

❖ Epithelial pathology

LEUKOPLAKIA (LEUKOKERATOSIS; ERYTHROLEUKOPLAKIA)

Oral **leukoplakia** (*leuko* = white; *plakia* = patch) is defined by the World Health Organization (WHO) as “a white patch or plaque that cannot be characterized clinically or pathologically as any other disease.”

As with most oral white lesions, the clinical color results from a thickened surface *keratin* layer, which appears white when wet, or a thickened *spinous* layer, which masks the normal vascularity (redness) of the underlying connective tissue.

CAUSEES

The cause of leukoplakia remains unknown, although hypotheses abound.

- TOBACCO
- ALCOHOL
- SANGUINARIA
- ULTRAVIOLET RADIATION
- MICROORGANISMS
- TRAUMA

CLINICAL FEATURES

Leukoplakia usually affects persons older than 40 years of age. Approximately 70% of oral leukoplakias are found on the lip vermillion, buccal mucosa, and gingiva. Early and mild lesions appear as slightly elevated gray or gray-white plaques, which may appear somewhat translucent, fissured, or wrinkled and are typically soft and flat .

HISTOPATHOLOGIC FEATURES

Microscopically, leukoplakia is characterized by a thickened keratin layer of the surface epithelium (**hyperkeratosis**), with or without a thickened spinous layer (**acanthosis**).

The keratin layer may consist of parakeratin (**hyperparakeratosis**), orthokeratin (**hyperorthokeratosis**), or a combination of both .

With parakeratin, there is no granular cell layer and the epithelial nuclei are retained in the keratin layer. With orthokeratin, the epithelium demonstrates a granular cell layer and the nuclei are lost in the keratin layer.

Carcinoma in situ is defined as dysplastic epithelial cells that extend from the basal layer to the surface of the mucosa (“top-to-bottom” change).

TREATMENT

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Because leukoplakia represents a clinical term only, the first step in treatment is to arrive at a definitive histopathologic diagnosis. Therefore, a biopsy is mandatory and will guide the course of treatment. Complete removal can be accomplished with equal effectiveness by surgical excision, electro cauterly, cryosurgery, or laser ablation.

ERYTHROPLAKIA (ERYTHROPLASIA; ERYTHROPLASIA OF QUEYRAT)

erythroplakia is defined as a red patch that cannot be clinically or pathologically diagnosed as any other condition.

Almost all true erythroplakias demonstrate significant epithelial dysplasia, carcinoma *in situ*, or invasive squamous cell carcinoma.

The point prevalence rate of oral erythroplakia has been estimated as 1 per 2500 adults.

CLINICAL FEATURES

Erythroplakia is predominantly a disease of middle-aged to older adults with no significant gender predilection. The floor of mouth, tongue, and soft palate are the most common sites of involvement, and multiple lesions may be present. The altered mucosa appears as a well-demarcated erythematous macule or plaque with a soft, velvety texture. It is usually asymptomatic and may be associated with an adjacent leukoplakia (**erythroleukoplakia**).

HISTOPATHOLOGIC FEATURES

histopathologically represent severe epithelial dysplasia, carcinoma *in situ*, or superficially invasive squamous cell carcinoma. The epithelium shows a lack of keratin production and often is atrophic. This lack of keratinization, especially when combined with epithelial thinness, allows the underlying microvasculature to show through, thereby explaining the red color.

TREATMENT

As with leukoplakia, the treatment of erythroplakia is guided by the definitive diagnosis obtained by biopsy.

SMOKELESS TOBACCO USE AND SMOKELESS TOBACCO KERATOSIS (SNUFF POUCH; SNUFF DIPPER'S LESION; TOBACCO POUCH KERATOSIS; SPIT TOBACCO KERATOSIS)

The three main types of smokeless tobacco used in the United States include chewing tobacco, moist snuff, and dry snuff.

CLINICAL FEATURES

One of the most common local changes is a characteristic painless loss of gingival tissues in the area of tobacco contact that may be accompanied by destruction of the facial surface of the alveolar bone.

Dental caries also has been reported.

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A brown-black extrinsic tobacco stain is typically found on the enamel and cementum surfaces of the teeth adjacent to the tobacco. In addition, halitosis is a frequent finding in chronic users.

A characteristic white plaque, the **smokeless tobacco keratosis**, also is produced on the mucosa in direct contact with snuff or chewing tobacco.

The lesion is confined to areas in direct contact with spit tobacco. It is typically a thin, gray or gray-white, almost “translucent,” plaque with a border that blends gradually into the surrounding mucosa .

The altered mucosa typically has a soft velvety feel to palpation, and stretching of the mucosa often reveals a distinct “pouch” (**snuff pouch, tobacco pouch**) caused by flaccidity in the chronically stretched tissues in the area of tobacco placement.

HISTOPATHOLOGIC FEATURES

The histopathologic appearance of smokeless tobacco keratosis is not specific. The squamous epithelium is hyperkeratinized and acanthotic. Parakeratin **chevrons** may be seen as pointed projections above or within superficial epithelial layers .

TREATMENT

Treatment depend on the histopathologic diagnosis , Without microscopic evidence of dysplasia or malignancy, keratoses are not treated.

Alternating the tobacco-chewing sites between the left and right sides will eliminate or reduce the keratotic lesion.

Significantly, habit cessation leads to a normal mucosal appearance (usually within 2 weeks) in 98% of smokeless tobacco keratosis .

NICOTINE STOMATITIS (NICOTINE PALATINUS; SMOKER’S PALATE)

Once a common mucosal change of the hard palate, **nicotine stomatitis** has become less common as cigar and pipe smoking have lost popularity. Although this lesion is a white keratotic change obviously associated with tobacco smoking, it does not appear to have a premalignant nature, perhaps because it develops in response to heat rather than the chemicals in tobacco smoke.

CLINICAL FEATURES

Nicotine stomatitis most commonly is found in men older than 45 years of age. the palatal mucosa becomes diffusely gray or white; numerous slightly elevated papules are noted, usually with punctate red centers . Such papules represent inflamed minor salivary glands and their ductal orifices. The mucosa that covers the papules frequently appears whiter than the surrounding epithelium. The whiteness usually involves marginal gingiva and interdental papillae. A heavy brown or black tobacco stain may be present on the teeth.

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HISTOPATHOLOGIC FEATURES

Nicotine stomatitis is characterized by hyperkeratosis and acanthosis of the palatal epithelium and mild, patchy, chronic inflammation of subepithelial connective tissue and mucous glands. In cases with papular elevation, hyperplastic ductal epithelium may be seen near the orifice.

TREATMENT

Nicotine stomatitis is completely reversible, even when it has been present for many decades. The palate returns to normal, usually within 1 to 2 weeks of smoking cessation.

ACTINIC CHEILOSIS (ACTINIC CHEILITIS)

Actinic cheilosis is a common premalignant alteration of the lower lip vermilion that results from long term or excessive exposure to the ultraviolet component of sunlight.

CLINICAL FEATURES

It has a strong male predilection, with a male-to-female ratio as high as 10:1. The lesion develops so slowly that patients often are not aware of a change. The earliest clinical changes include atrophy of the lower lip vermilion border, characterized by a smooth surface and blotchy pale areas. Blurring of the margin between the vermilion zone and the cutaneous portion of the lip is typically seen. As the lesion progresses, rough, scaly areas develop on the drier portions of the vermilion.

HISTOPATHOLOGIC FEATURES

Actinic cheilosis is usually characterized by an atrophic stratified squamous epithelium, often demonstrating marked keratin production. Varying degrees of epithelial dysplasia may be encountered. A mild chronic inflammatory cell infiltrate commonly is present subjacent to the dysplastic epithelium. The underlying connective tissue invariably demonstrates a band of amorphous, a cellular, basophilic change known as **solar (actinic) elastosis**, an ultraviolet light-induced alteration of collagen and elastic fibers.

TREATMENT

Use lip balms with sunscreens to prevent further damage.

In clinically severe cases without obvious malignant transformation, a lip shave procedure (**vermilionectomy**) may be performed.

SQUAMOUS CELL CARCINOMA

Approximately 94% of all oral malignancies are **squamous cell carcinoma**.

ETIOLOGY OF ORAL CANCER

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The cause of oral squamous cell carcinoma is multifactorial. No single causative agent or factor (carcinogen) has been clearly defined or accepted, but both extrinsic and intrinsic factors may be at work.

Extrinsic factors include such external agents as tobacco smoke, alcohol, syphilis, and (for vermilion cancers only) sunlight.

Intrinsic factors include systemic or generalized states, such as general malnutrition or iron-deficiency anemia.

CLINICAL AND RADIOGRAPHIC FEATURES

There is minimal pain during the early growth phase, and this may explain the delay in seeking professional care.

Oral squamous cell carcinoma has a varied clinical presentation, including the following:

- Exophytic (mass forming; fungating, papillary, verruciform)
- Endophytic (invasive, burrowing, ulcerated)
- Leukoplakic (white patch)
- Erythroplakic (red patch)
- Erythroleukoplakic (combined red-and-white)

INTRAORAL CARCINOMA

The most common site for intraoral carcinoma is the tongue, usually the posterior lateral and ventral surfaces. appear as painless, indurated masses or ulcers of the posterior lateral border.

Individualized TNM classifications are used for most human cancers. This staging protocol depends on three basic clinical features:

1. T—Size of the primary tumor, in centimeters
2. N—Involvement of local lymph nodes
3. M—Distant metastasis

Once the three parameters are determined, they are tallied together to determine the appropriate stage.

The higher the stage classification, the worse the prognosis

HISTOPATHOLOGIC FEATURES

Squamous cell carcinoma arises from dysplastic surface epithelium and is characterized histopathologically by invasive islands and cords of malignant squamous epithelial cells.

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Invasion is represented by irregular extension of lesional epithelium through the basement membrane and into subepithelial connective tissue. Invading cells and cell masses may extend deeply into underlying adipose tissue, muscle, or bone, destroying the original tissue as they progress.

Histopathologic evaluation of the degree to which these tumors resemble their parent tissue (squamous epithelium) and produce their normal product (keratin) is called **grading**.

Lesions are graded on a 3-point (grades I to III) or a 4-point (grades I to IV) scale. The less differentiated tumors receive the higher numerals.

TREATMENT

The clinical stage of the disease guides the treatment of intraoral squamous cell carcinoma, which consists of wide (radical) surgical excision, radiation therapy, or a combination of surgery and radiation therapy.

VERRUCOUS CARCINOMA (SNUFF DIPPER'S CANCER; ACKERMAN'S TUMOR)

Verrucous carcinoma is a low-grade variant of oral squamous cell carcinoma. Some of these lesions might be associated with the use of smokeless tobacco.

CLINICAL FEATURES

Verrucous carcinoma is found predominantly in men older than 55 years of age (average age, 65 to 70 years).

The most common sites of oral mucosal involvement include the mandibular vestibule, gingiva, buccal mucosa, tongue, and hard palate.

The lesion appears as a diffuse, well-demarcated, painless, thick plaque with papillary or verruciform surface projections. Lesions are typically white but also may appear erythematous or pink.

HISTOPATHOLOGIC FEATURES

Verrucous carcinoma has a deceptively benign microscopic appearance; it is characterized by wide and elongated rete ridges that appear to "push" into the underlying connective tissue. Lesions usually show abundant keratin (usually parakeratin) production and a papillary or verruciform surface.

Parakeratin typically fills the numerous clefts or crypts (parakeratin plugs) between the surface projections. These projections may be long and pointed or short and blunted. The lesional epithelial cells generally show a normal maturation pattern with no significant degree of cellular atypia.

TREATMENT

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Because metastasis is an extremely rare event in verrucous carcinoma, the treatment of choice is surgical excision without radical neck dissection.