

### **2.10 Verruca Vulgaris (Figs. 41, 42)**

This is the oral counterpart of the lesion seen more commonly on the skin and caused by HPV types 2 and 4.

The squamous epithelium typically shows papillomatosis, acanthosis and variable hyperkeratosis, primarily of the parakeratotic type. It often has a prominent granular layer with cells containing large keratohyaline granules and cells with pyknotic nuclei surrounded by a halo of clear cytoplasm ("koilocytes") in the superficial layers. The rete-ridges at the periphery of the lesion are usually bent inwards towards the centre. If tangentially cut, a verruca vulgaris may resemble early well-differentiated squamous cell carcinoma.

### **2.11 Condyloma Acuminatum**

Condyloma acuminatum (venereal wart) occurs most frequently on anogenital skin and mucosa and is caused by HPV.

Several cases of intraoral occurrence have been reported, caused by oro-genital contact. These are largely associated with HPV types 6 and 11.

Histologically, the lesions show hyperplastic epithelium arranged in a papillomatous pattern, mostly without keratinization. There is often vacuolization of the epithelial cells of the spinous cell layer and koilocytes are frequently seen.

## **3 Precancerous Lesions (Clinical Classification)**

*A morphologically altered tissue in which cancer is more likely to occur than in its apparently normal counterpart.*

### **3.1 Leukoplakia (Figs. 43–47)**

*A predominantly white lesion of the oral mucosa that cannot be characterized as any other definable lesion.*

Over the years the term leukoplakia has been used for lesions having a whitish appearance as the common denominator

and some of which have proved to be precancerous. Studies have shown that such whitish lesions may have widely different aetiological backgrounds, which may be related to their malignant potential.

Whitish patches or plaques for which a local cause can be identified should be classified according to the established cause and not be included among leukoplakias. Examples are lesions associated with friction, dental restorations, cheek-biting, and glassblowing (see below). Lesions with a white appearance that cannot be clearly diagnosed on clinical examination as any other disease of the oral mucosa should be provisionally diagnosed as oral leukoplakia. A definitive diagnosis of oral leukoplakia is made as a result of the identification, and if possible elimination, of suspected aetiological factors and, in the case of persistent lesions, histopathological examination.

The term "hairy leukoplakia" has recently been introduced to describe a characteristic white lesion that almost exclusively occurs bilaterally on the borders of the tongue in some HIV-infected individuals. This terminology is potentially misleading as it does not coincide with the definition of leukoplakia (as given above) and in itself carries no risk of malignant transformation.

According to their *clinical* appearance, leukoplakias may be classified as either homogeneous or non-homogeneous. The latter comprise about 10 % of all leukoplakias. Table 1 gives a classification based upon clinical criteria.

*Homogeneous leukoplakias* may be found in all regions of the oral mucosa. The lesion is white or whitish with a surface that may be flat, corrugated, cracked, wrinkled, or pumice-like.

The corrugated type is especially found in the floor of the mouth, and is sometimes called the "ebbing-tide" type of leukoplakia. The anatomical location of the lesion may influence its morphology.

Wrinkling of the mucosal surface is characteristic of the type seen only in individuals using snuff intraorally. The intensity of

**Table 1.** Clinical classification of leukoplakias

<i>Homogeneous leukoplakias</i>	<i>Non-homogeneous leukoplakias</i>
Flat	Verrucous
Corrugated	Nodular
Wrinkled	Ulcerated
Pumice-like	Erythroleukoplakia

wrinkling has been used in grading the severity of the lesions in studies in Sweden and the USA. The openings of minor salivary gland ducts on the surface may be present as red punctate features. This type only very rarely exhibits dysplasia.

The fourth type of homogeneous leukoplakia is the pumice-like type. It is characterized by delicate white striae and appears to be a specific reaction of the oral mucosa that may be caused either by smoking tobacco or by snuff usage.

Often a mixed pattern of the above clinical types may be observed.

*Non-homogeneous leukoplakias* may also be found on any oral mucosal surface. They are predominantly white with verrucous, nodular, ulcerated or erythematous features and are more dangerous when found to be indurated on palpation. In general terms, they present a greater risk of malignant change than the homogeneous types. The verrucous type is characterized by a warty appearance and may be difficult to distinguish from squamous papilloma or verrucous carcinoma. A rare type is characterized by being multifocal, slow growing and with a propensity to recur after excision. Some have described this type as *proliferative verrucous leukoplakia*; in the past it has sometimes been called oral florid papillomatosis. Nearly all cases of proliferative verrucous leukoplakia eventually undergo malignant transformation at multiple sites. The nodular type of leukoplakia, originally described as speckled leukoplakia, possesses the important clinical feature of white nodular excrescences. In between the predominating nodules, the mucosa is often erythematous (erythroleukoplakia).

A homogeneous leukoplakia that becomes infected with *C. albicans*, which is often the case, may change its clinical appearance and become ulcerated or more erythematous. Such a lesion may eventually develop into a nodular leukoplakia. Non-homogeneous leukoplakias treated with local antifungal agents may correspondingly revert to the homogeneous type.

The term erythroleukoplakia is used when a lesion is composed of a mixture of white areas, often in the form of white nodules, and red areas.

### 3.2 Erythroplakia (Fig. 48)

*A fiery red patch that cannot be characterized clinically or pathologically as any other definable lesion.*

Some erythroplakias are smooth and some are granular or nodular. Often there is a well-defined margin adjacent to mucosa of normal appearance. The soft palate, ventral surface of the tongue and floor of the mouth are the most likely sites to be involved, but any part of the oral mucosa may be affected. Erythroplakias are high-risk lesions for the subsequent development of carcinoma.

### 3.3 Palatal Keratosis Associated with Reverse Smoking (Fig. 49)

*A diffuse whitening of the palatal mucosa in reverse smokers.*

This occurs with or without the following features: elevated white patches, red areas, ulcerations and hyper-pigmented or non-pigmented areas. In several countries cigars or cigarettes are smoked with the glowing end inside the mouth. The largest number of reverse smokers is found in certain areas of India, but the habit is also practised in some Latin American countries, in Sardinia and in the Philippines.

## 4 Precancerous Lesions (Histological Classification)

Although leukoplakia is a clinical term and its use carries no implications with regard to histological findings, a histological report should always include a statement on the presence or absence of epithelial dysplasia and, if present, an assessment of its severity. Sometimes malignancy develops in association with an oral leukoplakia for which earlier biopsies have not demonstrated epithelial dysplasia.

The majority of homogeneous leukoplakias show hyperorthokeratosis and acanthosis (Fig. 50) without signs of epithelial dysplasia. Inflammation may or may not be present in the lamina propria.

Those leukoplakias that are not hyperorthokeratotic exhibit hyperparakeratosis (Fig. 51). The mitotic activity of hyperparakeratotic leukoplakias is usually higher than in the hyperorthokeratotic types but this, by itself, should not be interpreted as a sign of dysplasia. Characteristically, hyperparakeratotic lesions usually have a much thicker epithelium than those with hyperorthokeratosis.

A special form of hyperkeratinization is the so-called chevron type of parakeratosis that is confined to non-keratinized oral mucosa (Fig. 52) and seems to be a specific reaction of the oral mucosa to tobacco. It is characterized by streaks of parakeratosis with a chevron-like pattern. The streaks are often raised beyond the adjacent layers, giving the surface a fingerprint-like appearance clinically.

Non-homogeneous leukoplakias are often associated with epithelial dysplasia, carcinoma in situ or squamous cell carcinoma. The same is true for erythroplakias and erythroleukoplakias.

#### **4.1 Squamous Epithelial Dysplasia (Figs. 53–55)**

*A precancerous lesion of stratified squamous epithelium characterized by cellular atypia and loss of normal maturation and stratification short of carcinoma in situ.*

The general disturbance of the epithelium is designated dysplasia and the potential for developing invasive carcinoma increases with the severity of dysplasia.

The changes that may occur in epithelial dysplasia are listed in Table 2, and the more prominent or more numerous they are, the more severe the grade of dysplasia. It will, of course, be appreciated that not all these changes are necessarily seen in any one case and that there is considerable subjectivity involved in their recognition and the interpretation of their significance in various combinations and forms. It should also be noted that some cellular atypia, usually of minor degree, is often present in inflammatory conditions and in regenerating epithelium. Sometimes epithelial dysplasia may be seen in lichen planus and in candidiasis.

The relationship of epithelial dysplasia in its various grades (commonly divided into mild, moderate and severe) to the subsequent development of cancer has not been fully clarified. However, it is generally believed that any degree of epithelial