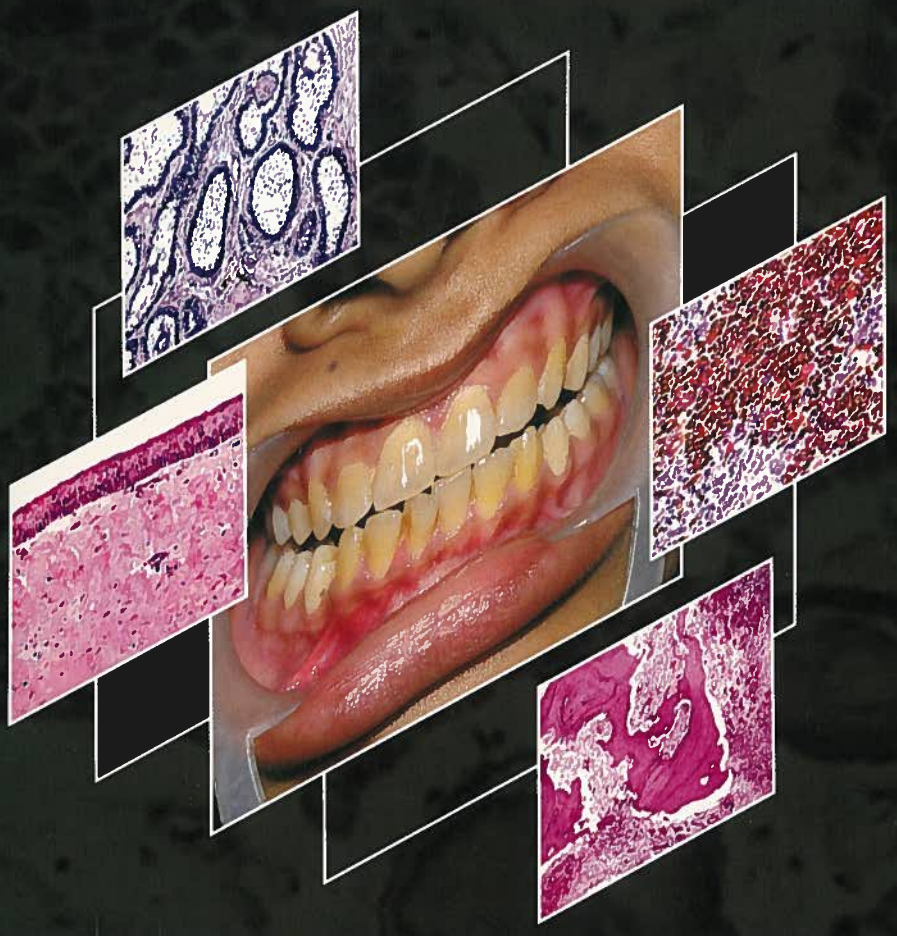

THIRD EDITION

Essentials of ORAL PATHOLOGY

Swapan Kumar Purkait

Forewords
RR Paul
Jay Gopal Ray
Tamal Kanti Pal

JAYPEE

Essentials of Oral Pathology

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Contents

CHAPTER 3

Oral Precancerous Lesions and Conditions

Oral cancers are sometimes preceded by some clinically visible lesions, which are noncancerous to begin with and have therefore been termed as "precancers". However, it is widely understood that neither do all the precancerous lesions progress to cancer, nor all cancers necessarily originate from such lesions.

According to the World Health Organization (WHO), the oral precancerous state is divided into two board groups: (i) precancerous lesions and (ii) precancerous conditions.

PRECANCEROUS LESION

A precancerous lesion is defined as **'a morphologically altered tissue in which cancer is more likely to occur than in its apparently normal counterpart'** -WHO 1978.

- **Leukoplakia, erythroplakia, stomatitis nicotina, chronic candidiasis**, etc. are the common examples of precancerous lesions found in the oral cavity.

PRECANCEROUS CONDITION

A precancerous condition is defined as **'the generalized state of the body, which is associated with a significantly increased risk of cancer'**- WHO 1978

- **Oral submucous fibrosis, sideropenic dysphagia (mucosal atrophy with chronic iron deficiency anemia), syphilis and oral lichen planus**, etc. fall into this category.

Examples of precancerous lesions and conditions

Precancerous lesions:	• Erythroplakia • Stomatitis nicotina • Chronic candidiasis • Leukoplakia
Precancerous conditions:	• Syphilis • Oral lichen planus • Oral submucous fibrosis • Sideropenic dysphagia

It is important to note that all these precancerous lesions and conditions mentioned above, produce a wide variety of clinical and histopathological features, but the most important criteria for evaluating their malignant potential is the microscopic study of "epithelial dysplasia". It has been reported by a large number of investigators that the "dysplastic" lesions carry a risk of malignant transformation, which is nearly 15 times higher than the non dysplastic lesions.

LEUKOPLAKIA

DEFINITION

Leukoplakia can be defined as a **"white patch"** or **"plaque"** in the oral cavity, which cannot be scrapped off or stripped off easily and more over, which cannot be characterized clinically or pathologically as any other disease"- WHO 1978.

This definition was revised five years later at the International Conference and the new definition states that "leukoplakia is a white patch or plaque in the oral cavity, which cannot be scrapped off or stripped off easily and which cannot be characterized clinically or pathologically as any other disease and it is not associated with any physical or chemical agents except the use of tobacco"

PRELEUKOPLAKIA

This is a grayish or grayish-white, slightly lobular lesion of oral mucosa with ill-defined borders.

ETIOLOGY OF LEUKOPLAKIA

The exact etiology of leukoplakia is unknown but a large number of factors have been implicated for their occurrence, which are known as the "predisposing" factors. The common predisposing factors for leukoplakia are tobacco, alcohol,

candidiasis, dietary deficiency, syphilis, viral infections, hormonal imbalance, chronic irritation, galvanism and actinic radiation, etc.

Among these, tobacco is considered to be the single most important factor.

Etiological factors of leukoplakia

- Tobacco (in smoking and smokeless forms)
- Alcohol
- Candidiasis
- Dietary deficiency
- Syphilis
- Viral infections
- Hormonal imbalance
- Chronic irritation
- Actinic radiation
- Galvanism

Tobacco

- It is used by large number of people in various forms, such as smoking of cigarettes, cigars, pipes and beedes (country-made cigarettes), tobacco chewing and snuff dipping, etc.
- All these types of tobacco habits are important for the development of leukoplakia and it has been confirmed that the people those who use tobacco in any form, develop leukoplakia more often than the people those who do not use them.
- Furthermore, the leukoplakic lesions (Fig. 3.1) regress significantly more often when the tobacco habits are discontinued or reduced, as compared to when the habits remain unchanged or continued.
- It is believed that during smoking a significantly large amount of tobacco end products are produced in the oral cavity, these products in association with the heat, (generated during smoking) cause severe irritation to the oral mucous membrane and finally results in the development of leukoplakia.
- An important observation in this regard is the higher rate of occurrence of leukoplakia among the "reserve smokers" (those who keep the burning end of the cigarettes inside the mouth).
- Finally, it is important to note that the risk of development of leukoplakia in a person depends upon the frequency and duration of the tobacco habits, and the age and sex of the person concerned.

Alcohol

Alcohol itself is not an important risk factor for leukoplakia but many people may develop leukoplakia who consume alcohol as well as use tobacco in some form. Therefore, it is believed that the synergistic effect of tobacco and alcohol both, increase the risk of leukoplakia more often than in cases where a single habit is practiced.

Candidiasis

Chronic candidal infections are often associated with leukoplakia, however, it is not very clear whether the fungi are directly responsible for the initiation of the disease or they are only producing secondary infections in a pre-existing leukoplakia. However, it has been observed that the Candida associated leukoplakias develop more epithelial dysplasia than the non candidal lesions.

Dietary Deficiency

Deficiency of Vitamin A causes metaplasia or hyperkeratinization of the epithelium, which may eventually result in the development of leukoplakia. Deficiency of vitamin B complex may also cause leukoplakic changes in the mucosa, but the exact pathogenesis is not clear.

Syphilis

In the older literatures, syphilis was considered to be a very important predisposing factor in the development of leukoplakia, especially the tertiary stage of the disease, which presents mucous patches over the tongue and buccal mucosa. However, recent reports indicate that the syphilitic infections play only a minor role in the causation of leukoplakia.

Viral Infections

Experimental studies indicate that, oral mucosal infections caused by the herpes virus hominis type I (HSV–I) and human papilloma virus

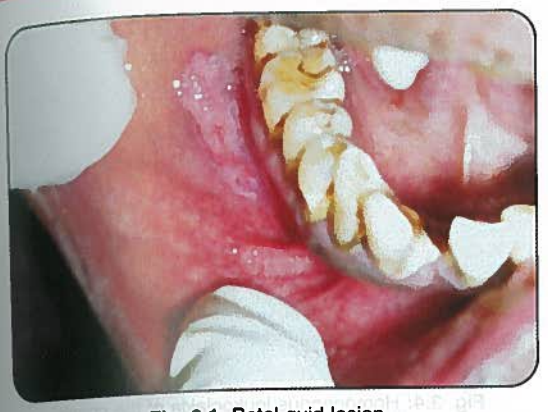

Fig. 3.1: Betel quid lesion

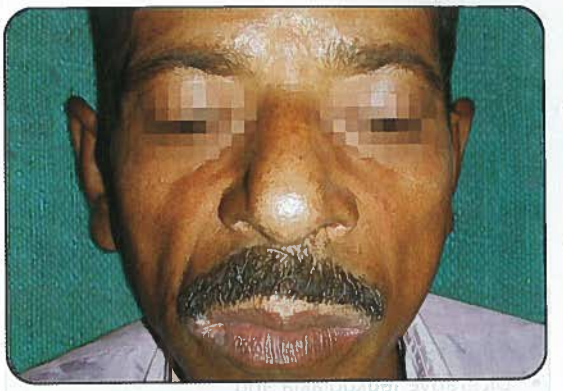

Fig. 3.2: Leukoplakia at commisure

may have some role in the development of leukoplakia.

Hormonal Imbalance

Imbalance or dysfunctions of both male and female sex hormones may induce some keratogenic changes in the oral epithelium and these changes may ultimately lead to the development of leukoplakia.

Chronic Irritation

Chronic irritation to the mucosa by ill-fitting dentures, sharp cuspal edges of teeth and hot or spicy foods, etc. may cause leukoplakia.

Actinic Radiation

Actinic or solar radiation may bring about some hyperkeratotic changes in the oral mucosa, especially the lip mucosa and this can be a predisposing factor for leukoplakia in rare cases.

Galvanism

Galvanic reactions may occur in the oral cavity when there is difference in the electrical potential between two dissimilar metallic restorations. These reactions often lead to the development of leukoplakia in the oral mucosa.

CLINICAL FEATURES OF LEUKOPLAKIA

Age: Usually, the lesion occurs in the fourth, fifth, sixth and seventh decade of life. Only about 5 percent lesions occur below the age of 30 years.

Sex: Leukoplakia occurs more often in males than females. However, this trend is changing very fast due to the gradual increase in the tobacco related habits among females, with subsequent increase in the incidence of leukoplakia among them.

Site: Buccal mucosa and commissural areas are the most frequently affected sites (Fig. 3.2), followed by alveolar ridge, tongue, lips, hard and soft palate, floor of the mouth and gingiva, etc. Multiple areas of involvement may be seen in few cases.

CLINICAL PRESENTATION

- Oral leukoplakias often present solitary or multiple **"white patches"**. They can be nonpalpable, faintly translucent, white areas over the mucosa.
- Many lesions can be **thick, fissured, indurated or papillomatous** in nature.
- The size of the lesion may vary from a small, welllocalized patch measuring about few millimeter in diameter to a diffuse large lesion, covering a wide mucosal surface.
- The surface of the lesion may be **smooth or finely wrinkled or even rough** on palpation, and the lesion cannot be removed by scrapping.
- The lesions are usually **white or grayish or yellowish-white** in color and in some cases, due to the heavy use of tobacco, they may take a brownish- yellow color.
- Some lesions may exhibit a **pumice-like surface**, which occurs due to the presence of multiple discrete keratotic striae on the surface of these lesions.

- Leukoplakia of the floor of the mouth sometimes has an ebbing-tide pattern of appearance.
- The thickness of the patch may vary from only faint to considerably thick.
- In most of the cases, leukoplakias lesions are asymptomatic, however, in some cases they may cause pain, a feeling of thickness and burning sensations, etc.

Clinical classification of leukoplakia

- Homogenous leukoplakia
- Ulcerative leukoplakia and
- Nodular or speckled leukoplakia.

The homogenous leukoplakia clinically presents extensive white patch having uniformly smooth, flat or corrugated surface with an irregular margin. These lesions usually maintain a relatively consistent pattern throughout the clinical course (Figs 3.3 and 3.4).

- These lesions are mostly associated with the oral use of snuff.
- They can be either non elevated or slightly elevated and the margin is not well-demarcated from the surrounding normal epithelium.

The ulcerative leukoplakia clinically exhibit either predominantly white or mixed red and white lesions, in which there is a central ulceration (Figs 3.5 to 3.7).

- The ulcerated center of the lesion appears red and it may have a yellowish fibrin coating.
- White patches are seen at the periphery of these lesions.

The nodular or speckled leukoplakia clinically present mixed red and white lesions; the mucosa

Fig. 3.3: Homogenous leukoplakia

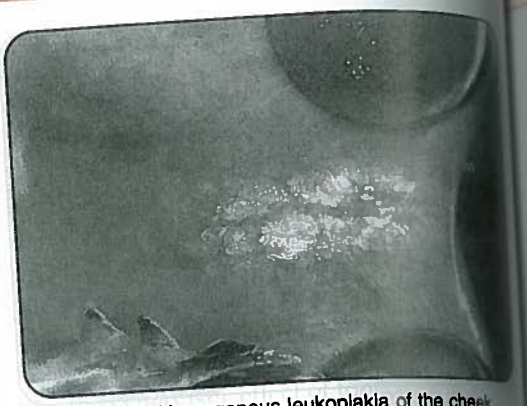

Fig. 3.4: Homogenous leukoplakia of the cheek

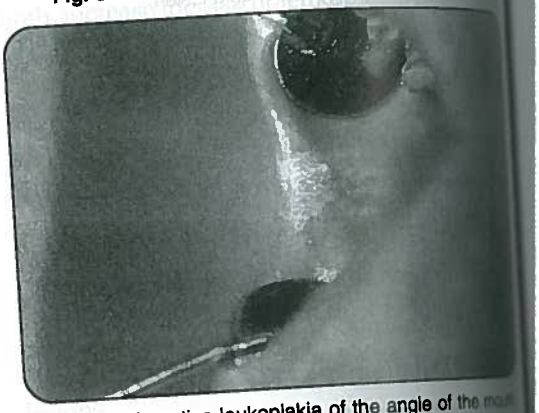

Fig. 3.5: Ulcerative leukoplakia of the angle of the mouth

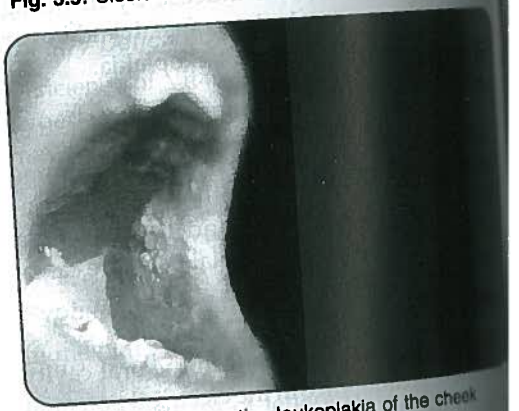

Fig. 3.6: Ulcerative leukoplakia of the cheek

is in which multiple small, slightly rai
rounded, keratotic nodules or granules are s
scattered through out the erythematous base
3.8).

- This variety of leukoplakia often carries
maximum risk of malignant transformat

HISTOPATHOLOGY

Under microscope leukoplakia generally
sents **hyperorthokeratinization or hyper**

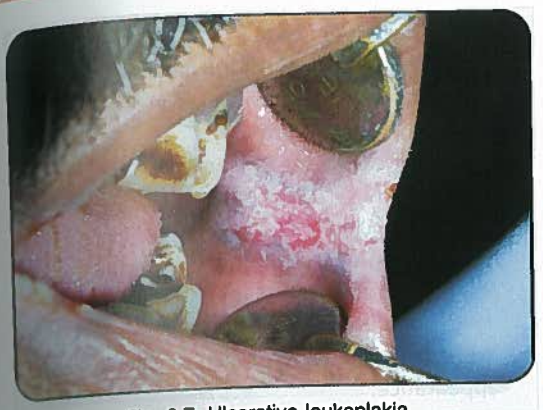

Fig. 3.7: Ulcerative leukoplakia

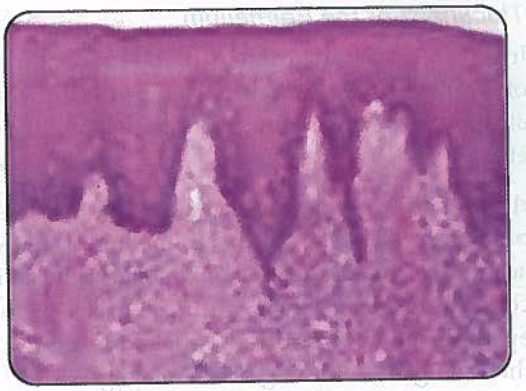

Fig. 3.9A: Normal stratified squamous epithelium

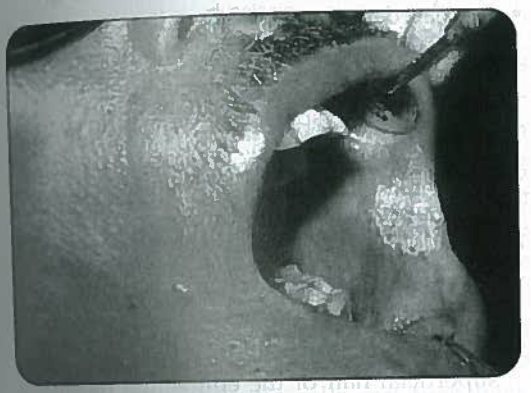

Fig. 3.8: Nodular leukoplakia of the cheek

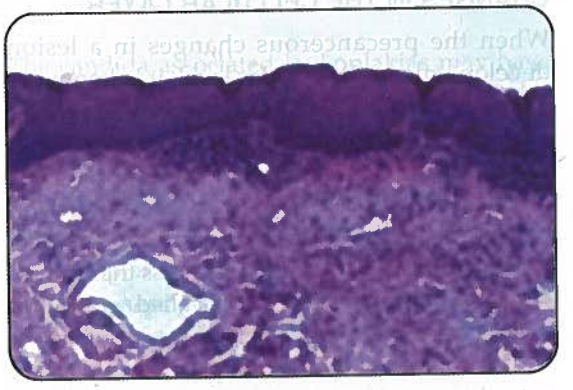

Fig. 3.9B: Photomicrograph of mild epithelial dysplasia

keratinization or both, with or without the presence of epithelial dysplasia.

Normal epithelium (Fig. 3.9A) shows a variety of histologic changes in terms of the following factors- (a) keratinization pattern (b) changes in the cellular layers (c) thickness of the epithelium and (d) alterations in the underlying connective tissue stroma.

CHANGES IN THE KERATINIZATION PATTERN

Hyperkeratinization of the epithelium refers to formation of keratinized layers in the epithelium which are normally nonkeratinized or abnormal increase in the thickness of the existing keratin layer in the epithelium, which are normally keratinized.

Hyperorthokeratinization

Orthokeratin is a homogenous layer of keratin present on the superficial part of the epithelium, which does not contain any nuclear remnants. In case of leukoplakia, an abnormal increase in the thickness of orthokeratin layer is seen in the areas of epithelium which are usually keratinized. Besides this, some degree of orthokeratinization may also be seen in the areas of epithelium, which are usually nonkeratinized.

Hyperparakeratinization

When there is an increase in the thickness of parakeratin layer (keratin that contains some nuclear remnants) on the epithelium, it is called hyperparakeratinization. An important histologic criteria of leukoplakia is the presence of hyperparakeratinization of the normally keratinized epithelium, or some amount of parakeratin deposition in the areas of epithelium which are usually non-keratinized. Epithelial dysplasia is more frequently associated with hyperparakeratinized lesions.

In few lesions of leukoplakia, both hyperorthokeratinization and hyperparakeratinization may be seen.

Thickness of the Epithelium

In leukoplakia, the thickness of the epithelium is often altered and it occurs in the form of epithelial atrophy or epithelial hyperplasia or acanthosis, etc.

Acanthosis: An abnormal increase in the thickness of stratum spinosum of the epithelium is called acanthosis. In case of leukoplakia, acanthosis is commonly observed in multiple areas of the epithelium, which often causes elongation, thickening and blunting of the retepegs.

CHANGES IN THE CELLULAR LAYER

When the precancerous changes in a lesion develop only at the cellular level, it is known as **'cellular atypia'**. At this situation, the overall alterations in the tissue in the direction of precancerous changes are not fully expressed.

When the precancerous changes in a lesion worsen further and the changes (both physical and morphological) begin to express themselves in the overall tissue levels, it is called **'epithelial dysplasia' (Fig. 3.9B)**.

The degrees of epithelial dysplasia in a lesion may change with time.

Dysplasia (dys–abnormal, plasia–formation)

Epithelial dysplasia is the hallmark in the histological changes seen in the epithelium, in case of leukoplakia and its presence is an important indicator of the precancerous nature of the disease.

The features of epithelial dysplasia include the following:

- Nuclear hyperchromatism (large and deeply stained nuclei)
- Cellular pleomorphism (altered size and shape of cells)
- Irregular epithelial stratifications (normal orientation of cell layers disturbed)
- Increased nuclear–cytoplasmic ratio (size of nucleus increases and volume of cytoplasm decreases; in normal epithelial cells the ratio is 1:4 and in dysplastic cells the ratio changes to 1:1)
- Poikilocarynosis or division of nucleus without division of cytoplasm
- Loss of polarity of basal cells.
- Increased number of mitotic figures (abnormal mitosis may also be present)
- Presence of mitotic activity even in the superficial half of the epithelium (normally it is seen in the basal layer)
- Individual cell keratinization
- Dyskeratosis (abnormal expression of keratin production in the superficial as well as in deep layers of epithelium)
- Enlarged nucleoli
- Diminished intercellular adherence
- Drop-shaped rete-pegs with basal cell hyperplasia
- More than one layer of cells having "basaloid" appearance.

Key points of features of epithelial dysplasis

- Nuclear hyperchromatism
- Cellular pleomorphism
- Irregular epithelial stratifications
- Increased nuclear–cytoplasmic ratio
- Poikilocarynosis or division of nucleus without division of cytoplasm
- Loss of polarity of basal cells.
- Increased number of mitotic figures
- Presence of mitotic activity even in the superficial half of the epithelium
- Individual cell keratinization
- Dyskeratosis
- Enlarged nucleoli
- Diminished intercellular adherence
- Drop-shaped rete-pegs with basal cell hyperplasia
- More than one layer of cells having "basaloid" appearance.

Types of Dysplasia

Depending upon the degree and the extent to which the dysplastic changes have developed in a lesion of leukoplakia; epithelial dysplasias can be divided into three categories namely the

- **Mild epithelial dysplasia (Fig. 3.9B),**
- **Moderate epithelial dysplasia (Fig. 3.10)**
- **Severe epithelial dysplasia (Fig. 3.11)**

The degree of dysplasia is of immense value in predicting the malignant potential of a precancerous lesion.

Fig. 3.10: Photomicrograph of moderate epithelial dysplasia

The **severe dysplasia** in a lesion means it has more chances of undergoing malignant transformation; similarly **mild dysplasia** in a lesion means it carries the least chance of undergoing malignant transformation and likewise the **moderately dysplastic** lesion falls between the two extreme categories in terms of its risk for malignant transformation.

However, the dysplastic changes in a lesion are reversible and if the predisposing factors are removed, the dysplastic cells can turn back towards normal.

Factors determining the degree of epithelial dysplasia in leukoplakia

- Age and sex of the individual having precancerous lesion in the mouth
- Frequency and duration of oral habits
- Types of oral habits (tobacco, alcohol, snuff)
- Types of tobacco used and mode of consumption (smoking, chewing or others)
- Any synergism (combination) of multiple habits or not,
- Location of the lesion in the oral cavity (lips, tongue, floor of the mouth)
- Presence or absence of secondary infections (candidiasis, syphilis , HPV or HSV)
- Systemic health of the individual (hormonal factors/nutritional status).

Candidal Hyphae

Histologic sections of leukoplakia often reveal the presence of candidal hyphae in the epithelium.

Fig. 3.11: Photomicrograph of severe epithelial dysplasia

The candida associated leukoplakias may have an increased tendency for malignant transformation.

Reduction in thickness of basement membrane

In leukoplakia, there is a gradual reduction in the thickness of basement membrane of the epithelium, with the increase in the severity of the epithelial dysplasia.

CHANGES IN THE UNDERLYING CONNECTIVE TISSUE

Chronic Inflammatory Cell Infiltration

In leukoplakia, there are often variable degrees of destruction of the collagen fibers and moreover chronic inflammatory cell infiltration is also present in the underlying connective tissue stroma.

SPECIAL INVESTIGATIONS IN LEUKOPLAKIA

In leukoplakia, the presence of epithelial dysplasia and the malignant transformation potential of the lesion can not always be assessed properly with the help of simple histopathology alone. In such cases, special investigative techniques should be employed which are as follows:

- Histochemistry
- Enzyme histochemistry

- Immunohistochemistry
- Exfoliative cytology
- Cell proliferation study
- Stereological techniques
- DNA histograms
- *In vitro* testing of living tissue.

DIFFERENTIAL DIAGNOSIS OF LEUKOPLAKIA

- Lichen planus
- Candidiasis
- Frictional keratosis
- Verrucous carcinoma
- White sponge nevus
- Chemical burns
- Discoid lupus erythematosus
- Leukoedema
- Syphilitic patches
- White sponge nevus.

Key points of leukoplakia

- Leukoplakia is a common precancerous lesion of the oral cavity.
- It appears as a "white patch" or "plaque" in the oral mucosa, which cannot be scraped off or stripped off easily and more over, which cannot be characterized clinically or pathologically as any other disease.
- Clinically, it presents well defined solitary or multiple "white patches". They can be non-palpable, faintly translucent, white areas over the mucosa.
- The surface of the lesion may be smooth or finely wrinkled or even rough.
- The lesions are usually white or grayish or yellowish-white in color.
- Clinically, leukoplakias are divided into three types—homogenous leukoplakia, ulcerative leukoplakia and nodular or speckled leukoplakia.
- Under microscope, leukoplakia generally presents hyperorthokeratinization or hyperpara-keratinization or both, with or without the presence of epithelial dysplasia.
- The epithelial dysplasia may be of mild, moderate and severe types.
- The overall malignant transformation rate of leukoplakia is about 3 to 6 percent.
- Treatment includes surgical excision of the lesion or cryosurgery along with stoppage of all oral habits.

MALIGNANT TRANSFORMATION IN LEUKOPLAKIA

According to WHO, the overall malign transformation rate of leukoplakia is about 3 6 percent. The malignant potentiality of leukoplakia lesion also depends upon sever factors like the age and sex of the patient, ty and duration of habits, frequency of habit of the lesion, clinical type of leukoplakia pres and whether treatment provided or not etc.

Usually, the nodular leukoplakias show highest rate of malignant transformation amo all the clinical types. Malignant transforma in leukoplakia will lead to squamous ce carcinoma.

Generally, the homogeneous leukoplakias an leukoplakias of the palate have the least chance of malignant transformation.

Risk of malignant transformation increase with older age of the patients and in lesions persis ting or remaining untreated for longer duration

Leukoplakias of floor of the mouth and ventra surface of the tongue carry the highest risk fo malignant transformation.

Women carry higher risks of malignan transformation, if they have leukoplakia a compared to men.

TREATMENT OF LEUKOPLAKIA

Stoppage of all oral habits, surgical excision o the lesion or cryosurgery and administration o heavy dose of vitamin A, etc.

ORAL HAIRY LEUKOPLAKIA

DEFINITION

Oral Hairy leukoplakia is a **HIV-associate mucosal disorder** and is considered as a reliable marker for the presence of HIV virus in the bod and is also a precursor of full blown AIDS.

Homosexual men with HIV (human immuno deficiency virus) infection may develop thes white patchy lesions in the oral cavity. Moreover these lesions can also be seen in other HIV/AID risk individuals like patients with hemophilia an other common transfusion recipients, etc.

CLINICAL FEATURES

- Clinically, oral hairy leukoplakia occurs mo frequently on the **lateral borders** and ventra

surface of the tongue. However, it can also occur on the floor of the mouth, buccal or labial mucosa and palate, etc.

- The lesion often appears as a **slightly raised, white plaque with vertically corrugated, irregular surface.**
- The oral hairy leukoplakias characteristically exhibit an irregular surface with numerous linear vertical folds or projections on it and these projections are sometimes so marked as to resemble **"hairs"** (hence, the name hairy leukoplakia has been coined).
- The lesions vary in size from few millimeters to 3 centimeter in maximum dimension and they can not be rubbed off or scraped off from the surface.
- Some lesions are small and have a finely corrugated surface.
- Hairy leukoplakias are asymptomatic lesions, whenever they occur on the buccal mucosa.
- The lesions are nearly always colonized by *Candida albicans*, but the etiology of the disease itself is viral.
- Hairy Leukoplakia probably occurs due to opportunistic infection in immunosuppressed individuals; being caused by Epstein Barr virus.
- In HIV infected patients, presence of hairy leukoplakia indicates progression of the disease from asymptomatic seropositive states into the full blown AIDS.
- There is no evidence of malignant transformation in this form of leukoplakia.

HISTOPATHOLOGY

- In oral hairy leukoplakia, the **parakeratin layer is thick** and is often colonized by **candidial organisms.**
- A very characteristic finding in oral hairy leukoplakia is the presence of a sub corneal (below the keratin layer) upper spinus layer zone, made up of cytopathically altered keratinocytes. These are large, **pale staining epithelial cells,** which are often called **'balloon cells'.**
- These cells exhibit clear cytoplasm, vesicular nuclei with margination of the chromatin (peripheral condensation of chromatin along the nuclear membrane).
- No dysplastic changes are seen in oral hairy leukoplakia and neither there is evidence of any malignant transformation.
- The submucosa does not exhibit much inflammatory cell infiltration.

Key points of oral hairy leukoplakia

- Oral Hairy leukoplakia is a HIV–associated mucosal disorder, which clinically presents a slightly raised, white plaque with vertically corrugated, irregular surface.
- The lesion mostly develops on the lateral border and ventral surface of the tongue.
- Hairy leukoplakia often characteristically has numerous linear vertical folds or projections on the surface, which are sometimes so marked as to resemble "hairs".
- Presence of hairy leukoplakia indicates progression of the disease from asymptomatic seropositive states into the full blown AIDS.
- Histologically, the lesion shows a markedly thickened superficial parakeratin layer and below the surface layer large, pale staining epithelial cells are seen, which are often called **'balloon cells'.**
- No dysplastic changes are seen in oral hairy leukoplakia.

DIFFERENTIAL DIAGNOSIS

- Chronic candidiasis
- Lichen planus
- White sponge nevus
- Geographic tongue
- Verrucous leukoplakia
- Chronic tongue biting habits.

SPECIAL INVESTIGATION

Hairy leukoplakia is diagnostically confirmed by using DNA *in situ* hybridization with an Epstein Barr virus molecular probe on processed tissue section. It reveals positive staining of the upper spinus layer of cells.

TREATMENT

No treatment is specifically required since hairy leukoplakia is an asymptomatic lesion. However, it subsides after acyclovir therapy is given to the patient.

LEUKOEDEMA

DEFINITION

Leukoedema or preleukoplakia is an alteration of the oral epithelium characterized by intra-

cellular accumulation of fluid (edema) within the spinus cell layer.

ETIOLOGY

The etiology of leukoedema is not known. According to many investigators, the condition is a variation of normal epithelium rather than a disease.

CLINICAL FEATURES

- Leukoedema more commonly occurs among black population; age of occurrence is about 45 years.
- The oral mucosa exhibits an asymptomatic, **diffuse, translucent, grayish–white area** with a **filmy appearance.**
- It is commonly seen on the buccal mucosa (often bilaterally) near the occlusal plane. However, some lesions can occur on the lateral border of the tongue and inner surface of the lips.
- The affected mucosa may be wrinkled or corrugated in extreme cases.
- When the mucosa is stretched, the lesion often disappears or is greatly decreased.
- Few such lesions may turn into leukoplakia in future.

HISTOPATHOLOGY

- Histologically, leukoedema is characterized by thickening of the epithelium with mild degree of parakeratosis and acanthosis.
- Within the spinus cell layer, large amount of **intracytoplasmic fluid and glycogen** often accumulate, which results in enlarged spinus cells with pyknotic nuclei and clear cytoplasm.
- The rete-pegs are often broad and the underlying connective tissue is normal.
- The epithelium never exhibits any dysplastic changes.

TREATMENT

No treatment is necessary.

CARCINOMA *IN SITU*

DEFINITION

Carcinoma *in situ* is a **laterally spreading, intra-epithelial type of superficial carcinoma,** which mostly occurs over the skin and sometimes in the mucosa, including that of the oral cavity.

It is the most severe stage of epithelial dysplasia, which involves the entire thickness of the epithelium, however the **basement membrane remains intact** in this lesion.

These mucosal lesions resemble leukoplakia in all respects except that the dysplastic features are very pronounced and involve almost all layers of the epithelium. The most striking feature of carcinoma *in situ* is that dysplastic epithelial cells do not invade into the underlying connective tissue stroma.

CLINICAL FEATURES

Age: Elderly.

Sex: More common among males than females.

PRESENTATION

- Clinically, the lesions may appear either as **white plaques** or as **ulcerated, eroded** or **reddened** areas over the oral mucosa.
- The common sites of occurrence of these lesions are the **floor of the mouth, tongue or lips,** etc.
- The lession may sometimes clinically appear either as leukoplakia or erythroplakia.
- In some other lesions, combined features of both leukoplakia and erythroplakia are found.

HISTOPATHOLOGY (FIG. 3.12)

- Histologically, hyperkeratosis may or may not be present on the surface of the lesion and if it is present, it will usually be the hyperparakeratosis.

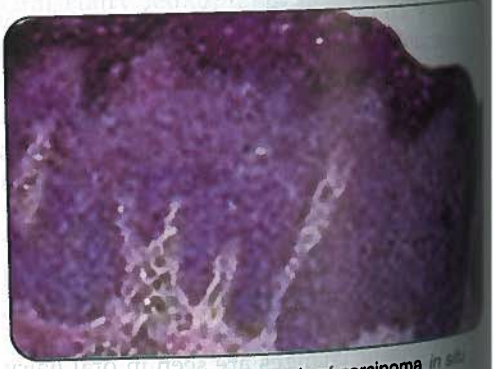

Fig. 3.12: Photomicrograph of carcinoma *in situ*

- The epithelium is generally **hyperplastic** or sometimes it can be atrophic.
- The features like individual cell keratinization and keratin pearl formation, etc. are exceedingly rare.
- In fact, if keratin pearls are found, invasive carcinoma should be suspected rather than carcinoma *in situ*.
- One of the most consistent features of carcinoma *in situ* is the **loss of orientation and loss of polarity of the dysplastic epithelial cells.**
- A **sharp line of division** between the normal and the dysplastic epithelium is always present, which extends from the surface up to the connective tissue.
- Basement membrane of epithelium always remains intact.
- Cytologically, carcinoma *in situ* is similar to squamous cell carcinoma except that architecturally the **epithelial basement membrane is intact** and no invasion of the dysplastic cells into the underlying connective tissue has occurred.
- Sometimes, multiple lesions of carcinoma *in situ* may develop in a single surface of epithelium, being separated from one another by the normal epithelium.

Key points of carcinoma *in situ*

- Carcinoma *in situ* is the most severe stage of epithelial dysplasia and is also called laterally spreading, intra-epithelial type of superficial carcinoma.
- The dysplastic process involves the entire thickness of the epithelium, However, the basement membrane remains intact.
- It commonly develops in the floor of the mouth, tongue or lips, etc.
- Histologically, the epithelium is generally hyperplastic or sometimes it can be atrophic
- The lesion often characteristically exhibits loss of orientation and loss of polarity of the dysplastic epithelial cells.
- Since the basement membrane is intact, there is no invasion of the neoplastic cells into the underlying connective tissue.

- Since, there is no invasion of the neoplastic cells into the underlying connective tissue, metastasis does not occur in carcinoma *in situ*.

TREATMENT

Treatment is done by surgery, radiotherapy or elctrocautery, etc. The untreated cases will eventually transform into invasive squamous cell carcinoma.

ERYTHROPLAKIA

Erythroplakia is a clinical term, which refers to "a **red patch or plaque** in the oral mucosa, which can not be characterized clinically or pathologically as any other condition and which has no apparent cause" (WHO-1978).

It was first reported by Queyrat in 1911 as a red, velvety lesion on the mucosa of the glans penis of elderly males. Oral erythroplakias represent the most severe type among all oral precancerous lesions and histologically, these lesions almost always exhibit dysplastic changes.

ETIOLOGY

The exact etiology is not known. However, excessive use of tobacco (cigarette or beede smoking) and heavy drinking of alcohol are believed to be responsible for the disease.

CLINICAL FEATURES

Prevalence rate: About 0.09 percent in U.S.A and 0.02 percent in India.

Age: Fifth, sixth and seventh decade of life.

Sex: Males and females are almost equally affected.

Site: Floor of the mouth and retromolar areas are most frequently involved. The other intraoral sites are buccal mucosa, gingiva, tongue (ventral and lateral surfaces) and soft palate, etc.

The gingiva and alveolar ridge lesions are more frequently seen among females.

PRESENTATION

Clinically, erythroplakia appears as a small or extensive, red, velvety lesion with clearly defined margins. The redness is not always a prominent feature of this disease since the color may not be uniformly present in all parts of the lesion. The oral erythroplakias are always clinically and histologically similar to those seen in the genitalia.

CLINICAL TYPES

Erythroplakia clinically presents **three distinctive patterns**, which are as follows:

Homogenous Erythroplakia

This type of lesion appears as bright red, velvety, soft areas on the oral mucosa, with an irregular but well defined margin.

Erythroplakia Interspersed with Patches of Leukoplakia

In this type of erythroplakia, there is presence of multiple, irregular erythematous areas in the oral epithelium and along with that few white leukoplakic patches are also present. The erythematous areas are not as red as those seen in the homogenous type.

Speckled Erythroplakia

These lesions are similar to the speckled leukoplakias of the oral cavity and are characterized by the presence of soft, irregular, raised, erythematous areas in the epithelium with a granular surface. There are some tiny, focal white plaques distributed all over the red surface.

HISTOPATHOLOGY

- Erythroplakia should be viewed with high degree of alert, since most of the lesions (80 to 90 percent) exhibit features of invasive epidermoid carcinoma or carcinoma *in situ* or at least severe epithelial dysplasia.
- The areas which clinically appear red histologically exhibit atrophy of the epithelium with reduction in the keratin production. Moreover, there is also an increase in the vascularity of the submucosal connective tissue.
- The underlying connective tissue shows intense chronic inflammatory cell infiltration.

DIFFERENTIAL DIAGNOSIS

- Erosive lichen planus
- Early squamous cell carcinoma
- Atrophic candidiasis
- Kaposi's sarcoma

Key points of erythroplakia

- Erythroplakias represent the most severe type among all oral precancerous lesions, with extreme risk of malignant transformation.
- Clinically, it appears as a small or extensive, red velvety lesion with clearly defined margins.
- The disease has three distinct clinical types: homogenous erythroplakia, erythroplakia interspersed with patches of leukoplakia and speckled erythroplakia.
- Histologically, erythroplakia often exhibits features of invasive epidermoid carcinoma or carcinoma *in situ* or at least severe epithelial dysplasia.
- Deep and wide surgical excision of the lesion is the treatment of choice.

- Stomatitis associated with nutritional deficiency or denture irritation
- Contact allergy
- Palatal erythema due to heavy smoking.

TREATMENT

Deep and wide surgical excision of the lesion, regular follow-up examinations are mandatory.

STOMATITIS NICOTINA

DEFINITION

Stomatitis nicotina (**smoker's keratosis**) is a tobacco-related keratosis of the oral mucosa and is commonly seen in the palate of the excessive pipe or cigar smokers. The severity of the condition is directly related to the intensity and duration of smoking.

CLINICAL FEATURES

- The condition affects both **hard and the soft palates**, however, if the patients hard palate is covered with a denture then only the soft palate is affected (Fig. 3.13).
- The disease represents two separate abnormalities simultaneously; one is the **hyperkeratosis** of the epithelium and the other is the **inflammatory swelling of the palatal mucous glands.**

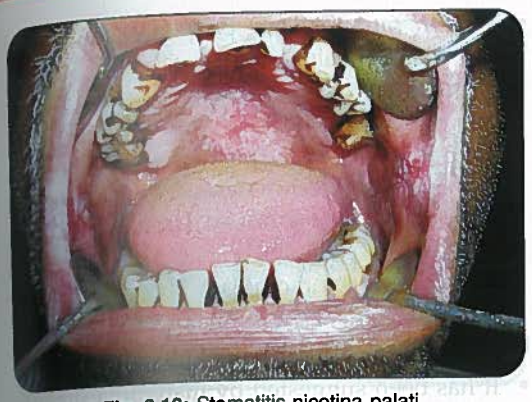

Fig. 3.13: Stomatitis nicotina palati

- Initially, the palatal mucosa becomes red and later on, it becomes white due to increased thickening and hyperkeratosis of the epithelium.
- On the surface of the lesion, few **red, dot-like areas** are seen, which are **surrounded by elevated, white keratotic rings**. These red dots represent the inflammed duct openings of the palatal minor salivary glands.
- The white background of the palatal mucosa may have a rough surface and it may be even fissured or wrinkled.
- In severe cases, the palatal mucosa may become completely ulcerated.
- Similar lesions can sometimes be seen over the buccal mucosa, particularly on that side of the mouth where the pipe or cigar is held.
- The lesion subsides to a great extent once the pipe smoking habit is discontinued.

HISTOPATHOLOGY

- The histopathology of stomatitis nicotina shows hyperorthokeratosis and acanthosis of the surface epithelium.
- The palatal mucous glands are **inflammed and swollen.**
- The ductal epithelium of the palatal minor salivary glands often exhibits **squamous metaplasia.**
- Sometimes, the minor salivary glands themselves exhibit partial or complete atrophic changes.
- Moderate degree of inflammatory cell infiltration is often seen in the connective tissue adjacent to the palatal minor salivary glands.
- Dysplastic changes may sometimes be seen either in the palatal surface epithelium or in the ductal epithelium of the minor salivary glands.

TREATMENT

Complete stoppage of all oral habits and observation. The malignant transformation of this lesion is rare, unless the patient is a reverse smoker. Palate is the least common site for the development of oral cancer. However, pipe smokers can develop cancer not directly in the palate but in the lingual retromolar areas.

ORAL SUBMUCOUS FIBROSIS (OSF)

DEFINITION

Oral submucous fibrosis (Figs 3.14 and 3.15) is the most predominant precancerous condition arising in the oral cavity, oropharynx, nasopharynx and esophagus, etc. The disease is

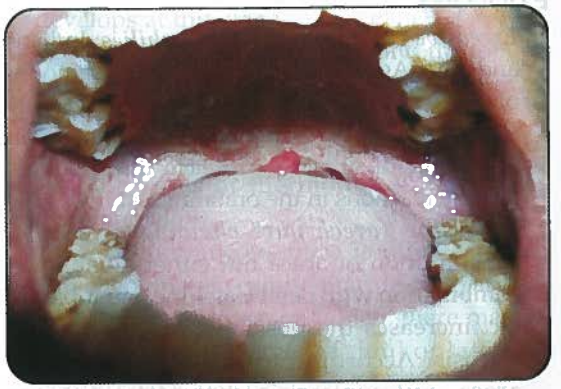

Fig. 3.14: Submucous fibrosis-I

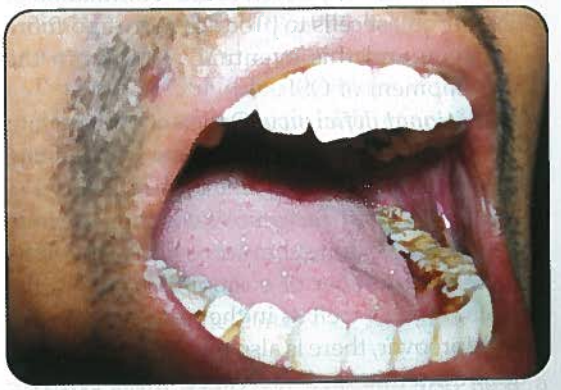

Fig. 3.15: Submucous fibrosis-II

characterized by juxta-epithelial inflammatory reaction in the oral mucosa, followed by a fibro-elastic transformation of the lamina propria leading to mucosal atrophy, rigidity and trismus.

The condition was first reported by Schwartz (1952) in the name of "Atrophia idiopathica (tropica) mucosae oris". The present name oral submucous fibrosis was coined by Dr Joshi from Bombay in the year 1953.

EPIDEMIOLOGY

The disease is more common among the people of South-East Asian countries, especially the Indians, Bangladeshis, Nepalese, Burmese, Vietnamese and South Africans, etc. The extreme climatic conditions in these regions and adherence of the people to more spicy foods, is believed to the main reason behind the higher incidence of the disease. Oral submucous fibrosis may undergo malignant transformation and develop squamous cell carcinoma in the mouth.

ETIOLOGY

- ***Excessive consumptions of red chilies:*** Indians and other Asiatic people consume large amount of chilies regularly because they like foods duly seasoned with hot peppers. Chilies contain an active ingredient called 'capsaicin' that produces allergic reactions in the oral mucosa.
- ***Excessive "areca nut" chewing:*** Excessive consumption of areca nut either alone or in combination with betel leaf, lime and tobacco, etc. increases the possibility of submucous fibrosis. According to many investigators, areca- nut contains a chemical substance called 'arecoline', which causes stimulation of the fibroblast cells to produce more and more collagen and this eventually results in the development of OSF.
- ***Nutritional deficiency:*** Deficiency of vitamin A, B complex and C, etc. as well as the deficiency of iron and zinc in the diet.
- ***Immunological factors:*** According to some investigators, oral submucous fibrosis exhibits increased number of eosinophils both in the circulation as well as in the tissue.

  Moreover, there is also presence of gamma-globulinemia and increased mast cell response, etc. All these factors indicate an immunologic background of the disease.
- ***Genetic factors:*** Some people are genetically more susceptible to this disease.
- ***Protracted tobacco use:*** Excessive use of chewable tobacco.
- ***Deficiency of micronutrients:*** Patients with deficiency of selenium, zinc, chromium and other trace elements may fail to prevent the free radical injury in the body and can therefore develop oral submucous fibrosis.

PATHOGENESIS

- It has been suggested by many investigators that the chronic exposure to areca nut, chilli peppers along with prolonged deficiency of iron, zinc and vitamins, etc in the diet cause an alteration in the oral mucosa, which increases the risk of hypersensitivity to many other potential irritants.
- The hypersensitivity reaction to the oral epithelium often results in an juxta-epithelial inflammation and a fibrotic change in the lamina propria.
- Moreover, increased fibrosis in the sub-epithelial connective tissue cause atrophy of the oral mucosa, which in turn may be more and more vulnerable to irritants (For example tobacco, alcohol, betel nut and other agents) and may eventually undergo malignant transformation.

CLINICAL FEATURES

Age: 20 to 40 years of age.

Sex: Female are affected more often than male.

Site: In submucous fibrosis, fibrotic changes are frequently seen in the buccal mucosa, retromolar area, uvula, soft palate, palatal fauces, tongue, lips, pharynx and esophagus, etc.

It is believed, that the disease initiates from the posterior part of the oral cavity and then gradually spreads to the anterior locations.

PRESENTATION (FIGS 3.16 TO 3.18)

- The onset of the disease is either insidious and it may develop gradually over a period of 5 years.
- Initially, the patient complains of burning sensations in the mouth, particularly during taking hot and spicy foods.

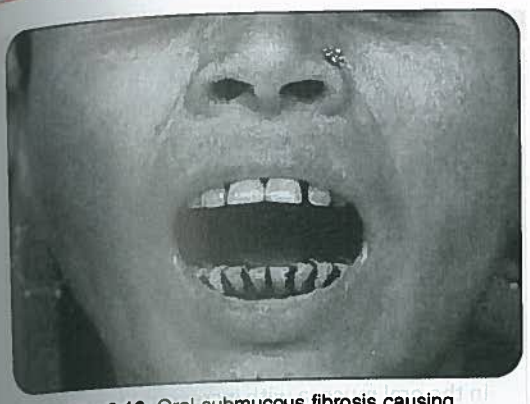

Fig. 3.16: Oral submucous fibrosis causing difficulty in mouth opening

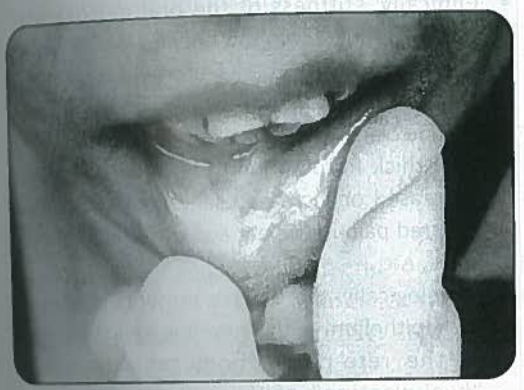

Fig. 3.17: Blanched appearance of mucosa with ulceration in submucous fibrosis

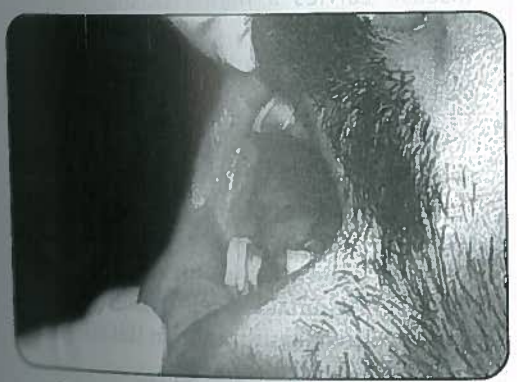

Fig. 3.18: Oral submucous fibrosis turning into squamous cell carcinoma

- This is often accompanied or followed by the formation of multiple vesicles over the palate or ulcers or inflammatory reactions in other parts of the oral mucosa.
- There can be either excessive salivation or decreased salivation (xerostomia) along with recurrent stomatitis. Patients also develop defective gustatory sensation.
- In the initial phases of the disease, palpation of the mucosa elicits a "**wet-leathery**" feeling.
- Petechial spots may also be seen in the early stages of the disease over the mucosal surfaces of tongue, lips and cheek, etc
- Oral mucous membrane is very painful upon palpation at this stage.
- One of the most important characteristic features of oral submucous fibrosis is the gradual stiffening of the oral mucosa with progressive reduction in the mouth opening **(trismus)** (Fig. 3.16).
- The stiffness of the oral mucosa and the subsequent trismus develops gradually within a few years after the development of the initial symptoms.
- In the advanced stage of OSF, the oral mucosa losses its resiliency to a great extent and it becomes blanched and stiff. Severe trismus develops at this stage.
- Because of stiffness of the lips and the tongue patients are unable to blow whistles or even blow out a candle.
- The oral mucosa is symmetrically affected on both sides of the mouth and it shows extreme pallor.
- The oral submucous fibrosis often causes a blanched opaque (**white marble-like**) appearance of the mucosa, on which, there may be occasional presence of leukoplakic or erythroplakic patches (Fig. 3.17).
- Palpation of the mucosa often reveals many vertical white fibrous bands on the inner aspect of the cheek.
- Patients of OSF often develops difficulty in deglutition, referred pain in the ear or deafness and nasal intonation of voice.
- Depapillation of the tongue with recurrent or sometimes persistent glossitis occurs. Later on the tongue becomes stiff and shows restricted movements.
- In mild cases, there may be white areas on the soft palate, but in severe cases, it shows restricted movements. Patients also have a 'bud-like' shrunken uvula.

- Thinning and stiffening of the lips causing microchelia and presence of circumoral fibrous bands.
- Areas of hypo or hyperpigmentations are seen in the oral mucosa.
- Loss of stippling occurs in the gingiva, and it becomes depigmented and fibrotic.
- Floor of the mouth becomes blanched and it gives a leathery feeling during palpation.
- Palate presents several fibrous bands, which are radiating from the pterygomandibular raphe to the anterior faucial pillars.
- The faucial pillars may be thick and short and the tonsils are often placed between them.
- When the disease progresses to the pharynx and esophagus, it causes extreme difficulty in deglutition.

HISTOPATHOLOGY

Microscopically, submucous fibrosis reveals the following features:

- The overlying hyperkeratinized, **atrophic**, epithelium often shows **flattening and shortening of the rete-pegs.**
- There can be variable degrees of cellular atypia or epithelial dysplasia.
- In oral submucous fibrosis, dysplastic changes that are found in the epithelium include marked irregular epithelial stratifications, nuclear pleomorphism and severe intercellular edema, etc.
- This type of dysplastic features are not seen in leukoplakia and instead there will be features like nuclear hyperchromatism, increased mitosis and basilar hyperplasia, etc.
- In the early stage of submucous fibrosis, the connective tissue stroma exhibits finely fibrillar collagen, inter cellular edema and increased fibroblastic activity.
- The stromal blood vessels in this stage are dilated and congested and there can be areas of hemorrhage.
- The underlying connective tissue stroma in the advanced stage of the disease shows "**homogenization**" and "**hyalinization**" of the collagen fibers (this is one of the most important features of the disease).
- Besides this, decreased number of fibroblast cells and narrowing or obliteration of the blood vessels due to '**perivascular fibrosis**' also present.
- There can be presence of signet cells in some cases.
- **Degeneration of the muscle fibers** and chronic inflammatory cell (lymphocyte and plasma cell, etc.) infiltration in the connective tissue are commonly seen.
- The malignant transformation rate of OSF is about 4.5 to 7.6 percent.

Key points of oral submucous fibrosis

- Oral submucous fibrosis (OSF) is the most predominant precancerous condition arising in the oral cavity, oropharynx, nasopharynx and esophagus.
- The disease frequently occurs among the people of Indian subcontinent and is often related to factors like excessive consumption of red chillies, excessive areca nut chewing and nutritional deficiency, etc.
- These agents cause juxta-epithelial inflammation in the oral mucosa with increased fibrosis of the underlying connective tissue.
- Clinically, stiffness of the oral mucosa with gradual reduction in the opening of the mouth (trismus) is the hallmark features of the disease.
- The other important features of the disease include blanched opaque appearance of mucosa with thick fibrotic bands, burning sensation, decreased or increased salivations, dysphagia, referred pain in the ear and nasal intonation of voice, etc.
- Histologically, the disease presents atrophy of the epithelium with flattening and shortening of the rete-pegs; "homogenization" and "hyalinization" of the collagen fibers and degeneration of the muscle fibers, etc. The disease carries a high risk of malignant transformation.
- Treatment includes intralesional injections of collagenease, corticosteroids and fibrinolysins, etc.

ULTRASTRUCTURAL CHANGES

Following ultrastructural changes are found in submucous fibrosis:

- Fragmentations of the collagen fibers.
- Increased amount of fine immature collagen fibrils and interfibrillar matrix.

- Defective polymerization and maturation of collagen.
- Degeneration of mitochondria and nuclei of the muscle cells.
- Altered staining reaction of the collagen.
- PAS positive materials in the connective tissue.

LABORATORY INVESTIGATIONS

- Raised ESR
- Anemia
- Eosinophilia
- Hypergammaglobulinemia
- Increased serum alkaline phosphatase levels
- Alteration in the zinc and iron ratio in the tissue as well as in the blood
- Decreased serum vitamin A levels
- Scanning and transmission electron microscopy.

TREATMENT

Stoppage of all habits, grinding and rounding of sharp cuspal edge of teeth, routine extraction of all third molars are the preliminary steps in the treatment plan.

The definitive treatment of OSF includes intralesional injections of collagenase, corticosteroids and fibrinolysins, etc.

Systemic administration of steroids is also done in severe cases.

Biopsy is mandatory before treatment and if the dysplastic features are present in the epithelium, steroids should be avoided from the treatment schedules.

SIDEROPENIC DYSPHAGIA

DEFINITION

Sideropenic dyphagia or Paterson-Brown-Kelly syndrome (or Plummer-Vinson syndrome) occurs primarily due to chronic iron deficiency and this disease is often associated with a high risk of cancer of the oral cavity and the aerodigestive tract.

In developing countries, iron deficiency is common problem, which may occur either due to nutritional deficiency or due to hookworm infestations

Increased numbers of oral cancer cases are often found in the geographic areas, where iron deficiency is common.

CLINICAL FEATURES

- Sideropenic dysphagia is found more often among the middle aged females.
- Patients often suffer from weakness and generalized fatigue.
- Difficulty in swallowing is a common problem, which occurs as a result of formation of esophageal webs.
- Angular cheilosis, mucosal pallor with atrophy and a depapillated, smooth, glossy, tongue is frequently present.
- Buccal mucosa is pale in appearance and it also exhibits atrophic changes.

INVESTIGATIONS

- Examination of blood reveals the presence of severe iron deficiency anemia.
- Histological examination of oral and aerodigestive tract mucosa often exhibits mucosal atrophy and increased mitotic activity.

SIDEROPENIC DYSPHAGIA AND ORAL CANCER

- Sideropenic dysphagia is often associated with an increased risk of cancer.
- Malignant transformation of sideropenic dysphagia leads to the development of squamous cell carcinoma, which often occurs in relation to the tongue, buccal mucosa and the aerodigestive tract, etc.
- Although, the exact pathogenesis of the disease is unclear, it is believed that chronic iron deficiency causes atrophic changes in the mucosa and also causes suppression of the reprative potential of the mucosal tissue. This results in an increased susceptibility of the tissue towards malignancy when it is subjected to common irritants.

LICHEN PLANUS

DEFINITION

Lichen planus is a rather common chronic mucocutaneous disease, which probably arises due to an abnormal immunological reaction and

the disease have some tendency to undergo malignant transformation.

ETIOPATHOGENESIS

- The exact etiologic factors causing lichen planus are unknown, however psychological stress often aggravates the condition.
- It is believed that an abnormal recognition and expression of basal keratinocytes of the epithelium as foreign antigens by the Langerhans cells, induces an autoimmune reaction in the body, which results in the initiation of this disease.
- Initially, Langerhans cells recognize an antigen, which is similar to the antigens on the epithelial keratinocytes of the susceptible patient with certain classes of major histocompatibility antigens (MHA).
- Thereafter, during the processing of antigens and subsequent stimulation of the T-lymphocytes by the langerhans cells, some lymphocytes which are cytotoxic to the epithelial keratinocytes are produced.
- These cytotoxic T-lymphocytes accumulate in the subbasilar connective tissue region of the epithelium and interact with the basal keratinocytes and eventually cause 'liquefaction degeneration' of these cells.

CLINICAL FEATURES

Incidence: Lichen planus is a common skin disease and it occurs in about 1% of the population. The cutaneous lesions alone occur in about 35% cases, the mucosal lesions alone occur in about 25% cases, however, 40% patients exhibit both mucosal and cutaneous lesions together.

In India, the average incidence rate of lichen planus is about 2.1 per 1000 men and 2.5 per 1000 women.

Age: Lichen planus occurs among the middle aged or elderly people. Rarely, it can affect children.

Sex: Both sexes are affected but there is often a slight predilection for females.

Site: Lichen planus can involve several areas of the body and important among those areas or sites are as follow:

- *Cutaneous lesions*: Lichen planus of the skin usually involves (a) fexor surface of the wrist and forearms, (b) inner aspect of the knee and thigh, (c) upper part of the trunk, (d) scalp, nail beds and genitalia, etc.
- *Oral lesions:* Oral lesion of lichen planus commonly occurs on the mucosal surfaces of the buccal mucosa, vestibule, tongue, lips and gingiva, etc. palate and floor of the mouth are the least affected sites (Fig. 3.25).

In many cases, oral lesions develop bilaterally.

PRESENTATION

Cutaneous Lesions of Lichen Planus

- The cutaneous lesions of lichen planus clinically appear as clusters or diffuse areas of raised, purplish or reddish papules, which are covered by a white glistening scale (or a white keratotic **"cap").**
- These lesions often occur in a **bilaterally symmetrical** pattern.
- Lichen planus lesions increase in size, if it is subjected to some irritation.
- As the skin lesions produce itching sensation, patients often produce linear excoriations which result in the development of linear pattern of additional lesions along the scratch marks.
- ***Koebner phenomenon:*** It refers to the development of skin lesions of lichen planus, which are extending along the areas of injury or irritation.
- Cutaneous lesions of lichen planus sometimes exhibit periods of regression and recurrence.

Oral Lesions of Lichen Planus (Figs 3.19 to 3.22)

- The classic form of oral lichen planus clinically exhibits numerous interlacing white keratotic lines, which often produce a typical **'lace-like' or 'annular' pattern,** against an erythematous base.
- A tiny white elevated dot like structure is frequently present at the point of intersection of the white lines, which is known as **"sign of Wickham".**
- Oral lesions are generally asymptomatic although few lesions can cause pain or burning sensation while taking hot or spicy foods.

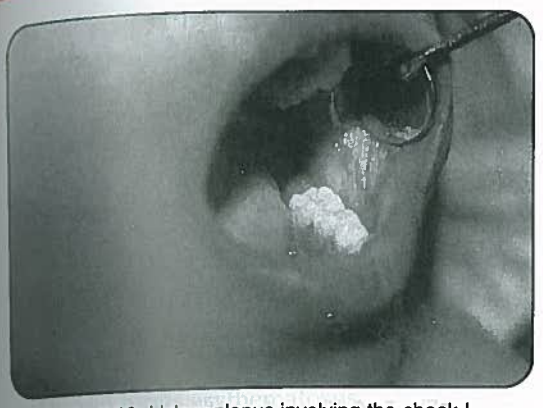

Fig. 3.19: Lichen planus involving the cheek-I

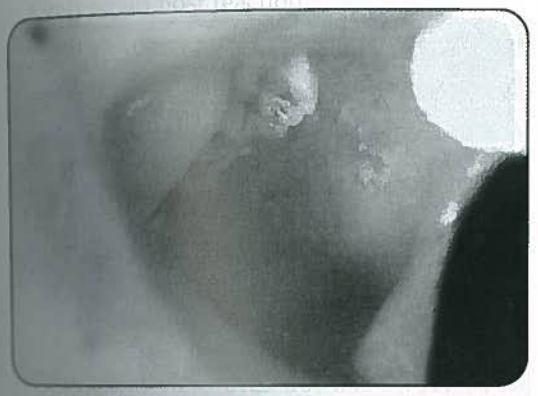

Fig. 3.20: Lichen planus of the cheek in another patient-II

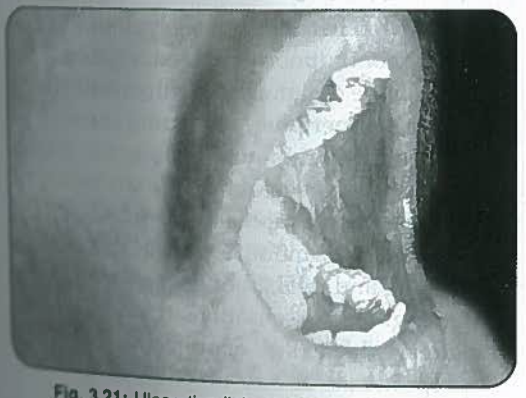

Fig. 3.21: Ulcerative lichen planus of the cheek

- These lesions also normally occur in a bilaterally symmetrical pattern.
- In some cases, patients with lichen planus may also simultaneously have other mucosal lesions like submucous fibrosis and leukoplakia, etc. in the oral cavity.

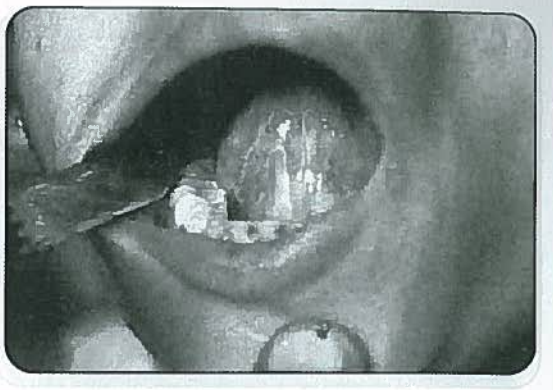

Fig. 3.22: Ulcerative lichen planus of the undersurface of tongue

CLINICAL TYPES OF LICHEN PLANUS

Clinically, lichen planus often presents several distinct clinical forms or types, which often correlate closely to the severity of the disease process.

Reticular Type

Reticular type of lichen planus of the mucous membrane produces a unique and distinctive clinical appearance.

- It usually consists of numerous raised, thin, snowy-white lines, which produce a lacework or a reticular appearance and they radiate from a central erythematous area.
- The lines are usually wavy, parallel and non-elevated.
- Reticular lichen planus commonly occurs on the buccal mucosa and buccal vestibule. Sometimes, they can occur on the mucosal surfaces of the tongue and gingiva.
- These lesions are usually asymptomatic and they often occur bilaterally.
- In some cases, reticular lichen planus may occur in association with the erosive form of the disease.

Erosive Type (Fig. 3.23)

- The erosive form of lichen planus exhibits shallow irregular areas of epithelial destructions.
- Clinically, the lesion presents a mixture of erythematous, ulcerated and white areas, which are often covered with a yellowish-white pseudomembranous coating.

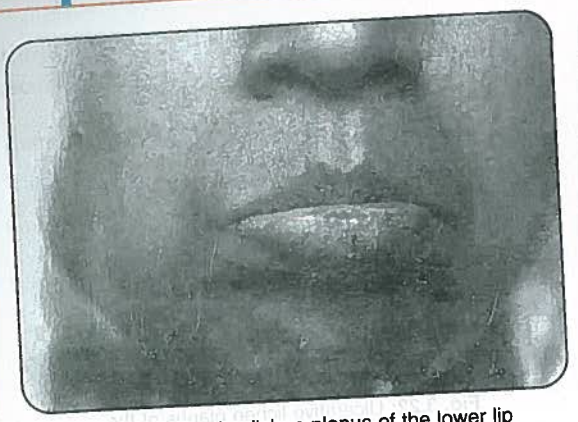

Fig. 3.23: Erosive lichen planus of the lower lip

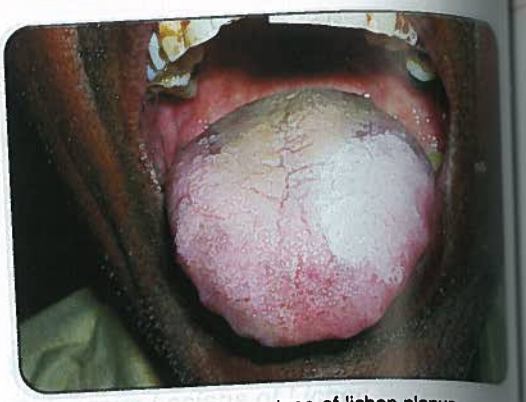

Fig. 3.24: Plaque type of lichen planus

- There can also be atrophic erythematous areas with central ulceration (Fig. 3.22).
- A faint white zone resembling radiating striae is frequently seen at the junction where the erosive area meets with the normal epithelium.
- Most of the lesions develop on the buccal mucosa and the vestibule.
- When the epithelial atrophy and ulcerations are confined only to the gingival area, the condition is referred to as 'desquamative gingivitis'.
- Patients with erosive lichen planus often complain of severe pain and burning sensation in the mouth, at the time of taking hot or spicy foods or during taking alcoholic beverages.
- In some cases, patients restrict themselves to only the bland liquid diet.
- Palpation of the affected mucosa often elicits pain and bleeding.
- The areas of mucosa where the lesion has already healed up exhibit melanotic hyperpigmentations.
- The margin of the lesion may be slightly depressed due to fibrosis and healing at the periphery.

Plaque Type (Fig. 3.24)

- The plaque type of lichen planus clinically presents a raise or flattened, white area on the mucous membrane.
- Dorsal surface of the tongue is mostly affected, where it produces irregular, white, smooth or raised plaques.
- These forms of lichen planus lesions often clinically resemble leukoplakias.

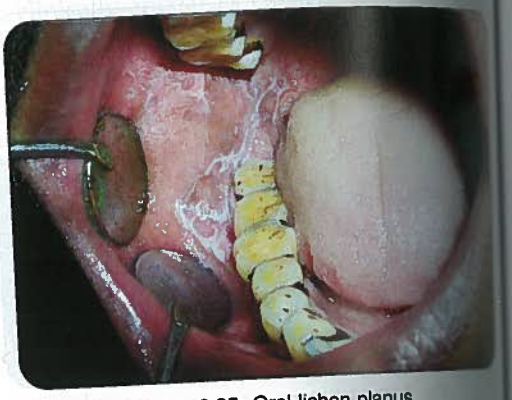

Fig. 3.25: Oral lichen planus

Atrophic Type (Fig. 3.25)

- Atrophic lichen planus often clinically pre sents smooth, poorly defined, erythemato areas on the oral mucosa, with or without th presence of peripheral radiating striae.
- The condition commonly affects the gingi or the buccal mucosa.
- Patients often complain of pain and burnin sensation in the mouth especially during toot brushing and taking hot or spicy foods.
- The aggravated sensations to hot and spic foods are due to lack of protective function the epithelium as a result of thinning.

Bullous Type

- It is a rare form of lichen planus and characterized by the formation of large vesic or bullae (size ranges between 4 mm to 2 in diameter) on the oral mucosa.
- The lesions usually develop within erythematous base and they rupture alm

immediately after their formation, thereafter leaving painful ulcers on the mucosal surface.
- Bullous lichen planus usually have peripheral radiating striae and these lesions are often seen over the posterior part of the buccal mucosa.

DIFFERENTIAL DIAGNOSIS

- Leukoplakia
- Candidiasis
- Mucous membrane pemphigoid.
- Discoid lupus erythematosus
- Syphilis
- Graft *versus* host reaction
- Erythema multiforme.

Key points of lichen planus

- Lichen planus is a common skin disease, which often affects the mucous membrane and the disease arises probably due to some immunlogical abnormality.
- Oral lichen planus clinically exhibits numerous interlacing white keratotic lines, which often produce a typical 'lace-like' pattern, against an erythematous base.
- A tiny white elevated dot like structure is frequently present at the point of intersection of the white lines, which is known as "striae of Wickham".
- Oral lesions are generally asymptomatic, although few lesions can cause pain and burning sensations while taking hot or spicy foods.
- Clinically, lichen planus has several types, which include reticular, erosive, bullous, ulcerative, plaque and atrophic, etc.
- Histologically, the disease presents hyperortho or hyperparakeratinization of the epithelium with thickening of the granular cell layer and acanthosis.
- A characteristic finding of the disease is the necrosis and liquefaction degeneration of the basal cell layer of the epithelium, which brings the spinus cell layer of epithelium directly in contact with the connective tissue.
- Thick 'band-like' infiltration of chronic inflammatory cells (predominantly lymphocytes) occurs in the juxta-epithelial region.
- Local and systemic steroid therapy is the main treatment.

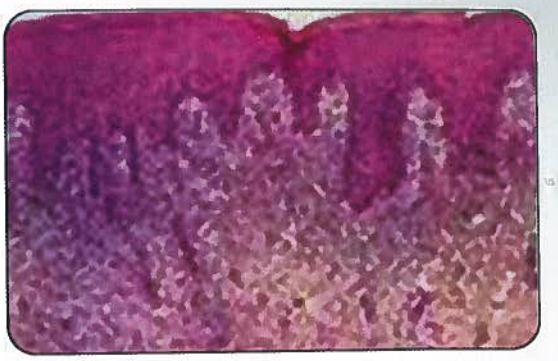

Fig. 3.26: Photomicrograph of lichen planus

HISTOPATHOLOGY

Microscopically lichen planus often reveals the following features (Fig. 3.26):
- The overlying surface epithelium exhibits hyperorthokeratinization or hyperparakeratinization or both.
- Thickening of the granular cell layer.
- Acanthosis or thickening of the spinus cell layer.
- Intercellular edema in the spinus cell layer.
- Shortened and pointed rete-pegs of the epithelium, which often produces a so called **"saw-tooth"** appearance. This appearance is not often seen in histologic sections of oral lesions of lichen planus rather it is more commonly seen in the skin lesions.
- One of the most important histologic features of lichen planus is the presence of **"necrosis and liquefaction (hydropic) degeneration"** of the basal cell layer of the epithelium.
- Due to the liquefaction degeneration of the basal cell layer, the epithelium becomes thin and the spinus cell layer often comes in direct contact with the underlying connective tissue.
- In erosive type of lichen planus, the epithelium is often extremely thin and it shows areas of complete loss of rete-pegs formation. Moreover, chronic inflammatory cells may often extend into the middle or upper layer of the epithelium.
- In lichen planus, few round or ovoid, amorphous, eosinophilic bodies are sometimes present within the epithelium, which are known as **"civatte bodies"**.

- These civatte bodies probably represent apoptotic (dead) keratinocytes or other necrotic epithelial components, which are transported to the connective tissue for phagocytosis.
- A **thick 'band-like' infiltration** of chronic inflammatory cells (predominantly lymphocytes) in the juxta-epithelial region is often seen.
- In lichen planus, the affected epithelium exhibits dysplastic changes in about 4 percent cases, out of which about 0.3 to 10 percent cases may undergo malignant transformation.

SPECIAL INVESTIGATIONS

- Direct immunofluorescent test demonstrates deposition of fibrinogen along the basement membrane of the epithelium with vertical extensions into the immediate underlying connective tissue.
- In immunofluorescent tests, all forms of lichen planus lesions are usually negative for IgG, IgA and IgM antibodies but positive for fibrinogen.
- Immunohistochemical study by using the antibody to S–100 protein, indicates an increase in the langerhans cells in the mid layers of the epithelium.

TREATMENT

Small lesions of lichen planus are treated well with topical steroids, e.g. fluocinonide.

In more resistant cases, systemic administration of methyl prednisolone is effective either alone or in combination with topical steroids. Intralesional injections of steroid have been used with some degree of success but are often not well tolerated by the patient.

Patient's psychological balance must be restored.

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