

FDA
Dermatologic and Ophthalmic Drugs
Advisory Committee

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Study Designs of Trials in the
Treatment of Myopia

Briefing Document

For Public Disclosure Without Redaction

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List of abbreviations

AMD	Age-related macular degeneration
BCVA	Best-corrected visual acuity
BSVA	Best-spectacle corrected visual acuity
CDRH	Center for Devices and Radiologic Health
CNV	Choroidal neovascularization
COMET	Correction of Myopia Evaluation Trial
D	Diopters
ETDRS	Early Treatment Diabetic Retinopathy Study
FDA	Food and Drug Administration
HANES	National Health and Nutrition Examination Survey
ICH	International Committee on Harmonization
IOP	Intraocular pressure
LASIK	LAser in Situ Keratomileusis
NEI	National Eye Institute
PAL	Progressive Addition Lenses
RSVP	Refractive Status and Vision Profile
SD	Standard deviation
SE	Standard error
SEM	Standard error of the mean
SER	Spherical equivalent refractive error
UCVA	Uncorrected visual acuity
UK	United Kingdom
US	United States
VA	Visual acuity
WHO	World Health Organization

1 Purpose

The main purpose of this document is twofold. It is to:

- Provide background information on myopia
- Provide a rationale and study design for a pharmacological treatment for juvenile onset myopia.

Novartis has been studying myopia for many years and considers it a serious ocular condition that warrants the development of new therapies. Based upon discussions with various experts around the world, as well as with Health Authorities including the Food and Drug Administration (FDA), we are proposing a clinical trial design that we believe is adequate to assess the safety and efficacy of a pharmacological treatment of myopia.

2 Background

2.1 Introduction to myopia

Juvenile onset myopia, or shortsightedness, is defined as refractive error where parallel rays of light come to focus in front of the retina due to axial elongation of the eyeball, resulting in blurred vision. This does not include myopia secondary to other ocular, systemic, or neurodevelopmental conditions which are outside the scope of Novartis' research. Juvenile onset myopia usually occurs during the ages of 6 to 16 years (school-age myopia) with mean cessation ages ranging from 14.44 to 15.28 years for females and 15.01 to 16.66 years for males ([Goss and Winkler 1983](#)).

The axial elongation results from uncontrolled growth of the sclera and leads not only to the refractive error in the optical system of the eye but also to stress on the tissues of the eye due to the resulting anatomical defect ([Figure 1](#)). Depending on the degree, this stress can lead to serious ocular complications later in life. While refractive error is most significant to the myopic patient, this defect is merely a symptom of the underlying pathophysiologic changes. These changes have the potential to lead to long-term complications such as retinal detachment, retinal degenerative changes, glaucoma, and cataracts. The stages of myopia have commonly been categorized as low (-0.50 to less than -3.00 diopters (D)), moderate (-3.00 to less than -6.00 D), and severe (more than -6.00 D).

Myopia is highly prevalent, increasing with age until maturity ([Negrel, et al 2000](#)). Refractive errors are one of the most common causes of impaired vision in the United States (US), affecting approximately 25% of persons aged 12 to 54 years old ([Sperduto, et al 1983](#), [Wang, Klein, and Moss 1994](#)). Myopia is a significant problem, not only because of its high prevalence, but also because it can contribute to visual morbidity and increase the risk of vision-threatening conditions. Although many researchers agree that children's refractive status is in part genetically determined, evidence shows that visual experiences early in life (i.e., amount of near work) may affect ocular growth and eventual refractive status ([Mutti, et al 2002](#)).

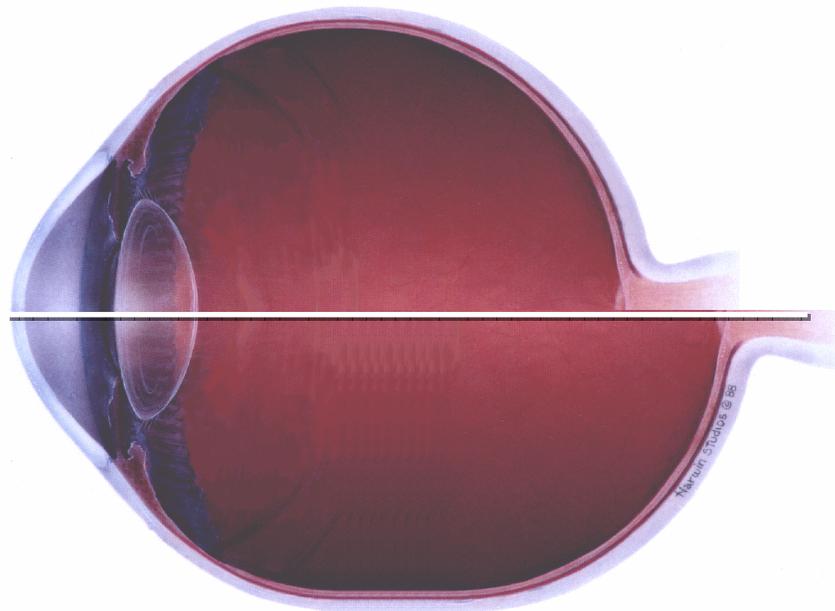
As the fifth most frequent cause of registrable blindness in developed countries ([Curtin 1985](#)), myopia is recognized as an important health concern by many public health organizations.

The World Health Organization (WHO) has selected five conditions to study with the goal of eliminating avoidable blindness. Refractive error is one of these conditions. Indeed, patients with myopic retinopathy are legally blind for an average of 17 lifetime years, compared to 5 lifetime years of blindness due to diabetes and age-related maculopathy, and 10 lifetime years from blindness in glaucoma (Green, Bear, and Johnson 1986).

The National Eye Institute (NEI) has included support for myopia-related research in its 5-year strategic program. The NEI plans to “identify human risk factors of myopia and abnormal eye growth and evaluate promising treatments for preventing the onset of or slowing the progression of myopia, such as special spectacles or contact lenses or pharmacological treatments” (National Advisory Eye Council 1998). The annual cost of myopia in the US is approximately \$4.8 billion” (PolyTech University-Hong Kong 2003).

Figure 1 **Normal versus myopic eye**

Shorter / Rounder Emmetropic Eye



Longer / Oval Shaped Myopic Eye

2.2 Prevalence of myopia

As part of HANES (National Health and Nutrition Examination Survey) conducted by the National Center for Health Statistics in the US from 1971 to 1972, eye exams were performed on 9,882 of the 14,147 person sample. From this dataset, the prevalence of myopia in the US, in persons aged 12 to 54 years old, was estimated to be 25% (Table 1). Whites had substantially higher rates than blacks, and women had significantly higher rates than men up

to the age of 35. Interestingly, the prevalence of myopia increased as family income rose and also increased markedly for all age groups as the number of years of school completed rose. With respect to geography, the prevalence of myopia seems to vary by country (Table 2; [Wilson et al 1989](#)).

Table 1 **Prevalence of myopia in the US**

Race and Sex	All ages	Age 12-17	Age 18-24	Age 25-34	Age 35-44	Age 45-54
All Races						
Both sexes	25.0%	24.0%	27.7%	24.2%	24.5%	24.8%
Men	22.8%	21.7%	22.5%	20.2%	26.1%	24.4%
Women	27.1%	26.4%	32.5%	27.8%	23.2%	25.1%
Whites						
Both sexes	26.3%	25.8%	29.7%	25.6%	24.9%	25.5%
Blacks						
Both sexes	13.0%	12.0%	10.4%	12.3%	14.8%	17.3%

Source: [Sperduto, et al 1983](#)

Table 2 **Prevalence of myopia by country**

Country	Myopia %
China	70%
US	25%
UK	27%
Sweden	33%
India	22%
Israel	18.4%
Germany	13.8%

Source: [Wilson and Woo 1989](#)

2.3 **Natural history of myopia**

Progression of myopia is highly variable among individuals. Once myopia appears in a child, it almost always increases in severity ([Bücklers 1953](#)). Generally, a progression rate of -0.45 D per year is observed in juvenile Caucasians (8 to 12-year-old) ([Goss and Cox 1985](#)). For juvenile onset myopia in Asians, the rate of progression typically observed is twice that in Caucasians ([Saw, et al 2002](#)).

A correlation has been observed between the age of onset and final refractive status, where earlier onset seems to lead to a higher final amount of myopia ([Goss and Cox 1985](#), [Mäntyjärvi 1985](#), Table 3). An important aspect of this trend may be the consideration of puberty, where onset of myopia prior to puberty may result in greater final myopia.

Table 3 Earlier onset leads to higher levels of myopia

Age of the onset of myopia (years)	Mean diopters at age 15 to 16
7 to 8	5.00
9	4.43
10	4.16
11	3.16
12	2.75
13	2.54
14	2.11
15	1.15

Source: [Mäntyjärvi 1985](#)

2.4 Risk factors for developing myopia

Generally, the causes of myopia are classified in terms of either genetic or environmental. ([Mutti and Zadnik1995](#), [Zadnik 2002](#), [Mutti, et al 2002](#)). Studies have shown that the prevalence of myopia in children with 2 myopic parents is 32.9%, decreasing to 18.2% in children with 1 myopic parent, and to less than 6.3% in children with no myopic parents (Table 4). The most common environmental factor cited is near work, where a statistical association between myopia, increasing education and higher amounts of near work has been observed.

Table 4 Association between myopia in parents and children

Parental Myopia	Prevalence of children with myopia	Univariate odds ratios (95% CI)
None	6.3 %	---
1 myopic parent	18.2 %	3.31 (1.32-8.30)
2 myopic parents	32.9 %	7.29 (2.84-18.7)

Source: [Mutti, et al 2002](#)

2.5 Quality of life issues associated with myopia

In trying to better understand the impact of myopia from the perspective of the patient on daily life, it is useful to consider 2 concepts, namely, the far point and the effect that myopia has on loss of visual acuity (VA). The far point is the furthest point at which a person can see clearly. For myopes, this point moves closer and closer to the eye, as the degree of myopia increases. For example, the far point of -1.00 D myope = 40 inches; for a -2.00 D myope, the far point = 20 inches. Objects beyond the far point are recognizable, however, they become progressively more “blurred” with increasing distance. This change in the far point is what gives rise to the phenomenon of high myopes (-6.00 D or more of myopia) holding books very close to their face to read when they are not wearing their spectacle correction.

To appreciate the magnitude of the impact of myopia with respect to loss of uncorrected visual acuity (UCVA), we can consider a “rule of thumb” relationship that is used by many

clinicians when they refract patients (Table 5; [Bennett and Rabbetts 1989](#)). This provides an approximate relationship between unaided vision and spherical myopia.

Table 5 Relationship between acuity and refractive error

Visual Acuity*	Spherical Error (D)
20/20	-0.25
20/30	-0.50
20/40	-0.75
20/60	-1.00
20/80	-1.50
20/120	-2.00
20/200	-2.00 to -3.00

*Uncorrected

Based on this relationship, a -2.00 D myope would have an unaided VA of approximately 20/120. To better understand the significance of this decay in unaided VA, consider the following subjective clinical overview of vision requirements for various activities and professions (Table 6). This list was compiled based on Novartis' discussions with clinicians working in the field of myopia research.

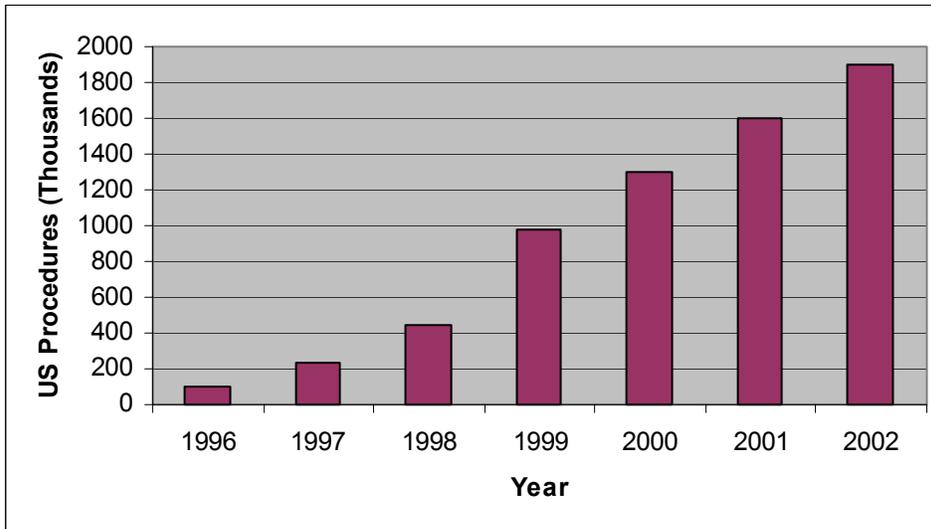
Table 6 Visual requirements for certain activities and professions

Activity	Minimum Vision Required					
	20/20	20/25	20/30	20/40	20/50	20/60
Hit an overhand baseball	X					
Obtain a pilot license	X					
See chalk board from back of class room		X				
Interpret coach/director instructions from field or stage			X			
Obtain an unrestricted drivers license in most states				X		
See necessary distances for diving and swimming				X		
Scan full distance of soccer or football field				X		
Perform near work at comfortable distance					X	
Recognize faces across a crowded room						X

In light of the effect of myopia on the far point as well as unaided VA, it is noteworthy to consider the significant number of people with myopia who have opted to undergo laser refractive surgery (Figure 2). The fact that so many myopic patients choose this alternative when non-invasive treatment options exist appears to be reflective of the significance of

myopia on their daily quality of life and their dissatisfaction with these treatment options (Market Scope Research, 2003).

Figure 2 US LASIK procedures by year

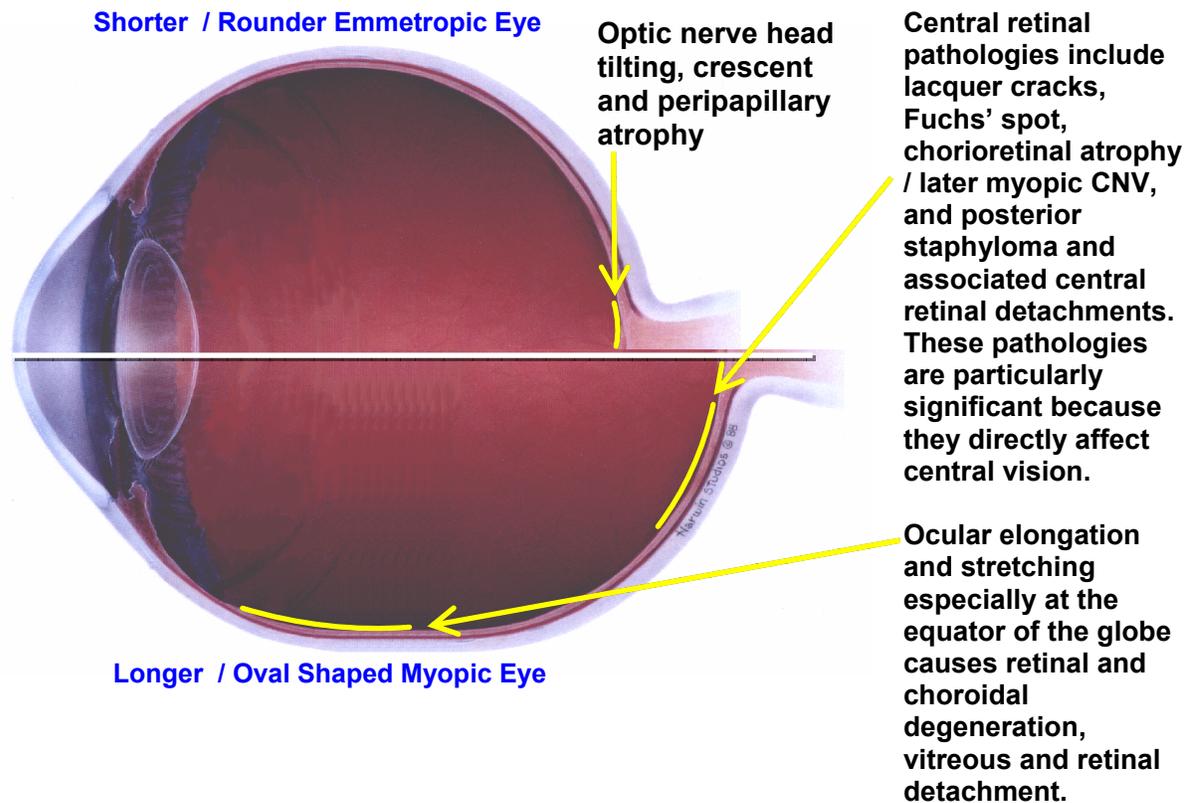


Quality of life measures are often difficult to quantify, and indeed, it is very difficult to find published studies in this regard with respect to myopia. However, in the United Kingdom (UK), a study was performed to assess the effect of degree of myopia on quality of life. The control group for this study was a group of keratoconus patients who were being treated with optical correction. Quality of life was assessed using the VF-14 questionnaire as well as data from interviews. It was determined that high myopes (more than -10.00 D) experienced an impaired quality of life similar to patients with keratoconus (Rose, et al 2000).

2.6 Complications associated with myopia

This section summarizes the main medical complications associated with myopia. As seen in Figure 3, the effect of significant axial elongation on the structure of the eye can result in various complications which typically manifest later in life.

Figure 3 Potential complications of myopia



2.6.1 Retinal disease and myopia

2.6.1.1 Myopic retinopathy

Myopic retinopathy has long been recognized as a serious cause of blindness. Myopic retinopathy is characterized by a variety of degenerative retinal changes. Progressive and excessive elongation of the eye associated with high myopia results in various fundus changes within the peripheral and central retina (Rabb and LaFranco Garoon 1981, Noble and Carr 1982, Curtin 1985, Steidl and Pruett 1997). These changes include chorioretinal atrophy, lacquer cracks, subretinal hemorrhage, choroidal neovascularization (CNV), Fuchs' spot (Levy, Pollock, and Curtain 1977, Hotchkiss and Fine 1981, Jalkh, et al 1987, Hayasaka, Uchida, and Setogawa 1990), and posterior staphyloma (Curtin and Karlin 1971, Curtin 1985). Among the various myopic fundus lesions, macular CNV is the most common vision-threatening complication of high myopia (Fried, Siebert, and Meyer-Schwickerath 1981, Hampton, Kohen, and Bird 1983, Avila, et al 1984).

Myopic retinopathy has been surveyed infrequently in population-based studies. However, the population-based Blue Mountains Eye Study determined prevalence rates of myopic retinopathy in a population aged 49 years or older (Table 7; Vongphanit, Mitchell, and Wang 2002). In this population, the prevalence of myopic retinopathy increased markedly with increasing levels of myopia. This observation is consistent with other studies showing a

higher prevalence of pathologic signs at greater axial lengths ([Curtin and Karlin 1971](#) and [Gozum, et al 1997](#)).

Table 7 Prevalence of myopic retinopathy

Spherical equivalent refraction (D)	Myopia n (%)	Myopic retinopathy n (%)
> -1.00	3179 (87.0)	10 (0.3)
-1.00 to -2.99	295 (8.1)	2 (0.7)
-3.00 to -4.99	101 (2.8)	3 (3.0)
-5.00 to -6.99	44 (1.2)	5 (11.4)
-7.00 to -8.99	14 (0.4)	4 (28.6)
< -9.00	21 (0.6)	11 (52.4)

Source: [Vongphanit, Mitchell, and Wang 2002](#)

2.6.1.2 Lattice degeneration and myopia

Estimates of the prevalence of lattice degeneration due to myopia range from 6% to 8% ([Byer 1979](#), [Straatsma, et al 1974](#)). In eyes with retinal detachment due to myopia, ([Straatsma and Allen 1962](#)) previously found that 30% of eyes had lattice degeneration. Törnquist had similar findings and noted patients experiencing retinal detachment with lattice degeneration were more likely to be younger and myopic ([Törnquist, Törnquist, and Stenkula 1987](#)).

2.6.1.3 Retinal detachment

Myopic eyes are at an increased risk for retinal detachment ([Perkins 1979](#), [Ogawa and Tanaka 1988](#), [The Eye Disease Case-Control Study Group 1993](#)). This increased risk occurs even at low degrees of myopia and increases in patients with higher myopia. As one example, The Eye Disease Case-Control Study found that the risk for retinal detachment in eyes with -1.00 D to -3.00 D of myopia is more than 4 times that compared to no myopia, whereas this risk for an eye with more than -3.00 D of myopia is nearly 10 times that of an eye with no myopia. In another case-controlled study, similar risks were found for mild and moderate levels of myopia compared to no myopia. For eyes with severe myopia, the risk of retinal detachment is 26 times that of an eye with no myopia ([Ogawa and Tanaka 1988](#)).

While the incidence of retinal detachment is relatively low, the cost of treatment and impact on vision are high. ([Burton 1982](#)) observed that only 40% of treated eyes recover to 20/50 or better acuity when the detachment involved the macula.

2.6.2 Glaucoma and myopia

An association between myopia and glaucoma has been recognized for decades. Larger recent studies support a relationship between the two, even for low degrees of myopia. In the Blue Mountains Eye study ([Mitchell, et al 1999](#)), an association was observed between degree of myopia and prevalence of glaucoma. In this population-based study, persons with low myopia (-1.00 to -3.00 D) were twice as likely to have glaucoma (OR, 2.3; 95% CI 1.3 to 4.1) whereas those with moderate myopia (-3.00 D and greater) were 3 times as likely to have glaucoma (OR, 3.3; 95% CI 1.7 to 6.4). Other studies have shown a correlation between

myopic refraction and increasing intraocular pressure (IOP) and an increased odds of having glaucoma in persons with myopia (Wong, et al 2003).

2.6.3 Cataract and myopia

An association between cataract and myopia has been reported in cross-sectional population based studies (Wong, et al 2001, Younan, et al 2002). In the Blue Mountains Eye study, the strongest association was reported between high myopia and nuclear cataract, moderate to high myopia and posterior subcapsular cataract, and any myopia and cataract surgery. In the Beaver Dam Eye Study, an association between any myopia and cataract surgery was reported, however, an association between nuclear, cortical and subcapsular cataracts was not observed.

2.7 Current treatments for myopia

The current treatments for myopia include spectacles with single-vision lenses, contact lenses, and refractive surgery. These treatments only correct the refractive error due to myopia. They do not address the underlying pathophysiologic changes associated with excessive axial elongation of the eye. A recently published article reinforces this point:

“Popular (refractive) procedures seem almost irrelevant to the discussion of high myopia. These procedures improve cosmesis, but provide no relief for the pathological process of high myopia” (Bell 1993).

Reports of interventions attempting to retard the progression of myopia have included progressive addition and bifocal spectacles, contact lenses and eyedrops including atropine and the topical beta-blocker, timolol maleate (Saw, et al 2002, Gwiazda, et al 2003). Studies involving bifocal spectacle lenses with various additions, progressive addition lenses (PAL), topical tropicamide and topical timolol have not demonstrated clinically significant effects with respect to slowing either the progression of refractive error or the increase in axial length growth. Reports involving topical atropine in concentrations of 0.5% and 1.0% have demonstrated statistically significant effects. However, the side-effects associated with topical atropine are generally considered unacceptable for long-term therapy, and therefore, topical atropine has not been accepted as a treatment for slowing progression of myopia. In a recent review of all published interventions for slowing the progression of myopia, it was noted that “the latest evidence from randomized clinical trials does not provide sufficient information to support interventions to prevent the progression of myopia” (Saw, et al 2002).

3 Proposal and rationale of a study design for a pharmacologic treatment of myopia

3.1 Indication

Novartis is proposing the following indication based on the population and primary variable being proposed for study: Reduction of progression of myopia in patients diagnosed with juvenile onset myopia.

3.2 Population

Eligible patients will be diagnosed with juvenile onset myopia, aged 6 to 12 years, and meet the following criteria:

- Refractive status as determined by cycloplegic autorefraction: -1.00 to -4.00 D
- Astigmatism: ≤ 1.25 D in either eye
- Anisometropia: ≤ 1.00 D (spherical equivalent between eyes)
- No known ocular, systemic, or neurodevelopmental condition that might affect refractive development.

3.3 Study design

Prospective, randomized, double-masked, placebo controlled study. For the purposes of registration, Novartis proposes a period of 30 months on-drug as being an adequate period of time to establish efficacy and safety.

Given the patient population being studied, it is appropriate to have additional safety data resulting from an extended exposure period. The length of exposure being proposed is consistent with feedback from experts in the myopia treatment community and exceeds the ICH guideline regarding the exposure period required for drugs intended for long-term treatment of non-life-threatening conditions (i.e., this guideline stipulates that 300 to 600 patients should have exposure data for 6 months and a minimum of 100 patients should have exposure data for 12 months).

An “off drug” period of 6 months is also being proposed to address the potential concern regarding rebound associated with discontinuation of therapy. It is important to understand that cessation of therapy during the period of life where myopia is naturally progressing, will result in a resumption of progression of myopia. This phenomenon is not a rebound effect. The concern regarding rebound centers around the potential for an acceleration of progression of myopia to occur upon cessation of therapy. A period of 6 months is considered adequate for the manifestation of any rebound effect.

3.4 Primary outcome measure

The primary outcome measure is progression of myopia as expressed by the change from baseline in spherical equivalent refractive error (SER) assessed using cycloplegic autorefraction.

3.5 Efficacy variables

3.5.1 Primary

Novartis proposes a primary efficacy variable based on a comparison of the proportion of patients in the treated versus placebo groups whose myopia progresses by -2.00 D or greater at a predetermined time point.

3.5.2 Secondary

The proposed secondary efficacy variable is a comparison of change in axial length between treated and untreated groups.

3.6 Rationale for the primary efficacy variable and treatment period

3.6.1 Rationale for outcome measure

The progression of myopia can be characterized as having 2 primary outcomes that are significant to the patient. These are the change in refractive error that reduces unaided VA and the development of ocular complications. The development of ocular complications results from the stress on the ocular system arising from axial elongation of the ocular globe due to increased vitreous chamber length. The increased axial length of the ocular system leads to the change in refractive status of the system and results in the most immediate impact to the patient, a reduction in the ability to see clearly. Using refractive error as assessed by cycloplegic autorefraction is the best method for assessing the refractive status of the ocular system. It is an objective measure with minimal variability and is the approach generally accepted by experts in the field as being most relevant for clinical research. Thus, change in refractive status as assessed by change in refractive error is a clinically significant outcome measure for a treatment of juvenile onset myopia.

3.6.2 Rationale for magnitude of change

To use change in SER as a primary measure of efficacy, we must define the magnitude of change that is clinically meaningful. We will address this by defining:

- The change in refractive error considered to be clinically significant based on objective criteria. This change = 0.75 D.
- The change in refractive error considered to be clinically significant based on subjective criteria. This change = 1.00 D to 2.00 D.

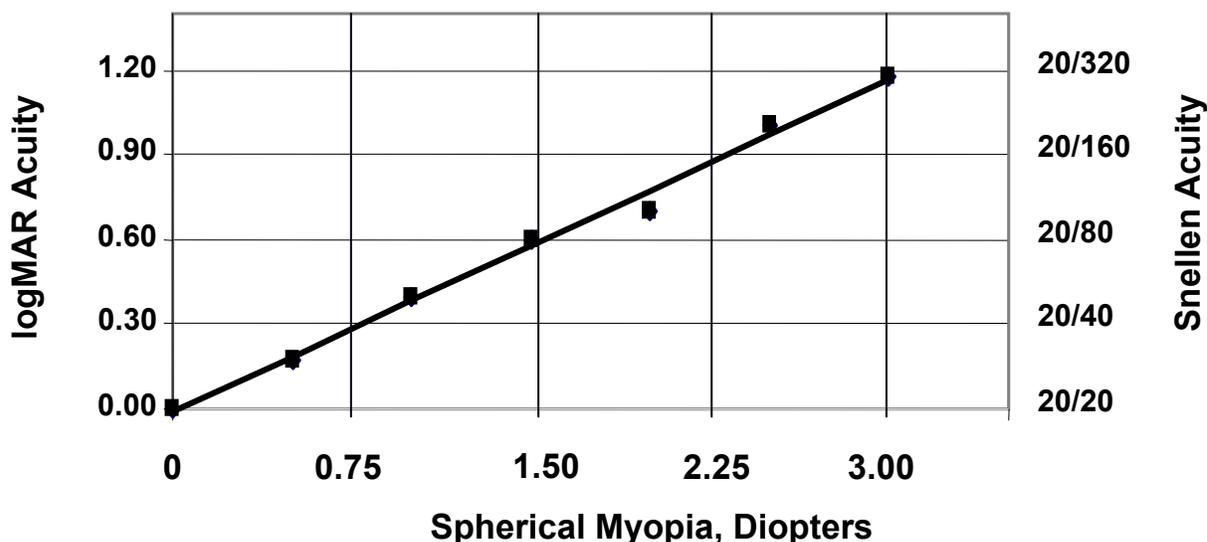
3.6.2.1 Change in refractive error considered to be clinically significant based on objective criteria

When either best-corrected visual acuity (BCVA) or UCVA have been used as endpoints to approve new treatments in ophthalmology, a change that corresponds to a doubling of the visual angle has been considered clinically significant.

- For Drugs—a 3-line loss in BCVA on an Early Treatment Diabetic Retinopathy Study (ETDRS) chart has been accepted by the FDA as clinically significant for the purpose of approving new drugs for age-related macular degeneration (AMD); this change corresponds to a doubling of the visual angle.
- For Devices—lasers approved for laser refractive surgery, the effectiveness endpoint based on VA defined in the FDA guidance document is “percentage of eyes with UCVA 20/40 or better ([best-spectacle corrected visual acuity (BSVA)] 20/20 or better preoperatively).” Thus, for eyes in which it is possible to correct to 20/20, a primary endpoint is based on the percentage of eyes whose UCVA does not decay beyond a doubling of the visual angle.

The change in refractive error that corresponds to a doubling of the visual angle can be calculated to be 0.75 D. This number arises from evaluating VA decay with refractive error changes. For this evaluation, we used a dataset of 45,206 physical examination records where 7,482 refraction records were reviewed (Pincus 1946). Figure 4 presents the UCVA data prior to dilation in the subset of patients that exhibited spherical myopia on cycloplegic refraction.

Figure 4 Relationship between uncorrected visual acuity and refractive error



Source: [Pincus 1946](#)

In addition to criteria that have been defined for VA changes that can be considered as clinically significant, the following criteria have been defined in the Center for Device and Radiologic Health's (CDRH) guidance document for Refractive Surgery Lasers with respect to refractive error changes that are part of the definitions of effectiveness. Based on the inclusion of these criteria, changes of these magnitudes are considered to be clinically significant:

Percentage of eyes that achieve predictability (attempted versus achieved) of manifest refraction spherical equivalent of ± 2.00 D, ± 1.00 D, and ± 0.50 D.

3.6.2.2 Change in refractive error considered to be clinically significant based on subjective criteria

Two subjective criteria have been chosen to support a determination of clinical significance, a patient-driven treatment decision option and a measure of quality of life associated with change in refractive status. Based on these criteria, a change in refractive error of 1.00 to 2.00 D can be considered clinically significant.

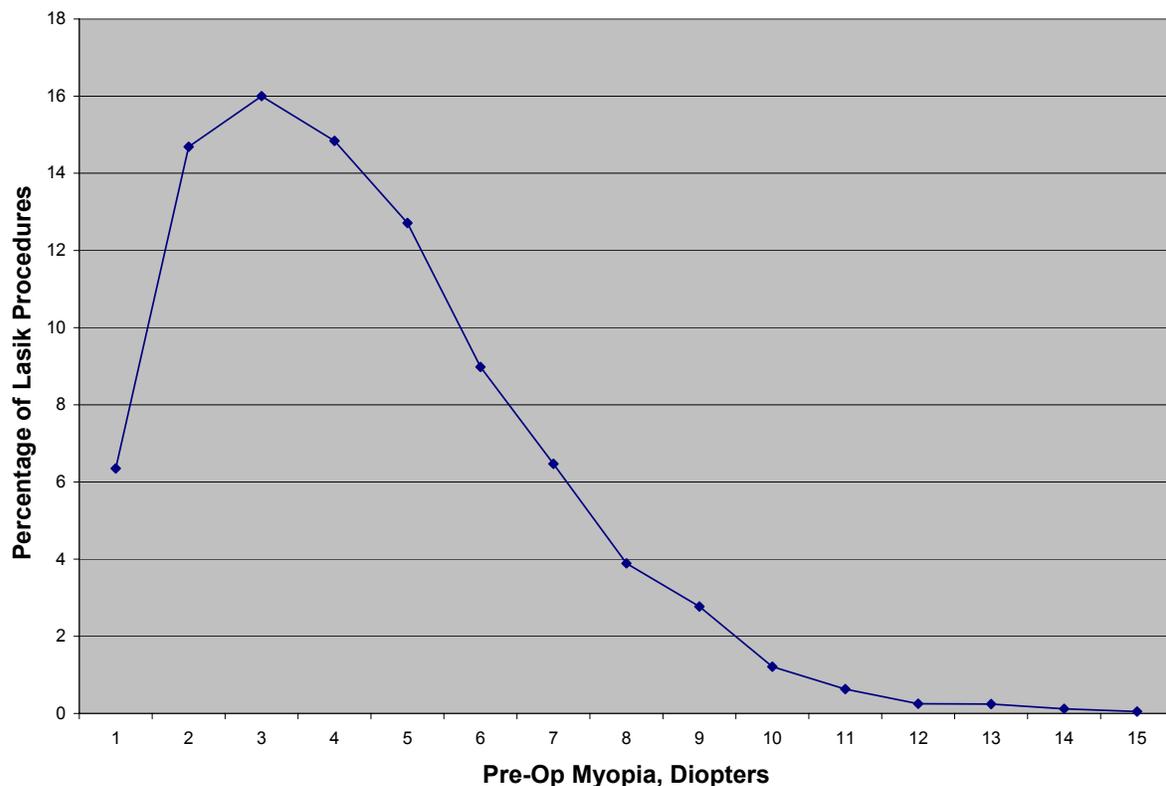
3.6.2.2.1 Patient-driven treatment option

When considering options to pursue for correction of the optical defect associated with myopia, patients have a variety of non-invasive and invasive treatments from which to

choose. We considered the choice of a patient to pursue an invasive treatment option such as laser refractive surgery to be a significant indication of their dissatisfaction with their refractive status.

We used the most prevalent form of laser refractive surgery (i.e., LAser in-Situ Keratomileusis (LASIK)) and a sample of over 6,000 LASIK patients undergoing this procedure during the years 1996 to 2002. In considering the distribution of the percent of patients undergoing LASIK as a function of pre-operative myopia, a significant rise in the incidence occurs as the pre-operative refractive status approaches -2.00 D. This rise does not occur as the pre-operative refractive status approaches -3.00 D or -4.00 D. It is important to note that the prevalence of myopia in the population is highest at lower levels and is similar in the 2.00 to 5.00 D range. Using this subjective criteria, a 2.00 D change in refractive error can be considered clinically significant.

Figure 5 **Percent of LASIK refractive procedures compared to pre-operative refractive status**



Source: Market Scope Research, 2003

3.6.2.2.2 Quality of Life Measure Associated with Change In Refractive Error

The Refractive Status and Vision Profile (RSVP) is a validated questionnaire designed specifically to measure self-reported vision-related health status via evaluation of symptoms, functioning, expectations and concern in persons with refractive error.

The RSVP includes 8 subscales, and an overall score which assess physical-social functioning, driving, psychological functioning, symptoms, optical problems, glare, problems with corrective lenses, and expectations (specifically, expectations related to post-surgical outcome associated with refractive surgery).

When the effect of changes in SER were considered in terms of reported patient satisfaction in patients who have not undergone laser refractive surgery, it was found that for every additional diopter of SER (i.e., with increasing severity of myopia), people are significantly more likely to report being dissatisfied with their vision, even after adjustments for age, gender, lens type (spectacles or contact lenses), and RSVP subscale quality of life measures. As expected, for every additional 2.00 D of change in SER, the reduction in satisfaction is even more pronounced (Vitale, et al 2000).

3.6.3 Rationale for a dichotomous versus continuous variable

Novartis is proposing a dichotomous variable as the primary variable because we believe it better reflects the treatment effect of a therapy for juvenile onset myopia.

Given the population we are proposing to study, a dichotomous variable of 2.00 D reflects the treatment effect in preventing the progression of the population through significant steps of myopic progression (Table 8). It reflects the difference between the treated and untreated groups in the percent of patients who progress from mild to moderate and from moderate to severe myopia.

Table 8 Change in stage of myopia with –2.00 D progression

Baseline myopia (SER) (D)	Progression of 2.00 D and greater	Stages reflected
-1.00 to less than -3.00 D	-3.00 to less than -6.00 D	Mild to moderate
-4.00 D	-6.00 D and greater	Moderate to severe

Definitions of Stages of Myopia:

- 1.00 D to less than -3.00 D = Mild myopia
- 3.00 D to less than -6.00 D = Moderate myopia
- 6.00 D and greater = Severe myopia

If a continuous variable were to be required, it would not be reasonable to impose a requirement of demonstrating a 2.00 D difference between groups at 30 months. Novartis does not believe a continuous measure is a clinically meaningful as a dichotomous measure, but if it were to be required a different threshold for clinical significance should be applied. To better understand what this threshold should be, we undertook a statistical modeling experiment.

We used as the basis for our modeling the recently published data (Gwiazda, et al 2003) from the Correction of Myopia Evaluation Trial (COMET). This study enrolled a population that is very similar to the population we are proposing to study. These data were collected from a double-masked, randomized sample based in the US.

When the sample size was determined for the COMET study, a potential treatment effect of 33% was assumed as part of the calculation. This magnitude of treatment effect was

considered clinically significant by the COMET study group. We used this same assumption to model the theoretical difference in mean refractive error that could be achieved if a treatment exhibited a 33% treatment effect each year for a period of 3 years. Additionally, we considered the potential treatment effect in the model if a 50% treatment effect were achieved (Tables 9 and 10).

Table 9 Estimated changes from baseline (slopes) in mean refraction assuming active reduces myopic progression by 33%

Interval	Active	Control	Annual Treatment Effect	Cumulative Treatment Effect
0-1 Year	-0.40	-0.60*	0.20	0.20
1-2 Year	-0.33	-0.49*	0.16	0.36
2-3 Year	-0.26	-0.39*	0.13	0.49
Total	-0.99	-1.48	0.49	--

*Estimated values from COMET SVL group (N=234; Mean age = 9.4 yrs; Mean refraction = -2.37 D).

Table 10 Estimated changes from baseline (slopes) in mean refraction assuming active reduces myopic progression by 50%

Interval	Active	Control	Annual Treatment Effect	Cumulative Treatment Effect
0-1 Year	-0.30	-0.60*	0.30	0.30
1-2 Year	-0.25	-0.49*	0.24	0.54
2-3 Year	-0.20	-0.39*	0.19	0.73
Total	-0.75	-1.48	0.73	--

*Estimated values from COMET SVL group (N=234; Mean age = 9.4 yrs; Mean refraction = -2.37 D).

As can be seen from Table 9, a treatment of myopia that can maintain a 33% year-over-year improvement versus the control group will result in a treatment difference of - 0.49 D after 3 years of treatment. As seen in Table 10, a treatment of myopia that can maintain a 50% year-over-year improvement versus the control group will result in a treatment difference of - 0.73 D after 3 years of treatment. Based on an assumption of a reasonable treatment effect, namely 33% and 50%, it would not be possible to achieve a treatment effect difference (i.e., difference in mean refractive error between groups) of 2.00 D, even if the clinical study were to involve 3 years of treatment. It may be possible, however, to achieve a treatment effect of 0.75 D, which is consistent with the clinically significant effect we defined based on objective criteria.

4 Conclusion

The condition of myopia continues to be a problem in society. The issues surrounding myopia can be characterized by the following:

- Myopia has been recognized by governmental health agencies as a significant public health condition requiring research and new treatments.

- Patients diagnosed with myopia continue to search for treatments to alleviate this condition. This is reflected by the significant growth in laser refractive surgery over the last decade, even when many non-invasive treatment options exist.
- Current available treatments address only the optical defect associated with myopia, they do not affect the underlying pathophysiologic changes that lead to long-term complications.
- An association between myopia and significant long-term complications has been reported by many investigators. These complications include retinal detachment, myopic retinopathy and glaucoma.
- Evidence also suggest an increasing risk for developing certain of these complications with higher degrees of myopia.
- Patients diagnosed with myopia continue to search for treatments to alleviate this condition. This is reflected by the significant growth in laser refractive surgery over the last decade, even when many non-invasive treatment options exist.

A pharmacological approach to treatment represents the only avenue for addressing both the optical defect associated with myopia as well as the underlying pathophysiologic changes resulting from excessive axial elongation.

Because the significant complications associated with myopia do not generally manifest until later in life, but the physiologic defect leading to these complications occurs early in life, a clinical development program based on the development of a complication associated with myopia is not feasible. Therefore, another outcome measure is needed if new therapies are to be developed.

Refractive error associated with myopia is the optimal alternative. It represents the aspect of myopia that is most relevant to patients, has the greatest immediate impact on their life and is reflective of the underlying pathophysiologic changes that are occurring.

Novartis has presented a proposal for an endpoint based on using change in refractive error as an outcome measure. We have defined a clinically significant change in this parameter which can be used to measure a treatment effect based on various criteria and have proposed a treatment period that addresses the safety concerns reflective of the population being studied.

We believe this approach represents the best balance between measuring a treatment effect using a parameter which is clearly important to the patient but also allows for the reasonable development of new treatments in a safe manner.

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NOTE: Selected references are provided in Appendix 1.

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Appendix 1 Publications

Natural History of Choroidal Neovascularization in Degenerative Myopia

MARCOS P. AVILA, MD, JOHN J. WEITER, MD, ALEX E. JALKH, MD,
CLEMENT L. TREMPPE, MD, RONALD C. PRUETT, MD, CHARLES L. SCHEPENS, MD

Abstract: We studied 354 eyes with myopic chorioretinal degeneration by means of standard clinical evaluation and fluorescein angiography. The eyes were classified on the basis of the degree of chorioretinal degeneration found in the posterior pole. Lacquer cracks (breaks in Bruch's membrane) were noted in 82% of the 149 eyes with choroidal neovascular membranes (CNM) and in 96% of the 58 eyes with isolated subretinal hemorrhages. These hemorrhages were reabsorbed without adverse visual sequelae in 32 eyes that were followed; in 14 of these eyes that were followed closely, the average time of reabsorption was 6.4 weeks. Seventy eyes with CNM were followed for an average of 40.9 months. In 96% of these eyes the CNM remained stable or regressed, leaving an atrophic, nonexudative scar. This study indicates that CNM in degenerative myopia is usually self-limited. [Key words: Bruch's membrane, choroidal neovascular membrane, chorioretinal degeneration, degenerative myopia, lacquer cracks, laser photocoagulation.] *Ophthalmology* 91:1573-1581, 1984

Simple myopia may be caused by a small increase in the globe's axial length or an increase in the refractive power of the eye; such eyes demonstrate near-normal anatomy. In contrast, degenerative myopia (also called pathological, progressive, or pernicious myopia) is an ocular disease characterized by excessive axial length, abnormal visual functions, and a number of changes in the ocular tissues. Chorioretinal degeneration is the most prevalent posterior fundus change noted.¹ Degenerative myopia ($> -6D$), the seventh leading cause of blindness in adults in the United States,² is present in about 0.5% of the general population in Europe³ and is estimated to represent 2% of all types of myopia.⁴

The pathogenesis of the degenerative changes in the macula of the highly myopic eye is the subject of this

study. We used fluorescein angiography to elucidate the natural course of some of these macular changes, particularly the development of a choroidal neovascular membrane (CNM).

MATERIALS AND METHODS

PATIENTS

We reviewed the records of 188 patients (354 eyes) with degenerative myopia, examined by the Retina Associates between 1970 and 1982. Eighty-six patients (46%) were men and 102 (54%) were women; their average age at initial visit was 48.8 years (range, 14-80 years). The refractive error (in spherical equivalents) ranged from -6.50 to -24.50 diopters. Patients were referred for further examination when macular changes were suspected or identified. Thus, this group of selected patients does not necessarily reflect the general prevalence of myopic macular changes. Patients with a history of retinal detachment surgery, diabetes, retinal vascular disease, glaucoma (intraocular pressure >20 mmHg), senile macular degeneration, or ocular injury were excluded.

From the Eye Research Institute of Retina Foundation and Retina Associates, Boston.

Presented at the Eighty-eighth Annual Meeting of the American Academy of Ophthalmology, Chicago, Illinois, October 30-November 3, 1983.

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Fig 1. Left eye of a 46-year-old woman with V_1 choroidal neovascular membrane and grade M_3 degenerative myopia. *Left*, early fluorescein transit shows hyperfluorescence associated with filling of the choroidal neovascular membrane. *Right*, late transit shows minimal leakage confined to choroidal neovascular membrane borders.

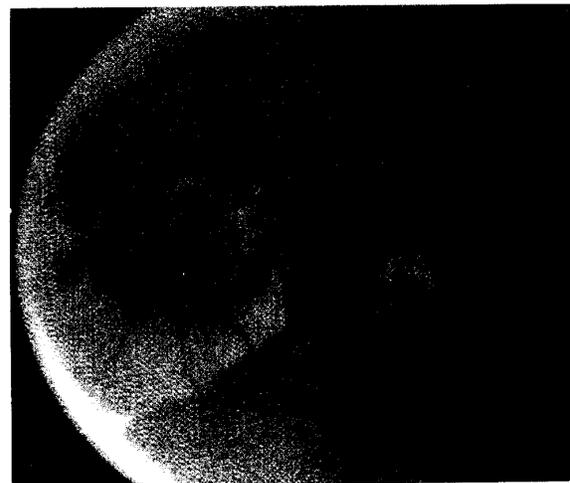
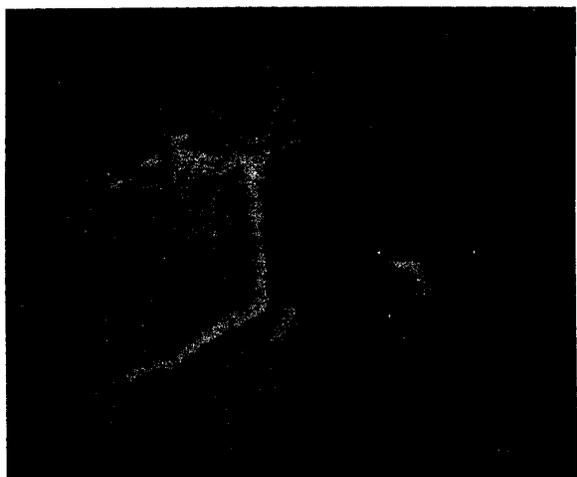


Fig 2. Left eye of a 61-year-old woman with V_2 choroidal neovascular membrane and grade M_2 degenerative myopia. *Left*, early fluorescein transit shows hyperfluorescence associated with filling of the choroidal neovascular membrane. *Right*, late transit shows marked leakage which extends beyond choroidal neovascular membrane borders.

PROCEDURES

The initial evaluation included a detailed fundus drawing using indirect stereoscopic ophthalmoscopy, fluorescein angiography, and stereoscopic fundus color photographs. These procedures were repeated as necessary during follow-up visits. Best corrected visual acuity was measured at each visit using the same standard equipment for visual acuity testing.

We made note of the following conditions whenever they were present in the posterior pole: fundus pallor and tessellation (terms used synonymously with choroidal thinning), diffuse or focal chorioretinal atrophy, posterior staphyloma, and lacquer cracks. These myopic changes (M) were graded retrospectively on a scale of increasing

severity from 0 to 5, as follows: Grade M_0 (4 eyes), normal-appearing posterior pole; Grade M_1 (25 eyes), choroidal pallor and tessellation; Grade M_2 (39 eyes), choroidal pallor and tessellation, with posterior pole staphyloma; Grade M_3 (201 eyes), choroidal pallor and tessellation, with posterior pole staphyloma and lacquer cracks; Grade M_4 (75 eyes), choroidal pallor and tessellation, with posterior pole staphyloma, lacquer cracks, and focal areas of deep choroidal atrophy; Grade M_5 (10 eyes), posterior pole showing large geographic areas of deep choroidal atrophy ("bare sclera").

Since lacquer cracks are subtle changes frequently missed in routine examination, we projected 35-mm slides from color, monochromatic, and fluorescein angiography photographs to aid in their detection.

The angiograms were individually reviewed by three authors; when a CNM was diagnosed at an initial or follow-up visit, its new vessels (V) were classified into one of two types. In V₁ CNMs, the area of hyperfluorescence associated with filling of the CNM in early transit did not increase significantly throughout the transit, indicating that the leakage was minimal or absent. This leakage was confined to the CNM borders (Fig 1). In V₂ CNMs, the leakage was marked, resulting in extension of dye beyond the boundaries of the neovascular net that was delineated in the early fluorescein transit (Fig 2).

We also recorded the presence of isolated, round, coin-like macular hemorrhages, without CNM detectable by fluorescein angiography, which we called "coin lesions."

Between 1972 and 1977, 14 highly myopic eyes (14 patients) with CNM were treated with laser photocoagulation. These eyes were analyzed separately from the 354 eyes considered for the natural history. A monochromatic argon green laser (514.5 nm) was used in spot sizes of 50 to 100 μm, at power settings of 50 to 250 mW, and durations of 0.2 to 0.5 seconds. We used low intensity levels and fairly long exposures to prevent hemorrhage. The entire neovascular membrane was covered with confluent photocoagulation burns.⁵

P values were computed using Pearson's chi-square test.⁶ A finding was considered statistically significant if the P value was less than 0.05 (P < 0.05). The data were analyzed in two fashions: (1) prevalence of a determined phenomenon at the first visit (cross-sectional survey), and (2) incidence of a phenomenon in follow-up patients (longitudinal survey).

FOLLOW-UP

Seventy eyes of 58 patients with CNM were followed for periods ranging from ten to 108 months (average, 40.9 months). The average age of these patients was 52.2 years (range, 20–80 years). The remaining 79 cases of CNM could not be followed for various reasons (eg. patients lived far away or were referred only for fluorescein angiography). No clinical characteristics at the initial visit distinguished cases that were followed from those that were not. The sample of 70 eyes was considered, therefore, to be representative of the 149 eyes with CNM. Forty-six eyes of 44 patients without CNM but with posterior pole staphyloma (grades M₂–M₅), were followed for periods ranging from eight to 84 months (average, 31.7 months).

Thirty-two eyes of 24 patients with coin lesions were observed for three to 60 months (average, 22 months). Fourteen of these eyes were observed closely at one- or two-week intervals and were used to determine the natural course of this lesion. The interval between onset of symptoms and the first visit was also recorded. The sizes, in disc diameters, of coin lesions and CNMs (as seen in the early fluorescein transit) were evaluated at each visit.

Table 1. Distribution of the Two Types of Choroidal Neovascular Membrane (CNM) Found in Various Grades of Degenerative Myopia

CNM Type†	Grade of Degenerative Myopia*					
	M ₀	M ₁	M ₂	M ₃	M ₄	M ₅
V ₁ (139 eyes)	0	0	12	76	49	2
V ₂ (10 eyes)	0	5	3	2	0	0
Total (149 eyes)	0	5	15	78	49	2

* See Methods for explanation of grades.

† V₁, fluorescein angiography shows no leakage beyond border of CNM. V₂, fluorescein dye leaks beyond CNM.

The post-treatment follow-up period for the 14 eyes with CNM treated by photocoagulation ranged from 11 to 108 months (average, 30.2 months). Because of the disappointing preliminary results obtained from photocoagulation, no eyes were treated from 1977 to the end of the study period. The average age of the 14 patients was 52.9 years (range, 31–78 years).

RESULTS

CROSS-SECTIONAL SURVEY

CNMs were detected at the first visit in the macular area of 149 eyes (116 patients); 72 patients (62%) were women and 44 (38%) were men (P < 0.01). Their average age was 51.1 years (range, 19–80). Table 1 shows the distribution of the two types of CNM over the various grades of degenerative myopia. V₁ CNM (139 eyes, 93%) was found significantly more frequently (P < 0.001) than V₂ CNM (10 eyes, 7%). Lacquer cracks were identified in 122 (82%) of the 149 eyes with CNM. They were seen either at the site of CNMs (Fig 3) or in their immediate vicinity. The size of CNM varied from one quarter to two disc diameters. Large CNMs (two disc

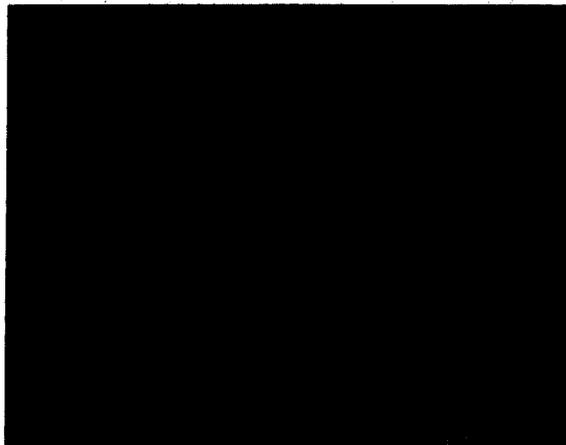


Fig 3. Left eye of a 52-year-old man. Fluorescein angiography shows CNM associated with lacquer crack.

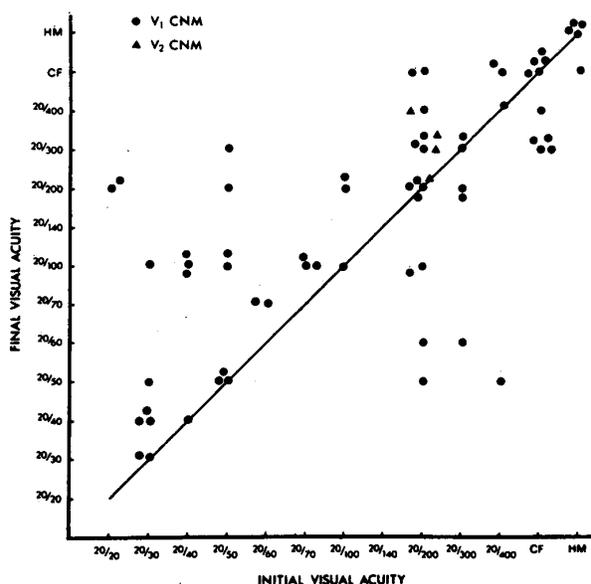


Fig 4. Initial and final visual acuities in 70 eyes with untreated CNM (average follow-up, 40.9 months). Dots on the line indicate unchanged visual acuity, dots below the line indicate improvement, and dots above the line indicate worsening.

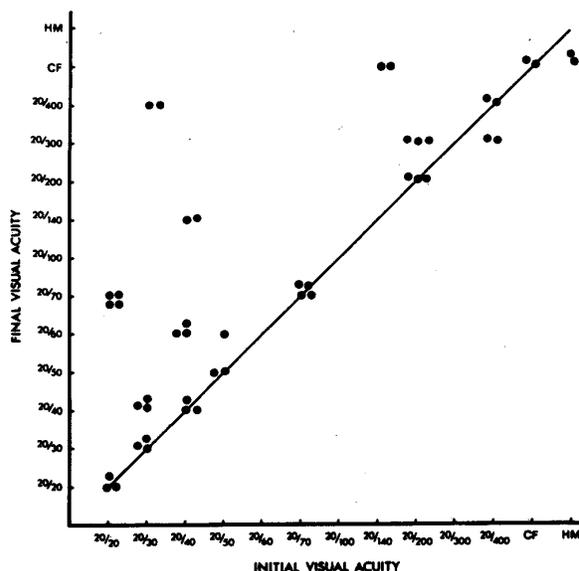


Fig 5. Initial and final visual acuities in 46 eyes with posterior pole staphyloma (grades M_2 - M_5) but without CNM (average follow-up, 31.7 months). Dots on the line indicate unchanged visual acuity, dots below the line indicate improvement, and dots above the line indicate worsening.

diameters) were uncommon and occurred in both V_1 and V_2 types.

Coin lesions (isolated macular hemorrhages without evidence of CNM on fluorescein angiography) were seen in 58 eyes of 46 patients; 30 (65%) were men and 16 (35%) were women ($P < 0.05$); their average age was 38.4 years (range, 14-66 years).

Coin lesions were associated with lacquer cracks in 56 of 58 eyes (97%); they were seen along the course of the lacquer cracks in 52 eyes and in the cracks' immediate vicinity in four. There were some eyes in which multiple, minute coin lesions were seen along the same lacquer crack. In other eyes, coin lesions were seen at different locations in the posterior pole.

LONGITUDINAL SURVEY

Three cases that had no CNM and grade M_2 fundus changes at the initial visit developed CNM during the follow-up period. Fundus changes characteristic of grade M_3 (lacquer cracks) appeared concomitantly.

Seventy eyes with CNM were followed; 66 had V_1 CNM and four had V_2 CNM. The eyes with V_1 CNM showed nonexudative atrophic scars at the end of the follow-up period; in 22 of these eyes (33%) a suggestion of residual CNM could be detected. None produced exudative fibrovascular scars. Some scars were small, whitish, and slightly elevated, but most were small, flat, and pigmented (Fuchs' spot). Small areas of RPE degeneration usually surrounded the scars. Of the four eyes with V_2 CNM, one showed a whitish, mildly elevated,

atrophic scar. The remaining three eyes showed organized exudative fibrovascular scars that had extended beyond the edge of the initially detected CNM. The retina overlying these lesions was elevated. Thus, 67 eyes (96%) showed atrophic nonexudative scars at the end of follow-up.

Figure 4 shows the initial and final visual acuities of the 70 eyes with CNM. Figure 5 shows the initial and final visual acuities in the 46 eyes with posterior staphyloma (grades M_2 - M_5) but no CNM.

Of the 14 eyes that received photocoagulation treatment for CNM, 11 had V_1 CNM and three had V_2 CNM. Following treatment, all eyes had complete closure of CNM documented by fluorescein angiography. The visual acuities for this group are depicted in Figure 6. Immediately after treatment or one year later, nine eyes with V_1 CNM had visual acuities the same as or better than pretreatment vision. By the end of the follow-up, however, visual acuities had deteriorated in six of these eyes. In the three eyes with V_2 CNM, the final visual acuity was found to be improved or stable. In all 14 eyes, the dry atrophic scars noted after treatment had enlarged considerably over time; the scars associated with V_1 CNM were especially large by the end of the follow-up (Fig 7).

Table 2 shows the change in visual acuity in treated and untreated eyes during the follow-up period. Of the 70 eyes with untreated CNM that were followed, 38 (54%) had visual improvement or stabilization after CNM resolution.

In the 32 eyes with coin lesions that were followed, the lesions were reabsorbed partially or completely (Fig 8); in the 14 eyes that were followed closely, the time from initial complaint to reabsorption ranged from two to eight weeks (average, 6.4 weeks). The initial complaint in most of these cases was a visual disturbance referred to as a "black dot" in front of the vision. In six of the 32 eyes that were followed, decreased visual acuity appeared directly associated with the coin lesions. In all these eyes, visual acuity improved after reabsorption. Four patients had a history of vigorously rubbing their eyes on the day, or within four days, of the appearance of the "black dot."

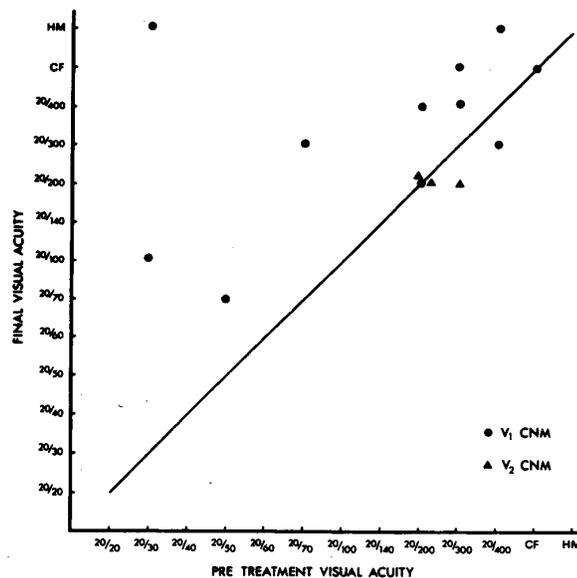
New coin lesions often appeared at different locations in the same eye during the follow-up. Coin lesions varied in size from one-tenth to one disc diameter; larger lesions generally took longer to be reabsorbed. In all eyes but one that were followed, fluorescein angiography revealed no further deterioration. In one eye a small V_1 CNM was noted after the blood reabsorbed. This ultimately became a small, flat, pigmented, atrophic scar.

DISCUSSION

The pathogenesis of chorioretinal degenerative changes of the fundus of highly myopic eyes is unknown,⁷ but the basic abnormality in degenerative myopia is excessive axial elongation.¹ This enlargement, attributed mostly to distension of the posterior segment,^{7,8} results in an ocular volume that is about 50% greater than that of a normal eye.⁸ Progressive distension⁹ of the posterior pole is believed to stretch the ocular coats, as evidenced by straightening of the temporal retinal vessels, by the appearance of a supertraction crescent, which is the simplest evidence of a disproportion between the scleral shell and its choroidal and retinal contents, and by thinning of the retina and choroid.^{7,8,10-12} Mechanical tissue strain and vascular changes occur^{10,13} secondary to the stretching. The severity of degenerative myopia (M_0 - M_5) is determined by this progressive distension of the posterior pole.

The term "Fuchs' spot" has been used to characterize small pigmented subretinal lesions in the posterior pole of eyes with degenerative myopia. With the advent of fluorescein angiography, neovascularization extending from the choroid into the subpigment epithelial space has been found to be associated with Fuchs' spot,^{1,7,14-17} which represents the end stage of CNM in degenerative myopia. The reported incidence of CNM in highly myopic eyes varies from 4 to 11%.^{10,18,19}

Continued stretching and degeneration of the choroid causes eyes with severe myopia to develop linear breaks in Bruch's membrane (lacquer cracks).^{17,20} Several studies have suggested a relationship between lacquer cracks and the development of CNM.^{7,8,15,17} Hotchkis and Fine²⁰ found the incidence of lacquer cracks to be higher



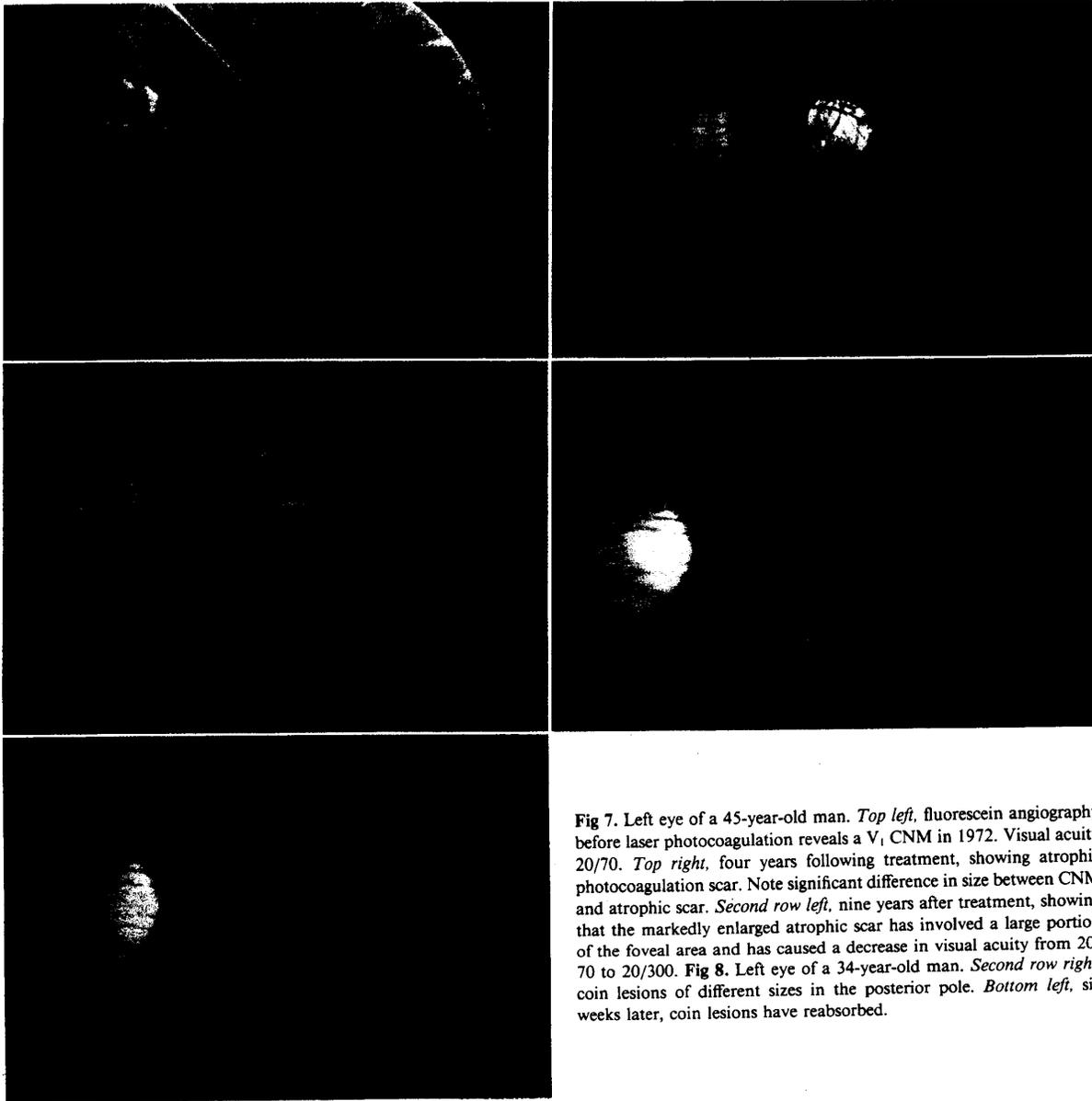


Fig 7. Left eye of a 45-year-old man. *Top left*, fluorescein angiography before laser photocoagulation reveals a V_1 CNM in 1972. Visual acuity 20/70. *Top right*, four years following treatment, showing atrophic photocoagulation scar. Note significant difference in size between CNM and atrophic scar. *Second row left*, nine years after treatment, showing that the markedly enlarged atrophic scar has involved a large portion of the foveal area and has caused a decrease in visual acuity from 20/70 to 20/300. **Fig 8.** Left eye of a 34-year-old man. *Second row right*, coin lesions of different sizes in the posterior pole. *Bottom left*, six weeks later, coin lesions have reabsorbed.

generative myopia are expected to show little or no leakage of fluorescein. This concept is supported by the observation that, of the 149 eyes in which a CNM was detected at the first visit (cross-sectional survey), 91% of V_1 CNMs (Fig 1) were found in eyes with severe grades of myopic chorioretinal degeneration (M_3 - M_5), and 80% of the V_2 CNMs (Fig 2) were seen in eyes with mild myopic chorioretinal degeneration (M_1 and M_2) (Table 1). This difference is significant ($P < 0.01$).

Because of their clinical behavior, V_2 CNMs might be considered "aggressive" and V_1 CNMs "nonaggressive." The aggressiveness of CNM thus appears to be

inversely related to the degree of degenerative myopia: the greater the degeneration and the thinner the choroid, the less aggressive the CNM. Because of this relationship, methods for measuring choroidal thickness, such as sophisticated ultrasonic techniques,²² might be useful in determining the long-term prognosis for eyes with CNM. The concept of new vessel aggressiveness should also be applicable to other entities associated with CNM, such as senile macular degeneration.

Degenerative myopia is so frequently associated with serious visual loss that it has often been called malignant myopia.⁷ Posterior pole staphylomas are associated with

poor visual prognosis.^{1,7,23} In 403 highly myopic eyes with posterior staphyloma, Curtin¹⁸ found a 34% prevalence of legal blindness. We found posterior pole staphyloma, which accounts for poor visual performance, in the great majority of eyes (97%) with CNM. The main cause of central vision loss in the untreated eyes with CNM seemed to be profound chorioretinal degeneration caused by stretching; exudation from the CNM seemed much less important. If we consider three groups—untreated eyes with CNM (Fig 4), eyes with treated CNM (Fig 6), and eyes without CNM but with posterior pole staphyloma (Fig 5)—we find that visual acuity deteriorated by the end of follow-up in all of these eyes. Among these three groups there was no statistically significant difference in the percentage of eyes with improved, stabilized, or worsened visual acuity (Table 2). It is interesting that after spontaneous remission of CNM, 38 (54%) of the 70 eyes with untreated CNM had improved or stabilized visual acuity by the end of the long-term follow-up. Fried et al²⁴ recently reported similar observations.

Laser photocoagulation of CNM may be indicated when exudation from the CNM reduces, or threatens to reduce, central vision by causing serous or hemorrhagic detachment of the RPE and sensory retina. This treatment modality has been successful in some patients who showed CNM associated with various ocular disorders, mostly senile macular degeneration.²⁵⁻²⁸ Although serous or hemorrhagic senile macular degeneration often results ultimately in exudative subretinal fibrovascular organization,²⁹ our long-term follow-up of 70 eyes with CNMs in high myopia has shown that most (96%, 67 eyes) developed nonexudative, atrophic scars. This benign course that we and others,^{7,8,16,24,30} have noted in followed cases of CNM in highly myopic eyes indicates that such lesions do not generally require laser treatment. In the rare instance of macular involvement due to a large amount of exudation from an aggressive (V₂) CNM, photocoagulation may be of value.

The increase that we noted in the size of atrophic macular scars following laser therapy (Fig 7) is easily explained by the progressive distension of the posterior pole of eyes with degenerative myopia. In four instances these scars eventually reached the foveal area and were directly associated with loss of central vision, although there was initial improvement or stabilization of visual acuity after laser treatment. Some atrophic, untreated, posterior pole scars also enlarged progressively, but to a lesser extent than the treated ones. Thermal damage may have caused a weakness in the already injured and stretched ocular coats. This enlargement of atrophic macular scars in the long term should be considered in the decision to apply photocoagulation to CNM in high myopes. In a few cases (V₂ CNM), however, the probability of developing large post-photocoagulation scars may be less damaging to vision than the immediate deleterious effects of exudation from the CNM. In fact, in the three eyes with V₂ CNM that we treated, the final visual acuity was the same as or better than the pretreatment level (Fig 3). Low-vision aids may benefit

Table 2. Final Visual Acuity Compared with Initial* or Pretreatment† Acuity in Eyes with Degenerative Myopia

Final Visual Acuity	No. Patients in Each Group		
	1* (%)	2† (%)	3* (%)
Improved	14 (20)	2 (14)	4 (9)
Stable	24 (34)	4 (29)	22 (48)
Worse	32 (46)	8 (57)	20 (43)
Total	70	14	46

* Group 1, eyes with untreated CNM; † group 2, eyes with CNM treated with laser photocoagulation; group 3, eyes without CNM and with posterior pole staphyloma. The differences among the three groups are not statistically significant ($P = 0.34$).

highly myopic patients, but since the size of atrophic macular scars is directly related to visual acuity,³¹ eyes with large, post-photocoagulation scars would benefit less from such devices.

Sattler³² was the first to point out that isolated macular hemorrhages, which we call coin lesions, are not uncommon in high myopia. The exact source of these hemorrhages has not been clearly established.⁸ Klein and Curtin³³ observed one or more such hemorrhages along the course of lacquer cracks in seven eyes. In our series, of the 58 eyes with coin lesions noted at the first visit, 97% (56 eyes) were associated with lacquer cracks. The most plausible explanation for the origin of coin lesions relates to the intimate anatomic relationship between Bruch's membrane and the choriocapillaris. Small breaks in Bruch's membrane (lacquer cracks) may also cause minute tears in the choriocapillaris. A coin-shaped hemorrhage would result, and multiple such hemorrhages may develop as lacquer cracks worsen slowly. The appearance, in some large coin lesions, of a dark point in their center and a lighter periphery suggests a concentration gradient of red blood cells centered on a single tear. Some coin lesions were associated with microtraumas to the eye, mostly rubbing. In myopic eyes, further distension of existing cracks could cause small tears in the choriocapillaris. Ophthalmologists should instruct patients with high myopia to avoid causing such microtraumas to their eyes.

We and others,^{8,15,33,34} have noted that coin lesions are relatively innocuous, and that prognosis for the retention of central vision after their resolution is good. In the 14 eyes that were followed closely, coin lesions were reabsorbed in an average of 6.4 weeks after the initial symptom occurred. The maculae returned to normal, functionally and anatomically (Fig 8), in all but one of the 32 eyes that were followed. In one case only, a small V₁ CNM was identified after reabsorption.

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Discussion

by

Brian J. Curtin, MD

Dr. Avila and his colleagues have reported an unusual fundus study of highly myopic eyes. Ophthalmoscopy, fundus photographs, and fluorescein angiography were used in the evaluation of 354 eyes. This study design is unique and, as expected, some very interesting data have been retrieved in this retrospective study.

These authors observed, among other things, that rubbing of the eyes in patients with highly myopic eyes produces

fundus hemorrhages, that subretinal neovascularization that does not leak beyond its perimeter is self-limited and does not require photocoagulation, and that Fuchs' spots have a guarded prognosis in respect to visual acuity.

There can be no disputing the malignant effect of acute or, for that matter, chronic elevations of intraocular pressure in highly myopic eyes. With sudden increases fresh tears in Bruch's membrane or the extension of old tears may occur with resultant hemorrhage. Unfortunately, high myopes are often dedicated to frequent and enthusiastic eye rubbing and they should be warned of the potentially harmful effects of this pursuit. Sustained increases in ocular tension decrease the perfusion pressure in the nonautoregulated choroidal vessels.

From the Myopia Clinic, Manhattan Eye, Ear & Throat Hospital, New York.

At our Myopia Clinic we have found a greater loss of choroidal circulation and retinal degeneration in glaucomatous eyes.

The finding of a relatively benign course of subretinal neovascular membranes with limited leakage is of considerable interest. Should this phenomenon be confirmed, it will give the clinician a more clear-cut indication for the photocoagulation treatment of these lesions.

Lastly, our essayists have noted that eyes with typical Fuchs' spots, indeed, have a guarded prognosis for the retention of central vision. A number of papers have intimated that these eyes improve in visual acuity as the acute changes of transudation and/or hemorrhage resolve. This is certainly true but if these same eyes are followed for several years an area of the surrounding retina, usually that which was involved in the "high water mark" of the transudation, will be seen to undergo atrophy. With this "areolar" atrophy, the fixation point is

often moved further away from the fovea with proportional loss of vision.

I congratulate Dr. Avila and co-workers for an extensive and innovative study. We need many more pieces such as these to fit into the puzzle before our treatment of this serious disease can be more effective. If I have any misgivings, they would concern the lack of distinction made between "subretinal neovascular membranes" and "Fuchs' spots". One is not synonymous with the other, and this lack of distinction makes a valid interpretation of the results difficult. There is also the matter of age. In pathologic myopia, patient age is crucial to the clinical findings. Subretinal hemorrhages in a teenager are usually a benign event, quickly absorbed with complete restoration of vision. These are mechanical in origin. Those in mid- and late-adult life are more often a consequence of neovascularization and are of much greater consequence.

Biomechanical considerations in high myopia: Part III - Therapy for high myopia

GARY R. BELL, O.D., M.S.Ed.

ABSTRACT: Clinical procedures for the treatment of high myopia are updated in this third part of a report on high myopia. After a discussion of testing techniques and refractive approaches for high myopia, an examination of therapeutic drug experiences shows their relative merits. The author believes that more investigation of beta blocker and epinephrine topical solutions is needed pertaining to the treatment of high myopia. Theoretically, such agents could improve deficient arterial perfusion of the highly myopic eye, and could be helpful in retarding scleral creep. Lifestyle recommendations include patient advice on accommodative reduction and proper exercise techniques. Low impact aerobics may have merit for highly myopic patients since the improved cardiovascular efficiency they can provide may improve the deficient arterial perfusion of their retinas. A summary of the three-part report on high myopia concludes the article. The physiological patterns of high myopia dovetail into the biomechanical considerations showing that a scleral pathogenesis hypothesis of myopic development is a viable working theory. The author's clinical procedures reflect the influence of that theory. If research were redirected from deprivation studies to investigating biomechanical considerations and pharmacological approaches to high myopia, the author contends that dramatically improved treatment regimens could result.

KEY WORDS: pseudomyopia, myopic exophthalmos, atropine, hypotensive agents, sphygmous pulse amplitude.

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A new commitment to the prevention of vision loss is needed in high myopia therapy. I will address a more aggressive pattern in treating this anomaly, looking at the realms of refractive therapy, pharmacological therapy, lifestyle alterations, and surgical interventions.

Refractive therapy

In my investigation of myopia, I have found no breakthrough approaches in the refractive treatment of high myopia. These patients merely need meticulous care in the techniques we already use. This is particularly true when it comes to refraction. While many high myopes can be adequately refracted with noncycloplegic, binocular refraction techniques, there are certain subgroups that may benefit from cycloplegic refractions. These subgroups include; very young congenital myopes, monocular amblyopic high myopes, high myopes with cataracts, and high myopes with reduced acuity. One should always carefully check the vertex distance of the refracting instrument and the chosen spectacle frame. A check of the change of refraction using Halberg or Jannelli Clips over the patient's old prescription is a wise idea. Accurate cylinder correction is thought to be beneficial to the course of high myopia.¹ Duke-Elder recommended undercorrection for high myopes, citing their frequent discomfort with full correction.² Curtin states, "The most acceptable lenses for highly myopic patients are the weakest that can adequately meet their visual requirements."³ Probably the best policy is a special emphasis on "plus bias" with the refraction without fogging the distance vision. Any correction that induces "squinting" should be thought of as undesirable, since such obicularis squeezing can raise the IOP in spikes.⁴ For similar reasons, rubbing of the eyes should be discouraged. Bifocals may be indicated in nonpresbyopes if a sizeable near point esophoria is present.⁵ Base in prism has been advocated, but substantial amounts would be needed to significantly reduce convergence and such amounts would likely spur rejection of the prescription in many cases.

Contact lenses have optical merit for these patients, increasing retinal image size and reducing the prismatic effects of spectacles, while providing cosmetic improvement. Myopic exophthalmos can increase the difficulty in obtaining a successful fit, as can increased lens thickness. Gas permeable lenses have been found to have partial effectiveness in arresting myopia, and are widely used for that purpose.⁵ Corneal flattening tendencies are certainly part of the explanation of the decreases in progression found in such fits. Contact lenses may alter behavior somewhat, as they reduce the comfort of reading for myopes. Kelly has suggested that the movement and gentle massage exerted by rigid lenses causes an increase in aqueous outflow, aiding myopia.⁶ This interesting hypothesis is without experimental confirmation.

A few notes should be made about ophthalmoscopy. Direct ophthalmoscopy is of limited value in high myopia, due to the high magnification and small field of view in such cases. The Reichart Monocular Indirect Ophthalmoscope is a nice substitute for the direct ophthalmoscope in high myopia. Few other patient groups need binocular indirect ophthalmoscopy more than high myopes, with their high incidence of peripheral retinal defects. Techniques to allow examination beyond the equator with higher powered condensing lenses and scleral depression also are invaluable. The new, high powered convex fundus lenses, combined with a slit lamp, provide an excellent way to evaluate the posterior pole binocularly. Periodic retinal photography of fundus defects is recommended to monitor the progression of the pathological process.

Special consideration needs to be given to visual fields in high myopia. Blatt found a variety of field defects associated with high myopia,⁷ including central defects, paracentral defects, arcuate scotomas, concentric contraction, annular scotomas, hemianopic and quadrantanopic defects. The high refractive error and staphylomas can lead to the false detection of field defects. Contact lenses are thought to provide the most reliable method of optically preparing the highly myopic eye for fields testing.⁸ If the practitioner finds an unexpected field defect with a high myope, retesting with a disposable soft lens (or other high-minus soft lens) in place may reveal improved performance.

Pharmacological therapies

The use of topical ophthalmic pharmaceutical preparations in the treatment of high myopia is an area of growing interest. International investigations of various drug interventions are currently in progress.⁹

A considerable body of evidence has been collected on the use of cycloplegic agents in the treatment of myopia, both in humans, mammals, and even in chicks.¹⁰ Atropine has been the most widely studied cycloplegic, and has shown some effectiveness in arresting myopic progression.¹¹ Atropine has long term treatment problems that include; sustained mydriasis, risk of radiation injury, ciliary and zonular atrophy, contact dermatitis, toxic responses, intense photophobia, poor patient compliance, and post-treatment "catch up" progression. Atropine therapy for myopia has existed since the 19th century and never has become popular within the medical community, probably due to the myriad of problems associated with its use. The atropine research is of value in what it can tell us about myopia. As noted earlier, it points to an accommodative role in myopic progression. While well known for its inhibition of aqueous outflow at the trabeculae, atropine increases uveoscleral outflow in the vitreous chamber, which may be helpful in axial myopia.¹²

Hypotensive agents would seem to possess positive characteristics for highly myopic patients. Drugs already in use for glaucoma are currently being investigated for myopia, primarily outside the U.S. Substantial evidence cited here and in other sources suggests that the scleras, choroids, and retinas of high myopes are being exposed to harmfully high levels of biaxial tensile stress. With lowered IOP, stress on the ocular coats should be reduced with concomitant declines in scleral creep and enhanced retinal and choroidal arterial perfusion. To buttress this concept, a review of Tarkanen's monocular congenital glaucoma studies is revealing.¹³ The affected glaucomatous globe usually had significantly greater axial length than the unaffected eye. Successful glaucoma surgery in these cases resulted in post equatorial axial length decreases of up to 0.8 mm as pressures were lowered in these eyes.

Investigations of timolol maleate are in progress. Giovannini et al. found improved choroidal sphygmous pulse amplitude in high myopes using timolol.¹⁴ This finding could hold considerable promise for high myopes facing choroidal and retinal degeneration. Another study of timolol used for grammar school aged myopes in Denmark found that the treated group had little improvement in progression rates compared to a control.¹⁵ Commenting on individual chartings of children in this study, Jensen and Goldschmidt noted that many children did not show a significant hypotensive effect using 0.25 percent timolol twice daily.¹⁶ Another study found that a different beta blocking agent, Labetalol, (not yet approved in the U.S. by the FDA) showed some effectiveness in retarding myopic progression over a 4-month period.¹⁷

Phenylephrine hydrochloride has been used in two studies of myopia control, and demonstrated partial success in arresting the error.^{18,19} Phenylephrine has adrenergic effects similar to epinephrine, although its hypotensive effects are not substantial. In prolonged usage, phenylephrine is toxic to the epithelium, and this is a deterrent to its value as a myopia control agent.²⁰

Weiner recommended instillations of 1/1000 solutions of epinephrine three times a day for progressive myopia, claiming a 50 percent arrest rate.²¹ Macdiarmid and Hamilton found Weiner's regimen to be effective when used in children under 7 years of age.²² Epinephrine has several actions that could be beneficial to high myopia; it increases aqueous outflow while also suppressing aqueous formation, it reduces IOP, it slightly inhibits accommodation, and it provides mild mydriasis.²³ Although not investigated yet, its hypotensive effects probably increase choroidal sphygmous pulse amplitude also. Dipivefrin (Propine) is a prodrug that is transformed into epinephrine once in the eye. Propine is noted for decreased stinging and side effects, which enhanced absorption compared to L-epinephrine.

This drug should be investigated for therapeutic use in high myopia.

The drugs known as miotics include pilocarpine, carbachol, demecarium, echothiaphate, and others. These drugs substantially lower IOP, but should not be used for myopia control for a number of reasons. These drugs usually cause accommodative spasms that increase myopia. They also reduce ocular rigidity, decrease uveoscleral outflow,²⁴ and increase the risk of retinal detachment.

One type of pharmaceutical agent that investigators are looking for is an agent that would increase scleral resistance to stretch. Fledelius and Goldschmidt have predicted the development of a fibroblast growth factor that would help stimulate the growth of new scleral collagen in the posterior pole.²⁵ Other approaches that might strengthen the sclera include agents that would help calcify posterior pole collagen, or agents that catalyze the formation of the aldehyde cross-links between collagen molecules. Such scleral strengthening agents theoretically should produce superior myopia control therapy, but they only exist hypothetically at present.

One final note on pharmaceutical agents in the treatment of high myopia: Investigators should not judge the efficiency of such drugs based solely on the drug's effect on the progression rate. Improved sphygmous pulse amplitude and choroidal arterial profusion might be very important factors in reducing the degenerative processes of high myopia, making drugs such as timolol potentially important even without refractive improvement.

Lifestyle changes for high myopia

Many years ago environmental changes were introduced into western schools due to concern about "school myopia." It's time to update our guidance for high myopes; introducing lifestyle changes that should help them retain useful vision. Myopes frequently seem to be prolific readers. They also tend to work at near point occupations.²⁶ Optometrists often have been inhibited in telling people to limit reading or other near point activities. After all, such activities are enriching and stimulate the intellect. Optometry should be looking into innovative ways to reduce accommodative overloads for myopic children, such as using opaque projectors to project the reading material onto a wall, or projection computers that would reduce computer associated asthenopia. Conversely to near point occupations, hard manual labor seems to be hazardous to high myopia,²⁷ as we may hypothesize that the extreme straining of such occupations probably increases IOP.

Certain types of exercises seem indicated for high myopes, such as low impact aerobics, while other exercises should be avoided. Exercises that induce intense straining, such as weight lifting, may cause an upward

spike in IOP. Boxing is obviously hazardous. High board diving may also be excessively risky. Low impact aerobic activities seem to lower IOP somewhat,²⁸ and as improved conditioning occurs, cardiovascular efficiency gains will probably extend to the choroidal and retinal vasculature. This conditioning effect may be superior to the improved arterial flow caused by hypotensive drugs, since conditioning effects last for months whereas hypotensive drugs last a maximum of 12 hours.

Dietary change for high myopia is an area of complexity and confusion. There seems to be a consensus that modern nutrition has contributed to a reduced rate of high myopia in Northern Europe during the last 100 years.²⁹ Goldschmidt compared a large sample of modern (1964) military conscripts to a similar sample provided by Tscherning in 1882. Although the rates of simple myopia were very similar, the frequency of high myopia was 2.8 times higher in Tscherning's sample. Vitamin supplements, used in modest amounts with broad vitamin and mineral ingredients, may be of benefit in high myopia, until the nutritional picture becomes clearer. Nutrient deficiencies that have been implicated in progressive myopia include vitamins A, B, C, D, E, chromium, copper, and amino acids in protein.³⁰ None of these deficiencies has been repeatedly verified as a cause of myopia. Zinc deficiency has been implicated in macular degeneration, which occurs with increased frequency in high myopia.³¹ Vitamin C is of interest because it directly participates in the formation of collagen, and in its presence, collagen has greater tensile strength.³² Additionally, ascorbate has been found to have hypotensive effects.³³ The eye has an ascorbate pump, which is evident from the high levels of intraocular sodium ascorbate compared to mean plasma levels.³⁴ But, increasing the ascorbate in the blood doesn't increase ocular ascorbate beyond a maximum level. Because of these pump characteristics, steady low doses of Vitamin C should be more effective at attaining optimal intraocular levels than large uneven doses. One potential pitfall with Vitamin C supplements is that the nutrient is an antioxidant, which could work against the formation of oxidative cross links that increase scleral stretch resistance. Research on the effects of Vitamin C on the sclera is needed.

Surgery for myopia

Ophthalmology has been rapidly expanding the surgical procedures available for myopia. As already mentioned in Part I, lasers are increasingly being used to treat retinal breaks, and seal neovascular nets. A report on disciform degeneration with patients having Forster-Fuchs spots recommends laser coagulation of subretinal neovascular nets.³⁵ Their conclusion was based on a poorer than previously thought prognosis for this condition. Ernst noted that laser therapy in these cases, as



Figure 1: Several characteristics of high myopia are shown in this photo; an extensive temporal, chorio-retinal crescent, straightening of the retinal vessels, and an early Forster-Fuchs spot. The yellow-whitish branching streaks of the retina are lacquer cracks in Bruch's membrane.

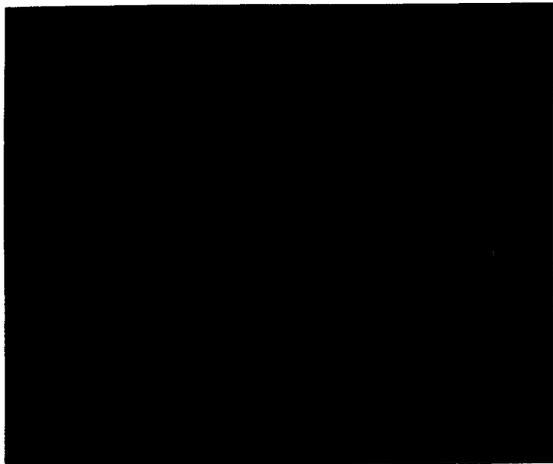


Figure 2: This photo demonstrates a double myopic crescent. Somewhat difficult to see is macular degenerative changes in this 39-year-old male. At 4:30 position below the disc some whitish lacquer cracks are evident. These represent fissures in the retinal pigment epithelium-lamina vitrea-choriocapillaris complex.

in age-related macular degeneration, is only effective in a few patients who have active neovascular membranes distant from the fovea³⁶

Curtin reports discouraging results from scleral reinforcement surgery at the Sprague Myopia Clinic in New York.³⁷ Pavan recommends surgical insertion of autografts of fascia lata or homografts of sclera for degenerative myopia.³⁸ It seems likely that with increased emphasis on surgery for high myopia, inventive

surgeons will perfect scleral reinforcement in the near future, improving the prognosis for the gravest cases of high myopia.

Popular radial keratotomy and keratomileusis procedures seem almost irrelevant to the discussion of high myopia. These procedures improve cosmesis, but provide no relief for the pathological processes of high myopia. With increased surgical skills and the probable development of sophisticated sculpturing lasers, more myopes will probably be placing their eyes in the hands of the surgeons in the future. This probability heightens the need for optometry to become a source of myopia prevention, with therapeutic drugs aiding such an expansion of services.

Summary

In this series, I have surveyed the biomechanical considerations of high myopia in some detail. The scleral distensibility (mesodermal) theory of myopia development was reviewed in Part I. The theory is both hereditary and environmental in nature, and is gaining adherents internationally. I have examined the puzzling relationship between glaucoma and high myopia. A simple relational statement can be made about open angle glaucoma and axial high myopia; in both conditions the eyes have excessive amounts of aqueous in them. From the evidence of excessive stress loads on the choroid, retina, and sclera, I would hypothesize that reducing the excess aqueous volume should aid the health of the highly myopic eye, just as it does the glaucomatous eye. In any case, practitioners need to be aware that highly myopic ocular hypertensive patients are about eight times as likely to develop glaucoma as nonmyopic ocular hypertensives.³⁹

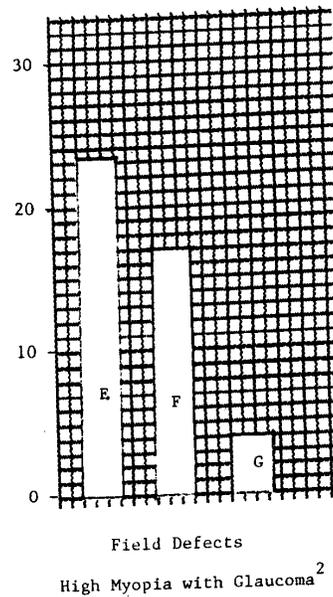
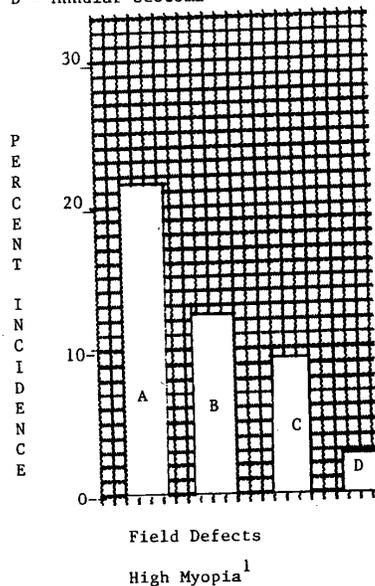
Animal visual deprivation studies are yielding dramatic results, although the data are hard to apply directly to most clinical cases of myopia. An underlying current in the discussion of the results of the animal deprivation studies is that retinal mechanisms control the global distension that was produced in these experiments. Studies found a retinal depletion of dopamine in visually deprived monkeys and chicks.^{40,41} In contrast, a Japanese study of three lid-sutured monkeys found scleral alterations pointing to a scleral distensibility causation.⁴² This upsurge in research of myopia is very encouraging.

As noted in Part II, the analysis of balloon expansion dynamics should cause investigators to reanalyze the use of Laplace's law in calculating scleral stress loads. The stress-strain testing of strips of sclera from different regions of the globe shows the lack of homogeneity of the sclera, further discouraging the use of Laplace's law.⁴³ According to those results, the staphylomas of high myopia most likely should occur in the posterior pole region, which is most often the case. Thus, more evidence in favor of the scleral distensibility

TABLE 1: FIELD DEFECTS IN HIGH MYOPIA

A - Concentric contraction
 B - Central scotoma
 C - Hemianopia/quadrantopia
 D - Annular scotoma

E - Enlarged blind spot
 F - Temporal fiber-bundle defect
 G - Superotemporal defects



- 1 Blatt N, Gesichtsfeldveränderungen bei hochgradig Myopen. *Klin Monatsbl Augenheilkd.* 145:680, 1964
- 2 Greve EL, Furuno F, Myopia and Glaucoma. *A Von Graefes Arch Klin Exp Ophthalmol.* 213:33, 1980.

theory of myopia development seems revealed. The cycled stress elongation of several strips of pig sclera could represent an experimental example of how myopic scleral creep takes place.⁴³ A plateauing of stress measurements occurred in these pig scleras that showed permanent elongation, in a manner somewhat similar to the balloon expansion phenomena.

Coleman's theory of accommodation was reevaluated, and this hypothesis is worthy of much more experimental attention. We need to know whether the pressure increases in the vitreous chamber during accommodation. Young has provided us with evidence that it does.⁴⁴ It would appear that the rheo-oculography techniques of Giovannini et al.⁴⁵ could be used to test this theory, as changes in the choroidal sphygmous pulse amplitude during accommodation could reflect vitreous chamber pressure dynamics.

Greene has caused one of the oldest theories of myopic development to reemerge—scleral stretching caused by extraocular muscle contractions.⁴⁶ Moses et al. have given this theory added impetus, pointing out that a large part of the resistance in IOP is provided by

the EOM, especially at the equator.⁴⁷ The only modestly successful treatment mode in retarding myopic progression, atropine dosage, tends to point away from an important role of the extraocular muscles.

According to calculations based on Darcy's law, the uveoscleral outflow of highly myopic eyes may be much higher in amount than that of other refractive groups. This finding should be tested experimentally. Whether or not increased uveoscleral outflow influences the clinical course of myopia is not known. Increased uveoscleral outflow may help explain enigmatic cases of high myopia with normal levels of IOP, but decreased levels of outflow facility.

I have explored treatment methods in Part III that include optical correction techniques, lifestyle changes, and the investigation of the possible usage of hypotensive drugs. Hypotensive drugs may improve the arterial perfusion of highly myopic eyes and, if the mesodermal theory of myopic development is valid, discovery of an optimal agent should help reduce myopic progression rates. In investigating lifestyle changes in high myopia, I believe we may be underestimating the value of low

impact aerobic conditioning on choroidal and retinal health. At the same time, we need to warn the high myopes about sports and occupations that could adversely affect their condition. Nutritional and hormonal contributions to high myopia remain an area of darkness. We need to start over from "square one" to investigate this important arena of eye research.

The other theory of myopic development, the ectodermal theory, with an aberrant retinal pigment epithelium being the underlying control of axial distension, holds out fewer possibilities for pharmacological alteration than the mesodermal theory. The finding of a dopamine deficit in the retinas of deprived animals may provide an avenue by which myopic degeneration can be treated under this theoretical basis. Efficiently delivering dopamine to the RPE could prove to be a formidable obstacle. Since it holds more potential for ocular alteration, the mesodermal theory deserves equal research attention, which it currently doesn't seem to be getting.

It is hoped that optometry will get involved in the new interest in research concerning myopia. With the scope of optometric practice expanding, optometrists could become a trusted source of real help for our highly myopic patients. Progress in research in high myopia also could lead to progress in the treatment of less severe forms of myopia, and other refractive errors. ■

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Clinical Visual Optics

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Subjective refraction

Introduction

A patient may wish to have an eye examination for one of many reasons such as poor vision either at distance or in close work, asthenopic symptoms such as head or eye aches or for a general check on the state of his eyes. An eye examination consists of four main parts: checking the health of the eyes, measuring any optical errors of focusing, evaluating the efficiency with which the two eyes work together and deciding whether to prescribe some form of optical correction or treatment (such as orthoptic training) to improve the binocular functioning of the eyes.

The patient's refractive error, or refraction as it is often called, may be estimated by two broad methods: objective and subjective. The former requires no help from the patient except to look in a certain direction or into an instrument, the adjustments being made by the examiner (*see* Chapters 17 and 18). Subjective refraction requires the co-operation of the subject and many of the specific techniques will be discussed in this chapter. Although it is based on scientific principles, the experienced refractionist realizes that subjective work is partly an art; the ability to know which method to use for a particular patient and the ease with which understanding is established with patients can come only with experience.

In general, a patient's refractive error is first estimated objectively. There may be errors involved in an objective measurement, so the refraction is usually checked subjectively in order to refine it. There are patients, for example, young children, with whom it is not possible to make a

satisfactory subjective examination, in which case the prescriber relies on the objective results alone. In order to impart a thorough understanding of the methods of subjective work, it is better, however, to describe subjective refraction without assuming an initial objective assessment. The later parts of this chapter will describe how the various subjective techniques are normally linked with a prior objective refraction. Some of the more sophisticated methods of balancing the monocular findings will then be discussed.

Unaided vision and refractive error

The first step in measuring a refractive error is to determine the patient's unaided vision with each eye separately and then binocularly. As shown in Chapter 4, myopia will cause a reduction in distance vision from a standard which is usually taken as 6/6 or better. A hypermetropic error may also cause a reduction in vision, depending on the ability of the eye to increase its refractive power by accommodation. In a young person there is usually ample accommodation and such a patient with a small or medium hypermetropic error will be able to read the small lines on the test chart. Even so, prolonged use of the eyes for detailed vision may cause discomfort since more than the usual amount of accommodation is required. The maximum power of accommodation declines with age (*see* Chapter 7), therefore an older person with even a small hypermetropic error of one or two dioptries will have reduced vision.

An astigmatic error may be combined with either myopia or hypermetropia. With myopia or

high hypermetropia, both the astigmatic and spherical components of the error reduce the unaided vision. When astigmatism is combined with a low hypermetropic error in a young patient, accommodation can be brought into action so as to place either of the focal lines or the circle of least confusion on to the retina. Even so, vision is usually reduced. With a small astigmatic error, the vision may be almost normal, but if either focal line may be brought on to the retina, accommodation is unstable and asthenopic symptoms often result. Paradoxically, a larger astigmatic error may cause less asthenopia, because the vision is too poor to stimulate alternations of the level of accommodation between the two astigmatic foci. Moreover, the change in accommodation required may be too great for easy adjustment. If the axes of the error are approximately horizontal or vertical, unaided vision is often reduced less than with an oblique error; this is because most letters are composed of vertical and horizontal strokes.

Table 6.1, which is based on the studies plotted in Figure 4.22, gives the approximate relationship between unaided vision and spherical and astigmatic ametropia. With modern apparatus using non-serif letters and higher luminances, the predicted ametropia may be slightly higher than the figures tabulated. For example, a score of 6/12 (20/40) is often possible with ametropia of 1.00 D.

The predicted vision in astigmatism is tabulated on the assumption that the circles of least confusion lie on or close to the retina, either naturally or with the aid of accommodation or trial lenses. The vision with a given dioptric value of astigmatism is better than for the same amount of spherical ametropia (compare equations 4.17 and 5.9). For a patient already wearing spectacles, or halfway through a subjective routine, Table 6.1 can be used to predict the remaining error.

This table is reasonably accurate for a pupil size of about 4 mm. With much larger pupils, which can occur in young patients or in low illumination, the same deterioration in vision will be caused by a smaller error. Conversely, a patient with small pupils, about 2 mm, will be able to see better than predicted for the refractive error. A patient who is used to being under-corrected may see far better than expected from the size of the error, because he or she is used to interpreting blurred images, whereas a person who has recently broken his spectacles will be

Table 6.1 Expected vision in various ametropic states

Vision	Refractive error (D)	
	Spherical*	Astigmatic
6/6 (20/20)	small	small
6/9 (20/30)	0.50	1.00
6/12 (20/40)	0.75	1.50
6/18 (20/60)	1.00	2.00
6/24 (20/80)	1.50	3.00
6/36 (20/120)	2.00	4.00
6/60 (20/200)	2.00 to 3.00	high

* Myopia or absolute hypermetropia.

Note The predicted vision in astigmatism is on the assumption that the circles of least confusion lie on or close to the retina.

more greatly handicapped and may accordingly be led to the erroneous conclusion that the spectacles have made the sight worse.

Some people habitually squeeze their eyelids together in order to see clearer: reducing the effective pupil size decreases the retinal blurs. This habit or manoeuvre is sometimes erroneously called 'squinting'.

The practitioner can make use of the pinhole disc to test whether reduced vision is due to poor focusing or to a retinal defect such as amblyopia or macular degeneration. If the pinhole – about 1 or 1.5 mm diameter – improves the vision, then in general there is ametropia to be corrected. An exception to this rule occurs when opacities in the ocular media produce an irregular focusing effect. In this case the pinhole may give a better acuity than a lens alone if it isolates a small region which is sufficiently homogeneous to give a good focus.

Basic equipment for refraction

The distance test chart has already been discussed in Chapter 3. By convention, the normal testing distance is 6 metres or 20 feet but is sometimes varied slightly to suit the size of the consulting room. To enable the patient to adopt a comfortable posture, the chart should be placed at an average eye-level. Frequently, a reversed or indirect chart is used, viewed by the patient in a mirror. In this case, the mirror and image of the chart should be at the patient's eye level, the mirror being angled if necessary to enable the test chart or cabinet to be placed at a greater height convenient for the practitioner.

It is important that the mirror should be large enough so that the test-chart surroundings are visible even to patients not of average height or tending to sit to one side. If the mirror is framed, the colour of the frame should merge with the surrounding wall. This reduces any tendency on the patient's part to accommodate for the distance of the mirror instead of attempting to relax his accommodation as fully as possible.

The room illumination should be at a comfortable indoor level: pupils dilate in the dark and a refraction under these conditions will be influenced by the aberrations due to the peripheral parts of the eye's optical system. The correction found under these conditions may not be the best for use in daylight out of doors with a normal size pupil. A trial case of separate lenses is a necessity, even if a refracting unit (or phoropter) is normally in use. Trial case lenses are placed in a trial frame (*Figure 6.1*) worn by the patient, or, less frequently, supported by a wall bracket. They may either be full aperture, about 38 mm diameter, or of a reduced aperture of 20 mm or so in a full-size mount. The larger lenses enable the practitioner to obtain a better view of the patient's eyes and similarly give the patient a larger field of view. On the other hand, reduced-aperture lenses are lighter and thinner. They are better protected by the wide rim and less likely to break if dropped. The wide rim also tends to prevent finger marks on the lenses and permits clearer power markings. A further advantage is that the trial sets are available in a more extensive range of fractional powers than full-aperture trial sets.

In a refracting unit, discs of reduced-aperture lenses are so mounted that any spherocylinder combination can quickly and easily be placed before the patient's eye.

Such units are large and must be mounted mechanically. As a result, the patient's head has to be kept pressed against the unit, which can be uncomfortable. Also, in some designs the unit cannot be tilted, which means that near vision testing has to be undertaken in a horizontal plane. Nevertheless, refracting units have many practical advantages.

The designs of trial lenses, whether for use with a trial frame or in a refracting unit, raises several problems arising from effectivity, that is, the effect of lens form, thicknesses and separations on the vergence of the emergent pencils of light. As far as distance vision is concerned, these problems can be overcome by designs based on the principle of

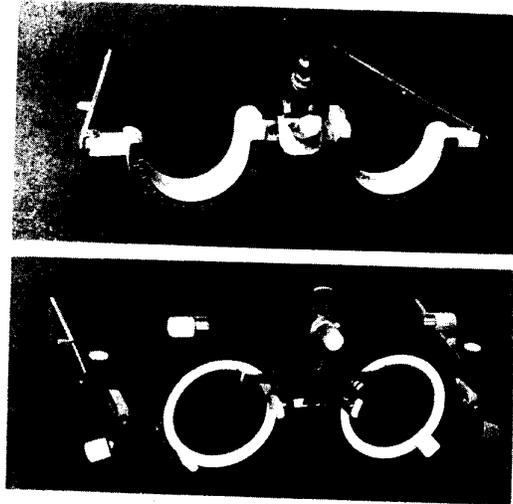


Figure 6.1. Oculus drop cell and rotating cell trial frames.

additive vertex powers, but in near vision the full-aperture symmetrical and reduced-aperture curved forms are generally superior (*see also Report of a Ministry of Health Committee (1956) and Bennett, 1968*).

The trial frame or refracting unit should be carefully centred to the patient's inter-pupillary distance (abbreviated to PD). There are specialized instruments for measuring the PD (*see page 266*) but reasonable accuracy may be obtained with a simple ruler, or better still, a rule with a fixed cursor at the zero of the scale and a movable cursor. The rule is held in the spectacle plane and the patient is directed to look at the examiner's right eye. Using this eye, the examiner lines up the zero cursor with the centre of the patient's left pupil. With the rule still held in this position, the patient's attention is redirected to the examiner's left eye, and using this eye the second cursor is lined up with the centre of the patient's right pupil. This gives the distance PD. The near PD is measured by asking the patient to look at one of the examiner's eyes, the examiner leaning forward so that the distance from patient to practitioner is the same as the usual working distance. The cursors are lined up with this eye alone, the rule again being held in the spectacle plane.

Available trial case accessories include centring discs, which can be used in a similar manner to adjust the trial frame directly to the patient's PD.

They also facilitate the vertical adjustment* which is no less important than the horizontal centration. Another necessary adjustment, made by angling the sides, is to set the plane of the lenses at right-angles to the line of sight.

Finally, the projection of the trial frame should be adjusted so that the vertex distance, as far as can be judged, will be little changed if spectacles are subsequently worn. Because of effectivity considerations, the strongest spherical lens needed should be placed in the rear cell, with any weaker auxiliary lenses in front of it. When the lens power exceeds about 5 D, the vertex distance should be measured and recorded as part of the prescription. At the dispensing stage, when the frame and lens type have both been chosen, the vertex distance with these spectacles can then be estimated. If it differs from that recorded in the prescription, calculation as in Chapters 4 and 5 or reference to tables will show what alteration, if any, to the original prescription should be made to reproduce the same effect at the eyes.

The vertex distance may be measured with special calipers, by placing a stenopaic slit in the rear cell of the trial frame and pushing a thin card scale through it to meet the patient's closed eyelid, or, less accurately, by viewing from the side with a rule held against the side of the head.

Since trial frames are relatively heavy, it is more comfortable for the patient if the frames are removed occasionally during the refraction, for example, when writing down the objective findings and later the subjective results for distance.

The many other items of equipment in general use will be described in the relevant places.

Measurement of a spherical ametropia

A standard routine

Although the possibility of astigmatism should never be excluded, it is simpler initially to assume

* Trial frames and many refractor heads cannot be adjusted to compensate for a marked vertical difference in eye and pupil positions. With some patients, the final spectacles may be best fitted off the horizontal so as to match the brow line; in this case the trial frame may be similarly tilted. In other cases, the spectacles and trial frame or refractor head should remain horizontal. An allowance for induced prism, much as discussed on pages 317–318, may then be needed.

that any ametropia present is purely spherical. The first stages in the routine apply in either case. The unaided vision will give some guide as to the possible size of any error. If the vision is good, for example 6/9 or better, it indicates a small amount of myopia, emmetropia or hypermetropia. If hypermetropia, there could be a small absolute error in a middle-aged person, or a medium or large error in a young patient. While the patient is still observing the distant test chart, with the other eye occluded, add +1.00 DS. If the vision is made worse, try +0.50 DS; if the vision again deteriorates, the patient is emmetropic or myopic. Then try -0.50 DS; if the vision improves, the patient is myopic. From *Table 6.1*, -0.50 DS should improve the vision from 6/9 to 6/6, but some patients with 6/9 vision may need slightly more negative power.

If the initial +1.00 DS made a slight improvement or no difference to the vision, hypermetropia is confirmed. Since accommodation can overcome all or part of a hypermetropic error, positive sphere should continue to be added until the vision no longer continues to improve. Initially, the plus power should be increased in whole dioptre steps until the next addition of +1.00 DS causes a reduction in vision. At this stage, half and quarter dioptre steps should then be used.

Now suppose the patient's unaided vision to be 6/24. *Table 3.1* predicts an error of about 1.50 D, so a +1.50 DS lens should be tried initially. If this improves vision, continue adding positive spherical power as in the previous example until no more is accepted, that is, further addition causes blurring. On the other hand, if the initial positive lens made the vision even worse, then a minus lens, say -1.00 DS, should be tried next. This should improve the vision to about 6/9, and a little more negative sphere should then give the best VA. The change in minus sphere should be consistent with the improvement in acuity; for example, it should not require -4.00 DS to improve the vision from 6/24 to 6/6. Over-minusing an eye merely stimulates accommodation without improving vision and makes the eye effectively hypermetropic.

It is, however, a familiar fact that if a myopic eye is slightly over-corrected (too much minus power) or a hypermetropic eye is slightly under-corrected, the test letters or symbols generally appear smaller and blacker. The accepted rule is that the highest positive or lowest negative power that gives the best acuity should be regarded as

the ametropic error. Other factors have to be taken into consideration, and we shall discuss this rule later in greater detail.

In order to verify the refractive findings so far determined, check tests must be applied. The simplest test is to add positive power to the correction, whether the patient is hypermetropic or myopic. If the patient's acuity is 6/6, then addition of +0.25 DS should blur the line fractionally, but without rendering it illegible. An addition of +0.50 DS should blur the vision back to 6/9, and a +1.00 DS to 6/18, as predicted by *Table 6.1*. If the patient can still read 6/9 through an extra +1.00 DS then either the first result is incorrect or the patient has either a smaller pupil or greater ability in interpreting blurred images than average. Normally, this check test is carried out only with a +1.00 DS.

A disadvantage of increasing positive power from zero when refracting a hypermetropic patient is that accommodation is then brought into play until the ametropia is fully corrected. Some patients, however, find it difficult to make the accommodation relax once it has been exerted. Accordingly, an alternative approach is to start by obtaining the best spherical lens, as described above. The +1.00 DS check test is then applied. Next, this extra lens power is reduced* by a quarter of a dioptre at a time until the best line is again read. Perhaps only half a dioptre need be removed if some relaxation has taken place. This method is called 'fogging'.

Unfortunately, some eyes will react to a 'fogged' image by accommodating, even though this makes the retinal image worse. Ward (1987) showed that this reaction does not usually occur unless the eye is fogged by more than +1.5 to 2.0 D. The resulting vision of about 6/30 is then too blurred to control accommodation which may then drift towards its resting state (*see the discussion on inadequate stimulus myopias in Chapter 7*). The binocular methods of refraction to be described later are greatly superior.

* During these lens changes, add the new lower powered lens before removing the original lens or use the other hand as an occluder. Accommodation will be stimulated if the patient is allowed to see the chart with less than the full correction in the trial frame.

Bichromatic (duochrome) methods

The human eye is not corrected to focus light of different wavelengths at the same image point, that is, it suffers from both axial and transverse chromatic aberration. The axial aberration may be used to help determine the spherical component of the refractive error. If yellow light is focused exactly on the percipient layer of the retina, the blue-green focus will lie in front of the retina and the red focus behind it.

One of the earliest tests based on this principle and suitable for clinical use was designed by Clifford Brown and patented in 1927. It used carefully selected red and green glass filters and was marketed under the trade-name 'duochrome'. More recently, the word 'bichromatic' has become an accepted generic term for tests of this kind, though 'dichromatic' is said to be etymologically more correct.

Although the retina is most sensitive to light of a greenish hue in photopic conditions, Ivanoff (1953) found that for distance vision the eye tends to select a yellow focus in preference to green. The choice of filters takes this into account, together with the spectral distribution of energy of the typical tungsten-filament light source and the spectral luminous efficiency curve of the eye. Thus, green filters conforming to the British Standard* have their peak luminosity at wavelength approximately 535 nm and the red at approximately 620 nm. Relative to a best focus in the yellow at 570 nm, these filters give a green focus about 0.20 D forward and a red focus at about 0.24 D behind (Bennett, 1963). Another property of these filters is that they appear of approximately equal brightness to the observer with normal colour vision (*see also pages 346-347*).

Since the red and green foci are equally spaced about the yellow, an emmetrope (or corrected ametropes) should see black test objects on the two coloured backgrounds equally clearly (*Figure 6.2a*). Bichromatic test panels may show a series of Snellen letters on each colour, a series of concentric rings (usually in the 4.5, 12 and possibly 24 m sizes) or a pattern of dots. Since the 'white' focus for a low myope falls a short distance in front of the retina, a myope will see the pattern

* BS 3668: Red and Green Filters used in Ophthalmic Dichromatic and Dissociation Tests.

on the red background clearer; and, conversely, a hypermetrope will prefer the green. This means that if the red is seen clearer a minus lens is required (*Figure 6.2b*) and a plus lens if the green pattern appears clearer.

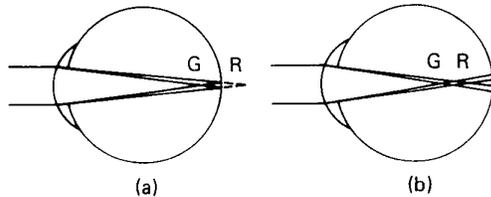


Figure 6.2. (a) Principle of the bichromatic (duochrome test). G indicates the focus for green light, R the focus for red light. When yellow light is in focus, these should lie approximately equidistant from the retina, one in front and one behind. (b) In the myopic eye, the red focus lies closer to the retina.

The bichromatic panel may be used as another check test: the patient is asked whether the pattern appears clearer (or blacker) on the red or the green background. It sometimes has to be stressed that no attention must be paid to any apparent brightness difference. The trial lenses are adjusted to make both rings equally clear, or if this is not possible, clearer just on the red or just on the green, according to the purpose of the examiner.

Where the ametropia is considerable, the patterns on both colours will be grossly out of focus and the test will be unreliable. (This is probably the reason for the indecisive findings of O'Connor Davies, 1957, when recording the bichromatic preference of uncorrected subjects.) When the correction is within about 1 D of the optimum, the bichromatic test does appear to work satisfactorily. If the best acuity is poorer than the detail size of the test pattern the contrast of the frame surrounding the test panel can sometimes be used though the test is generally omitted in these circumstances.

With older patients, the crystalline lens becomes markedly yellow, blue-green light being partially absorbed and scattered. This gives a marked red bias to the test and it sometimes becomes impossible to obtain apparent equality. Where it is obtained in such cases, too much minus lens power has usually been added and on returning to the black and white Snellen chart, an addition of about +0.50 DS may well be preferred, improving the acuity. Colour defectiveness

should not upset this test too much, since the sharpness of focus is not affected, only the appearance of the colour. The protanopic or strongly protanomalous patient has a reduced sensitivity to the red end of the spectrum and this can cause difficulty since the red background will appear much dimmer than the green.

Determination of the astigmatic error

There are two main methods of determining the astigmatic component of the refraction. The older method, using a special 'fan' chart of radial lines, will be described first since it illustrates the nature of the refractive asymmetry extremely well. The newer method, using a specially mounted cross cylinder, is now used more often because of its advantages, but not all patients respond satisfactorily and it is useful to be able to return to the older technique.

The fan and block method

In *Figure 5.4*, we can see that the first focal line of an astigmatic pencil is parallel to the weaker or more hypermetropic β meridian of the eye, while the second focal line is parallel to the more myopic α meridian. This figure illustrates diagrammatically the convergent astigmatic pencil where the principal meridians are horizontal and vertical.

They may, of course, be oblique. Suppose that an eye with simple myopic astigmatism has its more powerful principal meridian along 45° (*Figure 6.3*). The axis of the minus correcting cylinder is thus at 135° . Since the focal line on the retina

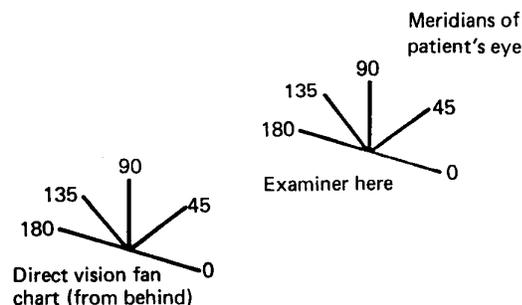


Figure 6.3. Three-dimensional view of fan chart and meridional notation of a patient's eye. Viewed from behind, the direct vision fan chart has the same meridians as the eye.

lies along the 45° meridian, this must also be the direction of the clearest line seen. According to standard axis notation (*Figure 5.3*), meridians are numbered anti-clockwise from the horizontal. Nevertheless, from the examiner's position between the patient and the fan chart, the line on the chart which is parallel to the patient's 45° meridian appears to be 45° clockwise from the horizontal. A reverse numbering is thus required for fan charts viewed directly (*Figure 6.4a*).

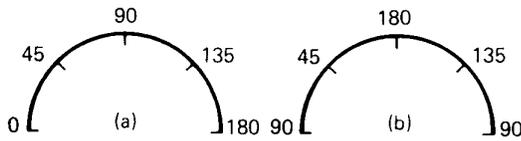


Figure 6.4. (a) Direct vision fan chart, giving a reversed protractor, being the examiner's view of the chart in *Figure 6.3*. (b) Indirect fan chart, numbered to indicate the required minus trial cylinder axis, for viewing by reflection in a mirror.

When a mirror is used, this reverse numbering is no longer required but, despite this, a different system is commonly used for convenience. The principle is to assume each line in turn to be the clearest and to number it with the axis direction of the minus correcting cylinder, which is always perpendicular to the given line. The resulting scheme is shown in outline in *Figure 6.4(b)*.

The complete fan chart is illustrated in *Figure 6.5*. Radial lines of thickness about the limb width of an 18-metre letter are spaced at 10° intervals

around a central panel carrying an arrowhead and two sets of mutually perpendicular lines. The arrow or V is due to Maddox and is used to refine the determination of the axis of the astigmatism. Thus, if the patient says the group of lines near the top of the chart are the clearest, the arrow is rotated to point at the clear group. Suppose that, as in *Figure 6.5*, the right-hand side of the arrowhead appears the clearer: this side is more nearly parallel to fan lines on the left of the arrow tip.* Thus, to find the axis of the astigmatism more accurately, the arrow is rotated away from its clearer side until equality is obtained.

The patient's attention is then directed to the two sets of lines or 'blocks' and he is asked which is the clearer: this should be the set parallel to the clearest line on the fan chart. Negative cylinder power is then brought into play, the axis being at right angles to the lines of the clearer block, until the two sets of lines are equally clear.

Using this method, the refraction of an astigmatic eye may be undertaken as follows.

- (1) Occlude the second eye and measure the unaided vision of the first eye.
- (2) Determine the sphere giving the best vision obtainable with spherical lenses alone by the methods on pages 114–115. This lens is called the 'best vision sphere'. If the resulting vision is 6/12 or better, a bichromatic test may also

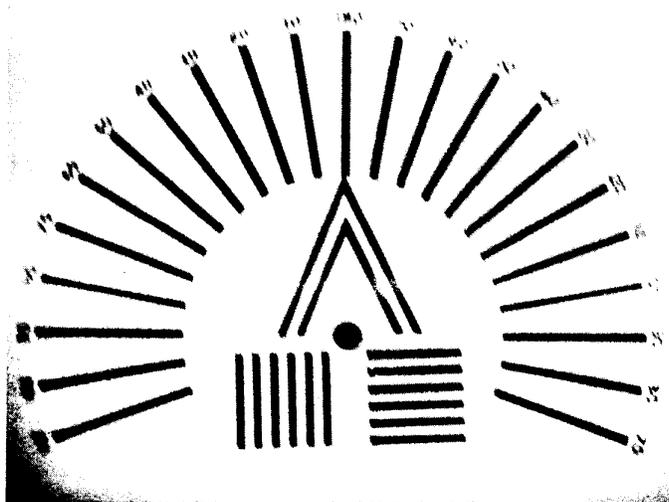


Figure 6.5. Photograph of a fan and block chart taken through a plus cylinder at axis 20°. The unequal clarity of the limbs of the Maddox V shows that an anti-clockwise rotation is needed to give equality and identify the axis.

* When the patient views the chart in a mirror, his left will be the refractorist's right for both the Maddox V and the blocks.

be used. This new vision is then noted, and from *Table 6.1* the amount of astigmatism present may be estimated. It is assumed that the best vision sphere puts the circle of least confusion on the retina. Hence, in order to bring the eye into a state of simple myopic astigmatism:

- (3) Add a positive sphere equal to half the estimated amount of astigmatism, (since the circle of least confusion lies dioptrically midway between the two focal lines) or add +1.00 DS if vision at this stage is 6/9 or better.
- (4) Refer the patient to the fan chart and ask which line or group of lines appear clearest and darkest. This gives the approximate direction of the astigmatic error. However, a simple check test should be made by temporarily adding an extra +0.50 DS in order to confirm that the eye is in a state of simple myopic astigmatism. The blackest lines should blur, but if not, more positive sphere should be added until they do. (In some cases the clearest lines will change through 90°, indicating that the eye had been in a state of simple hypermetropic astigmatism, with the anterior focal line near the retina. In this case, continue adding positive sphere until this new set of lines just begins to blur.)
- (5) Direct the attention to the Maddox arrow and rotate it away from its blacker limb until both limbs appear equally blurred. This gives the axis of the astigmatism, but care must be taken to ensure that the patient's head is upright.
- (6) Directing attention now to the blocks, add negative cylinder at the appropriate axis until the second becomes as clear as the first. If this is not quite possible, it is better to just under-correct than over-correct the astigmatic error, that is, leaving the first group of lines the clearer or blacker of the two.
- (7) Make a second check test by again adding +0.50 DS, or, if the patient is a critical observer, +0.25 DS. Both blocks should blur equally, but if the blackest lines change over, the astigmatism has been over-corrected. If the originally darker block again becomes blacker, the original sphere from step (4) was wrong and must be re-checked.
- (8) Return to the letter chart and determine the sphere giving best acuity, the cylindrical element remaining as just determined. As usual,

a positive lens should be tried first, but a weak minus lens will most frequently be required.

If in step (4) no lines appear blacker than the others, there may be no astigmatism present, but other possibilities are that the eye is excessively fogged, has the circles of least confusion on the retina or is in a state of compound hypermetropic astigmatism. The +0.50 DS check test will show up either of these last two conditions, by making some lines darker. On the other hand, if the eye is already fogged, extra positive power will blur the lines even more, whereas the addition of minus power will make some lines blacker in the presence of astigmatism, or all equally black if there is no astigmatism.

To summarize the technique:

- (1) Obtain sphere giving best vision.
- (2) Estimate power of astigmatic error from the vision at this stage.
- (3) Assuming that the lens found in (1) was that putting the circle of least confusion on the retina, add plus spherical power equal to half the estimated minus cylinder.
- (4) Find the clearest line(s) on the fan. Temporarily add an extra +0.50 DS to check that the blackest lines blur.
- (5) Refine the cylinder axis using the V.
- (6) Equalize the clarity of the blocks with minus cylinders.
- (7) Ensure that the eye is not spherically under-corrected by adding +0.50 DS and checking that the blocks are equally blurred or at least not reversed in clarity from the original appearance. If necessary, adjust cylinder power.
- (8) Refine sphere with Snellen or bichromatic chart.

The present writer's (RBR's) redesign of the V and blocks is described on pages 125–126.

The cross cylinder

Introduction

This is an astigmatic lens in which the two principal powers are numerically equal but opposite in sign, the mean power thus being zero. According to the relevant British Standard,* the

* BS 3521: Glossary of Terms relating to Ophthalmic Lenses and Spectacle Frames.

CHANGES IN REFRACTION DURING LIFE*

BY

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It is well known that the refraction of the eyes may change in the course of a lifetime, but we do not know the reasons and the rhythm that rule such changes of shape and function. The interest of research workers has long been exclusively focused on the question of the origin of short-sightedness. On this there are two opinions: the endogenous theory that considers the germ-plasma as the basis for the development of the eye and its parts, and the exogenous theory that attributes short-sightedness to the observation of close objects and other mechanical factors.

If we talk of refraction we mean total refraction. However, this does not mean a degree which is directly measurable, but a figure that results from the proportion of all optical constant values to the length of the eye's axes. This fact and the approximate value of any subjective measurement explain the difficulties that hinder work in this field.

The first step was an investigation of the frequency of different stages of refraction among certain sections of the population. Long-sightedness and short-sightedness, like all biological characteristics, exist in innumerable finely graduated degrees. The proportion of the different states of refraction found at various stages of life confirm that myopia increases more rapidly in the course of the school years than later in life. Until recently it has been maintained that learning to read and write is the chief cause of the development of myopia.

In contrast to the study of large-scale statistics, the investigation of refraction-changes during the lives of individuals has a more personal character. It is an important condition that a series of patients should visit the same oculist over a long period.

Material

In my practice in Hanover, I was lucky enough to find continuous notes made by my predecessors (Stölting and Agricola) going as far back as the year 1886. Thus I was able to draw individual curves of refraction for several patients. The horizontal scale in each graph gives the patient's age, and the vertical scale gives the refraction in dioptries.

* Received for publication May 22, 1953.

Fig. 1 illustrates the principle on which the graphs have been drawn. The subject, whose sight could be examined for 40 years, showed in both eyes an equal long-sightedness and a considerable astigmatism. I took only the right eye, which had full visual power. At the age of 4 years, when he came as a boy to be examined for the first time, the correction required was $+3.5$ combined cylinder -1.0 . While the spherical component remained nearly constant during his youth, the cylindrical component rose by the 12th year from 1 to 3 dioptries, and the position of the axis of the cylinders turned from 10° to 55° . In the following years the astigmatism remained nearly constant but the spherical component went down in spite of the decline in accommodation.

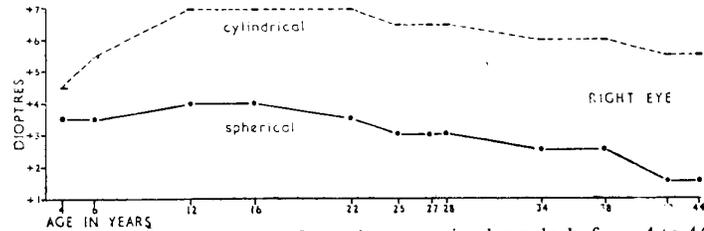
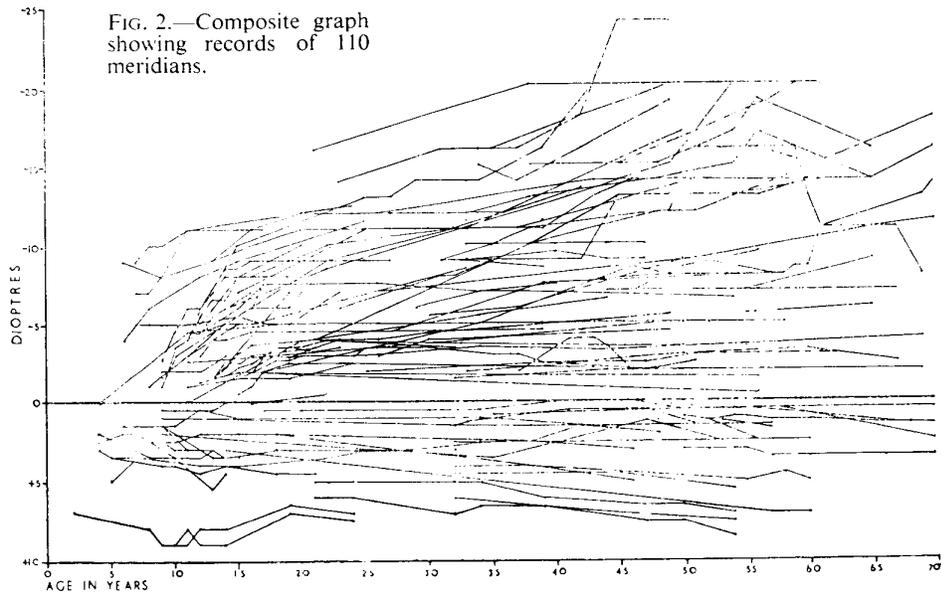


FIG. 1.—Records of the right eye of a patient examined regularly from 4 to 44 years.

Fig. 2 shows a synopsis of refraction change in 110 eyes, or rather 110 meridians, of persons who could be examined periodically for at least two or three decades. As we are consulted more especially by people who show a rather complicated fault of refraction, there are many cases of astigmatism among them. In order to keep the graph clear, only the spherical component has been recorded.



The short-sighted patients are entered above the zero-line of the graph, and the long-sighted patients below. Therefore the increase of long-sightedness is graphically expressed by a descending line. The number of the hyperopes remains

far less than that of the myopes. The reason may be that the patients were selected by chance and that long-sighted people visit the oculist generally later and less frequently. In the course of a lifetime, a numerical progression can be stated on the myopic as well as on the hyperopic side of the graph, but the number of these results is too small to establish a biological law.

Observations

Fig. 2 confirms the well-known fact that with short-sighted people the curve of refraction shows a steeper ascent during the two first decades. Towards the end of growth, that is at about 20 years of age, the lines of the curves flatten. Generally, the earlier and the higher myopia begins, the greater the tendency towards a quick and steady increase, but this rule is not without exceptions. One case of myopia of 5 D begins at the age of 7 and remains constant over a longer period and others come to a standstill by the age of 13 or 15, while growth is still in progress. In these cases the curves tend to become horizontal. Blegvad (1918) demonstrated that these stationary periods at an early age are not restricted to the lower degrees of myopia, but also apply to the higher degrees of 9 or 10 dioptres and more.

On the other hand, there are degrees of refraction that after remaining stationary up to the 5th or 6th decade show a sudden and distinct increase. We shall discuss the reasons for this atypical course later on. Now and then we also see a certain lessening of myopia in the course of a lifetime, for example from 2.0 at the age of 15 to 0.5 at 65, or from 7.5 at the age of 17 to 6.5 at 54.

Some cases of excessive short-sightedness show an exceptional tendency to decrease at a later age. In one case myopia decreased in the seventh decade in one eye from 19 to 16, and in the other from 17 to 14 dioptres. With another patient we even found a decrease by steps from 17 to 8, a decline of 9 dioptres in 13 years. Such exceptions cannot be explained by a change in the length of the axis, but only by the diminution of the refraction of the cornea or the crystalline lens.

Long-sighted people show fewer dramatic changes. Here we also find steeper increases for a few years in youth, but generally the stationary forms predominate.

Individual Cases

In the entanglement of lines in Fig. 2, a good many curves coincide or cross each other, so that there is no clear view of any individual change of refraction, but we will also consider a few isolated cases.

Fig. 3 shows the curve of a slight myopia with astigmatism. It is the right eye of a doctor whose refractions on both sides were approximately equal. At the age of 11 the short-sightedness was 1.25 D; it then increased slowly to 3.5 and remained stationary from his 19th year for the following three decades. This is a classical example of the typical evolution of a simple myopia. The astigmatism was constant during all this time.

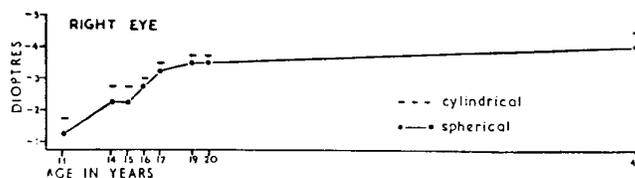
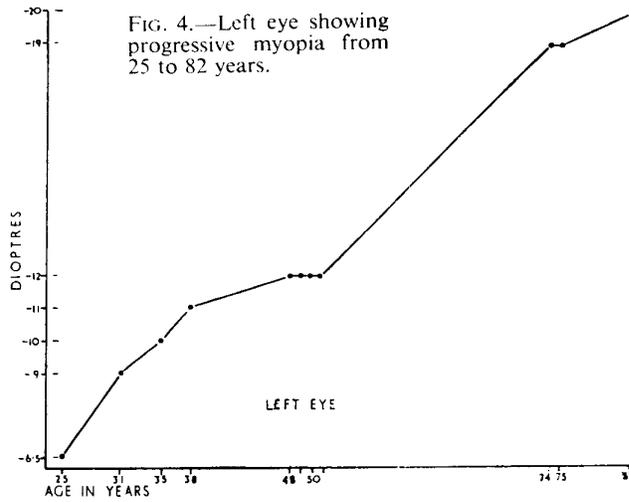
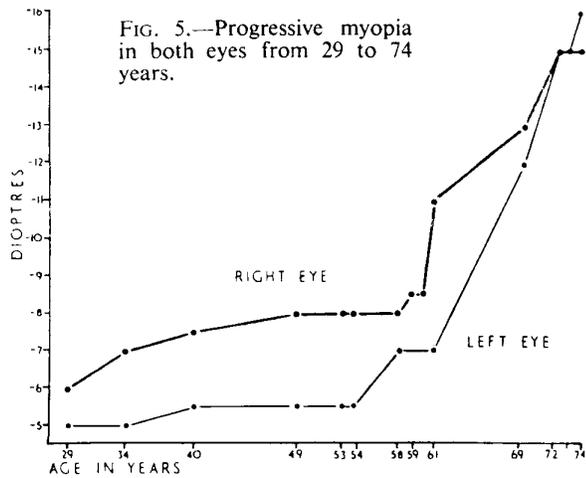


Fig. 3.—Right eye showing slight myopia with astigmatism from 11 to 47 years.



As contrasted with this form of myopia which becomes stationary at the end of the period of growth, Fig. 4 shows a progressive myopia that was 6.5 D during the 3rd decade, and ascended almost continuously up to 20 D in the 9th decade. Both eyes showed not only the same refraction but also very bad myopic degeneration of the retina. The right eye was blind towards the end of the patient's life and only the left eye is represented in this graph.

Fig. 5 demonstrates the curve of a woman teacher. When she was about 30 years old we found a myopia of 6 D in the right eye and 5 D in the left. In the following decades the short-sightedness increased very slowly until her 60th year. Then there was a sudden rapid increase in both eyes, so that at 74 years of age 15 and 16 D were found. Such a result at this age cannot be explained by an increasing length of the axis but only by a change in the optical system. Indeed, just at the time of this remarkable rise there developed a cataracta



nuclearis, that is, the crystalline lens in each eye resembled a bull's-eye window-pane. As such nuclei have a higher index of refraction, the result is an additional myopia.

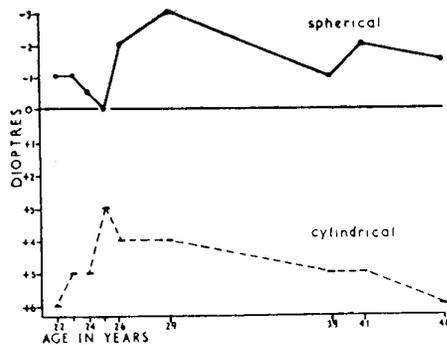


Fig. 6 demonstrates the change of refraction in an eye with keratoconus, that is, accompanied by a high degree of astigmatism. At the age of 22 the refraction in the horizontal meridian was -1.0 D and in the vertical +6.0. In the middle of the third decade, the refraction in both meridians declined remarkably, but very soon it rose again to above the previous level, and remained at 7 D until the fifth decade.

A state of refraction, which can be demonstrated perfectly by the graphic method, is anisometropia. This form of different refraction in each eye is the very touchstone of all theories about the origin of myopia. Fig. 7 is taken from a housewife, who was already suffering at 21 years of age from a myopia of 12 D in the right eye and 5 D in the left. In this case the refraction of the better eye remained for decades absolutely constant, and in the more myopic eye, which was weak-sighted, the refraction increased

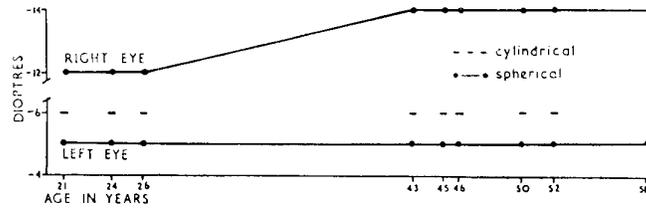


FIG. 7.—Development of anisometropia from 21 to 58 years.

only by 2 D, so that the difference remained the same during her lifetime. By contrast, Fig. 8 shows a striking “disharmony” in the change in refraction. While in the right eye the small degree of short-sightedness of 2 D remained constant during

the whole of the patient’s life (and even declined somewhat towards the end), the myopia of the left eye, which was higher from the beginning, ascended steeply and had attained 20 D when the patient reached the age of 62.

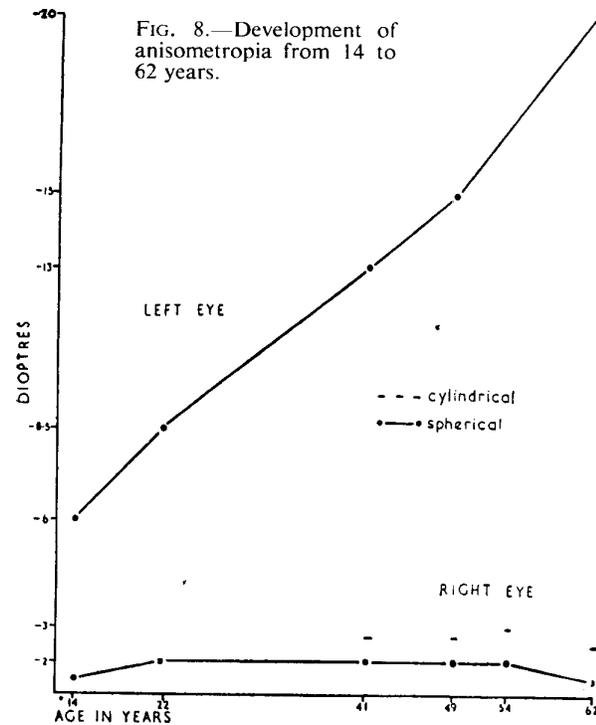


FIG. 8.—Development of anisometropia from 14 to 62 years.

Such cases demonstrate that the change in refraction for each eye is determined from birth to death by endogenous factors and cannot possibly be explained by external influences.

These few examples illustrate what can be said about individual changes in refraction when the notes of many years are available. Our question was not “why” but “how” changes in refraction occur

during the lifetime of certain persons. The results therefore do not offer a basis for defending or attacking the different interpretations of the character and origin of short-sightedness. But they call for the solution of other questions seen from an ontogenetic point of view. One of these is the relation between the growth of the eye and that of the rest of the organism, especially the numerical correlations between the magnitude of the different parts of the eye and the length of the body. The refraction

curves of twins and the testing of all these problems on growing animals remain to be examined. When these questions have been explored it may be found whether outside (that is, parakinetic) influences may change the shape and function of the eye, or whether it is only hereditary factors which decide its evolution and refraction.

REFERENCE

BLEGVAD, O. (1918). *Ugeskr. Laeg.*, **80**, 287.

RECOVERY OF VISUAL ACUITY AFTER RETINAL DETACHMENT INVOLVING THE MACULA*

BY *Thomas C. Burton, MD*

INTRODUCTION

INTUITIVELY, PERHAPS, MORE THAN BY ANY OTHER METHOD, OPHTHALMOLOGISTS have thought that prompt surgery for retinal detachment would provide optimal visual recovery. It has been long observed, and more recently confirmed, that visual results are best when the macula has not become involved in the detachment process.¹⁻⁵ Unfortunately, in most large retinal detachment series the macula is involved about 75% of the time, a figure which has changed little over a period of many years.⁶⁻¹¹ Predetachment or early detachment symptoms obviously are not alerting patients adequately, or often their physicians, to the urgent need for thorough retinal evaluations.

Notwithstanding dramatic improvements in diagnostic and therapeutic techniques, functional recovery of the reattached retina has remained distressingly poor, with only about 40% of cases achieving 20/50 acuity or better.^{2,6-9,12,13} Comparisons of visual results in large detachment populations several years apart, even from the same institution, fail to demonstrate improvement expected with refined techniques.^{2,3,8} However, this observation does not account for attempts to operate on detachments of increasing complexity. Now, of course, cases, which a few years ago would have been considered inoperable, are being restored anatomically. On the other hand, the functional results in this class of detachments are very poor, tending to reduce the average visual recovery.

Unquestionably, the preoperative visual acuity provides the best prognostic index of anatomic success rates and final visual recovery.^{5,6,13-17} A preoperative acuity of 20/20 to 20/50 implies a limited detachment with the macula spared or only flatly detached. As a consequence of pre-existing ocular pathology; not every detachment with macular sparing presents with good visual acuity.^{5,15}

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Similar appearing detachments have widespread variations in final visual acuity.¹⁸ Some authors believe that functional recovery is governed largely by factors beyond the influence of the retinal surgeon.^{2,3} Kaufman¹⁹ determined that 85% of variation in visual acuity was explained by nine factors, only one of which (duration of detachment) might be manipulated. Similarly, Burton and Lambert¹³ isolated at least 22 factors (including age of patient, presenting visual acuity, type of detachment, pre-retinal membrane formation, vitreous membranes, macular cyst or hole, senile cataract, or history of glaucoma) none of which could be altered readily.

Tani et al⁶ found 14 factors related to favorable functional results, the most important of which were preoperative acuities of 20/50 or better, less than total detachments, anterior tears, operative technique, and absence of the following: giant retinal tears, preoperative ocular hypotony, and untreated ocular hypertension.

Over the past several years there has been renewed interest in the study of functional recovery in retinal detachments involving the macula. The evidence concerning the importance of duration of macular detachment is conflicting. Important, if not critical, durations of macular detachment, after which the prognosis for visual recovery becomes worse, have been estimated at one week (Kreissig,¹⁰ Davies²⁰) two weeks (Hudson,⁷ Marquez²¹), one month (Tani et al,⁶ Charamis and Theodossiadis,¹¹ Davidorf et al²²) and two months (Norton,² Grupposo,¹⁵ Jay,¹⁸ Cleary and Leaver^{23,24}). Gundry and Davies^{25,26} have indicated there is a progressive decline in recovery from day one onward, while Hughes²⁷ stated there seemed to be no influence on final vision as long as the retina had not been detached longer than six months.

Such inconsistent information tends to produce casual attitudes about the urgency of managing detachments which involve the macula. Surgical delays of several days, often desirable for a variety of reasons, might seem more acceptable. It appears prudent, however, on the basis of current information, to encourage prompt surgery rather than permit unnecessary delay.

The following study was designed to characterize the role of macular detachment in recovery of visual acuity, and, further, to determine the degree to which duration of detachment influences the final visual result.

MATERIALS AND METHODS

Nine hundred and fifty-three consecutive cases of primary rhegmatogenous retinal detachment, evaluated between January 1, 1975 and Decem-

ber 31, 1978, provided the data base for this study. There were 548 phakic cases (57.5%) and 405 aphakic cases (42.5%).

Demarcations with argon laser photocoagulation, xenon arc photocoagulation or transconjunctival cryopexy were performed in 58 cases (6.1%) with peripheral detachments. On the remaining cases, several types of scleral buckling procedures were performed, consisting of episcleral solid silicone rubber (81.3%), episcleral silicone sponge (6.9%), intrascleral solid silicone rubber (3.0%), and combinations of the preceding (2.7%). Cryopexy produced the chorioretinal reaction in all scleral buckling operations.

Visual acuities were recorded by trained technicians, utilizing Sloan or Snellen distance visual acuity charts, employing ± 0.50 diopter (D) and ± 1.00 D spheres over previous known corrections, in the same visual screening area under similar lighting conditions. To minimize the effect of duration of follow-up observations, final visual acuities were obtained, whenever possible, in the postoperative interval from three to six months. Acuities obtained later than six months were utilized only if patients had not been observed during the three to six month interval. Cycloplegic refractions were done routinely on patients with postoperative acuities less than 20/50.

The macula was defined clinically as a circular area approximately 1.5 mm in diameter, corresponding to the anatomic fovea or fovea centralis.²⁵ The preoperative macular status was ascertained by indirect ophthalmoscopy and confirmed by fundus biomicroscopy utilizing a three-mirror Goldmann contact lens. No attempt was made to characterize features, other than visual acuity, which differentiate patients with macular sparing from those with macular involvement.

Patients with postoperative visual acuities of 20/60 or less were routinely evaluated with a direct ophthalmoscope and fundus contact lens for macular pathology. Fluorescein angiography was not performed regularly.

Statistical analyses on postoperative visual acuity without regard to duration of macular detachment were limited to cases undergoing a single operation with a minimum follow-up period of three months, and consisted of those which were anatomically cured and those which were regarded as primary failures with persistent inoperable detachments. Patients with a follow-up time of less than three months were excluded. Also excluded were patients who experienced primary failures, but who underwent subsequent operations.

An effort was made to determine, as accurately as possible, the day of onset of macular symptoms. Durations of macular detachment were considered inaccurate and excluded from statistical analysis for the following reasons: (1) when impaired visual acuity had been discovered inadvertent-

ly; (2) when only a crude range of duration could be established; and (3) when a patient was regarded as a poor historian.

In the analysis of effect of duration of macular detachment on final visual acuity, several classes of patients were eliminated due to coexisting ocular pathology, which could affect adversely the final visual acuity. These included a history of congenital cataract surgery, nystagmus, amblyopia ex anopsia, retrolental fibroplasia, pars planitis, central corneal scarring, history of penetrating injury, senile cataract formation sufficient to obscure visualization of the central fundus, glaucoma with extensive disc cupping, retinal vascular occlusive disease, detachments due to macular holes, and macular scarring secondary to trauma, inflammatory disease, degenerative myopia, heredomacular degeneration or senile macular degeneration. Patients with preoperative macular cyst or hole formation and those with preoperative macular puckering were retained, since the two complications might be related to duration of detachment.

The single operative complication that resulted in exclusion of patients was subretinal hemorrhage in the macula (15 cases). Postoperatively, extensive vitreous opacities resulted in excluding two cases. Assuming the retina remained reattached, no other patient was excluded because of a postoperative complication (including anterior segment ischemia, angle closure glaucoma, open angle ocular hypertension, infection, or morphologic disturbances in the macula).

Data from phakic and aphakic eyes were combined, since several investigations have demonstrated similar visual recovery patterns in reattached cases.^{2,6,13,17,19,22}

Statistical analyses were done using the SAS²⁹ software package with an IBM/168 Computer. Significance of differences among frequencies was determined by chi-squared analysis with Yates' continuity correction applied when appropriate. Linear regression analysis was accomplished with a general linear models procedure using the Proc GLM program. Non-linear regression was accomplished with the Proc N-LIN program. Given original estimates of the non-linear model, Proc N-LIN uses an iterative process to improve continually the estimates until the error sums of squares is minimized. Both linear regression and non-linear regression provide least square estimates of their parameters.

For both linear and non-linear regression analysis distance visual acuities were converted to a decimal notation to provide a linear scale for visual function (Table I). Extremely poor visual acuities of finger counting and hand motion or light perception arbitrarily were assigned values of 0.01 and 0.001, respectively.

TABLE I: CONVERSION OF SLOAN OR SNELLEN
DISTANCE VISUAL ACUITIES TO
DECIMAL NOTATION

DISTANCE VISUAL ACUITY	DECIMAL EQUIVALENT
20/20	1.00
20/25	0.80
20/30	0.67
20/40	0.50
20/50	0.40
20/60	0.33
20/70	0.29
20/80	0.25
20/100	0.20
20/125	0.16
20/160	0.12
20/200	0.10
15/200	0.075
10/200	0.050
5/200	0.025

RESULTS

PREOPERATIVE MACULAR STATUS

Nine hundred and fifty-three primary retinal detachments entered the study of which 70% included the macula (Table II). Opacities of the media or very flat detachments prevented determination of the macular status approximately 1% of the time. Macular sparing was not associated invariably with intact visual acuity, a situation explained by coexisting ocular pathology. Further, excellent vision was preserved in a small proportion of cases with obvious macular detachments (Table III). Nevertheless, differences in preoperative visual acuities between cases with macular sparing and those with macular involvement were highly significant ($P < 0.0001$).

SURGICAL RESULTS

After a single operative procedure, 738 cases (77.4%) were cured anatomically for a minimum of three months. Eighty-six cases (9.0%) represented primary failures and had no further surgery, usually due to inoperable

TABLE II: PREOPERATIVE MACULAR STATUS IN 953
PRIMARY RETINAL DETACHMENTS

MACULAR STATUS	NO CASES	PERCENT
Attached	283	29.7
Detached	662	69.5
Indeterminate	8	0.8

TABLE III: CORRELATION OF PREOPERATIVE MACULAR STATUS WITH INITIAL VISUAL ACUITY IN 936* PRIMARY RETINAL DETACHMENTS

PREOPERATIVE MACULAR STATUS	INITIAL VISUAL ACUITY					
	20/20-20/50		20/60-20/200		< 20/200	
	NO CASES	%	NO CASES	%	NO CASES	%
Attached	235	85.1	27	9.8	14	5.1
Detached	20	3.1	96	14.7	536	82.2
Indeterminate	3	37.5	2	25.0	3	37.5
			$P < 0.0001$			

*The initial visual acuity was not obtained in 17 cases.

massive periretinal proliferation, but occasionally because patients declined additional procedures. There were 93 patients (9.8%) who experienced primary surgical failures, but underwent secondary operations. An additional 36 cases (3.8%) were followed postoperatively for less than three months.

POSTOPERATIVE VISUAL RECOVERY

Of the 824 cases for which a single operation was performed, 27% had preoperative acuities of 20/50 or better. Postoperatively, 38% of this group, including failures, had acuities of 20/50 or better (Table IV).

A highly significant correlation ($P < 0.0001$) was found between final visual acuity and the surgical result (Table V). Postoperatively, there was a pronounced shift away from acuities less than 20/200, but only 42% of reattached cases achieved 20/20 to 20/50 acuity. Five percent of surgical failures maintained 20/20 to 20/50 acuity for at least three months, because the detachments remained limited to the periphery.

Macular detachment exhibited a strong negative influence on recovery of central vision (Table VI). Twenty percent of cases involving the macula regained 20/50 or better vision compared to 82% in which the macula was spared, a difference which was highly significant ($P < 0.0001$).

TABLE IV: COMPARISON OF PREOPERATIVE AND POSTOPERATIVE VISUAL ACUITIES IN 824 RETINAL DETACHMENTS HAVING ONE OPERATION

DETACHMENT STATUS	VISUAL ACUITY					
	20/20-20/50		20/60-20/200		< 20/200	
	NO CASES	%	NO CASES	%	NO CASES	%
Preoperative	221	26.8	103	12.5	500	60.7
Postoperative	317	38.5	281	34.1	226	27.4
			$P < 0.0001$			

TABLE V: CORRELATION OF SURGICAL RESULT WITH FINAL VISUAL ACUITY IN 824 RETINAL DETACHMENTS HAVING ONE OPERATION

POSTOPERATIVE RETINAL STATUS	FINAL VISUAL ACUITY					
	20/20-20/50		20/60-20/200		< 20/200	
	NO CASES	%	NO CASES	%	NO CASES	%
Attached	313	42.4	280	37.9	145	19.6
Detached	4	4.7	1	1.2	81	94.2
			$P < 0.0001$			

The preoperative visual acuity had a highly significant correlation with final acuity ($P < 0.0001$). Eighty-nine percent of the cases presenting with 20/20 to 20/50 acuity maintained that level of vision postoperatively. In contrast, 47% of the cases presenting with 20/60 to 20/200 acuity and only 15% of cases initially less than 20/200 recovered vision of 20/50 or better. Sixty-two percent of the cases with a final acuity of 20/20 to 20/50 were accounted for by the group with 20/20 to 20/50 acuity preoperatively (Table VII). In the group with an initial visual acuity range of 20/20 to 20/50, 9% dropped to the 20/60 to 20/200 range and another 3% fell below 20/200 postoperatively. Similarly, in the group with an initial visual acuity range of 20/60 to 20/200, 14% dropped below 20/200 following surgery.

DURATION OF MACULAR DETACHMENT

In this study, approximately one-third of the patients were able to provide adequate information regarding the onset of macular involvement. After excluding cases with pre-existing ocular disease, macular hemorrhage and vitreous opacities, there remained 205 patients, each with a primary retinal detachment, able to provide an accurate history, reattached with a single scleral buckling procedure, and followed for a minimum of three months. Including hospitalization time required for preoperative evaluations, most patients experienced macular detachments of relatively short duration. Forty-two percent were operated within 9 days of subjective symptoms,

TABLE VI: CORRELATION OF PREOPERATIVE MACULAR STATUS WITH FINAL VISUAL ACUITY IN 516* RETINAL DETACHMENTS HAVING ONE OPERATION

PREOPERATIVE MACULAR STATUS	FINAL VISUAL ACUITY					
	20/20-20/50		20/60-20/200		< 20/200	
	NO CASES	%	NO CASES	%	NO CASES	%
Attached	197	82.4	20	8.4	22	9.2
Detached	117	20.3	259	44.9	201	34.5
			$P < 0.0001$			

*The macular status was indeterminate in eight cases.

TABLE VII: CORRELATION OF INITIAL VISUAL ACUITY WITH FINAL VISUAL ACUITY IN 824 RETINAL DETACHMENTS HAVING ONE OPERATION

INITIAL VISUAL ACUITY	FINAL VISUAL ACUITY					
	20/20-20/50		20/60-20/200		< 20/200	
	NO CASES	%	NO CASES	%	NO CASES	%
20/20-20/50	196	88.7	19	8.6	6	2.7
20/60-20/200	48	46.6	41	39.8	14	13.6
< 20/200	73	14.6	221	44.2	206	41.2
			$P < 0.0001$			

77% within 19 days and 88% within 29 days. The remaining 12% were distributed over an additional 45 days (Fig 1).

Ninety-one percent (186/205) of the postoperative visual acuities were recorded during the interval from three to six months. Nineteen patients (9%) had their final acuities recorded from 7 to 30 months postoperatively. The mean observation period was four and one-half months for the entire group.

Fifty-three percent (46/87) of the cases operated within 9 days achieved 20/20 to 20/50 acuity, a proportion which diminished to 34% (24/70) of those operated from 10 through 19 days and to 29% (14/48) of those operated beyond 19 days. Macular involvement of 9 days or less was associated significantly more often with final acuities of 20/50 or better than durations of 10 through 19 days ($P < 0.05$) and durations of 20 days or more ($P < 0.05$). The frequencies of 20/20 to 20/50 acuity were not significantly different between durations of 10 through 19 days and 20 days or more ($P > 0.05$).

Only four patients (2%), all operated within five days of macular detachment, regained 20/20 acuity. Eleven cases (5.4%) recovered 20/25 acuity, but none after 21 days of macular detachment. Twelve cases (5.9%) recovered 20/30 acuity, but none after 19 days. Thirty cases (14.6%) recovered 20/40 acuity, but only two after 28 days. An additional 27 cases (13.2%) recovered 20/50 acuity, but only 2 after 21 days. Therefore, 84 cases (41%) regained a visual range of 20/20 to 20/50. The average visual acuity for the entire group of 205 patients was approximately 20/60.

Since more than three-fourths of the patients were operated within 19 days of macular detachment, a scatter plot, displaying every postoperative visual acuity with a conventional linear scale indicating duration, resulted in crowding of observations toward the lower end of the time scale (Fig 2). By visual inspection, it was impossible to determine a trend relating visual acuity to duration of macular detachment or to devise a line (or curve) which would be representative of the population. Linear regression analy-

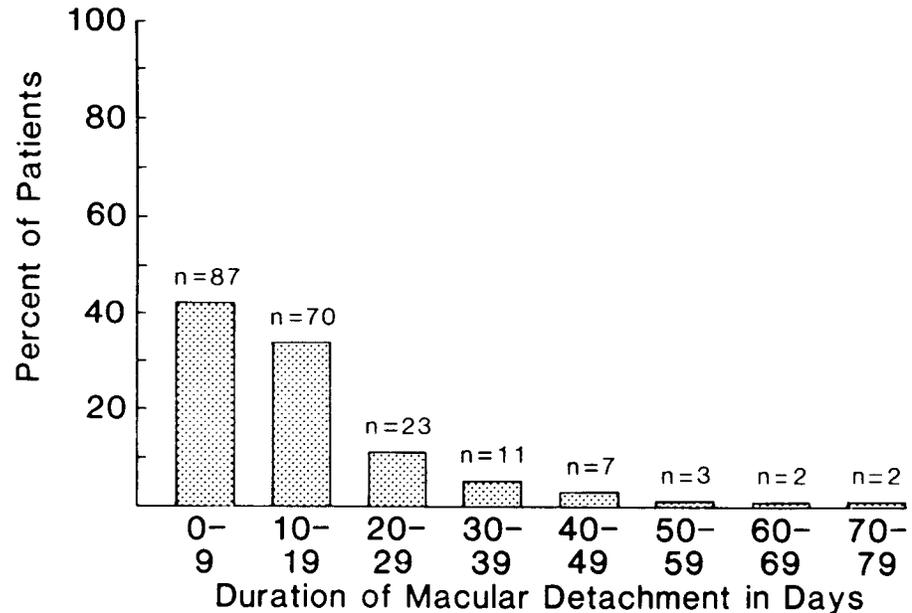


FIGURE 1

Frequency distributions of durations of macular involvement in patients with primary retinal detachment. ($n = 205$.)

sis indicated that a straight line did not describe adequately the trend in distribution of postoperative visual acuities.

When the observations were plotted on a semi-log graph, the downward trend in visual recovery with increasing duration was recognized (Fig 3). Although there was considerable scatter of the data, especially after about 12 days, the negative influence of increasing duration on visual recovery was emphasized by similarly plotting the means of the observations for each day (Fig 4).

When the mean observations were plotted on a conventional linear scale, the variation in the data was evident (Fig 5).

A non-linear regression model was designed to estimate the trend in visual recoveries, using duration as the only modifying factor (Fig 6). The r-square value of the mathematical model was 0.71. Therefore, 71% of the variation in final visual acuities observed in this study was explained by the effect of duration of macular detachment alone.

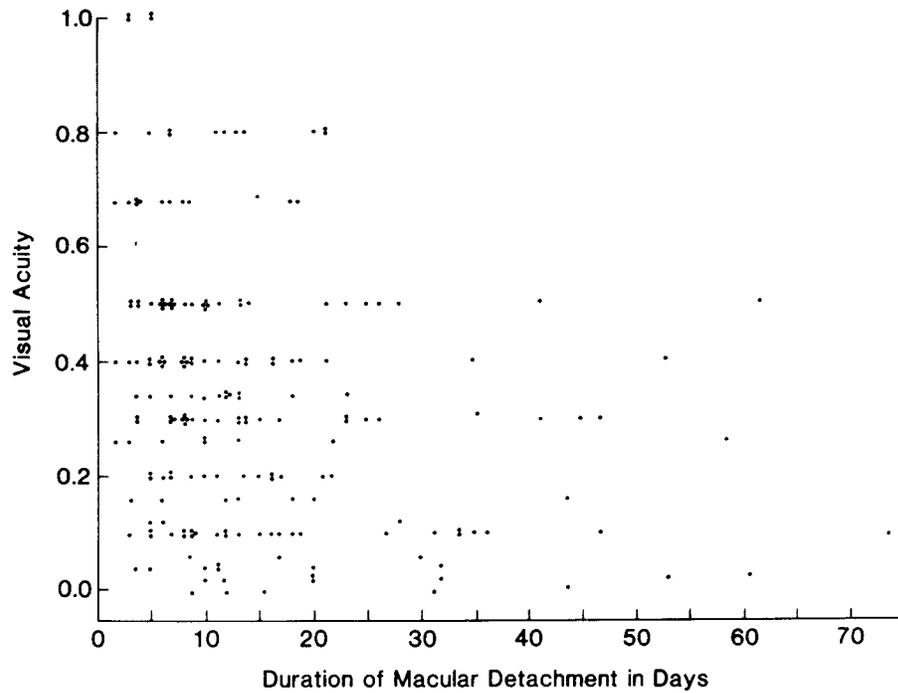


FIGURE 2

Linear scale graph of postoperative visual acuities results in crowding of observations. Relationship between visual acuity and duration cannot be represented by a straight line. ($n = 205$.) (See Table I for Conversion of Visual Acuity.)

The regression line can be expressed mathematically by the exponential equation: $y = ae^{-bx}$, where

- y = postoperative visual acuity,
- $a = .44$ (the calculated y intercept),
- $e = 2.718$ (base of natural logs),
- $b = -.022$ (calculated constant exponent),
- x = duration in days.

The negative value for the constant exponent indicates a progressively declining value in visual recovery with increasing duration of macular detachment, but reaching the zero point only after an infinitely long period of time.

For each day of duration, the model also yielded limits of one standard deviation above and below the mean for single observations (Fig 7). By five days of duration, visual recovery averaged 20/50. By 13 days of duration, the average acuity declined to 20/60. Visual recoveries averaged 20/70 at 20

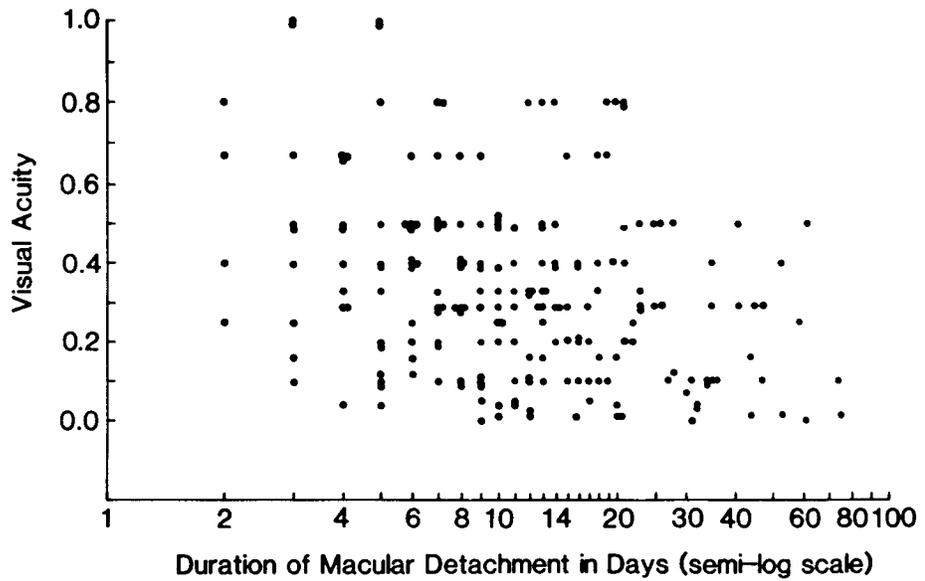


FIGURE 3
Semi-log graph of postoperative visual acuities overcomes crowding of observations and indicates decreasing visual recovery with increasing duration. (n = 205.)

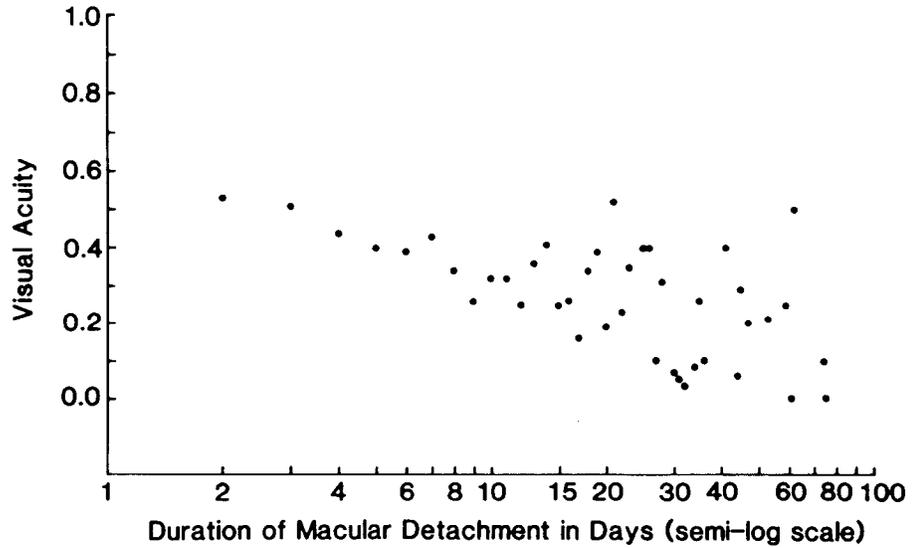


FIGURE 4
Semi-log graph of means of postoperative visual acuities emphasizes decreasing visual recovery with increasing duration. (n = 205.)

Visual Acuity

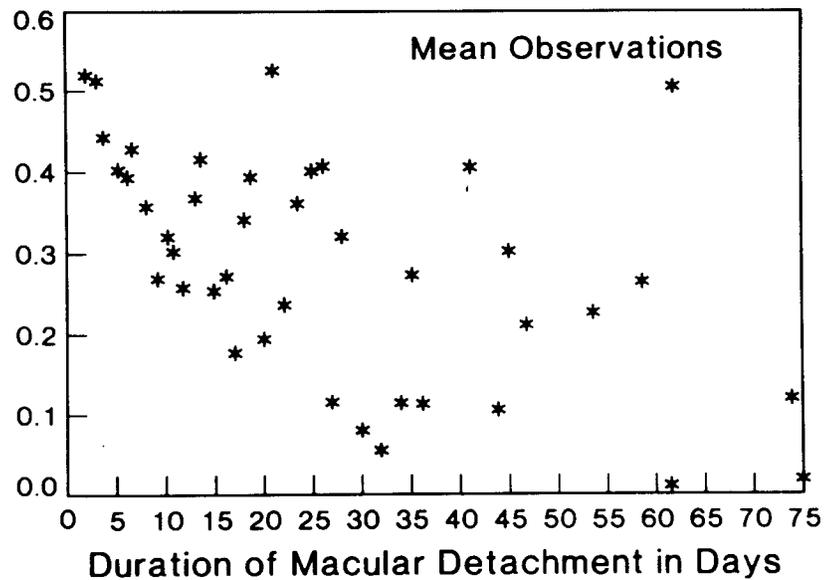


FIGURE 5
Linear scale graph of means of postoperative visual acuities emphasizes variation in data.
($n = 205$.)

days, 20/80 at 27 days, 20/100 at 37 days, 20/125 at 47 days, 20/160 at 58 days and 20/200 at 69 days.

Given the duration of macular detachment, the estimated final visual acuity for any individual in this study can be calculated from the preceding equation. Alternatively, the postoperative visual range can be estimated with 67% accuracy for an individual case by utilizing Figure 7 as a nomogram.

POSTOPERATIVE MACULAR CHANGES

Visual acuities of less than 20/50 were recorded in 47% (41/87) of patients with durations of macular detachment of 9 days or less, in 66% (46/70) of patients with durations of 10 to 19 days, and in 71% (34/48) of patients with durations of 20 days or more (Table VIII). Some form of macular pathology was observed in 45% of cases with final acuities of less than 20/50. Macular pucker occurred most frequently (26%), but was not related to duration of detachment ($P > 0.05$). Macular pigmentation occurred in 13% of the cases, but was not related to duration of detachment ($P > 0.05$). Six percent

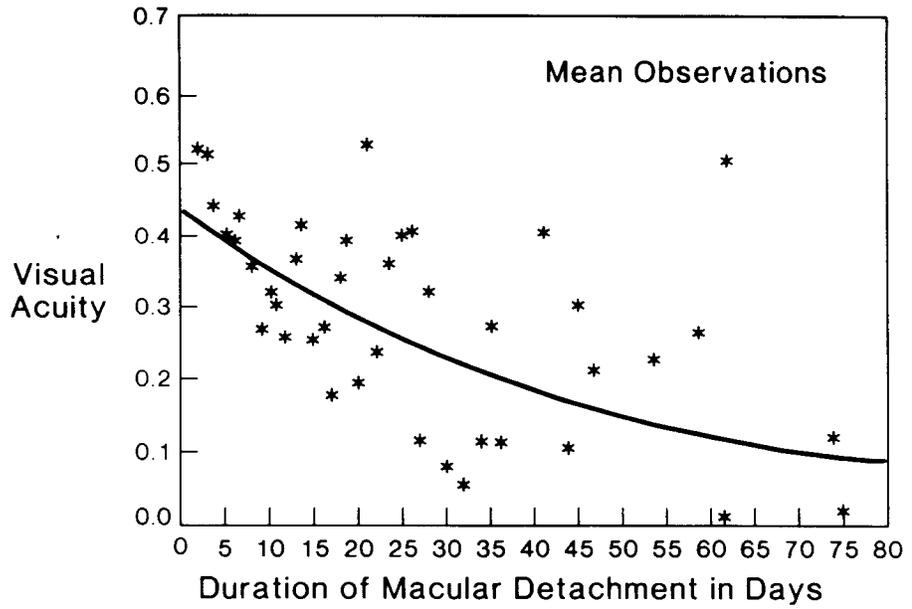


FIGURE 6

Non-linear regression curve superimposed on means of postoperative visual acuities. Equation $y = ae^{-bx}$ describes negative exponential relationship between visual recovery and duration of macular detachment. ($n = 205$.)

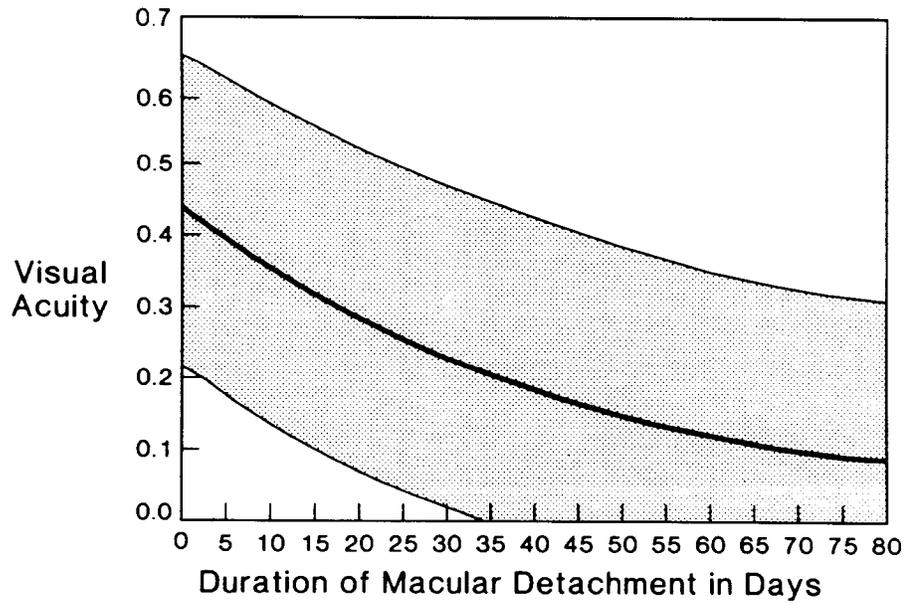


FIGURE 7

Non-linear regression curve \pm one standard deviation indicates expected range of visual recovery for durations of macular detachment of 1 to 80 days for individual patients.

TABLE VIII: MACULAR CHANGES IN 121 PATIENTS WITH DETACHMENTS OF KNOWN DURATION AND FINAL VISUAL ACUITIES OF LESS THAN 20/50

DURATION IN DAYS	POSTOPERATIVE MACULAR ALTERATION											
	PUCKER		PIGMENTATION		CYST/HOLE		NONE					
	NO CASES	%	NO CASES	%	NO CASES	%	NO CASES	%				
0-9	11	26.8	5	12.2	3	7.3	22	53.7				
10-19	11	23.9	4	8.7	2*	4.3	29	63.0				
> 19	9	26.5	7	20.6	3	8.8	15	44.1				

*One case of macular cyst was diagnosed preoperatively.

of cases appeared to have macular cysts or holes, one of which was observed preoperatively in the 10 to 19 day duration group.

The 31 cases of macular pucker had visual acuities ranging from 20/60 to hand motion with a mean of 20/160. The 16 cases of macular pigmentation had visual acuities ranging from 20/60 to finger counting with a mean of approximately 20/125. The eight cases of macular cyst or hole had visual acuities ranging from 20/70 to finger counting with a mean of approximately 20/160.

DISCUSSION

In 1934 Dunnington and Macnie¹ observed that once the macula had become involved in the detachment process, reattachment of the retina failed to restore central visual acuity. Reese³⁰ (1937), later reviewing the data of Dunnington and Macnie, wrote that 38% of successfully operated cases that had been detached for less than one month recovered at least 20/30 acuity, compared to 26% of cases detached over one month. He concluded that duration of detachment was a factor in determining the final visual result.

Reporting the collaborative results of numerous retinal surgeons in 1952, Hughes²⁷ found that detachment of the macula did not necessarily indicate a poor visual prognosis, since nearly one-third of patients with preoperative acuities of 20/200 or worse recovered to 20/40 or better. He suggested the ultimate prognosis for at least 20/40 vision was unaffected by a history of detachment less than six months old.

In 1963 Norton² determined that poor visual acuity was explained by three principal factors: vitreous traction, macular detachment and duration of macular detachment. When the macula was detached only 38% of cases recovered 20/50 acuity or better, compared to 84% in cases sparing the macula. While patients with durations exceeding two months had a much poorer prognosis, the visual results were similar for those operated before two weeks and from two to eight weeks.

Jay¹⁸ (1965) concluded that as long as the macula had not been detached longer than two months, the final visual acuity, which averaged 6/18 (20/60), was not dependent on duration. After two months, the final acuity was dependent on duration, with very little recovery of macular function observed in cases exceeding six months.

In contrast, Hudson⁷ (1968) observed that surgery within two weeks of macular detachment provided better visual results, with reattached cases averaging approximately 20/60 acuity. After two weeks, there was little influence of duration on final acuity, averaging about 20/120 even in cases beyond six months.

If cryopexy had produced the chorioretinal reaction in eyes with macular detachment, Hilton et al.⁸ (1969) found that 60% recovered at least 20/50 acuity, when the duration was less than two weeks, compared with 38% for durations of two to eight weeks and 25% for durations exceeding two months.

Jacklin¹² (1972) reported that 37% of macular detachment cases recovered at least 20/50 acuity. No data were presented to support his contention that duration of macular involvement determined the degree of recovery.

Charamis and Theodossiadis¹¹ (1972) found less favorable results when macular detachments exceeded one month in duration, but observed no significant variations in final visual acuities for durations ranging from 15 to 30 days.

Davies²⁰ (1972) concluded that the final visual acuity was dependent on duration of macular detachment and development of recognizable postoperative complications, such as macular hemorrhage, choroidal hemorrhage, uveitis, macular pigmentation and macular pucker. The highest rate of visual recovery occurred in detachments with durations less than seven days, after which there was only a gradual decline for six months.

Cairns³¹ (1973) found that 20% of cases with macular involvement achieved at least 6/18 (20/60) acuity compared with 71% of cases with macular sparing. In the macular detachment group operated within seven days there was a 38% recovery to at least 6/18 acuity, compared with 33% and 16% for those operated at one to four weeks and one to six months, respectively.

In cases of macular detachment operated during the first week, Gundry and Davies^{25,26} (1974) showed a decline in final vision from day one onward. After the first week the advantage of early surgery was less evident, until the stage of six months, when there appeared to be a dramatic fall in visual recovery. Improper construction of the graphic model, in which the time scale was arbitrarily non-linear, resulted in erroneous interpretation of the data. There was no basic unit of time. Durations of 0 to 7 days, 14 to 28 days, 1 to 3 months, 3 to 6 months, and anything beyond 6 months all were assigned equal intervals on the abscissa. If a linear or semi-log scale had been employed, the apparent precipitous fall in visual recovery would have been eliminated and replaced by gradually declining values for increasing durations.

In a study of 179 eyes, Grupposo¹⁵ (1975) found that not until after eight weeks of macular detachment was there a significant reduction in recovery of macular function. The conclusion may have been influenced by the division of visual acuity into broad classes (rather than using a linear scale) and comparison of proportions of eyes regaining 20/70 acuity or better.

Neither length of follow-up nor the postoperative interval during which final acuities were obtained was reported. Further, although reported in 1975, all the cases had been operated 10 to 16 years earlier, when other surgical methods, such as lamellar scleral dissection and partial penetrating diathermy, were conventional.

Davidorf et al²² (1975) reported that duration of macular detachment made little difference in visual acuity until after one month. Included were cases with pre-existing ocular pathology, which could have influenced visual recovery adversely. Patients with preoperative acuities of better than 20/400 were excluded, under the assumption that such cases had only partial macular involvement. Average visual recoveries were displayed graphically with non-linear scales for both visual acuity and duration of detachment, which resulted in an artifactitious slope of the curve. Apparently, most of the final visual acuities were obtained from referring physicians, a nonstandardized method which must be regarded with suspicion.

Kreissig¹⁰ (1977) identified four factors influencing postoperative macular functions: extent and height of macular involvement, duration of macular detachment, age of patient, and degree of myopia. Visual recovery in cases involving the macula was optimal with durations of seven days or less. Macular detachments lasting one to two weeks had no better prognosis than those lasting from two weeks to one year, beyond which there appeared to be a further decrease in visual recovery.

Noting numerous factors which could affect the final visual result, Marquez²¹ (1979) indicated that early detachment surgery, especially in cases of macular sparing, resulted in a better prognosis. Visual acuity recovered up to 0.40 (20/50) with durations of macular detachment less than two weeks. Visual recovery declined to 0.15 (approximately 20/125) with durations of two weeks to six months and to 0.10 (20/200) after six months.

Tani et al⁶ (1975) reported that 41% of cases with macular detachments less than one month in duration recovered 20/50 or better acuity compared with 28% of cases with durations exceeding one month.

Paralleling the recovery patterns in visual acuity are alterations in other psychophysical measurements. Retinal sensitivity, determined by static perimetry, diminishes in proportion to duration of macular detachment.^{10,32-34} Color discrimination, measured by the Farnsworth-Munsell 100 hue test, decreases with increasing duration of detachment.^{32,33} The Haidinger phenomenon is impaired progressively by detachments of longer duration.³⁴ Abnormalities in Amsler grid responses have been recorded in up to 85% of reattached cases, even in eyes with visual acuity of

5/5 (20/20).³⁵ Amsler grid defects have been correlated with extent or height, as well as duration, of macular detachment.^{10,34}

Four principal weaknesses in design recur among the foregoing studies: (1) a non-linear scale for visual acuity; (2) a non-linear scale for duration of detachment; (3) variation in time of recording postoperative acuities; and (4) the assumption that all patients provide accurate histories establishing the onset of macular symptoms.

Conversion of Snellen or Sloan notations into decimal equivalents avoids excessively long (or arbitrarily divided) scales and the need to combine various acuities into broad classes, such as 20/60 to 20/200. However, difficulties will remain with acuity notations of finger counting, hand motion or light perception. A semi-log graph legitimately overcomes the crowding phenomenon encountered when one of the scales, such as duration, is excessively long and most of the observations are located at one of the extremes.

In this study, two-thirds of the patients were judged to be unable to provide accurate histories regarding the onset of macular symptoms. Many patients, who suddenly discovered impaired central vision by inadvertently occluding the uninvolved eye, were excluded. Patients for whom only a crude range of duration could be estimated were excluded. Typical of this problem was the recently aphakic individual who had not received a corrective lens and who apparently had developed a retinal detachment between consecutive visits to the primary ophthalmologist. Many patients simply were poor historians. It was axiomatic that histories became progressively vague and unreliable with detachments of increasing duration. The factors of improper graphic display of data and inclusion of data from unreliable patients largely have been responsible for the variation in conclusions about the effect of duration of detachment on visual recovery.

This study indicates that visual recovery, in response to increasing duration of detachment, declines in exponential fashion, similar to the decay curve of a radioactive material. Seventy-one percent of the variation in visual acuity was explained by duration of macular detachment alone. Assuming the duration to be known and patient selection similar to the manner described in this study, the final visual acuity can be estimated by the equation: $y = ae^{-bx}$. Alternatively, there is a 67% chance that the final visual acuity for any individual patient will fall within the shaded area in Figure 7, which can be used as a nomogram. However, the mean visual acuity obtained from several detachment patients, all having the same duration, will approach the value represented by the corresponding point on the regression line.

In this study, 29% of the variation in visual recovery was attributed to unknown factors, which probably include pre-existing ocular disease, patient age, refractive status, type of detachment, preretinal membrane formation, operative complications, postoperative complications, macular pathology and length of follow-up observations. Following successful detachment surgery, visual acuity may continue to improve for six months to five years.^{9,14,25,26,32,33} The majority of cases have stable acuity three to six months postoperatively.^{10,11,22,32,33,35} Declining vision occurs in a small percentage of reattached cases, usually from cataract formation, macular pucker or senile macular degeneration.^{9,11,18,22} Utilizing a multiple regression model, Kaufman¹⁹ found no significant correlation between final visual acuity and length of follow-up. However, a study of patients recalled 10 to 39 years after surgery revealed 44% with visual acuity worse than at discharge due to cataracts and macular degeneration.³⁶ The potential effect of length of follow-up on final acuity was minimized in the current study. While the mean observation period of four and one-half months may seem modest, 90% of the visual acuities were obtained during a three month postoperative interval.

Attention to surgical detail and avoidance of complications, such as choroidal hemorrhage, will enhance visual recovery. Likewise, careful observation during the immediate postoperative phase will permit recognition and appropriate treatment of vision threatening problems, such as angle closure glaucoma, anterior segment ischemia and severe infections. It should be obvious that meticulous postoperative refractions with attention to changes in axial length of the globe and corneal curvature will improve late visual results.^{14,37-41} Nevertheless, the simple expedient of refraction often is neglected.

A high proportion of cases with poor visual recovery can be explained by morphologic changes of the retina, consisting predominantly of preretinal membrane formation (macular pucker), macular cysts, cystoid macular edema, subretinal pigment migration and retinal pigment epithelial atrophy.^{9,18,23,24,30,42-48} Fundus contact lens examination and fluorescein angiography may be required to detect subtle changes.

Gross retinal pigment epithelial atrophy has been attributed to long standing macular detachment.^{11,36} Cystoid macular edema is not related to duration of detachment.⁴⁷ The effect of retinal pigment epithelial fallout is disputed, but since that complication results from a surgical maneuver, there is no correlation with duration of preoperative detachment.⁴⁹⁻⁵²

Among the 205 patients with detachments of known duration, 59% failed to recover visual acuity better than 20/60. Approximately half of those patients were found to have macular pathology in the form of macular

pucker, macular pigmentation, or degenerative cyst or hole formation. Since patients with visual acuities of at least 20/50 were not subjected to the same ophthalmoscopic examinations, it is likely that milder forms of preretinal membrane formation (surface wrinkling retinopathy) were undetected.^{53,54} Therefore, an accurate estimate of the incidence of macular pucker for the entire group of patients cannot be established. It is possible that some of the cases diagnosed as macular cysts or holes actually represented cystoid macular edema, a differentiation which would have been improved by regularly obtaining fundus fluorescein angiography.

Experimental detachments in owl monkeys produce cystoid spaces within the retina and progressive degeneration of outer receptor segments.⁵⁵ Both changes are reversed by retinal reattachment.⁵⁶ The preceding observations have led several investigators to invoke the possibility that faulty realignment of receptor cells might explain impaired visual function in the absence of grossly visible retinal pathology.^{9,17,23,24,32,33} Gradual realignment of receptors could account for some cases of slowly improving visual acuity.⁵⁷ Fitzgerald et al⁵⁸ have demonstrated corresponding improvements in Stiles-Crawford function, Snellen acuity and interferometric acuity after detachment surgery, although the importance of their observations remains uncertain.

SUMMARY

Nine hundred and fifty-three primary retinal detachments were analyzed to establish the effects of macular detachment on final visual acuity. Nearly 90% of cases with preoperative acuities of 20/20 to 20/50 maintained the same level of vision postoperatively. Over 80% of cases with macular sparing achieved 20/50 acuity or better, compared with 20% of cases with macular involvement. Two percent of patients with macular detachment of known duration regained 20/20 acuity. Similar to several previous reports, the overall visual results in this study were disappointing. Forty-two percent of all reattached cases recorded at least 20/50 acuity.

After macular involvement occurs, duration of macular detachment becomes the most important factor in determining final visual acuity. In this study, duration of macular detachment alone accounted for 71% of the variation in final visual acuities. Clearly, the macula does not fail to recover function after a specific time limit. Similarly, there is no duration beyond which visual acuity is lost precipitously. Instead, visual recovery behaves as a function of a biological system, declining rapidly during the initial stages of the detachment and more slowly as the detachment becomes chronic. The relationship between visual acuity and duration of macular

detachment is analogous to the decay curve of a radioactive material and can be expressed by the exponential equation: $y = ae^{-bx}$.

Given a detachment of known duration, the estimated final acuity can be derived from the preceding equation. The graphic display of the non-linear regression curve and limits for one standard deviation above and below the mean can be used as a nomogram to estimate the likely postoperative visual range for individual patients.

Few of the numerous factors affecting visual acuity in retinal detachment disease are subject to regulation. The time a macula is permitted to remain detached is an exception. Every reasonable effort should be made to minimize duration of macular involvement. There is no excuse for unnecessary delay of detachment surgery, whether for the convenience of the patient, surgeon, anesthesiologist or operating room schedule.

Since visual decline is a continuous process, there are no definite intervals when surgery is more or less advisable. Emergency status probably should be assigned to patients with macular symptoms of recent onset. In this study, no patient regained 20/20 vision with a macular detachment exceeding five days, a time when an average of 20/50 acuity is anticipated. Patients with macular detachments of longer duration still should be regarded with urgency. After 5 days, approximately one line of vision will be lost for each additional 7 days until 27 days. Beyond 4 weeks one line of vision will be lost for each additional 10 to 11 days of macular detachment, at least until approximately 70 days, when 20/200 will be the average visual recovery.

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REVIEW

Lattice Degeneration of the Retina

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Abstract: Lattice degeneration of the retina is the most important of all clinically distinct entities that affect the peripheral fundus and are related to retinal detachment. The purpose of this review is to survey the extensive literature, to evaluate the many diverse opinions on this subject, and to correlate and summarize all the known facts regarding this disease entity. The disease is fully defined and described, both clinically and histologically. Some aspects of the disease are still poorly understood, and some remain controversial, especially in the area of management. For this reason, the indications for treatment are discussed under eight subsections, with a view toward providing practical guidelines for recommendations in management. (*Surv Ophthalmol* 23:213-248, 1978)

Key words. cryotherapy • diathermy • heredity • lattice-degeneration
• prophylactic therapy • retinal detachment

The disease known in English as lattice degeneration of the retina is acknowledged to be the most important clinically recognizable vitreoretinal abnormality known to be a precursor of rhegmatogenous retinal detachment. In the 50 years that it has been known to ophthalmologists, it has received a large variety of designations, relating to anatomic location, to one or another morphologic feature (either clinical or histologic), or to differing ideas of pathogenesis.

I. Historical Background

A. TERMINOLOGY

The terms *snail-track degeneration* (Sneckenspuren), *palissades* (Palisaden), and *etat givre* have generally been ascribed to Gonin. In addition, the following names have been applied: cystoid degeneration,^{220 222} lattice-like degeneration,^{183,184} distinctive

chorioretinopathy,^{149,150} sclerotic areas,¹⁶³⁻¹⁶⁶ equatorial degeneration,¹⁴⁶ milkyway-like or galaxy bands,⁹⁰ retinal erosion,¹⁷⁷ local retinal excavation,⁸³ and vitreous base excavation.^{84,200}

Describing and naming entities or phenomena is an important cultural and scientific duty, and should be done cautiously, precisely and accurately; the foregoing terms are attempts in this direction. Names should also serve the practical purpose of enhancing clear communication among those concerned with a particular disease. The above rather confusing array of labels has not always served this end, but has in some ways, though quite unintentionally, hindered clear communication.

B. EARLY DESCRIPTIONS

Incomplete descriptions of peripheral retinal lesions probably representing lattice degeneration were mentioned by Gonin in

1920⁹³ and by Vogt in 1924.²¹⁹ Rehsteiner in 1928¹⁷¹ gave an undoubted description of the typical branching white line feature of lattice degeneration in four patients, as an incidental part of his large study of fundus changes in myopic and senile eyes.

In 1930, Gonin⁹⁴ briefly described in one patient a "brilliant white trellis" appearance in an equatorial lesion; he also described several other eyes which had equatorial lesions probably representing lattice degeneration with features other than white lines. Vogt,²²⁰ however, in 1930 published the first detailed and accurate drawings of its clinical appearance and supplied by far the best and most complete early description of the clinical manifestations.^{221,222} Vogt proved^{221,222} that the white lines represented blood vessels, showing filled blood columns posterior to, anterior to, and continuous with individual white lines. Astutely, he realized that white lines were not essential to the diagnosis, and stated that they were absent in the majority of lesions. Although this latter question has continued to be a controversial subject,¹⁸⁶ there is a strong body of evidence which gives confirmation to Vogt's early view, and the accuracy of his early perception shows him to have been a man ahead of his times. Many other clinical descriptions and studies have followed.^{1,11,12,20,21,32,35,37,46,49,75,76,90,95,105,146,147,149,150,156,157,164,177,178,183-185,190,200,202,204,205,217,218}

C. "CYSTOID DEGENERATION" OF VOGT

Vogt's designation of the condition as cystoid degeneration of the retina^{221,222} was unfortunate and was evidently the result of his mistaken assumption^{222 (p.106)} that the clinical entity he was describing corresponded to the histologic entity of peripheral cystoid degeneration of the retina, which had been described by Blessig²² and by Iwanoff.¹¹⁴ However, neither cysts nor cystoid spaces have been shown to be components of the histologic picture of lattice degeneration of the retina. Actually, as correctly stressed by Pau,^{163,164,166} lattice degeneration is entirely unrelated to peripheral cystoid degeneration of the retina. As pointed out by Meyer-Schwickerath,¹⁴⁷ the tiny circumscribed reddish areas within lattice lesions are not cysts, but tiny areas of retinal thinning. Ricci¹⁷³ is correct in maintaining that the term "cystoid" should no longer be used in reference to

lattice degeneration.

Vogt's mistaken idea led him into an erroneous concept of the pathogenesis of the retinal holes and tears associated with lattice degeneration. He believed that by the rupture of their thin walls these "cysts" could form holes, or could become confluent with other "cysts," thus leading to the formation of horseshoe tears. The influence of his views has continued to be seen in the frequent references to these supposed cysts or cystoid spaces by other writers.

II. Clinical Definition

A. MORPHOLOGIC FEATURES

One of the areas of greatest disagreement in regard to lattice degeneration is the clinical definition of the entity. The wide variety of dissimilar designations given to the disease is an indication of the multiplicity of its clinical manifestations (Figs. 1-6).

The following features, which may be observed either singly or in all possible combinations, are listed according to the approximate frequency of their occurrence: localized round, oval or linear shaped retinal thinning; pigmentation; whitish-yellow surface flecks; round, oval or linear white patches; round, oval or linear red craters; small atrophic round holes; branching white lines; yellow atrophic spots (depigmentation of pigment epithelium); and rarely tractional tears at the ends or posterior margins of lesions. Usually one, but sometimes two or three, of these features predominate in each individual lesion. Differences between one lesion and another, however, are sometimes so striking that some observers have been inclined to think that they may represent basically different entities. Thus, a number of classifications and other reports of peripheral retinal diseases^{1,49,75,89,90,105,112,118,119,125,126,229} have been published in which lesions, undoubtedly representing different manifestations of lattice degeneration, have been regarded as separate disease entities.

B. CRITERIA FOR DEFINING CLINICAL LATTICE DEGENERATION

Any lesion in the peripheral retina which is consistent with lattice degeneration in its shape, location, and orientation must be examined carefully with scleral indentation. If, with indirect ophthalmoscopy and scleral indentation, the examiner can demonstrate at

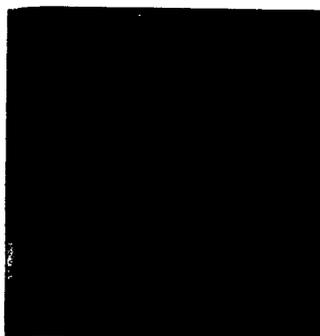


FIG. 1. Lattice degeneration, showing combined features of white lines, snail-track, and reddish base.



FIG. 2. Lattice degeneration with marked pigmentation plus white lines.



FIG. 3. Lattice degeneration with marked depigmentation of pigment epithelium (without scleral indentation).

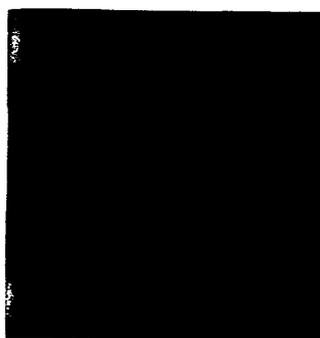


FIG. 4. Same lesion as Figure 3 (with scleral indentation) showing typical white line.

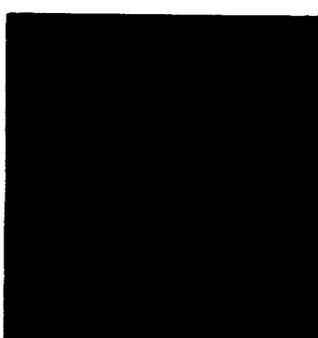


FIG. 5. Lattice degeneration, showing snail-track feature (with scleral indentation).



FIG. 6. Lattice degeneration, showing only a reddish excavation (with scleral indentation).

the borders of such a lesion an abrupt, discrete irregularity of the otherwise smooth surface of the retina, the lesion should be regarded as lattice degeneration, in spite of variations in pigmentation or other morphologic features.

C. NONESSENTIAL PRESENCE OF WHITE LINES

Some¹⁸⁶ have maintained that the presence of white lines (Fig. 1) is a sine qua non for the diagnosis of lattice degeneration and have therefore considered lesions with white lines as a separate entity, differentiating them from similar lesions lacking the white line feature. This feature is the most striking and unusual clinical feature, but it is arbitrary to state that its presence is mandatory. Vogt,²²² Byer,^{32,35,37} Ricci,¹⁷³ and Straatsma et al²⁰⁵ agree that white lines are not essential to the diagnosis. There are at least three reasons why a broader definition is required.

1) Histologic surveys^{29,61,76,202,205} showing a prevalence rate for lattice degeneration in the

general population of 8%, 5%, 9.5%, 6%, and 10.7% are in close agreement with clinical surveys^{32,35,101} which have found a prevalence rate of 7.1%, 8%, and 6%. The autopsy report of Okun giving the much lower rate of 1.2%¹⁵⁶ was evidently the result of his exclusion of cases without white lines. This would correspond almost exactly with the prevalence of cases with white lines in my two clinical studies where it was found that 1.23% (17.4% \times 7.1%)³² and 1.45% (18.2 \times 8%)³³ showed them respectively.

2) It has been shown that many lesions that do not exhibit white lines nevertheless do show an earlier stage of vascular change, namely, the presence of narrowing of vessels within or near the borders of the lesions. Such lesions are much more common (by a ratio of 5.7 to 1³⁷) than those showing actual white lines.

3) When patients with lattice degeneration are observed over a period of time without surgical intervention, new white lines

can be seen to appear. This was documented in 14% of 204 patients so observed.³⁵ Among 54 involved lesions, new white lines developed in 30 lesions which had initially shown none by microscopic examination with Goldmann lens, and additional white lines appeared in the remaining 24 lesions which had had white lines previously. This is sufficient proof to permanently settle the controversy that has existed, confirming that lesions in which white lines are absent represent the same disease process as those lesions with white lines. The white lines have been identified in 12% of lesions and 30% of patients in a large series.³⁵

Several peripheral retinal lesions (to be discussed) are considered by some authors to be possibly different entities, namely so-called "pigmentary degeneration;" "snail-track degeneration," "retinal erosion" or "vitreous base excavation." However, white lines can occasionally be found in all of these lesions as I have shown in fundus photographs³⁷ and I believe that they are to be regarded as variations of lattice degeneration. The use of a somewhat more restricted definition of lattice degeneration (or "equatorial degeneration") may account for the report of a much higher prevalence of white lines (80%) in these cases.¹⁴⁷

D. "PIGMENTARY DEGENERATION"

Some authors have drawn a distinction between lattice degeneration and a form of pigmentary degeneration (Fig. 2) which they have classified as a separate entity and which they believe is a precursor of rhegmatogenous retinal detachment. Everett⁷⁵ stated that much overlapping occurred between lattice degeneration and pigmentary degeneration, and later,⁷⁶ although still using the latter term as a separate classification, he strongly suggested that it should be questioned as a definite pathologic entity.

I am not aware of any histologic reports that would substantiate the existence of any such entity that is separate from lattice degeneration. The pigmentary changes associated with the peripheral degeneration of high myopia are very irregular and non-descript and are not in themselves rhegmatogenic. It is very important in this regard to remember that pigmentary changes are among the most prominent features of lesions of lattice degeneration, having been reported in 81.7%³² and 92%²⁰⁵ of lesions. These pigmentary changes probably do not represent

part of the primary pathologic process in lattice degeneration, as thought by Michaelson,^{149,150} but are secondary and non-specific changes that occur in the pigment epithelium.^{61,166} There are at least four different types of pigmentation that occur in association with lattice lesions.³⁷

1) Pigment may be found in scattered clumps or granules, or may be diffusely distributed throughout the lesion. This may be so heavy that almost no other features are apparent.

2) Pigment may be distributed in alignment with the blood vessels passing through the lesion.

3) When a tiny round atrophic retinal hole is present within a lattice lesion, usually there is also a narrow adjacent concentric cuff of elevation of retina within or sometimes extending very slightly beyond the lesion. Typically, this round area of detachment is of a uniform dusky gray appearance, which is produced by a subtle diffuse secondary pigment migration within or from the pigment epithelium, and limited in extent exactly to the round zone of detached retina. In examining the peripheral retina, one can frequently observe such round gray zones, even without scleral indentation. In my opinion, they are a pathognomonic sign of the presence of a tiny atrophic retinal hole which may be difficult to perceive, but which can be found with careful scleral indentation or slitlamp examination with the Goldmann contact lens.

4) Frequently, in the same area that contains a tiny hole with concentric adjacent detachment, there is also a neat necklace-like row of more obvious pigment granules, demarcating the outer limit of the elevated area.

In association with these secondary pigment changes seen in lattice lesions one also frequently sees, as might be expected, discrete yellowish atrophic areas of depigmentation. Figures 3 and 4 show an exaggerated example. Attention has been called to the similarity in appearance of these areas to those of pavingstone degeneration.¹⁶⁶ From their clinical appearance, one would surmise that their histologic picture would be similar to, or identical with, that of pavingstone degeneration. They are commonly seen adjacent to lattice lesions and appear to be secondary and nonspecific changes, as identical lesions have been reported in association with senile retinoschisis.³⁴

The confusion concerning this pseudo-entity of pigmentary degeneration could, I think, be removed if the diagnostic criteria outlined in Section II, B were observed. It is probable that failure to examine such lesions in this way accounts for the idea of the existence of a separate pigmentary degenerative entity which is thought to be capable of giving rise to retinal breaks.

E. "SNAIL-TRACK DEGENERATION"

Snail-track degeneration (Sneckenspuren) is a term used by many authors to designate another peripheral retinal manifestation (Fig. 5) thought to represent an entity possibly distinct from lattice degeneration. However, there is evidence which strongly suggests that this morphologic appearance is yet another of the various clinical manifestations of lattice degeneration.

Gonin⁹⁵ (in his Tab. XXXIII) showed a good illustration of such a lesion which contained in one end a tiny round atrophic hole of the type typical of lattice degeneration. Vogt²²² (in his Abb. 140-141) published an illustration of a snail-track lesion with a typical tractional horseshoe tear which developed on the posterior edge and around both ends of the lesion. The term "snail-track" is a useful and well-chosen morphologic descriptive clinical label for lesions with usually abrupt discrete borders having the characteristic shape, location, and orientation of lattice lesions.

The essential ingredients of the snail-track appearance are the tiny glistening yellow-white flecks which are seen in large multitudes either on the surface of the retina or suspended just above the retinal surface in the most peripheral (external) vitreous layers. These flecks are also seen in the absence of other characteristics of lattice degeneration, and the term "snail-track" should probably be avoided in these situations. They are a prominent feature of senile retinoschisis,^{34,194} where they are found in 70% of lesions.³⁴ They may also be seen adjacent to meridional retinal folds and to retinal rosettes in the peripheral retina,⁶² and adjacent to retinal tears not caused by lattice degeneration.³² Large areas of these flecks are sometimes seen covering a quadrant or more of the peripheral retina with very indistinct borders which gradually merge into normal retina. Such an appearance is also designated as "etat givre" and is illustrated well by

Heinzen¹⁰⁵ (p. 187, Abb. 138). However, this is not to be confused with lattice degeneration. According to Eisner,⁷³ when these "glistening retinal dots" are the only retinal change and the surrounding retina appears normal, abnormal vitreoretinal adhesions are not present, since the vitreous detaches at these sites without complication. He also states that these dots may disappear following a posterior vitreous detachment. These were formerly thought to possibly represent cholesterol deposits.^{95,105} Daicker,⁶² however, has extensively investigated the histologic nature of areas of snail-track appearance in 21 eyes using trypsin digestion and concluded that the individual glistening particles represented microglia cells containing lipid or lipoprotein material. He found the retina in the area of the snail-track was always primarily or secondarily atrophic.

Streeten and Bert²⁰⁶ also used trypsin digestion in studying lattice lesions and found that the basement membrane was absent from the surface of all lesions. The surface showed instead variable PAS-staining coarse fibers with round PAS-staining discs attached to the fibers. They stated that these were identical to hyaline bodies often seen in digestions of degenerated peripheral retina, and suggested that they might correspond to the yellow-white surface flecks seen clinically.

Straatsma, et al²⁰⁵ studied lattice lesions using trypsin digestion and electron microscopy and demonstrated dense granules of PAS-staining material within and at the margins of lesions. They believed this to represent extracellular products of cell breakdown and fibrosis, and correlated it with the tiny surface particles seen clinically. Possibly this also corresponds to the collections of pink-staining hyaline material, staining positively with PAS, which Straatsma and Allen described briefly in an earlier report.²⁰² Typical snail-track lesions tend to have a "white-without-pressure" appearance, and frequently may also exhibit a rather marked increase of whiteness when scleral pressure is applied. (The term "white-with-pressure," however, should be used in a more strict sense, describing a well-defined "geographic" type of fundus whiteness which is produced with pressure and which is entirely different from any form of snail-track appearance).

The condition reported by Gärtner⁹⁰ and designated as "milkyway-like" or "galaxy-like" degeneration undoubtedly falls within

the group of "snail-track" lesions.

It is my opinion that the term "snail-track degeneration" should no longer be used, since it implies a distinct pathologic entity. Neither should the word "snail-track" be used to differentiate a lesion in the fundus from the disease we know as lattice degeneration of the retina. For the following reasons, the term should be limited to describing simply one variation or manifestation of lattice lesions.

1) Writers who use the term have consistently drawn attention to the fact that snail-track lesions closely resemble the shape, location, and orientation of lattice lesions.

2) The essential white flecks of the snail-track appearance occur to varying degree in 80% of lattice lesions.³²

3) The snail-track appearance is frequently combined with other classic features of lattice lesions such as round atrophic holes,^{1,37,90,95,105,222} horseshoe tractional tears,^{105,222} or white lines and reddish base as shown in Fig. 1.

In summary, the yellow-white retinal flecks probably represent, as Daicker⁶² concludes, a non-specific expression of primary retinal processes which are slowly atrophic-degenerative in nature.

F. "RETINAL EROSION," "LOCAL RETINAL EXCAVATION," "VITREOUS BASE EXCAVATION"

There is another lesion which has the typical shape, orientation, and location of lattice lesions and is characterized by a sharply demarcated excavation and a uniform reddish base (Fig. 6); I have regarded this as a variation of lattice degeneration.³² It has also been called retinal erosion,¹⁷⁷ local retinal excavation,⁸³ and vitreous base excavation.^{84,200}

Foos et al⁸⁴ state that this lesion probably represents a variant of lattice degeneration which is modified by its location within the area of the vitreous base. Rutnin and Schepens¹⁷⁷ express doubt as to its exact nature, but suggest the possibility that this lesion, while having the basic characteristics of early lattice degeneration, may be nonprogressive, stating they have never seen it progress to a typical lattice-like lesion. They illustrate such a lesion showing associated pigmentation and also overlying white flecks. I have also shown³⁷ that such lesions may have white lines and particularly may develop small atrophic holes. I believe that the preponderance of evidence would support the

inclusion of this lesion as simply another clinical variation of lattice degeneration.

G. "DISTINCTIVE CHOROIDORETINOPATHY" (CHORIORETINOHYALOIDOPATHY)

The term "distinctive choroidoretinopathy"^{149,150} (chorioretinohyaloidopathy)⁴⁹ would seem to imply a specific role of the choroid in the pathogenesis of this condition; however, the choroidal alterations in lattice degeneration are often absent and when present, are probably nonspecific secondary changes.^{61,134,166}

H. RELATION TO POST-EQUATORIAL RADIAL PERIVASCULAR CHORIORETINOHYALOIDOPATHY (WAGNER'S HEREDITARY VITREORETINAL DEGENERATION)

In attempting to define the clinical appearance of lattice degeneration, it is necessary to discuss another lesion which has been the source of considerable confusion. It may be designated "post-equatorial radial perivascular chorioretinohyaloidopathy." It has been included in the category of clinical manifestations of lattice degeneration by several authors.^{49,142,205} Cibis⁴⁹ refers to it as "post-equatorial (pigmented) lattice degeneration," and McPherson¹⁴² calls it "familial lattice degeneration." Its fundus picture appears to be the same as the one now becoming recognized as an important component of Wagner's vitreoretinal degeneration. Although the distinctive appearance was not noted in the earliest reports of Wagner's disease,^{25,223} a patchy perivascular form of pigmentation was reported soon thereafter,^{86,116,172} and has since been more fully described.^{3,15,107,217}

Other authors have presented descriptions and photographs of lesions very closely resembling and probably identical with this particular component of Wagner's disease. Cibis⁴⁹ described familial cases of what he called "post-equatorial (pigmented) lattice degeneration" or "post-equatorial chorioretinohyaloidopathy," and stated that he was inclined to consider it identical with Wagner's hereditary hyaloideoretinal degeneration. Hagler and Crosswell¹⁰⁰ reported 33 patients with a very similar fundus appearance which they termed "radial perivascular chorioretinal degeneration." However, because of certain differences between their cases and

some of those reported with Wagner's disease, it was their opinion that their cases probably represented a distinct familial entity. For example, Hagler and Crosswell found a very high incidence of retinal detachment (67%) in their cases, whereas retinal detachments have been notably absent among the patients reported by Wagner, even following cataract extraction.^{24,124}

Urrets-Zavalía²¹⁸ has also reported a pedigree of four cases similar to those of Hagler and Crosswell.¹⁰⁰ The fundus lesion described by the various foregoing authors has an ophthalmoscopic appearance which is, in most respects, decidedly different from that of lattice degeneration as defined in this review. This lesion, which we may call post-equatorial radial perivascular chorioretinohyaloidopathy, is characterized by a typical radial orientation, symmetrically arranged around a major blood vessel which appears to form the central core of the lesion. There are usually large coarse clumps of black pigment which often form a prominent black sheath around the vessel. The lesions are very broad with ill-defined margins merging imperceptibly with normal retina. There tends to be a broad zone of depigmentation of the pigment epithelium and of atrophy of the choriocapillaris. The lesions are also very long and posterior, sometimes extending back to the optic disc.^{3,100}

Typical lattice degeneration has, however, been reported in association with post-equatorial radial perivascular chorioretinohyaloidopathy.^{3,49,100,107,218} In four of these reports,^{3,100,107,218} the two conditions are differentiated from each other.

I. "EQUATORIAL DEGENERATION"

The term, "equatorial degeneration,"¹⁴⁶ enjoys great popularity and serves a useful purpose in emphasizing the interrelationships among some of the various clinical forms of lattice degeneration. However, it has the disadvantage of not being sufficiently specific, since there are a number of other degenerative processes which involve the equatorial zone but have no relationship to lattice degeneration.

III. Histologic Features

A. HISTORICAL BACKGROUND

In 1904, Gonin⁹² briefly described the histologic appearance of an equatorial retinal

lesion in a patient with retinal detachment. Although his description is somewhat confusing, the published drawing of this lesion (Fig. 3, page 38) which is immediately anterior to a tractional retinal tear, does show features which are consistent with lattice degeneration. This probably is a lattice lesion and, as such, represents the earliest histologic documentation of this disease of which I am aware. Gonin stated that it resembled a focus of choroiditis. Later (in 1930), when Gonin⁹⁴ gave a brief clinical description of lattice degeneration, he expressed the opinion that it probably corresponded to the type of histologic lesion he had reported earlier.⁹²

In 1929, Kümmell¹²⁸ studied an eye removed seven days after the onset of a retinal detachment. His published photomicrographs reveal a number of the typical features of lattice degeneration. Arruga, in his 1936 text,¹² presents histologic sections from the eye of a patient of Sourdille which show an entirely typical lattice lesion. The description of the lesion, however, is very scanty, stating only that it shows "retinal atrophy with post-inflammatory pigmentary residue."

The first clear histological description with supporting illustrations of specimens was given by Lindner¹³⁴ in 1937. His report indicates that he recognized all the salient histologic features of the disease that are known today, including thinning of the inner retinal layers, adjacent vitreous liquefaction, attachment of condensed vitreous fibrils to the edges of the lesion, and glial proliferation. He calculated the length of the lesions by measurements of serial sections and therefore emphasized the broad "apron-like" nature of pathologic vitreoretinal attachments, a concept which is still not widely enough understood today. He also pointed out the notable absence of choroidal involvement. His important contribution has received insufficient notice in the literature. Although he demonstrated histologically that the lattice lesion could be the site of a tractional retinal tear, he also showed that posterior vitreous detachment can coexist with an intact retina at such sites of abnormal vitreoretinal attachment.

However, it is an interesting question whether Lindner realized that the histologic entity he described corresponded to the clinical disease we now know as lattice degeneration, for in discussing Michaelson's paper¹⁴⁹ on clinical lattice degeneration 17

years later, he made no mention of his own earlier work. It seems quite possible that the dominant influence of Vogt's mistaken view that clinical lattice degeneration (or "cystoid degeneration") arose from Blessig's cysts (peripheral cystoid degeneration) may have obscured the importance and correct interpretation of Lindner's discovery.

Other histologic reports followed later.^{5,6,29,61,76,150,156,157,164-166,202,205,206}

B. MORPHOLOGIC FEATURES

Straatsma et al²⁰⁵ studied 800 consecutive autopsy cases, finding 86 (10.7%) with lattice degeneration. All the 286 lesions found in these cases showed three invariable features; retinal thinning; vitreous liquefaction overlying the area of thinned retina; and vitreous condensation and exaggerated vitreoretinal attachments at the borders of the lesions. Almost all of the autopsy reports mention the presence of a new-formed cellular component of the lesions thought by most to represent glial proliferation.^{61,134,164,202,205,206} Some have thought that this new tissue might have originated from the pigment epithelium,^{60,164,166} vascular connective tissue,^{164,166} or even from cortical cells of the vitreous.^{156,166}

C. TRYPSIN DIGESTION STUDIES

Trypsin digestion studies have been carried out by several investigators,^{61,62,205,206} and have been commented on in Section II.E.

D. ELECTRON MICROSCOPIC STUDIES

Two investigators have studied lattice degeneration with electron microscopy.^{205,206} Straatsma et al²⁰⁵ demonstrated thinning of the retina, fibrosis of blood vessels, loss of retinal neurones, accumulation of extracellular (glial) material, pigment abnormalities, and alterations of the inner limiting lamina. All these changes, as one would expect, were found to be progressively more advanced toward the center of the lesions. Streeten and Bert²⁰⁶ demonstrated an absence of basement membrane over the surfaces of lesions, which showed instead the presence of glial cells which they identified as astrocytes.

IV. Methods of Clinical Examination

The particular features of lattice lesions which will become apparent during clinical examination depend markedly on the method of examination employed, and on the skill and experience of the examiner. The very

peripheral location of the lesions makes them largely inaccessible to direct ophthalmoscopy. Slitlamp examination with the Goldmann contact lens, especially when used in conjunction with Eisner's⁷³ independently movable scleral indentation, gives good visualization of the periphery and reveals details, particularly of the vessels and vitreoretinal relationships, which cannot be seen by any other method. However, binocular indirect ophthalmoscopy with scleral indentation, utilizing less magnification, permits examination of a larger field, reveals better color contrast, permits visualization of any lesion in multiple profiles, and provides a better perspective of the disease as a whole than does any other method. Furthermore, many lesions cannot be detected except by scleral indentation. Dependence on less adequate means of examination may account for the comment by Pau¹⁶¹ that some lesions seen in autopsy eyes cannot be seen clinically; it may also account for the impression of some^{111,130} that lattice lesions frequently seem to progress suddenly and change their appearance in a short period of time, even among older patients.

V. Clinical Features

A. SUMMARY OF NEW DATA

Many of the clinical characteristics of lattice degeneration have already been discussed (Section II). To shed further light on its clinical appearance, I would now like to present previously unpublished data³³ (Table I) assembled in 1966 from a study which I conducted on 1700 consecutive patients. These patients represented a different series than the one I previously reported,³² but they were selected with the same criteria. That is, the patients were not referred by another ophthalmologist, did not present with retinal symptoms, and had no known history of retinal disease or intraocular surgery. Of the 1700 patients surveyed, 137 (8%) had lattice degeneration which involved 195 eyes, being

TABLE I

Clinical Survey of 1700 Patients (3400 Eyes)

Number	Patients	Eyes	Lesions
w/ Lattice	137 (8%)	195	393
w/ Round Holes	40 (29.2%)	46 (23.6%)	64 (16.3%)
w/ White Lines	25 (18.2%)	30 (15.4%)	47 (11.9%)

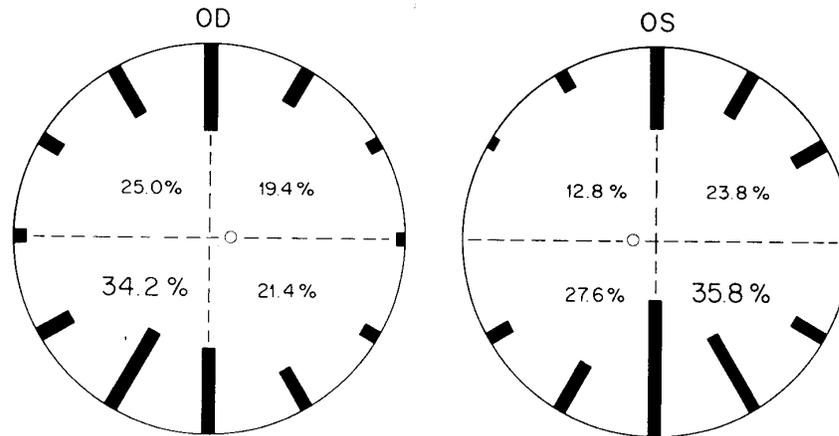


FIG. 7. Distribution of lesions of lattice degeneration by quadrant and meridian in 137 consecutive patients.

bilateral in 58 (42.3%). There were 393 lesions representing two lesions per eye. The distribution of lesions by meridian and quadrant is shown in Fig. 7. Forty patients (29.2%) had one or more round holes in one or more lesions, and 25 patients (18.2%) had white lines in one or more of their lattice lesions. Of the 25 patients with white lines, 9 (6.6% of total patients with lattice) had the white line lesion as their only lattice lesion. The 25 patients had 115 lesions, only 47 (41%) of which showed white lines. These 47 lesions with white lines represented 11.9% of the total 393 lesions studied.

B. GENERAL FEATURES

Lattice degeneration is not known to show any racial preference, having been reported commonly among Caucasians, Orientals^{125, 126, 179-181, 195, 209, 229} and Africans.¹⁴ The distribution is not statistically different for males and females.^{32, 205}

The refractive index of eyes with lattice has been reported to be shifted significantly to the myopic side,^{32, 152a, 205} but some²¹³ believe it is not a contributory factor. Hyams and Neumann¹¹² found either "lattice" or snail-track lesions in 15% of myopic eyes of -1.00 D or more. Cambiaggi⁴⁰ reported palisade degeneration in 19% of myopic eyes, and an increased prevalence in those over -8.00 D. Kirker and McDonald¹²² found lattice in 8%-22% of myopic eyes over -6.00 D, but the definition of their categories is unclear. Karlin and Curtin,¹²¹ in their study of myopic eyes and axial length, found an increased

prevalence of lattice degeneration associated with increased axial length, reaching a prevalence of 15% in the longest eyes.

The disease appears to reach its maximum prevalence prior to the age of 10 years³² and clinical surveys have reported this prevalence to be between 6% and 8%.^{32, 33}

Bilateral involvement has been reported in 33.7%,³² 48.1%,²⁰⁵ and 42.3%.³³ In bilateral cases, there is frequently a striking symmetry in the location and appearance of individual lesions. The average number of lesions per eye has been found to be 2.4,³² 2.3,²⁰⁵ and 2,³³ but the actual number may vary from 1-19 or more.^{32, 205}

The length and width of individual lesions is very variable. Clinically, the length has been reported to vary between $\frac{1}{2}$ and 12 disc diameters (DD)³² and, in an autopsy study, from $\frac{1}{6}$ to 12 DD.²⁰⁵ However, they may occasionally be much longer. The width has been reported by the same studies to be $\frac{1}{4}$ to $\frac{2}{3}$ DD³² and $\frac{1}{10}$ to $2\frac{1}{3}$ DD with the average being $\frac{1}{2}$ DD.²⁰⁵ However, they may sometimes be so narrow as to appear as only thin lines, especially in the case of some new lesions making their first appearance.³⁵ Lesions may be linear, oval, or, if very small, even round in shape.

The large majority of lesions have an orientation approximately parallel with the ora serrata, but some are somewhat obliquely placed at various angles.^{32, 205} The most common location for lesions in the anterior-posterior plane is slightly posterior to the midway point between ora and equator.^{32, 205}

It is not uncommon to find two lesions situated parallel to each other, one more anterior and one more posterior. Occasionally, as many as four or five lesions exhibit this adjacent parallelism in such a manner that each lesion is situated progressively more posterior than the previous one; also, each lesion is displaced progressively slightly more laterally than the previous one. When this occurs, a straight line drawn through the series of lesions would lie in an oblique plane in relation either to the equator or to the anterior-posterior plane.

C. DISTRIBUTION OF LESIONS

The opinion has been almost universally held that lattice degeneration has a predilection for the upper temporal quadrant. Not until the lesions began to be studied according to meridian^{32,33,205} was it realized that lattice lesions tend to be clustered between the 11 to 1 o'clock and 5 to 7 o'clock meridians rather than in any particular quadrant. These areas contained 66% of the 286 lesions in the autopsy study by Straatsma et al,²⁰⁵ and 78.6% of the 393 lesions in my clinical study.³³ However, when the 393 lesions in my study were analyzed as to quadrant (Fig. 7), it was found that the lower temporal quadrant was the most common one involved.

The reason that lattice degeneration has been so widely thought to be most common in the upper temporal quadrant is not difficult to understand. Most patients in whom lattice degeneration is discovered have sought out the ophthalmologist because of acute retinal symptoms. In a series of 100 such eyes showing symptomatic retinal breaks with retinal detachment, Dumas and Schepens⁷² found that 30 of the eyes had lattice degeneration and that each of these had at least one retinal tear closely related to a lattice lesion. These 30 eyes showed 33 horseshoe tears associated with lattice, and 54.5% of these were located in the upper temporal quadrant, a much higher percentage than was found in any other quadrant. This is consistent with the long known fact that among retinal detachment patients, the upper temporal quadrant is the commonest quadrant for the occurrence of retinal breaks. Therefore, it is this infrequent complication that originally brings the lattice degeneration to the attention of the physician and when it does, the upper temporal quadrant is most often the one affected.

D. SPECIFIC MORPHOLOGICAL FEATURES

1. Pigmentation

Pigmentation is observed to some degree in 82% of lattice lesions,³² and has been thoroughly discussed in Section II D.

2. Whitish-yellow Flecks

The whitish-yellow flecks, which lie either on the surface of many lattice lesions or are suspended slightly superficial to lesions in the vitreous attachments, have also been discussed previously (Section II E). They are more prominent on the posterior edge of the lesions and have been found in 80% of lesions.³²

3. White Lines

The classical white lines of lattice lesions were proven by Vogt²²¹ to represent altered blood vessels when he showed that they were continuous with the normal vascular pattern with a visible blood column connecting to each end of such white lines. Pseudo "white lines" may also be seen³² but on examination with the Goldmann lens they can always be differentiated from true white lines. The pseudo white lines are caused by a linear arrangement of the whitish-yellow flecks discussed previously, and not by blood vessels.

True white lines have been reported in 12% of lesions³³ (Table 1) and affect venules more frequently than arterioles.⁷² The earliest preceding vascular change is a localized narrowing of the vessel and many lesions evidently remain in this arrested state;³⁷ some, however, progress to show parallel white sheathing, and some progress beyond this to the classical white lines. White lines are uncommon in young patients, being found in 3.3% in the 10-19-year age group, but increase with age, reaching a prevalence of 42.9% after 50 years of age.³² Although lattice lesions are slightly more common in the inferior half of the eye, lesions with white lines are statistically more common in the superior half.³⁵ The reason for this is unknown. The specific presence of white lines in superiorly located lattice lesions probably does not explain the marked predominance of symptomatic retinal breaks in general for the superior half of the fundus. Several reported series of such breaks have shown that 95%,³⁷ 73%,⁷² and 82%⁶³ occurred in the upper half.

4. Tractional Retinal Tears

Among horseshoe tears which were direct-

ly associated with lattice lesions, and which were also symptomatic and had led to a retinal detachment, Dumas and Schepens⁷² found that 88% were superiorly located. This great predilection of symptomatic tears for the superior fundus is undoubtedly more accurately explained by the marked gravitational dragging forces that occur with posterior detachment of the vitreous than by the fact that lesions with white lines are more common superiorly. Since every lattice lesion is characterized by a firm vitreoretinal attachment histologically,²⁰⁵ each lesion is a potential site for the occurrence of a tractional tear. This fortunately occurs very infrequently, and was seen in only 1.5% of cases in a large clinical study³⁵ and in 2.4% of eyes in a large autopsy study.²⁰⁵ Tending to confirm the above explanation is the illustrative case in my study³⁵ in which an acute posterior vitreous detachment produced a horseshoe tear at the site of a superior lattice lesion with no white lines, while a nearby lesion with white lines was not involved.

5. Atrophic Retinal Holes

The small atrophic retinal holes which occur in lattice lesions are not the result of tractional forces, but appear to be caused by the gradual progressive thinning of the retina until a tiny perforation is finally produced. Prior to the actual formation of the hole, it is frequently possible to observe a tiny round discrete reddish spot for several years where the retina has become extremely thin, giving greater visibility of the orange-red color of the choroid. These reddish spots have frequently been interpreted to represent tiny "cysts" which are believed to rupture, thus producing the holes. As discussed previously, this erroneous view probably represents the continuing influence of a mistaken earlier concept of the pathogenesis of these lesions promulgated by Vogt. It is possible, however, to make a differentiation between such reddish spots and actual holes by indirect ophthalmoscopy combined with scleral indentation, and also by slitlamp examination with the Goldmann contact lens. The existence of an actual hole can be verified by the presence of a very sharp and distinct border and also by a more marked contrast between the color of the hole and that of the immediately surrounding retina. An additional diagnostic point of great significance is the fact that the

color of this hole (which is usually slightly detached) immediately changes in relation to the surrounding retina when the arcuate "shadow" of the advancing edge of the scleral indentation is made to pass beneath it.

Almost all atrophic holes in lattice lesions are small, usually less than $\frac{1}{4}$ DD and only rarely reaching a diameter of one DD.³⁵ Many in fact are in the range of $\frac{1}{15}$ DD (0.1 mm) and are difficult to identify. However, since most atrophic retinal holes in lattice lesions produce a tiny adjacent circumscribed area of retinal detachment very soon after their appearance, this becomes a diagnostic point of great significance. If the observer sees a tiny, usually round, zone of slightly detached retina within a lattice lesion or slightly wider than the lesion, and with a slightly grayer, more dusky hue than the rest of the lesion, this is a pathognomonic sign of the presence of a tiny retinal hole near the center of this area, even though it is so small that it initially escapes notice. Although most holes in lattice lesions are solitary, they may be multiple.

Atrophic holes within lattice lesions have been reported in 18.2% of 22 lesions observed clinically by Rutnin and Schepens.¹⁷⁷ In the autopsy study of 1588 eyes by Straatsma et al,²⁰⁵ 24.9% of the 125 eyes with lattice had round holes, as did 18.2% of the 286 lesions. In my clinical study of 1700 patients (3400 eyes)³⁵ atrophic holes occurred in 29.2% of the patients with lattice, in 23.6% of the eyes with lattice, and in 16.3% of lesions (Table 1). Of the total series, 2.3% of the patients and 1.35% of the eyes had lattice lesions with holes. Foos⁸² has surveyed 5600 autopsy eyes and found 2.4% of them to contain holes of trophic origin (not associated with flap or operculum). He found the round holes of lattice to comprise 75% of all holes in his series. Of his total series, 3% of the cases and 1.84% of the eyes had lattice lesions with holes, figures in close agreement with my series.

Retinal holes are already present in 13.3% of patients in the 10-19-year age group, the prevalence then steadily increasing in older age groups. Statistically, there is a highly significant preponderance of holes in the inferior half of the fundus — a ratio of more than two to one as compared to the upper half.³⁵ The strongly preferred quadrant is the lower temporal.^{1,35,210} The prognosis of these holes will be discussed later.

VI. Changes in Lesions with Increasing Age

In histologic studies^{61,202,205} a differentiation has sometimes been made between "early" and "late" lesions, depending on the severity of the histologic alterations. Based on his study of many autopsy eyes, Daicker^{60,61} has outlined a progressive series of histologic changes, beginning with a localized area of vitreous liquefaction adjacent to a localized retinal area where only the innermost layers are degenerated. This then progresses to increased vitreoretinal adhesions at the periphery of the lesion, increased thinning and degeneration of the center of the retinal lesion, eventually destroying the outer nuclear layer and sensory cells, and finally involving the pigment epithelium in both atrophic and proliferative changes. Finally, the whole area tends to become converted into a fibrous gliosed plate into which pigment epithelial cells migrate and clumps of pigment become irregularly dispersed. Daicker,⁶¹ however, was not able to clearly correlate progressive severity of lesions with increasing age of the cases in his histologic study. Straatsma et al²⁰⁵ found no age-related trend in regard to the size, location, or orientation of lesions, but they did find with advancing age of the autopsy eyes in their series a statistically significant increase in degree of vitreoretinal attachments and prevalence of pigment abnormalities, white lines, retinal holes, posterior vitreous detachment and retinal tears.

From a clinical standpoint, however, it is not possible to draw any conclusion as to the age of a particular lesion on the basis of its clinical appearance, even though certain changes can be documented in individual lesions observed over a period of time.³² There is often a marked disproportion between the age of a patient and the severity of the lattice lesions; older patients frequently show very mild lesions and, conversely, young patients sometimes have lesions which exhibit the most advanced degrees of severity. This disproportion is due to a notable tendency for lattice lesions to remain clinically arrested throughout life, the great majority showing no noticeable change over a period of years.³⁵ Changes in lesions, when they appear, occur extremely slowly, except in the case of tractional tears.

Lattice lesions have been observed histologically as early as 17 months of age,⁴

and the maximal prevalence of the condition is already attained by the beginning of the second decade.^{32,205} However, additional new lattice lesions can occasionally occur. They have been documented in 5% of patients already having lattice degeneration. Most (95%) of these new lesions occur before the age of 19 years,³⁵ 95% of such new lesions occurring, however, before the age of 19 years.³⁵ Difficult to correlate with this data is a disturbing report¹³⁰ of 13 eyes in which new lesions or new extensions of old lesions were observed. Half of the patients were 50 years of age or older, and the authors stress the rapidity with which new lesions may occur, even in as short a period as one month. To evaluate this report, it is crucial to know the method of examination, which is not stated. Many lattice lesions are subtle and scleral depression is essential in verifying their presence or absence. Hyams et al¹¹¹ observed 873 eyes for periods ranging from one to six years in a group of patients thought to be prone to retinal detachment, and 95% of whom were over 30 years of age. The authors reported numerous cases in which new areas of lattice or snail-track lesions were believed to have appeared. However, I believe that the method of examination, with only slitlamp biomicroscopy and Goldmann 3-mirror contact lens, probably explains this finding, since without the use of scleral indentation, lattice lesions frequently remain clinically invisible, and may have been missed on earlier examination.

New atrophic retinal holes have been documented in lattice lesions,^{35,37} having appeared in 12.7% of patients observed over a period of years. Interestingly, 65% of these new holes appeared prior to age 35, whereas only 31% of new white lines (which appeared in 14.2% of patients) occurred before that age. New holes, as is the case with preexisting ones, are markedly more frequent in the inferior half of the fundus. New white lines, conversely, are slightly more common superiorly. Atrophic holes do not tend to enlarge with the passing of time. I observed enlargement in only two of 137 holes over a period of years.³⁵

The most serious and, fortunately, the least common change in lattice lesions is the development of a tractional horseshoe tear in the adjacent retina, either posteriorly or extending also from the posterior margin around one or both ends of the lesion. In a series of 86 autopsy cases, Straatsma et al²⁰⁵

found this in 3.5% (2.4% of eyes) with lattice. In a clinical series of 204 patients observed over a period of years,³⁵ I found such a tear in 1.5% (or 1% of eyes).

VII. Fluorescein Angiography of Lattice Lesions

The fluorescein angiographic appearance of lattice lesions has been reported by a number of authors.^{7,8,44,175,179,181,195,205,209,211-213,224,225} Some of these studies are of limited usefulness because they were performed in patients who had lattice degeneration associated with an existing retinal detachment.

The most informative report is that by Sato et al¹⁸¹ who studied 49 eyes with lattice degeneration without retinal detachment. From this large group, they were able to compile statistical data on the relative frequency with which various angiographic abnormalities are seen. In all cases, they observed leakage of dye from choroidal vessels in the area of the degenerative lesion and avascularity in and proximal to the lesion. The retinal vessels proximal to the lesion exhibited extravasation of dye in 61%, delayed filling in 54%, arteriovenous shunts in 33%, capillary dilatation in 33%, and formation of microaneurysms in 16% of eyes. These investigators interpreted their findings to indicate that in a majority of cases of lattice degeneration the retinal circulatory disturbance may be the primary cause of the disease, and that choroidal changes may also play some role in the etiology.

Wessing²²⁵ found that veins which appear ophthalmoscopically normal may actually be occluded peripherally, and that in these cases the posterior branches of these veins may fill by side branches, thus creating "rectangular" patterns which are angiographically characteristic of lattice degeneration. He also noted the occasional occurrence of fan-shaped formations similar to those seen in sickle cell disease, Eales' disease, or Coats' disease. He stated that the vascular changes observed in lattice degeneration probably represent a repair mechanism in a degenerative process with a very protracted course.

Tolentino et al,²¹² also studying only cases without an associated retinal detachment, found that eyes with early or mild retinal changes did not reveal remarkable findings. They observed that branches of arterioles supplying the unaffected retina around the le-

sion showed normal filling with dye, and interpreted this to indicate a pathologic process which was involving only a segment of these vessels. They also found that retinal venules peripheral to the lesion were patent, suggesting that there was retinal perfusion peripheral to the lattice lesion.

VIII. Heredity

There has been little study of the influence of heredity on lattice degeneration as an individual entity; the only definite published report of which I am aware is Gärtner's.⁹⁰ His pedigree showed a probably autosomal dominant mode of transmission. There is one older and somewhat doubtful report by Jaeger,¹¹⁵ who described a pedigree of 9 individuals, four of whom he said showed retinal vascular changes "exactly like those Vogt had described," and most of which were in the inferior temporal quadrant. However, a drawing of the fundus lesion of one of the patients shows no resemblance to lattice degeneration.

A number of pedigrees of familial retinal detachment have been published, and in many of these the association with cases of true lattice degeneration has also been studied. These include the report of Cibis⁴⁹ (Figs. 119, 121, and possibly 124) and those of nine other authors^{1,15,41,49,66,77,96,103,131} Lattice degeneration may have been associated with certain other pedigrees.^{88,91} The hereditary pattern in some of these families is unclear, but in a number of them^{41,49,66,77,103} the transmission appears to be of an autosomal dominant type, either regular or irregular. Falls⁷⁸ believes that lattice degeneration is transmitted as a recessive trait, but exhibiting the phenomenon of pseudodominance. He bases this view on the known high prevalence rate of lattice degeneration in the general population, which provides a ready opportunity for the intermarriage of homozygous and heterozygous individuals whose offspring would therefore be expected to show the condition in approximately 50% of cases. Ricci¹⁷³ agrees that as a rule the hereditary pattern is recessive autosomal pseudodominant, but he believes that in certain families also affected with hereditary retinal detachment, the pattern is probably autosomal dominant.

The above mentioned pedigrees indicate that lattice degeneration is sometimes strongly associated with later retinal detachment. This is not to say that lattice is

necessarily the cause, for some of the families also showed a high association with other chorioretinohyaloidopathy or myopia. The cause may in fact be one or more still unknown factors which predispose to both lattice degeneration and retinal detachment. The fact that almost all the published pedigrees of families with lattice degeneration also show a fairly high prevalence of retinal detachment tends to give a very false impression of the danger of this complication among patients who have lattice degeneration. This is due largely to the almost complete absence in the literature of hereditary studies of lattice degeneration as an individual entity. It is common to observe various patients with this condition in a family which has no history of retinal detachment. It is accurate to assume that the recorded pedigrees of families in which lattice degeneration is strongly associated with retinal detachment comprise not more than 1% of patients in the general population who have the former condition.^{32,35}

The genetic origin of lattice degeneration is also substantiated by the report of Jesberg,¹¹⁷ who studied Turner's Syndrome (gonadal dysgenesis), which is a disease with typical chromosomal abnormalities. He found that 17 of 21 cases (81%) also had chorioretinal degeneration, which took the form of lattice degeneration with white lines in 67% of the involved eyes, and lattice without white lines in 33%.

IX. Association with Other Conditions

A. TURNER'S SYNDROME

The high association of lattice degeneration with Turner's Syndrome was discussed in the previous section.

B. EHLERS-DANLOS SYNDROME

Pemberton, Freeman and Schepens¹⁶⁷ reported a pedigree of seven individuals, including six who had myopia with retinal detachment, four who had Ehlers-Danlos Syndrome, and three who had lattice degeneration.

C. WAGNER'S HEREDITARY VITREORETINAL DEGENERATION

Typical lattice degeneration has been reported in association with Wagner's Disease by Cibis,⁴⁹ Alexander and Shea,³ Hagler and Crosswell,¹⁰⁰ Urrets-Zavalía,²¹⁸

and Hirose et al.¹⁰⁷ The histologic nature of Wagner's Disease has still not been sufficiently clarified to permit us to know what relationship, if any, it bears to typical lattice degeneration.

D. CHRONIC RESPIRATORY DISEASE

Gottlieb et al.⁹⁷ measured the first-second vital capacity (FSVC) in 187 patients with retinal detachment, comparing 55 members of this group who had lattice degeneration to 132 who did not. They found that 44% of the group with lattice degeneration had a FSVC of less than 70% while only 33% of the group without lattice had a FSVC this low. While the authors stated the difference was not statistically significant, they speculated that a larger series might prove it to be so.

E. ATHEROSCLEROSIS

In Okun's historic study of pathology in autopsy eyes,¹⁵⁶ the three patients who had lattice degeneration (with white lines) all had far-advanced atherosclerosis. The ages of these patients is not given and the significance of this finding is not known.

F. SURFACE WRINKLING RETINOPATHY

In a study of the finding of surface wrinkling retinopathy (SWR) in a large series of autopsy eyes, Roth and Foos¹⁷⁶ found lattice degeneration associated with this entity in 18.5% of the involved cases and in 14.3% of the involved eyes. This is substantially higher than the prevalence of lattice degeneration among autopsy eyes studied in the same laboratory²⁰⁵ which was found to be 10.7% of cases and 7.9% of eyes. All cases of SWR were associated also with a cellular epiretinal membrane. At the present time there is no other known relationship between SWR and lattice degeneration, and no known clinical significance to the association of the two conditions.

X. Pathogenesis

The pathogenesis of lattice degeneration is still not well understood. Although various hypotheses have been advanced, none has yet achieved the status of general consensus. Newer methods of investigation have given added information as to the nature of the lesion — namely, fluorescein angiography, trypsin digestion, and electron microscopy. The hereditary basis of the disease was deduced by Vogt²²² because of the frequent

bilateral symmetry of the lesions. However, the mechanism by which this influence is mediated has been a subject of varied points of view, most prominent among which are that it is a developmental, a degenerative (abiotrophic), or an ischemic process. Specific proposed concepts of pathogenesis are described below.

A. CYSTOID DEGENERATION OF THE RETINA

The earliest well formulated view of pathogenesis was that of Vogt,²²⁰⁻²²² who believed that the peripheral cystoid "edema" of Blessig²² and Iwanoff¹⁴ was responsible. This view has already been discussed in this review (Section IB).

B. CHOROIDOPATHY

Michaelson^{149,150} has postulated a series of pathological events, beginning with a pigmented choroidopathy which leads to a local retinal phlebosclerosis and finally to the typical clinical appearance of the lattice lesion. He theorizes that this occurs by localized loss of nourishment from the choriocapillaris to the outer portion of the retina as the initial abnormality. This view suggests, therefore, that ischemia of the outer layers of the retina accounts for the later pathologic changes. Contrary to this view, it has been observed^{134,164,166} that the choroid is often not involved in lattice lesions. Also, other histologic studies^{60,61,205} have indicated that the earliest and most severe changes occur at the level of the inner retinal layers. Daicker⁶¹ therefore believes that the choroidal changes that are sometimes seen are secondary.

C. LANGE'S FOLD

The peripheral retinal fold of Lange,¹²⁹ originally described by Lange in 1893, has been proposed²⁰² as a possible site from which the lattice lesion originates. However, various authors^{61,139,159,228} have pointed out that this finding is probably a post-mortem histologic artefact. Kalina's definitive study¹¹⁸ found the fold in nearly all of 120 infant autopsy eyes, but in none of 185 living infant eyes, even though most eyes in both groups were premature. He came to the conclusion that such folds do not exist during life.

D. EMBRYOLOGICAL VASCULAR ANASTOMOSES

Pau^{160,162,164,165} hypothesized that the

characteristic vitreoretinal adhesions of lattice lesions are the result of rests of embryologic vascular anastomoses between vitreous and retinal vessels. Gärtner⁹⁰ agrees with this hypothesis and believes that the type of lattice lesion he reported (ora-parallel bands) is related to certain embryologically determined structures of the retinal surface, the "separation zones of the folded membrane of Pau in the posterior limiting membrane of the vitreous." Heinen¹⁰⁵ feels, however, that the origin of these "folded membranes" from original vitreous vascular rests remains hypothetical, and that they are not a convincing explanation for these adhesions.

E. VITREOUS TRACTION

The theory that lattice degeneration is primarily a vitreous disease, the retinal lesion being the result of localized vitreoretinal traction, was mentioned by Tolentino et al.²¹³ Presumably traction is exerted at paravascular vitreoretinal attachments, causing sclerosis of the retinal vessels. These authors feel this concept may be supported by 1) the localized involvement of the retina, 2) the early involvement of the inner retinal layer and late involvement of the outer layer, including the choroid, and 3) the presence of localized vitreous body changes which are associated with traction.

F. RETINAL ISCHEMIA

Heinen¹⁰⁵ held the view that lattice degeneration was caused by perisclerosis of small vessels. On the basis of fluorescein angiographic findings, several authors^{7,179,181} also favor the view that the primary etiological factor in lattice degeneration is a disturbance of the retinal circulation. Straatsma et al.²⁰⁵ utilizing additional data from trypsin digestion and electron microscopic studies, also postulate a primary vascular etiology. They view the process as beginning with initial vascular structural abnormalities which lead to vascular insufficiency, then to a secondary retinal ischemia which affects the inner retinal layers first, and finally results in all the typical histopathology which is characteristic of the disease.

Several authors, however, believe that the theory of retinal ischemia does not correctly explain the etiology of lattice degeneration. Daicker⁶¹ states that a vascular origin can be excluded because of the independence of the course of the blood vessels, and that the visi-

ble vascular changes are secondary. Wessing²²⁵ believes that the vascular changes observed with fluorescein angiography probably represent a repair mechanism in a degenerative process with a very protracted course. Tolentino et al²¹² also presented angiographic data that cast doubt on the vascular hypothesis. They reported that cases with early or mild retinal changes did not reveal remarkable findings. They also found that branches of arterioles supplying the unaffected retina around the lesion showed normal filling of the eye, indicating a pathological process that involved only a segment of these vessels. It is also the opinion of this reviewer that the typical discrete configuration of lattice lesions, surrounded as they are by apparently normal retinal tissue and almost always lying in an orientation concentric with the ora serrata, is not satisfactorily explained by the vascular theory, and that the vascular abnormalities which have been described must be secondary to some preceding pathological process.

G. INTERNAL LIMITING LAMINA (INTERNAL LIMITING MEMBRANE) ABNORMALITY

Ricci¹⁷³ proposed that lattice degeneration may be related to an anomaly of development, in the form of an aplasia or an absence of the internal limiting membrane. Daicker⁶¹ also hypothesized that it may be due to a local disturbance in the maturation of the retina, especially the inner parts, which could then lead to a progressive secondary degeneration of that zone and possibly also of the overlying vitreous.

In an interesting and significant study, Streeten and Bert²⁰⁶ examined lattice lesions by electron microscopy and also by trypsin digestion, using a modification of the Kuwabara-Cogan method in which there was no prior washing or removal of any vitreous or internal limiting membrane. They found that there was no surface membrane over any lesion after digestion, and this was confirmed by electron microscopy. They state that the sharpness of the edges with upward tear-like corners suggested mechanical factors in this loss of basement membrane rather than gradual erosion. Straatsma et al²⁰⁵ also reported that electron microscopy revealed thinning and intermittent absence of the inner limiting lamina in the center of lattice lesions.

In my opinion, the concept of a localized defect in the internal limiting membrane as the initial structural abnormality in lattice degeneration best explains the known facts regarding the histologic and clinical features and the progression of lattice lesions. If this concept is correct, it points to the fibers of Müller's cells as the locus of the defect in this disease. According to Mann,¹⁴⁰ the internal limiting membrane is formed embryologically by the union of adjacent footplates which represent expansions of protoplasmic processes (fibers) of Müller's cells; this process is already discernible by the 12 mm (5 week) stage of embryologic development. Whether this pathologic process is developmental (e.g. a localized aplasia) or degenerative (abiotrophic) in nature can not be known with certainty.

XI. Prognosis

The clinical significance of lattice degeneration resides solely in its potential to bring about retinal detachment in some patients. This can occur (1) by means of a tractional tear adjacent to the lattice lesion, or (2) by means of an atrophic retinal hole within a lesion. Although both complications are statistically rare considering the high prevalence of lattice degeneration in the population, retinal detachment more frequently results from a tractional tear than from an atrophic hole. Risks from these two types of retinal break will be discussed separately.

The percentage of patients in retinal detachment populations who also have lattice degeneration have been reported variously as 20%,¹⁴⁹ 30%,^{35,53,72} 31%,²⁰² and 31.8%.¹⁵⁴ Graether⁹⁸ found that 30% of 100 consecutive retinal detachment patients under age 50 also showed "equatorial degeneration, with or without lattice" (i.e., white lines). In a combined group of patients with either retinal detachment or retinal tears without detachment, Meyer-Schwickerath¹⁴⁶ found "equatorial degeneration" in 65% of the affected eyes. Morse and Scheie¹⁵⁴ found that among 129 phakic retinal detachment cases, 48 (37%) had lattice, while among 94 aphakic retinal detachments only 23 (24.5%) had lattice lesions. Hyams et al¹¹³ studied 103 myopic aphakic eyes and stated that the prevalence of lattice and snail-track degeneration was similar to the prevalence of these lesions in myopic phakic eyes, which they had

studied previously. Detachments caused by lattice degeneration with round holes have been reported to be 2.8% by Tillery and Lucier²¹⁰ and 13.9% by Morse and Sheie,¹⁵⁴ leaving those caused by lattice with tractional tears or mixed breaks in the range of 16% to 27% of all primary detachments. However, among the large population of patients who have lattice degeneration, the risk of developing a detached retina has been estimated to be in the range of 0.3% to 0.5%³⁵ based on the data of Böhringer²³ and Okun.¹⁵⁶ Hyams et al¹¹¹ followed 278 eyes which had either lattice (with white lines) or snail-track degeneration for periods ranging from one to six years and four of these (1.4%) developed retinal detachment.

A. TRACTIONAL RETINAL TEARS

Tractional tears originate at the ends or along the posterior margins of lattice lesions as a result of posterior vitreous detachment, as illustrated by Tasman.²⁰⁷ They occur suddenly and are often, but not always, associated with symptoms. The size may vary considerably from small to very large. This propensity to form tears has led many ophthalmologists to refer to lattice lesions as "weak areas" of the retina. However, this terminology is mistaken, for as Pau^{164,166} quite correctly points out, because of the glial proliferation that is one of their typical components, lattice lesions have considerable strength and are more resistant to tearing forces than is the surrounding retina. The tear occurs not because the retina is weak, but because as the posterior vitreous detaches, there is a sudden concentration of tractional forces exerted on the vitreoretinal adhesion of the lattice lesion, causing a tear to occur in the normal retina just posterior to the lesion. It can easily be confirmed both clinically and histologically that virtually never does the tear rupture the island of the lattice lesion proper.

The potential of a lattice lesion for producing a tractional tear at the time of posterior vitreous detachment depends on its precise location with relation to the vitreous base, i.e., whether the lesion is extrabasal, juxtabasal, or intrabasal as classified by Foos.⁸⁰ Flap tears occur at the posterior border of the vitreous base because of traction exerted by the detaching posterior vitreous on posteriorly directed irregularities in the

posterior border of the vitreous base. This has been well described by Foos^{79,80} and also discussed and shown schematically by Slezak.¹⁹⁶ The natural corollary of this is that lattice lesions that are situated within the vitreous base (i.e., intrabasal) are protected from the risk of developing a tractional tear. This does not imply that in the clinical examination of an eye the posterior border of the vitreous base can be clearly identified, or that it can be accurately determined whether a particular lattice lesion is situated in an intrabasal, juxtabasal, or extrabasal location. The posterior border of the vitreous base can, however, be accurately identified under certain circumstances, for instance, when the downward gravitation of blood behind a detached posterior vitreous demarcates this border. It can also be identified when juxtabasal retinal tears have led to a retinal detachment, and the detached posterior vitreous responsible for the tears has slightly elevated a narrow equatorial fold which is exactly in line with the flaps of the tears and the posterior border of the vitreous base. Similarly, the posterior border of the vitreous base may sometimes be demarcated by a white line in the presence of a posterior vitreous detachment, but in the absence of a retinal detachment. These phenomena have been discussed and illustrated by Dobbie and Phillips⁶⁷ and Hawkins.¹⁰⁴ They are also well shown in drawings of autopsy specimens by Okun,¹⁵⁷ in drawings of the living eye by Cockerham and Schepens⁵² and in the photographs of autopsy specimens by Boniuk and Butler,²⁸ Spencer et al,²⁰⁰ and Foos.⁷⁹

It is important to remember that in eyes with lattice degeneration, not all horseshoe tears occur at predictable sites, i.e. adjacent to lattice lesions. Dumas and Schepens⁷² studied 100 consecutive patients with symptomatic retinal breaks and recent retinal detachment, 30% of whom had lattice degeneration. Of the 40 horseshoe tears found in these 30 lattice eyes, 82.5% were adjacent to lesions of lattice. In the study by Davis et al of fellow eyes,⁶⁴ 15 eyes with lattice each developed a new retinal break. Of these 15 new breaks, only 10 (67%) were limited to sites of lattice lesions, while the remaining 5 (33%) occurred in previously normal appearing areas of the fundus. The author therefore surmised that in these five eyes prophylactic treatment probably could not have prevented

subsequent detachment because the normal-appearing areas would not have been treated. But in an autopsy series of 4812 eyes, 89 of which had tractional tears, Foos⁸⁰ found that, of those with flap tears, only 17% had lattice, and of the tears found in these lattice-eyes only 20% were actually adjacent to lattice lesions. In a recent update of this same autopsy series (now numbering 6800 eyes), Foos⁸¹ found that of the 139 eyes with tractional tears, 18% also had lattice, and that only 28% of the tears in these lattice-eyes were located adjacent to lattice lesions.

Therefore, it becomes obvious that in eyes with lattice degeneration vitreoretinal traction tends to be a widespread phenomenon and the danger of tractional tears can not be thought of as being limited only to those areas of visible lesions, for the majority of such tears in lattice-eyes will arise in other areas removed from these lesions.

The frequency with which such tractional tears occur in relation to lattice lesions is apparently very low. They were found in only 1% of a clinical series of 289 eyes with lattice degeneration which were followed for 3-10 years.³⁵ A histologic survey of 125 eyes with lattice²⁰⁵ revealed an incidence of 2.4%.

What is the prognosis of such tears? Two good studies^{57,63} of symptomatic tractional tears in general have reported that 28% and 35%, respectively, progress to retinal detachment. In my longterm natural history study,³⁵ only three eyes developed tractional tears. None of these detached, but one (33%) might have if left untreated. Although not all flap tears produce symptoms when they occur, the above figures may be accepted as the most accurate data available to express the risk of retinal detachment from the tractional tears of lattice degeneration.

B. ATROPHIC RETINAL HOLES

Although these small holes are much more common than the tractional tears previously discussed, they lead to retinal detachment much less frequently. They tend to be tiny, appear usually near the ends of lattice lesions, and are statistically more common inferiorly. They characteristically occur early in life and without producing symptoms, because they are caused by a localized dissolution of tissue in the very thin base of the lesion and not by sudden traction of a detaching posterior vitreous.

Even though they rarely progress to a

clinical retinal detachment, most of the holes very soon after their appearance collect a tiny amount of subretinal fluid from the overlying liquified vitreous which elevates a circular cuff of retina around them.³⁵ There is a real, though weak, bond between the sensory retina and the pigment epithelium which coincides with the border of the lattice lesion, and this bond is usually sufficient to limit the area of detachment which results from these small holes to the exact boundaries of the lattice lesion. Occasionally, however, this subretinal fluid may extend a fraction of 1 DD beyond the edge of the lesion where it generally develops a pigmented demarcation line and remains stationary. In some cases, the fluid may extend farther than one DD and fall within the definition of a subclinical detachment, as given by Davis.⁶³ Even in this latter circumstance, which was seen in only 1.5% of cases of lattice followed over a period of years,³⁵ this small area of detachment has a strong tendency to remain stationary and nonprogressive. The most likely explanation for this is that the source of the fluid is the overlying pocket of liquified vitreous, and that this pocket is not in direct communication with the main body of liquified vitreous in the eye. However, when such a communication does occur, it becomes possible for a progressive clinical retinal detachment to result.

Eisner⁷⁴ performed slitlamp examination on unfixed autopsy eyes with lattice degeneration, and found large fissures in the condensed vitreous covering which typically lines the pockets of liquified vitreous over lattice lesions. However, because clinical retinal detachments caused in this way are infrequent, Eisner concluded that even this free communication is usually not sufficient in itself to bring about a detachment.

Although none of the 137 such holes found in my longterm clinical study³⁵ led to clinical retinal detachment, it is well-known that they may occasionally do so. In a large survey of primary retinal detachments, Tillery and Lucier²¹⁰ found that 2.8% were caused by the round holes of lattice degeneration. In the smaller series of Morse and Sheie,¹⁵⁴ 13.9% of the primary detachments were caused by these round holes.

Tillery and Lucier²¹⁰ also provided a good description of the typical features of this type of detachment. Half the patients were under age 30, more than 75% had myopia exceed-

ing -3.00 diopters, inferior detachments were most common (often with evidence of slow progression), and prognosis for successful surgical repair was excellent.

Of particular interest is the young age at which this type of detachment tends to occur. Whereas in the detachment population as a whole, Schepens and Marden¹⁸⁹ showed that more than 85% occurred after age 40, Tillery and Lucier found not only that 50% of detachments caused by round holes of lattice occurred before age 30, but also that the absolute number of patients in each decade above 30 was less than that in each of the two decades below 30. This compares interestingly with my finding³⁵ that 65% of patients who develop new retinal holes are under age 35. It is well-known that various factors which theoretically would tend to make detachment more likely, namely an increased number of retinal holes, increasing liquefaction of the vitreous, and a higher prevalence of posterior vitreous detachment, are all more common with advancing age. In spite of this, it is apparent that there is not only a relative, but also an actual, decrease in retinal detachments due to round holes of lattice with increasing age. We may therefore conclude that a patient who has lattice with round holes has a lesion which actually becomes less and less dangerous as he grows older! Conceivably, this might be due to a gradual increase in the strength of the bond between sensory retina and pigment epithelium at the borders of the lattice lesion that is brought about by the progressive secondary histologic changes which affect this junction. Even though this bond is admittedly weak, it may be strong enough to resist the ingress of fluid vitreous into the subretinal space.

Whatever the cause may be, it is an indisputable clinical fact that subretinal fluid entering the subretinal space through a atrophic retinal hole almost always remains confined to the area of the lattice lesion or extends no more than a minute distance beyond it. This is one of the prominent features of the clinical behavior of lattice lesions.

Foos⁸² has reported that the round holes of lattice degeneration comprise 75% of all atrophic (nontractional) holes found in 5600 autopsy eyes, and concluded that they are an uncommon cause of retinal detachment. In Davis' long-term study⁶³ of retinal breaks, 22 eyes had lattice and also round holes, and two (9%) of these progressed to detachment. It is

not stated whether these were clinical or sub-clinical, but 80% of this group were "fellow eyes" of patients with detachment of the retina, and this category may possibly have a somewhat altered prognosis.

The view is widespread among ophthalmologists that lattice lesions with holes represent a substantially increased risk of retinal detachment compared to lattice lesions without such holes. It is imperative in our thinking about the prognosis of lattice degeneration in general and of lattice lesions with holes in particular that we be circumspect in our interpretation of the available data.

We may assume a 30% prevalence rate for lattice degeneration among primary retinal detachment patients. Based on Tillery and Lucier's²¹⁰ study, 9.3% of this lattice-detachment group

($\frac{.028}{.30}$) had lattice with holes only.

Combining this with Morse and Sheie's higher figure of 43.7%,¹⁵⁴ we would arrive at an average of 26.5% for that portion of the group of lattice-detachment patients who had lattice with holes only. However, since statistically only about 0.3% of patients with lattice degeneration can be expected to have an associated retinal detachment,³⁵ the portion of lattice patients who would be likely to have a retinal detachment because of lesions with atrophic holes can be computed to be .08% (.265 \times .003), or one in 1250 lattice patients. However, since only 29.2 of lattice patients actually have lesions with holes, this risk is spread over only this portion, and = .274% ($\frac{100}{29.2} \times .08$), or one in 365 patients who have lattice lesions with holes.

Although the reports of Morse and Sheie¹⁵⁴ and Tillery and Lucier²¹⁰ rightly remind us that lattice lesions with round holes can lead to retinal detachment and that they comprise a real, though small, portion of the total retinal detachment population, we must avoid hastening to the conclusion that the prognosis of lattice lesions with holes is therefore unfavorable or that these lesions are dangerous. This is an entirely different question and to answer it we must look elsewhere, simply comparing the prevalence of lattice lesions with holes to the expected risk of retinal detachment in these eyes, as has just been done in the preceding computation. It is simply not generally realized how very com-

mon lattice lesions with holes are in the general population. It is therefore disturbing to read the warning of the danger of these lesions given by Morse and Sheie¹⁵⁴ who, it appears, have not taken this high prevalence into account.

C. FELLOW EYES

Among fellow eyes of patients whose first eyes had suffered retinal detachment, Meyer-Schwickerath¹⁴⁶ found that 35% had equatorial degeneration. Davis et al⁶⁴ reported that only 9.2% of their series of 680 fellow eyes showed lattice degeneration. This disparity is probably explained by differences in the diagnostic criteria of the authors.

In general, fellow eyes of patients whose first eyes have had primary retinal detachment have an overall risk of about 10% of suffering the same fate, thus giving rise to the category of bilateral detachments. If the vulnerable eyes could be identified prior to that event, then a reasonable basis for prophylactic treatment could be established. Thus it is important to attempt to ascertain to what degree lattice degeneration participates in the risk of fellow-eye detachments. There is not much information available on this question, but the following reports are pertinent, even though the methods and approaches used were varied.

Studying the natural history of retinal breaks in a group of which 80% were fellow eyes, Davis⁶³ observed 22 eyes with lattice lesions with associated holes, and found that 2 (9%) of them detached. This corresponds to the estimated risk of fellow eyes in general. In the most instructive study on this subject Davis et al⁶⁴ retrospectively surveyed 680 untreated fellow eyes and found that 10 of 63 (16%) with lattice degeneration developed retinal detachment. Of this group, 9 of 38 (24%) with "typical" lattice (i.e., with white lines) detached and only 1 of 25 (4%) with "atypical" lattice (i.e., without white lines) detached.

In a report more difficult to interpret because the authors use a different definition of lattice degeneration, Merin et al¹⁴³ observed 719 untreated fellow eyes, 44.5% of which had either lattice-like, snail-track, or pigmentary degenerative changes. Of these, 67 (9.3%) developed retinal detachment.

Everett⁷⁶ studied 200 retinal detachment patients, 65% of whom were first-eye detachments and 35% of whom were fellow-eye detachments. Of the first-eye group, 8.5%

had lattice, and of the fellow-eye group, 24.3% had lattice.

Smolin¹⁹⁷ studied 951 consecutive patients with retinal detachment. Of 846 unilateral cases, 9.3% had lattice lesions. Of 105 bilateral cases, lattice was found in 24.7%, but it was not stated whether lattice lesions were present in the fellow eyes.

Kojima¹²⁶ compared the fellow eyes of retinal detachment patients with fellow eyes of a control group who had equatorial degeneration but no detachment in the primary eye. His data are very difficult to interpret because of his classification of equatorial degeneration. He states that the order of incidence of degeneration is the same in both groups.

XII. Management

The existence of lattice degeneration as such does not interfere with visual function. If, however, it leads to retinal detachment this must be treated surgically utilizing currently acceptable procedures.

A. HISTORY AND BASIS OF PROPHYLACTIC TREATMENT

Ever since it became established that a retinal break is an essential stage in the development of a retinal detachment, the concept of prophylactic treatment has been very appealing to ophthalmologists. It was logical to believe that a retinal break or a retinal lesion thought capable of producing a retinal break should be surrounded by a surgically created chorioretinal scar so that the onset of a retinal detachment could be prevented. The enthusiasm that has been engendered by these concepts may be judged by the literature which has become so voluminous that it can scarcely be completely reviewed, and I do not claim that the more than 90 publications on this subject which I am including in this review cover all the reports which have been published. While not making reference to each of these contributions individually, I will attempt to glean from them important emphases and observations and to discern significant trends that have occurred in our thinking on this subject during the past 20 years. Relevant reports not cited specifically in this section are listed here.

2, 10, 16, 21, 26, 28, 30, 32, 38, 45, 47, 49, 51, 55, 57, 65, 68, 70, 72, 75, 76, 99, 102, 105, 106, 108, 110, 120, 123, 127, 136, 137, 141, 143, 145, 148, 151, 152, 154, 155, 164, 169, 170, 174, 193, 198, 199, 202, 205, 208, 213, 214, 216, 227, 230, 233

In discussions of prophylactic treatment there is usually an important overlapping between the categories of retinal breaks and lattice (equatorial) degeneration, which may or may not be associated with retinal breaks. Some authors do not clearly differentiate between these two groups in reporting their data, but in most of the papers the category of lattice degeneration represents the largest single group of patients treated prophylactically.

Prophylactic treatment was at first recommended purely on theoretical grounds because no detailed knowledge of the natural history of retinal breaks or other retinal lesions existed, and there had been no documentation of possible risks of treatment. Experience soon began to accumulate as physicians followed individual cases in which either no retinal detachment occurred, or, conversely, in which it did occur, sometimes soon after treatment and apparently as the result of new retinal breaks not present before treatment. These early clinical impressions tended either to encourage or to restrain the enthusiasm of retinal surgeons in recommending such treatment.

In 1932, the use of electrodiathermy was separately reported by Larsson, Weve and Safar, and for the next two decades this method with its various modifications was the preferred mode of prophylactic treatment. The general attitude toward prophylaxis during this period has been described by ten-Doesschate⁶⁸ as "reserved." In 1956, Meyer-Schwickerath introduced the use of Xenon photocoagulation and, in general, this was quickly and enthusiastically received as being an improvement over diathermy for prophylactic purposes. Heinzen¹⁰⁵ stated that photocoagulation "revolutionized the indications" for prophylactic treatment. In the *Symposium on Preventive Treatment of Idiopathic and Secondary Retinal Detachment of the International Ophthalmological Congress* in 1958, a wide range of opinions was expressed.^{9,18,19,58,59,69,85,135,144,168,185,191,226} These varied from the view of Meyer-Schwickerath¹⁴⁴ that lattice (equatorial) degeneration was a particularly urgent indication for prophylaxis to that of Schepens¹⁸⁵ who stated that in the present state of knowledge, operation on fundus changes without retinal breaks was definitely unjustified, and that so-called prophylactic surgery gave a very doubtful protection against retinal detachment.

While the new modalities of cryotherapy and argon laser have more recently been introduced into this field, considerable diversity in opinions regarding prophylactic treatment has continued to exist. Lincoff¹³² pointed out in 1961 that decisions in regard to prophylaxis were based on clinical impression because the vulnerable lesions could not be identified, and Malbran¹³⁸ in 1966 correctly observed that the arguments for prophylactic treatment were largely speculative. This diversity was again clearly apparent in the Houston Conference in 1965, entitled *New and Controversial Aspects of Retinal Detachment*,^{42,56,158,187,188,192,201} and has continued to be seen in many subsequent publications. It is understandable that in the absence of reliable data on the natural history of retinal lesions, the indications for prophylactic treatment must necessarily be to a large extent arbitrary. But it must also be expected of us as responsible ophthalmologists to exercise a large measure of discreet restraint in recommending treatment until controlled clinical studies can provide a valid scientific basis for more carefully defining acceptable indications.

While it may not be possible in an absolute sense to establish rigid criteria,²⁰³ it cannot be denied that the only alternative to arbitrary dicta is the collection of statistical data by observing pure sub-groups of patients with unmolested retinal lesions over a period of years. It is not possible to reconstruct the natural history or calculate the risk of any type of retinal lesion by analyzing a population of retinal detachment patients as suggested by Morse,¹⁵³ because this provides no information on the size of the population pool from which the lesion originated. Natural history studies are slow and painstaking projects, but a few have been reported in very recent years.^{35,64} These studies have provided certain very relevant data that bear directly on the question of indications for treatment of lattice degeneration.

B. COMPLICATIONS OF PROPHYLACTIC TREATMENT

It is undoubtedly true that it will never be possible to prevent all detachments of the retina, and it is also true that no method of prophylaxis has yet been introduced that is free of complications. This is largely explained by the fact that the most dangerous factor within the eye (i.e., vitreoretinal traction) against which prophylactic measures are

directed, tends itself to be exacerbated to some degree by all methods of prophylaxis. Following the example of Meyer-Schwickerath,¹⁴⁶ it has become customary for many writers, especially in Europe, to attempt to differentiate between those retinal detachments that occur "because of" prophylactic treatment from those that occur "in spite of" it. While it may in some cases seem possible to make this differentiation, I tend to agree with tenDoesschate⁶⁸ who said that an answer to this question always contains much speculation. There are statistical grounds for concluding that in some cases the very event we are trying to avoid (retinal detachment) is specifically brought on by the "preventive" treatment itself. This is not meant to depreciate the tremendous contribution that photocoagulation, and the more recent modalities of cryotherapy and argon laser, have made in the field of prophylactic treatment in carefully selected cases.

I will attempt to avoid the whole controversy regarding "because of" and "in spite of" categories by simply including them all under the title of sequelae of prophylactic treatment. The conclusions of 32 reports on this subject are tabulated in Table 2. The data from these reports are quite diverse and many of the writers have not stated the numbers of eyes treated for various indications, nor the exact groups in which later sequelae arose. All the reports included cases of lattice degeneration among the indications for treatment, and in most of them this was the largest single category. As is readily apparent, all modalities carry a significant risk of complications that are important in regard to visual function. The most important of these are retinal detachment, new retinal breaks and maculopathy.

1. Diathermy

In summarizing those cases in Table 2 treated with diathermy for various indications, the risk of retinal detachment is calculated to be 6.4%. Colyear,⁵⁴ in comparing two groups of his own cases, found the risk of later detachment to be 7.5% with diathermy and 4.4% with photocoagulation.

2. Photocoagulation (Xenon)

Meyer-Schwickerath¹⁴⁸ has summarized his large amount of data on patients treated with photocoagulation and concluded that the risk of later retinal detachment (combining

his two categories) was 5% and that of maculopathy was 1%. Okun and Cibis¹⁵⁸ treated 65 eyes with lattice degeneration and found that 6% later developed detachment. Boniuk et al³⁰ presented well-analyzed data on 101 eyes with lattice degeneration treated only with photocoagulation and found later retinal detachment in 5.9% and maculopathy in 3%.

3. Cryotherapy

In summarizing those cases in Table 2 treated with cryotherapy for various indications, the risk of retinal detachment is calculated to be 2.1%. Boniuk et al,³⁰ treating a pure group of 221 eyes with lattice degeneration found the risk of later retinal detachment to be 3.2% and of maculopathy to be 1.8%. Tasman and Jaegers²⁰⁸ treated a pure group of 222 eyes with lattice and found later detachment in 3.6%.

C. INDICATIONS FOR PROPHYLACTIC TREATMENT

1. Lattice Without Retinal Breaks

Prophylactic treatment of lattice lesions should never be given in cases in which 1) the fellow eye has not had a retinal detachment, 2) there is not a strong family history of retinal detachment, and 3) the eye with lattice lesions does not have symptomatic retinal breaks and is not highly myopic, aphakic, or soon to become aphakic.

This criterion should not be altered because of the extensiveness, location, or appearance of the lattice lesions nor by any other clinical impression or theoretical argument. Some reports, in stressing the serious nature of lattice degeneration in general, have not made this distinction and have either stated or implied that any and all lattice lesions are eligible for treatment. However, it has been shown^{32,35} based on the prevalence rate of retinal detachment as calculated by Böhringer²³ and Okun¹⁵⁶ as compared to the prevalence of lattice degeneration (even including lesions with round holes), that the expected risk of detachment would be 0.3%.^{32,35} When this risk has been studied by a different method, by actual natural history studies over a long period of time,³⁵ the danger has been found to be 0.5%, almost exactly agreeing with the earlier prediction. This means that only one out of 200-300 patients with such lattice lesions would develop retinal detachment.

TABLE 2
Sequelae of Prophylactic Treatment

Author	Year	Eyes	# with Degeneration	# Mixed	% Retinal Detachment	% New Breaks	% Maculopathy	Dia-thermy	Photo-coag.	Cryo-therapy	Laser
Meyer-Schwickerath	1960	465		465	1.7				All		
Meyer-Schwickerath	1959	490		490	2.8				All		
Colyear	1965	200		?	7.5	8.5		All			
Straatsma, et al	1965	107		107	1.8			3	93		
ten Doesschate	1965	51		51	13.9				All		
Harms, et al	1966	207		207	6.7		.48	178	26		
Böke	1966	184	140		3.8	.5	.54		All		
Chudzinski	1966	180		180	4.4		2.7		All		
Söllner	1966	377		377	4.0	.5	1.4		All		
Guillaumat & Krebs	1966	88	34		10.0			17	70		
Linnen	1966	325	183		1.8				All		
Topalis	1966	91	37		4.4				All		
Dufour & Thiiges	1966	60		60	8.3			+	+		
Mortimer	1966	200		200	1.0		1.0		All		
Colyear	1968	230	230		4.4	7.4	.43		All		
Okun & Cibis	1968	65	65		6.0	4.5			All		
Abraham & Shea	1968	475		475	.4		0.0				All
Witmer	1971	140	140		5.7			25	74	10	
Meyer-Schwickerath	1971	?			5.0		1.0		All		
Böke & Voigt	1971	53	53		1.9		0.0		All		
Kreissig & Sbaiti	1971	116	32		0.0						All
Merin, et al	1971	247	mostly		5.0				?		
Boniuk, et al	1972	367	367		4.1	5.4	2.2		101	221	
Tasman & Jaegers	1972	232	232		3.9				10	222	
Robertson & Norton	1973	301		301	6.0	8.3	1.7		183	110	
Ramsay & Eifrig	1973	62	31		5.0					62	
Chignell & Shilling	1973	231	112		5.2		0.8		62	129	
Fisni	1973	176	33		0.0	0.0	0.0	48		128	
Morse & Sheie	1974	231	95		0.0	0.0	0.0			All	
Kanski & Daniel	1975	701	298		4.7	8.0	.57		520	90	
Zweng & Little	1977	123		123	0.7		0.7				All
Delaney & Oates	1978	135		135	7.0				+	+	

2. Lattice With Round Atrophic Holes

Many writers have listed lattice lesions with holes among the specific indications for prophylactic treatment.^{2,21,42,72,142,153,154,158,208,231,233} Although a few authors favor observation of such lesions without treatment,^{32,63,174,187} there seems to be a widespread feeling that lattice lesions with holes represent a greater risk than do lesions without holes. However, this clinical impression is not substantiated by statistics, which suggest that only about one out of 365 patients with such holes later has detachment from this cause (see previous section, XI B).

In my series³⁵ of 50 patients whose non-fellow eyes had 96 atrophic holes in lattice lesions followed from three to ten years, none led to a clinical detachment. Although in Davis⁶³ series of 22 such eyes (most of which were fellow eyes), 9% became detached, he compares his data to that of the treated series of Okun and Cibis¹⁵⁸ and concludes that the prophylactic treatment provided only an insignificant improvement in outcome. He

further stated that prophylactic treatment of eyes with asymptomatic breaks without detachment must be highly effective and attended by virtually no complications to prove superior to a policy of periodic observation.

Okun and Cibis¹⁵⁸ treated a pure group of 65 eyes with lattice with holes, and 6% later detached. Tasman and Jaegers²⁰⁸ treated a pure group of 176 such eyes, 2.8% of which later detached. For these reasons I do not believe that the presence of holes in lattice lesions constitutes a sufficient reason for treatment. Such patients should merely be informed of possible retinal symptoms and asked to return for re-examination in one year.

3. Lattice with Tractional Tears

Tractional tears occurring adjacent to lattice lesions may be symptomatic or asymptomatic and probably have as serious a risk of detachment as such tears in general. For symptomatic tears this risk is from 28%⁵⁷ to

35%,⁶³ and for this reason such tears undoubtedly represent the best of all indications for prophylactic retinal surgery. Davis⁶³ found that asymptomatic horseshoe tears without detachment in phakic eyes had a 10% risk of leading to retinal detachment. In my series³⁶ of 26 asymptomatic flap tears in non-fellow eyes followed from three to nine years, no instance of detachment occurred.

It should also be borne in mind that horseshoe tears associated with lattice may carry a higher risk of the post-treatment complication of retinal detachment than other horseshoe tears. In a study of 219 eyes with horseshoe tears which underwent prophylactic treatment, Robertson and Norton¹⁷⁴ observed lattice degeneration in only 8.7%. However, among 17 of these treated eyes which later progressed to retinal detachment, six (35%) also had lattice degeneration, and in each of these the original tears were symptomatic.

4. Lattice in Fellow Eyes

The practice of treating the fellow eyes of patients in whom the first eye has suffered a retinal detachment originated as the result of three clinical observations: 1) retinal detachments are frequently bilateral; 2) the fellow eye often shows the presence of lesions thought capable of causing retinal breaks or detachment; and 3) lesions can be surrounded by surgically produced chorioretinal adhesions.

The rationale for treatment has been based on several assumptions regarding the following observations: a) the incidence of bilaterality of retinal detachment is in the range of 20% to 30%; b) the visible lesions in the fellow eye represent the sites from which retinal detachment will arise; and c) the prophylactic treatment of these lesions will significantly reduce the incidence of retinal detachment in the fellow eye and, therefore, the bilateral occurrence of detachment. I shall now attempt to evaluate these assumptions.

a. *Bilaterality of retinal detachment* is reported to vary from 9% to 34%,¹⁸⁹ figures that are obtained by simply counting the number of bilateral cases in a given retina clinic population.

As Schepens and Marden¹⁸⁹ have noted, bilateral cases tend to be seen more often in specialized retina clinics. This view is further supported by the report of Törnquist,²¹⁵ who found that among patients from Gothenburg

where there was only one eye clinic, the bilaterality was 11.2%, whereas among patients referred from other places and who often had severe and previously treated detachments, the rate was 18.4%. We may probably assume therefore that the higher reported figures are the least accurate for the true bilaterality of retinal detachment.

The best way to learn the true bilaterality is to follow for a long period of time a group of patients who have had detachments. This has been done in the classic, though retrospective, study by Davis et al⁶⁴ who followed 680 such patients for 6 months to 16 years and found that 7.9% later detached in the fellow eye. Longer follow-up may increase this figure somewhat. On the other hand, the true figure may actually be lower, because these patients were all referred to a retinal center and some of them may have been referred because they were thought to be more difficult cases.

In a quite different type of study, the National Cooperative Study in Israel^{151,152} has tabulated all detachments occurring in a large closed group of patients in a population reported racially to have a higher than average incidence of retinal detachment.¹⁸⁹ At the beginning of their study, they found the bilaterality rate to be 10.9%. It is probable that the true bilaterality rate of idiopathic, rhegmatogenous retinal detachment is in the range of 9% to 10%.

b. *Degenerative changes of the lattice or "equatorial" type* have been reported in fellow eyes with prevalence rates of 9%,⁶⁴ 24%,^{75,76,143} and 35%.¹⁴⁶ In the series of Davis et al,⁶⁴ there were 38 eyes with "typical" lattice (with white lines) of which nine (24%) detached. Of the 25 eyes with "atypical" lattice (without white lines), only one (4%) detached. Therefore, of 63 fellow eyes with lattice degeneration 10 (16%) eventually had a retinal detachment. There were 15 fellow eyes with lattice lesions that developed new retinal breaks, but in 1/3 of these the breaks occurred in normal appearing areas away from the lattice lesions. The authors state that prophylactic treatment probably could not have prevented retinal detachment in these eyes since treatment would not have been applied to the normal appearing areas.

In Foos' autopsy study,⁸⁰ 15 eyes with lattice lesions had 29 tears, but only 6 (20.7%) of these were adjacent to a lattice lesion. In his later update of this material,⁸¹ 24 eyes had lat-

tice with tears, but of 42 tears only 12 (28%) were directly related to lattice lesions.

Schepens¹⁸⁵ reported that in 55% of eyes with subclinical retinal detachment, some of the breaks occur in unpredictable sites. Other authors^{71,72,188,201} have emphasized this same point as an important reason for conservatism in recommending prophylactic treatment.

In a recent study of second eye detachments, Delaney and Oates⁶⁵ found that in 43% of the cases the causative breaks were associated with previously observed degenerative areas, but that in 57% of the cases the causative breaks occurred in unsuspected areas of normal appearing retina.

c. The proposition that the systematic prophylactic treatment of degenerative lesions in fellow eyes can statistically reduce the incidence of bilateral retinal detachment has been tested by two studies.

On the basis of the prior bilaterality rate in the Bonn Clinic, Söllner,¹⁹⁸ assumed the expected bilaterality rate to be 20%. He treated a series of 307 fellow eyes and during a follow-up period of five years observed that 2% of these patients developed a second retinal detachment. He, therefore, concluded that the treatment had been effective. However, as shown above, if his finding is compared to the more accurate expected bilaterality rate of around 9%–10%, the effectiveness of the treatment would appear more doubtful.

In 1969, Michaelson et al¹⁵¹ reported the results of the first seven years' experience of the National Cooperative Study in Israel, designed in part to prevent retinal detachment by the prophylactic treatment of suspicious lesions in fellow eyes. They concluded that their program of treatment had reduced fellow eye detachments in Israel from 10.88% to 4.2%, which they felt was probably a nearly irreducible minimum. However, in an updated report of this study in 1972,¹⁵² the bilaterality rate had again risen to 9.1%, despite continuation of the prophylactic program. The authors therefore concluded that there had been no notable drop in the incidence of retinal detachment despite these preventive measures. Boniuk et al³⁰ treated lattice lesions in 262 fellow eyes and observed subsequent retinal detachment in 12 (4.58%).

Summary. The foregoing data can be summarized by the following statements.

1) The incidence of bilateral (fellow eye)

retinal detachment is in the range of 9%–10%.

2) The prevalence of lattice degeneration among fellow eyes is around 24%.

3) The incidence of retinal detachment among fellow eyes with lattice is 16%, and these eyes therefore account for about 4% of fellow eye detachments in general ($.16 \times .24$).

4) The routine prophylactic treatment of lattice degeneration in fellow eyes might therefore, theoretically, be expected to reduce the incidence of fellow eye detachments from 9%–10% to 5%–6%, if we may assume that such prophylactic treatment were entirely without complication, and also entirely effective in preventing detachment.

5) The incidence of retinal detachment among fellow eyes treated prophylactically, whether from complication or failure of the treatment, is in the range of 4%–6% with Xenon photocoagulation, and 2%–3% with cryotherapy.

6) Among fellow eyes with lattice, new retinal tears may occur in 33% of eyes in "normal" appearing unsuspected retinal areas, and among eyes in general with lattice, as many as 72% of tractional tears may occur in such areas, unassociated with lattice lesions.

In conclusion, we may say that the accumulated evidence has not yet shown prophylactic treatment of lattice lesions in fellow eyes to be of more than negligible value in preventing retinal detachment. Prophylactic treatment is clearly indicated in symptomatic tractional tears associated with lattice, and may be justified in cases in which the first eye had retinal detachment surgery which failed. In this more serious situation, treatment of the fellow eye is probably justified to gain even a small therapeutic advantage, which statistically amounts to only a few percentage points.

New additional data on the subject of lattice degeneration in fellow eyes would be very beneficial, and should be in the form of detailed prospective clinical studies.

5. Lattice in Aphakia

Scheie et al¹⁸² found the prevalence of retinal detachment among aphakic patients 40 years of age or older to be 2.2%, a figure which agrees well with the literature that they reviewed. The data of Böhringer,²³ as analyzed by Okun,¹⁵⁶ showed the prevalence of retinal detachment to be .07% in the general population and .14% in those over 40 years of age. Thus, detachment in aphakic

patients is more common than among the general population by a factor of 31.4 to 1; among patients over 40 years of age, it is more common by a factor of 15.7 to 1.

Ashrafzadeh et al.¹³ found peripheral degeneration (including lattice degeneration and "retinal vascular degeneration") in 44.4% of phakic retinal detachments, but in only 34.2% of aphakic detachments. Likewise Morse and Scheie¹⁵⁴ found lattice degeneration in 37.2% of eyes with phakic detachment, but in only 24.5% of eyes with aphakic detachment.

Hawkins¹⁰⁴ compared two equal-sized groups of phakic and aphakic retinal detachment, and found 36 retinal breaks related to lattice in the phakic group, but only 20 such breaks in the aphakic group.

In the large series of eyes with lattice degeneration treated prophylactically by Boniuk, et al³⁰ 10 later underwent cataract extraction, and 2 (20%) of these subsequently detached.

Benson et al¹⁶ reported a series of patients who had aphakic retinal detachment in the primary eye and eventual aphakia in the second eye. Prophylactic treatment was carried out in 24 of the fellow eyes, and 2 (8%) of these detached. Of 100 fellow eyes which contained no suspicious lesions and therefore remained untreated, retinal detachment later appeared in 19 (19%), and in at least 16 (84%) of these the detachment arose from breaks which appeared in clinically normal areas. This strong tendency for retinal breaks in aphakic retinal detachments to occur in clinically normal areas had led to the recommendation for complete (360 degree) circumferential prophylactic treatment in such eyes.^{39,43} Benson et al¹⁶ feel, however, that until such treatment is proven to be more effective and safe, it is not necessary to recommend it for treating normal areas of the fundus. Unfortunately the above study did not include a control group in which the fate of lattice lesions in aphakic fellow eyes left untreated could be studied.

Although Davis⁶³ concluded from his data that asymptomatic breaks in aphakic eyes have a 50% risk of leading to detachment, we do not at this time have comparable natural history data regarding the risk of lattice lesions per se in aphakic eyes.

It seems evident that lattice degeneration does not play as important a role in the onset of aphakic detachment as in phakic detach-

ment. This is consistent with the conclusion of Ashrafzadeh et al¹³ that a loose chorioretinal adhesion is relatively more important than vitreous traction in causing retinal detachment in aphakic cases.

In summary, we may draw the following conclusions:

a) Retinal detachment is much more common in aphakic than in phakic eyes.

b) Breaks in clinically normal areas are more common in aphakic retinal detachment than in phakic detachment.

c) Lattice degeneration and retinal breaks associated with lattice lesions are both less common in aphakic retinal detachment than in phakic cases.

d) Reported failure rates of prophylactic treatment in aphakic eyes in which subsequent retinal detachment occurred are 20%³⁰ and 8%,¹⁶ which is somewhat higher than in phakic cases.

The role of prophylactic treatment of lattice lesions in association with aphakia has not yet been clearly established.

6. Lattice in Myopia

Although lattice degeneration has an increased prevalence among patients with either myopia or retinal detachment, and although retinal detachment is more common in patients with myopia (especially of higher degree), I know of no clinical reports purporting to show that myopic patients who also have lattice degeneration are more prone to retinal detachment than myopic patients who do not have lattice. Nevertheless, because of the indirect association various authors have stated that lattice degeneration in the presence of myopia, particularly of higher degree, deserves prophylactic treatment for that reason. While this may eventually be found to be true, at the present time the reasons for believing it are theoretical.

7. Lattice with Family History of Retinal Detachment

The etiologic role of lattice degeneration in cases of familial retinal detachment is often not easy to prove. Most of the published pedigrees of families in which both conditions appear show a relatively few cases with true lattice degeneration, or are quite small pedigrees. Some pedigrees show a strong relationship between the two conditions, such as those Cibis⁴⁹ illustrated in his Figures 120.

121, and 123. However, in Cibis' large pedigree (Figure 124), the hyaloideochorioretinopathy which he designated "pigmented lattice"^{48,49} and which was strongly associated with retinal detachment that was usually bilateral, may actually be a different disease entity (see Section II H, on post-equatorial, radial, hyaloideochorioretinopathy).

If there is a strong family history of retinal detachment with a fairly consistent association of lattice lesions with the causative retinal breaks, prophylactic treatment of such lesions found in relatives who have not yet had retinal detachment should be considered. However the mere finding of sporadic cases of retinal detachment in families who also exhibit lattice degeneration does not necessarily justify such treatment.

8. Extensiveness of Lattice Lesions

The degree of involvement of the retina with lattice degeneration may vary from a small solitary lesion to extensive areas covering almost the complete circumference of the peripheral retina. Diverse opinions are held with regard to how this variable degree of involvement affects the criteria for prophylactic treatment.

Dumas⁷¹ and Dumas and Schepens⁷² have noted that short islands of lattice were more frequently related to retinal tears than were long ones, and also that the tears around such small islands tended to be larger than tears associated with extensive lesions.

Tasman and Jaegers²⁰⁸ stated that the extent of involvement was seldom a major criterion in their series, but that in many instances they did tend to treat small isolated lesions more often than cases with nearly circumferential involvement. On the other hand, more extensive involvement is thought by some authors^{2,51,154,231,232} to signify a higher risk of retinal detachment, and they therefore advocate prophylactic treatment in such cases. Everett,⁷⁵ however, was of the opinion that even in cases of fellow eyes with extensive involvement of all quadrants, few surgeons would suggest photocoagulation covering 360 degrees in all such cases, and that some logical guide to selective treatment should be sought.

In addition to the opinion that extensive involvement with lattice is more dangerous, there is also the realization that retinal tears commonly occur in previously normal-

appearing areas of the retina, and this may seem to provide justification for circumferential treatment extending 360 degrees around the periphery. Following the introduction of Xenon photocoagulation by Meyer-Schwickerath, Lindner¹³⁵ stated that this new method could be used to prophylactically treat the entire retinal periphery at one time. Various other authors have either reported or recommended 360 degree circumferential treatment (usually however in a sequence of several separate treatments) using various modalities as follows: diathermy,³⁹ Xenon photocoagulation,^{138,198} cryotherapy,^{133,170} cryotherapy combined with encircling silicone band,¹¹⁰ and Argon laser photocoagulation.^{31,231-233}

However, enthusiasm for this form of treatment should probably be tempered by a strong impulse to therapeutic restraint in view of the very significant potential for complications.

Söllner¹⁹⁸ reported an increased rate of complications which was correlated with treatment of an increased number of quadrants. Whereas treatment of only one quadrant was attended by a complication rate of 4%, photocoagulation of all four quadrants led to complications in over 20% of eyes. For this reason he stated that circumferential treatment should be avoided if possible.

Spira²⁰¹ stated that photocoagulation should never be used if the degeneration extends around the entire periphery because of the danger of precipitating a retinal detachment.

McPherson¹⁴¹ pointed out that extensive treatment with cryotherapy was also dangerous, especially if the amount of coldness was excessive, and could lead to massive preretinal retraction. Freeman⁸⁷ reported a disastrous end result in the only eye of a 15-year-old boy who had been treated with circumferential photocoagulation and who developed a 360 degree retinal tear, with later complete retinal detachment, densely organized vitreous, and blindness.

In summary, the view that extensive involvement with lattice degeneration is more dangerous than solitary lesions has not been substantiated by any report of which I am aware, either in fellow eyes or non-fellow eyes. There is also no proven increased risk for eyes with parallel lattice lesions, which have been regarded as more serious in one study.²

XIII. Summary

Lattice degeneration is a common degenerative disease of the peripheral retina and vitreous which has a very early onset in life. It is characterized by very typical histologic features, but clinically it manifests itself in a myriad of polymorphous forms.

Although the vast majority of cases are non-progressive or very slowly change throughout life, a small number may lead to clinical retinal detachment. When this occurs, it usually does so by the sudden, usually symptomatic, development of a tractional tear, secondary to an acute posterior vitreous detachment. Less commonly, retinal detachment ensues as the result of the gradual asymptomatic appearance of an atrophic retinal hole within a lattice lesion. The pathogenesis and heredity of lattice degeneration are still unclear.

The role of prophylactic treatment of symptomatic tractional tears associated with lattice degeneration is undisputed and this is clearly the best of all indications in the field of prophylaxis of retinal diseases. The place of prophylactic treatment of lattice degeneration in various other circumstances remains controversial and in doubt, and is associated with a disturbing potential for significant complications — most notably the precipitation of retinal detachment and maculopathy. These hazards not infrequently render our prophylactic expectations self-defeating. The reason for this is simply that the real enemy lurking within the disease called lattice degeneration is vitreoretinal traction, and it occasionally happens that our carefully planned surgical attack, rather than achieving our objective of neutralizing this enemy, may instead transform it into a more hostile and destructive foe, by aggravating and accelerating the vitreoretinal tractional forces which are always present with this disease.

Lattice degeneration is the most important of all clinically distinct entities which affect the peripheral fundus and which are related to retinal detachment. An intimate knowledge of this fascinating and sometimes temperamental disease is essential for our wise counseling of the many patients who are afflicted with it.

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Outline

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XIII. Summary

The Myopias

BASIC SCIENCE AND CLINICAL MANAGEMENT

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Chapter 1

Significance and Perspectives

DEFINITION

Myopia is defined as that state of refraction in which parallel rays of light entering the eye at rest are brought to focus in front of the retina. In this situation, distant objects cannot be perceived distinctly. Myopic eyes have a finite far point in space from which divergent rays of light are brought to a focus on the retina without accommodative effort. (See Fig. 6-1.) This far point often coincides with the preferred reading distance. The handicap of defective distance vision is therefore partially compensated by an advantage of clearer near vision, especially in later life. This advantage has been cited as one important reason for the myope's superior reading skills and academic achievement.

HISTORY

The word *myopia* is thought to be derived from New Latin which, in turn, was derived from the original Greek word *mūopia*, which means contracting or closing the eyes. This is an apt description of the typical facial attitude of the uncorrected myope as he attempts to obtain clear distance vision. Until the general introduction of spectacles, squinting the lids, with the resultant production of a horizontal stenopeic slit, was the only practical means whereby clear distance vision could be achieved.

In ancient times the myope was reliant upon others with normal vision for both the

spoils of the hunt and protection in war. In prehistoric times this dependency must have been considerably greater. With the advent of civilization and the emergence of agriculture, handicrafts, and the written word, the near-sighted at last found a place of worth in society. As knowledge and fine skills have become increasingly important in our advancing culture, this place has been continually expanded.

The evolution of our knowledge of myopia has been marked by occasional giant strides based on careful investigations and their impartial analysis. All too often the contributions to this subject have been bewildering in their protocols, their results, and their conclusions. A tendency toward advocacy rather than investigatory curiosity can be seen to checker the early literature. Incredibly, myopia remains to this day not only one of the major causes of visual disability and blindness about which little is known, but also a subject that is considered to be almost "beneath" a serious scientist's efforts. As a result, myopia continues to be a problem of major proportions.

It is an old problem, and there are a number of fine reviews of the history of myopia.^{2, 6, 9, 10, 33, 42} Aristotle is generally thought to be one of the first to consider the problem seriously. He noted the tendency of the myope to blink the lids and write in small script. Galen, whose concepts so totally dominated the early years of medicine, thought that ocular refraction was dependent upon the composition and quantity of the eye fluids (animal spirit). From Aristotle's time it was held that the eye itself was the source of vision rays, an

idea finally dispelled by Alhazin (AD 1100). The optical correction of myopia evolved very slowly. Although Nero is believed to have watched gladiator battles through a concave ruby, correcting spectacles did not make their appearance until near the end of the 13th century. These lenses were convex, and the myope was to wait some two centuries before the general introduction of minus lenses. Even then, there were few people who wore them or advised wearing them.

The optics and image formation of refraction were poorly understood in those times. Porta (1558?–1593) thought that the image fell on the anterior surface of the lens, whereas his contemporary, Maurolycus (1575), deduced that the lens was involved in focusing the image and that it was more convex in myopia and flatter in hyperopia. He made no mention of the retina, however, and placed the focal plane on the optic nerve. Adding to the confusion was the problem of obtaining an upright image in the eye, an accomplishment that earlier workers considered indispensable for normal vision. A dramatic step forward was initiated by the contribution of Kepler, who by virtue of his background in both mathematics and myopia seemed eminently suited to address this subject. In 1604 he was able to demonstrate the image formation of the eye and the role played by the cornea and lens. He placed the inverted image at the retina and defined the action of convex and concave lenses upon this system. Somewhat later, in 1611, he noted that in myopic eyes parallel rays of light fell in front of the retina. He also wrote about accommodation, but in this area there was a considerable degree of confusion as a result of an inability to appreciate the fact that presbyopia occurred in both myopia and hyperopia. Kepler further attributed the ability to see clearly at both distance and near to alterations in the shape of the eye. He went on to propound the "near-work" hypothesis for myopia by stating that study and fine work in childhood rapidly accustoms the eye to near objects. With advancing years this adaptive mechanism produces a permanent, finite far point such that distant objects are seen poorly,

a theory that is still very much in evidence today.

With Newton's (1704) concept of hyperopia as a condition due to parallel rays of light converging behind the retina, the stage was set for the acceptance of the axial length of the eye as the sole determinant of refraction. Anatomical proof of increased axial lengthening of the eye was first provided by Plempius (1632). Boerhaave (1708) confirmed this lengthening while citing another cause of myopia: increased convexity of the refractive surfaces. Other causes that had been postulated were an increase in the thickness of the lens, an increase in its refractive index, and a change in its position.

In the absence of the instrumentation necessary to measure these corneal and lenticular variables, there were a number of studies confirming the variability of axial length. Included in these were the studies of Morgagni (1761), Guerin (1769), Gendron (1770), and Pichter (1790). The first anatomical description of posterior staphyloma in two female eyes followed shortly after in a study by Scarpa in 1801 (Fig. 1-1). Von Ammon (1832) pointed out that posterior staphyloma was not rare and was due to a distention of the posterior pole, although he did not make the association between this lesion and myopia. This association was postulated by von Graefe (1854) in a combined ophthalmoscopic and anatomical study of two eyes measuring 29 mm and 30.5 mm in length. Von Jaeger (1854) had also understood the ophthalmoscopic changes of myopia to be due to a distention of the posterior segment of the eye. It was Arlt (1856), however, whose anatomical studies convinced the scientific world of the intimate association of myopia with axial elongation of the globe at the expense of the posterior pole.

As a consequence of these studies the greatest efforts of the ophthalmologic community were concentrated on a search for the causes of increased axial length of the eye. That this search became indiscriminate and almost irrational can be appreciated by a review of the early theories of the etiology of myopia. It is apparent, in retrospect, that this central tenet

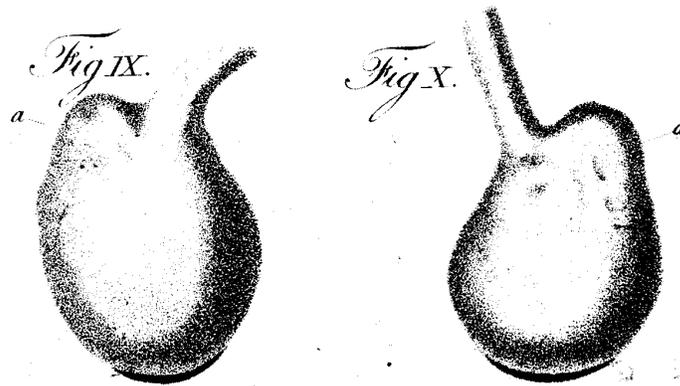


FIGURE 1-1. The earliest depiction of the pathologically myopic eye as contained in the text of Antonio Scarpa. (Scarpa A: A Treatise on the Principal Diseases of the Eye, 2nd ed. Briggs J (trans): London, Cadell and Davies, 1818)

of the older school would eventually be challenged. That axial length was not the sole determinant of refraction was appreciated by Donders and undoubtedly many others. Schnabel and Herrnheiser (1895) had found axial diameters varying from 22.25 mm to 26.24 mm in 23 emmetropic eyes and postulated that emmetropia was determined by the relation between axial length and total refraction. It remained, however, for Steiger (1913), in a large statistical study of corneal power in children, to deemphasize the importance of axial length as the only determinant of refraction. Although his biomathematical study was large (5000 children), his experimental method was somewhat faulty in that he assumed lens power to be a constant and thus calculated the axial length of the eye from total refraction in this manner. The variability of lens power had been alluded to as early as 1575 by Maurolycus, and variations in lens thickness, refractive index, and position had been enumerated as possible causes of myopia prior to Donders' time. Furthermore, actual lens power measurements, albeit in small samples, had been demonstrated by von Reuss (1887–1890), Awerbach (1900), and Zeeman (1911) to show considerable variations. Steiger's corneal measurements gave a binomial curve extending from 39 D to 48 D. He failed to note any set value of corneal power in emmetropia. He further fashioned a distribution curve of from +7 D to -7 D using his corneal values and then calculated axial lengths found in emmetropia (21.5 mm–25.5 mm). Steiger saw emmetropia

and refractive errors as points on a normal distribution curve, with corneal power and axial lengths as free and independent variables. Vulnerable as they were, these concepts brought an entirely new approach to the study of myopia.

Tron (1934–1935) followed shortly with a study of 275 eyes in which the pitfalls of Steiger's work were carefully avoided. The only optical element not measured directly was axial length, which was calculated from the refraction, corneal power, lens power, and anterior chamber depth. Tron confirmed the wide range of axial lengths in emmetropia (22.4 mm–27.3 mm). He further deduced that axial length was the determinant factor of refraction only in the range beyond +4 D and -6 D. He obtained essentially binomial curves for all the elements of refraction except axial length. With the elimination of myopic eyes of more than 6 D, the curve for axial length also assumed a normal distribution. Stenstrom (1946) was able to measure the ocular axial length directly by x-rays owing to the development of this technique by Rushton (1938) in the interim. Stenstrom undertook a study of 1000 right eyes and, in these, confirmed the results Tron had obtained in the smaller series. Both of these biometric studies found essentially normal distribution curves for corneal power, depth of anterior chamber, lens power, and total refraction. Both showed a peaking (excess) for axial length above the binomial curve as well as an extension of the limb toward increased axial length (skewness). It was

noted by Stenstrom that the distribution curve of refraction had basically the same disposition as that of axial length, featuring both a positive excess at emmetropia and a skewness toward myopia.

This deviation in the population refraction curve had been noted previously by Scheerer and Betsch (1928–1929), who had attributed this to the incorporation of eyes with crescent formation at the optic nerve. When these eyes were deleted from the data, a symmetric curve was obtained for the distribution of refraction. In the analysis of these data it was pointed out that a positive excess still persisted in the “corrected” curve. Stenstrom’s refractive curve after the removal of eyes with crescents also demonstrated an excess. This central peaking was attributed to two factors: the first was the effect of component correlation in the emmetropic range as postulated by Wibaut (1928) and Berg (1931) and the second was the direct effect of axial length distribution upon the curve of refraction. Sorsby and co-workers (1957) were later to again confirm the results of both Tron and Stenstrom and to further explore the variables in the correlations between the optical components in various refractions. This had been done to a limited extent by Berg. Sorsby and co-workers demonstrated conclusively in their study of 341 eyes that “emmetropization” effect was noted in distribution curves of refraction as a result of a correlation of corneal power and axial length. In ametropias of ± 4 D and above, this correlation appeared to break down. Their study also indicated that neither the lens nor the chamber depth was an effective emmetropization factor.

A large number of more recent studies in this same vein have been added by Japanese authors such as Otsuka and Kondo, Ohno, Sugata, Tokoro, and Araki.³² In all of their investigations the dominant finding was the high correlation of total refraction with axial length. This is true especially in the emmetropic range of refraction in which the correlation of corneal power diminishes the impact of axial length upon the refraction. The latter remains, for the most part, as the primary determinant even in this range of refraction.

CLINICAL TYPES

It is important, at this point, to note that the symptom of blurred distance vision and the diagnosis of myopia are common denominators of what have been described as two different clinical entities: physiologic myopia and pathologic myopia. Physiologic (simple, school) myopia is an optical condition of the eye in which a chance combination of normal refraction components renders the eye nearsighted. An increase in curvature of the surfaces of the cornea or lens (decrease in radius of curvature) or an increased axial diameter of the eye *attained by normal growth* are factors each of which is capable of producing myopia unless proportional compensatory changes are present in the other components.

Pathologic (degenerative, progressive, malignant) myopia is a direct consequence of an abnormal component of refraction. In its general usage and as a strict diagnostic term, it indicates those cases associated with an abnormal lengthening of the eye. This process is generally attributed to the stretching of the scleral wall. The condition may be generalized and involve the entire posterior sclera as far forward as the insertions of the recti muscles. This diffuse process is usually associated with a herniation of an area of the posterior pole, which yields the dramatic picture of a posterior staphyloma. Technically, the term pathologic myopia, in its broadest sense, can be applied to such myopias as those found in keratoconus and spherophakia. To avoid confusion these entities are probably best termed “curvature” myopias. In this text the term *pathologic myopia* will be used only in the strict sense to mean a myopia due to abnormal axial lengthening of the eye accompanied by staphyloma formation.

Part 2 of this volume will consider at some length the inadequacies of a “physiologic–pathologic” classification for myopic eyes. There is clearly a large group of myopic eyes that cannot be classified as physiologic because they show evidence of abnormally increased axial lengths. On the other hand, they should not be classified as pathologic, since they do not display the classic degenerative fundus

changes of this disease. These eyes shall be classified as "intermediate" in type.

SOCIOECONOMIC EFFECTS

Visual Disability

Myopia, except in its lowest grades, presents a socioeconomic problem of significant magnitude. Throughout life the myope has the financial burden of purchasing, and the inconvenience of servicing, a variety of visual aids. These may take the form of spectacles or corneal lenses. The myope accounts for a large share of the optical aid market in the United States, which in recent years has exceeded 4 billion dollars in annual sales. In a recent survey conducted on youths aged 12 to 17 inclusive,³³ it was found that 34% wore correcting lenses. Myopes accounted for an increasing proportion of these patients, progressing from 72% of those using visual aids at age 12 to 87% at age 17. This increase was associated

with a proportional drop in hyperopic corrections in the same age group.

Blindness

If myopia merely caused a significant dependence upon optical corrections, it would be a problem of major dimensions. Of greater importance is the severe reduction in corrected vision that is associated with the pathologic form of myopia. In a detailed study of visual disability in the United States (1976), the National Eye Institute found myopia to be the fifth most frequent specific cause of impaired vision (Table 1-1), the eighth most frequent cause of severe visual impairment (Table 1-2), and the seventh most frequent cause of legal blindness (Table 1-3).⁴⁴ A somewhat older study by the National Society for the Prevention of Blindness also found myopia to be the

TABLE 1-1. Estimates of Prevalence of Impairment from Visual Disorders: Impaired Vision

Type of Eye Affection	Impaired Vision (Numbers in Thousands)
Glaucoma	1,070
Cataract (prenatal, other)	1,711
Retinal disorder (prenatal, diabetic, other)	815
Retrolental fibroplasia	19
Myopia	715
Cornea or sclera	294
Uveitis	285
Optic nerve disease	121
Multiple affections	90
Refractive errors with lesser disability	1,662
Other affections	3,656
Unknown	221
Total (all affections)	10,659

(Support for Vision Research. Washington, DC, Dept of Health, Education and Welfare Publication No. [NIM] 76-1098, 1976)

TABLE 1-2. Estimates of Prevalence of Impairment from Visual Disorders: Severe Visual Impairment

Type of Eye Affection	Severe Visual Impairment (Numbers in Thousands)
Glaucoma	207
Cataract (prenatal, other)	217
Retinal disorder (prenatal, diabetic, other)	392
Retrolental fibroplasia	19
Myopia	36
Cornea or sclera	67
Uveitis	67
Optic nerve disease	107
Multiple affections	90
Refractive errors with lesser disability	0
Other affections	103
Unknown	179
Total (all affections)	1,483

(Support for Vision Research. Washington, DC, Dept of Health, Education and Welfare Publication No. [NIM] 76-1098, 1976)

TABLE 1-3. Estimates of Prevalence of Impairment from Visual Disorders: Legal Blindness

Type of Eye Affection	Legal Blindness (Numbers in Thousands)
Glaucoma	56
Cataract (prenatal, other)	64
Retinal disorder (prenatal, diabetic, other)	118
Retrolental fibroplasia	10
Myopia	14
Cornea or sclera	22
Uveitis	23
Optic nerve disease	41
Multiple affections	23
Refractive errors with lesser disability	0
Other affections	45
Unknown	53
Total (all affections)	468

(Support for Vision Research. Washington, DC, Dept of Health, Education and Welfare Publication No. [NIM] 76-1098, 1976)

seventh cause of blindness in patients 20 years of age and over (Fig. 1-2).¹³ These data may be somewhat misleading, however. Pathologic myopia is a single disease entity, and in these tabulations it is ranked behind such disease groupings as "cornea or sclera," "uveitis," "optic nerve disease," "prenatal," "vascular," and the like. It is apparent that as a single cause of visual loss, pathologic myopia is underestimated to a significant extent by some of these surveys.

An equally important aspect in the consideration of the visual loss produced by myopia is its relatively early onset. The Model Reporting Area studies on blindness conducted by the US Department of Health, Education, and Welfare indicate that, in addition to ranking seventh as a cause of blindness (1969-1970),²¹ the incidence of myopic blindness increased from 0.1% in children under 5 years of age to 0.6% in the aged. The sharpest increase could

be noted to occur in the middle of the fifth decade. This rise is particularly ill-timed in that it coincides with that period of life in which the talents and productivity of those affected are at a maximum. It also coincides with that time at which there is a peak in financial responsibility; thus, the impact of this blindness upon the family is particularly severe.

Nor do the young escape the visual privations of myopia. A recent investigation in the United States attributes 5.6% of blindness among school children to myopia,¹⁸ making it the fifth most frequent cause of blindness after retrolental fibroplasia, cataract, optic nerve atrophy, and the combined category of anophthalmia-microphthalmia.

The prevalence of world blindness in general and myopic blindness in particular varies widely with the parameters used in different surveys. Unfortunately, there has been wide variance in the definitions of blindness and, specifically, myopic blindness. In some surveys, the blindness of a myopic eye due to glaucoma, for example, may be reported as myopic in nature. Conversely, blindness due to retinal detachment in eyes with substantial degrees of myopia is reported as due to retinal and not myopic causes. The classic example of this is the relatively homogeneous population of Germany. Reports from the Federal Republic of Germany find myopia to be the seventh most frequent cause of blindness (6.6% of cases). The neighboring Democratic Republic to the east finds myopia to be either the first or second most frequent cause in two surveys (14.7% and 13.9% of cases respectively).²⁴ More reliable data will be forthcoming when international health agencies can standardize such reportage. In spite of the obvious shortcomings of these surveys at the present, the prevalence of myopia as a blinding disease is most impressive. In Europe a large number of such studies have been conducted. The data from Great Britain is of particular note because of Sorsby's interest in myopia. In an early survey of blindness in England and Wales, he found myopia to be the second most frequent cause of blindness in persons between the ages of 30 and 49 years.⁴⁰ In the next age-group

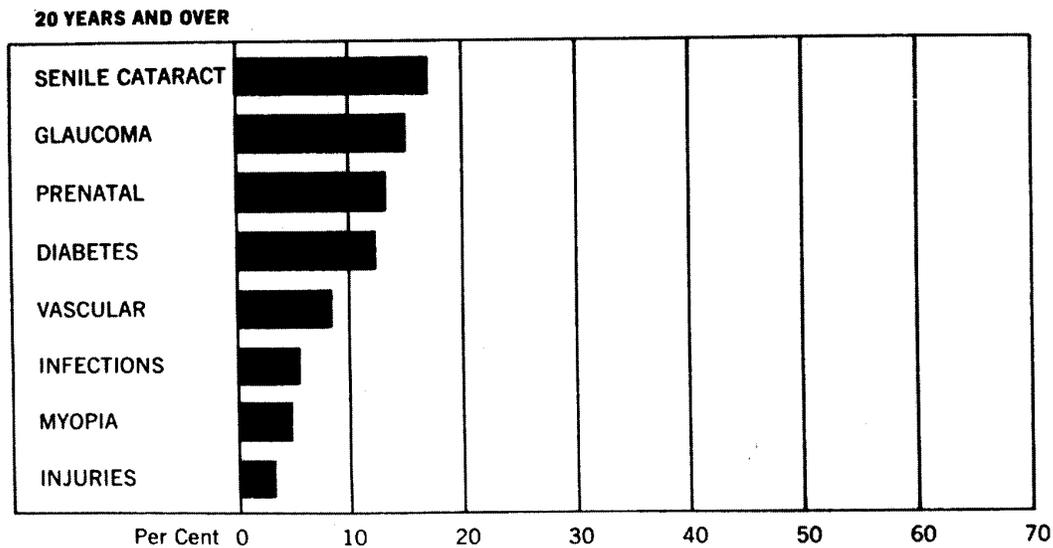


FIGURE 1-2. The eight major causes of blindness in the United States: population 20 years of age and above. (Estimated Statistics on Blindness and Vision Problems. New York, National Society for the Prevention of Blindness, 1966)

(50–69 years) it ranked second only to cataract. Overall, myopia was ranked as the third most prevalent cause behind cataract and glaucoma.⁴⁰ In a more recent study of the same population, Sorsby⁴¹ found myopic atrophy and retinal detachment to be the cause of 14% of blindness in all age-groups behind diabetic retinopathy and cataract. It would appear that in Scotland the problem of myopic blindness is even more grave. Here it has been found as the single greatest cause in persons in the fifth decade of life. According to surveys conducted in 1942²⁶ and 1946,⁸ it was ranked second only to cataract among all age-groups. The combination of these data revealed a significantly earlier onset of blindness among myopic persons (mean, 52.1 years) as compared with persons with blindness due to other causes (Table 1-4). In these surveys blindness secondary to cataract as well as retinal detachment in myopic eyes was reported as myopic in nature. The inclusion of the former is of questionable validity, and a somewhat exaggerated picture of the importance of myopia emerges from this review.

Other European studies, in addition to those

of West Germany and East Germany, have noted the significant prevalence of myopic blindness (Table 1-5). Other surveys that have been included in an extensive review of the world's major blinding conditions are those of Japan, in which myopia ranks fourth as a cause of blindness (8.4%); Hong Kong, fifth leading cause of blindness (8%); and Sri Lanka, one of five principal causes of blindness.²⁴

Older surveys are also of interest in this regard. Two German reports (1925–1926) noted myopia as the seventh most frequent cause of blindness.^{14, 15} In France, myopia in combination with other errors of refraction was cited in 1937 as the second most prevalent cause.³⁹ In Greece, a 1939 study showed a ranking of ninth,⁵ whereas a similar investigation 3 years earlier had found myopia to be the fourth leading cause in Hungary.⁴ Two reports have been published from Canada. In 1946 myopia was noted to be the fifth most frequent cause of blindness,³ whereas in a later study (1965) it was ranked third (9% of blindness) behind cataract (15%) and glaucoma (10%). This latter survey included 24,605 persons and ex-

TABLE 1-4. Mean Ages of Onset and Blindness as Related to Major Causes of Blindness in Scotland

Cause of Blindness	Number of Cases	Mean Age of Onset	Mean Age of Blindness
Myopia	1089	14.1	52.1
Abiotrophy	300	17.0	36.7
Cataract	1246	60.7	65.3
Diabetes	93	56.7	60.8
Glaucoma	594	58.3	61.9
Vascular Disease	263	60.3	63.6

(Dickson RM: A statistical analysis of persons certified blind in Scotland. *Br J Ophthalmol* 30:381, 1946; Marshall J, Seiler HE: A statistical analysis of 3,219 persons. *Br J Ophthalmol* 26:337, 1942)

cluded retinal detachment as a cause of myopic blindness.²⁵

In certain areas of the world there can be observed a decrease in the relative importance of congenital anomalies and degenerative diseases as blinding conditions with a commensurate rise in the frequency of infection, malnutrition, and cataract.²⁹ A 1971 study in Jerusalem found myopia to be the sixth most frequent cause of blindness (9.3%). Myopic blindness was slightly more common among non-Jews than among the Jewish population.¹ An Egyptian survey of the same year studied the causes of blindness in urban and rural populations. In the former, myopia was the third most frequent cause of blindness, affecting more males than females in a ratio of

3:2.³⁶ Oddly this survey failed to find any cases of blindness attributable to myopia among the rural population. It would be hazardous to postulate that this discrepancy between the two populations is the result of differences in occupation, diet, and the like. It is probably more accurately attributed to the fact that the rural myope would find it advisable to live where ophthalmic care and visual aids, in addition to increased opportunities for employment, were available.

MYOPIA AND PERSONALITY

The psychological effects of myopia are operative, to the most part, during the crucial

TABLE 1-5. Myopia as a Cause of World Blindness

Country or Territory	Ranking as Cause of Blindness	Percentage of Population Affected
United States	7th	3
Hong Kong	5th	8
Japan	5th	8.4
Sri Lanka	5th	Not reported
Denmark	3rd	Not reported
Germany, Democratic Republic	1st or 2nd	14.7 or 13.9
Germany, Federal Republic	7th	6.6
Malta	1st	19.4
Poland	3rd	11
Union of Soviet Socialist Republics	2nd	Not reported

(Lim AS, Jones BR: World's major blinding conditions. *Vision* 1:101, 1981)

periods in the development of personality. The gradual loss of efficient distance vision tends to concentrate the interest and energies of these patients more and more on near tasks. This obligatory shift to near is capable of producing subtle as well as striking changes in the attitudes and aptitudes of the individual. Justly or not, the myope has always been considered the introverted, bookish, nonathlete who is the academic bane of his more outgoing emmetropic and hyperopic fellows. Rice³⁴ also noted the tendency of the myope to become finicky, painstaking, and scrupulous. It will come as a relief to note that these characterizations were more the impressions of the author and were unsupported by scientific data. Rice noted that use of correcting lenses, as in the case of Theodore Roosevelt, could prevent the development of such an intolerant personality.

There is, however, more than fragmentary evidence that this impression is true, at least to a limited extent. In an early study of college students,³⁰ it was found that myopes did indeed show a slight but consistent tendency toward introversion when compared with normally-sighted colleagues. The average difference as measured by the Bernreuter Personality Inventory was not statistically significant and, in addition, was unaffected by the degree of myopia and the duration of the use of corrective lenses. A number of other tests consistently show differences in the mental makeup and attitudes of the myope. Schapero and Hirsch,³⁸ using the Guilford–Martin Temperament Test, found myopes to be more prone to emotional inhibition and disinclined toward motor activity. These authors noted that the myope was inclined toward social leadership. A later study by Stevens and Wolff,⁴³ using a test for the evaluation of leveling-sharpening mentation, showed a significant correlation with refraction. Myopia was associated with highly differentiated memories as a result of minimal perceptual interaction. In 1967 Young⁵⁰ used the Edwards Personal Preference Schedule and found that myopes scored higher than nonmyopes in achievement, introspection, abasement, heterosexuality, and aggression needs. Nonmyopes scored higher in deference, order, exhibitionism, dominance, and

change. Statistical significance was achieved only in abasement (guilt feelings, willingness to accept blame), exhibitionism (need to be noticed), and change (the desire to vary or avoid routine). Using the Rorschach test, Rosanes³⁵ compared the myope with the emmetrope and hyperope with the hypothesis that myopia might be a protective or adaptive mechanism, a reaction pattern to anxiety. She theorized that myopia might be one of a series or constellation of tendencies or reactions to stress by a certain type of personality configuration. This study concluded that myopes have a statistically significant increase in covert anxiety, with a decrease in motor activity compared with other refractive groups ($P < 0.01$). She also noted the fact that both hyperopes and myopes demonstrate less variability in exhibiting anxiety than do emmetropes ($P < 0.01$). These two groups also showed less variability in exhibiting hostility compared with those who were emmetropic ($P < 0.01$). Rosanes concluded that myopes have a high tolerance for anxiety and exhibit excessive control. They are less likely to place themselves in a situation where they can be attacked. They are innately cautious and use compromise generously. She found that the typical attitude of the hyperope could be characterized as “fight” and that of the myopes as “flight.” An earlier Rorschach test survey conducted by van Alphen² had found that myopes demonstrated a unique system of abstract thinking but had a deep-seated anxiety pattern. From these results it would appear that myopia is associated with certain differences in cerebration that are accompanied by distinguishing personality traits. Guilt feelings, anxiety, and introversion are frequently cited in this regard, and these emotions may have much to do with the greater achievements of the myope.

MYOPIA AND INTELLIGENCE

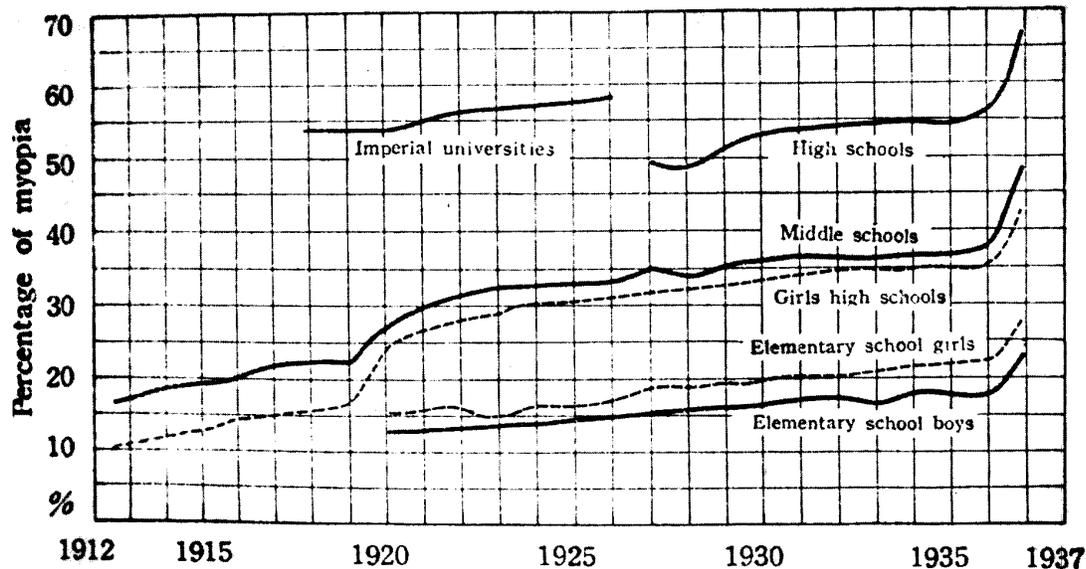
The remarkable academic success of the myopic population has naturally raised questions regarding the association of myopia and intelligence. At this time there is no body of scientific evidence to support or refute this con-

cept. Although numerous studies have found the intelligence quotient (IQ) of the myope to be somewhat higher than that of nonmyopes, statistical significance has not been established. What does appear to be functional in this regard is a superior reading ability and, possibly, greater attention to detail. The association of myopia and occupations of the intellect has been noted by a number of investigators. These include Tscherning,⁴⁸ Landolt,²³ Heinonen,¹⁹ and von Moers-Messmer.²⁷ This relationship was seen, alternately, as cause and effect,¹⁹ adaptive,²³ and even ontogenetic wherein the overdeveloped eye is part of the overdeveloped brain.²⁷ The earliest and most extensive reports on this subject were those of Cohn⁷ in Germany. He found 1.4% of children in the primary grades to be nearsighted. This increased to 26.2% at the university level. Cohn compiled an extensive, international survey of the relationship between myopia and academic achievement.

In Japan this same phenomenon has been seen. A very large 1937 study found that myopia increased in the school population from

27% in the elementary grades to about 46% in middle grades to a high of 67% in high schools (Fig. 1-3).^{32, 37} Goldschmidt made a careful survey of school children in the Danish population in 1968.¹⁶ He noted a significant plurality of myopes in the academic "streams" as compared with the other two, intellectually less rigorous, comprehensive and general streams. He also noted that whereas the frequency of this condition was about the same in the normal school populations and in schools for emotionally disturbed children and those for the deaf, the frequency of myopia was significantly less among retarded children. In the United States, Dunphy, in 1970,¹¹ found a disproportionately high frequency of myopia in 200 graduate students attending the Harvard schools of business and law. In Britain it has been noted that nearsighted students score about 5% higher in tests of reading, mathematics, and verbal intelligence. This phenomenon was not seen in nonverbal intelligence testing, however.¹² A study of the Icelandic population shows a general prevalence of myopia of 9% among persons age 30 to 50 years.

FIGURE 1-3. The prevalence of myopia in various schools of Japan over a 15-year period. The prevalence increases with the intensification of education. (Sato T: The Causes and Prevention of Acquired Myopia. Tokyo, Kanehara Shuppan, 1957)



In contrast, the prevalence among honor graduates, notably those in mathematics, is 35%.²²

A variety of tests have demonstrated a measurable difference in the IQ of persons with various refractive states. The myope usually scores perceptibly higher than the emmetrope and hyperope. Nadell and Hirsch,³¹ administering the California Test of Mental Maturity (CTMM) to 414 students, demonstrated a data trend that indicated that myopes were generally more intelligent, but not to a significant degree. One year later Hirsch published the results of another study in which he administered the Stanford–Binet test to children 6 to 7 years of age and the CTMM to older pupils.²⁰ Five hundred forty-four students were tested. He found no statistical difference in scores among youngsters 6 to 9 years of age, but among those age 10 to 13, myopes scored higher ($P < 0.001$). In these data there was an almost linear increase in IQ from students with hyperopia of greater than +2 D to myopic students of greater than -2 D. These results were seen as being the result of several possible mechanisms: an overdeveloped eye associated with greater cerebral development, the effect on test scores of reading experience and proficiency, the tendency of intelligent children to read more and thereby become myopic, and the superior reading ability of myopes leading to an increase in their scores.

Young⁴⁹ later studied 251 students using both the Stanford–Binet and the CTMM. All correlations were low and negative. The larger differences favoring myopes were contained in the results of the CTMM, which requires greater reading ability. Young then tested the reading ability of 117 students and found that myopes were significantly better readers than the emmetropes. Grosvenor¹⁷ studied 707 white New Zealand students using a verbal (Otis self-administered) test, and to 290 of them also administered a nonverbal (Raven-Matrix intelligence) test. With the first test he found no significant difference between myopes and emmetropes and emmetropes and hyperopes. He did find a statistical difference ($P < 0.05$) between myopes and hyperopes, however. In a nonverbal test, which uses a

minimum of reading and language skills, no significant differences among the three groups could be demonstrated, although myopes did average four points higher than emmetropes and nine points better than hyperopes. This same study also noted the overrepresentation of myopes among the high and medium academic streams ($P < 0.05$).

In summary it may be said that myopes generally score higher on intelligence tests, although not to a significant degree. Part of this, but not all, can be attributed to their demonstrably superior reading ability and their personality traits. Given the hereditary background of myopia, scholarship reinforcement is also more likely to be present at home. The myopic student more often has a similarly affected parent, often of academic achievement, who would stress intellectual pursuits and academic hobbies. Even the very wearing of spectacles may play a small part in the tendency to regard myopes as more intelligent. Thornton^{45, 46} found that merely wearing glasses can give the impression of intelligence.

Additional observations of those with short sight have included the allegation that they are essentially night people who like to stay up late. This is said to be related possibly to the greater security felt by the myopic child at night, at which time the darkness neutralizes his handicap to some degree. If dimness of the external world of the myope retards the development of an extroverted, gregarious personality, it appears to be a superb catalyst for the development of artistic skills. An unusual number of outstanding individuals have in common a period of time in their lives during which they were forced by circumstances to retire within themselves to develop a philosophy and plan of life. Pulmonary tuberculosis was the classic disease in this regard, and many have descended from Mann's tubercular "Magic Mountain" after a period of physical rest and intellectual stimulation to attain great success in life. These include, among many others, Goethe, Voltaire, and Descartes.²⁸ Myopia may provide a somewhat similar intellectual environment, and it is not surprising, therefore, to find the myope disproportionately

represented among the successful in the fields of literature, music, and art. Among these can be listed, such names as Goethe, Schiller, Schopenhauer, Schubert, Wagner, Beethoven, Bach, Tennyson, Alexander Pope, Edward Lear and Annette VonDroste–Hulshoff. Both Milton and Johnson have also been cited as myopic. Myopia is well represented among artists. These include Monet, Cézanne, Renoir, Degas, Pissarro, and Craig. Some of the greatest exponents of the school of impressionism are included in these names and one cannot help but speculate that this school evolved not only from the collective genius of these men but also their undercorrected myopia. Other artists who are presumed to have had myopia are Dufy, Derain, Braque, Vlaminck, Segonzac, and Matisse. In sculpture no less a giant than Rodin can be found among the nearsighted.⁴⁷ To these we may add the names of Shostakovich and three outstanding Irish writers: W. B. Yeats, Sean O’Casey, and James Joyce.

It has been said that “success dwells in the silences.” It is conceivable that myopia provides just such a “silence” for the young it afflicts.

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TABLE 13-13. Cataract Types Observed in 53 Eyes With Pathologic Myopia Preoperatively

Cataract Type	No. of Eyes
Nuclear	29 (54.7%)
Nuclear-posterior subcapsular	10 (18.8%)
Posterior subcapsular	9 (17.0%)
Posterior subcapsular-cortical	3 (5.7%)
Nuclear-cortical	2 (3.8%)

(Curtin BJ: Cataract extraction in pathological myopia. *Ophthalmol Surg* 7:65, 1976. Published by SLACK Incorporated, Medical Publishers, copyright 1976.)

tation of patients with this degree of myopia. Perkins^{239A} recently has confirmed the presence of an elevated prevalence of myopia among 388 cataract patients. Of these patients, 13.7% were also diabetic.

Nuclear cataract, in spite of its frequent occurrence in high myopia, is often an overlooked diagnosis. The increasing myopia in these patients is attributed to active progression and the diminished visual acuity to retinal degeneration. The poor fundus view obtained with direct ophthalmoscopy, which is characteristic of high myopia, also deprives the examiner of the ability to note subtle changes in the transition zones of the lens. Slit-lamp examination should include a careful study of the lens nucleus in any adult showing active "progression" of his myopia. Its cause is more likely the effect of advancing nuclear sclerosis. The progression of pathologic myopia has been found to be due, in some cases, to increases in lens power in the absence of nuclear sclerosis.^{214, 255} Increases in the power of a clear crystalline lens, especially in high myopia, should always suggest the possibility of subluxation. One study²⁴⁹ reports myopia as the fourth most frequent cause of ectopia lentis requiring surgery. With the exception of those conditions in which pathologic myopia is associated with subluxation of the lens, as in Marfan syndrome, the lens dislocation in high myopia appears to be the result of a degeneration of the zonules, which is usually associated with degeneration of the vitreous.²²⁵ Apollonio and Weigelin report the incidence of subluxation of the lens in their series of highly myopic eyes to be 0.7%.²¹⁵

The Fundus

Careful examination of the fundus of the myopic eye is most important. Its findings establish the diagnosis of pathologic myopia as well as form the most reliable basis for the prognosis of the disease. Both the central and peripheral fundi must be evaluated. Stereopsis is indispensable in these studies. Direct ophthalmoscopy is of limited value. The enlarged, poorly defined image can be improved by asking the patient to wear correcting lenses, but the panorama of fundus changes is difficult to appreciate with this method of examination. However, fine fundus details can be studied in this way, and slit-lamp biomicroscopy is also of great value for this purpose. The monocular indirect ophthalmoscope, which yields an upright image, can be very useful in the examination of highly myopic eyes, but the absence of stereopsis relegates its use to an ancillary status. Binocular indirect ophthalmoscopy has the disadvantage of the reversed inverted image, but its wide field of view and excellent stereopsis make it by far the best method of evaluating these fundi. The use of lower powered condensing lenses, 14 D or 16 D, enhances the examination of the posterior fundus because of the increased image brightness and better stereopsis they afford.

The early changes that are found in the pathologically myopic fundus, central or peripheral, are both developmental and mechanical in nature. In the earliest stages the posterior fundus may reveal only a localized thinning or hypoplasia of the retinal pigment epithelium. This is seen as an area of tessella-

tion and pallor of a fundus area conforming in distribution to that of a primary posterior staphyloma. It should be recalled that the retinal pigment epithelium is generally thought to induce the formation of both its contiguous choroid and sclera. (See Chap. 3, The Development of Refraction). A defective retinal pigment epithelium induces a defective choroid and sclera such that the prerequisite conditions for subsequent staphyloma development and chorioretinal degeneration are present. Typical choroidal colobomas are the classic example of this sequence. In this disease the absence of the retinal pigment epithelium is associated with a marked underdevelopment of the choroid and extensive ectasia of the hypoplastic sclera.

With time, ectasia of the pale, tessellated fundus areas of early pathologic myopia usually ensues. This ectasia may be quite slow, but in occasional cases can be alarmingly rapid. With advancing years superimposed mechanical changes play an increasingly important role in the prevalence and severity of the various degenerative phenomena of myopia.

The peripheral fundus changes in the myopic eye remain poorly understood. They appear to be related to the degree of expansion of the eye as well as to age. Some, like RPE hypoplasia of the posterior fundus, may also have a hereditary basis. It is equally important to determine the type and extent of peripheral as well as posterior fundus changes in the myopic eye. The markedly high incidence of retinal detachment in pathologic myopia argues eloquently to this point.

THE POSTERIOR (CENTRAL) FUNDUS

Roughly three stages of pathologic myopia can be distinguished on the basis of central fundus changes. The ophthalmoscopic characteristics that mark these stages are localized tessellation and pallor, development of ectasia, optic nerve changes, and a variety of chorioretinal degenerative phenomena. The early stages are dominated by developmental alterations. With time, the mechanical aspects associated with

ectasia of the fundus become more pronounced. Middle age and the years beyond are marked by an increasing loss of choroidal circulation and fundus atrophy.

Early Changes (Birth to Age 30)

In many young patients the only fundus changes indicative of pathologic myopia are a localized area of hypoplasia of the retinal pigment epithelium and optic nerve crescent. Tessellation and pallor of a fundus area around or to one side of the disc are seen (Fig. 13-12; Color Fig. 13-2). The area of retinal pigment epithelium thinning conforms in distribution to that of a primary posterior staphyloma, but ectasia of the affected fundus is often not discernible. Optic nerve crescent is present and is usually located on the same side of the disc as the tessellated area. These same fundus changes, also without ectasia, may be found in a small percentage of adult myopia patients. (See Chap. 14, Clinical Course.)

For the majority of patients with pathologic myopia, however, a variable degree of ectasia of the affected area ensues with time. This causes an added spreading of the thinned retinal pigment epithelium, with stretching of the lamina vitrea and choroidal vasculature.

Posterior Staphyloma

Five varieties of primary posterior staphyloma have been described.²⁸⁶ Each affects a different area of the fundus and while one or two are oddities, all are important. Even in those varieties in which the macula is not involved, the visual acuity may be subnormal. (See Visual Acuity earlier in this chapter.) The prevalence of each type of primary (types I to V) and compound (types VI to X) staphyloma can be found in Table 13-14.

The most frequent and the most important type of primary staphyloma is that affecting the posterior pole (Type 1; Fig. 13-13). Tessellation and pallor extend in a horizontal elliptical area from 2 disc diameters to 5 disc diameters nasal to the optic nerve to the macula area. With further development of the

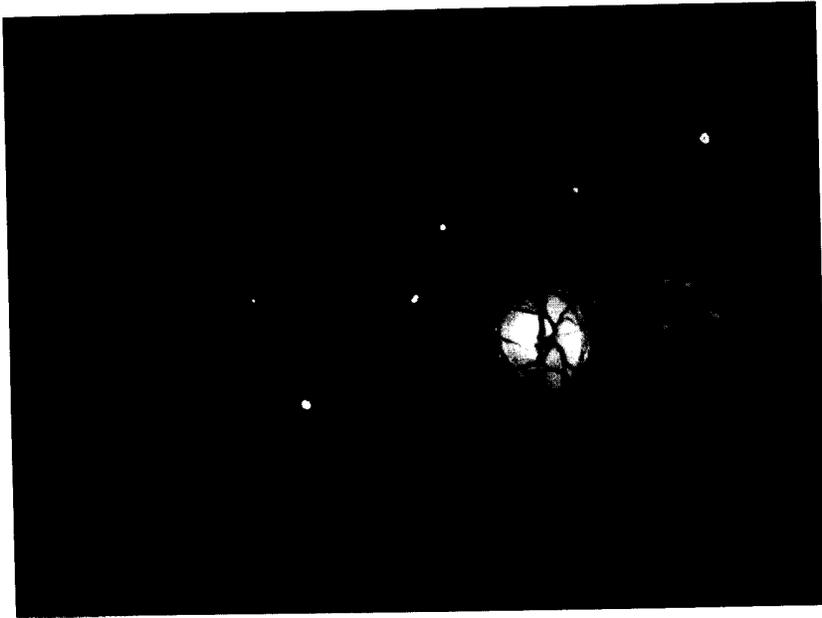
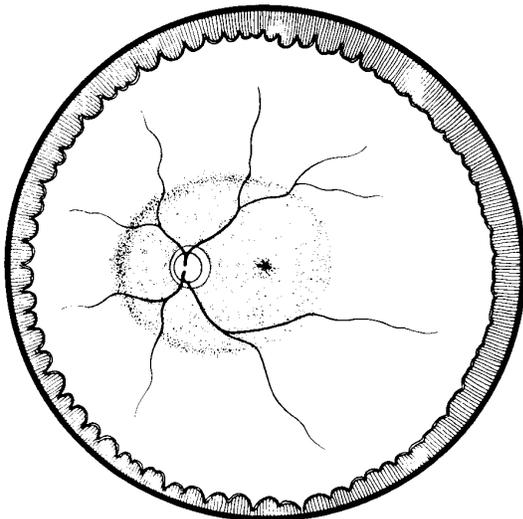


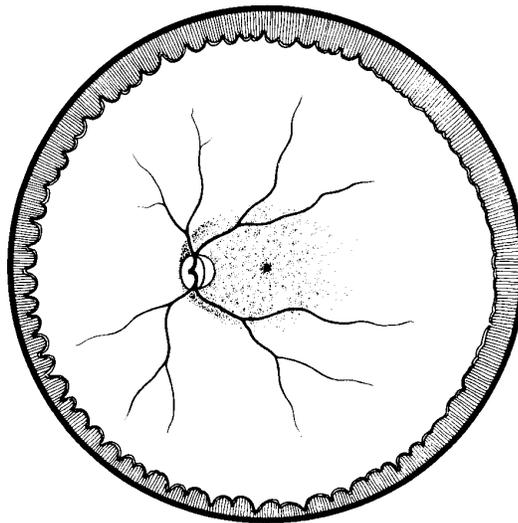
FIGURE 13-12. The fundus as it appears early in the course of pathologic myopia in a 10-year-old Hispanic female, right eye. Tessellation and pallor are observed about the optic nerve, which shows a circumpapillary retraction of the lamina vitrea complex.

FIGURE 13-13. Drawing of type I, or posterior pole, staphyloma. (Curtin BJ: The posterior staphyloma of pathologic myopia. *Trans Am Ophthalmol Soc* 75:67, 1977)



TYPE I

FIGURE 13-14. Drawing of type II, or macular, staphyloma. (Curtin BJ: The posterior staphyloma of pathologic myopia. *Trans Am Ophthalmol Soc* 75:67, 1977)



TYPE II

TABLE 13-14. Prevalence of Primary and Compound Staphylomas in Eyes of 250 Patients

Type of Staphyloma	Age of Patients (yr)				Total
	3-19	20-39	40-59	60-86	
Primary					
I	65	68	61	55	249
II	28	4	2	4	38
III	2	0	0	5	7
IV	2	2	5	13	22
V	4	0	2	6	12
Compound					
VI	8	3	4	3	18
VII	0	0	2	1	3
VIII	6	6	10	7	29
IX	6	11	11	8	36
X	1	10	16	12	39
Without staphyloma	16	11	1	7	35
Detached retina	0	1	2	5	8
Phthisis	0	0	2	2	4

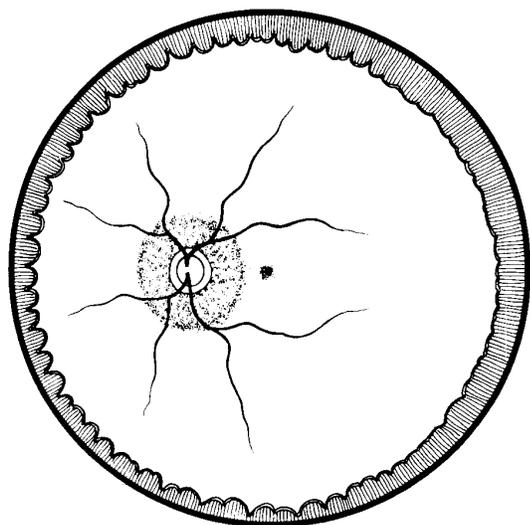
(Curtin BJ: The posterior staphyloma of pathologic myopia. *Trans Am Ophthalmol Soc* 75:67, 1977)

staphyloma, tessellation and pallor may ultimately extend well temporal to the macula. This staphyloma can attain great degrees of ectasia, with its nasal wall usually having the sharpest margin and the greatest slope. (Color Fig. 13-3). A large volume of literature has been devoted to reports of this staphyloma.^{291, 292, 307, 308, 318, 322, 334, 335, 337-339, 351, 357, 362, 375-377}

The earliest descriptions using monocular indirect ophthalmoscopy are the most comprehensive. Later reports using the monocular direct method refer principally to a vertical, crescentic shadow located nasal to the optic nerve with a substantial difference in dioptric correction for the fundus areas on either side of its dark, concave arc. This shadow corresponds to the sharp nasal margin of the staphyloma. Its concavity therefore faces the disc.

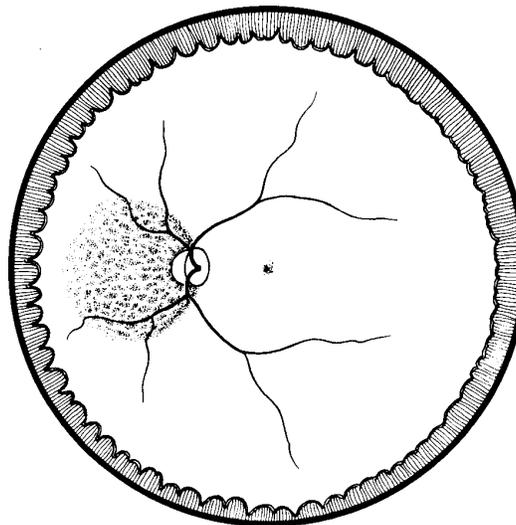
The second staphyloma, the macular staphyloma (Type II), involves a smaller elliptical area from the optic nerve to a variable distance to the temporal aspect of the macula (Fig. 13-14). This is the second most common primary staphyloma and characteristically is limited in its ectasia. It may reach substantial degrees of herniation, however. This staphyloma is important because of its macular involvement. It has not received the attention in the literature commensurate with this importance, however. Only one reference can be found.³²⁰

The least common primary staphyloma, the peripapillary staphyloma (type III), involves a sharply circumscribed, circular area about the optic nerve (Fig. 13-15). In spite of its rarity, it appears in an unusually large number of case reports.^{282, 310, 316, 321, 337, 360, 361} Interest in this



TYPE III

FIGURE 13-15. Drawing of type III, or peripapillary, staphyloma. (Curtin BJ: The posterior staphyloma of pathologic myopia. *Trans Am Ophthalmol Soc* 75:67, 1977)



TYPE IV

FIGURE 13-16. Drawing of type IV, or nasal, inverse staphyloma. (Curtin BJ: The posterior staphyloma of pathologic myopia. *Trans Am Ophthalmol Soc* 75:67, 1977)

type of staphyloma has been stimulated by its occasional contractile qualities^{319, 381} or associated respiratory pulsations³⁶³ as well as by its unusual appearance and depth.

Staphylomas of the nasal, and often the inferonasal, aspect of the fundus originate at the optic nerve and as a rule involve an elliptical area with minimal ectasia. These nasal staphylomas, type IV (Fig. 13-16), have been reported in a number of studies.^{284, 301, 330, 349} This staphyloma is often associated with inversion of the retinal vessels.²⁸¹ It has been designated as "inverse myopia" by Fuchs,^{298, 299} who also noted its increased prevalence among women. Nasal staphylomas are of special interest because of the visual-field changes they may produce. The bitemporal hemianopia seen in bilateral cases can be mistaken for chiasmal lesions by the unwary.^{342, 343, 346}

The fifth and last primary staphyloma involves an elliptical area below the optic nerve. This also tends to be a shallow lesion. The inferior, or type V staphyloma (Fig. 13-17), is

commonly considered a forme fruste of the choroidal coloboma. It has been reported by a number of authors.^{298, 327, 348} Table 13-15 outlines the ophthalmoscopic characteristics of the primary staphylomas.

Although the associated phenomena of fundus tessellation and pallor in the myopic eye have been described by many authors and specifically linked to staphyloma formation,³³⁷ it is the Japanese who have been especially interested in these changes. The "tigroid fundus," as reported by Otsuka and Kondo,³³³ has been found to be an indication of elongation of the axial diameter; the greater the axial length of the eye, the more likely that this fundus change will be seen. These findings have been confirmed by Tanaka.³⁶⁶ The tigroid fundus also appears to be a hereditary trait.^{332, 367}

The five compound varieties of posterior staphylomas are essentially variations of the primary type I. They may consist of a combination of a type I with another type such as type II, type VI (Fig. 13-18) or with type III,



COLOR FIGURE 13-1. The normal eye compared with the distended, highly myopic eye. The myopic eye exhibits a large semitransparent posterior staphyloma. Note dimpling of sclera at area of greatest thinning: the equator in the normal eye and the posterior pole in the myopic specimen.



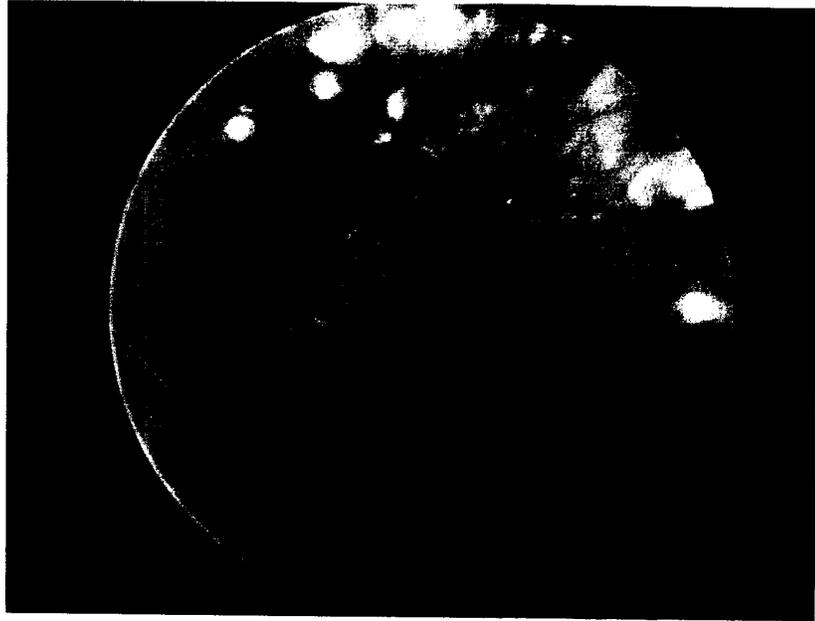
COLOR FIGURE 13-2. Fundus appearance early in the course of pathologic myopia. Marked thinning of the retinal pigment epithelium is present in a localized fundus area corresponding to that of a type I (posterior pole) staphyloma.



COLOR FIGURE 13-3. Grade 2 posterior pole staphyloma with tessellation and pallor in staphyloma area. A gentle sloping of the nasal wall and a shallow ectasia of the area nasal to the disc are present. One focal area of atrophy is seen on the temporal border of the staphyloma.



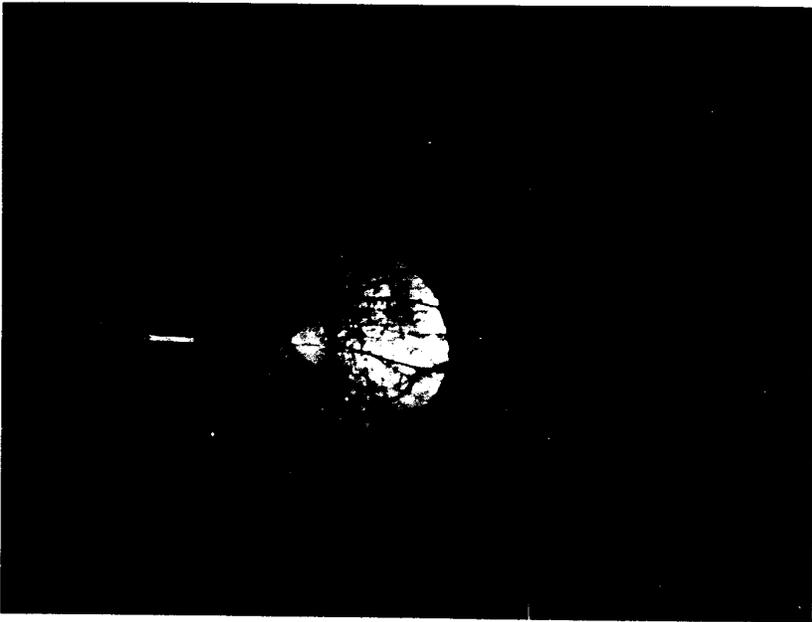
COLOR FIGURE 13-4. Fresh lacquer cracks associated with subretinal hemorrhages at the posterior pole.



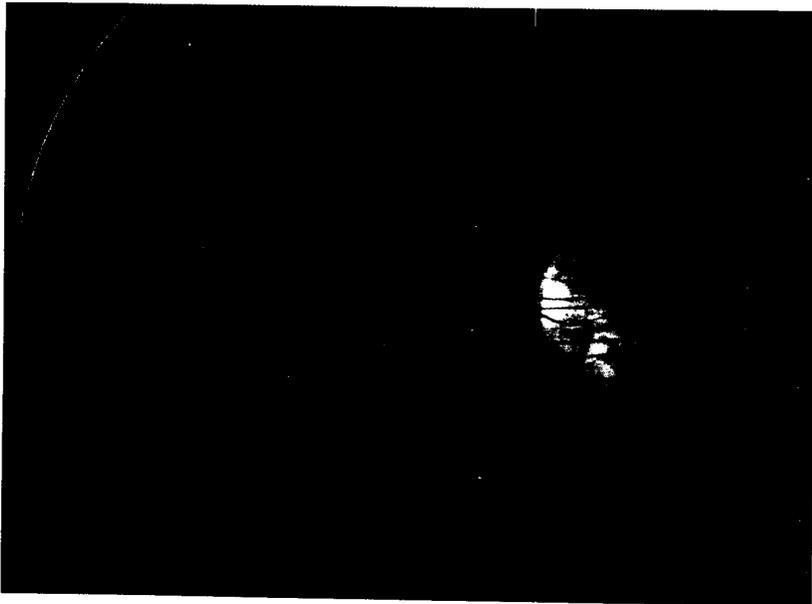
COLOR FIGURE 13-5. The inferotemporal border of a well-advanced posterior pole staphyloma (grade 5). Note the lightening of the fundus in the upper ectatic area as well as the numerous focal areas of atrophy within the staphyloma perimeter. A large pigmented lesion lies on the staphyloma margin.



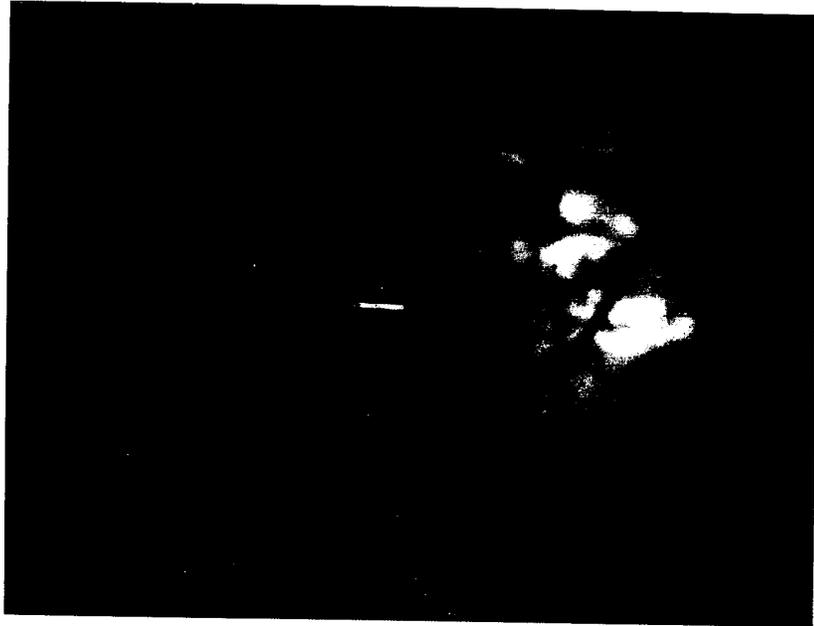
COLOR FIGURE 13-6. The nasal staphyloma. Extensive degeneration of the ectatic fundus nasal to the optic nerve can be observed. This condition has a distinct predilection for females and, where bilateral, produces bitemporal hemianopic visual-field defects. This condition has also been termed "myopia inversa."



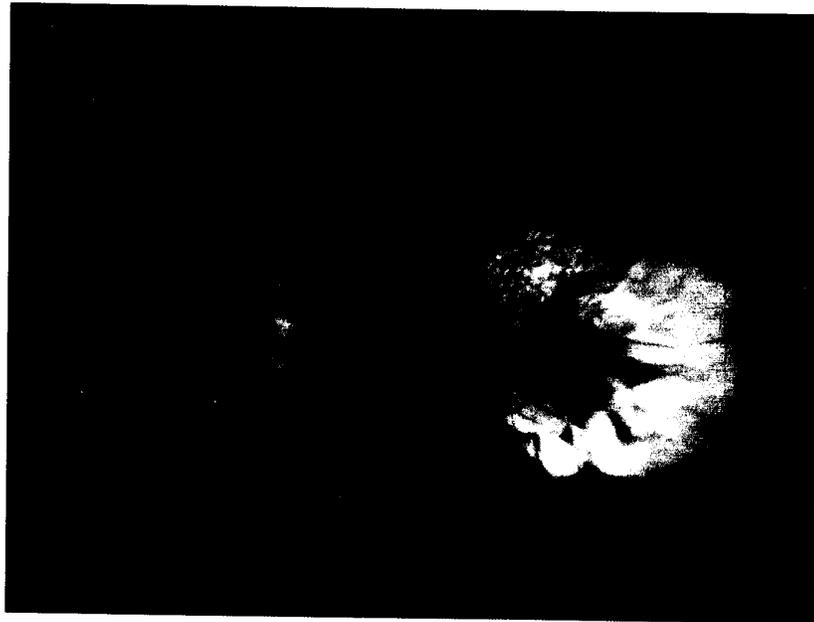
COLOR FIGURE 13-7. The picture of "choroidal sclerosis" in a young Hispanic female. A very large temporal crescent extends towards the macular area, where numerous lacquer cracks are present.



COLOR FIGURE 13-8. An unusual double Fuchs' spot in a highly myopic eye. Note the extremely large temporal crescent, the tessellation and pallor of the ectatic fundus, and the incipient chorioretinal degeneration contiguous with the pigment spots.



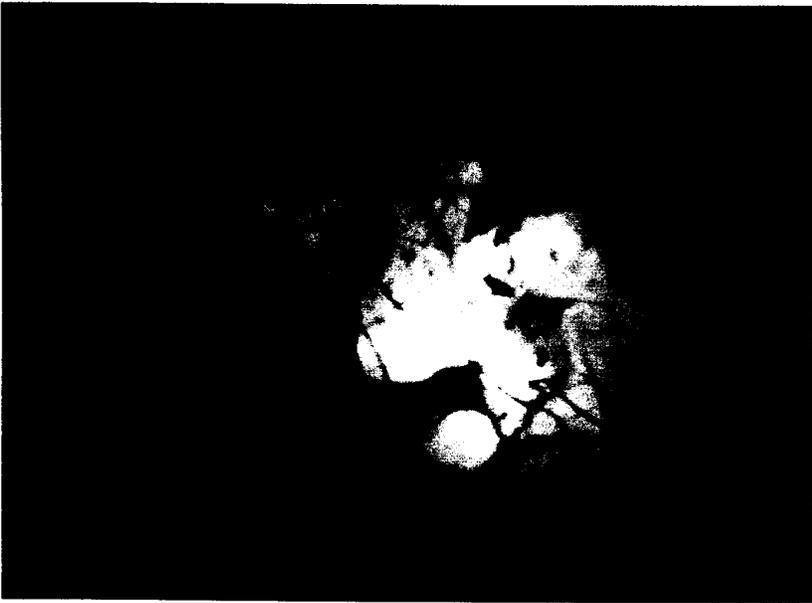
COLOR FIGURE 13-9. A fresh Fuchs' spot with associated hemorrhage. Note the gray color in contrast to the two lesions in Color Figure 13-8.



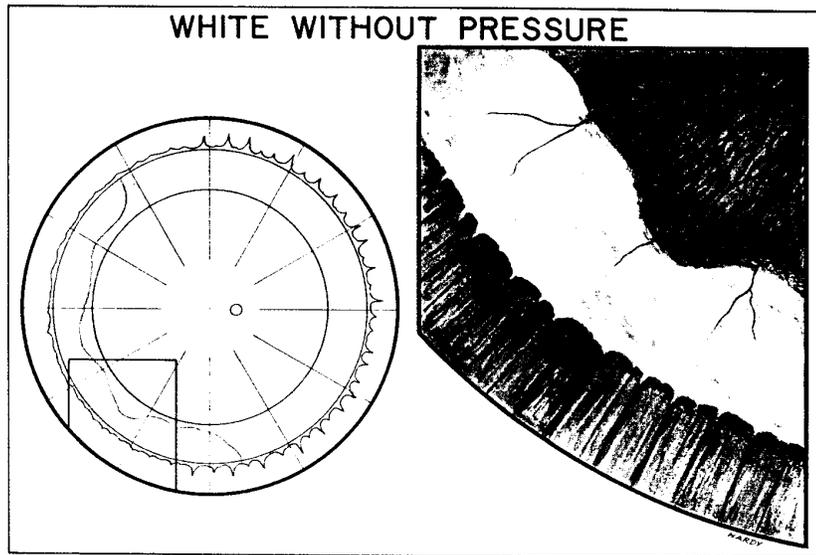
COLOR FIGURE 13-10. An old Fuchs' spot with a green-gray color. The spot has disintegrated to a considerable degree and its "halo" of atrophy is well developed.



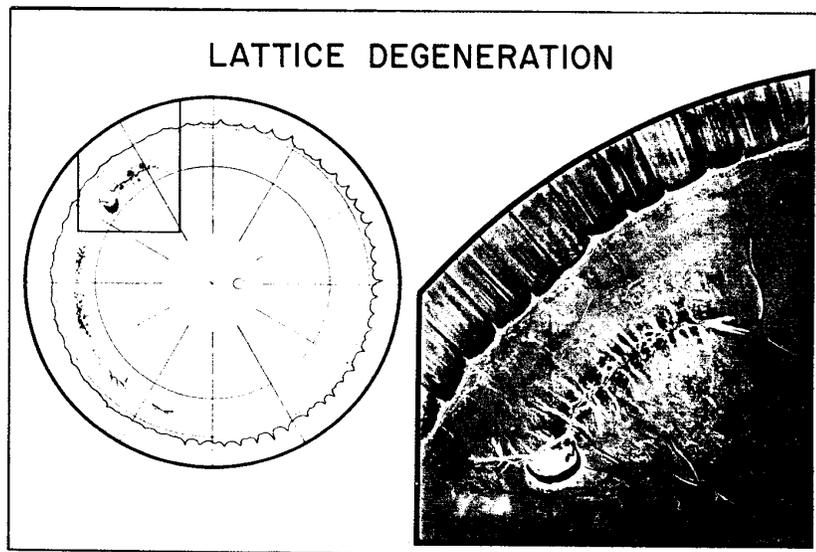
COLOR FIGURE 13-11. Advanced myopic degeneration. The peripapillary atrophy has begun to merge with the area of degeneration of the macular region. The macula is ectopic, being situated more inferior than normal.



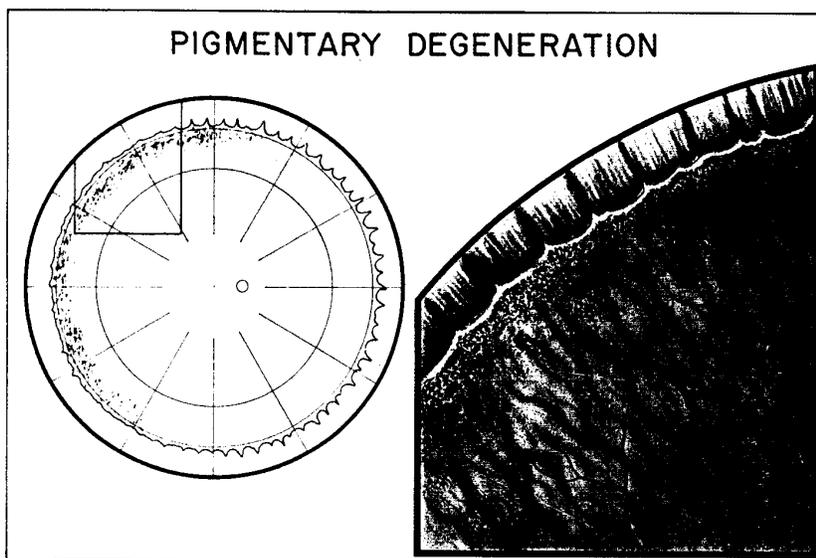
COLOR FIGURE 13-12. The same eye as in Color Figure 13-11 about 8 years later, wide-field photograph. The extent of the staphyloma can be discerned. There has been further loss of choroid and outer retina, representing the usual end stage of myopic chorioretinal degeneration. This picture has been referred to as "bare sclera." Observe the three steps on the nasal margin of this type VIII staphyloma.



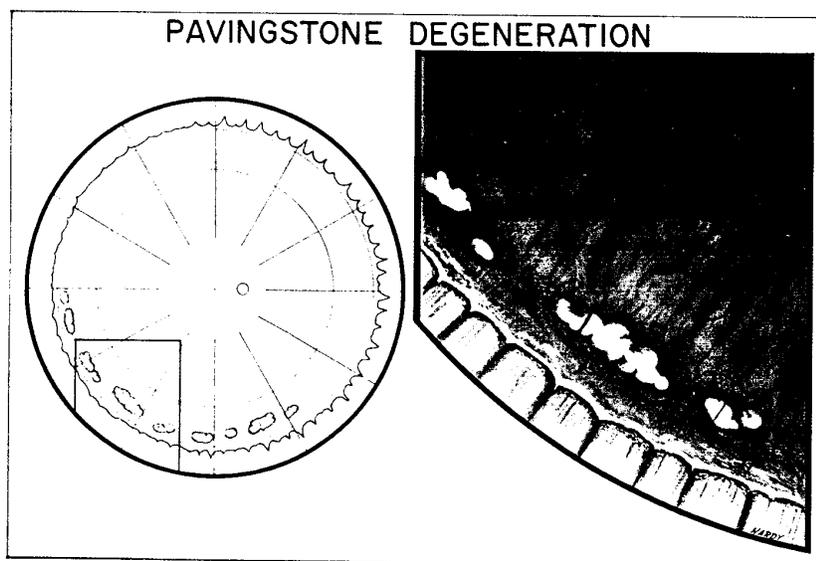
COLOR FIGURE 13-13. White-without-pressure. Lesion may be flat or appear to be elevated and involves the peripheral fundus from the ora posteriorly to a variable extent. The temporal quadrants, notably the inferior, are most often involved. (Karlín DB, Curtin BJ: Peripheral chorioretinal lesions and axial length of the myopic eye. *Am J Ophthalmol* 81:625, 1976. Published with permission from The American Journal of Ophthalmology. Copyright by The Ophthalmic Publishing Company.)



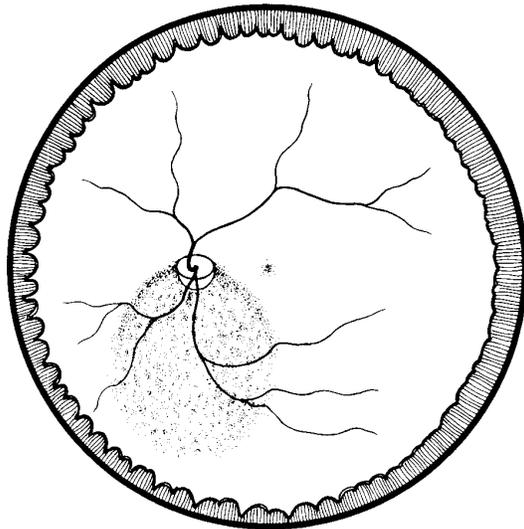
COLOR FIGURE 13-14. Lattice degeneration. These lesions present at or anterior to the equator in spindle-shaped areas that may be pigmented or nonpigmented. The temporal quadrants, notably the superior, are affected most frequently. (Karlín DB, Curtin BJ: Peripheral chorioretinal lesions and axial length of the myopic eye. *Am J Ophthalmol* 81:625, 1976. Published with permission from The American Journal of Ophthalmology. Copyright by The Ophthalmic Publishing Company.)



COLOR FIGURE 13-15. Pigmentary degeneration. These changes vary from a light dusting of fine particles to large pigment clumps. The temporal quadrants, especially the superior, are involved preferentially. (Karlín DB, Curtin BJ: Peripheral chorioretinal lesions and axial length of the myopic eye. *Am J Ophthalmol* 81:625, 1976. Published with permission from The American Journal of Ophthalmology. Copyright by The Ophthalmic Publishing Company.)

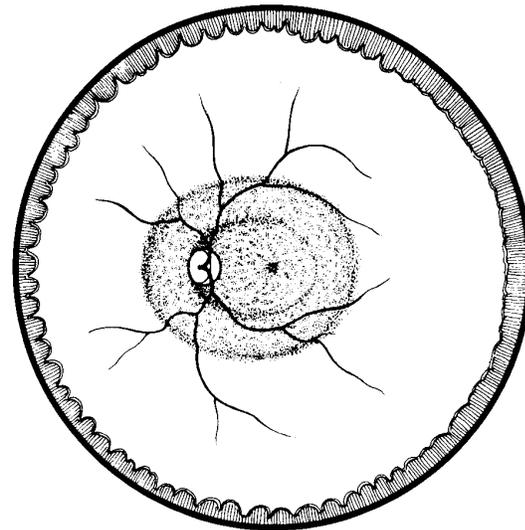


COLOR FIGURE 13-16. Pavingstone degeneration. Sharply demarcated, confluent lesions are seen to form in a line parallel with and one or two disc diameters posterior to the ora serrata. The lower quadrants are most commonly involved, the temporal more often than the nasal. (Karlín DB, Curtin BJ: Peripheral chorioretinal lesions and axial length of the myopic eye. *Am J Ophthalmol* 81:625, 1976. Published with permission from The American Journal of Ophthalmology. Copyright by The Ophthalmic Publishing Company.)



TYPE V

FIGURE 13-17. Drawing of type V, or inferior, staphyloma. (Curtin BJ: The posterior staphyloma of pathologic myopia. *Trans Am Ophthalmol Soc* 75:67, 1977)



TYPE VI

FIGURE 13-18. Drawing of compound staphyloma, type VI. Both staphyloma types I and II are present. (Curtin BJ: The posterior staphyloma of pathologic myopia. *Trans Am Ophthalmol Soc* 75:67, 1977)

type VII (Fig. 13-19). Type VIII staphylomas show steps or terraces along the nasal slope of the ectasia (Fig. 13-20). Descriptions of this type of fundus are not uncommon.^{337, 351, 357} In Type IX staphylomas (Fig. 13-21) a prominent, broad, vertical septum in the region of the optic nerve separates two deeper areas of ectasia. In the presence of extensive choroidal atrophy, a bright, vertical light reflex may originate from its convex surface. Although this type of staphyloma may be a variant of type I, there is at least an equal possibility that it may represent two distinct staphylomas, one macular (II) and the other nasal (IV). (See stereophoto, Fig. 13-48.) The precise morphogenesis of this staphyloma has not been established. In the case of the fifth type of compound staphyloma, type X (Fig. 13-22), the ectatic area is compartmentalized by one or more plicae. These thin, elevated ridges originate at the disc and extend to the staphyloma margin. A retinal vessel is usually found coursing along the top of the plication. In the plicated area fundus degeneration is usually re-

duced. When multiple, these plicae give rise to the most usual fundus pictures.

During the first 3 decades of life, staphyloma development can be found to vary substantially from patient to patient. Compound staphylomas are not usually seen, however. In general only primary types I and III can eventually develop any great degree of ectasia. The deeper the staphyloma development, the sharper or more abrupt its margins become.

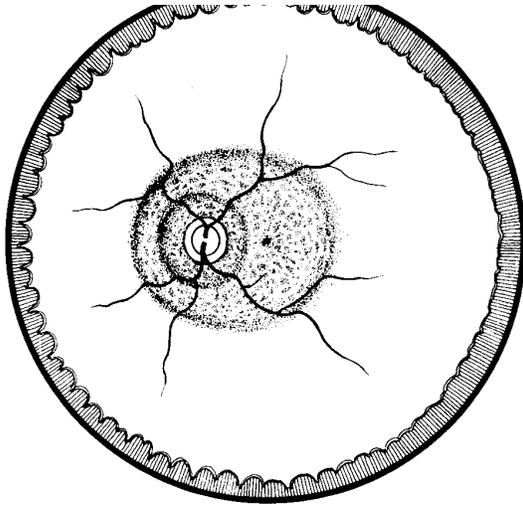
Considering the difficulty in appreciating shallower staphylomas, especially with monocular direct ophthalmoscopy, it is not unusual that the prevalence of these lesions has been, with only notable exceptions, grossly underestimated. An exception is Otto^{334, 335} who reported 55 staphylomas among 355 myopic eyes (16%). He found that all patients with myopia of -20 D or more demonstrated this lesion. Even in patients showing -15 D to -20 D of myopia, he found almost all eyes to be also affected, and among eyes with myopia as low as -11 D and -11.5 D, half showed these lesions. In the absence of stereopsis, Otto

(Text continues on p. 308.)

TABLE 13-15. Fundus Characteristics of Primary Staphylomas

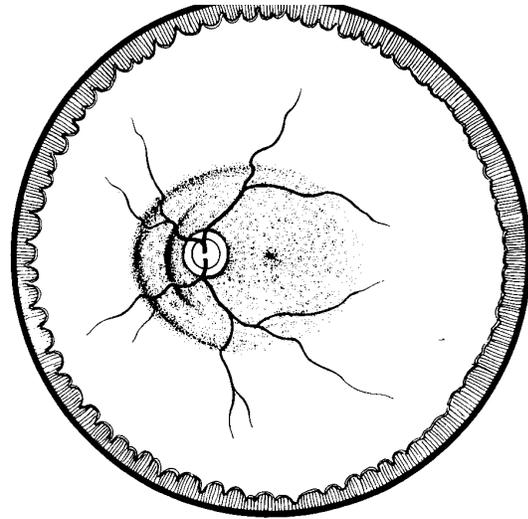
Type Staphyloma	Area of Ectasia	Shape and Depth	Margins	Disc	Retinal Vessels
Type I (posterior pole)	From 2-5 DD nasal to optic nerve temporally to macula or several DD temporal to it	Horizontal oval to almost circular; variable depth usually increasing with age	Nasal margin steepest; may be abrupt through 360°, can be excavated nasally	Lies flat within ectasia; temporal crescent with peripapillary extension or peripapillary crescent usual	Straightened within staphyloma; often a length of central artery and vein seen lying on disc
Type II (macular)	From disc to macula or somewhat beyond; temporal vascular arcades lie on upper and lower walls	Horizontal oval; shallow	Graduated; steepest at disc	Tilted temporally with elliptical shape; temporal crescent; nasal supertraction may be seen in youth	Exit disc in temporal direction; nasal vessels curve back
Type III (peripapillary)	1-2½ DD radius about optic nerve	Circular; may be deep	Variable, may be sharp throughout 360°; may be excavated occasionally	Usually lies flat at base of ectasia; may be eccentric; peripapillary crescent	Radiate out from disc
Type IV (nasal)	Optic nerve nasally for variable distance	Vertical oval; shallow	Graduated; steepest at disc	Tilted nasally with elliptical shape; nasal crescent	Exit disc in nasal direction; temporal vessels curve back
Type V (inferior)	Optic nerve, or slightly above it, inferiorly for variable distance	Vertical oval; shallow	Graduated; steepest at disc	Tilted inferiorly with elliptical shape; inferior crescent; superior supertraction rare	Exit disc in inferior direction; superior vessels curve back

DD, disc diameters.
 (Curtin BJ: The posterior staphyloma of pathologic myopia. Trans Am Ophthalmol Soc 75:67, 1977)



TYPE VII

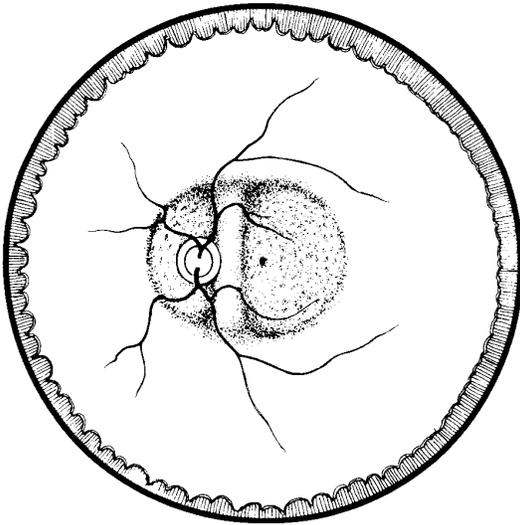
FIGURE 13-19. Drawing of compound staphyloma, type VII. Both staphyloma types I and III are present. (Curtin BJ: The posterior staphyloma of pathologic myopia. *Trans Am Ophthalmol Soc* 75:67, 1977)



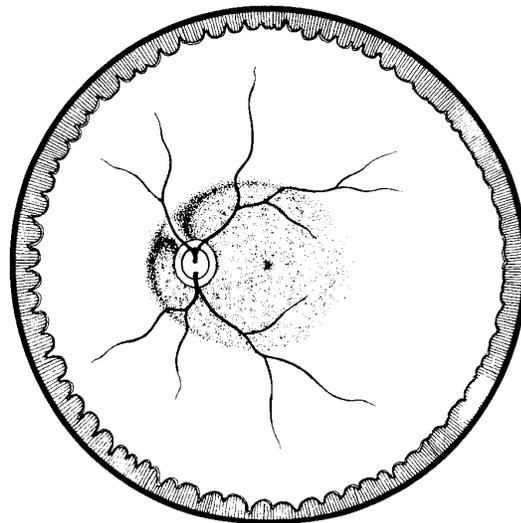
TYPE VIII

FIGURE 13-20. Drawing of compound staphyloma, type VIII. The nasal staphyloma wall exhibits tiers or a steplike morphology. (Curtin BJ: The posterior staphyloma of pathologic myopia. *Trans Am Ophthalmol Soc* 75:67, 1977)

FIGURE 13-21. Drawing of compound staphyloma, type IX. A vertical septum is present at or in the immediate vicinity of the optic nerve. In some eyes this gives the appearance of combined, deep types II and IV staphylomas. (Curtin BJ: The posterior staphyloma of pathologic myopia. *Trans Am Ophthalmol Soc* 75:67, 1977)



TYPE IX



TYPE X

FIGURE 13-22. Drawing of compound staphyloma, type X. These staphylomas are marked by foldlike plicae that radiate out from the disc. They usually have a retinal blood vessel coursing along their top. Occasional eyes may be seen to contain a number of these that divide the staphyloma into compartments. (Curtin BJ: The posterior staphyloma of pathologic myopia. *Trans Am Ophthalmol Soc* 75:67, 1977)

was forced to base the diagnosis upon parallax, the dark crescentic nasal reflex, the course of the retinal vessels, especially their bending at the staphyloma margin, and the dioptric changes between normal and ectatic fundus areas, a difference that can amount to as much as 10 D in some cases.

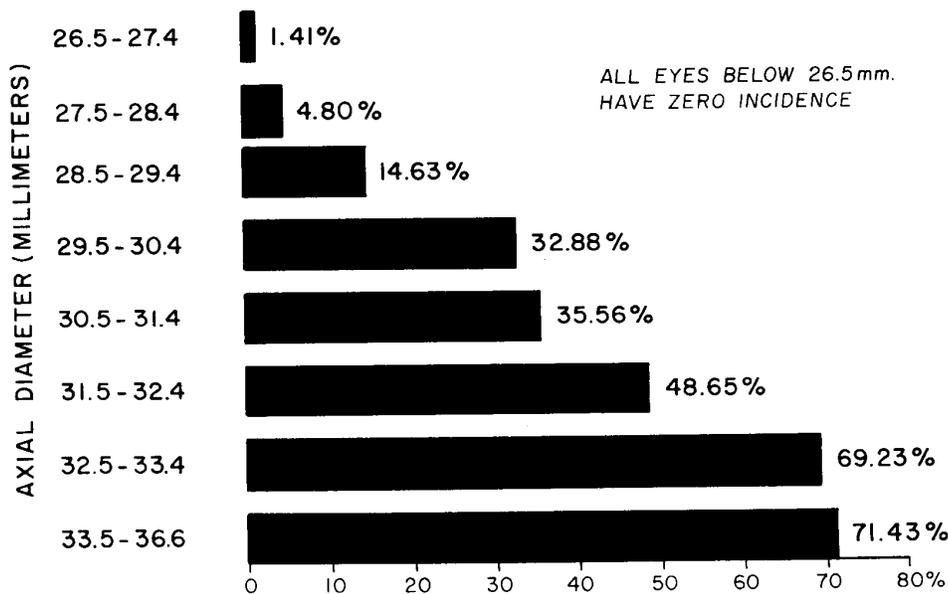
Other authors report staphyloma frequencies to be much lower.^{284, 318} This discrepancy would appear to be a tribute to Otto's thoroughness of examination, since modern stereoscopic funduscopy reveals that, indeed, posterior staphyloma is the rule rather than the exception in the higher orders of myopia. Infrequently it is found in eyes with spherical equivalent refractions as low as -3.25 D and axial diameters as small as 25.1 mm.²⁸⁶ A report of this lesion in an eye with a refraction of $-0.25 -2.00 \times 90$ has also appeared.³³⁹ In eyes of increased axial diameter (≥ 26.5 mm), posterior staphyloma with sharp margins has been found to affect 19% of patients. As

the axial diameter of the myopic eye increases, the prevalence of this lesion rises to 71% (Fig. 13-23).²⁸⁹ This also is a deceptively low incidence, since a large number of patients with shallow staphylomas were not included in this classification. It is our current impression at the Myopia Clinic of the Manhattan Eye, Ear and Throat Hospital that probably all cases of pathologic myopia have a posterior staphyloma of some type at some stage of development. It is unquestionably the quintessential lesion of pathologic myopia.

Optic Nerve Changes

Crescent formation, tilting, and supertraction are the three principal changes noted at the disc in early myopia. These changes are for the most part a consequence of the location and degree of development of the posterior staphyloma. With type I staphylomas, temporal crescent, usually with peripapillary extension, or,

FIGURE 13-23. Prevalence of posterior staphyloma at each axial diameter. Only staphylomas with sharp borders and distinct ectasia were included. (Curtin BJ, Karlin DB: Axial length measurements and fundus changes of the myopic eye. *Am J Ophthalmol* 71:42, 1971. Published with permission from the American Journal of Ophthalmology. Copyright by The Ophthalmic Publishing Company.)



less commonly, typical peripapillary crescents are found. With advanced development of ectasia, peripapillary extension of a temporal crescent is almost always seen. Type II staphylomas show temporal crescents. These enlarge with staphyloma development, and the disc is seen to tilt temporally on its vertical axis. Nasal supertraction may ensue. Peripapillary staphylomas show peripapillary crescents, while nasal staphylomas have nasal crescents. If the latter have any degree of ectasia, a nasal tilting of the optic nerve may be seen, but temporal supertraction has not been reported in these eyes. Type V staphylomas often show tilting of the disc on the horizontal axis, with crescent formation below and sometimes supertraction above.

Besides increasing their size, crescents may also change in color. Staphylomas that display limited ectasia postnatally, such as types IV and V, have crescents that are relatively small and white. In eyes with active postnatal staphyloma development, the crescent enlarges and choroidal elements may be found within its borders. A double crescent, an inner scleral and outer choroidal, can often be seen in these cases. Pigment proliferation at the crescent border may also occur. "Choroidal" crescents vary markedly in pigmentation. In blacks and Orientals they are heavily pigmented as a rule. In blond Caucasians they are often indistinguishable from the original scleral crescent except for their choroidal vascular elements.

Supertraction may give rise to light reflexes, which are seen best by direct ophthalmoscopy. Then thin streaks appear near the nasal border of the disc, with their concavity toward the nerve head. They have been called "Weiss streaks" after the author who initially reported them in detail.^{374, 377} Weiss attributed these streaks to reflections from the detached posterior vitreous surface. Goldmann, however, has placed them at the concave vitreoretinal surface where the supertraction mound starts (see Fig. 8-7). In an occasional eye a double reflex is seen. The second reflex is temporal to the larger Weiss reflex and usually crosses vertically upon the optic nerve surface. This reflex appears to originate from the convexity of the

supertraction. These phenomena are more likely seen in youth. With advancing myopia and expansion of the posterior fundus, there is a flattening of the supertraction mound and their light reflexes disappear.

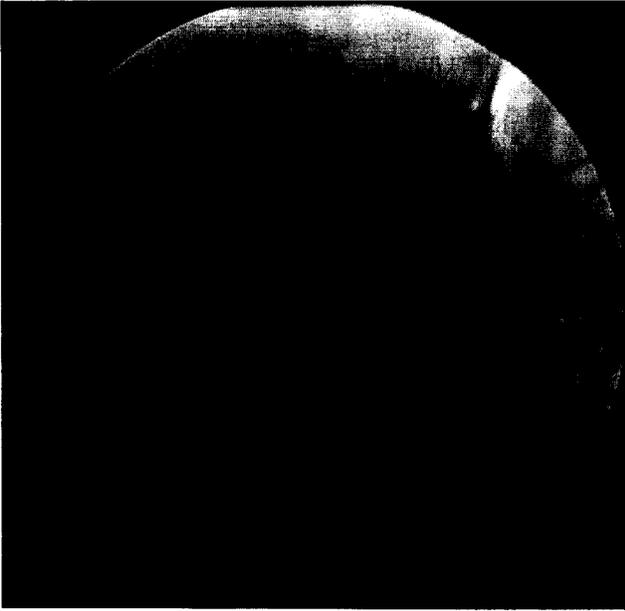
Chorioretinal Changes

Three important fundus changes may also make their appearance during the first 3 decades of life. These are retinal hemorrhages, lacquer cracks, and small focal areas of atrophy.

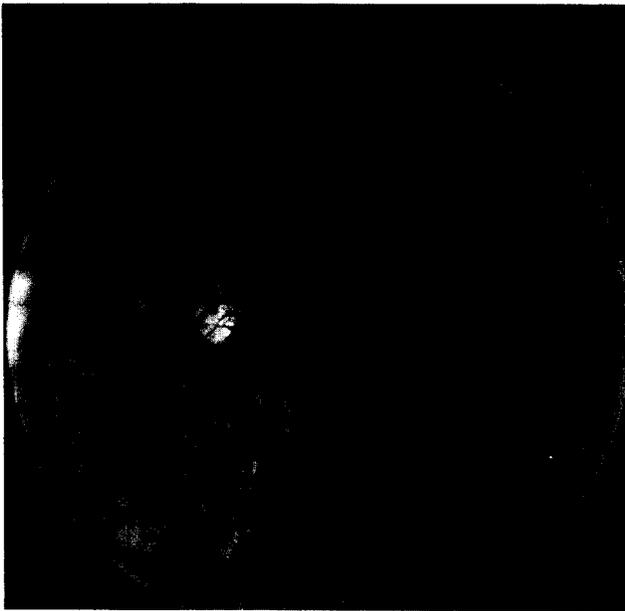
"Choroidal" hemorrhages may occasionally be seen during the early course of pathologic myopia. They may occur as isolated findings, especially in the macular area,²⁶⁷ but are also found in conjunction with fresh lacquer crack formation (Fig. 13-24). The term *choroidal* is used because the location of these hemorrhages has not been fully established. They may lie between the retinal pigment epithelium and lamina vitrea, especially if subretinal neovascularization is present. Fluorescein angiography in these young eyes usually does not confirm the presence of such vascular networks, however. The absence of rebleeding and the rapid absorption of these hemorrhages with the restoration of retinal function tend to indicate that the hemorrhages are, more likely, related to ruptures in the lamina vitrea. The choriocapillaris is involved in this event because of the intimate relationship between the two structures. Hemorrhages that occur in this way would come to lie on either side of the lamina vitrea and tend to have a round shape. When they are more extensive, irregular forms may be seen. If these hemorrhages occur in the macula, a variable degree of visual loss and metamorphopsia may ensue. In youth the prognosis is good; among our clinic population these types of hemorrhages usually absorb over a period of weeks with little or no aftereffect. Such "coin" lesions are not uncommon findings in highly myopic eyes. Blach²⁷¹ obtained an incidence of 6.5% in his study of 77 patients.

Lacquer cracks are seen as yellow white lines of irregular caliber that course across the posterior pole (Fig. 13-25). They are usually

(Text continues on p. 312.)



A



B

FIGURE 13-24. (A) A large subretinal hemorrhage coincident with lacquer crack formation. The hemorrhage is round and may be somewhat elevated at its center. (B) Two small retinal hemorrhages in the process of absorption. Numerous lacquer cracks and one focal area of chorioretinal degeneration are also present.



A



B

FIGURE 13-25. (A) A solitary lacquer crack passing across the fundus and the macular region. It is yellow white, somewhat irregular in caliber. The rent in the lamina vitrea complex exposes the large choroidal vessels beneath. (B) Numerous lacquer cracks with a predominantly horizontal orientation over the posterior pole.

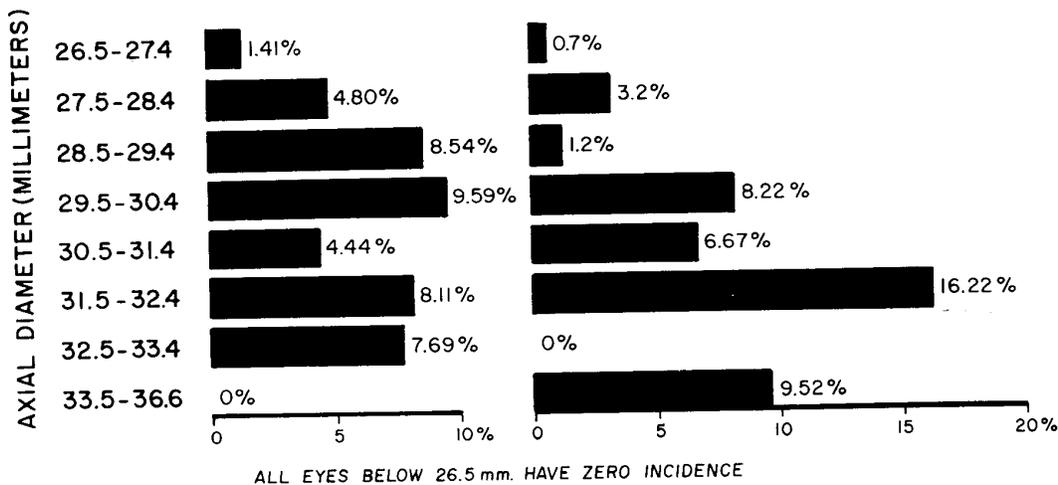


FIGURE 13-26. Prevalence of Fuchs' spots (*left*) and lacquer cracks (*right*) at each axial diameter. (Curtin BJ, Karlin DB: Axial length measurements and fundus changes of the myopic eye. *Am J Ophthalmol* 71:42, 1971. Published with permission from the American Journal of Ophthalmology. Copyright by the Ophthalmic Publishing Company.)

associated with posterior pole staphylomas³¹⁷ and may show some predilection for males.²⁸⁹ In one study lacquer cracks were found to affect patients ranging in age from 19 to 51 years, with the majority noted during the third and fourth decades of life. In this same study, 4.3% of eyes with an axial diameter of 26.5 mm or more were affected (Fig. 13-26).³¹⁷ These lines are usually multiple and often are horizontally oriented. They may also form crisscross patterns.^{299, 337} In addition to posterior staphyloma, these lesions are found in association with choroidal hemorrhages (32%) (Color Fig. 13-4) and chorioretinal atrophy (23%).³¹⁷ Slit-lamp biomicroscopy reveals these cracks to lie in the deepest layers of the retina. Larger choroidal vessels frequently traverse the lesions posteriorly. No apparent disturbance of the inner retina is evident. Significant visual dysfunction can rarely be attributed to these phenomena. Visual fields in these eyes demonstrate some degree of concentric contraction as a rule, but scotomata related to the lacquer cracks cannot be demonstrated. An acquired yellow-blue color-vision deficiency is a common finding.

Fluorescein angiography shows early pseu-

dofluorescence, but there is no intraretinal or subretinal leakage of dye. In the late angiographic phase only a faint hyperfluorescence can be detected.^{317, 373}

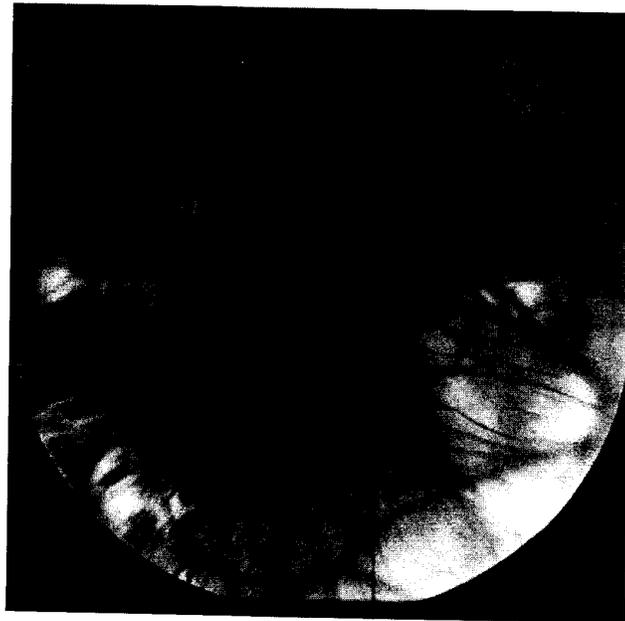
Lacquer cracks are generally considered to represent fissures in the retinal pigment epithelium–lamina vitrea–choriocapillaris complex. They are thought to originate as mechanical tears in these tissues. A degenerative etiology has also been postulated.²⁹³ In this regard, one recent study has found a statistically significant increase in the association of these cracks with angioid streaks.³⁶⁵ Lacquer cracks have also been said to represent sclerosed choroidal vessels.³⁵¹ Their association with fresh hemorrhaging would argue strongly against the concept, however.

The importance of lacquer cracks lies mainly in their prognostic significance. Their declining prevalence with age indicates that the fundus areas in which they occur are extremely prone to extensive degeneration. The presence of such associated lesions as subretinal hemorrhages, Fuchs' spots, and, especially, focal degenerative lesions along their course lends added weight to the seriousness of their nature (Figs. 13-27 and 13-28). Lacquer cracks, par-



FIGURE 13-27. Wide-field photograph of fundus in Figure 13-25, B 2 years later. A small hemorrhage is present above and nasal to the ectopic macula, which now exhibits a small Fuchs' spot as well as numerous lacquer cracks.

FIGURE 13-28. Lacquer cracks in association with numerous areas of focal chorioretinal degeneration. Degeneration frequently occurs at or in the immediate vicinity of lacquer cracks, which commonly become unidentifiable as chorioretinal atrophy advances.





A

FIGURE 13-29. Progressive chorioretinal degeneration in a 28-year-old Hispanic female. (A) Fine lacquer cracks are present over the posterior pole at and below the macula. Focal atrophy is present inferiorly with pigmentation. A small subretinal hemorrhage is above the inferotemporal arteriole (1972). (B) Numerous punched-out areas of fresh atrophy appear in upper fundus (1975).



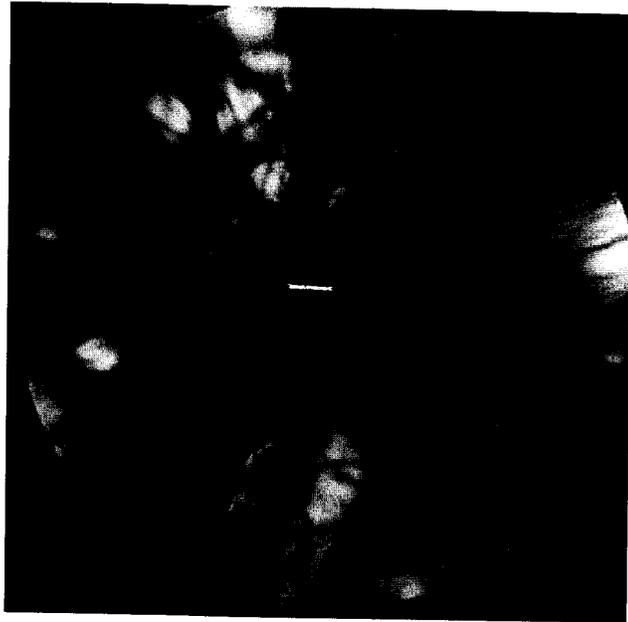
B

particularly when they involve the macular area, impart a guarded prognosis for central vision in later life.³¹⁷

The small, discrete, punched-out areas of

atrophy that are referred to as focal chorioretinal atrophy; may be seen as independent lesions or may occur in conjunction with lacquer cracks. They are usually round and white

FIGURE 13-29. (continued) (C) In addition to several new, fine atrophic areas, the older lesions show expansion and increased pigmentation (1980). (D) Wide-field photograph shows further expansion and coalescence of lesions (1983). The atrophy at the crescent margin is now greatly enhanced. In addition there is added thinning of the pigment epithelium.



C



D

to yellow white. Pigment clumping may be noted at their margins. Usually they are found in eyes of young patients with advanced staphyloma development (Fig. 13-29). These le-

sions differ somewhat from the chorioretinal degeneration of older myopic eyes. In older persons the lesions are considerably larger and tend toward confluence with one another. The

small diameter of the areas in youth, usually well short of the .6 mm to .8 mm diameter of the choroidal lobules at the posterior pole,³⁶⁹ indicates that they probably are caused by small dehiscences in the lamina vitrea rather than choroidal vascular occlusions or areas of involuted subretinal neovascular membranes. Some may represent focal abiotrophic degeneration of the retinal pigment epithelium.

Macular Changes

The macula in high myopia often shows an unusual degree of hyperpigmentation. This is present very early in life²⁷⁷ (see Fig. 13-12) and is possibly the result of hyperplasia of the retinal pigment epithelium in the macular area. The pallor of the surrounding fundus also has a tendency to accentuate the macular pigmentation by contrast.²⁸⁵ With active staphyloma development involving the macular region (types I and II), a dispersion or spreading out of the macular pigment occurs and a granular appearance is seen. If hemorrhaging has occurred, the pigmentary changes of migration and clumping may appear. These changes may be reflected by a moderate reduction in visual acuity.

Intermediate Changes (Ages 30 to 60 Years)

During the intermediate period in the evolution of pathologic myopia, particularly the fifth and sixth decades, there is progression of the various pathologic processes seen in earlier years. Added to these are more serious events that reflect the aging process and consist of the loss of choroidal circulation and its sequelae.

Posterior Staphyloma

The advanced grades of staphyloma development emerge during this time. Ectasia of these lesions becomes more manifest in many cases, and an increased percentage of deeper lesions with expanded margins and sharply sloping walls is seen.²⁸⁸ The compound forms of staphyloma increase sharply in frequency also.

Among patients attending our myopia clinic, the level of intraocular pressure appears to play some role in the progression of posterior staphyloma development. Staphylomas of greater area and depth are usually found in greater frequency among eyes with higher intraocular pressures. Extensive staphyloma development can occur in the absence of elevated pressure, however. (See Chap. 14.)

Optic Nerve Changes

Although the general appearance of the disc remains the same, two changes mark this stage. The first is essentially mechanical. Within the deepening staphyloma the retinal blood vessels are seen to straighten in their course. This is also associated with a widening of the intervascular spaces in the choroid, an observation made originally by Donders.²⁹² The expansion of the staphyloma also produces an eversion of the inner aspect of the optic nerve and a forward movement of the lamina cribrosa. (See the section Intraocular Pressure earlier in this chapter.) These forces, the traction on the retinal vessels and eversion of the inner nerve, have the effect of exposing the central retinal artery and vein for a variable distance posterior to their primary bifurcations (Figs. 13-30 and 13-31). They assume the configuration of a horizontal letter T or Y.²⁸⁷ When acquired, this "T" or "Y" sign is indicative of high degrees of scleral ectasia with eversion of the posterior scleral foramen.

The second change is degenerative in nature. It is the appearance of atrophy in the peripapillary area. The margin of the crescent is usually involved first. Its previously sharp edge becomes fragmented and irregular. Gray white areas, usually with soft margins, form along its border (Fig. 13-32) and may cause a slight enlargement of the blind spot, but the patient is unaware of any visual changes. This is generally the first evidence of chorioretinal degeneration. In some cases this will be the only area of degenerative involvement but, unhappily, in most eyes it is the initial stage of more extensive choroidal atrophy. With advancing years these degenerative changes may



FIGURE 13-30. The "T" sign. With eversion of the inner aspect of the optic nerve and traction upon the retinal vessels secondary to posterior segment expansion, the vessels present on the disc surface. The artery bifurcates at 180° to give the appearance of the letter T.

become so great that the optic nerve comes to lie within a large surrounding area of atrophy (Fig. 13-33). This event causes a decided increase in the size of the blind spot, but central vision again is not affected. Unfortunately

these changes, especially when they are extensive, are very likely to occur in conjunction with similar lesions at the posterior pole. These we will consider presently. The involvement of the crescent margin in early degenerative

FIGURE 13-31. The "Y" sign. The process outlined in Figure 13-30 has eventuated such that both the central retinal artery and vein bifurcate acutely while lying flat on the temporal disc surface. The letter Y is formed.





FIGURE 13-32. Incipient degeneration along the midzone of a temporal crescent. This is usually the earliest presenting degenerative lesion in pathologic myopia.

changes is thought to result from two pathogenetic mechanisms. The first is mechanical in nature and involves the increased stress and strain of the lamina vitrea complex (retinal

pigment epithelium–lamina vitrea–choriocapillaris) as it is displaced from the disc. The second is attributed to circulatory causes. The displacement of the complex from the disc re-

FIGURE 13-33. Advanced circumpapillary chorioretinal degeneration. This area and the macular region are preferentially involved in the degenerative process.



moves the only barrier against the invasion of the subretinal space by choroidal vessels.

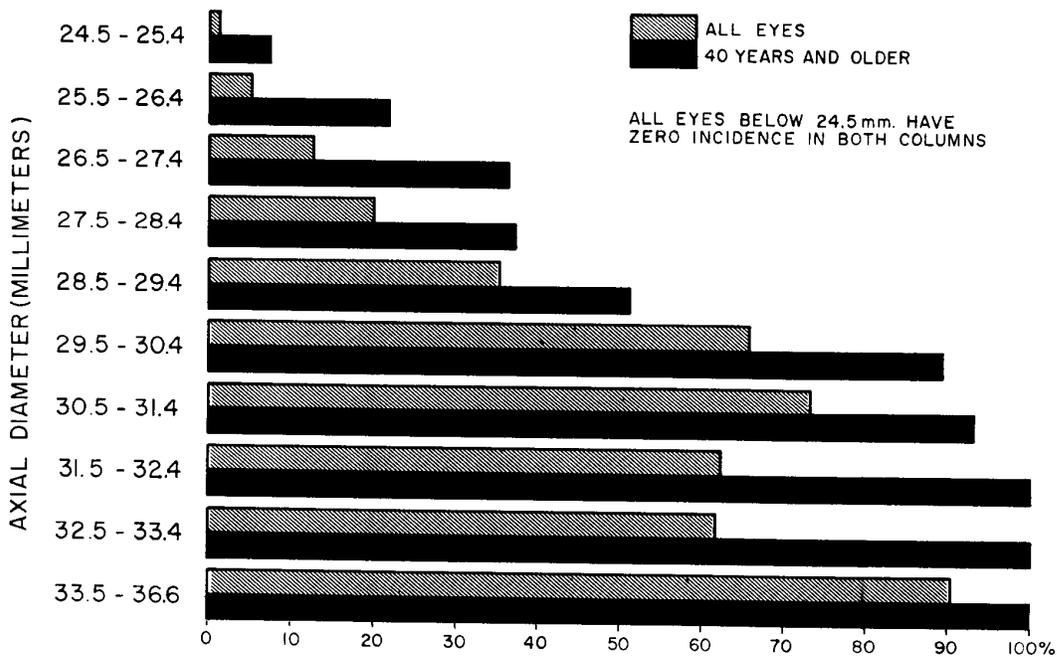
Chorioretinal Changes

Aging has a deleterious effect upon the abnormal retinal pigment epithelium and choroid of the myopic eye. An increasing avascularity of the choroid also becomes apparent with time. Ischemia of the outer layers of the retina in the presence of numerous dehiscences in the lamina vitrea sets the stage for the formation of subretinal neovascular networks.^{265, 303, 304} From these membranes serious subretinal hemorrhages, transudates, and Fuchs' spots may follow.

Chorioretinal Atrophy. In adult eyes with typical tessellation and pallor but no demonstrable ectasia of the fundus, areas of mild degeneration can occasionally be observed. These

are confined to the area about the disc and present as breakdowns of the crescent margin or as peripapillary atrophy. The classic isolated, focal atrophic lesions have only rarely been observed at the myopia clinic in the absence of ectasia. When extensive ectasia is present, there is pervasive evidence of extensive choroidal decompensation. The prevalence of chorioretinal atrophy therefore can be correlated with increased axial diameter of the eye (Fig. 13-34). The areas of choroidal avascularity occur almost exclusively within the confines of the posterior staphyloma. Each type of staphyloma is affected, but the appearance of the atrophic areas can vary with the choroidal vascular pattern in the affected area (Figs. 13-35, 13-36, and 13-37). The edge of the staphyloma, when sharp, can also be involved and, infrequently, lesions can also be found just outside the perimeter of the staphyloma. These are always in immediate proximity to the

FIGURE 13-34. Prevalence of chorioretinal degeneration at each axial diameter. The significant effect of age is demonstrated by the increased prevalence in persons 40 years and older. (Curtin BJ, Karlin DB: Axial length measurements and fundus changes of the myopic eye. *Am J Ophthalmol* 71:42, 1971. Published with permission from the American Journal of Ophthalmology. Copyright by The Ophthalmic Publishing Company.)



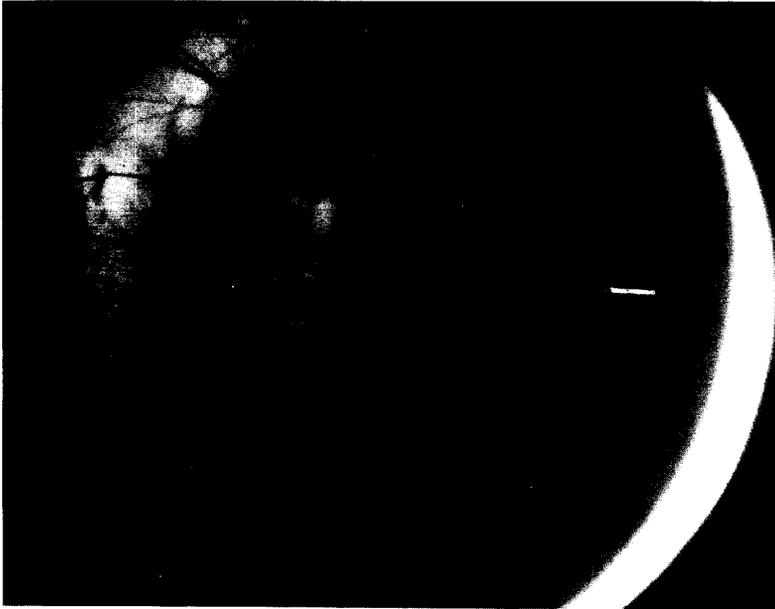


FIGURE 13-35. Chorioretinal atrophy in the peripapillary (type III) staphyloma. There is virtually a complete obliteration of the lamina vitrea complex within the staphyloma, and even the border areas of the fundus are involved.

FIGURE 13-36. Chorioretinal atrophy in the nasal (type IV) staphyloma, left eye. Extensive degeneration involves the nasal, ectatic tissues. These staphylomas usually do not show substantial degrees of ectasia. Although the maculae in these eyes appear normal, they occasionally undergo degenerations, which include Fuchs' spot formation.

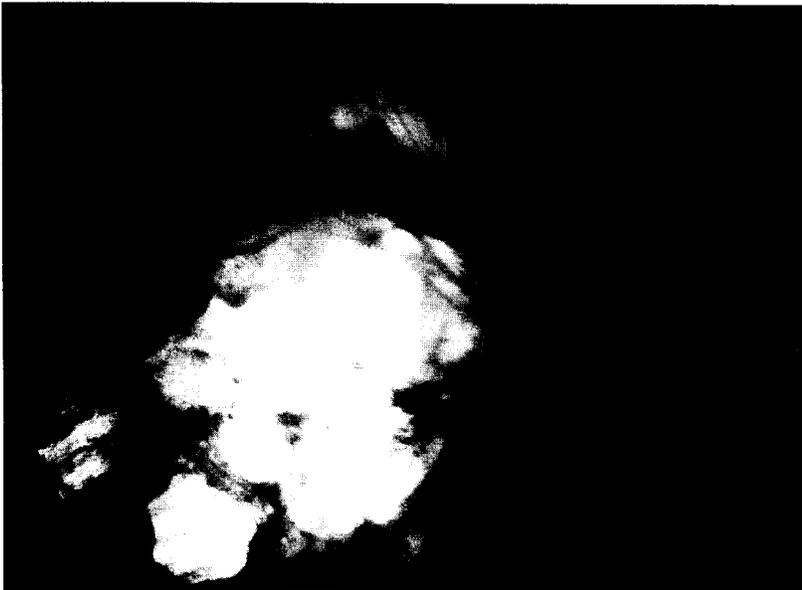




FIGURE 13-37. Chorioretinal atrophy in the inferior (type V) staphyloma. The disc is tilted inferiorly and the lower fundus is ectatic. There is extensive degeneration contiguous to the inferior crescent. This extends inferiorly along the course of a retinal vessel.

staphyloma margin, however (Color Figs. 13-5, 13-6).

The small, round areas of atrophy with sharp margins that are characteristic of the myopic fundus in youth eventually give way to more sweeping changes. The lesions in adults are larger in diameter and are compatible in size with the diameter of one or more lobules of the choriocapillaris. Some areas may have sharp margins while others do not. With time, all these areas demonstrate a strong tendency to join together into larger lesions, which can assume rather bizarre shapes. A variable amount of pigment may form at the margins of these areas, or clumps of pigment may come to rest within an area of coalescing lesions (Fig. 13-38; also stereophoto Figs. 13-49 and 13-50).

It has been noted previously that these atrophic zones are depressed, punched-out areas that show a loss of choroidal circulation. (See Chap. 11.) This loss is complete except for the survival of large-sized vessels, which

can be seen ophthalmoscopically to cross behind these areas. Retinal pigment absorption, migration, and proliferation are seen histologically with disorganization of the outer layers of the sensory retina. The pathologic change that is generally considered to be the basis for these extensive degenerative phenomena is the occlusion of choroidal end-arterioles. There is a generous collateralization of the choroidal circulation at the posterior pole.^{344, 369} This is especially so in younger persons.³⁷⁸ Age changes, with the loss of the collaterals, would impart a greater morbidity to choroidal arterial occlusions.

Even in the absence of frank arterial occlusions, the choroidal circulation is abnormal in high myopia. Fluorescein angiography and ocular pulse studies all reveal a retardation and diminution of choroidal blood flow in this disease.^{261, 266, 290, 306, 368, 382} The level of intraocular pressure may also play a role in the reduction of choroidal circulation. This circulation, unlike that of the retina, is not auto-



FIGURE 13-38. Wide-field photograph of "geographic" chorioretinal degeneration, left eye. Peripapillary atrophy with extension nasally over the tiered nasal wall of a compound (type VIII) staphyloma. Pigment clumping is present within and on the borders of the lesion.

regulatory; that is, it does not respond to increases in intraocular pressure by corresponding increases in its intravascular blood pressure. As a result, in the presence of increased intraocular pressure there is a reduction in choroidal perfusion pressure.²⁷⁰ Fluorescein studies reveal a susceptibility of the choroidal circulation to increases in intraocular pressure,^{264, 268, 275, 364, 379} a susceptibility most evident in the peripapillary area.^{274, 276} The glaucomatous peripapillary halo of atrophy has been attributed to this.^{340, 347, 380}

It would be a serious error to ignore the possible role of abiotrophic degeneration in pathologic myopia, however. Chapters 3 and 5 review the importance of the retinal pigment epithelium in the development of its contiguous choroid and sclera as well as the implications of a derangement of this process upon ocular development. Based upon such data, Blach²⁷² concluded that degenerative myopia is possibly one of "the commonest of the tapeto-retinal dystrophies." Jain and Singh³¹⁵ wrote of a gene for myopic degeneration that is distinct from that for axial elongation. Meyer³³¹ and Vontobel³⁷² also have ascribed a hereditary nature to the degenerative phenomena of pathologic myopia. In addition, recent laboratory experiments have indicated that destruction of the retinal pigment epithelium can

produce, in turn, atrophy of the choriocapillaris. Korte and colleagues^{318A} injected sodium iodate systemically in rabbits and caused patchy areas of retinal pigment epithelial breakdown. This was associated with loss of contiguous choriocapillaris, which showed degeneration of endothelial cells and the proliferation of dense pericapillary collagenous tissue.

One change that can be observed in the myopic eye that suggests a true heredodegenerative effect is the picture of choroidal sclerosis. The larger sized choroidal vessels in these eyes are clearly visible. They are pink or white and may be sheathed or have irregular lumina (see Color Fig. 13-7). However, it must be remembered that myopia frequently accompanies retinal pigment epithelial diseases. Choroideremia, gyrate atrophy, retinitis pigmentosa, and choroidal coloboma are examples of this. (See Chap. 5.) In a recent paper Giovannini and Colombati³⁰⁵ reviewed a number of cases of myopia in association with heredodegenerative disease. They concluded that the fundus lesions seen in these varieties of hereditary fundus degenerations are separate and distinct from lesions associated with ocular elongation.

Another pathogenetic pathway for the chorioretinal degeneration of high myopia re-

cently has been brought into clearer focus. Avila and co-workers^{266A} studied a large number of eyes with degenerative myopia by fluorescein angiography. They found that 42% of these eyes showed active subretinal neovascular membranes. In this longitudinal study a number of these membranes failed to provoke the formation of typical Fuch's spots, but remained nonpigmented. These were seen to involute eventually and form localized atrophic scars. This mechanism can account for some of the myopic degenerative changes of the macula and the region of the optic nerve, two areas in which neovascular membranes most commonly form.

Age is an indisputable factor in the pathogenesis of myopic degeneration; the older the patient, the more likely he is to show these changes.^{278, 289, 290, 351, 358, 371} The same can be said regarding the malignant effects of the degree of myopia. In recent years fundus degeneration has been specifically correlated with the increased axial diameter of the eye.^{279, 289, 352} It should be noted here, however, that in "axial length" measurement the depth of the posterior staphyloma is of prime importance. Donders,²⁹² with his usual perspicacity, recognized this well over 100 years ago. Recent studies at our myopia clinic confirm Donders' impression. All eyes of patients 40 years of age or older having posterior staphyloma have been found to display some degree of chorioretinal degeneration.²⁸⁹ Other studies at our clinic reveal that the level of intraocular pressure may also be related to the extent of cho-

rioretinal degeneration. Eyes with clearly elevated pressures have often been found to be disproportionately associated with extensive, "geographic-type" chorioretinal degeneration.

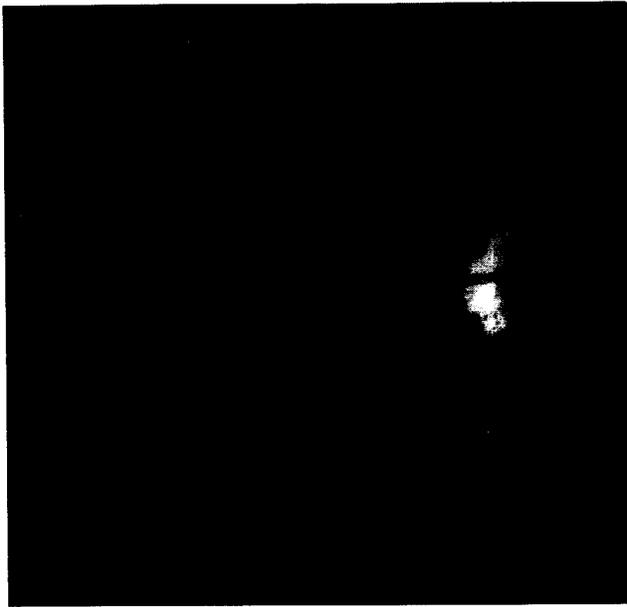
Reports of the prevalence of atrophy among myopic populations vary considerably as a result of the above factors; prevalences of 7.1%,³¹⁵ 23%,²⁸⁹ 36%,³⁴⁵ 38%,²⁷¹ 45%,²⁶² and 85%²⁶³ have been reported. In one study at our clinic all eyes of 31.5 mm and above in patients 40 years of age and older were affected. The relationship between myopic atrophy, age, and axial length is particularly evident in Table 13-16.

Subretinal Neovascularization. The formation of neovascular membranes between the retinal pigment epithelium and the lamina vitrea is a serious complication in high myopia. The thin-walled vessels and fibrous tissue that invade the subretinal space from the choroid through defects in the lamina vitrea are seen ophthalmoscopically as dirty gray patches at the posterior pole. These new vessels frequently leak a transudate or give rise to frank hemorrhage. The onset of transudation or hemorrhage is often associated with metamorphopsia. Extensive hemorrhage will usually produce a central scotoma and, while eventual absorption can take place, these episodes often act as trigger mechanisms for Fuchs' spot formation. These spots are round or elliptical black lesions that, as a general rule, occur in the macular area. Occasionally they may be eccentric to the macula, even occurring in the

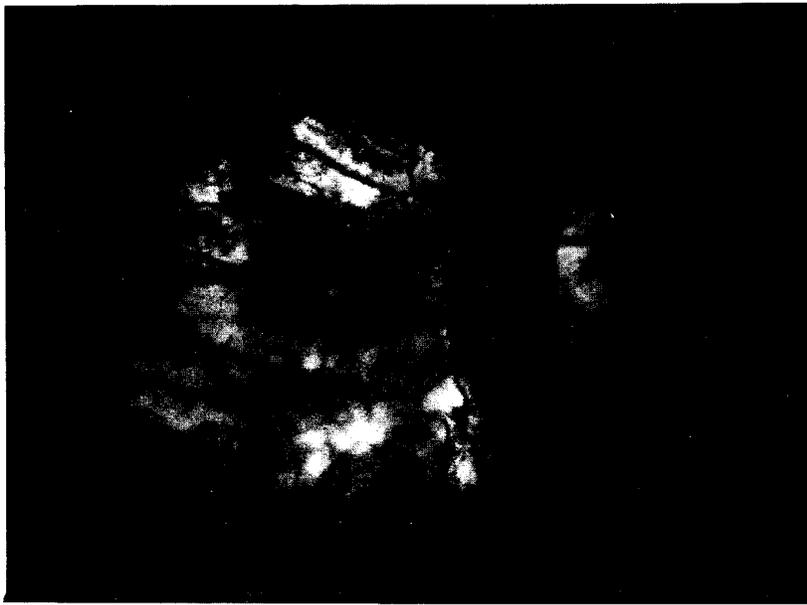
TABLE 13-16. Prevalence of Chorioretinal Degeneration in Myopic Eyes: Effects of Age and Axial Length of Eye

Axial Length (mm)	19 and below	Age (Yr) 20-39	40 and Above
27	0/76 (0%)	2/15 (13%)	16/44 (36%)
28	0/44 (0%)	5/26 (19%)	20/54 (37%)
29	1/18 (5.6%)	7/25 (28%)	20/39 (51%)
30	1/10 (10%)	6/17 (35%)	41/46 (89%)

(Curtin BJ, Karlin DB: Axial length measurements and fundus changes of the myopic eye. *Am J Ophthalmol* 71:42, 1971. Published with permission from The American Journal of Ophthalmology. Copyright by The Ophthalmic Publishing Company.)



A



B

FIGURE 13-39. (A) Fuchs' spot with extensive hemorrhaging from subretinal neovascular membrane in macular (type II) staphyloma. (B) Five years later an area of degeneration well in excess of the original hemorrhage now surrounds the remains of a lightly pigmented Fuchs' spot.

nasal fundus.²⁹⁹ They are usually slightly elevated and sharply circumscribed and vary in size from a fraction of a disc diameter to measurements well in excess of this (Color Fig. 13-8). The original clinical description of these lesions was contributed by Forster.²⁹⁶ Donders²⁹² also described this lesion in his text a few years later. It was Fuchs³⁰⁰ who gave the most comprehensive report of this entity, however.

At their onset the initial metamorphopsia may rapidly give way to loss of central vision. Subretinal hemorrhage, seen as a "rim" of subretinal blood about the lesion, is frequently observed with fresh lesions (Color Fig. 13-9). This finding was initially reported by Fuchs,³⁰⁰ and recent studies indicate that 65%³¹¹ to 78%²⁹⁷ of new cases are associated with hemorrhages (Fig. 13-39). Subretinal neovascular membranes may be demonstrated by fluorescein angiography in the majority of these eyes (Fig. 13-40).^{287, 297, 311, 324} Angiography may also reveal transmission defects and single or multiple serous leaks.³²³ Fuchs' spots appear in eyes with increased axial length, particularly those with posterior staphyloma.

The Fuchs' spot is caused by hyperplasia of retinal pigment epithelial cells over the subretinal neovascular membrane. Pigment absorption and migration may occur in time, together with changes in the hemorrhagic blood elements. Fibrosis of the neovascular membrane eventually takes place. Detachment of the overlying neurosensory retina may also occur early in the course of this lesion. All these events produce a number of changes in the morphology of Fuchs' spots. Their black color may change to gray. Yellow and reddish hues are sometimes seen.^{269, 280, 300} Emerald green spots, probably the result of hemoglobin changes, have been reported.³⁵⁹ Of all of these other colors, gray is seen most commonly; this has been thought to be the result of cystic degeneration.³²⁶ A more probable explanation is that this color is due to an overlying detachment of the neurosensory retina. For this reason gray Fuchs' spots tend to be larger than the darker variety.^{323, 324} Over a period of years Fuchs' spots undergo a gradual breakdown in

structure. The well-demarcated, elevated lesion flattens, its margins become indistinct, and pigmentation is lost. Frequently it becomes surrounded by a halo of fundus atrophy³²⁴ (Color Fig. 13-10).

At the end of its active course, the Fuchs' spot often lies within a large area of chorioretinal degeneration. The only evidence of its previous existence may be a certain amount of clumped pigment in the macular area (Fig. 13-41).

Fuchs' spots occur also in the absence of myopia. Their increased frequency in myopia may be related to the unusual macular hyperpigmentation that is often seen in these eyes early in life. The greater the degree of myopia, the greater the risk of their occurrence. Age is also a factor since these lesions usually affect persons over the age of 35. Fuchs' 50 patients ranged in age from 16 to 71 years, with an average of 42. Campos²⁸³ found an age range of 19 to 84 years, and his patients showed a myopia of from -8 D to -20 D. In younger patients, Campos noted that these lesions affected only highly myopic eyes. In the elderly, they occurred in eyes with relatively low myopia. At our clinic, 79% of affected patients were 40 years of age or older. These pigmented spots occurred only in eyes with an axial length of 26.5 mm or more (see Fig. 13-26). In a recent study from West Germany,²⁹⁷ an age range of from 14 to 66 years (median 41 years) was reported. In this series, age and the degree of myopia could be statistically correlated to show that these lesions occur earlier in eyes with higher myopic errors ($P < 0.05$).

Although Fuchs did not note a sex difference in his original report, most study populations of this lesion show a predominance of females: 4:1,²⁸³ 2:1,^{289, 297} and 3:2.^{266A, 311}

Fuchs spots are not uncommon among myopic populations. They are generally believed to affect from 5% to 10% of these patients. In Campos' large series of 950 patients with myopic correction of 5 D or more, 107 of these lesions occurred in one or both eyes (9.6%). Blatt²⁷³ found five cases of Fuchs' spot formation among 109 high-grade myopes (4.6%). If axial diameter is used as the criterion of



A

FIGURE 13-40. (A) Fuchs' spot with associated subretinal hemorrhage. (B) Fluorescein angiogram of same eye showing extensive late staining of lesion.



B

pathologic myopia (≥ 26.5 mm), 5.2% of eyes were found to be affected.²⁸⁹ Hotchkiss and Fine³¹¹ report 33 of 81 highly myopic patients (40.7%) to demonstrate subretinal neovascularization in their study. Dalkowska²⁹⁰ has re-

ported a 3% prevalence of Fuchs' spots and an additional 1.2% of patients with "serious maculopathy." Fuchs' spots do not appear to affect either eye preferentially.²⁸³

Frequently these lesions affect both eyes.



FIGURE 13-41. Involving Fuchs' spot. The original disciform lesion is now flat, and its pigmentation is mottled and irregular. Contiguous atrophy has appeared.

The length of the follow-up period can alter the reported frequency of bilaterality, however. Binocular Fuchs' spots have a reported incidence of 12%,³¹¹ 18%,²⁸⁹ 24%,³⁰⁰ 28%,²⁸³ and 41%.²⁹⁷ Involvement of the fellow eye may occur within a matter of days or years. Fuchs reported its occurrence to take place within a 5-year period. Campos²⁸³ obtained a range of from 1 month to 15 years. Fried and co-workers²⁹⁷ noted an average interval of 2.4 years between the formation of these lesions, with a maximum of 8 years. In cases of anisomyopia, the more myopic eye has a significantly higher risk of being affected ($P < 0.05$). Relatively lower degrees of myopia do not protect the fellow eye completely, since 44% of these eyes showed eventual involvement.²⁹⁷ In cases of high unilateral myopia, the outlook is quite different: Campos found that the emmetropic eye in such patients was not involved.

In view of the diffuse pathology found in the highly myopic eye, the association of other important fundus changes with Fuchs' spots is not unexpected. In addition to subretinal neovascular networks and hemorrhage, chorioretinal atrophy (84%), lacquer cracks (57%), and posterior staphyloma (43%) were reported

in one study.³¹¹ Another study reported 89% chorioretinal degeneration, 4% lacquer cracks, and 32% abrupt posterior staphyloma in eyes with Fuchs' spots.²⁸⁹

Since Fuchs' first report, the visual prognosis in eyes with pigment spots has been considered poor. There may be, and usually is, some degree of visual improvement after the acute process has passed. This can best be attributed to the absorption of the transudate and hemorrhage about the base of the lesion together with the establishment of a point of eccentric fixation closer to the fovea. With time, the breakdown of the spot and the appearance of a halo of atrophy around it produces an expansion of the central scotoma. This usually obliterates the retinal area used for eccentric fixation and necessitates the use of another area further removed from the fovea. This in turn causes a proportionate loss of visual acuity, often to the level of legal blindness (Fig. 13-42).

Two recent investigations appear to indicate that the prognosis for these eyes is not totally devoid of hope, however. Hotchkiss and Fine³¹¹ found that the final visual acuity could be related to the location of the subretinal neovascularization. In half of eyes with this mem-



A

FIGURE 13-42. Fuchs' spot with consecutive "halo" atrophy in a 35-year-old black female. (A) Fuchs' spot 6 months after initial appearance. A surrounding hemorrhage has absorbed. (B) Seven years later a distinct zone of chorioretinal degeneration has formed about the lesion, which exhibits depigmentation and a loss of definition at its margins.



B

brane located outside the foveal zone, the acuity reached 0.5 (20/40) or better. As the new vessels approached the fovea, the prognosis worsened, but even with this, 21% of affected eyes had visions of 0.5 or better. The follow-

up for this study was somewhat short, however—25.5 months.

A second study with a median 5-year follow-up of 36 patients reports an improvement in vision in 35%, a deterioration in 37%, and



FIGURE 13-42. (*continued*) (C) Four years later. The process of halo degeneration has continued at a reduced pace.

C

stable vision in the balance of eyes.²⁹⁷ This study found that the visual prognosis was related not to the degree of myopia but rather to three other factors: foveal involvement of the subretinal neovascularization, the recurrence of subretinal hemorrhage, and the persistence of subretinal neovascularization. Involvement of the fovea, that is, the normal avascular zone of the central retina, by the disease process occurred in 50% of eyes and reduced the vision to levels of 0.1 (20/200) or less. With resolution of the acute lesion the vision improved in 27% of these eyes to an average of 0.25 (20/80). On the other hand, progression of extrafoveal subretinal neovascularization may occur. This was seen to eventually involve the fovea in 22% of such eyes, followed by a reduction in vision to 0.1 or less.²⁹⁷

Rebleeds from subretinal neovascularization membranes were noted in 27% of eyes in this same study, and visual reduction followed as a consequence in more than half the affected eyes. Persistence of subretinal neovascularization was seen in 38% of eyes, and of these about three-fourths suffered further loss of acuity. This study also noted that the visual

prognosis was slightly better in youth ($P < 0.01$). These authors felt that the Fuchs' spot carries a relatively benign visual prognosis inasmuch as 41% of affected eyes retain acuities of 0.2 (20/100) or better, 70% retain 0.1 (20/200) or better, and 85% retain 0.05 (20/400) or better after an average 5-year follow-up.

This unfortunately has not been the experience of our myopia clinic population. In a large number of these eyes, long-term follow-up study reveals the disorganized Fuchs' spots to eventually lie within an enlarging halo of central chorioretinal degeneration. In these eyes, vision of 0.2 (20/100) or better is not common. In view of this we regard the long-term visual prognosis of eyes with Fuchs' spots to be guarded. A somewhat poorer prognosis has also been found in a study at Moorfield's Hospital. Hampton and co-workers³⁰⁹ report that 60% of all Fuchs' spots resulted in visions of equal to or less than 0.1. This study noted that the prognosis was worse with central neovascular membranes and better when these membranes were located a distance from the fovea.

Macular Changes

During this crucial intermediate stage of fundus alterations in myopia, the macula may show several changes. It has already been noted that the macula is frequently involved in the sudden and dramatic transudation or hemorrhage from subretinal neovascular networks. It may also be involved in the classic "myopic" chorioretinal atrophic process. In fact, the macula, in spite of its more generous choroidal blood supply, appears to be especially prone to the formation of atrophic lesions.³⁵⁴ The previous occurrence of lacquer cracks in the macular region may predispose the eye to these later degenerative changes, a sequel that has been noted earlier.

The least of the changes that affect the macula at this time is an increase in pigment granularity, which occurs with or without some degree of pigment clumping.²⁷³ The foveal reflex may also be considerably more difficult to discern. This can be attributed to retinal thinning and flattening in eyes with progressive staphyloma development at the posterior pole.

Macular degeneration in myopia occurs on an average of 16 years earlier than senile macular degeneration. It is often bilateral and appears to affect females more frequently.³⁰² Schweizer³⁵⁴ found 6.3% of all myopes to demonstrate degeneration of the macula, but in myopes of -20 D or more, all eyes were affected. Pigment rarefaction with small areas of degeneration was seen to affect 20.6% of myopic eyes in another recent study. An additional 4.7% showed extensive atrophy of the macula.²⁹⁰

Late Changes (Age 60 Years and Above)

It is during the later years of life that the chorioretinal degenerative process dominates the myopic fundus picture.

Posterior Staphyloma

Even with advancing age the myopic eye is not exempt from further development of the posterior staphyloma. The staphyloma may increase in depth with the formation of sharp

margins over a greater portion of the staphyloma perimeter.²⁸⁸ Primary staphyloma types I and II as well as all the compound varieties can be involved in this progression.

Optic Nerve Changes

With further expansion of the posterior segment there tends to be a continued flattening of the supertraction tissues. For this reason the Weiss streak is seldom seen. There is also an accentuation of the peripapillary atrophy, which commenced along the border of the crescent. The entire peripapillary area is now usually involved in all eyes with primary or compound staphylomas that involve the posterior pole. The disc, which earlier might have appeared somewhat pale, takes on pinker color compared with the surrounding white of the peripapillary bare sclera.

Chorioretinal Changes

Although the elongation of the majority of highly myopic eyes will stabilize, for the most part increasing age tends to enhance the fundus atrophy of the earlier stages. In addition to the accentuation of peripapillary atrophy, there is a confluence of atrophic areas at the posterior pole. The ultimate picture of myopic fundus degeneration is produced by the conjunction of the expanding atrophy in two primary areas: peripapillary and posterior pole (Figs. 13-43 and 13-44; Color Figs. 13-11 and 13-12). This process yields the classic fundus picture of bare sclera, which occurs within posterior staphylomas, especially those with marked ectasia (Figs. 13-45 and 13-46; also stereophoto Figs. 13-51, 13-52, and 13-53).

Macular Changes

The macular area in eyes with extensive posterior pole degeneration may occasionally be identified only by pigment clumping or the remains of a previous Fuchs' spot. In these latter cases a yellow cystlike area may sometimes be discerned. In eyes in which the posterior staphyloma does not involve the macula,

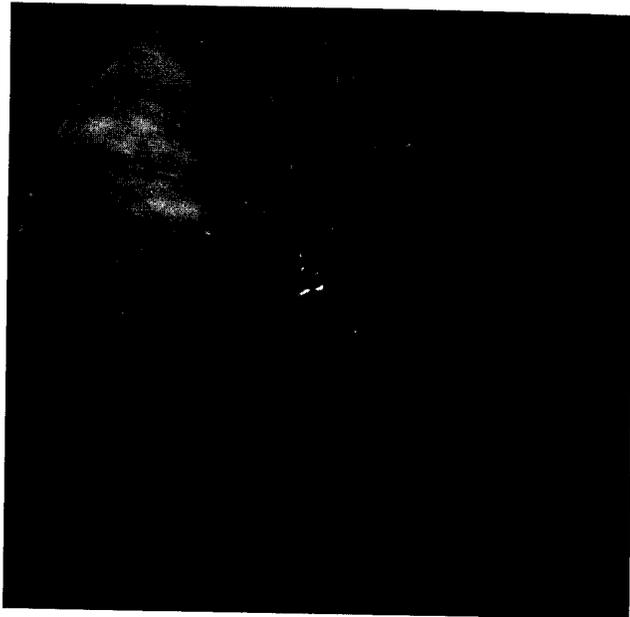
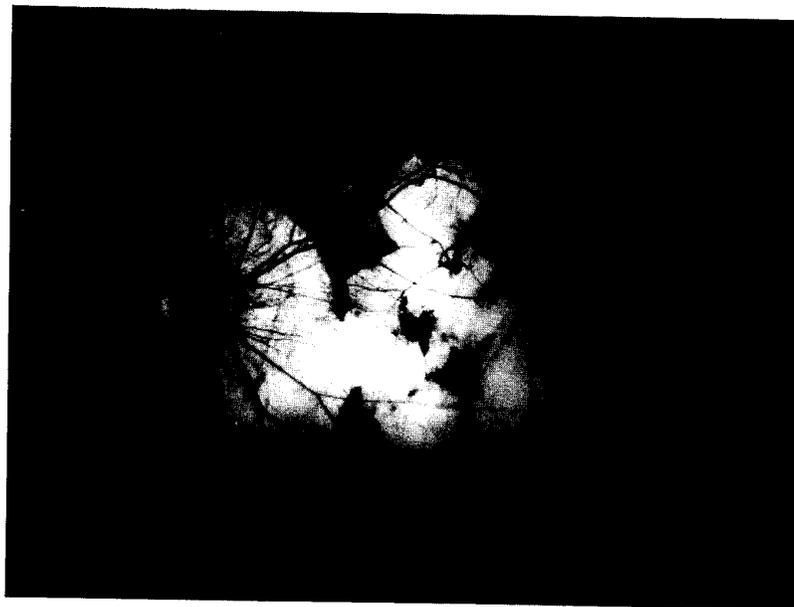


FIGURE 13-43. Progressive chorioretinal degeneration in a 50-year-old Caucasian, left eye. There is extensive atrophy extending out from the crescent area nasally. A large area of macular atrophy is also present, containing two large clumps of pigment on "bare sclera." A small island of intact choroid separates the two areas of atrophy.

FIGURE 13-44. Wide-field photograph of the same fundus shown in Figure 13-43, 14 years later. The two areas of atrophy, papillary and macular, have coalesced to form one extensive bilobular atrophic zone with irregular borders. The interlesional island of useful retina has been obliterated.



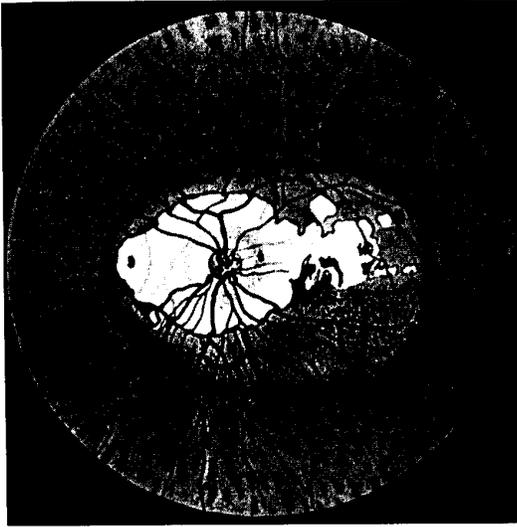
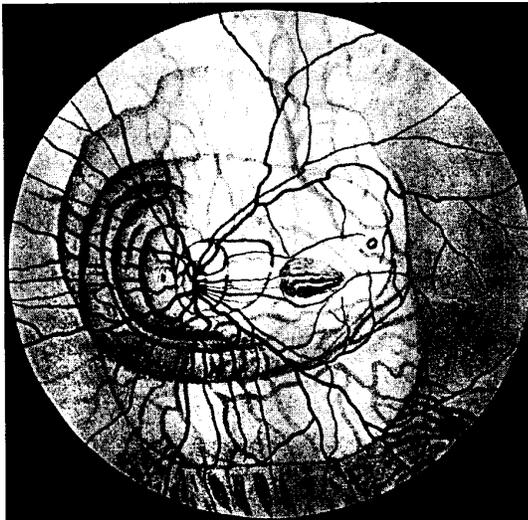


FIGURE 13-45. Artist's conception of a fully developed (grade 5) posterior pole (type I) staphyloma. Note the extensive chorioretinal degeneration within the confines of the staphyloma perimeter. In this eye there appears to be the typical merging of peripapillary and macular atrophic zones. (Siegrist A: *Refraktion und Akkommodation des Menschlichen Auges*. Berlin, Julius Springer, 1925)

FIGURE 13-46. Artist's conception of a compound (type VIII) staphyloma with an unusual degree of step development on the nasal wall of the lesion. (Siegrist A: *Refraktion und Akkommodation des Menschlichen Auges*. Berlin, Julius Springer, 1925)



such as types IV and V, the macula usually retains relatively normal function, although rarely a Fuchs' spot may occur in such eyes.

Ocular pathophysiology, being the important variable that it is in all eye disease, may greatly modify the character of myopic fundus changes. Rarely do bilateral cases show the same degree of staphyloma development, the same associated fundus changes, or the identical complications in both eyes. The stages of myopic fundus changes that have been reviewed here are arbitrary distinctions at best. The examiner must be prepared occasionally to find a Fuchs' spot in a 14 year old or lacquer cracks in late adult life. Only one constant affects all these eyes and that, unfortunately, is the grave threat of gradual or precipitous visual loss with advancing years.

Posterior Retinal Holes

Hole formation in the posterior segment of highly myopic eyes may occur at the macula or, less frequently, the juxtapapillary area. Rarely the staphyloma margin may be involved.

Round lamellar holes of the macula are not unusual in nonmyopic eyes. They occur as a consequence of aging, ocular vascular disease, inflammations, degenerations, epiretinal membrane formation, trauma, and glaucoma.²⁹⁴ They are not thought to have a significantly increased incidence in high myopia, but when present they do have a tendency to perforate.^{294, 328} A full-thickness defect such as this at the macula in the presence of the ubiquitous posterior vitreous detachment of myopic eyes sets the stage for posterior detachment of the retina.^{259, 295, 353} In one large study retinal detachments with macular breaks were seen almost twice as frequently in myopic eyes as in nonmyopic eyes.³²⁸ These full-thickness breaks are also seen with trauma and aphakia. Another factor that predisposes the myopic eye to posterior detachments is the staphyloma itself.^{339, 355, 356, 383}

Posterior detachments account for 1% or slightly less of all retinal detachments.^{328, 356}

Females may be slightly more predisposed to these incidents.³⁸³ In the nonmyopic eye, posterior detachments are, as a rule, self-limited. In highly myopic eyes they tend to be more extensive. Macular holes are associated with diminished visual acuity, and some degree of surrounding detachment can be found in a large number of these patients.²⁸⁷ The diagnosis can be facilitated by monochromatic fundus photography or biomicroscopy. Fluorescein angiography fails to reveal either leakage or pooling of dye.

Juxtapapillary breaks are rare and when seen occur in highly myopic eyes. These tears are small and usually located inferonasally to the disc margin in the vicinity of a retinal vessel. They have been attributed to vitreous pull upon adhesions to the retina in the area margegiani.³⁴¹ The retinal detachment is shallow and, if not stationary, shows only slow progression.

Rarely tears may occur at the margin of the posterior staphyloma. Phillips and Dobbie³³⁹ report such an instance among their nine cases of posterior retinal detachment. They attributed this break to vitreoretinal adhesions. Of their eight remaining cases, six were associated with macular holes and two with those in the juxtapapillary area. A posterior staphyloma was not present in two of these eyes (Fig. 13-47).

Fundus Abnormalities Secondary to Extraocular Disease

In view of the diversity and severity of fundus alterations in pathologic myopia, it is of interest that a number of morbid processes of the eyegrounds show a reduced incidence in these eyes. Such conditions are generally of a vascular nature, and it appears that the relative avascularity of the highly myopic eye protects it, in some measure, from the adverse effects of other diseases. Of greatest interest in this regard is diabetic retinopathy, which shows a markedly reduced incidence in myopic eyes.^{260, 314, 350, 370} In addition to diabetes, Paller and co-workers³³⁶ have also found a re-

duced frequency of hypertensive retinopathy, venous thrombosis, and, to a lesser extent, arterial occlusions in myopia. These authors also noted a reduction of such optic nerve derangements as papilledema.

The ophthalmologist is often asked about the potential untoward effects of pregnancy and labor upon the highly myopic eye. Some reports indicate that a normal pregnancy, *per se*, does not produce any deleterious effects.^{325, 384} Other reports indicate that a considerable morbidity can be associated with pregnancy and, especially, childbirth. Masci³²⁹ found an increase in the degree of myopia during pregnancy. This was proportional in some degree to the amount of myopia. Ivanov³¹² could detect no change in the refractive error of 100 highly myopic females during pregnancy. Repeated fundus studies, however, have demonstrated fresh atrophic areas in 6%, fundus hemorrhages in 2%, and rhegmatogenous retinal detachment in 2% of patients (192 eyes).³¹³

It is not unreasonable to assume that during a prolonged and difficult labor with Valsalva maneuvers and related activities, sharp, intermittent increases in the intraocular pressure occur, increases that can easily distend the ocular wall. This distention can have serious consequences in eyes with peripheral retinal changes and posterior staphyloma with preexistent stretching of the sclera and choroid. Link and Hudemanns³²⁵ suggestion of the routine use of forceps in the delivery of infants of highly myopic mothers would seem a prudent course of management in patients with portentous fundus changes.

THE PERIPHERAL FUNDUS

The chorioretinal changes occurring at the posterior pole of the myopic eye are very important, since they frequently reduce central vision to a level of legal blindness. The peripheral vision that is retained is usually sufficient for safe travel in familiar environs and, surprisingly, the patient may also be able to read. The

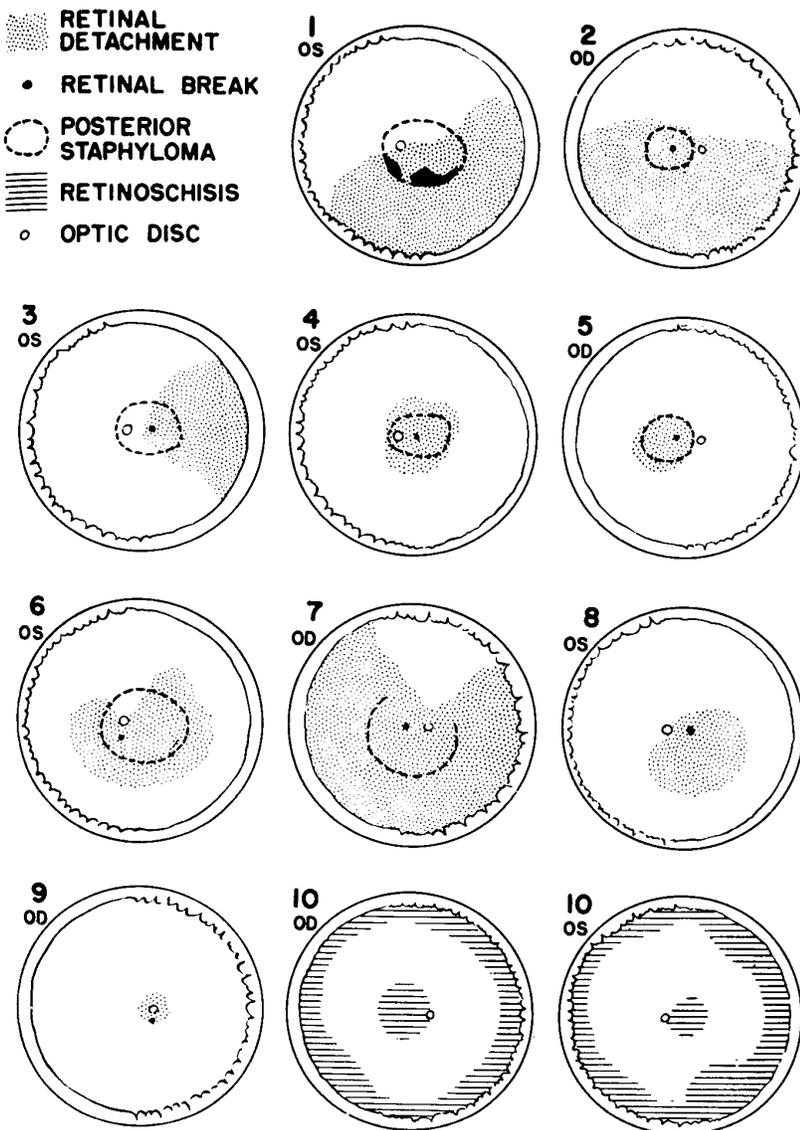


FIGURE 13-47. Location of retinal breaks and areas of retinal detachment in seven eyes with posterior staphyloma. (Phillips CI, Dobbie JG: Posterior staphyloma and retinal detachment. *Am J Ophthalmol* 55:332, 1963. Published with permission from the American Journal of Ophthalmology. Copyright by the Ophthalmic Publishing Company.)

fundus changes seen in the periphery of the myopic eye pose a more serious threat to vision. Many of these lesions can lead to total retinal detachment and the complete loss of vision, an event much more tragic than the loss of central field.

Predisposition to Retinal Detachment

It has been noted previously that the normal postnatal expansion of the eye involves principally the oraequatorial area.^{462, 466} It has also been noted that the deepest of posterior staph-

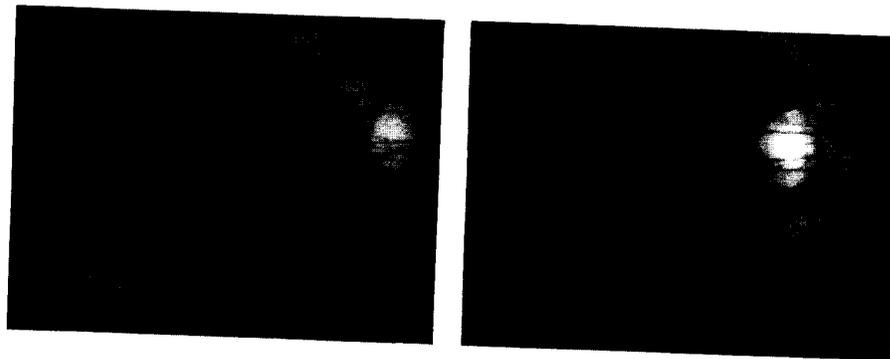


FIGURE 13-48. Stereophotographs of highly ectatic temporal segment of a compound type IX staphyloma in the right eye of a 28-year-old man. The vertical septum passes next to the temporal disc margin. Note the incipient fine focal areas of chorioretinal atrophy over the posterior pole.

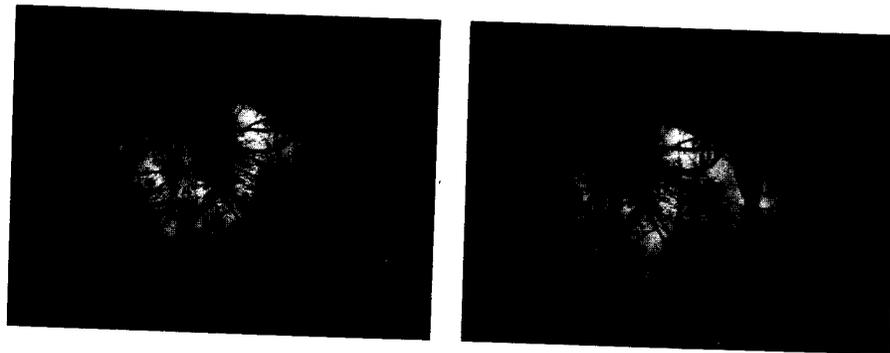


FIGURE 13-49. Left eye of a 52-year-old woman. Wide-field stereophotographs of compound staphyloma show steplike nasal wall as well as a plica that involves the superonasal retinal vessels. Note the reduced degeneration of the less ectatic fundus of the plica.

FIGURE 13-50. Right eye of a 58-year-old man. Wide-field stereophotographs of compound staphyloma that shows gradations in nasal wall ectasia and two plicae of the nasal vessels.



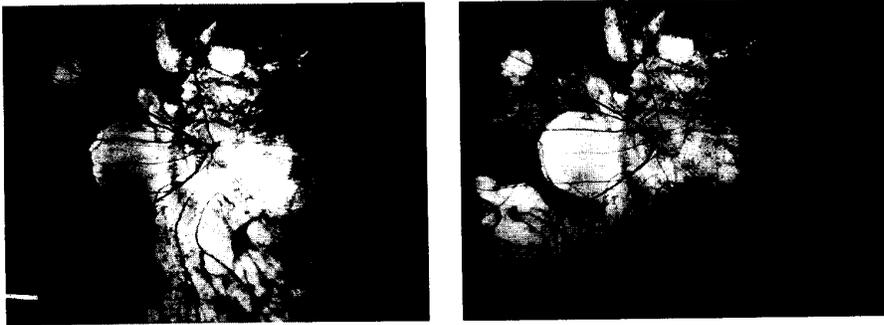


FIGURE 13-51. Wide-field stereophotographs of compound type IX staphyloma in the right eye of a 64-year-old woman. A vertical septum can be seen temporal to the disc, dividing the posterior staphyloma into nasal and temporal segments. The nasal segment appears the deeper of the two.

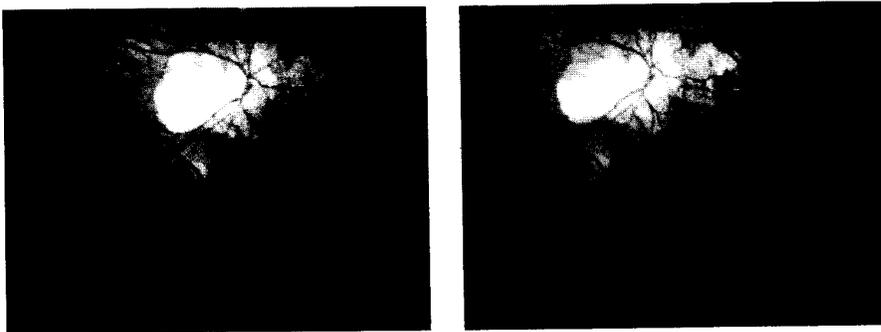
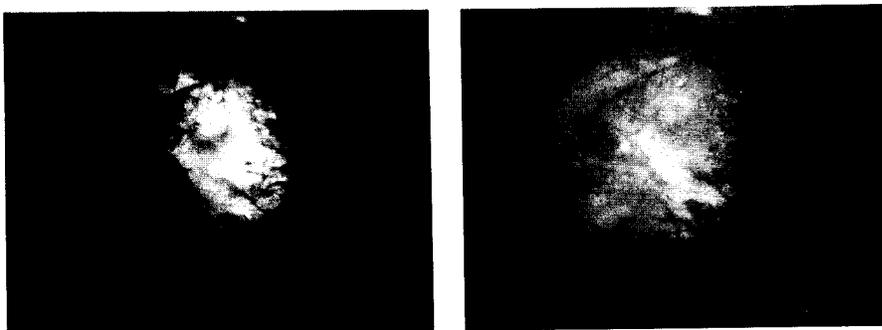


FIGURE 13-52. Wide-field stereophotographs of deep posterior pole (type I) staphyloma in the right eye of a 63-year-old man. Note marked tessellation and pallor of posterior pole as well as extensive peripapillary degeneration.

FIGURE 13-53. Wide-field stereophotographs of end-stage staphyloma development and chorioretinal degeneration in the left eye of a 67-year-old man. Almost the entire choroidal circulation has been lost in this advanced, deep type I staphyloma. This patient also gave a history of poorly controlled glaucoma.



ylomas rarely measure more than about 6 mm. For globes with increased axial diameters, there must be an extensive expansion of the oraequatorial zone even in the presence of a very deep staphyloma. This expansion process is associated with important changes that are seen in the periphery of the fundus. A number of these changes are associated with retinal breaks. These breaks, under certain circumstances, may lead to retinal separation. Autopsy and clinical observations indicate that about 6% or 7% of eyes have retinal breaks. Since the yearly incidence of phakic retinal detachment is only about 5 to 10 persons per 100,000 population (0.005%–0.010%),³⁹⁰ it is apparent that not all eyes with retinal breaks will undergo retinal separation. Other ancillary factors increase the probability of detachment. Among the most important of these are posterior vitreous detachment and retinal traction. The myopic eye, as we know, undergoes posterior vitreous detachment earlier than other eyes. By virtue of its increased incidence of lattice degeneration and its increased association with a number of other vitreoretinal diseases, the myopic eye is also more likely to have areas of vitreoretinal adhesions. Other factors may also predispose the myopic eye to detachment. Choroidal ischemia, a common finding in high myopia, is sometimes found in areas of retinal breaks,⁴⁶⁵ and the characteristically thinned myopic retina enhances the likelihood of full-thickness breaks.^{390, 446} Glaucoma is also generally acknowledged to be a predisposing factor to retinal detachment.⁴¹⁰ The increased prevalence of this disease in myopia has already been reviewed. Genetic factors may also increase the representation of myopia in detachment populations. A pedigree of hereditary high myopia with retinal detachment has been reported by Gillespie and Covelli.⁴¹⁸ Four generations of 138 patients demonstrated a 35% prevalence of high myopia. One third of these myopic patients suffered detachment of the retina (16 patients), whereas only two others in the pedigree detached. An autosomal dominant transmission appeared likely (see Fig. 5-26).

In view of the above, it is little wonder that

retinal detachment has been repeatedly found to be a frequent complication of myopia since the days of von Graefe. A large number of authors have noted the disproportionately high representation of myopic refractions among detachment populations. Prevalences of 35%,⁴⁵³ 42%,³⁸⁹ 48%,³⁹² 51%,⁴⁵⁵ 53%,⁴⁶⁴ 58%,³⁸⁷ 60%,⁴⁴² 61%,⁴⁶⁸ 62%,⁴⁵⁷ 64%,⁴⁴⁷ 65%,⁴³⁴ 67%,⁴¹³ and 79%⁴²⁰ have been reported. These figures are far in excess of the normal representation of myopic refractions in the general population.

Other investigators have studied the incidence of retinal detachment among myopes. Detachments have been found to affect substantial proportions of myopic persons: 0.7%,⁴⁴⁸ 1%,^{417, 422} 1.2%,³⁹³ 2.5%,⁴⁵⁴ 3.2%,⁴²¹ 3.5%,⁴²⁵ 4%,³⁹⁴ 5%,³⁸⁷ and 6.6%.⁴²⁷ Bohringer³⁹⁴ estimates the lifetime risk of retinal detachment in a person with myopia of greater than -5 D who lives to age 60 to be 2.4% compared with .06% for the emmetrope. In a study of asymptomatic myopic eyes, full-thickness retinal breaks were found in 11%.⁴²⁶ Perkins⁴⁴⁷ has dramatically demonstrated the increased risk of detachment in myopia. The substantial increase in the risk of detachment in the higher grades of myopia is clearly evident in his data (Tables 13-17 and 13-18).

There appears to be general agreement that the higher the myopia, the greater the probability of retinal detachment, although the studies of Cambiaggi⁴⁰⁰ and Schepens and Marden⁴⁵³ did not find the dramatic effects of the highest grades of myopia reported by Gonin⁴²⁰ and Arruga.³⁸⁷ These latter studies found that 52% and 55% of myopes with detachments showed refractions of over -8 D. The expected proportion of this level of myopia in the general population is less than 1%. Schepens and Marden⁴⁵³ found an elevated prevalence of detachment of 25% among highly myopic eyes in their study (Table 13-19). These same authors noted that highly myopic males were significantly more likely to develop retinal detachment and that these myopic detachments occurred earlier than in the general population. Kaufmann⁴³¹ has also found an increased representation of higher

TABLE 13-17. Probability of Retinal Detachment for Various Refractions

Refraction (D)	Number of Patients	Number of Detachments
+5.00	1,540,000	24.2
0 to +4.75	47,025,000	961.4
0 to -4.75	5,714,000	857.7
-5.00 to -9.75	715,000	535.6
≥ -10.00	55,000	371.6

(Perkins ES: Morbidity from Myopia. Sight Sav Rev 49:11, 1979)

TABLE 13-18. Detachments per Year in Population of 55 Million

Refraction	No. at Risk of 100,000	Incidence of Detachment	Probability of Detachment
+5.00	2,800	0.044	1/63,636
0 to +4.75	85,500	1.748	1/48,913
0 to -4.75	10,390	1.5595	1/6,662
-5.00 to -9.75	300	0.9735	1/1,335
≥ -10.00	100	0.675	1/148

(Perkins ES: Morbidity from Myopia. Sight Sav Rev 49:11, 1979)

TABLE 13-19. Comparison of the Incidence of Retinal Detachment and Degree of Myopia in Three Study Populations

Degree of Myopia (D)	Myopia and No Retinal Detachment		Myopia and Retinal Detachment					
			Arruga ³⁸⁷		Gonin ⁴²⁰		Schepens and Marden ^{453*}	
	No.	Percent	No.	Percent	No.	Percent	No.	Percent
≤4.0	9,935	73.6	96	24.1	39	16.5	241	45.2
Over -4.0 to -8.0	2,226	16.6	83	20.9	75	31.6	166	31.2
> -8.0	1,344	9.8	219	55.0	123	51.9	126	23.6
Total	13,505	100.0	398	100.0	237	100.0	533	100.0

* A total of 13,505 eyes from four studies cited by Schepens and Marden.

(Schepens CL, Marden BA: Data on the natural history of retinal detachment. Am J Ophthalmol 61:213, 1966. Published with permission from The American Journal of Ophthalmology. Copyright by The Ophthalmic Publishing Company.)

grades of myopia in retinal detachment, in addition to its earlier onset. Meyer-Schwickerath and Gerke^{438A} have contributed a recent study of particular interest in this regard. They measured the relationship between axial length,

equatorial diameter, and ocular volume in four groups of eyes: emmetropic, emmetropic with retinal detachment, moderately myopic with retinal detachment, and highly myopic with retinal detachment. They observed that eyes

with detachment, regardless of refraction, differed significantly in their dimensions from the emmetropic controls. Eyes with detached retinas were of substantially greater size, but in particular, they showed a significant increase in equatorial diameter. This study would indicate that measurement of equatorial diameter is equally important as measurement of axial diameter in the evaluation of the myopic eye.

Bilateral detachment of the retina has been found to involve from 8% to 32% of myopic patients. These high incidences may be due to the fact that persons seen at the clinic have been referred by their physicians, since more recent reports indicate a lower incidence of about 10% in nonreferral populations.^{405, 407, 436} The prevalence of bilateral retinal detachment is also seen to increase in the higher orders of myopia. Cambiaggi⁴⁰⁰ found 14% of persons with myopia of -8 D and less to have bilateral detachments compared with 20% of those whose refractions are above this level.

Peripheral Retinal Changes

Four types of peripheral fundus abnormalities are found in association with increased axial elongation of the eye. These are white-without-pressure, lattice degeneration, pigmentary degeneration, and pavingstone degeneration. Each has a distinctive morphology that tends to change with time. Some are frequently associated with retinal breaks and detachments, while others are not.

White-Without-Pressure

The term white-without-pressure refers to geographic, gray or white areas that tend to run circumferentially in wide swathes about the retinal periphery (see Color Fig. 13-13). They may be flat or they may have an elevated appearance much like a beach or snowbank. They often show bizarre shaped, irregular distributions that cover almost the entire periphery, but small focal patches may also be found, notably in the region of the vitreous base and

at the ora serrata. The temporal quadrants, particularly the inferior, are most likely to be involved. These lesions, when flat, may be found well posterior to the equator and even reach the retinal vascular arcades at the posterior pole. They often are covered by glistening yellow white dots and fine lines. These dots are similar to those described in the overlying vitreous of lattice lesions,³⁹⁷ retinoschisis,⁴⁵⁸ and snowflake degeneration.⁴²³

This unusual fundus picture was first described by Schepens,⁴⁵² and it is considered by many to be an advanced form of white-with-pressure, a characteristic blanching of the affected retina when subjected to scleral indentation.⁴⁵⁰ White-with-pressure is almost invariably found in areas of lattice degeneration and about small retinal breaks. It is also seen in the attached retina of eyes with detachments and in their "normal" fellow eye as well as in eyes with posterior vitreous detachment.⁴⁶⁹

Nagpal and co-workers⁴⁴¹ found that all their patients with white-without-pressure had posterior vitreous detachment but not in the affected areas. Here the vitreous appeared to be in contact with the retina.

In addition to vitreoretinal adhesions, a substantial number of retinal disorders are capable of giving rise to this picture. These are extensive cystoid degeneration, separation of the vitreous cortex from the retina with the production of new collagen fibrils in the interspace,⁴¹⁶ alterations of the retinal internal limiting membrane and posterior hyaloid membrane with increased light reflection,⁴³⁸ condensations of the cortical vitreous,⁴⁰⁴ as well as retinoschisis, pars planitis, retrolental fibroplasia,⁴⁶³ snowflake degeneration,⁴²³ and flat retinal detachment. Most retinal specialists attribute white-without-pressure as seen in most eyes to vitreoretinal traction.

Figure 13-54 demonstrates the increased prevalence of this disorder from 0% in the shortest eyes to levels as high as 54% at the 33 mm length. The dramatic association of this lesion with patients under 20 years of age is also demonstrated. In these younger patients, all eyes measuring 33 mm or more showed this change. The overall prevalence of white-

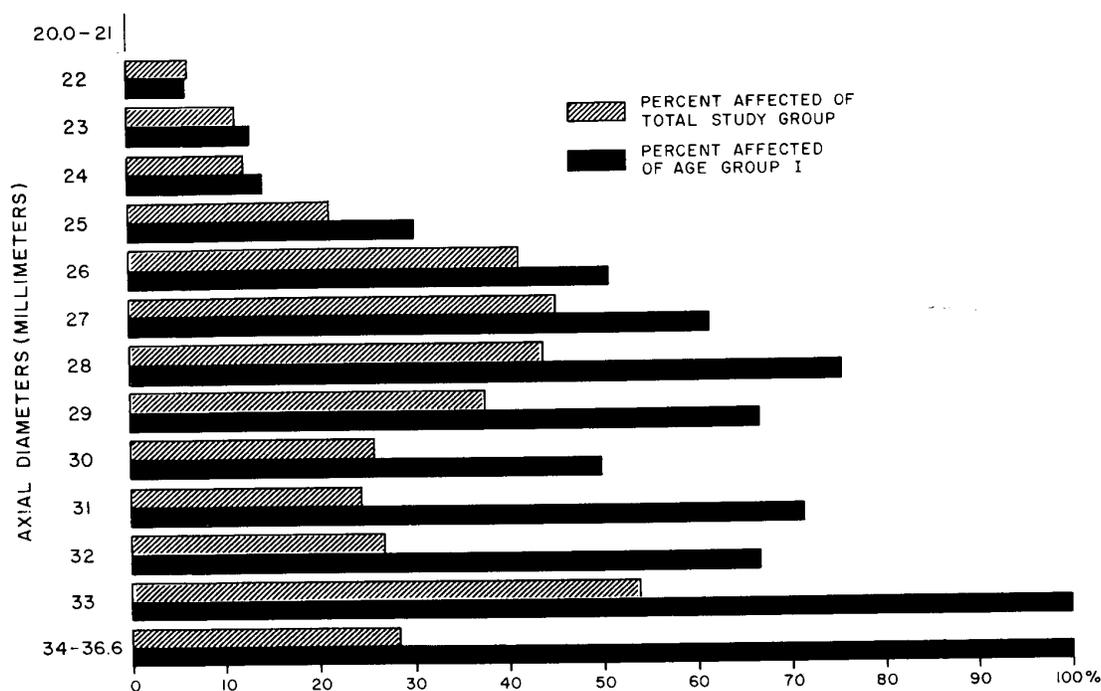


FIGURE 13-54. The prevalence of white-without-pressure in eyes of various axial diameters. Hatched bars indicate percent affected in entire study population; the solid bars indicate the percent affected in the age-group of greatest prevalence, those under 20 years. (Karlin DB, Curtin BJ: Peripheral chorioretinal lesions and axial length of the myopic eye. *Am J Ophthalmol* 81:625, 1976. Published with permission from the American Journal of Ophthalmology. Copyright by The Ophthalmic Publishing Company.)

without-pressure in eyes of patients below age 20 has been found to be 36%, and an almost equal number of patients, 35%, are affected between the ages of 20 and 40 years. The prevalence is reduced sharply in patients over 40, of whom 9.5 are affected.⁴³⁰ This sharp reduction suggests that this lesion may change with time, and Nagpal and co-workers⁴⁴¹ have noted the migratory tendency of these lesions in patients with hemoglobinopathies. In addition, this type of lesion has been found in a large number of patients with sickle cell anemia and in a smaller number of controls by Condon and Serjeant.⁴⁰⁴

Areas of white-without-pressure tend to be isolated fundus findings, but when associated with other changes they are most likely to be seen with lattice degeneration. This is particularly so in the young, in whom lattice lesions

are usually located along the posterior border of the white-without-pressure area or, less commonly, within it and oriented parallel with its posterior margin. White-without-pressure has an increased prevalence among blacks and prematures.

This peripheral change is essentially a benign lesion. When elevated, however, as in retinoschisis, small round holes may form within these areas and lead to retinal detachment. These detachments tend to progress slowly and contain a viscous subretinal fluid.⁴²⁹

Lattice Degeneration

Unquestionably, the changes that are classified as lattice degeneration are the most important lesions of the peripheral retina in myopia. Al-

though it is the least frequent of the four major peripheral changes, it is closely associated with retinal breaks and detachment.

Lattice degeneration was first described by Gonin in 1904.⁴¹⁹ It appears as linear or spindle-shaped areas at, or peripheral to, the equator. These patches are sharply demarcated and oriented circumferentially. A variable amount of pigment is seen with these lesions, which is probably due to proliferation into the inner retina of retinal pigment epithelium.³⁹⁰ An extensive range of pigmentation can be seen. Some lesions show no pigment whatsoever, while others become heavily pigmented. (See Color Fig. 13-14.)

The affected areas show retinal thinning early in their evolution, and there is liquefaction of the overlying vitreous. Condensations or irregular strands of vitreous are found attached to their well-defined borders. With time these vitreous adhesions become more apparent, and round holes also appear within the lesion. White interlacing lines are seen to cross the affected areas in some eyes. These correspond to retinal vessels with thickened or hyalinized walls and produce the classic lattice-like or pallsading appearance of the lesion.^{460, 461} Biomicroscopy often reveals glistening yellow white flecks on the surface of or adjacent to these areas. Lattice lesions have been observed to enlarge circumferentially, and new lesions may also form,⁴³⁵ especially in young patients.³⁹⁹

Lattice degeneration shows no progressive increase in prevalence with age and fails to show a sex preference. It is often bilateral (34%,³⁹⁷ 40%,⁴³⁰ 50%,⁴⁶⁰ 63%⁴⁴⁰) and preferentially affects the temporal quadrants, notably the superior^{388, 412, 430, 460} (See Color Fig. 13-14). The 12 o'clock and 6 o'clock meridians have also been found to be frequently affected.^{397, 399}

When present, lattice lesions are usually multiple, with the average number ranging from a high of 4.5 lesions at ages 20 to 29 to a low of two at 60 years and above.³⁹⁷ Their bilateral occurrence in patients with high unilateral myopia has suggested a hereditary etiology that is variably expressed with my-

opia.⁴⁷¹ Linear nonpigmented lesions that have a glistening, frostlike appearance suggestive of slime have been termed snail tracks, the "schnecken spurren" of Gonin. In general these lesions are considered to be a variant of lattice degeneration because they share the same location in the fundus as well as the tendency toward contiguous vitreous liquefaction, vitreoretinal adhesions, and retinal breaks. Aaberg and Stevens³⁸⁵ point out, however, that these lesions are not commonly seen with typical lattice degeneration and that they also lack both the pigmentation and white lines seen with such lesions. In addition, they are less common than lattice but pose a greater risk of retinal detachment.⁴⁰² Snail tracks may well constitute a separate pathologic entity, but in our clinic they have been classified as lattice lesions. This appears to be a common clinical practice,⁴⁴⁰ since the classic appearance of lattice with true white lines can be found in only 9% to 12% of eyes.^{397, 399} It has recently been suggested that snail-track degeneration is either a variant or an early stage of lattice.⁴⁵⁹

Lattice degeneration has been found in 6% of autopsy eyes⁴⁶⁰ and in 7% of asymptomatic eyes.³⁹⁷ Cambiaggi⁴⁰¹ has found prevalences of 4.5% in normals and 19% in myopic eyes. A Canadian study has noted lattice degeneration in 22% of highly myopic eyes.⁴³² It has been detected in 11% of eyes measuring 26.5 mm or more in axial length.⁴³⁰ Conversely, eyes with lattice degeneration show an increase in prevalence of the myopia: 63%⁴⁴⁰ and 73%.³⁹⁷ Fluorescein angiography reveals poor or absent perfusion in the affected retina, with occlusion of the retinal vessels at the posterior edge of the lesion.⁴⁶⁵

Lattice lesions form not only round holes within the confines of the lesion but also are prone to tears at the posterior margin and ends of the lesion. In one large study the majority of eyes demonstrating retinal breaks (55%) showed lattice degeneration.³⁹⁸ These breaks frequently lead to detachment of the retina. Retinal holes in lattice lesions are less likely to cause detachments (45%) than are tears (55%).³⁹¹ Retinal detachment secondary to retinal holes is commonly seen in the younger,

high myope, whereas detachments due to tears are more apt to be seen in the older, less myopic patient.³⁹¹ The detachments that occur secondary to atrophic holes in lattice degeneration show a distinctly more benign course than those due to traction breaks. A Japanese study notes that atrophic hole detachments are, as a rule, insidious in onset with only slow progression of a shallow detachment. The formation of demarcation lines is not uncommon in these cases. The risk of detachment in lattice degeneration with round holes was estimated at about 1 in 90.^{440A} Detachment of the retina can therefore be readily appreciated as a frequent sequel to lattice degeneration. Numerous studies of retinal detachment populations indicate an unusually high prevalence of lattice degeneration: 20%,⁴³⁹ 29%,³⁹¹ 30%,^{403, 412} and 38.5%.⁴⁴⁰ Among patients undergoing surgery for detachments or prophylaxis for retinal breaks, the proportion of lattice eyes has been

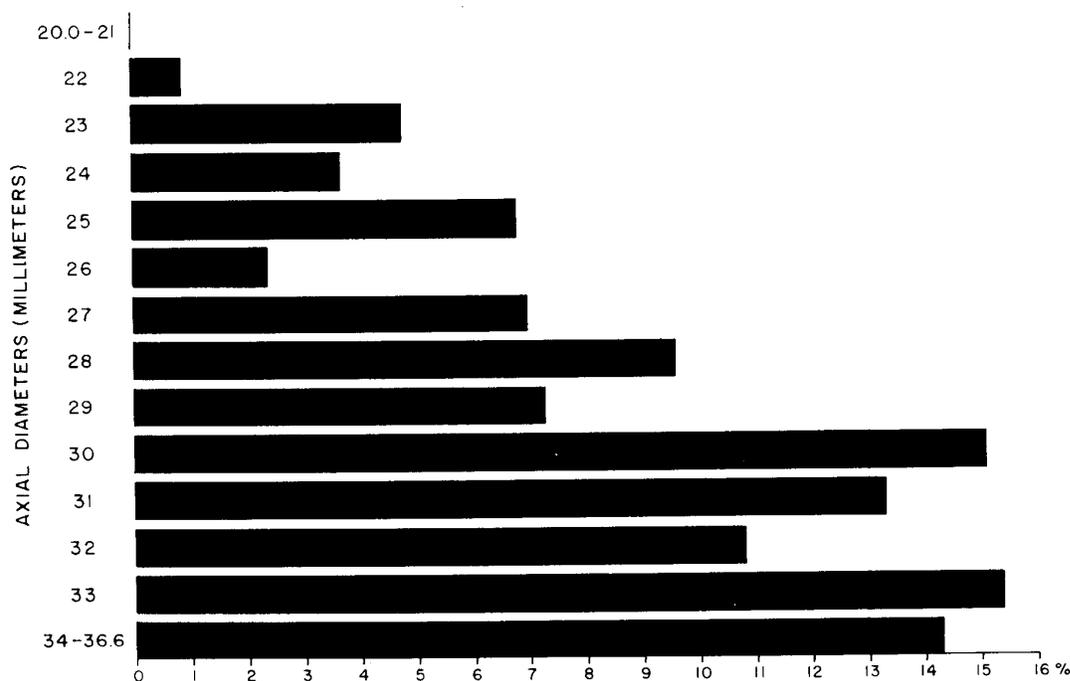
reported at 31%⁴⁶⁰ and even 65%⁴³⁷ Axial length measurements show that lattice lesions occur with increasing frequency in eyes of greater axial diameter (Fig. 13-55) ($P < 0.01$).⁴³⁰

Lattice degeneration frequently is seen in the presence of other forms of peripheral degeneration. In early life it is commonly associated with white-without-pressure. In midlife it is seen with both white-without-pressure and pigmentary degeneration. Over age 40 it is most frequently found in eyes with paving-stone degeneration.⁴³⁰

Pigmentary Degeneration

Of the various types of peripheral changes commonly found in myopic eyes, probably the least studied, and therefore the least understood, is pigmentary degeneration. It is found to affect an increasing proportion of eyes as

FIGURE 13-55. Prevalence of lattice degeneration at each axial length in patients of all ages. (Karlin DB, Curtin BJ: Peripheral chorioretinal lesions and axial length of the myopic eye. *Am J Ophthalmol* 81:625, 1976. Published with permission from the American Journal of Ophthalmology. Copyright by The Ophthalmic Publishing Company.)



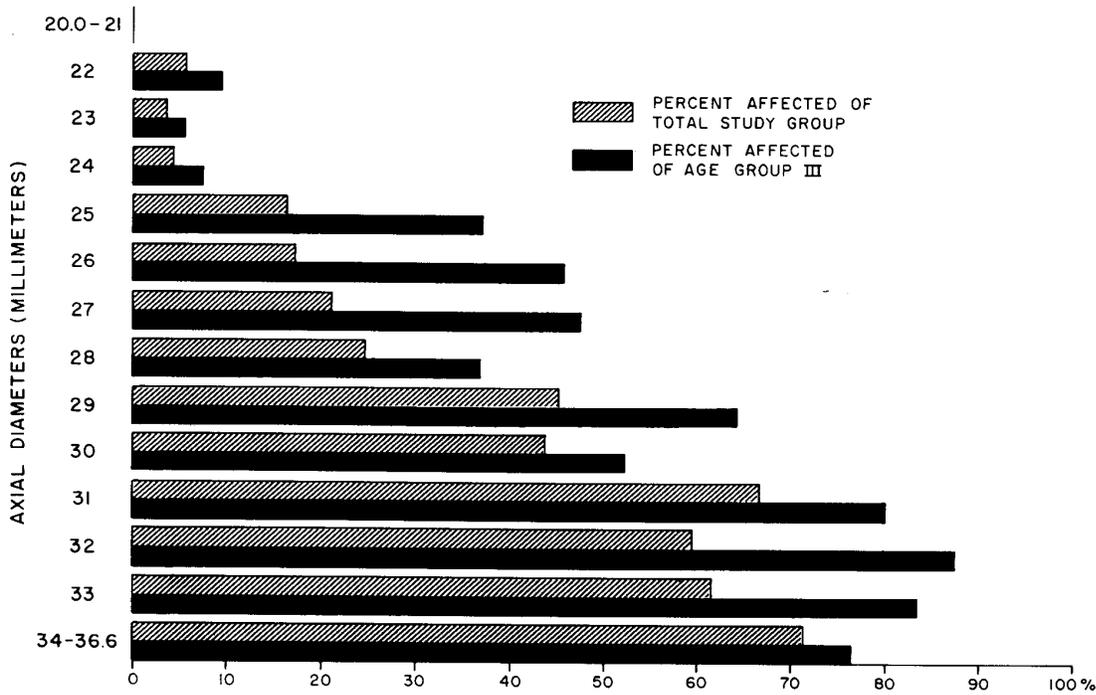


FIGURE 13-56. Prevalence of pigmentary degeneration at various axial lengths. Hatched bars indicate percent with such changes in total study population; solid bars are percentages for the most commonly involved age-group, those patients 40 years and older. (Karlin DB, Curtin BJ: Peripheral chorioretinal lesions and axial length of the myopic eye. *Am J Ophthalmol* 81:625, 1976. Published with permission from the American Journal of Ophthalmology. Copyright by The Ophthalmic Publishing Company.)

the axial diameter increases, progressing from a zero prevalence at 21 mm to 75% at the longest diameters ($P < 0.01$) (Fig. 13-56). Age is also an important factor in the development of these lesions, since they are encountered in only 6% of eyes in youth and 41% of patients age 40 and above ($P < 0.01$).⁴³⁰ In addition to age, vascular, inflammatory, and toxic agents may also play a role in their pathogenesis. Rehsteiner, however, noted this lesion in only 5% of myopic fundi. This figure probably reflects the findings that could be obtained by the examination methods that were available over 50 years ago.

With these lesions, a variable degree of pigmentation is seen in the extreme periphery. This pigmentation may vary from a fine diffuse darkening of the fundus to the presence of large discrete pigment clumps. The posterior

margin may extend several disc diameters from the ora and is usually indistinct. The border may be contiguous with a relatively depigmented zone of the fundus. (See Color Fig. 13-15.) This type of peripheral fundus change has a tendency toward bilaterality and apparently shows no sex preference. One study has found an increased prevalence of pigmentary degeneration in the myopic male, however.⁴³³ It has a slight tendency to be found with white-without-pressure in the younger patient, but in those over age 40 it is most commonly found with lattice degeneration.⁴³⁰ When seen in the presence of white-without-pressure, it gives the appearance of the lesion that Rutnin and Schepens⁴⁵⁰ term moderate or severe chorioretinal degeneration. The temporal halves of the peripheral retina are most commonly affected, especially in the superior quadrant. Lo-

calized pigmentation may also be noted anterior to the dichotomous terminal branching of the retinal vessels and, less often, in linear distribution alongside the retinal vessels peripheral to the equator.³⁸⁸ Some cases of focal pigmentation have been found to be bilateral and familial.³⁹⁶

The pigmentary deposition that is characteristic of this fundus change has been attributed to the migration and proliferation of retinal pigment epithelium. Biochemical irritation and retinal traction have been specifically incriminated as etiologic factors,⁴²⁴ while other authors have postulated a developmental anomaly of the pigment epithelium as its cause.⁴¹¹

Pigmentary degeneration of the retina can be associated with both retinal holes and tears.⁴²⁹ In Everett's⁴¹⁴ study of fellow eyes in patients with retinal detachment, 32% with this disorder were found to have breaks. Of itself it appears to be essentially a benign lesion, however, and its morbidity may be attributed more to unidentified areas of pigmented lattice and focal chorioretinal pigment clumping within these pigmented areas. Both these entities are prone to the formation of retinal breaks.

Pavingstone Degeneration

Pavingstone degeneration has been termed discrete chorioretinal atrophy⁴⁵⁰ punched-out chorioretinal degeneration,⁴¹⁴ and cobblestone degeneration.⁴³⁷ In the United States this phenomenon is generally referred to as pavingstone degeneration as designated by Meyer-Schwickerath.⁴³⁷ It was first described by Donders⁴⁰⁹ in 1855, and later Rehsteiner⁴⁴⁹ noted its clinical features also. Typically it is seen as small depressed, circular, yellow white areas located one disc diameter or two disc diameters posterior to the ora. These may measure from 0.1 disc diameter to 1.0 disc diameter in size. They may occur singly or in groups. With the latter, a tendency toward confluence can be found such that these lesions take on a linear shape with irregular scalloped borders. A variable amount of pigment is seen at their

margins, and large patent choroidal vessels often are seen to pass behind these areas (See Color Fig. 13-16). The inferior retinal quadrants, notably the temporal, are affected most frequently. Pavingstone degeneration is bilateral in 38%³⁸⁶ to 57%⁴³⁰ of cases. There does not appear to be a strong sex preference for this change, although one study has found males to be three times more likely to be affected.⁴⁵⁰

The prevalence of these lesions has a clear, statistically significant association with increased axial length of the eye ($P < 0.01$) as well as age ($P < 0.01$). In young persons, fewer than 1% of eyes are affected, whereas in myopic patients over 40 years of age, 40% show these lesions⁴³⁰ (Fig. 13-57). At autopsy 27% of persons over 20 years of age demonstrate these changes, and clinically they are seen in 30% of the general population over age 60.⁴⁴⁵

The cause of the pavingstone lesion is apparently vascular. The retina is thinned and shows a loss of rods and cones. The choriocapillaris is absent, especially in the center of the lesion. There is a union of the sensory retina and its underlying tissues. These adhesions often serve to delimit the progression of retinal detachments. No vitreous changes are noted in association with them. The retinal pigment epithelium is lost within their borders, and these cells are seen to proliferate at their margins.^{386, 445}

Pavingstone degeneration is a benign lesion of the peripheral retina and is not associated with retinal breaks. Everett's finding⁴¹⁴ that this lesion was present in 23% of the fellow eyes of eyes with retinal detachment reflects the normal frequency of this lesion in a group of patients with an average age of 53 years.

Retinal Holes and Tears

Retinal breaks are not uncommon in the general population. Autopsy studies reveal a substantial number of eyes to have these defects. Okun⁴⁴⁴ found 2.4% of eyes (4.8% of cases) affected, Boniuk and Butler³⁹⁵ reported 6.8% of eyes (8.7% of cases) involved, and Foos and Allen⁴¹⁵ 10.6% of eyes (18% of cases) with

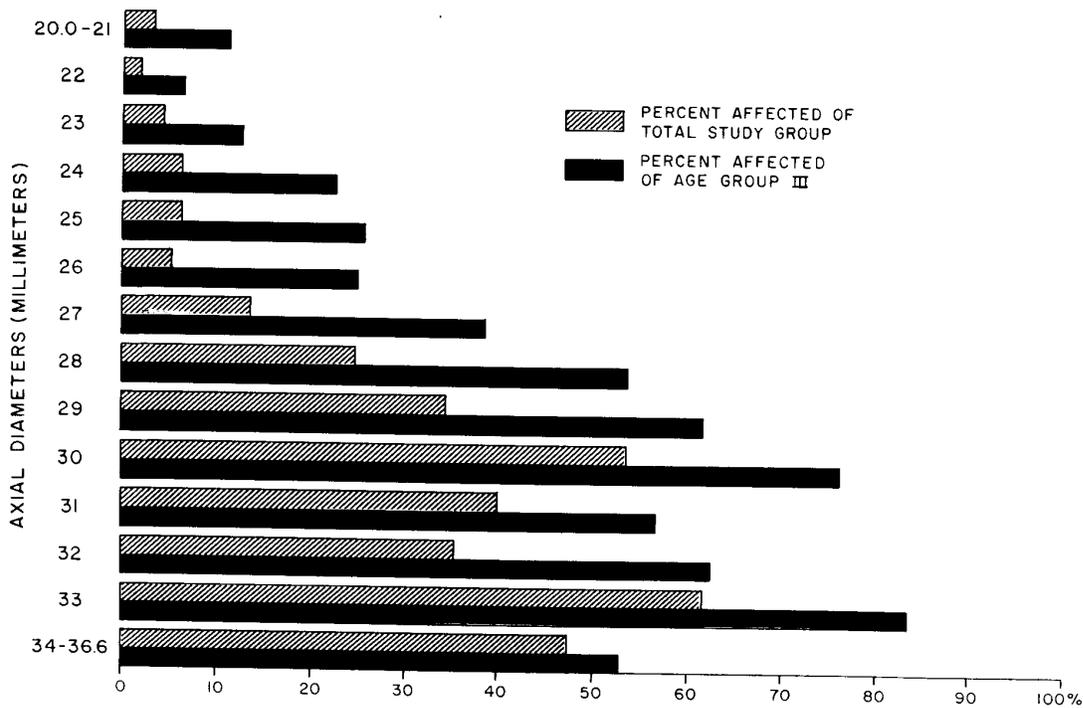


FIGURE 13-57. Prevalence of pavingstone degeneration at various axial lengths. Hatched bars represent percent of eyes with lesions in entire study population; solid bars are percentages for the age-group with the greatest frequency, those 40 years and above. (Karlin DB, Curtin BJ: Peripheral chorioretinal lesions and axial length of the myopic eye. *Am J Ophthalmol* 81:625, 1976. Published with permission from the American Journal of Ophthalmology. Copyright by The Ophthalmic Publishing Company.)

breaks. Clinical studies have obtained prevalences of 5.8%³⁹⁸ and 13.7%⁴⁵⁷ for randomly selected patients. Round holes have been found to outnumber tears by ratios of 1.4:1⁴⁵⁶ and 2.3:1.⁴⁶⁷

Of the four types of peripheral retinal changes that are commonly found in myopia, all but pavingstone degeneration may give rise to breaks. Cystoid degeneration is usually benign, but hole formation can occur in these areas.^{412, 426} Lattice areas, as has been noted, often give rise to round holes within the lesion as well as tears along its posterior margin and at its ends. Both holes and tears are seen in the presence of pigmentary degeneration.⁴²⁹ The retinal breaks in myopia tend to occur more frequently in the temporal quadrants.^{408, 429, 467} Breaks that are associated with symptoms (photopsia, vitreous floaters, smoky

vision) are usually associated with retinal traction. These breaks may be of the horseshoe (arrowhead) variety or they may be holes with overlying, avulsed opercula. The former were found to outnumber the latter in one study by almost 6:1, and one quarter of these eyes with symptomatic breaks may progress to detachment.⁴⁰⁵ Hyams and Neumann⁴²⁶ found 37 of a total of 332 asymptomatic myopic eyes to have retinal breaks (11.1%). The schematic analysis of the 48 breaks found in this study appears in Figure 13-58: 13 horseshoe tears and 35 round holes (9 with opercula). These breaks were related to age and, to a lesser extent, the degree of myopia (Table 13-20). In Tulloh's⁴⁶⁷ study of 451 patients with detachment, round holes were found in 344 myopic eyes and 172 nonmyopic eyes. Tears were noted in 37 nonmyopic and 185 myopic eyes.

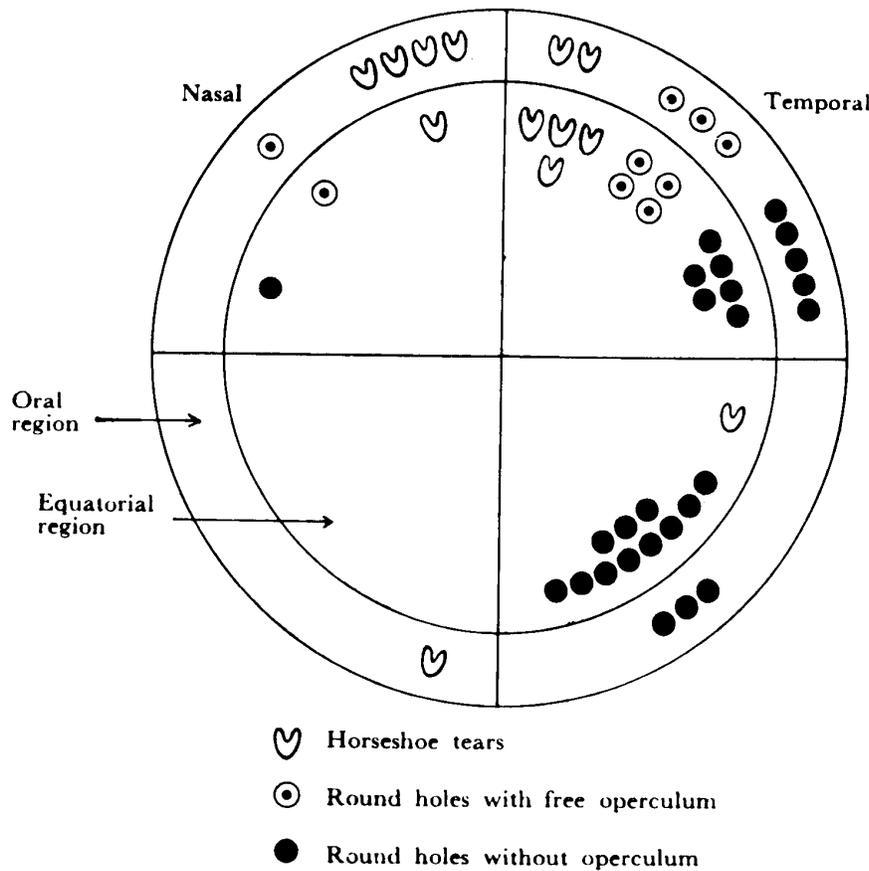


FIGURE 13-58. Schematic analysis of 48 asymptomatic retinal breaks (37 eyes, 34 subjects) detected on routine examination of 332 myopic eyes. Type of break and positions are indicated. (Hyams SW, Neumann E: Peripheral retina in myopia with particular reference to retinal breaks. *Br J Ophthalmol* 53:300, 1969)

The increased prevalence of tears in the myopic eye versus the nonmyopic eye (5:1) compared with holes (2:1) is indicative of the more serious vitreoretinal pathology of the peripheral retina in this condition.

Retinal breaks have been found to be related to increased axial diameter of the eye. In one study they were found in about 3% of eyes measuring between 22 mm and 25 mm. Above this level 11% of eyes were involved (Fig. 13-59).⁴²⁹

Giant retinal tears, those that extend for one or more retinal quadrants, may show an association with myopia. Norton and co-workers⁴⁴³ found 83% and Kanski⁴²⁸ found

71% of patients with giant tears to be myopic. Furthermore, in the latter series the myopia was exceeding high, greater than -20 D in 20% of the eyes.

Retinal dialysis, usually located in the inferotemporal quadrant, was found by Tulloh⁴⁶⁷ to affect 46 eyes of 451 patients with retinal detachment. Of these, 11 (24%) were myopic. In general these large disinsertions of the retina are the result of trauma, although congenital weakness of the retina, as in retinoschisis, may also be an etiologic factor.

One might also expect that retinal detachment associated with equatorial staphyloma of the sclera might be more prevalent in the my-

TABLE 13-20. Prevalence of Retinal Breaks in Myopic Eyes: Tabulation by Age and Degree of Myopia

Age (yr)	Degree of Myopia (D)			Total
	1-3	3.25-6.00	> 6	
10-20	0/19	5/60	1/15	6/94 (6.4%)
21-40	4/47	4/44	3/29	11/120 (9.2%)
41-65	7/39	7/46	6/33	20/118 (16.9%)
Total	11/105 (10.5%)	16/150 (10.7%)	10/77 (13%)	37/332 (11.1%)

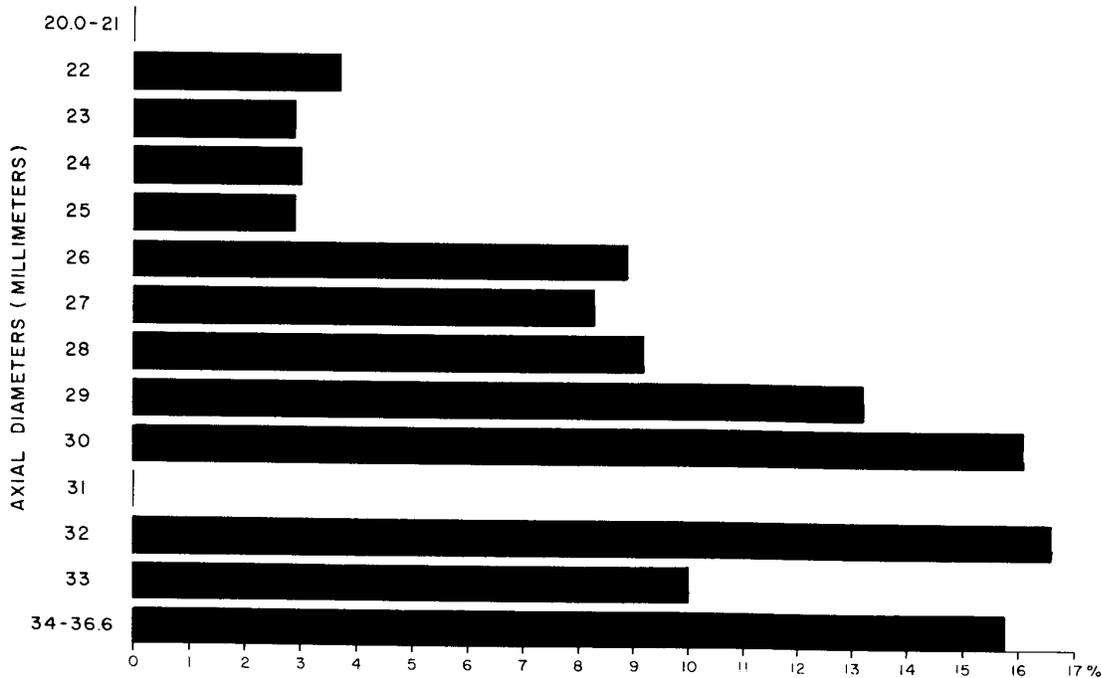
(Hyams SW, Neumann E: Peripheral retina in myopia with particular reference to retinal breaks. Br J Ophthalmol 53:300, 1969)

opic eye. This does not appear to be the case, however. Two studies have found the prevalence of myopia in these detachments to be 11%.^{406, 470} This figure is well below the expected prevalence of myopia in a detachment population.

The ophthalmologist must take pains to

carefully evaluate the retinal periphery in all patients with high myopia and in all myopic patients in midlife or beyond. One unusual finding that can be encountered in highly myopic eyes warrants mentioning here. This is the unusual configuration of the peripheral fundus in the horizontal midline. With extreme gen-

FIGURE 13-59. Prevalence of retinal holes at each axial diameter in patients of all ages. (Karlin DB, Curtin BJ. In Pruett RC, Regan CDJ [eds]: Retina Congress, p 639. New York, Appleton-Century-Crofts, 1974)



eralized ectasia of the sclera, the posterior ciliary nerves and vessels, resisting the ectatic process to some degree, indent the retina. This can give the appearance of the bow of a ship and might be mistaken for a vitreous band.

Examination of the highly myopic eye presents a special challenge to the conscientious ophthalmologist. The detection of retinal breaks and early detachments is substantially more difficult in the presence of fundus changes that are produced by widespread atrophy of the peripheral choroid and retina. Scleral depression and triple-mirror biomicroscopy become indispensable aids in the study of these eyes.

Visual Fields

Visual-field studies play an important role in the evaluation of pathologic myopia. They are of both diagnostic and prognostic value and of particular worth during the early stages of the disease. In actuality, visual-field changes are often the first and most serious functional derangement of these eyes.⁴⁷⁶ The changes are

not proportional to the degree of myopia but rather to the condition of the retina, the position and depth of posterior staphylomata, and the integrity of the optic nerve. Careful evaluation of visual field changes in the light of existing fundus findings can avoid the erroneous diagnosis of such ocular diseases as low tension glaucoma and atypical retinitis pigmentosa in addition to neurologic disorders.

Accurate measurement of the visual field in pathologic myopia is complicated by the high refractive error of the patient. Some types of visual-field changes can be markedly improved or eliminated by proper optical correction.^{474, 475, 495, 500, 501, 510} Jayle and Bérard⁴⁹⁰ noted the disappearance of field defects in 11 of 24 myopes (46%) with the correction of their refractive error. This is particularly true of hemianopic^{486, 505} and sector⁴⁷⁷ defects. An increase in minus spectacle eliminates or reduces these losses by virtue of producing an improved retinal focus in ectatic areas of the fundus^{481, 498} (Fig. 13-60). The minus spectacle lens itself is a source of visual field distortion, however. By effectively reducing the size of the test object by image minification, it gives rise to a certain degree of concentric contraction.⁵¹²

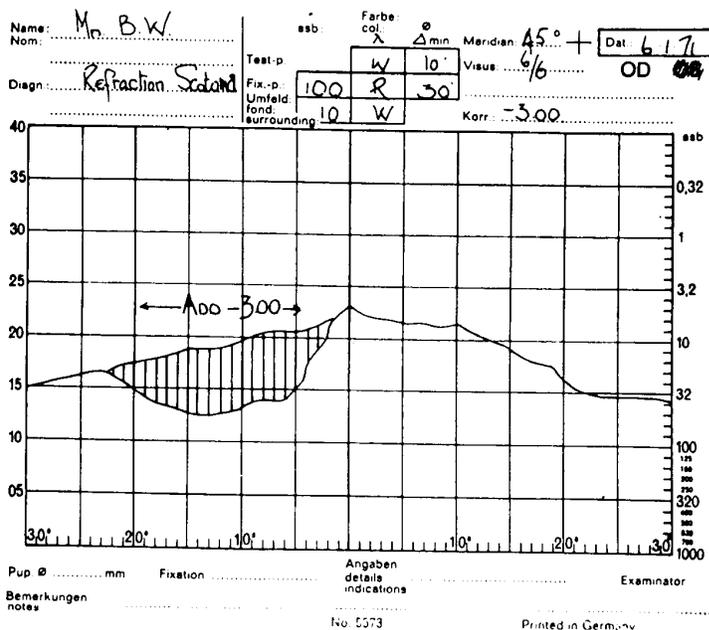


FIGURE 13-60. Minus spectacle correction of scotomatous field defect produced by local fundus ectasia. (Maguire C: Ametropia in the visual field. *Trans Ophthalmol Soc UK* 91:663, 1971)

The best method of correction for visual-field accuracy is the contact lens. Using this approach, Blach⁴⁷⁴ found that the field changes corresponded strictly with visible fundus lesions. No hemianopias or quadrantanopias could be detected in his small series of six patients. The effect of optical correction can best be appreciated by the report of Jayle and Ourgard.⁴⁹¹ These authors report a case in which a bitemporal hemianopia was plotted when no correction was used. With the patient's glasses, an enlarged blind spot and a superotemporal depression was found. With a contact lens, however, no defects could be discerned.

The visual-field defects in pathologic myopia have been attributed to a number of factors in addition to optical effects. Focal chorioretinal degeneration produces an absolute scotoma due to the destruction of retinal neuroepithelial elements. Disorientation of these cells, as on the sloping walls of a deep staphyloma, is another potential cause of scotomata. These would be in arcuate or annular forms. Retinal hypoplasia is another cause of visual-field depression in myopia. The reduction of neuroepithelial cells in these localized areas of the retina gives rise to relative scotomatous defects.^{486, 517} Lastly there is the question of optic nerve changes in the etiology of centrocecal and sector defects found in pathologic myopia. Hayreh⁴⁸⁸ has indicated that the prelaminar portion of the optic nerve circulation is derived from the peripapillary choroid. This area shows extensive ischemic atrophy in many cases of advanced myopia, and there is a conviction among some authors that certain defects, such as Bjerrum scotomata, are a result of this change.^{488, 516}

The stage of myopia may therefore have a great impact upon the severity of the field defects. With time there is an increasing amount of chorioretinal atrophy as well as the added occurrence of such central lesions as Fuchs' spots. Furthermore, the ectasia of the various posterior staphylomas also has a tendency to increase the disorientation of sentient cells and to further complicate the optical correction of the eye for visual-field testing. Accordingly,

one extensive longitudinal study found that early relative scotomata became absolute over a period of several years.⁴⁷⁶

The visual-field examination in myopia can be conducted under photopic or scotopic conditions. Tokoro and associates⁵¹² have found that the Goldmann targets of V/4, IV/1, III/1, II/1, and I/1 are of greatest value in myopia. Scotopic field testing may have particular merit in high myopia.^{489, 496, 497} In an occasional patient quadrant defects may be discovered that are not found under photopic conditions. These defects are independent of the refraction, adaptation, and fundus changes.⁴⁸⁹ Stargardt⁵¹⁵ was unable to find an appreciable difference in the results obtained with these two methods, however. Color fields do not appear to have any specific value. One study reported a reduction of retinal sensitivity to the longer wave lengths of light,⁵¹⁶ whereas another obtained a concentric contraction of the fields to both red and blue, the latter color showing a considerable increase in this effect.⁴⁹²

The visual-field defects found in high myopia are both central and peripheral. There are, in fact, few types of field changes that are not found in myopic eyes.

CENTRAL-FIELD DEFECTS

The defects of the central field of vision that present in eyes with high myopia are enlargement of the blind spot and central, paracentral, and arcuate defects.

Enlargement of the Blind Spot

Enlargement of the blind spot is an inconstant finding in myopia. Donders⁴⁸⁰ noted that a small stimulus placed upon the crescent of the myopic eye was not observed by the patient. He also found that in some cases the scotoma was somewhat smaller than the crescent and also that small crescents failed to demonstrate scotomatous defects. A number of investigators have drawn attention to the inconsistency of blind spot enlargement in myopia.^{472, 485, 503} There is little that is mysterious about this in-

consistency. Unless the disc is relatively flat or has a crescent of some size, it is not likely that an enlarged blind spot can be plotted. An oblique disc with a relatively small crescent in the absence of peripapillary atrophy will not project an increase in size. Parsons,⁵⁰⁷ citing Landolt, Dobrolowsky, and Volpe, indicates that the distance between the fovea and the center of the blind spot is reduced in myopia. This is attributed to a lateral displacement of the blind spot due to temporal crescent formation. Anatomical measurements in myopic eyes indicate that while there is a definite increase in the distance between the fovea and the disc margin, the distance between the fovea and the edge of the pigment epithelium is normal.⁵⁰⁷ The position of the blind spot must take into account the increased distance of the disc from the posterior nodal point, scleral stretching, and the obliquity of the retinal surface.⁵⁰⁷ Enlargement of the blind spot commonly occurs in association with depression of the superotemporal quadrant.^{484, 494, 502} These changes have been described as "typical" for myopia by Jayle and Bérard.⁴⁹⁰

Central-Field Scotomata

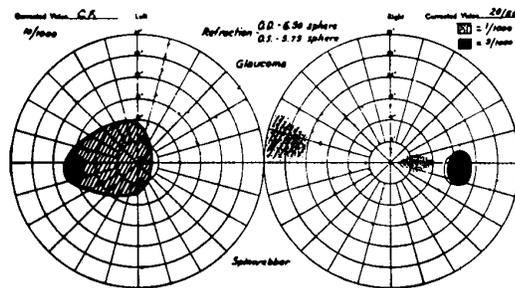
Central-field scotomata in myopic eyes are a consequence of myopic degeneration of the macula as well as Fuchs' spot formation. Blatt⁴⁷⁶ found these defects in 13 (12%) of 109 patients. In ten the scotoma was absolute and in three it was relative. These scotomata were usually round, involved from 5° to 20° of the field, and were seen only in myopia of more than 8 D. Campos⁴⁷⁸ noted that in its early stages, the Fuchs' spot produced a positive scotoma.

Paracentral Scotomata

Paracentral scotomata, when caused by small focal areas of myopic atrophy, may be seen as gray spots by the patient and, with small fixational movements, the acuity may vary noticeably. This causes a "glimmering" of vision. It may also produce the paradox in which the

patient is better able to read fine print, since with large-sized print only a part of the word may be visible.⁴⁸⁰ A more uncommon but serious paracentral defect is the centrocecal scotoma.^{490, 514} Traquair⁵¹³ calls attention to juxta-cecal scotomata, which may be annular or arcuate. These are not considered an effect of nerve fiber defects. He also has noted the importance of quantitative perimetry in the evaluation of the temporal crescent margin in high myopia. A sloping of the margin of the blind spot scotoma toward the fixation point is indicative of progressive chorioretinal degeneration. Conversely a sharp edge is associated with relative stability. Paracentral scotomata tend to occur in the presence of glaucoma. Carroll and Forbes⁴⁷⁹ found myopia in three of their five cases of centrocecal scotoma in glaucomatous eyes and suggested that myopic changes at the papilla, notably vascular, might be a factor in the production of these lesions. Cupping and pallor of the temporal disc were observed in those eyes. The field defect may vary considerably in size and shape (Fig. 13-61). Blatt⁴⁷⁶ concluded that paracentral scotomata are likely to indicate organic changes in the optic nerve, but careful optical correction may make some disappear, indicating a functional basis.⁵⁰⁰

FIGURE 13-61. Centrocecal scotoma in myopia accompanied by glaucoma in a 53-year-old man. Refraction: OD, -6.50 D; OS, -5.75 D. Corrected vision: OD, 20/50; OS, counting fingers. Disc cupping: OD, mild; OS, marked. Visual fields: OD, nasal step plus scotoma between fixation and blind spot; OS, dense centrocecal scotoma. (Carroll FD, Forbes M: Centrocecal scotomas due to glaucoma. *Trans Am Acad Ophthalmol Otolaryngol* 72:643, 1968)



Arcuate Defects

Arcuate defects are classically associated with glaucoma but may also be encountered in myopia.⁴⁷⁶ They tend to affect the superior field.⁵⁰⁸ These probably represent optic nerve changes of an ischemic nature, but glaucoma must be carefully ruled out in each case.

PERIPHERAL-FIELD DEFECTS

A wide variety of peripheral defects can be found in the myopic eye. Among these are concentric contraction, ring and arcuate scotomata, hemianopic and quadrantic defects, and peripheral scotomata.

Concentric Contraction

Concentric contraction is one of the more consistent field defects in myopia. In Blatt's⁴⁷⁶ series it was found in 22% of cases. It could not be correlated with the degree of myopia but rather with the extent of the fundus changes. It is present for white and colored test objects,^{506, 507, 515} particularly blue⁴⁹² (Fig. 13-62). It does not disappear when contact lenses are worn.⁴⁷⁴ Concentric contraction may progress to tubular fields, and Blatt⁴⁷⁶ found three patients (2.8%) who showed this change, a finding that was thought to suggest the presence of glaucoma.

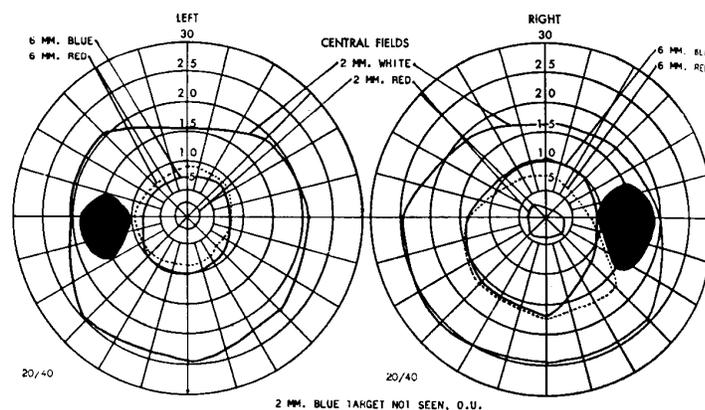
Ring or Annular Scotomata

Ring or annular scotomata are also common findings in highly myopic eyes.^{476, 507} The ring is plotted nearer to the fixation point than that seen in retinitis pigmentosa^{493, 504, 515} and is often incomplete or irregular such that crescentic or arcuate scotomata are seen. The cause of these unusual field changes is unknown. Jarry,⁴⁸⁹ using scotopic perimetry, has found that the annular scotoma corresponds in location to the angioscotomata of the retinal vascular arcades. It is also possible that these scotomata correspond to the acutely sloping walls of the posterior staphyloma. In this situation the malalignment of the photoreceptor cells gives rise to the Stiles-Crawford effect, with demonstrable loss of sensitivity in these areas.⁴⁹² Traquair⁵¹³ feels that ring scotomata, especially when multiple, may have a functional basis.

Hemianopic and Quadrantic Defects

Hemianopic and quadrantic defects are of particular interest. Although incongruous homonymous and binasal hemianopia can be seen occasionally, the most common reported type of hemianopic field defect is bitemporal^{473, 476, 482, 505, 508} (Fig. 13-63). This stems from the fact that such fields can be misinterpreted as chiasmal lesions, and fruitless neurological evaluation and even cranial explora-

FIGURE 13-62. Concentric contraction in pathologic myopia, blue greater than red. (Klein RM, Curtin BJ: Lacquer crack lesions in pathologic myopia. *Am J Ophthalmol* 79:386, 1975. Published with permission from The American Journal of Ophthalmology. Copyright by The Ophthalmic Publishing Company.)



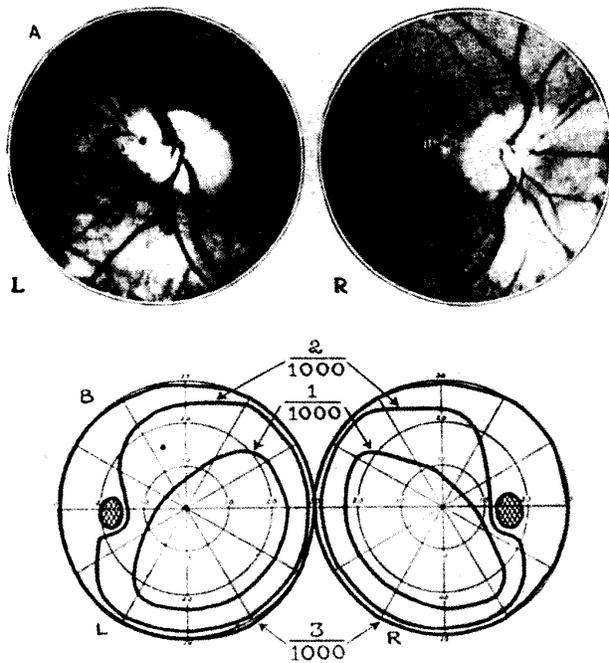


FIGURE 13-63. Bitemporal hemianopia in patient with bilateral tilted discs and inferonasal fundus ectasia with chorioretinal degeneration. (Rucker WC: Bitemporal defects in the visual fields resulting from developmental anomalies of the optic disks. *Arch Ophthalmol* 35:546, 1946. Copyright 1946, American Medical Association.)

tion may be undertaken in these cases.⁴⁸⁶ As with chiasmal lesions, the superior temporal fields are affected preferentially.⁴⁸⁹ These defects may disappear when larger-sized test objects are used,⁵⁰⁸ and they can best be differentiated from those of chiasmal lesions by their tendency to slope across the midline and by their lack of progression.⁴⁸⁶ There is general agreement that these field changes are a consequence of bilateral nasal (type IV), inferior (type V), or inferonasal posterior staphylomas. It should be remembered that these staphylomas are often associated with tilting of the disc toward the ectasia and with tessellation and pallor of the staphyloma area. The visual-field defect can be attributed to the difference in refraction of the ectatic fundus and to the hypoplasia of its retina.^{486, 517} The clinical findings in these patients include myopic astigmatism, situs inversus, congenital conus, inferonasal thinning of the retinal epithelium and choroid, in addition to the temporal hemianopia. This has been termed the "tilted disc syndrome" by Young and co-workers.⁵¹⁷ Their report included the histopathologic study of

the eyes of one patient. Hypoplasia of the choroid was evidenced by a reduction in the number of choroidal vessels. Although there was an equal sex distribution among their 12 patients, a significant excess of females was noted in another slightly larger series.⁴⁸⁶ Altitudinal defects have also been reported in myopia,^{514, 517} and in our patients at the myopia clinic this defect is more likely to be seen with inferior staphyloma (type V).

As with several other field changes in high myopia, there is always the increased possibility of the presence of glaucoma with quadrantic and hemianopic defects. Graham and Wakefield⁴⁸⁶ found this in two of their patients (13%). Monocular quadrantic defects of myopic eyes are most commonly found superotemporally,^{476, 509} and their association with enlarged blind spots has already been noted.^{490, 502} Superonasal defects and even depressions of the lower fields can be found.^{476, 483} Nasal field loss was found in 8.3% of cases by Blatt.⁴⁷⁶ In three of these, glaucoma was present. Manor⁴⁹⁹ reported nine cases of nasal disc tilting with temporal field

loss. Four of these patients displayed a tendency toward chronic glaucoma. Greve and Furuno⁴⁸⁷ report a number of myopia-induced field changes in a glaucoma population. These include enlarged blind spots, which are related to the degree of myopia (18%–30%), relative superotemporal defects (2%–6%), frequent atypical nerve fiber-bundle defects, which are rare in nonmyopic eyes, and a variety of irregular changes produced by myopic fundus degeneration. Temporal fiber-bundle defects were detected in 18% of these eyes. In addition to neurologic disease and glaucoma, the possibility of subclinical retinal detachment must also be considered in hemianopic, quadrantic, and altitudinal field defects in myopic eyes.

Peripheral Scotomata

Peripheral scotomata in association with myopia require painstaking perimetry. They are uncommon and, unless large, difficult to detect.⁴⁷⁶

Color Vision

The acquisition of blue-yellow dyschromatopsia in eyes with progressive myopic changes of the fundus has been recorded by a number of authors.^{521, 522, 524–528} Francois and Verriest⁵²³ noted that this was a frequent finding in high myopia and added that acquired red-green defects also could be found but with much less frequency. Total achromatopsia may also evolve in myopic patients with extensive retinal degeneration.^{518, 529} Presumably, this is related to the associated visual loss.

In Blach's⁵¹⁸ study, using the Hardy–Rand–Rittler (HRR) plates, 52 myopic patients were examined. The results appear in Table 13-21. Somewhat better than one half of his patients had normal color perception (58%). The balance showed blue-yellow and red-green defects in addition to two patients with total achromatopsia. These latter two patients had very poor visual acuity. Of the patients with red-green defects only, 2 of the 11 did not also

TABLE 13-21. Color Vision in 52 Patients with Pathologic Myopia

Color Vision	No. of Patients
Normal	30
Blue-yellow defect	18
Red-green defect	11
Total color defect	2

* Number of patients with both blue-yellow and red-green defects.

(Blach RK: The nature of degenerative myopia: A clinico-pathologic study. Master's thesis, University of Cambridge, 1964).

have a blue-yellow dyschromatopsia, confirming the higher prevalence of blue-yellow as compared with red-green defects. Blach⁵¹⁹ points out that color perception in myopia can be affected by the clarity of the media, notably the lens, the presence of fundus degeneration, and, possibly, the amount of macular pigmentation. The importance of the media in color vision appraisal is underscored by one of his patients in whom a blue-yellow defect was present in the cataractous eye but the fellow, aphakic eye showed no dyschromatopsia.⁵¹⁸ He could not correlate the visual acuity with blue-yellow dyschromatopsia, since he found these defects in eyes with acuities of 1.0 (20/20).

In Cox's⁵²² small study of six myopic patients, a battery of color discrimination tests was used. Of these, the Farnsworth 100 Hue Test proved of most value. Two patients revealed tritanopia. Both were over 70 years of age and showed macular degeneration. Five of her six patients demonstrated macular changes. It is interesting that all six could pass the Ishihara and Farnsworth D-15 tests. The HRR test did detect a tritanopia in one patient (Table 13-22). Bozzoni⁵²⁰, using both the Farnsworth D-15 panel and 100 Hue Test, found the axis of confusion to be located close to that of acquired tritanopia. Francois and Verriest⁵²³ employing the Farnsworth 100 Hue Test, located the axis between deuteranopia and tritanopia, (Fig. 13-64). These authors also found a displacement of the Rayleigh equation

AXIAL LENGTH MEASUREMENTS AND FUNDUS CHANGES OF THE MYOPIC EYE

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The posterior fundus changes of the myopic eye are as striking as they are unique. They are the clinical basis for the diagnosis of pathologic myopia and can effect an incapacitating loss of vision in the later stages of the disease.

These fundus changes have generally been assumed to be the consequence of increased axial elongation of the globe with the attendant mechanical tissue strain and vascular changes which occur secondary to a process of stretching. A definite parallel between the degree of myopia and the severity of its fundus changes has never been established, however. Partly because of this, the concept of a biomechanical pathogenesis for these changes has been increasingly challenged and their origin ascribed rather to abiotrophy.^{1,2}

This problem is not solely academic for the nature of these changes determines the possibility of their prevention and response to various therapeutic approaches.

The degree of refractive myopia, in general, reflects the ocular axial length. Although axial length is the primary determinant of refraction, the effect of variations in corneal power and lens power, each in the order of approximately ± 5 diopters, are such that a parallel between the degree of myopia and fundus changes due to axial elongation could be difficult to demonstrate.

Prior to the clinical use of ultrasound, the measurement of the axial length of the eye by optical or roentgenologic methods was

From the Sprague Myopia Clinic of The Manhattan Eye, Ear and Throat Hospital. This work was supported by USPHS Grant N-3408 and was presented at the 106th meeting of the American Ophthalmological Society, May 28-30, 1970, Hot Springs, Virginia, and will appear in the Transactions of the Society.

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complex and, in the case of the latter method, potentially dangerous. The ultrasonic method has proven at least as accurate and considerably more simple than these older methods.³⁻⁵

With the availability of this method of axial measurement it was possible to undertake a large scale study to statistically determine the relationship between axial elongation and the fundus changes of myopia.

MATERIAL AND METHODS

The clinical material in this investigation consisted of patients referred to the Myopia Clinic of the Manhattan Eye, Ear and Throat Hospital. Approximately one hundred randomly selected hyperopic and emmetropic patients were included in the study group to obtain samples in eyes of shorter axial lengths. Each eye was dilated and the fundus examined by both direct and binocular indirect ophthalmoscopy. Biomicroscopic fundus study was added in selected cases. The axial length of each eye was measured by ultrasound.

The ultrasound equipment employed has been described in detail elsewhere.^{6,7} Both 8 MHz and 10 MHz focused transducers were used with delay columns or, in the earlier stages of the study, in direct contact with the cornea. The ultrasonic receiving and display unit was modified so as to permit direct millimeter readouts of each axial length component. In this investigation only a composite reading was taken using an acoustic velocity of 1532 meters per second. This introduces a small error due to the presence of the lens.⁸

There were 1437 eyes examined in this manner. The eyes were divided on the basis of age into three groups. Group 1 consisted of eyes of individuals up to and including 19

years of age, in Group 2 were those of persons aged 20 to 39 years inclusive, and in Group 3 those of 40 years and above. All cases in which a complete examination could be performed were included in this study with no attempt made to obtain a balanced sampling of eyes. This produced a disproportionately high representation of girls of the age classified as Group 1 (Table 1).

RESULTS

Five fundus changes were found to be associated with increased axial length of the eye. These were: optic nerve crescent, chorioretinal atrophy, the central pigment spot (Fuchs'), lacquer cracks, and posterior staphyloma.

PART I. INCIDENCE AND CHARACTERISTICS OF MYOPIC FUNDUS CHANGES

Crescent—Retraction of the lamina vitrea complex (pigment epithelium-lamina vitrea-choriocapillaries) from the optic nerve

margin was seen in 1032 eyes. The types of crescents seen and their prevalence are set forth in Figure 1. Chorioretinal atrophy at the optic nerve has the tendency to be peripapillary and have sharp borders. This could result in an erroneously high number of annular crescent forms. When eyes displaying atrophy at the optic nerve were eliminated from consideration, the percentage of eyes with temporal crescent increased to 71% while that for annular crescent decreased to 17%.

The incidence of crescent formation in eyes of different axial lengths is seen in Figure 2. It demonstrates a steady rise from 0% in eyes of 20.0-21.4 mm diameter to 100% in all eyes of 28.5 mm length and above. The regression coefficient for the prevalence of crescent in eyes measuring from axial lengths of 21 mm to 35 mm is highly significant ($p < .01$).

As the axial length increased the tendency towards annular crescent formation in-

OPTIC NERVE CRESCENT: TYPE AND INCIDENCE						
APPEARANCE (LEFT EYE)						
NAME	TEMPORAL	ANNULAR	NASAL	TEMPORAL-ANNULAR	INFERIOR	TEMPORAL-INFERIOR
ALL CRESCENTS TOTAL 1032	62%	25%	3%	2.7%	2.5%	2.3%
CRESCENTS WITHOUT PERIPAPILLARY ATROPHY 841 TOTAL	71%	17%	2.9%	2.4%	2.7%	2.2%
APPEARANCE (LEFT EYE)						
NAME	NASAL-INFERIOR	TEMPORAL-INF-NASAL	NASAL-ANNULAR	INFERIOR-ANNULAR	SUPERIOR	TEMPORAL-NASAL
ALL CRESCENTS TOTAL 1032	<1%	<1%	<1%	<1%	<1%	<1%
CRESCENTS WITHOUT PERIPAPILLARY ATROPHY 841 TOTAL	<1%	<1%	<1%	<1%	<1%	<1%

Fig. 1 (Curtin and Karlin). Types and incidence of crescent formation.

TABLE 1
MYOPIA STUDY GROUP—AGE AND SEX DISTRIBUTION

Classification	Axial Length mm													
	20.0 to 21.4	21.5 to 22.4	22.5 to 23.4	23.5 to 24.4	24.5 to 25.4	25.5 to 26.4	26.5 to 27.4	27.5 to 28.4	28.5 to 29.4	29.5 to 30.4	30.5 to 31.4	31.5 to 32.4	32.5 to 33.4	33.5 to 36.6
Age distribution:														
Group 1 (19 years and less)	22	64	75	125	116	175	83	45	18	10	7	6	2	1
Group 2 (20 through 39 years)	0	11	22	28	25	26	15	26	25	17	8	15	5	3
Group 3 (40 years and above)	9	31	48	39	35	48	44	54	39	46	30	16	6	17
Sex distribution:														
Male	7	31	52	80	61	119	61	57	37	38	23	28	9	11
Female	24	75	93	112	115	130	81	68	45	35	22	9	4	10

creased. This could be noted in the lowest age group (Group 1) where the annular crescent became predominant over the temporal form at the axial diameter of 30.5 mm and remained so above this level. This same effect was present in the oldest age group (Group 3) but here the temporal crescent was exceeded at 27.5 mm. This three millimeter discrepancy is probably caused by peripapillary atrophy. All crescents regardless of position tended to be larger in size as the axial length of the globe increased.

Chorioretinal atrophy—Areas of circumscribed chorioretinal degeneration were noted most often to involve the vicinity of the optic nerve and the posterior pole. The earliest degenerative changes usually involved the crescent edge with peripapillary atrophy seen as a later development. Posterior pole involvement in the early stages consisted of focal patches of absent pigment epithelium and choriocapillaries associated with a variable amount of pigment clumping within, or on the border of, the lesion. These regions later became confluent with the formation of large geographic areas of atrophy often merging with an enlarged peripapillary degenerative zone.

There were 23% of all eyes above 24.5 mm that demonstrated atrophy with a pre-

valence which increased from 1% in the 25 mm eye to a high of 90% at the greatest diameters. The regression coefficient for the incidence of chorioretinal atrophy in eyes of this axial length range is significant not only for Group 3 ($p < .01$) but also in combined Groups 1 and 2 ($p < .01$). The effect of age also was evident in the incidence of this change. Figure 3 compares the incidence of atrophy in eyes of all ages to that of the age group classified as Group 3.

Although the effect of age can be strikingly demonstrated in this manner it is of greater interest to consider the occurrence of atrophy in eyes of each group at several axial diameters. Table 2 illustrates in this way the marked effect of age as well as axial elongation on the pathogenesis of this fundus change. When the regression coefficient of the prevalence of atrophy in eyes measuring from 23.5 to 36.6 mm for Groups 1 and 2 is compared to that of Group 3 the difference between the two coefficients is statistically significant ($p < .01$).

In age Group 3 patients the area of atrophy was greater in eyes of highest axial diameters. The eyes of female patients displayed an 8 to 20% greater incidence of atrophic changes at axial lengths below 27.4 mm. Above this diameter the incidence of

such changes became about equal although slightly greater for eyes of females. The youngest patient to demonstrate atrophy was a 14-year-old boy with Marfan's syndrome.

Central pigment spot (Fuchs')—A rounded, black area of variable diameter at the macula occurred in a total of 28 eyes of 26.5 mm or more axial length. This represents an incidence of 5.2% in such eyes. It was bilateral in four patients. The eyes of females were affected more frequently than males in almost a two to one (18:10) proportion. The overwhelming majority, 22 cases, occurred in the third age group. The youngest patient in which this change was noted was a 31-year-old woman.

Figure 4 presents the frequency of the central pigment spot at various axial lengths. The regression coefficient for the incidence of the Fuchs' spot in eyes measuring 25.5 to 36.6 mm showed no statistical significance.

Lacquer cracks—Yellow-white lines of variable orientation and diameters were seen at the posterior pole in 23 eyes of 26.5 mm

diameter or more. This corresponds to an incidence of 4.3%. The eyes of males were affected more often than those of females in a proportion of almost two to one (15:8). The greatest incidence of lacquer cracks was noted in the second age group where they were found in 13 eyes. The youngest patient to exhibit this change was a 19-year-old boy and the oldest, a 51-year-old man. The lacquer cracks were bilateral in seven patients. Its occurrence at each axial length is found in Figure 4. The regression coefficient for the incidence of lacquer cracks in eyes measuring 25.5 to 36.6 mm showed no significance.

Posterior staphyloma—A posterior ectasia or staphyloma is probably present in all eyes of great axial lengths. As a recognizable ophthalmoscopic entity, however, a sharp or abrupt edge is necessary for this classification. There were 102 eyes of 26.5 mm axial length or more that demonstrated this fundus change (19%). Three varieties of posterior staphyloma were seen. In one eye a peripa-

INCIDENCE OF CRESCENT AT EACH AXIAL DIAMETER

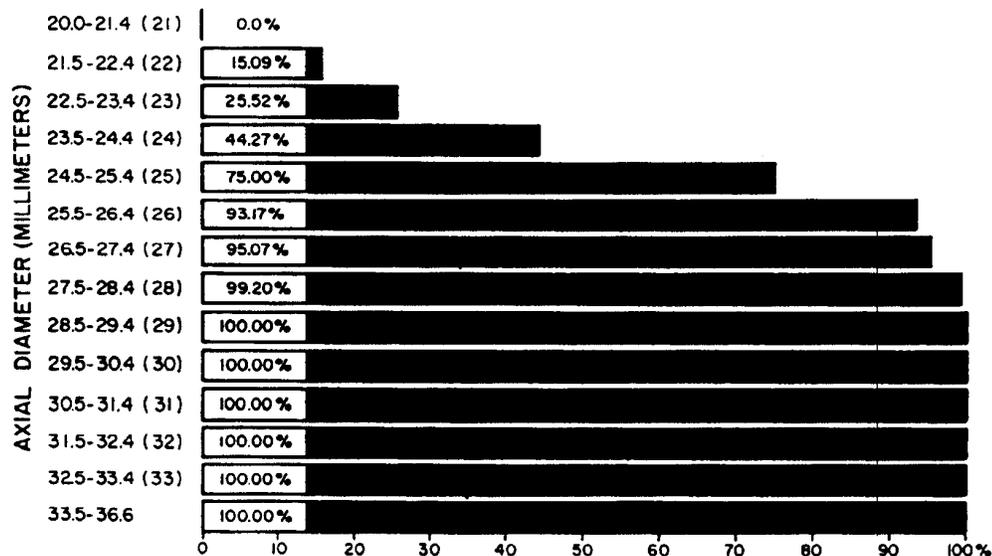


Fig. 2 (Curtin and Karlin). Incidence of crescent at each axial diameter.

INCIDENCE OF CHORIO-RETINAL ATROPHY AT EACH AXIAL DIAMETER

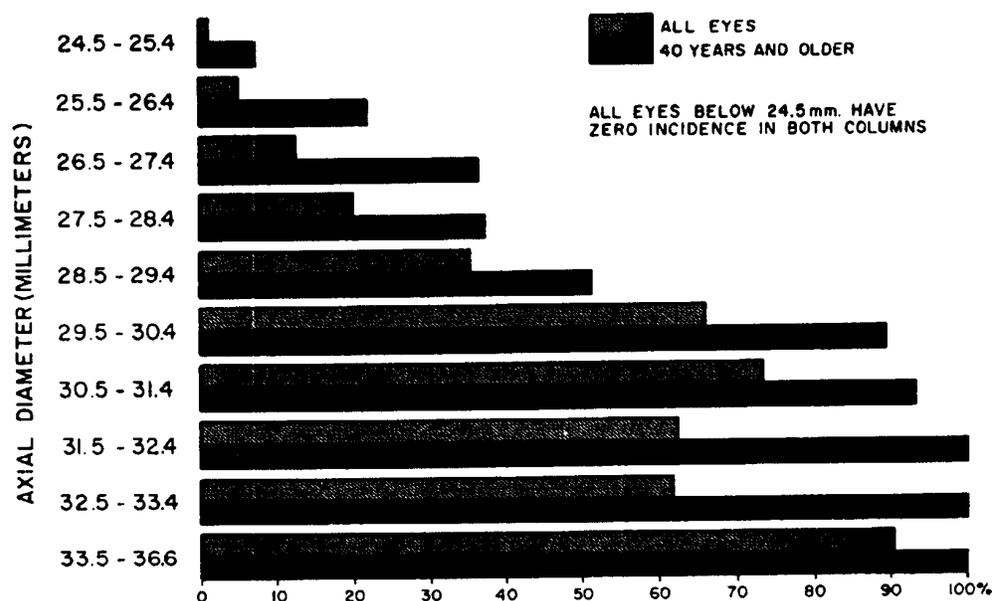


Fig. 3 (Curtin and Karlin). Incidence of chorioretinal atrophy at each axial diameter.

pillary staphyloma was noted and in two others nasal staphylomas were present. In the latter instance the staphyloma edge was seen at the temporal border of the optic nerve with the ectasia involving the nasal fundus. In the remaining eyes, the staphyloma originated at, or more commonly, one to four disk diameters nasal to the border of the optic nerve in an abrupt out-pouching. Step-like configurations were frequently encountered. The sharp edge of the staphyloma was usually lost as it was followed temporally above and below the region of the optic nerve. In a few instances, however, a recognizable edge could be followed about the entire posterior pole. This staphyloma edge, if present temporally, was considerably less abrupt and could be followed as far anteriorly as the equator of the globe. The ectatic area of the fundus was pale with a prominently visible choroidal vasculature in comparison to the rest of the fundus.

Staphylomas were seen in males slightly more often than in females (55:47), were

bilateral in 36 patients, and could be detected in all age groups. The youngest case was a four-year-old boy. The greatest prevalence was found in the third age group where 30%

TABLE 2
MYOPIC CHORIORETINAL ATROPHY—AGE GROUP
INCIDENCE AT FOUR AXIAL LENGTHS

Axial Length (mm)	Age Group 1	Age Group 2	Age Group 3
27	$\frac{0}{76}$ (0%)	$\frac{2}{15}$ (13%)	$\frac{16}{44}$ (36%)
28	$\frac{0}{44}$ (0%)	$\frac{5}{26}$ (19%)	$\frac{20}{54}$ (37%)
29	$\frac{1}{18}$ (5.6%)	$\frac{7}{25}$ (28%)	$\frac{20}{39}$ (51%)
30	$\frac{1}{10}$ (10%)	$\frac{6}{17}$ (35%)	$\frac{41}{46}$ (89%)

of eyes over 26.5 mm length exhibited this change. Group 2 had an incidence of 25% while in Group 1 it was seen in only 4.6% of eyes.

The frequency of posterior staphyloma formation at various axial lengths of the eye is set forth in Figure 5. This increased steadily from a low of 1.4% at the 27 mm diameter to a high of 71% in eyes with greatest axial diameters. The regression coefficient for the incidence of staphyloma in eyes measuring 25.5 to 36.6 mm is highly significant ($p < .01$).

PART II. INTERRELATIONSHIPS OF MYOPIC FUNDUS CHANGES

The interrelationships of eyes exhibiting myopic fundus changes are set forth in Table 3.

Crescent formation was present in every eye with chorioretinal atrophy. There also was noted a tendency for these atrophic changes to involve that area of the fundus ipsilateral to the sector crescent. This occur-

red not only at the crescent margin but also in fundus areas beyond the immediate vicinity of the disk. Hence the eye with temporal crescent tended to show atrophy at the posterior pole. With a nasal crescent the fundus areas nasal to the optic nerve were preferentially involved while with the inferior crescent the lesions were found in the area below the optic nerve. Chorioretinal atrophy was most commonly associated with annular type crescents (56%). In general, a positive relationship between size of crescent and degree of chorioretinal atrophy also could be discerned.

The Fuchs' spot was always accompanied by crescent formation with the annular crescent forms most commonly encountered (64%). All eyes exhibiting lacquer cracks had crescent formation. Here, however, the temporal crescent was most frequently seen (48%).

All eyes with staphylomas were noted to have crescents. The annular form predominated and was seen in 59% of these eyes.

INCIDENCE OF FUCHS' SPOT AT EACH AXIAL DIAMETER

INCIDENCE OF LACQUER CRACKS AT EACH AXIAL DIAMETER

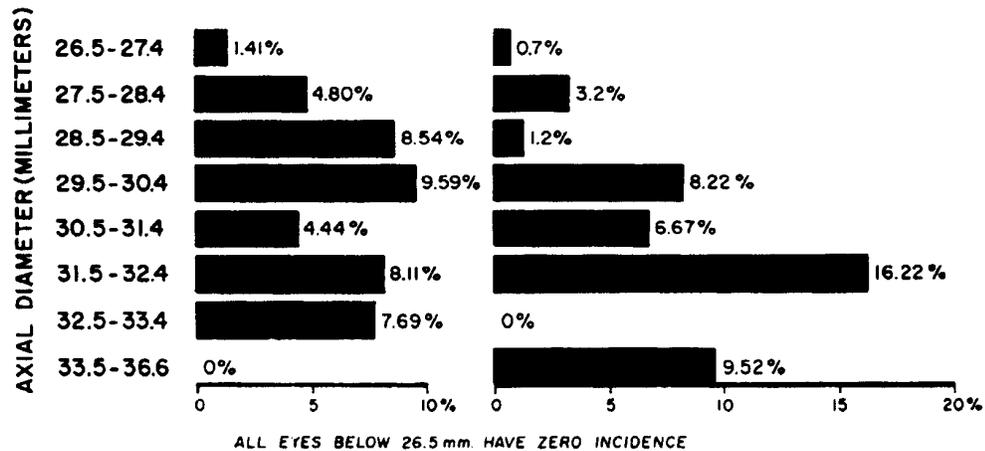


Fig. 4 (Curtin and Karlin). Incidence of pigment spot (Fuchs') and lacquer cracks at each axial diameter.

POSTERIOR STAPHYLOMA AT EACH AXIAL DIAMETER

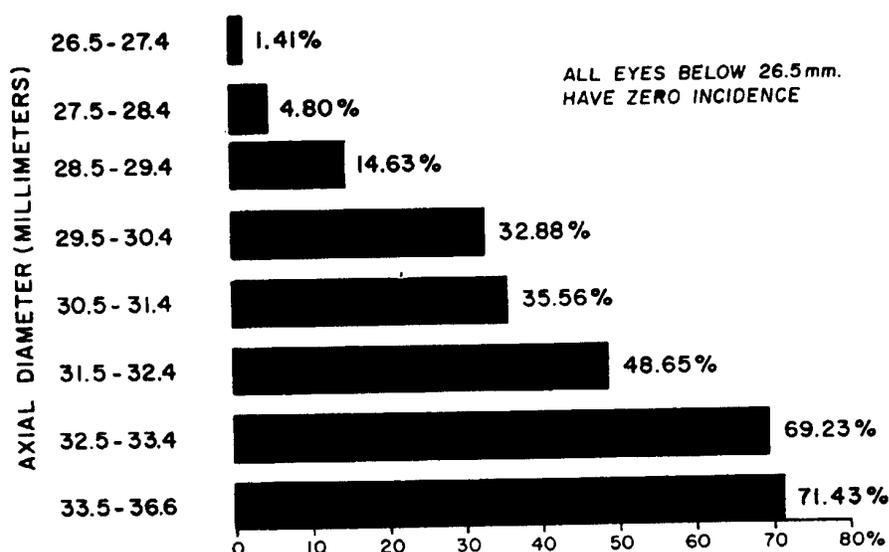


Fig. 5 (Curtin and Karlin). Incidence of posterior staphyloma at each axial diameter.

Twenty-five of the 28 eyes with the Fuchs' spot also showed chorioretinal atrophy (89%). The atrophy tended to involve both the peripapillary and posterior fundus areas concomittantly. Fuchs' spots occurring in Group 3 eyes were associated with chorioretinal atrophy in all but one eye, that of a 48-year-old woman.

Nine of 23 eyes with lacquer cracks showed atrophy (39%). Seventy-nine eyes with staphyloma showed chorioretinal atrophy (77.5%) which usually involved both the peripapillary region and the fundus area of the staphyloma. No eyes with staphyloma were seen without accompanying atrophy in patients above the age of 40. The atrophy in these eyes was extensive as a rule. In the reverse relationship 36% of eyes having atrophy also had staphyloma formation. Eyes with lacquer cracks were found to have a slightly greater incidence of staphyloma formation (39%).

Only one case of lacquer cracks and a coincident Fuchs' spot was encountered.

COMMENTS ON RESULTS

The close association of crescent formation with increased axial diameters of the globe found in this investigation agrees with the studies of Stenstrom⁹ and Otsuka and Kondo.¹⁰ In these, however, a less abrupt rise in incidence was noted in the intermediate axial lengths. For example, in this series at 25 mm axial length 75% of eyes show crescents whereas in the two earlier studies this figure was not reached until the eyes measured about 26.5 mm. This discrepancy is attributable to three factors:

1. *Crescent classification*—In this study any degree of retraction of the lamina vitrea complex from the border of the optic nerve as detected by direct ophthalmoscopy was classified as crescent formation. This alone could have the effect of increasing the incidence of this change considerably.

2. *Age of the patient examined*—Of the patients in this series at the lower and intermediate axial lengths (20.0-26.4 mm), 64%

were in the lowest age group (Group 1). It is more probable that an immature eye will show crescent formation at the same intermediate axial length than a mature eye. For example, at the axial length of 24 mm 49% of Group 1 eyes displayed crescents as compared to only 27% of age Group 3 eyes.

3. *The predominance of female eyes in the low and intermediate axial lengths*—The eye of the female, being significantly shorter than that of the male,^{11,12} could be expected to demonstrate a higher incidence of crescent formation in the intermediate range of axial lengths.

In this study 60% of the eyes in the diameter range of from 22.5-26.4 mm were of female patients.

In this investigation the incidence of temporal crescents, 71% in eyes not exhibiting chorioretinal atrophy, is between the 54% incidence of Vossius¹³ and the 79% incidence recorded by Hertel.¹⁴ Von Szily's¹⁵ incidence of 87% also included the temporal-annular type and is considerably higher than a combined incidence of 73% of the two forms for this study.

The association of increased axial length with larger temporal crescents as well as both the simple and combined forms of annular crescents agrees with a number of previous studies.¹⁶⁻¹⁸ It is also in indirect agreement with studies in which a greater amount of myopia was associated with these crescent types.^{19,20}

Whereas two recent studies have detected the greater association of chorioretinal atrophy with the higher grades of myopia,^{21,22} this study demonstrates a close correlation of this atrophy with increasing axial length. The importance of age in the production of this fundus change, has been widely recorded in the ophthalmic literature, and is confirmed by the results of this investigation.

No significant difference in the incidence of atrophy between the sexes could be discerned, however. The increased incidence noted in eyes of females in the intermediate axial lengths, does not indicate their increased susceptibility to this change so much as the axial length difference between eyes of both sexes. The almost equal incidence

TABLE 3
INTERRELATIONSHIPS OF MYOPIC FUNDUS CHANGES

	Crescent	Chorioretinal Atrophy	Fuchs' Spot	Lacquer Cracks	Posterior Staphyloma
Eyes with crescent Total 1032	—	$\frac{218}{1032} = 21.1\%$	$\frac{28}{1032} = 2.7\%$	$\frac{23}{1032} = 2.2\%$	$\frac{102}{1032} = 9.9\%$
Eyes with chorioretinal atrophy Total 218	$\frac{218}{218} = 100\%$	—	$\frac{25}{218} = 11.5\%$	$\frac{9}{218} = 4.1\%$	$\frac{79}{218} = 36.2\%$
Eyes with Fuchs' spot Total 28	$\frac{28}{28} = 100\%$	$\frac{25}{28} = 89.3\%$	—	$\frac{1}{28} = 3.6\%$	$\frac{9}{28} = 32.1\%$
Eyes with lacquer cracks Total 23	$\frac{23}{23} = 100\%$	$\frac{9}{23} = 39.1\%$	$\frac{1}{23} = 4.4\%$	—	$\frac{9}{23} = 39.1\%$
Eyes with posterior staph. Total 102	$\frac{102}{102} = 100\%$	$\frac{79}{102} = 77.5\%$	$\frac{9}{102} = 8.8\%$	$\frac{9}{102} = 8.8\%$	—

found in eyes of greater axial diameter does not confirm the purported susceptibility of the female eye to myopic chorioretinal degeneration.²³

The incidence of Fuchs' spots in this series, 5.2% of eyes 26.5 mm and above, is slightly greater than Blatt's²² figure of 4%. The correlation between Fuchs' spots and increasing axial length is not as dramatic as with other myopic fundus changes nor can a statistical significance be demonstrated between the two in the affected range of axial lengths (26.5 to 36.6 mm). This may be due to the fact that this lesion changes in morphology with time to the extent that it can become unrecognizable as an ophthalmoscopic entity. Fuchs'²⁴ original description of the pigment spot noted an equal incidence between the sexes. The 2:1 plurality of the female in this series agrees more with Campos'²⁵ large series in which eyes of females were affected in a 4:1 proportion over those of males. Fuchs' report, furthermore, noted an absence of related fundus changes with the pigment spot. This study reveals an invariable association with crescent formation, an almost equally strong association with chorioretinal atrophy (89%) and, to a lesser extent, one with posterior staphyloma formation (32%).

Lacquer cracks were detected predominantly in males and at a younger average age than Fuchs' spots. Only 35% of lacquer cracks were found in age Group 3 eyes. Like the pigment spot it has erratic prevalence levels at increased axial diameters, so that a statistical significance with increasing axial length in the range of 25.5 to 36.6 mm could not be demonstrated. The coincidence of early chorioretinal atrophy in these younger eyes and the decreased incidence of lacquer cracks in older eyes suggests the clinical progression of these lesions with their eventual incorporation into larger areas of chorioretinal atrophy wherein they, like the Fuchs' spot, also become unrecognizable.

Axial elongation of the eye would appear to play some role in the occurrence of both

Fuchs' spots and lacquer cracks, however. The regression coefficients for these fundus changes in the total axial length range of 20.0 to 36.6 mm shows significance in both instances (Fuchs' spot $p < .05$; lacquer cracks $p < .01$).

Posterior staphyloma showed a strong correlation with increasing axial length and was considerably more common than either Fuchs' spots or lacquer cracks. It was always associated with crescent formation usually of the annular type (59%) which is decidedly less than the invariable association of these two changes found in Weiss' small series.²⁶ The association of staphyloma with chorioretinal atrophy is particularly marked in eyes of patients over 40 years (100%). It is the frequent occurrence of staphylomas in young eyes prior to the age at which degeneration would be expected to supervene, which accounts for the fact that chorioretinal atrophy is often absent in these eyes.²⁷

The increase in the incidence of staphylomas with age would concur with the natural history of the disease insofar as there is the tendency towards gradual progression of pathologic myopia during the patient's life.^{28,29}

DISCUSSION

Although this study demonstrates a strong correlation between increasing axial length of the eye and at least three myopic changes of the fundus, it does not rule out the possibility of another common correlating factor. Such a factor could be a derangement of the retinal pigment epithelium. During embryologic development, the pigment epithelium induces the formation of both the choroid and sclera.^{29,30} An abnormal retina may induce the formation of a sclera deficient in quantity, quality or both with resultant ectasia under the stress of normal intraocular pressure.³¹ In this way abiotrophic degeneration of the retina could ensue independent of the enlargement of the scleral shell.

There are aspects of this study which indicate that biomechanical factors are operative

to some degree in these fundus changes, however. The crescent which is so strongly associated with myopia, of itself, cannot be considered an abiotrophic entity. It can be seen in emmetropic and even hyperopic eyes and is usually found in the absence of ocular disease. The myopic crescent, being closely associated with increased axial length, must be considered the result of a disparity in area between the scleral shell on one hand and the lamina vitrea complex on the other.

The origin of myopic chorioretinal atrophy is not indicated clearly by this study. The frequent onset of atrophy at the edge of the crescent, where the greatest biomechanical stress could be expected, and the high correlation of chorioretinal atrophy with increased axial length, crescent and staphyloma would suggest at least some element of biomechanics is involved in this disease process. The association of atrophy and crescent is further remarkable in that the incidence and severity of the chorioretinal degenerative changes are related to crescent type and size. In addition, the occurrence of myopic degeneration in a connective tissue disease such as Marfan's syndrome must also be noted.³² Although atrophic changes in myopia must continue to be considered possibly abiotrophic in nature, this study strongly suggests at least some element of biomechanical effect.

No conclusion as to the origin of Fuchs' spots or lacquer cracks can be deduced from this material. Although strongly associated with crescent and to a moderate degree with staphyloma formation, these changes could be abiotrophic in nature.

Posterior staphyloma, as previously noted, could be the result of a congenitally defective sclera and, indirectly, an abiotrophic defect. The progressive increase in incidence of this change with age as detected in this series is more compatible with the concept of a scleral disease process, however, as are their frequent step-like configurations. It must also be noted that the occurrence of anterior staphylomas is associated with acquired scleral disease and cannot be attrib-

uted to abnormalities of the ciliary epithelium. In this series one eye with the posterior staphyloma and two with chorioretinal atrophy were observed in three patients with Marfan's syndrome and high axial diameters. The occurrence of these changes in this study and the previous report of posterior staphyloma formation in the Ehlers-Danlos syndrome³³ are also more consistent with a connective tissue disease. In view of these considerations, it is difficult to ascribe the occurrence of *acquired* posterior staphylomas to retinal abiotrophy.

Identical twin studies can be of considerable help in the delineation of a genetic abiotrophic disease process. Two reports in the literature are of particular interest in this relation. Orth³⁴ has reported identical twins, one of whom was emmetropic with no fundus abnormalities while the brother's refraction was RE: -26.00, LE: -25.00 D. These myopic fundi showed peripapillary crescents with stretching changes at the posterior pole of both eyes. Marchesani³⁵ reported uniovular twins with identical corneal power and astigmatism in all four eyes. The refraction of three of these eyes was -18.00 diopters and their fundi showed large annular crescents with macula degenerative changes. The remaining eye at -10.00 diopters showed only a small temporal crescent without degenerative macula changes. Marchesani concluded that these myopic changes were dependent upon stretching and were not heredodegenerative in nature.

The myopia of prematurity also can be of value in resolving this question. Although at the present time these patients are too young to exhibit the late changes associated with high myopia, their posterior fundus changes are indistinguishable from pathological myopia in the early stages of the disease. Crescent, as well as pallor, tessellation and fine pigment mottling of the fundus all can be detected in youngsters with a history of premature birth with oxygen treatment in the absence of a family history of myopia. If other myopic changes, notably chorioretinal

atrophy, supervene in later years their biomechanical pathogenesis will be strongly indicated. Prematurity is an important factor in producing a discordance of refraction in uniovular twins²⁶ and it is this mechanism which possibly accounts for the refraction disparities contained in the twin studies of both Orth and Marchesani.

SUMMARY

In this study of the relationship of myopic fundus changes and axial length in 1437 eyes the following results were obtained: Crescent formation was demonstrated as directly related to increased axial length in incidence ($p < .01$) as well as type and size. Chorioretinal atrophy was demonstrated to be related to increased axial length ($p < .01$) but age also plays an important role in the production of this defect ($p < .01$). Fuchs' spots and lacquer cracks, although occurring in eyes of greater axial length, cannot be directly correlated with increasing axial length. This is possibly the result of changes in the morphology of these lesions with age. Posterior staphyloma is directly related to increased axial length ($p < .01$). Crescent formation is present in all eyes exhibiting other myopic fundus lesions. Chorioretinal atrophy occurs very frequently in eyes with Fuchs' spots. Chorioretinal atrophy usually of an extensive degree occurs in eyes of patients above the age of 40 years who have posterior staphyloma.

Although these results do not conclusively rule out abiotrophy in the pathogenesis of myopic fundus changes the significant correlation of crescent formation, chorioretinal atrophy and posterior staphyloma with increased axial length is strongly suggestive of some element of biomechanical effect. The occurrence of these myopic changes in patients with the connective tissue diseases of Marfan's syndrome and Ehlers-Danlos syndrome also tend to indicate the involvement of biomechanical factors.

This conclusion is further supported by two previous uniovular twin studies and

tentatively, by the fundus changes in the myopia of prematurity.

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Risk Factors for Idiopathic Rhegmatogenous Retinal Detachment

<EDCCSG 93>

The Eye Disease Case-Control Study Group

The objective of this case-control study of idiopathic retinal detachment was to evaluate previously suggested hypotheses about risk factors for retinal detachment and to investigate whether new ocular or systemic risk factors could be identified. Between 1986 and 1990, data were obtained at five US clinical centers on 253 patients with idiopathic retinal detachment and 1,138 controls. Patients with pathologic myopia were excluded. Data were collected from interviews, clinical examinations, and laboratory analyses of blood samples. Only one clearly relevant risk factor, myopia, emerged from the analyses. An eye with a spherical equivalent refractive error of -1 to -3 diopters had a fourfold increased risk of retinal detachment compared with a nonmyopic eye; if the refractive error was greater than -3 diopters, the risk was increased 10-fold. The data suggest that almost 55% of nontraumatic detachments in eyes without previous surgery are attributable to myopia. The etiology of retinal detachment appears to be related to the architecture of the eye. The study found no evidence that systemic factors, particularly cardiovascular factors, play a role. *Am J Epidemiol* 1993;137:749-57.

cardiovascular diseases; myopia; retinal detachment; risk factors

The incidence of idiopathic rhegmatogenous retinal detachment in persons over 50 years of age is approximately 30 per 100,000 population per year (1). Only cataracts and glaucoma cause more hospitalizations for

eye disorders in persons over 45. In spite of improvements in diagnostic and therapeutic techniques, only about 40 percent of treated eyes recover with 20/50 acuity or better (2).

Several case series have provided hy-

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potheses as to risk factors for retinal detachment. Myopia has consistently been noted as being more common among cases than expected (3-6). Vascular insufficiency has been suggested as a possible mechanism for retinal detachment (7-9), and prevalences of coronary artery disease and systemic hypertension were found to be higher than expected in one series of cases (9).

Two studies included comparison groups along with cases. Ogawa and Tanaka (10) confirmed the higher prevalence of myopia in their cases. Austin et al. (11) noted self-reported myopia to be associated with a threefold increased risk of retinal detachment. They also found an unexpected reduced risk of idiopathic rhegmatogenous retinal detachment in current smokers, but no association with a history of myocardial infarction or hypertension.

We felt that there was a need for evaluation of these hypotheses and included idiopathic rhegmatogenous retinal detachment in the Eye Disease Case-Control Study, a multicenter study of five retinal disorders (12). Other diseases studied in the Eye Disease Case-Control Study included age-related macular degeneration, macular holes, branch retinal vein occlusion, and central retinal vein occlusion. Features of the Eye Disease Case-Control Study, including use of similar protocols and a single large pool of controls for the five disorders, made it convenient to evaluate not only previously suspected risk factors but also several factors not previously reported to be associated with risk of retinal detachment.

MATERIALS AND METHODS

Identification of study subjects

Rhegmatogenous retinal detachment was one of five retinal diseases studied in the Eye Disease Case-Control Study. All cases and controls were selected from patients seen at five large eye care centers between May 1986 and December 1990: the University of Illinois in Chicago, Illinois; the Medical College of Wisconsin in Milwaukee, Wisconsin; the Massachusetts Eye and Ear Infirmary in Boston, Massachusetts; the Manhattan Eye,

Ear, and Throat Hospital in New York City; and the Wilmer Eye Institute at the Johns Hopkins Hospital in Baltimore, Maryland.

Cases were identified by clinic coordinators who screened surgical records. Since nearly all persons with retinal detachment had surgery, this screening strategy was designed to enroll a high percentage of eligible patients. Each clinic developed an algorithm for using medical records to systematically select control patients. The controls were identified by the clinic coordinators using sources within the clinics that were similar to the sources from which the cases came. An eligibility form was completed for all potentially eligible cases and controls who were identified in the screening process. Eighty-one percent of the cases and 70 percent of the controls identified as eligible for the study agreed to participate. Reasons for nonparticipation were similarly distributed in cases and controls and included lack of interest, being too busy or too sick, being unable to miss work, and various other reasons.

We expected sufficient overlap in the age-sex distribution of the five diseases studied to permit use of a single large pool of controls. The combined case group and the controls were frequency-matched on age, sex, race, and clinic. Balance between cases and controls with regard to the matching characteristics was monitored on a quarterly basis by the Coordinating Center, and when imbalances were noted, the clinics were directed to change the selection criteria for controls to correct the imbalances. For example, when it was noted that too few older controls were being enrolled, the coordinators were directed to raise the minimum age cutoff for controls. The frequency matching provided approximate balance between cases and controls with respect to the matching characteristics. We used a multiple logistic regression model in the analyses to adjust for residual imbalances in the matched characteristics, as well as differences in the proportions of cases and controls enrolled at the five clinics.

Cases had to be 21-80 years of age, residents of the local clinic area (as defined by

zip code), and diagnosed in the year prior to enrollment. A senior examiner certified that subjects identified by the clinic coordinators met the study's eligibility requirements. Examinations or retinal drawings that had been done prior to surgery were used to verify that a detachment of the sensory retina at least one disc diameter in size was present. Examinations or retinal drawings were also used to note the type of break (tractional or atrophic) and whether lattice degeneration was present in the cases. Cases with a history of significant trauma, previous cataract or other intraocular surgery, and any congenital vitreoretinal abnormalities were excluded. A history of trauma was used as an exclusion criterion only when the examiner determined there was a clear-cut history of direct trauma to the globe, orbit, or mid-facial area in the year prior to detachment.

Controls were persons aged 21–80 years who resided in the local clinic area and were free of current evidence or a past history of retinal detachment or any of the other eye diseases included in the Eye Disease Case-Control Study (exudative macular degeneration, macular holes, branch retinal vein occlusion, and central retinal vein occlusion).

Excluded from both the case and the control groups were persons with pathologic myopia (moderate to high myopia accompanied by a posterior staphyloma or spherical equivalent refractive error less than -8 diopters), vasoproliferative disease, or intermediate or posterior intraocular inflammatory disease.

Data collection

A limited physical examination, a standardized questionnaire, and laboratory analysis of serum samples provided data on possible risk factors for retinal detachment. The variables included in this analysis are listed in table 1.

Iris color was graded by clinical and photographic assessments (13). Cup/disc ratios were estimated from stereoscopic fundus photographs. The photographic assessments of iris color and the cup/disc measurements

TABLE 1. Risk factors included in an analysis of idiopathic rhegmatogenous retinal detachment, Eye Disease Case-Control Study, 1986–1990

Personal factors
Alcohol consumption (never, former, and current)
Cigarette smoking (never, former, and current)
Daily coffee consumption (no. of cups)
Education (≥ 12 th grade or < 12 grade)
Lifetime sunlight exposure
Percentage of time wearing sunglasses outdoors (4-point scale)
Place of work (mainly indoors, equally indoors and outdoors, or mainly outdoors)
Summer leisure time spent outdoors (3-point scale)
Winter leisure time spent outdoors (3-point scale)
Marital status (married/unmarried)
Photographic and clinical assessments of iris color (5-point scales)*
Subjective impression of physical activity in the past (5-point scale)
Subjective impression of present physical activity (5-point scale)
Vigorous physical activity (no. of times/week)
Medical and physiologic factors
Body mass index† at interview
Diabetes history (yes/no)
Cardiovascular disease history (yes/no)
Systolic blood pressure (mmHg)
Diastolic blood pressure (mmHg)
Hypertension‡ (yes/no)
Biochemical data (from serum measurements)
Albumin (g/dl)
Albumin:globulin ratio
Alpha-1-globulin (g/dl)
Alpha-2-globulin (g/dl)
Antithrombin III (%)
Beta-globulin (g/dl)
Fibrinogen (mg/dl)
Gamma-globulin (g/dl)
Glucose (mg/dl)
Hematocrit (%)
High density lipoprotein cholesterol (mg/dl)
Sedimentation rate (mm/hour)
Total cholesterol (mg/dl)
Total protein (g/dl)
Triglycerides (mg/dl)
Ocular measurements
Horizontal and vertical cup/disc ratios, corresponding eye
Intraocular pressure (mmHg), corresponding eye
Refractive error (spherical equivalent in diopters), study eye
Factors pertaining to women only
Estrogen use (never, former, and current)
Hysterectomy (yes/no)
Parity (≥ 1 child vs. 0)
Ever use of oral contraceptives (yes/no)

* Whites only.

† Weight (kg)/height (m)².

‡ Systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 90 mmHg, or use of antihypertensive medication.

were done by masked examiners at a Reading Center. Laboratory analyses were also conducted at a central laboratory without knowledge of whether specimens were obtained from cases or controls.

Analysis

Step 1. We screened the data for each possible risk factor using a logistic regression model with the presence of retinal detachment as the dependent variable, and with the risk factor entered with one coefficient for ordered and continuous variables and $K - 1$ coefficients for variables with K categories without a natural ordering. Included in the regression equation were sex, race, clinic, and age in five groups (<45, 45-54, 55-64, 65-74, and ≥ 75 years) with four coefficients. All risk factors were screened separately for an association with retinal detachment at the <0.05 level of statistical significance. Sample sizes varied for the risk factors, depending on the available data. Of the 253 cases, the number included in any analysis ranged from 253 to 236; of the 1,138 controls, the number included ranged from 1,138 to 1,079. In analysis of risk factors for women only, there were 100 cases and 631 controls.

Step 2. Each continuous variable that was significant at the <0.05 level upon screening was divided into three categories to facilitate interpretation. Odds ratios and confidence intervals were calculated for these groups, as

well as p values for the association with retinal detachment. These p values were obtained, as in the screening analysis, from a logistic regression analysis including age, sex, race, and clinic. We used the same regression model to evaluate the interaction of retinal detachment-associated factors with age, race, or sex.

RESULTS

A total of 253 cases were enrolled in the study (table 2). All but three cases were enrolled prospectively after the study began. The study examination was conducted within 1 month of diagnosis in 35 percent of the cases, 1-6 months after diagnosis in 54 percent of the cases, and more than 6 months after diagnosis in 11 percent of the cases. The affected eyes were evenly divided between the right and the left (table 3). Twenty percent of the eyes had tractional breaks, and 69 percent had atrophic breaks. Lattice degeneration was noted in 61 percent. Nearly half of the eyes had a visual acuity of 20/40 to 20/160. Only 19 percent had a visual acuity of 20/20 or better.

Table 4 presents the distribution of diagnoses in the control patients. The most com-

TABLE 2. Characteristics of cases and controls in a study of idiopathic rhegmatogenous retinal detachment, Eye Disease Case-Control Study, 1986-1990

	Cases		Controls	
	No.	%	No.	%
Race				
White	216	85	922	81
Nonwhite	37	15	216	19
Age (years)				
<45	57	22	119	10
45-54	39	15	111	10
55-64	85	34	312	27
65-74	63	25	457	40
≥ 75	9	4	139	12
Sex				
Male	153	60	507	45
Female	100	39	631	55
Clinic				
Baltimore, Maryland	36	14	173	15
Boston, Massachusetts	64	25	254	22
Chicago, Illinois	51	20	274	24
Milwaukee, Wisconsin	68	27	221	19
New York, New York	34	13	216	19
Total	253		1,138	

TABLE 3. Ocular characteristics of cases in a study of idiopathic rhegmatogenous retinal detachment, Eye Disease Case-Control Study, 1986-1990

	No.	%
All cases	253	100
Eye		
Right	125	49
Left	128	51
Retinal signs prior to surgery		
Tractional breaks		
Absent	203	80
Present	50	20
Atrophic breaks		
Absent	75	30
Questionable	4	2
Present	174	69
Lattice degeneration		
Absent	97	38
Questionable	2	1
Present	154	61
Best corrected visual acuity		
20/20 or better	47	19
20/25 to 20/32	45	18
20/40 to 20/160	111	44
20/200 or worse	48	19
Not recorded	2	1

TABLE 4. Diagnoses of controls in a study of idiopathic rhegmatogenous retinal detachment, Eye Disease Case-Control Study, 1986-1990

	No.	%
Lid disorders	356	31
Conjunctivitis	183	16
Corpus vitreum disorders	160	14
Cataract	145	13
Corneal disorders	108	9
Retinal disorders	55	5
Miscellaneous other disorders	131	12
Total	1,138	100

mon diagnoses involved abnormalities of the lids, the conjunctiva, the corpus vitreum, and the lens. Each of these diagnostic categories comprised a diverse group of disorders.

We screened for a large array of potential risk factors for retinal detachment (table 1). These included personal variables, medical and physiologic variables, biochemical variables, ocular variables, and variables pertaining to women only. Of the factors included in screening, few achieved statistical signifi-

TABLE 5. Variables associated with idiopathic rhegmatogenous retinal detachment in the Eye Disease Case-Control Study, 1986-1990*

Factor	p
Ocular	
Refractive error, study eye	<0.0001
Clinical assessment of iris color†	0.008
Horizontal cup/disc ratio (corresponding eye)	0.04
Photographic assessment of iris color†	0.02
Biochemical	
High density lipoprotein cholesterol (mg/dl)	0.01
Low density lipoprotein cholesterol‡ (mg/dl)	0.005
Total cholesterol (mg/dl)	0.008

* Each factor was analyzed in a logistic regression analysis that included age, sex, race, and clinic.

† Whites only.

‡ Computed: low density lipoprotein cholesterol = total cholesterol - (high density lipoprotein cholesterol + (triglycerides/5)).

cance at a probability level less than 0.05 (table 5). Risk increased with decreasing spherical equivalent refractive error and decreased with darker irides, larger horizontal cup/disc ratios in the corresponding eye, and higher levels of total cholesterol and its components.

The odds ratio for myopic eyes (table 6) suggested a nearly eightfold greater risk of retinal detachment than for hyperopic eyes. Emmetropic eyes did not show a statistically significant increase in risk compared with hyperopic eyes. The association for myopic eyes was unambiguous: The lower bound of the 95 percent confidence interval was 5.0. For the grouped case series consisting of macular holes, central retinal vein occlusion, and branch retinal vein occlusion, there was no suggestion of an association of refractive error with risk of disease. There was also no evidence that refractive error was a risk factor for any of these diseases individually. Clearly, the sizeable association with myopia is unique to retinal detachment among the five ocular diseases we investigated.

We were concerned that the retinal detachments seen at the referral centers that participated in the study might be unusually severe and that the retinal detachment-

TABLE 6. Odds ratios for idiopathic rhegmatogenous retinal detachment, according to level of refractive error, Eye Disease Case-Control Study, 1986-1990

Refractive error: spherical equivalent	No. of subjects			RD* cases vs. controls		Non-RD cases vs. controls	
	RD cases	Non-RD cases†	Controls	Adjusted‡ OR*	95% CI*	Adjusted‡ OR	95% CI
Greater than +1 diopter (hyperopia)	31	302	402	1.0		1.0	
-1 diopter to +1 diopter (emmetropia)	62	314	480	1.3	0.8-2.1	0.9	0.7-1.1
Less than -1 diopter (myopia)	147	119	178	7.8	5.0-12.3	1.0	0.7-1.3
	240	735	1,060				
Test for trend (χ^2 , 1 df)				$p < 0.0001$		$p = 0.65$	

* RD, retinal detachment; OR, odds ratio; CI, confidence interval.

† Idiopathic macular hole, idiopathic central retinal vein occlusion, or idiopathic branch retinal vein occlusion.

‡ Adjusted for age (<45, 45-54, 55-64, 65-74, and ≥ 75 years), sex (male/female), race (white/nonwhite), and clinic (Baltimore, Boston, Chicago, Milwaukee, or New York).

myopia relation might be unique to these severe detachments. Using visual acuity as a crude surrogate for severity, we examined the odds ratios for retinal detachment and refractive error separately for visual acuity better than 20/40 and visual acuity equal to or less than 20/40 (table 7). Myopia remained an important risk factor for both levels of acuity; odds ratios were 8.2 and 12.0 for better and worse visual acuity, respectively, in the most myopic eyes.

Although significant trends were seen among white patients in the odds ratios for photographic and clinical assessments of iris color (table 8), the odds ratios decreased only modestly for persons with darker irides. Overall, the trends in risk were similar for the two assessment methods.

Odds ratios for horizontal cup/disc ratio grouped according to the 20th and 80th percentiles of the control group did not deviate far from 1 and were not statistically significant (data not shown).

When the serum measurements that achieved statistical significance were grouped using the 20th and 80th percentiles of the controls as cutpoints, higher levels of total cholesterol and high density lipoprotein cholesterol were associated with decreased risk of retinal detachment at marginal levels of significance. Significance was not achieved for low density lipoprotein cholesterol (data not shown).

In a multivariate logistic regression model that included refractive error, iris color, total

cholesterol level, age, sex, and clinic, there was a statistically significant protective effect for darker irides using the clinical assessments of iris color but not the photographic assessments. Increasing myopia and lower levels of total cholesterol were associated with increased risk in the multivariate model (data not shown).

DISCUSSION

In this study, myopia emerged as the most striking risk factor for idiopathic rhegmatogenous retinal detachment. An eye for which the refractive error was in the range -1 to -3 diopters had a risk more than four times that of an eye with no myopia. If the refractive error was beyond -3 diopters, the risk was nearly 10 times that for an eye with no myopia (table 7). The implications of these findings are dramatic. We have no way of knowing how representative our cases were of other cases in the population, but if they were representative, then almost 55 percent of retinal detachment cases are attributable to myopia ($(7.8 - 1.0)/7.8 \times (147/240)$ in table 6). Studies by Ogawa and Tanaka (10) and Austin et al. (11) also showed a markedly increased risk of retinal detachment with myopia.

Burton (14) concluded from his series that retinal detachment tends to occur at an earlier age in patients with myopia than in other patients. We computed the odds ratios for risk of retinal detachment by age (<45, 45-

54, 55-64, and ≥ 65 years) in order to evaluate this relation (data not shown). Odds ratios were similar for the first three age groups, ranging from 7.5 to 8.2, and the odds ratio decreased to 4.5 for the oldest age group. The increased risk remains sizeable for all age groups, however, such that persons with myopia remain at higher risk throughout the age range included in our study.

Degenerative changes in the peripheral retina and corpus vitreum are thought to predispose the myopic eye to retinal detachment. Retinal breaks and lattice degeneration, important risk factors for retinal detachment, are reportedly more common in myopic eyes (15). It has been suggested that elongation of the ocular globe, a characteristic of many myopic eyes, may result in stretching of the retina, making it more prone to breaks and degenerative changes and less resistant to traction. Degenerative changes in the corpus vitreum, including a higher incidence of posterior detachment in myopic eyes, may result in increased tractional stress in these eyes.

The protective effect of darker irides in whites is seen largely at grades 4 and 5 (table 8). Neither the gradient in odds ratios nor the level of statistical significance is as great as was seen for refractive error. Austin et al. (11) noted a similar trend in their study, but it was not significant.

Although there was a significant association for horizontal cup/disc ratio in our initial analytic screen, the trend was modest and nonsignificant when cup/disc ratios were grouped according to the 20th and 80th percentile levels.

An association of retinal detachment with cardiovascular disease or its risk factors is not supported by these data. Higher levels of cholesterol showed a modest protective effect, with marginal statistical significance. No association with a history of cardiovascular disease was seen, a finding also reported by Austin et al. (11). The unexpected finding by Austin et al. of a protective effect for current smokers was not confirmed in our data set. Neither physical activity, blood

pressure, nor fibrinogen level yielded a significant association.

It is well to remember that this study was restricted to eyes with no history of serious trauma, intraocular surgery, or pathologic myopia, all clearly important additional causes of retinal detachment.

In summary, although we screened for a wide array of potential risk factors through interview, physical examination, and analysis of serum specimens, we found only one factor, refractive error, to be clearly relevant to retinal detachment. Moreover, the majority of our cases can be explained by this one variable. The etiology of retinal detachment seems to be rooted largely in the architecture of the eye. Evidence did not emerge for the influence of systemic effects, particularly cardiovascular disease, on the risk of retinal detachment.

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NATURAL HISTORY OF FUCHS' SPOT: A LONG-TERM FOLLOW-UP STUDY

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ABSTRACT

Basic data on 206 eyes of 145 patients with Fuchs' spot and follow-up results on 55 eyes of 36 patients were reported to elucidate the nature and natural course of this condition.

Fuchs' spot is not a rare occurrence, affecting 5–10% of myopes over –5. D. Sex bears an influence on incidence, women being twice as often affected as men. Fuchs' spot tends to develop in both maculas in a considerable percentage (20–50%) during a short interval. There is a marked effect of age, refraction and axial length on incidence with peaks of manifestation between 40–50 years, around –12.0 D and between 26.5 to 31.4 mm of axial length.

In unilateral cases affected eyes are usually more myopic than non-affected eyes. Anisomyopia is no protection for the less myopic eye against Fuchs' spot. In unilateral cases usually the higher myopic eye will be affected. There is a tendency to earlier manifestation with rising degree of myopia. Patients with Fuchs' spot are almost exclusively juvenile myopes with a high percentage of myopia in their families.

The follow-up study revealed in general a relatively benign visual prognosis, especially for near vision. Fuchs' spot seems to be largely a non-progressive, relatively stationary condition for about 2/3 of patients. The high percentage of spontaneous scarring of subretinal neovascularisation (SRN) is of favourable prognostic significance. SRN in high myopes seem to possess a less active potential than SRN in emmetropes, probably due to the atrophic changes that take over. The course of this condition is mostly self-limited. Spontaneous cicatrization of SRN and stabilization or slight improvement of vision in 2/3 of cases characterize the natural course of Fuchs' spot.

INTRODUCTION

The ophthalmoscopic appearance of a pigmented lesion of the macula in highly myopic eyes is well known since its first description by Förster (1862) and its detailed analysis by Fuchs (1901). In their honour it has been termed

Table 1. Study population of patients with Fuchs' spot from the Essen University Eye Hospital during the years 1957 to 1980.

	No. of patients	No. of eyes
Group A*	145	206
Group B**	36	55

*Includes all patients documented to have Fuchs' spot.

**Patients answering to a follow-up call in 1980.

Group B is part of Group A.

Förster-Fuchs' spot. Its histologic features have first been studied by Lehmus (1875) and valuable clinical reports have been produced by various authors (Aiello and Master 1953; Lloyd 1954; Campos 1957, D'Hoine *et al.* 1974). Gass (1967) first interpreted this lesion as a disciform, neovascular process associated with breaks in Bruchs' membrane. This notion gained universal acceptance and has found confirmation in further fluorescein angiographic studies by Levy, *et al.* (1974, 1977). Ultrasonic data of eyes with Fuchs' spot were first produced by Curtin and Karlin (1971).

However, the question regarding the visual prognosis and natural course has received little systematic attention. We report herein the findings in this regard based on a retrospective follow-up study with a final reexamination at the end of the observation period.

The purpose of this study was to evaluate the natural course of visual acuity, changes in fundus appearances, frequency of recurrences and involvement of the second eye.

SUBJECTS AND METHODS

For this purpose the fundus slides and records of all patients with the diagnosis Fuchs' spot at the Essen University Eye Hospital were reviewed in 1980. 206 eyes of 145 patients were documented to have Fuchs' spot (Group A) and up to date 36 patients living within a reasonable travel distance answered to our follow-up call (Group B). (Table 1). A complete ocular examination, including fundus photography, fluorescein angiography and ultrasonic biometry was performed. Follow-up ranged from three to 15 years, with a median of five years. A follow-up of at least three years was considered sufficient to meet the natural history criteria.

RESULTS AND DISCUSSION

Women were twice as often affected as men, the female – male ratio being 2:1. One explanation for the predominance of females is that women are more prone to higher degrees of myopia (Duke-Elder 1976).

Patients with Fuchs' spot are almost exclusively juvenile myopes (94,4%), myopia developing before the age of 15 years (mean $9,6 \pm 5,2$ years).

Table 2. Frequency of unilateral and bilateral cases of Fuchs' spot.

	Unilateral	Bilateral
Group A	86/145 (59,3%)	59/145 (40,7%)
Group B	17/36 (47,2%)	19/36 (52,8%)

At the same time, the frequency of myopia in their first degree relatives is quite high, reaching 29,68%. 58,3% of their parents were myopic.

Age of manifestation of Fuchs' spot varies largely in individual cases. In our series the youngest was a 14-year old boy and the oldest men and women 66 years of age. There is a strong predilection for the 30 to 60 years age group, the median being 41 years. Males and females show no significant differences regarding age at manifestation.

Bilaterality

The frequency of Fuchs' spot in both eyes was 40–52% in our series, which is higher than in other reports. (Fuchs (1901) = 24%; Campos (1957) = 28–42%; Curtin and Karlin (1971) = 18,2%). This figure depends very much on length of follow-up and reflects the fact that referral centers see the more desperate cases. (Table 2).

The follow-up group revealed rising bilaterality with length of follow-up. The time interval between involvement of the first eye and the second eye may vary largely from days to many years. The average time interval in this study was 2.4 years, with a range from 0–8 years and the median being one year. Fuchs (1901) in his original article mentioned a time interval of up to five years. We confirm, that in the majority of susceptible individuals both maculas may be affected during a short course.

Refraction

This study corroborates that Fuchs' spot affects mainly moderately high myopes around – 12,0 D.

However, a comparison with the refraction curve of Betsch (1929) shows that the incidence of myopia decreases as the degree of myopia increases. In other words, excessive high myopes are infrequent and so are Fuchs' spot in such eyes as well.

The importance of degree of myopia in the pathogenesis of Fuchs' spot becomes apparent in that affected eyes are significantly more myopic than non-affected eyes in the same individuals ($-12,47 \pm 5,08$ D vs $-10,52 \pm 5,5$ D; $p < 0.01$).

Anisomyopia as such is no protection against Fuchs' spot, since 44,6% of anisomyopes were bilaterally affected. On the other hand, in anisomyopia the more myopic eye is significantly more frequently affected than the less myopic eye ($p < 0.05$).

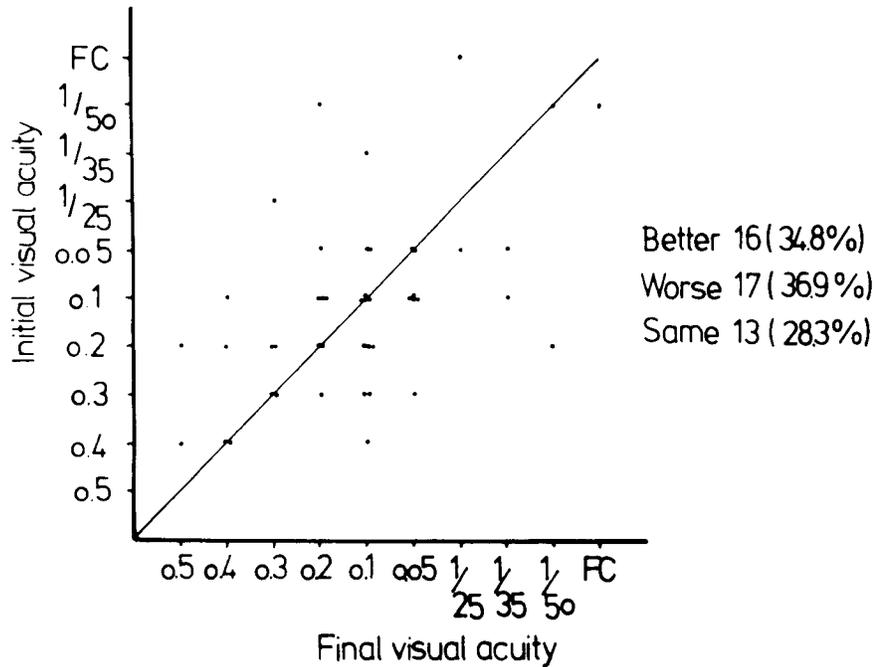


Fig. 1. Scattergram comparing initial visual acuity and final visual acuity in the follow-up group.

Age of onset of Fuchs' spot and degree of myopia are significantly related in such a way, that manifestation tends to occur earlier with rising degree of myopia, the correlation coefficient being $r = -0,44$; $p < 0,001$.

The same relation exists between age of onset of Fuchs' spot and axial length ($r = -0,33$; $p < 0,05$).

All this proofs the fundamental role of the degree of myopia in the pathogenesis of Fuchs' spot.

Visual prognosis

When initial visual acuity is plotted against final visual acuity apparently 34,8% of eyes improve, 36,9% deteriorate and 28,3% retain unchanged visual acuity (Figure 1). This is to say, that in about 2/3 or 63% of eyes visual acuity was stabilized or improved untreated during follow-up. Almost as many eyes improved spontaneously as deteriorated. The overall distribution of visual acuity changes very little during follow-up. Median visual acuity at begin and at end of study was unchanged 0,1.

Visual prognosis is slightly better in the younger age group ($r = -0,36$; $p < 0,01$). Visual prognosis is not related to the degree of myopia. Unilateral and bilateral cases do not differ in their visual outcome.

Group B n = 46 eyes

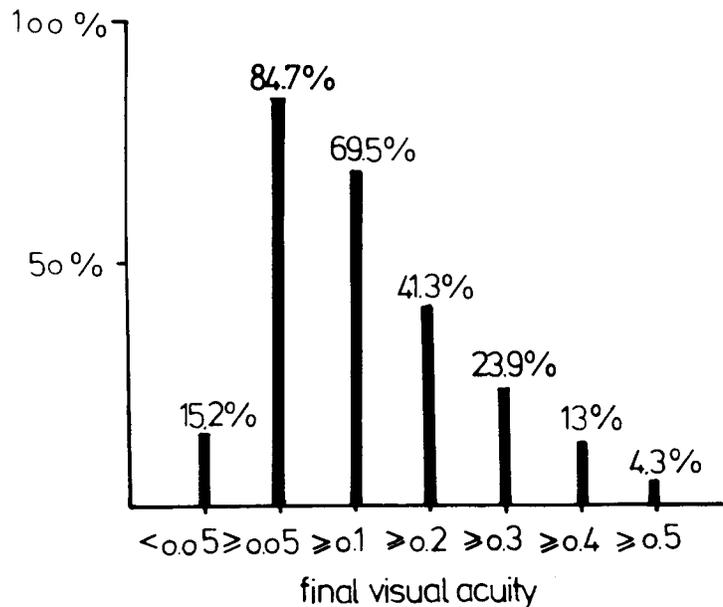


Fig. 2. Histogram showing the cumulative final visual acuity in the follow-up group.

Interestingly, near visual acuity recorded at the most favourable reading distance is usually better than distance visual acuity (67,3% of eyes; $p < 0,001$). Most eyes with Fuchs' spot retain some reading vision ability. This reflects the fact, that in most cases not the whole fovea is involved and that myopes benefit from their own magnification as they approach the reading text.

On the whole, Fuchs' spot seems to carry a relatively benign visual prognosis. Visual acuity of 0,2 or more was retained by 41,3% of eyes, of 0,1 or more by 69,5% and of 0,05 or more by 84,7% of eyes. Legal blindness resulted in three out of 46 eyes (6,5%) (Figure 2).

Regarding visual prognosis Fuchs' spot seems to be a non-progressive, relatively stationary condition. After the initial visual impairment chances for moderate improvement or stabilization are good.

Morphology

Fuchs (1901) in his original article gave a distinctive clinical description of the typical pigmented lesion of the macula, which he thought was due to the accumulation of pigment and not related to hemorrhage. Fuchs had observed hemorrhage in only nine of his 50 cases and considered it to be a merely accidental association. He stressed to have seen many macular hemorrhages in myopes not resulting in a pigmented lesion.

In this report we were able to detect fresh macular hemorrhage in 78% and subretinal neovascularization (SRN) on fluorescein angiography in 77% of macular lesions. We also noted lacquer cracks in 54,5% at the posterior pole. Lacquer crack lesions are due to rupture of Bruchs' membrane and may provide the entry for subretinal neovascularization. (Klein and Curtin 1975). The high percentage of chorioretinal atrophy found (90,9%) is another clue to the pathogenesis.

The course of these fresh hemorrhagic macular lesions due to SRN is, however, quite variable. During the subsequent course the clinical appearance is to a high degree changeable. Many turn into this heavily pigmented, sharply demarcated black lesion. Others tend to develop pigment dispersion as the acute hemorrhage resolves. Increase in chorioretinal atrophy (75%) during the course is a prominent feature, sometimes dissolving the typical Fuchs' spot.

When visual prognosis is related to morphology the single most important variable is foveal involvement. Involvement of the fovea was defined as an area roughly equivalent to the normal retinal avascular zone using a transparent overlay grid. Involvement of the fovea was noted initially in 26 of 46 eyes reducing visual acuity to 0,1 or less. As the acute lesion resolved seven eyes regained visual acuity above 0,1 (range 0,2–0,4; mean 0,25). There is a decent chance of improvement as the acute lesion resolves. On the other hand ten of 46 eyes with an extrafoveal lesion initially developed foveal involvement during follow-up reducing visual acuity to 0,1 and less.

A second factor of significance is recurrent hemorrhage which we observed in 15 of 55 eyes (27,3%). Such recurrency led to further deterioration in eight of 15 eyes (53,3%), while in five of 15 eyes acuity improved and in two of 15 eyes remained unchanged despite recurrency of bleeding.

A third factor of significance regarding visual acuity is persistence of SRN (as documented by fluorescein angiography) with or without recurrent hemorrhage. Persistent SRN were detected in 11 of 29 eyes (37,9%). In such cases vision deteriorated further in 72,7% (8 of 11 eyes).

Spontaneous scarring of SRN was seen in 72,4% (21 of 29 eyes) and increase in chorioretinal atrophy in 75% (22 of 29 eyes) of eyes. In such eyes vision improved in 50% and stabilized in 60–80% in due course. Spontaneous scarring of SRN coincident with increase in chorioretinal atrophy is frequent and turned out to be of favourable prognostic significance. SRN in high myopic eyes seem to possess a less active potential than in emmetropic eyes, probably due to atrophic changes that take over. In no case did we note such enormous disciform responses as may be seen in the presumed ocular histoplasmosis syndrome or in senile disciform macular degeneration (Junius Kuhnt).

This might explain the relatively benign course Fuchs' spot has. Progressive visual loss, recurrent hemorrhage and persistent growth of SRN are absent in about 2/3 of all patients. Spontaneous cicatrization of the SRN and stabilization or slight improvement of visual acuity in about 60% characterize the natural course of Fuchs' spot.

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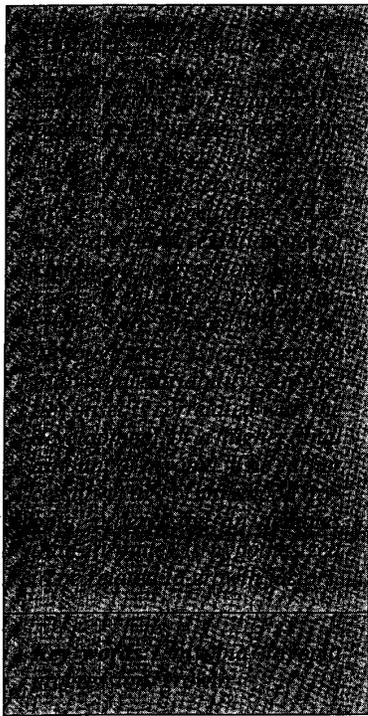
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Trends in the change of clinical refractive error in myopes

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Refractive error changes are generally greater in young myopes than in young hyperopes.¹⁻³ The phenomenon of increases in myopic refractive error is often referred to as myopia progression. The purpose of this paper is to describe the patterns and characteristics of myopia progression. Throughout the paper minus changes in refractive error represent increases in myopia and plus changes decreases in myopia.

Previous literature

Age of myopia onset

Hirsch,⁴ in a study of Ohio school children, and Young et al.⁵ in a study of eastern Washington school

children, found that the prevalence of myopia continued to increase throughout the school age years. Hirsch's⁴ data showed the prevalence to increase most at 11-12 years of age in girls, and 13-14 years in boys. Young et al.⁵ found the greatest increase in prevalence of myopia to be at 9-10 years of age in girls, and 11-12 years in boys.

Fletcher⁶ presented evidence to suggest that the earlier the age of onset the greater the amount of myopia which developed. She used what were presumably clinical records. She presented a table showing at what age 1 D of myopia first appeared, with the corresponding average myopia at various yearly intervals thereafter. For example, for 13 children with age of onset at 4-8 years, the average myopia 6 years later (10 to 14 years of age) was 4.32 D. This can be compared to 1.75 D of myopia at ages 15 to 19 years for a group of 15 children with age of onset ranging from 11 to 15 years, and to 2.56 D of myopia at ages 13 to 14 years for a group of 24 children with age of onset at 9 to 10 years. A source of ambiguity in these results is the fact that the gender distribution of the sample was not given. Rosenberg and Goldschmidt,⁷ using data from files of an ophthalmological practice in Denmark, noted a slight tendency toward greater myopia increase in the two years following onset, for subjects with the earlier onset ages. This held for both boys and girls.

Childhood myopia progression

Using retinoscopic data from a twice yearly screening of southern California school children and using two graphical visual inspection tests and two statistical tests, Hirsch³ judged that 84 to 90% of the chil-

dren had a linear change in refractive error with age. Using subjective visual inspection and an F-test for linearity on similar data from an Ontario, Canada school, Langer⁸ found 93% of children to change linearly by one or both of these tests. Both samples included both hyperopes and myopes, but Langer stated that linearity was more common among myopes than hyperopes.

Using subjective refraction data from three optometric practices in the central USA, Goss⁹ found that rates of childhood myopia progression were most commonly around -0.45 D/yr, although there was considerable individual variation. Both Goss⁹ and Rosenberg and Goldschmidt⁷ noted a slight tendency for higher rates of progression to occur more often in females than in males. For instance, Rosenberg and Goldschmidt reported that of the 108 boys and 144 girls in their sample, 5% of the boys and 10% of the girls increased in myopia more than 2 D in the two years after its onset. This is comparable to Hirsch's¹⁰ observation that of 5,201 randomly selected records of patients aged 18 to 50 years from the former Los Angeles College of Optometry clinic, the ratio of females to males with myopia greater than 6 D was 2:1, while for myopia less than 6 D it was 4:5. Hirsch's data presumably included all types of myopes, not exclusively those who had simple childhood progression.

The work of several investigators, including Sorsby,¹¹ Tokoro and Suzuki,¹² and Fledelius¹³ has shown that the major anatomical component alteration responsible for childhood myopia progression is axial elongation.

Many treatment systems, most notably bifocals, have been employed in an attempt to reduce my-

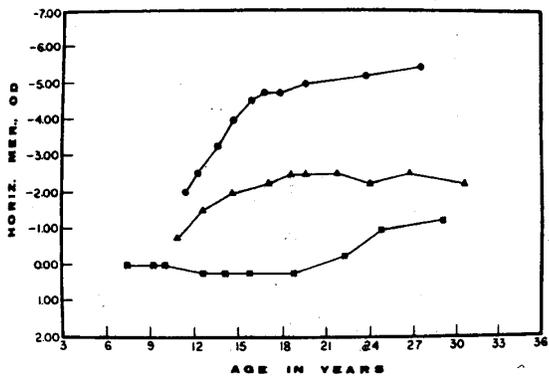


Figure 1: Examples of young adulthood myopia progression patterns based on the classification system of Goss, Erickson, and Cox.¹⁹ Each set of common symbols represents refractive data (refractive error in the principal meridian nearest horizontal in the right eye) for one subject. Filled circles—adult continuation; filled triangles—adult stabilization; filled squares—adult acceleration.

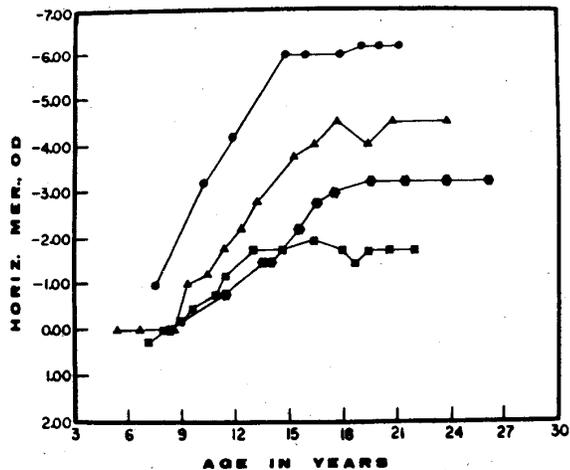


Figure 2: Plots of four males selected as typical and considered to be representative of myopia progression trends in the sample. Age in years is plotted on the x-axis, and refractive error (diopters) in the principal meridian nearest horizontal for the right eye is on the y-axis. Each set of common symbols represents one individual.

opia progression rates, but none of them has been found to be consistently and universally effective.^{14,15}

Cessation of childhood myopia progression

Ophthalmic clinicians are aware that myopia progression most often becomes less pronounced during the middle to late teens. Goss and Winkler¹⁶ investigated this on a quantitative basis using four graphical and statistical techniques, to derive index values for the ages at which childhood myopia progression ceased or slowed appreciably. The mean cessation age was significantly lower for females than for males, although there was considerable individual variability. The second method employed by Goss and Winkler¹⁶ defined the cessation age as the point at which a regression line of refractive error versus age for points below 15 years of age intersected a line with zero slope through the mean amount of myopia at points after 17 years of age. The mean (\pm SD) cessation ages

using this method were 16.7 (\pm 2.1) years for males and 15.2 (\pm 1.7) years for females.

Young adulthood myopia progression

Young adulthood is generally a time of relatively stable refraction,² although some myopes have increases in their myopia,² and some emmetropes become myopic.^{17,18} Using longitudinal records of optometric practice patients (the same sample as the present paper), Goss, Erickson, and Cox¹⁹ characterized patterns of young adulthood refractive changes in myopes as adult stabilization, adult continuation, and adult acceleration. Examples based on this categorization are illustrated in Figure 1. Adult stabilization features rapid myopia increases during childhood and/or early adolescence, followed by slight or no change in adulthood. In adult continuation, myopia progression is also present in adulthood, but generally at a slower rate than in childhood. In adult acceleration, myopia progres-

sion accelerates in adulthood. Adult stabilization was the most common pattern (87% of females and 68% of males), and adult acceleration was the least common (0% of females and 6% of males). The most common adulthood rate of progression was about -0.05 D/yr, with males tending to show higher rates. For all the adult continuation and adult acceleration subjects for whom there was sufficient keratometric data for analysis (11 subjects) there was an increase in power of the anterior corneal surface. The coefficient of correlation of the rate of refractive error change to the rate of anterior corneal radius change was 0.58. The cornea did not show comparable changes during childhood myopia progression in these individuals, even though the rates of childhood myopia progression were greater than the rates of young adulthood progression in most of the subjects. Adult stabilization subjects did not show consistent changes in corneal power. Goss, Erickson, and Cox¹⁹ therefore suggested that corneal steepening plays an important part

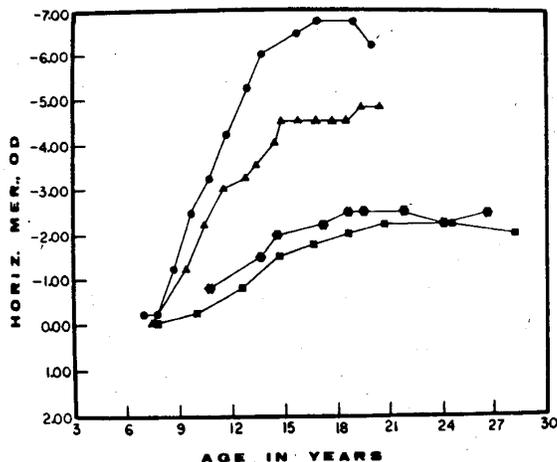


Figure 3: Plots of four females selected as typical and considered to be representative of myopia progression trends in the sample. Age in years is plotted on the x-axis, and refractive error (diopters) in the principal meridian nearest horizontal for the right eye is on the y-axis. Each set of common symbols represents one individual.

in the increases of myopia which occur in some young adults. Measurements of the other ocular dioptric components were not available.

Subjects and methods

The data used in this study were derived from longitudinal records of 559 patients from five optometric practices on the basis of the following criteria: (1) at least four examinations between the ages of 6 and 24 years, (2) myopia of at least 0.50 D sometime during the course of the clinical record, (3) astigmatism never manifested in excess of 2.50 D, (4) no strabismus or amblyopia, (5) no contact lens wear prior to the last refractive data recorded for use in this study, (6) no ocular pathology, and (7) no systemic pathology which might affect ocular findings. These practices were located in the north central and south central United States: (1) a small town in northwestern Iowa surrounded by an agricultural area settled mainly by people of Scandinavian extraction (n = 74); (2) a small town in southern Indiana with agricultural,

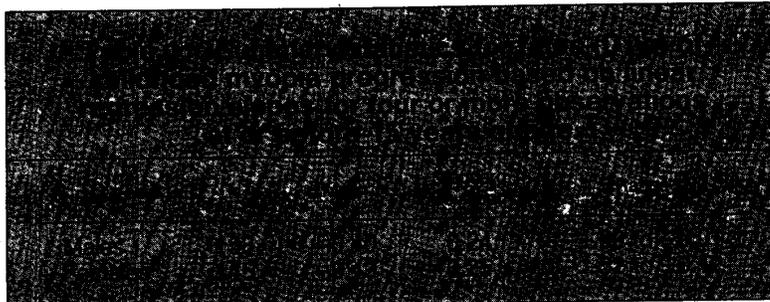
lumbering, and furniture industries, and settled primarily by Germans (n = 141); (3) small city in northern Illinois with a large university, some industry, and some surrounding rural area, with a predominantly Caucasian population of diverse national descent (n = 190); (4) a metropolitan area of a large city in northeastern Oklahoma, the practice serving mainly black people (n = 95); and (5) a medium sized city in northeastern Oklahoma, the practice serving primarily a Caucasian population (n = 59).

The refractive data used in this study consisted of the refractive error in the principal meridian nearest

horizontal in the right eye as derived from the subjective refraction recordings. Typical graphs of refractive error versus age are shown in Figures 2 and 3.

Additional plots that are representative of this sample, have been presented elsewhere, in studies of childhood myopia progression,^{9,16} and a study of adulthood myopia progression.¹⁹ The high degree of linearity which appears to be present in the childhood and adulthood segments of the plots, and the findings of Hirsch³ and Langer⁸ discussed above, have led us to adopt a linear model to define various parameters of myopia progression. We used linear regression slopes (D/yr) to derive rates of childhood myopia progression, using points at or before 15 years of age in those cases where four or more refractions were recorded during that age span. An index of myopia onset age was obtained by extrapolating the line to zero refractive error. The final amount of myopia after childhood progression was derived by averaging the amounts of myopia found at examinations after 17 years of age. Cessation ages were found by determining the age at which the childhood progression line intersected a zero slope line through the final amount of myopia. This is the same technique used as cessation age determination method 2 by Goss and Winkler.¹⁶

We also calculated an average amount of myopia for males and females at half-year intervals. For individuals who did not have examinations at the exact age levels



studied, an amount of refractive error at these half year intervals was obtained by linear interpolation between the next lower age and the next higher age observations. Means were calculated at each of these age levels.

In two of the practices from which data were taken, spectacle corrections consisted primarily of single vision lenses with full correction of the myopic refractive error, while in the other three locations bifocal lenses were used almost as often as single vision lenses. For a smaller portion of this sample, single vision lens wearers and bifocal lens wearers did not differ significantly in cessation age¹⁶ or rate of childhood progression.⁹

Results

Rates of childhood progression

Four or more refractions at and before the age of 15 years were available for 158 males and 145 females in the sample. The mean rates of childhood myopia progression were -0.40 D/yr for males, and -0.43 D/yr for females. There was considerable variability in rates with standard deviations of about 0.25 (see table 1). Rates of about -0.4 D/yr were most common, while positive rates and rates more minus than -1.00 D/yr were quite uncommon (see table 2).

Onset age

An index of the age of onset of myopia as defined above (under Subjects and Methods) was correlated with other parameters of myopia progression. As shown in Table 3, onset age showed a significant correlation with average refraction for visits after 17 years of age (referred to herein as the final amount of myopia). The coefficient of correlation is greater for females. This correlation supports the hypothesis that the earlier the age at which myopia appears the greater the amount of myopia which is likely to develop during childhood. The correlation of onset age and cessation age is not statistically significant (see table 3), suggesting that the duration of childhood progression is not consistent from one individual to another.

Average refractive error for sample

A plot of mean amount of myopia as a function of age is given in Figure 4. This graph supports some of the general trends noted by study of the individual data. Most notable is the fact that the plot of average myopia for females levels off before that of males.

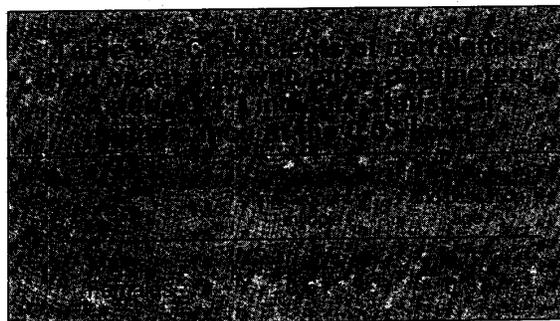
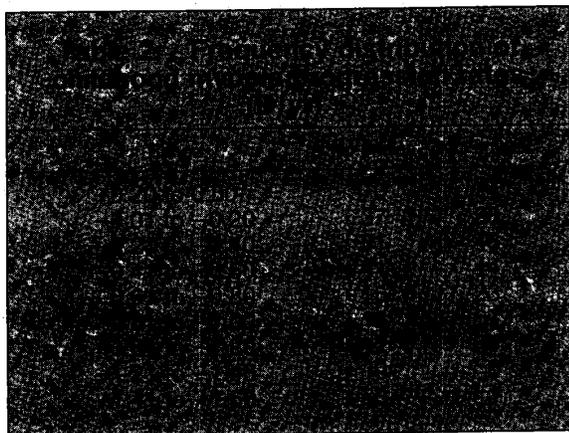
The gender difference in cessation age parallels gender differences in general body growth. We did not have data on the stature or weight

of the subjects in this sample, but assuming that they represent a good cross-section of at least a portion of the USA, it would be valid, for certain limited purposes, to compare mean refractive data from our sample to national norms for stature. Such a comparison can be made in Table 4 in which median height from norms given by Lowrey²⁰ is entered. Average myopia shows relatively small changes after about 16.5 years for males, and after about 14.5 years for females (see table 4). It may be noted that these ages correspond closely to the ages after which median height shows less change. The coefficient of correlation of average myopia and median height at corresponding ages was 0.99 for females and 0.97 for males.

Discussion

Based on the previous literature cited and the present study, we can note several gender differences in myopia progression. Females tend to have earlier onset, earlier cessation, a higher prevalence of high myopia, and less likelihood of adulthood progression. The earlier cessation age of childhood myopia progression in females than in males parallels the earlier cessation of growth in stature in females.

It is possible that the hormonal influences leading to the termination of long bone growth may make



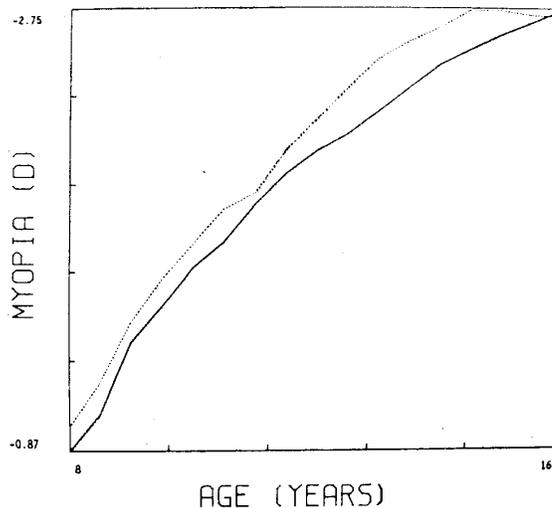


Figure 4: Average of individual refractive errors in the principal meridian nearest horizontal for the right eye plotted with respect to age. The plot for females is represented by the dotted line, that for the males by the solid line.

the sclera less distensible, thus rendering endogenous and exogenous factors responsible for axial elongation less effective. This might mark the transition from childhood myopia progression with its typical rates of about -0.4 D/yr, to young adulthood myopia progression with its typical rates of about -0.05 D/yr. It is also compatible with data from the previous literature which would suggest that the most important ocular component change in childhood progression is axial elongation, while corneal power increases may be most significant in adulthood progression.

Summary and conclusions

Longitudinal records of 559 myopic patients were obtained from five optometric practices, in order to study characteristics and trends of myopia progression. A linear regression model was employed to describe various parameters in the change of the clinical refractive error with age.

Table 4: Average amount of myopia from the present study and 50th percentile of height from Lowrey.²⁰ For the myopia data the number of subjects from which the average was determined is given in parentheses.

Age in Years	Mean Amount of Myopia in diopters		Median Height from Lowrey in cm. (see text)	
	Males	Females	Males	Females
8	-0.87 (64)	-0.93 (58)	130.0	128.0
8.5	-1.01 (81)	-1.12 (73)	132.8	130.5
9	-1.32 (102)	-1.37 (94)	135.5	132.9
9.5	-1.47 (119)	-1.57 (112)	137.9	135.8
10	-1.64 (135)	-1.71 (129)	140.3	138.6
10.5	-1.75 (152)	-1.86 (151)	142.3	141.7
11	-1.91 (168)	-1.93 (162)	144.2	144.7
11.5	-2.04 (180)	-2.11 (171)	146.9	148.1
12	-2.12 (192)	-2.26 (189)	149.6	151.9
12.5	-2.19 (195)	-2.40 (196)	152.3	154.3
13	-2.29 (200)	-2.52 (205)	155.0	157.1
13.5	-2.40 (207)	-2.59 (204)	158.9	158.4
14	-2.50 (205)	-2.65 (194)	162.7	159.6
14.5	-2.55 (203)	-2.73 (191)	165.3	160.4
15	-2.62 (201)	-2.74 (185)	167.8	161.1
15.5	-2.67 (204)	-2.71 (177)	169.7	161.7
16	-2.72 (200)	-2.71 (167)	171.6	162.2
16.5	-2.78 (193)	-2.71 (158)	172.7	162.4
17	-2.77 (184)	-2.75 (144)	173.7	162.5
17.5	-2.77 (175)	-2.77 (134)	174.1	162.5
18	-2.82 (158)	-2.90 (121)	174.5	162.5

The following conclusions can be drawn from this study:

- The most common rates of childhood myopia progression in this sample were around -0.4 D/yr. Considerable individual variability was noted, with standard deviations of about 0.25.
- If an individual develops myopia at an early age, it is likely that that person will develop a high amount of myopia.
- Gender differences should be taken into account in theories of myopia etiology.
- The childhood progression of myopia tends to cease earlier in females than in males. It is hypothesized that this is related to growth factors. Future studies that investigate this possible relationship are needed. ■ ■

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Progression of Myopia in Youth: Age of Cessation

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ABSTRACT

Patient records of young myopes were collected from three optometry practices. An index of the age at which increases of myopia in young people cease was derived using four different graphical and statistical methods. The results suggest that myopia stops increasing earlier in females than in males. There is, however, a great deal of individual variability in cessation age. Some implications for clinical practice and clinical research are discussed.

Key Words: myopia, myopia progression, refractive error

It is widely acknowledged among ophthalmic clinicians that once a youngster becomes myopic, he will most likely become more myopic, and that this increase in myopia will stop or slow down sometime in the teenage years or later.¹ Moreover, several studies support the notion that myopia progression ceases in the middle or late teens. Brown^{2,3} and Slataper,⁴ using clinical records including both hyperopes and emmetropes as well as myopes, indicated lower mean rates of changes in refractive error after 20 years of age, as compared to the rates of change in childhood and teenage years. Bücklers,⁵ from records from his practice, noted that myopic subjects show rapid increases in myopia up to about 20 years of age, where the change is not as great. Hofstetter⁶ obtained data from an optometric practice in Bloomington, Indiana, and calculated the change in refractive error per month for various age levels. He found that mean refractive changes were close to zero in

the 21- to 34-year age range. In Japan, Tokoro and Suzuki⁷ found the mean change in refractive error for 56 myopic eyes was greatest before 15 years of age, less between 15 and 20 years, and even lower but still positive between 20 and 25 years.

The purpose of this paper is to derive index values to represent the ages at which progressive increases of myopia in youth may be considered to have ceased or to have slowed down so appreciably as to be negligible for statistical purposes, to examine and compare the age differences for the cessation index values in the two sexes, and to compare different methods for determining these values.

SUBJECTS AND DATA

Records of 299 patients were selected from three optometry practices on the basis of the following criteria: (1) at least four refractive examinations between the ages of 6 and 24 years, (2) myopia of at least one-half diopter sometime during the course of the record, (3) astigmatism never manifested in excess of 2.5 D, (4) no strabismus or amblyopia, (5) no contact lens wear before the last examination data used in this study, (6) no ocular pathology, and (7) no systemic pathology which might affect ocular findings. The records were obtained from optometry practices in the following locations: (1) a small town in Northern Iowa surrounded by an agricultural area settled primarily by people of Scandinavian extraction (N = 74); (2) a small town in Southern Indiana with agricultural, lumbering, and furniture industries, settled mainly by Germans (N = 141); and (3) a small city in Northern Illinois with a large university, some industry, and surrounding rural area, with a predominantly Caucasian population of diverse national descent (N = 84). These data were collected for other studies as well, and many of the subjects' records did not include adequate data for the derivation of the theoret-

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ical termination points or cessation ages of the progression of myopia, as will be described below.

The data used consisted of the subjective refraction findings recorded in the optometrists' clinical files, i.e., the lens formulas which represented the examiner's subjectively determined cylindrical correction combined with the least minus lens sphere permitting the maximum attainable visual acuity. Different optometrists might consistently get slightly different values by this procedure, but the potential error should be negligible in terms of this investigation because for almost every subject all measurements were made by the same optometrist. For the present purposes, each subject's degree of myopia was represented in two ways for separate analyses: (1) by the refractive error of the right eye in the principal meridian nearest the horizontal, and (2) by the computed mean spherical equivalent for the two eyes.

In two of the three practices, the age at the time of each examination, rather than the birthdate, was recorded. Thus, the exact age could not be determined for many subjects. In those cases, a precise age was assigned for each patient at each examination in a manner similar to that used by Mandell.⁸ All subjects were examined at least four times. By noting the months in which a given subject was seen and the ages reported,

it was possible to narrow the precise date of birth to within a range of a few months. The birthdate was then taken as the midpoint of that range.

METHODS

Determination of the age at which the progressive increase of myopia may be considered to have ceased was made by four different methods. One of the methods is a graphical technique with visual inspection, one is a statistical technique using simple linear regression analysis, and the other two involve a more sophisticated statistical model involving a switching regression.

Method 1

The first method was a graphical technique involving visual inspection. For each subject, the refractive error in the principal meridian nearest horizontal in the right eye was plotted against age. Fig. 1 illustrates representative plots from the male sample and Fig. 2 illustrates plots selected from the female sample. The great majority of curves showed an increasing degree of myopia into the middle teens and a relatively flat, horizontal segment beginning in the late teens. The graphical procedure of Method 1 was to draw (1) a best fit straight line by visual

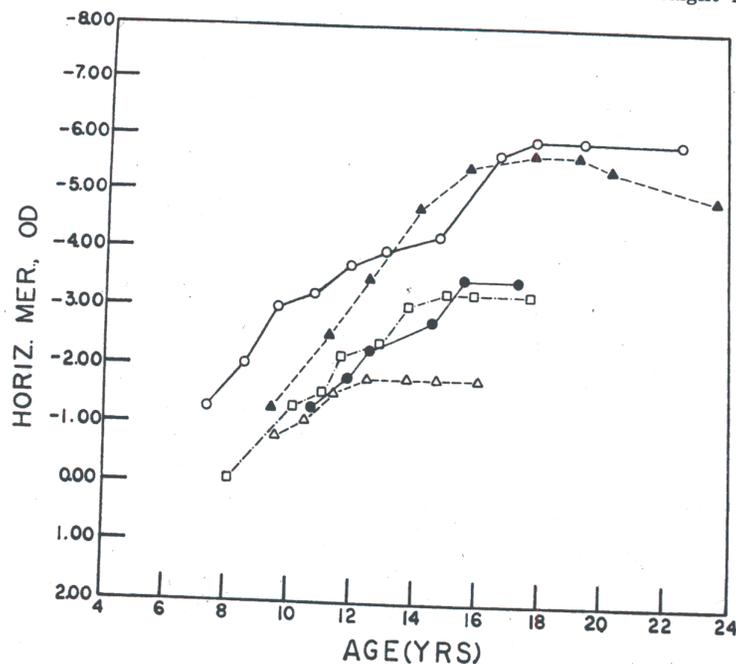


Fig. 1. Graphs of five male subjects selected as typical and representative of the sample. Each trace represents one subject.

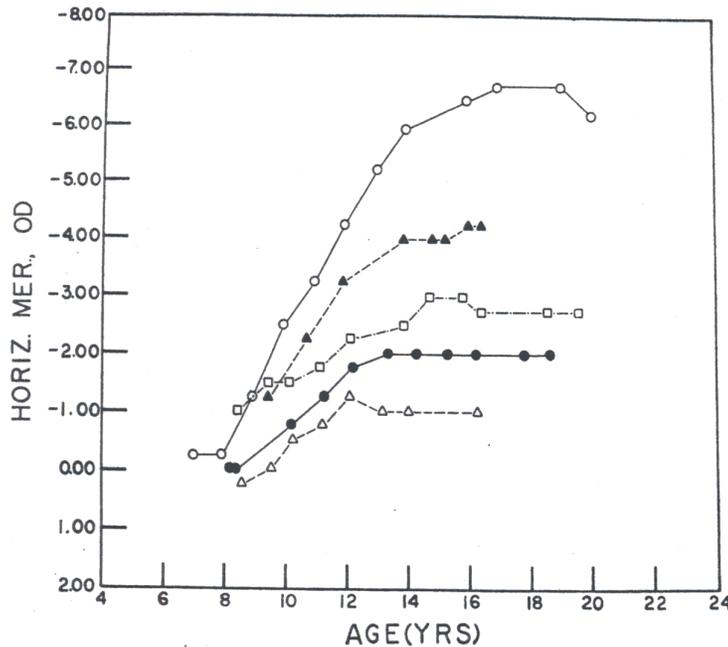


Fig. 2. Graphs of five female subjects selected as typical and representative of the sample. Each trace represents one subject.

inspection through three or more points under about 15 years of age, and (2) a horizontal line through the mean refractive error at points after about 17 years of age. The cessation age from Method 1 was then taken to be the age at which these two lines intersected. This technique is illustrated in Fig. 3, in which the cessation age would be 14.25 years.

In only a few instances did the myopia obviously cease to increase before age 15 or obviously continue to increase past age 18, by evidence of several points. In general, Method 1 was not used in instances in which there were fewer than three points under 15 years of age or fewer than two points after 18 years, except when the age intervals between points were sufficiently large to provide slope values that seemed as reliable as might be obtained by more points closer together.

Method 2

This method performed essentially the same analysis as Method 1, using a statistical technique rather than a graphical technique. The line representing the ascending portion of the graph of amount of myopia vs. age was determined by linear regression analysis.⁹ The age at which this regression line intersected the zero slope line through the mean amount of myopia

at points after 17 years of age was taken as the cessation age of the progression of myopia as determined by Method 2. The age guidelines for the use of Method 2 were the same as those for Method 1. However, Method 2 allowed the determination of the cessation age in some cases in which Method 1 was not used due to ambiguity in the placement of the ascending portion of the graph by visual inspection.

Method 3

This method used all of the data points in the plot of the refractive error in the principal meridian nearest horizontal in the right eye as a function of age. A switching regression model developed by Ferreira¹⁰ was used to generate a piecewise linear regression model consisting of two regression lines. In essence, this model finds the pair of regression lines providing the best overall fit to the data. The age at which these two lines intersected (i.e., the point at which the regression model "switched") was taken as the cessation age of the progression of myopia as determined by Method 3. To be included in this analysis, individual cases had to meet two criteria: (1) the record must have continued to at least 16 years of age, and (2) the record must have started at 11 years or earlier or 12.5 years or earlier if 0.25 D of myopia appeared after 11

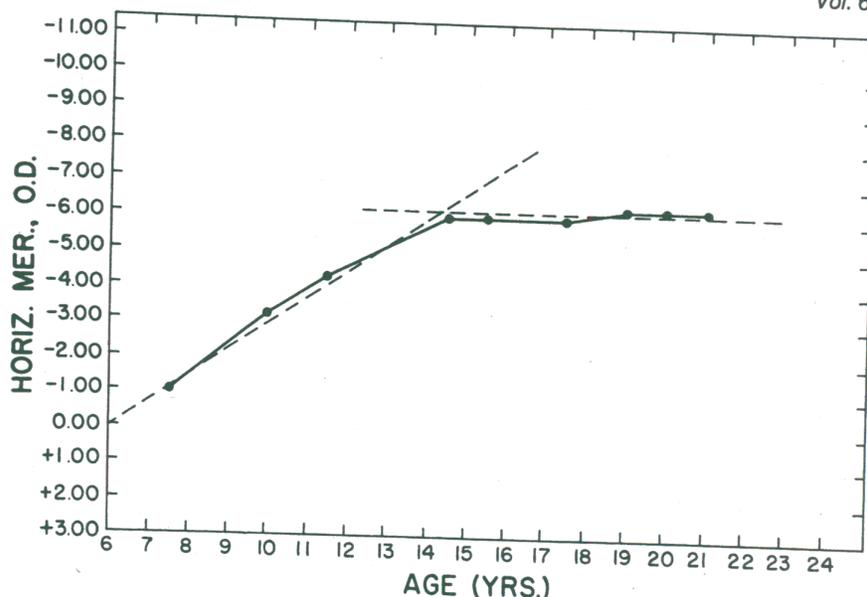


FIG. 3. An illustration of the graphical visual inspection method of determining the cessation age of the progression of myopia. Each solid circle indicates a single observation. The diagonal dashed line is a regression line fitted by visual inspection. The other dashed line is a horizontal (zero slope) line through the mean refractive error of points after 17 year age.

years, if the record continued beyond 20 years of age, or if the record continued beyond 18 years of age and there were at least six observations. When there were many points after 24 years of age, the record for this analysis was stopped at 24 years. Hyperopic points before the appearance of myopia were eliminated because refractive error change appears to accelerate markedly when a subject crosses the line from hyperopia into myopia.

Method 4

Method 4 is identical to Method 3 except that the mean of the spherical equivalent refractive errors of the two eyes was used instead of the refractive error in the principal meridian nearest horizontal in the right eye. As in Method 3, the age at which the two regression lines intersected in the switching regression model was taken as the cessation age of the progression of myopia. In Methods 3 and 4, unlike Methods 1 and 2, the separation of the data into two regimes corresponding to the progression of myopia and the period with relatively stable myopia was done strictly in a mechanical fashion dictated by the switching regression model, as opposed to being done in an ad hoc fashion.

Inherent in the analysis by both graphical and statistical techniques is the assumption that the refractive error progresses linearly with age.

Whether this assumption is warranted, at least for the period of myopia progression, is being examined in another study.

RESULTS

The distributions of myopia progression cessation ages determined by the four different methods for those subjects meeting inclusion criteria are presented in Figs. 4 to 7. Each of these figures displays two cumulative distributions, one for males and the other for females. Some summary statistics are given in Table 1.

The cumulative curves for females in Figs. 4 to 7 are generally to the left of those for males, suggesting that females tend to have lower cessation ages. The four methods gave mean cessation ages ranging from 14.44 to 15.28 years for females and from 15.01 to 16.66 years for males. For each method, the mean cessation age was higher for males than for females, as can be seen in Table 1. The difference in means varied from 0.57 years (Method 3) to 1.45 years (Method 2), and all differences were statistically significant except for the difference from Method 3.

For both males and females, there was a considerable variability in cessation age. The ranges of the distributions in Figs. 4 to 7 are all in the neighborhood of 10 years. The SD of cessation age was near 2 years for each sex and each method (Table 1).

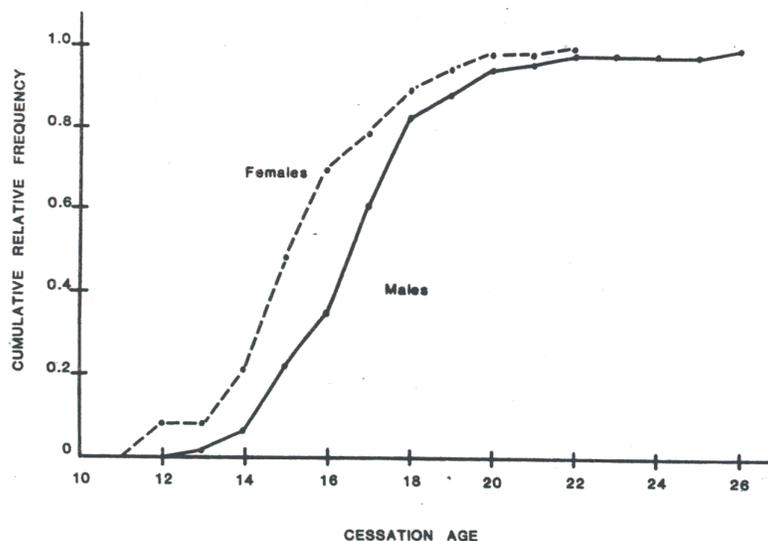


Fig. 4. Cumulative distributions of cessation ages determined from Method 1 for males and females.

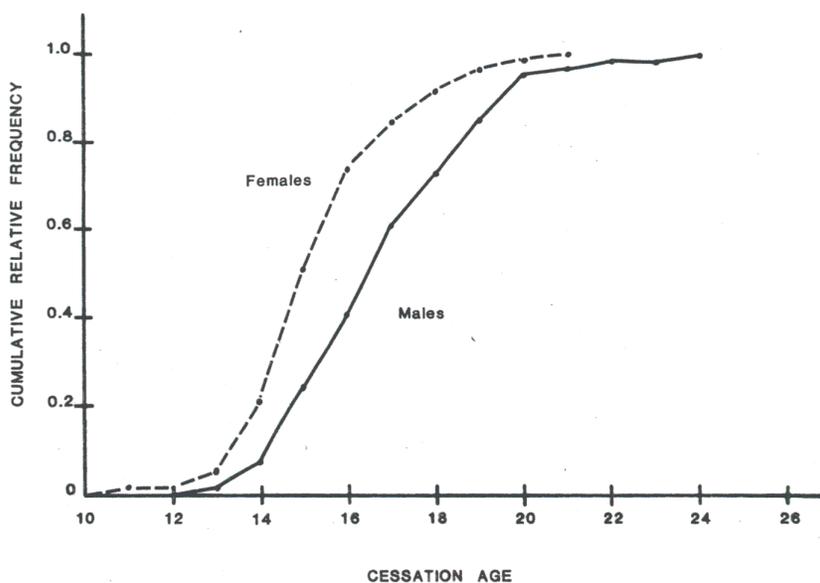


Fig. 5. Cumulative distributions of cessation ages determined from Method 2 for males and females.

Table 2 indicates how the cessation ages from the different methods were correlated. The highest correlations were between Methods 1 and 2 and between Methods 3 and 4, although the other correlations are also reasonably high (and significantly different from zero). Methods 1 and 2 generally yielded higher cessation ages than Methods 3 and 4 because the former methods restricted the slope of the second line segment

to zero (e.g., see Fig. 3). In Methods 3 and 4, no such restriction was made, and a low positive slope (further slight increase in myopia) was more common for the second line segment than was a zero or negative slope. (A positive slope in graphs such as Fig. 3 corresponds to a negative rate of change in diopters per year, that is, to an increase in myopia.) The average value of the second slope was about 0.10 for both sexes and

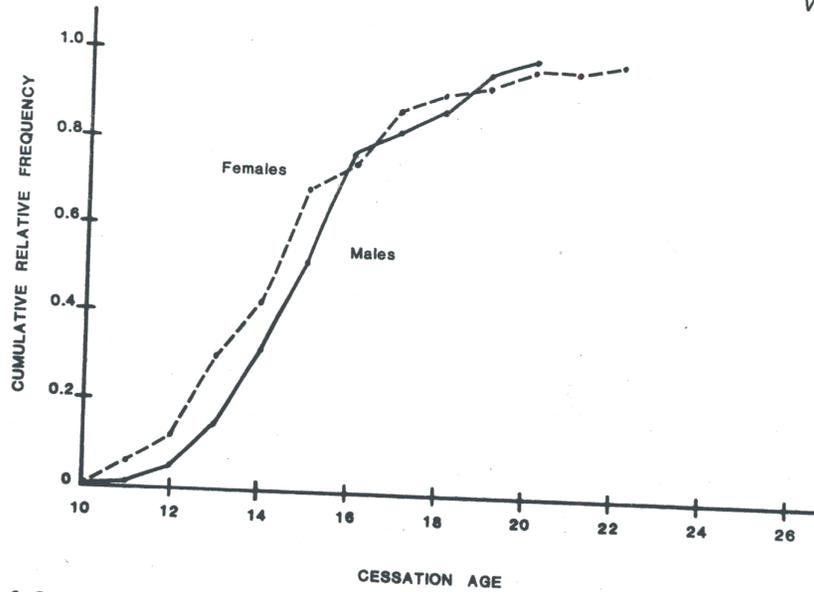


Fig. 6. Cumulative distributions of cessation ages determined from Method 3 for males and females.

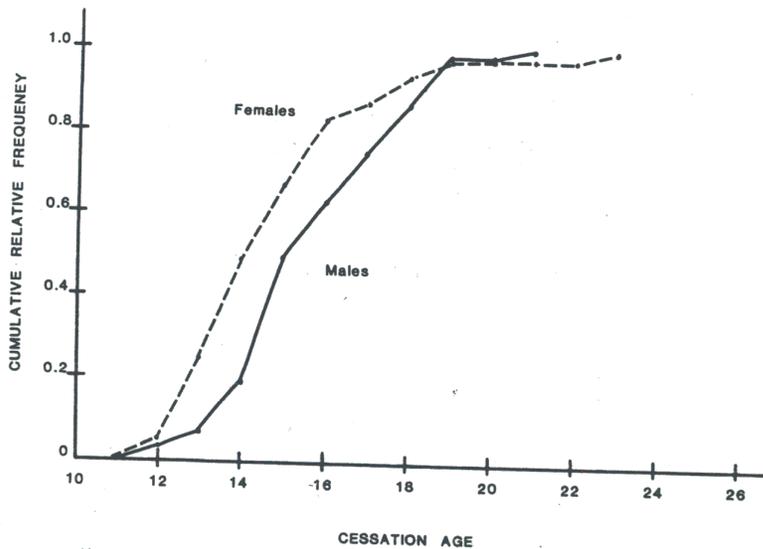


Fig. 7. Cumulative distributions of cessation ages determined from Method 4 for males and females.

both methods (3 and 4). For a given first line, a positive slope for the second line means that the two lines intersect at an earlier age than if the slope of the second line had been zero. It is worth noting that the lack of statistical significance of the difference in mean cessation ages determined by Method 3 for males and females can be explained, in part, by this lowering of the cessation age when the second line segment

shows a further, albeit at a lesser rate, increase in myopia. The second line segment had a positive slope for 76.3% of the males in Method 3, as compared with 67.3% of the females. The reasonably close agreement of the means and the high correlation between Methods 3 and 4 suggest that astigmatism changes are relatively unimportant in the determination of cessation ages.

TABLE 1. Mean cessation ages, SD's, and levels of significance of difference of mean cessation ages for males and females.

Method	Sex	N	Mean	SD	t	Significance
1	M	59	16.53	2.11	3.21	0.0014
	F	56	15.28	2.04		
2	M	66	16.66	2.10	4.16	0.0001
	F	57	15.21	1.74		
3	M	59	15.01	2.01	1.34	0.18
	F	49	14.44	2.34		
4	M	59	15.53	1.93	2.34	0.02
	F	45	14.57	2.18		

TABLE 2. Coefficients of correlation of cessation ages given by different methods for males (females).

Method	Method		
	2	3	4
1	0.91 (0.88)	0.59 (0.63)	0.59 (0.46)
2		0.63 (0.77)	0.62 (0.64)
3			0.74 (0.90)

TABLE 3. Means (SD's) of rates of increase of myopia before cessation age.

	Method		
	2	3	4
M	-0.45 (0.22)	-0.50 (0.26)	-0.46 (0.24)
F	-0.50 (0.23)	-0.56 (0.30)	-0.54 (0.27)

In terms of the slopes of the first line segment, representing rates of increase of myopia before the age of cessation, the regression lines from Methods 2 to 4 were very similar. The average rates, given in Table 3, were all near -0.50. Moreover, the rates from different methods for the same subjects were very highly correlated, as can be seen from Table 4. The rate tended to be positively correlated with the cessation age, as the correlation coefficients in Table 5 demonstrate. These correlations are significantly different from zero, but they are of moderate size, with most in the neighborhood of 0.40.

In two of the practices from which data were collected, both single vision lenses and bifocals were used for young myopes. Whether bifocals have an effect on myopia progression is controversial.^{11,12} Cessation ages were investigated for those subjects who wore one or the other type of lens the entire time from the first observation to the cessation age; summary statistics are given in Table 6. Among both males and females,

mean cessation ages for single vision lens wearers and bifocal lens wearers were not significantly different, although the sample size is quite small. Preliminary work¹³ on the rates of increase of myopia indicates that the rates for single vision and bifocal wearers are not significantly different.

DISCUSSION

If myopia progression tends to end earlier in females than in males, this may suggest that it is growth-related because general body growth tends to cease earlier in females. This would not, however, provide us with any answers concerning the heredity vs. environment controversy about the etiology of refractive errors. That is, the genetically determined changes in refractive error may cease when growth tends to cease, or environmental determinants of refraction may no longer be effective after a certain age which varies from individual to individual.

The variation among methods can be related to different notions about the progression of myopia. The methods were similar in terms of the first line segment but not in terms of the second line segment. The imposition in Methods 1 and 2 of a zero slope for the second line

TABLE 4. Coefficients of correlation of regression slopes (representing rates of increase of myopia before cessation age) given by Methods 2 to 4.

	Methods		
	2, 3	2, 4	3, 4
M	0.92	0.82	0.83
F	0.87	0.81	0.98

TABLE 5. Coefficients of correlation of cessation ages and rates of increase in myopia before cessation age.

	Method		
	2	3	4
M	0.37	0.37	0.46
F	0.04	0.47	0.43

TABLE 6. Mean cessation ages and SD's (from Method 4) for single vision lens (SV) and bifocal lens (BF) wearers.

Lens	Sex	N	Mean	SD
SV	M	9	15.74	1.76
BF	M	14	14.63	1.32
SV	F	6	14.73	2.20
BF	F	9	14.10	1.58

segment suggests a relatively sudden cessation in the increase of myopia. Relaxing this constraint, as in Methods 3 and 4, allows the model to reflect a possible shift to a lesser degree of increase of myopia as opposed to a sudden cessation.

A correlation was observed between the rate of increase of myopia before cessation and the age of cessation. Thus, whereas a high rate of increase of myopia may tend to indicate an eventual high degree of myopia, some subjects with high rates of increase may stop increasing sooner than others with lesser rates of increase, thereby arriving at similar "final" levels.

The results of this study may be useful to the practitioner in answering a patient's or parent's inquiries about when myopia will stop increasing. For example, if we use the results from Method 2, we can say that boys tend to stop at about 16½ years and girls at about 15¼ years, although deviations of up to 2 or 3 years in either direction from these ages are not at all unusual and even more extreme deviations are possible. The curves in Figs. 4 to 7 can be used to provide some general guidelines as to when the progression of myopia is likely to cease.

It has been suggested¹¹ that research on therapies designed to slow the rate or progression of myopia in young people should have experimental and control groups matched in age and should use subjects with ages lower than that at which myopia would be expected to stop increasing. The mean rate for a group may be affected by improper age matching, obscuring the effect of the experimental technique. Thus, it was proposed,¹¹ based on the graphical visual inspection technique (Method 1), that males should not be used for these studies after about 14.4 years of age and females after about 13.2 years. Using the mean minus 1 SD with the results from Method 2, this cut-off age would be 14.6 years for males and 13.5 years for females.

SUMMARY AND CONCLUSIONS

The purpose of this paper is to derive index values to represent the ages at which progressive increases of myopia in youth may be considered to have ceased or to have slowed down so appreciably as to be negligible for statistical purposes, to examine and compare the age differences for the cessation index values in the two sexes, and to compare different methods for determining these values. Patient records of young myopes were collected from three optometry practices. Estimates of the age at which increases of myopia in young people cease were developed using four different graphical and statistical techniques. The progression of myopia tends to continue to a later age for males than for females. There is, however, a high variability in cessation

ages for both males and females. Differences in results from the different methods can be related to underlying assumptions about the nature of the progression and cessation of the progression of myopia.

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The burden of genetically determined eye disease

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SUMMARY We determined the underlying aetiology of blindness for the registered blind population of the Province of Newfoundland and Labrador. In both 1981 and 1984 single-gene disorders accounted for 30% of total blindness and congenital defects for another 10-11%. Genetically determined conditions, diabetes, and senile macular degeneration (SMD) were the three leading causes of registration in each year, 1980-4. We calculated mean ages of registration and mean ages of death over the last four years for five major aetiological groups. Patients with genetic conditions were registered at a much younger age and had a correspondingly longer duration of blindness (21 years as compared with 5 years for either diabetes or SMD). Total 'person-years of blindness' was then calculated from the product of this duration of blindness and the total numbers registered in each group. This index shows that the overall individual and population impact of monogenic blindness is overwhelmingly greater than that of other causes (6849 person-years compared with 270 for diabetes and 430 for SMD). In view of this frequency and duration of monogenic blindness, and also of the substantial hereditary liability to relatively common causes of blindness such as glaucoma, diabetic retinopathy, and high myopia, we suggest that more attention needs to be paid to elucidating the genetic contribution to blindness.

There is a growing awareness of the importance of genetic disease as a cause of blindness. For example, a recent paper from Saudi Arabia¹ reported a changing pattern of aetiology, so that fully 84% of childhood blindness in that country is now caused by hereditary conditions.

Three years ago we reported on the causes of registered blindness in Newfoundland at the end of 1981.² Our aim was to determine as accurately as possible the underlying aetiology of blindness in each case, based on a review of the files of all persons registered with the Canadian National Institute of the Blind (CNIB) and examination of as many as possible of those cases for which the reported cause of registration was ambiguous. Single-gene disorders accounted for at least 30% of all registered blindness.

We have now brought this review of records up to date, tabulating the new registrations for the past three years. We present here analyses comparing 1981 and 1984. We are also interested in the relative burden to the population of different causes of blindness, and therefore determined 'person-years of

blindness' for the different categories as an index of the personal and population impact of each.

Patients and methods

The Canadian Province of Newfoundland and Labrador has a total population of approximately 580 000, the majority of whom live in relatively isolated, scattered coastal communities. The legal responsibility for the registration of blindness rests with the CNIB. Registration is not obligatory at present. The criteria for registration, only one of which need be met, are (a) corrected visual acuity of 6/60 or worse in the better eye, and (b) a total visual field of less than 10° from fixation using a white target 10 mm in diameter at a distance of 1 m.

The files of all persons registered on 31 December 1981 had previously been analysed in detail to determine the aetiological category.² Persons newly registered in each of the years 1980-4 have now been analysed in the same way. If there was some ambiguity in the diagnosis or aetiological code, an attempt was made to examine the patient. We have examined a total of 350 of the 1041 registered

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patients. In the case of retinal dystrophies and related conditions this examination included colour vision testing, dark adaptation, and electroretinography. Although glaucoma, diabetic retinopathy, and high myopia may have a strong genetic component, these entities were tabulated separately, not under established or presumed genetic disease.

The ages of death of all registrants dying in the years 1981-4 were obtained, as were their ages at registration. From these numbers were calculated the mean ages of registration for each major aetiological category, the duration of blindness to the nearest whole year of each deceased registrant, and the mean duration of blindness for each major aetiological category. For comparison the mean ages of registration for all registrants and for those first registered in the last five years were calculated. The determination of mean years of blindness is possible only for the period 1981-4, during which CNIB files have been monitored, as no continuing record is kept of age at registration and age at death of those deceased in earlier decades.

For each aetiological category we multiplied mean duration of blindness for deceased registrants (1981-4) by the overall number of patients in the category as at 31 December 1984 to arrive at 'person-years of blindness', an indicator of the relative burden to the population of each major cause of blindness.

Results

As at 31 December 1984, 1041 individuals were registered blind in the Province. Two hundred and fifty-three (24%) of these were blind because of single-gene disorders such as the retinal dystrophies, albinism, aniridia, or autosomal dominant cataracts, established by examination (Table 1). Another 5% were presumed to have genetic disorders on the basis of family history of such conditions as nystagmus or optic atrophy, but were not seen by us. The congenital group included some unidentified simplex cases of the genetic forms of cataract, coloboma, or microphthalmos. Senile macular degeneration (SMD), diabetic retinopathy, and glaucoma (each of which may be regarded as being multifactorial in aetiology), which are frequently noted elsewhere as leading causes of blindness, occurred much less often in this Newfoundland series than did monogenic blindness.

Between 1981 and 1984 there was only a small increase in the total number registered, from 1013 to 1041 (Table 1). The genetic and congenital proportions were unchanged, comprising over 40% of registrations. The proportions of myopia and glaucoma were also unchanged. There was an

increase in the number of cases of senile macular degeneration. Blindness from infectious disease and trauma had decreased slightly in frequency. There were more deaths of elderly affected patients in these groups than new registrations. Fewer diabetics were registered now than previously; this reflects only imperfectly the high mortality in this group (see below).

Table 2 shows the registrations in each of the past five years. Except in 1983, when few diabetics were registered, senile macular degeneration, genetic conditions, and diabetic retinopathy were consistently the top three causes of registration.

The mean age at registration for the new registrants of the past five years was similar to that of the total registrations in each of the five major aetiological groups (Table 3). The mean ages of registration of

Table 1 Causes of blindness in all persons registered with the Canadian National Institute for the Blind in Newfoundland and Labrador on 31 December 1981 and 31 December 1984

	1981		1984	
	Number	%	Number	%
Genetic established	243	24.0	253	24.3
Genetic presumed	56	5.5	56	5.4
Congenital: cataract and multiple anomalies	110	10.9	116	11.1
High myopia	100	9.9	100	9.6
Senile macular degeneration	60	5.9	86	8.3
Infectious disease	88	8.7	77	7.4
Trauma and poisoning	67	6.6	62	6.0
Diabetic retinopathy	59	5.8	54	5.2
Glaucoma	48	4.7	49	4.7
Vascular and other systemic disease	41	4.0	42	4.0
Senile cataract	34	3.4	29	2.8
Tumour	22	2.2	21	2.0
Other	61	6.0	68	6.5
Undetermined	24	2.4	28	2.7
Total	1013	100.0	1041	100.0

Table 2 Causes of blindness registration in each of the years 1980-4

	1980	1981	1982	1983	1984	Total
Senile macular degeneration (SMD)	11	18	12	18	11	70
Genetic (established and presumed)	15	13	10	17	9	64
Diabetic retinopathy	15	11	10	3	13	52
Congenital	7	8	3	4	4	26
Glaucoma	3	6	3	8	3	23
Trauma and poisoning	5	7	5	1	2	20
High myopia	6	6	4	2	1	19
Vascular and other systemic disease	0	1	4	5	6	16
Senile cataract	5	3	2	3	2	15
Infectious disease	2	3	1	2	1	9
Tumour	1	0	1	0	1	3
Other and undetermined	7	4	5	6	3	25
Total	77	80	60	69	56	342

Table 3 Mean ages at registration in five selected aetiological categories (years \pm SD)

	Total registration (n=1041)	New registrations 1980-4 (n=342)	Persons dying 1981-4 (n=175)
Diabetes	56 (\pm 16)	53 (\pm 18)	61 (\pm 14)
SMD	74 (\pm 9)	77 (\pm 7)	77 (\pm 7)
Glaucoma	62 (\pm 17)	73 (\pm 17)	71 (\pm 12)
Myopia	46 (\pm 16)	57 (\pm 17)	58 (\pm 11)
Genetic	25 (\pm 16)	25 (\pm 20)	46 (\pm 19)

Table 4 Mean years of blindness in five aetiological categories of those registered blind persons who died during 1981-4

	Number of deaths	Mean age at registration	Mean age at death	Mean years of blindness
Diabetes	39	61	66	5
SMD	23	77	82	5
Glaucoma	15	71	81	10
Myopia	7	58	75	17
Genetic	22	46	67	21
	Total deaths 175			

Table 5 Expected total 'person-years of blindness' in five aetiological categories, based on blind population registered on 31 December 1984

	Number registered	Mean years of blindness	Person-years of blindness
Diabetes	54	5	270
SMD	86	5	430
Glaucoma	49	10	490
Myopia	100	17	1700
Genetic	309	21	6489

those who died within the past four years were also comparable, except for the genetic category; in this case the mean age of registration was 46 years, compared with 25 years for recent registrations and total registrations.

One hundred and seventy-five registrants died during 1981-4 (Table 4). The deaths in the diabetic retinopathy group were markedly out of proportion to their representation in the total sample; of 79 diabetics registered at some time during 1981-4, 39 died within that interval. During the same time 23 of 102 with senile macular degeneration died and only 22 of 326 with genetic conditions.

Persons with diabetic retinopathy and senile macular degeneration experienced on average five years of blindness, persons blind owing to high myopia 17 years, and persons blind due to monogenic conditions 21 years (Table 4). In the total registered blind population the 'person-years of blindness' attributable to diabetes were 270, to SMD 430, and to genetic diseases 6489 (Table 5).

Discussion

In analysing the records of all the registered blind persons in the Province our first goal was to determine as accurately as possible the underlying aetiology of the blindness. As has previously been discussed, in 15% of cases either the recorded cause of blindness or the aetiology code was found to be incorrect.² However, by undertaking this study in a geographic area with a relatively small and stable population we could establish family histories relatively easily and frequently examine patients with ambiguous records to establish diagnoses.

The high frequency of genetic blindness in Newfoundland is not a reflection of ascertainment due to our research interests. Rather than a recent increase in the proportion of monogenic blindness we are demonstrating a continued high prevalence. Single-gene disorders accounted for 30% of total blindness in our initial study in 1981, reflecting the high prevalence of this type of blindness over previous years.

The increase in senile macular degeneration in the 1981-4 interval may indicate improved ascertainment or a real increase as the life expectancy of the general population increases. In this interval there have been few new registrations in the categories of infection and trauma, presumably because of improved treatment, and the overall representation of these categories has decreased. New cases of blindness in younger people due to infection and trauma are unlikely to have escaped detection and registration in this well defined population. The cases which are more likely to escape registration at the appropriate level of vision are those due to slowly progressive diseases in older people—senile macular degeneration, diabetic maculopathy, and glaucoma.

It may be asked whether the high proportion of genetically determined blindness in Newfoundland is explained by the Province's population genetic structure. The population derives primarily by natural increase from settlers who arrived before 1835, drawn from highly circumscribed areas of south-western England and southern Ireland. Hundreds of small communities have grown up around Newfoundland's many natural harbours. At present about 50% of the population of the Province reside in communities of fewer than 2500 inhabitants, and 41% reside in communities of fewer than 1000. These small subpopulations remain genetically isolated (Bear JC, Nemeč TF, Kennedy JC, *et al.*, unpublished data). The low levels of migration into these communities and of genetic exchange between them contrast with observations from numerous studies of European isolates of comparable size where there has been increasing genetic exchange in

this century. Thus frequencies of specific recessive disorders may be increased owing to inbreeding. Because closely consanguineous unions tend to be avoided, the matings are usually between distant relatives, and the frequency of a recessive disorder is reasonably ascribed to founder effect (the chance presence of an allele in relatively few original settlers of a genetically isolated population). Several instances of locally raised frequencies of autosomal dominant and X-linked ocular disorders, such as von Hippel-Lindau disease and ocular albinism, have also been described, again reasonably attributed to founder effect. Conversely, just as some deleterious alleles are found in unusually high frequency, it is to be expected that some will be infrequent or absent, and indeed no examples of Best's macular dystrophy or of choroideraemia have been identified.

It must be emphasised that a high proportion of blindness due to hereditary disease is also indicated in studies elsewhere. In a county in Norway 29.6% of blind people (vision 6/60 or less) had hereditary or probably hereditary diseases.³ Genetically determined conditions accounted for 77% of childhood blindness in Lebanon,⁴ 79% in Cyprus (of which half were autosomal recessive),⁵ and 84% in Saudi Arabia as already noted.¹ We have previously shown that the prevalence of genetic eye disease in Newfoundland was underestimated because of errors and ambiguities in coding at the time of registration of blindness.² This underestimation could also apply to other studies where it was not possible to review all files in detail or examine as many of the patients when there was ambiguity in the coding.

Persons with monogenic blindness, as a group, are registered much younger than other blind persons, and consequently have a much longer duration of blindness. Although the mean years of blindness calculated for the group of 22 who died in 1981–4 was 21 years, higher than for other groups, this none the less greatly underestimates the usual duration of monogenic blindness. The mean age of registration for the most recent registrants in the genetic group is 25 years (Table 3), not 46 years as in the small group who died recently. The mean years of blindness of the genetic group as a whole may therefore be expected to be around 42 years rather than 21 years and attributable 'person-years of blindness' about 13 000. Not only are monogenic conditions the leading cause of blindness, but also in 'person-years of blindness', the overall individual and population impact of monogenic blindness is overwhelmingly greater than that of other forms of blindness.

The mean duration of blindness attributed to SMD and diabetes was five years. Senile macular degeneration causes blindness primarily in elderly people with a short life expectancy. Although the mean age of

registration for diabetics is lower, sometimes in the interval 20–30 years, life expectancy of this group is unfortunately very poor. In fact, of the 15 diabetics registered in 1980, 10 were deceased by 1985, compared with six of the 62 registered for other causes in 1980. Several young juvenile-onset diabetics died within one or two years of registration.

It is noteworthy that the genetic group appears to have a relatively low mean age of death (67 years), only one year higher than diabetics (66 years). If premature mortality among blind people with genetic disease is substantiated in studies of larger numbers of registrants, it will be important to try to determine what factors contribute to this. (Perhaps SMD and glaucoma registrants seem relatively long lived because these disorders are associated with advanced age.)

Regardless of the exact proportion of monogenic blindness in a particular country, the extra 'person-years of blindness' are relevant in all countries in which infectious and nutritional causes of blindness are adequately controlled. Moreover, the total genetic contribution to blindness extends well beyond the category of monogenic blinding disorders. Diabetes and glaucoma each show familial aggregation, and the genetic component in the liability to each is substantial. High myopia frequently seems strikingly familial.

While it remains of great importance to provide support through low-vision services, itinerant teachers for the visually impaired, and employment counselling, much more attention should be paid to elucidating the genetic component of blindness. This includes accurate diagnosis to provide specific recurrence risks for genetic counselling, clarification of the natural history and prognosis of individual disorders to provide specific advice for affected persons, and genetic linkage studies, to allow carrier detection and presymptomatic identification of affected individuals.

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Relationship between retinal lesions and axial length, age and sex in high myopia

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ABSTRACT: We analysed the relationship between central and peripheral retinal lesions and axial length (AL), patient's age and sex with myopia greater than 6 diopters. A total of 212 eyes of 109 patients with high myopia underwent detailed funduscopy and A-scan ultrasonography. AL was measured, and central and peripheral retinal lesions were noted. Results were analysed using Student's t-test. Sixty-one patients (118 eyes) were female and 48 (94 eyes) male. Mean age was 31.00 ± 13.67 years, and mean AL was 28.31 ± 2.02 mm. Chorioretinal atrophy, Fuchs' spot, posterior staphyloma and posterior vitreous detachment increased significantly with AL and age. Fuchs' spot was more common in females. White-without-pressure (WWP) was inversely correlated with AL and age, and was more common in males. The high frequency of WWP in younger patients and moderate AL suggests that these lesions result from vitreoretinal tractions. Lattice degeneration was also a frequent finding in high myopia, and tended to increase with AL and age, though without reaching statistical significance. (Eur J Ophthalmol 1997; 7: 277-82)

KEY WORDS: High myopia, Retinal lesions, Axial length, Age

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INTRODUCTION

Pathologic myopia is a subgroup of myopia where axial length (AL) of the eyeball is excessive, and degenerative changes take place in the central and peripheral retina (1). It is one of the leading causes of blindness in the young population (1-5). Along with the oreoquatorial elongation there is also localised ectasia in the posterior pole, namely posterior staphyloma (6). Its prevalence has been reported to be between 0.2% and 9.6% (1, 7-9). In pathologic myopia, refraction is normally -6.00 diopters (D) or more. However, some studies use limits as high as -8.00 D or as low as -4.00 D (1, 7, 10-14). Since refractive power does not fully reflect axial elongation, biometric measurement of AL is more valuable (1, 2, 15).

Curtin (12) reported that central retinal lesions like crescent, chorioretinal atrophy (CRA) and posterior staphyloma increase with AL. Peripheral retinal lesions are also common in pathologic myopia. The relation-

ship between lattice degeneration and retinal detachment has been repeatedly shown (13, 16-18). In a study on 1437 eyes, Karlin (13) reported that peripheral retinal lesions and lattice degeneration increased with AL. Pierro (19) supported these findings. However, Celorio (14) found that lattice degeneration was frequent in moderate myopia and decreased with AL.

This study was planned to investigate the frequency of central retinal lesions which have a bearing on the visual prognosis and of peripheral lesions associated with retinal detachment, and to see how these lesions were related with AL, age and sex in eyes with -6.00 D or more myopia.

PATIENTS AND METHODS

A total of 212 eyes of 109 patients with -6.00 D or more myopia presenting at the Department of Ophthalmology, Istanbul University, Faculty of Medicine be-

tween 1992 and 1994 were included in the study. Eyes with systemic and/or previous or present ocular disease were excluded in order to avoid any confusion or misinterpretation of the lesions.

Patients underwent routine ophthalmic examination, and a detailed fundus examination with indirect binocular ophthalmoscopy and biomicroscopy with a Goldmann three-mirror lens together with scleral indentation. Crescent, chorioretinal atrophy (CRA), Fuchs' spot, lacquer crack, clinically significant posterior staphyloma and posterior vitreous detachment (PVD) were noted as posterior pole lesions and four major peripheral retinal degenerations (lattice, paving stone, white-without-pressure (WWP), pigmentary degeneration) and retinal breaks as peripheral lesions.

Axial lengths were measured with an Allergan-Humphrey Model 820 ultrasonic biometer using a standardized A-scan 10-Mhz frequency probe. Mean AL

measurements of eyes with retinal lesions were compared with those without lesions using Student's t-test in order to analyse the relationship between retinal lesions and AL. The relationships between age and retinal lesions were also analysed.

Eyes were divided into five groups according to AL (Group 1 24.00-25.99 mm, Group 2 26.00-27.99 mm, Group 3 28.00-29.99 mm, Group 4 30.00-31.99 mm), and the distribution of retinal lesions in these groups was checked.

Patients were divided into four age groups (Group 1 ≤ 19 years, Group 2 20-39 years, Group 3 40-59 years, Group 4 ≥ 60 years), and the distribution of retinal lesions in each group was studied.

The relationships between various parameters were statistically evaluated. Pearson correlation coefficients (r) were calculated for the variable of degree of myopia (Diopters), AL and age, and statistical significance (p) was evaluated.

TABLE I - CENTRAL AND PERIPHERAL RETINAL LESIONS

Retinal lesion	No.	%
Crescent	141	66.5
Chorioretinal atrophy	13	6.1
Fuchs' spot	14	6.6
Lacquer crack	2	0.5
Posterior staphyloma	50	23.6
Posterior vitreous detachment	68	32.1
Lattice	35	16.5
Paving stone	19	9.0
White-without-pressure	43	20.3
Pigmentary degeneration	11	5.2
Tear/hole	11	5.2

RESULTS

There were 61 females and 48 males. Mean age was 31.00 ± 13.64 years, range 9-70. Mean refraction was -12.34 ± 5.34 D, range between -6.00 D and -32.00 D. Mean AL was 28.31 ± 2.02 mm, range 24.63-34.00 mm. There was a positive correlation between degrees of myopia and AL ($r=0.8059$; $p<0.001$). There was no correlation between age and myopia and AL ($r=0.1128$; $p=0.051$; $r=0.0967$, $p=0.080$, respectively).

The frequency of retinal lesions is shown in Table I. Crescent was the most frequent and lacquer crack the

TABLE II - RELATIONSHIP BETWEEN RETINAL LESIONS AND AXIAL LENGTH

Lesions	Mean axial length (mm)		t	p
	With lesions	Without lesions		
Crescent	29.00 ± 1.89	26.94 ± 1.50	7.98	$p<0.001^{**}$
Chorioretinal atrophy	30.19 ± 1.54	28.18 ± 1.99	3.56	$p<0.001^{**}$
Fuchs' spot	30.73 ± 1.35	28.14 ± 1.95	4.89	$p<0.001^{**}$
Posterior staphyloma	30.00 ± 2.11	27.78 ± 1.68	7.65	$p<0.001^{**}$
Posterior vitreous detachment	29.64 ± 1.99	27.68 ± 1.71	7.38	$p<0.001^{**}$
Lattice	28.71 ± 2.22	28.23 ± 1.97	1.27	$p=0.204$
Paving stone	29.37 ± 2.29	28.20 ± 1.97	2.43	$p=0.016^*$
White-without-pressure	27.74 ± 2.03	28.45 ± 2.00	-2.07	$p=0.039^*$
Pigmentary degeneration	29.47 ± 1.99	28.24 ± 2.01	1.97	$p=0.051$
Tear/hole	28.74 ± 2.12	28.28 ± 2.02	0.72	$p=0.469$

* $p<0.05$: significant; ** $p<0.001$ highly significant

rarest central retinal lesion, while WWP was the most frequent and pigmentary degeneration the least frequent peripheral retinal lesion.

AL were significantly longer for eyes with crescent, CRA, Fuchs' spot and PVD ($p < 0.001$). AL was significantly longer in eyes with paving stone degenerations ($p = 0.016$) and significantly lower in WWP ($p = 0.039$). No association was shown between AL and retinal breaks (Tab. II).

Table III shows the distribution of retinal lesions in

AL groups. Central retinal lesions, PVD and paving stones were significantly more frequent in long AL eyes (Tab. III).

No correlation was found between age and AL ($r = 0.0967$, $p > 0.05$). On the other hand, age was significantly higher in crescent, CRA, Fuchs' spot, posterior staphyloma and PVD cases. Paving stones were more common in older and WWP more frequent in younger groups (Tabs. IV and V).

Fuchs' spots were more common in females ($p < 0.001$)

TABLE III - DISTRIBUTION OF RETINAL LESIONS IN RELATION TO AXIAL LENGTH

Lesions	Axial length (mm)					Total	p
	24-25.99	26-27.99	28-29.99	30-31.99	32-34.00		
Crescent	3 (12.5%)	40 (51.9%)	58 (86.6%)	27 (87.1%)	13 (100%)	141 (66.5%)	<0.0001
Chorioretinal atrophy	— (0%)	— (0%)	7 (10.4%)	4 (12.9%)	2 (15.4%)	13 (6.1%)	0.0105
Fuchs' spot	— (0%)	— (0%)	4 (6.0%)	4 (12.9%)	6 (46.2%)	14 (6.6%)	<0.0001
Lacquer crack	— (0%)	— (0%)	1 (1.5%)	— (0%)	1 (7.7%)	2 (0.9%)	—
Posterior staphyloma	2 (8.3%)	6 (7.8%)	15 (22.4%)	18 (58.1%)	9 (69.2%)	50 (23.6%)	<0.0001
Posterior vitreous detachment	1 (4.2%)	15 (19.5%)	23 (34.3%)	18 (58.1%)	11 (84.6%)	68 (32.1%)	<0.0001
Lattice	4 (16.7%)	9 (11.7%)	11 (16.4%)	8 (25.8%)	3 (23.1%)	35 (16.5%)	n.s. (0.4554)
Paving stone	1 (4.2%)	6 (7.8%)	5 (7.5%)	2 (6.5%)	5 (38.5%)	19 (9.0%)	0.0045
White-without-pressure	9 (37.5%)	15 (19.5%)	14 (20.9%)	3 (9.7%)	2 (15.4%)	43 (20.3%)	n.s. (0.1471)
Pigmentary degeneration	— (0%)	3 (3.9%)	2 (3.0%)	5 (16.1%)	1 (7.7%)	11 (5.2%)	0.0414
Tear/hole	1 (4.2%)	3 (3.9%)	4 (6.0%)	1 (3.2%)	2 (15.4%)	11 (5.2%)	n.s. (0.4955)

N.S.: not significant

TABLE IV - RELATIONSHIP BETWEEN AGE AND RETINAL LESIONS (right eye)

Lesions	Mean age (years)		t	p
	With lesions	Without lesions		
Crescent	33.65 ± 14.76	25.88 ± 9.27	3.31	p=0.001**
Chorioretinal atrophy	40.69 ± 16.38	30.36 ± 13.24	2.68	p=0.008**
Fuchs' spot	39.50 ± 13.77	30.39 ± 13.46	2.44	p=0.015*
Posterior staphyloma	35.36 ± 14.25	29.65 ± 13.20	2.62	p=0.009**
Posterior vitreous detachment	44.66 ± 13.72	24.54 ± 7.45	11.32	p<0.001***
Lattice	33.65 ± 12.84	30.47 ± 13.76	1.26	p=0.208
Paving stone	47.89 ± 15.99	29.33 ± 12.22	6.13	p<0.001***
White-without-pressure	22.58 ± 7.98	33.14 ± 14.20	-6.50	p<0.001***
Pigmentary degeneration	36.63 ± 11.95	30.69 ± 13.68	1.41	p=0.160
Tear/hole	37.72 ± 13.90	30.63 ± 13.56	1.69	p=0.093

* p<0.05: significant; ** p<0.01: highly significant; *** p<0.001: very highly significant

TABLE V - DISTRIBUTION OF RETINAL LESIONS IN RELATION TO AGE

Lesions	Age (years)				Total	p
	19 ≤	20-39	40-59	60≥		
Crescent	24 (60.0%)	79 (62.7%)	30 (83.3%)	8 (80.0%)	141 (66.5%)	n.s. (0.0727)
Chorioretinal atrophy	1 (2.5%)	5 (4.0%)	6 (16.7%)	1 (10.0%)	13 (6.1%)	0.0275
Fuchs' spot	— (0%)	9 (7.1%)	4 (11.1%)	1 (10.0%)	14 (6.6%)	n.s. (0.2347)
Lacquer crack	— (0%)	1 (0.8%)	— (0%)	1 (10.0%)	2 (0.9%)	—
Posterior staphyloma	5 (12.5%)	30 (23.8%)	11 (30.6%)	4 (40.0%)	50 (23.6%)	n.s. (0.1580)
Posterior vitreous detachment	3 (7.5%)	23 (18.3%)	32 (88.9%)	10 (100%)	68 (32.1%)	<0.0001
Lattice	3 (7.5%)	25 (19.8%)	4 (11.1%)	3 (30.0%)	35 (16.5%)	n.s. (0.1416)
Paving stone	1 (2.5%)	6 (4.8%)	7 (19.4%)	5 (50.0%)	19 (9.0%)	<0.0001
White-without-pressure	14 (35.0%)	28 (22.2%)	1 (2.8%)	— (0%)	43 (20.3%)	0.0018
Pigmentary degeneration	1 (2.5%)	6 (4.8%)	4 (11.1%)	— (0%)	11 (5.2%)	n.s. (0.2899)
Tear/hole	1 (2.5%)	6 (4.8%)	2 (5.6%)	2 (20.0%)	11 (5.2%)	n.s. (0.1644)

N.S. Not significant

TABLE VI - DISTRIBUTION OF RETINAL LESIONS IN THE TWO SEXES

Lesions	Sex		Total	p
	Female	Male		
Crescent	82 (69.5%)	59 (62.8%)	141 (66.5%)	p=0.376
Chorioretinal atrophy	9 (7.6%)	4 (4.3%)	13 (6.1%)	p=0.466
Fuchs' spot	14 (11.9%)	— (0%)	14 (6.6%)	p=0.001*
Lacquer crack	— (0%)	2 (2.1%)	2 (0.9%)	—
Posterior staphyloma	27 (22.9%)	23 (24.5%)	50 (23.6%)	p=0.914
Posterior vitreous detachment	42 (35.6%)	26 (27.7%)	68 (32.1%)	p=0.279
Lattice	21 (17.8%)	14 (14.9%)	35 (16.5%)	p=0.704
Paving stone	11 (9.3%)	8 (8.5%)	19 (9.0%)	p=0.837
White-without-pressure	13 (11.0%)	30 (31.9%)	43 (20.3%)	p<0.001*
Pigmentary degeneration	9 (7.6%)	2 (2.1%)	11 (5.2%)	p=0.138
Tear/hole	4 (3.4%)	7 (7.4%)	11 (5.2%)	p=0.311

* p<0.001: Highly significant

and WWP more common in males (p<0.001). Other lesions were equally distributed (Tab. VI).

DISCUSSION

AL is high both in intermediate and pathologic myopia in the classification of Curtin (1, 6, 20). Who reported the lower limit of pathologic myopia as an AL of 24.50 mm (11). Generally, pathologic changes become apparent above 26.5 mm (1, 12). We included in this study myopic eyes with spherical equivalents of -6.00 D and higher. This group includes, apart from pathologic myopia, also intermediate myopia with -10.00 D as the upper limit. Therefore, it would be more appropriate to use the term high axial myopia.

The most frequent central retinal finding was crescent (66.5%) followed by posterior staphyloma (23.6%), Fuchs' spot (6.6%), CRA (6.1%) and lacquer crack (0.5%). Curtin (12) also found crescent was the most frequent central retinal lesion. He reported that a zero incidence of crescent in AL of 20-21.5 mm, increasing to 75% in AL of 24.5-25.4 mm and 100%

above 28.5 mm. Crescent was equally frequent in both sexes.

This study found that the incidence of crescent increased with AL and age, and was similar in both sexes. These findings support the idea that myopic crescent is an important demonstration of mechanical stretching in the posterior pole (1, 9, 12).

CRA involves an atrophic region corresponding to a choriocapillaris locus in the posterior pole, and its incidence ranges between 7.1% and 85% in pathologic myopia (1, 12). Curtin (12) showed a significant correlation between CRA and AL and age. Our incidence of CRA was lower, but increased significantly with AL and age ($p < 0.001$ and $p = 0.0105$, respectively).

The incidence of posterior staphylomas, which are essential lesions of pathologic myopia, has been reported to be 19% in eyes with AL more than 26.5 mm (12). We found the incidence of posterior staphyloma was 23.5%, increasing with AL and age. Fuchs' spot, which is an area of retinal pigment epithelial hyperplasia over a subchoroidal neovascular membrane in the macula, is seen in 5.2-10% of eyes with high myopia (9, 12). We found the incidence was 6.6% which increased with age and AL, and it was more common in females (Tab. VI).

The fact that the incidence of central retinal lesions increases with AL suggests that biomechanical factors are important in its pathogenesis. The increased incidence with age shows that these lesions continue to progress throughout life.

WWP was a frequent (20.3%) peripheral retinal lesion in this study. Its incidence was markedly higher in young age; it was slightly more frequent in eyes with moderate AL and was common in males. Pierro (19) found its incidence was 22.8% in eyes with AL more than 24.5 mm, and reported that its incidence decreased with age. Karlin found similar results (13). The decreasing incidence with age suggests that this is a preliminary lesion which undergoes changes in time. Its high incidence in young eyes when PVD has not yet developed and in eyes with moderate AL supports the idea that vitreoretinal adhesions are important in its pathogenesis (19).

Lattice degeneration which is the main peripheral lesion in myopes and is closely associated with retinal tears and detachment (13, 16-18) has an incidence of 6-8% in the population. The rate is higher in myopia (14, 19). This study found an incidence of 16.5%, but

no significant relationship between the incidence and AL, age or sex. Karlin (13) and Pierro (19) reported that lattice increased with AL but Celorio (14) found its incidence increased in moderate myopia. Although this study found no significant relation between lattice and AL, the incidence of 16.5% is way above its incidence in emmetropes. Furthermore, it tended to increase with AL, being highest in the 30-34 mm range, without reaching statistical significance. On the other hand, the absence of a relationship between lattice and AL supports the idea that hereditary factors may also be active in its etiopathogenesis (14).

This study showed no relationship between retinal breaks and AL and age. While Pierro (19) reported similar results, Karlin (14) found that retinal breaks increased with AL and age.

In conclusion, this study once more confirms that crescent, CRA, posterior staphyloma and Fuchs' spot increase with AL and age, thus reflecting mechanical stretching forces upon the posterior pole. On the other hand lattice, which was also a frequent finding in high myopia, tended to increase with AL and age, without this reaching statistical significance. In this study, WWP stands out as a preliminary lesion seen in young males and undergoes changes with time. This information may be clinically valuable when evaluating patients with high myopia.

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A Randomized Clinical Trial of Progressive Addition Lenses versus Single Vision Lenses on the Progression of Myopia in Children

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PURPOSE. The purpose of the Correction of Myopia Evaluation Trial (COMET) was to evaluate the effect of progressive addition lenses (PALs) compared with single vision lenses (SVLs) on the progression of juvenile-onset myopia.

METHODS. COMET enrolled 469 children (ages 6–11 years) with myopia between -1.25 and -4.50 D spherical equivalent. The children were recruited at four colleges of optometry in the United States and were ethnically diverse. They were randomly assigned to receive either PALs with a $+2.00$ addition ($n = 235$) or SVLs ($n = 234$), the conventional spectacle treatment for myopia, and were followed for 3 years. The primary outcome measure was progression of myopia, as determined by autorefractometry after cycloplegia with 2 drops of 1% tropicamide at each annual visit. The secondary outcome measure was change in axial length of the eyes, as assessed by A-scan ultrasonography. Child-based analyses (i.e., the mean of the two eyes) were used. Results were adjusted for important covariates, by using multiple linear regression.

RESULTS. Of the 469 children (mean age at baseline, 9.3 ± 1.3 years), 462 (98.5%) completed the 3-year visit. Mean (\pm SE) 3-year increases in myopia (spherical equivalent) were -1.28 ± 0.06 D in the PAL group and -1.48 ± 0.06 D in the SVL group. The 3-year difference in progression of 0.20 ± 0.08 D between the two groups was statistically significant ($P = 0.004$). The treatment effect was observed primarily in the first year. The number of prescription changes differed significantly by treatment group only in the first year. At 6 months, 17% of the PAL group versus 30% of the SVL group needed a prescription change ($P = 0.0007$), and, at 1 year, 43% of the PAL group versus 59% of the SVL group required a prescription change

($P = 0.002$). Interaction analyses identified a significantly larger treatment effect of PALs in children with lower versus higher baseline accommodative response at near ($P = 0.03$) and with lower versus higher baseline myopia ($P = 0.04$). Mean (\pm SE) increases in the axial length of eyes of children in the PAL and SVL groups, respectively, were: 0.64 ± 0.02 mm and 0.75 ± 0.02 mm, with a statistically significant 3-year mean difference of 0.11 ± 0.03 mm ($P = 0.0002$). Mean changes in axial length correlated with those in refractive error ($r = 0.86$ for PAL and 0.89 for SVL).

CONCLUSIONS. Use of PALs compared with SVLs slowed the progression of myopia in COMET children by a small, statistically significant amount only during the first year. The size of the treatment effect remained similar and significant for the next 2 years. The results provide some support for the COMET rationale—that is, a role for defocus in progression of myopia. The small magnitude of the effect does not warrant a change in clinical practice. (*Invest Ophthalmol Vis Sci.* 2003;44:1492–1500) DOI:10.1167/iovs.02-0816

Myopia is a significant public health problem that affects at least 25% of adults in the United States¹ and a much higher percentage of people in Asia.² It is a predisposing factor for retinal detachment, myopic retinopathy, and glaucoma, thus contributing to loss of vision and blindness. As might be expected for such a prevalent condition, treatment costs are high, with annual estimates in the United States for eye examinations and correction by spectacles and contact lenses ranging from \$2.5 to \$4.6 billion.³ If interventions to retard the progression of myopia are successful, these costs should be reduced.

At present, the mechanisms involved in the etiology of myopia are unclear, and methods for prevention are unproven. Even without a sound scientific rationale, many options for slowing the progression of myopia have been evaluated. Most of the intervention studies have had methodological limitations, such as unmasked examiners and nonrandom assignment to treatment groups. Results of most previous studies in which lenses, mainly bifocals, were used have been equivocal or have applied to restricted populations. Recently, the use of bifocals in children with near-point esophoria was reported to slow progression of myopia by 0.25 D over 30 months, compared with children randomized to SVLs.⁴ PALs, sometimes referred to as no-line bifocals or multifocal lenses, have been reported to slow significantly the progression of myopia by approximately 0.50 D after 2 years in one study of 80 Chinese children,⁵ but not in two other studies of Chinese children.^{6,7} The mean difference in progression after 18 months was 0.21 D in 217 children in Taiwan⁶ and was 0.14 D after 2 years of follow-up in 254 children in Hong Kong.⁷

The Correction of Myopia Evaluation Trial (COMET) is a National Eye Institute/National Institutes of Health-supported multicenter clinical trial designed to evaluate whether PALs

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TABLE 1. Inclusion Criteria

Ages 6 to 11 years inclusive at baseline
Refractive criteria determined by cycloplegic autorefraction
Spherical equivalent: between -4.5 D and -1.25 D inclusive in both eyes
Astigmatism: ≤ 1.50 D in either eye
Anisometropia ≤ 1.0 D (spherical equivalent between eyes)
Visual acuity (with distance correction): 0.20 logMAR units or better (Snellen equivalent 20/32)
No strabismus by cover test at far (4 m) or near (33 cm) wearing distance correction, or at 33 cm wearing $+2.0$ over distance correction.
Birth weight ≥ 1250 g
No known ocular, systemic, or neurodevelopmental condition that might affect refractive development
No use of medications that might affect refractive development
No prior wear of progressive addition or bifocal lenses
No prior wear of contact lenses

slow the rate of progression of juvenile-onset myopia when compared with conventional correction with SVLs. The rationale for COMET was based on reports in animal and human studies suggesting that increased retinal defocus is a factor in the pathogenesis of myopia.⁸⁻¹⁰ Many studies have documented that the eyes of animals exposed to continuous retinal defocus become myopic.^{8,9} In humans, high accommodative lag at near has been associated with myopia.^{10,11} Insufficient accommodation when children are engaged in near-work activities may result in retinal defocus, and accurate accommodation may be critical to reduce excessive defocus and thus slow axial elongation.¹⁰ One of the major unknowns is how much defocus must occur and over what period, to stimulate eyes to elongate. Providing children who have myopia with lenses that produce clear vision over a range of viewing distances from near to far, as PALs do, could reduce defocus and slow the progression of myopia.

This report presents 3-year outcome measurements of refractive error and ocular components from children enrolled in the COMET and randomized to either PALs or SVLs.

METHODS

Details of the study design and demographic characteristics of the study population have been presented previously and are briefly summarized herein.^{12,13} Four clinical centers located at schools and colleges of optometry in Birmingham, Alabama; Boston, Massachusetts; Houston, Texas; and Philadelphia, Pennsylvania, enrolled 469 children between September 1997 and September 1998, and took measurements from them for at least 3 years. Children enrolled in COMET met the inclusion criteria listed in Table 1. Before the baseline examination, children and parents agreed to accept either SVLs or PALs as assigned by the randomization scheme, attend follow-up appointments semiannually for at least 3 years, and refrain from wearing contact lenses throughout the study. Children agreed to wear their COMET glasses during all waking hours. The COMET study and protocols conform to the tenets of the Declaration of Helsinki. The institutional review boards of each participating center approved the research protocols. Informed consent (parents) and assent (children) were obtained after verbal and written explanation of the nature and possible consequences of the study.

Study Design

Study Organization. COMET represents a collaborative effort involving a Study Chair, a Coordinating Center, four Clinical Centers, and the National Eye Institute (see Appendix). Three committees (Executive, Steering, and Full Investigator) composed of study investigators provided leadership to the study and reviewed its progress

regularly. Overall study performance and child safety were reviewed by a Data and Safety Monitoring Committee (DSMC).

Intervention. Myopia in children was corrected either with SVLs (the standard treatment) or PALs (Varilux Comfort lenses with a $+2.00$ D addition; Essilor of America, St. Petersburg, FL). This add power was chosen because it was shown to be more effective than $+1.50$ D in slowing progression of myopia in a study by Leung and Brown,⁵ and because in pilot testing it brought the focal plane of children with myopia, who often show accommodative insufficiency, to the plane of the test target (0.33 m). All lenses were polycarbonate. PALs were fitted with the top of the channel, 4.0 mm above the pupil, allowing at least 11 mm for distance vision.¹⁴ The fitting protocol was designed to encourage the children to use the near-addition portion of the lenses, because unlike adults with presbyopia, for whom the glasses are typically prescribed, children can accommodate and thus have no need for a near addition for close work.

Randomization. Children were randomized to either PALs or SVLs. The randomization scheme was stratified by clinical center, using a random permuted block design. Randomization assignments were allocated centrally by the coordinating center after eligibility criteria were verified. A child was considered to be enrolled in COMET once the randomization assignment and study number were issued and the child received the assigned lenses.

Masking. Several steps were taken to preserve and monitor masking of study optometrists who collected outcome data. The following highlights the main measures, which have been reported previously.^{12,13} Study optometrists did not know the lens assignments; therefore, parents and children were told not to discuss any issues related to the study glasses with the COMET optometrists and not to wear study glasses in their presence. A consulting optometrist, with knowledge of lens assignment and not involved with collection of outcome data, was available to handle any issues regarding visual symptoms or child safety that could lead to unmasking of the study optometrists. An effort was made to mask children and parents by having all lenses fit as though they were PALs and providing uniform wearing instructions based on PALs.

Procedures. Cycloplegic autorefraction was used to assess progression of myopia, the primary outcome measure. As with all data-collection procedures, autorefraction was performed in both eyes by experienced optometrists who were trained and certified on study protocols (Hyman L, Hussein M, Gwiazda J, and the COMET Study Group, ARVO Abstract 4348, 1998). An autorefractor/autokeratometer (ARK 700A; Nidek, Gamagori, Japan) was used to take five consecutive reliable readings, both before and after cycloplegia. The cycloplegic agent was 2 drops of 1% tropicamide, administered 4 to 6 minutes apart, after corneal anesthesia was obtained with either proparacaine or benoxinate. The COMET protocol specified that cycloplegic autorefraction measures be taken 30 minutes after administration of the second drop of 1% tropicamide. Tropicamide (1%) was found to be an effective cycloplegic agent in this group of children with myopia, as documented by residual accommodation measurements taken at baseline by autorefractor (model R-1; Canon USA, Lake Success, NY).¹⁵

After cycloplegic autorefraction, ocular component dimensions (anterior chamber depth, lens thickness, vitreous chamber depth, and overall axial length [AL]) were measured by ultrasonography (A-2500; Sonomed, Lake Success, NY). Five individual measures were attempted per eye, with at least three measures per eye necessary to qualify for inclusion in the study. Five measures were obtained for 96% of eyes at all visits.

Subjective refraction was completed before cycloplegia according to a standard protocol.^{12,13} At baseline, all children received new glasses based on the distance prescription. At follow-up visits they received new glasses if their myopia correction, determined by subjective refraction, had increased by at least 0.50 D spherical equivalent from their current prescription in at least one eye. Smaller prescription changes were made if clinically indicated.

Sample Size and Power. A sample of 450 children was selected, based on detecting a projected 33% reduction in the amount of progression among the PAL versus the SVL group, assuming that the SVL group would progress by a mean of 1.50 D (SD 1.10–1.35 D) after 3 years. This estimate was also based on using a two-sided 1% α level to achieve 84% power, allowing for 20% attrition.

Outcome Measures

The primary outcome for COMET was progression of myopia, defined as the change in spherical equivalent refractive error (SER) relative to baseline (a continuous measure). A summary measure of SER was calculated for each of the five autorefraction measurements per eye, and the mean of the five SER measures was then computed. Progression of myopia was analyzed by expressing refractive error as three components: M (spherical equivalent), J_0 (dioptric power of a Jackson cross cylinder at axis 0°), and J_{45} (dioptric power of a Jackson cross cylinder at axis 45°), as determined by Fourier decomposition.¹⁶ Because oblique astigmatism is often mirror symmetric in the two eyes, the average J_{45} values were calculated by transforming the axis values between 91° and 180° to values between 0° and 90° for each eye and then averaging them between the two eyes. The secondary outcome for COMET was change in AL during follow-up relative to baseline measured by A-scan ultrasonography. Before the beginning of data collection, study examiners showed good consistency of both autorefractor and AL measurements with those of a gold standard examiner.¹⁷

Additional Measures

The study design also included an evaluation of changes in ocular components (i.e., anterior chamber depth, lens thickness, and vitreous chamber depth), by A-scan ultrasonography. Corneal curvature was measured using the keratometry setting of the autorefractor (Nidek). Accommodation at near (33 cm) and far (4.0 m) and concomitant measures of phoria were taken using the autorefractor (Canon R-1), with an attached motorized Risley prism operated by the child. Phoria at near and far also was measured, with the cover test. These procedures have been described in detail.^{12,13}

Three measurements of each child's normal reading distance for standardized age-appropriate text were taken by the opticians at each visit. The protocol called for measurement from the child's eye to the page of a book with a tape measure marked in inches. Additional data collected at the annual visits included an assessment of adherence to the use of COMET glasses based on both children's and parents' answers to a questionnaire administered separately and monitoring of child safety.

Statistical Analyses

The balance of baseline clinical and demographic characteristics between the two treatment groups was evaluated by *t*-tests or the Wilcoxon test for continuous variables and the χ^2 test or the Fisher exact test for categorical variables. Follow-up data were analyzed by applying an intent-to-treat principle according to the child's original lens assignment and the last known value of the outcome measures. For the seven children lost to follow-up and thus without data at the third annual visit, progression information from the latest follow-up visit was used.

The primary analysis for progression of myopia in COMET was child based, using the average of both eyes to evaluate the magnitude of change in SER between follow-up and baseline (Pearson correlation coefficient between the eyes at 3 years = 0.90). The analytic strategy was similar for SER and AL. Univariate analyses were conducted to guide the selection of variables to be included in subsequent multivariate analyses for the overall treatment effect. These analyses used general linear modeling of the multiple linear regression approach,¹⁸ to allow adjustment of the potentially most prognostic covariates: age, gender, ethnicity, baseline refractive error, axial length, accommodative response, and phoria, all chosen because of their known relationship to progression of myopia. In addition, interaction analyses adjusting for multiple comparisons were conducted, using specific macros

(developed in SAS software; SAS, Inc., Cary, NC) to obtain preliminary estimates of a possible differential effect of PALs among categories of these selected covariates. The unadjusted and adjusted annual rates of change were calculated for each year of follow-up. Linear modeling techniques were used to evaluate the association between changes in SER and AL.

RESULTS

Four hundred sixty-nine children were enrolled in COMET, with 235 randomized to PALs and 234 to SVLs, as shown in Figure 1. Each of the four clinical centers enrolled between 108 and 133 children. Three-year retention was excellent, with only seven children, six in the PAL group and one in the SVL group, who did not return for the 3-year visit. Two children changed lens assignments, both from SVLs to PALs, due to binocular vision problems. Of 2939 possible study visits of the children with 3-year visits, only 10 (4 in the PAL group and 6 in the SVL group) were missed. Baseline characteristics were balanced, with no statistically significant differences between treatment groups, as shown in Table 2.

Primary Outcome

At baseline the SER was the same in the two treatment groups. Mean change in SER and astigmatism (J_0 and J_{45}) at each annual visit is plotted in Figure 2. The difference in progression of myopia between the PAL and SVL groups occurred in the first year, as illustrated by the dashed lines in Figure 2a. The treatment effect based on the adjusted (for age, gender, ethnicity, baseline SER, accommodative response, and near point phoria) annual rate of change between baseline and 1 year was 0.18 D ($P < 0.0001$). This difference persisted but did not increase over the next 2 years, with the mean difference in the change between treatment groups from year 1 to year 2 equal to 0.04 D and from year 2 to year 3 equal to -0.02 D. The addition of these three annual differences resulted in an adjusted 3-year treatment effect of 0.20 ± 0.08 D, which is statistically significant (95% confidence interval [CI]: 0.06–0.33; $P = 0.004$).

J_0 , which was close to zero in both groups at baseline, increased at each annual visit. Figure 2b shows that the change in the first year was slight, but significantly greater in the SVL than the PAL group (mean difference = 0.04 D, $P = 0.002$). This difference was maintained in the second year (mean difference = 0.04, $P = 0.05$), but not at 3 years (difference = 0.01, $P = 0.74$). As shown in Figure 2c, the change in J_{45} in children in both the PAL and SVL groups was close to zero at all annual visits. Overall, the mean amount of astigmatism increased by slightly more than 0.25 D over 3 years, with no significant difference between treatment groups.

Table 3 presents the adjusted 3-year mean progression rates for both treatment groups and the corresponding adjusted mean differences for each baseline characteristic in the table. Significant differences between treatment groups were observed in children with lower baseline myopia (0.30 ± 0.11 D; 95% CI: 0.04–0.55; $P = 0.0097$) and lower baseline accommodative response (0.33 ± 0.11 D; 95% CI: 0.07–0.58; $P = 0.005$). Table 3 also shows that the 3-year adjusted SER increased from baseline by 1.28 ± 0.06 D in the PAL group and 1.48 ± 0.06 D in the SVL group, resulting in the overall adjusted 3-year treatment effect of 0.20 D.

Interaction analyses were conducted to identify whether the treatment effect differed within any of the baseline characteristics included in Table 3 (e.g., was there a greater treatment effect in children with lower versus higher baseline accommodative response?). A significant interaction was found between treatment and baseline accommodative response, with the treatment found to be more effective by 0.26 D ($P =$

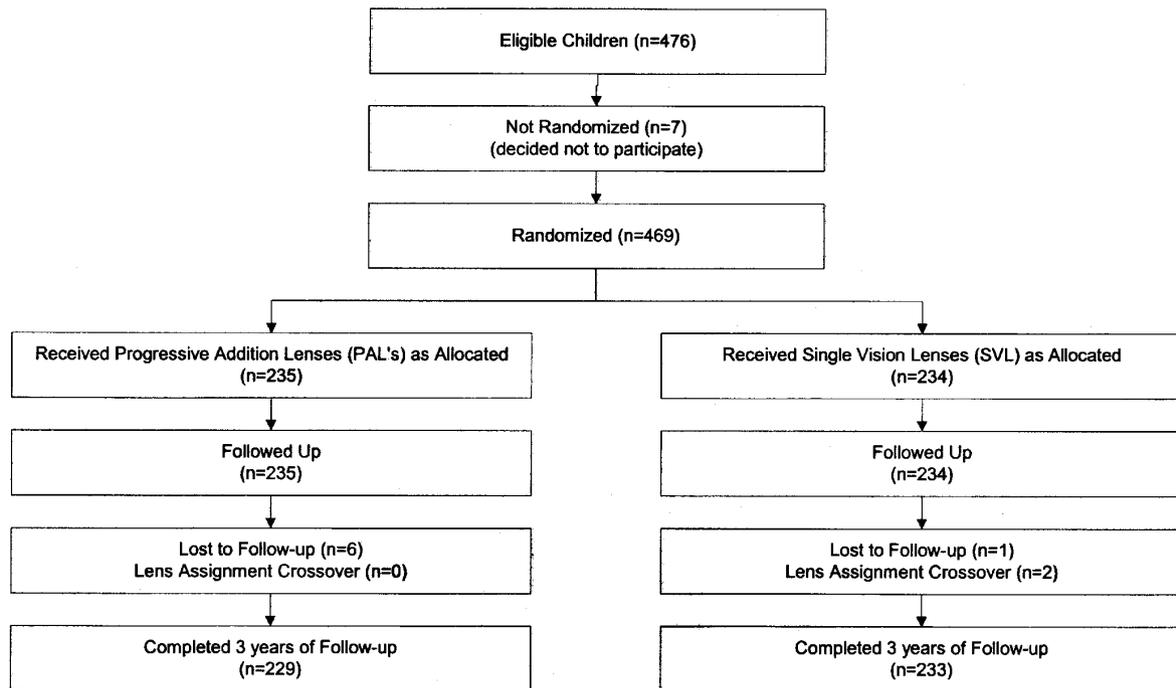


FIGURE 1. Participant flow and randomization assignment of COMET children.

0.03) in children with lower versus higher accommodative response. There was also a significant interaction between treatment and baseline myopia, with the treatment more effective by 0.20 D ($P = 0.04$) in children with lower versus higher myopia.

Progression is presented in Figure 3 for baseline myopia and accommodative response, the only factors that showed statistically significant interactions with treatment. The unadjusted mean progression of myopia in the PAL and SVL groups is plotted for lower (Fig. 3a) and higher (Fig. 3b) baseline myopia,

and lower (Fig. 3c) and higher (Fig. 3d) baseline near accommodative response. At each annual visit, the difference between treatment groups was larger in children with lower than in those with higher baseline myopia, with a 3-year difference of 0.32 ± 0.11 D in children with lower baseline myopia and 0.07 ± 0.10 D in those with higher myopia. Similarly, at each annual visit the difference between treatment groups was larger for children with lower compared with higher accommodative response, with a 3-year difference of 0.34 ± 0.11 D in the lower accommodative response group and 0.02 ± 0.10 D in the higher accommodative response group.

TABLE 2. General Baseline Characteristics of COMET Children by Study Group

Characteristic/Variable	PAL Children (n = 235)		SVL Children (n = 234)		P
	%	Mean ± SD	%	Mean ± SD	
Gender					
Female	52		53		0.85
Ethnicity					
White	46		47		0.75
African American	26		26		
Hispanic	14		15		
Asian	9		6		
Mixed/Other	5		6		
Age (y)		9.3 ± 1.30		9.4 ± 1.30	0.63
Cycloplegic autorefraction (D)					
Spherical equivalent		-2.40 ± 0.75		-2.37 ± 0.84	0.38
J ₀		0.03 ± 0.25		0.05 ± 0.24	0.51
J ₄₅		-0.02 ± 0.07		0.00 ± 0.08	0.15
Axial length (mm)		24.10 ± 0.72		24.14 ± 0.72	0.56
Accommodative response at near (D)		2.47 ± 0.67		2.48 ± 0.60	0.91
Phoria at near (PD)		1.86 ± 6.49		2.57 ± 6.88	0.25

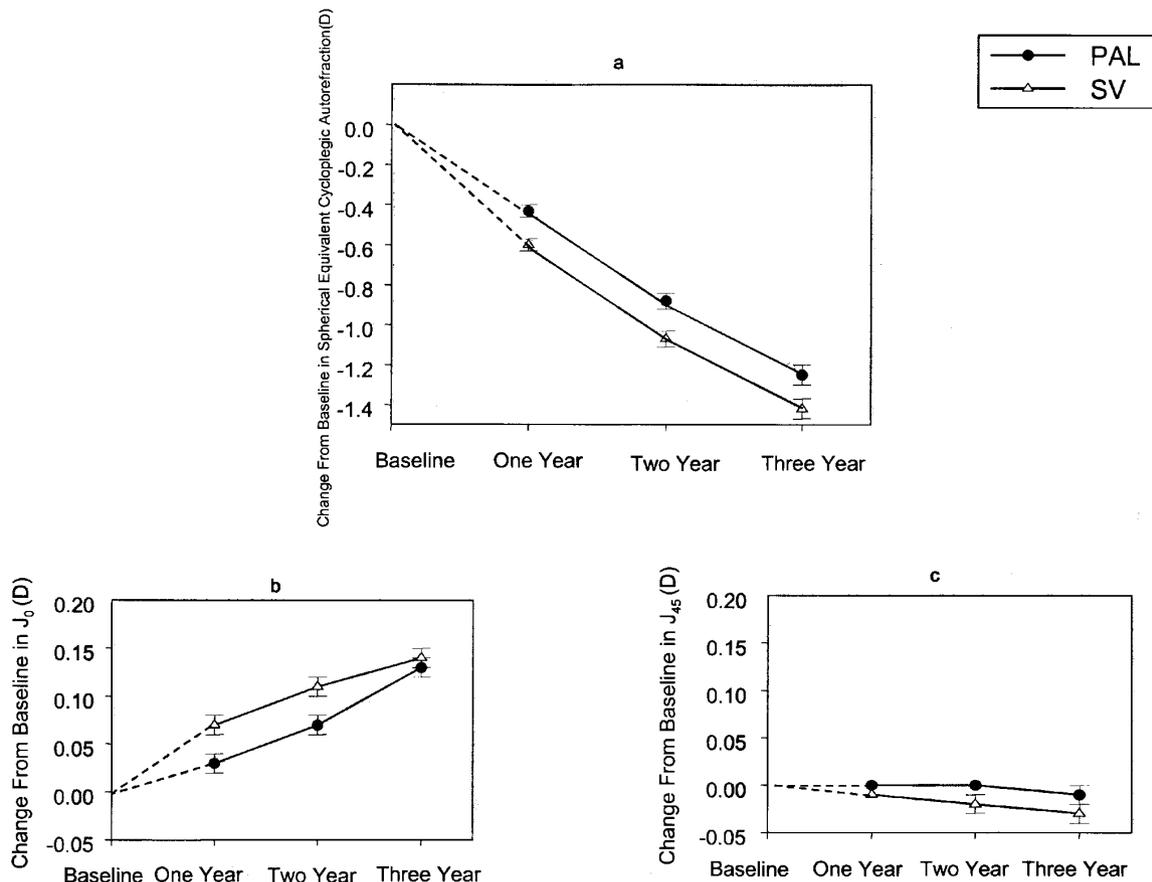


FIGURE 2. Mean change in (a) spherical equivalent refractive error (M), (b) J_0 , and (c) J_{45} at each annual visit in the PAL and SVL groups. Dashed lines are included for illustrative purposes to demonstrate the similarity of the two treatment groups at baseline. Error bars, SE.

In a separate analysis, the treatment effect was found to be larger in children with a reading distance closer than the median of 12 in. In this group, the mean difference in progression of myopia between the PAL and the SVL groups was 0.22 D at 1 year ($P < 0.0001$), 0.26 D at 2 years ($P = 0.002$), and 0.23 D at 3 years ($P = 0.03$). In the group with reading distances greater than 12 in., the treatment effect was 0.11 D ($P < 0.01$), 0.15 D ($P = 0.03$), and 0.13 D (NS) for each year, respectively. As with the other measurements, the main effect was observed in the first year.

Consistent with the overall treatment effect occurring in the first year, the number of prescription changes also differed significantly by treatment group at both the 6-month and 1-year visits. At 6 months 17% of the PAL group versus 30% of the SVL group required one change in prescription, a statistically significant difference ($P = 0.0007$). At 1 year, the pattern was similar and also statistically significant ($P = 0.002$), with 43% of the PAL group versus 59% of the SVL group requiring a prescription change. At 3 years, however, there was no statistically significant difference in the number of prescription changes between treatment groups. Overall, 86% of the PAL group versus 91% of the SVL group had at least one prescription change.

Secondary Outcome

The adjusted mean AL increased from baseline to 3 years by 0.64 ± 0.02 mm in the PAL group and 0.75 ± 0.02 mm in the

SVL group, resulting in an overall adjusted 3-year treatment effect of -0.11 ± 0.03 mm ($P = 0.0002$; 95% CI: -0.16 to -0.05). Figure 4 shows mean increases in the AL of eyes of children in the PAL and SVL groups at each annual visit. The mean change in AL was greater in the SVL group at the first annual visit, and the magnitude of the difference between groups increased through the second year. The adjusted annual rate of change showed a statistically significant benefit of PALs versus SVLs from baseline to the first year (difference = -0.07 ± 0.02 mm; $P < 0.001$) and a reduced but still significant effect between the first and second years (difference = -0.03 ± 0.01 mm; $P = 0.022$). No additional treatment benefit occurred between the second and third years (-0.01 ± 0.01 mm; $P = 0.34$).

Progression and treatment effects for AL varied within some baseline characteristics, similar to those reported in Table 3 for SER. Significant differences between treatment groups were observed in children with baseline characteristics of low myopia (-0.15 ± 0.05 mm, 95% CI: -0.25 to -0.04), lower accommodative response (-0.18 ± 0.05 mm; 95% CI: -0.28 to -0.07), orthophoria by cover test (-0.16 ± 0.05 mm; 95% CI: -0.28 to -0.03), and in girls (-0.12 ± 0.04 mm; 95% CI: -0.22 to -0.01). Results of phoria measurements by the Maddox rod-Risley prism were similar to those reported for both AL and SER in the cover test. Interaction analyses revealed a statistically significant interaction between treatment and baseline accommodative response, with the treatment more effec-

TABLE 3. Adjusted 3-Year Myopia Progression and Mean Difference between Study Groups by Baseline Characteristics

Baseline Characteristics	PAL		SVL		Difference ± SE†	Simultaneous 95% CI
	n	Adjusted Mean ± SE*	n	Adjusted Mean ± SE*		
Age (years)						
6-9	120	-1.59 ± 0.08	112	-1.78 ± 0.08	0.19 ± 0.11	(-0.06 to 0.45)
10-11	115	-0.97 ± 0.08	122	-1.17 ± 0.08	0.20 ± 0.11	(-0.05 to 0.46)
Gender						
Male	113	-1.18 ± 0.08	110	-1.39 ± 0.08	0.21 ± 0.11	(-0.05 to 0.47)
Female	122	-1.38 ± 0.07	124	-1.57 ± 0.08	0.19 ± 0.11	(-0.06 to 0.44)
Ethnicity						
Asian	22	-1.22 ± 0.16	14	-1.61 ± 0.20	0.39 ± 0.26	(-0.41 to 1.19)
African American	62	-0.96 ± 0.10	61	-1.27 ± 0.10	0.31 ± 0.14	(-0.12 to 0.73)
Hispanic	33	-1.51 ± 0.13	35	-1.39 ± 0.13	-0.12 ± 0.18	(-0.69 to 0.44)
White	107	-1.27 ± 0.08	111	-1.49 ± 0.07	0.22 ± 0.11	(-0.10 to 0.53)
Mixed	11	-1.50 ± 0.23	13	-1.64 ± 0.21	0.14 ± 0.31	(-0.83 to 1.10)
Cycloplegic autorefraction (D) [§]						
Less myopia (≥ -2.25)	109	-1.17 ± 0.08	127	-1.47 ± 0.08	0.30 ± 0.11	(0.04 to 0.55)
More myopia (< -2.25)	126	-1.38 ± 0.07	107	-1.48 ± 0.08	0.10 ± 0.11	(-0.15 to 0.36)
Accommodative response to 3 D demand (D) [§]						
Low (≤2.57)	115	-1.27 ± 0.08	119	-1.60 ± 0.08	0.33 ± 0.11	(0.07 to 0.58)
High (≥ 2.57)	120	-1.28 ± 0.08	115	-1.36 ± 0.08	0.07 ± 0.11	(-0.18 to 0.33)
Baseline near point (33 cm) Phoria (Δ) (cover test)						
Exo (≤2)	45	-1.43 ± 0.11	37	-1.38 ± 0.13	-0.05 ± 0.17	(-0.52 to 0.43)
Ortho (-1 to 1)	93	-1.27 ± 0.09	108	-1.57 ± 0.08	0.30 ± 0.12	(0.00 to 0.60)
Eso (≥2)	97	-1.18 ± 0.08	89	-1.39 ± 0.09	0.20 ± 0.12	(-0.11 to 0.52)
Overall	235	-1.28 ± 0.06	234	-1.48 ± 0.06	0.20 ± 0.08	(0.06 to 0.33)

*Adjusted for all other covariates presented in this table.

† (PAL - SVL).

‡ Adjusted for multiple comparison and interaction.

§ Statistically significant treatment effect ($P < 0.01$).

|| Statistically significant interaction ($P < 0.05$).

tive by 0.14 mm ($P = 0.03$) in children with lower versus higher accommodative response. Overall, the Pearson correlation coefficient between the change in AL and the change in SER was 0.86 in the PAL group and 0.89 in the SVL group.

Mean (±SD) 3-year changes in ocular component measurements in the eyes of children in the PAL and SVL groups, respectively, were 0.06 ± 0.11 and 0.07 ± 0.09 mm (anterior chamber), -0.01 ± 0.10 and -0.01 ± 0.08 mm (lens thickness), and 0.56 ± 0.33 and 0.65 ± 0.34 mm (vitreous chamber). The 3-year difference in vitreous chamber depth was significant between groups (difference = -0.09 ± 0.03 mm, 95% CI: -0.15 to -0.03; $P = 0.002$), but the differences in lens thickness and anterior chamber depth were not significant. Mean (±SD) changes in corneal radii were 0.03 ± 0.03 D in the PAL group and 0.03 ± 0.07 D in the SVL group in the horizontal meridian, and -0.01 ± 0.05 D in the PAL group and -0.01 ± 0.05 D in the SVL group in the vertical meridian. These values did not differ by treatment group.

Adherence and Masking

Self-reported adherence to wearing glasses was excellent, as assessed by answers to questionnaires administered separately to both children and parents at all visits. The number of children and parents responding to the questions varied slightly at each visit. Overall, at any visit, at least 211 (93%) of 229 of the PAL group and 224 (96%) of 234 of the SVL group reported wearing their glasses most or all the time. Parental reports of adherence were similar.

Masking of study optometrists regarding treatment assignment was preserved for most children (464/469; 99%) during the 3 years of follow-up, with unmasking being slightly more frequent in the PAL (4/235; 1.7%) than in the SVL group (1/234; 0.04%).

Data on the success of masking children and parents regarding their lens assignment will be collected when they are informed of the study results.

Safety Outcomes

No serious adverse events were reported during the 3 years of COMET. Protocol deviations occurred relatively infrequently and included children wearing the wrong glasses or contact lenses and the PAL group being given frames that did not meet the fitting protocol.

DISCUSSION

Synopsis

The COMET results demonstrate a statistically significant 3-year treatment effect of PALs ($P = 0.004$), with an adjusted mean difference in 3-year SER between the PAL and the SVL group of 0.20 D, which occurred in the first year. This difference is not clinically significant, suggesting that PALs should not be routinely prescribed for children with myopia as is common in some practices. The projected overall benefit in the PAL versus the SVL group in the design of COMET was 33%, yet the observed overall benefit, although statistically significant, was 14%. Changes in AL between the PAL and SVL groups were similar to those in SER, and the progression of myopia was highly correlated with changes in AL.

Possible Mechanisms

Although the mechanism regulating eye growth is poorly understood at present, the current data provide clues on the possible involvement of active and passive models (i.e., the roles of defocus and lens thinning), two of the prominent

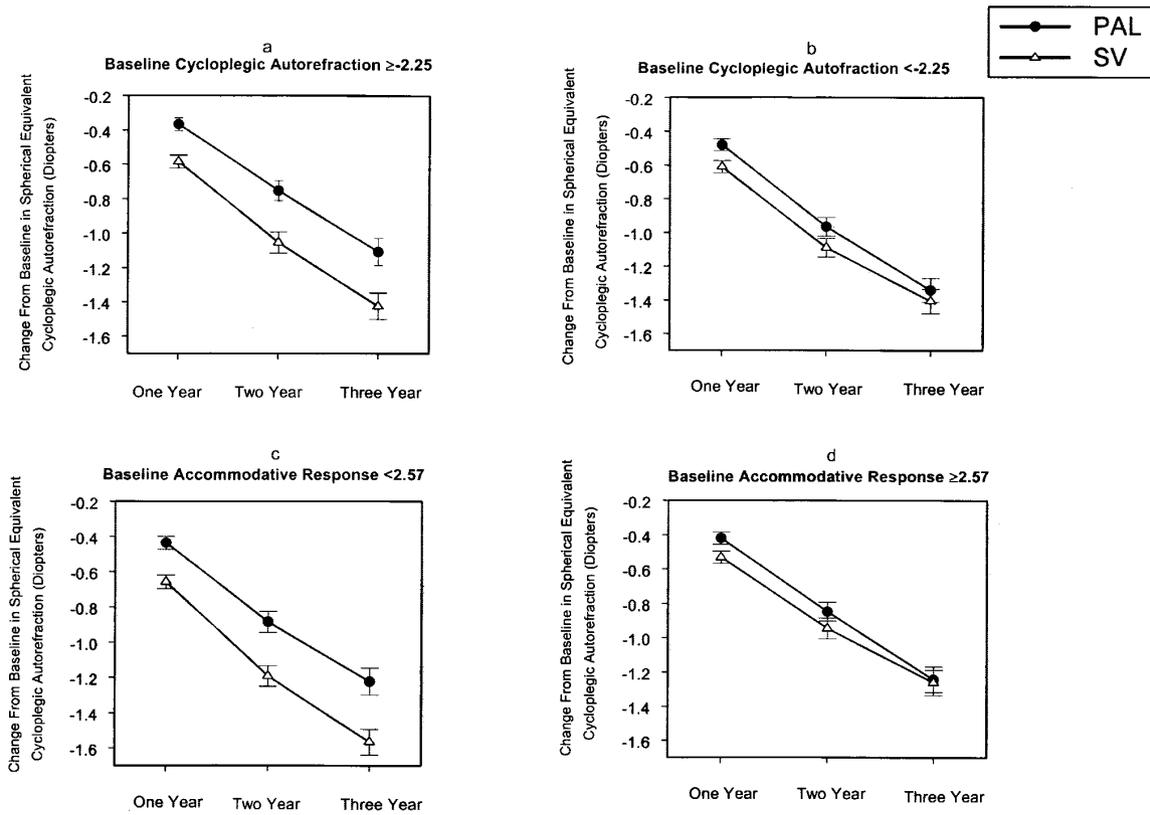


FIGURE 3. Mean progression of myopia in the PAL and SVL groups for two of the covariates, baseline myopia (a, b) and baseline accommodative response (c, d). Error bars, SE.

hypotheses proposed to account for human myopia. The difference between treatment groups in both SER and AL was larger in children with poorer accommodative response and lower amounts of myopia at baseline. An additional exploratory analysis combining these two significant covariates showed a 3-year treatment effect of PALs of 0.55 D in children

with both poor accommodative response and low baseline myopia. These results suggest a possible role for defocus in human myopia, consistent with the rationale for COMET. Retinal defocus resulting from insufficient accommodation when children with recent onset of myopia are engaged in close work may be a stimulus for increased axial elongation leading

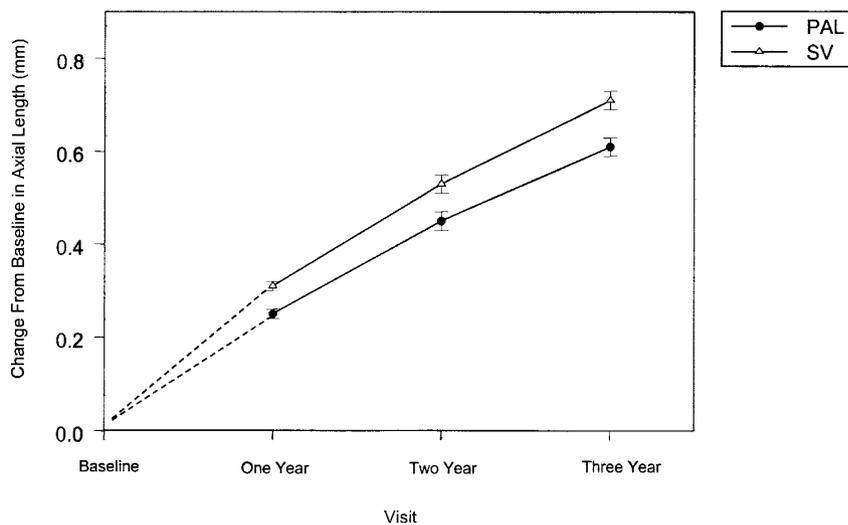


FIGURE 4. Mean increases in the axial length of eyes of children in the PAL and SVL groups at each annual visit. Dashed lines are included for illustrative purposes, to show the similarity of the two treatment groups at baseline. Error bars, SE.

to myopia, similar to animal models. The larger treatment effect found in children with a closer reading distance and a preliminary analysis suggesting that the treatment effect was larger in children with more hours of weekly near work are also consistent with this hypothesis. A recent model suggests that the interaction of accommodative response, the target's closeness, and time spent in near viewing could be important factors in determining whether eyes become myopic or whether extant myopia progresses.¹⁹

Lens thinning cannot account for the differential progression of myopia in the two treatment groups; we found no evidence of lens thinning in COMET children during the 3 years of follow-up. This finding was unexpected, given the reports of crystalline lens-thinning between 6 and 10 years of age in a sample of children most of whom did not have myopia.²⁰ This does not support a role for crystalline-lens-based interactions with eye growth in children with myopia.

One factor that has not been investigated in COMET but could be related to the size of the treatment effect is familial myopia. There is good evidence suggesting that myopia, especially high myopia, may be inherited.²¹⁻²³ Most persons with myopia, including COMET children, have a moderate refractive error that is probably the result of a combination of genetic and environmental influences. Whether the effectiveness of an intervention that manipulates the visual environment is associated with familial myopia remains to be determined.

For both of COMET's outcome measures, the treatment effect occurred in the first year. There are several possible reasons that PALs slowed progression of myopia more than SVLs during the first year. One is that there may be limitations on the ability of an environmental intervention to restrain progression, and these limitations may be exceeded after 1 year. To the extent that genetic and environmental factors are involved in development of myopia, PALs or other potential treatments may be able to affect progression by only a certain amount. If PALs reduce defocus, the mechanism may not be straightforward. It is known that ocular aberrations are larger in eyes with more myopia and that higher-order aberrations cannot be corrected with conventional spectacles.^{24,25} Also, aberrations inherent in spectacles increase with minus lens power. After 1 year, some children in the PAL group may have reached a level of myopia such that the reduction in defocus during near work produced by the PALs was counteracted by increased defocus from other sources.

Comparison with Other Studies

Several recent studies also have evaluated whether spectacle interventions (bifocals or PALs versus SVLs) can slow the progression of myopia. The size of the treatment effect in COMET is similar to that reported in other studies, ranging from slightly less than 0.25 D in COMET (and in Refs. 4,6,7) to slightly more than 0.50 D.⁵ The other studies had some methodological limitations, including unmasked examiners and a relatively small sample size,⁵ high losses to follow-up unevenly distributed across treatment groups,⁶ and inadequate statistical analysis of the data.⁷ Even with limitations and with differences in study design, the similar magnitude of the treatment effect across studies suggests that a spectacle lens intervention may have a limited effect. The early effect of an intervention to slow myopia is not restricted to COMET, although to our knowledge it has not been addressed previously. Other reports of an effect occurring in the first 6 to 12 months include recent investigations of PALs,⁷ atropine plus PALs,⁶ and RGP contact lenses.²⁶ This result is important for guiding future myopia interventions and has implications for mechanisms of myopia pathogenesis, as has been discussed.

Strengths and Weaknesses

An evaluation of COMET results should consider methodologic strengths of the trial. COMET recruited an ethnically diverse group of children with moderate myopia from four different geographic locations, suggesting generalizability of the results. COMET had outstanding retention of children, with only 7 of 469 children lost to follow-up by the 3-year visit, resulting in complete ascertainment of the study outcomes on 98% of enrolled children. Balance by lens assignment was found at baseline in all critical study measures. The protocol provided standardization of key outcome measures across clinical centers and was designed to maintain masking of treating clinicians and family members. Very few examiners became aware of a child's lens assignment. Study personnel were certified according to a standard protocol before collecting data. Reliability of the outcome measurements, monitored throughout the trial, was high. There were no serious adverse events and very few protocol deviations.

A weakness is that COMET was not powered to look for differences in progression of myopia between the PAL and the SVL groups by ethnicity. In addition, aside from white children who were represented at all four centers, most of the children in the other ethnic groups were clustered at one or two clinical centers, making it difficult to separate ethnic from possible center differences. Future multiethnic investigations should ensure adequate representation of each ethnic group at each center.

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APPENDIX

COMET Study Group

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COMMITTEES: *Data and Safety Monitoring*: Robert Hardy (Chair), Argye Hillis, Don Mutti, Richard Stone Sr., Carol Taylor. *Executive*: Jane Gwiazda (Chair), Donald Everett, Leslie Hyman, Wendy Marsh-Tootle. *Steering*: Jane Gwiazda (Chair), Donald Everett, Mohamed Hussein, Leslie Hyman, M. Cristina Leske, Daniel Kurtz, Ruth Manny, Wendy Marsh-Tootle, Mitchell Scheiman, Thomas Norton.

Visual Prognosis of Disciform Degeneration in Myopia

G. ROBERT HAMPTON, MD, DAVUT KOHEN, MD, ALAN C. BIRD, MD, FRCS

Abstract: A retrospective study was done on a consecutive series of patients presenting to the Moorfields Eye Hospital with visual reduction secondary to angiographically proven subretinal neovascularization associated with myopia (Förster-Fuchs' spot), with a short history of visual loss, and free of other ocular disease. The visual acuity at follow-up was compared to that at presentation, and related to size and location of the neovascular complex, as well as patient age, and duration of follow-up. The results show a generally poor prognosis in that 43% of the patients lost two or more lines of vision, while 60% were $\leq 6/60$ at last follow-up. As expected there was a direct relationship between visual acuity and the distance of the neovascular tissue from the fovea, and an inverse relationship between acuity and the size of the lesion. There seems to be a short neovascular growth phase, with early visual loss. [Key words: disciform, Förster-Fuchs', macula, myopia, natural history, neovascularization.] *Ophthalmology* 90:923-926, 1983

It is generally accepted that the pigmented lesion described by Fuchs¹ and the hemorrhagic lesion of Förster² are different stages of the disciform process in myopia.³ Disciform degeneration in myopia (Förster-Fuchs' Spot) is reported to develop in 5 to 10% of eyes with an axial length of more than 26.5 mm.^{4,5} Previous studies of natural history have been somewhat conflicting in reporting final visual outcome following onset of Förster-Fuchs'. In one series of patients Fried noted that the acuity stabilized or improved in 63% of the patients studied.⁶ Subretinal neovascularization, however, was not detected by fluorescein angiography in 33% of his patients. In another study, Hotchkiss and Fine⁷ documented subretinal neovascularization in 23 patients and demonstrated a worse prognosis, as visual acuity deteriorated in approximately 51% of their study eyes, and 44% progressed to 6/60 or worse.⁷ However, this was not a pure natural history study because 22% of their study eyes underwent laser photocoagulation.

These disparate results combined with our clinical

impression that disciform degeneration in myopia has a relatively favorable course prompted us to undertake a retrospective study of visual outcome following subretinal neovascularization of recent onset in myopia.

SUBJECTS AND METHODS

We reviewed the clinical records, color photographs, and fluorescein angiograms of 96 patients seen at Moorfields Eye Hospital between 1972 and 1982 with the diagnosis of Förster-Fuchs' Spot. Thirty-five patients were eliminated due to lack of follow-up, another 22 were removed from the study because their duration of symptoms was too long at presentation (over 6 months), the fluorescein angiogram revealed no subretinal neovascularization, they had undergone laser photocoagulation, or they had other unrelated ocular conditions reducing vision. There remained 42 eyes of 39 myopic patients with angiographically proven subretinal neovascularization symptomatic for 3 months or less in most patients (6 months in four patients).

Refractive error was available on 27 patients, of these 18% were -5 to -9 diopters, 60% were -10 to -15 diopters, and 22% were -16 to -25 diopters. The remaining cases were considered myopic degeneration with findings such as laquer cracks, peripapillary atrophy, and lacunar atrophy.

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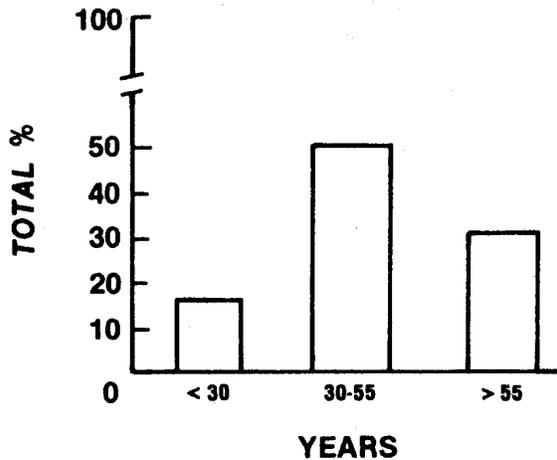


Fig 1. Histogram—patient age at presentation.

Figure 1 shows distribution of age into three groups that range from 12 to 96 years, and follow-up duration is summarized in Figure 2 for all patients.

Patients were assigned a level of visual acuity from 0-10 where each level corresponds to a line on the Snellen chart (Table 1).⁸

Fluorescein angiograms were reviewed carefully, and the subretinal neovascular complex measured and localized with respect to the center of the foveal avascular zone. The case was considered subfoveal if any portion of the new vessel system was under the center of the fovea and juxtafoveal if the edge of the new vessels were within 100-300 microns of the foveal center. Others were termed extrafoveal.

RESULTS

The neovascular tissue was subfoveal in 58% of the eyes at time of first visit, in 23% it was juxtafoveal, and in 19% extrafoveal. Seventy-eight percent of all complexes were $\geq 400 \mu\text{m}$ in diameter.

At time of last visit the vision had improved in 1 (2%) eye, was unchanged in 11 (27%), and had deteriorated in 29 (71%) (Fig 3). As a group the patients showed an average loss of 1.6 lines after presentation. Table 2 shows average initial acuity and average amount of visual loss

Table 1. Visual Acuity Group Levels

Acuity	Group No.	Acuity	Group No.
6/5	0	6/36	6
6/6	1	6/60	7
6/9	2	Finger count	8
6/12	3	Hand motion	9
6/18	4	Light percep	10
6/24	5		

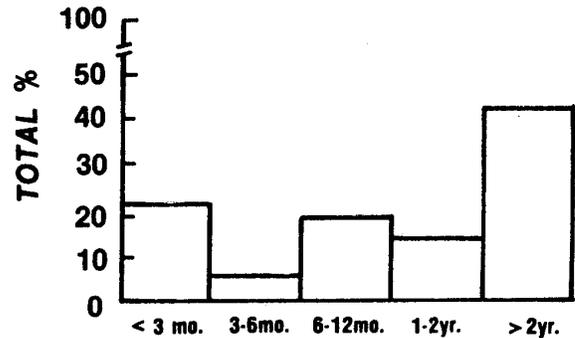


Fig 2. Histogram—follow-up duration.

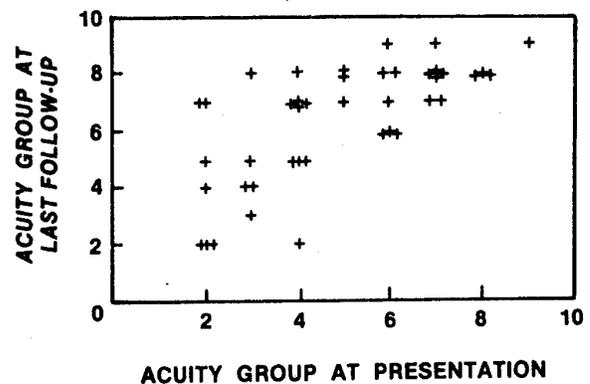


Fig 3. Scattergram comparing acuity group—presentation vs last follow-up.

in relation to original location of the subretinal neovascular membrane. Although the average number of lines lost remains essentially the same between groups (non-significant at $P < 0.05$ by analysis of variance), there was a direct relationship between visual acuity and distance of neovascular tissue from the fovea. There was an inverse relationship between presenting visual acuity and size of neovascular complex (Table 3). The vast majority of eyes had complexes larger than $400 \mu\text{m}$, and in these there was a statistically significant reduction in visual acuity at last follow up, using a paired T-test. Additionally, the larger the neovascularization, the more likely it will be subfoveal (Table 4).

There was no significant difference between the acuity at presentation of the three age groups by analysis of

Table 2. Initial Acuity and Visual Loss Relative to Location of Subretinal Neovascularization

Neovascular Location	% Total Eyes	Initial Acuity Grade	Lines Lost at Follow-up	T-Test
Extrafoveal	19	3	-1.4	NS
Juxtafoveal	23	4	-1.8	<.01
Subfoveal	58	6	-1.4	<.001

Table 3. Initial Acuity and Visual Loss Relative to Size of Neovascular Complex

Neovascular size (μm)	Presentation Acuity Grade	Average Acuity Loss	T-Test
≤ 200	3.7	-0.7	NS
$>200-\leq 400$	3.5	-1.8	NS
$>400-\leq 1000$	4.3	-1.6	$<.001$
>1000	5.9	-1.5	$<.01$

NS = not significant.

Table 4. Distribution of Neovascular Complex Sizes

Neovascular Size (μm)	% Total Eyes	% Eyes Subfoveal
≤ 200	7	0
$>200-\leq 400$	15	17
$>400-\leq 1000$	39	57
>1000	39	93

variance. The younger age group tended to have less acuity loss at their follow up visit, which was nonsignificant change by T-test (Table 5). However, those patients over 30 years of age had significant reduction in their vision at follow-up.

There was no statistically significant difference related to length of follow-up confirming that acuity is stable after initial loss (Table 6).

Forty-two percent of eyes were potentially treatable when first seen. Of these, only 35% subsequently became untreatable with an overall average visual loss of -2 lines.

DISCUSSION

Contrary to our clinical impression of a favorable visual outcome, and the relatively mild course implied by Fried,⁶ disciform degeneration in myopia has a poor

Table 5. Initial Acuity and Visual Loss Relative to Patient Age

Age-Yrs	Presentation Acuity Grade	Average Acuity Loss	T-Test
<30	4.9	-0.9	NS
31-55	4.6	-1.7	$<.001$
>55	5.5	-1.7	$<.05$

Table 6. Length of Follow-up Relative to Visual Loss

Length follow-up	<3 mo	3-6 mos	6-12 mos	1-2 yrs	>2 yrs
Average total lines lost	1.4	1.5	1.7	1.5	1.4

visual prognosis. The different behavior recorded in Fried's patients compared with those of the present study may be due to the inclusion in the former series of patients without subretinal new vessels. The loss of two or more lines in 43% of our patients and poor outcome ($\leq 6/60$) in 60% accords with the results of Hotchkiss and Fine.⁷ That more of their patients recovered vision may be explained by laser photocoagulation done on 22% of their cases with subretinal new vessels. This is in contrast to our group of untreated patients, in which only one improved spontaneously. These results indicate that visual loss with myopic disciform lesions is similar to disciform degeneration in the elderly, and that from presumed ocular histoplasmosis. In untreated cases, 68% of patients with senile disciform degeneration, and 50% of those with presumed ocular histoplasmosis, where the neovascular complex is within 0.25 disc diameters of the fovea would be expected to have final acuity $\leq 6/60$.^{9,10} Our results show that despite a similar final visual outcome between disciform disease in myopia and senile macular degeneration, the final level of vision is reached earlier in myopia. Disciform lesions in myopia tend to be smaller and originate more frequently at a foveal or parafoveal site than in age related disease. These features would tend to early determination of the final vision.

Predictably the visual prognosis in myopic disciform seems to be determined by the location of subretinal new vessels. There was a direct relationship between the distance of the fovea from the neovascular complex and final vision, and an inverse relationship to the size of the disciform lesion. With larger neovascular complexes on presentation, there is an increasing frequency of these new vessels being subfoveal. In the majority of patients, after presentation the acuity decreases further or remains stable. There was no correlation between age and presenting acuity, but those patients less than 30 years tended to lose less vision at follow-up (0.9 average lines lost).

The concept that laser treatment in these patients is not necessary because there is generally a good outcome is not supported by these results, although few of the treatable patients had significant visual loss after their first visit. The therapeutic options are clearly limited by the short growth phase of the subretinal neovascular tissue.

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Discussion

by

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Along with diabetic retinopathy, senile macular degeneration, and glaucoma, pathologic myopia is one of the major causes of severe visual loss in Western society. Sorsby has estimated that nearly 10% of persons on the blind registries of the United Kingdom suffer from pathologic myopia.¹ And among those blinded by myopia, chorioretinal degeneration in the posterior pole, including disciform degeneration, is the most frequent immediate cause of poor visual acuity.

In 1971, Curtin and Karlin suggested that, in myopic eyes, axial length was more important than refractive error in determining the likelihood of pathologic changes at the posterior pole.² They reported, for example, that 90% of persons over 40 years of age with an axial length greater than 29.5 mm were found to have chorioretinal atrophy. They concluded from these observations that the pathologic changes were a reflection of biomechanical stress rather than abiotrophy.

Although the Forster-Fuchs' spots and the neovascular membranes are part of the spectrum of chorioretinal degeneration in the posterior pole, it has not been shown convincingly that these specific changes are directly related to increased axial length. In fact, in the series of patients reported by Hotchkiss and Fine, this relationship could not be detected.³ Furthermore, we do not understand why choroidal neovascularization occurs in myopia anymore than we understand why it develops in other neovascular maculopathies. To state that the disciform response occurs because there are breaks in Bruch's membrane, or lacquer cracks, through which vessels can grow begs the question. As in other conditions characterized by breaks in Bruch's membrane, such as SMD and angioid streaks, the frequency of breaks exceeds the frequency of neovascularization. So the why remains paramount.

The authors have stated that the visual prognosis in myopic eyes with neovascular membranes is worse than they anticipated. Their data indicate that 43% of eyes lost two or more Snellen lines and that 60% were legally blind. They also noted the direct relationship between visual acuity and distance of the membrane from the fovea, the inverse relationship between visual acuity and size of the membrane, and the direct relationship between membrane size and subfoveal position, a relationship also noted in SMD.⁴

While the authors are to be congratulated for adding valuable information on the natural course of neovascular mac-

ulopathy in high myopia, their data provide no clear indications regarding management.

Two-thirds of their patients were under age 55, and nearly 60% were followed-up for less than 2 years. Ratner, working in our group, has just developed data to suggest a reasonable visual recovery rate in eyes with histoplasmic neovascular maculopathy, especially in younger individuals.⁵ It is conceivable, therefore, that longer follow-up would witness improved acuity.

Even if the visual prognosis were exactly as observed, however, a convincing case cannot be made for immediate photocoagulation treatment. Indeed, Hotchkiss and I reported that photocoagulation for neovascular maculopathy in myopia was successful in preserving acuity in only 50% of cases.

Where do we proceed from here? We are dealing with a major cause of serious visual loss. When there exists legitimate doubt about proper management for a well-defined condition that is a major public health problem, then a clinical trial is the most reasonable way to resolve that therapeutic question, in this case, concerning the value of photocoagulation for myopic neovascular maculopathy.

But an even higher priority is our need to understand the pathogenesis of chorioretinal degeneration in myopia. Is it abiotrophy or does it result from biomechanical stress at the posterior pole? And of what relevance to the human condition are the observations on experimentally induced myopia? These are the questions that must be answered if pathologic myopia is to be removed from the list of most common causes of blindness.

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Subretinal hemorrhages with or without choroidal neovascularization in the maculas of patients with pathologic myopia

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Abstract. We examined 20 patients (24 eyes) who had refractive errors of -8 diopters or more and subretinal hemorrhages at the initial visit. They were divided into two groups according to fluorescein angiographic findings: 15 eyes without choroidal neovascularization (CNV) and 9 eyes with CNV. Subretinal hemorrhage without CNV was frequent in patients aged 20–39 years (mean, 36.8 years). CNV was common in patients aged 60–79 years (mean, 61.0 years). No relationship was noted between refractive error and type of hemorrhage. In the eyes without CNV, the subretinal hemorrhages disappeared spontaneously after a few months. The visual acuity of these patients was variable at the initial visit (range, 0.01–0.8), and was unchanged or improved during the follow-up period. In the eyes with CNV, the visual acuity was less than 0.1 at the initial visit and was unchanged or worse during the follow-up period.

Introduction

Ocular changes such as crescents, posterior staphylomas, retinochoroidal degeneration, lacquer cracks, and subretinal or choroidal hemorrhages are common in pathologic myopia [1–12]. Two types of subretinal hemorrhages, with and without choroidal neovascularization (CNV), have been reported in pathologic myopia as well [1, 2, 7]. Results of a recent study have recommended that pathologic myopia be considered a refractive error of -8 diopters or more in adult Japanese patients [12]. We therefore examined adult patients who had refractive errors of -8 diopters or more for subretinal hemorrhages with or without CNV.

Subjects and methods

We reviewed the clinical records of adult Japanese subjects with pathologic myopia and selected patients with refractive errors (in

spherical equivalent) of -8 diopters or more who had subretinal hemorrhages at their initial visit. The patients were divided into two groups according to fluorescein angiographic findings: with and without choroidal neovascularization (CNV). Subretinal hemorrhage without CNV appeared ophthalmoscopically as a 1/4–

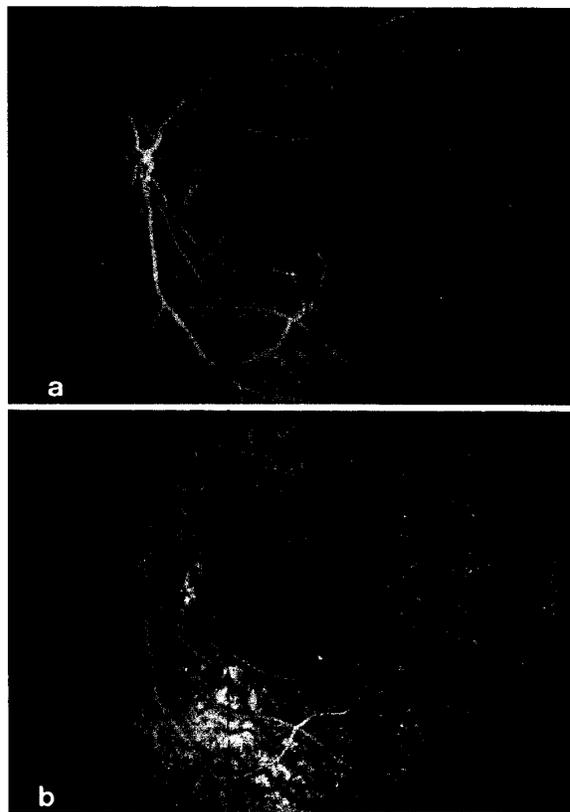


Fig. 1 a, b. Fluorescein angiograms of subretinal hemorrhage without choroidal neovascularization (CNV) in a 34-year-old woman with a refractive error of -8 diopters show: **a** the blockage of choroidal fluorescence in the early phase; **b** no leakage in the late arteriovenous phase

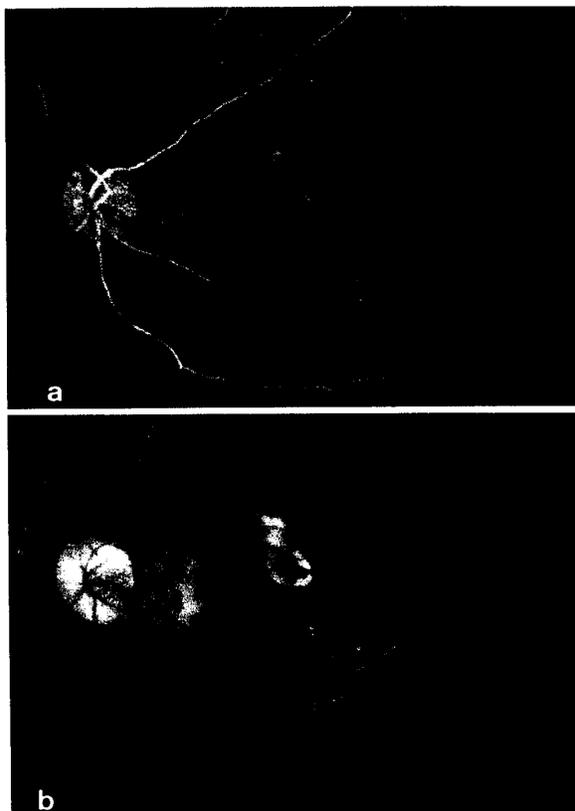


Fig. 2a, b. Fluorescein angiograms of subretinal hemorrhage with CNV in a 39-year-old man with a refractive error of -9 diopters reveal a patch of irregular hyperfluorescence in the early phase and b leakage of the dye in the late arteriovenous phase

1 disc diameter, round, red patch in the macula. On fluorescein angiography (Fig. 1), no leakage of the dye was found within or near the patch.

Subretinal hemorrhage with CNV appeared ophthalmoscopically as a red patch of variable size and shape that was associated with exudate, fibrovascular tissue, and/or exudative or hemorrhagic retinal detachment. On fluorescein angiography (Fig. 2), CNV was defined as a patch of lacy or irregular hyperfluorescence at the level of the pigment epithelium in early arteriovenous phase, leakage of dye from the lesion in a late arteriovenous phase, and staining of the lesion with fluorescein in a late phase. All patients were followed up for at least 4 months by us and for more than 1 year by the referring ophthalmologists.

Patients with age-related macular degeneration, macular hole, angioid streaks, choroidal ruptures, systemic hypertension, diabetes mellitus, glaucoma, and other ocular diseases were excluded from the present study.

Results

Twenty patients (24 eyes) with refractive errors of -8 diopters or more had macular hemorrhages at the initial visit (Table 1). Of these, 15 eyes had hemorrhages without CNV, and 9 had bleedings with CNV. Sixteen patients had a unilateral involvement, and 4 had bilateral lesions. A 39-year-old man had a subretinal hemor-

Table 1. Patients with pathologic myopia and subretinal hemorrhages

Age (years)	Sex	No. of patients	No. of affected eyes	Subretinal hemorrhages	
				Without CNV	With CNV
20-39	Male	5	7	6	1
	Female	3	4	4	0
40-59	Male	1	1	0	1
	Female	5	5	3	2
60-79	Male	2	2	0	2
	Female	4	5	2	3
20-79	Male	8	10	6	4
	Female	12	14	9	5
Total		20	24	15	9

CNV, Choroidal neovascularization

rhage without CNV in the right eye and a bleeding with CNV in the left eye. No sexual predilection by type of hemorrhage was found. Subretinal hemorrhages without CNV were frequent in patients aged 20-39 years (mean, 36.8 years). The CNV was common in patients aged 60-79 years (mean, 61.0 years).

The relationship between refractive error and initial visual acuity was evaluated (Fig. 3). Mean value of the refractive errors in 15 eyes without CNV was 12.8 diopters, and that in 9 eyes with CNV was 11.1 diopters. There was no correlation between refractive error and type of hemorrhage. The eyes without CNV had various initial visual acuities, ranging from 0.01 to 0.8, which depended in part on the location and extent of the hemorrhage. The eyes with CNV had poor initial visual acuities of less than 0.1. In these eyes, all foveas were involved by the hemorrhage. The size of CNV was not associated with visual acuity and refractive error.

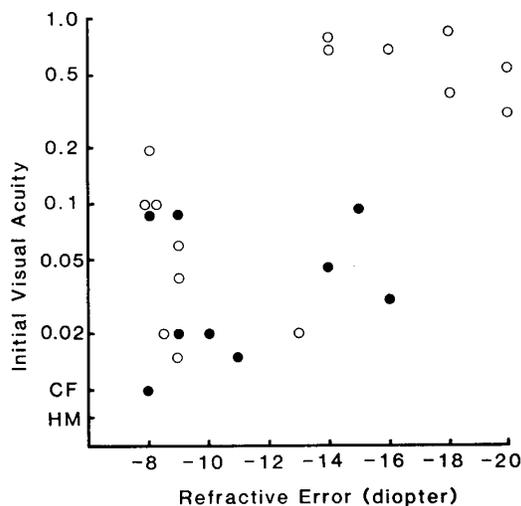


Fig. 3. Refractive errors and initial visual acuities are plotted in eyes with subretinal hemorrhages (○) without CNV and (●) with CNV. CF, counting fingers; HM, hand motion

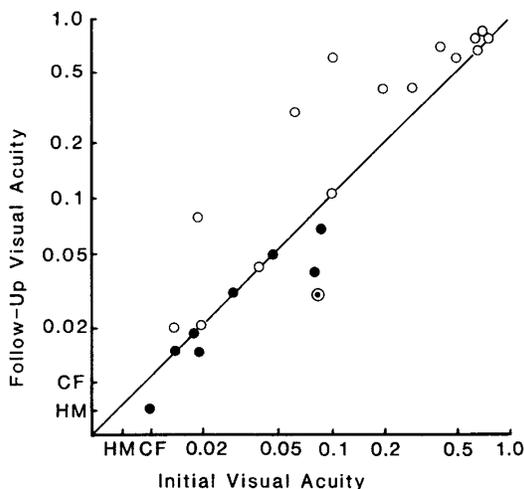


Fig. 4. Changes in visual acuity during the follow-up period. The follow-up for eyes with (○) subretinal hemorrhage without CNV was determined 3 months after the initial visit. The follow-up visual acuity (●) for those with subretinal hemorrhage with CNV was measured 1 year after the initial visit. One eye (◐) with CNV was treated with laser photocoagulation 1 month after the initial visit. The follow-up visual acuity was determined 1 year after the treatment. *CF*, Counting fingers; *HM*, hand motion

The mean value of the axial lengths measured in eight eyes without CNV was 28.05 mm and that in four eyes with CNV was 27.55 mm.

The eyes without CNV were followed up for 4 months to 6 years (mean, 10 months) by us. The hemorrhages in these eyes resorbed almost completely within 3 months. After resorption, some eyes manifested no atrophic change, while others demonstrated small round, atrophic scars. In two eyes the subretinal hemorrhage recurred 4 months later, and in one eye the hemorrhage redeveloped 5 years later. The recurrent bleeding disappeared almost completely within 3 months. No other eyes had recurrences during the follow-up period. The visual acuities in the eyes without CNV were unchanged or improved after 3 months of follow-up (Fig. 4). The visual acuities 1 year after the initial visit, determined by the referring ophthalmologist, were reportedly the same as those at 3 months.

The eyes with CNV were followed up for 1–4 years (mean, 2 years). The hemorrhages in these eyes changed to organized tissues or recurred during the follow-up period. The visual acuities in some eyes improved transiently, when the hemorrhages and exudates decreased. The visual acuities in the eyes with CNV 1 year after the initial visit were unchanged or worse (Fig. 4).

One eye with extrafoveal CNV was treated with focal photocoagulation. Despite the treatment, the visual acuity decreased (Fig. 4).

Discussion

In most cases, it was not difficult to classify the subretinal hemorrhages into types with the use of repeated fluo-

rescein angiography for the detection of CNV. Occult neovascular membranes in the eyes with apparently simple hemorrhages were clinically excluded because of evidence of no fluorescein leakage in these eyes after resolution of the bleeding. Other previous investigators defined pathologic myopia as refractive errors greater than -6.25 or -6.5 diopters [1, 7]. In the study of Tokoro and associates [12], however, eyes with higher refractive errors of -8 diopters or more were chosen. The authors demonstrated that eyes with refractive errors of -8 diopters or greater have axial lengths that are over 3 S.D. more than those in the adult Japanese population [12]. We, therefore, selected the eyes with refractive errors of -8 diopters or more. We excluded some eyes in elderly people with soft drusen and macular hemorrhages from the present study, even if their refractive errors were over -8 diopters.

The types of subretinal or choroidal hemorrhages have been previously reported in pathologic myopia. Blach [2] described simple macular hemorrhages and a disciform response. Hayashi and associates [7, 8] reported on macular hemorrhages with or without neovascular tissue. Avila and coworkers [1] found isolated macular hemorrhages without evidence of choroidal neovascular membrane on fluorescein angiography (which they called coin lesions) and choroidal neovascularization.

Previous investigators indicated that macular hemorrhages without CNV in pathologic myopia are usually associated with lacquer cracks, and that they commonly resorb a few months later and sometimes recur [1, 2, 4, 7, 8, 10, 11]. Similarly in the present study, macular hemorrhages without CNV were found along the course of lacquer cracks. These resorbed in all eyes and recurred in a few eyes. This type of hemorrhage was noted in young people [7]. It is possible that the elongation of the eyeball in young people with pathologic myopia may induce the rupture of Bruch's membrane and choriocapillaris (lacquer cracks), resulting in a small subretinal or choroidal hemorrhage without CNV. The visual prognosis in such eyes may be fair unless hemorrhage recurs, atrophic scars develop, or retinohoroidal degeneration progresses.

In accordance with other studies [3, 7], our findings showed that subretinal hemorrhages with CNV usually occur in elderly people. It is possible that CNV in pathologic myopia may be associated with aging, as in age-related macular degeneration. To our knowledge, it is unclear whether there may be a difference in pathologic myopia and age-related macular degeneration between the Japanese and Caucasian populations. Laser photocoagulation therapy is reportedly useful in treating neovascular membranes outside the foveal avascular zone [9]. Extrafoveal CNV was observed in only one eye in this study, and the visual outcome was poor. In eyes with pathologic myopia and CNV, visual prognosis may be poor.

We believe that the classification of subretinal hemorrhages in pathologic myopia into two types, with or without CNV, may be useful to assess the subsequent visual prognosis.

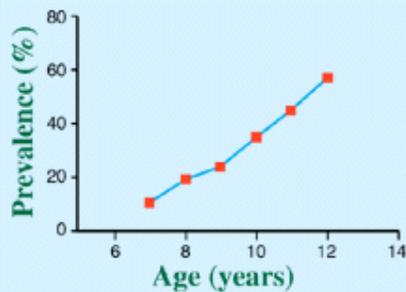
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Community Need

About 70 % of 17-year old school children in Hong Kong are short-sighted or myopic. If the population of China develops myopia to the same degree, some 700 million people in China will become myopic in the next 20-40 years. Myopic degeneration is the second highest cause of low vision in Hong Kong. A treatment for myopia would improve the quality of life for more than half a billion Chinese, and have considerable positive economic implications for the country. The annual cost of myopia in the US is in the region of US\$4.8 billion. China will soon have 18 times more myopes than the US.

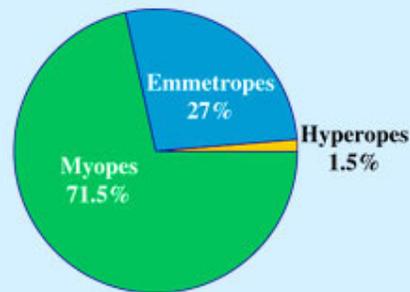
Prevalence of Myopia in Hong Kong Children



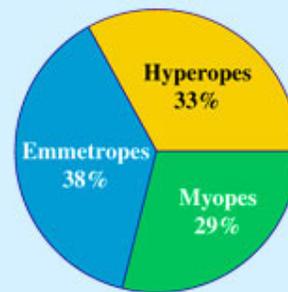
(Edwards, 1999)

The Changing Prevalence of Myopia

The huge increase in the prevalence of myopia in the younger compared with the older generation in HK (see below) demonstrates an environmental influence.



Prevalence of Myopia
(age 19 - 39 years)



Prevalence of Myopia
(age 40 - 75 years)

(Goh and Lam, 1994; Lam et al., 1994)

PATHOLOGIC MYOPIA AND CHOROIDAL NEOVASCULARIZATION

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Pathologic myopia involves a progressive elongation of the globe accompanied by degenerative changes of the retina and choroid. This condition is the seventh leading cause of blindness in adults in the United States. It is especially common in the Orient and in the Middle East.¹

Previous studies have suggested that 5% to 10% of eyes with an axial length of more than 26.5 mm develop choroidal neovascularization.^{2,3} This study was designed to add new data on the clinical progression of eyes with pathologic myopia and choroidal neovascularization.

SUBJECTS AND METHODS

We reviewed clinical records, color photographs, and fluorescein angiograms of 81 patients with severe myopia who were examined here between 1970 and 1979. All but three patients had a refractive error of -6 diopters or more; three patients had a refractive error between -5 and -6 diopters with fundus changes typical of pathologic myopia.

Of the 81 patients with severe myopia, 33 had a choroidal neovascular membrane at the posterior pole (Group A). In four of these 33 patients, neovascularization had occurred in both eyes. None of these patients had any signs of other degenerative diseases of the posterior segment. Follow-up information was obtained on 23 of the 33 patients with choroidal neovascular membranes; 17 of these 23 patients were re-examined by

us. Follow-up information for the other six patients was obtained from the original referring ophthalmologists. In 16 of the 23 follow-up cases, the fellow eye was also evaluated. All 16 eyes in this "contralateral group" had pathologic myopia but had not developed neovascular membranes (Group B).

From the group of 48 patients with severe myopia who did not have choroidal neovascularization, we selected 11 control patients who lived close to Baltimore, and re-examined them (Group C).

At the initial evaluation, we measured corrected visual acuity. A pinhole was used to improve visual acuity.

In the follow-up evaluations, a manifest refraction was performed in each case by one of us (M. L. H.). After dilating the pupils, we performed direct and indirect ophthalmoscopy and slit-lamp biomicroscopy with the Goldmann contact lens. Stereoscopic color photographs and fluorescein angiograms were obtained for all patients. We noted the following conditions whenever they were present: temporal crescent formation, diffuse or focal chorioretinal atrophy, posterior staphyloma, lacquer cracks, and retinal hemorrhage. In each patient re-examined here, we determined global axial length with an A-scan ultrasonoscope at a wave velocity of 1,545 m/sec. Three separate readings were taken for each globe and the values were averaged. This method is accurate to within 0.2 mm on either side of the averaged reading.^{4,5}

RESULTS

Initial examination—Group A included a higher proportion of women than Group C did (Table 1). The difference may be clinically significant in some way not

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TABLE 1
AGE AND SEX OF PATIENTS AND CONTROLS

	Group A	Group C
No. of patients	33	11
Men	13	8
Women	20	3
Age at onset of visual symptoms (yrs)		
Mean	45	42
Range	19 to 73	10 to 64
Under age 50 yrs	21	9

TABLE 2
REFRACTIVE ERROR

Refractive Error	Group A	Group B	Group C
No. of eyes	37	21	22
Mean	-11.27	-12.10	-13.50
Median	-9.00	-12.25	-12.90
Range	-5.50	-5.50	-7.75
to	-20.50	-20.00	-21.50
to			

evaluated in this study. Patients in both groups first developed visual symptoms at similar ages.

Table 2 shows the mean, median, and range of refractive errors for all three groups. The mean refractive errors were similar for all three groups. However, the median refractive error in Group A was less severe than in Groups B and C.

The pathologic conditions of the three groups are shown in Table 3. Lacquer cracks were more common in Groups A and B. Retinal hemorrhages were found almost exclusively in Group A. The remaining conditions occurred with similar frequency in all the groups.

To analyze visual acuity data, we classified the eyes with neovascularization according to the location of the new vessels with respect to the foveal avascu-

lar zone. Using stereoscopic color photographs and fluorescein angiograms, we classified neovascular membranes as being outside the foveal avascular zone, extending to the edge of the foveal avascular zone, or within the foveal avascular zone. In Group A, the neovascular membrane was located inside the foveal avascular zone in 21 eyes, extended to the edge of the foveal avascular zone in six eyes, and was outside the foveal avascular zone in ten eyes.

Follow-up examination for Group A—We obtained follow-up information for 27 of the 37 eyes with neovascular membranes. Twenty-one of these eyes were re-examined by both of us. Referring ophthalmologists supplied clinical information, stereoscopic color photographs, and fluorescein angiograms for the remaining six eyes. The average

TABLE 3
RETINAL FINDINGS IN SEVERE MYOPIA

Finding	Group A	Group B	Group C
No. of eyes	37	21	22
Temporal crescent	20	11	10
Chorioretinal atrophy	28	16	19
Diffuse	23	16	10
Focal	11	4	8
Posterior staphyloma	16	10	8
Lacquer cracks	21	11	8
Retinal hemorrhage			
Foveal	16	1	0
Parafoveal	8	1	0

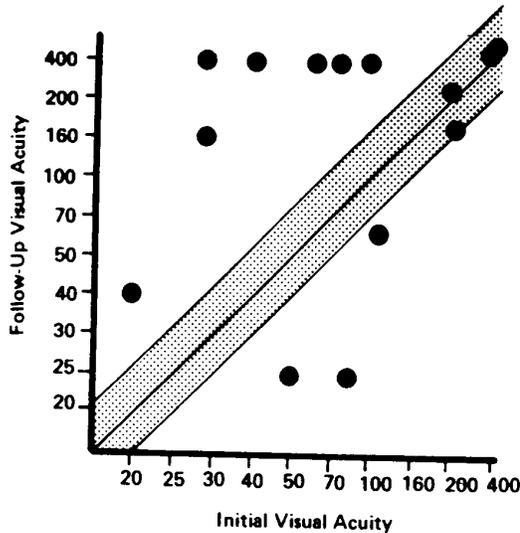


Fig. 1 (Hotchkiss and Fine). Change in visual acuity for the 14 eyes in Group A that had new vessels inside the foveal avascular zone.

follow-up interval was 25.5 months. The mean axial length of the eyes in Group A was 28.05 mm.

NEOVASCULAR MEMBRANES INSIDE THE FOVEAL AVASCULAR ZONE—We obtained follow-up information for 14 of the 21 eyes with neovascular membranes within the foveal avascular zone. These data are

summarized in Figure 1. Three of the 14 eyes improved two or more lines on the Snellen chart; visual acuity remained the same in four eyes; and seven eyes lost two or more lines on the Snellen chart.

Although the presence of a new vessel membrane within the foveal avascular zone caused visual loss in most patients, the visual outcome was not uniformly poor. One patient, for example, had a seven-month history of visual loss in the left eye. The left eye had a refractive error of -9.50 diopters, and her visual acuity was 6/24 (20/80). New vessels were present beneath the fovea of the left eye (Fig. 2). Five years later, visual acuity in the left eye had improved to 6/9 (20/30) with no apparent change in the size of the neovascular membrane.

Photocoagulation was not used to treat any eye containing a neovascular membrane within the foveal avascular zone.

NEOVASCULAR MEMBRANES EXTENDING TO THE EDGE OF THE FOVEAL AVASCULAR ZONE—We obtained follow-up information for five of the six eyes that initially had a neovascular membrane extending to the edge of the foveal avascular zone. In all five cases, the new vessels had

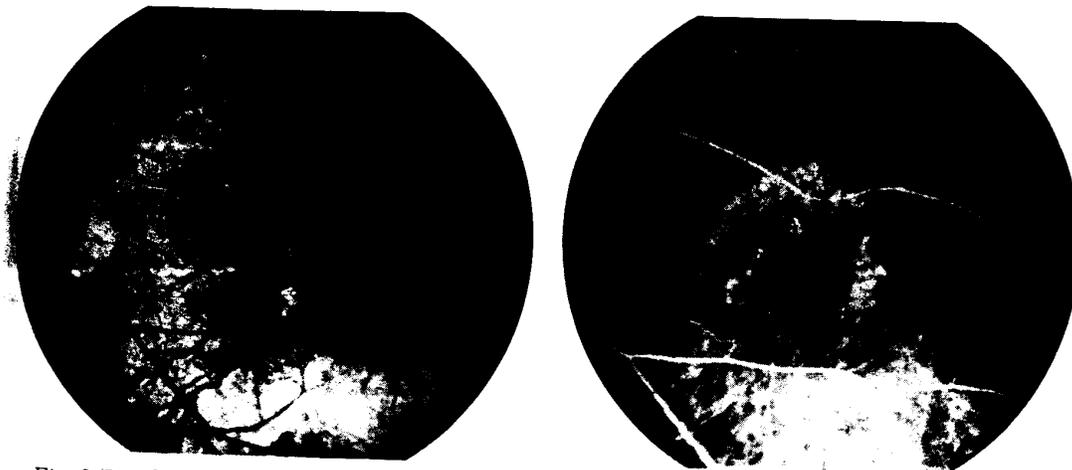


Fig. 2 (Hotchkiss and Fine). A 40-year-old woman had had visual blurring in her left eye for seven months. Visual acuity was 6/24 (20/80). Left, A neovascular membrane was present in the macula. Right, Fluorescein angiography showed the neovascular net beneath the fovea.

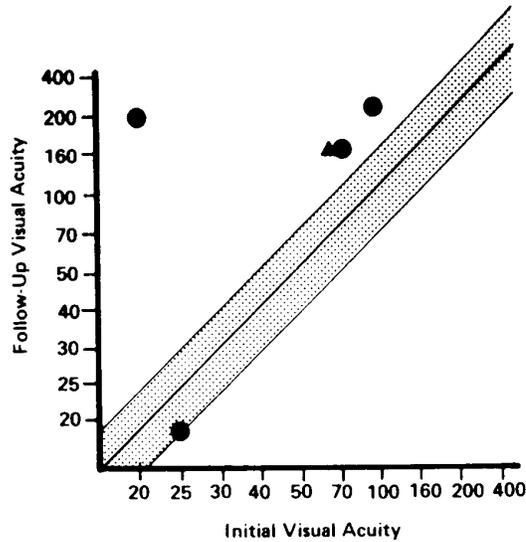


Fig. 3 (Hotchkiss and Fine). Change in visual acuity in the five eyes in Group A that had neovascular membranes extending to the edge of the foveal avascular zone. Triangular figure represents case in which the laser photocoagulation was used to treat the membrane.

advanced to within the avascular zone. Figure 3 summarizes the changes in visual acuity for these eyes. Visual acuity remained the same in one eye; the remaining four eyes lost two or more lines

on the Snellen chart. One patient had received argon-laser photocoagulation to the new vessel at the time of initial examination. Pretreatment visual acuity was 6/22.5 (20/75) (Fig. 4, left). One year later, the membrane had advanced inside the avascular zone and visual acuity was 6/48 (20/160) (Fig. 4, right).

NEOVASCULAR MEMBRANES OUTSIDE THE FOVEAL AVASCULAR ZONE—We obtained follow-up information for eight of the ten eyes with neovascular membranes outside the foveal avascular zone. These data are summarized in Figure 5. Visual improvement occurred in only one eye and involved the use of eccentric fixation. Visual acuity remained the same in four eyes and decreased at least two Snellen lines in three eyes.

Five of the eight eyes for which follow-up data were obtained had been treated with argon-laser photocoagulation. In three of the five eyes, an initial visual acuity of 6/6 (20/20) was preserved. One eye retained a visual acuity of 6/60 (20/200). One treated eye progressed from 6/7.5 (20/25) to 6/60 (20/200) during an 18-month period.

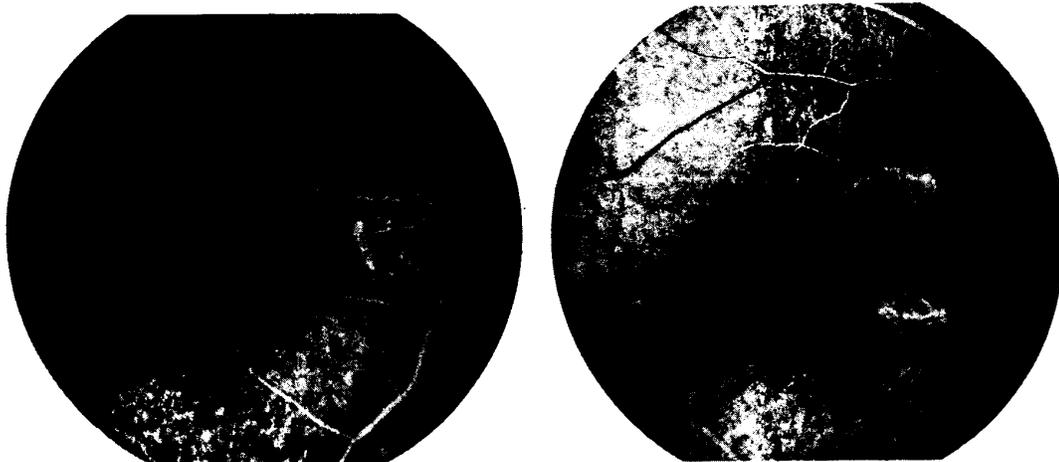


Fig. 4 (Hotchkiss and Fine). A 34-year-old man had a four-week history of decreased visual acuity in his right eye. Visual acuity was 6/22.5 (20/75). Left, A neovascular membrane extending to the edge of the avascular zone was treated with argon-laser photocoagulation. Right, Angiogram taken one year after photocoagulation of the membrane. Despite initially successful treatment, new vessels ultimately grew inside the avascular zone. Visual acuity was 6/48 (20/160).

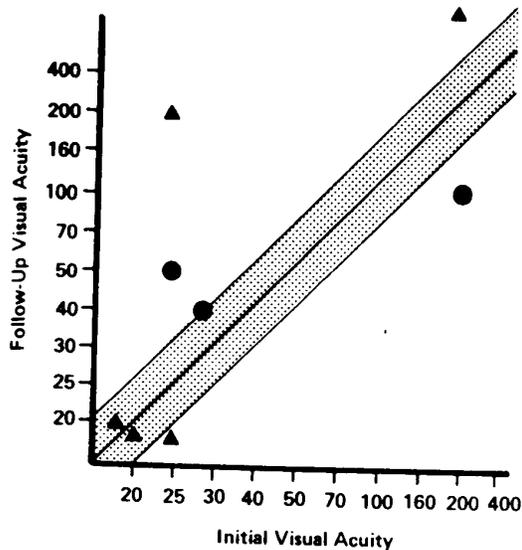


Fig. 5 (Hotchkiss and Fine). Change in visual acuity in the eight eyes in Group A that had new vessels outside of the foveal avascular zone. Triangular figures represent those cases treated with argon-laser photocoagulation.

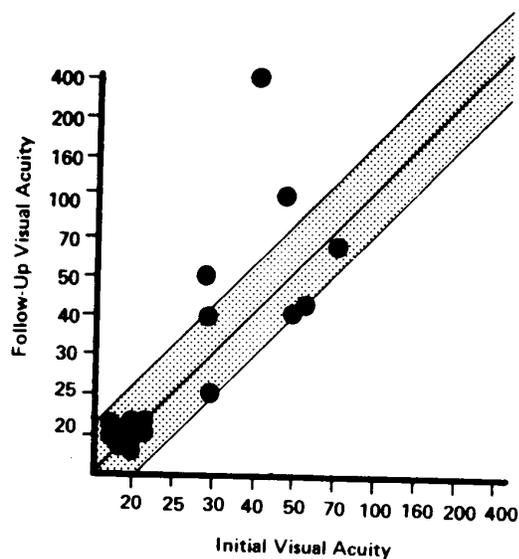


Fig. 6 (Hotchkiss and Fine). Change in visual acuity in the 16 eyes in Group B.

Follow-up examination for Groups B and C—We obtained adequate follow-up information for 16 eyes in Group B. The average axial length was 28.31 mm. Figure 6 summarizes the changes in visual acuity for these eyes. Three eyes lost two or more lines on the Snellen chart. In 13 eyes, initial visual acuity was unchanged.

We obtained follow-up information for 16 eyes in Group C. The average follow-up interval was 31.8 months. Axial length measurements averaged 28.92 mm. Visual acuity data are summarized in Figure 7. Five eyes improved two or more lines on the Snellen chart and visual acuity remained the same in 11 eyes.

DISCUSSION

Choroidal neovascularization has been described in association with a number of conditions, including senile macular degeneration, ocular histoplasmosis, angioid streaks, and traumatic choroidal rup-

ture.^{6,7} A break in Bruch's membrane precedes the development of neovascularization in each of these conditions. Histologic changes of a degenerative, calcific, inflammatory, or neoplastic nature are usually present within the cho-

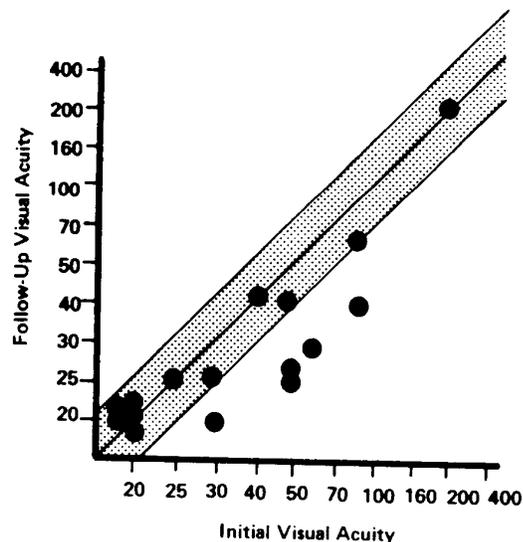


Fig. 7 (Hotchkiss and Fine). Change in visual acuity in the 16 eyes in Group C that were highly myopic but without neovascularization.

roid, adjacent to the defect in Bruch's membrane. Once established, the break in Bruch's membrane permits neovascular proliferation from the choriocapillaris into the subretinal pigment epithelial space.

A similar process has been proposed for severe myopia.^{8,9} Fluorescein angiographic studies have shown that choroidal and retinal circulations are slowed in severe myopia. Conceivably, vascular compromise predisposes the eye to choroidal degeneration.^{10,11} Continued stretching and degeneration of the choroid causes eyes with severe myopia to develop breaks in Bruch's membrane. Large breaks in Bruch's membrane, called lacquer cracks, allow choroidal neovascular growth. These lacquer cracks were present in 21 of the 37 eyes in Group A. However, in 16 eyes, choroidal neovascularization developed in the absence of lacquer cracks. Microscopic defects in Bruch's membrane might have been present in these cases. The other features of myopic degeneration, including temporal crescent formation, diffuse and focal chorioretinal atrophy, posterior staphylomas, and axial length, did not correlate with the development of choroidal neovascular membranes.

We evaluated eyes in Groups B and C separately to avoid masking a possible genetic predisposition towards choroidal degeneration and neovascularization. Indeed, lacquer cracks were more common in Groups A and B.

In five of the 16 eyes in Group C, visual acuity had increased two or more Snellen lines at the follow-up examination. Because manifest refraction had not been performed at the initial examination, we cannot exclude the possibility that refraction may account for this improvement. Results of fluorescein angiography in these eyes were also unchanged from the initial evaluation.

SUMMARY

In 14 of 27 eyes with choroidal neovascular membranes associated with severe myopia, visual acuity deteriorated two or more lines on the Snellen chart. Twelve of the 27 eyes became legally blind.

Final visual acuity may be related to the position of the neovascular membrane within the posterior pole. Four of the eight eyes with new vessels outside of the foveal avascular zone had follow-up visual acuities of 6/12 (20/40) or better. Only one of five eyes with new vessels extending to the edge of the avascular zone had a final visual acuity of 6/12 (20/40) or better. Three of 14 eyes with a neovascular membrane beneath the foveal avascular zone had visual acuities of 6/12 (20/40) or better.

Neovascularization associated with severe myopia clearly jeopardizes central visual acuity. Laser photocoagulation therapy may be useful in treating neovascular membranes outside the foveal avascular zone or extending to the edge of the perifoveal capillary network. A larger prospective study is needed to determine the guidelines for and efficacy of such treatment for patients with severe myopia who develop choroidal neovascularization.

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Fifty years ago this month in The Journal:

We might say that the myopic eye of such a child is overgrown, and that if we put it at rest by means of atropin for such a period, while the body continues to grow and the child lives an outdoor life, the body can in a measure catch up with the eye. My experience in many such cases is that the myopia remains stationary or improves a little from June to September, and that most myopias increase about three quarters of a diopter during the school year. The special value of continued attention to the earliest stages of myopia in the young child should be repeatedly stated to the mother and teacher, and the pediatricist should aid in this education.

De Wayne Hallett: The Prevention of Myopia
Am. J. Ophthalmol. 14:146, 1931

Choroidal Neovascularization in Degenerative Myopia: Role of Laser Photocoagulation

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ABSTRACT

Laser photocoagulation of extrafoveal choroidal new vessels was performed in 19 eyes with degenerative myopia. Sixteen eyes required only one treatment. Three eyes required more than one because of incomplete closure of the new vessels after the first treatment. Choroidal new vessel formation did not recur during the post-treatment follow-up period (average 29.2 months), and a dry, atrophic photocoagulation scar was achieved in all eyes. Visual acuity improved in only two eyes (11%), stabilized in four eyes (21%), and deteriorated in 13 eyes (68%). All except two eyes showed spontaneous progressive enlargement of the atrophic photocoagulation scar, which worsened visual acuity in 13 eyes (68%).

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The authors thank J. Wallace McMeel, M.D., and Felipe I. Tolentino, M.D., who allowed inclusion of their patients.

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Degenerative myopia (≥ 6 diopters) is characterized by increased axial length associated with vitreous liquefaction and chorioretinal degeneration.¹ Several degrees of chorioretinal degenerative changes have been described,² and choroidal neovascularization can occur as a complication.^{3,4} Choroidal new vessels are often related to lacquer cracks^{5,6} and their natural course is usually self-limited,^{2,7} a finding we have confirmed previously.

Although photocoagulation for choroidal neovascularization has been successful in many diseases, particularly senile macular degeneration,^{8,9} it has produced poor results in degenerative myopia.²

This retrospective study describes the immediate and long-term effects of photocoagulation of choroidal new vessels in degenerative myopia.

PATIENTS AND METHODS

We reviewed the records of 19 patients (19 eyes) with degenerative myopia who underwent photocoagulation of extrafoveal choroidal new vessels. The patients included eight men (42%) and 11 women (58%), ranging in age from 27 to 68 years (average 50.2 years). The refractive errors in the 19 eyes ranged from -6.25 diopters (D) to -21.5 D in spherical equivalent. We excluded patients with a history of photocoagulation, cryotherapy, or retinal detachment surgery, as well as those with diabetes, retinal vascular disease, glaucoma, senile macular degeneration, or ocular trauma.

All 19 eyes had fluorescein angiographic evidence of



FIGURE 1: Early fluorescein transit of left eye with degenerative myopia showing choroidal new vessels nasal to fovea.

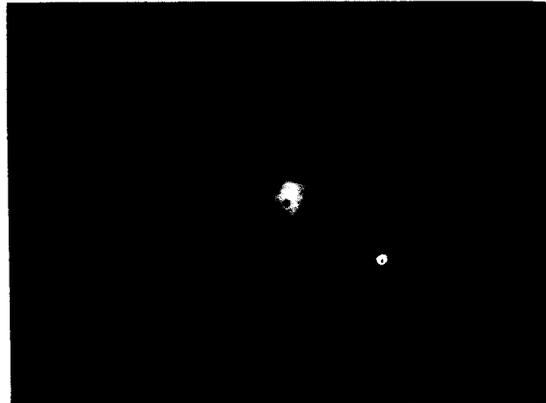


FIGURE 2: Late fluorescein transit of same eye in Figure 1 showing minimal leakage from choroidal new vessels (V_1 , new vessels).

extrafoveal choroidal neovascularization. Three of us separately reviewed angiograms for presence, location, and leakage of choroidal new vessels. To be considered for photocoagulation, the new vessels had to be located clearly outside the foveal avascular zone. The new vessels were graded as follows: V_1 , if the area of hyperfluorescence associated with filling of choroidal new vessels in the early transit did not increase significantly in the late transit, indicating minimal leakage; V_2 , if hyperfluorescence in the late transit extended well beyond the margins of the new vessels, indicating moderate to marked leakage.

At each visit, best corrected visual acuity was measured using the same standard equipment for visual acuity testing and preferably the same examiner. Central visual field testing was also performed, using the Autoplot apparatus and 1-mm and 6-mm white test objects at 1 m.

A dry, atrophic, subretinal scar was defined as a scar associated with a flat retina, showing no leakage by fluorescein angiography. Worsening or improvement of visual acuity was defined as a change of one or more lines on the Snellen chart. Stabilization of visual acuity meant no change on the Snellen chart.

Photocoagulation was performed with the green monochromatic argon laser. The entire choroidal neovascular membrane was covered with confluent photocoagulation burns of 50 to 100 μm . Relatively low power settings (100 to 250 mW) and long duration (up to 0.5 sec) were used to prevent hemorrhage and to minimize damage to the choroidal structures, including Bruch's membrane. Photocoagulation was judged optimal when post-treatment fluorescein angiography showed a homogeneously hypofluorescent patch in the area of photocoagulation, particularly in the early transit, indicating complete closure of the new vessels.

After treatment, fluorescein angiography was repeated at 1 week, 1 month, and 3 months after photo-

coagulation, and as needed thereafter. Post-treatment follow-up ranged from 21 to 52 months (average 29.2 months).

A finding was considered statistically significant if the probability that it would have occurred by chance was less than 5%.

CASE REPORT

A 63-year-old woman had a 2-week history of decreased visual acuity in the left eye. She was highly myopic and had undergone retinal detachment surgery for repair of a macular hole in the right eye 4 years previously.

Visual acuity in the right eye was counting fingers at 2 feet with a correction of $-14.75 - 0.5 \times 15^\circ$, and in the left eye 20/100 with a correction of $-10.25 - 0.50 \times 10^\circ$. The intraocular pressure was 18 mmHg in each eye. Indirect ophthalmoscopy showed a large, macular, atrophic, subretinal scar in the right eye and a small, subretinal hemorrhage in the macular area of the left eye. Both eyes showed moderate myopic chorioretinal degeneration, but no retinal breaks. In the left eye, central visual field examination revealed a paracentral scotoma to a 1-mm test object, and fluorescein angiography showed a small choroidal neovascular membrane located at the nasal edge of the fovea (Figure 1). The choroidal new vessels showed minimal leakage in the late transit (Figure 2).

The patient underwent photocoagulation with a green monochromatic argon laser, 100- μm spot size, 125 mW power setting, of 0.3-sec duration. The choroidal neovascular membrane was covered entirely with a total of 63 applications.

Fluorescein angiography of the left eye, which was repeated 1 week after treatment, revealed a homogeneously hypofluorescent patch in the early transit, indicating complete closure of the photocoagulated choroidal new vessels (Figure 3).

Four months later, visual acuity in the left eye had improved to 20/60, and the central visual field revealed a significant reduction of the paracentral scotoma.



FIGURE 3: Fluorescein transit of same eye in Figure 1, 1 week after photocoagulation, showing complete closure of new vessels.

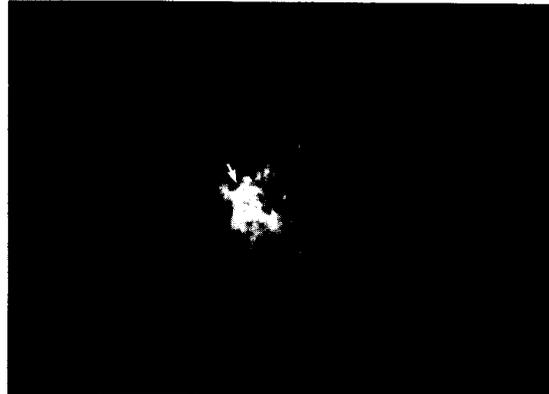


FIGURE 4: Red-free monochromatic photograph of same eye in Figure 1, 7 months after photocoagulation, showing whitish, atrophic scar nasal to fovea (arrow).

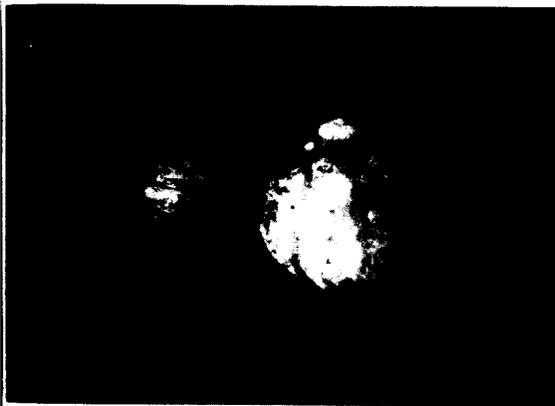


FIGURE 5: Red-free monochromatic photograph of same eye in Figure 1, 17 months after treatment, showing marked enlargement of photocoagulation scar.



FIGURE 6: Fluorescein transit of same eye in Figure 1, 17 months after treatment, showing large, atrophic, subretinal scar in macula.

Four successive eye examinations at 3-month intervals showed stable visual acuity at 20/60 and unchanged central visual fields. A small, dry, atrophic, subretinal scar was present at the nasal edge of the fovea (Figure 4) with no evidence of new vessels by fluorescein angiography.

Seventeen months after treatment the patient began experiencing decreasing visual acuity associated with a deteriorating central visual field. Successive fluorescein angiography showed progressive enlargement of the atrophic photocoagulation scar. No recurrent choroidal new vessels were seen at any time.

The last follow-up visit revealed a best corrected visual acuity of 20/200 in the left eye. The paracentral scotoma had become significantly larger. Fluorescein angiography showed a large, atrophic, subretinal scar associated with deep choroidal atrophy in the area of photocoagulation (Figures 5 & 6). The scar involved the fovea, but no choroidal new vessels were detected.

RESULTS

All the choroidal neovascular membranes were extrafoveal with diameters ranging from $\frac{1}{4}$ to 1 disc. Sixteen eyes had V_1 choroidal new vessels associated with minimal or no leakage by fluorescein angiography, and three eyes showed V_2 choroidal new vessels with moderate leakage. After photocoagulation the new vessels were closed completely in all eyes. In 15 of the 16 eyes with V_1 new vessels, complete closure was achieved with one treatment; one eye required two treatments. In the three eyes with V_2 new vessels, two eyes required three successive treatments because of incomplete closure of the new vessels, and one eye required only one treatment. When the new vessels were judged to be completely closed by photocoagulation, there were no recurrences. The follow-up period ranged from 21 to 52 months (average 29.2

months), and a dry, atrophic, subretinal scar was obtained in all eyes after photocoagulation.

Of the 19 eyes treated, visual improvement at the end of the follow-up period was seen in only two eyes (11%), stabilization in four eyes (21%), and visual deterioration in 13 eyes (68%). Progressive enlargement of the atrophic photocoagulation scar, resulting in a wide ring of deep choroidal atrophy around the initial area of photocoagulation, was seen in 17 eyes (89%) after an average period of 13.4 months (range 11 to 19 months) following photocoagulation. The two eyes that did not show enlargement of the photocoagulation scar had V₂ new vessels; the visual acuity improved in one eye and stabilized in the other. Of the 17 eyes with an enlarged scar, 16 eyes had V₁ new vessels; visual acuity had deteriorated in 13 eyes, stabilized in three eyes, and improved in one eye.

DISCUSSION

Axial elongation in eyes with degenerative myopia¹ causes progressive distension of the posterior pole¹⁰ and stretching of the ocular coats. This process results in thinning of the retina and choroid accompanied by vascular and degenerative changes in the choroid.¹¹ In a study of 354 eyes with myopic chorioretinal degeneration, we demonstrated that in 96% of 149 eyes showing choroidal neovascularization, the new vessels had a self-limited course and involuted into atrophic nonexudative scars.² We attributed the benign course of these choroidal new vessels to changes in choroidal hemodynamics, secondary to diffuse choroidal thinning and degeneration. These changes caused severe circulatory disturbances of the choriocapillaris, from which the choroidal new vessels originated. This process may explain why, in the present study, most of the choroidal new vessels showed little or no leakage.

Argon and krypton laser photocoagulation have been used successfully to treat choroidal neovascular membranes associated with senile macular degeneration.^{8,9,12} In degenerative myopia, however, photocoagulation is not indicated if choroidal new vessels do not show significant leakage.² This retrospective study confirms our preliminary findings² and demonstrates that in degenerative myopia, although closure of the new vessels by photocoagulation is usually easy, the resulting atrophic subretinal scar progressively enlarges and often is associated with visual deterioration.

Because of the questionable benefit of laser photocoagulation in treating choroidal neovascularization associated with degenerative myopia, only membranes located outside the foveal avascular zone were treated. The new vessels, particularly those of the V₁ type, were easy to close permanently by photocoagulation; 15 of the 16 eyes (94%) with V₁ new vessels required only one treatment, and none showed recurrence of the new vessels after an average follow-up period of 29.2

months. Although the number of eyes with V₂ choroidal new vessels was too small for statistical analysis, two of three eyes with V₂ new vessels (66.6%) required more than one treatment for permanent closure, whereas additional treatments were required in only one of 16 eyes (6.25%) with V₁ new vessels. These observations further confirm the benign behavior of choroidal new vessels, particularly those of the V₁ type, in degenerative myopia.² These findings are distinctly different from those in senile macular degeneration in which permanent closure of choroidal new vessels often requires several treatments.

Despite the absence of choroidal new vessel recurrences after treatment, 17 of 19 eyes (89%) showed progressively enlarging atrophic subretinal scars. These scars resulted in large rings of deep choroidal atrophy surrounding the previously photocoagulated areas. This atrophy appears to be related to a laser-induced weakening of the choroid, which is also stretched continuously by progressive degenerative myopia. The enlarged scars caused decreased function in 13 eyes (68%) due to involvement of the fovea by the atrophic changes. The clinical differentiation between V₁ and V₂ choroidal new vessels by fluorescein angiography is important for management because enlargement of the photocoagulation scar, often associated with visual deterioration, was seen in all eyes with V₁ new vessels but in only one of the three eyes with V₂ new vessels. This may indicate a weaker choroid in eyes with V₁ than in those with V₂ new vessels.

We have shown that the natural course of V₁ choroidal new vessels in degenerative myopia is self-limited. In 38 of 70 eyes (54%) with untreated choroidal new vessels, visual improvement or stabilization occurred.² In the present series of 16 photocoagulated eyes with V₁ choroidal new vessels, visual acuity stabilized or improved in only three eyes (19%). These results are significantly worse than those observed in the natural history of the condition (P<0.05), indicating that photocoagulation is not beneficial in treating choroidal neovascularization of type V₁ associated with degenerative myopia.

Because the natural course of choroidal new vessels of type V₁ in degenerative myopia is self-limited,² and because in these cases the photocoagulation scar often enlarges and causes functional deterioration, photocoagulation should be applied with extreme caution. Thus far, we have not observed enough cases with choroidal new vessels of type V₂ in degenerative myopia to recommend specific treatment.

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The Fuchs' Spot: An Ophthalmoscopic and Fluorescein Angiographic Study

A correlation of fundusoscopic and fluorescein angiographic findings in the Fuchs' spot of high myopia is presented. A variety of ophthalmoscopic changes indicate that both serous and hemorrhagic detachments of the retinal pigment epithelium and neurosensory retina are associated with this lesion. Fluorescein angiography, however, reveals subretinal neovascularization from the choroid as the basic underlying disease in most cases reviewed. Wide variations in the ophthalmoscopic appearance of the pigmented maculopathy of high myopia necessitate a more descriptive approach than that indicated by the term "Fuchs' spot." Fluorescein angiography becomes a necessity to delineate neovascular lesions as paracentral tufts may possibly be treated with laser photocoagulation to reduce progression.

In a recent survey, pathologic myopia has been found to be the seventh cause of adult blindness in the United States.¹ The Fuchs' spot is of special interest in this regard because of the marked effect it has upon central vision and because it tends to occur at an age when visual acuity is essential for employment. Fuchs,² in his original description, noted a dark spot at the macula, fre-

quently with a surrounding macular hemorrhage. The lesion has been noted to vary in color and, in addition to black, both green and grey spots have been described.

Campos³ has placed the incidence of this condition as high as 10% in myopes of greater than 5 diopters. In a recent study by Curtin and Karlin,⁴ Fuchs' spots were found to affect 5.2% of eyes with an axial length of 26.5 mm or more.

The recent development of fluorescein angiography has presented the ophthalmologist with an invaluable diagnostic tool for the study of fundus diseases.

From the Sprague Myopia Clinic, the Fluorescein Clinics, and the Photocoagulation Clinic of the Manhattan Eye, Ear and Throat Hospital, New York, NY.

Reprint requests to: 1938 Grand Concourse, Bronx, NY 10457 (Dr. Levy).

Thus far, only one reference to the fluorescein angiographic changes in Fuchs' spot has been made. Gass⁵ has indicated that the Fuchs' spot may be the result of 2 different stages in the development of hemorrhagic disciform macular degeneration and probably represents a disciform lesion in nature. In the first stage an acute hemorrhagic detachment ensues and during the second stage there is organization of the subneuroepithelial hemorrhage which may be accompanied by proliferation of the pigment epithelium resulting in a dark spot in the macula. It has been the purpose of this study to evaluate a large number of Fuchs' spots with fluorescein angiography so as to correlate the fundusoscopic and angiographic findings in this disease process.

Materials and Methods

The diagnosis of Fuchs' spot was made clinically in patients referred for fluorescein angiography from the Sprague Clinic for Myopia at the Manhattan Eye, Ear and Throat Hospital over a 10 month period. Axial lengths were measured as previously reported by one of us (B.J.C.).⁶ Fluorescein angiography was performed as described in a previous article by another (J.H.L.).⁷

Seventy-two eyes were examined in 36 patients and the following observations were made. Age ranged from 24 to 67 years. There were 24 women and 12 men. The degree of myopia in spherical equivalents was -6.75 to -23.50 diopters. Axial lengths were 27.0 to 34.0 mm. Best corrected visual acuities ranged from 20/20-1 to finger counting at one foot.

Results

Despite the range of vision and of size and shape of the pigmented area in the highly myopic patient, most of the Fuchs' spots were noted to be associated with neovascularization extending from the

choroid into the subpigment epithelial space. The pathologic neovascularization at times was present by itself and at other times was present with serous pigment epithelial detachments, with or without serous neurosensory detachments, and on occasion, with hemorrhagic detachments. Late stage lesions appear to contain widespread fibrosis and atrophy in addition to macular hyperpigmentation.

Case Reports

Case 1. A 48-year-old white man noted metamorphopsia OD 2 months before examination. Best corrected vision was 20/40— with $-18.00 +1.00 \times 140$ OD. Axial diameters were 34.0 mm OU. Fundusoscopic examination revealed a peripapillary myopic conus, lacquer cracks and a flat area of macular hyperpigmentation OD (Color fig 1).

Fluorescein Angiography. A small area of central neovascularization extending from the choroid into the subpigment epithelial space is noted in the venous phase with diffusion of dye in the late photograph. The neovascular tuft is most characterized in the early phase by the serrated pattern (Fig 1).

Case 2. A 56-year-old black woman gave a history of metamorphopsia in the left eye for 3 to 4 years before examination. Best corrected vision was 20/20-1 with $-12.00 -1.75 \times 85$ OS. Axial length was 29.8 mm OS. Fundusoscopic examination revealed a temporal myopic conus with a small area of hyperpigmentation in the inferotemporal portion of the macula with adjacent areas of hemorrhage and depigmentation (Color fig 2).

Fluorescein Angiography. Multiple areas of hyperfluorescence were first noted in the arterial phase and persisted well into the post fluorescent phase. The serrated pattern of a neovascular tuft is again seen and best noted in Figure 2c. The small hemorrhage blocked choroidal fluorescence throughout the study (Fig 2). This picture is again consistent with a choroidal neovascular tuft extending under the pigment epithelium.

Case 3. A 65-year-old white woman noted sudden onset of decreased vision



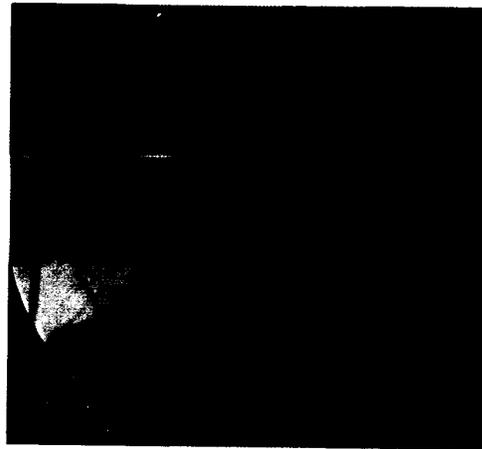
COLOR FIG 1



COLOR FIG 2



COLOR FIG 3



COLOR FIG 4



COLOR FIG 5

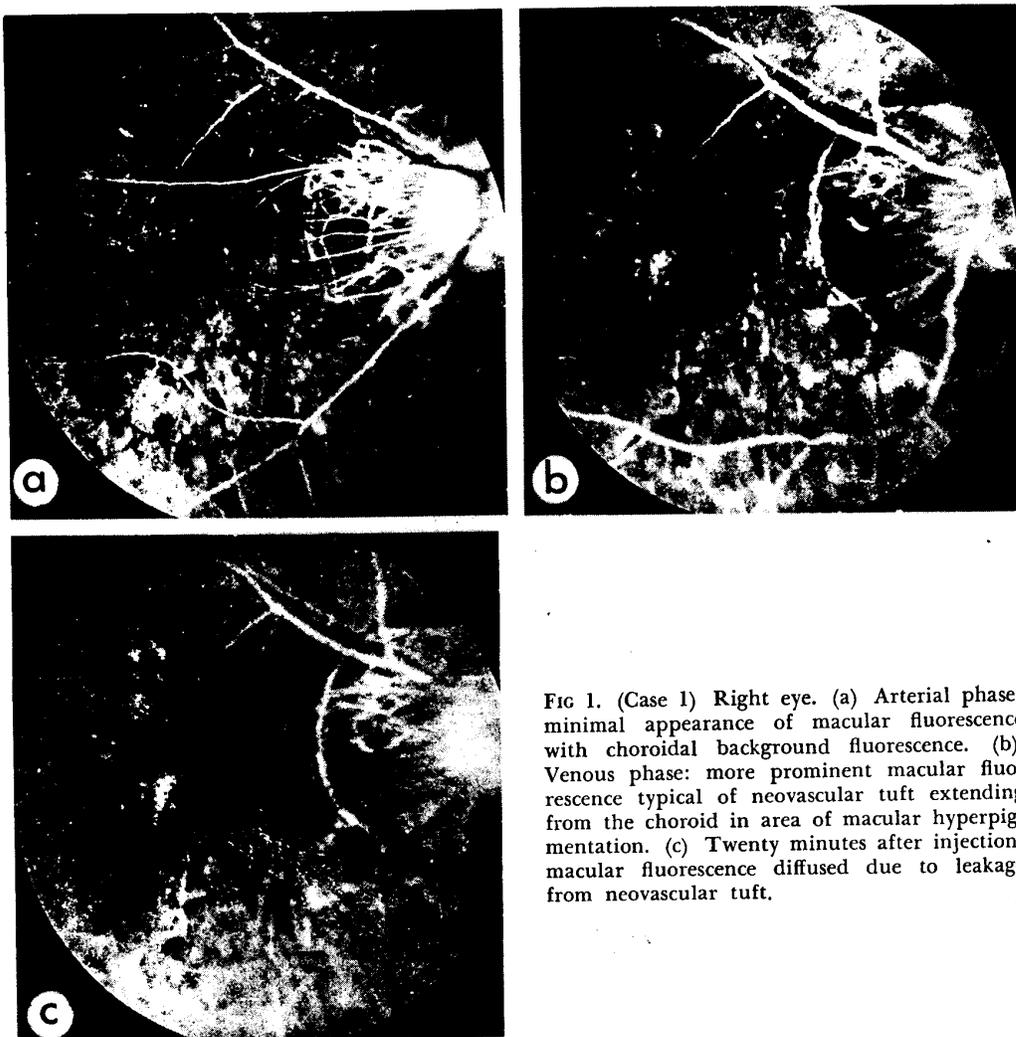


FIG 1. (Case 1) Right eye. (a) Arterial phase: minimal appearance of macular fluorescence with choroidal background fluorescence. (b) Venous phase: more prominent macular fluorescence typical of neovascular tuft extending from the choroid in area of macular hyperpigmentation. (c) Twenty minutes after injection: macular fluorescence diffused due to leakage from neovascular tuft.

and metamorphosis 2 days before examination. Best corrected vision was 20/70 with $-12.00 -1.00 \times 180$ OS. However, 2 months previously, she had had a documented visual acuity of 20/40 in that eye. Axial length was 28.6 mm OS. Funduscopic examination revealed a solitary doughnut-shaped area of hyperpigmentation in the macular area of the left eye (Color Fig 3).

Fluorescein Angiography. Leakage and pooling of dye into a disciform detachment of the pigment epithelium was seen. This began in the early arteriovenous phase, with persistence of fluorescein into the late phase, and ultimate diffusion of the dye into the subretinal space. Areas of transmitted fluorescence

indicative of defects in the pigment epithelium also were noted superotemporal to the macula. No definite neovascular tuft into the retinal pigment epithelial detachment could be noted, but filling with dye was so rapid, this might be present and have been missed (Fig 3).

Case 4. A 67-year-old white man presented with poor vision OU since childhood with additional loss more recently OS. Best corrected vision was finger counting at one foot with -22.50 OD and 20/300 with $-11.50 -0.75 \times 10$ OS. Axial lengths were 30.2 mm OU. Funduscopic examination OD revealed almost total loss of chorioretinal tissue in the posterior pole, but no Fuchs' spot, while

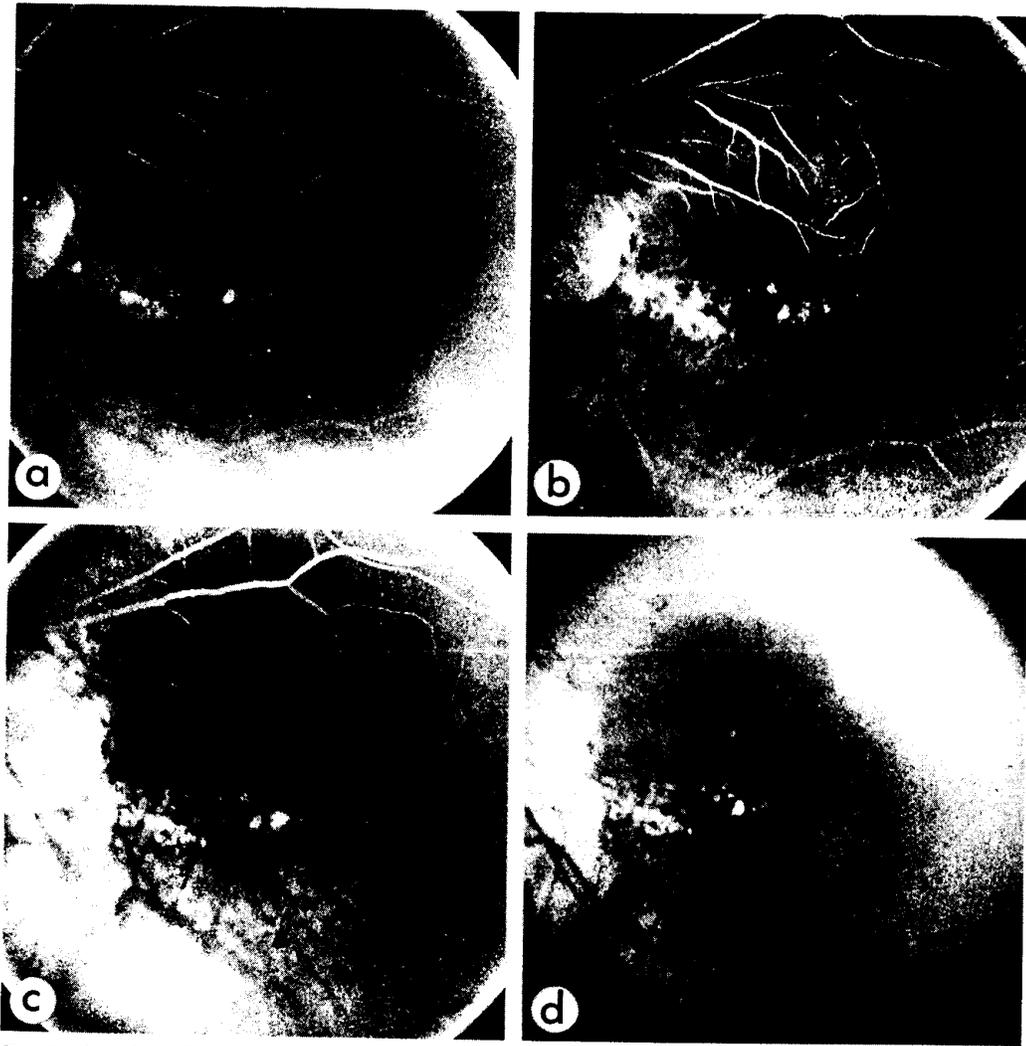


FIG 2. (Case 2) Left eye. (a) Arterial phase: multiple small areas of prominent fluorescence corresponding to areas of depigmentation and hyperpigmentation on funduscopy. Area of hemorrhage remains dark. (b) Early venous phase: persistence and increased prominence of fluorescence, now in typical serrated pattern of choroidal neovascularization. (c) Recirculation phase: continued prominence of fluorescence, more apparent as neovascular tuft. (d) Twenty minutes after injection: further persistence of multiple areas of fluorescence with some diffusion of dye indicating leakage from neovascular tuft.

OS there was a 360° myopic conus with macular hyperpigmentation surrounded by hemorrhage (Color Fig 4).

Fluorescein Angiography. There was prominent fluorescence in the typical serrated pattern in the disciform peripapillary area from choroidal neovascularization underlying the retinal pigment epithelium with blocked fluorescence from the surrounding subretinal hemorrhage. Two focal areas of leakage under the pigment epithelium were noted superotemporally (Fig 4).

Case 5. A 46-year-old black woman with longstanding visual impairment noticed definite visual decrease OD 3 years prior to examination. Best corrected vision was 20/400 with a $-14.50 - 1.00 \times 180$. Axial length was 29.2 mm. Funduscopy revealed lacquer cracks in the macular areas of both eyes with an elevated lesion with surrounding pigmentation at the macula (Color Fig 5).

Fluorescein Angiography. The elevated disciform area at the macula again shows

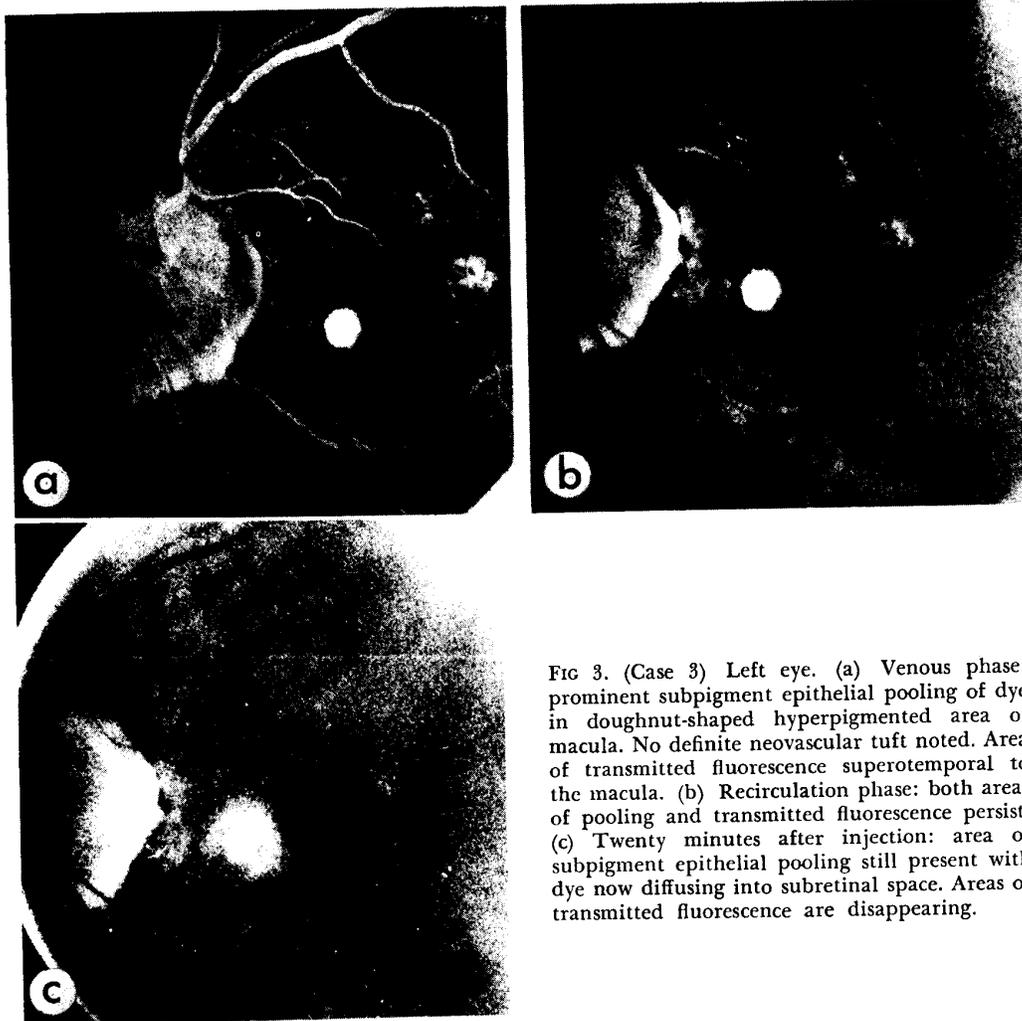


FIG 3. (Case 3) Left eye. (a) Venous phase: prominent subpigment epithelial pooling of dye in doughnut-shaped hyperpigmented area of macula. No definite neovascular tuft noted. Area of transmitted fluorescence superotemporal to the macula. (b) Recirculation phase: both areas of pooling and transmitted fluorescence persist. (c) Twenty minutes after injection: area of subpigment epithelial pooling still present with dye now diffusing into subretinal space. Areas of transmitted fluorescence are disappearing.

the typical serrated pattern of choroidal neovascularization in addition to a similar pattern at the temporal end of the peripapillary myopic conus (Fig 5).

Discussion

Since Fuchs' original description in 1901,² common usage of the term "Fuchs' spot" has included any dark spot at the macula in patients with high myopia. These dark spots, however, may be extremely varied in ophthalmoscopic appearance as seen in this study. They may be of uniform consistency, dark with pale centers, round or elliptical, elevated or flat, and surrounded by normal retina

or bare sclera. Visual acuity may range from normal to complete loss of central vision.

The fluorescein abnormalities described in this study appear to demonstrate certain recurring pathologic aspects of the pigmented maculopathy of high myopia known as the Fuchs' spot. These are serous and hemorrhagic detachments of the retinal pigment epithelium and/or the neurosensory retina which are frequently, but not always, associated with choroidal neovascularization extending into the subretinal pigment epithelial space. It is probable

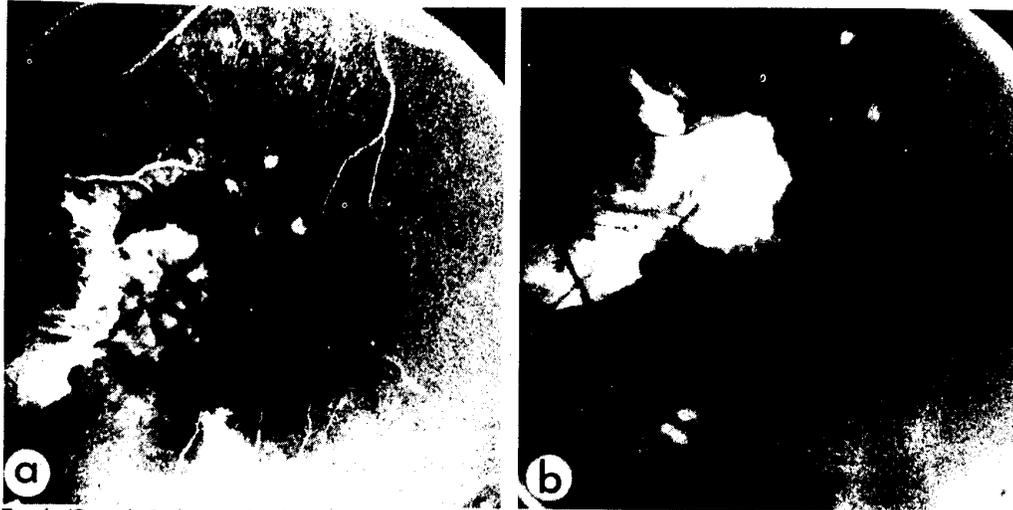


FIG 4. (Case 4) Left eye. (a) Arteriovenous phase: fluorescence of typical serrated pattern of choroidal neovascularization from the peripapillary area into the subretinal pigment epithelial space surrounded by blocked fluorescence due to subretinal blood. Two focal areas of leakage into subretinal space noted superotemporal to macula. (b) Twenty minutes after injection: diffusion of dye from peripapillary neovascular tuft noted and focal leaks superotemporal persist. Staining of bare sclera in myopic conus also is prominent.

that choroidal neovascularization precedes the hemorrhagic detachments although the serious detachments may either follow or precede the actual neovascular process.

The multiplicity of fluorescein angiographic abnormalities found in this study is similar to that seen in serous and hemorrhagic detachment of the macula in the senile nonmyopic eye, however, with 2 exceptions. These are: (1) its tendency toward greater pigmentary deposition; and (2) the associated circumscribed chorioretinal atrophy of the myopic eye. While both are unique to the myopic eye, it is the former which gives the classic picture of the Fuchs' spot. Angiographically, choroidal neovascular tufts into the subretinal pigment epithelial space are noted in both disease processes. The essential lesion of the Fuchs' spot as seen in this study consists of frank serous or hemorrhagic detachments of the pigment epithelium and/or the neurosensory epithelium associated with this neovascu-

larization. Identical counterparts exist in the nonmyopic eye in serous and hemorrhagic disciform macular degeneration, but usually without the characteristic hyperpigmentation of the myopic macula. While the end stage lesion of serous or hemorrhagic senile disciform macular degeneration is often a glial scar, the pigmented maculopathy of high myopia appears to progress to complete atrophy of tapetoretinal tissue. This atrophy occurs even if a previous subretinal hemorrhage has occurred, which in other instances might lead to glial proliferation.

The reason for the unusual pigmentary response of the myopic macula is unknown. Fuchs'² believed that the proliferation of pigment epithelium at the macula occurred without relation to other pathology. Salzmann⁸ has called attention to breaks in the lamina vitrea and Lloyd⁹ to stretching of the choriocapillaris as being causative factors. Hyperpigmentation of the macula is especially common in congenital myopia.

Because of widespread ophthalmol-

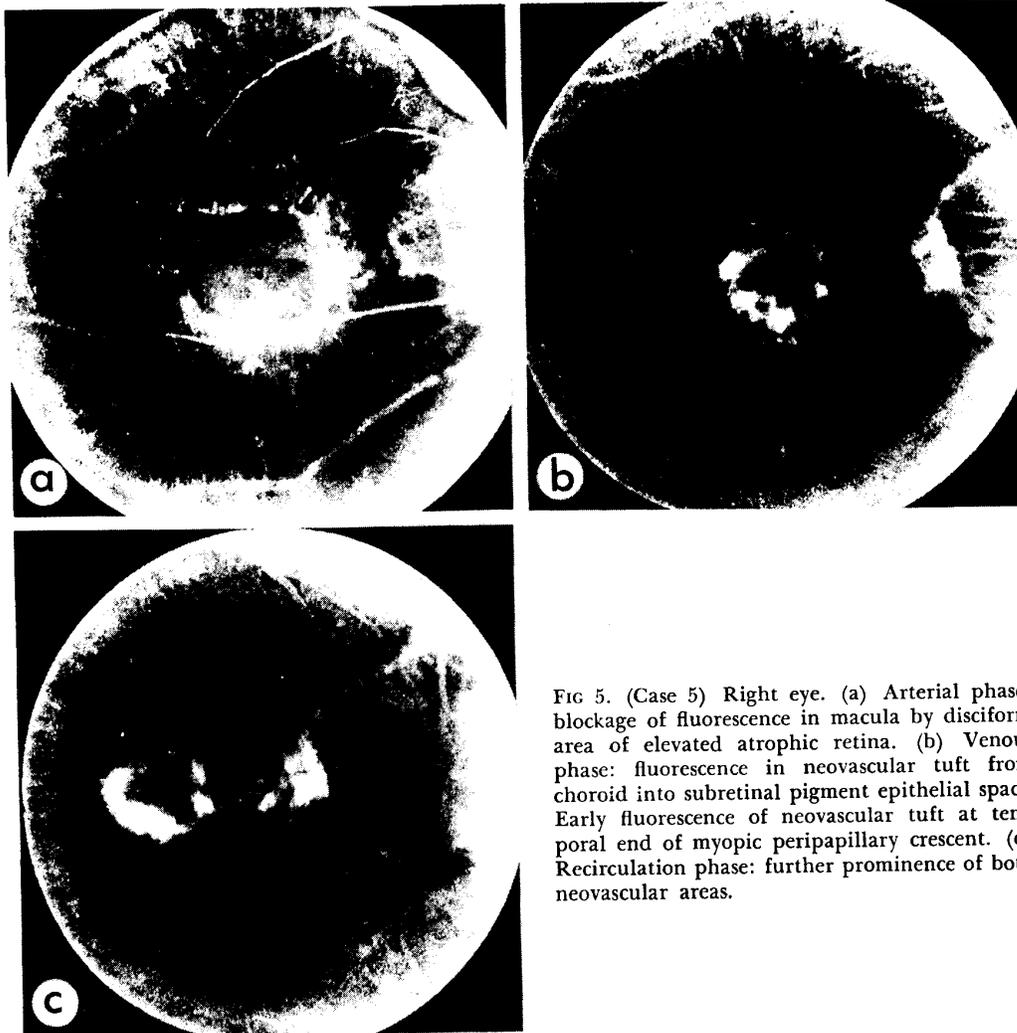


FIG 5. (Case 5) Right eye. (a) Arterial phase: blockage of fluorescence in macula by disciform area of elevated atrophic retina. (b) Venous phase: fluorescence in neovascular tuft from choroid into subretinal pigment epithelial space. Early fluorescence of neovascular tuft at temporal end of myopic peripapillary crescent. (c) Recirculation phase: further prominence of both neovascular areas.

scopic range in the pigmented maculopathy associated with high myopia, the authors believe that the diagnosis of "Fuchs' spot" incompletely describes the functional anatomic variations which may be present. Therefore, it is the current practice at this facility to classify pigmented maculopathies both by ophthalmoscopic appearance and fluorescein angiographic abnormalities.

The presence of subretinal neovascularization in the macular area of the myopic eye demonstrated in this study serves to alert physicians to the impor-

tance of complaints of visual blurring or distortion of such a patient. Such an eventuality should not be regarded as an initial stage in the inevitable loss of central vision. Paracentral progressive lesions may, as in the nonmyopic eye, be treated with laser photocoagulation. Such a study is now in progress.

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Rudolph Ellender Medical Foundation Course

The Rudolph Ellender Medical Foundation (an AMA-approved Course in Continuing Medical Education) will present its Eighteenth Annual Instruction Course in Contact Lens Fitting by the Ophthalmologist in New Orleans March 9-11, 1978. This course will be immediately followed by the Second Annual OphthalmologyCryosurgical Seminar to run concurrently with the Fourth Annual DermatoCryosurgical Seminar, March 11 and 12, 1978.

Intraocular Microsurgery Workshop Including the OCUTOME and FRAGMATOME TECHNIQUE

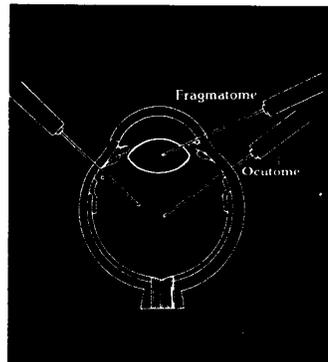
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Predicting of Myopia Progression in School Children

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ABSTRACT

Myopia in 214 school children has been followed from one to nine years. The children have been divided in groups according to the age of onset of myopia and the amount of final myopia at the age of 15 or 16 has been recorded. If myopia started before puberty (at the age of 10 or younger) 70% of the children ended up with myopia of -3.0 to -5.75 D, only 12.5% remained under -3.0 D, and 17.5% had myopia -6.0 D or more. If myopia began at the ages of 11-15, 66.7% remained under -3.0 D, 32.2% reached -3.0 to -5.75 D, and only 1.1% of the children had myopia of -6.0 D or more. Of all the 214 children, 95.8% had myopia less than -6.0 D at the age of 15-16 years.

However, the individual variation is very wide, and it is difficult to predict the final amount of myopia in school years in an individual case.

In the course of school years over 20% of children can become myopic.^{1,2} The incidence of new cases of myopia depends on age; it is highest (about four cases per 100 per year) between 11 to 13 years of age.² In following years myopia usually progresses until it reaches a stable level.

Although myopia has been widely studied for over 100 years, there is still no agreement of the relative effect of genetic or environmental factors on its etiology.^{3,4} Various

treatments to prevent the progression of myopia have not been adequately proven effective.⁵ Therefore, worried parents of myopic children would like to know how long and how far myopia will progress.

The purpose of this study of myopic school children was to find out whether it is possible to predict how many diopters myopia will reach, on the average, by the age of 15 or 16 years when the progression of myopia usually ends.⁶

Subjects and Methods

The refraction of 214 myopic school children aged seven to 15 years was followed from one to nine years. There were 136 girls and 78 boys in the study group. The children were divided into groups according to the age of onset of myopia as is seen in Table 1. The refraction of the children was followed up to the age of 15-16 years, in most cases by examinations annually or once in two years.

The ophthalmological examination consisted of testing the vision and phorias as well as biomicroscopy, ophthalmoscopy, and retinoscopy with cyclopentolate HCl, 1%.

The refraction of the right eye was used in the calculations. The astigmatic refractions were recorded as their spherical equivalents.

Results

The distribution of the final refractions of all the 214 children is shown in Figure 1. Of all the refractions 95.8% remained less myopic than -6.0 D.

The mean of the final recordings of myopia according to the age of onset of myopia is shown in Table 1.

It has been suggested that myopia has a different progression depending upon whether it begins before or after puberty.^{7,8} Therefore, the final refraction of the children

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TABLE 1
THE MEAN AMOUNT OF MYOPIA AT THE AGE OF 15-16 YEARS ACCORDING TO THE AGE OF THE ONSET OF MYOPIA

Age of the onset of myopia, yrs.	Final refraction		No of cases	
	Mean	SD		
7-8	Girls	-6.17	1.20	3
	Boys	-4.42	2.04	6
	Total	-5.00	1.94	9
9	Girls	-4.91	2.52	8
	Boys	-4.06	0.95	9
	Total	-4.43	1.87	17
10	Girls	-4.00	1.14	8
	Boys	-4.33	0.88	6
	Total	-4.16	1.04	14
11	Girls	-3.27	1.26	32
	Boys	-3.00	1.40	15
	Total	-3.16	1.30	47
12	Girls	-2.82	1.06	34
	Boys	-2.63	1.14	15
	Total	-2.75	1.08	49
13	Girls	-2.59	0.95	20
	Boys	-2.42	0.77	6
	Total	-2.54	0.90	26
14	Girls	-2.09	1.18	16
	Boys	-2.13	0.94	12
	Total	-2.11	1.07	28
15	Girls	-1.23	0.67	15
	Boys	-1.00	0.52	9
	Total	-1.15	0.62	24

who became myopic before or after the age of 11 years are shown separately in Tables 2 and 3.

Of the children whose myopia started before puberty (at the age of 10 years or younger) 70% reached a myopia of -3.0 to -5.75 D. In only 12.5%, myopia remained under -3.0 D and 17.5% reached myopia of -6.0 or more.

Of the children whose myopia began at puberty or later, 66.7% had myopia less than -3.0 D, 32.2% had myopia from -3.0 to -5.75 D, and only 1.1% had -6.0 D or more of myopia.

Figure 2 shows the great amount of individual variation in the progression of myopia among some children whose myopia had begun at the same age.

Table 4 shows the prediction of final refraction at the age of 15-16 years in children whose myopia had begun at a given age. Calculated from the present material, the range of final myopia in 68% of cases (Mean ± one SD) is from -2.83 to -6.09 D if the onset of myopia is 7-10 years, from -1.72 to -4.02 D if the onset is at 11-13 years, and from -0.66 to -2.66 D if the onset is at 14-15 years of age.

Discussion

Duke-Elder⁹ states that the simple myopia appearing in the school years usually does not exceed 5-6 D. This study agrees with that statement; 95.8% of the refractions of the children in this study remained less myopic than -6.0 D (Figure 1).

However, if we focus on those children whose myopia began before puberty, we notice that almost one fifth of them had become myopic -6.0 D or more, and over two thirds of them had reached myopia of -3.0 to -5.75 D. Those children whose myopia started at the age of 11-15 years usually progressed to a lower degree of myopia (under -3.0 D), and only 1/100 of them ended up with myopia over -6.0 D. This finding confirms the observation of Rosenberg and Goldschmidt⁷ that myopia starting before puberty has a tendency to exhibit stronger progression than myopia beginning in the later school years.

In the study of Lecaillon-Thibon,⁸ most cases of myopia starting before the age of seven were between -3 and -7 D

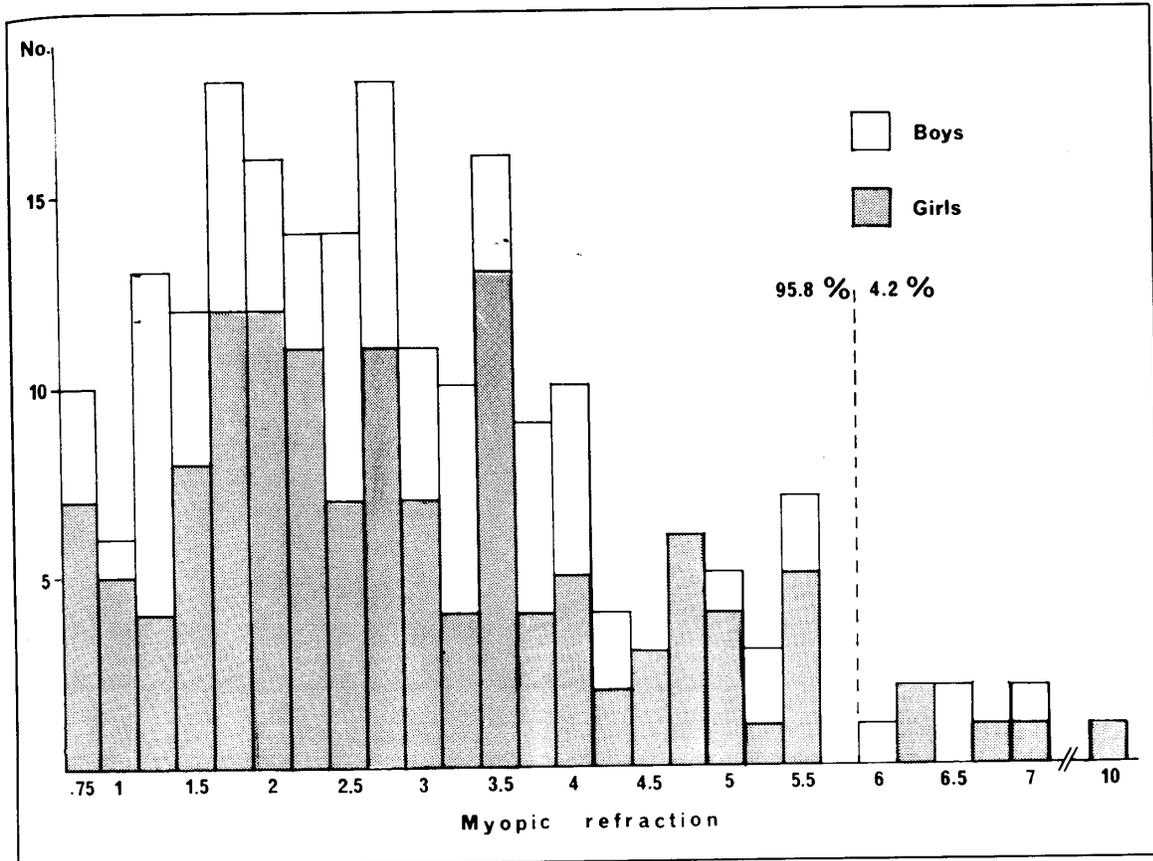


FIGURE 1: Distribution of the amount of myopia at the age of 15-16 years in 214 myopic school children.

Myopia at the age of 15-16 years	Girls	Boys	Total	%
-2.0 to -2.75	3	2	5	12.5
-3.0 to -5.75	13	15	28	70.0
-6.0 to -10.0	4	3	7	17.5
	20	20	40	

Myopia at the age of 15-16 years	Girls	Boys	Total	%
-0.75 to -2.75	74	42	116	66.7
-3.0 to -5.75	41	15	56	32.2
-6.0 to -7.0	1	1	2	1.1
	116	58	174	

at the age of 15. Children whose myopia began in the ages of nine and 12 reached 2-5 D of myopia, and a myopia starting after age 14 reached 1-3 D. The present study confirms these results (Table 4).

Goldschmidt¹⁰ found that of school children aged 13-14, only 3-4% had myopia more than -6.0 D. The prevalence of

4.2% found in the present study agrees well.

Figure 2 shows the progression of myopia in some children whose myopia began at the same age. The graphs illustrate how strong the individual variation can be. The development of refraction is due to the changes in different parts of the eye: the axial length, the lens, and the cornea.

PREDICTING MYOPIA

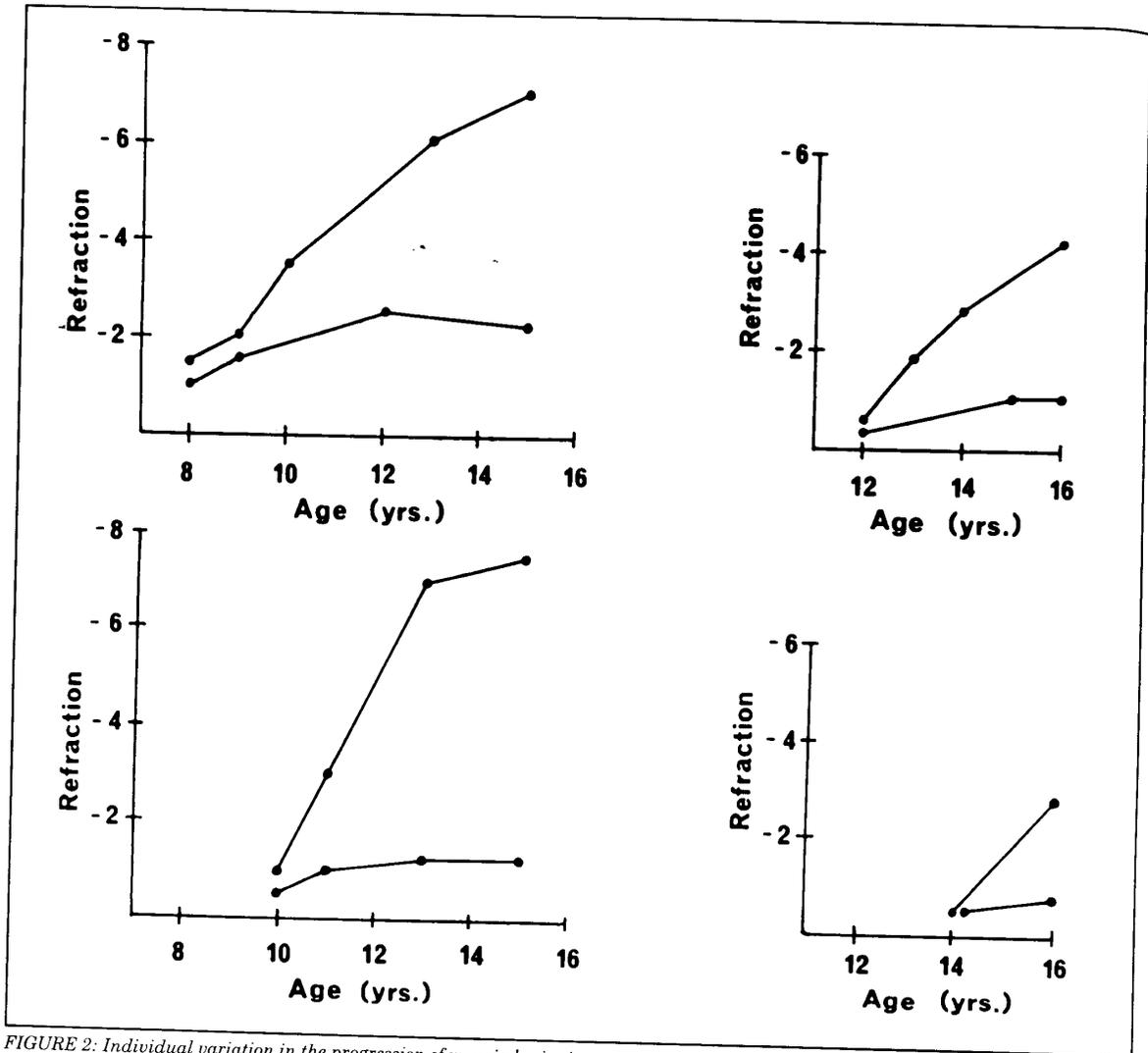


FIGURE 2: Individual variation in the progression of myopia beginning at the same age.

TABLE 4
PREDICTION OF THE FINAL MYOPIA ACCORDING TO THE AGE OF ONSET OF MYOPIA

Age of onset of myopia, yrs	No. of cases	Final refraction		Predicted range of myopia at the age of 15-16 years*
		Mean	SD	
7-10	40	-4.46	1.63	-2.83 to -6.09
11-13	122	-2.87	1.15	-1.72 to -4.02
14-15	52	-1.66	1.00	-0.66 to -2.66

* Mean final refraction plus or minus one SD corresponding to a probability of 68%.

Each of these components can change differently, and the final outcome of the refraction after the period of growth, ie, after puberty, can be very different, even if the starting point in the refraction before puberty had been the same.¹¹ Table 4 shows how wide the range of the final refraction can be.

It is very difficult to predict the progression of myopia in the school years. We can only say that the changes in the development of the eye are completed, for the most part, by the age of 14,^{12,13} but small changes could occur until the age of 20. The age of cessation of myopia has been calculated from 15¼ years (girls) to 16¾ years (boys) but a deviation of up to two to three years in either direction from those ages is not unusual.⁶ As for the final amount of myopia, we can calculate the mean values according to the age of onset of myopia (Table 1); however, a more practical presentation may be the one in Tables 2 and 3: if myopia begins before puberty it will likely end up between -3.0 and -5.75 D, but if it starts at or after puberty, the myopia often remains under -3.0 D.

The considerable individual variation in the progression of myopia in school children living in the same environment, having about the same amount of schoolwork, and sharing at least one meal every school day (at school), strongly suggests that hereditary factors must primarily be involved in the development of myopia in the school years.

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The Relationship between Glaucoma and Myopia

The Blue Mountains Eye Study

Paul Mitchell, MD, FRCOphth, Fleur Hourihan, BSc, MPH, Jen Sandbach, MB, FRACO, Jie Jin Wang, MB, MMed (ClinEpi)

Objective: To quantify the relationship between myopia and open-angle glaucoma, ocular hypertension (OH), and intraocular pressure (IOP) in a representative older population.

Design: Cross-sectional population-based study of 3654 Australians 49 to 97 years of age.

Methods: Subjects with any myopia (≥ -1.0 diopter [D]) were identified by a standardized subjective refraction and categorized into low myopia (≥ -1.0 D to < -3.0 D) or moderate-to-high myopia (≥ -3.0 D). Glaucoma was diagnosed from characteristic visual field loss, combined with optic disc cupping and rim thinning, without reference to IOP. Ocular hypertension was diagnosed when applanation IOP was greater than 21 mmHg in either eye in the absence of glaucomatous visual field and optic disc changes.

Main Outcome Measure: General estimating equation models were used to assess associations between eyes with myopia and either glaucoma or OH.

Results: Glaucoma was present in 4.2% of eyes with low myopia and 4.4% of eyes with moderate-to-high myopia compared to 1.5% of eyes without myopia. The relationship between glaucoma and myopia was maintained after adjusting for known glaucoma risk factors, odds ratio (OR) of 2.3, and 95% confidence intervals (CI) of 1.3 to 4.1 for low myopia. It was stronger for eyes with moderate-to-high myopia (OR, 3.3; CI, 1.7–6.4). Only a borderline relationship was found with OH, OR of 1.8 (CI, 1.2–2.9) for low myopia, and OR of 0.9 (CI, 0.4–2.0) for moderate-to-high myopia. Mean IOP was approximately 0.5 mmHg higher in myopic eyes compared to nonmyopic eyes.

Conclusions: This study has confirmed a strong relationship between myopia and glaucoma. Myopic subjects had a twofold to threefold increased risk of glaucoma compared with that of nonmyopic subjects. The risk was independent of other glaucoma risk factors and IOP. *Ophthalmology* 1999;106:2010–2015

An association between myopia and primary open-angle glaucoma has been recognized for decades^{1–3} and documented in numerous case series^{4–9} and in most,^{10,11} but not all,¹² case-control studies. Other reports have highlighted the high frequency of myopia in young adults presenting with open-angle glaucoma.¹³ Some studies have found the relationship only in patients with high myopia.⁹

Myopia has also been found to have an influence on intraocular pressure (IOP).^{14–20} In a large case-control study, myopic refractive error was found to be strongly associated with ocular hypertension (OH).¹⁶ An Israeli study of 2403 subjects documented a significant relationship between myopia and increasing IOP, particularly in persons

of North African or Asian origin.¹⁷ Other studies have reported higher applanation pressures in myopic subjects,¹⁵ including children,¹⁹ or in subjects with increased axial length.¹⁴ However, no relationship with IOP was found in a United Kingdom study¹⁰ or in myopic anisometropia,²¹ whereas one study reported an association between myopia and low-tension glaucoma.²²

Selection bias could account for some of the reported association between glaucoma and myopia in case series and case-control studies, as myopic subjects are likely to seek ophthalmic care more frequently and glaucoma is a relatively underdiagnosed condition in the community.^{23,24} This bias may be lessened in population studies, in which the diagnosis of disease is based on a masked assessment of diagnostic characteristics.

To date, however, no large population-based studies have examined the role and relative strength of myopia as a risk factor for glaucoma. The "use of eyeglasses for reading" was assessed in the Barbados Eye Study, but the relationship between open-angle glaucoma and myopia was not assessed.²⁵ We therefore aimed to investigate associations between myopia and open-angle glaucoma, OH, and IOP in a well-defined older population, in which both re-

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fractive error²⁶ and glaucoma prevalence²⁴ were assessed and other glaucoma risk factor data were collected.

Methods

The Blue Mountains Eye Study is a population-based survey of age-related eye diseases in residents of an urban population in the Blue Mountains region, west of Sydney, Australia. Survey methods were described previously.^{24,26,27} All permanent noninstitutionalized residents 49 years of age or older were identified in a door-to-door census. Of 4433 eligible residents, 3654 (82.4%) were examined from 1992 to 1994. After excluding persons who died or left the area during the survey and could not be examined, the response rate was 87.9%. The study was approved by the Western Sydney Area Human Ethics Committee, and written, informed consent was obtained from all participants.

An interviewer-administered questionnaire included demographic characteristics, medication use, visual function, and medical history including diabetes, hypertension, and migraine. Subjects underwent a detailed eye examination, which included applanation tonometry, Humphrey automated perimetry, stereoscopic optic disc photography, slit-lamp examination, and subjective refraction.^{24,26} The Humphrey 76-point suprathreshold visual field test (Allergan Humphrey, San Leandro, CA) was performed in 3241 (89%) participants, of whom 352 persons (9.6%) were classified as glaucoma suspects, either from defects on the 76-point test or because optic disc signs suggested glaucoma. All were asked to return for Humphrey full-threshold 30-2 visual fields, of whom 336 (9.2% of the population) completed the test. Stereo optic disc photographs of both eyes (30°) were performed in 98% of subjects.

Open-angle glaucoma (here termed *glaucoma*) was diagnosed by the presence of matching optic disc cupping with rim thinning (cup-disc ratio ≥ 0.7 or cup-disc asymmetry ≥ 0.3) and characteristic visual field loss on automated perimetry, after excluding rubeotic, secondary, or angle-closure glaucoma with gonioscopy. The diagnosis of glaucoma was made without reference to IOP.²⁴ Characteristic glaucomatous field loss was defined as an abnormal Humphrey 30-2 Glaucoma Hemifield Test with one or more of the following defects not explained by ocular or neurologic causes: (1) arcuate or paracentral scotoma, at least four contiguous points on the pattern deviation plot depressed at $P < 0.5\%$ level; (2) nasal step at least two horizontal points in width (10°) on the pattern deviation plot depressed at $P < 0.5\%$ level; or (3) advanced glaucomatous field loss. The OH was defined as an IOP greater than 21 mmHg in either eye, but without diagnostic visual field and optic disc signs, after excluding persons with open-angle or other forms of glaucoma.

A Humphrey autorefractor (Model 530) was used to obtain an objective refraction. Subjective refraction was then performed using the Beaver Dam Eye Study modification of the Early Treatment Diabetic Retinopathy Study protocol with a logarithm of the minimum angle of resolution (LogMAR) chart.²⁶ Spherical equivalent refractive error was calculated as (sphere + cylinder/2) measured in diopters (D). Myopia was defined when myopic spherical equivalent of the eye (SEq) was -1.0 D or greater, hyperopia if SEq was greater than $+1.0$ D, and emmetropia when SEq was in the range from -0.99 to $+1.0$ D. Low myopia was defined in eyes with a myopic SEq of -1.0 D or greater to less than -3.0 D. Moderate-to-high myopia was defined in eyes with a myopic SEq of -3.00 D or greater. For analyses involving persons, SEq was calculated as the mean value of the two eyes.

Diabetes was diagnosed from history or an elevated fasting blood glucose of 7.8 mmol/l or greater (140 mg %).²⁷ Hyperten-

sion was defined as a history of hypertension with current use of antihypertensive medication or elevated blood pressure (systolic ≥ 160 mmHg or diastolic ≥ 95 mmHg). The questionnaire assessed family history of glaucoma, history of typical migraine,²⁸ and history of inhaled or systemic steroid use.²⁹ Pseudoexfoliation was assessed from the slit-lamp examination.

Statistical Analysis System (SAS; SAS Institute, Cary, NC) was used for statistical analyses, including Mantel-Haenszel chi-square test for trend and generalized linear models. Associations between glaucoma and myopia were assessed for individual eyes, because of the asymmetry of refractive error, glaucomatous damage, or IOP in some subjects. The Liang and Zeger general estimating equation method,³⁰ which takes into account the correlation between eyes, was used to assess relationships between these variables. Analyses by subject were also performed using logistic regression. Age and IOP were used as continuous variables. Odds ratios (OR) and 95% confidence intervals (CI) are presented.

Results

Definite or probable glaucoma was diagnosed in 108 persons (3%); the prevalence increased exponentially with age.²⁴ Among persons diagnosed with glaucoma, 72 (66.7%) had typical glaucomatous field loss in the right eye and 88 (81.5%) had field loss in the left eye (total, 160 eyes). After nonphakic eyes were excluded, a total of 126 eyes had diagnostic glaucomatous field loss and could be used for analysis. The OH was found in 135 participants, a prevalence of 3.7% (CI, 3.1-4.3) but with no significant age-related increase in prevalence.²⁴ Among persons with OH, 124 (91.9%) had elevated IOP in the right eye and 109 (80.7%) had elevated IOP in the left eye (total, 233 eyes). After excluding nonphakic eyes, a total of 211 eyes had OH and were available for analysis.

After nonphakic eyes were excluded, 866 eyes (12.5%) with any myopia (SEq ≥ -1.0 D) were available for analysis (Table 1). Low myopia (≥ -1.0 D to < -3.0 D) was present in 524 eyes (7.6%), and moderate-to-high myopia (SEq ≥ -3.00 D) was found in 342 eyes (4.9%). A higher age-adjusted prevalence of myopia was found in women than in men (OR, 1.4; CI, 1.0-2.0), and the prevalence decreased significantly with increasing age ($\chi^2_{trend} = 10.73$, 1 degree of freedom, $P < 0.001$).

A strong association was found between low myopia and glaucoma, as shown in Table 2. Glaucomatous damage to the optic disc and visual field was more than twice as frequent in eyes with low myopia (4.2%) than in eyes without myopia (1.5%) (OR, 2.1; CI, 1.2-3.8) after adjusting for age and gender. This relationship remained after simultaneously adjusting for other known glaucoma risk factors as well (e.g., glaucoma family history, diabetes, hypertension, history of typical migraine, steroid use, and presence of pseudoexfoliation) (OR, 2.3; CI, 1.3-4.1). It was also consistently present across the age groups examined, apart from the youngest age group, which had inadequate statistical power because of small numbers.

A stronger association was found between moderate-to-high myopia and glaucoma, also shown in Table 2. Glaucoma was almost threefold as frequent in eyes with moderate-to-high myopia (4.4%) than in eyes without myopia (1.5%) (OR, 3.3; CI, 1.7-6.4) after adjusting for other known glaucoma risk factors. Again, it was consistently present across the age groups.

A weaker association was found between low myopia and OH, as shown in Table 3. The OH was more frequent in eyes with low myopia (4.8%) than in eyes without myopia (2.9%) (OR, 1.7; CI, 1.1-2.7) after adjusting for age and gender. This relationship remained after simultaneously adjusting for other known glaucoma risk factors as well (OR, 1.8; CI, 1.2-2.9). The magnitude of this

Table 1. Prevalence of Low and Moderate to Severe Myopia in Participant Eyes by Age Group and Sex, after Excluding Nonphakic Eyes

Age Group (yrs)	Women (3927 eyes) Myopic Eyes (%)	Men (2986 eyes) Myopic Eyes (%)	Either Sex (6913 eyes) Myopic Eyes (%)
Low Myopia (≥ -1.0 to < -3.0 D)			
<60	110 (10.4)	94 (11.4)	205 (10.9)
60-69	71 (5.4)	75 (6.8)	146 (6.0)
70-79	58 (5.8)	60 (8.6)	118 (7.0)
80+	33 (10.1)	22 (10.1)	55 (10.0)
All ages	272 (6.9)	252 (8.4)	524 (7.6)
P for trend	0.04	0.21	0.02
Moderate to High Myopia (≥ -3.0 D)			
<60	81 (7.1)	47 (5.3)	128 (5.9)
60-69	75 (5.3)	31 (2.7)	106 (4.2)
70-79	39 (3.8)	38 (5.2)	77 (4.4)
80+	19 (5.4)	12 (3.6)	31 (5.4)
All ages	214 (5.4)	128 (4.3)	342 (4.9)
P for trend	0.006	0.87	0.12

relationship, however, varied across the age groups examined, ranging from OR 0.5 to 3.9. No association was found between moderate-to-high myopia and OH. Similar prevalence rates for OH were found in eyes with moderate-to-high myopia (3.5%) to eyes without myopia (2.9%) (OR, 0.9; CI, 0.4-2.0) after adjusting for other known glaucoma risk factors.

Associations between myopia and glaucoma or OH were also assessed in subjects in the multivariate model using mean refractive error of the two eyes and the presence of glaucomatous damage or elevated IOP in either eye. For glaucoma, a similar magnitude of association was found for subjects with any myopia (SEq ≥ -1.0 D) (OR, 2.4; CI, 1.5-4.0). Age-specific prevalence rates for glaucoma in subjects with and without myopia are compared with overall glaucoma prevalence rates, as shown in Figure 1. Myopia was associated with a substantially increased risk of glaucoma at all except the youngest age group.

Table 4 shows that the mean IOPs of both right (16.51 mmHg) and left (16.40 mmHg) eyes with myopia were approximately a half-millimeter higher than emmetropic eyes (16.01 and 16.00 mmHg, respectively), a small difference that was statistically significant by Student's *t* test. The mean IOP for myopic eyes was 16.45 mmHg. Hyperopic eyes had a similar mean IOP (16.03 mmHg for the two eyes) as emmetropic eyes (16.00 mmHg). Eyes with moderate-to-high myopia (≥ -3.00 D) also had a similar mean IOP of 16.47 mmHg to eyes with low myopia (≥ -1.00 D to < -3.0 D), which had a mean IOP of 16.44 mmHg.

The role of IOP in the association between glaucoma and myopia was also assessed by adjusting for IOP (continuously) in the multivariate model. The associations found with glaucoma were similar with OR of 2.1 (CI, 1.2-4.4) for low myopia and OR of 2.6 (CI, 1.3-5.2) for moderate-to-high myopia. This suggests that the relationship between glaucoma and myopia is independent of IOP.

Table 2. Associations between Glaucoma and Low Myopia (spherical equivalent ≥ -1.0 to < -3.0 diopters) or Moderate to High Myopia (spherical equivalent ≥ -3.00 diopters), Stratified by Age and Adjusted for Confounders

Age Group (yrs)	Glaucoma in Eyes with Low Myopia [No. (%)]	Glaucoma in Eyes without Myopia [No. (%)]	Sex-adjusted OR (95% CI)	Multivariate-adjusted OR (95% CI)*
<60	1 (0.3)	4 (0.2)	1.7 (0.2-13.9)	Insufficient data
60-69	5 (4.0)	16 (0.7)	2.5 (0.8-7.5)	2.6 (0.9-7.7)
70-79	7 (5.9)	41 (2.6)	2.1 (0.8-5.9)	2.1 (0.8-5.7)
80+	9 (16.7)	28 (5.7)	2.4 (1.0-5.4)	2.6 (1.1-6.2)
All ages	22 (4.2)	89 (1.5)	2.1 (1.2-3.8)†	2.3 (1.3-4.1)†
	Glaucoma in Eyes with Moderate to High Myopia [No. (%)]	Glaucoma in Eyes without Myopia [No. (%)]	Sex-adjusted OR (95% CI)	Multivariate-adjusted OR (95% CI)*
<60	0 (0.0)	4 (0.2)	Insufficient data	Insufficient data
60-69	5 (4.7)	16 (0.7)	7.0 (2.0-24.8)	4.7 (1.0-22.6)
70-79	4 (5.3)	41 (2.6)	2.7 (1.0-7.4)	2.4 (0.9-6.8)
80+	6 (19.4)	28 (5.7)	4.1 (1.4-12.1)	5.2 (1.7-15.8)
All ages	15 (4.4)	89 (1.5)	3.7 (2.0-6.9)†	3.3 (1.7-6.4)†

OR = odds ratio; CI = confidence interval.

* Adjusted for sex, family history of glaucoma, diabetes, hypertension, typical migraine history, steroid use, and presence of pseudoexfoliation.

† Adjusted also for age.

Table 3. Associations between Ocular Hypertension and Low Myopia (spherical equivalent ≥ -1.0 to < -3.0 diopters) or Moderate to High Myopia (spherical equivalent ≥ -3.00 diopters), Stratified by Age and Adjusted for Confounders

Age Group (yrs)	Ocular Hypertension in Eyes with Low Myopia [No. (%)]	Ocular Hypertension in Eyes without Myopia [No. (%)]	Sex-adjusted OR (95% CI)	Multivariate-adjusted OR (95% CI)
<60	10 (4.9)	34 (2.0)	2.0 (0.7-4.2)	2.2 (1.0-4.5)
60-69	2 (1.4)	74 (3.2)	0.5 (0.1-2.1)	0.5 (0.2-1.2)
70-79	8 (6.8)	45 (2.9)	2.7 (1.2-6.4)	2.8 (1.2-6.4)
80+	5 (9.3)	21 (4.2)	2.0 (0.6-6.9)	3.9 (1.1-14.4)
All ages	25 (4.8)	174 (2.9)	1.7 (1.1-2.7)†	1.8 (1.2-2.9)†

Age Group (yrs)	Ocular Hypertension in Eyes with Moderate to High Myopia [No. (%)]	Ocular Hypertension in Eyes without Myopia [No. (%)]	Sex-adjusted OR (95% CI)	Multivariate-adjusted OR (95% CI)*
<60	6 (4.7)	34 (2.0)	1.9 (1.3-2.7)	1.8 (0.5-6.3)
60-69	5 (4.8)	74 (3.2)	1.4 (0.5-3.9)	0.9 (0.3-2.7)
70-79	4 (5.3)	45 (2.9)	Insufficient data	Insufficient data
80+	1 (1.3)	21 (4.2)	Insufficient data	Insufficient data
All ages	12 (3.5)	174 (2.9)	1.1 (0.5-2.2)†	0.9 (0.4-2.0)†

* Adjusted for sex, family history of glaucoma, diabetes, hypertension, typical migraine history, steroid use, and presence of pseudoexfoliation.

† Adjusted also for age.

Discussion

This population-based study of an Australian white community has found a strong relationship between open-angle glaucoma and myopia, after taking into account the effects of other known glaucoma risk factors. This association was present for eyes with low myopia (OR, 2.3) and was stronger (OR, 3.3) for eyes with moderate-to-high myopia, suggesting a dose response. The consistency of these findings provides support for the hypothesis of a true relationship between the two conditions.

It may be deceptive to describe people with normal discs and fields but elevated IOP by a different term (OH), as IOP elevation may have been present for too short a period and the visual field test may be too insensitive to detect early

damage.³² The likelihood that some people with OH have an early stage of glaucoma is consistent with our finding of a relatively weak association between OH and myopia, which was only found with low myopia. This weak association probably is reflected by the slightly higher (half millimeter) IOPs of myopes.

Although many clinic-based and case-control studies have suggested a relationship between glaucoma and myopia, no previous population-based studies have examined the association in detail while taking into account the effects of other known glaucoma risk factors. Our findings are relevant, as the population-based design is likely to have minimized the possibility of selection bias affecting the results. Confirmation that myopia is a frequent risk factor for glaucoma (one in four glaucoma cases in this age group) should help to identify this group, whose participants need earlier and regular ophthalmic screening and closer follow-up.

Could our findings of a strong association between glaucoma and myopia be confounded by measurement error or misclassification of either the glaucoma or myopia status of persons in this older population? Such misclassification could bias the findings and lead to an overestimation of any relationship between the two conditions.

The overall glaucoma prevalence reported from our study (3.0%)²⁴ is higher than in some other recent population-based prevalence studies, including Beaver Dam³² and Rotterdam.³³ However, these two studies examined either a younger age range³³ or had a lower proportion of subjects in the oldest age group.³³ Given the exponential increase in glaucoma prevalence with age found in our study, such age differences could have a marked effect on the overall prevalence.

More likely sources of misclassification are the documented changes in the appearance of the optic disc in myopia.³⁴ These could either result in the overclassification

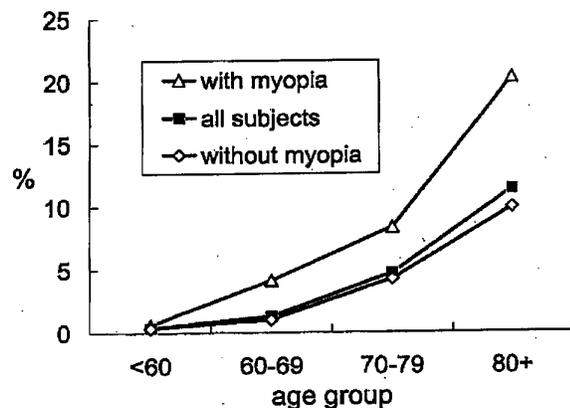


Figure 1. Prevalence of glaucoma by age group in myopic and nonmyopic subjects compared to prevalence in the overall Blue Mountains Eye Study population.

Table 4. Mean Intraocular Pressure of Right and Left Eyes by Refractive Error Status, Using Spherical Equivalent Refraction (SEq) Measured in Diopters (D)*

Mean Intraocular Pressure (mmHg \pm SE)	Myopia SEq ≥ -1.00 D	P	Emmetropia SEq -0.99 D to $+1.00$ D	P	Hyperopia SEq $> +1.00$ D
Right eyes (n = 3355)	16.51 (± 0.13)	0	16.01 (± 0.07)	0.22	16.14 (± 0.07)
Left eyes (n = 3374)	16.40 (± 0.13)	0	16.00 (± 0.07)	0.46	15.93 (± 0.07)

* Adjusted for age, sex, diabetes and systolic blood pressure, after excluding nonphakic eyes plus eyes with pseudoexfoliation and secondary or angle-closure glaucoma.

of nonglaucomatous field defects resulting from tilted discs as glaucomatous or underclassification of glaucoma because of the difficulties in grading the cup-disc ratio and neuroretinal rim in some myopic eyes. Tilted discs may cause visual field defects, but these are predominantly temporal and often cross the vertical meridian.³⁵ Patients with myopia may also develop enlarged blind spots, superotemporal defects, and irregular defects from myopic retinopathy.³⁶ Great care was taken in the adjudication of field defects to include only those defects that were typically glaucomatous.²⁴ Patients with myopia also tend to have larger optic discs³⁴ and cups.³⁷ The stereo optic disc photographs from all myopic eyes classified as having glaucomatous field defects were also carefully reviewed. Disc cupping, which matched the field defects, was confirmed in these glaucoma cases, although rim thinning was occasionally more difficult to evaluate, because of the flatter nature of some myopic discs.

Care was taken in the assessment of myopia to include only phakic eyes, as cataract surgery would affect measurement of the underlying refractive state. Although the myopia prevalence rates in this study are slightly lower than in comparable United States studies,^{38,39} these differences may be due in part to small differences in myopia definition.

The 0.45-mmHg IOP difference found in our study between myopic and emmetropic eyes is slightly lower than in some previous reports, which have reported differences ranging from 0.75 to more than 1.0 mmHg.^{5,15,40} We were also unable to confirm a trend with increasing levels of myopia, which has been demonstrated previously.^{17,40} The small difference found between myopic and nonmyopic eyes, although statistically significant, is unlikely to be important clinically.

A number of mechanisms have been postulated to explain the link found between glaucoma and myopia.³ The optic nerve head in myopic eyes may be structurally more susceptible to glaucomatous damage from elevated or normal IOP^{5,7,9,34} than in nonmyopic eyes. Quigley³¹ has proposed that shearing forces exerted by scleral tension across the lamina cribrosa may be important in the pathogenesis of glaucomatous damage. Cahane and Bartov⁴¹ calculated that myopic eyes have higher scleral tension across the lamina than in eyes with shorter axial length, even when IOP is the same, with the difference even more marked in eyes with thinner sclera. Similar connective tissue changes may also occur in glaucoma and myopia.^{3,42}

Both glaucoma and myopia have a strong familial basis and may share a common genetic link. An early report

indicated that people with high myopia are more likely to be steroid responders than those in the general community.⁴ Recently, the gene coding for a trabecular meshwork-induced glucocorticoid response protein in the GLC1A locus on chromosome 1q21-q31 was identified and found in 3.9% of a glaucoma population compared to 0.3% of a general population.⁴³ It is possible that this and other glaucoma genes may be represented more frequently in persons with myopia.

In summary, these data from the Blue Mountains Eye Study have confirmed the strong relationship between glaucoma and myopia in an older white population sample. Subjects with myopia had a twofold to threefold increased risk of glaucoma compared with that of nonmyopic subjects. This risk was independent of other glaucoma risk factors and IOP. Myopic eyes had slightly higher IOPs than emmetropic or hyperopic eyes, and we found only a borderline association between myopia and OH.

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Parental Myopia, Near Work, School Achievement, and Children's Refractive Error

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PURPOSE. To quantify the degree of association between juvenile myopia and parental myopia, near work, and school achievement.

METHODS. Refractive error, parental refractive status, current level of near activities (assumed working distance-weighted hours per week spent studying, reading for pleasure, watching television, playing video games or working on the computer), hours per week spent playing sports, and level of school achievement (scores on the Iowa Tests of Basic Skills [ITBS]) were assessed in 366 eighth grade children who participated in the Orinda Longitudinal Study of Myopia in 1991 to 1996.

RESULTS. Children with myopia were more likely to have parents with myopia; to spend significantly more time studying, more time reading, and less time playing sports; and to score higher on the ITBS Reading and Total Language subtests than emmetropic children (χ^2 and Wilcoxon rank-sum tests; $P < 0.024$). Multivariate logistic regression models showed no substantial confounding effects between parental myopia, near work, sports activity, and school achievement, suggesting that each factor has an independent association with myopia. The multivariate odds ratio (95% confidence interval) for two compared with no parents with myopia was 6.40 (2.17-18.87) and was 1.020 (1.008-1.032) for each diopter-hour per week of near work. Interactions between parental myopia and near work were not significant ($P = 0.67$), indicating no increase in the risk associated with near work with an increasing number of parents with myopia.

CONCLUSIONS. Heredity was the most important factor associated with juvenile myopia, with smaller independent contributions from more near work, higher school achievement, and less time in sports activity. There was no evidence that children inherit a myopigenic environment or a susceptibility to the effects of near work from their parents. (*Invest Ophthalmol Vis Sci.* 2002;43:3633-3640)

Of all the issues surrounding myopia in children, there is probably none so contentious yet crucial as understanding the relative contributions of environment—primarily near

work—and heredity. Several clinical studies have documented an association between myopia and higher levels of children's near work.¹⁻⁴ Level of education is often used as a surrogate measure for near work with more myopia among the more educated.⁵⁻¹⁰ Researchers in Asia point to their rigorous schooling system and the long hours children spend studying as being responsible for the high rates of myopia in Asia, rates that may be on the increase.¹¹⁻¹⁴ Support for an important role for near work also comes from animal studies that have demonstrated the plasticity of refractive error in response to environmental stimuli. Neonatal chicks, tree shrews, or monkeys experience increased ocular growth and become myopic or less hyperopic after wearing minus lenses, presumably to compensate for the hyperopic defocus produced by these lenses.¹⁵⁻¹⁸ Hyperopic defocus from a deficient accommodative response in juvenile myopes is theorized to be the connection between near work in human myopia and the minus lens results from animal studies.¹⁹ The current environmental model derived from these clinical and experimental studies is that exposure to hyperopic defocus from accommodative lag during prolonged near work leads to excessive growth of the eye and a myopic refractive error.

An equally strong case can be made for the view that refractive error is determined genetically. Parents who have myopia tend to have children with myopia. The prevalence of myopia in children with two parents with myopia is 30% to 40%, decreasing to 20% to 25% in children with one parent with myopia and to less than 10% in children with no parents with myopia.²⁰⁻²² An increasing number of parents with myopia significantly elevates the odds of being myopic, with an odds ratio of 5.09 reported for having two versus no parents with myopia.²³ Monozygotic twins tend to resemble each other in refractive error more than do dizygotic twins. Heritabilities for refractive error calculated from twin data are typically very high, on the order of 0.82 or greater.²⁴⁻²⁶ Refractive error and the axial length of children's eyes are more closely related to parental refractive error than to children's near-work habits.⁴ To date, genetic loci have been associated with pathologic myopia^{27,28} but not with juvenile myopia.²⁹

Two hypotheses may reconcile these divergent views. The first is a theory of inherited environment. The tendency for myopia to run in families may be due to a shared intense near-work environment within a family, rather than because of shared genes. Parents with myopia would pass on their own academic standards or love of reading to their children rather than passing on a myopic refractive error itself. The same argument would apply to twin data. Monozygotic twins may share a more similar environment, as well as identical genes, than do dizygotic twins, perhaps falsely inflating estimates of heritability.

Another theory that may reconcile genetic and environmental evidence is that there is a genetic susceptibility to the effects of environment. Both heredity and environment are important, but the trait inherited is sensitivity to the myopigenic effects of near work, rather than myopia itself. A child could perform intense near work but would not have myopia

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without the susceptibility genes. Another susceptible child who performs the same level of near work would have a higher risk of myopia. This theory has been suggested by several investigators^{8,26,30,31} but rarely formally evaluated.³² Modification of the risk of near work by parental history of myopia should be detectable as a statistical interaction, with near work having the strongest association with myopia when there are two parents with myopia and the weakest association when there are no parents with myopia.

Further complicating the task of unraveling the role of near work is the association between myopia and intellectual ability. Children with myopia tend to have higher intelligence test scores^{10,33-38} and higher achievement test scores,³⁹ with better vocabularies and grades in school, than do nonmyopes.⁴⁰ It is conceivable that children with a special aptitude for schoolwork may be inclined to engage in more near work over a longer time. Perhaps a child's cognitive skills are more closely related to refractive error than is near-work behavior. This association also underscores the difficulty in using the highest level of education achieved as a surrogate for near work. Brighter children are more likely to do more near work⁴¹ and to pursue higher education.

Untangling the relative importance of near work, heredity, and intellectual ability is impossible without assessing all three factors in the same subjects. To our knowledge, this analysis has not been performed in a previous study. The purpose of the present study is to evaluate the association between children's myopia and three important factors: parental myopia, children's visual activities, and children's performance on a standardized achievement test. In addition, the hypotheses of inherited environment and inherited susceptibility to the environment will be evaluated. A preliminary analysis of a subset of these data has been reported previously.⁴²

SUBJECTS AND METHODS

Subjects for this study were children in the eighth grade who participated in the Orinda Longitudinal Study of Myopia (OLSM), a community-based cohort study of risk factors for predicting the onset of juvenile myopia. Participants in OLSM included first through eighth graders, but the increase in the prevalence of myopia with age required restricting the age of participants.^{43,44} Only data from eighth graders were used in this analysis to maximize the likelihood that any myopia that would occur had occurred, thereby minimizing participation by premyopes—children without myopia in whom it develops later. Parents gave consent for their child's participation after all study procedures were explained in accordance with the Declaration of Helsinki. Consent was obtained once for participation in OLSM and separately at a later date to obtain achievement test scores. The Orinda Union School District also gave permission to the investigators to obtain the achievement test scores of participating children. There were 394 of 467 eligible OLSM eighth grade participants in 1991 to 1996 whose parents consented to the release of their children's achievement test scores, a participation rate of 84%. Of these, four had incomplete OLSM examination data, and 24 had incomplete achievement test data, leaving 366 children for this analysis. The average age (\pm SD) of the sample was 13.7 ± 0.5 years. The sample was 45.5% female and predominantly white (89.1%), with smaller proportions of Asian-American (8.7%), Hispanic (1.9%), and African-American (0.3%) subjects. There was no difference in refractive error between participants and nonparticipants (*t*-test, $P = 0.0954$). The mean spherical equivalent for participants was -0.17 ± 1.56 D, and the mean for nonparticipants was -0.51 ± 1.85 D. There was, however, a difference between the two groups in the proportion of parents with myopia (χ^2 test, $P = 0.033$). Among the participants, 47% of the children had one parent with myopia, and 25% had two parents with myopia. In the group of

children who did not participate, 38% had one parent with myopia and 20% had two parents with myopia.

Myopia was defined as at least -0.75 D and hyperopia as at least $+1.00$ D in each principal meridian on cycloplegic autorefraction. This definition was chosen to reduce the number of false-positive results for myopia, to exceed the 95% limits of agreement of the autorefractor,⁴⁵ to reach a level of myopia likely to produce clinical symptoms, and to maintain consistency with the definition used in previous reports of this project.⁴⁶ Children in the eighth grade in 1991 to 1996 who participated in this analysis enrolled in OLSM either as sixth graders in 1989 to 1991, as third graders in 1989 to 1991, or as first graders in 1989.

The variables in this analysis were children's refractive status (myopic, emmetropic, or hyperopic), the number of parents with myopia (none, one, or two), time spent in various activities, and standardized achievement test scores. Children's refractive error was measured each fall by autorefraction (R-1; Canon USA., Lake Success, NY, no longer manufactured) under tropicamide 1% cycloplegia. Tropicamide has been found to be an effective cycloplegic for the measurement of refractive error in this protocol.^{47,48} The measurement protocol has been described in detail elsewhere.⁴⁹ Parents' refractive status was determined for each parent by a survey filled out by parents at study entry asking whether glasses were worn, for what purpose, and at what age they were first prescribed. Each parent was classified as myopic if he or she wore glasses only for distance viewing, or if glasses were worn for both distance and near, as long as the glasses were first prescribed before age 16 years. This method has been shown to classify myopia correctly with a sensitivity of 0.76 and a specificity of 0.74.⁵⁰ Children's near work was assessed each spring after OLSM testing by a survey completed by parents asking how many hours per week outside of school the child spent in five activities: (1) reading or studying for school assignments; (2) reading for pleasure; (3) watching television; (4) playing video/computer games or working on the computer at home; and (5) engaging in sports activities. These activities were analyzed separately and as a composite variable for near work weighted by the dioptric equivalent of an assumed working distance for activities 1 to 4. The purpose of this weighting was to quantify exposure to near work not just in terms of time, but also in terms of the accommodative effort required during each activity.⁴ This diopter-hours (Dh) variable was defined as: $Dh = 3 \times (\text{hours spent studying} + \text{hours spent reading for pleasure}) + 2 \times (\text{hours spent playing video games or working on the computer at home}) + 1 \times (\text{hours spent watching television})$.

The survey completed by parents when their children were in the eighth grade was used as the measure of the current level of near work in all analyses. Near-work activity during school was not quantified. Parents are not in a position to report on the details of near work while children are in school. The reliability of children as a source of near-work survey information has not been established, although agreement between parents' and children's near activities survey responses is rated as only fair.⁵¹ We assumed that time spent in near work during school did not add substantially to the variability in near work for children of the same grade within the same school.

Achievement test scores were obtained from Form G of the Iowa Tests of Basic Skills (ITBS; Riverside Publishing Company, Chicago, IL), administered each spring by the Orinda Union School District, independently from the OLSM. The national percentile score from the test administered during each child's eighth grade academic year constituted the primary ITBS data used in this analysis. The local percentile scores, normed using students in the Orinda district alone, were available and also analyzed for a subset of 306 children in 1991 to 1995. The ITBS tests the mastery of skills important for school achievement in three areas: reading, language, and mathematics. Correlations between ITBS scores and those from IQ tests, such as the Wechsler Intelligence Scale for Children, are moderate, ranging from a low of 0.26 in third grade to high of 0.49 in fifth grade.⁵² The three areas of the ITBS are intended to measure distinct skills,⁵³ but the intercorre-

TABLE 1. Hours Spent per Week in Various Activities Outside of School

Activity	All Subjects (<i>n</i> = 366)	Myopes (<i>n</i> = 67)	Emmetropes (<i>n</i> = 271)	Hyperopes (<i>n</i> = 28)
Studying	9.4 ± 5.7	11.2 ± 7.2*	8.9 ± 5.2	9.4 ± 4.9
Reading for pleasure	4.4 ± 4.5	5.8 ± 4.8†	4.1 ± 4.6	3.6 ± 2.9
Watching TV	8.3 ± 5.9	9.2 ± 6.8	8.3 ± 5.7	6.6 ± 4.5
Video games/computer	2.3 ± 3.3	2.7 ± 4.1	2.2 ± 3.2	1.4 ± 1.8
Diopter-hours	53.8 ± 26.8	65.1 ± 34.1†	51.5 ± 24.4	48.2 ± 21.2
Sports	9.3 ± 6.4	7.4 ± 6.7†	9.7 ± 6.2	9.8 ± 7.9

Wilcoxon rank-sum test comparing myopes or hyperopes with emmetropes. Wilcoxon testing was used because of the non-normal distribution of variables. None of the comparisons between emmetropes and hyperopes was significant. Comparisons between myopes and emmetropes were significant as marked. Data are expressed as mean hours ± SD.

* $P < 0.05$.

† $P < 0.005$.

lations between sections are significant.⁵⁴ This may be because each section uses similar sets of cognitive skills or psycholinguistic abilities. Each ITBS section correlates with numerous sections of the Illinois Test of Psycholinguistic abilities, such as auditory vocal association and visual motor association.⁵² Although there are three sections to the ITBS, factor analysis reveals that most of the variance in ITBS scores is accounted for by one variable, termed general scholastic ability,^{53,55} which has been more specifically characterized as general reading ability.⁵⁴ The emphasis of the ITBS on reading ability make it particularly well suited for determining whether cognitive skills important for success in reading confound the relation between near work (primarily reading) and myopia in children.

RESULTS

Of the 366 children in the sample, 67 (18.3%) were myopes, 28 (7.7%) hyperopes, and 271 (74.0%) emmetropes (Table 1). The axial nature of the refractive errors can be seen by the correlation between axial length and spherical equivalent ($r = -0.48$, $P < 0.0001$). Survey results from parental report accounted for an average of 33.7 hours per week outside school (Table 1). On average, children spent nearly as much time studying as they did watching television or engaging in sports activities. Reading for pleasure occupied less than half the number of hours children spent studying. Children spent the least amount of time playing video games or working on a computer at home. The time spent in these visual activities varied as a function of refractive error. Consistent with previ-

ous reports, children with myopia spent more time engaged in near activities (1 to 4) and less time engaged in sports³⁶ ($P = 0.0003$), compared with emmetropes (Wilcoxon rank-sum test comparing myopes and emmetropes; Table 1). In particular, these near activities were studying for school assignments ($P = 0.024$) and reading for pleasure ($P = 0.0019$). As a result, the composite near-work variable of diopter-hours was also significantly greater for myopes than for emmetropes ($P = 0.0015$). Watching television and playing video games or working on the computer at home did not differ between myopes and emmetropes. Myopes also spent more time reading for pleasure ($P = 0.034$) and less time in sports ($P = 0.049$) and had a higher number of diopter-hours per week than hyperopes ($P = 0.032$; Wilcoxon rank-sum test comparing myopes and hyperopes). Emmetropes and hyperopes spent comparable amounts of time in all the various activities.

Study participants scored approximately 30 percentile points higher on average than the national norm and approximately 5 percentile points higher than the local norm in the three main areas tested by the ITBS (Table 2). Despite this good performance, variability was not severely compressed: One standard deviation in scores was roughly one-fifth to one-third of the entire possible range of scores. Again, consistent with previous reports,^{10,33-35,37-40} myopes scored higher than emmetropes in both national and local percentile scores in the areas of Reading ($P < 0.013$) and Total Language ($P < 0.0069$; Wilcoxon rank-sum test comparing myopes and emmetropes; Table 2). Myopes also scored higher than hyperopes in national

TABLE 2. ITBS National and Local Percentile Scores

ITBS Subtest	All Subjects (<i>n</i> = 366)	Myopes (<i>n</i> = 67)	Emmetropes (<i>n</i> = 271)	Hyperopes (<i>n</i> = 28)
National				
Reading	79.6 ± 23.2	82.9 ± 23.7*	79.2 ± 23.1	75.3 ± 22.9
Total Language	82.8 ± 19.0	86.6 ± 17.7†	82.2 ± 19.2	79.0 ± 20.2
Mathematics	83.8 ± 19.8	84.1 ± 21.4	83.5 ± 20.0	86.3 ± 13.6
Local				
Number of test scores	306	58	229	19
Reading	53.7 ± 29.6	62.5 ± 31.0*	52.6 ± 28.9	41.5 ± 26.6
Total Language	55.1 ± 28.8	64.2 ± 29.7†	53.2 ± 28.1	52.2 ± 29.2
Mathematics	54.5 ± 28.5	57.4 ± 29.6	53.6 ± 28.4	59.7 ± 26.7

Wilcoxon rank-sum test comparing myopes or hyperopes with emmetropes. Wilcoxon testing was used because of the non-normal distribution of variables. None of the comparisons between emmetropes and hyperopes was significant. Comparisons between myopes and emmetropes were significant as marked. Data are expressed as the mean score ± SD.

* $P < 0.05$.

† $P < 0.01$.

TABLE 3. Proportion of Children with and Children without Myopia as a Function of Number of Parents with Myopia

Parental Myopia	Child with Myopia (n = 63)	Child without Myopia (n = 276)
None (n = 95)	6.3 (6)	93.7 (89)
One parent (n = 159)	18.2 (29)	81.8 (130)
Two parents (n = 85)	32.9 (28)	67.1 (57)

$\chi^2_2 = 21.0$; $P = 0.001$; $n = 339$. Data are percentage of each parental myopia group, with the number of children in parentheses.

Reading ($P = 0.011$) and local Reading ($P = 0.0095$), in national Total Language ($P = 0.018$), but not local Total Language ($P = 0.099$); Wilcoxon rank-sum test comparing myopes and hyperopes). Hyperopes have been reported to score lower in reading achievement and IQ tests.^{38,56,57} The lower scores for hyperopes compared with those of emmetropes in this study did not achieve statistical significance, perhaps because the number of hyperopes was small at this age, limiting statistical power. Mathematics achievement test scores were not different between any of the refractive groups. The higher scores for myopes in Reading and Total Language seem unlikely to be the result of greater visual comfort during testing. The similar scores in Mathematics suggest that each refractive group could see the test equally well, but that the groups may differ in skills specific for language.

Consistent with previous reports of associations between refractive errors in parents and children,²⁰⁻²² parents with myopia tended to have children with myopia ($\chi^2_2 = 21.0$; $P = 0.001$; Table 3). This tended to follow a dose-dependent pattern. Of the children in families with two parents with myopia, 32.9% had myopia compared with 18.2% of the children in families in which only one parent was myopic and 6.3% of the children in families with no parents with myopia.

Table 4 shows the univariate odds ratios calculated to quantify the association between children's myopia and the factors identified as significant in Tables 1 through 3. Having either one (OR = 3.31; 95% confidence interval [CI] = 1.32-8.30) or two parents with myopia (OR = 7.29; 95% CI = 2.84-18.7) significantly increased the odds of being a myope, in a dose-response fashion. As suggested by the numeric values in Table 1, myopes tended to engage in more near work (OR = 1.018; 95% CI = 1.008-1.027) and to spend less time engaged in sports activities (OR = 0.936; 95% CI = 0.892-0.983). Myopia was significantly associated with local ITBS Reading (OR = 1.013; 95% CI = 1.003-1.024) and Total Language scores (OR = 1.014; 95% CI = 1.004-1.025), but not with national

scores. This inconsistency, depending on the source of the score, suggests that the association between myopia and reading achievement as measured by the ITBS may be weak.

One of the difficulties in assessing these risk factors is their interconnection, and therefore their potential, for confounding the association with myopia. Perhaps myopes read more because they have better cognitive skills and therefore greater potential for achievement. Perhaps myopes score higher on school achievement tests because they study more. The most important potentially confounding association is between near work and parental refractive error. Perhaps parents with myopia have children with myopia only because they pass along a myopigenic environment with intense near-work demands. There were significant Spearman correlations between diopter-hours and all ITBS scores and between diopter-hours and hours of sports per week, indicating their potential for confounding the association between each of these factors and refractive error (Table 5). The number of diopter-hours did not differ significantly as a function of the number of parents with myopia ($P = 0.31$), indicating little potential for confounding, because parents with myopia did not appear to pass along a more intense near-work environment to their children.

Confounding was assessed in a multivariate logistic regression model (Table 4). The association between myopia and the number of parents with myopia, near work in diopter-hours per week, the number of hours spent in sports activities per week, and local ITBS Reading scores was adjusted for the effects of each other factor in this model. ITBS local Total Language was not significant in the multivariate model and was therefore excluded from the multivariate results in Table 4. Despite their correlations, the risk factors had very little confounding effect on the association with myopia—that is, univariate values were virtually unchanged when adjusted for the other factors in the multivariate model (Table 4). The odds ratio for having two compared with no parents with myopia decreased by only 12% when adjusted for near work, sports activities, and local ITBS Reading scores. Again, this suggests that the association between children's and parents' myopia may be due to heredity rather than to greater near-work demands being placed on children with myopia by parents with myopia. The odds ratio for near work did not change when adjusted for the number of parents with myopia, sports activity, and school achievement. Near work appears to have an independent association with myopia that is not explained by greater academic aptitude in myopes or myopia in parents. Similarly, myopes score higher in reading achievement independent of the greater amount of time they spend in near work.

TABLE 4. Univariate and Multivariate Odds Ratios and Confidence Intervals for the Association between Children's Myopia and the Various Risk Factors

Risk Factor	Univariate Odds Ratios	Multivariate Odds Ratios	P (Multivariate)
One myopic parent	3.31 (1.32-8.30)	3.32 (1.18-9.37)	0.023
Two myopic parents	7.29 (2.84-18.7)	6.40 (2.17-18.87)	0.0008
Diopter-hours per week	1.018 (1.008-1.027)	1.020 (1.008-1.032)	0.0013
Sports (h/wk)	0.936 (0.892-0.983)	0.917 (0.864-0.974)	0.0045
ITBS Reading local percentile score	1.013 (1.003-1.024)	1.014 (1.002-1.027)	0.0276
ITBS Total Language local percentile score	1.014 (1.004-1.025)	Not in multivariate model	NS

Data are odds ratios with confidence intervals in parentheses. The multivariate model adjusts for all other factors listed.

TABLE 5. Spearman Correlations between Diopter-Hours and ITBS or Hours of Sports per Week

Variable	Correlation with Diopter-Hours	P
ITBS Reading (national)	0.231	<0.0001
ITBS Total Language (national)	0.242	<0.0001
ITBS Math (national)	0.192	<0.0001
ITBS Reading (local)	0.243	<0.0001
ITBS Total Language (local)	0.266	<0.0001
ITBS Math (local)	0.224	<0.0001
Sports (h/wk)	0.123	0.0210

The hypothesis of inherited susceptibility to near work can be evaluated statistically by testing whether there is significant interaction between near work and parental history of refractive error. We modeled this interaction with near work as a categorical and a continuous variable. Near work was dichotomized into high and low levels of near work split at the median level (50 Dh). Odds ratios associated with being in the higher compared with the lower level of near work were then calculated at each level of parental myopia history (none, one, or two parents with myopia). If the inherited susceptibility hypothesis is true, the odds ratio associated with near work should be the highest for two parents with myopia and the lowest for no parents with myopia. As seen in Table 6, the odds ratios were consistent across number of parents with myopia. When modeled as an interaction term in a logistic regression with near work as a continuous variable and parental myopia in three categories, there was also no evidence of statistically significant interaction ($P = 0.67$ for the interaction term, diopter-hours \times number of parents with myopia).

Having found significant independent effects for parental history of myopia and near work, it would be useful to compare their relative impact. The total range of near work performed by children can be approximated by four standard deviations for diopter-hours, or roughly 100 Dh (4×26.8 Dh; Table 1). A child would have to increase the time spent in near work by more than half the total range of time in near work (61.3 Dh) to equal the effect of one myopic parent on the risk of myopia. Nearly the entire range of near work (94.7 Dh) equals the effect of two parents with myopia on the risk of myopia. Myopes and emmetropes differ by an average of only 13.6 Dh of near work (Table 1). This suggests that the smaller differences in near work that are likely to occur between children have less impact on refractive error than do hereditary influences.

DISCUSSION

In this study, both heredity and near work were significantly associated with myopia, with heredity being the more important factor. We also found no evidence to support the theory that heredity is important only because parents with myopia have children who do more near work. Children of parents without myopia did as much near work as children of parents with myopia. This is consistent with previous studies that report on both near work and parental history of refractive error. Bear et al.⁵⁸ found little change in correlations between the refractive errors of family members after adjustment for the current level of near work, suggesting a strong genetic component independent of near work. Although Wong et al.⁵⁹ reported significant odds ratios for both hours per day of reading and familial tendency toward myopia, they did not assess the effect of each variable on the other by comparing univariate and multivariate odds ratios. In a sample of Singa-

porean conscripts with a highly myopic average refractive error of -6.1 D, Saw et al.⁶⁰ found that parental myopia was significantly related to myopia, but neither past nor current near work was a confounding variable, because near work was not associated with myopia. Parental myopia became nonsignificant when adjusted not for near work, but for educational level and placement in a program for the gifted in school.

Individual components of near work had different effects. The strongest associations between myopia and near-work activities were for studying and reading for pleasure (Table 1). In contrast to the concerns of parents, watching television, playing video games, or working on a computer at home were not associated with myopia. Having a television before the age of 12 for 1 to 3 years⁵⁹ and watching television from a close distance have been associated with myopia in Asia.⁶¹ The risk did not behave in a dose-response fashion, however; having a television for longer periods was not associated with myopia.⁵⁹ The nearly universal exposure to television in the United States may make this a different variable than in Asia, where it may be more related to socioeconomic status. National prevalence estimates for myopia suggest that the impact of television is low. Adults who were born between 1917 and 1927 (presumed minimal exposure to television as children) had a prevalence of myopia as 45- to 54-year-old adults in 1971 to 1972 nearly identical with those who were born between 1947 and 1960 (12-17 years old in 1971 to 1972) with a greater exposure to television as children.⁹ A decrease in the prevalence of myopia with age has been hypothesized to be due to increasing near-work demands in more recent decades. For example, prevalence estimates from the Framingham Offspring Eye Study show that 52% of adults aged 35 to 44 years are myopic, whereas only 20% of adults aged 65 to 74 years have myopia.⁶² Our comparison of studies conducted nearly two decades apart argues against this assumption, indicating that this decrease in prevalence is due to age rather than increasing near-work demands placed on children with a more recent year of birth.⁶³

Children with myopia also tended to engage in a lower amount of sports activity. This result could be due to a more introverted personality among myopes,^{64,65} limitations to physical activities because of wearing glasses, or perhaps a true protective effect for sports activities. An impractical clinical trial randomizing children to various levels of sports activities would be needed to establish such an effect. The positive association between sports activity and diopter-hours in Table 5 is counterintuitive, considering that myopia is related to higher levels of near work and lower levels of sports activity. The correlation is driven by the positive correlation between diopter-hours and sports activity in nonmyopes (Spearman $r = 0.18$, $P = 0.002$), but not in myopes (Spearman $r = 0.016$, $P = 0.90$).

We also find no evidence that children inherit a susceptibility to the environment. In two previous studies, investigators have examined gene-environment interactions. Saw et al.³² examined data for Singaporean children aged 7 to 9 years, finding that the proportion of children with more than -3.00

TABLE 6. Odds Ratios and Confidence Intervals for Myopia Associated with Performing 50 Dh or More of Near Work Compared with less than 50 Dh per Week

Parental Myopia	Odds Ratio for ≥ 50 Dh
None	2.09 (0.364-12.0)
One parent	2.22 (0.941-5.25)
Two parents	1.57 (0.60-4.09)

Data are odds ratios with 95% confidence intervals in parentheses.

D of myopia was higher if children read more than two books per week than if they read two or fewer books. This increase in myopia due to reading more books also varied by the number of parents with myopia. It is important to note, however, that this increase did not follow the dose-response pattern of the susceptibility hypothesis. The greatest increase associated with reading more than two books per week was with one parent with myopia (a factor of 4.46 times) with little difference between two and no parents with myopia (factors of 2.12 and 2.44 times, respectively). The interaction term in their model was significant, but the absence of a dose-response relation provides no clear support for an inherited susceptibility hypothesis.³² Alternatively, near work and heredity may operate differently in Asian children than in the predominantly white sample in Orinda. Chen et al.⁶⁶ reported a study from Taiwan that showed a significant interaction between genes and environment, but the hereditary factor in that study was zygosity, not parental history of myopia. Therefore, that study sheds no light on the hypothesis of inherited susceptibility to near-work. However, their twin study offers some perspective on the relative importance of near work and heredity. They found that twins who are concordant in near-work habits are also concordant in refractive error more often than discordant twins, but by a greater amount if the twins are fraternal (by 24.2 percentage points) compared with identical (by 13.3 percentage points).⁶⁶ This may represent a ceiling effect, considering that the overall concordance rate in refractive error for identical twins was already high: 89.1% compared with 51.2% for fraternal twins. The relative effects of near work and heredity may be inferred by comparing the concordance rate among identical twins with similar near-work habits (92.4%) with the concordance rate for identical twins with discordant habits (79.1%). If the difference of 13.3 percentage points is the effect of environment and 79.1% is the effect of heredity, the ratio is 5.9:1.⁶⁶ Consistent with the present study, heredity may also be more important than near work in this sample of Asian twins.

Despite a long history of association with myopia, near work describes very little of the variance in refractive error compared with heredity. Models of refractive error with near-work variables generally have an R^2 between 2% and 12%.^{1,2,4,7} This compares poorly with heritabilities of at least 0.82 in twin studies.²⁴⁻²⁶ A limited role for near work is also supported by the modest effect of bifocal spectacles in children with myopia with esophoria at near. The progression of myopia is reduced by only 20% in children wearing bifocals compared with children wearing single-vision glasses.⁶⁷ The higher prevalence rates for myopia in Asia are consistently related to education^{11,12,59,60} but have only been weakly associated with near work.^{60,68,69} A recently reported significant odds ratio for near work in Chinese schoolchildren is difficult to interpret, because it is unclear whether it represents the effect of near work or an urban versus rural site.⁷⁰ Location may be an important confounding variable. After adjustment for location in a subsequent study, as well as for age, night-light use, and parental myopia, the only significant association between myopia and near work in a sample of Singaporean and Chinese children was for the number of books read per week, but not for hours of reading per day, a near-vision task index, additional classes, or computer use.⁷¹ Similar to the present study, odds ratios for parental myopia were higher (3.44 for two compared with no parent with myopia) than for near work (1.43 for reading more than two compared with less than two books per week).⁷¹ It may be that universal exposure to near work in Asian schooling makes it less important as a risk factor. As Saw et al.⁶⁰ have suggested, education may be a surrogate for intellectual ability rather than near work. Intellectual ability may be a more

important risk factor than near work.^{40,41} The impact of intellectual ability may be underestimated in the present study, because the OLSM sample was from a district where the average ITBS scores were above the national average and most students go to college. Alternatively, ITBS scores may be an imperfect marker for general intellectual ability, because they are only moderately correlated with IQ scores⁵² and heavily emphasize skills important for reading.^{53,54}

One limitation to the present study is that the survey used may be a crude estimate of the true near-work activity of children. Despite the greater detail of a survey conducted in Asia where near work has been presumed to play a greater role in myopia, the magnitudes of the association reported here and in Asia are similar. For example, if reading more than two books per week is taken to be a split at the median level of near work, the odds ratio of 1.43 in the Singapore-China study⁷¹ compares well with our estimate of roughly 2.0 in Table 6. The issue of how much detail is needed and which detail is the most relevant has not been resolved. As stated earlier, books read per week seems to be the single critical feature of near work in studies in Asia.^{69,71} Future research may benefit from measuring more specific components of near work and intelligence in a more detailed fashion in both parents and children to understand what is being transmitted genetically or environmentally and what role these factors play in myopia.⁷²

A further limitation of this study is that results are cross-sectional rather than longitudinal, modeling the odds ratios associated with being a myope rather than with becoming a myope. Longitudinal follow-up analyses are needed to clarify the relative roles of near work and heredity in the onset of myopia. Our estimates of risk may also be affected by sampling at only one age. Although in most cases myopia initially occurs by the eighth grade,⁴⁵ some myopia has its onset in high school, college, and early adulthood. Our sample of emmetropes no doubt contains some future myopes. This may bias some of our estimates of risk toward the null.

We concluded from our cross-sectional data that both heredity and near work are associated with myopia, but that heredity is by far the more important factor. We also found no evidence to support two alternate theories, either that children with myopia resemble their parents because they do more near work or that they inherit a susceptibility to the environment.

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The Utility of Three Predictors of Childhood Myopia: a Bayesian Analysis

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Any treatment to prevent the onset of juvenile myopia will require predictive tests in order to determine which children should receive treatment. Three risk factors for myopia were evaluated for their ability to predict myopia: (a) refraction at school entry; (b) refraction in infancy; and (c) parental history of myopia. Bayes' theorem was used to estimate these conditional probabilities. Refraction at school entry had twice the power to predict myopia (probability of juvenile myopia given the child is near emmetropia at school entry = 0.53) compared to either infant refraction (0.21-0.28) or parental myopia (0.20-0.25). While a history of any parent having myopia had the highest test sensitivity (probability of a positive family history of myopia given juvenile myopia in the child = 0.90) and refraction at school entry the highest test specificity (probability of more hyperopia than +0.50 D at school entry given no juvenile myopia = 0.91), none of these three factors had high values for both sensitivity and specificity. Further work is required to develop a battery of tests which could predict the onset of juvenile myopia with both adequate sensitivity and specificity.

Myopia Refractive error Risk factors Bayes' theorem

INTRODUCTION

Because pharmacological intervention in the abnormal eye growth of juvenile onset myopia may be possible in the twenty-first century (Stone, Lin & Laties, 1991; McBrien & Cottrill, 1993), there is renewed interest in predicting the onset of childhood myopia. In order to apply any potential treatment in a meaningful way and in order to evaluate that treatment's efficacy, the clinical community would insist on specific, accurate guidelines as to who was most likely to develop myopia. Previous proposed therapies for myopia, e.g. bifocal spectacles (Mandell, 1959; Roberts & Banford, 1967; Oakley & Young, 1975; Goss, 1986; Grosvenor, Perrigin, Perrigin & Maslovitz, 1987; Parssinen, Hemminki & Klemetti, 1989) rigid contact lenses (Baldwin, West, Jolley & Reid, 1969; Stone, 1973, 1976; Perrigin, Perrigin, Quintero & Grosvenor, 1990), and topical cycloplegic agents (Bedrossian, 1979; Yen, Liu, Kao & Shiao, 1989) have been applied to prevalent myopes in the hope of retarding myopia progression. An optimal treatment would begin before the onset of myopia; therefore, how and when to identify pre-myopes is an essential part of the development of any truly preventive treatment regimen.

In the early 1960s, Hirsch (1964) observed that children with less hyperopic refractions by non-cycloplegic retinoscopy at school entry were more likely

to develop juvenile onset myopia during the ensuing school years. More recently Gwiazda, Thorn, Bauer and Held (1993) have claimed that non-cycloplegic, near retinoscopy results in infancy can predict school-age refractive error: specifically, that babies with myopic near retinoscopy measures are more likely to be myopic by ages 9-13 yr.

Parents frequently ask eye care practitioners whether their hyperopic or emmetropic child will eventually develop myopia. This is especially true when the parents themselves are myopic. From studies conducted in the United States and Europe, the best estimates of the prevalence of myopia among children of myopic parents are on the order of 30-40% when both parents are myopic, 15-25% when either parent is myopic, and 10% when neither parent is myopic (Goldschmidt, 1968; Ashton, 1985; Gwiazda *et al.*, 1993). Thus there may be some predictive power in knowing the parental refractive error history.

Although these studies of putative risk factors may provide some information about the etiology of myopia, the analysis methods used in these investigations do not evaluate the utility of these factors in predicting myopia onset. For example, none of these analyses calculate the sensitivity and specificity of their particular risk factor(s) for predicting myopia onset. Further, risk factors as predictors must be evaluated in light of the probability of the condition in the population at risk (Hill, 1987). Bayes' theorem is a basic statistical tool which can be used to obtain these predictive probabilities.

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TABLE 1. Re-analysis of Hirsch's data on non-cycloplegic retinoscopy at school entry and prediction of the onset of juvenile myopia (Hirsch, 1964)

	Juvenile myope at age 13 or 14 yr (Sph eq: -0.50 D or more myopia)	Not a juvenile myope at age 13 or 14 yr (Sph eq: -0.49 D or less myopia emmetropia, or any hyperopia)	Total
Retinoscopy at school entry: Sph. eq. refraction of any minus, emmetropia, or hyperopia less than $+0.50$ D	54	61	115
Retinoscopy at school entry: Sph. eq. refraction of $+0.50$ D or more plus power	38	613	651
Total	92	674	766

Prevalence of myopia: $92/766 = 12\%$.

The purpose of this report is to re-analyze the data of Hirsch (1964), Gwiazda *et al.* (1993), and new data on parental refractive error history from the Orinda Longitudinal Study of Myopia (Zadnik, Mutti, Friedman & Adams, 1993). We use sensitivity and specificity analysis and Bayesian statistics to critically evaluate the relative and absolute utility of refraction at school entry, infant refraction, and parental refractive error history in the prediction of future juvenile myopia.

METHODS

Data on refractive error at school entry and in infancy were taken from two published reports (Hirsch, 1964; Gwiazda *et al.*, 1993). Hirsch's Table 4 presents his retinoscopic findings from 261 eyes out of 766 eyes of 383 children refracted at school entry and again at ages 13–14 yr. Hirsch (1964) randomly selected 100 emmetropic eyes for presentation in this table from a pool of 605 emmetropes in the study, hence the missing 505 eyes. Multiplying the frequencies for emmetropes by 6.05 to recreate Hirsch's entire data set should minimally distort the estimate of predictability obtained in this analysis, assuming that the frequencies of initial refractions for these 100 emmetropic eyes are randomly represented. Use of the full sample is conservative since excluding these emmetropes would overestimate the predictive power of Hirsch's data.

Initial spherical equivalent refraction was divided into two groups based on Hirsch's claim that initial refractions of less than $+0.50$ D were the most predictive of future myopia: (1) any myopia, emmetropia, or hyperopia up to but not including $+0.50$ D; and (2) hyperopia of $+0.50$ D or more. Ultimate refraction at age 13 or 14 years was also dichotomized, with eyes either myopic (-0.50 D spherical equivalent or more myopia) or non-myopic (-0.49 D or less myopia, emmetropia, or any hyperopia). Frequencies used may be found in our Table 1.

Gwiazda *et al.* (1993) report on a group of 65 out of 72 children in a longitudinal study for whom infant refractive status was determined within the first 6 months of life. Of the 31 children with spherical equivalent non-cycloplegic near retinoscopic findings as infants of any minus power, 42% became myopic as children (criterion for juvenile myopia not stated). Of the 20

children with retinoscopic findings as infants of $+0.50$ D or more hyperopia, 10% became myopic as children. We therefore use $n = 13$ (42% of 31) and $n = 2$ (10% of 20), respectively, for the number of children in each childhood refractive error group. The eventual refractive status of another group of 14 children with infant refractions between 0.00 and $+0.49$ D are not reported by Gwiazda *et al.* (1993). While it seems probable that these emmetropic infants became myopic as children at some rate between 10 and 42%, we will examine the sensitivity and specificity of these data in two ways: (1) the 14 emmetropic infants became myopic at the same rate as the hyperopic infants (10%, $n = 1$); and (2) the 14 emmetropic infants became myopic at the same rate as the myopic infants (42%, $n = 6$). The frequencies used in these two analyses may be found in Tables 2 and 3, respectively.

Data on the effect of parental history of refractive error on the prevalence of myopia in children are taken from the Orinda Longitudinal Study of Myopia (OLSM), a study of refractive error and ocular component development in children 6–14 yr of age (Zadnik *et al.*, 1993). Data from 333 children in grades 6–8 were analyzed both for whether the child was myopic by cycloplegic autorefraction (at least -0.75 D in both principal meridians) or was not myopic (less myopia than -0.75 D, emmetropia, or any hyperopia in both principal meridians), and for the parents' history of refractive error. Two children did not have parental refractive history in the data base, resulting in $n = 331$. Informed consent was obtained from the parents of study participants after all procedures were explained. Children's refractive error was measured with a Canon

TABLE 2. Re-analysis of data from Gwiazda *et al.* (1993) on non-cycloplegic retinoscopy in infancy and prediction of myopia onset assuming the 14 emmetropic infants became myopic at a rate similar to hyperopic infants (10%)

	Myopia in childhood	No myopia in childhood	Total
Myopia in infancy (any minus power)	13	18	31
No myopia in infancy (plano to any plus power)	3	31	34
Total	16	49	65

Prevalence of myopia: $16/65 = 25\%$.

TABLE 3. Re-analysis of data from Gwiazda *et al.* (1993) on non-cycloplegic retinoscopy in infancy and prediction of myopia onset assuming emmetropic infants became myopic at a rate similar to myopic infants (42%)

	Myopia in childhood	No myopia in childhood	Total
Myopia in infancy (any minus power)	13	18	31
No myopia in infancy (plano to any plus power)	8	26	34
Total	21	44	65

Prevalence of myopia: 21/65 = 32%.

R-1 autorefractor following tropicamide 1% cycloplegia. The efficacy of tropicamide as a cycloplegic in children of this age and the repeatability of the Canon autorefractor are dealt with in other reports (Egashira, Kish, Twelker, Mutti, Zadnik & Adams, 1993; Mutti, Zadnik, Egashira, Kish, Twelker & Adams, 1994; Zadnik, Mutti & Adams, 1992). Only children in the sixth, seventh, and eighth grades were included in the analysis because the majority of juvenile myopia has developed by this age (Blum, Peters & Bettman, 1959).

Parents themselves were not examined, but they completed a questionnaire on when they first received glasses and whether their glasses or contact lenses were used primarily for distance or near vision, or were equally important for both. Parents were classified as myopes if they used their correction primarily for distance vision, or if it was equally important for both distance and near viewing as long as they first started wearing spectacles before age 16 yr. Misclassification is bound to occur, with some astigmats and high hyperopes being included as myopic parents. This should only reduce the predictive power of parental refractive history in this analysis, making the reported estimate a conservative one. Data on test sensitivity and specificity are analyzed in two ways: (1) when both parents are myopic (Table 4); and (2) when either one or both parents are myopic (Table 5).

Test sensitivity is defined as the number of true positives, those with a positive test result who developed juvenile myopia divided by the number of children with myopia (Table 6). This yields the conditional probability $P(T+|M+)$, or the probability of a positive test result ($T+$), i.e. myopia in infancy, given that the subject was myopic ($M+$) in childhood. Test specificity is defined as

the number of true negatives, those with a negative test result who did not develop juvenile myopia divided by the number of non-myopic children, giving the conditional probability of a negative test result given no myopia in childhood, $P(T-|M-)$. The sensitivities and specificities for each risk factor are summarized in Table 6.

While test sensitivity and specificity are useful probabilities that can be obtained directly from the results reported in Tables 1-5, they are not on an absolute scale and therefore cannot solely represent the utility of a test. Sensitivity and specificity are relative measures whose value depends on the prevalence of the condition a test is designed to detect. A certain "high" sensitivity and specificity for a test of a more common disease may indicate that the test is good, while the same level of sensitivity and specificity might be inadequate for a test of a rare disease (Hill, 1987).

The conditional probability which together with sensitivity and specificity expresses the utility or worth of a test is its predictive power; for myopia, this would be the probability that myopia occurs given that the test result was positive, $P(M+|T+)$ (Hill, 1987). This may be thought of as the level of confidence the clinician has in a particular test, its diagnostic value, or the likelihood that the patient with a positive test result will actually go on to develop the condition. It cannot be obtained directly from these retrospective studies, however, because the prevalence of myopia in the study sample may not equal the prevalence in the population of interest. Differences in the prevalence of myopia between the study sample and population would proportionally distort, or bias, any estimate of $P(M+|T+)$ obtained directly from Tables 1-5. As in this example adapted from Hill (1987), the probability that one would measure elevated intraocular pressure in a patient known to have glaucoma is virtually the same whether the test is conducted in a general practice or a glaucoma clinic, despite vast differences in the prevalence of glaucoma in these two settings. The probability that a patient with elevated intraocular pressure has glaucoma, however, is quite different depending on the prevalence of glaucoma in the sample being tested. Therefore, for $P(M+|T+)$ to apply to a population rather than the test sample only, it must be normalized to the prevalence of myopia in the population of interest.

The probability $P(M+|T+)$ may be obtained from $P(T+|M+)$ and $P(T+|M-)$ from the study data if

TABLE 4. Frequency of juvenile myopia as a function of whether or not both parents are myopic

	Myopia in childhood (at least -0.75 D in both meridians)	No myopia in childhood (less myopia than -0.75 D, emmetropia, or hyperopia in both meridians)	Total
Both parents myopic	24	54	78
One or no parents myopic	38	215	253
Total	62	269	331

Prevalence of myopia: 62/331 = 19%.

Data are taken from cycloplegic autorefraction of children and survey of parents' refractive status as part of the Orinda Longitudinal Study of Myopia (Zadnik *et al.*, 1993). See the text for the definition of parental myopia.

TABLE 5. Frequency of juvenile myopia as a function of whether any parent, one or both, or neither parent is myopic

	Myopia in childhood (at least -0.75 D in both meridians)	No myopia in childhood (less myopia than -0.75 D, emmetropia, or hyperopia in both meridians)	Total
Any parent myopic	56	173	229
Neither parent myopic	6	96	102
Total	62	269	331

Prevalence of myopia: 62/331 = 19%.

Data are taken from cycloplegic autorefracton of children and survey of parents' refractive status as part of the Orinda Longitudinal Study of Myopia (Zadnik *et al.*, 1993). See the text for the definition of parental myopia.

one knows $P(M+)$, the prevalence of myopia in the population of interest, by the use of Bayes' theorem (Hill, 1987):

$$P(M+|T+) = \frac{P(M+) * P(T+|M+)}{\{P(M+) * P(T+|M+)\} + \{P(M-) * P(T+|M-)\}}$$

Similarly,

$$P(M-|T-) = \frac{P(M-) * P(T-|M-)}{\{P(M-) * P(T-|M-)\} + \{P(M+) * P(T-|M+)\}}$$

Since the prevalence of myopia varies as a function of age and ethnicity (Working Group on Myopia Prevalence and Progression, 1989), we calculated estimates of $P(M+|T+)$ and $P(M-|T-)$ for a range of myopia prevalences, $P(M+)$, from 0.10 to 0.25 (Sperduto, Siegel, Roberts & Rowland, 1983). The probability of no myopia, $P(M-)$, is equal to $1 - P(M+)$.

RESULTS

Test sensitivities, probabilities for a positive test result given that a child is myopic, range from a high of 0.90 for any parent, one or both, being myopic to a low of 0.39 for both parents myopic (Table 6). Test specificities, probabilities for a negative test result given that a child is not myopic, range from a high of 0.91 for refraction at school entry, to a low of 0.36 for any parent being

TABLE 6. The sensitivity and specificity of various predictive tests

Predictive test	Test sensitivity	Test specificity
Refraction at school entry	0.59	0.91
Infant refraction (10%)	0.81	0.63
Infant refraction (42%)	0.62	0.59
Both parents myopic	0.39	0.80
Any parent myopic	0.90	0.36

Sensitivity is the proportion of future myopes (15% of the population) whose myopia is correctly predicted from the test results. Specificity is the proportion of future non-myopes (85% of the population) who are identified correctly based on the results of the predictive test. Predictive tests are: (1) refraction at school entry; (2) refraction in infancy assuming 10% of emmetropic infants become myopic; (3) refraction in infancy assuming 42% of emmetropic infants become myopic; (4) history of myopia in both parents; and (5) history of myopia in any parent.

myopic. Prevalences of myopia in these studies ranged from a high of 32% for Gwiazda *et al.* (1993) to a low of 12% for Hirsch (1964) (Tables 1-5).

Probabilities $P(M+|T+)$ and $P(M-|T-)$ obtained from Bayes' theorem are shown as a function of the prevalence of myopia in Fig. 1. As expected, $P(M+|T+)$ increases and $P(M-|T-)$ decreases with higher prevalences for each test. If 15% is taken as a typical prevalence for myopia (Blum *et al.*, 1959), then the greatest power for the prediction of juvenile myopia [highest $P(M+|T+)$], 0.53, is obtained from refraction at school entry (see arrow on Fig. 1). Infant refraction has approximately half the power to predict myopia as refraction at school entry, 0.21-0.28. Parental history of myopia has similar predictive power to infant refractive error, 0.25 if both parents are myopic and 0.20 if any parent is myopic. The probabilities for predicting

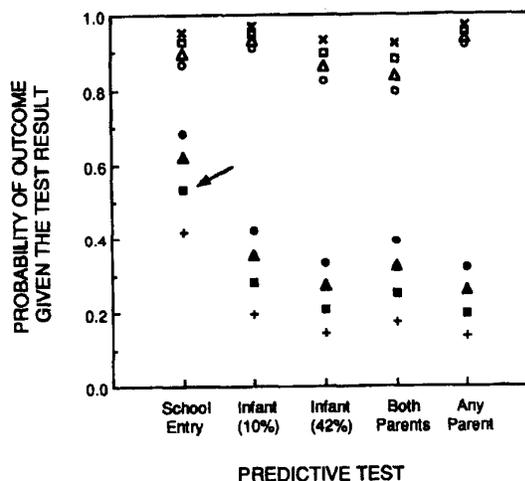


FIGURE 1. The probabilities of myopia as a child given a positive test result $\{P(M+|T+)\}$ are depicted by the solid symbols, ● for a prevalence of myopia of 25%, ▲ for 20%, ■ for 15%, and + for 10%. The probabilities of no myopia given a negative test result $\{P(M-|T-)\}$ are depicted by the open symbols, ○ for a prevalence of myopia of 25%, △ for 20%, □ for 15% and × for 10%. Predictive tests are: (1) refraction at school entry; (2) refraction in infancy assuming 10% of emmetropic infants become myopic; (3) refraction in infancy assuming 42% of emmetropic infants become myopic; (4) history of myopia in both parents; and (5) history of myopia in any parent.

no myopia given a negative test result, $P(M-|T-)$, occur in a narrow range, from 0.88 to 0.95 (Fig. 1).

The criteria for the dichotomization of risk factor data in the preceding analyses were based on the recommendations made in the original papers. The effect of changing the criteria for dichotomization may be seen in Table 7. Hirsh (1964) provides data on various levels of refraction at school entry, but refraction at age 13 or 14 is a fixed classification. These data can be used to illustrate the effects of changing the criterion for the risk factor. There is a reciprocal relationship between sensitivity and specificity as the criterion for initial refraction is altered (Table 7A). Large improvements in sensitivity come at the expense of specificity when the criterion for refraction at school entry is hyperopia less than +1.00 D and vice versa if the criterion is hyperopia less than +0.25 D. The probability $P(M+|T+)$ generally increases as the criterion for refraction at school entry is shifted toward less hyperopia, again at the expense of sensitivity.

Characterization of parental history in the OLSM data is also fixed, but the effects of changing the criterion for outcome, defining children's myopia as refractive error in both meridians from -0.25 to -1.00 D, are shown in Tables 7B and C. The main effect is a shift in the prevalence of myopia in the sample. Performance characteristics, sensitivity, specificity, and $P(M+|T+)$, are relatively unaffected by changes in sample prevalence

since the results are normalized for a population prevalence of 15%. Data from Gwiazda *et al.* (1993) are not available in a form which allows for an analysis of the effects of changing criteria for dichotomization of either risk factor or outcome.

The prevalence of myopia in parents of OLSM participants was 46% (307/662), lower than the 62-65% prevalence found by Gwiazda *et al.* (1993) in their sample. Of the 229 OLSM children with myopic parents, 151 had one myopic parent and 78 had two myopic parents. The prevalence of myopia in children with no myopic parents was 5.9% (6/102), increasing to 21.2% (32/151) if one parent was myopic, and 30.8% (24/78) if both parents were myopic. These prevalences as a function of parental refractive history are similar to those found by Gwiazda *et al.* (1993) as well as Ashton (1985).

These results can also be used to estimate the probability of myopia given information on two tests: (1) parental history of myopia; and (2) refraction at either infancy or entrance to school, $P(M+|T_1+, T_2+)$. The probability of myopia given a single test result will become the new prevalence of myopia used in calculating the probability of myopia given the result on the second test (Hill, 1987). Assuming a prevalence of myopia of 15%, the conditional probabilities of myopia given the results from two tests are depicted in Fig. 2. This analysis also assumes that the two tests are independent, that

TABLE 7. The effect of changing criterion for dichotomization of the the risk factor refraction at school entry (A) and the outcome measure (criterion level for juvenile myopia) for both parents myopic (B) and any parent myopic (C)

(A) Refraction at School Entry					
Retinoscopy at School entry: Sph. eq. refraction of hyperopia less than:	Test sensitivity	Test specificity	$P(M+ T+)$	$P(M- T-)$	
0.00	0.11	1.00	1.00	0.86	
+0.25	0.18	0.95	0.37	0.87	
+0.50	0.59	0.91	0.53	0.93	
+0.75	0.82	0.61	0.27	0.95	
+1.00	0.98	0.22	0.18	0.98	
(B) Both Parents Myopic					
Myopia in childhood (at least this amount in both meridians)	Test sensitivity	Test specificity	$P(M+ T+)$	$P(M- T-)$	$P(M+)$
-0.25	0.34	0.80	0.23	0.87	0.27
-0.50	0.38	0.80	0.25	0.88	0.22
-0.75	0.39	0.80	0.25	0.88	0.19
-1.00	0.36	0.79	0.23	0.88	0.17
(C) Any Parent Myopic					
Myopia in childhood (at least this amount in both meridians)	Test sensitivity	Test specificity	$P(M+ T+)$	$P(M- T-)$	$P(M+)$
-0.25	0.83	0.36	0.19	0.92	0.27
-0.50	0.83	0.35	0.18	0.92	0.22
-0.75	0.90	0.36	0.20	0.95	0.19
-1.00	0.91	0.35	0.20	0.96	0.17

Results in (A) demonstrate the reciprocal relationship between changes in sensitivity and specificity as the criterion for the risk factor are altered. Changing outcome criteria in (B) and (C) only affect the prevalence of myopia in the sample, to which the results are quite robust.

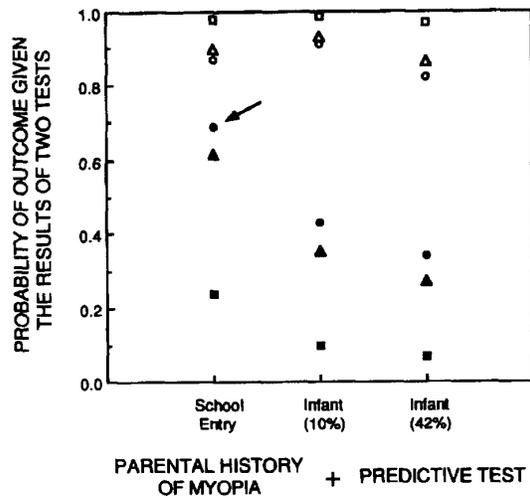


FIGURE 2. The probabilities of myopia as a child given a positive result on two tests $\{P(M+|T_1+, T_2+)\}$, parental history of myopia and either refraction on school entry or infant refraction, are depicted by the solid symbols, ● if both parents are myopic, ▲ if any parent is myopic, and ■ if neither parent is myopic. The probabilities of no myopia given a negative result on two tests $\{P(M-|T_1-, T_2-)\}$ are depicted by the open symbols, ○ if both parents are myopic, △ if any parent is myopic, and □ if neither parent is myopic. The prevalence of myopia is assumed to be 15%. Predictive tests are: (1) refraction at school entry; (2) refraction in infancy assuming 10% of emmetropic infants become myopic; and (3) refraction in infancy assuming 42% of emmetropic infants become myopic.

$P(T_2+|M+)$ is the same regardless of the outcome of the results for T_1 (see Discussion).

Having information on whether any or both parents are myopic increases the probability of myopia compared to knowing only refraction at school entry or in infancy. This probability is highest if refraction at school entry is more myopic than +0.50 D and both parents are myopic, 0.69 (see arrow on Fig. 2). While knowing that both parents are myopes also increases the likelihood of myopia given a myopic refraction in infancy, the probability remains less than that for refraction at school entry, 0.34 to 0.43.

DISCUSSION

Bayesian analysis allows for risk factors associated with myopia to be expressed as probabilities which can then be compared for their ability to predict myopia. The best single predictor of myopia as a child is a refraction more myopic than +0.50 D at school entry (0.53 for a prevalence of myopia of 15%). Infant refraction and parental history of myopia have a lower and roughly similar power to predict myopia (0.20–0.28). This represents only a small to moderate increase in predictive power over the 0.15 prevalence-based estimate one would have with no test information at all.

Other elements should be considered, however, before making a judgment about which test is the most "useful", or the most suitable for predicting the onset

of myopia and, someday, directing treatment. One is the prevalence of the risk factor. A relatively rare finding, such as a refraction of plano at school entry, even if highly predictive, would be a poor basis for making decisions. Likewise, positive findings which apply to many children but which have poor predictive power also would have little utility. The ideal situation would be to have a test or battery of tests that has the predictive power as well as the sensitivity and specificity to correctly discriminate the future myopes in the population from the non-myopes.

Unfortunately, none of these three factors alone has all of these characteristics. Table 6 lists the sensitivity, $P(T+|M+)$, and specificity, $P(T-|M-)$, of each factor. A positive test result would indicate the need for treatment and a negative result no treatment. Therefore, $P(T+|M+)$ is also the probability of correctly treating the future myope and $P(T-|M-)$ the probability of correctly not treating the future non-myope. A refraction at school entry more myopic than +0.50 D would identify only 59% of those who became myopic. It is more effective at identifying the non-myope, with a specificity of 92%. A myopic refraction in infancy identifies from 62 to 81% of future myopes (depending on how many of the emmetropic infants became myopic; Gwiazda *et al.*, 1993), but it would recommend unnecessary treatment for 37–41% of non-myopes. Infant refraction appears to add a negligible to modest increase in sensitivity coupled with a large decrease in specificity compared to refraction at school entry. The most myopes are identified on the basis of any parent having myopia, 90%. This is clearly a poor basis for a treatment decision, however, since 64% of non-myopes would also receive treatment by this criterion.

In contrast to the statement from Gwiazda *et al.* (1993) "... children who develop school-age myopia can be predicted from their infantile manifest refraction", the results from this analysis suggest that infant refraction has limited predictive power and is not sufficiently specific to be used as a basis for predicting juvenile myopia. Refraction at school entry has nearly twice the predictive power, somewhat less sensitivity, and much greater specificity when compared to refraction in infancy. Improved predictive power and specificity may come from infant refractions if the criterion for dichotomization of refraction in infancy is modified, but it is likely that this will come at the expense of sensitivity, as illustrated for refraction at school entry (Table 7A).

The age at testing could affect the predictive power and specificity of infant refractions as Gwiazda *et al.* (1993) found greater correlations between refractions at age 1 yr and those after the age of 5 yr than those done at age 3 months. Results from Hirsch (1964) may be the upper limit to this improvement, however. Cycloplegia may also have an impact on the utility of infant refractive measures as predictors of eventual refractive error. Accommodative responses are immature in infants under 2 months of age (Haynes, White & Held, 1965; Braddick, Atkinson, French & Howland, 1979; Banks, 1980); thus measures of tonic accommodative posture

may confound non-cycloplegic retinoscopy in infants under 6 months of age. Longitudinal cycloplegic refractive data are being collected in infants (Atkinson, 1993; Wood & Hodi, 1992), although the duration of follow-up has not yet extended to adolescence.

If single tests fail, results presented in Fig. 2 suggest that combining test results could improve predictive power. The validity of Fig 2, however, depends on whether the probability of a refraction of less than +0.50 D at school entry is similar in children who became myopic and had myopic parents to that in children who became myopic and had no myopic parents. The degree of this correlation is not known from any published data. If the tests are correlated, $P(T_2 + |M+)$ will obviously increase for the second test if the result is positive on the first test. For example, if two color vision tests were used to detect glaucoma, the probability of failing the second color test would be clearly higher if there were failure on the first test. Given that distortion, it would be inappropriate to use the probability of glaucoma given a positive result on the first test as the new prevalence of glaucoma for the second test. Rather than to provide a firm estimate for predictive power, however, Fig. 2 is meant to illustrate the improvement in predictive power which results from the use of two or more tests assumed to be largely independent. Considering the inadequacy of single predictive tests, such approaches would be worthwhile in the future.

If predictive tests are identified and an effective treatment is available, the timing of treatment is an important consideration. Dedicating resources to predict juvenile myopia from infant refraction is problematic since infancy would be an inappropriate time to begin treatment to prevent myopia. Therapies such as bifocal spectacles or contact lenses could not be used. Any pharmaceutical intervention intended to slow eye growth would not be advisable since substantial normal eye growth occurs between infancy and the age of 8 yr when the prevalence of myopia begins to increase (Larsen, 1971; Blum *et al.*, 1959). Any emmetropization which may occur during that time should not be interrupted. A more effective battery of tests for predicting myopia might be better used closer to the time when the majority of eye growth is complete, but before the onset of myopia.

Another factor to consider is the impact of the treatment itself, both in terms of the inconvenience to the parent or child, the chance of significant side effects, and the financial cost to parents, insurers, or government. These factors determine what level of sensitivity and specificity are required of any predictive tests for myopia. If both the cost of treatment and its morbidity are low, poorer specificity becomes acceptable. As specificity becomes worse, however, the need for performing any testing at all also decreases, especially if the prevalence of the condition to be treated is high. For example, all children drink fluoridated water without any testing for a risk of dental caries. If the prevalence of myopia were very high, as

in Asia (Lam & Goh, 1991), and treatment morbidity and cost were low, predictive testing might be less important.

A more likely scenario in the United States, with a prevalence of myopia in children between 10 and 25% (Sperduto *et al.*, 1983), is that the cost of any efficacious pharmaceutical treatment for myopia will be high and that tests for myopia with a high predictive power will be required by the clinical community. A sensitivity near 90%, equal or greater specificity, and a predictive power near 90% might be reasonable goals for such a battery of predictive tests. At present, however, which tests to perform and when to perform them in order to achieve these levels are not known.

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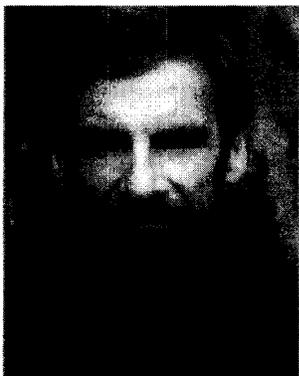
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VISION RESEARCH

A NATIONAL PLAN: 1999-2003

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL EYE INSTITUTE

A Report of the National Advisory Eye Council



Roy H. Steinberg, M.D., Ph.D.

Not long after the creation of the National Eye Institute (NEI) by Congress in 1968, a young, promising vision research scientist named Roy Steinberg received one of the first NEI Research Career Development Awards. This marked the beginning of

a long and productive association between the NEI and a researcher who served the vision community in many ways.

With his great breadth of knowledge and sharp mind, Roy had a clearer grasp than most of the many facets of retinal research, both clinical and laboratory. Most productive scientists establish a single theme to their research program during their career. Roy was different, adapting to new ideas and seeking challenging new avenues through which to pursue his numerous research interests. His early work led to a greater understanding of the complex active and passive ionic mechanisms governing retinal pigment epithelium (RPE) cell transport properties. He showed how the RPE contributes to the electroretinogram and controls the environment surrounding the photoreceptor cells.

In the late 1980's, while maintaining an interest in retinal physiology, Roy and his colleagues at the University of California at San Francisco became interested in growth factors and their potential use in slowing or preventing retinal degenerations. Roy was instrumental in demonstrating that basic fibroblastic growth factors could act as a survival-promoting neurotrophic factor in hereditary retinal degenerations. At the time of his death, Roy was involved in experiments he believed could lead to treatment of blinding diseases like retinitis pigmentosa and macular degeneration.

Roy's great intellect, careful experimental approach, and keen scientific insights earned him the MERIT Award from the NEI and the Friedenwald Award from the Association for Research in Vision and Ophthalmology. While maintaining an active and vigorous vision research program, Roy also found time to serve as an adviser to the National Institutes of Health and the NEI. He was a member and later Chair of the Visual Disorders Study Section, the forerunner of today's Visual Sciences C. He served as Chair of the Retinal Diseases Panel for the NEI's Vision Research—A National Plan: 1987 Evaluation and Update and as a consultant to the 1978–1982 and the 1994–1998 national plans. He authored the highlights and recommendations from two NEI-sponsored workshops—the first on the Cell Biology of Retinal Detachment in 1986, and the second on Repair and Replacement to Restore Sight in 1991. In 1994, he was appointed to the National Advisory Eye Council, where he served with great distinction until his death.

The NEI and the vision community have lost a dear friend. We are deeply indebted to Roy for his unselfish service and loyalty. The NEI is proud to dedicate *Vision Research—A National Plan: 1999–2003* in his memory.

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Programs and Research Priorities

The research projects supported by the National Eye Institute (NEI) address the leading causes of blindness and impaired vision in the United States. The NEI supports a broad range of basic and clinical research, clinical trials and other epidemiologic studies, and research training and career development in the sciences related to vision.

A detailed description of NEI program priorities and funding policies is contained in the report of the National Advisory Eye Council, *Vision Research - A National Plan: 1999-2003*. The research objectives given below are representative only, and are not intended to be an all-inclusive compilation of areas of interest to the NEI. Investigators are strongly encouraged to contact one of the [NEI extramural program directors](#) to discuss their research, training, or career development plans. All Division of Extramural Research staff members may be reached at 301-451-2020.

Retinal Diseases

- Explore the pathophysiological heterogeneity of age-related macular degeneration (AMD) to hasten development of the tools needed for improved diagnosis, prevention and therapy.
- Investigate the pathogenesis of vascular diseases of the retina and choroid including diabetic retinopathy, AMD, and retinopathy of prematurity; develop better methods of prevention and therapy.
- Identify novel causes of inherited retinal degenerations; further examine the cell and molecular mechanisms whereby identified gene defects cause retinal degenerations.
- Further develop and critically evaluate therapies involving gene delivery, growth factors, and transplantation for the treatment of retinal disease.
- Explore the cell and molecular basis of the response to retinal injury.
- Identify the factors that dictate the unique properties of intraocular immunity and inflammation and alter systemic immunity to intraocular antigens.
- Develop diagnostic methods and therapeutic approaches that distinguish among infectious immunopathogenic and autoimmune posterior segment inflammation.
- Analyze the mechanisms underlying light adaptation and recovery following phototransduction.
- Study how visual information is transformed by successive layers of the neural retina and the mechanisms involved.
- Identify and characterize factors important in retinal cell fate determination and differentiation.
- Catalog and map genes expressed in the retina and choroid and begin to determine the cellular sites of retinal gene expression in health and disease.
- Probe the control of the retina's microenvironment through studies of Bruchs membrane, the interphotoreceptor matrix, the retinal pigment epithelium, glia, choroid and vitreous.

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Corneal Diseases

- Explore the molecular basis of corneal transparency.
- Analyze the molecular nature of corneal inflammation and wound healing.
- Delineate the pathogenesis of corneal developmental anomalies and dystrophies.
- Improve the understanding of ocular surface physiology.

Program Director:

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Lens and Cataract

- Determine if there are novel markers that differentiate the normal aging process from the diseased (cataractous) state.
- Definitively test hypotheses of cataract.
- Map, identify, and characterize genes which when mutated cause congenital or age-related cataract; determine if there are genetic factors that interact with environmental factors to confer susceptibility to age-related cataract.
- Identify genes and pathways that control eye development, especially those critical for lens induction and cell fate determination.
- Define the contributions of crystallins to normal lens function.
- Characterize, at the molecular level, the ion channels, transporters and gap junction proteins needed to maintain lens homeostasis; determine what roles perturbations in these systems play in cataract formation.
- Define the mechanisms that regulate the cellular and sub-cellular architecture of the lens, with special emphasis on the contribution of minor constituents and their progressive modification during aging and opacification.
- Understand the basis of lens accommodation and presbyopia at the molecular and mechanistic levels

Program Director:

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Glaucoma

- Identify genes and genetic loci contributing to glaucoma, especially those responsible for the common forms of the disease, and to characterize the function and interaction of their gene products.
- Define the molecular and biochemical mechanisms that lead to retinal ganglion cell death in human glaucoma and in relevant animal models of related optic nerve injury.
- Enhance understanding of the structure and function of the aqueous humor outflow pathways at the cellular and molecular level.
- Develop a better understanding of anterior segment immunology.
- Improve our understanding of the nature and course of glaucoma, incorporating studies of co-morbidity, natural history, and genetics with special emphasis on Hispanic, Native American, and African-American populations.
- Develop improved diagnostic techniques encompassing measures of visual function, optic nerve and nerve fiber layer structure, in situ and for clinical applications of

genetics.

- Identify neuroprotective strategies that could prevent retinal ganglion cell death.

Program Director:

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Strabismus, Amblyopia, and Visual Processing

- Identify the visual error signals that govern eye growth during correction for refractive error; identify human risk factors for myopia and abnormal eye growth; and evaluate promising treatments for preventing the onset of or slowing the progression of myopia, such as special spectacle or contact lenses or pharmacological treatments.
- Investigate the effectiveness of immuno-modulating therapies in halting disease progression in optic neuritis, and identify the unique characteristics of ocular muscles that render them vulnerable to Graves' ophthalmopathy, myasthenia gravis, orbital myositis, and chronic progressive external ophthalmoplegia.
- Discover how topographic gradients are generated and read out to form ordered visual structures, and identify the sites and mechanisms of action of axon guidance molecules.
- Determine the role of peptide growth factors, such as neurotrophins, in the development, plasticity and regeneration of the visual pathways; to determine how critical periods are regulated; manipulate the molecular signals underlying this regulation to enhance the adaptive and regenerative properties of the adult brain.
- Elucidate the mechanisms by which spontaneous patterns of electrical activity, present before the onset of visual experience, guide the formation of visual structures, prior to visual experience.
- Characterize the clinical problems of amblyopia and impaired stereoscopic vision more precisely, and clarify their relationship to strabismus, anisometropia and other related conditions.
- Study the development and plasticity of neural mechanisms affected in strabismus and amblyopia, including studies in animal models and normal and abnormal human populations.
- Develop innovations in the detection and treatment of strabismus and amblyopia.
- Develop functional magnetic resonance imaging (fMRI) and related technologies as useful, quantitative tools for exploring the neural basis of human visual processing.
- Understand how neural computations are accomplished and stored within the central visual system.
- Understand plastic mechanisms in the oculomotor system that ensure accurate gaze shifts, precise alignment of the two eyes, steady fixation which can be affected by nystagmus, and a stable visual world during self-movement.
- Extend studies of eye alignment to include vertical and torsional eye movement control; gain insight into the pathogenesis of cyclo-vertical strabismus.
- Discover how visual information contributes to perceptual decisions, object recognition, internal representations of external space, transformations between different spatial frames of reference, and to the formation of neural signals appropriate for guiding behavior.
- Understand the cellular mechanisms that give rise to changes in visual sensitivity associated with attention and perceptual learning.

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Visual Impairment and Its Rehabilitation

- Develop a theoretical understanding of normal visual functioning that can be extended to understanding and treating the disabilities experienced by people with low vision.
- Understand the visual requirements of everyday tasks.
- Develop effective assistive devices and techniques to maximize residual vision and/or substitute for visual information.
- Develop environmental designs and modifications that enhance independence among the visually impaired.
- Evaluate the effectiveness of rehabilitation in the visually impaired.
- Ascertain the prevalence and incidence of visual impairment and visual disability in the United States and identify subpopulations at heightened risk for visual impairment and disability.
- Create an effective infrastructure for research on visual impairment and rehabilitation.

Program Director:

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Collaborative Clinical Research

The NEI supports single center and multi center clinical trials and other epidemiologic and health services research. Collectively, these projects are directed toward furthering knowledge about the predictors for and natural history of visual system diseases and disorders and developing better prevention and management strategies for these conditions.

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Refractive Error Study in Children: Sampling and Measurement Methods for a Multi-Country Survey

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- **PURPOSE:** The Refractive Error Study in Children was designed to assess the prevalence of refractive error and vision impairment in children of different ethnic origins and cultural settings.
- **METHODS:** Population-based cross-sectional samples of children 5 to 15 years of age were obtained through cluster sampling. Presenting, uncorrected, and best-corrected visual acuity, along with refractive error under

See also pp. 427-435, 436-444, 445-454, and 525-527.

cycloplegia, were the main outcome measures. Amblyopia and other causes of uncorrectable vision impairment were determined.

- **RESULTS:** Study design and sample size calculations, survey enumeration and ophthalmic examination methods, quality assurance monitoring, and data analyses and statistical methods are described.
- **CONCLUSIONS:** The study design, sample size, and measurement methods ensure that the prevalence of age-specific and sex-specific refractive error can be estimated with reasonable accuracy in the target populations. With commonality of methods, a comparison of findings between studies in different ethnic origins and cultural settings is possible. (Am J Ophthalmol 2000;129:421-426. © 2000 by Elsevier Science Inc. All rights reserved.)

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THIS ARTICLE DESCRIBES THE METHODS USED FOR AN international study of refractive error and other visual disorders in school-age children, the Refractive Error Study in Children, conducted in China, Nepal, and Chile. Study methodology, which was common across the three sites, is presented in this article. Findings from each of the surveys are reported in three companion articles.¹⁻³

Clinical evidence suggests that refractive errors, along with amblyopia and strabismus, are common in children. Refractive error can place a substantial burden on the individual. School-age children constitute a particularly vulnerable group, because uncorrected refractive error may have a dramatic impact on learning capability and educational potential. Despite the recognized importance of correcting refractive anomalies in children, available data are incomplete concerning the prevalence of refractive error, its variation with sex, age, and race, the extent to which it is being corrected, and whether its prevalence is changing over time. Moreover, it remains particularly difficult to compare the prevalence of refractive error in different geographic areas for a number of reasons: definitions of emmetropia, myopia, and hyperopia are not uniform across studies; populations with limited representativeness have been studied (surveys have generally dealt with convenience samples, such as school children or military recruits, rather than population-based samples); procedures used to assess refraction status are different (refractions may have been performed with or without cycloplegia); and the demographic makeup of the studied populations is often dissimilar (age and sex composition in particular).

Table 1 provides an overview of some of the worldwide literature on the prevalence of refractive error in children.⁴⁻¹² Additionally, a recent review of myopia studies in Scandinavia reports prevalences ranging from 1% in 7 to 8 year olds to 33% in young adults.¹³ Attempts to compare prevalence rates are problematic for the reasons mentioned above.

The purpose of the Refractive Error Study in Children

TABLE 1. Prevalence of Refractive Error in School-Age Children

Authors	Country	Sample Size	Age Range	Myopia		Hyperopia	
				Definition	Prevalence (%)	Definition	Prevalence (%)
Angle and Wissmann ⁴	United States	13,536	12-17	VA < 20/20*	31.8	NA	NA
Grosvenor ⁵	Vanuatu	788	6-19	≤ -0.5 D	2.9	≥ 1.25 D	0.25
Lin and associates ⁶	Taiwan	2,353	13-16	NA	49.6	>2 D	0.6
Au Eong and associates ⁷	Singapore	110,236	15-25	VA ≤ 6/18*	44.2	NA	NA
Zadnik and associates ⁸	United States	716	6-14	≤ -0.75 D	7.5	NA	NA
Auzemery and associates ⁹	Madagascar	1,081	8-14	VA ≤ 6/9*	0.92	VA ≤ 6/9*	1.11
Kassir ¹⁰	Lebanon	935	5-18	NA	15.7†	NA	15.7†
Cummings ¹¹	United Kingdom	1,809	8-10	VA ≤ 6/9*	24.4	VA ≤ 6/9*	0.6
Preslan and Novak ¹²	United States	680	4-7	< -0.5 D	3.1	>4 D	0.9

D = diopters; NA = not available; VA = visual acuity.

* Refers to unaided visual acuity that corrects with refraction.

† Refers to ametropia percentage (myopia and hyperopia combined).

was to assess the age-specific and sex-specific prevalence of refractive error and the prevalence and causes of visual impairment in children of different ethnic origins and cultural settings using consistent definitions and common methods. China and Nepal were selected as study sites because of the availability of investigators who had recent experience in similar adult surveys. Chile was selected to provide another developing country population with characteristics distinctly different from each of the other two sites.

Human subject research approval for the study protocol was obtained from the World Health Organization Secretariat Committee on Research Involving Human Subjects. Approval to conduct the study was obtained from the local health authorities.

METHODS

GENERAL ECONOMIC STATUS AND ETHNIC COMPOSITION in common with a major segment of the population, familiarity with health and other authorities in the community, and geographic proximity to the study institution were considered in identifying the specific target population within each country. Population-based, cross-sectional samples of the target population were selected through random sampling of children ages 5 through 15 years. For logistical practicality, cluster sampling with geographically defined clusters of approximately equal population size was used. Cluster size was chosen to correspond to a typical village population size in China and Nepal, with 200 to 300 children ages 5 to 15 years. The need to group small villages and subdivide large ones in creating clusters of approximately equal size was, thus, minimized. In Chile, a single large urban area was subdivi-

vided into clusters, of approximately 200 children, by grouping community blocks.

Sample size was calculated to estimate an anticipated 22% prevalence of refractive error in 15-year-olds within an error bound of 20% with 95% confidence. The sample size requirement with simple random sampling was 340, as calculated by

$$n \approx Z^2(\rho)(1 - \rho)/B^2,$$

where $\rho = .22$, $B = .20 \times .22 = .044$ with a 20% error bound, and $Z = 1.96$ for a 95% confidence interval. With no oversampling at any particular age, and assuming a uniform age distribution across the 11-year age interval, a total of 3,740 children were required. After adjusting for an anticipated 10% absenteeism and nonparticipation rate, and allowing for an arbitrary 25% increase in sample size to accommodate possible inefficiencies associated with the cluster sampling design, the sample size requirement increased to 5,194 children. In the absence of reliable prevalence data from the study areas, the same sample size was used at each of the three sites.

Households within each of the randomly selected clusters were identified, and all children inclusive of 5 to 15 years of age and resident in the selected clusters were enumerated by name, age, and sex. The only exclusions were transient residents (visitors/guests) and institutionalized children or others who had been away for more than 6 months. The school currently attended, the child's grade level, and the educational level of both the father and mother were obtained. In Chile and Nepal, an identification and physical mapping of all houses within cluster boundaries preceded the house-to-house enumeration. In China it was possible to identify households and enumer-

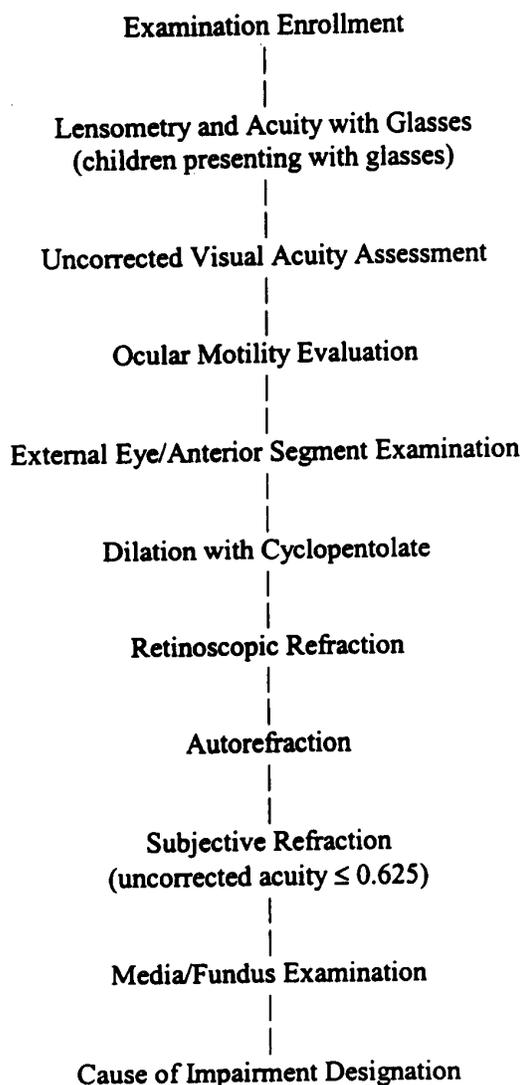


FIGURE 1. Ophthalmic examination flow diagram.

ate all eligible children using official village residence registers.

The testing and examination protocol included lensometry, visual acuity measurements, ocular motility and alignment evaluation, cycloplegic retinoscopy and autorefraction, and examination of the external eye, anterior segment, media, and fundus (Figure 1).

Distance visual acuity was measured with a retroilluminated logMAR chart, with five tumbling "E" optotypes on each line (Precision Vision, Villa Park, Illinois). Visual acuity measurements began at a distance of 4 meters with the top line (20/200). If the orientation of at least four of the five optotypes was correctly identified, the child was

then tested by dropping down to line 4 (20/100). If one or less optotypes were missed, the testing resumed at line 7 (20/50), continuing to line 10 (20/25) and finally line 11 (20/20). If at any level the child failed to recognize four of the five optotypes, the line immediately above the failed line was tested, until successful. If the top line at 4 meters was missed, the child was advanced to 1 meter with progression down the chart as described above. The lowest line read successfully was assigned as the visual acuity for the eye undergoing testing. The right eye was tested first, then the left eye, each time occluding the fellow eye. The child was requested to indicate the direction of the E optotype either by pointing with his/her hand or by calling the direction. The child was observed to prevent squinting (pinhole effect) while reading the optotypes. If the child presented with glasses, the power of the lenses was measured using a Zeiss SBM 70 Focimeter lensometer (Carl Zeiss Jena GmbH, Jena, Germany). For these children, visual acuity was measured first with and then without glasses.

Strabismus was diagnosed and quantitated with cover testing and observation of the corneal reflex both at 0.5 meters and 4.0 meters. After the child fixated on an object with both eyes open, the right eye was covered while observing the fellow eye to detect any correcting movement (tropia). After a few seconds with no cover, the left eye was checked for tropia with the same procedure. Tropias were categorized as esotropia (outward movement of the fellow eye), exotropia (inward movement), or vertical (downward or upward movement). Tropias were distinguished from phorias, movement of the covered eye after the cover is removed. The 4.0-meter cover test was important in identifying intermittent exotropia, which is usually worse with distance fixation. The degree of tropia was measured using the corneal light reflex (Hirschberg's method). A reflex within the pupillary margin, approximately 2 mm from the pupillary center, was noted as 15 degrees or less; reflex beyond the pupillary margin but in the mid-iris region, approximately 4 mm from the pupillary center, was noted as 16 to 30 degrees; and reflex near or at the limbus was noted as greater than 30 degrees.

The anterior segment was examined using a magnifying loupe ($\times 2.5$). The lids, conjunctiva, cornea, iris, and pupil were examined and abnormalities noted.

Both pupils were dilated. Two drops of cyclopentolate 1% were administered 5 minutes apart to each eye. After 20 minutes, if a pupillary light reflex was still present, a third drop was administered. The light reflex and pupil dilation were checked after an additional 15 minutes. Dilating and light reflex status were recorded between 40 to 60 minutes after the first drop. Cycloplegia was considered complete if the pupil dilated to 6 mm or greater and a light reflex was absent.

Cycloplegic refraction was performed using a streak retinoscope in a semidark room, with the examiner at a distance of 0.75 meters and a +1.5-diopter lens in the trial

frame. The spherical and cylindrical power and axis necessary to neutralize the shadow movement were noted, first for the right eye and then the left eye.

Cycloplegic autorefraction was carried out using a handheld Nikon Retinomax K-Plus (Nikon Corporation, Tokyo, Japan). Calibration of the autorefractor was performed at the beginning of each working day using an eye model (+4.00 to +5.50 diopters). After the alignment process, eight measurements were taken for each eye. Repeat measurements were taken if there was excessive eye movement or if the machine-calculated acceptance value was low. An average of the eight measurements and one representative keratometry reading were produced in printed form.

Subjective refraction was performed on children with an uncorrected visual acuity 0.625 or worse (20/32), using retinoscopy and autorefraction values as a starting reference.

After refraction, the eye examination was completed with indirect or direct ophthalmoscopic examination of the lens, vitreous, and fundus. Specific abnormalities were noted. Finally, for eyes with uncorrected visual acuity 0.625 or worse, a principal cause of reduced vision was designated by the examining ophthalmologist using a seven-item list (refractive error, amblyopia, corneal opacity resulting from trachoma, other corneal opacity, cataract, retinal disorder, other causes).

Arrangements were made for dispensing spectacles at no cost to the patient and providing medical treatment.

Study staff underwent training for familiarization with the Refractive Error Study in Children protocol, equipment use, measurement methods, and data collection forms. Field operations were tested in a pilot study immediately preceding the actual study. Quality assurance was monitored in a preselected 20% of the study clusters. All children with uncorrected visual acuity 0.625 or worse in either eye and 10% of those with normal vision in both eyes were evaluated twice for visual acuity, retinoscopic refraction, and autorefraction in these quality assurance clusters. Repeat evaluations were done independently by a second examiner. Reproducibility of visual acuity measurements was evaluated with kappa statistics. Reproducibility of both methods of refraction was investigated by calculating 95% upper and lower limits of agreement around the mean of the differences found by subtracting the second measurement from the first one.¹⁴ Assuming that these differences follow a normal distribution, 95% would be expected to lie between limits defined by the mean difference ± 1.96 times the standard deviation of the differences. Refraction measurements, expressed as spherical equivalents, were calculated as the algebraic sum of the spherical measurement and 0.5 times the cylindrical power.

Completed household enumeration forms and eye examination forms were edited for accuracy and missing values in the field. Data entry and computerized verifica-

tion were conducted at study headquarters. This verification included checks on cluster, household, and child identification numbers, measurement-data range and frequency checks, and consistency checks for related measurements. Data common to the household and examination forms, such as age and sex, were also checked for consistency. Original data forms were reviewed when discrepancies were noted. The final data sets were translated into system files for statistical analysis using Stata software.¹⁵

The prevalence of vision deficits was calculated for uncorrected visual acuity, presenting visual acuity, and best-measured visual acuity using five vision categories. The latter measurement considered that obtained with subjective refraction for those with reduced uncorrected visual acuity. The vision categories were defined using visual acuity measurements from both eyes: 0.625 (20/32) or better in both eyes, 0.625 or better in only one eye, 0.50 (20/40) or worse to 0.32 (20/63) or better in the better eye, 0.25 (20/80) or worse to 0.125 (20/160) or better in the better eye, and 0.10 (20/200) or worse in the better eye.

Confidence intervals for prevalence estimates were calculated using two methods: a normal distribution approximation with standard errors adjusted for clustering effects, and the exact binomial distribution ignoring cluster effects.^{15,16} Although existing software readily allows for cluster design effects to be taken into account with the normal approximation, the accuracy of the confidence interval obtained by this approximation is compromised when prevalences are near zero. With very low prevalences, the confidence interval is shifted downward from that calculated with the exact binomial, which can result in a negative lower value. Accordingly, the confidence interval based on the binomial distribution was substituted when the upper value of this estimate was above that obtained with the normal approximation, which was common for prevalences below 1%. This approach ensured that the upper confidence interval value would not be overly conservative.

The age-specific and sex-specific prevalences of myopia -0.5 spherical equivalent diopters or less and of hyperopia 2 spherical equivalent diopters or greater were calculated. Individuals were considered myopic if one or both eyes were myopic and hyperopic if one or both eyes were hyperopic, so long as no eye was myopic. Emmetropes were children with neither eye myopic or hyperopic. Confidence intervals were calculated using variance estimators for proportions, with adjustment for cluster design effects. The prevalence of astigmatism was assessed at two levels: greater than or equal to 0.75 to less than 2 cylinder diopters, and greater than or equal to 2 diopters.

Agreement between spherical equivalent values obtained by retinoscopic refraction versus autorefraction was investigated using 95% limits of agreement, as was done in investigating reproducibility within each of the two methods.

The relationship between refractive error and uncorrected visual acuity was investigated, using eyes with uncorrected visual acuity 0.8 (20/25) or better—clearly normal vision—and those with reduced vision that corrected to this level with subjective refraction. Eyes where something other than refractive error might have contributed to vision reduction were, thus, excluded from the analysis.

Refractive error was reported as the cause of reduced vision for all eyes improving to 0.625 or better with refraction. The principal cause of impairment, as assigned by the examining ophthalmologist, was used in categorizing eyes not improving to this level. Amblyopia was reported as the cause of impairment only for children with no apparent organic lesion and satisfying one or more of the following criteria: 1) esotropia, exotropia, or vertical tropia at 4 meters fixation, or esotropia or vertical tropia at 0.5 meters (strabismic amblyopia); 2) anisometropia 2 spherical equivalent diopters or greater (anisometropic amblyopia); or 3) bilateral ametropia of +6 spherical equivalent diopters or greater. Cases with uncorrectable vision loss designated by the examiner as “amblyopia” in the absence of any organic lesion were tabulated as being of unexplained causes if they did not meet these explicit criteria.

DISCUSSION

SAMPLING WAS CARRIED OUT IN SUCH A WAY THAT EACH child living within the target population had an equal chance of being selected for inclusion in the survey. The size of the cluster within which the child resided did not influence the chance of being selected. Drawing the sample from children in schools, instead of from geographically defined populations, would not have produced *population-based* estimates of refractive error—not just because some children may not be attending school, but the age structure and sex structure present in the target area cannot be easily replicated without population-based sampling. Without a representative sample from the target population, study samples may overestimate or underestimate the prevalence of refractive error and other disorders. Although study findings pertain only to the target population, generalization to a larger segment of the country may be appropriate because, in each survey, the target population was considered to be representative of a significant proportion of the country.

The upper age limit of 15 years was chosen because there would have been difficulty in achieving an acceptably high response rate above this age. Fifteen years of age generally coincides with the last year of school attendance and expected residence in the community. The lower age limit, 5 years, coincides with the lowest age at which it was considered possible to use a single visual acuity measurement method across the entire study population. It was

expected that this age interval would encompass the age at which myopia begins to develop as a significant public health problem.

Clustering of refractive error at the family level¹⁷ was ignored in sample size calculations and in the calculation of prevalence confidence intervals. Ignoring possible familial effects is of no consequence; however, if the familial structure in the study sample is similar to that in the target population at large. There is no reason to believe otherwise. In any event, familial clustering should have minimal effect on age-specific prevalence analyses, because all children within a 1-year age interval are likely to come from different families. Clustering effects associated with measurements in eyes from a single individual were dealt with by generally reporting right eye and left eye findings separately.

Adequate sample size requirements, appropriate study methods, and quality assurance in data collection ensure that reliable and comparable data regarding the prevalence of refractive error and vision impairment are obtained from Refractive Error Study in Children surveys. Furthermore, by selecting distinctly different populations in each survey, potentially interesting comparisons between study findings are possible. Refractive Error Study in Children surveys are being planned for two locations in India. Surveys in other regions would also be of interest.

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Pathologic Myopia

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There are a number of pathologic abnormalities of the retina and choroid associated with the axial elongation of the globe in myopia. While the exact pathogenesis of these are unclear, they probably result from a combination of two interrelated factors: (1) progressive elongation of the globe with stretching, thinning, and atrophy of tissue; and (2) an inherited abiotrophy or dystrophy of the retina and choroid.

In its milder expression, the thinning of the retina and choroid results in easy visibility of the choroidal vessels, referred to as "tigroid" or "tessellated" fundus. With progressive atrophy, the choroidal vessels appear yellowish or whitish, and the term choroidal "sclerosis" is used (although choroidal atrophy is more correct) (Fig 1). Further chorioretinal atrophy results in patchy areas of bare sclera that can occur in the posterior pole or the periphery (Fig 2). When confined to the periphery it may be confused with the inherited choroidal dystrophy gyrate atrophy.

The presence of a posterior staphyloma, a localized

ectasia, is virtually pathognomonic for pathologic myopia. The depth and size of the staphyloma is best appreciated with the stereopsis of indirect ophthalmoscopy. Staphyloma involving the macula are usually associated with subnormal vision, whereas staphyloma in other locations in the posterior pole may have no effect on central vision (Fig 3).

Associated to a high degree with posterior staphyloma are "lacquer cracks," fine, irregular, yellowish-white lines that represent linear breaks in Bruch's membrane (Fig 4). These breaks are probably implicated in the development of subretinal choroidal neovascularization that can result in a hemorrhagic maculopathy (Fig 5). Resolution of this maculopathy with pigment proliferation represents the lesion described by Foerster and Fuchs that bears their name (Fig 1).

The vitreous also undergoes a degenerative process with liquefaction and posterior vitreous detachments occurring more frequently at an earlier age. These vitreal abnormalities undoubtedly are contributing factors in the increased incidence of retinal breaks, retinal detachments, and macular holes.

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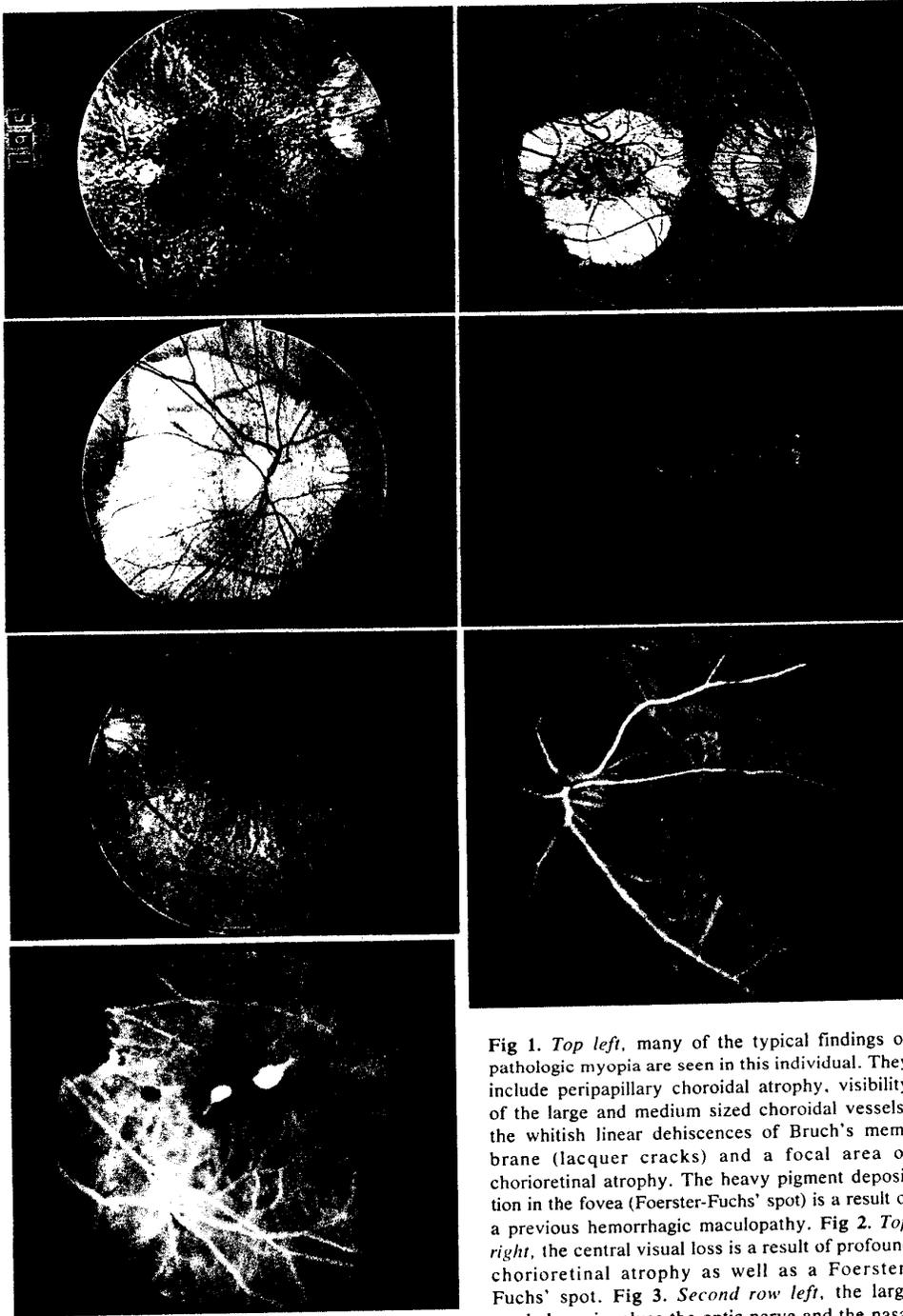


Fig 1. *Top left*, many of the typical findings of pathologic myopia are seen in this individual. They include peripapillary choroidal atrophy, visibility of the large and medium sized choroidal vessels, the whitish linear dehiscences of Bruch's membrane (lacquer cracks) and a focal area of chorioretinal atrophy. The heavy pigment deposition in the fovea (Foerster-Fuchs' spot) is a result of a previous hemorrhagic maculopathy. Fig 2. *Top right*, the central visual loss is a result of profound chorioretinal atrophy as well as a Foerster-Fuchs' spot. Fig 3. *Second row left*, the large staphyloma involves the optic nerve and the nasal portion of the macula. Fig 4. *Second row right*, the lacquer cracks involve the fovea and are associated with a mild degree of chorioretinal atrophy. Fig 5A-C. A, *third row left*, the subretinal hemorrhage in the fovea is a result of subretinal choroidal neovascularization which is occurring in two separate locations (Band C, *third row right and bottom left*).

THE RELATIONSHIP BETWEEN REFRACTIVE ERRORS AND RETINAL DETACHMENT —ANALYSIS OF 1,166 RETINAL DETACHMENT CASES—

Akihiko OGAWA* and Minoru TANAKA**

Summary: We compared 1,166 eyes with retinal detachment to 11,671 eyes of patients without retinal detachment in order to clarify the distribution of refraction ranges and the relative frequency in incidence of retinal detachment for each range.

In the retinal detachment group, hyperopia was detected in 8.58%, emmetropia in 9.26% and myopia in 82.16%, and the corresponding ratios in the control group were 24.29%, 41.30% and 34.41%, respectively. The retinal detachment group thus exhibited a high frequency of myopia, as has been known.

The relative frequency of retinal detachment for each range of refraction was 0.35 for hyperopia, 0.22 for emmetropia and 0.83 for myopia in the range -0.75 to -2.75 D. The relative frequency increased with an increase of severity in myopia up to the range of higher than -15.0 D, where the frequency was 68.6 times higher than for the hyperopic range.

Key Words: Retinal detachment, refractive errors, myopia, relative frequency

Introduction

A number of Japanese reports show that most of the patients with retinal detachment are myopic. Duke-Elder² reported that myopia occurred in about two-thirds of patients with retinal detachment. However, we have found few reports comparing the refraction of a retinal-detachment group with a general population. Gernet³ and Kaufmann⁴ compared their data for patients with retinal detachment with the distribution of refraction in a general population reported by Betsch¹. In Japan, only Tokoro¹¹ has conducted such a study.

Tokoro¹¹ compared the distribution of the refraction in 586 eyes with retinal detachment and a known degree of refraction from patients with retinal detachment excluding traumatic aphakia or macular hole to the distribution of refraction in 1,407 inhabitants of Naruse-mura, Kanagawa Prefecture, reported by Ohyama⁶, in 12,000 outpatients at Tubraingen University by Betsch¹ and in 16,438 eyes of outpatients at the Department of Ophthalmology, Tokyo Medical and Dental University. He concluded that the incidence of retinal detachment increased in proportion to the severity of myopia.

We have compared the distribution of refraction in patient groups with or without retinal detachment, and determined the incidence of myopia.

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Table 1. Subjects of this study

	Retinal detachment*	Control**
Number of eyes	1,166	11,671

*without aphakia and unknown refraction

**patients over age of 6

Materials and Methods

1. Materials

There were 1,325 eyes diagnosed as having retinal detachment at the Department of Ophthalmology of our university hospitals between April 1961 and December 1984. Refraction was determined for 12,735 eyes in patients without retinal detachment who were examined at the Juntendo Urayasu Hospital between May 1984 and November 1985. Of the 1,325 eyes with retinal detachment, 1,166 eyes with known refraction were assigned to the retinal detachment group. Aphakic retinal detachment cases were excluded. Of the 12,735 eyes from patients without retinal detachment and with known refraction, 11,671 were from patients over the age of 6. These were used as controls (Table 1). The retinal detachment was due to a break in all cases. Cases of traumatic and secondary retinal detachment were not included in the study.

2. Methods

Refractive values were obtained by subjective tests based on objective tests. When this measurement was not available, the refraction of the glasses worn by the patient, or the premorbid data in the patient's chart was used. Refraction was divided into the ranges of hyperopia (+0.75 D), emmetropia (+0.5 to -0.5), and five stages of myopia (-0.75 to -2.75, -3.0 to -5.75, -6.0 to -8.75, -9.0 to -14.75 and <-15.0). The distribution was determined for each range in each group.

To compare the relative frequency of each range in the two groups, the frequency of the retinal detachment group was divided by that of the control group.

Results

The age distribution of the patients with retinal detachment (1,325 eyes) was bimodally distributed with the first peak in the 20's and the second in the 50's. Patients between 0 and 19 years of age constituted about 37% of the controls (Figure 1).

We analyzed the distribution of refractive range in the retinal detachment (1,166 eyes) and control (11,671) groups. In the retinal detachment group, 100 eyes (8.58%) were in the range of >+0.75 D; 108 eyes (9.26%), +0.5 to -0.5; 190 eyes (16.30%), -0.75 to -2.75; 305 eyes (26.16%), -3.0 to -5.75; 212 eyes (18.18%), -6.0 to -8.75; 181 eyes (15.52%), -9.0 to -14.75; and 70 eyes (6.0%), <-15.00. In the control group, these respective ranges were observed in 2,835 (24.29%), 4,820 (41.30%), 2,225 (19.06%), 1,249 (10.70%), 363 (3.11%), 150 (1.29%) and 29 (0.25%) eyes (Table 2).

Thus, the control group showed a peak of the refractometry distribution in the emmetropia range and a gradual decrease in proportion to the increase in the severity of myopia. In contrast, the distribution in the retinal detachment group was greatest on the

Table 2. Frequency of eyes with retinal detachment and control group with these respective refractive errors

Diopter	Retinal detachment 1,166 eyes (n)	Control 11,671 eyes (N)	$\frac{n}{N}$
~+0.75	8.58	24.29	0.35
+0.5 ~ -0.5	9.26	41.30	0.22
-0.75 ~ -2.75	16.30	19.06	0.83
-3.0 ~ -5.75	26.16	10.70	2.44
-6.0 ~ -8.75	18.18	3.11	5.85
-9.0 ~ -14.75	15.52	1.29	12.03
-15.0 ~	6.00	0.25	24.00
	100(%)	100(%)	

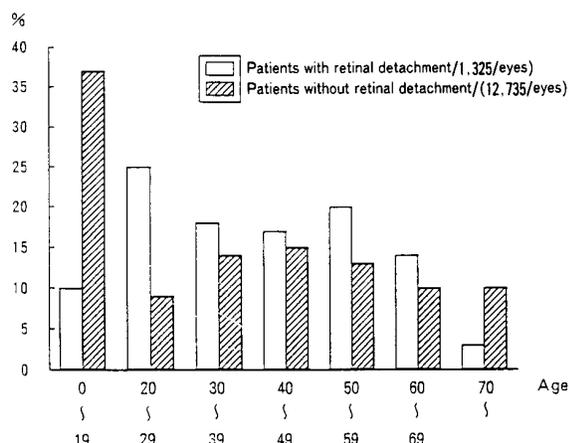


Figure 1. Age distribution of patients with retinal detachment was bimodally distributed with first peak in 20's and second in 50's.

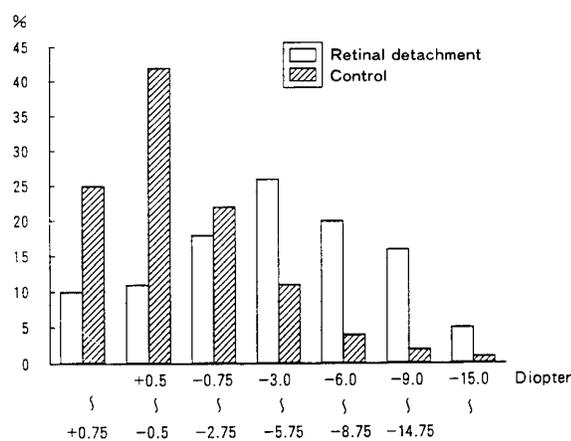


Figure 2. Distribution of refractive errors of patients with retinal detachment and control group. Distribution in retinal detachment group is greatest on myopic side with peak in -3.0 to -5.75 D range.

myopic side with a peak in the -3.0 to -5.75 D range and a low frequency in the emmetropia range (Figure 2). To calculate the incidence of retinal detachment for each range of refraction in the retinal detachment group, the frequency of each range in the retinal detachment group was divided by that in the control group. The frequency curve showed an increase starting at 0.35 for >+0.75, 0.22 for +0.5 to -0.5, 0.83 for -0.75 to -2.75, 2.44 for -3.0 to -5.75, 5.85 for -6.0 to -8.75, 12.03 for -9.0 to -14.75 and 24.0 for <-15.0 (Table 2 and Figure 3).

Discussion

We compared the refraction data of the retinal detachment group and the control group without retinal detachment. Patients over the age of 6 had been chosen for the control group because retinal detachment seldom occurs in individuals under the age of 6, and the youngest patient in the present study was 7 years old.

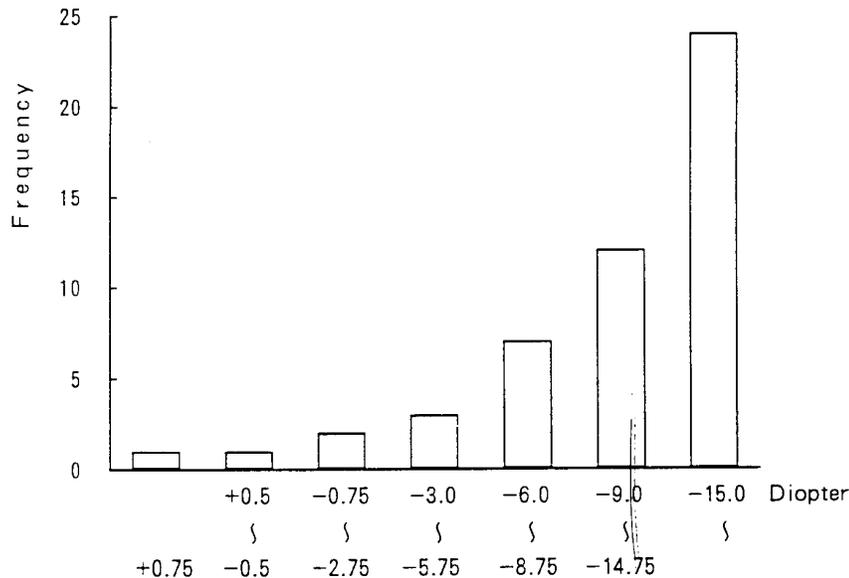


Figure 3. Relationship between retinal detachment and refraction errors shows frequency curve indicating linear increase.

Patients without retinal detachment under 19 years of age represented about 37% of the control group. We investigated whether or not this age distribution influenced the distribution of the refraction ranges in the control group. The control group included no patient under the age of 6, and no appreciable difference was detected between the distribution among the patients with retinal detachment over the age of 20 and the distribution in the control group for any studied range of refraction. Therefore, there was no influence of the age distribution.

In the control group, hyperopia was found in 24.29%; emmetropia, in 41.30%; and myopia as a whole, in 34.41%. The control group thus exhibited a lower ratio of myopia and a higher ratio of emmetropia than the retinal detachment group.

In the retinal detachment group, hyperopia was detected in 8.58%, emmetropia in 9.26% and myopia, as a whole, in 82.16%. This ratio appears higher than the ratios of myopia among patients with retinal detachment reported by Suzuki¹⁰ (68.1%) and Sato⁸ (73.0%). This is probably due to differences in the classification of refraction; our retinal detachment group included no aphakic eye.

Kaufman⁴ observed that the range -3.0 to -8.0 D of refraction constituted 30.63% of the myopic eyes with retinal detachment (70.25%). According to Sanada⁷, 27.80% of the myopic eyes with retinal detachment (67%) fell within this range. We also observed a high ratio of moderate myopia in the present study.

Tokoro¹¹ analyzed the distribution of refraction ranges among 586 eyes with retinal detachment and found hyperopia in 6.3%, emmetropia in 19.6% and myopia in 74.1%. In addition, he divided the ranges of refraction at intervals of one diopter to obtain a distribution curve of refraction. This curve was asymmetric with a peak in emmetropia and a long skirt on the myopic side. Ogino⁵ noted two ranges of myopia in a similar curve in incidence of retinal detachment. One of the ranges showed two peaks, one in emmetropia and another around

Table 3. Refractive frequency of retinal detachment

Diopter (D)	Control 13,505 eyes (N)	Arruga (1933)		Gonin (1934)		Schepens (1966)	
		398 eyes (n)	n N	237 eyes (n)	n N	533 eyes (n)	n N
	(%)	(%)		(%)		(%)	
~-4.0	9,935 (73.6)	96 (24.1)	0.32	39 (16.5)	0.22	241 (45.2)	0.61
-4.0~8.0	2,226 (16.6)	83 (20.9)	1.26	75 (31.6)	1.90	166 (31.2)	1.88
-8.0~	1,344 (9.8)	219 (55.0)	5.61	123 (51.9)	5.30	126 (23.6)	2.41

-5.0 D. The remainder occurred between -8.0 D and around -20 D with no definite peak, indicating advanced myopia. The distribution in our study had no definite peak in emmetropia because refraction was not graduated at intervals of one diopter, and the ranges were different from those reported by others.

Using 13,505 myopic eyes without retinal detachment as controls, Schepens⁹ determined the relative frequency of retinal detachment for each range of refraction in comparison with the values by Arruga and Gonin. Calculation of relative frequencies on the basis of these data revealed that the frequencies for the range -8.0 D were about 20 times higher than those for -4.0 D in Arruga's and Gonin's series and about four times Schepens' cases. Our value was close to those of Arruga and Gonin (Table 3).

The relative frequency of retinal detachment increased with the increase in severity of myopia: hyperopia in 0.35 and the range -15.0 in 24.0. The incidence of the most severe myopia was about 68.6 times that of hyperopia. Tokoro¹¹ calculated the relative frequency of retinal detachment for each range of refraction, using Ohyama's 1,407 patients, Betsch's 12,000 and 16,438 eyes from outpatients at the Department of Ophthalmology, Tokyo Medical and Dental University, as controls. In Ohyama's series, the frequency of the range -13.0 to -14.0 D was about 124 times that of emmetropia, and in Betsch's series, the frequency of the range -15.0 to -16.0 was about 97 times that of emmetropia. Our value was close to theirs; the frequency of the range -15.0 was about 109 times that of emmetropia. The series from Tokyo Medical and Dental University also showed an increasing frequency of retinal detachment with increasing severity of myopia but to a lesser degree. This was probably because ametropia was a chief complaint in many of their patients.

Early detection and treatment is essential for retinal detachment. The results of the present study confirmed the importance of a complete examination of the fundus in patients with advanced myopia and an explanation of this condition.

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. . . even the lower degrees of myopia are associated with conditions resulting in significant ocular morbidity

Morbidity from Myopia

E. S. Perkins, M. D.

High myopia is recognized as a significant cause of ocular disease, but most ophthalmologists look upon lower degrees of myopia as little more than a mild social disability without any serious consequences. It is the purpose of this paper to review the morbidity of myopia and to suggest that even the lower degrees of myopia are associated with conditions resulting in significant ocular morbidity.

Registrable Blindness from Myopia

Sorsby^{1,2} analyzed the causes of blindness leading to registration in two groups of patients. The first comprised patients of all ages who were registered during the years 1955-1960 and he found that degenerative myopia was responsible for 8.4% and myopic retinal detachment for 0.4% of blind registration. Other important causes of blindness were senile macular generation, cataract, glaucoma, and diabetic retinopathy (Table 1). Myopia was the fourth most common of these causes. However, if age is taken into account (Table 2), myopia emerges as the most important cause of blind registration in

the age group 50-59 and is second only to diabetic retinopathy in the 60-69 age group.

TABLE 1 MAJOR CAUSES OF BLIND REGISTRATION IN ALL AGE GROUPS (1955-1960)

Clinical classification	% Total
Senile macular degeneration	26.9
Cataract	22.8
Glaucoma	12.8
Myopia	8.8
Diabetic retinopathy	7.1

The second series of blind registration analyzed by Sorsby covered the years 1963-1968 but gave details only for patients up to the age of 65. In this series, myopic chorioretinal atrophy and detachment were responsible for 14.0% of blind registrations, a figure

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TABLE 2 CAUSES OF BLINDNESS AS A % OF BLIND POPULATION BY AGE AT REGISTRATION (1955-1960)

Clinical classification	0-14	15-29	30-49	50-59	60-69	70 and over
Myopia	1.6	5.2	11.3	18.1	18.1	5.9
Retinitis pigmentosa	2.0	12.4	11.8	6.2	2.0	0.4
Diabetic retinopathy	0.0	4.3	10.8	15.2	16.7	4.4
Cataract	0.0	0.0	0.0	7.9	15.8	27.9
Glaucoma	0.0	1.2	3.3	8.6	14.5	13.7
Senile macular degeneration	0.0	0.0	0.0	1.2	8.3	38.1

exceeded only by congenital defects and diabetic retinopathy (Table 3). If age is taken into account, myopia is the second most common cause of blind registration in the age groups 50-59 and 60-64 (Table 4).

TABLE 3 MAJOR CAUSES OF BLIND REGISTRATION IN PATIENTS UP TO THE AGE OF 65 (1963-1968)

Clinical classification	% Total
Diabetic retinopathy	15.7
Congenital defects	14.2
Myopia	14.0
Glaucoma	7.2

Unlike diabetes, there is no evidence that myopic degeneration has any effect on life span, so myopia is considerably more important than diabetic retinopathy in terms of years of blindness. Unfortunately, it is not possible from these figures to relate the risk of blindness to the degree of myopia. If,

however, we assume that the myopia was -5.00 D or more and that this degree of myopia occurs in 1.4% of the population³, it is possible to estimate the risk of blind registration for people with this degree of myopia. Sorsby¹ gives the rate for 100,000 of the population for blind registration due to myopia in different age groups. For those individuals 70 and over, this rate is 13.3. We should expect from the distribution of refractive errors that 1.4% of 100,000 people would have a refraction of -5.00 D or more, ie, 1,400, so that the rate of 13.5 per 100,000 of the population means that nearly 1% of patients of 70 or over with this degree of myopia are likely to be registered as blind.

There is little doubt that the higher the refractive error the greater the risk of blindness, but the work of Curtin and Karlin⁴ strongly suggests that because variations in corneal power and lens power can in themselves alter

TABLE 4 SOME CAUSES OF BLINDNESS AS A % OF BLIND POPULATION BY AGE AT REGISTRATION (1963-1968)

Clinical classification	0-14	15-29	30-49	50-59	60-64
Myopia	1.5	5.4	13.0	18.2	17.5
Retinitis pigmentosa	1.9	13.3	12.2	6.8	3.8
Diabetic retinopathy	0.0	6.0	15.4	19.3	20.8
Cataract	0.9	1.2	3.2	7.2	11.8
Glaucoma	0.1	0.7	3.0	8.7	12.9

Unlike diabetes, there is no evidence that myopic degeneration has any effect on life span, so myopia is considerably more important than diabetic retinopathy in terms of years of blindness

refraction by ± 5 diopters, the measurement of the axial length is a more sensitive indicator of risk than refraction.* They showed clearly that there was a significant correlation between axial length and the incidence of atrophy of the choroid and retina, crescent formation, and posterior staphyloma (localized thinning and bulging of the coats of the eye).

In their study, over 20% of eyes from patients over the age of 40 with axial lengths between 25.5 mm and 26.4 mm showed chorioretinal atrophy. Stenstrom's⁹ figures suggest that 80% of eyes with axial lengths of from 25.5 mm to 26.1 mm have refractions of less than -5.00 D and 15% of these will be between +1.00 and 0 diopter. In the face of these figures, it is difficult to accept that myopia can be divided into simple (ie, uncomplicated) and pathological types on the grounds of refractive error alone. There can be no denying, however, that the greater the axial length the more severe the chorioretinal changes and in Curtin and Karlin's series, over 90% of eyes from those aged 40 and over with an axial length exceeding 29.5 mm showed chorioretinal atrophy. Their results strongly support the theory that the degenerative changes in myopia are the result of

*The axial length is the distance from the front of the eye to the posterior pole. Eyes which are shorter than normal tend to be hypermetropic (farsighted) and eyes which are longer than normal, myopic (nearsighted). See Figure.

biomechanical forces rather than an associated abiotrophy.

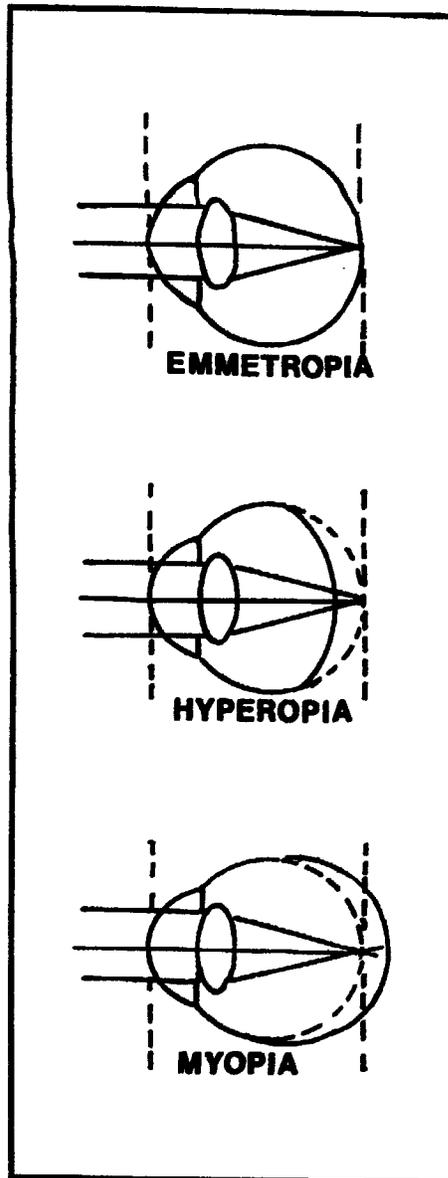


TABLE 5 DISTRIBUTION OF REFRACTIVE ERRORS IN THE NORMAL POPULATION AND IN PATIENTS WITH RETINAL DETACHMENT

Refraction	Idiopathic detachment (%)	Traumatic detachment (%)	Normal population (%)
+ 5.0	0.88	0.0	2.8
0 to +4.75	34.98	45.24	85.5
0 to -4.75	31.19	19.05	10.39
-5.0 to -9.75	18.47	14.29	1.3
-10.0 to -14.75	8.41	9.52	
-15.0 to -20.0	3.98	9.52	
> -20.0	1.11	2.38	0.1

TABLE 6 PROBABILITY OF DETACHMENT FOR DIFFERENT REFRACTIONS

Refraction	No. at risk out of 100,000	Incidence of detachment	Probability of detachment
+ 5.00	2800	0.044	1/63636
0 to +4.75	85,500	1.748	1/48913
0 to -4.75	10,390	1.5895	1/6862
-5.0 to 9.75	1300	0.9735	1/1335
> -10.0	100	0.675	1/148

Retinal Detachment and Myopia

Retinal detachment is not a common cause of bilateral blindness resulting in blind registration. In Sorsby's first series,¹ retinal detachment of unknown cause (idiopathic) was responsible for 0.7% of blind registration and 1.7% in the second series.² Only in the first series is a separate figure (0.4%) given for detachment due to myopia, and this may be an underestimate as the refractive errors of the patients with idiopathic detachment were not known. Although bilateral blindness from retinal detachment is now uncommon, thanks partly to improved surgical techniques and prophylactic treatment of the second eye, unilateral visual loss of some degree is inevitable if the macula becomes detached.⁴

Retinal detachment is relatively common, affecting about one in 20,000 of the population each year and although myopia has long been recognized as a

predisposing factor, in the modern literature it is surprising how little emphasis is placed on the refractive error of patients with detachments.

An analysis of patients seen in the Retinal Detachment Unit of Moorfields Eye Hospital, London, England, showed that 64% of 452 cases of idiopathic detachment had a myopic refraction and 55% of 42 cases diagnosed as traumatic detachment were also myopic. The distribution of the refractive errors and the expected distribution in the normal population³ are shown in Table 5.

Assuming an annual incidence of detachment of 1/20,000, it is possible to calculate the relative risk of developing a retinal detachment for different refractive errors. Table 6 shows the numbers of persons with a given refractive error in a population of 100,000 and the proportion of five detachments which would be found assuming the distribution of refractive errors as in

TABLE 7 DETACHMENTS PER YEAR IN POPULATION OF 55 MILLION

Refraction	Number in population	Probability of detachment	Number of detachments
+5.00	1,540,000	1/83636	24.2
0 to +4.75	47,025,000	1/48913	961.4
0 to -4.75	5,714,000	1/6982	857.7
-5.0 to -9.75	718,000	1/1335	535.8
> 10.0	55,000	1/148	371.6

the Moorfields' series. The final column gives the risk of detachment for the different refractive groups. As expected, the risk increases with higher degrees of myopia but it should be noted that the risk of detachment is over seven times higher for low myopes than hypermetropes. A similar figure was reported by Böhlinger.⁷

If these probabilities are applied to a population of 55,000,000, it becomes apparent why the increased risk from myopia is not so obvious. Because the distribution of a refractive errors in the population is so biased towards hypermetropia, 36% of all detachment cases will have a hypermetropic refraction (Table 7) and only 34% will have refractive errors of -5.00 D or more.

As with the degenerative fundus changes in myopia, it is likely that the incidence of detachment would show a better correlation with axial length than refractive error. The prerequisites for a detachment are collapse of the vitreous and peripheral degenerative changes and the latter have been shown by Karlin and Curtin⁸ to be closely linked with increased axial length and it is

probable that there is a maximum volume which the vitreous can attain and beyond which collapse occurs.

There are two other types of retinal detachment in which myopia plays a significant role: (1) aphakic detachment and (2) retinal detachment resulting from miotic treatment. Hyams *et al*⁹ found retinal breaks in 18.4% of 103 aphakic eyes with a myopia of -6.00 D or more and stressed the special risk of aphakic detachment in relatively young patients with myopia. Retinal detachment occurred in 6.7% of 136 myopic eyes after cataract surgery compared with 0.28% in emmetropic eyes. Other authors have suggested that between 30 and 60% of aphakic detachments occur in myopic eyes.

Pape and Forbes¹⁰ reported 34 eyes in 31 patients in whom retinal detachment occurred during miotic therapy. Eight eyes had myopia of less than -3.00 D and 13 myopia of -3.00 D or more.

Myopia and Glaucoma

The evidence for an association between myopia and open-angle glau-

... in the modern literature, it is surprising how little emphasis is placed on detachments

coma is based on the following observations:

1. The incidence of myopia in open-angle glaucoma is higher than would be expected particularly in younger patients.¹¹
2. Data from a myopia clinic¹² shows a close relationship between axial length in myopic eyes and the incidence of glaucoma. In myopes with an axial length below 26.5 mm, the incidence of glaucoma was 3%; with axial lengths between 26.5 and 33.5 mm, the incidence rose to 11%; and above 33.5 mm glaucoma occurred in 28%.
3. Patients with pigmentary glaucoma are almost all myopes.

We do not know whether the myopia is the cause of the glaucoma or vice versa but from the clinical aspect it is important to recognize that a myopic eye has an increased risk of developing glaucoma. This may be of particular value in helping to distinguish which patients with ocular hypertension are likely to develop field defects.

Refraction	Open Angle glaucoma (%)	Ocular hypertension (%)
Myopic	31	11
Emmetropic	33	23
Hypermetropic	36	66

A retrospective analysis of patients diagnosed as having open-angle glaucoma during a glaucoma survey carried out in the town of Bedford,

England¹³ showed that 31% had a myopic refraction of -1.00 D or more, 33% were emmetropic ($< \pm 1.00$ D), and 36% hypermetropic ($< + 1.00$ D). The refractive state of a similar number of ocular hypertensives who had failed to show any evidence of glaucoma after prolonged (7 years) follow-up is shown in Table 8.

If the incidence of glaucoma in the population is assumed to be 1% and the refraction of the ocular hypertensives is representative of a random population sample, the comparative probability of having glaucoma can be calculated in a similar manner to that used above for retinal detachments. The results are shown in Table 9 and it can be seen that a myope is twice as likely to have open-angle glaucoma as a normal individual (emmetrope) and five times as likely as a farsighted individual (hypermetrope).

Refraction	Probability of glaucoma
Myopic	1/35
Emmetropic	1/70
Hypermetropic	1/183

A random sample of patients from the Glaucoma Clinic at the Institute of Ophthalmology in London was analyzed in the same way with similar results (Table 10). Drance¹⁴ kindly supplied me with figures of the refractive state of patients with ocular hypertension and open-angle glaucoma seen in Vancouver, British Columbia, Canada, and these were also analyzed with the result shown in Table 11. In this series,

TABLE 10 PROBABILITY OF GLAUCOMA FOR DIFFERENT REFRACTIONS (INSTITUTE OF OPHTHALMOLOGY)

Refraction	Patients (%)	Probability of glaucoma
Myopia	32	1/34
Emmetropia	40	1/57
Hypermetropia	28	1/235

the distribution of refractions of the glaucoma patients is almost identical to that of the London series but among the ocular hypertensives were more emmetropes. However, the myopes still have the highest probability of glaucoma.

TABLE 11 PROBABILITY OF GLAUCOMA FOR DIFFERENT REFRACTIONS (VANCOUVER)

Refraction	Glaucoma (%)	Ocular Hypertension (%)	Probability of glaucoma
Myopia	29	14	1/49
Emmetropia	45	53	1/85
Hypermetropia	26	34	1/128

The difference is even more striking if age is taken into account as the figures from Vancouver for those under the age of 50 (Table 12) show a sevenfold difference between myopes and hypermetropes. Drance *et al*¹³ have since shown by discriminant analysis that refraction is one of the seven variables most useful in separating patients with chronic simple glaucoma from normals.

The actual refractive error of the patients on the Bedford Survey was not recorded but it is very unlikely that they were all high myopes as in only one case

was a note made of high myopia. The mean refraction of the myopes in the Institute series was -4.45 D with a range of -1.00 D to -15.00 D so that although, as the figures from New York show, the high myopes have a one in four chance of developing glaucoma, the risk is not insignificant for more moderate myopes.

TABLE 12 PROBABILITY OF GLAUCOMA FOR PATIENTS UNDER AGE OF 50

Refraction	Glaucoma (%)	Ocular hypertension (%)	Probability of glaucoma
Myopia	48	11	1/23
Emmetropia	48	52	1/171
Hypermetropia	4	7	1/175

Myopia and Cataract

Myopia is cited in some textbooks as predisposing to cataract but such an association has been largely, ignored in the modern literature and I have been unable to find any recent statistics. A preliminary analysis of the pre-operative refraction of patients admitted to Moorfield's Eye Hospital for extraction in one year showed a wide range of refractive errors with a median value of approximately -3.75 D with an approximately equal distribution on either side of this figure.¹⁴ The preponderance of myopic refractions can in part be due to an increased refractive power of the cataractous lens and, from a perusal of the notes, Weale concludes that this could account for three to four diopters of myopia before surgery was done. Even if allowance is made for this factor, the results do sug-

**. . . from the clinical aspect it is important to recognize
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has an increased risk of developing glaucoma**

gest that a higher proportion of myopes require cataract extraction than would be expected from the prevalence of myopia in the population.

Discussion

The following conclusions can be drawn from the evidence presented above:

1. Myopic chorioretinal degeneration is a major cause of blindness and its incidence can be correlated with the axial length of the eye.
2. The risk of idiopathic, traumatic, and aphakic retinal detachment is higher in myopic eyes. Even low myopes are seven times more likely to develop a detachment than hypermetropes.
3. Open-angle glaucoma is more likely to be diagnosed in myopic eyes than in emmetropic or hypermetropic eyes.

Recognition of a problem, although an essential preliminary, does not automatically provide a solution. It should however stimulate interest in a solution and even if we do not understand the etiology of myopia, the risks of visual loss in myopia are sufficiently high to warrant serious attempts to reduce its adverse effects. The only widespread efforts in this direction are in the prophylactic treatment of fellow eyes in patients who have already developed a detachment in one eye, and the routine pretreatment of the retinal periphery of myopic eyes before cata-

ract surgery to reduce the incidence of aphakic detachment.

The problem of unrecognized glaucoma in high myopes has been partly solved by the use of applanation tonometry instead of indentation methods so that falsely low tensions due to the low scleral rigidity of such eyes are eliminated. Assessment of cupping and field defects in highly myopic eyes still present some problems and require further study. The prognostic value of the refraction (or perhaps axial length) in patients with ocular hypertension which is suggested by the results presented here deserves further evaluation.

The most serious complication of myopia is chorioretinal degeneration. If, as the evidence of Curtin and Karlin⁴ suggests, this is the result of mechanical stretching of the retina, reinforcement of the sclera seems logical. Useful results have been reported by a few surgeons in the United States and England^{17,19} and it is used more widely in the USSR. Although this method sometimes results in visual improvement the main success has been in preventing deterioration. The criteria for surgical intervention before visual loss are therefore of great importance and deserve further study. The surgical techniques are probably capable of further refinement but scleral reinforcement is the most helpful procedure yet devised for prevention of blindness from myopic chorioretinal degeneration providing it is used in an early stage of the condition.

Summary

Myopic chorioretinal degeneration is one of the major causes of blindness but myopia is also a factor in ocular morbidity due to retinal detachment, glaucoma, and possibly cataract. Although the risks increase with the degree of myopia, evidence is presented that even myopia of less than -5.00 D increases the probability of retinal detachment and glaucoma. Myopes of this degree have a sevenfold risk of detachment compared with hypermetropes and a threefold risk of glaucoma.

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g cataract extraction, but smaller hemorrhages had no deleterious effect.

(6) Vitreous hemorrhage occurred in of 140 eyes operated on, an incidence of 7 percent. In only one case was there reuuction of vision directly attributable

to the vitreous hemorrhage.

(7) Postoperative hypotonia was encountered in 2.1 percent of 140 cases and lacerations of Descemet's membrane in 5 percent. In no case did these result in a reduction of final visual acuity.

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UNAIDED VISUAL ACUITIES CORRELATED WITH REFRACTIVE ERRORS

A STUDY

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INTRODUCTION

With the passage of the Selective Service Act, in 1940, and especially after the attack on Pearl Harbor by the Japanese, many men and women, the volunteers as well as those who were called to serve their country, came to the Army Induction Stations and General Dispensaries for their physical examinations.

These centers were overtaxed with applicants. Complete and impartial physical examinations had to be conducted with the meager means at hand, and opinions had to be given regarding the fitness or unfitness of the individual for military duty. Sometimes these opinions were made hurriedly, sometimes under extreme pressure.

The ocular examinations came to be regarded as of great importance. Many applicants who desired to enter the military service tried to hide visual defects, either by not mentioning them or by attempt-

ing to evade their detection. A few who wished to evade military service entirely as well as those anxious to obtain a non-combatant classification exaggerated a known visual defect or stated that one existed.

It is pertinent to mention these two groups—negative and positive ocular malingers—because the writer found that their existence created a very definite need for some systematized method of correlating the unaided visual acuity with the refractive error, provided the correcting lenses brought the visual acuity of the eyes to the accepted Snellen standard of 20/20, when no organic disease was present.

For example: If three individuals possessing correcting lenses of $-1.50D.$ sph. $\ominus -1.00D.$ cyl. ax. 180° , which gave them normal vision, presented themselves for examination, and the unaided visual acuity of one was 20/200, of the sec-

ond 20/100, and of the third 20/300, an average uncorrected visual-acuity reading of 20/200 would be obtained. It would then be reasonable to expect an unaided visual-acuity reading in the vicinity of 20/200 from others who possessed correcting lenses of that power, provided no organic ocular lesion was present.

As has been stated, the unaided visual acuity of any group of persons who possess the same corrective power of lenses would vary. Numerous factors—such as age, fatigue, foci of infection, malnutrition, accommodative power—would cause such variations, but there would be a reasonable range of such variation.

A chart or charts containing the average unaided visual-acuity data and the visual ranges for each of the corrective lenses most commonly encountered would materially aid an examiner in the detection of malingerers, and in classification.

The opportunity for such study presented itself in two ways. The great majority of the men and women who came for the physical examination prior to induction to the service were applying as officer candidates. The general average-intelligence level of these people was somewhat above that of the average inductee, and their responses during the ocular examination were somewhat more reliable. This, however, does not exclude a considerable portion of this group from the two classes of ocular malingering mentioned previously. Secondly, when the Army began to issue spectacles to its personnel, requests for refractions increased by leaps and bounds. The officers and enlisted men presenting themselves for an ocular examination and refraction, as a whole, no longer had any reason to be positive or negative malingerers. Many came because they were told that they needed glasses; a number came because they thought that this was a good oppor-

tunity to have their spectacles changed; others, because they desired an ocular examination.

METHODS

The physical-examination records of 45,206 men and women as well as 7,482 refraction records were reviewed for this study. Since each square of the presented charts represents the unaided visual acuity of an eye that obtained standard vision with the corresponding correcting lens or lenses, all records that showed vision correctable to 20/20 in the absence of organic disease were retained for tabulation.

All of the examinations were performed at an Army General Dispensary. The author personally examined more than half of these individuals, and the remainder were examined by associates trained in his routine methods of examination.

Each examinee, whether present for a routine physical examination or for an ocular examination and refraction, was impressed with the fact that squinting would not be permitted.

The American Optical Company Projecto-Scope and Screen were used throughout these examinations. Visual acuities were tested at 20 feet from the screen. The unaided visual acuity of each eye as well as binocular vision was recorded. Individuals who had unaided visual acuity of less than 20/400 in one or both eyes, were slowly walked up to the 400 figure until it was accurately identified. The distance between the examinee and the screen was then recorded as the numerator and 400 as the denominator. No one chart or figure was used consistently. Four different Projecto-Scope charts were used interchangeably, so that no one could familiarize himself with nor memorize them.

Each eye was then examined for patho-

logic lesions and a notation made of any existing abnormality. Following this, the spectacles (if any) of the examinee were neutralized, and the vision of each eye, separately, and the binocular vision with the glasses were noted. If the vision in each eye was not corrected to 20/20, a rapid retinoscopic examination was performed with the aid of the trial-case frame and lenses. The best visual acuity obtained for each eye and the strength of the correcting lenses in the trial-case frame were recorded on the physical-examination sheet. Fundus studies were made on all whose vision in either eye was not correctable to 20/20; on all whose unaided visual acuity was 20/100 or worse; and on all who gave a history of ocular pathologic change.

All military personnel under the age of 40 years, with no contraindications noted, received a cycloplegic examination. The manifest refraction of those over 40 years was recorded. Fundus studies were made in every instance.

METHOD OF TABULATION

Fifty charts for each refractive group, exactly as those presented, were attached to a large board. The upper row represented the Hyperopic group, the middle row represented the Myopic group, and the lower row the Mixed-Astigmatism group.

As each record was reviewed, the refractive error was noted, and the square corresponding closest to that error was filled with the unaided visual acuity, and the age of the individual. As the squares of the lower refractive errors quickly filled the 50 charts of each group, additional charts were attached in order to include all such unaided visual acuities.

With the review of records completed, loose-leaf pages, each marked consecutively to correspond to the refractive errors, were made up in book form—one

book for each refractive group.

Each page had the refractive error, age groups, and axes arranged in the manner shown in table 1. The recorded unaided visual acuities were then transposed to the proper pages and inserted under the correct age-group and axes columns.

These columns were individually added, and the total divided by the number of figures in that column. This gave the average unaided visual acuity for that particular refractive error and age group. Immediately below each column the extremes of unaided visual acuity were recorded and enclosed in parentheses.

Since the average unaided visual-acuity figures are impracticable for use by the average examiner, the writer converted them to the nearest Snellen equivalent.

For example: In table 1 the average unaided visual acuities are: 35, 32, 38, 37, 44, 41, 52; 50, 52, 49, 61, 57. When converted to the nearest Snellen equivalent they become: 30, 30, 40, 40, 40, 40, 50, 50, 50, 60, 60.

RESULTS

Table 2 represents the average unaided visual-acuity findings of eyes, with no organic pathologic lesions which are correctable to 20/20 by the corresponding lens corrections in the three main refractive-error groups.

The great majority of the unaided visual-acuity readings are accounted for in the triangular region of 0 to 4.00D. spheres and 0 to 3.00D. cylinders, singly, and in combination, in all refractive groups. Myopic corrections predominated. The vacant spaces noted appear particularly in the oblique-axis columns and signify that these corrective lenses were not encountered in this study.

The unaided visual acuities under the oblique-axis cylinder corrections are, as a rule, slightly less than those found under the horizontal or vertical meridians.

As the average age in the Hyperopic group increased, the average unaided visual acuity for the same correcting lenses became increasingly worse. This is physiologic and to be expected.

The age factor in the Myopic and in the Mixed-Astigmatism groups, apparently does not materially influence the results of the unaided visual acuity for the same correcting lenses.

nately, the methods of recording visual acuity are not uniform. Many letters of affidavit for applicants testify to such lack. Many ocular prescriptions for spectacles from military installations brought similar evidence.

To obtain a proper record of visual acuity the head and eyes of the examinee must squarely face the chart. No squinting, head tilting, nor turning must be per-

TABLE 1
TABULATION OF THE UNAIDED VISUAL ACUITIES FOR A REFRACTIVE ERROR WITH VARIOUS CYLINDER AXES, IN THE DIFFERENT AGE GROUPS*
Example: +1.50D. sph. C +0.50D. cyl.

18-29				30-39				40+			
1	2	3	4	1	2	3	4	1	2	3	4
40	40	40	40	40	40	70	50	50	50	50	50
30	30	40	30	50	40	30	40	50	40	50	70
30	30	30	30	50	40	30	50	70	40	70	70
50	25	30	50	40	30	50	70	40	50	100	50
30	40	40	40	40	30	40	40	50	50	50	50
40	40	30	30	5	220	5	260	4	210	40	50
30	25		40	40	50	50	50	52	40	6	370
30	40	6	230	40	40	40	7	350	40	70	50
40	30		30	44	40	52	50		61	8	460
9	320		40		40		50				
35	10	320	10	370	10	410		10	490		57
	32		37		41			49			
(30-50)	(25-40)	(30-50)	(30-50)	(40-50)	(30-50)	(40-70)	(40-70)	(40-70)	(40-70)	(50-100)	(50-70)

Figures 18-29, 30-39, 40+, represent the different age groups.
 Figures 1, 2, 3, 4, represent axes 45, 90, 135, and 180, respectively.
 The average unaided visual acuity is recorded at the base of each column.
 Each figure represents the denominator of the Snellen fraction, 20/.
 The figures in parentheses represent the range of unaided visual acuity.
 * The figures in each column represent but a fraction of the actual number tabulated for this refractive error.

The average unaided visual acuity of the Mixed-Astigmatism group, as a whole, was much better than that found in either of the other two groups.

In all groups, the average unaided visual acuities became worse as the refractive power of the correcting lenses increased.

As an interesting feature in this study, it was noted that Mixed-Astigmatism occurred more frequently in women.

COMMENT

Visual-acuity records, for the ophthalmologist, for the patient, and for statistics, are exceedingly valuable. Unfortu-

mitted. The vision should be tested both with and without glasses, provided glasses are worn, and the monocular as well as the binocular vision noted in each instance.

The Army physical-examination requirements specifically state that if the vision is within such and such range and correctable to such and such a value the individual will be classified thus, and so on. Any number of applicants are borderline problems, and an examiner is hard pressed to determine with a clear conscience just how to classify these individuals.

This study was undertaken because a need was felt for some simple expression

by which an examiner could rely on the answers given. Such information would be of value not only for mobilization and demobilization purposes, but for certain phases of civilian life as well.

Only eyes free from organic defects and with vision correctable to the accepted Snellen standard of 20/20 within the range of 0 to 6.00D. spheres and 0 to 6.00D. cylinders, in half-diopter increases, singly and in combination, in all three refractive-error groups, were selected for this study.

Thorington,¹ in his book on refraction, stated, "The visual acuity under definite conditions is an index of the strength of the necessary spherical lenses (plus or minus) which will give a vision of VI/VI or more. For instance, the question which has been decided is this: If a healthy eye, Hyperopic or Myopic, without astigmatism (or an eye with its astigmatism corrected with a cylinder) has the ability to see VI/VI, and has its ciliary muscle under the effect of 'drops,' what strength spheric lens would be required to give it normal vision? To begin with the writer had to work backward, so to speak, and in the following manner: The eyes were tested at six meters, and with the lenses which gave standard vision the eyes were tested to find out what the visual acuities would be when plus spheres were placed in front of the correcting lenses."

Agatston,² in his paper on "Ocular malingering," presented a table on the correlation of uncorrected visual acuity with the refractive error for myopia, myopic astigmatism, and compound myopic astigmatism based on the results of experiments with six Army men. "These subjects, each with less than 1 diopter of refractive error, had full correction, and, one eye being used at a time, the various refractive states were simulated by employment of plus lenses at the anterior fo-

cal plane. . . . If necessary, the examiner, using himself as a subject, may properly simulate any refractive error he may encounter."

In both instances, simulation was the method chosen. Though the conclusions are noteworthy, they were based on too few observations.

The author, with the help of his assistant, did simulate the different refractive errors. It was soon apparent, however, that no matter how truthful he attempted to be, he could not avoid recognizing figures or numbers which were blurred, and which would, no doubt, be unrecognizable to an individual whose unaided visual acuity was correctable to the normal value by the corresponding refractive corrections used.

In this study the recorded unaided visual acuities of more than 50,000 individuals, men and women, of different age groups were correlated with the refractive errors.

The great majority of the unaided visual-acuity readings were encountered in the region of 0 to 4.00D. spheres and 0 to 3.00D. cylinders, singly, and in combination, in both the Hyperopic and Myopic refractive groups. These average unaided visual-acuity readings are highly accurate. Beyond the 4.00D. spheres and 3.00D. cylinders, singly, and in combination, fewer readings for these corrective powers were obtained. Though fairly accurate, they do not possess the high degree of accuracy noted for the corrective-lens combinations mentioned previously. The empty spaces noted occur particularly in the oblique-axis columns and signify that such refractive errors were not encountered in this study. They could, however, be filled by interpolation. Other studies of this character, made on greater numbers of individuals, would help to fill these blank spaces and to corroborate

the work which has already been accomplished.

Armed with such information, an examiner would be aided materially in the detection of malingerers. It would help in classification and assignment of individuals entering the service. Many individuals will, no doubt, claim compensation for visual impairment aggravated by the stress and strain of war. Except for those with traumatic or organic pathologic lesions of the eyes, the truth or falsity of such claims in subjects who have unaided visual acuities correctable to 20/20, with lenses, the refractive power of whose eyes had not changed, would be readily determined. Positive malingerers will, of course, be tested with other corroborative methods.

In certain phases of civil life—for example, in the case of compensation work, civil suits, insurance—such information can be of great value.

Similar charts for the Navy can be constructed by using the Conversion Formula of Allen.³

CONCLUSIONS

A study, correlating the unaided visual acuities with the different refractive errors, obtained from a review of more than 50,000 physical examination and refraction records at an Army General Dispensary, is presented.

Only eyes free from organic defects and correctable to 20/20, within a range of 0 to 6.00D. spheres and 0 to 6.00D. cylinders, singly, and in combination, in all three refractive-error groups, were selected for tabulation.

This study was undertaken because a need was felt for some simple expression by which to determine and confirm the truth or falsity of answers given by applicants during the ocular examinations.

The importance of this study is reflected in the fact that, armed with such information, borderline individuals could be properly classified, and malingerers detected. Such information is of practical value not only for mobilization and demobilization purposes, but for certain phases of civilian life as well.

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Myopic Macular Degeneration

MAURICE F. RABB, IRA GAROON,
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Degenerative myopia is a severe disabling disease and is one of the leading causes of blindness in the world [10]. A major complication of high myopia is macular degeneration, which may subsequently lead to decreased central visual acuity; this occurs as a two-stage process. Developmental changes are the primary events, usually caused by a mechanical increase in the axial length of the eye. Degenerative changes are secondary to either vascular effects on a compromised eye, or as a second hypothesis suggests, an abiotrophic process [15].

Extensive studies of different age groups show a gradual increase in myopia from the newborn period to adulthood [3, 18, 19, 21, 22]. The incidence is thought to be equally divided between males and females; however, it is thought that women are slightly more likely to develop higher degrees of myopia as well as the subsequent degenerative changes [6]. Men tend to develop myopia later in life. Axial myopia greater than 4 diopters correlates well with axial length measurements above 25 mm. [20]. In myopia less than 4 diopters, only 17.5 percent had axial length measurements above 25 mm. Stromberg found that 0.5 percent of the population had axial length measurements greater than 26.75 mm. as well as having greater than 6 diopters of myopia [14].

CLASSIFICATION OF MYOPIA

Simple Myopia

Myopia may be divided into simple, high, and secondary categories. Simple myopia usually occurs when there is a refractive error

of less than 5 to 8 diopters, often develops during the first two decades of life, and fails to progress after maturation. The relatively low degree of refractive error is a result of the minor increase in the axial length of the globe and the increased curvature of the cornea or lens. There is usually no obvious pathological change in the posterior pole, with the exception of a myopic disc.

High Myopia

The three divisions of high myopia are congenital, pathological, and progressive. Congenital myopia tends to be stationary and does not develop the degenerative changes seen in the pathological condition. Curtin [4] has described 66 patients with this type of high myopia.

Pathological myopia is characterized by developmental or degenerative changes that occur in the posterior pole of severely myopic eyes. It results from extremely high axial elongation and is estimated to represent 2 percent of all types of myopia [16].

Progressive myopia is a developmental type in which the myopia and the axial length increase rapidly during adolescence. This increase in axial length may continue until the age of 50 years. Progressive myopia may be difficult to differentiate from simple myopia in the younger patient; however, as the condition progresses, characteristic changes in the sclera, retina, and choroid make the diagnosis quite clear.

Secondary Myopia

Another form that may be a type of high myopia is one that can occur in hereditary defects of the posterior pole, as in Wagner's disease, tapetoretinal dystrophies, atypical achromatopsia, and retinopathy of prematurity (retrolental fibroplasia). High myopia is commonly found in premature infants, regardless of whether there has been retinopathy. Approximately 10 percent of premature infants have myopia, and in approximately 10 percent of these it is greater than 6 diopters [7, 17].

Hereditary Disease

The hereditary condition plays an important part in both simple and degenerative myopia. Inheritance has been reported by Duke-

Elder to be autosomal recessive [6]. Hirsch and Ditmar found a correlation of 55 percent between children and parents with refractive errors greater than -7 diopters [12]. The simple condition has often been described as dominant in transmission [11]. Nevertheless, the hereditary pattern in myopia cannot be simply explained by Mendelian genetics, and may be multifactorial.

CLINICAL FINDINGS

Thinning of the sclera at the posterior pole is a frequent finding in high myopia, and sclera ectasia and posterior staphyloma are frequent complications.

Disc and Peripapillary Changes

The typical myopic disc is oval with a long vertical axis. The disc may appear tilted and oblique in configuration, with the temporal side flattened. The nasal side frequently has a very raised edge, sometimes called supertraction (Fig. 1). The course of the optic nerve through the canal usually is at a right angle to the surface of the eye, thus causing the disc to appear oblique. In the typical myopic eye the nerve entrance is oblique to the temporal side, and the disc appears tilted and the temporal side flattened. In addition, its temporal aspect is frequently surrounded by a concentric area of depigmentation, the so-called myopic conus or temporal crescent [1].

The myopic crescent may be present at birth, but most often occurs in later years, particularly in patients with myopia of 6 diopters or more. It usually appears as a white, sharply defined area on

FIGURE 1. Red-free photograph of myopic right disc showing large temporal crescent, sloping of the temporal retinal disc, and high elevation of the nasal portion of the disc (supertraction).





FIGURE 2. Red-free photograph of the left eye showing 360 degrees of peripapillary atrophy in retinal pigment epithelium and choroidal layers.

the temporal side of the disc where the inner surface of the sclera is seen distinctly. Absence of the retinal pigment epithelium and choroid allows visualization of the sclera. Because both layers fail to approach the temporal edge of the disc, this failure of the pigment epithelium and the choroid may be caused by a mechanical factor secondary to the progressive enlargement of the globe. Some temporal crescents are pigmented and some show vascular changes. This type of crescent results from the presence of choroidal vessels and choroidal pigmentation. The choroidal layer usually extends closer to the temporal edge of the disc than the pigment epithelium. Although most myopic crescents are located temporally, in 10 percent of cases they can surround the entire disc (Fig. 2). In other cases they can extend even into the macular region. In rare cases the myopic conus can be located on the nasal side of the disc, sometimes called inverse myopia. In other instances it may be present inferiorly in the form of an inferior crescent. The one factor separating a myopic from a temporal crescent is that the latter is stationary throughout life, whereas the former tends to progress in size and shape [1].

The Choroid

Choroidal atrophy frequently occurs in the posterior pole and is a common finding in severe degenerative myopia. Choroidal vessels

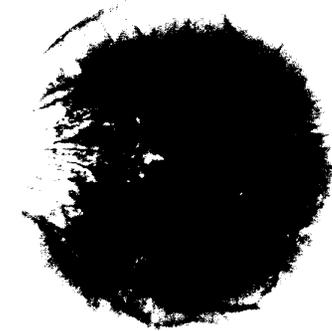


FIGURE 3. Red-free photograph of tessellated fundus with Fuchs' spot in fovea.

become quite visible because of the alteration and attenuation of the retinal pigment epithelium. Later, the choroidal vessels and melanocytes disappear, exposing numerous areas of discrete white sclera. Throughout the posterior pole may be proliferation of the pigment epithelium, with clumping in association with other areas of hypopigmentation. Frequently in myopic eyes there is a degree of pallor or tessellation of the fundus, where there is an increase in visibility of choroidal vessels through a thin retinal pigment epithelium (Fig. 3). This type of pallor is often seen inferior to the disc and the lower fundus; however, in very high myopes the degree of pallor may even cause the diagnosis of albinism to be considered [1].

The Retina

One of the most frequent changes seen in high myopia is a straightening of the retinal arterioles and venules. Other retinal changes involving the posterior pole are microcystic degeneration and generalized thinning, with a propensity for retinal hole formation and eventual detachment. Rhegmatogenous retinal detachment, one of the most common complications of high myopia, shows a tendency in those patients with the highest degree of myopia. The significant percentage of detachment is probably the result of peripheral retinal degeneration coupled with degeneration of the vitreous.

MACULAR FINDINGS

Those patients with the pathological type of high myopia will acquire developmental and degenerative changes in the macular area. Degeneration may be the result of aging plus secondary vascular changes. Developmental changes may be secondary to the biomechanical alterations in the eye, and include localized hypopigmentation, pigment clumping, posterior staphyloma, and lacquer cracks [23].

Lacquer cracks are some of the most important of the developmental changes. They represent breaks in the retinal pigment epithelium and Bruch's membrane. They are found exclusively in the posterior pole, frequently in association with a posterior staphyloma [13]. Their shape is linear or stellate, and bare sclera is often visible. Fluorescein angiography will show pseudofluorescence, with faint hyperfluorescence in the late venous stage. The lacquer cracks must be differentiated from two similar diseases of Bruch's membrane: angioid streaks and choroidal ruptures. Angioid streaks have a similar fluorescence; however, they usually emanate from the disc, and tend to be straighter. Choroidal ruptures are associated with a history of trauma, and are generally crescentic with the disc. Lacquer cracks may be the sources of subretinal neovascularization or hemorrhage (Fig. 4). These developmental changes may be related

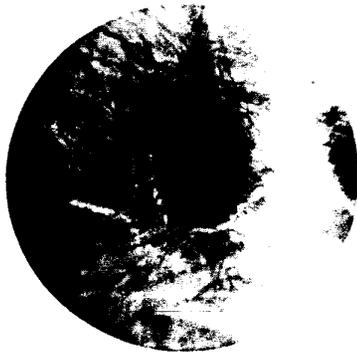


FIGURE 4. Red-free photograph demonstrating lacquer cracks (white lines). These lines, which often radiate from the macular region, represent small breaks in Bruch's membrane and the retinal pigment epithelium.



FIGURE 5. A myopic eye with generalized diffuse hypopigmentation of the macular region.

to decreased central visual acuity; however, the cause is often the degenerative change associated with lacquer cracks [13].

The finding of diffuse retinal pigment epithelial thinning is significant. It reflects the pathological distortion of the retinal pigment epithelium from the stretching of the neuroepithelial elements (Fig. 5). It is of interest to note that Black and associates found that the electrooculogram, a test that reflects the overall function of the retinal pigment epithelium, was diminished in the majority of high myopes [2]. Krill and Archer [14] state that the test has not been useful in differentiating between those children who will develop myopic degeneration from those who will remain stable. A reduced electroretinogram has been found in degenerative myopia, but not in the developmental stages. The scotopic function of the high myope is normal until the end stages.

Posterior staphylomas are of major significance. They represent an ectasia that includes all layers from the sclera to the retina (Fig. 6), usually located in the posterior pole [6]. Vision is generally decreased in patients with staphylomas in this area.

Focal areas of hypopigmentation can occur in the macula. If the foveal area is involved visual acuity may be affected.

Occasionally, a simple macular hemorrhage can occur in the 30- to 40-year age group in many myopes. This type of hemorrhage must be distinguished from Fuchs' spot, which carries a more



FIGURE 6. A highly myopic eye with staphyloma just temporal to the right disc. At the edge of the staphyloma is a discrete region of depigmentation (arrows).

guarded prognosis. The simple macular hemorrhage can absorb spontaneously, whereas Fuchs' spot is usually progressive (Fig. 7). If the foveal area is involved, central visual acuity may be affected.

Degenerative changes tend to be secondary either to aging and vascular changes affecting the posterior pole, or to an abiotrophy independent of the developmental changes. Degenerative changes

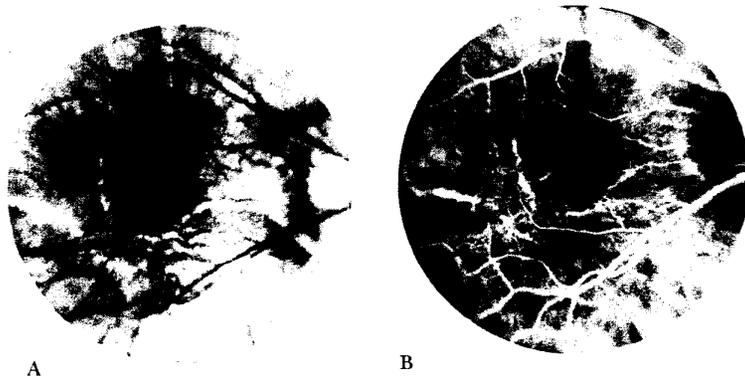


FIGURE 7. (A) Red-free photograph shows intraretinal hemorrhage and lacquer cracks. (B) Following spontaneous clearing of intraretinal hemorrhage, the fluorescein angiogram shows no evidence of subretinal neovascularization.

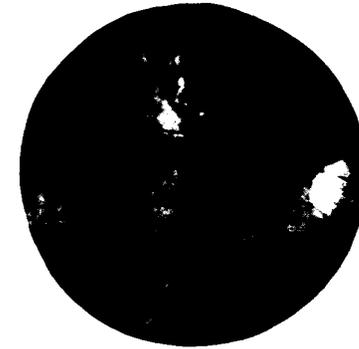


FIGURE 8. Red-free photograph shows Förster-Fuchs' spot associated with a choroidal hemorrhage in a tessellated fundus.

include pigmentary alterations in the macula, subretinal neovascularization, macular scars, and central macular atrophy of the retinal pigment epithelium (central areolar choroidal atrophy).

The Förster-Fuchs' spot is a dark spot in the macula that may be associated with a choroidal hemorrhage (Fig. 8). It was first described by Förster in 1862 [8] and later studied extensively by Fuchs in 1901 [9]. The color, shape, and size of Fuchs' spot may vary, depending on transudation, hemorrhage, and degree of degeneration of lipofuscin and melanin. In general, the younger the patient, the smaller the spot. As time progresses it can enlarge, depending on the size of the subretinal neovascularization (Fig. 9). Histopathologically, the lesion consists of a localized ingrowth of fibrovascular tissue from the choroid and proliferation of the pigment epithelium [10]. Hyperpigmentation without subretinal neovascularization may be present, although the reason for this is not known (Fig. 10). The fluorescein angiogram of a Förster-Fuchs' spot with subretinal neovascularization shows a serous or hemorrhagic pattern, with a subretinal neovascular net [15] (Fig. 11). Macular scars may be the residual of a Fuchs' spot (Fig. 12).

Central macular degeneration represents atrophic changes in the choriocapillaris, with visibility of the large choroidal vessels. The pathogenesis is believed to be atrophy of the larger and medium-sized choroidal vessels. This tends to lead to loss of the choriocapil-



FIGURE 9. (A) Red-free photograph of a myopic right eye with subretinal hemorrhage and generalized tessellation of the fundus. Note large choroidal vessel visible against white background. (B) Fluorescein angiogram of same eye shows large subretinal neovascularization.



FIGURE 10. Red-free photograph of pigment epithelial alterations and clumping in macular region, without the presence of subretinal neovascularization.

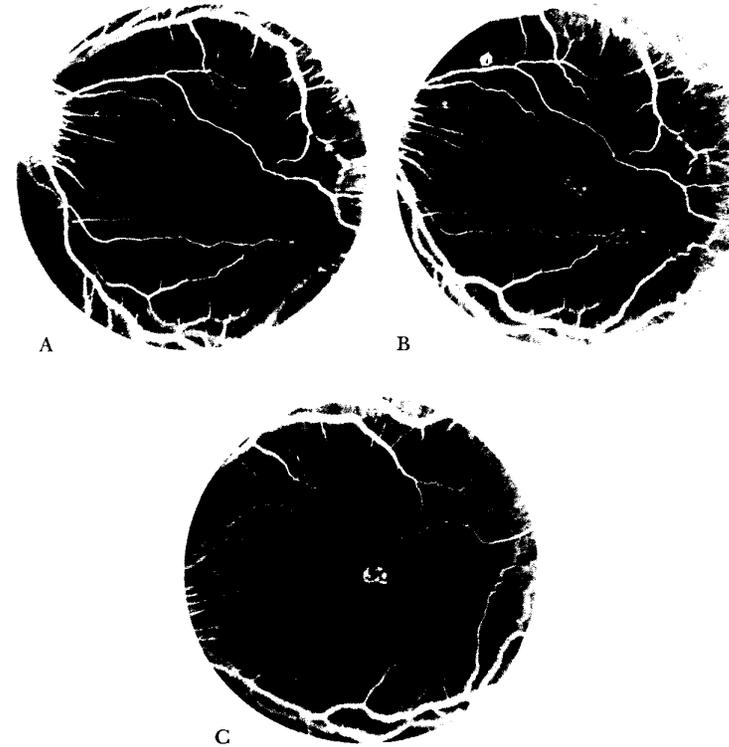


FIGURE 11. (A) Fluorescein angiogram of Fuchs' spot in eye depicted in Figure 3. (B) Early arteriovenous phase in same eye shows early hyperfluorescence in macular area. (C) Midvenous phase shows increased fluorescence in foveal area.

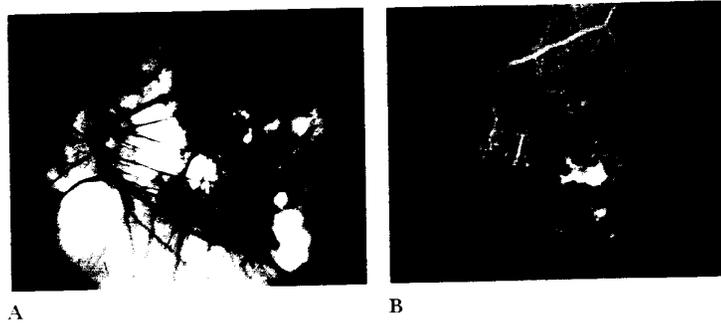


FIGURE 12. (A) Red-free photograph shows tessellation of the fundus, focal peripapillary areas of depigmentation at temporal and inferior portions of the disc, and atrophic areas in macular region in association with Fuchs' spot. (B) Fluorescein angiogram in late venous phase demonstrates hyperfluorescence of the fibrovascular scar in the foveal region.

laris, with resulting retinal pigment epithelial mottling and atrophy. An alternative hypothesis suggests that the initial change is in the retinal pigment epithelium, with secondary loss of the choriocapillaris and choroidal vessels (Figs. 13, 14, 15). The differential diagnosis of central areolar atrophy includes central areolar choroidal degeneration; macular holes in myopia are from the tractional effects of a posterior vitreous detachment [23].

We believe the occurrence of macular holes is rare in myopia; however, when holes do occur they may result in significant reduction in central visual acuity.

The schema depicted in Figure 16 was developed to show the possible relationship of the developmental and degenerative changes in myopia.

During the past five years, 85 patients have been referred for evaluation because of high myopia and decreased vision. Of these, 140 eyes had vision less than 20/60. Table 1 reflects the various pathological abnormalities present at the time of the evaluation. The most common abnormality in our series was thinning of the retinal pigment epithelium, which was present in every patient examined, and was found to be the only abnormality in 44.2 percent

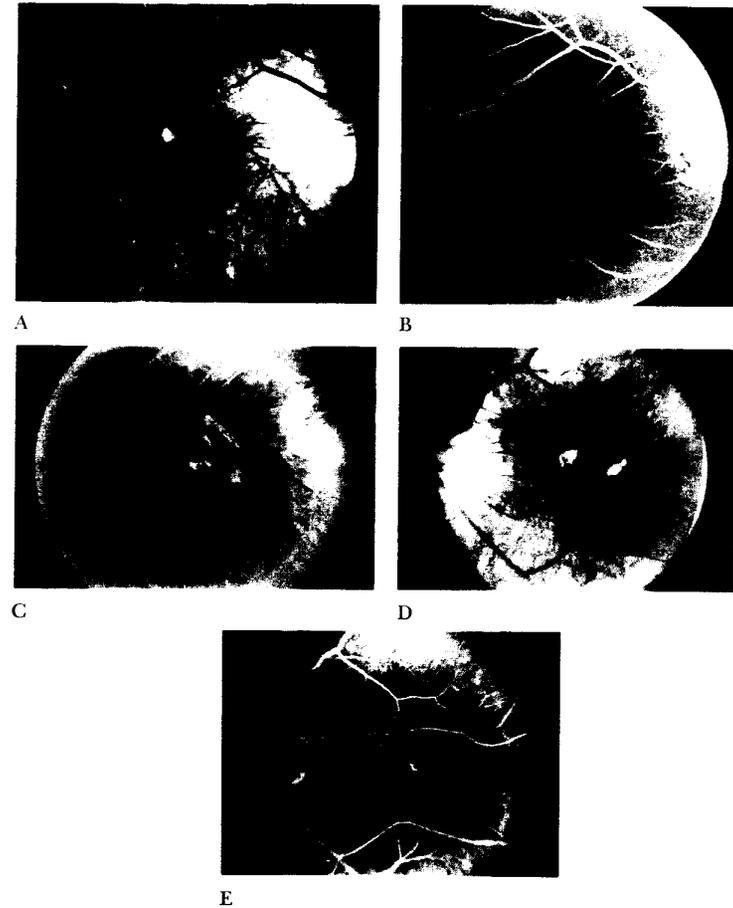


FIGURE 13. (A) Red-free photograph of the right eye shows an area of hypopigmentation surrounded by a circular area of pigmentation. There is some tessellation of the fundus inferior to the macular region. (B) Fluorescein angiogram of same eye shows pigment epithelial window defects from focal areas of hypopigmentation. (C) Same patient 4 years later showing a definite area of atrophy of retinal epithelium and choroidal capillaries with a central area of scarring, probably representing an old Fuchs' spot. (D) Same patient, baseline photograph of left eye at initial examination. Note 2 areas of focal depigmentation in macular region. (E) Fluorescein angiogram of same eye at initial examination shows 2 large areas representing pigment epithelial window defects.



FIGURE 14. Large area demonstrates loss of choriocapillaris with subretinal neovascularization.

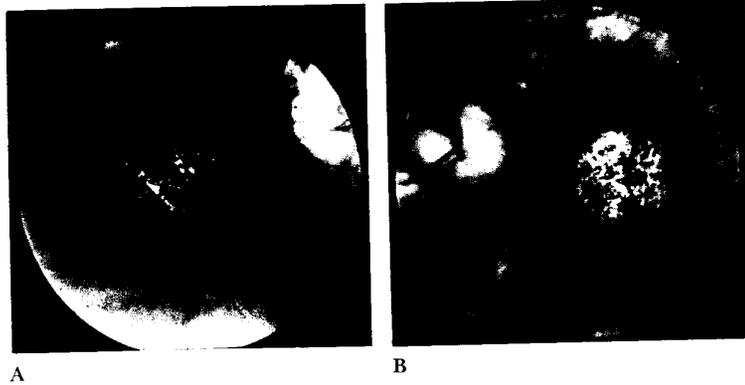


FIGURE 15. (A) Large, discrete geographical loss of the retinal pigment epithelium in the choriocapillaris. (B) Fellow eye of same patient, with symmetrical lesion in left macular area. Areas of pigment clumping are in center of geographical lesion.

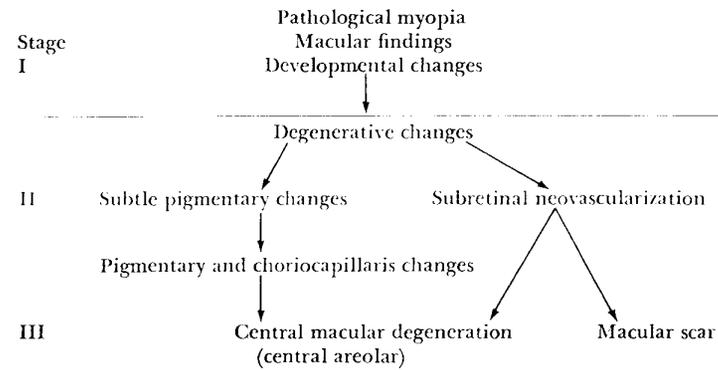


FIGURE 16. Relationship of developmental and degenerative changes in myopia.

of the referred patients. Fuchs' spots, lacquer cracks, and posterior staphylomas were the next most frequent findings. That no patients were referred for a macular hole associated with a myopic fundus is significant. According to Figure 16, overlap occurs because patients who may have lost some central vision in the earlier developmental stage were found to have a degenerative complication. This summary shows the relative incidence of each finding for a five-year period.

Our findings correlate with those of Curtin and Karlin [5], who studied the correlation of myopic fundus changes with axial length measurements. They found a Fuchs' spot in 5.2 percent of all patients; this amount increased in older persons. Posterior staphylomas were present in 19 percent of patients with axial lengths greater than 26.5 mm. They found lacquer cracks in 4.3 percent of all patients with axial lengths greater than 26.5 mm.

TREATMENT

Laser therapy has been successfully used to treat subretinal neovascularization when the foveal area has not been involved. In

TABLE 1. *Myopic macular degeneration*

Condition	No. of Patients	% All Patients
Total patients	85	
Unilateral myopia	30	35.2
Bilateral myopia	55	64.7
		% All Eyes
Total eyes	140	100
Fuchs' spot	25	17.8
Lacquer cracks	13	9.2
With neovascularization	3	2.1
Posterior staphyloma	31	22.1
RPE thinning only	62	44.2
Macular scar	5	3.5
Central macular degeneration	5	3.5
Macular holes	0	0

Figure 17 a subretinal neovascular net (Fuchs' spot) can be seen in the posterior pole and encroaching on the fovea. Visual acuity was reduced to 20/60 at this time. Fluorescein angiography shows leakage of dye into the foveal area (Fig. 18). The patient was treated with argon laser photocoagulation. Figure 19 shows the same patient, approximately two months after treatment. There is obliteration of the subretinal neovascularization, and no leakage of dye into the foveolar area. Central visual acuity improved to 20/40. Photocoagulation is only useful if the foveal area is not involved.

CONCLUSION

Myopia encompasses a variety of different entities ranging from simple myopia, which may be caused by small increases in axial length or changes in the curvature of the refracting tissues in the eye, to severe pathological myopia with large increases in the axial length and abnormal structural changes in the retinal and choroidal tissues. High myopia is a significant cause of blindness throughout



FIGURE 17. *Midvenous stage of fluorescein angiogram, showing hyperfluorescence from subretinal neovascularization.*

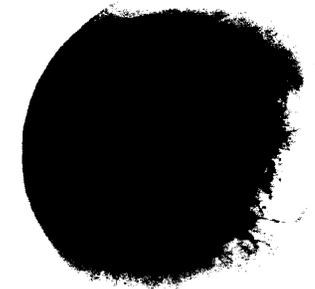


FIGURE 18. *Late venous stage of angiogram shows diffuse leakage of dye into foveal area, causing reduction in central visual acuity.*



FIGURE 19. *After treatment with argon laser photocoagulation there is obliteration of subretinal neovascularization.*

the world. We have found that while stretching of the retinal pigment epithelium may itself cause a decrease in central visual acuity, degenerative complications that may develop at a later stage are a more severe risk to central visual acuity. Continued observation of patients with developmental change is therefore important in high myopia, since a degenerative vascular change may be treatable with argon laser photocoagulation, preventing subsequent loss of vision.

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Quality of life in myopia

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Abstract

Background—The safety and predictability of refractive surgery for all degrees of myopia is now becoming established. It is therefore appropriate to evaluate whether there is a patient driven demand for such treatments and, if so, to establish guidelines for its provision within the National Health Service (NHS).

Methods—A comparative study was designed to assess the effect of degree of myopia on quality of life ("high" (n = 30) -10.00D, worse eye; "moderate" (n = 40) -4.00 to -9.75D, worse eye; "low" (n = 42) <-4.00D, worse eye) compared with a group of patients with keratoconus (n = 30) treated by optical correction. Data collection included binocular logMAR visual acuity, Pelli-Robson low contrast letter sensitivity, questionnaires to assess subjective visual function (VF-14) and effect on quality of life (VQOL), and semi-structured interviews.

Results—There were no significant differences in any of the measures between patients with a high degree of myopia and those with keratoconus, or between those with a low and those with a moderate degree of myopia. However, those with a high degree of myopia had highly significantly poorer logMAR, VF-14, and VQOL scores than those with low and moderate myopia (p<0.001). Interview data supported these findings with patients with a high degree of myopia and those with keratoconus reporting that psychological, cosmetic, practical, and financial factors affected their quality of life.

Conclusion—Compared with low and moderate myopia, patients with a high degree of myopia experience impaired quality of life similar to that of patients with keratoconus. Criteria should therefore be identified to enable those in sufficient need to obtain refractive surgical treatment under the NHS.

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Myopia affects 25% of the population in western industrialised societies and has a potentially negative effect on self-esteem, career choice, and ocular health.^{1,2} Despite the fact that the experience of being myopic appears to include a psychosocial component, the authors are unaware of published studies which indicate whether or not subjects with myopia feel that they have a significantly impaired quality of life.³

At present much of the interest in myopia centres around the nature versus nurture

debate⁴ and evaluation of new treatments such as photorefractive keratectomy (PRK), laser in situ keratomileusis (LASIK), and phakic lens implant. Although the evidence as to whether LASIK should replace PRK for any particular range of myopia is still not conclusive,⁵ most patients who present for laser treatment are seemingly satisfied with the outcome,⁶⁻⁸ including patients with higher degrees of myopia who undergo LASIK.⁹⁻¹¹

Patients who undergo such treatments are essentially a self selected group and therefore do not provide representative information on what it is like to live with myopia of different degrees or whether there is a patient driven need for provision of such treatments.

A study was therefore designed with the following objectives: (1) to assess the effect of myopia and its degree on quality of life in spectacle and contact lens wearers; (2) to compare the quality of life in patients with myopia with that in patients with keratoconus (a group of patients who suffer refractive change warranting ophthalmic management, including surgery, under the NHS); and (3) to inform future research into, and implementation of, alternative treatments for myopia.

Patients and methods

A comparative design was adopted consisting of the following four groups of adult patients aged between 18 and 65:

Group 1: High degree of myopia (refractive error ≥ -10.00 D, worse eye; ≥ -8.00 D, better eye; < 2.00 D anisometropia);

Group 2: Moderate degree of myopia (-4.00D to -9.75D, worse eye; ≤ 2.00 D anisometropia);

Group 3: Low degree of myopia (-1.50D to -3.75D, worse eye; at least -1.00D, better eye; ≤ 2.00 D anisometropia);

Group 4: Patients with bilateral keratoconus requiring correction by contact or spectacle lenses.

Data collection took place between February and October 1998. Patients in groups 1, 2, and 3 were recruited from five optometric practices covering areas of differing socioeconomic affluence in the Manchester area. Patients were eligible for inclusion if they had undergone a routine eye test in the previous 2 years, met a minimum best corrected visual acuity of 6/12 in the worse eye, and had not put themselves forward for laser treatment; those meeting the inclusion criteria were invited by letter to participate. In group 4, 32 consecutive patients attending the optometry department at Manchester Royal Eye Hospital (MREH) who met a minimum best corrected visual acuity of 6/18 in the worse eye and were deemed "stable" in

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that refitting of lenses had not been required for at least 6 months were invited to take part. In all groups patients with a history of ocular comorbidities, previous ocular surgery, or diabetes were excluded. Approval was obtained from the local research ethics committee.

Patients with myopia were assessed at their optometrist's practice and those with keratoconus at MREH. All the patients wore their habitual spectacle or contact lens correction for assessment so that the data might better reflect their "real world" visual experience.

The patients were assessed by a single researcher as follows: binocular logMAR visual acuity, Pelli-Robson low contrast letter chart (both charts illuminated to a minimum of 120 cd/m²), questionnaires evaluating subjective visual function (VF-14)¹² and vision related quality of life (VQOL),¹³ semi-structured interviews, and estimation of cost of prescriptions to patients.

The scoring ranges for the quantitative measures were as follows:

- (1) LogMAR: a score of 0.0 is equivalent to 6/6 vision, with minus scores indicating better vision and plus scores indicating poorer vision;
- (2) Pelli-Robson low contrast letter chart: scores range from 0.00, rising in intervals of 0.15 to 2.25, higher scores indicating more acute perception;
- (3) VF-14: score range 0–100. The lower the score, the more difficulty the respondent has performing activities tested;
- (4) VQOL: score range 0–5. High scores indicate poorer vision related quality of life.

The interviews consisted of a structured component where patients were asked about

their preferred form of optical correction, its cost, and about their knowledge of and interest in laser treatment of short sightedness. To complement the quantitative data collection methods¹⁴ patients were also asked the open question: "Do you feel that being short sighted has affected your work, your personal life or your social life in any way either now or in the past?"

Results

SAMPLE

One hundred and twelve patients with myopia who met the inclusion criteria were interviewed (28% response rate). These were divided into groups by degree of refractive error in the worse eye, as described above. Table 1 shows the numbers, age, sex, and mode of lens correction (spectacles or contact lenses) for each of the groups.

STATISTICAL RESULTS

The mean scores for binocular logMAR visual acuity, binocular Pelli-Robson low contrast letter sensitivity, VF-14, and VQOL are shown in Table 2. Statistical analysis of these variables showed that only the variable logMAR was normally distributed. A one way ANOVA (significant at the 0.05 level, 95% confidence interval) was used to test the differences in visual acuity between the four groups (Table 3). Patients in group 1 (high myopia) had highly significantly poorer binocular visual acuity than those with both low and moderate myopia ($p < 0.001$). Patients in group 4 (keratoconus) had significantly poorer acuity than those with low ($p = 0.001$) and moderate ($p = 0.028$) myopia. There was no significant difference in visual acuity between those with a high degree of myopia and those with keratoconus ($p = 0.189$), or between those with low and those with moderate myopia ($p = 0.636$).

All other variables were not normally distributed. Mann Whitney tests were employed at a reduced level of significance ($p < 0.01$) to reduce the likelihood of making a type I error. The following results are all presented at this level (Table 3).

There were highly significant differences ($p < 0.001$) between patients in group 1 (high myopia) and those in group 3 (low myopia) with respect to subjective visual function (VF-14) and vision related quality of life (VQOL), with those with a high degree of myopia being disadvantaged on both measures. Low contrast letter sensitivity was of borderline significance ($p = 0.01$), patients with a high degree of myopia scoring less well than those with a low level of myopia.

Patients with a high degree of myopia also fared worse than those with a moderate degree of myopia (group 2) with significantly poorer VF-14 and VQOL scores ($p < 0.001$) and a contrast sensitivity score again approaching significance ($p = 0.013$). There were no significant differences on any of the measures between patients in group 1 (high degree of myopia) and those in group 4 (keratoconus).

Compared with patients in group 3 (low myopia), patients with keratoconus had signifi-

Table 1 Age, sex, type of lens correction

	Age			Sex		Lens	
	Mean	Median	Range	M	F	Spectacle	Contact
Group 1 (n=30)	45	46	21–64	8	22	19	11
Group 2 (n=40)	42	43	18–65	12	28	26	14
Group 3 (n=42)	41	43	18–60	12	30	26	16
Group 4 (n=30)	35	32	24–60	22	8	3	27

Table 2 Mean and median scores by group for logMAR, low contrast letter sensitivity, VF-14, and VQOL

	Group 1	Group 2	Group 3	Group 4
logMAR				
Mean	0.12	-0.04	-0.08	0.05
Median	0.12	-0.03	-0.10	0.02
Contrast (range 0–2.25)				
Mean	1.77	1.89	1.89	1.81
Median	1.80	1.95	1.95	1.80
VF-14 (range 0–100)				
Mean	83.90	94.70	97.02	89.84
Median	89.25	95.05	98.10	93.05
VQOL (range 0–5)				
Mean	1.31	0.44	0.42	0.79
Median	1.20	0.25	0.20	0.60

Table 3 Between groups comparison of statistical significance of logMAR, low contrast letter sensitivity, VF-14, and VQOL

	Group					
	1 v 2	1 v 3	1 v 4	2 v 3	2 v 4	3 v 4
logMAR ($p < 0.05$)	<0.001	<0.001	0.189	0.636	0.001	0.028
Contrast ($p < 0.01$)	0.013	0.010	0.650	0.814	0.015	0.010
VF-14 ($p < 0.01$)	<0.001	<0.001	0.087	0.013	0.088	<0.001
VQOL ($p < 0.01$)	<0.001	<0.001	0.037	0.222	0.025	0.005

cantly poorer VF-14 scores ($p < 0.001$), a significantly poorer VQOL score ($p = 0.005$), and borderline lower contrast sensitivity ($p = 0.01$). However, compared with group 2 (moderate myopia), keratoconus patients showed no significant differences on any of the measures tested, although contrast sensitivity was reduced to a level approaching significance ($p = 0.015$). There were no statistically significant differences between patients in groups 2 and 3 (moderate and low myopia) on any of the variables.

INTERVIEW FINDINGS

All patients took part in interviews. These consisted of a structured part where patients were asked their preferred method of optical correction (Table 1) and how much this had cost (Table 4). It was found that patients with a high degree of myopia spent more money on spectacles than those with low or moderate myopia, even taking into account that they were entitled to vouchers to help with the cost of complex lenses. All groups were comparable in the amounts they spent on contact lenses and solutions, although it should be noted that patients with keratoconus tended to have to buy lenses more frequently than those with myopia because the fitting changed more rapidly as a result of disease progression.

All the patients with myopia were also asked whether they had heard of laser treatment for short sightedness and, if so, whether they would ever consider it themselves (Table 5). At least 90% knew that laser treatments existed, more in the groups with high and moderate degrees of myopia. These two groups of patients also expressed more interest in having the treatment, although many of those who were interested expressed reservations on the long term effects. In addition, the cost of such treatment was seen as prohibitive.

The unstructured part of the interviews was analysed qualitatively.¹⁵ Patients with a low degree of myopia were the most likely to make extreme statements about their short sight, while those with a moderate degree of myopia tended to play down the effect of their vision on daily functioning. Patients with a high degree of myopia and those with keratoconus were the most likely to cite concrete instances of how their eyesight adversely affected their lives. Examples fell into the following categories:

psychological, cosmetic, practical, and financial.

Many patients with a high degree of myopia reported that their eyesight dominated their lives from an early age. In many this led to a lack of self confidence because of teasing and feelings of inadequacy; this, in turn, could lead to social isolation and difficulties forming relationships. In others it led to a determination to succeed at activities that did not require perfect distance vision.

The psychological effects of a high level of myopia were augmented by cosmetic and financial factors. Many commented on their dislike of wearing thick spectacle lenses which were felt to be unsightly and a social handicap. Contact lenses were seen to have revolutionised the situation for those who could wear them, and wearers of high index spectacle lenses also commented on the positive cosmetic and social effects of their lighter, thinner lenses. However, the high cost of the latter, especially for higher prescriptions, limited the numbers who were able to take advantage of this option. The type of spectacle frame capable of supporting strong, complex lenses further restricted choice for those with a high degree of myopia, and several of the older individuals commented that years of wearing heavy glasses had damaged the skin on the bridge of the nose, further reducing options of what they could wear.

Both patients with a high degree of myopia and those with keratoconus commented that central distance vision was not the only factor in their visual experience. Practical difficulties were experienced in relation to discomfort in wearing contact lenses (especially patients with keratoconus), and with respect to peripheral vision (spectacle wearing patients with a high degree of myopia). In these groups the extreme dependence on optical correction for any kind of normal functioning was a constant daily concern. Difficulties in participating in sports such as swimming, football, cricket, and tennis were also frequently cited.

Discussion

SIGNIFICANCE OF FINDINGS

The quantitative results of this study show that higher degrees of myopia have an adverse effect on quality of life that is comparable to that of patients with an eye disease such as keratoconus which is widely accepted to be visually disabling and warranting management, including surgery, under the NHS. The visual disability of patients with a high degree of myopia and its effect on quality of life is further shown when comparisons are made with other groups. Both patients with keratoconus and those with a high degree of myopia were disadvantaged compared with those with a low degree of myopia. However, compared with patients with moderate myopia, those with keratoconus had no significant differences in any of the outcome measures while those with a high degree of myopia reported significantly reduced quality of life on all measures with the exception of low contrast letter sensitivity, which was borderline. The interview data sup-

Table 4 Average cost to patients per annum (by group) of purchasing habitual form of optical correction

	Spectacles	Contact lenses
Group 1	£230	Lenses £60, solutions £120
Group 2	£130	Lenses £80, solutions £95
Group 3	£90	Lenses £90, solutions £100
Group 4	£100	Lenses £140, solutions £120

Table 5 Patients with myopia aware of or willing to consider laser treatment

	Aware	Consider
Group 1 (n=30)	29 (97%)	16 (55%)
Group 2 (n=40)	38 (95%)	24 (60%)
Group 3 (n=42)	38 (90%)	9 (24%)

port the case that higher degrees of myopia are visually, personally, and financially disabling. The fact that patients with a high or moderate degree of myopia were much more likely to consider laser treatment also indicates that many of those who are significantly myopic feel that their needs are not being adequately met by current management methods.

LIMITATIONS OF STUDY

The low response rate among patients with myopia invited to participate in the study may have resulted in a bias towards those who are more conscious of their health and its effect on quality of life. Despite the fact that there appeared to be little variation between responders and non-responders in terms of age or post code, when evaluating the findings of the study it must be accepted that participants were to some extent a self selected rather than a representative group.

In assessing the significance of the results, the wide range of refractive error in the groups with a moderate and high degree of myopia should be considered. In addition, there is no "clear water" between groups so that those at the "high" end of one group may have a very similar degree of refractive error to those at the "low" end of another group.

The predominance of men (2:1) in the keratoconus group was predictable.¹⁶ The predominance of women in the myopia group is less easy to explain, although it was the researcher's impression that women were more flexible in arranging appointments and that more women may therefore have participated simply for logistical reasons.

One aspect of the study which merits further investigation is the findings related to binocular logMAR visual acuity. Despite the fact that the Snellen visual acuity entry criterion was included to ensure that all participants had broadly comparable best corrected distance vision, patients with a high degree of myopia exhibited significantly poorer binocular logMAR scores. One interpretation could be that the reduced performance of this group in relation to other variables was therefore simply a result of poorer corrected vision. However, this is countered to some extent by the fact that, although those with a high degree of myopia recorded poorer logMAR visual acuity scores than other patients with myopia, their results were comparable to the keratoconus group who had a less stringent Snellen acuity entry criterion, indicating that monocular Snellen acuity and binocular logMAR acuity may not be inextricably linked, but rather provide complementary information about visual status. In

addition, it should be remembered that, in the study, "real life" visual experience was the variable being measured rather than best possible achieved vision.

CONCLUSIONS

Research is needed to replicate and refine this study to elaborate the needs of this group of patients. In particular, studies are required which differentiate between the experiences of non-presbyopic and presbyopic patients with myopia.

The results of this study indicate that high myopia has an adverse effect on quality of life. If refractive surgery has reached an acceptable level of safety and predictability, then it can be argued that the time has come to define criteria which would facilitate treatment of patients with myopia according to need—that is, within the NHS.

Note added at proof stage:

The VQOL questionnaire is now referred to as the VCM1 (Frost NA, Sparrow JM, Durrant JS, et al. Development of a questionnaire for measurement of vision-related quality of life. *Ophthalmic Epidemiol* 1998;5:185–210).

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Interventions to Retard Myopia Progression in Children

An Evidence-based Update

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Topic: To evaluate the efficacy of interventions such as eyedrops, bifocal lenses, or contact lenses in retarding the progression of myopia in myopic children.

Clinical Relevance: Myopia is a common ocular disorder, and high myopia (myopia at least -6.0 diopters) is associated with potentially blinding conditions. At present, there are no general guidelines on interventions that may decrease myopia progression in children, but some interventions such as contact lenses are offered on an ad hoc basis.

Methods or Literature Reviewed: English and non-English language articles published from 1968 to 2000 were retrieved using a keyword search of MEDLINE, Embase, Cochrane Library, and Science Citation Index databases. Randomized controlled trials with comparisons of the effectiveness of interventions to decrease myopia progression in myopic children were reviewed.

Results: Ten clinical trials of different interventions to retard myopia progression were reviewed, including three trials that evaluated atropine and one trial that evaluated soft contact lenses. Atropine eye drops of 0.5% concentration were effective in clinical trials, but no significant effect was found for tropicamide or timolol eyedrops. Five of the six trials on bifocal spectacle lenses with various additions failed to show significant retardation, and results of the remaining trial were barely significant ($P = 0.047$). A trial of soft contact lenses failed to show significant effects.

Conclusions: The latest evidence from randomized clinical trials does not provide sufficient information to support interventions to prevent the progression of myopia. Long-term large-scale double-masked randomized clinical trials, including cycloplegic refraction, are needed before any recommendations about interventions in clinical practice to prevent high myopia in myopic children are considered. *Ophthalmology* 2002;109:415-427 © 2002 by the American Academy of Ophthalmology.

The prevalence rates of myopia are rising rapidly in several Asian countries.¹⁻³ In Taiwan, Hong Kong, and Singapore the prevalence rate of myopia in young adults is 60% to

80%; in the United States and Europe the prevalence rate in older adults is 20% to 50%.^{1,2,4-6} The rate of progression of myopia is highest in young children, and the average age of stabilization of myopia is approximately 16 years. The onset of myopia may occur at a relatively young age, leading to higher risks of high myopia (myopia at least -6.0 diopters [D]) in adulthood.¹ High myopia is associated with potentially blinding complications, such as retinal detachment and glaucoma.^{7,8} Often, the quality of life and daily visual activity of high myopes are compromised.⁹ Complications of high myopia impact individuals at a time when they are economically active. As such, the socioeconomic effects of high myopia are huge. These factors imply that the prevention of myopia is of utmost importance.

There are many hypotheses that attempt to explain the development and progression of axial myopia. Suggested mechanisms for the development of myopia include excessive accommodation and uncoordinated eye growth medi-

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ated by retinal signals as a response to prolonged near-work.^{10,11} In addition, the genetic basis of myopia has yet to be fully explained.

Various studies have suggested several interventions that may retard the progression of myopia in children, thereby decreasing the severity of myopia at maturity. Contact lenses may flatten the cornea or may retard axial elongation.¹² As a muscarinic antagonist, atropine may act through muscarinic receptors to paralyze accommodation; or it may have a direct effect on scleral growth.¹³ Adrenergic or β -blocking drugs may reduce raised intraocular pressure in high myopes.^{14,15} Bifocal lenses may reduce defective accommodative effort and improve retinal image quality in patients with high accommodative lag, thereby preventing potential aberrant eye growth.¹⁶

As conflicting results have been published in the literature, the clinician has been hard pressed to recommend any particular measure to prevent or retard the progression of myopia in children. The purpose of this study is to compile the latest evidence from all relevant randomized clinical trials evaluating interventions that could potentially decrease the progression rate of myopia in myopic children. Recommendations for each intervention have been made, and the strength of the evidence for each intervention is shown. Additional details will be presented in the Cochrane Review now in preparation.

Sources and Methods of Literature Search

Search Strategy for the Identification of Studies

A comprehensive search was conducted to identify all relevant randomized clinical trials with the primary objective of evaluating interventions to retard the progression of myopia in myopic children. Several databases (MEDLINE using PubMed, Embase, and Cochrane Collaborations) were searched (1968–2000) to identify English and non-English language articles on intervention studies in children to retard myopia progression. The search used the keywords *myopia*, *short-sightedness*, *near-sightedness*, or *myopia control*, combined with *progression of myopia* or *myopia prophylaxis* or *myopia prevention*. The publication type was limited to *clinical trials*. A total of 83 abstracts were found. Three different investigators (SMS, EC, AK) performed the search, and independent reviews of the abstracts were done. Two of the three reviewers were trained epidemiologists (SMS, EC), the third reviewer was an ophthalmologist (AK).

The bibliographies of existing reviews and retrieved articles were also reviewed to identify articles not captured by the different databases. Several drug companies involved in clinical trials for myopia control were contacted by mail or telephone to ask whether the company had conducted randomized clinical trials but had not reported their results. The proceedings of recent major international conferences on myopia research, such as the International Conference on Myopia and the Association for Research in Vision and Ophthalmology, were screened.

Criteria for Considering Studies for This Review

A total of 35 potentially relevant articles were retrieved. All three independent investigators (SMS, AK, EC) reviewed all articles to

identify randomized clinical trials conducted in myopic children with a main objective of the prevention of the progression of myopia. The investigators met to resolve any differences in the interpretation of the articles. Articles excluded from the study included retrospective studies, nonrandomized clinical trials, non-controlled clinical trials, short-term (<1 year) ocular outcome evaluations, or those in which the primary purpose of the trial was not the retardation of myopia progression. As a result, study interventions using behavioral vision training, ocular exercises, orthokeratology, prismatic lenses, monofocal convex lenses, and hydrogel lenses were excluded.^{17–20}

Data Extraction and Study Appraisal

Information on study design, conduct, outcomes, and analysis was documented on a data extraction form. Details include (1) study design: parallel or crossover randomized clinical trial; (2) masking: double, single or none; (3) method of randomization; (4) unit of randomization: eyes or patients; (5) description of intervention and control groups; (6) characteristics of study population; (7) similarity of the two groups at baseline; (8) equality of treatment for the two groups; (9) length of follow-up; (10) frequency of follow-up; (11) rate of loss to follow-up in each group; (12) whether intention-to-treat analysis was conducted; (13) eyes analyzed: right, left, worse, or average of two eyes; (14) outcome measures (e.g., change in refraction diopters per year [primary outcome]); and (15) adverse effects. Ten articles of randomized clinical trials were included, and, where necessary, we contacted the authors for further clarification and additional data. We grouped the articles according to the interventions: cycloplegic eyedrops, pressure-lowering eyedrops, bifocal spectacle lenses, or contact lenses. One article describing a randomized clinical trial of bifocal lenses and plus with prisms was not included, because the trial was conducted in adults (military academy students).²¹ The studies were appraised for methodologic quality using the recently revised Scottish Intercollegiate Guidelines Network methodology checklist for randomized controlled trials (Table 1).²²

Each article was rated according to the “strength of evidence” as recently defined by the American Academy of Ophthalmology’s glaucoma panel.²³ Level I indicates that the data provided strong evidence in support of the recommendation, that the design of the study addressed the issue in question, and that the study was performed in the population of interest and executed in a manner that ensured production of accurate and reliable data, using appropriate statistical methods. Level II indicates that the data provided substantial evidence in support of the recommendation but that the evidence lacked some qualities. Level III indicates a consensus of expert opinion in the absence of evidence that met the requirements of levels I and II. Recommendations for clinical outcomes were assessed as level A, B, or C.²³ Level A indicates that the recommendation is very important to clinical outcome; level B indicates that the recommendation is moderately important; and level C indicates that the recommendation is relevant but not critical.

Outcomes and Analysis

The primary outcome reported for subjects completing the study in each group was the mean progression rate of myopia (D per year) and its standard deviation. The progression of myopia was measured as the change in spherical equivalent cycloplegic

Table 1. Patient and Study Characteristics of the 10 Randomized Clinical Trials

Study	Study Score	Country	Methods	Masking	Total Randomized	Intervention
Eyedrops						
Yen 1989 ²⁴	+	Taiwan	Parallel RCT Baseline similar	No	247	1% atropine 1% cyclopentolate Normal saline*
Shih 1999 ²⁶	+	Taiwan	Parallel RCT Baseline similar	Single	200	0.5% atropine 0.25% atropine 0.1% atropine 0.5% tropicamide*
Shih 2000 [†]	+	Taiwan	Parallel RCT (central office)	Double	227	0.5% atropine Multifocals Single vision*
Schwartz 1981 ²⁷	+	USA (registry)	Baseline similar Parallel RCT in twins Baseline similar	Single (assessor)	26 pairs	1% tropicamide Single vision*
Bifocal lenses						
Grosvenor 1987 ³⁴	+	USA	Parallel RCT (random number table)	No	207	Bifocals + 2 D Bifocals + 1 D Single vision*
Parssinen 1989 ²⁵	+	Finland	Baseline similarity unknown Parallel RCT (sealed envelopes)	No	240	Bifocals + 1.75 D Single vision (distance only) Single vision*
Jensen 1991 ¹⁵	+	Denmark	Baseline similar Parallel RCT Baseline similar	No	150	Bifocals + 2 D Single vision + 0.25% timolol Single vision*
Fulk 1996 ²⁹	+	USA	Parallel RCT (sealed envelopes) Baseline similarity unknown	Single	32	Bifocals + 1.25 D Single vision*
Fulk 2000 ³⁰	+	USA	Parallel RCT Baseline similar	Double	82	Bifocals + 1.50 D Single vision*
Contact lenses						
Horner 1999 ³¹	-	USA	Parallel RCT Baseline similar	Single	175	Soft contact lenses Single vision*

*Control group.

[†]By Shih et al (Proceedings of the VIII International Conference on Myopia, 352-6, 2000).

D = diopters; RCT = randomized clinical trial.

refractive error and secondarily measured as a dichotomous variable (fast progressor: yes/no) in several studies. Fast progressors were defined as at least 0.25 D per year or at least 0.5 D per year.

Summary of Evidence

Of the 10 trials, 5 were three-arm parallel studies, 1 was a four-arm parallel study, 1 was a matched-pair (twin) study, and 3 were two-arm parallel studies (Table 1).^{15,24-34} There were seven comparisons of atropine eyedrops (three against tropicamide, one against cyclopentolate, and three against lenses), two comparisons of timolol eyedrops (against bifocals and single-vision spectacles); there were also seven comparisons of bifocals with various adds, one of multifocal lens alone and in conjunction with 0.5% atropine, and one of contact lenses (all against single-vision spectacles). All studies reported per protocol comparisons on subjects who completed the study. In seven studies the numbers analyzed were at least 80% (average, 91%; range, 83%-98%) of those randomized, with no significant differential dropout

rates among treatment groups. The three remaining studies analyzed fractions of 38%, 60%, and 74%, also with no significant differences across groups.^{24,31,34} The follow-up period varied from 1 to 3.5 years, with seven studies having at least 2 years of follow-up (Table 2). Frequency of follow-up visits varied from every 3 months to yearly (most common was every 6 months). We grouped the studies according to the interventions: cycloplegic eyedrops, pressure-lowering eyedrops, bifocal lenses, or contact lenses. We report on each separately.

Cycloplegic Eyedrops

An early study using a matched-pair design in 26 twins tested the combination of 1% tropicamide with bifocals against single-vision spectacles and found no significant difference (Table 2, Fig 1).²⁷ A range of atropine concentrations was tested in Taiwan; 1% atropine was quickly rejected from the experience of the Yen study (side effects of atropine included photophobia resulting in children stopping gymnastic classes and spending less time outdoors). Shih noted in a 1999²⁶ and a 2000 study (Proceedings of the

Table 2. Study Outcomes and Results of the 10 Randomized Clinical Trials

Study	Intervention	Cycloplegia?	Follow-up (years)	Group rates (Diopter/year)	Evidence*
Eyedrops					
Yen 1989 ²⁴	1% atropine	Yes	1.0	-0.22 (0.54) [†]	B, I
	1% cyclopentolate			-0.58 (0.49) [†]	
	Normal saline [‡]			-0.91 (0.58)	
Shih 1999 ²⁶	0.5% atropine	Yes	2.0	-0.04 (0.63) [†]	B, I
	0.25% atropine			-0.45 (0.55) [†]	
	0.1% atropine			-0.47 (0.91) [†]	
	0.5% tropicamide [‡]			-1.06 (0.61)	
Shih 2000 ⁸	0.5% atropine	Yes	1.5	-0.28 (0.05) [†]	B, I
	Multifocals			-0.79 (0.05)	
	Single vision [‡]			-0.93 (0.06)	
Schwartz 1981 ²⁷	1% tropicamide	Yes	3.5	Paired analysis	C, I
	Single vision [‡]				
Bifocal lenses					
Grosvenor 1987 ³⁴	Bifocals + 2 D	Yes	3.0	-0.32	C, I
	Bifocals + 1 D			-0.34	
	Single vision [‡]			-0.32	
Parssinen 1989 ²⁵	Bifocals + 1.75 D	Yes	3.0	-0.56 (0.3)	C, I
	Single vision (distance only)			-0.59 (0.3)	
	Single vision [‡]			-0.49 (0.3)	
Jensen 1991 ¹³	Bifocals + 2 D	Yes	2.0	-0.48 (0.28)	C, I
	Single vision + 0.25% timolol			-0.59 (0.30)	
	Single vision [‡]			-0.57 (0.36)	
Fulk 1996 ²⁹	Bifocals + 1.25 D	Yes	1.5	-0.39 (0.12)	C, I
	Single vision [‡]			-0.57 (0.11)	
Fulk 2000 ³⁰	Bifocals + 1.50 D	Yes	2.5	-0.40 (0.27) [†]	C, I
	Single vision [‡]			-0.50 (0.26)	
Contact lenses					
Horner 1999 ³¹	Soft contact lenses	No [§]	3.0	-0.36 (0.03)	C, II
	Single vision [‡]			-0.30 (0.03)	

*Importance to clinical outcome, strength of evidence.

[†]2 $P < 0.05$ for difference in myopia progression rates between the intervention and control group.

[‡]Control group.

[§]By Shih and colleagues (Proceedings of the VIII International Conference on Myopia, 352-6, 2000).

^{||}Noncycloplegic refractive measurements.

B = moderately important recommendation; C = relevant but not critical recommendation; D = diopters; I = strong evidence supporting recommendation; II = substantial evidence supporting recommendation but lacking some qualities required for strong support.

VIII International Conference on Myopia, 352-6, 2000) that a series of lower atropine concentrations were effective; the 0.5% atropine-bifocals group showed remarkably slow progression of myopia of -0.04 D per year compared with an average rate of -0.46 D per year for the 0.25% and 0.1% atropine groups.²⁶ Two children given 0.5% atropine in the Shih 1999²⁶ study complained of intolerable photophobia, but there were no notable side effects in the children given 0.25% and 0.1% atropine. Overall there is some evidence that regular application of atropine eyedrops can at least halve a baseline myopia progression of -1 D per year and halve the proportion of fast myopia progressors (progression at least -0.25 or -0.5 D per year). These studies need to be replicated in other countries with similarly high baseline myopia progression rates and in the West, where baseline rates seem to be less than half those recorded in the Taiwanese studies. Further studies on the short-term and long-term

side effects of the varying concentrations of atropine eyedrops are also needed.

Timolol Trial

The Danish study of 0.25% timolol maleate (a β -adrenergic blocking agent) against single-vision spectacles was reported twice and showed no retardation of progression (Table 2).^{15,32} Five children reported stinging sensations and discomfort of the eye; and one boy developed bronchial asthma.

Bifocal Lens Trials

A range of near vision additions (+1.00 to +2.00 D) was tested, but only the +2.00 D intervention was replicated^{13,34}; control group progression rates were similar among all studies (-0.32 to -0.57 D/year) (Table 2, Fig 1).^{32,34}

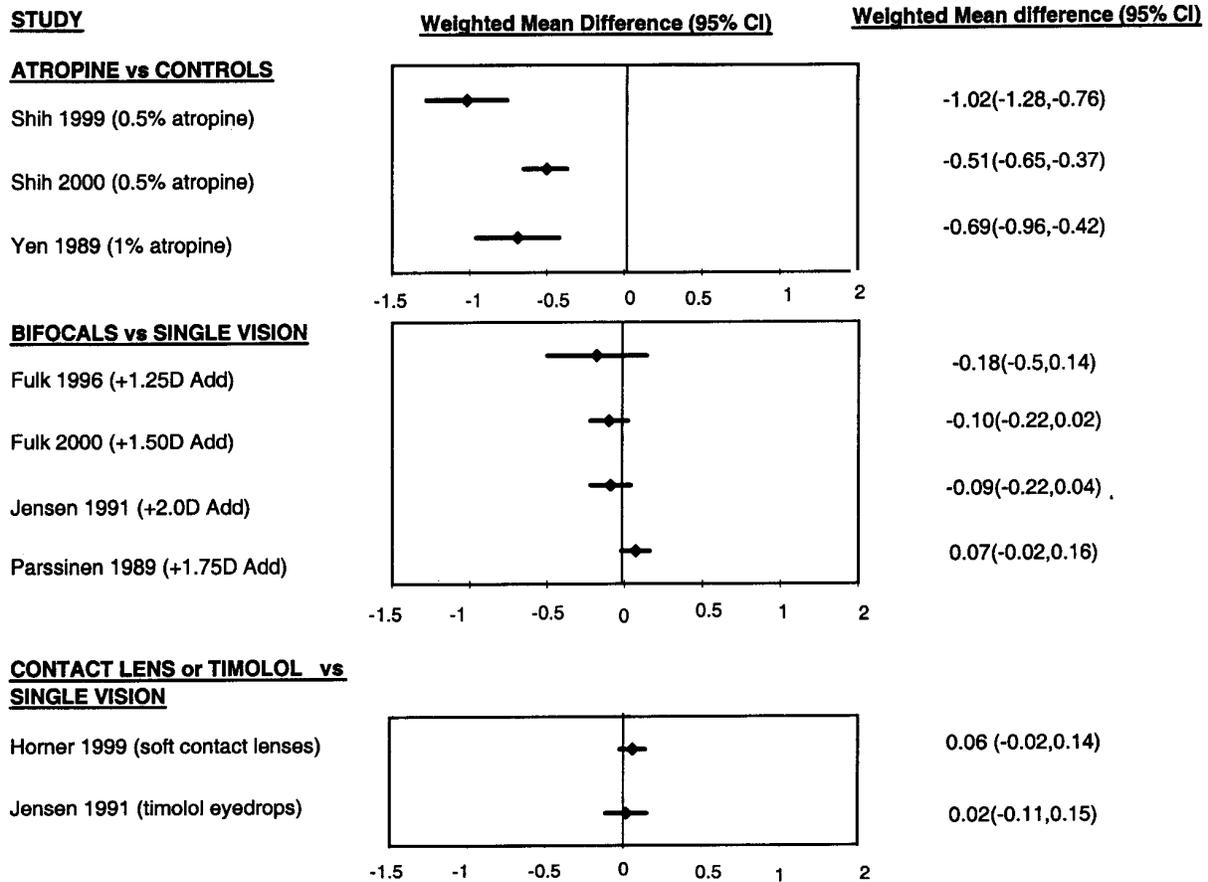


Figure 1. Forest-plot of randomized clinical trials. The Grosvenor study³⁴ is not included, because standard deviations of the myopia progression rates are not available. CI = confidence interval.

Note this is about half that in the Taiwanese studies. The Finnish study compared bifocal lenses with +1.75 D to two alternative single-vision spectacle-wearing regimens, continuous and distance-use only.^{25,33} Fulk et al^{29,30} compared bifocal lenses + 1.25 D in a small study of 32 subjects and later + 1.50 D in a larger study of 75 esophoric children. The latter study was barely significant (rate difference of 0.1 D/year, $P = 0.04$); the axial length increase was 0.16 mm/year in the bifocal lens group and 0.20 mm/year in the single-vision group.³⁰ The bifocal lens groups in the Jensen³² and two Fulk studies^{29,30} exhibited a trend in the direction of slower progression compared with single-vision spectacles. The latest study by Shih and colleagues (Proceedings of the VIII International Conference on Myopia, 352-6, 2000) showed an insignificant effect in favor of multifocals (-0.79 D per year versus -0.93 D per year, difference 0.12 D, 95% confidence interval, $-0.01, 0.29$). No side effects of bifocal or multifocal lenses were found.

Contact Lens Trial

Soft contact lenses were evaluated in one single-masked randomized clinical trial in the United States.³¹ There was

no statistically significant difference in myopia progression rates in the contact lens group (-0.36 D/year) compared with the single-vision lens group (-0.30 D/year) (Table 2, Fig 1). The refractive error measurements were, however, noncycloplegic, and 26% of the randomized subjects were dropped from the analysis. No side effects of contact lenses were reported.

In summary, three randomized clinical trials have demonstrated that 0.5% atropine eyedrops may lower the rate of progression of myopia; however, the long-term side effects are largely unknown. There is no evidence to suggest that bifocal lenses, pressure-lowering eyedrops, or soft contact lenses retard the progression of myopia, and further studies are needed.

Clinical Recommendations

The evidence for clinical recommendations is based on a systematic and comprehensive search of relevant articles and a consolidation of the best available evidence. Only

Table 3. Clinical Recommendations for the Different Interventions

Intervention	Recommendation	Evidence Rating
Atropine eyedrops	The routine use of atropine in children to reduce myopia is not recommended.	B, I
Bifocal lenses	Bifocal lenses are not recommended to retard myopia progression in children.	C, I
Soft contact lenses	Soft contact lenses are not recommended for retardation of myopia progression in children.	C, II

B = moderately important recommendation; C = relevant but not critical recommendation; I = strong evidence supporting recommendation; II = substantial evidence supporting recommendation but lacking some qualities required for strong support.

randomized clinical trials were included, because this "gold standard" study design provides the strongest evidence for efficacy of an intervention and a safeguard against biases. In randomized clinical trials, the nonpredictability of the treatment assignment for the next patient eliminates any selection bias on the part of investigators or patients. If the clinical trials were single- or double-masked, the results of the study would be even more rigorous. Because all studies evaluated were randomized clinical trials, the "strength of the evidence" for all recommendations was considered as I, except for soft contact lenses (II) (one small trial did not yield conclusive results) (Table 3). Recommendations regarding the use of atropine eyedrops were considered level B, moderately important to outcome. Bifocal lenses and soft contact lenses were considered to be level C, relevant but not critical to current patient care, because the interventions have not been clearly efficacious.

There is some evidence that atropine eyedrops retard myopia progression in three randomized clinical trials (B, I). The beneficial effects of atropine eyedrops have also been shown in retrospective studies, noncontrolled trials, and nonrandomized controlled studies.^{35,36} The efficacy of atropine is supported by animal experiments, demonstrating that muscarinic acetylcholine receptors may affect eye and scleral growth.^{37,38} However, there is little information on the exact mechanisms of action of atropine. Atropine eyedrops may not be recommended for all myopic children, because the possible long-term side effects such as cataract formation and retinal toxicity, are largely unknown. Few studies have evaluated the possible adverse effects and complications of the use of anticholinergic agents in growing eyes, especially over long periods of time. Thus, data on the safety of the drug are sparse. The possibility of reversal of myopia progression rates after termination of atropine eyedrops is still undetermined. Further randomized clinical trials are needed before considering the use of atropine in young children with rapid myopia progression rates (at least 1.0 D/year).

Bifocal lenses are not generally recommended for the

retardation of the progression of myopia in children (C, I). Despite several negative reports, we noted that Fulk and colleagues³⁰ reported significant results and no side effects from a recent randomized clinical trial. If the parents of a young child with progressive axial myopia request treatment with bifocal lenses, the parents should be counseled regarding the lack of evidence and possible side effects before bifocal lenses are prescribed. This hypothesis has to be confirmed by evidence from future well-designed randomized clinical trials. Alternatives to bifocal lenses include multifocal progressive lenses, which may be more acceptable cosmetically, and allow children to have clear vision at all distances. However, as the experience with pseudophakic adults has shown, adapting to the use of multifocal lenses is not always easy.

We do not recommend soft contact lenses for the retardation of the progression of myopia, because the evidence suggests that there is no significant retardation of the progression of myopia (C, II). Soft contact lenses are associated with a higher risk of ocular complications compared with rigid gas-permeable lenses. Soft contact lens wear is not without attendant risks such as ocular infections; the maintenance and care of contact lenses may be an inconvenience as well.

Other interventions, namely, part-time spectacle wear and hydrogel lenses, have been evaluated in retrospective case studies, nonrandomized controlled trials, and uncontrolled clinical trials.^{19,39} In addition, programs designed to decrease possible environmental risk factors such as near-work or night lights have not been evaluated in a systematic fashion. Evidence is lacking, and well-designed randomized clinical trials with low dropout rates are needed to answer the question: Do these interventions really retard the progression of myopia in children?

The best available evidence for myopia intervention in children is not conclusive, because the magnitude of effect of the intervention compared with the control group is small, dropout rates may be high, and compliance rates may be low. Use of 1% and 0.5% atropine eyedrops in children is associated with major side effects. Not all interventions have been evaluated using the "gold standard" study design of randomized clinical trials. Often, the primary purpose of the trials was not to evaluate the long-term retardation of the progression of myopia, but to evaluate short-term, possibly transient, effects. Several controlled trials did not use rigorous randomization techniques, such as random number tables, but opted for other means of treatment allocation such as "even" and "odd" number assignments or matching.⁴⁰ New research in this area should focus on large double-masked randomized clinical trials with optimal optical refraction data and adequate follow-up time. Long-term follow-up studies of atropine eyedrop instillation in humans or animals to determine the possible long-term side effects of atropine eyedrops are strongly advocated. Ongoing clinical trials of the efficacy of pirenzepine, a subtype-selective M1 antimuscarinic antagonist with possibly

fewer side effects compared with atropine, may provide useful and valuable information.

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Prevalence of Myopia in the United States

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• Data from the 1971 to 1972 National Health and Nutrition Examination Survey were used to estimate myopia prevalence rates for persons in the United States between the ages of 12 and 54 years. When persons were classified by the refractive status of their right eye, 25% were myopic. Significantly lower prevalence rates were found for male subjects than for female subjects and for blacks than for whites. Myopia prevalence rose with family income and educational level. The importance of income and educational level may result from their association with near work, a factor that has been implicated in the pathogenesis of myopia.

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Little is known about the distribution of myopia in the population of the United States. Most surveys of refractive error have dealt with select populations, such as students, army recruits, and eye clinic patients. As a result, knowledge of how the prevalence of myopia varies with sex, race, and age, for example, is incomplete.

Such prevalence data could be helpful in health care planning. In recent years, there has been growing interest in radial keratotomy, a surgical procedure aimed at correcting myopia.

To evaluate the potential medical and economic importance of this procedure, better prevalence data are required.

Prevalence data are also useful in searching for etiologic mechanisms.

Are early eye use habits of any importance? Information about the distribution of myopia in the population seems a useful place to start formulating an answer to this question.

We have used data from a general population study, the National Health and Nutrition Examination Survey (HANES), to report the prevalence of myopia for persons between the ages of 12 and 54 years in the United States. Rates are presented separately by age, sex, race, family income, and education.

SUBJECTS AND METHODS

As part of the HANES conducted by the National Center for Health Statistics in 1971 to 1972, a national probability sample of 14,147 persons, aged 1 through 74 years, was selected to represent the 192.7 million persons in the civilian noninstitutionalized population of that age at the time of the survey.¹ The probability that any person was included in the sample varied by race, age, and economic status. Weights that compensated for this oversampling and undersampling were assigned to each person sampled and permitted construction of valid estimates of population rates.

Between April 1971 and October 1972, eye examinations were performed on 9,882 (69.9%) of the 14,147 persons by 91 ophthalmologists in 35 geographic areas of the United States. A standardized eye examination included the following: determination of monocular distance visual acuity with current distance correction, if any, and with a pinhole test to measure correctability for eyes with visual acuity worse than 20/20; measurement of prescription in current correction; and detailed retinoscopy or spherical refraction for eyes with visual acuity worse than 20/40 (not including pinhole acuity).²

We classified eyes as nonmyopic or myopic and determined the degree of myopia. Nonmyopic eyes were not further classified. Refractive status was determined as follows:

For eyes with 20/20 visual acuity, a spherical equivalent was calculated from the current distance correction. If no correction was worn, the eye was classified as nonmyopic.

For eyes with 20/25 to 20/40 visual acuity, a group not refracted, a spherical equivalent was calculated from the current correction. If the spherical equivalent was negative and acuity improved with pinhole testing, the amount of myopia was adjusted according to the method described by Sloan.³

If no correction was worn and acuity improved with pinhole testing, the eye was excluded from the analysis because insufficient data were available for classification of refractive status. If no correction was worn and acuity did not improve with pinhole testing, the eye was classified as nonmyopic.

For eyes with visual acuity of less than 20/40 (not including pinhole acuity), a spherical equivalent was calculated from retinoscopy or spherical equivalent refraction.

We used these data to obtain national prevalence estimates of myopia for persons aged 12 to 54 years. The national probability sample included 7,401 persons within this age range. Although oversampling was used in certain population groups, rates were computed so as to provide representative national estimates. Of the 5,282 (71.4%) persons examined, insufficient data were available to classify the refractive status of 846 right eyes (16.0%) and 778 left eyes (14.7%).

Tables were prepared that allowed comparisons of national prevalence estimates according to age, sex, race, family income, and education. Income data were not available for 242 persons and educational level data were not available for 41 persons. In testing for differences between population proportions, we used SEs that took account of the complex sampling design used in the survey.

RESULTS

The prevalence of any degree of myopia among eyes of persons between 12 and 54 years was 25.0% and 24.3% for right and left eyes, respectively (Table 1). For all ages combined, prevalence rates were significantly less for men than for women ($P < .05$), but this difference in rates was not present after the age of 35 years (Table 1). Whites had substantially high-

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Table 1.—Estimated Prevalence of Myopia by Age, Race, and Sex in the United States From 1971 to 1972

Race and Sex	All Ages		Aged 12-17 yr		Aged 18-24 yr		Aged 25-34 yr		Aged 35-44 yr		Aged 45-54 yr	
	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE
All races												
Both sexes												
OD	25.0	1.1	24.0	1.6	27.7	2.1	24.2	1.6	24.5	2.0	24.8	2.2
OS	24.9	1.0	23.7	1.6	27.9	2.2	23.2	1.6	23.9	2.0	23.7	2.0
Men												
OD	22.8	1.5	21.7	2.1	22.5	2.6	20.2	2.2	23.1	3.7	24.4	2.6
OS	22.0	1.2	21.2	2.2	23.1	2.8	19.0	2.0	23.6	2.5	24.1	2.3
Women												
OD	27.1	1.2	26.4	2.9	32.5	3.1	27.6	2.4	23.2	1.6	25.1	2.2
OS	26.4	1.2	26.5	2.9	31.2	2.9	27.3	2.4	23.1	2.0	23.2	2.5
Whites, both sexes												
OD	26.3	1.2	25.8	1.8	29.7	2.6	25.6	1.8	24.9	2.3	25.5	2.3
OS	25.6	1.0	25.6	1.7	29.7	2.8	24.4	1.9	23.9	2.2	24.4	2.1
Blacks, both sexes												
OD	13.0	1.8	12.0	2.7	10.4	2.5	12.3*	3.5	14.8*	3.6	17.3*	7.1
OS	12.2	1.9	11.4	2.7	8.5*	2.6	13.4*	3.7	12.6*	3.6	16.8*	7.3

*Coefficient of variation is greater than 25%.

Table 2.—Estimated Prevalence (%) of Specific Levels of Myopia by Age in the United States From 1971 to 1972

Myopia, Diopters	All Ages	Aged 12-17 yr	Aged 18-24 yr	Aged 25-34 yr	Aged 35-44 yr	Aged 45-54 yr
<2						
OD	13.4	11.1	11.7	13.1	16.9	15.6
OS	13.2	11.0	11.6	13.4	14.9	15.4
2:7.9						
OD	11.4	12.5	15.8	10.7	8.4	8.9
OS	10.7	12.4	15.0	8.7	7.8	8.9
≥7.9						
OD	0.2	0.4	0.5	0.3	0.2	0
OS	0.4	0.4	0.7	0.2	0.7	0

Table 3.—Estimated Prevalence of Myopia by Age and Family Income in the United States From 1971 to 1972

Income	All Ages		Aged 12-17 yr		Aged 18-24 yr		Aged 25-34 yr		Aged 35-44 yr		Aged 45-54 yr	
	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE
<\$5,000												
OD	17.3	2.1	12.1	2.9	26.6	4.3	15.7	3.8	15.9*	5.2	10.0*	4.4
OS	17.1	2.2	13.1*	3.5	24.1	4.1	15.3	3.8	16.4*	5.5	12.1*	5.2
\$5,000-10,000												
OD	23.2	1.1	24.2	2.3	28.4	3.1	22.7	2.1	17.0	2.8	20.4	4.5
OS	22.2	0.9	21.8	2.1	27.9	3.0	21.3	1.8	18.4	2.7	19.8	3.8
>10,000												
OD	28.9	1.6	27.9	2.2	27.6	4.1	28.2	3.3	29.9	2.8	30.3	3.1
OS	27.8	1.4	28.0	2.2	28.0	4.2	27.5	3.2	27.7	2.3	27.8	2.8

*Coefficient of variation is greater than 25%.

or rates than blacks ($P < .01$). For whites and blacks, respectively, rates were 26.3% and 13.0% for right eyes and 25.6% and 12.2% for left eyes.

Although there was little variation in the overall rates with age, there was a progressive increase with age in the proportion of persons with less than 2 diopters of myopia and a corresponding decrease in those with 2 D or more of myopia (Table 2).

The prevalence of myopia increased as family income rose (Table 3). For the total population the rates increased from 17.3%, to 23.2%, to 28.9% for right eyes as family income increased from less than \$5,000, to \$5,000 to 10,000, to greater than \$10,000 per year. Corresponding rates for left eyes were 17.1%, 22.2%, and 27.8%.

Myopia prevalence increased markedly for all age groups as the number

of years of school completed rose from less than five years to greater than 12 years, another trend that was highly significant ($P < .01$) (Table 4).

The increase with age in the proportion of persons with less than 2 D of myopia and the corresponding decrease in those with 2 D or more of myopia persisted after standardization separately for income and education.

COMMENT

Most previous studies have dealt with select populations, making comparisons of prevalence estimates difficult. Our rates (about 25%) are higher than those in most published reports. Among British army recruits between 18 and 22 years of age, Sorsby et al¹ found an 11% myopia prevalence rate, whereas Goldschmidt² found a 14.5% rate for Swedish army recruits. In a population study of communal settlements in Israel, Hyams et al³ noted myopia in 18.4% of eyes in subjects 40 years of age or older. Leibowitz and associates⁴ found myopia to be present in 17.7% of eyes in the Framingham (Mass) Eye Study population, where age ranged from 52 to 85 years.

There were two important reasons for missing data in our analysis, but it seems unlikely that they explain the higher rates that we found. More than one quarter of the national probability sample was not examined. On the basis of the reasons given for nonparticipation and an analysis of the medical histories that were available for most of those not examined, the National Center for Health Statistics concluded that no sizable bias was introduced by these nonrespondents.⁴ Furthermore, one of the components of the weight assigned to an examined person was an adjustment for nonresponse. Though the analysis of the characteristics of those not examined is reassuring, the sizable proportion of nonexamined remains a potential source of bias in our estimates.

The inability to determine the refractive status of approximately 15% of examined eyes was a second source of missing data. This factor resulted from a failure of the examiner to record essential information or our inability to determine the refractive status of eyes with 20/25 to 20/40 visual acuity that had no correction but improved with pinhole testing. This group of eyes with missing data was known to be enriched with eyes that required glasses for distance or had decreased acuity. Tabulations were made available to us of the rates of missing data among those exam-

Table 4.—Estimated Prevalence of Myopia by Age and Highest Grade Level Completed in the United States From 1971 to 1972

Highest Grade Level Completed, yr	Aged 18-24 yr		Aged 25-34 yr		Aged 35-44 yr		Aged 45-54 yr	
	%	SE	%	SE	%	SE	%	SE
<6								
OD	8.1*	7.8	8.9*	8.3	5.5*	7.5	2.7*	2.3
OS	3.1*	7.8	4.0*	9.1	5.5*	8.1	2.8*	2.1
5-8								
OD	3.0*	2.7	13.2*	3.7	12.6*	5.4	10.2*	3.7
OS	2.9*	3.1	13.5*	3.5	10.1*	4.8	8.2*	3.6
9-12								
OD	29.0	2.4	22.0	1.9	20.3	1.9	24.2	3.0
OS	27.1	2.3	20.6	2.0	19.1	1.8	23.0	2.7
>12								
OD	31.4	3.3	32.3	4.4	39.2	4.7	39.5	5.0
OS	32.2	3.7	31.7	4.4	38.3	4.7	39.2	5.2

* Coefficient of variation is greater than 25%.

ined separately by age, by sex, and by race. Making some simple assumptions about the distribution of refractive errors among these, we concluded that the prevalence of myopia was likely to be underestimated by about 1% and that observations about major patterns were unaffected. We had no information on the proportion missing by income and education. As with the problem of the unexamined, although we were reassured by our analyses of potential bias from missing data, there is no substitute for complete ascertainment.

In our tests of significance, we used SEs that took into account the complex sample design of the survey.^{1,2} This step was necessary because we were interested in general population estimates, and oversampling of certain population groups was used in the survey.

Myopia prevalence remained remarkably constant from the ages of 12 to 54 years. However, there were progressively more low myopes and, correspondingly, fewer moderate-high myopes, with advancing age. In 1950, Slataper⁹ reported a slight but steady trend toward more positive (hypermetropic) mean refractive errors from the third to the seventh decades.

Richler and Bear¹⁰ also noted this trend toward decreasing mean refractive error among persons between the ages of 20 and 59 years in a population study in three communities in Newfoundland. Duke-Elder and Abrams^{11(6,22)} suggested that this is not the apparent increase in hypermetropia due to progressive failure of accommodation. Possible explanations for this trend toward hypermetropia include factors that decrease the power of the aging lens, such as a decreasing curvature of its surface as it grows throughout life or an increasing optical density of the cortex that makes the lens more uniformly refractive.^{11(6,22)} Alternately, this trend toward less severe myopia with advancing age in cross-sectional studies such as ours may be a cohort effect indicating that more recent birth cohorts are at a greater risk of the development of more severe myopia.

Duke-Elder and Abrams cited no sex difference in prevalence rates for refractive error. In a study of schoolchildren, Goldschmidt⁷ found a higher frequency of myopia in girls than in boys. Angle and Wissmann,¹² using data from the 1966 National Health Examinations Survey of 12- to 17-

year-olds, reported a 35.0% rate for girls and 27.4% for boys. Our data showed higher rates for female subjects than for male subjects between 12 and 35 years, but thereafter the rates for the two sexes were similar. In a 15- to 29-year age group, the Newfoundland study¹⁰ found that the shift to negative refraction occurred at an earlier age and was somewhat greater for women than men.

The association of myopia with both income and educational level has been noted in several previous reports. Among a US national probability sample of 12- to 17-year-olds, Angle and Wissmann¹² showed the frequency of myopia to increase from 16.8% to 35.1% as family income rose from less than \$500 to more than \$15,000 per year. Goldschmidt⁷ found a higher frequency of myopia among more educated Danish recruits, and British investigators¹¹ reported that myopia was more common in British children of nonmanual than manual workers.

The association with income and educational level may result from an association with near work. Angle and Wissmann¹² have shown that most of the variance in myopia explained by income level is eliminated when adjustments are made for near work. Educational status has been shown to be closely related to near work¹³ and is sometimes used as an indicator of near work in epidemiologic analyses. These observations can be used in support of the use-abuse theory of myopia, which postulates that accommodative effort in the developing eye causes the optic axis to elongate and the eye to become myopic. However, Goldschmidt⁷ has cautioned that genetic heterogeneity along social class lines may confound these observations.

Further analyses are needed to explore how the various factors, age, race, sex, education and income, relate to one another and how the association of myopia with one factor may be "explained" by another.

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Macular Complications Associated With Posterior Staphyloma

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- **PURPOSE:** To report macular abnormalities associated with posterior staphyloma in eyes with myopia.
- **METHODS:** In a retrospective study, we surveyed 116 eyes of 58 patients with myopic refractions. Myopic fundus abnormalities are related to clinically quantified posterior staphyloma formation.
- **RESULTS:** A posterior staphyloma was present in 88 (75.9%) of 116 eyes with myopic refractions of -3 diopters or more. Best-corrected visual acuity was decreased among eyes in all staphyloma grades. Eyes with the shallowest staphyloma depth (grade 1) displayed the largest drop in visual acuity as well as the greatest frequency of choroidal neovascular membranes and hemorrhages. A linear relationship was observed between staphyloma grade and conus formation ($P = .001$), retinal pigment epithelial defects ($P = .0001$), lacquer cracks ($P = .0001$), and chorioretinal atrophy ($P = .001$). All these variables were increased in staphylomatous eyes. A significant difference in means by staphyloma grade was observed for myopic refractive error ($P = .001$), axial length ($P = .001$), and best-corrected visual acuity (logMAR, $P = .0001$).
- **CONCLUSIONS:** There was an unexpected high

frequency of choroidal neovascular membranes, hemorrhage, and poor best-corrected visual acuity in the lower staphyloma categories. This suggests that the development of a choroidal neovascular membrane requires relative preservation of the choriocapillaris as present in eyes with less advanced stages of posterior staphyloma formation.

PROGRESSIVE MYOPIA CAN BE ACCOMPANIED BY A number of visually disabling complications. Among these are premature cataract formation, glaucoma, retinal detachment, and macular degeneration. Degeneration of the macula typically occurs slowly over a number of years, but significant impairment of central vision can occur during the productive time of life. Hallmarks of the process include lacquer cracks in Bruch's membrane, intermittent subretinal "coin" hemorrhages, choroidal neovascular invasion of the macula with secondary development of a Förster-Fuchs spot, and finally, expanding areas of choriocapillary and pigment epithelial atrophy. Less frequently seen are foveal cysts and holes; the latter is sometimes accompanied by a posterior retinal detachment.¹

The scleral shell of a highly myopic eye has increased elasticity and a tendency to expand gradually and to thin. Its collagen fibers are pathologically abnormal.^{2,3} In addition, the fibers in the posterior pole are smaller in diameter, appear immature, and may have less cross-linking than do emmetropic eyes.⁴ One hypothesis suggests that intraocular pressure and perhaps other forces, combined with scleral hyperelasticity, contribute to posterior staphyloma formation,^{5,6} the signature deformity of progressive myopia described by Scarpa⁷ in the early 19th century. In this model, the occurrence of cracks in Bruch's elastic lamina in the base of a staphyloma, their characteristic pattern, and the fact that their number and

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dimensions increase with time are considered strain-relieving responses to localized mechanical stress, perhaps exaggerated by the repetitive expansion wave induced by the choroidal vascular pulse. If these factors are operative, it would be expected that subsequent macular complications would not only be correlated with increased axial length and aging but that they also would be observed more frequently in eyes with staphylomatous distortion than in those with a more ovoid shape. This study was conducted to examine these relationships more closely and to search for features that might have prognostic value.

PATIENTS AND METHODS

IN A RETROSPECTIVE STUDY CONDUCTED IN A CONSULTATION practice, randomly selected records of patients with myopic refractions of -3 diopters or more, who were examined and followed up by the same vitreoretinal specialist (R.C.P.), were reviewed by another (S.M.S.). Chart drawings and notes, fundus photographs, fluorescein angiograms, and B-scan and A-scan ultrasonography records were used to grade severity of disease.

Staphyloma formation was graded from 0 to 4 based on contour change alone. Grade levels were determined from stereoscopic indirect ophthalmoscopic evaluation, stereo viewing of photographs and angiograms, and B-scan ultrasonographic data. In cases in which the entire eye was not included on B-scan imaging records, the staphyloma grade was based on the portion seen combined with clinical drawings. When a reliable determination of staphyloma size and shape could not be made, the eye was excluded from the study. A-scan axial length was compared to the recorded B-scan image, and the staphyloma depth was judged accordingly. An elongated eye with smooth scleral contour was given the designation of grade 0. A grade 1 staphyloma had a contour change of less than or equal to 2 mm. A grade 2 staphyloma had greater than 2 mm but 4 mm or less of contour change. A grade 3 staphyloma had greater than 4 mm but 6 mm or less of contour change. A grade 4 staphyloma showed greater than 6 mm of contour change.

We developed a grading scheme for categorizing chorioretinal atrophy that relied on an estimation of

the total area of atrophic involvement. Designation of chorioretinal atrophy required substantial loss of choriocapillaris and retinal pigment epithelium (grades 2 through 4). A grade 0 designation was given to eyes without evidence of atrophic change. Grade 1 eyes showed attenuated choroidal vessels, limited lacquer crack formation, and retinal pigment epithelial mottling, or combinations of these. Grade 2 eyes had a total area of geographic atrophy less than or equal to 2 disk areas. Grade 3 eyes had a total area of atrophy greater than 2 disk areas but less than or equal to 4 disk areas. Grade 4 eyes had a total area of atrophy greater than 4 disk areas. Area measurements were done using color photographs. Conus formation was included in the measurements of total area of atrophy.

Best-corrected visual acuities were determined using standard projected Snellen charts with current optical correction and pinhole testing. For the purpose of statistical analysis, visual acuity of counting fingers was given the Snellen equivalent of 20/1,600, and hand motion visual acuity was given the Snellen equivalent of 20/3,200. This was based on the degrees of arc required to recognize an object the width of an average human finger or hand.⁸ Before all calculations for visual acuity were made, visual acuity measurements were converted to logMAR units.

Statistical analysis was performed using SAS software (SAS Institute, Cary, North Carolina). Chi-square tests and Fisher's exact test were used to assess the association of categorical variables with staphyloma grade. Analysis of variance tests were used to compare the means of the continuous variables across the five staphyloma grades. To avoid the problem of multiple comparisons, Dunnett's two-tailed *t* test was used to compare staphyloma grades 1 through 4 with no staphyloma (grade 0). Chi-square tests for trend measured the linear association between staphyloma grade and these categorical variables. Multiple logistic regression was used to examine the independent effects of macular abnormalities with staphyloma, controlling for age, gender, and measures of myopic change.

RESULTS

WE REVIEWED THE RECORDS OF 116 MYOPIC EYES IN 58 patients, of whom 21 (36.2%) were male and 37

(63.8%) were female. Ages ranged from 12 to 90 years (mean \pm SD, 42.5 ± 16.9 years; median, 40.5 years), and although patients were randomly selected, all were white. The range of myopic refractive error was -3 to -38 diopters (mean, -14.9 ± 6.3 diopters). A posterior staphyloma was observed in 88 of the 116 eyes (75.9%). Mean myopic refractive error and mean axial length increased with increasing severity of staphyloma formation (Table 1). The means were significantly different in grades 2, 3, and 4 compared with grade 0 for refractive error and axial length. It should be noted that myopic refraction and axial length were highly correlated ($r = -.75$).

The average best-corrected visual acuity of 1.12 ± 0.63 (logMAR) observed in the grade 1 eyes was lower compared with the average visual acuity of 0.2 ± 0.2 (logMAR) observed in grade 0 eyes. This was probably because of the greater frequency of choroidal neovascular membranes and hemorrhages in grade 1 eyes. Evidence of choroidal neovascular membranes was found in the records of eight of 18 group 1 patients (44.4%) but in only two of 28 grade 0 eyes (7.1%). The difference in mean best-corrected visual acuity among groups with staphyloma formation was statistically significant for grades 1, 2, and 3 compared with grade 0 eyes. Hemorrhages were noted in only one of 28 grade 0 eyes (3.6%), whereas six of 18 grade 1 eyes (33.3%) were so affected.

Retinal pigment epithelial defects, lacquer cracks, and conus formation were increased in all categories of staphyloma formation compared with eyes without staphyloma formation. Retinal pigment epithelial defects were present in seven of 28 grade 0 eyes (25.0%). This increased to 17 of 18 (94.4%) in grade 1 eyes.

Chorioretinal atrophy increased in severity as the grade of staphyloma increased. Only staphyloma grade 4 had eyes in the most severe category. In contrast, 23 of 28 staphyloma grade 0 eyes (82.1%) had no evidence of chorioretinal atrophy.

Lacquer cracks were observed in only three of 28 grade 0 eyes (10.7%) but in 16 of 18 grade 1 eyes (88.8%). Conus formation also increased dramatically, from nine of 28 grade 0 eyes (32.1%) to 18 of 18 grade 1 eyes (100%). A conus was present in 65 of 70 eyes (92.8%) in staphyloma categories 2 through 4.

Glaucoma, macular holes, lattice degeneration, and posterior and peripheral retinal detachment were found in only a few cases in this study. The frequency

of occurrence of these lesions is summarized in Table 1. The difference in mean age by staphyloma grade was statistically significant ($F = 3.78$, $P = .0065$). The means were greater in staphyloma groups 1 through 4 and were significantly different for staphyloma grades 1 and 3 compared with grade 0. Gender also was associated with staphyloma formation, with women composing 27 of 30 patients (90.0%) of the grade 2 group.

In Table 2, data are displayed according to age groups. The frequency of staphyloma (grade 1 or greater) increased from 16 of 28 patients in the youngest group (57.2%) to 30 of 36 in the oldest (83.3%), and the grade of chorioretinal atrophy followed accordingly. The visual acuity scores decreased slightly from 0.41 ± 0.4 (logMAR) in the youngest group, a Snellen equivalent of 20/51, to 0.69 ± 0.6 (logMAR) in the oldest group, a Snellen equivalent of 20/98. There were no significant differences in mean refractive error, axial length, and best-corrected visual acuity by age. However, retinal pigment epithelial defects ($P = .001$), lacquer cracks ($P = .002$), conus formation ($P = .001$), and chorioretinal atrophy ($P = .002$) had a statistically significant association with age. Both posterior and peripheral retinal detachments were found only in the oldest age group, and this association was statistically significant.

After controlling for age, gender, axial length, and best-corrected visual acuity, conus formation and lacquer cracks were still significantly associated with having a staphyloma. Axial length was also associated with staphyloma after controlling for the other variables.

DISCUSSION

BECAUSE OF THE DIFFICULTY OF CLASSIFYING STAPHYLOMA formation, we utilized a grading system based on staphyloma depth, determined by B-scan and A-scan ultrasonography measurements combined with stereo ophthalmoscopic and photographic observations. This allowed an independent comparison of chorioretinal changes to staphyloma grade. Depth determinations required an approximation of what the normal eye contour should be in the area of the staphyloma. Staphyloma depth was easy to determine

Table 1. Descriptive Statistics by Staphyloma Grade

Variable	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
No. of eyes	28	18	30	30	10
Age (yrs)					
Mean \pm SD	34.0 \pm 18.5	49.6 \pm 17.9	39.2 \pm 14.9	46.6 \pm 12.0	48.6 \pm 20.3
Range	12-90	26-90	21-74	26-74	30-80
Gender (no. [%])					
Male	14 (50.0)	8 (44.4)	3 (10.0)	12 (40.0)	5 (50.0)
Female	14 (50.0)	10 (55.6)	27 (90.0)	18 (60.0)	5 (50.0)
Visual acuity (logMAR)					
Mean \pm SD	0.2 \pm 0.2	1.12 \pm 0.63	0.69 \pm 0.73	0.55 \pm 0.41	0.48 \pm 0.14
Snellen	20/32	20/264	20/100	20/71	20/60
Refraction (diopters), mean \pm SD	-9.1 \pm 3.1	-12.2 \pm 3.4	-15.3 \pm 4.6	-17.8 \pm 3.5	-26.9 \pm 6.6
Axial length (mm), mean \pm SD	26.8 \pm 1.9	28.0 \pm 2.6	30.3 \pm 2.6	31.6 \pm 1.7	34.9 \pm 1.8
IOP (mm Hg), mean \pm SD	14.5 \pm 3.8	12.7 \pm 2.7	14.5 \pm 3.0	14.0 \pm 2.7	16.7 \pm 2.9
Choroidal neovascularization (no. [%])	2 (7.1)	8 (44.4)	8 (26.7)	6 (20.0)	2 (20.0)
Hemorrhage (no. [%])*	1 (3.6)	6 (33.3)	5 (16.7)	9 (30.0)	2 (20.0)
Retinal pigment epithelial defect (no. [%])	7 (25.0)	17 (94.4)	24 (80.0)	29 (96.7)	10 (100)
Lacquer cracks (no. [%])	3 (10.7)	16 (88.8)	20 (66.7)	27 (90.0)	9 (90.0)
Conus (no. [%])	9 (32.1)	18 (100)	27 (90.0)	28 (93.3)	10 (100)
Cataracts (no. [%])	4 (14.2)	10 (55.5)	14 (46.6)	18 (60.0)	5 (50.0)
COAG (no. [%])	—	2 (11.1)	4 (13.3)	—	—
Macular hole (no. [%])	—	—	—	1 (3.3)	—
Lattice degeneration (no. [%])	1 (3.6)	—	3 (10.0)	2 (6.7)	2 (20.0)
Posterior retinal detachment (no. [%])	—	—	1 (3.3)	1 (3.3)	1 (10.0)
Peripheral retinal detachment (no. [%])	—	—	2 (6.7)	1 (3.3)	1 (10.0)
Chorioretinal atrophy (no. [%])					
Grade 0	23 (82.1)	1 (5.6)	6 (20.0)	5 (16.7)	—
Grade 1	4 (14.3)	7 (38.9)	15 (53.3)	17 (56.7)	—
Grade 2	1 (3.6)	4 (22.2)	3 (13.3)	4 (13.3)	3 (30.0)
Grade 3	—	6 (33.3)	6 (20.0)	4 (13.3)	5 (50.0)
Grade 4	—	—	—	—	2 (20.0)

COAG = chronic open-angle glaucoma; IOP = intraocular pressure
 *Preretinal, intraretinal, or subretinal hemorrhage

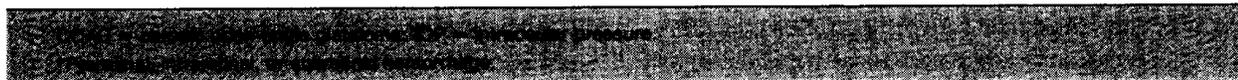
in the case of small staphylomas but became increasingly difficult as the area of staphyloma involvement increased. Particular difficulties arose when imaging did not show cuts through the deepest extent of the staphyloma. In addition, inconsistencies in serial A-scan measurements were common in patients with irregular posterior scleral contour, and in a number of cases, a best estimate based on serial readings was required to determine the axial length. We encountered a variety of different staphyloma patterns, including nasal, macula-centered, disk-centered, and tiered staphylomas. These formations were described by Curtin⁹ in his extensive study of posterior staphyloma.

Not all eyes with progressive myopia will develop a posterior staphyloma, but with increasing axial

length, staphyloma development appears to increase. In the present study, 88 of 116 eyes had a posterior staphyloma (75.9%). Staphyloma development appears to increase with age: a statistically significant different mean age by staphyloma grade was observed ($F = 3.78, P = .0065$). These mean differences were significantly greater in groups 1 and 3 compared with group 0. Other abnormalities associated with increasing axial length, such as conus and chorioretinal atrophy, have been reported.¹⁰ Our data show a significant increase in A-scan-measured eye length as well as myopic refraction in groups 2, 3, and 4 compared with grade 0 eyes. Chorioretinal atrophy ($P = .001$) and conus formation ($P = .001$) showed a linear association with the increasing staphyloma depth (Table 1). In some cases, it was difficult to



Variable	Age (yrs)		
	10-29	30-49	≥50
No. of eyes	28	52	36
Age (yrs), mean ± SD	22.8 ± 5.6	40.0 ± 5.5	63.8 ± 11.2
Gender (no. [%])			
Male	8 (28.6)	24 (46.2)	10 (27.8)
Female	20 (71.4)	28 (53.8)	26 (72.2)
Visual acuity (logMAR)			
Mean ± SD	0.41 ± 0.4	0.62 ± 0.6	0.89 ± 0.6
Snellen	20/51	20/83	20/98
Infravision (diopters), mean ± SD	-12.6 ± 3.6	-15.2 ± 8.5	-15.1 ± 6.7
Axial length (mm), mean ± SD	28.6 ± 2.4	30.7 ± 3.3	29.5 ± 3.5
ICL (mm), mean ± SD	13.7 ± 3.1	14.4 ± 3.4	14.5 ± 2.9
Choroidal neovascularization (no. [%])	3 (10.7)	13 (25.0)	10 (27.8)
Hemorrhage (no. [%])	3 (10.7)	13 (25.0)	7 (19.4)
Retinal pigment epithelial defect (no. [%])	13 (46.4)	42 (80.8)	32 (88.9)
Lacquer cracks (no. [%])	11 (39.3)	39 (75.0)	24 (66.7)
Conus (no. [%])	15 (53.6)	47 (90.4)	30 (83.3)
Cataracts (no. [%])	—	24 (46.2)	27 (75.0)
COAG (no. [%])	—	4 (7.7)	2 (5.6)
Macular hole (no. [%])	—	—	1 (2.8)
Lattice degeneration (no. [%])	1 (3.6)	4 (7.7)	3 (8.3)
Posterior retinal degeneration (no. [%])	—	—	3 (8.3)
Peripheral retinal degeneration (no. [%])	—	—	4 (11.1)
Staphyloma grade (no. [%])			
Grade 0	12 (42.9)	10 (19.2)	6 (16.7)
Grade 1	1 (3.6)	11 (21.2)	6 (16.7)
Grade 2	11 (39.3)	10 (19.2)	9 (25.0)
Grade 3	4 (14.3)	14 (26.9)	12 (33.3)
Grade 4	—	7 (13.5)	3 (8.3)
Chorioretinal atrophy (no. [%])			
Grade 0	15 (53.6)	14 (26.9)	6 (16.7)
Grade 1	13 (46.4)	17 (32.7)	13 (36.1)
Grade 2	—	9 (17.3)	6 (16.7)
Grade 3	—	10 (19.2)	11 (30.6)
Grade 4	—	2 (3.9)	—



determine whether progressive conus development was caused by mechanical stretching by an expanding eye wall or was part of progressive chorioretinal atrophy. When grading atrophy, we chose to consider conus formation as part of the chorioretinal atrophy. This minimized bias in interpretation but may have led to overestimates of chorioretinal atrophy when the area designated as atrophic in nature was atrophic primarily because of an expanding conus. This overestimate may have been somewhat offset by the fact that areas of early atrophy, as evidenced by mild retinal pigment epithelium changes, were not includ-

ed as atrophic change in the grading analysis (grades 2 through 4).

We observed an increase in female eyes in the grade 2 staphyloma category. Although Curtin and Karlin¹⁰ also describe a predominance of female eyes at axial lengths of less than 27.4 mm, their data are difficult to relate to our study because our ranges of data categorization are different.

Among patients with staphylomas, 51 of 116 eyes (43.9%) had a record of cataract formation. About one third of these (32%) had a cataract removed. Because increase in staphyloma size correlated with

increasing age, eye length, and myopic refraction, we suspect that much of the observed cataract formation reflects an association with increasing age.

A decrease in best-corrected visual acuity and an increase in hemorrhages and choroidal neovascular membranes were observed in the grade 1 staphyloma group. Choroidal neovascular membranes can cause hemorrhages, and both can affect vision. These findings offer grounds for speculation on the pathogenesis of progressive myopic visual changes. Subretinal neovascular membranes have been found in 30% of eyes with lacquer cracks and 75% of eyes with angioid streaks.¹¹ In this situation, mechanical damage to Bruch's membrane may be the stimulus to new vessel formation. It is possible that the grade 1 eyes may have a healthier and more metabolically active posterior pole with well-perfused chorioretinal tissue and good capacity to respond to injury by neovascular ingrowth. Up to a point, the incidence of neovascularization may increase with increasing chorioretinal damage. However, as chorioretinal atrophy becomes dominant, poor to absent circulation of both humoral and cellular components and a decrease in viable endothelial cells at the injury site may lead to a decrease in neovascular potential and a resulting decrease in membrane formation. Because the chorioretinal atrophy observed in grades 2 through 4 reflects only areas of easily visualized atrophy, we may have underestimated the extent of functionally abnormal tissue.

Caution should be exercised in interpreting data from retrospective chart reviews given the inherent bias in nonstandard data collection. We cannot rule out selection bias in our patient population as a contributing factor to the observation of increased neovascular complications in eyes with lower degrees of staphyloma formation. Although records were pulled at random, they were from a patient pool in a consulting practice. It is possible that symptomatic younger patients with membranes were more frequently referred than were older patients with long-term atrophic changes but who may have had a history of neovascular problems at an earlier age. The classic pigment spot of Förster-Fuchs can fade with the years, making its recognition at a later date difficult. In a study conducted in Germany, of 206 eyes with Fuchs' spots,¹² peak incidence was noted in patients between 40 and 50 years of age. An average refractive error of

-12.47 ± 5.08 diopters and an axial length of 26.5 to 31.4 mm was found in these eyes.

An interesting aspect of the serial B-scans evaluated was that in some cases, the staphyloma seemed to decrease in size with time. This was true despite the association of increasing axial length with age. An explanation might be that generalized progressive stretching of the sclera in the posterior pole can smooth the previously well-defined edge of a staphyloma.

The large ranges of refractions and axial lengths in our study suggest that these ranges, taken individually, are unreliable indicators of disease severity. Previous observations,⁹ as well as those described in this study, suggest an association between the development of posterior staphylomas and macular degenerative changes. The presence of a staphyloma, its grade and recorded progression, lacquer crack formation, a family history of similar disease, and the age of an individual patient must all be considered during formation of a prognosis for long-term central visual function. The outlook for young adults with many of these negative factors is guarded, whereas highly myopic individuals in their middle or late years, without significant staphyloma, can be offered modest reassurance. These study patients exhibited a high frequency of choroidal neovascular membranes, hemorrhage, and poor best-corrected visual acuity in the lower staphyloma categories, suggesting that the development of a choroidal neovascular membrane requires relative preservation of the choriocapillaris as present in eyes with less advanced stages of posterior staphyloma formation. Therefore, it is possible that patients with less advanced degrees of staphyloma formation may be at equal or greater risk of neovascular membrane development as well as of retinal hemorrhage formation and development of decreased visual acuity. These notions are derived from our data, which were obtained from an all-white, multiethnic, referred-patient pool. Because data were collected from both eyes of patients, the statistical significance of our findings may be overestimated. All data must be evaluated with this in mind. Also, extrapolation of these data to other populations for the purpose of developing a prognosis should be done with caution. Further quantitative studies are needed in African-American individuals, who are less affected by progressive myopia, and in Asians, who are often highly myopic.

Our current biomechanical model of posterior staphyloma evolution assists in the understanding of macular damage, but the basis of myopic change appears to be fundamentally molecular in origin and genetically driven. The myopic condition may be a common clinical outcome of a number of disorders, all of which result in ocular enlargement. Some well-established genetic abnormalities that cause myopia are characterized by multiple organ involvement, including the Ehlers-Danlos, Marfan, and Stickler syndromes. Others may be strictly ocular disorders with abnormalities in processes that secondarily regulate scleral growth, such as ciliary body-related intraocular pressure interactions,¹³ and pattern-modulated retinal signals,¹⁴ which attempt to maintain emmetropia. Mechanisms for growth regulation have recently been associated with scleral chondrocyte proliferation,¹⁵ retinal dopamine modulation,¹⁶ and direct chemical modulation by both basic fibroblast-derived growth factor and transforming growth factor-beta.¹⁷ The final determination as to the mechanism of staphyloma pathogenesis will require increased knowledge of environmental influences, such as nutrition, and the role of near work, as well as translation of valuable data now emerging from experimental occlusion models. Ultimately, it may be possible to propose cellular regulatory mechanisms to explain myopic macular degeneration.

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LATTICE DEGENERATION OF THE RETINA XXX EDWARD JACKSON MEMORIAL LECTURE

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The exciting advances of contemporary ophthalmology originate from many fields of science, a vast array of research accomplishments, and a host of dedicated scientists. Among the latter, Dr. Edward Jackson stands as a towering figure, with personal achievements related to research on refraction and as author, editor, teacher, and clinician.

To present this Jackson Memorial Lecture is a privilege and an honor that I wish to share with all past and present colleagues at the UCLA School of Medicine. This lecture, therefore, is concerned with a long-standing interest at UCLA, lattice degeneration of the retina. This distinct and important retinal disorder is considered in a clinicopathologic investigation that encompasses the spectrum from retinal ultrastructure to clinical practice.

In its typical form, lattice degeneration of the retina is a sharply demarcated, circumferentially oriented disease process located at or anterior to the equator and characterized by retinal thinning and abnormalities of the adjacent vitreous. This condition was recognized initially by Gonin in the early years of this century,¹⁻³ clearly illustrated

in the subsequent publications of Vogt⁴ and Arruga,⁵ and further described in more recent reports by Schepens,^{6,7} Michaelson,^{8,9} Meyer-Schwickerath,¹⁰ Heinzen,¹¹ Okun,¹² Straatsma,¹³⁻¹⁶ Allen,^{13,14} Byer,¹⁷ Cibis,¹⁸ and others.^{19,20}

Reflecting this long period of recognition and the attention of numerous investigators, the disease has been described by many names. For one form of the disorder, the term "Schnecken Spuren," or snail tracks, was used to denote a peripheral retinal band with a frosted appearance composed of fine yellow-white grains.¹⁻³ Vogt⁴ described another type of peripheral retinal disease as "zystoide Degeneration mit weissen Gefäßniennetzen" or cystoid degeneration with white blood vessel network, because of the interlacing white lines within the localized area of abnormal retina.

Subsequently, the alterations described as snail-track and white blood vessel network degeneration were identified as variations of a single disease,^{11,13,15,18} and this was reported under several names. Translated into English, the more common terms applied to this condition include cystoid degeneration with fibrils,³ superoexternal equatorial degeneration,⁵ cystoid retinal degeneration with obliterated white blood vessels,^{4,21} lattice degeneration,^{6,7} distinctive choroidoretinopathy,^{8,9} areolar sclerosis,¹⁹ equatorial degeneration,¹⁰ interlacing white line degeneration,¹⁰ palisade degeneration,¹¹ hyaloideoretinal degeneration,^{18,22} and rhegmatogenic chorioretinohyaloidopathy.¹⁸ Although no

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single name is concise, comprehensive, and fully descriptive, the term lattice degeneration of the retina, introduced by Schepens in 1952,^{6,7} is vivid, calls attention to a distinctive feature of the process, and is widely utilized in histopathologic investigations and clinical reports.

In studies of autopsy eyes, 6% had lattice degeneration associated with retinal thinning as well as with abnormalities of the adjacent vitreous. There is a predilection for bilateral occurrence, location anterior to the equator, and circumferential orientation. Additional variable distinguishing features include an arborizing network of interlacing white lines, alterations of retinal pigment, yellow-white particles on the surface of the retinal lesion, round holes, and tears that may develop along the posterior margin of degeneration.^{13-16,23,24}

Clinical studies of lattice degeneration indicate a comparable prevalence of 6%²⁵ to 7%,¹⁷ note similar major features,^{17,26} describe autosomal dominant transmission in some families,^{18,22,27-29} add angiographic information,³⁰⁻³⁶ and contribute data concerning clinical course and the relationship between lattice degeneration and rhegmatogenous retinal detachment.*

These reports provide substantial valuable information concerning lattice degeneration of the retina, but leave important questions unanswered. This investigation, therefore, utilizes autopsy eyes and surgical material to evaluate the major features, to define principal variations, and to establish the basic histopathology of lattice degeneration. This information is correlated with clinical observations on a series of patients with lattice degeneration to develop a concept of pathogenesis and to formulate recommendations concerning clinical management.

MATERIALS AND METHODS

Material incorporated in this investigation consisted of 800 autopsy cases, one surgical

case of lattice degeneration suitable for electron microscopy, and 100 patients with lattice degeneration.

The 800 consecutive autopsy cases excluded stillbirths but included all other autopsy cases. Both eyes were available from 788 cases, so a total of 1,588 eyes were studied.

Eyes were removed as soon as possible after death, fixed in formalin for seven days, and maintained in 50% ethanol thereafter. The principal diameters were measured with calipers, and the eyes were sectioned immediately superior to the horizontal plane. Gross examination was performed with a stereomicroscope and high-intensity light. Measurements were made with a vernier caliper or ocular reticule, and all findings were noted on gross examination records.

In these eyes, lesions of lattice degeneration were identified as discrete areas of retinal thinning with characteristic alterations in the adjacent vitreous. These lesions invariably demonstrated additional features indicative of lattice degeneration (e.g., oval or band shape and circumferential orientation) and no evidence of inflammation or other specific disease process. Whenever necessary, the diagnosis was confirmed with microscopic examination.

Based on this diagnosis, the prevalence of lattice degeneration was determined, and each significant gross morphologic feature was analyzed with computer procedures by case, by eye, by lesion, by decade of age, and by broader age groups (0 to 30, 30 to 60, and 60 to 87 years of age), to determine the range of gross morphology, frequency of specific features, and progression of the disease with age. Findings were analyzed for statistical significance by the One-Way Analysis of Variance method.

Representative specimens of lattice degeneration were processed by the trypsin digestion technique.^{42,43} In these specimens, washing with water was followed by incubation at 37°C in a solution of 3% trypsin and 0.1M Tris buffer (pH 7.8) for one to three

* References 1, 3, 4, 6, 8, 10, 11, 13, 17, 18, 20, 22, 26-28, 37-41.

hours. When the retina showed signs of disintegration, the incubation was terminated, the specimen was returned to water, and careful manipulation was used to remove tissue from the retinal vessels and intimately associated structures. After mounting and drying, the preparations were stained with PAS and hematoxylin.

Portions of lattice lesions subjected to trypsin digestion and other representative specimens of lattice degeneration were embedded in celloidin or paraffin, microsectioned, and stained with hematoxylin and eosin. Supplementary stains included Mason's trichrome, picroaniline blue, and PAS preparations.

The surgical enucleation specimen of lattice degeneration, examined with correlative light and electron microscopy, was from a 66-year-old white woman who underwent enucleation for a choroidal malignant melanoma that was confined to the posterior pole. The lattice degeneration lesion was diagnosed preoperatively, and fixation was accomplished immediately after surgical enucleation by rapid immersion in a solution of 2% paraformaldehyde and 2% glutaraldehyde containing 0.2M cacodylate buffer at pH 7.25. After fixation for five hours, the specimen was trimmed, rinsed in 0.2M cacodylate buffer, and postfixed for one hour in 2M osmium tetroxide containing the same cacodylate buffer. The specimen was then rapidly dehydrated in ethyl alcohol and embedded in Araldite. The tissue was systematically cut with alternating thick sections (1 μ) and thin sections (50 $m\mu$). Thick sections were stained with toluidine blue and examined with light microscopy. Thin sections were stained with lead citrate and examined with electron microscopy. This procedure provided for correlation between light microscopy and electron microscopy.

The 100 cases of lattice degeneration of the retina evaluated clinically constituted a representative sample of alphabetically selected patients examined by one of us (B.R.S.) and followed for a period of up

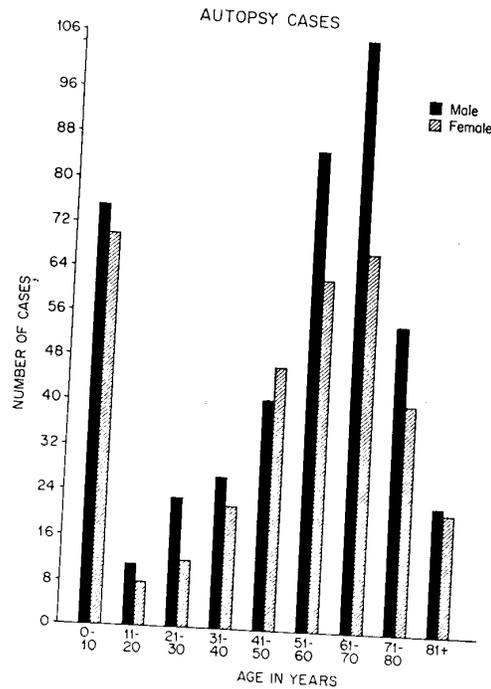


Fig. 1 (Straatsma, Zeegen, Foos, Feman, and Shabo). Age and sex distribution of 800 consecutive autopsy cases.

to 15 years. Every patient gave a detailed ophthalmic history and had a complete ophthalmic examination, including indirect ophthalmoscopy, scleral depression, and contact lens biomicroscopy. A number of patients also underwent ocular fundus photography and fluorescein photoangiography. Videotaping of angiography in several patients facilitated detailed analysis.

RESULTS

Autopsy and surgical specimen study—Figure 1 presents the age and sex distribution of the 800 consecutive autopsy cases.

Lattice degeneration of the retina, distinguished grossly and confirmed microscopically whenever necessary, was present in 86 cases (10.7%) with the age and sex distribution noted in Figure 2. Compared to the series as a whole, lattice degeneration was least common in the first decade, most common in the second decade, and distrib-

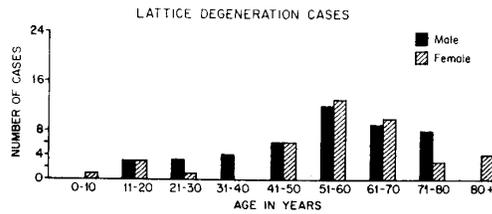


Fig. 2 (Straatsma, Zeegen, Foos, Feman, and Shabo). Age and sex distribution of 86 autopsy cases (10.7%) with lattice degeneration.

uted rather evenly throughout subsequent decades. The difference between the small incidence of lattice degeneration in the first decade and the greater incidence in the second decade was statistically significant (based on Fisher's Exact Test), but the difference in incidence of lattice degeneration in subsequent decades was not statistically significant.

Males accounted for 45 cases (52.4%) and females for 41 cases (47.7%). Both eyes were involved in 39 cases, the right eye was involved in 25 additional cases, and the left eye in 22 additional cases. Thus, there was no statistically significant preference for either sex or for either eye.

Both eyes were available in 81 cases; lattice degeneration was bilateral in 39 of these 81 cases (48.1%), and evident, therefore, in 125 of the 1,588 eyes (7.9%) in this series.

The 125 eyes with lattice degeneration contained a total of 286 separate lesions. Sixty-three eyes (50.4%) presented a single lesion and the remaining eyes contained from two to ten lesions (Fig. 3). When multiple, these lesions were often arranged in rows at different distances from the ora serrata.

Figure 4 shows the topographic distributions of the lesions, with lattice degeneration most commonly located adjacent to the vertical meridian superiorly and inferiorly. A total of 66.0% of the lesions were located in the clock-hours of 11:00 to 1:00 and 5:00 to 7:00.

All lesions of lattice degeneration pre-

sented as discrete areas of retinal thinning with characteristic alterations in the adjacent vitreous (Fig. 5). Invariably, these lesions demonstrated additional features associated with lattice degeneration such as oval or band shape, circumferential orientation, pigment epithelium irregularities, white particles within the lesion, interlacing white lines continuous with retinal blood vessels, retinal holes, and retinal tears. Each of these features was analyzed separately.

Most lesions of lattice degeneration were elliptical or oval in shape with the length greater than the width. There was substantial variation in length, however, from short lesions that encompassed less than a clock-hour to long bands that encompassed more than a quadrant (Fig. 6). Indicative of this, measurements of the 286 lesions in this series revealed a range in length from 0.25 mm to 18.50 mm with a mean length of

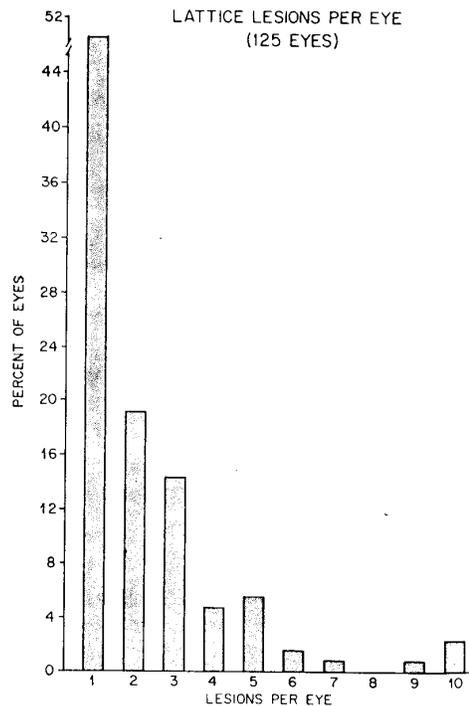


Fig. 3 (Straatsma, Zeegen, Foos, Feman, and Shabo). Number of lattice lesions in the 125 autopsy eyes with lattice degeneration.

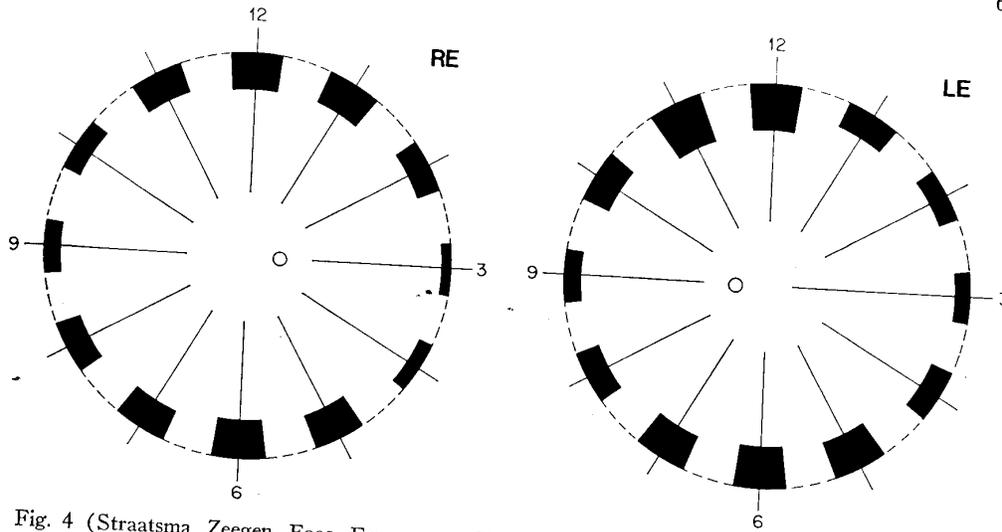


Fig. 4 (Straatsma, Zeegen, Foos, Feman, and Shabo). Meridional distribution of lattice degeneration in autopsy eyes.

2.12 ± 2.31 mm (Fig. 7). That is to say, the average lesion of lattice degeneration was slightly more than one optic disk diameter in length.

In anteroposterior width, there was variation from a narrow trough of degeneration

to a broad zone. Lesions ranged in width from 0.15 mm to 3.50 mm with a mean width of 0.77 ± 0.48 mm (Fig. 8). Width, moreover, was almost always less than length so that 91.6% of lesions were oval or band-shaped and only 8.4% were round.

The distance from the ora serrata to the anterior margin of the lattice degeneration was an extremely important feature. In some cases, lesions were very close to the ora serrata, while in other cases, they were encountered throughout the retinal portion of the vitreous base and were positioned

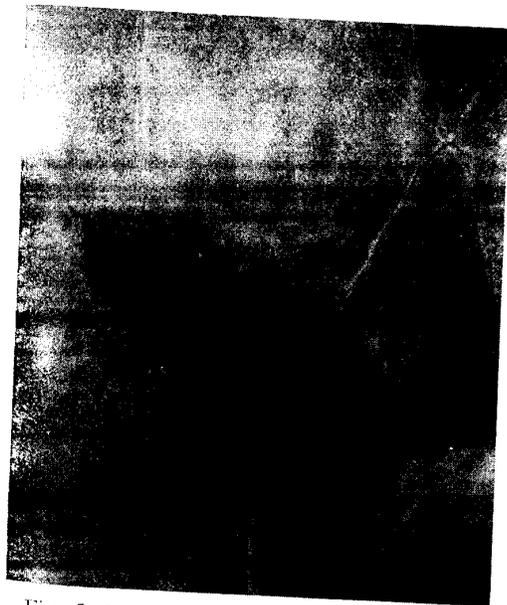


Fig. 5 (Straatsma, Zeegen, Foos, Feman, and Shabo). Lattice degeneration lesion with retinal thinning, characteristic vitreous alterations, and other typical features.



Fig. 6 (Straatsma, Zeegen, Foos, Feman, and Shabo). Lattice degeneration. Long, band-shaped lesion encompasses more than a quadrant.

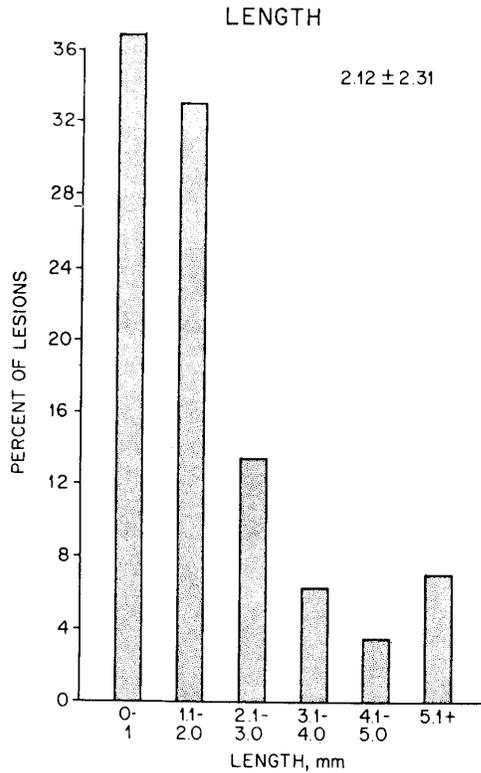


Fig. 7 (Straatsma, Zeegen, Foos, Feman, and Shabo). Length of lattice degeneration lesions; mean of 2.12 ± 2.31 mm.

posterior to the equator. Statistically, the distance from the ora serrata to the anterior margin of the lesion ranged from 0.10 mm to 9.00 mm with a mean of 2.18 ± 1.41 mm (Fig. 9). Stated another way, the average lesion was located somewhat more than one optic disk diameter posterior to the ora serrata.

Orientation of lattice degeneration lesions was also analyzed. In this series, the long axis of the lesion was generally parallel to the ora serrata, but lesions were also encountered at every angle so that some lesions were relatively radial and few were actually perpendicular to the ora serrata. Grouped to indicate orientation, the long axis of the lesion was essentially parallel to the ora serrata (i.e., at an angle of 5 degrees or less from parallel) in 195 lesions (68.2%), at an angle of 6 to 30 degrees in 27 lesions

(9.5%), at an angle of 31 to 60 degrees in 19 lesions (6.6%), and at an angle of 61 to 90 degrees in 21 lesions (7.3%) (Fig. 10). Additionally, 24 lesions (8.4%) were round in shape so that orientation could not be determined.

In essence, the overwhelming majority of lesions were parallel or nearly parallel to the ora serrata and thus conformed to the circumferential orientation characteristic of lattice degeneration.

Although length, width, distance from the ora serrata, and orientation were analyzed separately, these features were correlated in a general manner. Lesions close to the ora serrata tended to be linear, narrow, and circumferential in orientation; while lesions posterior to the equator tended to be oval,

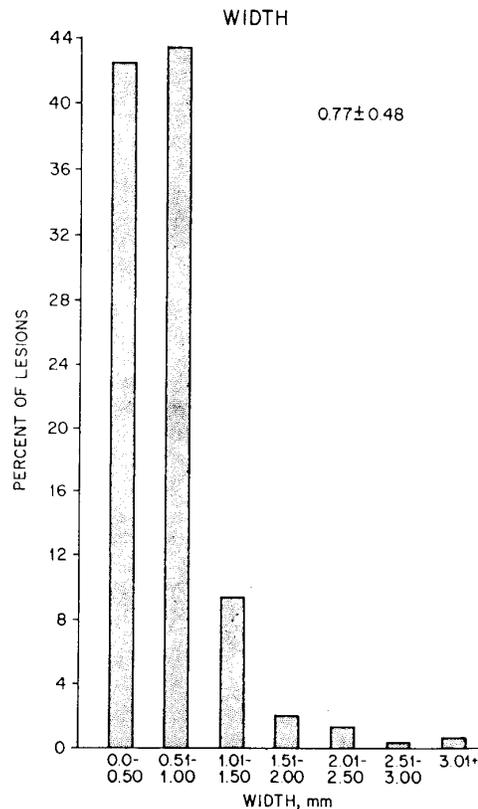


Fig. 8 (Straatsma, Zeegen, Foos, Feman, and Shabo). Width of lattice degeneration lesions; mean of 0.77 ± 0.48 mm.

wider, and more radial in orientation (Fig. 11).

In the lesions of lattice degeneration, retinal thinning was variable in degree and usually somewhat irregular. As a result, the retinal surface often appeared shaggy and frequently presented irregular, amorphous, gray-white particles. Vitreous liquefaction with corresponding loss of vitreoretinal attachments over the area of thinned retina was always present but, usually, was demonstrated only by manipulation of the specimen. Moreover, vitreous condensation at the margin of the liquefied pocket and exaggerated vitreoretinal attachments along the circumference of the thinned retina were variable in degree but always evident. In some instances, a cuff of exaggerated vitreoretinal attachments surrounded the central area of retinal thinning (Figs. 5 and 11).

Augmenting these invariable features, retinal pigment abnormalities corresponding to the lattice degeneration were noted in 263 lesions (92.0%) (Fig. 6). These consisted of focal loss of pigmentation and

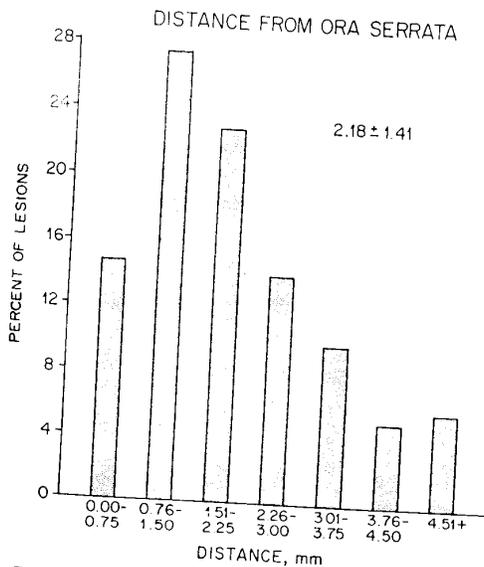


Fig. 9 (Straatsma, Zeegen, Foos, Feman, and Shabo). Distance of the anterior margin of lattice degeneration lesions from the ora serrata; mean of 2.18 ± 1.41 mm.

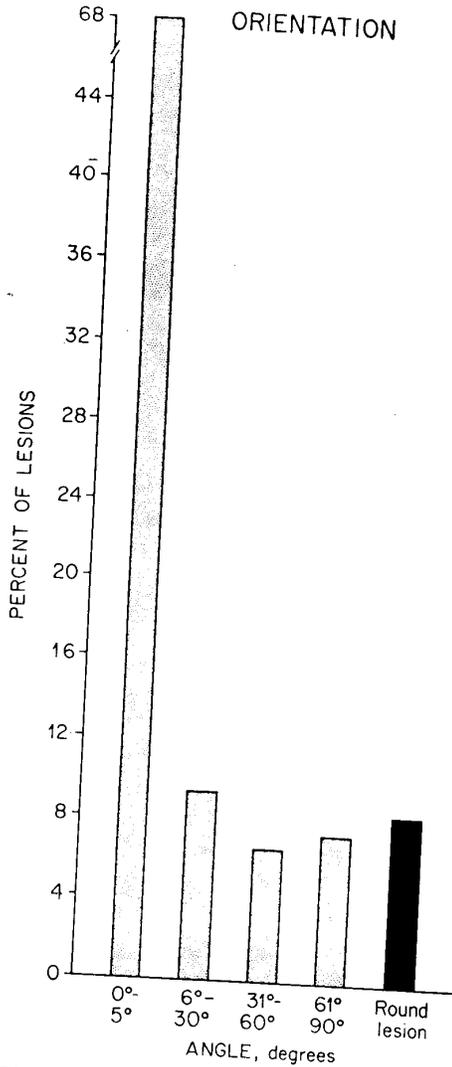


Fig. 10 (Straatsma, Zeegen, Foos, Feman, and Shabo). Orientation of lattice degeneration lesions by angle, in degrees, between the long axis of the lesion and the ora serrata.

clumps of hyperpigmentation in the retinal pigment epithelium, as well as migration of pigment into the retina, particularly into the perivascular space surrounding the retinal vessels.

Retinal vessel abnormalities within the foci of lattice degeneration were a conspicuous feature. Though grossly visible, only 131 lesions (45.8%) contained retinal vessels; vessels with abnormal fibrotic thicken-

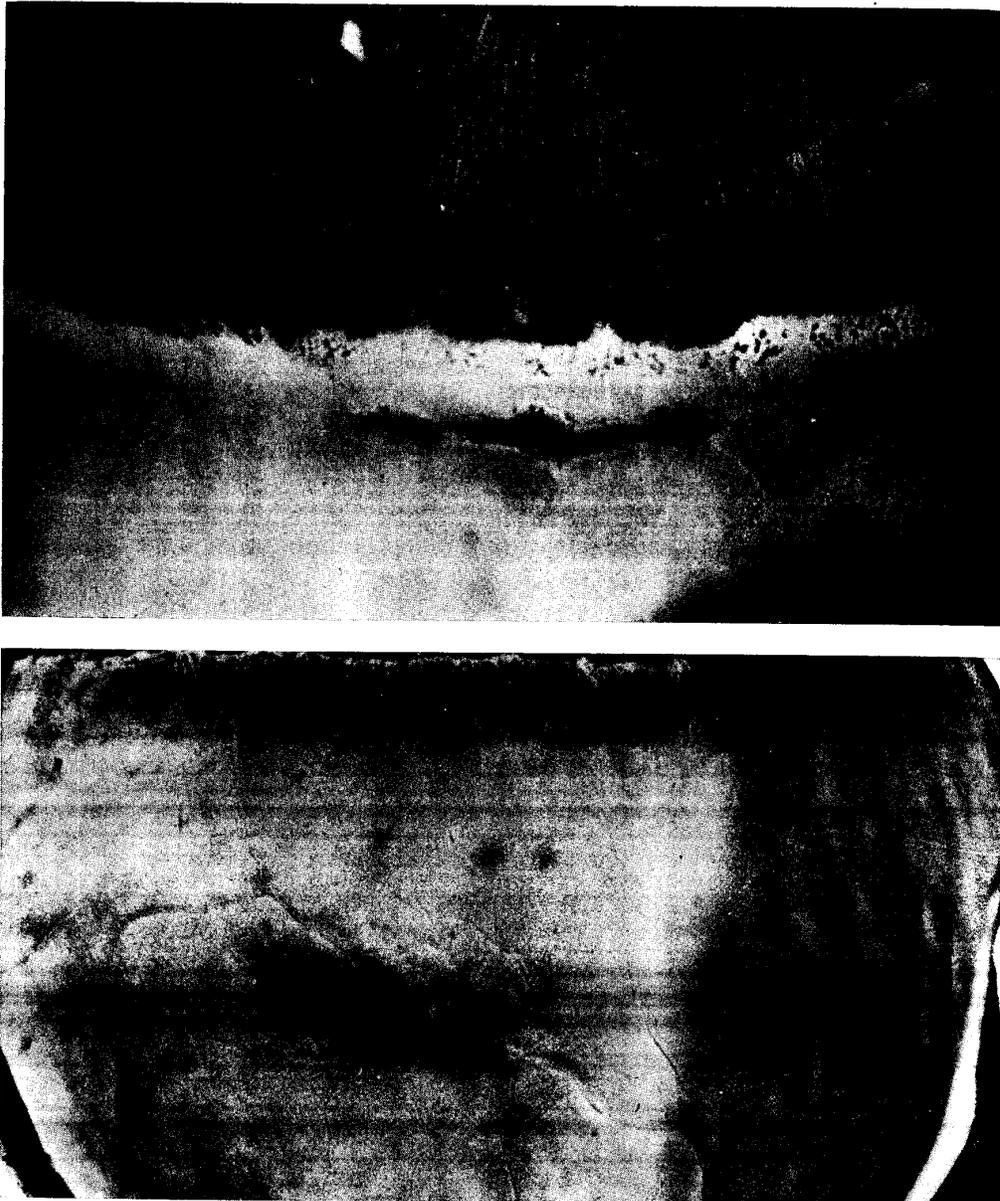


Fig. 11 (Straatsma, Zeegen, Foos, Feman, and Shabo). Lattice degeneration. Top, Lesion close to the ora serrata is linear, narrow, and circumferential in orientation, with focal thinning and a full-thickness retinal hole (PAS, $\times 125$). Bottom, Lesion posterior to the equator is oval, wide, and radial in orientation, with a paraxial vessel and gray-white particles in the adjacent retina.

ing sufficient to give a definite white line appearance occurred in 21 lesions (7.3% of the entire series) (Fig. 11, bottom). These vessel abnormalities were confined to the area of the lattice and were often accentuated by

the migration of pigment into tissue spaces immediately adjacent to the abnormal vessels.

Focal thinning of the retina within lattice degeneration occurred in 55 lesions (19.2%),

and 52 lesions (18.2%) contained round or oval full-thickness retinal holes. These round full-thickness retinal holes, present in 32 of the 125 eyes (24.9%) with lattice degeneration, were particularly apt to be located near the end of a lattice (Fig. 11, top).

In this series, retinal tears associated with lattice degeneration were encountered in only four lesions (1.4%). One eye demonstrated two separate tears, and two eyes were associated with a single tear; therefore, three of the 125 eyes (2.4%) contained retinal tears. In every instance, the tear extended along the posterior margin of the lattice lesion and progressed along one or both extremities of the lesion to produce an L-shaped or U-shaped retinal rupture. Significantly, all three eyes with retinal tears presented posterior vitreous detachment, clearly related to the traction-induced retinal tears.

To evaluate the course and progression of lattice degeneration, each gross morphologic feature was statistically analyzed by case, by eye, and by lesion, for each decade of age and for three major age groups (0 to 30, 31 to 60, 60 to 87 years of age). This analysis provided no statistically significant age-related trend in length, width, distance from the ora serrata, or orientation of the lesions. With advancing age, however, there was a statistically significant ($P < .05$) increase in the degree of exaggerated vitreoretinal attachments at the margin of the lesion and a statistically significant increase in the incidence of retinal pigment abnormalities, white line retinal vessels, full-thickness retinal holes, posterior vitreous detachment, and retinal tears. Retinal tears, as noted previously, were invariably associated with posterior vitreous detachment.

Trypsin digest preparations, light microscopy, and electron microscopy evaluated the pathologic characteristics of lattice degeneration. With trypsin digest preparations, lattice degeneration demonstrated (1) retinal thinning, (2) vitreous liquefaction with loss of vitreoretinal attachments over the area of

retinal thinning, (3) increased vitreoretinal attachments at the margin of the lesion, (4) extensive vascular abnormalities within the lesion, (5) accumulations of dense, amorphous, PAS-positive material, and (6) retinal pigment abnormalities.

When compared with the overall gross appearance of lattice lesions, trypsin digest preparations presented a corresponding, sharply demarcated area of retinal thinning that contained even, round defects corresponding to full-thickness retinal holes (Fig. 12). Liquefaction of the overlying vitreous was associated with an absence of vitreoretinal attachments, while exaggerated vitreoretinal attachments and vitreous condensation produced a densely staining cuff at the margin of the lesions.

All lesions had extensive vascular abnormalities. These were characterized by a decrease in the number of capillaries within the lesion, a relative acellularity of all vessels within the lesions, and an obliterative fibrosis of the large and small vessels within the areas of degeneration. Careful study of specific lesions revealed loss of capillaries, a decrease in the number of endothelial cells and intramural pericytes associated with vessels in the lesions, and a fibrosis that encroached on the lumen of all vessels within the areas of degeneration. Concomitantly, there were acellular PAS-positive strands, probably representing former capillaries, and irregular clumps of PAS-positive material throughout the lesions (Fig. 13). All of these abnormalities, progressively more severe with advancement from the periphery to the center of the lesions, were particularly evident when an area of lattice degeneration was compared with an adjacent uninvolved area of the peripheral retina (Fig. 14). Direct correlations, moreover, established that the white line appearance of retinal vessels was related to stromal fibrosis, acellular thickening of the vessel wall, and encroachment on the vessel lumen (Fig. 15). The irregular, amorphous, gray-white particles within and at the margin of the lat-

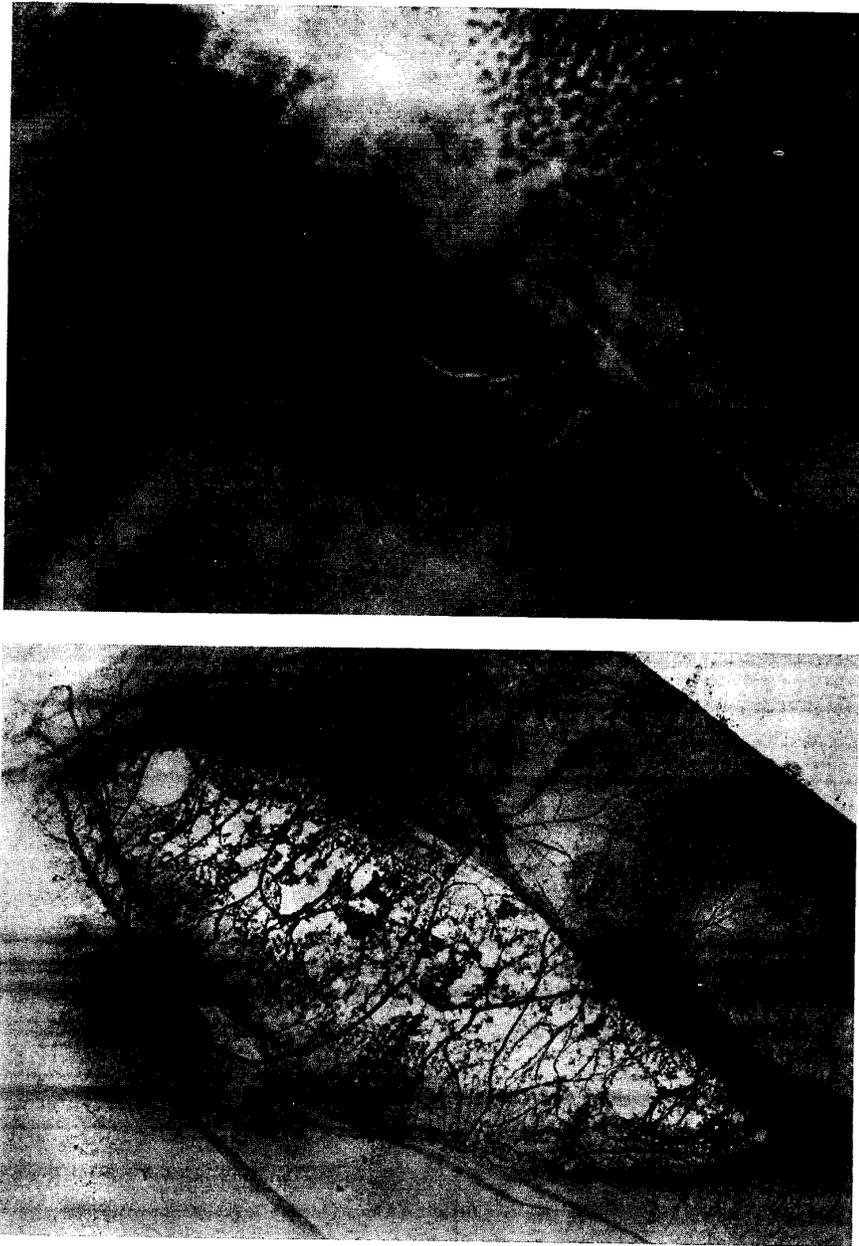


Fig. 12 (Straatsma, Zeegen, Foos, Feman, and Shabo). Lattice degeneration. Top, Lesion with sharply demarcated area of retinal thinning, exaggerated vitreoretinal attachments at the margin, white line vessels, pigment abnormalities, and a full-thickness retinal hole. Bottom, Trypsin digest preparation of same lesion emphasizes liquefaction of the overlying vitreous, dense vitreoretinal attachment at the margin of the lesion, vascular abnormalities, and the retinal hole ($\times 17$).

tice lesions were related to dense granules of PAS-staining material, shown by microscopy to represent extracellular products of

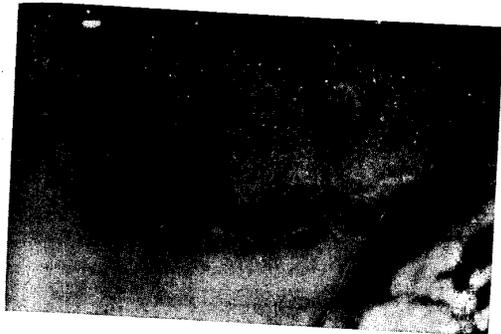


Fig. 13 (Straatsma, Zeegen, Foos, Feman, and Shabo). Lattice degeneration. Top, Lesion with characteristic features and extensive vascular abnormalities. Middle, Trypsin digest preparation of the right half of the same lesion ($\times 25$). Bottom, Trypsin digest preparation at higher magnification to illustrate loss of capillaries, decrease in endothelial cells and intramural pericytes, and fibrosis of all vessels. Acellular PAS-positive strands and irregular clumps are also evident ($\times 125$).

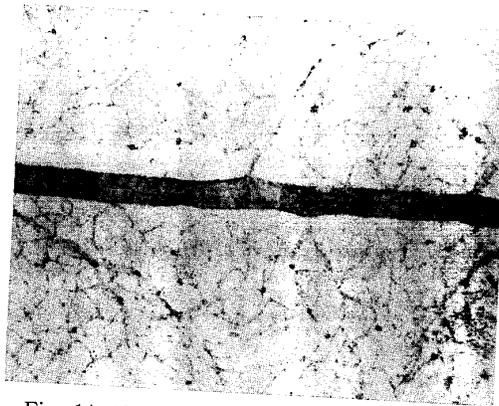


Fig. 14 (Straatsma, Zeegen, Foos, Feman, and Shabo). Trypsin digest preparation of normal control area adjacent to lattice degeneration lesion ($\times 75$).

cell breakdown and fibrosis. Pigment, when present in the retina, was usually perivascular and located within pigment-containing macrophages (Fig. 16).

Corroborating the trypsin digest studies and providing additional information, light microscopy studies of lattice degeneration revealed (1) retinal thinning, (2) vitreous liquefaction with loss of vitreoretinal attachments in the corresponding area, (3) increased vitreoretinal attachments at the margin of the lesion, (4) extensive vascular abnormalities, (5) degeneration of the retinal cells, (6) accumulations of PAS-positive particles, and (7) retinal pigment abnormalities.

All lesions of lattice degeneration, even mild examples of the condition, presented retinal thinning related to degeneration that was most severe in the inner retinal layers but affected all layers. In addition, there was vitreous liquefaction with loss of vitreous structure and an absence of vitreoretinal attachments immediately adjacent to the abnormal retina and exaggerated vitreoretinal attachments at the margin of the lesion (Figs. 11, top, and 17).

Advanced lesions demonstrated additional features such as generalized retinal thinning that seriously disrupted all layers, conspicuous vitreous condensation at the interface

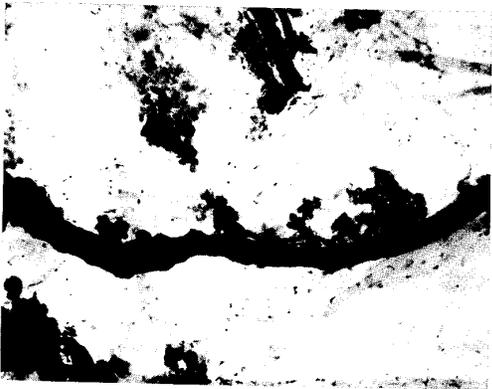
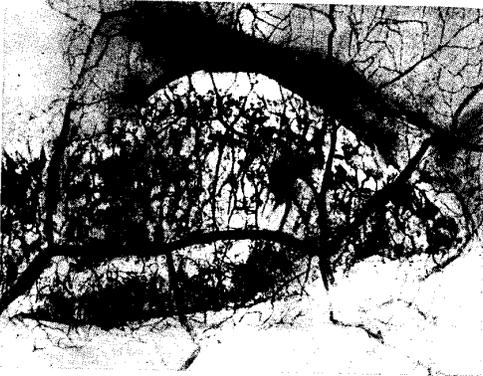
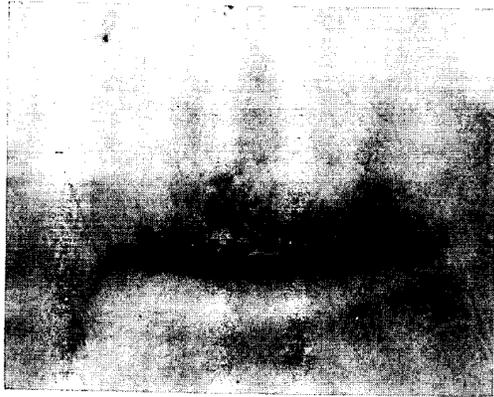


Fig. 15 (Straatsma, Zeegen, Foos, Feman, and Shabo). Lattice degeneration. Top, Lesion with white line appearance of retinal vessels. Middle, Trypsin digest preparation of the same lesion ($\times 35$). Bottom, Trypsin digest preparation at higher magnification shows fibrosis and acellular thickening of the vessel wall. Irregular clumps of PAS-positive material are in and adjacent to the fibrotic white line vessel ($\times 125$).

Fig. 16 (Straatsma, Zeegen, Foos, Feman, and Shabo). Lattice degeneration. Top, Lesion with severe pigment abnormalities. Middle, Trypsin digest preparation of the same lesion ($\times 25$). Bottom, Trypsin digest preparation at higher magnification shows vessel fibrosis, pigment in paravascular location, and pigment in macrophages at other sites in the retina ($\times 75$).

between liquid and formed vitreous, abnormal thickening of large vessel walls, irregular intraretinal deposits of eosinophilic and PAS-positive material representing cell breakdown products, and abnormal pigment within macrophages located in perivascular spaces or in the retina (Fig. 18).

In some advanced lesions of lattice degeneration, these histologic findings were supplemented by glial cell proliferation along the line of condensation at the interface between liquid and formed vitreous, glioses extending from retina into vitreous along this scaffold of condensed vitreous, severe obliterative fibrosis, and even occlusion of retinal vessels (Figs. 13, top, and 19).

More detailed information concerning the pathologic characteristics of lattice degeneration was provided by correlative light and electron microscopy. In the specimen, an advanced lesion of lattice degeneration, representative portions at the periphery, mid-periphery, and center of the lattice lesion were examined with both light and electron microscopy. With advancement from the periphery to the center of the lesion, these studies demonstrated (1) progressive thinning of the retina, (2) advancing fibrosis of retinal blood vessels, (3) increasing loss of retinal neurons, (4) mounting accumulations of extracellular material, (5) pigment abnormalities, and (6) significant alterations in the inner limiting lamina of the retina.

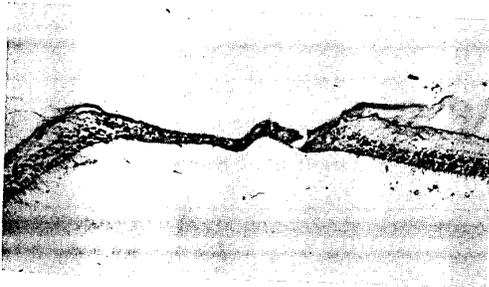


Fig. 17 (Straatsma, Zeegen, Foos, Feman, and Shabo). Lattice degeneration with retinal thinning, vitreous liquefaction over the lesion, and exaggerated vitreoretinal attachments at the margin. Gross appearance of the same lesion is shown in Figure 11, top (PAS, $\times 125$).

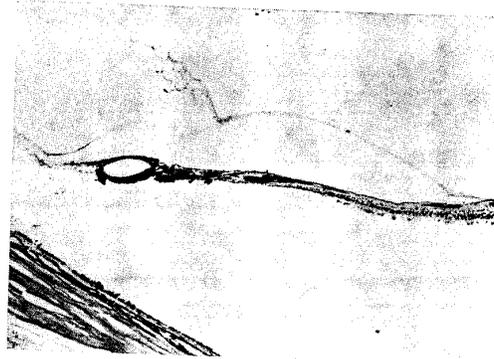
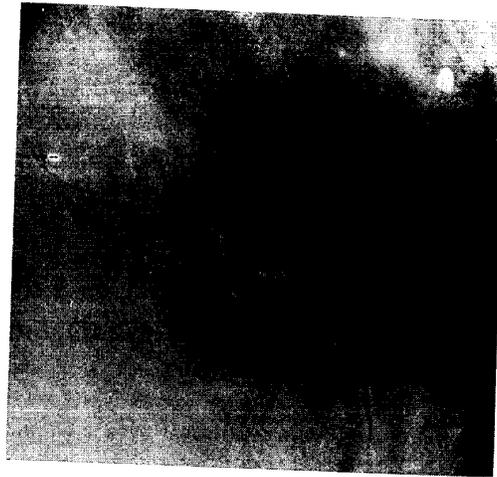


Fig. 18 (Straatsma, Zeegen, Foos, Feman, and Shabo). Lattice degeneration. Top, Postequatorial lesion with white line vessels and marked pigment alterations. Middle, Retinal thinning with description of all layers and conspicuous vitreous condensation at the interface of liquid and formed vitreous (PAS, $\times 75$). Bottom, Higher magnification illustrates abnormal thickening of vessel wall, intraretinal deposits of densely staining extracellular material and pigment within macrophages in perivascular spaces and adjacent retina (PAS, $\times 250$).

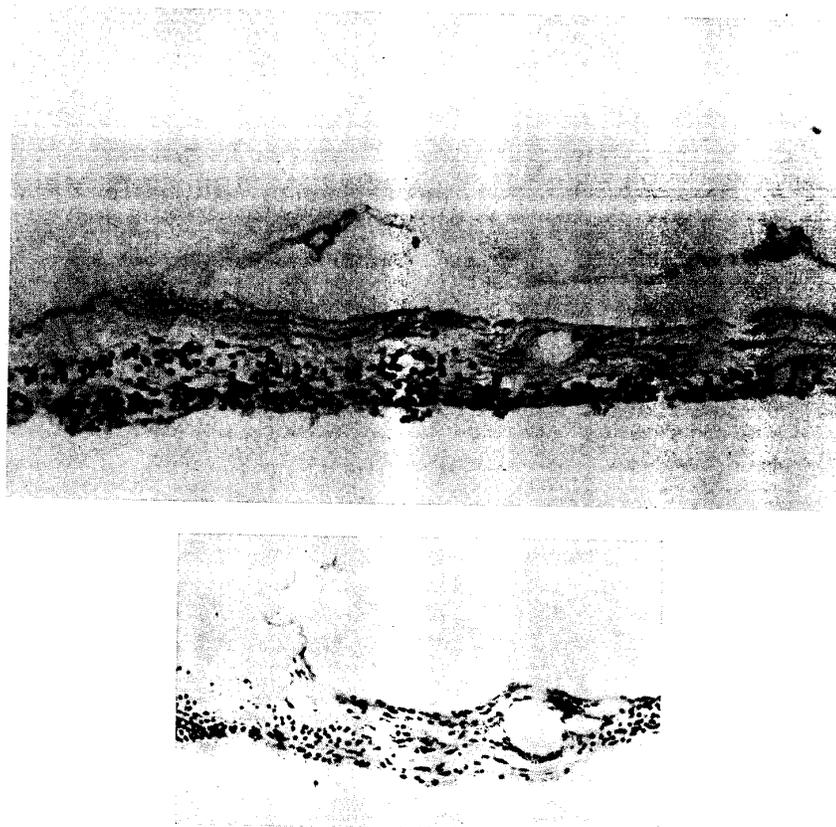


Fig. 19 (Straatsma, Zeegen, Foos, Feman, and Shabo). Lattice degeneration. Top, Glial proliferation along interfaces between liquid and formed vitreous (hematoxylin and eosin, $\times 250$). Bottom, Gliosis extending from retina into vitreous along scaffold of condensed vitreous and fibrotic occlusion of retinal vessel (hematoxylin and eosin, $\times 250$). Gross appearance of this lesion is shown in Figure 13, top.

Progressive thinning of the retina from the edge to the center of the lesion was evident by inspection of sections from the periphery, mid-periphery, and center of the lesion (Fig. 20). Increasing blood vessel alterations were also apparent in representative sections. At the periphery of the lesion, the walls of the vessels were structurally normal, and the lumina were open (Fig. 20, left). In the mid-periphery, blood vessel walls were thickened and the lumina partially obliterated (Fig. 20, center); in the center of the lesion, blood vessels were obliterated and the walls were replaced by dense cords of connective tissue (Fig. 20, right). These cords occasionally extended beyond the normal outlines of blood vessels into the

extracellular spaces of the degenerated retina or into the subretinal space.

Loss of retinal neurons, increasingly severe from the periphery to the center of the lesion, occurred in all retinal layers. In the mid-periphery, for example, electron microscopy demonstrated the cytoplasmic profiles of degenerating retinal neurons. Instead of normal intracellular organelles, these degenerating cells contained only a few scattered vesicles and mitochondria (Fig. 21). These degenerating neurons were surrounded by glial cells, many of which extended a myriad of cytoplasmic processes that appeared to fill the expanded extracellular spaces created by the shrinking neurons.

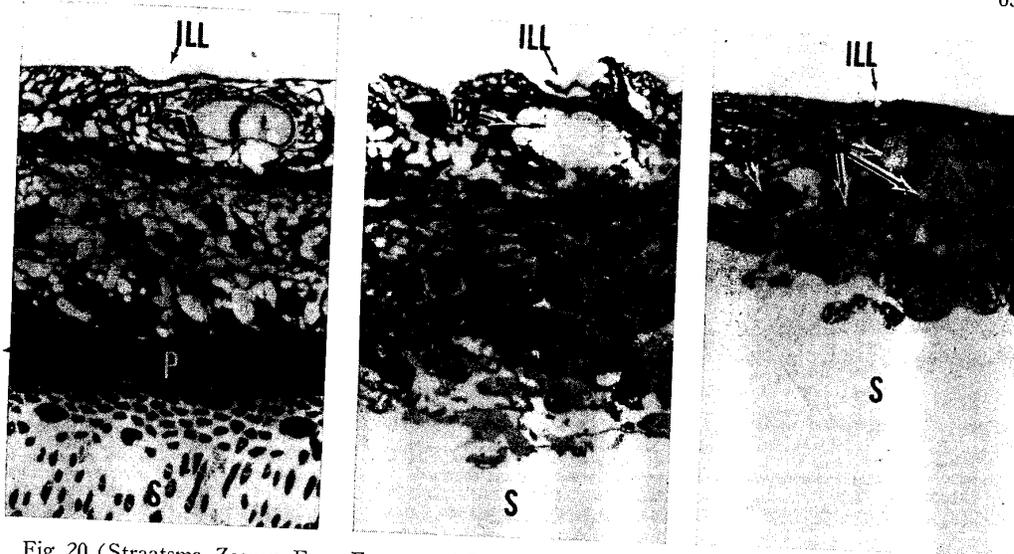


Fig. 20 (Straatsma, Zeegen, Foos, Feman, and Shabo). Lattice degeneration. Left, The periphery or margin of the lesion. Center, The mid-periphery. Right, The center of the lesion. Areas demonstrate several features of lattice degeneration. First, there is a progressive, marked thinning of the entire retina from the periphery and from the mid-periphery to the lesion center. Second, the blood vessels of the inner retina appear to be obliterated. In the periphery of the lesion (left), the lumina of the vessels (BV) appear normal in size and are surrounded by a thin rim of stromal connective tissue. Blood vessels in the mid-periphery (center) are partially obliterated, while those in the center of the lesion are absent and are replaced by dense, cord-like accumulations of connective tissue (CT) (right). These connective tissue masses extend beyond the vascular profiles into the intercellular spaces of thinned retina and occasionally project into the subretinal space (S) (right). Third, normal cellular spaces within the retina are absent with the residual structure composed of glial cell processes, scattered pigment containing macrophages (M), and interspersed fibrous connective tissue (right). Varying degrees of neuronal and photoreceptor (P) degeneration are present in the periphery and mid-periphery (left and center), but none of these cell types is present in the lesion center (right). Fourth, the inner limiting lamina (ILL) is intact in the periphery of the lesion (left). In the mid-periphery (center), the inner retinal surface is wrinkled, but the inner limiting lamina maintains its integrity. However, in the lesion center (right), the inner limiting lamina is thinned and discontinuous (1- μ plastic-embedded section; toluidine blue, $\times 650$).

In the mid-periphery, a comparable degeneration of retinal photoreceptors was also present. These cells demonstrated a decrease in the density of cytoplasmic processes and a diminution of intracellular organelles. However, the glial cell framework surrounding these cells was maintained.

Glial cells responded by filling the extracellular spaces, initially, with cytoplasmic processes (Fig. 21) and, subsequently, with extracellular material. Indicative of this were massive accumulations of extracellular glial connective tissue material (Fig. 22). Some of the extracellular masses contained maze-like patterns of basal lamina, which suggested that glial cell elements were incorpo-

rated in the relatively amorphous extracellular masses of connective tissue.

Offering insight into the development of this lesion, the inner limiting lamina of the retina demonstrated significant alterations. At the periphery of the lesion, this lamina was intact (Fig. 20, left). In the mid-periphery, this lamina was wrinkled but intact (Fig. 20, center). In the center, however, the inner limiting lamina was thinned and intermittently absent (Fig. 20, right). Thus, in some regions, there was no inner limiting lamina, and glial-cell processes extended toward the vitreous cavity (Fig. 23, left). In other areas, the inner limiting lamina was attenuated and bordered by abnormal glial



Fig. 21 (Straatsma, Zeegen, Foos, Feman, and Shabo). Lattice degeneration. Electron micrograph from the mid-periphery demonstrates degenerating cytoplasmic profiles of intraretinal neurons (N) that appear vacant except for scattered vesicles and mitochondria. These degenerating cells are surrounded by a framework of glial cells (G), many of which extend a myriad of cytoplasmic processes (CP) that appear to fill the extracellular spaces ($\times 22,657$).



Fig. 22 (Straatsma, Zeegen, Foos, Feman, and Shabo). Lattice degeneration. In the center of the lesion, glial cells (G) occasionally contain dense, round profiles resembling pigment granules (PG). Massive accumulations of extracellular connective tissue (CT) are present and some of these contain maze-like patterns of basal laminar material (BL). This "footprint" of basal laminar material suggests previous glial cell activity in the center of these scars ($\times 20,712$).



Fig. 23 (Straatsma, Zeegen, Foos, Feman, and Shabo). Lattice degeneration. The inner limiting lamina in the center of the lesion is discontinuous. In some regions (left), no inner limiting lamina is discernible and glial cells (G) of the inner retinal surface extend thin processes (arrows) toward the vitreous cavity. However, in other areas of the central lesion (right), an attenuated inner limiting lamina (ILL) can be identified and often borders discontinuous glial cell processes of the inner retinal surface ($\times 39,129$).

LATTICE DEGENERATION PATIENTS

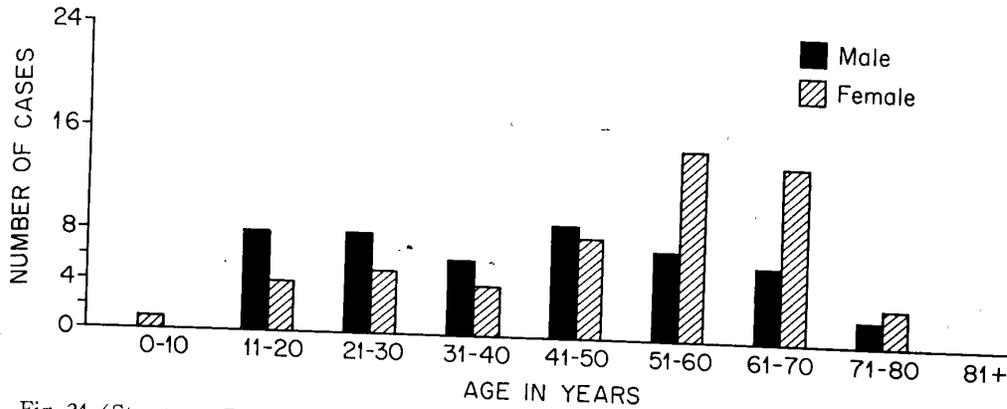


Fig. 24 (Straatsma, Zeegen, Foos, Feman, and Shabo). Age and sex distribution of 100 patients with lattice degeneration.

cell processes on one side and by structureless vitreous material on the other (Fig. 23, right).

Clinical study—In the clinical study, a representative sample of 100 alphabetically selected patients with lattice degeneration of the retina, examined by one of us (B.R.S.) and followed for up to 15 years, was reviewed. Although these physician-referred patients do not reflect the uncomplicated clinical course of lattice degeneration, this evaluation was carried out to correlate gross features and histopathologic findings with the clinical characteristics of lattice degeneration and to elucidate some of the variations in clinical course. Figure 24 details the age

and sex distribution of this group of 100 patients with lattice degeneration. The observation period ranged from a single consultation to a period of 15 years (Fig. 25).

Both eyes were available for examination in 95 patients, lattice degeneration was bilateral in 49 patients (51.6%) and evident, therefore, in a total of 149 eyes (76.4%).

The affected eyes varied in refractive error from a spherical equivalent of -22.00 to $+2.75$, with a significantly greater percentage of myopic refractive error than in the population as a whole (Fig. 26). Visual acuity in every eye, unless altered by an unrelated disease or a retinal detachment, was 20/30 or better.

The 149 eyes with lattice degeneration contained a total of 399 separate lesions with a range from one to 14 lesions in each affected eye. When lesions were multiple, they were often arranged in two, three, or even four rows at varying distances from the ora serrata.

Figure 27 shows the topographic distribution of the lesions with lattice degeneration most prevalent adjacent to the vertical meridian superiorly and inferiorly, less common in the temporal horizontal area, and least common in the nasal horizontal area.

On clinical examination, lattice degenera-

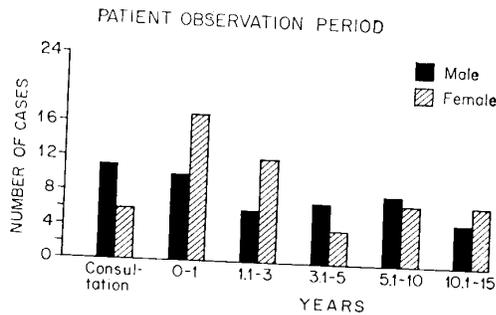


Fig. 25 (Straatsma, Zeegen, Foos, Feman, and Shabo). Observation period for 100 patients with lattice degeneration.

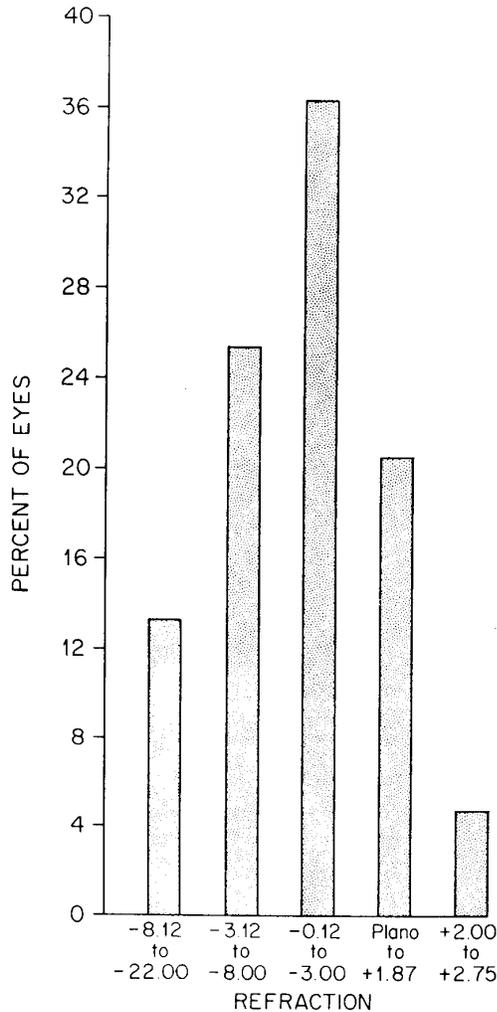


Fig. 26 (Straatsma, Zeegen, Foos, Feman, and Shabo). Refraction, in spherical equivalent, of patients with lattice degeneration.

tion presented a range of length, width, distance from the ora serrata, and orientation that corresponded with findings in the autopsy series. The characteristic lesion appeared as a sharply demarcated, preequatorial, circumferentially oriented area of retinal thinning, vitreous abnormalities, and pigment alterations. Vitreous liquefaction overlying the retinal lesion, condensation at the interface of liquid and formed vitreous, and exaggerated vitreoretinal attachments at the margin of the lesion were best seen with

contact lens biomicroscopy. This technique often revealed many tiny shimmering yellow-white reflexes corresponding to vitreous condensations overlying and at the margin of the retinal degeneration. Scleral depression, combined with contact lens biomicroscopy or indirect ophthalmoscopy, also emphasized the cuff of relatively dense, white-with-pressure, vitreoretinal attachments surrounding the area of retinal thinning.

The shaggy, irregular internal surface of the thinned retina was a conspicuous feature of both contact lens biomicroscopy and ophthalmoscopy. Irregular gray-white particles on the inner surface and within the thinned retina corresponded to the amorphous products of cell breakdown and extracellular fibrosis noted in the autopsy eyes and electron microscopy studies (Fig. 28).

Focal thinning and full-thickness retinal holes were seen in some cases. These holes were round or oval in shape and usually located near one or both extremities of a lesion. Scleral depression enhanced identification of these areas by increasing the translucency of the adjacent retina. By using contact lens biomicroscopy, indirect ophthalmoscopy, and scleral depression, differentiation between areas of focal thinning and full-thickness retinal holes was usually possible (Fig. 29).

Retinal tears that occurred with lattice degeneration were invariably associated with posterior vitreous detachment, and the rupture extended along the posterior border or lateral margins of the lesion to assume a linear, L-shaped, or U-shaped configuration.

All lesions of lattice degeneration studied with fluorescein photoangiography demonstrated retinal vascular abnormalities with relative avascularity in and adjacent to the lesion, or with abnormal vascular structures and flow dynamics within the lesion. Illustrating the latter is a postequatorial and radial area of lattice degeneration that contained a paraxial retinal vein (Fig. 30). This vessel was irregularly attenuated and surrounded by clumps of paravascular pig-

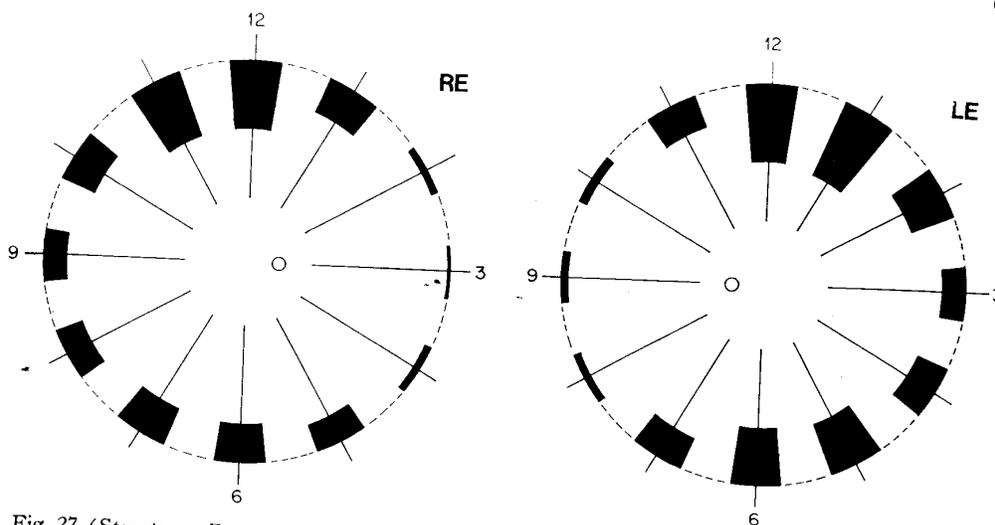


Fig. 27 (Straatsma, Zeegen, Foos, Feman, and Shabo). Meridional distribution of lattice degeneration in patients.

mentation. On fluorescein angiography, venous flow into the lesion was delayed, and when it occurred, the more posterior branches filled first and then drained into the paraxial vein (Fig. 31, top left). As this continued, fluorescein streamed posteriorly along the vessel wall in a laminar manner, but the central portion of the vessel remained filled with slowly moving blood from the more peripheral retina (Fig. 31, top right). After a few seconds, the more distal branches of the paraxial vein and, finally, the anterior portion of the paraxial vein were filled with fluorescein (Fig. 31, bottom left). Confirming the abnormally slow rate of flow, the paraxial vein remained hyperfluorescent for several seconds after the adjacent retinal veins had emptied (Fig. 31, bottom right).

Adjacent to the lattice lesions, arteriovenous connections were usually demonstrable. These connections, however, were of approximately capillary size and filled relatively late in the arteriovenous phase. Thus, these were small, low-velocity arteriovenous connections rather than high-velocity arteriovenous shunts.

On fluorescein angiography, all lattice lesions presented retinal pigment epithelium

irregularities that were evident early in the choroidal phase as areas of hyperfluorescence mixed with areas of hyperpigmentation (Figs. 30 and 31). The total area of pigment epithelium abnormality demarcated by fluorescein angiography was generally greater than the area of pigment abnormality discerned on color photographs. Significantly, sequential photographs did not reveal any evidence of fluorescein leakage from the choroid into the retina or any evidence of fluorescein leakage from retinal vessels.

Variations in the clinical course of lattice degeneration were evident in this series of 100 alphabetically selected, physician-referred patients. Although this atypical patient selection undoubtedly contributed to the high incidence of rhegmatogenous retinal detachment—affecting 51% of the patients in this series—and made detailed analysis inappropriate, general patterns of clinical progression were evident.

Patients with lattice degeneration unassociated with retinal holes or tears remained, almost always, clinically unchanged for extended periods. In a few instances, one or more full-thickness retinal holes developed, and rarely, posterior vitreous detachment

was associated with development of a retinal tear.

Patients with full-thickness retinal holes were also observed for extended periods. Infrequently, a localized retinal detachment formed adjacent to the retinal lesion, and this was usually treated with prophylactic retinal surgery. Rarely, a progressive extensive retinal detachment requiring retinal detachment surgery developed. When extensive detachment occurred, it usually was related to full-thickness holes located posterior to the vitreous base in eyes with significant myopia, aphakia, or other factors predisposing to retinal detachment.

Patients with retinal tears associated with lattice degeneration invariably presented posterior vitreous detachment. These traction-related retinal tears, particularly when located in the superior retina, were apt to cause retinal detachment, and they were treated prophylactically. In fact, traction tears of this type were responsible for the majority of progressive retinal detachments in this series. Requiring retinal detachment surgery, these detachments were particularly difficult to manage when retinal tears were adjacent to posterior, radially oriented lesions of lattice degeneration. Reflecting the relationship to posterior vitreous detachment, retinal tears adjacent to lattice degeneration were always posterior to the vitreous base, and usually were associated with significant myopia, aphakia, advanced age, or some other factor predisposing to posterior vitreous detachment.

The rather common occurrence of bilateral lattice degeneration in this series (51.6% of patients) and the usual symmetry of significant associated factors such as myopia, aphakia, and age-related vitreous degeneration contributed to the appreciable incidence of bilateral retinal detachment or unilateral detachment with contralateral prophylactic surgery in this series. Indicating the overall favorable prognosis for rhegmatogenous retinal surgery, no patient in this series was bilaterally blind (i.e., with a corrected vi-

sion of 20/200 or less) as a consequence of rhegmatogenous retinal detachment.

DISCUSSION

Although numerous aspects of this clinicopathologic study warrant attention, this discussion of lattice degeneration of the retina is confined to a consideration of pathogenesis, clinicopathologic manifestations, and management.

In regard to pathogenesis, this study indicates that lattice degeneration is a relatively common disorder that usually becomes evident in the second decade and evolves slowly thereafter.

Gross, microscopic, ultrastructural, and clinical observations emphasize the presence of retinal vascular abnormalities in all lattice lesions and note the correlation, in area and degree of involvement, between these vascular abnormalities and progression of the degenerative process. Initial structural changes affecting the vascular system are a decrease in the number of capillaries, a fibrotic degeneration of the larger vessels, and a diminution in the cellularity of capillaries and larger vessels within the lesion. Subsequently, an obliterative fibrosis decreases the lumina of all vessels within the lesion, and ultimately, severely affected vessels in the center of the lesion are replaced by solid cord-like structures of extracellular glial connective tissue.

Secondary to vascular insufficiency is retinal ischemia that, initially, has greatest effect on the inner retinal layers, progresses to involve all retinal layers, and eventually causes abnormalities of the pigment epithelium. The retina becomes thinned, neuronal cells decrease in size and number, and glial cells proliferate to occupy the expanded extracellular spaces with cytoplasmic processes. As the process continues, the glial cells produce the extracellular glial connective tissue that dominates the central portion of an advanced lattice lesion.

Ischemic degeneration of the inner retinal layers in the lattice lesion is responsible for

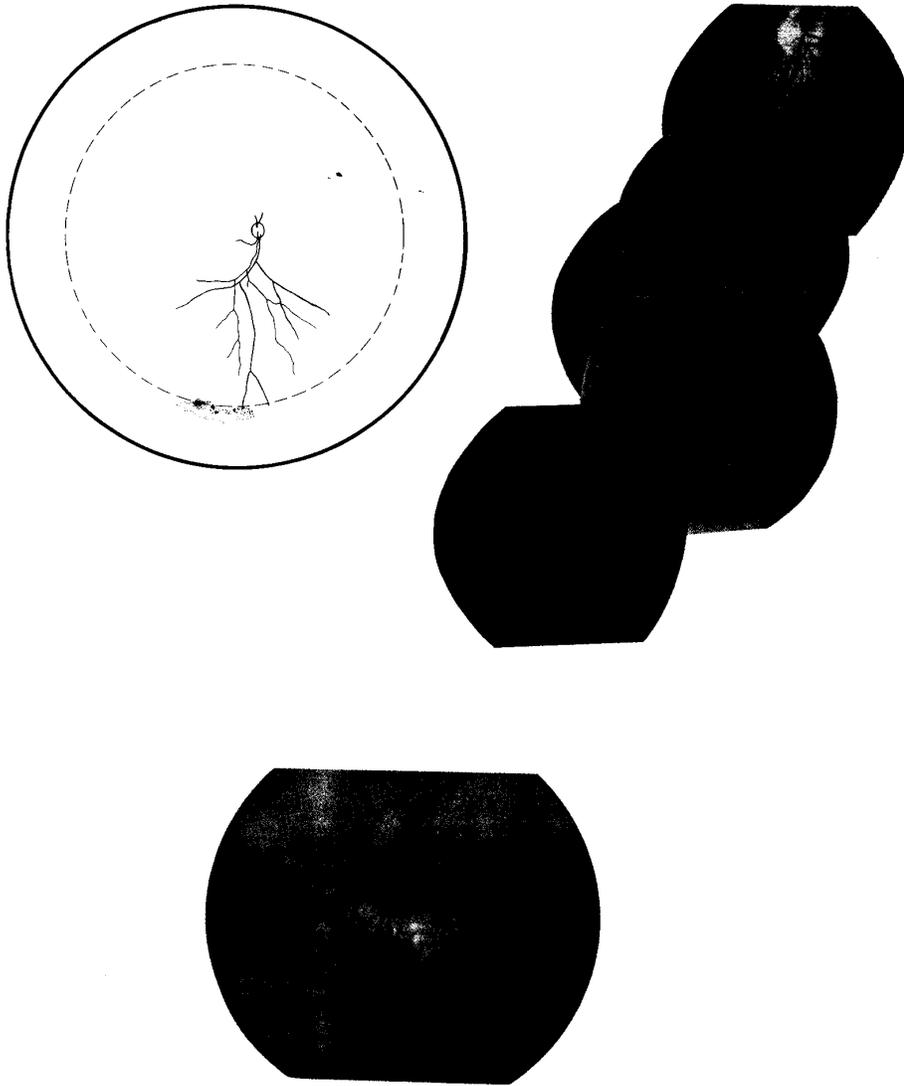


Fig. 28 (Straatsma, Zeegen, Foos, Feman, and Shabo). Lattice degeneration. Top, Oval-shaped, preequatorial, circumferentially oriented lesion in a 39-year-old white woman. Bottom, Clinical photograph illustrating pigment abnormalities and irregular gray-white particles on the surface of and within the thinned retina.

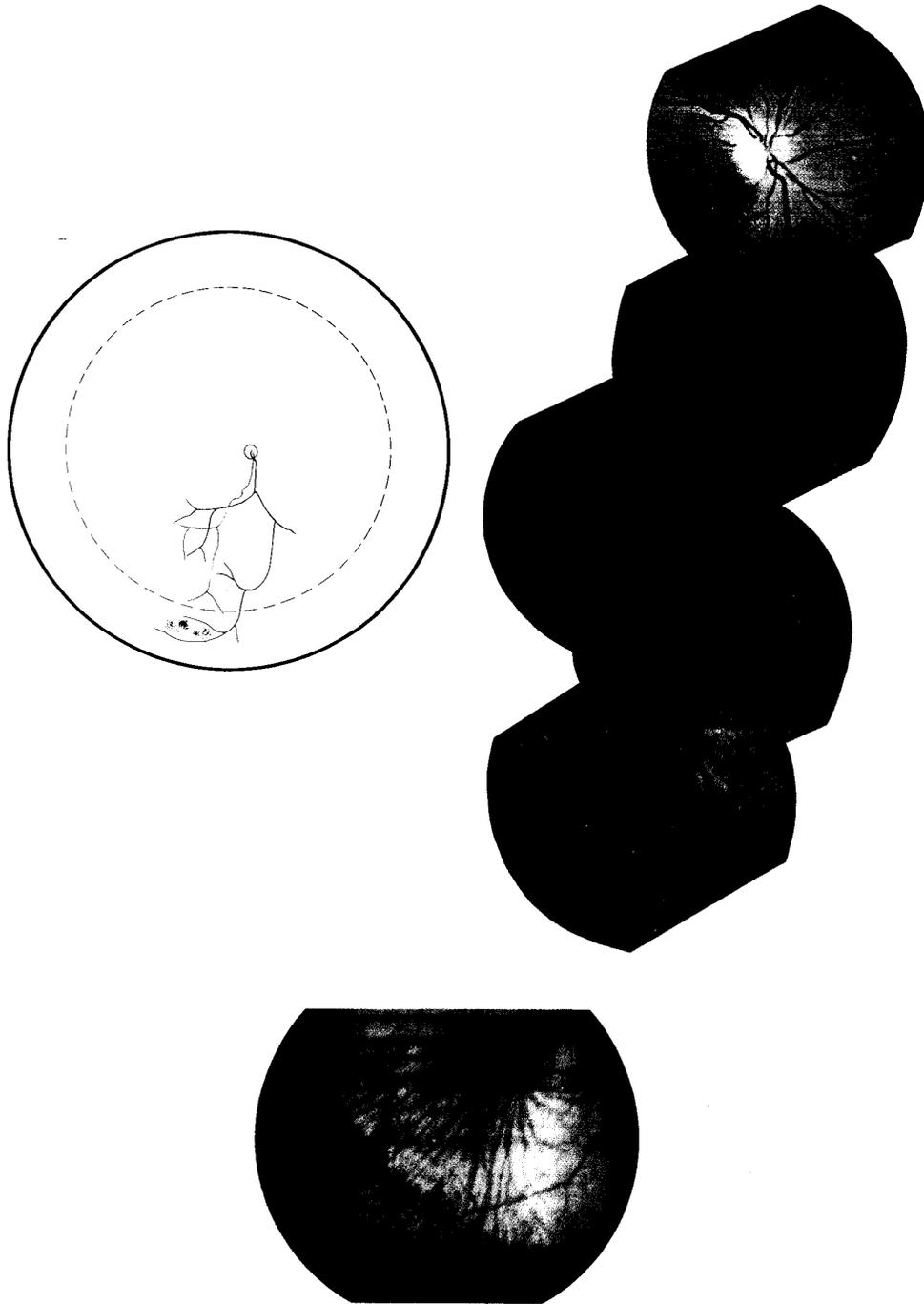


Fig. 29 (Straatsma, Zeegen, Foos, Feman, and Shabo). Lattice degeneration. Top, Oval-shaped, preequatorial, circumferentially oriented lesion in a 24-year-old white woman. Bottom, Clinical photograph illustrating focal retinal thinning, full-thickness retinal hole, and pigment irregularities.

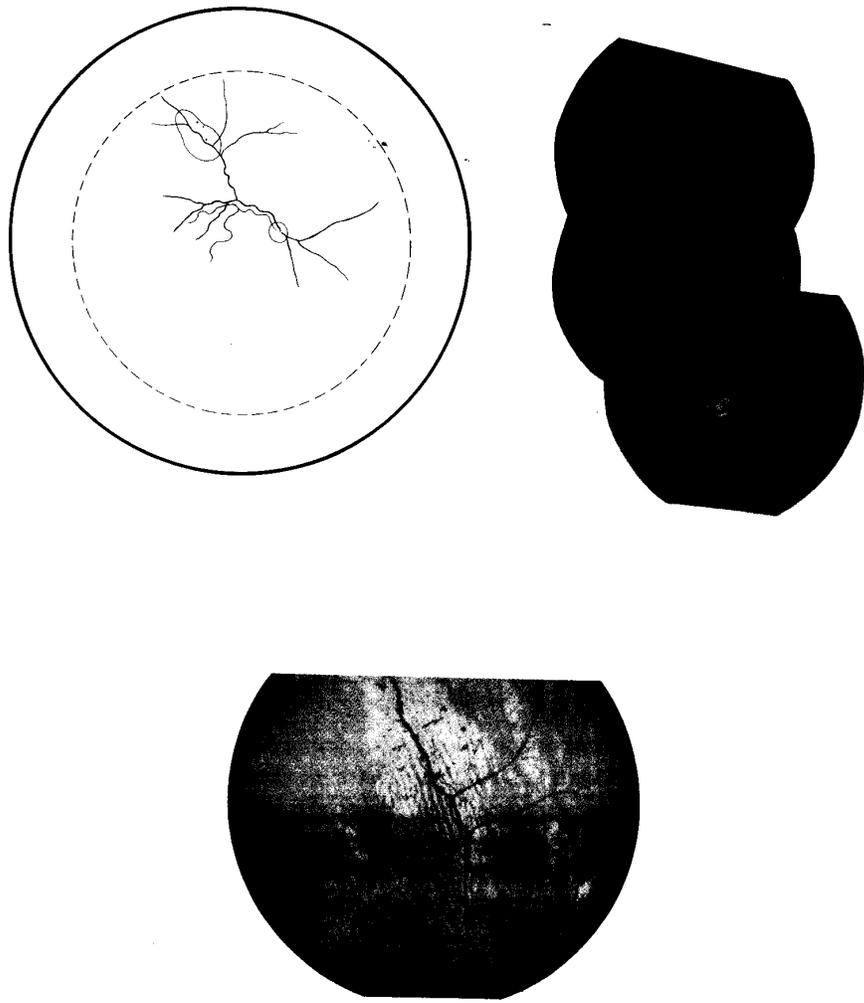


Fig. 30 (Straatsma, Zeegen, Foos, Feman, and Shabo). Lattice degeneration. Top, Widely oval, postequatorial, radially oriented lesion in a 51-year-old white man. Bottom, Clinical photograph of lesion with attenuated paraxial retinal vein and surrounding clumps of pigment.

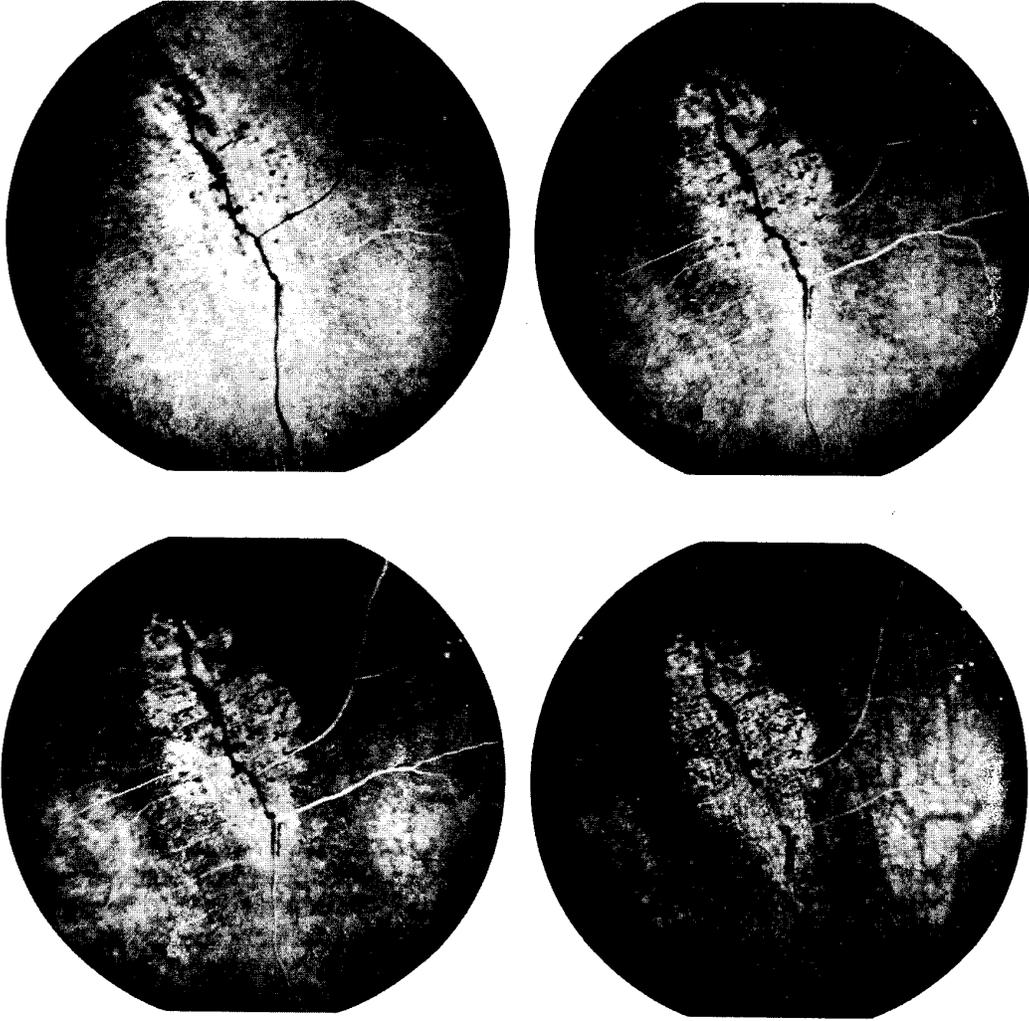


Fig. 31 (Straatsma, Zeegen, Foos, Feman, and Shabo). Sequential fluorescein angiography of lattice degeneration lesion illustrated in Figure 30. Refer to text for explanation.

intermittent disruption of the inner limiting lamina of the retina and for dissolution of the vitreoretinal attachments. This causes a pocket of structureless liquefied vitreous to form over the retinal lesion and stimulates condensation of vitreous structure at the junction of liquid and formed vitreous. Glial cells proliferating at the margin of the retinal degeneration may extend into the vitreous along the scaffold of vitreous condensation. This sequence of vitreoretinal dissolution, vitreous liquefaction, and glial reaction adjacent to an area of retinal ischemia is analogous to similar alterations noted in diabetic retinopathy, retrolental fibroplasia, and experimental embolic occlusions of retinal vessels with latex microspheres.^{44,45}

As the end product, lattice degeneration consists of a discrete area of ischemic degeneration in which the retina is thinned and collapsed as a consequence of cell loss and glial fibrosis. Internal to the degenerated retina, there is loss of vitreoretinal attachments and a pocket of liquefied vitreous surrounded by a condensation of vitreous structure and a cuff of exaggerated vitreoretinal attachments. Externally, retinal pigment epithelium is affected and foci of depigmentation alternate with clumps of hyperplastic pigmented cells.

Concerning clinicopathologic manifestations, lattice degeneration, according to the autopsy study, is present in 10.7% of the cases and bilateral in 48.1%. From one to ten lesions are present in each affected eye, and topographically, these are most prevalent adjacent to the vertical meridian.

Most lesions are oval or band shaped (with a mean length of 2.12 ± 2.31 mm and a mean width of 0.77 ± 0.48 mm), pre-equatorial (with a mean distance of 2.18 ± 1.41 mm from the ora serrata), and circumferential in orientation (with 68.2% of the lesions essentially parallel to the ora serrata). All of these features demonstrate substantial variations, but lesions close to the ora serrata tend to be linear, narrow, and circumferential; lesions posterior to the equa-

tor tend to be oval, wider, and more radial in orientation.

Lesions present retinal thinning and characteristic vitreous abnormalities in every instance, pigment alterations in 92.0%, white line vessels in 7.3%, focal thinning in 19.2%, and full-thickness retinal holes in 18.2%. Retinal tears are associated with 1.4% of the lesions, accompanied by posterior vitreous detachment, and located posterior to the vitreous base.

Recognizing the relationship of retinal tears to the vitreous base and posterior vitreous detachment, it should be noted that the vitreous base is a zone of firm vitreoretinal and vitreociliary attachments that measures about 3.20 mm in width, straddles the ora serrata, and extends about the circumference of the eye. The vitreoretinal or posterior portion of the vitreous base, composed of strong vitreoretinal attachments that prevent degenerative detachment of the vitreous from the retina, measures 3.03 ± 0.84 mm in the nasal horizontal meridian and 1.84 ± 0.64 mm in the temporal horizontal meridian and presents an irregularly undulating posterior border.^{46,47}

When posterior vitreous detachment occurs as a consequence of age-related vitreous body degeneration, surgical aphakia, high myopia, or other conditions, the vitreous separates, usually abruptly, from the retina posterior to the vitreous base. During this process, traction is exerted and retinal tears may be formed at the sites of exaggerated vitreoretinal attachments along the posterior and lateral margins of lattice degeneration. These tears may be linear, L-shaped, or U-shaped. Even giant tears extending along the margin of lattice degeneration for more than a full quadrant may occur with posterior vitreous detachment.⁴⁸

The vitreous base remains intact and is not involved in posterior vitreous detachment. Consequently, lattice lesions within the area of the vitreous base do not develop tears during the course of posterior vitreous detachment. Moreover, the relatively dense

collagen-like structure of the vitreous within the base decreases the extent of vitreous liquefaction in this area. Thus, there is less tendency for full-thickness retinal breaks to form in the vitreous base and to initiate a retinal detachment.

After posterior vitreous detachment, however, movement of the vitreous body exerts traction on the vitreous base and increases the likelihood of retinal tears at the margin of and within the vitreous base. This traction also increases traction adjacent to retinal holes within the vitreous base, so that after posterior vitreous detachment, retinal holes and tears within the vitreous base are more likely to precipitate rhegmatogenous retinal detachment.

These factors are of practical importance because the clinical management of lattice degeneration focuses on the prevention and treatment of rhegmatogenous retinal detachment. Viewed broadly, rhegmatogenous retinal detachment stems from (1) a basic predisposition caused by relative weakness of the bond between retinal pigment epithelium and sensory retina; (2) retinal anatomic factors, developmental variations and degenerations that combine to produce full-thickness holes, and a predilection for the formation of full-thickness tears; and (3) vitreoretinal attachments and vitreous degenerations that create traction and produce retinal tears. This basic pathogenetic mechanism is subject to infinite variation so that the incidence of retinal degenerations, holes, and tears is much greater than the incidence of retinal detachment.

Specifically, lattice degeneration of the retina is present in approximately 10.75% of the population, bilateral in about 48.1% of affected individuals, associated with retinal holes in about 24.9% of affected eyes, and combined with retinal tears in about 2.4% of affected eyes. In contrast, the incidence of rhegmatogenous retinal detachment in a large population is about one per 10,000 per year (0.01% per year).⁴⁹ Moreover, lattice degeneration is responsible for

only about 30% of the cases of rhegmatogenous retinal detachment.^{13,48} The incidence of lattice degeneration and associated retinal breaks, therefore, is much greater than the incidence of causally related retinal detachment. To form a basis for the prophylaxis of retinal detachment, this statistical discrepancy must be combined with clinical and laboratory observations concerning other factors contributing to the development of retinal detachment.

As an overall guide, estimation of the risk of development of retinal detachment is based on (1) specific ocular findings, (2) status of the opposite eye, (3) general condition of the patient, and (4) family history. In the category of specific ocular findings, retinal detachment is more likely to occur when the retinal break is a tear rather than a hole, associated with vitreous traction, symptomatic rather than asymptomatic, superior rather than inferior to the horizontal meridian, large rather than small, and posterior rather than anterior. Aphakia (associated with a 1 to 3% incidence of retinal detachment⁵⁰ that occurs within one year after cataract extraction in approximately half of the affected patients⁵¹), myopia of significant degree, and certain other ocular conditions also predispose to retinal detachment.⁴⁸

The status of the opposite eye is of great importance. Retinal detachment is bilateral in about 15% of patients,^{52,53} an incidence much greater than the percentage of retinal detachment in the general population. Moreover, because retinal degenerations, vitreous abnormalities, myopia, and other conditions are apt to be relatively symmetric, occurrence of a retinal detachment in one eye greatly increases the risk of retinal detachment in the opposite eye.

General condition of the patient is a factor; the risk of retinal detachment is increased in patients with Marfan's syndrome, Ehlers-Danlos syndrome, and other systemic disorders associated with retinal detachment. Age, sex, and life expectancy of the patient

are other general considerations.

Family history is pertinent. The risk of retinal detachment in patients with Wagner's hereditary hyaloideoretinal degeneration (a variant of lattice degeneration in at least some cases),¹⁸ in some families with high myopia, and in other specific pedigrees is clearly greater than the risk of retinal detachment in the general population.⁴⁸

To make these guidelines more specific, lattice degeneration of the retina usually warrants prophylactic therapy when it is (1) associated with full-thickness retinal tears; (2) discovered in a patient with a history of retinal detachment in the opposite eye due to similar lesion; (3) significant in degree, extent, or posterior location and present in an eye that is aphakic, or likely to require cataract surgery; or (4) encountered with full-thickness retinal holes and localized accumulation of subretinal fluid, high myopia, Marfan's syndrome, a history of retinal detachment in either eye, or a strong history of retinal detachment.

In following these guidelines, it is expected that prophylactic treatment will be administered to patients who would have progressed to retinal detachment as well as to some patients who would not have progressed to retinal detachment. Thus, the dual objectives of prophylactic treatment are to be maximally effective and to minimize any adverse effects or complications. Consistent with these goals, a series of 100 patients treated prophylactically to create a chorioretinal reaction surrounding lesions with a significant risk of progression to retinal detachment and followed for six months to six years after treatment included only two patients who developed retinal detachment despite treatment. Both of these achieved retinal reattachment and retained good vision with scleral buckling surgery. This series had no surgical complications.⁵⁴

Even with a reasonable program of prophylactic therapy, patients with lattice degeneration may present with rhegmatogenous retinal detachment when retinal tears

progress abruptly to the stage of retinal detachment or when undetected lesions progress slowly and asymptotically to retinal detachment. Consequently, prophylactic therapy reduces but does not eliminate the occurrence of retinal detachment.

When rhegmatogenous retinal detachment develops as a result of lattice degeneration, management is designed to detect retinal breaks and areas likely to form retinal breaks, to place these breaks and susceptible areas in contact with the pigment epithelium and choroid, and to maintain this apposition while a chorioretinal reaction forms a watertight adhesion that binds the sensory retina to the pigment epithelium and choroid. By appropriate application of a wide range of preoperative, operative, and postoperative measures, retinal reattachment is achieved in a high percentage of patients with rhegmatogenous retinal detachment related to lattice degeneration of the retina.

SUMMARY

In a series of 800 consecutive autopsies, lattice degeneration of the retina was present in 10.7% of the cases, bilateral in 48.1% of affected cases, and evident in 7.9% of the eyes examined.

Lattice lesions, though associated with a substantial range of features, were usually oval (with a mean length of 2.12 ± 2.31 mm and width of 0.77 ± 0.48 mm), preequatorial in location (with a mean distance of 2.18 ± 1.41 mm from the ora serrata), circumferential in orientation (with 68.2% of lesions essentially parallel to the ora serrata), and distributed adjacent to the vertical meridian (66.0% within one clock-hour of the vertical meridian).

All lesions presented a discrete area of retinal thinning, liquefaction of the overlying vitreous with loss of the corresponding vitreoretinal attachments, condensation of the vitreous at the border of the liquefied area, and exaggerated vitreoretinal attachments at the margin of the degeneration. Other features were pigment abnor-

malities (92.0%), white line appearing retinal blood vessels (7.3%), focal retinal thinning (19.2%), full-thickness retinal holes (18.2%), and retinal tears (1.4%).

With trypsin digest preparations, light microscopy, and electron microscopy, lattice degeneration was characterized by retinal thinning, vitreous liquefaction over the lesion with loss of vitreous structure, increased vitreoretinal attachments at the margin of the lesion, extensive retinal vascular abnormalities, loss of retinal neurons, glial cell reaction with production of extracellular connective tissue, and retinal pigment abnormalities.

Clinically, a series of 100 patients with lattice degeneration revealed comparable overall features, a predilection for association with myopia, significant abnormalities of vascular flow within the lesions, and a substantial incidence of bilateral rhegmatogenous retinal detachment in this physician-referred patient population.

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LATTICE DEGENERATION OF THE RETINA

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BY INVITATION

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IMPROVED methods for the prophylaxis and treatment of retinal detachment have directed attention to the processes which predispose to retinal breaks and separation. Of considerable significance in the pathogenesis of detachment is a distinctive retinal disease process termed *lattice degeneration*, which was clearly illustrated in the publications of Gonin,⁸ Vogt,²³ and Arruga³ more than twenty-five years ago, and further described in more recent reports of Schepens,^{18,19} Michaelson,^{14,15} Pau,¹⁷ Meyer-Schwickerath,¹³ Okun¹⁶ and Lincoff.¹²

Lattice degeneration in its typical form is a sharply demarcated, circumferentially oriented lesion that is located at or somewhat anterior to the equator. It is characterized by retinal thinning; an arborizing network of fine white lines which are often continuous with blood vessels; collections of pigment, frequently deposited along the white linear pattern, and vitreous abnormalities. Important additional distinguishing features include (1) a bilateral occurrence in many instances; (2) a predilection for location in the upper temporal quadrant; (3) the frequent association of multiple, round, punched-out areas of

retinal thinning or holes, and (4) a tendency for tears to develop along the posterior margin of the lesion.

It is evident, therefore, that the term *lattice* refers to only one of the features of this condition. It is not as descriptive as might be desired, and other names such as *equatorial* or *circumferential* degeneration have been considered. However, the name "lattice," introduced by Schepens¹⁸ in 1951, is vivid, calls attention to a distinctive feature of the disorder, and has the considerable advantage of widespread recognition and acceptance.

While this name is generally accepted and a number of characteristics are recognized, there is much concerning this process that is unknown. This study, therefore, incorporates observations of pathologic material and clinical cases to emphasize the frequency with which this condition occurs, trace the phases of its development, consider its relationship to retinal detachment, and suggest guides for clinical management.

PATHOLOGY

The eyes from 202 consecutive autopsy cases examined at the University of California Medical Center in a one-year period were surveyed. In this group there were 12 patients with lattice degeneration of the retina, an incidence of 6 per cent. The group included 109 males and 93 females with an average age of 40

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years at the time of death, and a range of age from birth to 80 years.

In addition to these cases, specimens of the lesion from three additional patients were obtained at University-affiliated hospitals. This total of 15 cases of lattice degeneration occurred in 8 males and 7 females with an age range from 3 to 79 years. Though two cases occurred in the first decade of life, most were noted in middle life, and the average age was 41 years. The cause of death was varied, including vascular, degenerative, and malignant disease, and no patient had a history of significant eye disorder.

Available material on these 15 cases comprised 25 globes: a single eye from each of 5 patients, and both globes from 10. In 5 of these 10 cases in which both eyes were examined, the lesion was bilateral. There was a distinct predilection for location of the process in the upper temporal quadrant; thirteen globes contained lattice in that sector, one in the inferior temporal, six in the superior nasal, and one in the inferior nasal quadrant.

Gross Appearance of Early Lesions

The earliest lesions appeared grossly as elongated areas of retinal thinning directed circumferentially, most often in the upper portion of the eye, and lying between the equator and the ora serrata (figs. 1 and 2). The margins of the lesion were sharp, and usually condensations or irregular strands of vitreous could be seen attached along the edges or over the base of the lesion. In contrast to the smooth and often glossy surface of the normal retina, the surface of the lesion was roughened, and at this site the retina was thinned in a trough-like fashion. Frequently there were punched-out areas of thinning in the base of the lesion, but microscopically



FIG. 1—Early lattice degeneration is present in the upper temporal quadrant of this specimen from a 9-year-old girl. The posterior margin of the lesion is partly obscured by overlying vitreous strands.



FIG. 2—The spindle-shaped lesion shown in figure 1 is a discrete area of retinal thinning. Vitreous bands attach along its margins and discrete punched-out areas are present in its base.

these did not prove to be holes. However, such lesions, even with the aid of a dissecting microscope, could not be distinguished with certainty from the true holes seen at later stages of the disease. Pigment deposition was not grossly apparent within the thinned area. Blood vessels, apparently uninvolved, coursed across the lesion from neighboring unaffected retina. At this stage of the dis-

ease, they did not present the striking and distinctive appearance which is so apparent later.

The details of the earliest lesions generally were softer in outline than those of later stages of development of the lattice lesion.

Gross Appearance of Late Lesions

Lesions at later stages of development retained, in general, their distinctive shape, and their outline appeared as an elongated oval or football, the long axis of which was directed circumferentially (figs. 2 and 3). The abnormal vitreous attachments were more apparent than in early stages, and often veil-like structures extended into the vitreous body from the margins of the lesion. Less commonly, such bands appeared to arise from the base of the lesion itself.

Throughout the extent of the lesion, the retina appeared obviously thinned, but not uniformly so. The far advanced lesions, without exception, showed punched-out areas, some of which were truly holes. Such holes seemed to occur along the posterior edge of the lesion, and in this material were discrete, within the lesion and not associated with rents or tears.

The most striking feature consisted of a distinctive network of fine white lines which were often continuous at the margin of the lesion with blood vessels (fig. 4). The pattern of the lines within the lesion itself resembled the vascular network in this portion of the retina. Late stages of the disease were characterized by irregular deposits of melanin, often distributed along and accentuating the plexiform appearance of the white lines.

Microscopic Appearance of Early Lesions

The histologic features of the earliest lesions correlate well with the gross characteristics. Where the process was least advanced, the inner retinal layers were absent, as if by erosion (fig. 5). In occasional areas, however, an abrupt excavated defect occurred. The degree of thinning was not uniform. At some areas the erosion involved only the inner limiting membrane and a portion of the nerve

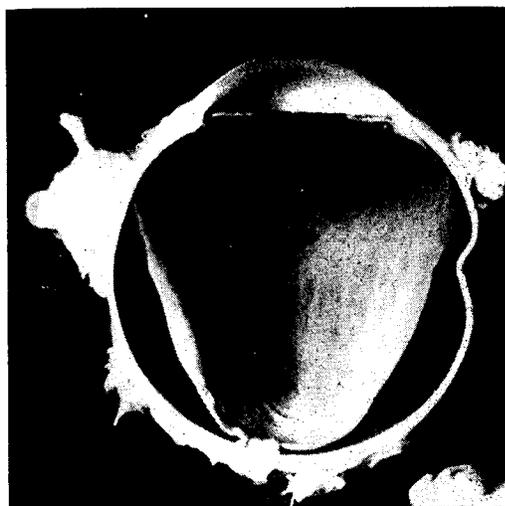


FIG. 3—A later stage of lattice degeneration is seen in this eye from a man aged 55 years. The posterior margin of the crescentic lesion is accentuated by artificial shrinking of the retina.

fiber layer. The foci of greatest thinning corresponded to the punched-out areas seen grossly, and at such sites all the inner layers of the retina had disappeared and the bottom of the lesion was formed by the outer nuclear layer or the outer limiting membrane.

The walls of the blood vessels within the lesion were thickened, but this change was much less marked than that seen in later stages of the disease.

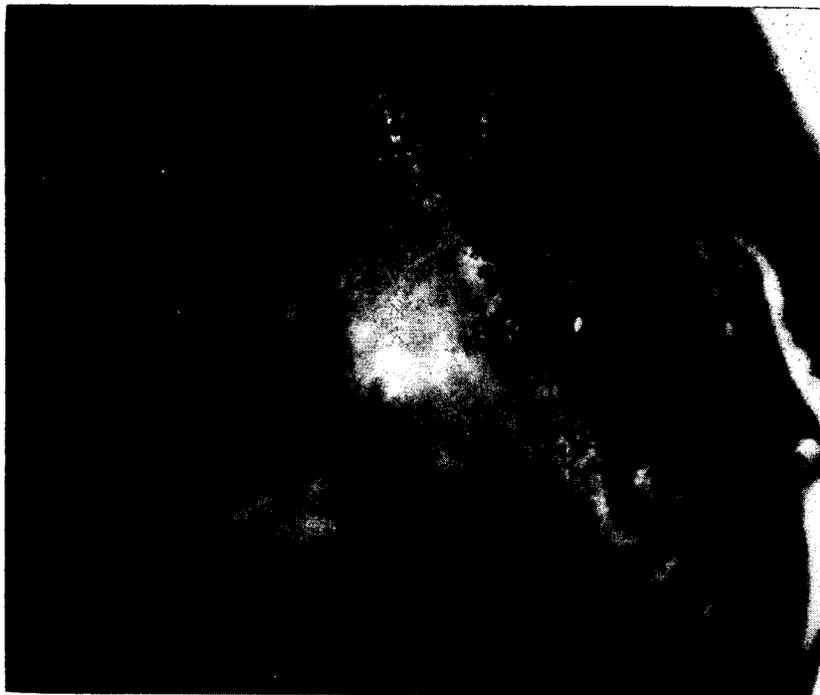


FIG. 4—The arborizing network of white lines can be seen within the lesion which is shown in figure 3. Focal collections of pigment are present within the thinned retina.

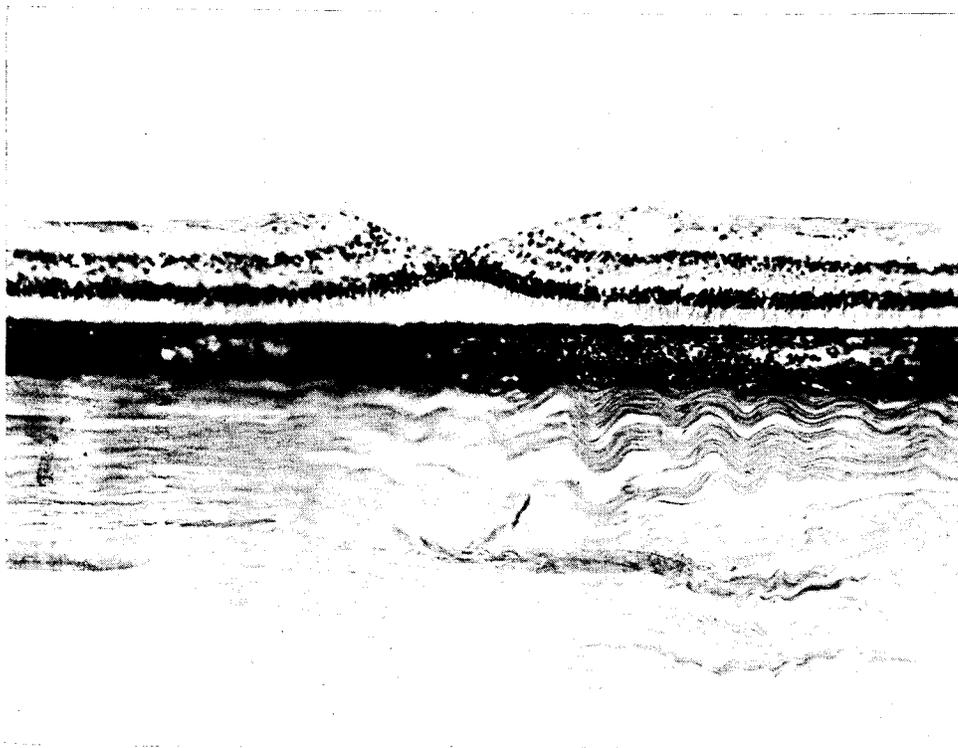


FIG. 5—A trough-like area of retinal thinning characterizes the early stages of retinal degeneration. In this example the inner retinal layers are gone, the outer plexiform layer forming the base of the lesion. (H & E. $\times 75$)

Changes in the adjacent vitreous body were apparent in all of the earliest lesions. Such changes consisted of a sharply circumscribed area in which all vitreous structure was lost. Adjacent to this area of liquefaction there was a

the adjacent retina, and there was patchy thickening of Bruch's membrane. From Bruch's membrane, focal thickening extended to involve the walls of the choriocapillaris, but obliteration of the capillaries was not present.

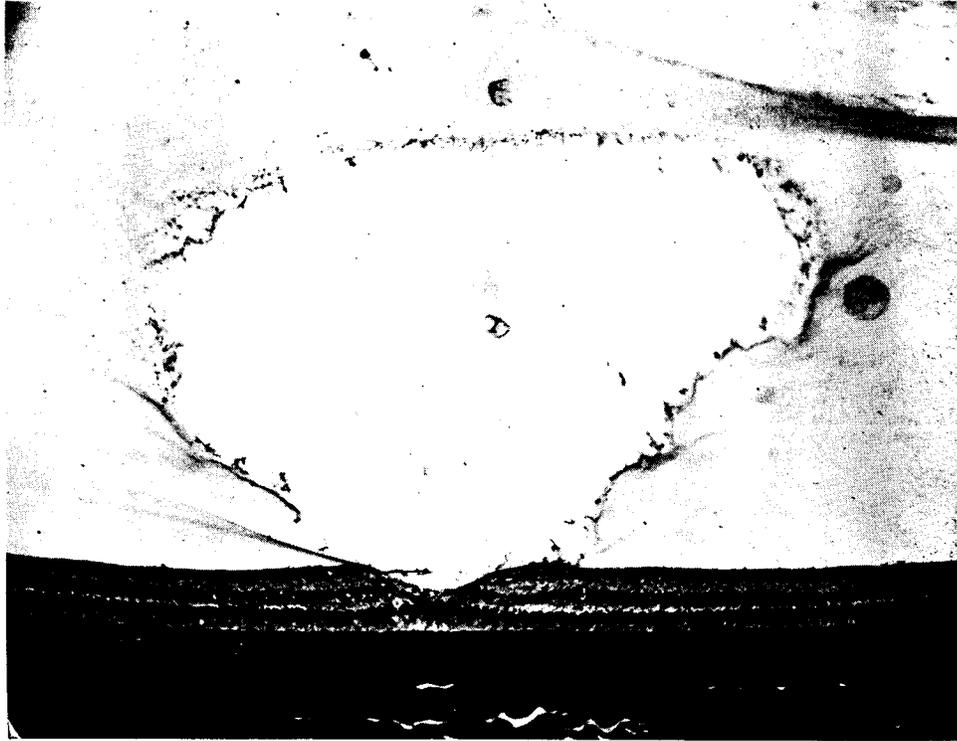


FIG. 6—Liquefaction of the vitreous body overlying an area of early lattice degeneration, as seen in this specimen, was a common finding. (Van Gieson, $\times 45$)

slight condensation of the vitreous body. At the margins of the lesion where the vitreous body was attached, the fibrillar structure of the vitreous was more dense and the inner retinal layers were drawn centrally as by traction (fig. 6).

In one case subtle changes were observed in the adjacent pigment epithelium and choroid. The pigment epithelial cells were irregular, occasional clumps of pigment granules were present within

Thus, even in the earliest lesions, distinct alterations were present within the retina and in the contiguous vitreous body and choroid.

Microscopic Appearance of Late Lesions

The lesion consists of a sharply circumscribed area of retinal thinning, in which all specialized elements of the retina are lost. Within the thinned area the

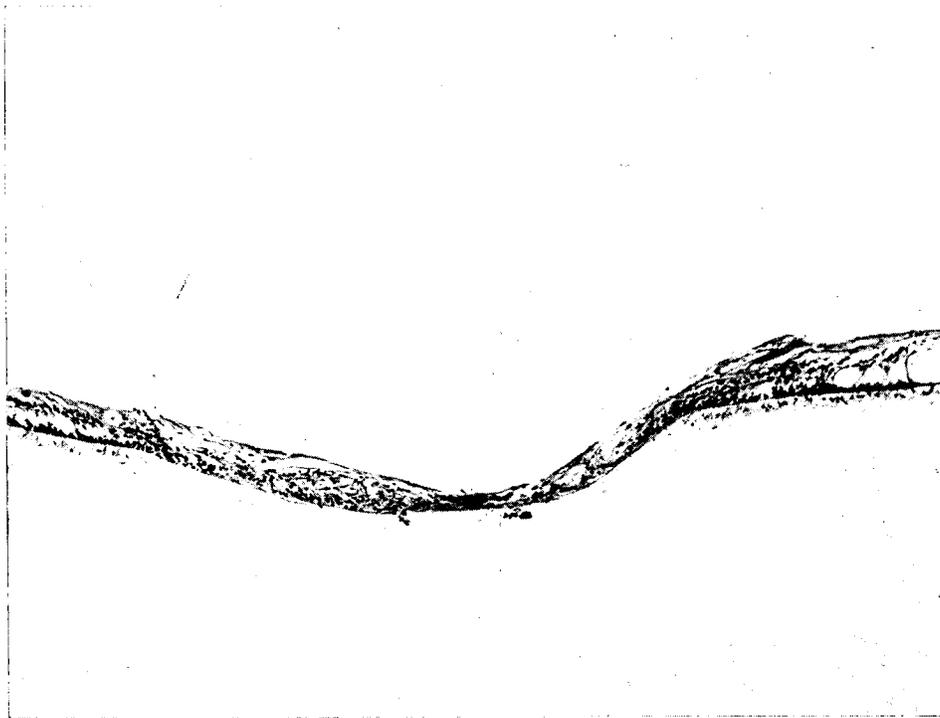


FIG. 7--The vitreous attachments define the margins of this area of lattice degeneration. Within the thinned area, thickened blood vessels, collections of hyaline material, and pigment may be present. (PAS, $\times 45$)

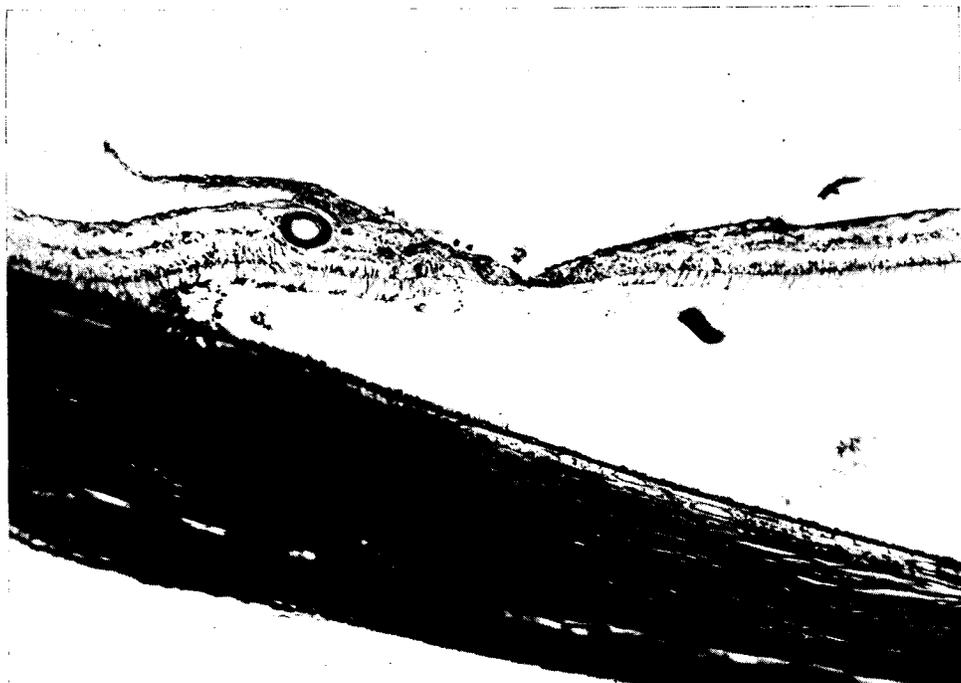


FIG. 8—At this site the lesion extends almost to the outer limiting membrane. Glial bands extend into the vitreous body from the edges of the lesion. (PAS-Aniline blue, $\times 45$)

blood vessels were greatly thickened, so much so that in some instances there was complete obliteration of the lumen. In addition, round collections of pink-staining hyaline material were present and superficially resembled obliterated small vessels, but were remarkable in that they stained positively with PAS (fig. 7). Deposits of pigment were present and were most often found in a perivascular location. The thinned segment of retina was only sparsely cellular, and most cells present appeared to be glia.

far advanced, holes were found. The holes were small and were generally along the posterior margin or at the ends of the lesion (fig. 9). Tears were not encountered in the pathological specimens.

The changes in the adjacent vitreous body which were seen in early phases of the disease were also present in the late stage. But, in addition, remarkable changes were noted where the vitreous

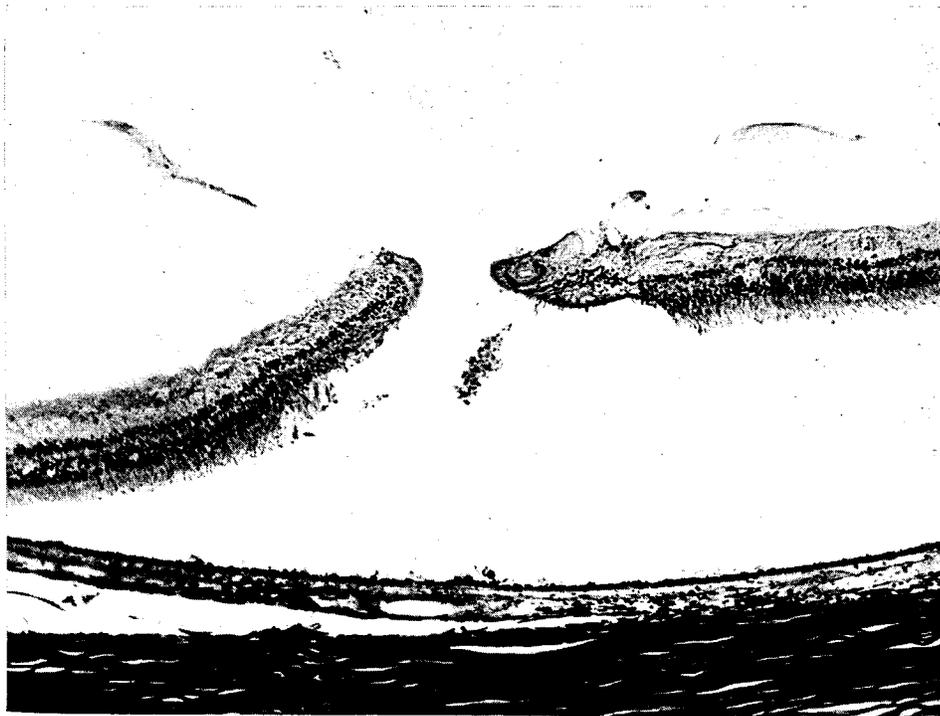


FIG. 9—A retinal hole is seen in an area of lattice degeneration. Pigment is deposited around a thickened blood vessel, and focal irregularity of the retinal pigment epithelium is present. (Van Gieson, $\times 45$)

There were focal areas where the retina showed abrupt thinning corresponding to the punched-out lesions observed at gross examination. Such lesions generally extended to the outer limiting membrane (fig. 8). However, in almost every instance in which the lesion was

body attached to both the anterior and posterior margins of the lesion. At these sites a broad curtain of glia extended into the vitreous body and, in general, followed the configuration of the vitreous liquefaction adjacent to the retinal lesion.

Abnormalities of the adjacent pigment epithelium were present in most instances. In several cases the pigment epithelium was focally absent and the thinned retina was adherent to Bruch's membrane. More commonly, however, the pigment epithelium was irregular and in some areas was heaped upon hyaline masses along the inner surface of Bruch's membrane. The walls of the choriocapillaris were thickened, but obliteration was not present.

CLINICAL OBSERVATIONS

Clinical observations emphasize the similar appearance of lattice degeneration in living patients and in eyes obtained at autopsy. The characteristic location and discrete outline of the lesions were readily apparent but the precise evaluation of vitreous abnormalities, retinal thinning, and round, punched-out defects often required direct and indirect ophthalmoscopy, scleral depression and special forms of biomicroscopy. Even these forms of examination, however, may fail to indicate the true extent of vitreous alterations or fall short of permitting differentiation between an area of focal thinning and a hole through the entire sensory retina.

Though these limitations exist, clinical observation does permit identification of lattice degeneration in its various phases. In the earliest stage it is a discrete, rather subtle, spindle-shaped lesion with a soft, slightly pigmented outline. The retina in the lesion is uniformly thinner than surrounding areas, but no punched-out defects are present and the vessels crossing the lesion maintain a normal red color (fig. 10).

At a more advanced stage, the lesion may be broader, longer and more sharply



FIG. 10—This early stage of lattice, detected in a 14-year-old girl whose other eye had a retinal detachment, is a discrete, slightly pigmented lesion. It is crossed by retinal vessels which appear normal.

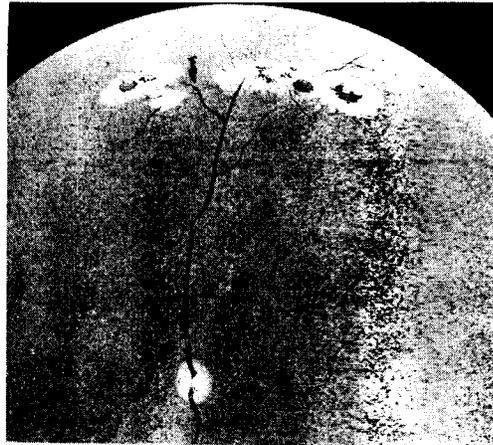


FIG. 11—At an advanced stage, the sharply delineated area of lattice degeneration contains arborizing white lines, irregular pigmentation and areas of apparent retinal hole formation.

delineated. Arborizing white lines, often continuous with retinal vessels, ramify within the lesion; pigmentation is variable but may be quite pronounced; and round or oval areas of extreme thinning or hole formation are evident (fig. 11). In some instances in which extended observation has been possible, a progression in the size and degree of the degeneration has been noted.

Holes within an area of lattice degeneration may be clinically indistinguish-

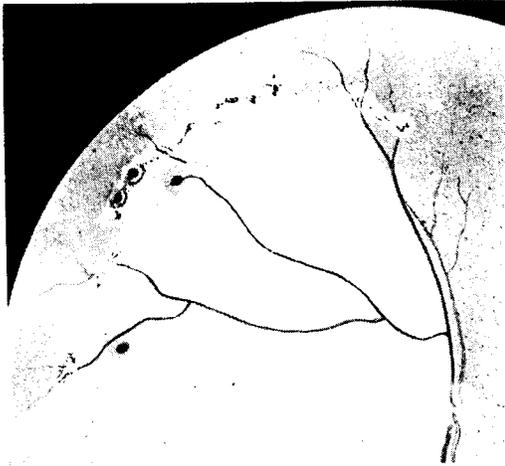


FIG. 12—Retinal holes within areas of lattice degeneration are responsible for retinal detachment in this aphakic patient.

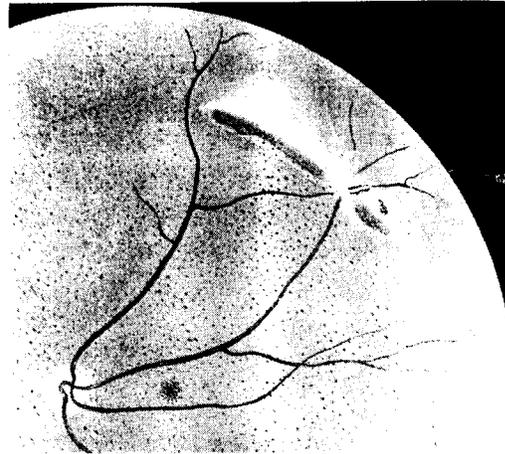


FIG. 13—Seen within six hours after the onset of light flashes and spots in the field of vision, these retinal tears along the posterior margin of an area with lattice degeneration have caused a localized detachment of the retina.

able from extreme thinning, but when present they may permit the passage of fluid and lead to retinal detachment (fig. 12). Detachment may also follow the formation of retinal tears along the posterior margin or ends of an area of lattice (fig. 13). This area is predisposed to rupture because of the general thinning of the retina and the increased traction of vitreous bands attached to the margin of the lesion. Once initiated, the tear may extend along a part of the entire length of the lattice degeneration. This type of break is associated with vitreous traction, often located in the superior quadrants of the eye and, therefore, prone to precipitate retinal detachment.

To evaluate the relationship between lattice degeneration and retinal separation, 100 patients operated upon consecutively for the prophylaxis or treatment of serous retinal detachment were reviewed. In this personally treated group there were 31 patients with lattice degeneration of the retina. These 31 patients required retinal detachment surgery on 20 eyes and prophylactic treatment on 14 eyes.

The group included 16 males and 15 females with an age range from 5 to 75 years and an average age of 49 years. Two patients reported a history of retinal detachment in other members of the family, 5 recalled a significant injury, and 7 patients had undergone cataract extraction prior to discovery of the retinal abnormality.

In this series, the refractive error was of distinct interest. No patient had a spherical equivalent more hyperopic than +2.50 D., and 21 had an error between +2.50 D. and -3.00 D., or the aphakic equivalent. Fundus changes characteristic of myopia seldom occur with a minus correction less than -3.00 D.,¹⁸ so these patients were considered as approximate emmetropes. In the group requiring minus lens correction greater than -3.00 D. were 10 patients; 8 of these were in the range between -3.00 D. and -10.00 D., one required -14.00 D., and one other needed a correction of -20.00 D.

A significant incidence of bilateral retinal disease was present in this group of

31 patients. Retinal detachment had occurred in both eyes of 8 patients; in 13 others retinal detachment was present in one eye and lattice degeneration in the second eye; 7 patients developed retinal detachment in one eye without abnormality of the other fundus, 2 had both

ferral. The degree of fundus scarring present in many treated eyes limited appraisal of the lattice degeneration and evaluation of its precise relationship to the retinal detachment.

However, in 28 previously untreated eyes with lattice degeneration, the extent

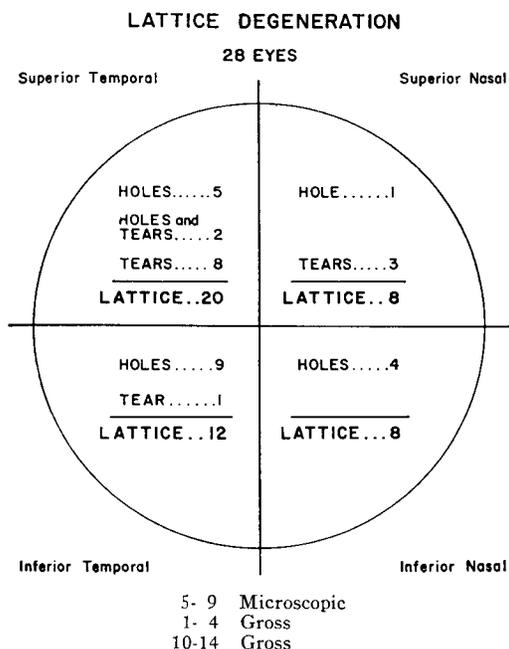


Chart 1—In 28 previously untreated eyes, the distribution of lattice degeneration and the localization of holes and tears is recorded.

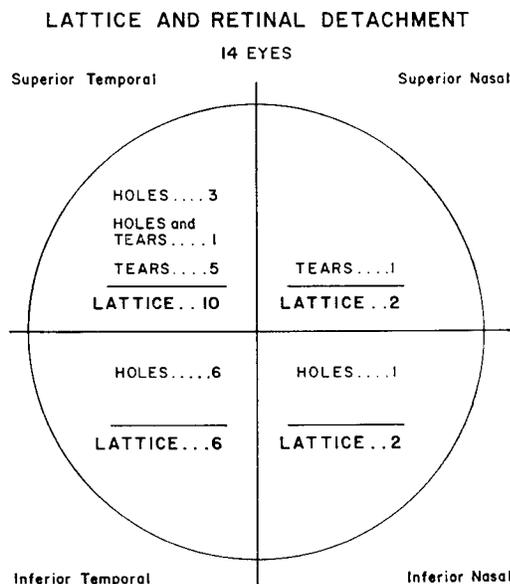


Chart 2—This chart indicates the distribution of lattice degeneration, holes and retinal tears in the 14 eyes of the previous group (Chart 1) in which a retinal detachment was present.

bilateral lattice degeneration and retinal holes, and a single patient was referred with lattice degeneration and holes in the retina of his only useful eye. The opposite eye of this last patient was phthisical as a result of an injury. Excluding this patient, it is evident that 23 out of a possible 30 patients, or 76 per cent of the group, had bilateral retinal disease. In the entire group, there were only 7 normal eyes.

The high incidence of bilateral disease, often developing over several years, undoubtedly contributed to the fact that 16 of these 31 patients had undergone retinal detachment surgery prior to re-

of the process could be determined. Charting this process by the quadrant in which it occurred (chart 1), and plotting the lesion in more than one sector if it extended to include 50 per cent or more of an adjacent quadrant, it is evident that 20 eyes contained degeneration in the superior temporal quadrant, 12 in the inferior temporal quadrant, 8 in the superior nasal sector, and 8 in the inferior nasal portion. The serious consequences of degeneration in the superior temporal quadrant of the eye were indicated by the occurrence of retinal tears in 8 eyes, tears and holes in 2 eyes, and

retinal holes in 5 other eyes. In the 12 instances of lattice degeneration, the inferior temporal quadrant contained one retinal tear and 9 examples of hole formation. Among the 8 eyes in which lattice degeneration occurred in the superior nasal sector, 3 tears were noted and retinal hole formation was detected in one eye. No tears and only 4 examples of retinal holes were apparent in the eyes with lattice degeneration in the inferior nasal quadrant.

To clarify further the relationship of lattice degeneration to serous detachment of the retina, a similar study was made on the 14 previously untreated eyes of this group in which an actual retinal separation was present (chart 2). This revealed 10 eyes with lattice degeneration in the superior temporal quadrant, 6 in the inferior temporal quadrant, 2 in the superior nasal quadrant, and 2 in the inferior nasal sector. Holes and tears in relation to this degeneration were the only retinal breaks in 9 patients, or 64 per cent of the group. Thus the importance of lattice degeneration in the development of retinal detachment cannot be questioned.

The treatment to be carried out in patients with lattice degeneration was selected with due regard for the previous history, the extent of retinal degeneration, the type and location of retinal breaks, the position of the retina, evidence of vitreous traction, clarity of the media, and the size of the dilated pupil. With consideration of these and other factors, operations on the 20 eyes with retinal detachment included photocoagulation, 3; the diathermy procedure, 3; the scleral buckle operation, 11; and the scleral buckle with silicone pillow procedure, 3. Prophylactic surgery in 14 eyes consisted of photocoagulation, 12, and the diathermy procedure, 2. Though patients in this series were deliberately chosen from a rather recently treated

group, the average follow-up is substantially more than six months. Surgery on all but two of the eyes was successful. One failure occurred in a 70-year-old woman with aphakia, glaucoma, retinal detachment and fixed folds; the other occurred in a 46-year-old man with a total retinal detachment and approximately one hundred retinal holes and tears related to extensive lattice degeneration.

DISCUSSION

A number of interesting and significant aspects of lattice degeneration merit consideration. However, this discussion will be confined to the etiology and progression of lattice degeneration, its relationship to retinal detachment and suggestions regarding therapy.

The cause of lattice degeneration is unknown. However, a number of suggestive factors may be important in causation. These include a genetic predisposition, a possible developmental factor related to Lange's fold in the peripheral retina of the very young, and specific anatomical features of the eye. Anatomical features of possible significance are the attachment of the vitreous body to the retina,^{7,21} the location of the vitreous base, the arborizing and often circumferentially directed vessels in the peripheral retina and the zone of transition between posterior and long ciliary arteries in the adjacent choroid. Though these factors may be of importance, gross, microscopic, and clinical observations emphasize the presence of vascular abnormalities in early lesions and a progression in these abnormalities as the process advances.

As vascular alterations increase, other degenerations involving the retina, vitreous and choroid progress. Histopathologic studies reveal retinal thinning, pigment disturbance, and vitreous degeneration in all cases but emphasize marked

differences in the extent of these changes. These implications of progression are confirmed by clinical observations which may reveal, on successive examinations, an increase in the size and degree of the degeneration. The course of the disease, however, is extremely variable. Lesions may remain without change for an extended, if not indefinite, period, or they may progress at an appreciable rate.

An awareness of the variation in rate of progression and the critical differences in the degree and extent of lattice degeneration is of aid in understanding the relationship between lattice and retinal detachment. Occurrence of retinal lattice in 6 per cent of the eyes examined at autopsy indicates that the disorder is far more common than retinal detachment. Comparing this frequency with the incidence of retinal detachment in a rather stable population⁴ makes it evident that the vast majority of patients with lattice degeneration do not develop detachment of the retina. Thus, the actual stage of the degeneration, the degree of vitreous traction and the strength of chorioretinal bond are factors in the actual development of detachment.

From a clinical point of view many authors^{3,8,22} have called attention to lattice degeneration in patients with retinal detachment. Michaelson¹⁴ emphasized the significance by reporting lattice degeneration in 20 per cent of the patients that he treated for detachment during 1953. Our series confirms the importance of lattice by noting it in 31 per cent of the patients. Furthermore, this incidence is made all the more significant by the fact that nearly three fourths of these patients had significant bilateral retinal disease.

The relative frequency of lattice degeneration in the general population and the distinct relationship to detachment

indicate the necessity for selecting, insofar as possible, cases that are likely to progress to retinal detachment. In general, the experiences with holes without detachment^{2,5,6,15,16} and with subclinical detachments^{12,18,20} serve as guidelines. Retinal detachment is more likely to develop when (1) there is a family history of retinal detachment, (2) the eye is subjected to frequent trauma, (3) retinal detachment has developed in the opposite eye, (4) the vitreous body shows degeneration, (5) lattice degeneration is in the superior temporal quadrant, and (6) lattice degeneration has advanced to the formation of holes or, more significantly, retinal tears. Altered pigmentation surrounding a retinal break may indicate a greater cohesiveness between retina and choroid,^{10,16} but this is not a reliable index of a reaction strong enough to prevent detachment.¹²

Though these factors are useful in selecting cases likely to progress to detachment, it is not possible to establish rigid criteria for prophylactic surgery. As noted at the XVIII International Congress of Ophthalmology¹ and in more recent reports by Guerry⁹ and Lincoff,¹² there is no unanimity regarding this type of surgery. Much remains to be learned about the evolution of fundus disease and the long-term results following prophylactic surgery. Each case, therefore, must be considered individually. However, when prophylactic treatment is carried out, it is important to use a minimum of photocoagulation or diathermy to avoid unnecessary scarring or shrinkage of retina, choroid and vitreous. Treatment should form a continuous band of reaction in the relatively healthy and thick retina surrounding the lesion (fig. 14). In some instances, buckling procedures may be indicated as an adjunct to diathermy or photocoagulation if traction is extreme or a subclinical detachment is present. Postoperatively, a controlled convalescence and



FIG. 14—A continuous band of photocoagulation reaction surrounds this area of advanced lattice degeneration in the superior fundus of a 36-year-old woman whose other eye developed retinal detachment related to lattice degeneration in a corresponding area. (See figure 11.)

careful observation are important, because prophylactic surgery has been known to precipitate retinal detachment.¹³ Rarely, lattice degeneration may be so extensive, and the amount of prophylactic surgery required and the likelihood of subsequent retinal detachment so great that observation, rather than operative intervention, is the treatment of choice.

It is equally difficult to establish guidelines for the management of lattice degeneration when it is present in an eye with a retinal detachment. However, both pathologic observations and clinical experience indicate that a break in relation to lattice requires treatment of the entire zone of degeneration—not just the break alone. An area of lattice apart from the detachment should be treated if there is marked retinal thinning, evidence of retinal breaks or the likelihood of significant vitreous traction. In scleral buckling procedures or other operations altering the shape of the globe, areas of lattice should be considered as zones of potential retinal break. Therefore, they should be placed on, or anterior to, the buckle whenever possible and not located

at the edge of a pillow or on the steep posterior slope of a buckle. As with prophylactic surgery, the management of lattice in an eye with a detachment requires individual evaluation and the use of surgical judgment.

SUMMARY

Lattice degeneration of the retina is a sharply demarcated, circumferentially oriented retinal lesion located at or somewhat anterior to the equator. It is usually bilateral, most commonly located in the superior temporal quadrant and characterized by retinal thinning, an arborizing network of white lines, variable pigmentation, vitreous abnormalities and choroidal alterations. These degenerative changes may progress to the formation of round, often multiple, retinal holes and tears along the posterior margin or ends of the lesion.

Detected in 6 per cent of 202 cases studied at autopsy and present in 31 per cent of eyes operated upon for retinal disease, lattice degeneration is a distinct pathological and clinical entity that often results in retinal detachment.

An understanding of the nature and behavior of this lesion will aid in the prophylaxis and treatment of retinal detachment.

ACKNOWLEDGMENTS

Grateful acknowledgment is due Miss Gwen Gloege for the clinical drawings, to Mr. W. H. Burnham for photographs of the gross specimens, to Mr. Lloyd Matlowky for photomicrographs. Special appreciation is accorded Miss Alice Arvin for the excellent histopathologic preparations.

DISCUSSION

DR. STRAATSMA: Dr. Allen and I find it most gratifying to learn of the agreement between our series and that reported by Dr. Colyear. It is also of distinct interest to hear of his experience in which a retinal break ap-

peared to be related to some manipulation of the scleral surface. This has not been noted in our patients, but it is not in the least surprising when one considers the extreme degrees of lattice degeneration and retinal thinning that may be present. One can only feel that such a patient as Dr. Colyear describes might well have developed a spontaneous break in the retina with the passage of time and further extension of the degeneration.

I believe that Dr. Colyear's independent observations of the correlation between lattice degeneration and retinal detachment emphasize the relationship between these two conditions. It is hoped that increased correlation of clinical findings and histopathology will add to our understanding of the basic causes of retinal detachment.

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Retinal detachment

A study of a population-based patient material in Sweden 1971-1981

II. Pre-operative findings

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Abstract. In a population-based material of patients with retinal detachment (RD), the pre-operative findings in different subgroups were studied. In traumatic cases flap tears and round holes were found in at least as high a frequency as oral dialysis, or even higher. In aphakic cases subtotal or total RD was often observed on admission for surgery. A high proportion of aphakic eyes without lattice degeneration exhibited no breaks. RD in myopic eyes was usually large, and round holes were frequently found. Full-thickness fixed retinal folds were more seldom seen pre-operatively in myopic than in non-myopic eyes. Lattice degeneration was usually observed in myopic RD patients of ages less than 30 years, but mainly in hyperopic or emmetropic eyes in patients over 60. In RD with lattice, multiple breaks were frequently found. A comparatively large group of RD cases without lattice were non-traumatic, phakic and non-myopic (40%). Most of these patients were 60 years and older. Flap tears were often seen, and the detachment was seldom large in this group.

Key words: retinal detachment - population-based study - predisposing factors - preoperative findings - retinal breaks.

The fundamental aetiology of idiopathic retinal detachment (RD) is the occurrence of a retinal break. However, various pathogenetic factors such as myopia, aphakia, peripheral retinal degeneration (e.g. lattice degeneration) and trauma may

contribute to the development of the break. Furthermore, the course and outcome of the disease may be influenced by these factors. An analysis of their relative importance requires an investigation of an unselected material of patients. In a previous population-based study (Törnquist et al. 1987) a classification taking into account these different factors was proposed. The purpose of the present paper is to describe the pre-operative fundus findings in RD with specific regard to these different subgroups.

Material and Methods

During 1971-1981 a population-based group of 538 patients (590 »cases«) were hospitalized for rhegmatogenous RD at the Ophthalmological Department of Örebro Medical Center Hospital. The patients were classified according to the pre-operative clinical profile into 7 subgroups (see Part I: Törnquist et al. 1987). For further characterisation of these subgroups, certain fundus findings were analysed, namely signs of pre-operative proliferative vitreo-retinopathy, extent of RD, and number, location and type of break.

Definition of »case« and statistical methods: see Part I (Törnquist et al. 1987).

Table 1.

Full-thickness fixed retinal folds (FRF) present pre-operatively in age and refraction groups. Cases with previous ocular surgery or trauma are excluded.

	Total No.	RD with FRF	
		No.	%
Age groups, years			
0-29	34	3	8.8
30-59	141	10	7.1
60+	250	30	12.0
Refraction groups			
Hyperopia > +2.0D & Emmetropia ± 2.0D	274	30	10.9
Myopia > -2.0D	130	4	3.1
Unknown, phakic	21	9	42.9
Total	425	43	10.1

Myopia vs non-myopic phakic refraction: $\chi^2 = 11.294$, df 1, $P < 0.001$ (Yates correction).

Table 2.

The size of the detached area in cases with different types of retinal detachment (RD), as specified in Table 8, Part I.

Type	No. of cases	Percentage of cases with				Detachment of the macular area
		RD of the indicated size				
		< 90°	90°-180°	180°-270°	> 270°	
T	37	18.9	35.1	27.0	18.9	56.8
A	78	3.8	38.5	26.9	30.7	56.4
AL	29	13.8	44.8	20.7	20.7	41.4
M	75	6.7	38.7	24.0	30.7	56.0
ML	63	23.8	39.7	23.8	12.6	34.9
L	72	23.6	26.4	30.6	19.4	58.8
S	236	14.4	41.9	24.2	19.5	63.1
Total	590	14.1	38.6	25.3	21.7	55.6

Size of RD:

A vs (Total - A): $\chi^2 = 10.409$; df = 3; $P < 0.02$

M vs (Total - M): $\chi^2 = 6.821$; df = 3; NS

L vs (Total - L): $\chi^2 = 9.015$; df = 3; $P < 0.05$

Macular detachment:

(AL + ML + L) vs (A + M + S): $\chi^2 = 12.732$; df = 1; $P < 0.001$

S vs (Total - S): $\chi^2 = 9.064$; df = 1; $P < 0.01$

Note: Since the χ^2 tests are not entirely independent of each others the P -values should be cautiously interpreted.

Results

Full thickness fixed retinal folds (FRF), as a sign of proliferative vitreo-retinopathy, were seen in 62 cases before the surgical intervention for the detachment. FRF were found in 10.8% of the traumatic and in 12.1% of the aphakic cases. In 43 cases in which no previous ocular surgery or trauma had taken place (Table 1) FRF were less frequent in myopia of >-2 D than in those with other refractive states. No association was found between FRF and either age or the average size of the largest retinal break but FRF were usually observed in cases with a large detachment (Table 3).

The sizes of the detached retinal area on admission are seen in Table 2. In the total material the detached area was less than one quadrant in 14.1% and more than three quadrants in 21.7%. A comparatively larger area was detached in type A and in the age group >60 years (Table 3), whereas a smaller detachment was typical in type L.

The macular area was detached in a high percentage in non-traumatic cases without lattice and specifically in type S.

The numbers of retinal breaks are given in Table 4 and 5. No break was seen in 12.0% and multiple breaks (two or more) in 38.8% of the total material. Type A showed fewer breaks mainly as a result of a high proportion of cases in which no break was seen (28.2%). In the youngest age group and in eyes with lattice degeneration a high frequency of multiple breaks was found.

The sites of the retinal breaks are illustrated in Fig. 1. In fewer than 10% of the cases one or more breaks were located in the inferior nasal quadrant. About 6 times more frequently breaks were found in the superior temporal quadrant. In the other two quadrants a break was seen in about 25% of the cases. Breaks were more frequently found in the temporal quadrant of the right eye than in that of the left eye (72% vs 64%, $P < 0.02$). A similar difference was noted when only flap tears were considered (71% vs 59%, $P < 0.02$). There was no significant sex difference in the distribution of the breaks among the four quadrants. At younger ages there was a high prevalence in the inferior temporal quadrant.

The distributions of breaks among the four

Table 3.
The size of the retinal detachment (RD) in non-traumatic cases. In the analysis of fixed retinal folds, cases with previous ocular surgery are excluded

	No. of cases	Percentage of cases with RD of the indicated size				Significance
		$< 90^\circ$	$90^\circ-180^\circ$	$180^\circ-270^\circ$	$> 270^\circ$	
Age groups, years						
0-29	37	8.1	56.8	16.2	18.9	$\chi^2 = 15.906$ df = 6 $P < 0.02$
30-59	164	18.3	43.9	21.3	16.5	
60+	352	12.8	34.7	27.8	24.7	
Lattice degeneration						
Yes	164	22.0	38.8	26.2	17.1	$\chi^2 = 13.768$ df = 3 $P < 0.01$
No	389	10.8	40.6	24.7	23.4	
Total	553	14.1	38.9	25.1	21.9	
Fixed retinal folds						
Yes	43	4.7	23.3	25.6	46.5	$\chi^2 = 23.732$ df = 3 $P < 0.001$
No	382	17.5	40.3	25.4	17.0	
Total	425	16.2	38.5	25.4	20.0	

Table 4.

The number of retinal breaks in different types of retinal detachments. For specification of types, see Table 8, Part I.

Type	No. of cases	Percentage of cases with the indicated numbers of retinal breaks		
		0	1	2+
T	37	10.8	56.8	32.4
A	78	28.2	46.2	25.6
AL	29	6.9	37.9	55.2
M	75	10.7	53.3	36.0
ML	63	4.8	30.2	65.1
L	72	4.2	38.9	56.9
S	236	12.3	57.2	30.5
Total	590	12.0	49.2	38.8

A vs (Total - A): $\chi^2 = 23.695$; $df = 2$; $P < 0.001$

quadrants in different types of RD are presented in Table 6. Breaks comprising more than one quadrant were especially found in cases with lattice degeneration. In type A, and to a lesser degree in type M, the breaks were more evenly spread among the quadrants.

Round atrophic holes were most frequently observed in the superior temporal quadrant (Fig. 1). In the younger age group (0-29 years) the round hole was the most common type of break in all

quadrants. It was more frequent in myopia, especially in high myopia ($> -5D$), than in other phakic refraction, in all quadrants. A high prevalence of round holes was also found in cases with lattice degeneration and in the inferior temporal quadrant in traumatic cases.

Flap tears (»horseshoe« tears or »arrowhead« tears) were the most frequent form of break, except in younger patients. They were preferably located in the superior temporal quadrant. In high myopia, however, they were more common in the superior nasal quadrant.

Oral dialyses were found especially in traumatic RD in young patients. They were mainly located in the inferior temporal retina. Only one patient had myopia of $> -2D$. No patient was older than 60 years.

Giant tears were found in only three cases and they were found partially or entirely located in the superior temporal quadrant.

Tears in the outer layer of a retinoschisis were found in 8 cases, in 6 of them in the inferior temporal quadrant.

A macular hole was seen in 6 patients, 1 male and 5 females. Changes simulating a hole in the macular area, »pseudoholes«, were more common and were observed in 30 patients, 12 males and 18 females.

A combination of breaks of different types was often found. The results reported above only include cases with one or more breaks of the same type in the quadrant in question.

Table 5.

The number of retinal breaks in non-traumatic cases.

	Total No.	Percentage of cases with the indicated numbers of retinal breaks			Significance
		0	1	2+	
Age groups, years					
0-29	37	2.7	43.2	54.0	$\chi^2 = 12.524$
30-59	164	8.5	46.3	45.2	$df = 4$
60+	352	14.8	50.3	35.0	$P < 0.02$
Lattice degeneration					
Yes	164	4.9	35.4	59.8	$\chi^2 = 43.548$
No	389	15.2	54.2	30.6	$df = 2$
					$P < 0.001$
Total	553	12.1	48.6	39.2	

Table 6.

Distribution of breaks in the four quadrants of different types of retinal detachments. ST and IT = superior and inferior temporal quadrants; SN and IN = superior and inferior nasal quadrants. For specification of the types, see Table 8, Part I.

Type	Percentage of cases				
	with any break in the indicated quadrant				with breaks in more than one quadrant (cases with no break excluded)
	ST	SN	IT	IN	
T	45.9	18.9	29.7	8.1	15.2
A	29.5	25.6	15.4	14.1	17.9
AL	69.0	44.8	24.1	6.9	55.6
M	53.3	30.7	25.3	18.7	43.3
ML	63.5	39.7	28.6	6.3	45.0
L	79.2	37.5	22.2	6.9	47.8
S	57.2	19.1	22.5	7.6	21.3

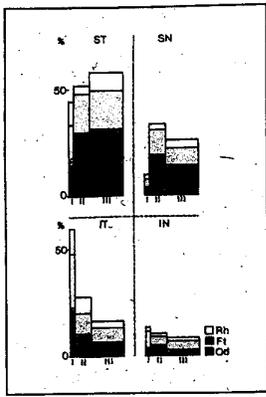
Discussion

The preponderance of the right eye in this material of RD (57.7% in the whole material and 55.6% in non-traumatic, phakic RD, Törnquist et al. 1987) is in accordance with some earlier publications (Smolin 1965; Everett & Katzin 1968; Haimann et al. 1982; Laatikainen et al. 1985a). Moreover, breaks (or specifically flap tears) were more frequently found in the temporal quadrant of the right eye than in that of the left eye in the present study. There is no obvious explanation for this higher proportion of RD in the right eye. Visual discomfort may possibly be more disturbing in the dominant eye, which usually is the right one, which may have meant that some cases of RD in the left eye may have been underdiagnosed in the present population. This possibility, however, cannot be proved or rejected on the basis of the present study. A theory to explain a higher morbidity in the right eye has been proposed by Everett & Katzin (1968). They considered the fast component of ocular movements from right to left while reading to be a possible pathogenetic factor. Pulling forces at the vitreo-retinal boundary layer acting in the temporal periphery of the right eye may be more hazardous than those acting in the nasal periphery of the left eye, which is probably less vulnerable. The definition of traumatic RD is difficult. Since the interval between trauma and symptoms of the detachment may be long (in one-third of the pa-

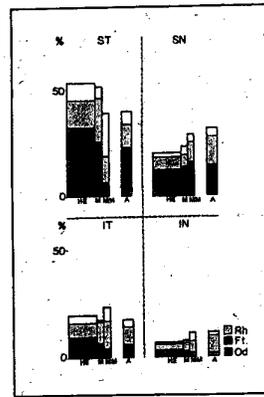
tients of the present study the symptoms of RD developed more than one year after the ocular trauma) the patient will sometimes doubt the association or may have forgotten about the trauma. The traumatic event may sometimes be unclear and opinions concerning the risk of certain forms of indirect trauma are confusing. In the present study only verified ocular trauma (penetrating injury and blunt trauma to the eye) were accepted as causative factors. Thus, an undefined number of cases may have been incorrectly excluded, and the number of patients of type T may be too low. Some of the younger patients of type S had clinical characteristics like those of the traumatic group (e.g. oral dialysis) in spite of a lack of any ocular trauma in their history.

More myopes than were expected from the population data were found in the traumatic group (Törnquist et al. 1987), suggesting that these eyes are more vulnerable to trauma. In view of the fact that oral dialysis is considered to be the most logical consequence of blunt trauma (Weidenthal et al. 1966), it is an interesting finding that flap tears and round holes were at least equally frequent in this material. Thus, different pathogenetic mechanisms are probably present in traumatic RD.

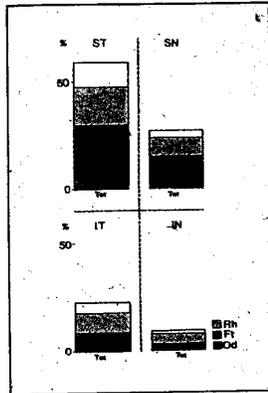
Aphakic RD is often large, either subtotal or total, on admission for surgery (Norton 1964; Ashrafzadeh et al. 1973; Stenkula & Törnquist 1977; Laatikainen et al. 1985b). In the present study a larger detached area was in fact found in



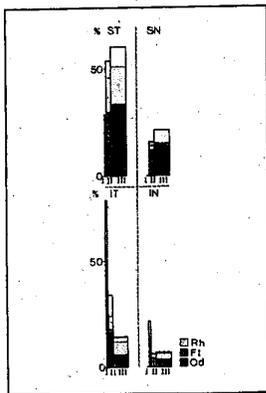
Age groups



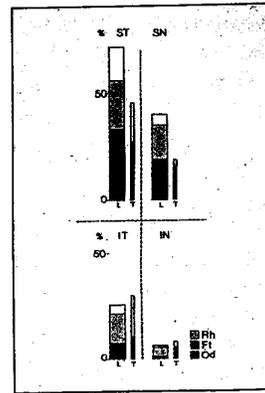
Refraction groups



Total material



Age groups in type S



Type L and type T

Fig. 1.

The distribution of breaks in the four retinal quadrants (ST = superior temporal, SN = superior nasal, IT = inferior temporal, IN = inferior nasal). The width of the bars is proportional to the size of the group in question. The height represents the proportion of cases with any break in this group. Only oral dialysis (red), flap tears (blue) and round holes (yellow) are specifically reported. The white areas at the top of the bars represent cases with a combination of different breaks or more infrequent types of breaks. The distributions in the total series, three age groups (I = 0-29 years, II = 30-59 years, III = 60 years and more), the same age groups in type S, refraction groups (HE = hyperopia and emmetropia ± 2 D, M = myopia -2.25 to -5.0 D, MM = myopia of more than 5.0 D, A = aphakia) and types L and T are shown.

type A. The interval between the first symptoms and surgery for RD was not significantly longer than in phakic RD. Thus, it seems that RD progresses relatively rapidly in the presence of aphakia.

Many authors have reported difficulties in detecting a retinal break in aphakic RD (Norton 1964; Everett & Katzin 1968; Edmund et al. 1974; Laatikainen et al. 1985b), and this was also documented in the present study. Opacities in the ocular media were not significantly more frequently found in aphakic than in phakic eyes in the present material (corneal opacities in 2.8% and 1.8%, and vitreous opacities in 70.1% and 65.5%, respectively).

The topographical distribution of detected breaks may also differ between the aphakic and phakic eye. Of all breaks, 64% were located in the temporal quadrants in aphakic and 70% in phakic RD. Although this difference is not significant, the figures are in accordance with those of Everett & Katzin (1968) and Ashrafzadeh et al. (1973), who found relatively more breaks in the nasal quadrants in aphakia.

About half of the cases with non-traumatic RD in this material were classified as type S. Types M, ML and L represented approximately one-third each

of the remaining half. The proportions were different in different age groups, however. Nearly every eye with lattice degeneration was myopic in the youngest patients, but in older ones these eyes were mostly non-myopic (Fig. 2). The maximum prevalence of lattice degeneration is probably reached prior to the age of 10 years (Byer 1965) and no age-related trend in regard to the size of lattice has been reported (Straatsma et al. 1974). The relative importance of lattice as a predisposing factor seems to decrease with age. Most authors have found a higher prevalence of lattice in myopes (see e.g. Byer 1979) as was also demonstrated in the present material (Törnquist et al. 1987). In patients older than 60 years, however, the majority of cases with lattice were non-myopic.

In eyes with lattice degeneration a smaller RD was more frequent. A significant difference in the size of RD was found between types M and L ($\chi^2 = 10.929$, $df = 3$, $P < 0.02$). The retinal breaks were more often numerous in type L than in type M, but this difference was not significant.

In moderate myopia (-2.25 D to -5.0 D) a flap tear was the most common type of break, but in myopia of > -5.0 D round holes outnumbered flap tears except in the superior nasal quadrant. Laatikainen et al. (1985b) reported that atrophic

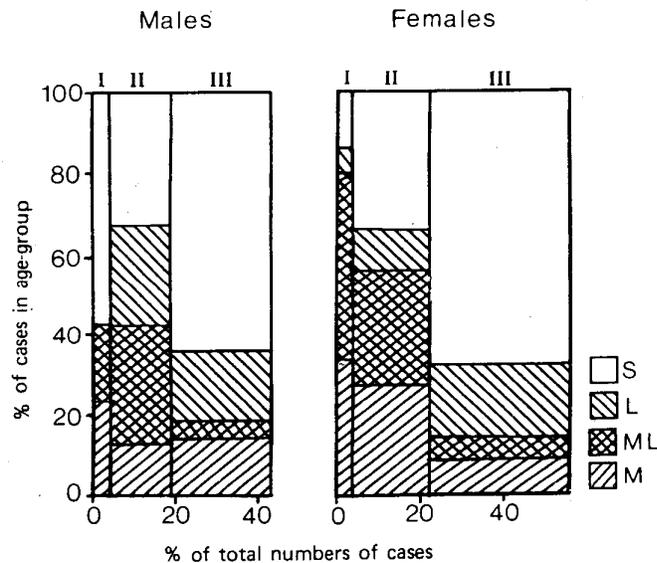


Fig. 2.

The distribution of the four types of non-traumatic, phakic retinal detachment (see Table 8, Part I) into age groups (I = 0-29 years, II = 30-59 years, III = 60 years and more) of both sexes. The areas are proportional to the number of cases.

round holes were more common in myopic than in non-myopic eyes, phakic or aphakic.

Full-thickness fixed retinal folds were found pre-operatively in 10.1% of cases with non-traumatic phakic RD. This figure is considerably lower than that reported by Ashrafzadeh et al. (1973) of 39.3%. However, it should be expected that the figure would be lower in our unselected patient material than in a group of more complicated cases with a poor prognosis.

In cases with giant tears, fixed retinal folds are a frequent finding (Törnquist, unpublished data), but in the present material with only three cases of tears larger than on quadrant, no association between the size of the largest tear of the eye and the incidence of fixed retinal folds could be demonstrated.

Summary

Type T was most common in young males. In eyes with oral dialysis ocular trauma was often reported by the patients, but in the total group of traumatic RD the frequency of flap tears and round holes was at least as high as that of oral dialyses, or even higher.

Type A: The RD was relatively often subtotal or total (30.7%). In a high frequency (28.2%) no break was found. The general tendency for breaks to be located in the superior and temporal parts of the retina was less pronounced.

Type AL: Lattice degeneration was present in 27% of the cases of aphakic RD. Among these cases only 6.9% displayed no break, and multiple breaks were nearly as common as in phakic eyes with lattice.

Type M: Round holes were common and the detachment was usually large. Fixed retinal folds were considerably less often seen pre-operatively (3.1%) than in the non-myopic group (10.9%).

Type ML: At younger ages lattice was more often found in myopic eyes than in other phakic or aphakic eyes. Multiple breaks were very frequent (65.1%).

Type L cases were characterized by a large number of breaks (more than one in 56.9% of this group), often located in more than one retinal quadrant, and a small detachment area.

Type S was the largest group (40%), and comprised mainly patients of older ages. In 57.2% of the type S cases only one break was found and most commonly a flap tear. Of the 64 cases in the younger age group 21 had an oral dialysis. A large

detachment was a comparatively in frequent finding, but a detachment of the macular area was significantly more common in this type than in other types of RD

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The Refractive Status and Vision Profile

A Questionnaire to Measure Vision-related Quality of Life in Persons with Refractive Error

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Objective/Background: To describe the Refractive Status and Vision Profile (RSVP), a questionnaire that measures self-reported vision-related health status (symptoms, functioning, expectations, concern) in persons with refractive error.

Design: Cross-sectional study by survey.

Participants: The RSVP was self-administered by 550 participants with refractive error (or history of refractive surgery) recruited from five refractive surgery practices and one optometric practice. Information on refraction, uncorrected and best-corrected visual acuity, and history of refractive surgery was obtained from physicians' records.

Methods: Internal consistency, test-retest reliability, agreement with global measures of vision (criterion validity), discriminant validity, content validity, and construct validity (associations of scale scores with patient status variables) were assessed using Cronbach's α , Spearman rank correlations, factor analysis, and multitrait analysis.

Outcome Measures: Scores on the overall RSVP scale (**S**) and on eight RSVP subscales (*functioning, driving, concern, expectations, symptoms, glare, optical problems, problems with corrective lenses*) were calculated based on 42 items.

Results: Cronbach's α was 0.92 for **S** and ranged from 0.70 to 0.93 for RSVP subscales, indicating good internal consistency. Satisfaction with vision was more strongly associated with **S** than with refractive error or with visual acuity. Individuals with more refractive error had significantly lower (worse) scores for **S** and for subscales *concern, functioning, driving, optical problems, and glare*. Scores for **S** and for subscales *concern, functioning, optical problems, and driving* remained significantly associated with satisfaction with vision after adjustment for age, gender, corrective lens type, and refractive error.

Conclusions: The RSVP measures a range of visual, functional, and psychologic impacts of refractive error that are likely to be important to patients. The RSVP would be a useful tool for evaluating interventions for correction of refractive error and may be useful for assessing refractive surgery candidates in clinical practice. *Ophthalmology* 2000;107:1529-1539 © 2000 by the American Academy of Ophthalmology.

Refractive error affects nearly 25% of adults in the United States.¹ Until recently, corrective lenses (contact lenses or

spectacles) were the only effective means of treating refractive error for most persons. Surgery to correct refractive error was introduced into the United States in the late 1970s. Today, surgical techniques that use the excimer laser predominate. With the increase in patients undergoing surgery for refractive error and the ongoing introduction of new approaches for treatment of refractive error, the importance of systematic evaluation of candidates for surgery and comparison of the outcomes associated with different therapeutic options has grown.

Traditional clinical measures of refractive status (refraction, uncorrected and best-corrected visual acuity [VA]) have been the primary considerations used in such evaluations and comparisons. However, research on cataract surgery has shown that patient-reported assessments of functioning, satisfaction, and symptoms capture aspects not detected by traditional clinical measures of the need for and outcomes of surgery.²⁻⁴ The National Eye Institute has recognized the need to "... study quality of life and functional status as perceived by the patient ... to assess the full impact of a treatment or disease process."⁵ Although vali-

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dated questionnaires to measure disease-specific^{2-4,6,7} and generic⁸ outcomes in ophthalmic research exist, these instruments may not be sufficiently sensitive or responsive (able to detect changes in status) for clinical use in persons with refractive error, especially those undergoing refractive surgery. In this report, we describe the development and properties of the Refractive Status and Vision Profile (RSVP), a questionnaire specifically designed to measure self-reported functioning, symptoms, health perceptions, and expectations in individuals with refractive error.

Methods and Participants

Overview

Potential items for inclusion in the questionnaire were identified from a review of items contained in published questionnaires,⁹⁻¹⁶ guided focus groups of eye care professionals and persons with refractive error, and unstructured interviews with additional individuals with refractive error. The focus group discussions were tape recorded and then subjected to content analysis. Specific wording that focus group participants used to describe problems with vision was maintained to the extent possible. A preliminary version of the questionnaire was pilot tested in a group of 306 individuals with refractive error, and factor analyses and multitrait scaling of the pilot test results were used to modify the questionnaire. The revised questionnaire was named the Refractive Status and Vision Profile (RSVP). The RSVP was tested in a new population of individuals, and a test-retest analysis was performed. Analyses of RSVP subscales, as well as the reliability and validity of an overall combined RSVP scale, are presented.

Identifying Areas of Health-related Quality of Life

Items identified from the transcripts were grouped into domains based on judgments regarding the particular aspect of health-related quality of life (HRQoL) they affected.¹⁷ The areas included functioning (ability to carry out activities in daily life), symptoms (sensations experienced by an individual), health perceptions (satisfaction with health, self-rating of health), and expectations (beliefs about future health states). Within each area, items were grouped into related topics (domains).

Formatting of Items and Response Options

Items. Items were worded to form short declarative statements (e.g., "I have problems watching TV"). Items were prefaced with the phrases "Because of my vision" and "In the past month."

Responses. For each item, the amount of difficulty or bother ("not at all," "mild," "moderate," "severe," "so bad that I don't use this type of correction") or frequency ("never," "rarely," "sometimes," "often," "all the time") was assessed. Responses of "not applicable" were permitted on both the pilot questionnaire and the RSVP.

Accounting for Corrective Lens Type. For all items relating to satisfaction with vision, rating of vision, visual symptoms, and visual functioning, patients were asked to respond for the corrective lens types that applied to them (i.e., with glasses, with contact lenses, and with no lenses). Persons who had not used a particular type of corrective lens for more than 1 hour during the past month were instructed to check "not applicable" for the panel of questions for that lens type.

Scoring and Scaling

Derivation of Item Scores. Scores for each satisfaction-, functioning-, or symptom-related item were based on the responses for the type of corrective lens currently used by the patient. For those who used both glasses and contact lenses, the score for either glasses or contacts responses that was worse was used. (In the initial phases of the analyses, we compared results obtained using the worse score to results obtained using the mean score for glasses and contact lenses. Results were nearly identical. We chose to use worse score in the final analyses because it seemed to be a clinically reasonable approach.)

Calculation of Scores. In the RSVP, all items had five response options (see Table 1). Responses were coded to values of 1 through 5, with 5 indicating the most severe or frequent trouble. For subscale and total scale (*S*) scores, the mean of values of nonmissing responses for each subscale was calculated, without weighting, because the standard deviations (based on identical number of response options) were very similar. Subscales for which all the items had missing responses were coded as missing.

Rescaling. The mean score for each scale and each individual was rescaled to a 0-to-100 metric by subtracting the minimum possible mean score (1) from the mean score for the scale, dividing this difference by the possible range of the mean score (5 minus 1), and multiplying by 100. Rescaling was performed to facilitate the interpretation of scale and individual scores as percentages of maximum difficulty. The total scale score, *S*, was calculated by taking the sum of the recoded responses as described above for all items included in all subscales of the RSVP and rescaling to a 0-to-100 scale.

Participants

Individuals. All participants gave oral consent to participate in the study. The study protocol was approved by the Johns Hopkins University Joint Committee for Clinical Investigation.

Clinical Information. Information on uncorrected and best corrected VA, manifest refraction, and history of ocular conditions and refractive surgery was obtained from the patient chart. Patients found to have nonrefractive ocular conditions that potentially affected vision or eligibility for refractive surgery (e.g., keratoconus, cataract, glaucoma) were excluded from analyses.

Evaluation of the Refractive Status and Vision Profile. Coordinators at participating sites (five refractive surgery practices and one optometric practice [see Appendix]) were asked to give the RSVP to consecutive patients undergoing refractive surgery evaluation between May and December 1997. Eligible individuals either had refractive error and no previous refractive surgery or were at least 3 months post refractive surgery. The RSVP consisted of a 64-item questionnaire that was self-administered by patients, taking, on average, 10 to 15 minutes to complete (additional questions to assess age, gender, and lens-wearing history are not included in the 64).

Test-retest Assessment

The 40 patients who completed an RSVP during the months of October or November 1997 who did not have intervening refractive surgery were asked to complete the RSVP questionnaire a second time within 1 day to 1 week of their original completion of the RSVP. Twenty-nine of the 40 completed a second RSVP. The interval between the first and second questionnaire administration ranged from 2 days to 3 weeks (and included their clinical evaluation for refractive surgery). A second assessment of test-retest reliability was carried out in a convenience sample of 16 persons with refractive error who were not undergoing evaluation for

Table 1. Domains of the Refractive Status and Vision Profile Questionnaire

Domain	No. Items	Items	Response Options
Function	12	Watching TV or movies; seeing an alarm clock; seeing clearly when first waking up; seeing a clock on the wall; doing activities outside; taking care of or playing with children; doing one's job; doing social activities; playing sports or recreational activities; near work; swimming	Not applicable (never use this type of correction); No difficulty at all; A little difficulty; Moderate difficulty; Severe difficulty; So much difficulty that I don't do the activity with this type of correction; Never do this activity for other reasons (not related to vision)
Driving	3	Driving at night, during rain, under glare conditions	Same as for function
Perceptions	7	Worry, concern, or frustration about vision; afraid to do some activities because of vision; feeling less self-sufficient because of vision; feeling vision held one back	Strongly agree; Agree; Neither agree nor disagree; Disagree; Strongly disagree
Symptoms	13	Eyes feeling irritated; drafts bothering eyes; pain in eyes; sensitivity to light; glare; seeing halo around lights; depth perception; seeing in dim light; things looking different out of one eye versus the other; judging distance when going up or down steps; things appearing distorted; vision being cloudy; change in vision during the day	Not applicable (never use this type of correction); No trouble at all; A little trouble; Moderate trouble; Severe trouble; So much trouble that I don't use this type of correction
Problems with corrective lenses	13	Wearing glasses or contacts bothers one, takes too much time; glasses getting dirty; glasses getting fogged up or wet; losing/looking for glasses; contact lenses moving around in the eye; losing a contact lens; not being able to wear contact lenses for as long as wanted to; being bothered by the sensation of a contact lens in the eye	Not applicable (never use this type of correction); No trouble at all; A little trouble; Moderate trouble; Severe trouble; So much trouble that I don't use this type of correction
Expectations	6	Frustrating to use glasses/contacts to get best possible vision; could accept less than perfect vision if didn't need glasses/contacts; only thing that would satisfy is to have very sharp vision without glasses/contacts; as long as could see well enough to drive without glasses/contacts, wouldn't mind having vision that was less than perfect; think vision will be worse in the future; think will always have some trouble with vision in the future	Strongly agree; Agree; Neither agree nor disagree; Disagree; Strongly disagree
Vision preference	1	Trade-off between distance vision and near vision	Excellent distance vision; poor near vision Distance vision good but not excellent; near vision good but not excellent Poor distance vision but not as bad as now; excellent near vision Keep my current vision
Satisfaction with vision	4	Satisfaction with current vision with glasses, with contact lenses, with no lenses, with near vision	Very satisfied; Satisfied; Neither satisfied nor dissatisfied; Dissatisfied; Very dissatisfied
Rating of vision	3	Rate vision with glasses, with contact lenses, with no lenses	Scale of 0 to 10 0 = completely blind 10 = perfect vision
General health	2	In general, would you say your health has been: How concerned about your health have you been during the past 1 month?	Excellent; Very good; Good; Fair; Poor 0 = Not at all concerned 10 = Very concerned

refractive surgery. The interval between the first and second RSVP administration for this second group ranged from 1 day to 1 week.

Domains of the Refractive Status and Vision Profile

Domains of the RSVP, items to assess them, and response options are shown in Table 1. Domains include physical-social functioning, driving, perceptions (psychological functioning and concern about health status), symptoms, problems with corrective lenses, and expectations (what patients expected regarding their postsurgical visual outcome). In addition, patients were asked to rate their vision and their satisfaction with vision separately for glasses, contact lenses, no lenses, and for near vision. The items on satisfaction and rating were used as global criteria for validating the RSVP and its subscales rather than to measure a domain of health perceptions. To assess the association between other patient characteristics and vision-related results, two global health items (concern about health and general rating of health) were included.

Additional questions to assess age, gender, and lens-wearing status were also included.

Analysis of Refractive Status and Vision Profile

Evaluation of Questionnaire Items. The frequency distributions of responses to each item were examined to identify problems and symptoms that caused no difficulty or trouble for nearly all patients or that caused severe difficulty or trouble for nearly all patients. Such items did not have sufficient variability to be useful in characterizing individuals. However, symptom items known to result potentially from refractive surgery (halos, starbursts) were retained, even if they were not frequently experienced before or after surgery, because they were judged to be important in evaluating outcomes of refractive surgery.

Identification of Subscales. Factor Analysis. Factor analyses (Statistical Analysis System, version 6.09, SAS Institute, Cary, NC) using squared multiple correlations as prior communality estimates were conducted to extract item groupings (factors) that fell into the broad categories of functioning, symptoms, and health

perceptions. The factor solutions were rotated using the varimax transformation¹⁸ to facilitate interpretation of factors. Items that had factor loadings less than 0.1 were excluded from further analyses. Items with factor loadings more than 0.9 were also excluded because they indicated excessive redundancy. Factor analyses were rerun on the remaining items, and the solutions were used to identify HRQoL subscales that could be used to characterize different subgroups of patients. The remaining items within each subscale were examined to assess their coverage of the intended domain ("face" or "content" validity).¹⁷

Multitrait Analysis. Multitrait analysis¹⁹ was used to assess the groupings of the items into subscales (based on the factors identified by factor analysis; Multitrait Analysis Program, Version 2.0, provided by J. E. Ware, Jr., New England Research Institute). This technique is based on calculating the corrected item-to-total correlation of each item with each subscale. Correlations of items within subscales were examined (correlations should be at least 0.4 to demonstrate convergent validity [also known as *internal consistency*]). Discriminant validity was assessed by comparing, for each item, the correlation of that item with its own subscale versus the correlation of that item with each of the other subscales. Items that did not have a correlation of at least 0.4 with any proposed subscale were removed. Items with lower (positive) correlations with their proposed subscale than with a different subscale were either removed or placed into the alternate subscale. Items with insufficient convergent or discriminant validity were either moved to a more appropriate subscale or dropped. A "successfully" scaled item is one whose correlation with its own subscale is greater than its correlation with any other subscale. Summaries of multitrait scaling are expressed, for each subscale, as the proportion of successful item-to-other-subscale comparisons. (The denominator is all possible item-to-other-subscale comparisons for items in that scale; i.e., [no. items in the subscale] × [total no. subscales - 1]). The result of the multitrait analysis identified the subgroup of items of the RSVP that comprised clinically meaningful and demonstrably valid subscales.

Assessment of Reliability and Validity. The internal consistencies of the overall RSVP scale, *S*, and of each subscale were assessed by calculating Cronbach's α , an average of corrected item-to-total correlations for the subscale.²⁰ Criterion validity was assessed by calculating Spearman correlations between each scale and variables that assess patient status; for example, spherical equivalent in the worse eye (absolute value, so that -3.5 diopters [D] would be more extreme than +3.0 D), overall satisfaction with vision, best corrected VA, and uncorrected VA. Associations between *S* scores, as well as subscale scores, and several demographic characteristics and traditional clinical measures were examined to determine whether median scores differed among subgroups in a manner consistent with hypothesized relationships (construct validity). The subgroups examined to assess construct validity were (1) those interested versus not interested in refractive surgery and (2) different corrective lens usage groups. In addition, the association of all subscales with age, gender, refractive error, and corrective lens type was assessed so that potential confounders of the association between subscales and satisfaction with vision could be identified and included in multiple regression models. Variables assessed as potential confounders included amount of refractive error, age, different corrective lens usage groups, and gender. Test-retest reliability was assessed using the intraclass correlation coefficient (ICC)²¹ and the standard error of measurement.²² The associations between the overall RSVP scale, *S*, as well as subscale scores and each of the global measures (satisfaction with vision and rating of vision) were evaluated by fitting multiple logistic or linear regression models, adjusting for traditional clinical measures and demographic variables. Associations for which the *P* value was less than 0.05 were considered statistically significant.

Table 2. Characteristics of Participants (N = 550)

Characteristic	Description
Age (yrs)	
Mean (standard deviation [SD])	37.2 (9.7)
Range	18-71
Spherical equivalent, worse eye	
Mean (SD)	-5.4 D (3.5 D)
Range	-18.375-+3.75 D
Health concern [†]	
Mean (SD)	1.6 (2.4)
Range	0-10
Rating of vision [‡]	
Mean (SD)	8.4 (1.4)
Range	0-10
Gender (n, %)	
Female	325 (59.1)
Source (practice type, n, %)	
Refractive surgery	508 (92.4)
Optometric	42 (7.6)
Corrective lens status (n, %)	
Glasses only	196 (35.6)
Contact lenses only	105 (19.1)
Glasses and contact lenses	234 (42.5)
No lenses*	13 (2.4)
History of refractive surgery (n, %)	
None	466 (84.7)
One eye	71 (12.9)
Both eyes	13 (2.4)
Best-corrected VA, both eyes (n, %)	
$\geq 20/20$ OU	472 (86.4)
$\geq 20/20$; 20/25-20/40	52 (9.5)
20/25-20/40 OU	22 (4.0)
Health rating (n, %)	
Very good or excellent	480 (87.9)
Satisfaction with vision (n, %)	
Satisfied or very satisfied	304 (56.2)

D = diopters, OU = both eyes.

*Two additional participants wore glasses for reading only.

[†]0 = not at all concerned; 10 = very concerned.

[‡]0 = completely blind; 10 = perfect vision.

Results

A total of 550 patients completed the RSVP questionnaire (Table 2). Most were female (59%). Nearly half used both glasses and contact lenses. Nearly all (96%) had best corrected VA of 20/20 or better in at least one eye, and 15% had a history of refractive surgery.

Refractive Status and Vision Profile Subscales

Factor analysis performed on all items revealed subscales (groupings of correlated items) consistent with domains chosen after the pilot test. The first factor related to physical-social functioning and optical problems. Other factors related to driving, ocular symptoms, concern, light and glare, expectations, problems with glasses, and problems with contact lenses. The eight subscale groupings suggested by the factor analysis were examined using multitrait scaling methods. Separate subscales were formed for physical and social functioning and optical problems. Items related to problems with glasses and problems with contact lenses were combined into a single subscale.

The final results of the multitrait scaling are shown in Table 3. Eight subscales comprising a total of 42 items were identified: *concern*, *physical-social functioning*, *expectations*, *driving*, *symp-*

Table 3. Subscales of the Refractive Status and Vision Profile (RSVP)

Name	No. Items	% Correctly Scaled*	α^{\dagger}	ICC [‡]	ICC (in stable group) [§]	2 × Standard Error of Measurement	Mean [¶]	Range
Concern	6	100	0.83	0.77	0.88	9.2	44.0	0–100
Driving	3	100	0.93	0.69	0.70	14.1	25.9	0–100
Expectations	2	100	0.70	0.42	0.91	13.3	58.7	0–100
Physical/social functioning	11	96.1;100	0.87	0.84	0.63	10.3	17.2	0–92.8
Symptoms	5	100	0.84	0.71	0.80	8.0	20.8	0–100
Optical problems	5	94.3;100	0.82	0.68	0.91	6.1	12.8	0–95
Glare	3	90.5;100	0.75	0.72	0.72	11.1	22.3	0–100
Problems with corrective lenses	7	100	0.82	0.76	0.78	13.1	34.0	0–100
S (overall scale)	42		0.92	0.61	0.88	5.5	26.6	0.7–100

ICC = intraclass correction coefficient.

*If all items within the subscale had significantly higher corrected item-to-total correlations with their own subscale than with any other subscale, this number would be 100%. If some items had higher (but not statistically significantly higher) corrected item-to-total correlations with their own subscale than with any other subscale, the first percentage indicates proportion with significantly higher correlations, and the second percentage indicates proportion with higher (regardless of whether significantly so) correlations.

[†]Cronbach’s α is a measure of internal consistency. Values of 1.0 indicate perfect internal consistency; values of 0 indicate no internal consistency. Values of 0.7 or higher are considered sufficient for comparing subgroups of persons.

[‡]Intraclass correlation coefficient to measure test–retest reliability. Measured in a subgroup of 29 participants who repeated the RSVP questionnaire within 2 days to 3 weeks after the first administration, with an intervening refractive surgery evaluation.

[§]Intraclass correlation coefficient to measure test–retest reliability. Measured in a convenience sample of 16 persons not from a refractive surgery practice who repeated the RSVP questionnaire within 1 day to 1 week after the first administration.

^{||}Two times the standard error of measurement (the reproducibility) represents the amount of change that would be required, after an intervention, to be statistically significant.²²

[¶]All subscale scores were rescaled to 0–100.

toms, optical problems, glare, and problems with corrective lenses. The number of items per subscale ranged from 2 to 11. The *functioning* subscale included items that involved distance and near vision tasks. Two items in the *functioning* subscale, swimming and social activities, had only moderate corrected-item-to-total correlations but were included because they increased the content validity of this subscale.

Performance of the Overall Refractive Status and Vision Profile Scale, S, and the Refractive Status and Vision Profile Subscales

Internal consistency of the total scale *S* and the RSVP subscales was high (Cronbach’s α range, 0.70–0.93; Table 3). The average *S* score was 26.6 (range, 0.7–100). Mean subscale scores ranged from 12.8 (*optical problems*) to 58.7 (*functioning*). The distribution of subscale scores tended to be skewed toward scores reflecting fewer problems, most markedly for *optical problems* and *functioning*. Discriminant and convergent validities of the subscales were excellent, with 90% to 100% of the item-to-total subscale comparisons rated as successful (Table 3), indicating that the scaling of the final 42 items into subscales was excellent.

Test–retest reliability of *S* in the 29 individuals recruited from refractive surgery practices was modest (ICC, 0.61) and less than that of seven of the eight subscales (ICCs, 0.68–0.84; the eighth subscale [*expectations*] ICC was 0.42). The test–retest reliability of *S* and of the subscales was in general higher in the convenience sample (except for *functioning*). The amount of change in score that would be required to detect a statistically significant change after an intervention (based on the standard error of measurement, an alternate measure of reproducibility²²) is shown in Table 3: for *S*, this number is 5.5; for the subscales, it ranged from 8 to 14.

To assess criterion validity (association of scale scores with

traditional clinical measures of patient status), Spearman correlations between *S*, the subscales, and each of the global measures (satisfaction with vision and rating of vision) were compared with Spearman correlations between each of the traditional clinical measures (absolute value of refractive error, VA) and the global measures (Table 4). The correlation between satisfaction with vision and *S* (–0.41) was greater than the correlation between satisfaction with vision and either uncorrected or best-corrected VA or absolute value of refractive error (0.05, 0.12, 0.15), indicating that *S* is more closely related to satisfaction with vision than are the traditional clinical measures. Similarly, the correlations between most RSVP subscales and satisfaction with vision were of a higher magnitude (–0.21 through –0.42; except *expectations* and *problems with corrective lenses*) than for traditional clinical measures. The correlation between rating of vision and *S* (–0.42) also was greater than the correlation between rating of vision and either uncorrected or best-corrected VA or refractive error (0.15, 0.19, 0.21). Similar patterns were seen for correlations with rating of vision (Table 4), indicating that *S* and most RSVP subscales are more closely related to the global measures than is VA.

Associations between S, the Refractive Status and Vision Profile Subscales, and Traditional Clinical Measures

Increasing age was associated with higher scores for *symptoms, optical problems, and problems with corrective lenses*. Type of corrective lens used was associated with *S, driving, functioning, symptoms, optical problems, glare, and problems with corrective lenses* (the subgroup using a combination of glasses and contact lenses consistently had the highest scores, except for *problems with corrective lenses*). Female gender was associated with higher scores for *S, driving, expectations, symptoms, optical problems,*

Table 4. Spearman Correlation Coefficients between RSVP Subscales versus Global Items and Traditional Clinical Measures

Traditional Measure	S [¶]	Concern	Expectations	Physical/Social Function	Driving	Symptoms	Optical Problems	Glare	Problems with Corrective Lenses	Satisfaction with Vision [§]	Vision Rating	General Health [†]	Health Concern [‡]
Visual acuity													
Uncorrected, better eye	-0.12*	-0.15*	-0.07	-0.16*	-0.13*	-0.05	-0.12*	-0.13*	0.01	0.05	0.15*	-0.05	0.03
Uncorrected, worse eye	-0.16*	-0.17*	-0.10*	-0.17*	-0.18*	-0.08	-0.16*	-0.16*	0.02	0.05	0.14*	-0.04	0.06
Best corrected, better eye	-0.05	-0.00	-0.07	-0.06	-0.16*	-0.00	-0.15*	-0.05	0.14	0.09*	0.19*	-0.06	0.02
Best corrected, worse eye	-0.10*	-0.05	-0.10*	-0.08	-0.18*	-0.01	-0.15*	-0.09*	0.09*	0.12*	0.18*	-0.09*	-0.00
Spherical equivalent													
Better eye	-0.19*	-0.23*	-0.11*	-0.19*	-0.24*	-0.07	-0.21*	-0.17*	0.06	0.12*	0.21*	-0.05	0.03
Worse eye	-0.21*	-0.27*	-0.13*	-0.20*	-0.25*	-0.05	-0.22*	-0.17*	0.08	0.15*	0.21*	-0.06	0.05
S (overall scale)										-0.41*	-0.42*	0.20*	0.23*
Concern										-0.21*	-0.16*	0.19*	0.21*
Expectations										-0.09*	-0.11*	-0.04	-0.03
Physical/social functioning										-0.42*	-0.44*	0.13*	0.16*
Driving										-0.39*	-0.47*	0.19*	0.13*
Symptoms										-0.22*	-0.31*	0.14*	0.19*
Optical problems										-0.39*	-0.45*	0.17*	0.16*
Glare										-0.22*	-0.26*	0.13*	0.12*
Problems with corrective lenses										-0.06	-0.02	0.11*	0.14*
Satisfaction with vision [§]												-0.10*	-0.08
Vision rating												-0.15*	-0.08

*Correlation coefficient differs significantly from 0 ($P < 0.05$).

†1 = excellent; 5 = poor.

‡0 = not at all concerned; 10 = very concerned.

§1 = very dissatisfied; 5 = very satisfied.

||0 = completely blind; 10 = perfect vision.

and glare, and with lower scores for *problems with corrective lenses*. A greater degree of refractive error was associated with higher scores for *S*, *concern*, *driving*, *functioning*, *optical problems*, and *glare*. Thus all these variables are potential confounders of the relation between satisfaction with vision and at least one of the subscales or *S*; hence, they were included in the multiple regression analyses described below.

In evaluating construct validity, we hypothesized that scores for *functioning*, *symptoms*, *optical problems*, and *problems with corrective lenses* would be higher among those wearing both glasses and contact lenses than among those wearing contact lenses only or among those wearing glasses only (Fig 1). This was found to be true for *S* ($P = 0.0001$ [glasses only]), for *functioning* ($P = 0.0001$ [glasses only]; $P = 0.0001$ [contacts only]), and for *symptoms* ($P = 0.0001$ [glasses only]; $P = 0.0001$ [contacts only]), but not for *problems with corrective lenses* (although wearers of contact lenses only were lower [$P = 0.04$], wearers of glasses only were higher, $P = 0.0001$) or *optical problems* ($P = 0.003$; $P = 0.08$, respectively). We also hypothesized that those undergoing refractive surgery evaluation would have higher scores than those from the optometric practice for subscales *concern*, *expectations*, *functioning*, and *problems with corrective lenses*. Indeed, scores for *S* ($P = 0.0001$), *concern* ($P = 0.0001$), *expectations* (more willing to accept less-than-perfect vision, $P = 0.0001$), and *problems with corrective lenses* ($P = 0.0001$) were

significantly higher, but not so for *functioning* ($P = 0.1$) or *symptoms* ($P = 0.5$).

Association between S, the Refractive Status and Vision Profile Subscales, and Satisfaction with Vision

Multiple logistic regression analyses were performed to examine the association between *S*, each of the RSVP subscale scores, and satisfaction with vision (defined as "satisfied" or "very satisfied"; Table 5). Age, lens usage, and spherical equivalent were consistently significantly associated with satisfaction with vision (older persons were less likely to be satisfied, those wearing glasses and contact lenses were less likely to be satisfied, those with more refractive error were less likely to be satisfied). After adjustment for age, gender, lens type, and refractive error, higher scores (more trouble) on *S* and on the subscales related to *concern*, *functioning*, *driving*, *symptoms*, *optical problems*, and *glare* were all significantly associated with lower odds of satisfaction with vision. There was a borderline association between higher scores (more trouble) on the *problems with corrective lenses* subscale and lower odds of satisfaction with vision. The *expectations* subscale was not associated with satisfaction with vision. Similar results were noted for

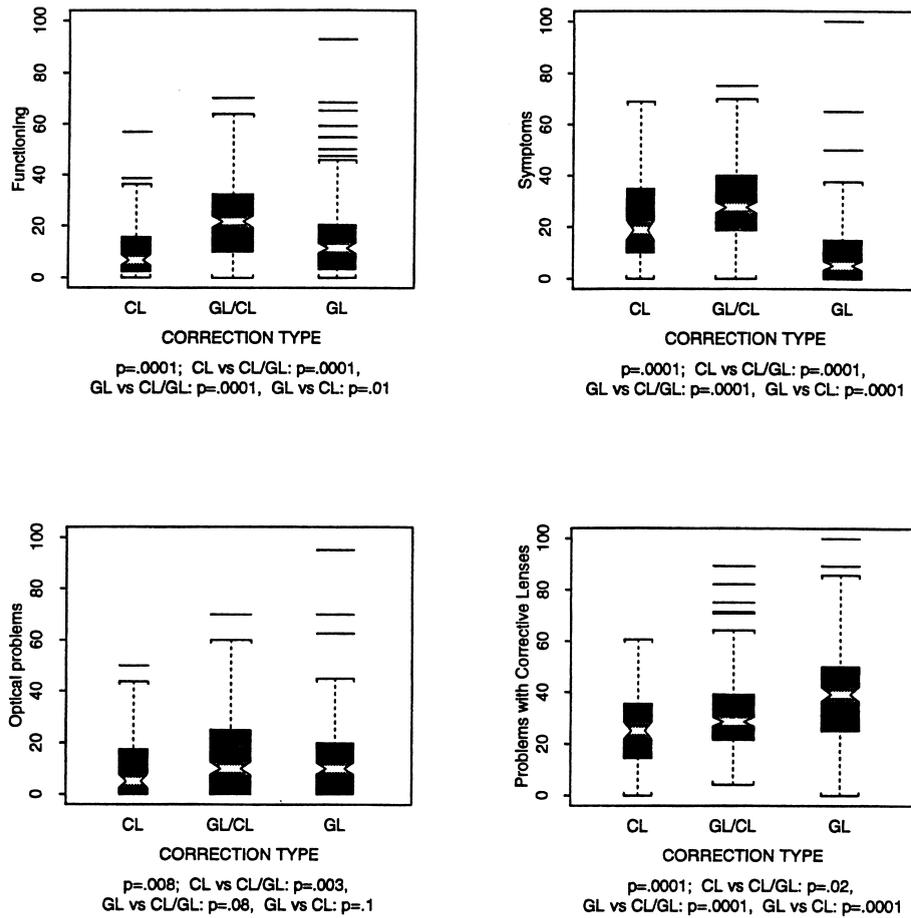


Figure 1. Association between Refractive Status and Vision Profile subscale scores and type of corrective lens used. Distribution of scale scores are expressed using box plots. The center white horizontal line represents the median. The shaded box extends from the 25th to the 75th percentiles. The vertical lines extending from the box cover the extent of the data within 1.5 times the interquartile range (length of the box). Values in the data beyond this range are indicated by horizontal solid lines. The indentations in the box centered on the median, in lighter shading, represent the extent of the 95% confidence interval for the median. The width of each box is proportional to the square root of the number of observations for that box. The distributions of scores are shown for each type of corrective lens (CL = contact lenses only; GL = glasses only; GL/CL = both glasses and contact lenses). The first P value listed is from the Kruskal-Wallis test assessing whether all three groups have the same median score for the subscale listed; the next P values are from Wilcoxon rank-sum tests assessing whether each pair of groups, respectively, have the same median score.

self-reported rating of vision (using multiple linear regression models with the 0–10 rating as the outcome variable).

Discussion

In ophthalmic research and practice, it is increasingly recognized that consideration of patients' own evaluation of their functioning and symptoms is important in assessing the need for and outcome after treatment. Patient-reported evaluations provide information complementary to that provided by traditional clinical measures, such as VA or refractive error.^{2,5} Measurements of patients' assessment of their health status should be valid and reliable. When used as outcome measures, they also should be sensitive (respon-

sive) to clinically meaningful changes in patients' status. Although generic instruments (i.e., those not specific to a particular condition) are a useful measure of patients' overall health status, they tend to be less sensitive than disease-specific instruments to clinically significant symptoms and to the specific functional impacts of a disease.²³

Most well-known validated questionnaires developed for use in an ophthalmologic setting were designed for use in individuals with cataract, are targeted mostly toward functioning (Visual Function-14-item,^{2,24,25} Activities of Daily Vision,^{3,26,27} Visual Activities Questionnaire,⁴ and others^{28,29}), and do not adequately address the problems or expectations of individuals with refractive error. One generic ophthalmic instrument, the National Eye Institute Visual Functioning Questionnaire,⁸ was developed based on

Table 5. Multiple Logistic Regression Analyses: Association between Each Refractive Status and Vision Profile Subscale Score and Satisfaction with Vision, Adjusting for Age, Gender, Lens Type, and Refractive Error

Scale Name	Odds of Satisfaction per Change in Scale Score* (per 10-Point Increase in Scale Score)	Change in Satisfaction per Change in Covariate				
		Age (per 10 yrs) [†]	Gender (M vs. F) [‡]	Lens Type (CL only vs. GL only) [§]	Lens Type (GL/CL vs. GL only) [§]	Spherical Equivalent (Worse Eye per Diopter)
Overall (S)	0.48 (0.40, 0.59) [¶]	0.66 (0.54, 0.82) [¶]	0.88 (0.59, 1.31)	1.51 (0.86, 2.66)	0.66 (0.42, 1.03) [¶]	1.09 (1.02, 1.16) [¶]
Concern	0.81 (0.73, 0.90) [¶]	0.68 (0.56, 0.83) [¶]	0.90 (0.62, 1.32)	1.60 (0.93, 2.74)	0.50 (0.32, 0.76) [¶]	1.10 (1.03, 1.17) [¶]
Expectations	0.95 (0.88, 1.03)	0.70 (0.58, 0.86) [¶]	0.90 (0.61, 1.31)	1.60 (0.94, 2.74)	0.51 (0.34, 0.78) [¶]	1.13 (1.06, 1.20) [¶]
Functioning	0.59 (0.51, 0.69) [¶]	0.68 (0.56, 0.84) [¶]	1.06 (0.71, 1.58)	1.29 (0.74, 2.26)	0.69 (0.44, 1.09)	1.09 (1.02, 1.16) [¶]
Driving	0.73 (0.66, 0.80) [¶]	0.68 (0.55, 0.84) [¶]	0.72 (0.48, 1.08)	1.38 (0.79, 2.42)	0.55 (0.36, 0.86) [¶]	1.08 (1.01, 1.15) [¶]
Symptoms	0.79 (0.70, 0.90) [¶]	0.68 (0.56, 0.83) [¶]	0.93 (0.63, 1.36)	2.14 (1.22, 3.76) [¶]	0.78 (0.48, 1.27)	1.13 (1.06, 1.20) [¶]
Optical problems	0.57 (0.49, 0.67) [¶]	0.72 (0.59, 0.89) [¶]	0.79 (0.53, 1.18)	1.44 (0.82, 2.53)	0.55 (0.35, 0.86) [¶]	1.09 (1.02, 1.16) [¶]
Glare	0.79 (0.71, 0.88) [¶]	0.70 (0.58, 0.86) [¶]	0.83 (0.56, 1.23)	1.65 (0.96, 2.83) [¶]	0.57 (0.37, 0.88) [¶]	1.11 (1.05, 1.18) [¶]
Problems with corrective lenses	0.89 (0.80, 1.00) [¶]	0.70 (0.58, 0.85) [¶]	0.96 (0.66, 1.41)	1.38 (0.79, 2.42)	0.46 (0.30, 0.71) [¶]	1.14 (1.07, 1.21) [¶]

CL = contact lenses; GL = glasses.

*An odds ratio less than 1.0 indicates that those who report more problems on the scale are less satisfied than those who report fewer problems. The odds ratio indicates the change in odds per 10-point increase in subscale score.

†An odds ratio less than 1.0 indicates that those who are older are less satisfied than those who are younger.

‡An odds ratio less than 1.0 indicates that males are less satisfied than females.

§An odds ratio greater than 1.0 indicates that those who wear only contact lenses are more satisfied than those who wear only glasses, or that those who wear glasses and contacts are more satisfied than those who wear only glasses (glasses only in the reference category).

||An odds ratio greater than 1.0 indicates that those who have worse refractive error are less satisfied than are those with less refractive error.

¶Statistically significant ($P < 0.05$).

¶Borderline statistically significant ($P < 0.07$).

Each row of the table represents a single logistic regression model with satisfaction with vision (satisfied or very satisfied) as the outcome, adjusting for the scale score in column 1 and the covariates in columns 3–7. Each table cell contains the estimated adjusted odds ratio and its 95% confidence interval.

evaluation of patients with glaucoma, cataract, age-related macular degeneration, cytomegalovirus retinitis, and diabetic retinopathy, conditions associated with either older age or a serious systemic disease. The types of impairment or concerns experienced by these individuals likely differ from those of persons who have refractive error and no other ocular condition. Another generic instrument that was specifically designed to be broadly applicable to many ocular conditions³⁰ also is, by design, likely to be insensitive to problems related to refractive error.

One instrument that was designed for use in persons with refractive error is targeted toward symptoms and satisfaction (the Prospective Evaluation of Radial Keratotomy [PERK] study,¹⁰ but includes only two items that assess physical functioning:⁹ whether the patient could read newspaper without corrective lenses and whether a patient could see a friend across the street without corrective lenses. The validation of the questions used in the PERK study has not been reported. In the PERK study, patient satisfaction 1 year after the procedure was assessed using a standardized Satisfaction Index.¹⁰ Patients who reported more trouble with fluctuation of vision and glare were significantly more likely

to be dissatisfied with the results of their refractive surgery than those who did not report such trouble. In a 6-year follow up to the PERK study,³¹ individuals who needed to use corrective lenses for reading or seeing a friend across the street were significantly more likely to be dissatisfied with the results of surgery. Another instrument used in persons with refractive error has had its validity reported³² and measures functioning, symptoms, and health perceptions, but consists of an impractically large number of items (more than 300) and was tested in a small group of patients (N = 45). We sought to develop an instrument brief enough to be used in clinical practice that would address the full range of problems related to refractive error and corrective lenses and that would measure the impacts of refractive surgery.

Other studies of patients undergoing refractive surgery have assessed patient-reported symptoms^{11,12,14–16,33–41} (typically glare, fluctuation of vision, halos, and ocular discomfort) and functioning,^{11,32,35,36} but did not use validated instruments to measure these HRQoL outcomes (except for one study³²). Presence and severity of glare and halo symptoms were found to be associated with less satis-

faction with vision in most of these studies as well as difficulty with night driving and continued dependence on corrective lenses. An instrument that seeks to measure the relevant aspects of HRQoL in persons with refractive error should address not only symptoms attributable to refractive surgery but also symptoms related to use of corrective lenses.

Because many individuals (nearly half in our study) used a combination of glasses and contact lenses and some functioned for at least part of the time without any corrective lenses, it is important to assess functioning, symptoms, and satisfaction separately for each type of corrective lens that could be used by a patient: glasses, contact lenses, both, or no lenses.

Instruments designed to assess HRQoL should address the most common areas of concern to patients. We attempted to do so by obtaining items for the RSVP from several sources, including eye care providers, individual patient interviews, and a focus group of patients with refractive error. We also searched preexisting reports of refractive surgery studies to identify additional items. Thus we believe that the items in the RSVP, which underwent a two-stage evaluation for their usefulness in distinguishing among clinically important subgroups, address most of the HRQoL-related problems that are likely to matter to individuals with refractive error.

The RSVP that we have developed is both valid and reliable. The RSVP *S* and RSVP subscale scores for *concern, functioning, driving, symptoms, optical problems*, and *glare* showed strong associations with satisfaction with vision. Of particular note is the fact that the RSVP subscales for *functioning, driving, symptoms, optical problems*, and *glare*, as well as the overall scale *S*, were more strongly correlated with satisfaction with vision and patients' overall ratings of vision than were VA or refractive error, even after adjusting for potential prognostic factors (refractive error, corrective lens usage, age, and gender). Thus the RSVP provides useful information regarding patient status that is not reflected in traditional clinical ophthalmic measures.

We examined the test-retest reproducibility of the RSVP in two groups of patients. In persons with refractive error who were not contemplating refractive surgery, the results of repeated administrations of the RSVP were highly reproducible, both for the overall RSVP and the subscale scores. Scores were less reproducible in the group of patients who were considering refractive surgery and who underwent an evaluation for refractive surgery between the first and second administrations of the RSVP. Rather than reflecting poor test-retest reproducibility, we believe these findings likely reflect patients' reactions to information they received during their office evaluation. This interpretation is supported by the finding that the subscale *expectations* had the lowest reproducibility in this group. We purposely included questions related to *expectations* because we thought that responses to these questions might help identify before surgery those patients who might be dissatisfied after surgery. It may be, however, that the domain *expectations* has

a limited role in direct comparisons of pre- and postrefractive surgery status. Nevertheless, these findings suggest that the timing of administration of the RSVP (i.e., before or after initial consultation with the refractive surgeon) may be important in establishing "baseline" functioning, symptoms, and perceptions for individuals considering refractive surgery. Data regarding changes in RSVP scores after refractive surgery are currently being analyzed. Preliminary findings (Vitale S, Schein OD, Steinberg EP. Invest Ophthalmol Vis Sci 1999; 40[Suppl]; S532) showed that the RSVP subscales are highly responsive to change, based on the standard error of measurement shown in Table 3. Future analyses on our pre- and postrefractive surgery data will allow a determination of which RSVP subscales are useful in identifying patients who experience a change in HRQoL after surgery as well as which are predictive of actual postoperative status. It is possible that subscales that are strongly associated with subgroups of interest in cross-sectional analysis will not be useful predictors of change in status²¹; conversely, subscales with limited usefulness in differentiating subgroups cross-sectionally may be responsive to clinically significant changes.²¹

As would be the case for any HRQoL instrument, our findings regarding the performance characteristics of the RSVP may reflect, in part, the population in whom the RSVP was studied. Our primary goal was to assess the properties of the RSVP in a population representative of those considering refractive surgery. A subgroup of persons not considering refractive surgery was also included to enhance the generalizability of conclusions to persons with refractive error who are not seeking surgery. Our study design called for the RSVP to be administered to consecutive eligible patients at each participating site. However, recruitment at some sites was lower than the stated patient volume because of coordinator absence, other demands on coordinators' time, patient refusal, and different patterns of scheduling surgery among practices. Our study design does not allow a rigorous assessment of representativeness. Nevertheless, subscale scores did not differ among the five refractive surgery sites (except for the *expectations* subscale, which was significantly lower for one site). Differences in practice patterns or surgical techniques may account for observed differences in spherical equivalent among refractive surgery sites. However, lens usage, rating of vision, and age did not differ in any substantial way among refractive surgery sites. This may indicate that variations in practice patterns and locales may not have a substantial effect on RSVP measurements; that is, that the RSVP will be useful for a broad spectrum of persons seeking treatment from a refractive surgery practice. Alternatively, it could be accounted for by homogeneity of patients at different refractive surgery sites.

In conclusion, the RSVP, in aggregate and in its subscales, has been demonstrated to be a valid questionnaire as measured by accepted standards for psychometric instruments. We believe the RSVP also is reliable and will be a helpful adjunct for use in studies to evaluate devices and procedures for correction of refractive error.

Appendix

Refractive Status and Vision Profile Study Clinical Sites and Investigators

Massachusetts Eye and Ear Infirmary, Boston, MA: Dimitri Azar, MD (CD); David Rees (SC).

Gimbel Eye Center and the Gimbel Foundation, Calgary, Alberta, Canada: Howard Gimbel, MD (CD); Maria Ferensowicz (SC).

Cornea & Laser Vision Institute, Teaneck, NJ: Peter Hersh, MD (CD); Bethann Hibbert (SC).

Washington Eye Physicians and Surgeons, Chevy Chase, MD: Roy Rubinfeld, MD (CD); Kate Kelly (SC).

Wilmer Eye Institute, Johns Hopkins Medical Institutions, Baltimore, MD: Terrence O'Brien, MD (CD); Nada Jabbur, MD (CI); Richard Schoen, OD (CI); Rebecca Scarborough (SC).

(Abbreviations: CD = clinic director; CI = co-investigator; SC = study coordinator.)

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Prevalence and Progression of Myopic Retinopathy in an Older Population

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Objective: To determine the prevalence and progression of myopic retinopathy in an older community-based population sample.

Design: Population-based epidemiologic study.

Participants: Eligible residents aged 49 years or older ($n = 3654$) who attended the Blue Mountains Eye Study, west of Sydney, Australia.

Methods: Participants had a detailed eye examination including measurement of logarithm of the minimum angle of resolution (logMAR) visual acuity, standardized refraction, and retinal stereophotography. All patients were invited to attend follow-up examinations after 5 years.

Main Outcome Measures: Myopic retinopathy was defined to include staphyloma, lacquer cracks, Fuchs' spot and myopic chorioretinal atrophy. β -peripapillary atrophy was assessed separately.

Results: Signs of myopic retinopathy were found in 67 eyes from 44 participants (1.2%), a prevalence of 1.4% in women and 1.0% in men; this increased from 1% in right eyes with myopia <3 diopters to over 50% in right eyes with myopia ≥ 9 diopters. There was a nonsignificant age-related trend in prevalence. The average spherical equivalent refraction was -6.1 diopters and the average visual acuity was 20/40 in eyes with myopic retinopathy. Visual impairment ($<20/40$) was present in 38.8% of affected eyes. Myopic retinopathy was bilateral in 52% of cases. Staphyloma was present in 26 participants (0.7%), bilateral in 35%, with a strong concordance of staphyloma location. Lacquer cracks were seen in 8 participants (0.2%), Fuchs' spot in 3 (0.1%), and chorioretinal atrophy in 7 (0.2%). Forty-six eyes (68.7%) with myopic retinopathy were reexamined after 5 years; 8.7% had new or increased numbers of lacquer cracks and 15.2% had new or expanded areas of chorioretinal atrophy. In those eyes developing lacquer cracks or chorioretinal atrophy, best-corrected visual acuity decreased by a mean of two LogMAR lines.

Conclusions: This study documented the age and sex-specific prevalence of myopic retinopathy and 5-year progression in an older white population. *Ophthalmology* 2002;109:704-711 © 2002 by the American Academy of Ophthalmology.

Myopic retinopathy refers to a cluster of signs that indicate degeneration of chorioretinal tissues associated with the excessive axial elongation of the myopic eye.^{1,2} Posterior pole changes consistent with myopic retinopathy include posterior staphyloma, lacquer cracks, Fuchs' spot, and chorioretinal atrophy. Peripheral retinal features of myopic retinopathy include lattice, paving stone, white-without-pressure, and pigmentary degenerations, as well as retinal tears.²⁻⁴ Cases with myopic retinopathy exhibited progressive elongation of the eye³ resulting in retinal complications³ and a poor visual prognosis.

Myopic retinopathy is an important cause of visual impairment.⁵ It is currently the leading cause of legal blindness in the 40-to-50 year age group in England^{6,7} and has been reported as the fourth to seventh most frequent cause of

blindness overall in different communities.^{6,8-10} The impact of myopic retinopathy on visual impairment is important because it is often bilateral^{11,12} and irreversible, and it frequently affects individuals during their productive years.^{13,14} It has been estimated that patients with myopic retinopathy are legally blind for an average of 17 years, a figure that nearly matches the mean duration of blindness from diabetes (5 years), age-related maculopathy (5 years), and glaucoma (10 years) combined.⁸ Myopic eyes also have a higher prevalence of cataract¹⁵ and glaucoma,¹⁶ as well as retinal detachment, which is strongly associated with myopia.¹⁷ These three diseases can all lead to visual impairment.

Despite the importance of degenerative myopia, the prevalence of myopic degeneration has not been documented in population-based studies.¹⁷ In an international survey of hospital clinics, Fuchs¹⁸ reported myopic retinopathy presentations in 0.3 to 9.6 of 100 patients per year. Tokoro¹⁹ reported a prevalence for myopic retinopathy of 2.2% in a Japanese hospital clinic sample and estimated the general population prevalence to be approximately 1.0%. Hu²⁰ screened a large Chinese population and reported a prevalence of 1.0%. To our knowledge, there have been no published population-based data on the prevalence of myopic retinopathy in older, largely white populations.

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There have been few reports on the progression rate of myopic degenerative changes. In Curtin's²¹ large series of 102 eyes with staphyloma, 35% progressed to a higher grade over 5 years. In a study of 66 eyes with lacquer cracks by Ohno-Matsui and Tokoro,²² 20% developed additional lacquer cracks and 38% developed choroidal neovascularization or atrophic changes during a 6-year mean follow-up. Avila et al²³ reported that 6.5% of 46 eyes with a staphyloma developed choroidal neovascularization over 2.5 years, whereas Fried et al¹² reported an increasing chorioretinal atrophy in 76% of 29 eyes with Fuchs' spot over 5 years.

The purpose of this report is to provide prevalent and progressive data for posterior pole myopic degenerative changes in a representative, older Australian population, including morphologic features, bilaterality, and relationship to refractive error.

Materials and Methods

The Blue Mountains Eye Study is a population-based survey of common eye diseases in an urban population aged 49 years or older, residing in two postcodes of the Blue Mountains region, west of Sydney, Australia. The survey methods and procedures have been described previously.²⁴ The study was approved by the Western Sydney Area Health Service Human Ethics Committee and written informed consent was obtained from all participants. A baseline eye examination study (BMES I) was performed from 1992 to 1994, with an overall participation rate of 82.4% (3654 participants). After excluding 543 participants (14.9%) who had died after the initial examination and before the 5-year follow-up examinations commenced, 2334 of the survivors (75.0%) participated in the follow-up study (BMES II) during 1997 to 1999. Of the remainder, 386 (12.4%) had moved from the area and 394 (12.6%) refused.

An interviewer administered detailed questionnaires to participants, which included past medical and eye histories, and performed comprehensive eye examinations. The retinal examination included dilated 30° stereoscopic photographs, taken with a Zeiss FF3 fundus camera (Carl Zeiss, Oberkochen, Germany), of the optic disc, macula, temporal retina, nonstereo photographs of the upper and lower temporal vascular arcades, and the nasal field.

Visual acuity was assessed using a logarithm of the minimum angle of resolution (logMAR) chart (Vectorvision CSV-1000, Vectorvision Inc, Dayton, OH) read at 8 feet. Participants who

could read ≥ 54 correct letters with each eye (Snellen equivalent, 20/20) were not refracted further, and their current spectacle correction, if worn, was recorded as their refractive error. If they were unable to correctly read 54 letters with each eye using current distant correction, then the autorefractor correction (Humphrey 530 automatic refractor, Humphrey Zeiss, San Leandro, CA) was placed in the trial lens frame, and a standardized subjective refraction was performed with both 0.5 diopter (D) and 0.25 D Jackson cross cylinders using the Beaver Dam Eye Study modification of the Early Treatment Diabetic Retinopathy Study protocol.²⁵ Cylindrical refractive errors were recorded in the negative form. The spherical equivalent refraction of each eye was calculated using the spherical diopters power plus half the cylindrical diopters power. Any visual impairment was defined as best-corrected visual acuity of 20/40 or worse, moderate impairment as 20/80 to 20/200, and severe impairment as worse than 20/200.

Retinal Photographs and Grading

The 350-mm retinal slides were mounted in clear plastic sleeves and examined using a Donaldson stereoviewer and a fluorescent viewing box, and then graded for signs of myopic retinopathy. The grader was masked to the participant's refractive error status to minimize bias, and signs were adjudicated by a retinal specialist (PM).

Myopic retinopathy was defined to include the following specific signs: staphyloma, lacquer cracks, Fuchs' spot and myopic chorioretinal thinning or atrophy. Staphyloma was diagnosed when the border of an ectasia was visualized. The staphyloma type was classified similar to the classification used by Curtin.¹⁴ Care was taken to distinguish staphyloma from coloboma; lacquer cracks from angioid streaks; Fuchs' spot from central pigmented lesions caused by age-related maculopathy or toxoplasmosis; myopic chorioretinal atrophy from the atrophic signs of age-related maculopathy, toxoplasmosis, or laser scars. Lacquer crack length was measured using a template of circles (Pickett small circles No.1203) overlaid on the fundus photograph.²⁶ The eye-camera magnification was corrected using the formula developed by Bengtsson and Krakau,²⁷ based on the spherical equivalent refraction, = $2.5/(1 - \{0.017 \times \text{spherical equivalent refraction}\})$.

Since β -peripapillary atrophy (β -PPA) has been described in association with myopia,^{1,2,4,28} its presence was also graded. Using Jonas et al's,²⁹ description of β -PPA, the width of its greatest involvement was measured in vertical disc diameters around the disc at 0°, 45°, 90°, 135°, 180°, 225°, 270°, and 315°.

The central retinal vessels were graded for presence of a T-sign (a distal bifurcation of the central retinal vessel at least 0.5 mm beyond the lamina cribosa).⁴ Cyclotorsion of the optic disc was

Table 1. Prevalence (%) of Myopia, Myopic Retinopathy and β -Peripapillary Atrophy in Right Eyes at Different Levels of Myopia

Spherical Equivalent Refraction (Diopters)	Myopia n (%)	Myopic Retinopathy n (%)	β -Peripapillary Atrophy* n (%)
> -1.00	3179	10 (0.3%)	420 (13.6%)
-1.00 to -2.99	295 (8.1%)	2 (0.7%)	85 (29.5%)
-3.00 to -4.99	101 (2.8%)	3 (3.0%)	46 (48.9%)
-5.00 to -6.99	44 (1.2%)	5 (11.4%)	16 (38.1%)
-7.00 to -8.99	14 (0.4%)	4 (28.6%)	11 (78.6%)
\leq -9.00	21 (0.6%)	11 (52.4%)	16 (76.1%)

*Excludes 99 right eyes with ungradable and unavailable photographs.

Table 2. Age- and Gender-specific Prevalence of Myopic Retinopathy

Age (Years)	Females (%)	Males (%)	Total (%)
49-59	6/569 (1.1)	3/438 (0.7)	9/1007 (0.9)
60-69	10/707 (1.4)	3/587 (0.5)	13/1294 (1.0)
70+	12/748 (1.6)	10/534 (1.9)	22/1282 (2.3)
All ages	28/2024 (1.4)	16/1559 (1.0)	44/3583 (1.2)
P for trend	0.40	0.06	0.07

assessed by determining the longest axis to the nearest 15°. Tilting of the disc around its horizontal or vertical axis was qualitatively noted.

At the 5-year follow-up examinations, similar interviews were conducted and the same retinal photographs taken of both eyes. Retinal photographs of eyes with myopic retinopathy were reexamined to assess new development or progression of lacquer cracks, new or enlarged areas of chorioretinal atrophy, as well as an increase in the area of involvement by β -PPA.

Statistical Analysis

Statistical Analysis System software V6.12 (SAS Institute, Cary, NC) was used for all statistical analyses. The *t* test was used to compare ages of subjects with and without myopic retinopathy. Mantel-Haenszel chi-square test statistics were used to assess trends. A generalized linear model was used to compare mean best-corrected visual acuity in the worse eye of persons with and without myopic retinopathy, adjusting for age. A generalized estimating equation model was used to examine associations between myopic retinopathy and other ocular diseases to take into account bilateral ocular involvement, age and gender. Odds ratios (OR) and 95% confidence intervals (CI) are presented. Data are presented both by subject and by right eye.

After 6 months, one author (JV) regraded a randomly selected, weighted sample of 20 eyes with myopic retinopathy and 40 eyes without myopic retinopathy. The following weighted kappa coefficients were found: 0.62 for staphyloma, 0.66 for lacquer cracks, 0.66 for Fuchs' spot, 1.0 for chorioretinal atrophy, 0.93 for an overall diagnosis of myopic retinopathy, 0.89 for tilted discs, and 0.70 for β -PPA.

Results

Of the 3654 participants, 71 (1.9%) were excluded because stereo photographs of both eyes were unavailable. The remaining 3583

participants comprised 2024 women (56.5%) and 1559 men (43.5%). Myopia (spherical equivalent refraction ≥ -1.0 D) was present in at least one eye of 603 participants (16.8%; 331 women and 272 men). High myopia (≥ -5.0 D) was present in at least one eye of 98 persons (2.7%; 60 women and 38 men). Table 1 shows the prevalence of myopia in right eyes by spherical equivalent refraction and indicates a diminishing proportion of cases with higher levels of myopia.

Myopic retinopathy was present in 67 eyes of 44 participants (1.2% of the population). Table 1 also shows myopic retinopathy prevalence in right eyes. The prevalence of myopic retinopathy increased with higher myopic spherical equivalent refraction, from 1.0% of right eyes with myopia < -3.0 D to 52.4% of right eyes with myopia of at least -9.0 D. Table 2 shows the age- and gender-specific prevalence of myopic retinopathy. An age-related trend was present, but this was not statistically significant, $P = 0.07$, and there was no gender difference ($P = 0.33$). The mean age of subjects with myopic retinopathy (67.7 years) and without myopic retinopathy (66.1 years) was similar ($P = 0.29$).

The mean spherical equivalent refraction of eyes with myopic retinopathy was -6.1 D; standard deviation (SD), 5.2; range, $+2.6$ D to -17.9 D. The mean cylindrical refraction was -1.5 D (SD, 1.5). Myopic retinopathy was graded as present in 16 eyes with no or minimal myopia (23.9% of all eyes with myopic retinopathy). In 10 eyes, a nonmyopic staphyloma was present, four eyes were pseudophakic and one eye had a -5.5 D cylindrical error with spherical equivalent refraction of -0.5 D. The remaining eye had a long axial length (29.3 mm), but its spherical equivalent refraction was $+1.1$ D.

After adjusting for age, the mean best-corrected visual acuity of the worse eye in participants with myopic retinopathy was 39 letters (Snellen equivalent, 20/40), which was significantly lower than the visual acuity in eyes without myopic retinopathy (49 letters; Snellen equivalent, 20/25; $P < 0.0001$). Mild, moderate, and severe visual impairment was present in 31.3%, 6.0%, and 1.5% of eyes with myopic retinopathy, respectively.

Table 3 shows the characteristics of eyes with the four posterior pole signs used to diagnose myopic retinopathy. Examples of the posterior pole signs are shown in Figures 1-5. Bilateral defects were infrequent for Fuch's spot and lacquer cracks, moderate for staphyloma and frequent for chorioretinal atrophy. Overall, bilateral involvement was present in 52.3% of participants.

Staphyloma (a type of scleral ectasia) was the most common myopic retinopathy sign graded, present in 35 eyes (52.2%). The distribution of staphyloma site and associated myopic retinopathy is shown in Table 4. The most frequent staphyloma site was

Table 3. Characteristics of Eyes (%) with Myopic Retinopathy and the Associated Changes

	Staphyloma (n = 35)	Lacquer Cracks (n = 9)	Fuchs' Spot (n = 3)	Chorioretinal Atrophy (n = 11)
<i>Characteristics</i>				
Participants: n (%)	26 (0.7)	8 (0.2)	3 (0.1)	7 (0.2)
Bilateral involvement n (%)	9 (34.6)	1 (12.5)	0 (0)	4 (57.1)
Women:Men	17:9	7:1	2:1	4:3
Mean corrected visual acuity (Snellen equivalent)	20/30	20/40	20/60	20/40
Mean spherical equivalent refraction (diopters) \pm SD	-4.3 ± 5.1	-7.2 ± 5.8	-11.7 ± 3.8	-7.5 ± 5.1
<i>Associated changes</i>				
Tilted disc (%)	20 (57)	4 (44)	1 (33)	5 (45)
β -Peripapillary atrophy	33 (94)	9 (100)	3 (100)	11 (100)

SD = standard deviation.

peripapillary, followed by posterior pole and macular sites. Inferior (4), nasal (2), inferonasal (2), and superonasal (1) staphylomas (grouped as other) were more often found in nonmyopic eyes. Their inclusion decreased the mean spherical equivalent refraction of all eyes with staphyloma. When present bilaterally, staphyloma location was highly symmetrical (78%).

Lacquer cracks were seen as pale thin lines with well-defined (sometimes pigmented) borders in the posterior pole of the fundus, as shown in Figures 1 and 2. Choroidal vessels within the pigmented choroid were visible through the defect. In eyes with lacquer cracks, the average number of cracks was 2.5 (SD, 0.7). Branching lacquer cracks (67%) were orientated horizontally and/or obliquely across the posterior pole. After correction for ocular magnification, the average length of lacquer cracks was 3.0 mm (SD, 1.3).

Fuchs' spot was seen in three eyes, with an example shown in Figure 3; they were gray (67%) or black (33%), irregular in shape (67%) and flat (100%), and surrounded by atrophic chorioretinal tissues (67%). Choroidal neovascularization was present in one case. Compared with other myopic retinopathy signs, eyes with Fuchs' spot had the poorest visual acuity and the highest myopic error (Table 3).

Chorioretinal atrophy was seen as a scallop shaped pale area with well-defined hyperpigmented borders, as shown in Figure 4. Large choroidal vessels overlaid the exposed sclera. This sign was most common in the nasal retina (8 of 11) but involved the macula in one eye. Chorioretinal atrophy was very commonly bilateral.

The prevalence of β -PPA increased with higher levels of myopia (Table 1) and was present in 13.6% of nonmyopic eyes, in 37.9% of myopic eyes and in 88.6% of eyes with myopic retinopathy. β -PPA was most common concentrically around the disc, then temporally and inferonasally in eyes with myopic retinopathy (Table 5). It was widest temporally and inferiorly at 0.4 vertical disc diameters, and was narrowest superiorly at 0.2 vertical disc diameters.

After adjusting for gender, age, and bilateral involvement of lesions in a generalized estimating equation model, no significant associations were found between myopic retinopathy and early age-related maculopathy (OR, 2.1; 95% CI, 0.2–2.1), glaucoma (OR, 1.1; 95% CI, 0.5–2.3) or posterior subcapsular (OR, 1.9; 95% CI, 0.6–6.2), nuclear (OR, 0.9; 95% CI, 0.6–1.4), or cortical cataract (OR, 1.2; 95% CI, 0.6–2.3).

In 48.6% of right eyes with myopic retinopathy and 79.8% of right eyes without myopic retinopathy, the long axis of the optic disc lay within 15° of the vertical meridian. A T-sign was observed

in 25.7% of right eyes with myopic retinopathy compared with 7.2% of right eyes without myopic retinopathy. The disc was tilted in 60% of right eyes with myopic retinopathy compared with 3% of right eyes without myopic retinopathy.

5-Year Progression in Eyes with Myopic Retinopathy

After a mean period of 61 months, 46 eyes (68.7%) with myopic retinopathy were reexamined. The mean spherical equivalent refraction improved by 1.0 D, but the best-corrected visual acuity deteriorated by 3 letters (half a logMAR line). Table 6 summarizes changes observed after 5 years. Significant progression of myopic retinopathy was observed in 8 eyes (17.4%) with an average reduced best-corrected visual acuity of 9 letters (nearly two logMAR lines). All 8 eyes showed β -PPA enlargement. New chorioretinal atrophy was observed in the perifoveal region in 4 eyes, and inferonasally in another eye. Chorioretinal atrophy developed in one eye with a Fuchs' spot (Fig 3) and in two eyes with lacquer cracks (Fig 2). No new Fuchs' spots were observed.

Discussion

In this study population, myopic retinopathy prevalence was 1.2%, a figure comparable with other reports: Hu²⁰ (0.95%), Fuchs¹⁸ (0.3–9.6%), and Tokoro¹⁹ (2.16%). Its prevalence increased markedly with higher levels of myopia, consistent with studies showing a higher prevalence of pathologic signs at greater axial lengths.^{2,28} Our finding of an age-related trend in myopic retinopathy is consistent with data from Curtin.⁴ Women had a nonsignificant higher prevalence of both high myopia (≥ -5 D) and myopic retinopathy than men, a gender difference found for all myopic retinopathy signs and also for bilateral involvement. Higher prevalence in women has been reported by some,^{2,5,7,21,30} but not all,⁴ past studies.

Our reported staphyloma prevalence is lower than in previous reports.^{1,2,28,31} However, it is possible that in our study, some staphylomas may have been overlooked if the 70° photographic field of the posterior pole was insufficiently wide enough to incorporate the ectatic wall or when

Table 4. Characteristics and Other Myopic Retinopathy Signs in Eyes (%) with Staphyloma

Staphyloma Site	Posterior Pole n = 6 (17.1)	Macular n = 4 (11.4)	Peripapillary n = 16 (45.7)	Other n = 9 (25.7)
Mean age (years)	67.6	63.8	72.5	67.0
Women:men	5:0	3:1	6:4	6:3
Mean corrected visual acuity (Snellen equivalent)	20/40	20/30	20/30	20/30
Spherical equivalent refraction (diopters \pm SD)	-7.5 \pm 6.5	-5.4 \pm 6.7	-4.8 \pm 4.5	-0.8 \pm 2.2
T-sign	3 (50)	0 (0)	4 (25)	8 (89)
Tilted disc	5 (83)	2 (50)	5 (31)	4 (44)
β -Peripapillary atrophy	5 (83)	4 (100)	15 (94)	9 (100)
Lacquer cracks	1 (17)	1 (25)	1 (6)	0
Fuchs' spot	1 (17)	0 (0)	0 (0)	0
Chorioretinal atrophy	1 (17)	0 (0)	1 (6)	1 (9)

SD = standard deviation.

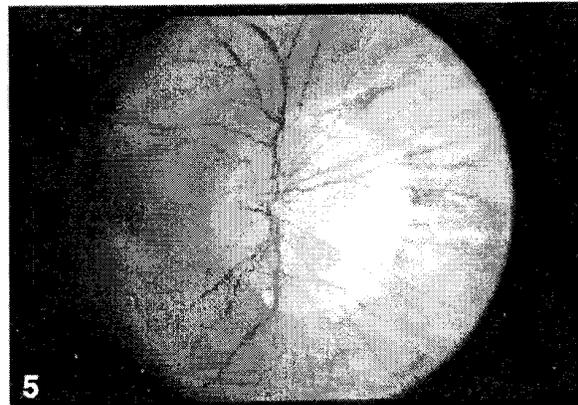
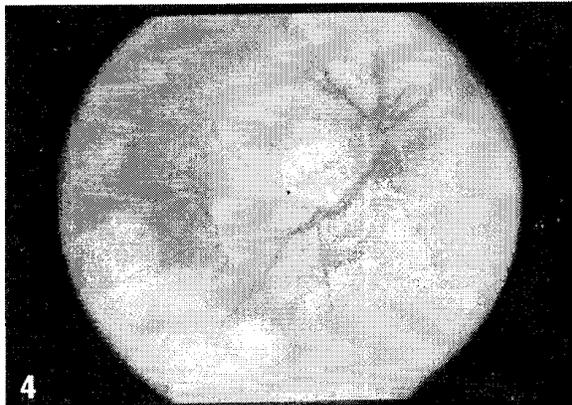
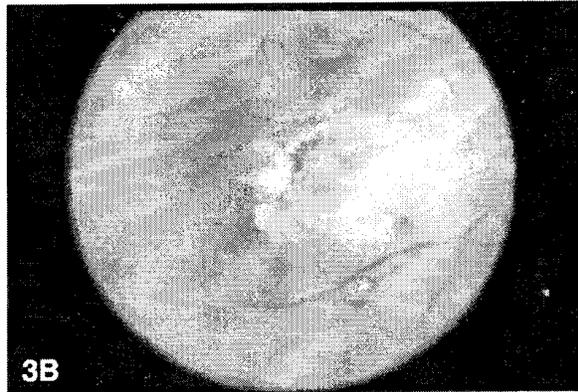
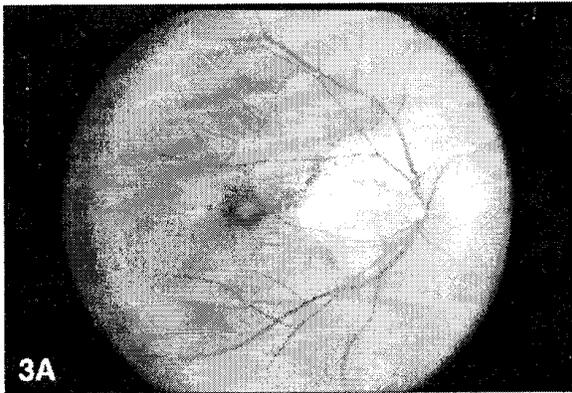
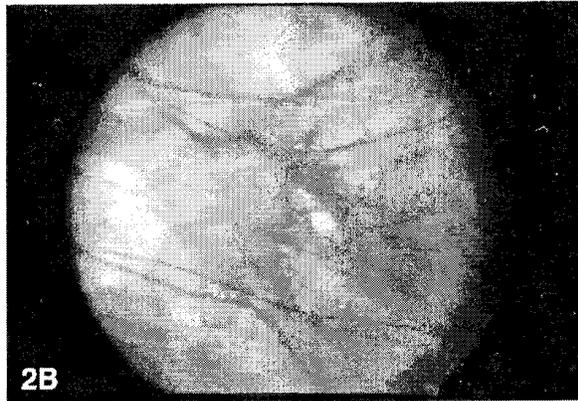
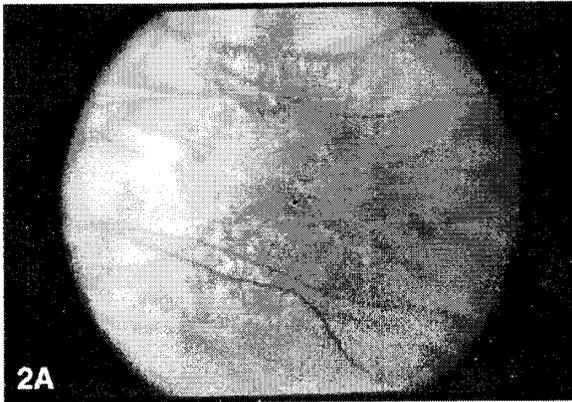
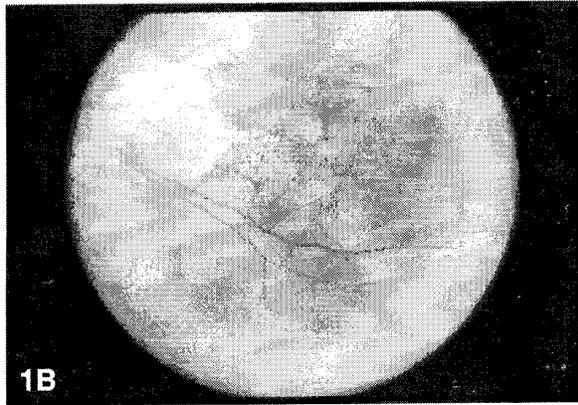
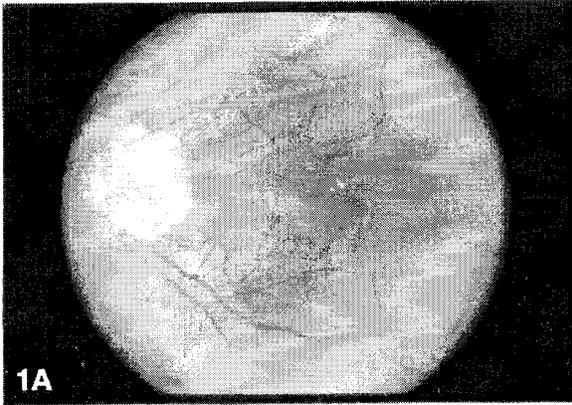


Figure 1. A, Branched lacquer cracks in the left eye of a 57-year-old woman with a spherical equivalent refraction of -10.75 diopters. B, Extension and development of lacquer crack in the eye after 5 years.

Figure 2. A, Branched lacquer cracks in the left eye of a 63-year-old woman with a spherical equivalent refraction of -18.0 diopters. B, Development of central chorioretinal atrophy in the eye after 5 years.

Figure 3. A, Fuchs' spot in the right eye of the same woman shown in Figure 1. The spherical equivalent refraction of this eye was -9.0 diopters. B, Development of central chorioretinal atrophy in this eye after 5 years.

Figure 4. Typical appearance of chorioretinal atrophy in advanced myopic retinopathy in the right eye of a 73-year-old woman with a spherical equivalent refraction of -16.0 diopters. Associated signs include retinal vessel straightening and annular β -peripapillary atrophy.

Figure 5. Nasal staphyloma in the right eye of a 52-year-old man with a spherical equivalent refraction of -0.25 diopters. The optic disc was tilted nasally and surrounded nasally by β -peripapillary atrophy. Tessellation and pallor of the nasal retina was present along with the T-sign. Pigmentary clumping was present inferonasal to the macula.

stereopsis from the stereophotographs was inadequate. Since the nasal retina is initially ectatic in early posterior pole staphylomas,²¹ detection of a low grade staphyloma was difficult if the stereoscopic nasal field was unavailable.

Posterior pole staphylomas have been reported to be the most common type of staphyloma.^{5,14} Peripapillary staphylomas have been considered relatively uncommon,^{4,14,32-34} despite numerous case reports.³²⁻³⁸ Some studies^{5,38} have reported a higher prevalence of peripapillary staphyloma than reported in Curtin's¹⁴ large series. Our findings suggest that peripapillary staphyloma may be more common than other types of staphyloma.

Eyes with peripapillary staphylomas have been noted to have poor visual function,^{32,33,37} with few published cases having normal vision.³⁴⁻³⁶ In our study, the mean corrected visual acuity in eyes with peripapillary staphyloma was 20/30, and only 3 eyes had a visual acuity $<20/40$ caused by macular hole, amblyopia and chorioretinal degeneration, nystagmus, and corneal scarring. This finding of near normal visual function suggests that people with peripapillary staphyloma may be less likely to visit an eye care practitioner and therefore, less likely to have this sign detected.

First described by Salzmann³⁹ in 1902, lacquer cracks are ruptures in the retinal pigment epithelium-Bruch's membrane-choriocapillaris complex.^{1,4,40} They have been observed to occur after subretinal hemorrhage.^{40,41} Lacquer cracks are potentially sight threatening^{11,22,41} as they precede development of Fuchs' spot, choroidal neovascularization, and chorioretinal atrophy.^{22,28} Previous reported prevalence of lacquer cracks has ranged from 0.6%¹ to 9.2%³¹ of highly myopic populations. In our study, this sign was relatively infrequent, found in only 8 participants (0.2%), including one bilateral case. The higher prevalence in women is consistent with previous studies.^{11,22,41} Fluores-

cein or indocyanine green angiography, not performed in our study, may have higher sensitivity in detecting lacquer cracks, particularly in cases with associated retinal hemorrhage.^{23,30,41}

Fuchs' spot was the least frequent myopic retinopathy sign observed in our study. Its reported prevalence ranged from 3.2%¹ to 20%³¹ of highly myopic populations and has most frequently been observed in middle age.^{4,6} The appearance of Fuchs' spot changes over time^{13,28} and may be obscured by the development of chorioretinal atrophy.⁴ The older age of our study population could partly explain the low prevalence observed. The female predilection, however, is consistent with previous reports.^{2,28,42} Eyes with Fuchs' spot had poor visual function with a mean visual acuity of 20/60, consistent with the guarded prognosis reported for this lesion.^{3,42}

Chorioretinal atrophy is the late stage of the myopic degenerative process. Visual function declines when it involves the macula. Chorioretinal atrophy has been observed to expand with time in degenerative myopia,⁴ as the atrophic area becomes confluent, leaving islands of viable retina in a sea of atrophy. In our study, chorioretinal atrophy was often bilateral and was always associated with β -PPA. Fuchs' spot and lacquers cracks may precede its development, but may also be seen in isolation at the border of a staphyloma.⁴

The β -PPA was more frequent with increasing levels of myopia^{2,28} and was nearly always present in eyes with myopic retinopathy. The distribution of β -PPA in eyes without myopic retinopathy resembles that reported by Curtin and Karlin,²⁸ predominantly temporal and inferotemporal. However, in eyes with myopic retinopathy, an annular distribution of β -PPA was most frequent, followed by a temporal location. Expansion of β -PPA was frequently seen in eyes with myopic retinopathy after 5 years (69.6%).

Table 5. Distribution of β -Peripapillary Atrophy in Right Eyes (%) of Participants with and without Myopic Retinopathy

	Eyes without Myopic Retinopathy (%)	Eyes with Myopic Retinopathy (%)
β -Peripapillary atrophy location ²⁸		
Temporal	319 (53.7)	8 (25.8)
Inferotemporal	73 (12.3)	2 (6.5)
Annular	66 (11.1)	9 (29.0)
Inferior	33 (5.6)	2 (6.5)
Nasal-inferior	23 (3.9)	4 (12.9)
Other	80 (13.4)	6 (19.4)

Table 6. Summary of Changes Observed after 5 Years in Eyes with Myopic Retinopathy

	Number of eyes (%)
Eyes reexamined	46 (68.7)
Expansion of β -peripapillary atrophy	32 (69.6)
New chorioretinal atrophy	5 (10.8)
Expansion of previous chorioretinal atrophy	4 (8.7)
New lacquer cracks	2 (4.3)
Increased numbers of lacquer cracks	2 (4.3)

Temporal tilting of the optic disc has been frequently described in association with asymmetrical temporal expansion of the myopic eye. In our study, eyes with myopic retinopathy frequently had a tilted and cyclotorted optic disc appearance compared with eyes without myopic retinopathy. Curtin⁴ described the T-sign of the central retinal vessel bifurcation, in association with eversion of the optic disc in myopic retinopathy. Although infrequent, this sign was more frequent in eyes with myopic retinopathy than in eyes without myopic retinopathy.

Progression of myopic retinopathy was observed in 17.4% of eyes after 5 years. Best-corrected visual acuity decreased by two lines to 20/60, confirming a poor visual prognosis. The level of myopia (using the spherical equivalent refraction) decreased as a result of cataract surgery in some and a hyperopic shift in other participants.⁴³ New lacquer cracks developed in 22% of participants with existing cracks, similar to the incidence reported by Ohno-Matsui and Tokoro²² (21% over 5 years). Development of focal chorioretinal atrophy from lacquer cracks was seen in two eyes (28.6%), also similar to the rate reported by Ohno-Matsui and Tokoro²² (22.7% over 5 years). New chorioretinal atrophy was also observed after resolution of a Fuchs' spot. Chorioretinal atrophy typically developed in the perifovea, with one case involving the macular center.

History of retinal detachment was twice as likely in persons with myopia (9 persons; 1.5%) than among those without myopia (23 persons, 0.8%).

In summary, this study has documented the age- and gender-specific prevalence of myopic retinopathy in an older Australian population. The prevalence and progression rates for myopic retinopathy in this community may provide useful baseline information for future intervention studies and in planning eye care and rehabilitation services.

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Refractive Status in the Beaver Dam Eye Study

Qin Wang, Barbara E. K. Klein, Ronald Klein, and Scot E. Moss

Purpose. To describe the prevalence of refractive errors in a population of adult Americans.

Methods. From 1988 to 1990, 4926 adults who were 43 to 84 years of age and living in Beaver Dam, Wisconsin at the time of the 1987-1988 census were examined. Refractions were performed according to a modification of the Early Treatment Diabetic Retinopathy Study protocol. Included in this study were 4533 people who had not undergone cataract surgery and who had a best corrected visual acuity better than 20/40 in at least one eye. Myopia was defined as a refractive error less than -0.50 diopters; hyperopia was defined as a refractive error greater than $+0.50$ diopters.

Results. Hyperopia was more frequent than myopia in the study group (age-adjusted rates of 49.0% and 26.2% in right eyes, respectively, $P = 0.0001$). The prevalence of hyperopia in the right eye increased with increasing age from 22.1% in those 43 to 54 years of age to 68.5% in those 75 years of age or older. The prevalence of myopia in the right eye decreased from 43.0% in those 43 to 54 years of age to 14.4% in those 75 years of age or older. There was a significant relationship between education level and refractive error (age adjusted $r = -0.32$, $P = 0.0001$). Neither household income nor occupation was associated with refractive error in our data.

Conclusion. These cross-sectional data indicate age-related differences in refractive status in an adult population and suggest that education is associated with myopia independent of age. Invest Ophthalmol Vis Sci. 1994;35:4344-4347.

Refractive error is a common condition necessitating the use of optical devices, usually spectacles, for optimum vision. The relationships of refractive errors to demographic and personal characteristics, such as age and education, have been evaluated in some clinical

and epidemiologic studies.¹⁻³ However, few studies have been performed of adult populations. The purposes of this report are to describe the distribution of refractive errors and to evaluate its associations with personal and demographic factors in data from an adult population in a typical midwest community.

MATERIALS AND METHODS. A private census of Beaver Dam, Wisconsin was performed from 1987 to 1988. Details of this census have appeared in a previous report.⁴ There were 5924 eligible people 43 to 84 years of age who were identified at the time of the census. Of these, 83.2% ($n = 4926$) participated in the examination, 4.7% ($n = 277$) permitted an interview only, 3.8% ($n = 226$) died before examination, 1.6% ($n = 92$) moved, 0.4% ($n = 23$) could not be located, and 6.4% ($n = 381$) refused to participate. Nonparticipants were more likely to be older women. The population was 99% white.

The institutional review board approved the protocol, which conformed to the tenets of the Declaration of Helsinki. Informed consent was obtained from each subject. A standardized evaluation of refraction was performed using the Humphrey 530 refractor.⁵ The correction was placed in a trial lens frame, and the best corrected visual acuity was remeasured using the Early Treatment Diabetic Retinopathy Study (ETDRS) protocol using Chart R and modified for a 2-m distance.⁶ If the best corrected visual acuity was 20/40 or worse, an ETDRS refraction was performed and the visual acuity was measured.⁶ For each eye, the visual acuity was recorded as the number of letters identified correctly (range, 0 [$<20/200$] to 70 [$20/10$]). Only persons whose visual acuity by either method was better than 20/40 (41 letters) in at least one eye are included in the following analyses.

For this report, myopia is defined as a refractive error less than -0.50 D. Hyperopia is defined as a refractive error greater than $+0.50$ D.

A standardized medical history was obtained at the study evaluation. Serum glucose and glycosylated hemoglobin from a casual specimen were measured for each subject. Diabetes was confirmed if the subject had a history of diabetes treated with either insulin, oral hypoglycemic agents, and/or diet ($n = 395$) or if the subject had a glycosylated hemoglobin level > 2 SD above the mean for the relevant age-sex group and a casual blood sugar > 11.1 mmol/l ($n = 50$).

An interview was conducted for each participant. Pertinent parts of the questionnaire included questions regarding education

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What was the highest year of school or college you completed?

household income

Which of these income groups: <\$1,000, \$1,000–4,000, \$5,000–9,000, \$10,000–19,000, \$20,000–29,000, \$30,000–44,000, \$45,000–59,000, and >\$60,000 best represents your own/your and your spouse's total household personal income for the past year? Please include all income, such as employment, rent, social security, disability, or retirement that you may be receiving?

and lifetime occupation

What kind of work have you done most of your adult life?

The subject's current age was defined as the age at the time of examination.

Of the 4926 persons completing the examination, 4767 were phakic in at least one eye. Of these 4767, 4533 were phakic and had best corrected visual acuity better than 20/40 in at least one eye and form the basis for those included in the data analyses. There were 4067 people with phakic best corrected visual acuity better than 20/40 in both eyes, 209 people with that best corrected visual acuity in the right eye only, and 257 people with it in left eye only. Therefore, analyses referring to the right eye are based on a total of 4275 people (4067 plus 209, minus 1 person whose refractor was missing).

The Statistical Analysis System was used for calculating the chi-square statistic and Student's *t*-test and nonparametric Wilcoxon test results. Tests for trends in proportions were performed with the Mantel-Haenszel procedure.

RESULTS. Table 1 shows the comparison of people who were included ($n = 4533$) and excluded ($n = 393$) from these analyses because of missing data, aphakia, or visual impairment. Those excluded were older, had lower body mass index, higher systolic blood pressure, lower diastolic blood pressure, higher glucose and glycosylated hemoglobin, were more likely to have diabetes, and were more likely to be women than those included ($n = 4,533$).

Increasing age is associated with decreasing frequency of myopia (or increasing frequency of hyperopia) in both men and women (Table 2, $P < 0.001$). Myopia is more prevalent in women than in men ($P < 0.001$). Because there are no differences in these trends or other relationships between right and left eyes, data are presented for right eyes only.

Table 3 describes the distribution of years of school completed by women and men. There was a greater proportion of women who finished high school or had a college education than men in those younger than 75 years of age. Men were more likely to have had either fewer than 12 years of school or to have received advanced degrees (16 to 26 school years). A greater proportion of younger people had completed more than 12 years of school than older people.

The number of years of school completed is associated with a higher frequency of myopia and a lower frequency of hyperopia (Table 4). The relationship is significant in most age and gender groups. There are no associations of household income or occupation (white collar, blue collar, farm) with refractive error (data not shown).

The mean refractive error for those with diabetes is not significantly different from those without diabetes at each age (data not shown). Among those with

TABLE 1. Comparison of People Included and Excluded in Refraction in the Beaver Dam Eye Study (1988–1990)

	Included (n = 4533)			Excluded* (n = 393)			P
	n	Mean	(SD)	n	Mean	(SD)	
Age	4533	61.0	(10.7)	393	74.2	(9.3)	0.0001
Body mass index (kg/m ²)	4511	28.2	(5.3)	367	27.3	(5.6)	0.003
Systolic blood pressure (mm Hg)	4532	131.8	(20.3)	391	136.3	(21.7)	0.0001
Diastolic blood pressure (mm Hg)	4532	77.8	(10.8)	391	72.1	(11.7)	0.0001
Glucose (mg/dl)	4519	105.6	(37.6)	389	119.4	(54.6)	0.0001
Glycosylated hemoglobin (%)	4516	6.1	(1.6)	387	6.6	(2.1)	0.0001
	n	%		n	%		
Diabetes (%)	4533	8.3		393	18.1		<0.0001
Sex: Female (%)	4533	55.3		393	65.1		<0.0001

* Because of incomplete or invalid data.

TABLE 2. Frequencies of Myopia and Hyperopia in Right Eye by Age and Sex in the Beaver Dam Eye Study (1988–1990)

Refractive Status	Frequency (%)				Age-Adjusted Frequency	P Value of Trend
	43–54 Years of Age	55–64 Years of Age	65–74 Years of Age	75+ Years of Age		
Female	n = 770	n = 660	n = 629	n = 295	n = 2354	
Myopia	47.5	26.5	15.9	13.6	28.1*	<0.001
Hyperopia	20.1	51.2	67.7	67.5	48.6	<0.001
Male	n = 698	n = 572	n = 460	n = 191	n = 1921	
Myopia	37.8	23.4	13.3	15.7	24.0*	<0.001
Hyperopia	24.4	49.0	66.5	70.2	49.4	<0.001
Total	n = 1468	n = 1232	n = 1089	n = 486	n = 4275	
Myopia	42.9	25.1	14.8	14.4	26.2	<0.001
Hyperopia	22.1	50.2	67.2	68.5	49.0	<0.001

* Difference of myopia in males and females was significant; $P < 0.001$.

diabetes, neither glycosylated hemoglobin (age-adjusted, $r = -0.05$, $P = 0.21$) nor duration of diabetes (age-adjusted, $r = 0.01$, $P = 0.55$) is associated with refractive error.

DISCUSSION. The finding of increasing frequency of hyperopia and decreasing frequency of myopia with increasing age has not been reported in any other population-based data. It has been postulated that relative changes in density of the cortex and nucleus occur during aging.⁷ This could lead to a hyperopic shift.⁷ Alterations in the tonic influences of the ciliary muscle and/or zonular fibers with increasing age could alter the position and curvature of the lens, although data from animal models suggest that this might lead to a myopic shift or no change in refraction in the nonaccommodated eye.⁸ Age-related increasing hyperopia is unlikely to be explained by residual accommodation because the youngest participant was 43 years of age. Another possible explanation is that the age relationship reflects a cohort phenomenon.

The finding that more education is associated with increased myopia has been reported in some other studies.^{2,3} We cannot determine whether there is a causal relationship between near vision tasks (for example, reading) and myopia or whether myopia is more common in those who pursue more education.

Refractive error, especially myopia, is postulated to be both genetically and environmentally related.^{2–3,9} A population-based Finnish Twin Cohort study⁹ showed that heritability for refractive errors, especially for myopia, was high. On the other hand, a study from National Health and Nutritional Examination Survey indicated that myopia prevalence rose with family income and education level.¹⁰ Although the relationship with income and education may result from their association with near work, a factor that has been implicated in the pathogenesis of myopia, they can both be related to other environmental and/or genetic factors. In our data, there was no significant difference in refractive error between people with or without diabetes. This finding is consistent with a study performed by Riordan et al.¹ In addition, in those with diabetes, duration was not associated with refractive error.

Radial keratotomy is a new procedure for the correction of myopia and is usually performed in younger people. If increasing hyperopia is a concomitant of aging, then more severe hyperopia may be an unexpected and unwanted outcome of this procedure.

In summary, refractive error, or deviation from emmetropia, is a common finding in the Beaver Dam Eye Study; only 11.5% of people are emmetropic. Refractive error is age related in these data. Education is associated with a higher frequency of myopia.

TABLE 3. Education* by Sex and Age Group in the Beaver Dam Eye Study (1988–1990)

Education	Frequency (%) Female				Age-Adjusted Rate	Frequency (%) Male				Age-Adjusted Rate
	43–54 (n = 785)	55–64 (n = 685)	65–74 (n = 682)	75+ (n = 352)		43–54 (n = 712)	55–64 (n = 593)	65–74 (n = 498)	75+ (n = 222)	
0–11 years	9.2	18.5	38.7	55.4	26.9	12.8	27.2	41.4	55.0	31.0
12 years	52.9	54.0	45.0	25.3	46.6	47.9	42.7	37.8	25.7	40.2
13–15 years	21.5	15.3	11.1	11.7	15.5	14.9	12.7	10.6	11.3	12.6
16–26 years	16.4	12.1	5.1	7.8	10.9	24.4	17.5	10.2	8.1	16.2

* Education status was missing in four people.

TABLE 4. Relationship of Education and Refractive Error in the Right Eye in the Beaver Dam Eye Study (1988 to 1990)

	Female			Male			Total		
	n	Refractive Error Mean (SD)	P*	n	Refractive Error Mean (SD)	P*	n	Refractive Error Mean (SD)	P*
Age 43-54									
Education									
0-11 (years)	71	-0.15 (1.87)	0.0001	87	0.13 (1.18)	0.0001	158	0.004 (1.53)	0.0001
12 (years)	404	-0.73 (2.21)		334	-0.37 (2.03)		738	-0.56 (2.14)	
13-15 (years)	167	-1.17 (2.32)		105	-0.81 (1.96)		272	-1.03 (2.19)	
16-26 (years)	126	-1.36 (2.22)		171	-1.55 (2.39)		297	-1.47 (2.32)	
Age 55-64									
Education									
0-11 (years)	120	0.91 (1.95)	0.02	154	0.66 (1.48)	0.001	274	0.77 (1.70)	0.0001
12 (years)	356	0.26 (2.24)		243	0.28 (1.89)		599	0.27 (2.10)	
13-15 (years)	104	0.14 (2.45)		74	0.13 (2.05)		178	0.14 (2.29)	
16-26 (years)	80	0.10 (1.92)		101	-0.35 (2.08)		181	-0.15 (2.02)	
Age 65-74									
Education									
0-11 (years)	247	1.40 (1.93)	0.002	184	1.19 (1.37)	0.01	431	1.31 (1.72)	0.0001
12 (years)	280	0.75 (2.13)		178	1.00 (1.58)		458	0.85 (1.94)	
13-15 (years)	69	0.93 (1.84)		50	0.40 (2.32)		119	0.71 (2.06)	
16-26 (years)	33	1.26 (1.86)		48	0.27 (1.86)		81	0.67 (1.91)	
Age 75+									
Education									
0-11 (years)	164	1.60 (1.98)	0.05	103	1.29 (1.57)	0.72	267	1.48 (1.84)	0.07
12 (years)	75	0.94 (2.25)		50	1.00 (1.79)		125	0.97 (2.07)	
13-15 (years)	32	0.95 (1.84)		23	0.92 (2.21)		55	0.94 (1.98)	
16-26 (years)	24	1.06 (1.66)		15	1.52 (1.64)		39	1.24 (1.64)	

* Kruskal-Wallis test (chi-square approximation).

† Education status was missing in three people (right eyes).

Key Words

refractive status, education, diabetes, cataract, population-based study

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A REVIEW OF THE PREVALENCE AND CAUSES OF MYOPIA

A Wilson, G Woo

ABSTRACT

In this study, we reviewed the prevalence of myopia by country. Different types of myopia are elaborated and the causes of myopia are presented. It appears that the origin of myopia is due to both environmental and genetic factors.

Keywords: Prevalence, nature and causes of myopia.

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PREVALENCE

For over a century, many studies of the prevalence of myopia have dealt with select populations making comparisons and generalizations difficult (1,2). Surveys of refractive error have been performed on students, army recruits, eye clinic patients, different age groups, and races. Such data are difficult to analyze due to different methods of refraction, methods of analysis, and definitions of myopia (3).

On the other hand, prevalence data can be useful in searching for etiologic mechanisms especially if the sample characteristics and sample size information are known. Changes with age and variations with race are especially important in this regard, as well as information as to general distribution.

Practitioners are not necessarily enlightened by lengthy lists of studies and statistics such as those provided in standard texts (4-6). The purpose of this review is therefore to present some of the most recent information on this subject and landmark studies rather than to be exhaustive.

Also, there is a general lack of agreement that myopia is a significant abnormality of health even though it was estimated that its annual cost in the mid-1980's in the U.S. was over \$4 billion (4).

In one of the largest early studies, Sheerer and Betsch published data from more than 12,000 clinical patients in 1928 and 1929 in Germany. The patients were over 25 and refractions were performed without cycloplegia (1,4-6). 13% were found to be myopic (4). The distribution curve was published by Duke-Elder and was subsequently analyzed by Stenstrom, who concluded that not only is it more leptokurtic than a

normal distribution but it is also skewed towards myopia. That is, there is a greater incidence of myopia than would be presented if refractive errors were normally distributed (1). Although the Sheerer and Betsch study only included a clinical sample, and we know those with refractive errors (especially myopia) are more likely to present themselves for vision care (3), it is often quoted in the literature as representing general populations.

Emmetropization is the term often employed to explain the finding that the frequency distribution of each of the dioptric components of the eye is substantially normal (6). The refractive curve of infants is almost normal (7) and yet the distribution of refractive powers of adult eyes is sharply peaked at or near emmetropia (8). However, the leptokurtic nature with a peak at emmetropia can be expected even on the basis of chance association (8,9). Some studies seem to indicate that the frequency distribution of human eyes peaks more nearly at about a diopter of hyperopia and that there is a slight favour toward a hyperopic design for the human eye (1,8,10).

Several recent studies of myopia in the U.S. are of interest. Leibowitz and associates found myopia to be present in 17.7% of eyes in the Framingham Eye Study population (11). The Framingham Eye Study of 1973-75 was a study of 2631 adults who were survivors of the Framingham Heart Study cohort in the town of Framingham, Massachusetts, and were therefore an ageing population. These subjects were not selected in terms of refractive status.

In 1971-81 as part of the US National Health and Nutrition Examination Survey (HANES), a national probability sample of 14,147 persons, aged 1 through 74 years, was selected to represent the 192.7 million persons in the civilian US population of that age at the time of the survey. Sperduto analyzed these data to obtain national prevalence estimates of myopia for persons age 12 to 54 years based on the refractions of 5282 persons (2). He found 25% were myopic, with significantly lower prevalence rates for male subjects than for females and for blacks than for whites (2). The incidence of myopia, that is, the number of persons who become myopic in a given period of time, was greatest between the ages of 12 and 17 years (2).

The incidence of myopia was given to Safir in 1979 as being 15-20% of the population (12). Young in 1980 showed that about 5% of the adult population has myopia greater than 4D (13).

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Differences in refraction between the sexes have been reported by a number of authors (1,3,4) indicating that higher degrees of myopia are predominant in females, but this is probably not true at all ages and with all ethnic groups (1,9,14).

Many investigators have noted that certain groups appear to have a high incidence of myopia. Historically, the highest incidence was reported among Chinese, Japanese, Egyptians, Germans, Jews and Middle Eastern peoples, and the lowest incidence was among Negroes, Eskimos and Indians (1,4,10,15). However for native populations, variations with age possibly due to changing lifestyle (15), schooling (16), or diet (17), and an excess of young persons in the sample can affect percentages reported. For example, Woodruff and Samek (17) report a mean refraction of about one-half a diopter of myopia in the Amerind population of Ontario, but they note an excess of myopia among teenagers and young adults, and a relative excess of hyperopia in older persons. 52% of their sample was made up of

children between ages 5 and 20.

A similar difference of refraction between age groups was reported in other native populations. Young et al report 30% myopia in Alaskan Eskimos (16) but 56% of their sample was 6 to 25 years, a group with much higher amounts of myopia than Eskimos of other ages. For example, there was virtually no myopia among the grandparents or parents, but approximately 58% of the offspring were myopic (16). Young also found a correlation between age and hypermetropia for the fathers but not for the mothers. In West Greenland where a written Eskimo language has been taught for 100 years, Alsbrink found the refraction of Eskimos over 15 years showed an emmetropic excess and a myopic skewness (15). Myopia greater than 1 diopter was present in 14.1%. In these Eskimos, Alsbrink observed that only females showed a trend to hyperopia with age (15).

Table I shows a few representative studies of the prevalence of myopia in various countries.

Table I
PREVALENCE OF MYOPIA BY COUNTRY

COUNTRY	% MYOPIA	AUTHOR	REFERENCE
China, students	53	Li (1920)	18
China, Peking	52	Dzen (1921)	19
Germany	13.8	Witte (1923)	20
US	19.6	Jackson (1932)	21
UK	27	Harman (1936)	22
China	70	Rasmussen (1936)	23
Sweden	33	Nordgren (1936)	24
US, army >-2.5 D	3.16	Downing (1945)	25
UK	24.2	Giles (1950)	26
UK, army	11	Sorsby (1960)	27
US	25-35	Hirsch (1964)	28
Fiji	0	Rose (1964)	29
India	22	Kuriakose (1967)	30
Sweden, army	14.5	Goldschmidt (1968)	31
Israel, communes	18.4	Hyams (1977)	32
US, Mass, age 52-85	17.7	Leibowitz (1980)	11
US, age 12-54	25	Sperduto (1983)	2

Crawford and Hammar conducted a screening of more than 50,000 school children in Hawaii (33). They reported myopia rates as follows: Chinese 17%, Koreans 13%, Japanese 12%, Caucasians 12%, Spanish 9%, Portuguese 7%, Filipinos 6%, Puerto Ricans 4%, partial Hawaiians 4%, Hawaiians 3% and others 3% (33).

Studies of refractive changes with age characteristically indicate a relative excess of hyperopia in infants, an increase in myopia between birth and adulthood, a stability of mean refractive status through early adulthood, then a change in mean refractive status towards less myopia or more hyperopia after age 40 (1,2,4,7,10,28,34-36).

The problem of determining refractive status of infants is complicated in that there can be wide variations in accommodative ability in infants. Also birth weight and time elapsed since birth has an effect on refraction (4). Thus the literature has reports both of high incidence of hyperopia and myopia, with and without cycloplegia. (1,7).

Gasson's 1932-33 study of changes of refractive state with age was divided into those showing hyperopia and those showing myopia (37). A marked difference between males and females appeared at 45-50 years, where male hyperopes showed a sharp trend toward a decrease in hyperopia and male myopes showed a decrease in myopia, while females showed

little mean change. At 60-65 years, male myopes showed a trend toward greater myopia (1). More recently, Grosvenor in 1977 published the data from a longitudinal study of refractive changes between ages 20 and 40 for 111 subjects. Grosvenor concluded that hyperopes tend to become more hyperopic and myopes tend to become more myopic during these years, also that the more myopic a subject was at age 20, the greater the increase in myopia which might occur by age 40. (34).

There appears to be a tendency to higher myopia in city as opposed to rural populations, and higher socioeconomic groups as opposed to lower (1,4). The association of myopia with both higher income and educational level has been noted in many reports, and is thought by some investigators to be closely related to nearwork (2,4,38,39). Further analyses are needed to explain how the various factors of age, race, sex, education and income related to one another and to myopia (2).

NATURE AND CAUSES

A study of refraction makes it clear that myopia has received the most attention (9,12). There are serious conditions associated with myopia, but it is not the only refractive condition associated with tissue destruction

or loss of function (12). It is however a symptom easily recognized, in contrast to hyperopia which is often hidden (12,40). In addition, myopia often makes its appearance during adolescence when so many things are changing rapidly. During this time, a great emphasis is placed on learning social functions, athletic skills and relating to members of the opposite sex. Also there is increasing demand for performance at school. The need to wear corrective lenses can create more difficulties for parents and children (12).

TYPES OF MYOPIA

Pathological myopia, which has been defined as progressive elongation of the globe with degeneration, is frequently associated with destructive choroidal and retinal lesions, as well as retinal detachment, and higher incidence of glaucoma and cataract (4,12,39,41). The axial elongation often causes peripheral fundus changes and posterior staphyloma because the elongation affects two areas – the ora-equatorial area and the posterior pole (42). There is a general agreement that high myopia is essentially a hereditary disease. (4).

In 1948 Stenstrom showed that the total refracting power of the eye had little or very slight correlation to the various dioptric elements of the eye, but axial length was different and showed a pronounced correlation (0.76 ± 0.014) with refractive error (43). He considered myopia of more than -8.00 diopters to be pathological, and believed that the skewness and frequency of extreme variables in the distribution of refractive error could be wholly explained by increased axial length, and many subsequent authors have agreed (39,40,44). The axial development of the vertebrate eye is the result of the interplay of intraocular pressure and scleral resistance; also included in the process of development is an element of stretch (45,46). The eye develops rapidly postnatally and this elongation would result in many eyes becoming myopic if it were not for compensating reduction in lens and corneal power (34,36,40,44,45,47), referred to as emmetropization. Pathologic myopia is readily distinguished from physiologic myopia for it is more likely to be a congenital condition in which excessive axial elongation can be detected at all stages of development (39). Nearwork is not thought to play a role in pathogenesis of high myopia (4,39).

Physiologic, or non-pathological myopia is thought to occur as the result of correlation failure of the refractive components of the normal eyes (4,9,12,39,44). The fundus appears normal in physiologic myopia (39). Every conceivable cause has been advanced to account for this condition (1,3,9,10). Various investigators have implicated convergence (4,39), head position (48), squeezing by the extraocular muscles (49,50), posture (4,48,51,52), illumination (4,48,51,53,54), higher levels of intraocular pressure (4,39,45), increased vitreous pressure (4,47,55), excessive pressure on the eye by eyelids or eye rubbing (4,40,49,56), scleral weakness (50), or congestion (4), motility imbalances (4), uncorrected corneal astigmatism or exophoria (4), contact lens over-correction of the non-dominant eye (57), dietary deficiencies (1,4,9,17), lack of calcium (1,4,58,59), eating excessive amounts of sugar and overcooked proteins (60), high urine concentrations of acid mucopoly saccharides (1), infectious disease (1,4,17), high incidence of dental caries (1,3,4,17) and "stretching of the posterior segment" (34). Morgan suggests a number of other possible causes of myopia including; endocrine imbalance, hypofunction of the thyroid, ratio of height to weight, protective mechanisms of introverted personality, and hybridization of genes of different races (9). Curtin in 1970 proposed three possible causative mechanisms; a

mesodermal mechanism, an ectodermal mechanism, and disparity in growth of ectoderm and mesoderm (61). More recently Curtin has argued for the division of the lower grades of myopia into "physiologic (low, simple)" and "intermediate", with temporal crescent formation as a sign of intermediate myopia (4).

In addition, myopia can be considered to be divided into functional or organic types. Organic changes can cause myopia of a transient or permanent nature at any age, for example; keratoconus, lens hydration, diabetes, dysentery, lens subluxation, nuclear cataract, drugs such as acetazolamide and oxytetracycline, as well as hyperbaric oxygen treatment and malnutrition (39). Some authors also divide functional into "pseudomyopia" which they consider to be reversible, and "simple", "true" or "school myopia" which is considered to be irreversible (4,47,62). Pseudomyopia has been attributed to accommodative spasm, edema of the ciliary body, swelling of the lens and transient increase of refractive index of the lens, vitreous or aqueous (4).

HEREDITY AND ENVIRONMENT

The inheritance of refractive error is generally agreed to be multifactorial (15,39) and polygenetic (4). That one basic determinant of refraction is heredity is borne out by a concordance of 70.6% to 90% between monozygous twins (4,44). There appear to be racial differences in the distribution of myopia. Unfortunately the results of studies of racial differences cannot be interpreted to attribute myopia to genetic causes (9,63).

Although heredity may be the primary cause for myopia, environment can have substantial effects, as is shown by the effect of maternal rubella, drugs and prematurity in causing myopia in the newborn (4,39,64,65). Young native people in North America who have attended school appear to be much more myopic than their parents (16,17); a trend which has been referred to as an epidemic of myopia in the youth (17). This evidence suggests a strong environmental influence (16,56).

NEARWORK AND ACCOMMODATION

Nearwork has been thought to be a cause of functional myopia since Cohn in 1867 presented the evidence that the percentage of German school children with myopia was directly related to the number of years in school (9,40,66). Tscherning, Wittte and Tiffin among many others have espoused this nearwork theory (4,9,15,56). Recent studies have found an unusually high incidence of nearsightedness among those whose occupations require them to do nearwork (40,58,63). For example, in 1979 Richler and Bear found myopia significantly correlated with nearwork for people ages 5 to 60 in three Newfoundland communities (36). However there is no indication whether the nearwork induced the myopia or the myopic individuals choose to do nearwork (9,40). Myopia does appear to develop during school years but it has not been conclusively shown whether nearwork influences its onset or development (9).

Many investigators have implicated accommodation as the cause of myopia (4,9,47,49,55,67). One theory is that accommodation leads to a permanent increase in the convexity of the lens surface since the ciliary muscle holds the lens in position as new lens fibres are laid down (55). There is also some evidence of increased vitreous pressure during accommodation which could cause an increase in axial length (4,47,68). Ciliary muscles spasm is said to be a common effect of nearwork in the adolescent and young adult (10,39).

Van Alphen felt that ciliary muscle tone was responsible for the emmetropization process and reduction of hyperopia postnatally, this process being controlled by a feedback loop through the Edinger Westphal nucleus (45,46). Dramatic effects have been reported with cycloplegia; there is a shift toward hyperopia and a reduction in the excess at emmetropia (47,69). Transient myopia after visual work has been shown to occur after as little as three hours of editing text at a video display terminal, which has been interpreted as a work-induced shift of accommodation toward the resting focus (70,71).

ANIMAL MODELS

Animal studies support the view the environment has an influence on myopia (4,40,41,49,54,72). There is evidence that myopia can be caused in laboratory animals by suturing eyelids shortly after birth (41,56) by elevated intraocular pressure with increased body temperature (73,74), by restricted visual space (54,56,75,76), and by gravitational effects caused by restriction of body position with the eyes facing downward (49,52). Young found that myopia did not develop in confined primates if that illumination was high or low, and attributed myopic changes to moderate levels of illumination (53).

Based on animal models it has been proposed that development of emmetropic refractive status is dependent on normal visual experience and early visual deprivation results in a shift toward myopia mediated by the nervous systems in a young animal, but can only be induced before eye growth is completed (4,40,41,48,54,56,77). Such visual deprivation could be caused in human infants by ptosis, hemangiomas of the eyelid, corneal opacities, congenital cataract, or retrolental fibroplasia (4,40,56,78). In different experiments employing lid suturing and injecting polystyrene beads into the corneal stroma, Raviola and Wiesel have found that some types of monkeys who were visually deprived developed myopia in the deprived eye, but myopia could be prevented with a daily application of atropine, or by rearing the animals in the dark (40). In other types of monkeys, myopia developed despite atropine and even if the optic nerve was cut or the visual cortex was removed (41,56). In these experiments one type of monkey who was visually deprived developed myopia and another type did not, under the same conditions. Raviola and Goss believe that the mechanisms leading to myopia in one type of animal may not be the same as that in another animal (41,54).

Raviola and Wiesel suggest that emmetropization is largely programmed on a genetic basis and that some sort of regulatory molecule may be released by the retina to fine-tune the eye growth, but that an abnormal visual experience can disrupt the process of postnatal eye growth and induce axial myopia (40,41). They believe that accommodation has only a small effect in determining the focal length of the eye at rest, and they further suggest that some children may be destined, like some types of monkeys, to develop myopia through excessive accommodation (40,41). Such myopia may be triggered environmentally or

genetically. These children may benefit from the use of atropine. But for children whose myopia is unrelated to accommodation, like the other type of monkeys studies, atropine would be useless (40).

OTHER CAUSES

Goss found myopia stops increasing earlier in teenage girls, which he attributes to the fact that general body growth tends to cease earlier in girls. His findings suggest that hormonal or growth related changes of adolescence are causative (35).

There are conflicting reports of the refractive status of amblyopic eyes and non-amblyopic "fellow" eyes. Lepard reported his findings of an unusual course of refraction in a longitudinal study of children with unilateral amblyopia (79). With normal use, the fixating non-amblyopic eye has found to undergo a steady drift toward myopia, whereas the refraction of the amblyopic fellow eye remained stable. This would seem to contradict other studies showing that the eye which is visually deprived becomes myopic (78,80,81). On the other hand, Woo in 1970 studied the refractive error distributions of monocularly amblyopic eyes, the non-amblyopic "fellow" eyes, and an equal number of amblyopia-free eyes in a cross sectional study of Ontario grade-school children. The refractive error distributions obtained for the three types of eyes were differently distributed. Also his results indicate the refractive error distribution of amblyopic eyes has a greater frequency of hyperopes than the distribution of non-amblyopic eyes, which in turn has more hyperopic eyes than the distribution of normal eyes (82). Woo and Irving repeated the study ten years later with subjects aged 5-55 and obtained essentially the same results. That is, the amblyopic eyes tend to have a greater frequency of hyperopia than normal eyes (83).

The trend toward progressively more low myopes and corresponding fewer moderate high myopes with advancing age has not been adequately explained. Possible explanations include a decrease in power of the lens, or a cohort effect in which more recent birth cohorts are at a greater risk of the development of more severe myopia (2). In addition, Morgan examined the possibility that earlier mortality for myopes might account for the reduced frequency of hyperopes in older population (9).

The evidence seems to be that both the environmental and the genetic schools are right (40). Environmental factors can and do affect refraction and if nearwork can cause myopia, it is only the physiologic variety (7,39).

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Refractive Errors, Intraocular Pressure, and Glaucoma in a White Population

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Objective: To examine the relation of refractive errors to glaucoma and intraocular pressure (IOP) in a defined white population.

Design: Population-based cross-sectional and follow-up study.

Participants: Persons aged 43 to 86 years living in Beaver Dam, Wisconsin (n = 4926).

Methods: All participants received a standardized assessment of refraction, IOP, and glaucoma at baseline (1988–1990), with IOP remeasured 5 years later (1993–1995). Refraction was defined at baseline as follows: myopia as spherical equivalent of -1.00 diopters (D) or less, emmetropia as -0.75 to $+0.75$ D, and hyperopia as $+1.00$ D or more.

Main Outcome Measures: Relation of baseline refraction to prevalent glaucoma (defined from IOP, optic disc, and visual field criteria) and incident ocular hypertension (defined as IOP more than 21 mmHg at the 5-year examination in eyes with IOP of 21 mmHg or less at baseline).

Results: A myopic refraction was correlated with increasing IOP at baseline ($P < 0.001$). After controlling for age and gender, persons with myopia were 60% more likely to have prevalent glaucoma than those with emmetropia (odds ratio [OR], 1.6; 95% confidence interval [CI], 1.1, 2.3). In contrast, controlling for age, gender, and baseline IOP, persons with hyperopia were 40% more likely to have incident ocular hypertension than those who were emmetropic at baseline (OR, 1.4; 95% CI, 1.0, 2.0). Myopia was not related to incident ocular hypertension.

Conclusions: In these population-based data, there was a cross-sectional association of myopia with higher IOP and prevalent glaucoma. Similar associations have been found in previous studies. Hyperopia may be associated with 5-year risk of ocular hypertension, a finding that needs further investigation. *Ophthalmology* 2003;110:211–217 © 2003 by the American Academy of Ophthalmology.

The relationship between refractive error, intraocular pressure (IOP), and glaucoma is uncertain.¹ Earlier studies have suggested that myopia, particularly high myopia, may be associated with risk of primary open-angle glaucoma,^{2–8} low-tension glaucoma,^{4,9} and ocular hypertension,^{10–13} but less is known regarding the relationship of mild and moderate levels of myopia or hyperopia to risk of glaucoma.¹⁴ Furthermore, existing evidence is derived mainly from clinic-based studies.^{2–14} Two population-based studies have

evaluated the association of refraction and glaucoma. In the Blue Mountains Eye Study in Australia, after adjusting for age, gender, and other risk factors, glaucoma was two to three times as frequent in eyes with myopia compared with eyes with emmetropia or hyperopia.¹⁵ In the Barbados Eye Study, a myopic refraction was one of several risk factors in adult black people with prevalent open-angle glaucoma.^{16,17} However, in both studies, a possible relationship between hyperopia and glaucoma was not examined.

The purpose of this study was to examine the relationship of refractive errors to IOP and presence of glaucoma among participants of a population-based study of white Americans. Additionally, we evaluated the relationship between refractive error and the change in IOP among study participants who returned for a five-year follow-up examination.

Materials and Methods

Study Population

The Beaver Dam Eye Study is a population-based study of ocular diseases in adults, with its population, research methodology, and findings described in detail elsewhere.¹⁸ Briefly, a private census of the population of Beaver Dam, Wisconsin, composed predominantly of white persons (99%), was performed from the fall of

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1987 through the spring of 1988. Of the 5924 people who were 43 to 86 years of age and were eligible for the study, 4926 participated in the baseline examination. Comparisons between participants and nonparticipants have been presented previously.¹⁸ Institutional Review Board approval was obtained at all examinations.

Assessment of Refractive Status

Procedures in the assessment of refraction have been described in detail elsewhere.^{19,20} Refraction was obtained by documenting the refraction in the participant's current prescription (if available). This was followed by a standardized refraction using an automated refractor. This estimate was refined subjectively according to a modification of the Early Treatment Diabetic Retinopathy Study protocol to obtain the best-corrected visual acuity in cases where the automated refraction yielded visual acuity of 20/40 or worse. The results of the automated refraction were used in the analyses for 96% of eyes at baseline, the results of Early Treatment Diabetic Retinopathy Study refraction were used in 4% of eyes, and refraction from the current prescription was used in the remaining people (<1% of eyes). Interexaminer and intraexaminer comparisons showed no significant differences.¹⁹

The refractive status of a particular eye was defined according to the baseline refraction. Myopia was defined as a spherical equivalent of -1.00 diopter (D) or less, hyperopia as a spherical equivalent $+1.00$ D or more, and emmetropia as a spherical equivalent of between -0.75 and $+0.75$ D.

Assessment of Baseline Intraocular Pressure and Glaucoma

The assessments and definitions of IOP and glaucoma in the Beaver Dam Eye Study have been described extensively.²¹⁻²⁴ As part of the baseline evaluation, each subject had a visual field screening test of each eye using a Henson CFS 2000 perimeter (Keeler Instrument Corporation, Broomall, PA). This device performed threshold-related suprathreshold static perimetry using multiple stimulus patterns.^{25,26} After establishing the threshold, the screening was performed using patterns of two, three, or four suprathreshold points within the central 25° of the visual field (26 stimuli in all).²¹ If any point was not seen at the first attempt, it was retested, with any point missed twice on three attempts defined as a confirmed miss, constituting failure of the screening test. Those who failed the screen were submitted to the full perimetric testing, involving testing 132 test points at 3° intervals across the central visual field.²¹ Insensitivity to a stimulus at any point was retested at progressively brighter light intensities, 0.5, 0.8, and 1.2 decibels higher than the initial testing level. For those passing the screening test, only the threshold was recorded.²¹

After visual field testing, the subject was examined at the slit lamp for anterior segment abnormalities and anterior chamber depth.²⁴ If the examiner determined that the angle was too narrow, the pupil was not dilated unless recent dilation was reported by the subject or eye care provider.²¹ The IOP was measured with a Goldmann applanation tonometer after instilling a drop of flouresscein (Flouress Barnes-Hind Armour Pharmaceutical Co, Kankakee, IL) in each eye.²² The tonometer was set to 10 mmHg before measuring the IOP in the right eye, with the value recorded only after the tonometer was moved back from the cornea. The tonometer was then reset to 10 mmHg for measurement in the left eye. If the examiner thought that the measurement was unreliable, it was indicated and excluded from these analyses.

While the pupils were dilating, subjects were interviewed about whether they had ever been told that they had glaucoma, were taking medicines for glaucoma, or had had surgery for glaucoma.^{21,24} When in doubt, the participant's ophthalmologist was

consulted. Photographs of the lens and fundus were then taken. Pertinent to this report, stereoscopic fundus photographs of field 1 (centered on the optic disc), as specified for the Early Treatment of Diabetic Retinopathy Study,²⁷ were taken with a Zeiss (Thornwood, NY) fundus camera. Photographs were processed and graded according to standardized protocols (see below).

There were 851 persons who completed the full visual field test.²¹ These fields were evaluated by four glaucoma specialists who were masked to subject characteristics, including refractive status, and to each other's gradings. The grading classifications were as follows: 1 = normal; 2 = suspicious (suggestive of glaucoma-related changes); 3 = mild to moderate nerve fiber layer-type defect; 4 = severe nerve fiber layer-type defect; 5 = neurologic-type visual field defect; 6 = other visual field abnormality. The consensus of three of four graders was obtained for 94.8% (807 of 851) of the visual fields.²¹ For this report, consensus grading scores of suspicious, mild to moderate nerve fiber layer-type defects, and severe nerve fiber layer-type defects were included as abnormal visual fields compatible with the diagnosis of glaucoma. Because full visual field testing was not performed on subjects who passed the screening test, these persons were not evaluated by the glaucoma experts.

Grading of optic discs and cups was performed according to a detailed standardized protocol.²³ The stereoscopic pairs were examined, and both vertical and horizontal disc and cup diameters were measured with a template of graded circles. Specific anatomic characteristics were used to define both the disc and cup margins.²³ Cup-to-disc ratios were computed for vertical and horizontal meridians in each eye. The vertical ratio was used for these analyses.

Criteria used to define the presence of primary open-angle glaucoma in Beaver Dam have been published.²¹ These included the following: 1 = visual field defect compatible with diagnosis of glaucoma; 2 = cup-to-disc ratio of 0.8 or more or a difference in the cup-to-disc ratio of 0.2 or more in the involved eye; 3 = IOP of 22 mmHg or more in the involved eye; 4 = a history of taking drops for or having surgery for glaucoma. The four factors in combination (or singly for history of glaucoma with treatment) were used to classify eyes as having definite or probable glaucoma. Eyes having at least two of the first three criteria were considered to be definite cases of glaucoma. Those with criteria four present and fewer than two of the other three criteria in the same eye were considered probable cases of glaucoma. Definite and probable cases of glaucoma were combined for this study, because previous analyses indicated these cases were similar.^{21,28} Cases that were determined to be primary angle-closure glaucoma were excluded from this analysis ($n = 2$).

Assessment of Change in Intraocular Pressure

All subjects identified during the initial census were invited for a second examination 5 years after the first.²⁹ Of the 4541 survivors from the baseline examination, 3684 (81.1%) returned for the follow-up examination from 1993 through 1995. Comparisons between participants and nonparticipants at the follow-up have been presented previously.²⁹ At the 5-year examination, IOP was reexamined for all subjects using the same standardized protocol.

We defined two summary variables to analyze change in IOP. A "significant IOP increase" was defined as an increase in IOP two standard deviations or more than the mean increase in IOP between the baseline and 5-year examination in the total population (an increase of 6.35 mmHg). Incident ocular hypertension was defined as an IOP of more than 21 mmHg at the 5-year examination in eyes with an IOP of 21 mmHg or lower at baseline.

Table 1. Baseline Characteristics Comparing Persons Included and Excluded

	Included		Excluded		P* Value
	No.	Mean (Standard Deviation) or %	No.	Mean (Standard Deviation) or %	
Systemic characteristics					
Age (yrs)	4,670	61.5 (11.0)	256	72.1 (10.3)	<0.001
Female gender (%)	4,670	56.1	256	56.3	0.24
Education (yrs)	4,665	12.0 (2.9)	255	11.2 (2.9)	0.39
Hypertension (%)	4,662	63.6	251	50.2	0.40
Diabetes (%)	4,648	9.8	251	20.3	<0.001
Systolic blood pressure (mmHg)	4,668	131.9 (20.5)	255	136.2 (20.7)	<0.001
Diastolic blood pressure (mmHg)	4,668	77.6 (10.9)	255	72.4 (11.5)	<0.001
History of cigarette smoking (%)	4,667	55.2	254	56.3	0.02
Ocular characteristics, right eyes					
Refraction (mean [diopters])	4,670	0.25 (2.35)	19	0.43 (2.09)	0.59
Intraocular pressure (mmHg)	4,661	15.4 (3.32)	179	15.4 (3.93)	0.19
Glaucoma (%)	4,512	3.1	186	15.6	<0.001

*P value comparing included and excluded, adjusted for age.

Other Variables

All other characteristics in this analysis were defined from baseline data. Age was defined as the age at the time of the baseline examination. Education level was defined as the number of years of completed education. Blood pressure was measured with a random-zero sphygmomanometer according to the Hypertension Detection and Follow-up Program protocol, and the average of the last two measurements of three was used for analysis.³⁰ Hypertension was defined as systolic blood pressure of 140 mmHg or more, diastolic blood pressure of 90 mmHg or more, or the combination of self-reported high blood pressure diagnosis and the use of antihypertensive medications at the time of examination. Diabetes mellitus was defined as a history of definite diabetes (treated with insulin or oral hypoglycemic drugs, or diet, or a combination thereof) or elevated glucose and glycosylated hemoglobin, based on specific criteria.³¹

Statistical Analysis

We analyzed data from right and left eyes separately. We also combined data from both eyes using the generalized estimating equation method described by Liang and Zeger³² and by Zeger et al,³³ which adjusts for the correlation between the two eyes in a single person. We compared mean baseline IOP by presence and severity of refractive error versus emmetropia. We used logistic regression to obtain the odds ratio and its 95% confidence intervals for prevalent glaucoma, a significant 5-year IOP change and incident ocular hypertension, by refractive status at baseline. All models were adjusted for age and gender. For analysis of IOP change, we also adjusted for baseline IOP. In multivariate models, we adjusted for education, hypertension, and diabetes, because these may be possible confounders. SAS software (SAS Institute, Inc., Cary, NC) was used for all analyses.

Results

Of the 4926 persons examined at baseline, we excluded 29 for whom refraction data was missing, 208 with aphakia or pseudophakia, and 19 with missing IOP or glaucoma data in both eyes, leaving 4670 included in this study. Comparison of persons included and excluded is presented in Table 1. In general, those

excluded were older, more likely to have diabetes and to have higher systolic and diastolic blood pressure, and to be cigarette smokers. Persons excluded also were more likely to have glaucoma, but they did not differ by refraction and IOP from those included.

In the study sample, 23.9% had myopia, 41.6% had hyperopia, and the remaining 34.5% had emmetropia (using refraction data in right eyes). The age- and gender-adjusted mean IOP was highest in eyes with myopia, followed by emmetropia and hyperopia, although the differences between groups were small (Table 2). When myopia and hyperopia were subdivided further into different severities, we found a progressive association between increasing myopia and IOP ($P < 0.001$, test of trend). The difference in IOP between eyes with refraction less than -3.00 D compared with refraction more than $+2.25$ D was 0.85 mmHg.

The prevalence and odds ratio of glaucoma according to the refractive status are shown in Table 3. In general, glaucoma was more frequent in eyes with a myopic refraction (2.9%) or a hyperopic refraction (3.7%) than in eyes with an emmetropic refraction (2.1%). After adjustment for age and gender, hyperopia was not associated with glaucoma, but eyes with myopia were 60% more likely to have glaucoma than were eyes with emmetropia. This association was similar for different levels of myopia (between -1.00 and -3.00 D and less than -3.00 D). Analyses adjusting for education, hypertension, and diabetes had no substantial impact on these results (e.g., OR, 1.6; 95% CI, 0.9, 2.6).

The mean IOP change between the baseline and 5-year examination in the population was 0.1 mmHg, which is consistent with our previous cross-sectional data that showed IOP was slightly higher in older people compared with younger people (IOP of 15.6 mmHg in people 75 years and older versus 15.0 mmHg in people 43–54 years).²¹ Myopia was not related to change in IOP or to the incidence of ocular hypertension (Table 4). In contrast, controlling for age, gender, and baseline IOP, eyes with a hyperopic refraction at baseline were 40% more likely to have a significant increase in IOP (two standard deviations or more than the mean increase) and incident ocular hypertension (more than 21 mmHg) at the 5-year follow-up than eyes that were emmetropic at baseline, although the absolute difference in risk between eyes with hyperopia and emmetropia was small (Table 4). The association between hyperopia and incident ocular hypertension persisted with further adjustment for education, hypertension, and diabetes (e.g., OR, 1.4; 95% CI, 0.9, 2.3). Results were similar after excluding people with glau-

Table 2. Intraocular Pressure by Refractive Status, Right Eyes and Two Eyes

Baseline Refractive Status	Right Eyes Only				Two Eyes			
	No. of Eyes	Age- and Gender-adjusted		P Value	No. of Eyes	Age- and Gender-adjusted		P Value
		Mean Intraocular Pressure (mmHg)	Spherical Equivalent			Mean Intraocular Pressure (mmHg)	Spherical Equivalent	
Myopia*	1114	15.71	0.10	0.02 [§]	2180	15.66	0.08	<0.001 [§]
Emmetropia [†]	1610	15.41	0.08	—	3230	15.34	0.06	—
Hyperopia [‡]	1937	15.22	0.08	0.10 [§]	3918	15.14	0.06	0.005 [§]
Refraction (diopters)								
Less than -3.00	358	16.09	0.18	<0.001	717	15.89	0.13	<0.001
-1.75 to -3.00	399	15.68	0.17		772	15.73	0.10	
-1.00 to -1.50	357	15.39	0.18		691	15.52	0.10	
-0.75 to +0.75	1610	15.41	0.08		3230	15.33	0.06	
+1.00 to +1.50	738	15.37	0.12		1492	15.17	0.07	
+1.75 to +2.25	558	15.31	0.14		1123	15.14	0.08	
More than +2.25	641	14.93	0.14		1303	15.04	0.09	

*Myopia = -1.00 diopters or less.

[†]Between -0.75 and +0.75 diopters.

[‡]+1.00 diopters or more.

[§]P value comparing intraocular pressure between myopia or hyperopia with emmetropia, adjusted for age and gender.

^{||}P value represents test of trend.

coma at baseline or after excluding people who had a cataract extraction between baseline and follow-up (data not shown).

Discussion

Because refractive errors (myopia and hyperopia) are extremely common conditions in the population,¹⁹ determining their relationship to potential ocular morbidity is an important goal in research. Myopia has long been linked to the risk of glaucoma,¹⁻¹⁴ although existing data have not shown a consistent picture, particularly with regard to the association of low and moderate levels of myopia and glaucoma.^{1,14} Furthermore, most previous studies examining these associations were conducted among clinic-based populations and may be subjected to selection biases (e.g., persons with myopia may be more likely to seek ophthalmic care and to have glaucoma diagnosed).

In this population-based study of white American persons aged 43 to 84 years, we found a cross-sectional association between myopia (defined as less than -1.00 D) and prevalent glaucoma. After taking into account the effects of age, gender, and other risk factors, persons with myopia were 60% more likely to have glaucoma than were those with emmetropia. We found that an increasing severity of myopia was associated with progressively higher IOP, although the difference in IOP between the extremes in refraction was modest (0.85 mmHg, comparing eyes with refraction less than -3.00 D and more than +2.25 D). However, after 5 years, we found that persons with hyperopia at baseline were 40% more likely to have a significant IOP increase (defined as more than two standard deviations of the mean increase) and incident ocular hypertension (defined as IOP more than 21 mmHg) than did those with emmetropia at baseline.

The association between myopia and glaucoma provides

Table 3. Prevalence and Odds Ratio of Glaucoma by Refractive Status, Right Eyes and Two Eyes

Baseline Refractive Status	Right Eyes Only			Two Eyes		
	No. of Eyes at Risk	% with Glaucoma	Age- and Gender-adjusted	No. of Eyes at Risk	% with Glaucoma	Age- and Gender-adjusted
			Odds Ratio (95% Confidence Interval)			Odds Ratio (95% Confidence Interval)
Myopia*	1073	3.0	1.6 (0.9, 2.6)	2118	2.9	1.6 (1.1, 2.3)
Emmetropia [†]	1583	2.2	1.0	3181	2.1	1.0
Hyperopia [‡]	734	4.0	1.1 (0.7, 1.7)	3766	3.7	1.0 (0.7, 1.4)
Refraction (diopters)						
Less than -3.00	339	3.0	1.7 (0.8, 3.5)	691	2.9	1.5 (0.8, 2.6)
-1.00 to -3.00	734	3.0	1.5 (0.9, 2.6)	1427	2.9	1.6 (1.1, 2.4)
-0.75 to +0.75	1583	2.2	1.0	3181	2.1	1.0
+1.00 to +2.25	1256	3.7	1.1 (0.7, 1.7)	2525	3.4	1.0 (0.7, 1.4)
More than +2.25	600	4.7	1.1 (0.7, 1.8)	1241	4.2	1.0 (0.7, 1.4)

*-1.00 diopters or less.

[†]Between -0.75 and +0.75 diopters.

[‡]+1.00 diopters or more.

Table 4. Change in Intraocular Pressure and Incident Ocular Hypertension between Baseline and 5-year Examination, by Refractive Status, Two Eyes

Baseline Refraction	5-year Intraocular Pressure Change				5-year Incident Ocular Hypertension		
	No. of Eyes at Risk	Mean Intraocular Pressure Change (mmHg)	% with Significant Intraocular Pressure Increase	Adjusted Odds Ratio (95% Confidence Interval)*	No. of Eyes at Risk	% with Incident Ocular Hypertension	Adjusted Odds Ratio (95% Confidence Interval)*
Myopia [†]	1681	0.13 (2.81)	1.37	1.0 (0.6, 1.6)	1616	2.66	1.0 (0.6, 1.6)
Emmetropia [‡]	2464	0.24 (3.12)	1.42	1.0	2368	2.24	1.0
Hyperopia [§]	2735	0.27 (2.80)	2.82	1.4 (0.9, 2.3)	2609	3.72	1.4 (1.0, 2.0)

*Adjusted for age, gender, and baseline intraocular pressure.

[†]−1.00 diopters or less.

[‡]Between −0.75 and +0.75 diopters.

[§]+1.00 diopters or more.

support to the findings from two other population-based studies, the Blue Mountains Eye Study of white Australian persons 49 to 97 years of age¹⁵ and the Barbados Eye Study of black persons 40 to 84 years of age living in Barbados.^{16,17} In the Blue Mountains, a stronger dose-response pattern was observed between increasing severity of myopia and prevalence of glaucoma.¹⁵ Controlling for age, gender, and other risk factors, persons with low myopia (between −1.00 to −3.00 D) were twice as likely to have glaucoma (OR, 2.3; 95% CI, 1.3, 4.1), whereas those with moderate to high myopia (less than −3.00 D) were three times as likely to have glaucoma (OR, 3.3; 95% CI, 1.7, 6.4) than those with emmetropia and hyperopia. In the Barbados Eye Study, a weaker association between myopia (less than −0.50 D) and glaucoma was found (OR, 1.5; 95% CI, 1.1, 2.0).¹⁷ In our current study, the association between myopia and glaucoma in white persons (OR, 1.6) was weaker than in the Blue Mountains Study, and a dose-response pattern with increasing myopia severity was absent. Possible explanations for these differences between the three studies may be related to racial variations and other differences in the study population (e.g., the participants in Blue Mountains Study were slightly older), as well as ascertainment of glaucoma (e.g., in the Blue Mountains and Barbados, all participants had definitive visual field examinations and glaucoma was defined without reference to IOP).

What are possible explanations for the association between myopia and glaucoma? First, this association may reflect a biologic relationship between myopia and a risk of glaucoma. The optic nerve head in myopic eyes appears to be more susceptible structurally to glaucomatous damage compared with nonmyopic eyes.¹ The cup-to-disc ratio is higher in myopes,³⁴ which may predispose more nerve fibers to damage at any level of IOP.^{7,35,36} Additionally, connective tissue changes and shearing forces in the lamina cribrosa have been observed to be exaggerated in eyes with longer compared with shorter axial length with the same IOP.³⁷ Second, both glaucoma and myopia may share common pathways. The two conditions show changes in the ocular connective tissue (in the sclera in myopia³⁸ and in the trabecular meshwork and lamina cribrosa in glaucoma³⁹), have a strong familial basis, and may share common genetic links.^{40–42} Third, it is possible that increased IOP contrib-

utes to axial elongation and myopia in a previously emmetropic eye, although this line of argument may be more relevant to juvenile glaucoma.^{43–45} Finally, the association may be an artifact. There is a tendency to overdiagnose visual field and optic disc characteristics as glaucomatous in myopic eyes. Myopic eyes are known to be associated with a variety of nonglaucomatous visual field defects (e.g., enlarged blind spots, superotemporal defects),^{46–48} and grading the cup-to-disc ratio and neuroretinal rim in some myopic eyes, particularly those with tilted optic discs, is extremely difficult.⁴⁹ However, this is minimized, perhaps because the examiners were masked to refractive status in our study.

In contrast, we are unable to offer adequate explanations for the finding that hyperopia at baseline was related to a greater subsequent increase in IOP and a higher risk of ocular hypertension. Unfortunately, we do not have a precise estimate of incident glaucoma in our 5-year follow-up examination to determine whether hyperopia (or myopia) was related to the risk of glaucoma. Hyperopia has been reported to be associated with primary angle-closure glaucoma, and it is possible that shallower anterior chamber depth at baseline predisposes a person to higher IOP at the 5-year follow-up.^{50,51} However, we note that primary angle-closure glaucoma was rare in our white population,²¹ and the two cases were excluded from analysis. Alternatively, it is possible that hyperopia may simply be a marker of biologic aging with regards to risk of ocular hypertension.⁵² In this regard, we have previously reported an association between hyperopia at baseline and a 5-year risk of incident nuclear and cortical cataract.⁵³ These data suggest that further research is warranted in understanding the ocular associations of hyperopia.

Strengths of this study include a large community-based population; use of data from both eyes; high response rate at both baseline and follow-up examinations; and standardized assessment of refraction, IOP, and glaucoma. Several important limitations warrant consideration. First, it is not clear whether measurement error or misclassification of either myopia or glaucoma may have influenced the results, because these data were based on single measurements (of refraction, IOP, optic disc, and visual fields) during the course of the study. Additionally, full visual fields were

performed only on participants who failed the screening visual field examination. Therefore, it is possible that glaucoma cases may have been underdiagnosed. However, the overall glaucoma prevalence reported in our study²¹ was similar to other population-based estimates on white persons,⁵⁴ and misclassification would tend to bias the findings toward the null. Second, refraction data were obtained in adults 43 to 84 years of age at the time of the baseline examination. As a result, these data do not reflect the effects of "axial" or "early onset" myopia and risk of glaucoma. Studies with ocular biometry would be useful in evaluating such associations. Third, the population is composed mainly of white American persons with a relatively low prevalence of myopia. Our data, therefore, may be inapplicable to other groups with a higher prevalence of severe myopia (e.g., Asians).⁵⁵ Finally, as in any observational studies, the inability to control for unmeasured factors may have masked some association and accentuated others.

In summary, we found a cross-sectional association of myopia with higher IOP and glaucoma, a relationship that has been seen in other clinic- and population-based studies. Additionally, we found a prospective association between hyperopia and five year risk of ocular hypertension, a finding that has not been reported previously. These data emphasize the need for future investigations to determine more precisely the potential ocular morbidities that may be associated not only with myopia but also hyperopia.

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OPHTHALMIC PATHOLOGY FELLOWSHIP

Research to Prevent Blindness and the American Ophthalmological Society-Knapp Fund is offering a two-year postgraduate fellowship for training in ophthalmic pathology with an annual stipend of \$52,500. Applicants must be graduates of a medical school accredited by the American Medical Association, citizens of the United States, and have plans for an academic career. Deadline for submission of applications: January 15, 2003 for fellowship starting in July 2003. Please direct all inquiries and requests for applications materials to:

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Refractive Errors and Incident Cataracts: The Beaver Dam Eye Study

Tien Yin Wong,^{1,2,3} Barbara E. K. Klein,¹ Ronald Klein,¹ Sandra C. Tomany,¹ and Kristine E. Lee¹

PURPOSE. To describe the relation between refractive errors and incident age-related cataracts in a predominantly white US population.

METHODS. All persons aged 43 to 84 years of age in Beaver Dam, Wisconsin, were invited for a baseline examination from 1988 through 1990 and a follow-up examination 5 years later from 1993 through 1995. At both examinations, participants had refraction and photographic assessment of cataract, according to a standardized protocol. Myopia was defined as a spherical equivalent of -1.0 diopters (D) or less, hyperopia as $+1.0$ D or more. The relations between refractive errors at baseline and cataract at baseline (prevalent cataract), 5-year incident cataract, and incident cataract surgery were analyzed by using generalized estimating equations.

RESULTS. When age and gender were controlled for, myopia was related to prevalent nuclear cataract (odds ratio [OR], 1.67; 95% confidence interval [CI], 1.23–2.27), but not to cortical and posterior subcapsular cataracts. Myopia was not related to 5-year incident nuclear, cortical, and posterior subcapsular cataracts, but was related to incident cataract surgery (OR 1.89; CI 1.18–3.04). Hyperopia was related to incident nuclear (OR 1.56; CI 1.25–1.95) and possibly cortical (OR 1.25; CI 0.96–1.63) cataracts, but not to posterior subcapsular cataract or cataract surgery. After further adjustment for diabetes, smoking, and education, the association between myopia and incident cataract surgery was attenuated (OR 1.60; CI 0.96–2.64), but the associations between hyperopia and incident nuclear and cortical cataracts were unchanged.

CONCLUSIONS. These data support the cross-sectional association between myopia and nuclear cataract seen in other population-based studies, but provide no evidence of a relationship between myopia and 5-year incident cataract. Hyperopia may be related weakly to incident nuclear and cortical cataract. (*Invest Ophthalmol Vis Sci.* 2001;42:1449–1454)

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The relation between refractive errors and risk of age-related cataract is not clear. Earlier studies have suggested that high myopia may be associated with development of cataract,^{1–3} but less is known regarding the association with mild and moderate levels of myopia or hyperopia. Existing data have been derived largely from clinic-based studies, which are subject to selection biases.^{4–7} To our knowledge, only one population-based study has attempted to specifically evaluate the relation between refractive errors and cataract in detail. In the Blue Mountains Eye Study in Australia, current myopic refraction and early-onset myopia (defined as self-reported history of distance spectacle use before age 20 years) were related to prevalent posterior subcapsular cataract.⁸ However, the cross-sectional study design cannot adequately differentiate cause and effect, which is particularly problematic when dealing with whether refractive errors are risk factors for cataract, because cataract (e.g., nuclear sclerosis) is also known to affect refraction (e.g., myopia).^{2,9}

The purpose of this study was to evaluate the relation between refractive errors and prevalent cataract, 5-year incident cataract, and incident cataract surgery, in the Beaver Dam Eye Study cohort.

METHODS

Study Population

The Beaver Dam Eye Study is a population-based study of ocular diseases in adults. Its population, research methodology, and findings described in detail in other reports.^{10,11} Briefly, a private census of the population of Beaver Dam, Wisconsin, was performed from fall 1987 through spring 1988. All 5924 people who were 43 to 84 years of age were invited for baseline examinations from spring 1988 through fall 1990. The population was composed of predominantly white persons (99%). Of eligible persons, 4926 participated in the baseline examination. All subjects identified during the initial census were invited for a second examination 5 years after the first. Of the 4541 participants from the baseline examination surviving, 3684 (81.1%) returned for the follow-up examination from spring 1993 through summer 1995. Comparisons between participants and nonparticipants at baseline¹⁰ and follow-up¹¹ have been presented elsewhere.

Procedures

The examination procedures for refraction and lens assessment at both baseline and follow-up were based on the same standardized protocol described in detail elsewhere.^{9,12–14} Tenets of the Declaration of Helsinki were followed. Refraction was obtained as follows: documentation of the refraction in the participant's current prescription (if available) was followed by a standardized refraction using an automated refractor. The refraction was then refined according to a modification of the Early Treatment Diabetic Retinopathy Study (ETDRS) protocol to obtain the best corrected visual acuity, when the automated refraction yielded visual acuity of 20/40 or worse.¹⁴ Interexaminer and intraexaminer comparisons showed no significant differences among examiners for the refractions obtained.

For the evaluation of cataracts, after pupil dilation, photographs were taken of the lens, by using slit lamp and retroillumination cameras.¹⁵ The photographs were subsequently graded for the presence and severity of cataract. The grading procedure was based on detailed codified decision rules, by graders masked to subjects' identities and characteristics (and presence or severity of lens opacities at baseline when grading photographs from the follow-up examination). Scores for nuclear sclerosis were based on comparisons with standard photographs that included a five-step level of severity based on opacity of the nucleus.¹⁵ Scores for cortical and posterior subcapsular cataracts were based on weighted estimates of degree of opacity of lens area as defined by a circular grid, divided into eight pie-wedged peripheral areas and a central circular area.¹⁵ In general, overall reproducibility was good and was similar for inter- and intragrader comparisons.^{12,13}

During the course of the standardized interview, questions were asked about education, diabetes status, and cigarette smoking, among other variables.

Definitions

Refraction status was defined according to refraction at the baseline examination.⁹ The results of the automated refraction were used in the analyses for 96% of eyes at baseline, the results of ETDRS refraction were used in 4% of eyes, and refraction from the current prescription was used in the remaining subjects (<1% of eyes). Eyes without a lens, with an intraocular lens, or with best corrected visual acuity of 20/40 and worse were excluded. For this analysis, myopia was defined as a spherical equivalent of -1.00 diopters (D) or less, hyperopia as a spherical equivalent of $+1.00$ D or more, and emmetropia as a spherical equivalent of between -0.75 and $+0.75$ D.

Definitions for lens opacity at the baseline (referred to as prevalent cataract) and follow-up examinations (5-year incident cataract, and 5-year progression of lens opacity) have been described in other publications.^{12,13} In summary, prevalent or incident cataract was defined according to the following specific criteria: nuclear sclerosis of level 4 or more, cortical opacities involving 5% or more of the lens surface, and posterior subcapsular opacities involving 5% or more of a grid segment. A prevalent cataract was a specific lens opacity of this severity at the baseline examination, whereas an incident cataract was based on the development of that opacity at the follow-up examination in eyes free of the specific lesion at baseline. Progression referred to an increase in the severity or involvement by that specific opacity, according to the following criteria: nuclear sclerosis as a change of one level and cortical and posterior subcapsular opacities as a change of 0.75 units or more after the square-root transformation of the data (to account for the increase in variability of estimated area of involvement as the base amount increased). The rationale and interpretation of the criteria for progression are described in more detail in other reports.¹³

Incident cataract surgery was defined as the absence of the lens in the follow-up examination, if the lens was present at baseline.¹⁶ Exceptions were lenses removed for a reason other than cataract.

All other characteristics in this analysis were defined from baseline data. Age was defined as the age at the time of the baseline examination. Diabetes mellitus was defined as a history of known diabetes (treated with insulin or oral hypoglycemic drugs and/or diet) or elevated glucose and glycosylated hemoglobin, based on specific criteria.¹⁷ Cigarette smoking was defined as having ever smoked (100 cigarettes or more in a lifetime) or having never smoked (fewer than 100 cigarettes). Education level was categorized into four levels (fewer than 12 years, 12 years, 13-15 years, and >15 years).

Statistical Analysis

Of the 4926 persons examined at the baseline examination, 4533 had phakic eyes and had best corrected visual acuity of 20/40 in at least one eye. Of these, 63 had evidence of direct trauma, ungradable lens, or missing lens data in both eyes, leaving 4470 persons available for the analysis of prevalent cataract. Analyses of 5-year incidence of cataract were based on the 3684 persons who participated in both baseline and

follow-up examinations. Persons were excluded if both eyes (1) had no lens, had an intraocular lens, had best corrected visual acuity of worse than 20/40 at baseline, or were missing refraction data ($n = 209$) or (2) had prevalent cataract at baseline, had an ungradable lens, or had missing lens data either at baseline or at follow-up ($n = 422$). This left 3053 persons for incident cataract analyses.

Initially, data from left and right eyes were analyzed separately. For regression models, we used data from both eyes, based on the generalized estimating equation method described by Zeger et al.¹⁸ and Liang and Zeger.¹⁹ This method allows use of data from both eyes, adjusting for the correlation between the two eyes in a single person. Age- and gender-adjusted odds ratio (OR) and its 95% confidence interval (CI) were calculated for a specific cataract type, in the presence of different severities of refractive errors compared with emmetropia. In multivariate models, we controlled for diabetes, smoking, and education—variables that were associated with the presence or development of cataract in our population. For models with cortical and posterior subcapsular cataract, we further adjusted for presence of nuclear cataract at baseline, because nuclear sclerosis increases the refractive index of the lens and lens power.⁹ All statistical analyses were performed by computer (SAS software; SAS Institute, Inc., Cary, NC).

RESULTS

Comparison of persons included ($n = 4470$) and excluded ($n = 456$) in the prevalent cataract analyses is presented in Table 1. In general, persons excluded were older, more likely to be women, and less likely to be smokers; had higher systolic and diastolic blood pressure and lower education and income; and had higher prevalence of diabetes at baseline. A similar comparison is shown for the 3053 persons included in the incident cataract analyses (Table 1). Persons excluded were also older and more likely to be women; had higher blood pressures and lower education and income; and had higher prevalence of diabetes at baseline.

Among persons included in the prevalent cataract analyses, the frequency of myopia and hyperopia (either eye meeting the definition at baseline) was 25.5% and 45.8%, respectively. In comparison, the corresponding frequencies were 26.9% and 42.5% among persons included in the incident cataract analyses. The prevalence of cataract (either eye meeting the definition at baseline) was 14.3% for nuclear, 14.4% for cortical, and 4.4% for posterior subcapsular.

The crude rates of nuclear, cortical, and posterior subcapsular cataracts, by refractive errors are shown in Table 2 (results shown on right eyes; results for left eyes were similar and are not presented). For these analyses, myopia and hyperopia were also divided into three categories, based on approximately equal frequency in each category. In general, hyperopia was associated with a higher prevalence and 5-year incidence and progression of cataracts. Increasing severities of hyperopia were also associated with increasing frequencies of nuclear and cortical, but not posterior subcapsular, cataracts.

The age- and gender-adjusted ORs for nuclear, cortical, and posterior subcapsular cataracts, by refractive error, are shown in Table 3. Myopia was related to prevalent nuclear (OR 1.67; CI 1.23-2.27), but not cortical and posterior, subcapsular cataracts. Myopia was not related to 5-year incidence or progression of nuclear, cortical, or posterior subcapsular cataracts.

Hyperopia was related to prevalence (OR 1.25; CI 0.99-1.57), 5-year incidence (OR 1.56; CI 1.25-1.95), and 5-year progression (OR 1.22; CI 1.07-1.39) of nuclear cataract. Hyperopia was also weakly related to incidence (OR 1.25; CI 0.96-1.63) and progression (OR 1.18; CI 0.99-1.41) of cortical cataract, but not of posterior subcapsular cataract. The age- and gender-adjusted relation between refractive errors and 5-year

TABLE 1. Comparison of Persons Included and Excluded from Analyses, by Baseline Characteristics

	Prevalent Cases		Incident Cases	
	Included (n = 4470)	Excluded (n = 456)	Included (n = 3053)	Excluded (n = 1873)
Age (y)*	60.8 ± 10.6	74.4 ± 9.0	58.8 ± 9.7	67.4 ± 11.4
Education (y)*	12.1 ± 2.8	10.5 ± 3.0	12.4 ± 2.8	11.2 ± 2.9
Smoking (pack y)*	17.6 ± 26.4	18.7 ± 32.0	16.4 ± 24.4	19.8 ± 30.7
Systolic BP (mm Hg)*	131.7 ± 26.3	136.5 ± 21.6	129.9 ± 19.1	135.8 ± 22.1
Diastolic BP (mm Hg)*	77.9 ± 26.4	72.1 ± 11.5	78.9 ± 10.3	75.6 ± 11.8
Gender, females†	2465 (55.2)	297 (65.1)	1371 (44.9)	1080 (57.7)
Annual income (\$US)†				
<10,000	593 (13.8)	167 (43.0)	303 (10.2)	457 (26.7)
≥45,000	690 (16.1)	19 (4.9)	552 (18.6)	157 (9.2)
Diabetes, yes†	277 (6.2)	71 (15.8)	145 (4.8)	203 (10.8)
Cigarette smoking, ever†	891 (20.0)	79 (17.4)	602 (19.7)	368 (19.9)

Myopia: -1.00 D or less; emmetropia: between -0.75 and +0.75 D; hyperopia: +1.00 D or more.

* Data expressed as means ± SD.

† Data expressed as number with percentage of total in parentheses.

incident cataract surgery is shown in Table 4. Myopia, but not hyperopia, was related to incident cataract surgery.

When diabetes, smoking, and education were controlled for, most associations were similar to the age- and gender-adjusted ORs (Table 5). Myopia was significantly related to prevalent nuclear cataract and possibly incident cataract surgery. Hyperopia was related to incidence and progression of nuclear, and possibly cortical, cataracts.

Finally, analyses with refraction treated as a continuous independent variable (0.25-D increments) showed no consistent patterns of association (data not shown).

DISCUSSION

Both refractive errors and age-related cataracts are common ocular conditions. In the United States, three quarters of adults

TABLE 2. Prevalence and 5-Year Incidence and Progression of Nuclear, Cortical, and Posterior Subcapsular Cataract, by Refractive Status

Refractive Status	Nuclear Cataract			Cortical Cataract			Posterior Subcapsular Cataract			Incident Cataract Surgery		
	At Risk	n	%	At Risk	n	%	At Risk	n	%	At Risk	n	%
Prevalence												
Emmetropia	1481	85	5.7	1484	113	7.6	1480	26	1.8	—	—	—
Myopia	976	85	6.9	972	46	4.7	976	18	1.8	—	—	—
-1.00 to -1.50	320	26	8.1	316	11	3.5	319	4	1.3	—	—	—
-1.75 to -3.00	357	22	6.2	355	16	4.5	357	3	0.8	—	—	—
-3.25 and less	299	19	6.4	301	19	6.3	300	11	3.7	—	—	—
Hyperopia	1676	230	13.7	1666	234	14.2	1666	60	3.6	—	—	—
+1.00 to +1.50	633	53	8.0	665	74	11.2	662	18	2.7	—	—	—
+1.75 to +2.25	496	70	14.1	492	79	16.1	488	24	4.9	—	—	—
+2.50 and more	517	107	20.7	509	83	16.3	516	18	3.5	—	—	—
Five-Year Incidence												
Emmetropia	1063	93	8.8	1044	56	5.4	1082	27	2.5	1195	22	1.8
Myopia	707	47	6.7	713	38	5.3	728	24	3.1	818	18	2.2
-1.00 to -1.50	222	16	7.2	224	11	4.9	225	6	2.7	261	6	2.3
-1.75 to -3.00	261	18	6.9	265	17	6.4	277	9	3.3	301	7	2.3
-3.25 and less	224	13	5.8	224	10	4.5	226	9	2.7	256	5	2.0
Hyperopia	1037	220	21.2	1031	120	11.6	1106	49	4.1	1290	40	3.1
+1.00 to +1.50	449	65	14.5	433	39	9.0	453	17	3.8	515	6	1.2
+1.75 to +2.25	293	75	25.6	298	36	12.1	312	18	5.8	373	18	4.8
+2.50 and more	295	80	27.1	300	45	15.0	341	14	4.1	402	16	4.0
Five-Year Progression												
Emmetropia	1105	525	47.5	1109	168	15.2	1089	17	1.6	—	—	—
Myopia	741	362	48.9	734	113	15.4	738	16	2.2	—	—	—
-1.00 to -1.50	2332	113	48.7	227	31	13.7	227	5	2.2	—	—	—
-1.75 to -3.00	276	134	48.5	275	51	18.6	280	4	1.4	—	—	—
-3.25 and less	233	115	49.4	232	31	13.4	231	7	3.0	—	—	—
Hyperopia	1159	583	50.3	1144	308	26.9	1126	35	3.1	—	—	—
+1.00 to +1.50	476	232	48.7	474	110	23.2	459	10	2.2	—	—	—
+1.75 to +2.25	332	168	50.6	329	91	27.7	319	14	4.4	—	—	—
+2.50 and more	351	183	52.1	341	107	31.4	348	11	3.2	—	—	—

Myopia: -1.00 D or less; emmetropia: between -0.75 and +0.75 D; hyperopia: +1.00 D or more. Data are for the right eye only.

TABLE 3. Age- and Gender-Adjusted Odds Ratios of Nuclear, Cortical, and Posterior Subcapsular Cataract, by Refractive Errors

Refractive Error versus Emmetropia	Nuclear Cataract			Cortical Cataract			Posterior Subcapsular Cataract		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Prevalence									
Myopia	1.67	(1.23, 2.27)	<0.001	0.84	(0.63, 1.13)	0.25	1.37	(0.84, 2.23)	0.20
-1.00 to -1.50	1.57	(1.04, 2.37)	0.03	0.50	(0.31, 0.81)	0.005	0.80	(0.32, 1.98)	0.62
-1.75 to -3.00	1.64	(1.08, 2.50)	0.02	0.83	(0.55, 1.24)	0.36	0.80	(0.37, 1.73)	0.58
-3.25 and less	1.83	(1.11, 3.01)	0.02	1.35	(0.88, 2.07)	0.17	2.65	(1.46, 4.79)	0.001
		P = 0.002*			P = 0.74*			P = 0.02*	
Hyperopia	1.25	(0.99, 1.57)	0.06	1.06	(0.86, 1.30)	0.62	1.41	(0.96, 2.07)	0.08
+1.00 to +1.50	1.01	(0.76, 1.34)	0.95	1.02	(0.79, 1.30)	0.89	1.11	(0.69, 1.79)	0.65
+1.75 to +2.25	1.08	(0.81, 1.44)	0.61	1.19	(0.92, 1.55)	0.19	1.61	(1.01, 2.55)	0.04
+2.50 and more	1.59	(1.21, 2.09)	<0.001	0.99	(0.76, 1.29)	0.97	1.50	(0.90, 2.51)	0.12
		P < 0.001*			P = 0.74*			P = 0.05*	
Five-Year Incidence									
Myopia	0.87	(0.64, 1.18)	0.38	1.04	(0.74, 1.45)	0.83	1.25	(0.79, 1.97)	0.35
-1.00 to -1.50	0.92	(0.59, 1.43)	0.71	0.87	(0.53, 1.43)	0.58	1.25	(0.66, 2.37)	0.50
-1.75 to -3.00	0.97	(0.65, 1.45)	0.90	1.06	(0.67, 1.67)	0.80	1.19	(0.62, 2.29)	0.59
-3.25 and less	0.70	(0.42, 1.18)	0.18	1.14	(0.69, 1.89)	0.61	1.29	(0.63, 2.63)	0.48
		P = 0.27*			P = 0.57*			P = 0.37*	
Hyperopia	1.56	(1.25, 1.95)	<0.001	1.25	(0.96, 1.63)	0.09	1.00	(0.70, 1.44)	0.99
+1.00 to +1.50	1.10	(0.84, 1.450)	0.47	1.12	(0.82, 1.55)	0.47	0.85	(0.55, 1.33)	0.48
+1.75 to +2.25	1.98	(0.49, 2.62)	<0.001	1.23	(0.87, 1.75)	0.24	1.32	(0.80, 2.19)	0.27
+2.50 and more	1.72	(1.27, 2.32)	<0.001	1.41	(1.00, 1.98)	0.05	0.92	(0.55, 1.540)	0.75
		P = < 0.001*			P = 0.02*			P = 0.89*	
Five-Year Progression									
Myopia	1.01	(0.88, 1.16)	0.92	0.95	(0.77, 1.18)	0.66	1.59	(0.93, 2.73)	0.09
-1.00 to -1.50	1.05	(0.86, 1.30)	0.61	0.88	(0.65, 1.20)	0.41	1.84	(0.90, 3.77)	0.09
-1.75 to -3.00	0.92	(0.76, 1.13)	0.43	1.00	(0.75, 1.33)	0.99	0.97	(0.41, 2.31)	0.95
-3.25 and less	1.04	(0.85, 1.27)	0.72	0.99	(0.72, 1.37)	0.96	2.08	(1.01, 4.27)	0.05
		P = 0.94*			P = 0.87*			P = 0.09*	
Hyperopia	1.22	(1.07, 1.39)	0.004	1.18	(0.99, 1.41)	0.06	1.32	(0.84, 2.09)	0.23
+1.00 to +1.50	1.17	(1.00, 1.38)	0.05	1.02	(0.82, 1.26)	0.87	1.05	(0.59, 1.86)	0.87
+1.75 to +2.25	1.35	(1.12, 1.63)	0.002	1.26	(0.99, 1.59)	0.06	1.69	(0.91, 3.14)	0.10
+2.50 and more	1.17	(0.96, 1.42)	0.12	1.30	(1.03, 1.66)	0.03	1.41	(0.78, 2.53)	0.25
		P = 0.03*			P = 0.007*			P = 0.14*	

Myopia: -1.00 D or less; emmetropia: between -0.75 and +0.75 D; hyperopia: +1.00 D or more.

* Test of trend.

have refractive errors,^{14,20} whereas one quarter have age-related cataracts.²¹ A number of population-based studies in different ethnic groups have demonstrated a strong and consistent cross-sectional association between myopia and age-related nuclear cataract.^{8,22-26} The association between myopia and prevalent nuclear cataract in our study is consistent

TABLE 4. Age- and Gender-Adjusted Odds Ratios of Incident Cataract Surgery, by Refractive Errors

Refractive Error versus Emmetropia	OR	95% CI	P
Myopia	1.89	(1.18, 3.04)	0.008
-1.00 to -1.50	1.46	(0.71, 2.99)	0.30
-1.75 to -3.00	1.52	(0.78, 2.96)	0.22
-3.25 and less	2.91	(1.47, 5.75)	0.002
		P = 0.003*	
Hyperopia	1.20	(0.80, 1.81)	0.38
+1.00 to +1.50	0.81	(0.47, 1.39)	0.44
+1.75 to +2.25	1.49	(0.90, 2.47)	0.12
+2.50 and more	1.27	(0.76, 2.14)	0.37
		P = 0.13*	

Myopia: -1.00 D or less; emmetropia: between -0.75 and +0.75 D; hyperopia: +1.00 D or more.

* Test of trend.

with these data. However, this association is difficult to explain and has been attributed in part to increasing lens power due to increasing density of lens nucleus with age.²⁷ In support of this hypothesis is the observation in Beaver Dam that persons with severe nuclear sclerosis at baseline were more likely to have a myopic change in refraction after 5 years, compared with no change or a hyperopic change in persons with only mild nuclear sclerosis.⁹

A more relevant and important issue is whether refractive errors are risk factors for age-related cataract. Anecdotal evidence and clinic-based studies have suggested that myopia, particularly severe and pathologic myopia, may increase the risk of cataract.¹⁻⁷ Few data are available from population-based studies regarding risk of cataract in persons with mild to moderate myopia or hyperopia. The Blue Mountains Eye Study recently looked at refractive errors and risk of age-related cataract in an Australian population.⁸ Early-onset myopia, defined as a self-reported history of distance spectacle use before 20 years of age and excluding eyes with hyperopia, was associated with a four times higher odds of posterior subcapsular cataract detected during the survey, when participants were 49 to 98 years of age. Further, a graded cross-sectional association was shown between increasing levels of myopia and odds of prevalent posterior subcapsular cataract. The authors therefore suggested that myopia could be a risk factor for the develop-

TABLE 5. Multivariate-Adjusted Odds Ratios of Nuclear, Cortical, and Posterior Subcapsular Cataract, by Refractive Errors

Refractive Error versus Emmetropia	Nuclear Cataract*			Cortical Cataract†			Posterior Subcapsular Cataract†			Incident Cataract Surgery†		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Prevalence												
Myopia	1.74	(1.28, 2.37)	<0.001	0.86	(0.64, 1.16)	0.34	1.23	(0.75, 2.03)	0.41	—	—	—
Hyperopia	1.21	(0.96, 1.53)	0.10	1.04	(0.84, 1.29)	0.69	1.33	(0.91, 1.96)	0.14	—	—	—
Five-Year Incidence												
Myopia	0.86	(0.63, 1.16)	0.32	1.08	(0.77, 1.51)	0.66	1.18	(0.73, 1.92)	0.49	1.60	(0.96, 2.64)	0.07
Hyperopia	1.55	(1.24, 1.93)	<0.001	1.27	(0.97, 1.66)	0.08	0.97	(0.66, 1.40)	0.85	1.22	(0.79, 1.89)	0.37
Five-Year Progression												
Myopia	0.99	(0.86, 1.14)	0.94	0.95	(0.77, 1.17)	0.62	1.59	(0.91, 2.77)	0.10	—	—	—
Hyperopia	1.24	(1.08, 1.41)	0.002	1.20	(1.01, 1.43)	0.04	1.24	(0.78, 1.97)	0.37	—	—	—

Myopia: $-1.00 D$ or less; emmetropia: between -0.75 and $+0.75 D$; hyperopia: $+1.00 D$ or more.

* Adjusted for age, gender, diabetes, smoking, and education.

† Adjusted for age, gender, diabetes, smoking, education, and prevalence of nuclear cataract at baseline.

ment of posterior subcapsular cataract. However, the study was cross-sectional in design, and the definition of early-onset myopia may be unreliable, because it was based on self-reported data, which are dependent on memory and interpretation of the interview question. In the Beaver Dam study, the relations between a history of wearing distance spectacles, age of first use of distance spectacles, and prevalent age-related cataracts were inconsistent.²⁸

This analysis provides objective documentation of the 5-year risk of age-related cataract in adults with mild and moderate severities of refractive errors. We could not find a clear association between myopia and 5-year incidence or progression of nuclear, cortical, and posterior subcapsular cataracts. Hyperopia may be related weakly to incidence (OR 1.55) and progression (OR 1.24) of nuclear cataract and possibly to incidence (OR 1.27) and progression (OR 1.20) of cortical cataract.

We are unable to explain the relation between hyperopia and incident nuclear or cortical cataract. In a previous analysis, we observed an association between thinner lens and incident cortical cataract.²⁹ A cross-sectional association between hyperopia and nuclear cataract has also been noted in the Blue Mountains Eye Study.⁸ Oxidative lens damage appears to occur early in myopic eyes, but it is not known whether similar changes take place in hyperopic eyes.^{30,31} Further research in this area is warranted. In any case, the associations we observed were weak, and it is possible that these results were related to chance.

We also found an association between myopia and 5-year risk of cataract surgery. The underlying reason is likely to be complex, because many factors are related to incident cataract surgery in our population.¹⁶ Because posterior subcapsular cataract was the most important lens opacity predicting the need for cataract surgery,¹⁶ it is possible that the higher risk of cataract surgery may be related to the development of posterior subcapsular cataract in myopic eyes during the 5-year interval. However, we cannot verify this. Another possible explanation is that persons with myopia may have had more frequent interactions with ophthalmologists and other eye-care providers, and may have been more likely to have cataract surgery during the 5-year interval between baseline and follow-up.

Significant strengths of this study include a large sample size and use of data from both eyes, high response rate at both baseline and follow-up examinations, standardized protocol for refraction and masked photographic grading of cataract, and ability to control for other known cataract risk factors. However, there are several important limitations that warrant con-

sideration. First, our definitions of myopia and hyperopia were based on refraction data obtained in adults 43 to 84 years of age at the time of the baseline examination. As a result, it is difficult to estimate the effects of axial and early- or childhood-onset myopia and risk of cataract. Studies with precise refractive data collected early in life or with axial length and keratometry data would be useful in evaluating these associations. Second, the population is composed mainly of white persons with a relatively low prevalence of myopia. We did not have a sufficient number of high myopes to examine its relation to incident cataract (number of persons with less than $-6.0 D$ in their right eyes; $n = 20$). Our data may therefore not be applicable to other groups (e.g., Chinese) with a higher prevalence of severe myopia.²⁵ Third, selection biases may have masked some association and accentuated others. For example, the failure to observe an association between myopia and cataract may be due to the excluded persons' having a higher prevalence of both hyperopia and cataract. Finally, as in any observational studies, we may be unable to control for unmeasured cataract risk factors or other confounders.

In summary, our study supports the cross-sectional association between myopia and nuclear cataract seen in other population surveys, but provides no evidence of an association between mild and moderate levels of myopia and 5-year risk of cataract. Hyperopia may be related to incident nuclear and cortical cataract. Other prospective studies in populations with a higher prevalence of severe refractive errors, perhaps supplemented with ocular biometry data, may yield further information regarding these associations.

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Myopia and Incident Cataract and Cataract Surgery: The Blue Mountains Eye Study

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PURPOSE. To assess whether an association exists between myopia and incident cataract and cataract surgery in an older population-based cohort study.

METHODS. The Blue Mountains Eye Study examined 3654 participants aged 49 years or more during 1992 to 1994 and then 2334 (75.1%) of the survivors after 5 years. A history of using eyeglasses for clear distance vision was obtained. Objective refraction was performed with an autorefractor, followed by subjective refraction with a logarithm of minimum angle of resolution (logMAR) chart. Emmetropia was defined as a spherical equivalent refraction between +1 D and -1 D, hyperopia as more than +1 D, and myopia as less than -1 D. Slit lamp and retroillumination lens photographs were graded for presence of cortical, nuclear, or posterior subcapsular cataract, according to the Wisconsin Cataract Grading System. Generalized estimating equation models analyzed data by eye.

RESULTS. There was a statistically significant association between high myopia (-6 D or less) and incident nuclear cataract (odds ratio [OR] 3.3, 95% confidence interval [CI] 1.5-7.4). Incident posterior subcapsular cataract was associated with any myopia (OR 2.1, 95% CI 1.0-4.8), moderate to high myopia (-3.5 D or less, OR 4.4, 95% CI 1.7-11.5), and use of distance glasses before age 20 (OR 3.0, 95% CI 1.0-9.3), after adjustment for multiple potential confounders, including severity of nuclear opacity. Incident cataract surgery was significantly associated with any myopia (OR 2.1, 95% CI 1.1-4.2) as well as moderate (-3.5 to more than -6D; OR 2.9, 1.2-7.3) and high myopia (OR 3.4, 95% CI 1.0-11.3).

CONCLUSIONS. These epidemiologic data provide some evidence of an association between myopia and incident cataract and cataract surgery, after adjustment for multiple confounders and severity of nuclear opacity. These data support other cross-sectional and longitudinal population-based findings. (*Invest Ophthalmol Vis Sci.* 2002;43:3625-3632)

Myopia is relatively common in older populations, with reports indicating prevalence rates ranging from 15% (in those 49 years and older)¹ to 38.7% (in those aged 40-79 years).² Cataract is also common in older age groups, with

increasing age associated with increased prevalence^{3,4} and incidence.⁵ High myopia is known to be associated with cataract,⁶ and a relationship between myopia and cataract has been suggested.^{7,8} Other reports reject the association with myopia, instead explaining that a trend to myopia is the direct consequence of the presence of nuclear cataract.⁹

To date, few population-based studies have attempted to assess the association between myopia and cataract. Cross-sectional data from the Blue Mountains Eye Study have provided such evidence, showing an association between myopia and both nuclear and posterior subcapsular cataract.¹⁰ The cross-sectional association between myopia and nuclear cataract was supported by data from the Beaver Dam Eye Study.¹¹ The longitudinal data from Beaver Dam, however, noted increased incident nuclear cataract, and possibly incident cortical cataract, in hyperopic eyes. In that study no relationship was found between myopia and 5-year incident cataract, but a higher incidence of cataract surgery was reported in myopes.¹²

A laboratory-based study identified reduced antioxidant properties in myopic eyes compared with those with typical age-related cataract.¹³ Increased levels of lipid peroxidation by-products have been found in cataractous lenses and in the vitreous of myopes compared with control subjects and non-myopic cataractous lenses.^{13,14} An association was also shown between the degree of retinal lipid peroxidation and lens opacity in rodents.¹⁵ These studies provide a plausible explanation for the association between myopia and cataract and suggest that increasing myopia may be related to increasing damage to rod outer segments, which could lead to potentially cataractous by-products.

Our purpose in the present report is to assess the association between myopia and incident cataract and cataract surgery in a group of older Australians for whom baseline and follow-up information had been collected over a 5-year interval. These data could add further epidemiologic evidence to the debate about whether an association exists between myopia and cataract and may serve to guide laboratory-based studies in the search for biological explanations of cataract risk factors.

METHODS

The Blue Mountains Eye Study is a population-based study of vision and common eye diseases in an urban population aged 49 years or older, resident in two postal codes of the Blue Mountains region, west of Sydney, Australia. The baseline survey methods and procedures have been described.^{16,17} The study was approved by the Western Sydney Area Health Service Human Ethics Committee and signed, informed consent was obtained from all participants. The research was conducted according to the recommendations of the Declaration of Helsinki. During 1992 to 1994 at the baseline examinations, 3654 (82.4%) of the 4433 eligible residents aged 49 to 97 years were assessed. Five-year follow-up examinations were conducted during 1997 to 1999, when 2334 (75.1%) of the survivors were reexamined. Of those not seen, 383 (12.3%) had moved from the area, and 394 (12.7%) refused the examination.

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Questionnaire and Definitions

An interviewer-administered questionnaire enabled documentation of a detailed general medical and ocular history, as well as general demographic information. A history of myopia was sought by asking each participant whether he or she currently wore glasses to see clearly in the distance (including bifocals or multifocals), or had previously done so. If worn, the participant was asked at what age glasses were first used for clear distance vision. Data from this question were used only for participants with eyes having a measured myopic refractive error at baseline. Objective refraction was performed with an autorefractor (model 530; Humphrey, San Leandro, CA). This was followed by subjective refraction according to the Beaver Dam Eye Study modification of the Early Treatment Diabetic Retinopathy Study (ETDRS) protocol using a logarithm of minimum angle of resolution (logMAR) chart.^{17,18}

Baseline refraction data were used for analyses. The baseline refractive state was defined as the spherical equivalent refraction (SER), calculated by the algebraic addition of the best corrected spherical refraction and half the cylindrical refraction. Emmetropia was defined as a SER between +1 D and -1 D, hyperopia as more than +1 D, and myopia less than -1 D. Myopia was further classified as low (less than -1 D to more than -3.5 D), moderate (-3.5 D or less to more than -6 D) and high (-6 D or less). For those known to be myopic at baseline, the age at which distance glasses were first worn was used as a proxy for the onset and therefore duration of myopia. Hyperopia was also divided into low (greater than +1 D to less than +2 D), moderate (+2 D to less than +4 D), and high categories (+4 D or greater).

Participants were asked whether they smoked or consumed alcohol and whether oral or inhaled steroids had been prescribed in the past. They were asked whether they had angina (also described as "chest pain from your heart"), stroke, diabetes, or hypertension diagnosed by a doctor. Systolic and diastolic blood pressure was measured with the subject seated, before the use of any eye drops. Hypertension was defined either by history and/or a systolic measurement above 160 mm Hg and/or a diastolic measurement above 95 mm Hg. Diabetes was defined either by history or a fasting blood glucose level of 7.0 mmol/L or more. All blood samples were collected at a subsequent visit and later analyzed at Westmead Hospital. Sun-related skin damage was estimated by a clinical examiner on a four-point scale (none, mild, moderate, and severe) by assessing the arms, hands, and face.¹⁹ Participants had their weight (after removal of shoes and heavy clothing) and height measured. Body mass index was calculated as weight/height squared in kilograms per square meter, with obesity defined as a body mass index of 30 or greater. Higher educational achievement was defined as attainment of a qualification (certificate, diploma, or degree) after leaving school.

Cataract Grading

Cataract was documented by both slit lamp (Topcon SL-7e camera; Topcon Optical Co., Tokyo, Japan) and retroillumination (CT-R cataract camera; Neitz Instrument Co., Tokyo, Japan) lens photographs. Details of the photographic technique and grading^{3,16} used in the Blue Mountains Eye Study have been reported. The grading closely followed the Wisconsin Cataract Grading System,²⁰ with good agreement found for assessments of both inter- and intragrader reliability.³ History of past cataract surgery was confirmed at both the examination and photographic grading. At the follow-up study, graders were masked to baseline cataract status.

Presence of nuclear, cortical, and posterior subcapsular cataract was assessed in each eye.²⁰ Presence and severity of nuclear cataract was defined on a five-level scale by comparison with a set of four standard slit lamp photographs. Participants with nuclear grades 1 to 3 at baseline who developed nuclear grade level 4 or 5 at 5-year follow-up were defined as having incident nuclear cataract. The percentage area involved by cortical or posterior subcapsular cataract in each eye was calculated from the estimated percentage area involved in each of nine segments of the lens divided by a grid.²⁰ Participants with

less than 5% cortical opacity at baseline who then developed 5% or more of the total lens area involved at follow-up were defined as having incident cortical cataract. Participants with no posterior subcapsular cataract at baseline with the presence of any posterior subcapsular cataract at follow-up were defined as having incident posterior subcapsular cataract. The definitions of each of these incident cataract types were not mutually exclusive.

Statistical Analysis

Because refraction is eye specific, analyses were run according to eye rather than subject. These were performed with all eyes combined using a generalized estimating equation method described by Zeger et al.²¹ and Liang and Zeger.²² This method allows data from both eyes to be used while accounting for the correlation between the two eyes of a single subject. Cataract was analyzed as a dichotomous variable. Because age is strongly associated with cataract incidence⁵ and both increased cataract prevalence^{3,4,23-25} and incidence^{5,26} has been noted in women, all odds ratios are age- and sex-adjusted, unless otherwise stated. For comparison, logistic regression analyses were also performed in right and then left eyes for both hyperopia and myopia. All presented results are from multivariate models that adjust for the same potential confounders as found in the tables, including level of nuclear opacity.

The variables included in multivariate generalized estimating equation models varied by cataract type. Variables considered for inclusion were: age (categorically), sex, smoking (ever versus never), current alcohol consumption (drinks per week), ever used inhaled steroids, dark brown iris color, educational achievement, sun exposure (none versus any sun-related skin damage), obesity, severity of nuclear opacity (levels 1-5), and history of diabetes, hypertension, stroke, or angina. Each model included only variables associated with that cataract type, either from our own age- and sex-adjusted incident analyses or from reports for prevalent or incident cortical,^{25,27-30} nuclear,^{25,27,29,31,32} or posterior subcapsular cataract,²³ as well as for cataract surgery.²⁵

Statistical analysis was performed on computer (Statistical Analysis System, ver. 6.12; SAS Institute Inc, Cary, NC). $P < 0.05$ was used to indicate statistical significance. Odds ratio (OR) and 95% confidence interval (CI) are presented.

RESULTS

Over the 5-year period, nuclear cataracts developed in 593 (23.4%) eyes, cortical in 350 (9.8%) eyes, and posterior subcapsular in 100 (2.5%) eyes, according to data from both eyes. During this same period, 211 (4.7%) eyes underwent cataract surgery. Baseline aphakia, pseudophakia, or enucleation was present in 139 (3.0%) eyes, which were excluded from these analyses. The reported data refer to participants who attended both examinations and had gradable photographs from both visits. Approximately 8.7% of eyes had missing baseline and/or follow-up data for cortical or posterior subcapsular cataract, because photographs were ungradable or were not taken. A higher proportion (35.7%) had missing data for grading of nuclear cataract, predominantly because of an intermittent camera malfunction, as described in our previous report.³ There were no significant differences, however, between participants with and without gradable photographs.³

Of participants who returned for the 5-year examination, baseline refraction data were available on 4663 (99.9%) eyes, including 2218 (47.6%) emmetropic, 1925 (41.3%) hyperopic, and 520 (11.2%) myopic eyes. The myopic eyes included 330 (63.5%) with low myopia, 115 (22.1%) with moderate myopia, and 75 (14.4%) eyes with high myopia. Information about the age at which distance glasses were first worn was available for 464 eyes of participants with myopia (89.2%). In 52.6%, the age was 40 years more, in 25.6% between ages 20 and 39 years and

TABLE 1. Baseline Characteristics of Participants Who Did and Participants Who Did Not Attend the 5-Year Follow-up Examinations in the Blue Mountains Eye Study

Baseline Characteristic	Participants in Both	
	Examinations Included in Analyses (%)	Survivors Who Did Not Attend Follow-up (%)
Total	2278	777
Age		
<60	712 (31.3)	260 (33.5)
60-69	928 (40.7)	255 (32.8)
70-79	529 (23.2)	191 (24.6)
80+	109 (4.8)	71 (9.1)
Sex		
Female	1309 (57.5)	472 (60.8)
Male	969 (42.5)	305 (39.3)
Right eye refractive error		
Emmetropia	1074 (47.3)	362 (47.3)
Hyperopia	944 (41.6)	304 (39.7)
Myopia	253 (11.1)	100 (13.1)
Baseline prevalent cataract		
Cortical	473 (20.8)	154 (19.8)
Nuclear	239 (10.5)	88 (11.3)
Posterior subcapsular	110 (4.8)	49 (6.3)
Education	854 (39.3)	321 (45.1)
Inhaled steroids	241 (11.2)	61 (8.7)
Dark brown iris color	229 (10.3)	80 (10.5)

in 21.8%, before 20 years. The hyperopic eyes included 961 (49.9%) with low hyperopia, 836 (43.4%) with moderate hyperopia, and 128 (6.6%) with high hyperopia.

Baseline characteristics of participants in the 5-year follow-up examination who were included in any analyses and survivors of the baseline examination who did not attend follow-up are shown in Table 1. There were no statistically significant differences ($P < 0.05$) between these two groups. Of the 2334 participants in both examinations, 56 were not included in any analyses (44 because of nongradable photographs at baseline and 12 because of nongradable photographs at follow-up).

No statistically significant associations were found between hyperopia or any myopia (compared with emmetropia) and incident cortical cataract in either the age- and sex-adjusted or multivariate-adjusted models (Table 2). The only statistically

significant age- and sex-adjusted association found was between incident cortical cataract and moderate myopia (OR 1.8, 95% CI 1.0-3.4). This finding, however, was not statistically significant after adjustment for multiple potential confounders. It is well known that nuclear cataract is associated with a myopic shift.⁹ We therefore repeated our multivariate analyses to adjust further for the severity of nuclear opacity. This indicated no statistically significant association between moderate myopia and incident cortical cataract. In logistic regression analyses for right and left eyes, hyperopia was associated with incidence of cortical cataract in an age- and sex-adjusted model (OR 1.4, 95% CI 1.0-2.0), but not in a multivariate model that also accounted for level of nuclear opacity (OR 1.3, 95% CI 0.9-2.0). No statistically significant association was found, however, between hyperopia and incident cortical cataract in left eyes (data not shown).

A statistically significant increased risk of incident nuclear cataract (OR 1.2, 95% CI 1.0-1.5) was found in hyperopic compared with emmetropic eyes, after adjustment for age and sex (Table 3). However, this was not statistically significant in the multivariate model. An association between moderate hyperopia and incident nuclear cataract was statistically significant in the multivariate model (OR 1.4, 95% CI 1.1-1.9). Analyses for right eyes also showed a statistically significant association between hyperopia and incident nuclear cataract in an age- and sex-adjusted model (OR 1.4, 95% CI 1.0-1.9), though not in the model adjusting for multiple potential confounders (OR 1.3, 95% CI 0.9-1.8). No statistically significant association was found for left eyes (data not shown). Although no association was found with low or moderate myopia, eyes with high myopia had a statistically significant higher risk of incident nuclear cataract, adjusting both for age and sex (OR 3.1, 95% CI 1.5-6.5) and in the multivariate model (OR 3.3, 95% CI 1.5-7.4).

We found stronger associations between baseline refractive status and incident posterior subcapsular cataract. The presence of any myopia was associated with more than a doubling of the risk (5.4% vs. 2.1%) of incident posterior subcapsular cataract (OR 2.9, 95% CI 1.7-5.2), after adjustment for age and sex (Table 4). This relationship was similar after adjustment for multiple potential confounders (OR 2.6, 95% CI 1.4-5.0). Analyses for left eyes also showed a statistically significant association between incident posterior subcapsular cataract and myopia in multivariate models (OR 3.5, 95% CI 1.3-10.1),

TABLE 2. Odds Ratios and 95% Confidence Intervals (CI) for the Association between Baseline Refraction and Incident Cortical Cataract in All Eyes

	Age and Sex Adjusted					Multivariate Adjusted*		Multivariate Adjusted†	
	Eyes at Risk (n)	Incident Eyes (n)	%	Odds Ratio	95% CI	Odds Ratio	95% CI	Odds Ratio	95% CI
Emmetropia	1776	151	8.5	1.0	Referent	1.0	Referent	1.0	Referent
Any hyperopia	1418	163	11.5	1.1	0.9-1.5	1.2	0.9-1.5	1.1	0.8-1.4
Hyperopia‡									
Low	737	80	10.9	1.1	0.9-1.5	1.2	0.9-1.6	1.1	0.8-1.6
Moderate	594	72	12.1	1.2	0.9-1.7	1.2	0.9-1.7	1.1	0.7-1.6
High	87	11	12.6	1.3	0.6-2.6	1.4	0.7-2.8	1.1	0.5-2.7
Any myopia	381	35	9.2	1.1	0.7-1.7	1.0	0.7-1.6	0.7	0.4-1.3
Myopia§									
Low	231	15	6.5	0.8	0.5-1.5	0.8	0.4-1.5	0.5	0.3-1.2
Moderate	96	14	14.6	1.8	1.0-3.4	1.7	0.8-3.3	1.3	0.5-3.2
High	54	6	11.1	1.3	0.6-3.1	1.0	0.4-2.5	0.5	0.2-2.0

* Adjusted for age, sex, education, alcohol, sun exposure, diabetes, obesity, and stroke.

† Also adjusted for severity of nuclear opacity.

‡ Low hyperopia, greater than +1 D to less than +2 D; moderate hyperopia, +2 D to less than +4 D; high hyperopia, +4 D or greater.

§ Low myopia, less than -1 D to more than -3.5 D; moderate myopia, -3.5 D to more than -6 D; high myopia, -6 D or less.

TABLE 3. Odds Ratios and 95% Confidence Intervals (CI) for the Association between Baseline Refraction and Incident Nuclear Cataract in All Eyes

	Age and Sex Adjusted					Multivariate Adjusted*	
	Eyes at Risk (n)	Incident eyes (n)	%	Odds Ratio	95% CI	Odds Ratio	95% CI
Emmetropia	1243	235	18.9	1.0	Referent	1.0	Referent
Any hyperopia	1036	312	30.1	1.2	1.0-1.5	1.1	0.9-1.5
Hyperopia†							
Low	536	134	25.0	1.1	0.8-1.4	1.0	0.8-1.3
Moderate	438	163	37.2	1.6	1.2-2.1	1.4	1.1-1.9
High	62	15	24.2	0.9	0.5-1.8	0.9	0.5-1.8
Any myopia	256	46	18.0	1.1	0.7-1.6	1.0	0.7-1.5
Myopia‡							
Low	151	21	13.9	0.8	0.5-1.3	0.7	0.4-1.2
Moderate	71	14	19.7	1.3	0.6-2.6	1.2	0.5-2.7
High	34	11	32.4	3.1	1.5-6.5	3.3	1.5-7.4

* Adjusted for age, sex, smoking, education, dark brown iris color, and inhaled steroids.

† Low hyperopia, greater than +1 D to less than +2 D; moderate hyperopia, +2 D to less than +4 D; high hyperopia, +4 D or greater.

‡ Low myopia, -1 D to more than -3.5 D; moderate myopia, -3.5 D to more than -6 D; high myopia, -6 D or less.

although this was not found for right eyes (OR 1.4, 95% CI 0.4-5.4). Although the odds for posterior subcapsular cataract were increased in low myopia, only the association with moderate or high myopia was statistically significant, after adjustment for age and sex (OR 5.7, 95% CI 2.8-11.6), and in the multivariate model (OR 5.4, 95% CI 2.5-11.9). After adjustment was made for severity of nuclear opacity, the associations between any myopia (OR 2.1, 95% CI 1.0-4.8) and moderate or high myopia (OR 4.4, 95% CI 1.7-11.5) remained strong and statistically significant (Table 4). There was no statistically significant association between hyperopia and incident posterior subcapsular cataract.

The presence of any myopia was strongly associated with incident cataract surgery in age- and sex-adjusted analyses (OR 2.8, 95% CI 1.8-4.5) and there were statistically significant associations of low, moderate, and high myopia with incident cataract surgery (Table 5). All findings remained statistically significant, after adjustment for multiple potential confounders. Multivariate models also showed statistically significant

associations between myopia and incident cataract surgery in logistic regression analyses for right (OR 2.3, 95% CI 1.0-5.6) and left eyes separately (OR 4.1, 95% CI 1.8-9.2). No significant associations were found between hyperopia and incident cataract surgery.

In attempting to quantify the effect of duration of myopia, we used the age that participants stated as that at which they had first worn glasses for distance vision. Duration of myopia was not associated with incident cortical or nuclear cataract (data not shown). Myopic subjects who began wearing distance glasses before age 40 had a significantly higher incidence of posterior subcapsular cataract after adjustment for age and sex. This was found both for those first wearing glasses before age 20 (OR 3.5, 95% CI 1.7-7.3) and for those first wearing glasses between ages 20 and 39 years (OR 4.5, 95% CI 1.8-11.5). The relationship, however, was only statistically significant for the subgroup wearing distance glasses for the longest period (Table 6), when multiple confounders were controlled for, including the level of nuclear opacity. Both the longest-

TABLE 4. Odds Ratios and 95% Confidence Intervals (CI) for the Association between Baseline Refraction and Incident Posterior Subcapsular Cataract in All Eyes

	Age and Sex Adjusted					Multivariate Adjusted*		Multivariate Adjusted†	
	Eyes at Risk (n)	Incident Eyes (n)	%	Odds Ratio	95% CI	Odds Ratio	95% CI	Odds Ratio	95% CI
Emmetropia	1925	41	2.1	1.0	Referent	1.0	Referent	1.0	Referent
Any hyperopia	1647	38	2.3	0.8	0.5-1.4	0.8	0.5-1.4	1.0	0.5-1.8
Hyperopia‡									
Low	825	21	2.6	1.0	0.6-1.7	1.0	0.6-1.8	1.3	0.7-2.5
Moderate	721	13	1.8	0.6	0.3-1.2	0.6	0.3-1.2	0.6	0.2-1.4
High	101	4	4.0	1.6	0.6-4.5	1.7	0.6-5.1	2.3	0.7-8.1
Any myopia	388	21	5.4	2.9	1.7-5.2	2.6	1.4-5.0	2.1	1.0-4.8
Myopia§									
Low	240	8	3.3	1.9	0.9-4.2	1.9	0.8-4.7	1.3	0.4-4.3
Moderate/high	148	13	8.8	5.7	2.8-11.6	5.4	2.5-11.9	4.4	1.7-11.5

* Adjusted for age, sex, education, obesity, and hypertension.

† Also adjusted for severity of nuclear opacity.

‡ Low hyperopia, greater than +1 D to less than +2 D; moderate hyperopia, +2 D to less than +4 D; high hyperopia, +4 D or greater.

§ Low myopia, less than -1 D to more than -3.5 D; moderate myopia, -3.5 D to more than -6 D; high myopia, -6 D or less.

TABLE 5. Odds Ratios and 95% Confidence Intervals (CI) for the Association between Baseline Refraction and Incident Cataract Surgery in All Eyes

	Age and Sex Adjusted					Multivariate Adjusted*		Multivariate Adjusted†	
	Eyes at Risk (n)	Incident Eyes (n)	%	Odds Ratio	95% CI	Odds Ratio	95% CI	Odds Ratio	95% CI
Emmetropia	2137	76	3.6	1.0	Referent	1.0	Referent	1.0	Referent
Any hyperopia	1875	84	4.5	0.8	0.5-1.1	0.8	0.6-1.2	0.8	0.5-1.3
Hyperopia‡									
Low	938	35	3.7	0.8	0.5-1.2	0.9	0.6-1.3	0.8	0.5-1.5
Moderate	827	44	5.3	0.8	0.5-1.2	0.8	0.5-1.4	0.9	0.5-1.6
High	110	5	4.6	0.9	0.3-2.4	1.3	0.5-3.1	0.9	0.2-4.1
Any myopia	479	50	10.4	2.8	1.8-4.5	3.2	1.9-5.3	2.1	1.1-4.2
Myopia§									
Low	294	30	10.2	2.5	1.4-4.5	2.7	1.3-5.3	1.5	0.5-4.3
Moderate	113	8	7.1	2.7	1.2-5.8	3.6	1.5-8.6	2.9	1.2-7.3
High	72	12	16.7	5.0	2.4-10.3	5.5	2.3-13.2	3.4	1.0-11.3

* Adjusted for age, sex, education, inhaled steroids, diabetes, dark brown iris color, and angina.

† Also adjusted for severity of nuclear opacity.

‡ Low hyperopia, greater than +1 D to less than +2 D; moderate hyperopia, +2 D to less than +4 D; high hyperopia, +4 D or greater.

§ Low myopia, less than -1 D to more than -3.5 D; moderate myopia, -3.5 D to more than -6 D; high myopia, -6 D or less.

and shortest-duration subgroups had statistically significant associations with incident cataract surgery after adjustment for age and sex and for multiple confounders, but not when the level of nuclear opacity was included in the model (Table 7).

DISCUSSION

Our previous report of cross-sectional associations between refractive error and cataract suggested a strong relationship between myopia and posterior subcapsular cataract that reflected the apparent duration of myopia.¹⁰ The present report of incident posterior subcapsular cataract provides support for this hypothesis. Because posterior subcapsular cataract rapidly progresses to cataract surgery, the significant relationship found between myopia and incident cataract surgery, particularly for long-duration myopes, adds further support.

An important limitation of this report is that using the age at which distance glasses were first worn as a proxy for onset of myopia does not take into account the many factors that impact on the decision to start wearing glasses. As pointed out by Wong et al.¹¹ in the Beaver Dam Eye Study report on the relationship between refractive errors and incident cataract, poor memory and interpretation of this question may be relevant factors and may have played a role in the reported inconsistencies between a history of wearing distance glasses, the age at first wearing, and prevalent age-related cataract.^{11,33}

Similarly, the decision to undergo cataract surgery, particularly on a second eye, takes into account many factors other

than severity of cataract. In our effort to counter the possibility that statistically significant associations with myopia may have been due to the presence of baseline nuclear cataract, interpretation of those adjusted results was limited by the fact that a significant proportion of participants had missing baseline data for nuclear cataract because of random camera malfunction (so reducing the power of our analyses). Our definitions of incident cortical and nuclear cataract may also pose a limitation. Presence of less than 5% baseline cortical opacity and baseline nuclear grades 1 to 3 were not considered to be cataract. Although we sought to encompass a level of clinically significant cataract to define cataract incidence, inclusion of any baseline cataract may have had a minor influence on our findings.

Strengths of our study include its high participation rate from a well-defined urban residential population. Information was collected about a large number of potential confounders as well as detailed information on refractive status.¹ Documentation of cataract status, based on reproducible grading of lens photographs according to the Wisconsin System, is a further strength. Graders of the prospective lens photographs were masked to refractive state and so could not be influenced by selection bias.

The development of age-related cataract is widely known to be associated with a myopic shift in refraction, principally by progression of the level of opacity within the lens nucleus.⁹ The Visual Impairment Project demonstrated a strong cross-sectional association between myopia and nuclear opacity,^{24,34}

TABLE 6. Odds Ratios and 95% Confidence Intervals (CI) for the Association between Baseline Age at Which Distance Glasses Were First Worn in Myopes and Incident Posterior Subcapsular Cataract in All Eyes

Age Distance Glasses First Worn (y)	Age and Sex Adjusted				Multivariate Adjusted*		Multivariate Adjusted†		
	Eyes at Risk (n)	Incident Eyes (n)	%	Odds Ratio	95% CI	Odds Ratio	95% CI	Odds Ratio	95% CI
Never	1925	41	2.1	1.0	Referent	1.0	Referent	1.0	Referent
40+	58	3	5.2	2.3	0.7-7.5	2.0	0.5-7.8	2.8	0.6-13.1
20-39	96	7	7.3	4.5	1.8-11.5	3.8	1.3-10.6	2.4	0.5-11.8
0-19	202	11	5.5	3.5	1.7-7.3	3.6	1.5-8.8	3.0	1.0-9.3

* Adjusted for age, sex, education, inhaled steroids, diabetes, dark brown iris color, obesity, and hypertension.

† Also adjusted for severity of nuclear opacity.

TABLE 7. Odds Ratios and 95% Confidence Intervals (CI) for the Association between Baseline Age at Which Distance Glasses Were First Worn in Myopes and Incident Cataract Surgery in All Eyes

Age Distance Glasses First Worn (y)	Age and Sex Adjusted					Multivariate Adjusted*		Multivariate Adjusted†	
	Eyes at Risk (n)	Incident Eyes (n)	%	Odds Ratio	95% CI	Odds Ratio	95% CI	Odds Ratio	95% CI
Never	2137	76	3.6	1.0	Referent	1.0	Referent	1.0	Referent
40+	86	23	26.7	4.7	2.3-9.4	4.9	2.2-11.1	2.2	0.8-6.3
20-39	112	5	4.5	1.3	0.3-5.6	1.4	0.2-8.8	1.1	0.1-13.0
0-19	238	15	6.3	2.5	1.3-4.8	3.0	1.5-6.3	2.0	0.8-5.3

* Adjusted for age, sex, education, inhaled steroids, diabetes, dark brown iris color, and angina.

† Also adjusted for severity of nuclear opacity.

as did the Barbados Eye Survey.³⁵ In the 5-year examinations of the Beaver Dam Eye Study, participants with the highest levels of nuclear opacity at baseline were more likely to have a myopic shift in refraction.³⁶

As cataract is frequently mixed, it is reasonable to adjust for the level of nuclear opacity when examining the impact of myopia on development of other cataract types. Our study indicates that myopia was related to incident posterior subcapsular cataract (as well as incident cataract surgery), after taking into account the effects both from multiple confounders plus the level of nuclear opacity. Adjustment for level of nuclear opacity, however, may be less important in assessing longitudinal associations, as we used the baseline refractive state to evaluate the impact of refractive error on development of cataract over time. The moderately strong relationship found between incident posterior subcapsular cataract and either moderate or high myopia at baseline argues that myopic shift may not be a relevant influence. It could be expected that further cataract-associated myopic shifts would be of a low magnitude.

The apparent relationship found in our study between duration of myopia and both incident posterior subcapsular cataract and incident surgery provides further support for a true association between myopia and this cataract type. This was seen for both longer-duration subgroups, but was strongest and statistically significant only in the fully adjusted model for those myopic subjects who reported wearing glasses for the longest period.

Apart from the association found with posterior subcapsular cataract, our data provide no evidence for a relationship between myopia, or other refractive error, and cortical cataract. Incident nuclear cataract was unrelated to baseline low or moderate magnitude myopia, but a relationship was found with high myopia, after adjustment for confounders. A weak relationship was observed between incident nuclear cataract and moderate hyperopia. There was, however, no statistically significant relationship with any hyperopia, and the odds ratios in the hyperopia categories did not show a dose-response relationship, suggesting that this finding could be spurious.

Although our prevalence findings suggested a protective influence of hyperopia for posterior subcapsular cataract,¹⁰ this was not supported longitudinally, either in our current data or from the Beaver Dam Eye Study data.¹¹ The Beaver Dam findings reported a significant trend ($P = 0.02$) for increasing myopia and higher prevalence of posterior subcapsular cataract. This was not, however, supported by their incidence data. In contrast, our longitudinal data supported the cross-sectional associations found with any myopia or high myopia and in persons with onset of myopia in their youth.

Small posterior subcapsular opacities may cause significant visual disturbance because of their central location in the visual axis. Because these opacities thus have a propensity to

progress to cataract surgery relatively quickly compared with nuclear or cortical opacities, it seems reasonable to consider incident cataract surgery as a surrogate for the development of posterior subcapsular cataract. The number of incident posterior subcapsular cataract cases may also be limited because of varying thresholds for cataract surgery.

The Beaver Dam Eye Study found a statistically significant association between baseline myopia and 5-year incident cataract surgery,^{11,12} as well as a significant trend ($P = 0.003$) for the relationship between increasing levels of myopia and increased incidence of cataract surgery.¹¹ Our longitudinal results provide strong support for this finding, with significant associations present between myopia at all levels and in all models examined, apart from low myopia in the multivariate model that adjusted for severity of nuclear cataract.

Our finding of a link between myopia and cataract is supported by data from several other studies.^{2,24,37-41} The Visual Impairment Project reported a statistically significant association between myopia (defined as ≥ 1 D) and cortical, nuclear, and posterior subcapsular cataract.^{24,37} The Melton Mowbray Eye Study reported a higher prevalence of cataract in myopes.³⁸ Participants who had worn eye glasses before age 20 (used as an indicator for myopia) had a higher relative risk (RR) for nuclear cataract in the Longitudinal Study of Cataract (RR 1.37, 95% CI 0.97-1.95),⁴⁰ and a higher risk of development of mixed cataract in the Lens Opacities Case-Control Study (OR 1.44, 95% CI 1.06-1.94).³⁹ In an Oxfordshire case-control study of patients who had had cataract surgery and control subjects aged between 50 and 79 years,⁴² a statistically significant increased risk of cataract was found in participants with a history of childhood myopia (RR 1.68, 95% CI 1.2-2.4). In several reports in which the records of patients who had undergone cataract surgery were reviewed,^{7,8} myopes were found to be more likely to undergo surgery than nonmyopes.

Biological plausibility of this association has been provided by a number of laboratory-based studies. Development of cataract in myopic lenses has been shown to be related to oxidative changes in lens proteins,⁴³ with glutathione a potential inhibitor of this oxidation.⁴⁴ Compared with healthy control subjects, cataractous lenses had lower levels of glutathione, with the lowest levels found in myopic lenses.¹³ Increased levels of malondialdehyde (MDA) have been found in cataractous lenses and in the vitreous of myopes compared with control subjects and nonmyopic cataract lenses.^{13,14} Because MDA is a breakdown product of lipid peroxidation, the vitreous finding suggests a retinal source. Rod outer segments are particularly susceptible to lipid peroxidation because of the high concentration of polyunsaturated lipid in their membranes.

One study has shown a correlation between degree of retinal lipid peroxidation and extent of lens damage.¹⁵ A subsequent study has shown a correlation between the level of

thiobarbituric acid reactive substances (also indicating lipid peroxidation) in the subretinal fluid of patients who undergo retinal detachment surgery and the degree of myopia.⁴⁵ These results suggest that increasing myopia may be related to increasing damage of rod outer segments and that by-products of this process may affect various ocular structures, including the lens. This could explain the higher prevalence and incidence, particularly of posterior subcapsular cataract and nuclear cataract, in myopic eyes.

Myopia increases the risk of glaucoma^{35,46} as well as retinal detachment, myopic retinal degeneration, visual impairment, and blindness.⁴⁷ The present study builds on our earlier finding¹⁰ in suggesting that myopia may increase the risk of posterior subcapsular cataract, one of the important predictors of cataract surgery. This finding is potentially important, given the increasing prevalence of myopia in East Asia,^{48,49} the United States,⁵⁰ and elsewhere.⁵¹

In this study, we assessed the association between baseline refraction and the 5-year incidence of cataract and cataract surgery. We have been able to provide epidemiologic evidence to confirm the previously noted increased risk of posterior subcapsular cataract in eyes with high myopia. We have also provided evidence to support the hypothesis that this type of cataract may develop more frequently in eyes with lower levels of myopia. These longitudinal data support our cross-sectional findings as well as the findings from some, but not all,¹¹ population-based reports. Previously, this association was considered because of the myopic shift from increasing nuclear opacity and was thought unlikely to be causally related.³⁷ Our data suggest the possibility of a causal relationship. Although some laboratory-based studies support a plausible biological basis, further studies are needed.

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MYOPIA AND HYPEROPIA IN CHILDREN: The Latest Wisdom

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BACKGROUND

Refractive error is the general term used to describe the "glasses prescription" of an eye. If the eye is perfectly focused for distance, that eye is emmetropic, and light from a distant object focuses on the retina at the back of the eye. The eye, then, naturally focuses (or "accommodates") for near until the age where a person needs reading glasses or bifocals (presbyopia).

Myopia, or nearsightedness, occurs with a general population prevalence as high as 25% in the United States, with much higher rates of myopia being reported in Asian countries. The underlying problem in myopia is that the length of the eye is too long for its focusing ability. In contrast to emmetropia, light from a distant object focuses in front of the retina, producing a blurry image on the retina itself. Glasses, contact lenses, or laser refractive surgery actually decrease the eye's optical power to move the focus back to the appropriate place on the retina. The field of myopia has generated considerable interest with the advent of laser refractive surgery, and the specific health care and general societal costs of myopia correction—however it is accomplished—are high, on the order of billions of dollars per year in the United States alone.

Hyperopia is, in some sense, the reverse of myopia. Hyperopic, or farsighted eyes, are too short for the eye's optics, and light from a distant object focuses in back of the retina. During childhood and young adulthood, many hyperopes do not need to wear glasses because the eye's natural focusing ability can "power up" the eye's optics and move the focus to the retina. As that focusing ability decreases with age, the person would notice he or she cannot see as well. The symptoms experienced by children who are significantly farsighted are not usually related to blur but instead

are the symptoms of eyestrain: headache, difficulty reading for a long time, eye turns, etc. **Figure 1** compares and contrasts the optics of emmetropic, myopic, and hyperopic eyes.

Causes of Myopia: The National Eye Institute, a division of the National Institutes of Health, has funded a portfolio of research on myopia in the past 15 years. As treatments for myopia have been pursued, there are conflicting theories about its cause. Classically, these theories can be summarized as nature versus nurture, i.e., a genetic theory versus an environmental theory in which near work and reading cause the axial ocular elongation of myopia.

The genetic argument is as follows. Myopic parents are more likely to produce myopic children (30–40% chance for two myopic parents, 25% chance for one myopic parent, <10% chance for no myopic parents). Identical twins' refractive error is more similar than fraternal twins or siblings. Children who are not yet myopic who have myopic parents have eyes that are anatomically long, like a myope, even before the children themselves develop myopia. The environmental risk factor most often cited is excess near work. There is evidence of statistical association between myopia and increasing education and higher amounts of near work. Work on animal models of myopia shows the profound influence the visual environment can have on the development of experimentally created myopia.

Diagnosis of Myopia: Juvenile onset myopia is most likely to develop between the ages of 8 and 14 years and progress to age 15–16 years; it stops sooner in girls than in boys. Children often are unaware that they are becoming nearsighted. They may notice that things are blurry far away, but they rarely report the observation to parents or teachers. Adults may notice that a child is squinting his or her eyes to see, or a teacher may find that a child pays better attention when seated in the front of the

class. These may be early signs of nearsightedness, or the diagnosis of myopia may simply be made during a vision screening at school or during a routine eye examination. A full eye examination is necessary to diagnose myopia and to prescribe appropriate spectacles or contact lenses. Children with myopia continue to progress (i.e., distant objects get blurry again after some time), and annual eye examinations are a must for the myopic child.

Treatment of Myopia: There are a number of studies just completed or underway that will yield more information about the treatment of juvenile onset myopia. Possible treatments fall into three main categories, all aimed at slowing the abnormal growth of the eye. First, antimuscarinic agents, topical eye drops that have been shown to react with the retina to modulate eye growth in animals, appear

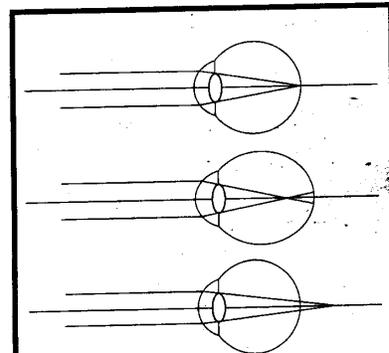


Figure 1. These drawings depict the eye in cross-section. The bulge at the front of the eye is the cornea, and the small oval represents the crystalline lens inside the eye. These two components bend light to focus it in the eye. The emmetropic eye (top) focuses light from a distant object on the retina. The myopic eye (middle) focuses light in front of the retina because the eye is too long. The hyperopic eye (bottom) focuses light behind the retina because the eye is too short.

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to slow eye growth (e.g., atropine). Unfortunately, these drops also dilate the pupil and paralyze the ability of the eye to focus up close. Bifocal spectacles have been associated with slowing the progression of myopia and so have rigid contact lenses.

There are clinical trials going on in the United States and Asia today with a new eye drop that may slow the growth of the eye without producing the unwanted side effects. The drug is called pirenzepine, and it is put in each eye twice a day. Results are pending from the first clinical trials of this eye drop in children (<http://www.valleyforgepharmaceuticals.com/qset2.html>).

A randomized clinical trial of bifocal spectacles in school-aged children was conducted at Northeastern University in Tahlequah, Oklahoma and published in 2000. It showed a 20% treatment effect, i.e., the children wearing bifocals had their myopic progression slowed by only 20% compared to the children wearing regular glasses to correct their myopia. A larger study, the Correction of Myopia Evaluation Trial (COMET), is expected to release its results within the next year or so (<http://www.nei.nih.gov/neitrials/static/study9.htm>). Bifocals for myopia control are designed to eliminate near work as a risk factor for myopia progression. If they work, the results will, in some ways, validate the "nurture" theory of myopia; if they are ineffective, the theory comes into question.

Rigid contact lenses have been touted as a way to slow the progression of myopia, through an unknown mechanism. There is a randomized clinical trial underway at Ohio State comparing the effect of rigid and soft contact lenses on myopia progression (<http://www.nei.nih.gov/neitrials/static/study81.htm>).

Despite layperson's claims to the contrary, there is no evidence that wearing glasses or contact lenses promotes myopia progression, and holistic methods to decrease myopia like the currently popular *See Clearly Method* are dubious. Although the idea that nursery illumination (i.e., night lights) before the age of two could cause myopia during childhood was raised several years ago, additional research has shown this risk factor to be unimportant. Laser refractive surgery is not recommended for people under the age of 21, mostly because eyes may still be developing in the late teens.

Diagnosis of Hyperopia: Hyperopia is much less common than myopia and is less studied. Children are not particularly reliable in reporting symptoms of eye strain, headache, or avoidance of near tasks. Farsightedness can be very difficult to de-

tect in children without a complete eye examination, primarily because of the ability of children's eyes to focus to compensate for the farsightedness. Uncorrected hyperopia is associated with inward eye turns (esotropia), so early detection, diagnosis, and treatment is important for affected children. Uncorrected hyperopia can make reading difficult, as the hyperopic child has to focus his eyes more and work harder than an emmetrope does to do near work. A dilated eye examination with measurement for glasses prescription after dilation is usually necessary to make a definitive diagnosis.

Treatment of Hyperopia: Hyperopia is treated with spectacles or contact lenses that decrease the optical power of the eye and keep the eye from having to focus to compensate for the farsightedness. Children with lower amounts of hyperopia who are symptomatic at near may be prescribed glasses just for reading. Children with higher amounts of hyperopia and/or an inward eye turn are prescribed glasses for constant wear. It is a common misconception that children may outgrow their farsightedness. We examined our data from a group of 33 moderate to high hyperopes between the ages of 6 and 14 and found that their farsightedness increased a small amount per year but did not decrease or resolve, with or without correction. This result argues for early correction of moderate to high hyperopia, even in the absence of an eye turn or marked symptoms on the part of the child.

The Orinda Longitudinal Study of Myopia and Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error in Children (CLEERE) Study (<http://www.nei.nih.gov/neitrials/static/study72.htm>, <http://spectacle.berkeley.edu/cleere/>): Our work in myopia and hyperopia in children focuses on prediction of myopia onset and assessment of risk factors in a diverse study group. The treatments outlined above for myopia in childhood all attempt to slow down the progression of myopia in already myopic children. If any of these treatments prove to be effective, it would be logical to extend them to include attempts to prevent the onset of myopia in children at risk for myopia. A clinical battery of tests that eye care practitioners could use to predict who is at risk for myopia is vital.

From 1989-2000, we conducted a longitudinal study of children between the ages of 6 and 14 in Orinda, California. We found that glasses prescription in third grade is highly predictive of myopia; the

closer a child is to being myopic at age 8 or 9, the more likely he or she is to develop full-blown myopia by age 14. Other clinical measurements of the eye, including its overall length, are also predictive of myopia.

In 1997, we enrolled 2,523 children (534 African American, 491 Asian, 463 Hispanic, 1,035 White) in school grades 1-8 from Eutaw, Alabama (through the University of Alabama at Birmingham School of Optometry); Irvine, California (through the Southern California College of Optometry); Houston, Texas (through the University of Houston College of Optometry); and Orinda, California (through The Ohio State University School of Optometry and the University of California, Berkeley School of Optometry). We have since added a site predominantly to recruit Native American children in Tucson, Arizona, through the auspices of the University of Arizona Department of Ophthalmology. In this study population, 9.2% of the children were myopic, 12.8% were hyperopic, and 28.4% were astigmatic. There were significant differences in the refractive error prevalences as a function of ethnicity (χ^2 , $p < 0.0001$), even after controlling for age and gender (polychotomous logistic regression, $p < 0.0001$). For myopia, Asians had the highest prevalence (18.5%), followed by Hispanics (13.2%). The Asians' risk of myopia compared to emmetropia did not differ from Hispanics ($p = 0.24$). Whites had the lowest prevalence (4.4%), which was not significantly different from African Americans (6.5%). For hyperopia, Whites had the highest prevalence (19.3%), followed by Hispanics (12.7%). Asians had the lowest prevalence (16.3%) and were not significantly different from African Americans (6.4%).

SUMMARY

In general, refractive error and its correction are important public health issues. The National Eye Institute stated that "...the loss of productivity and function due to refractive error may be said to rival that due to headache or the common cold." The popularity of laser refractive surgery among adults highlights the marked influence that myopia in particular has on lifestyles and everyday activities. Uncorrected refractive error during the elementary school years may affect school performance and influence a child's propensity for sports or physical activities. Education of parents so that they understand myopia, hyperopia, and the difference between the two, the importance of regular eye care, and the consequences of decisions they make about their children's eyes is warranted.