J Oral Pathol Med. 2007 Nov;36(10):575-80. doi: 10.1111/j.1600-0714.2007.00582.x.

Nomenclature and classification of potentially malignant disorders of the oral mucosa

S Warnakulasuriya [1], Newell W Johnson, I van der Waal

Affiliations + expand

PMID: 17944749 DOI: 10.1111/j.1600-0714.2007.00582.x

Abstract

At a workshop coordinated by the WHO Collaborating Centre for Oral Cancer and Precancer in the UK issues related to terminology, definitions and classification of oral precancer were discussed by an expert group. The consensus views of the Working Group are presented here. The term, 'potentially malignant disorders', was recommended to refer to precancer as it conveys that not all disorders described under this term may transform into cancer. Critically evaluating all definitions proposed so far for oral leukoplakia, the Working Group agreed that the term leukoplakia should be used to recognize 'white plaques of questionable risk having excluded (other) known diseases or disorders that carry no increased risk for cancer'. An outline was proposed for diagnosing oral leukoplakia that will prevent other oral white disorders being misclassified as leukoplakia. The Working Group discussed the caveats involved in the current use of terminology and classification of oral potentially malignant disorders, deficiencies of these complex systems, and how they have evolved over the past several decades. The terminology presented in this report reflects our best understanding of multi-step carcinogenesis in the oral mucosa, and aspires to engender consistency in use.

Nomenclature and classification

- **Definition**
- OPMDs refer to a group of lesions and conditions characterised by a variably increased risk of developing cancers of the lip (C00) and the oral cavity (C02-C06)

- ‘pre-cancer’, ‘precursor lesions’, ‘pre-malignant’, ‘intra epithelial neoplasia’ and ‘potentially malignant’ have been used in the international literature to broadly describe clinical presentations that may potentially become cancer.

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WHO classification 2005

- Classification of precancerous lesions and conditions

Precancerous lesions	Precancerous conditions
Leukoplakia	Submucous fibrosis
Erythroplakia	Actinic keratosis
Palatal lesions in reverse smokers	Lichen planus
	Discoid lupus erythematosus
	Hereditary disorders with increased risk: dyskeratosis congenita and epidermolysis bullosa

J Oral Pathology Medicine, Volume: 36, Issue: 10, Pages: 575-580, First published: 26 July 2007, DOI: (10.1111/j.1600-0714.2007.00582.x)

Review > Oral Dis. 2021 Nov;27(8):1862-1880. doi: 10.1111/odi.13704. Epub 2020 Nov 26.

Oral potentially malignant disorders: A consensus report from an international seminar on nomenclature and classification, convened by the WHO Collaborating Centre for Oral Cancer

Saman Warnakulasuriya [1], Omar Kujan [2], José M Aguirre-Urizar [3], José V Bagan [4 5], Miguel Ángel González-Moles [6 7], Alexander R Kerr [8], Giovanni Lodi [9], Fernanda Weber Mello [10], Luis Monteiro [11], Graham R Ogden [12], Philip Sloan [13], Newell W Johnson [14 15]

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PMID: 33128420 DOI: 10.1111/odi.13704

Free article

Abstract

Oral potentially malignant disorders (OPMDs) are associated with an increased risk of occurrence of cancers of the lip or oral cavity. This paper presents an updated report on the nomenclature and the classification of OPMDs, based predominantly on their clinical features, following discussions by an expert group at a workshop held by the World Health Organization (WHO) Collaborating Centre for Oral Cancer in the UK. The first workshop held in London in 2005 considered a wide spectrum of disorders under the term "potentially malignant disorders of the oral mucosa" (PMD) (now referred to as oral potentially malignant disorders: OPMD) including leukoplakia, erythroplakia, proliferative

WHO classification 2020

Remove from the 2021 classification due to limited evidence
Oral Epidermolysis Bullosa
Chronic hyperplastic candidosis
Exophytic verrucous hyperplasia/verrucous hyperplasia

Oral potentially malignant disorders: A consensus report from an international seminar on nomenclature and classification, convened by the WHO Collaborating Centre for Oral Cancer. Oral Dis. 2021 Nov;27(8):1862-1880. doi: 10.1111/odi.13704.

WHO classification 2020

Classification of oral potentially malignant disorders	Newly included in 2021 classification
Leukoplakia	Oral Lichenoid Lesion
Proliferative verrucous leukoplakia	Oral Graft versus Host Disease
Erythroplakia	**Remove from the 2021 classification due to limited evidence**
Oral submucous fibrosis	Oral Epidermolysis Bullosa
Oral lichen planus	Chronic hyperplastic candidosis
Actinic Keratosis (Actinic Cheilitis)	Exophytic verrucous hyperplasia/verrucous hyperplasia
Palatal changes in reverse smoking	
Oral Lupus Erythematosus	
Dyskeratosis Congenita	

Oral potentially malignant disorders: A consensus report from an international seminar on nomenclature and classification, convened by the WHO Collaborating Centre for Oral Cancer. Oral Dis. 2021 Nov;27(8):1862-1880. doi: 10.1111/odi.13704.

OPMD Epidemiology

- A recent systematic review included 22 epidemiological surveys that estimated a global prevalence of OPMDs at **4.47%** (95% CI = 2.43–7.08).
- It was noted that prevalence may vary between populations and was generally higher in Asians and males.

Prevalence of oral potentially malignant disorders: a systematic review and meta-analysis. J Oral Pathol Med 2018 Aug; 47: pp. 633-640.

Risk factors

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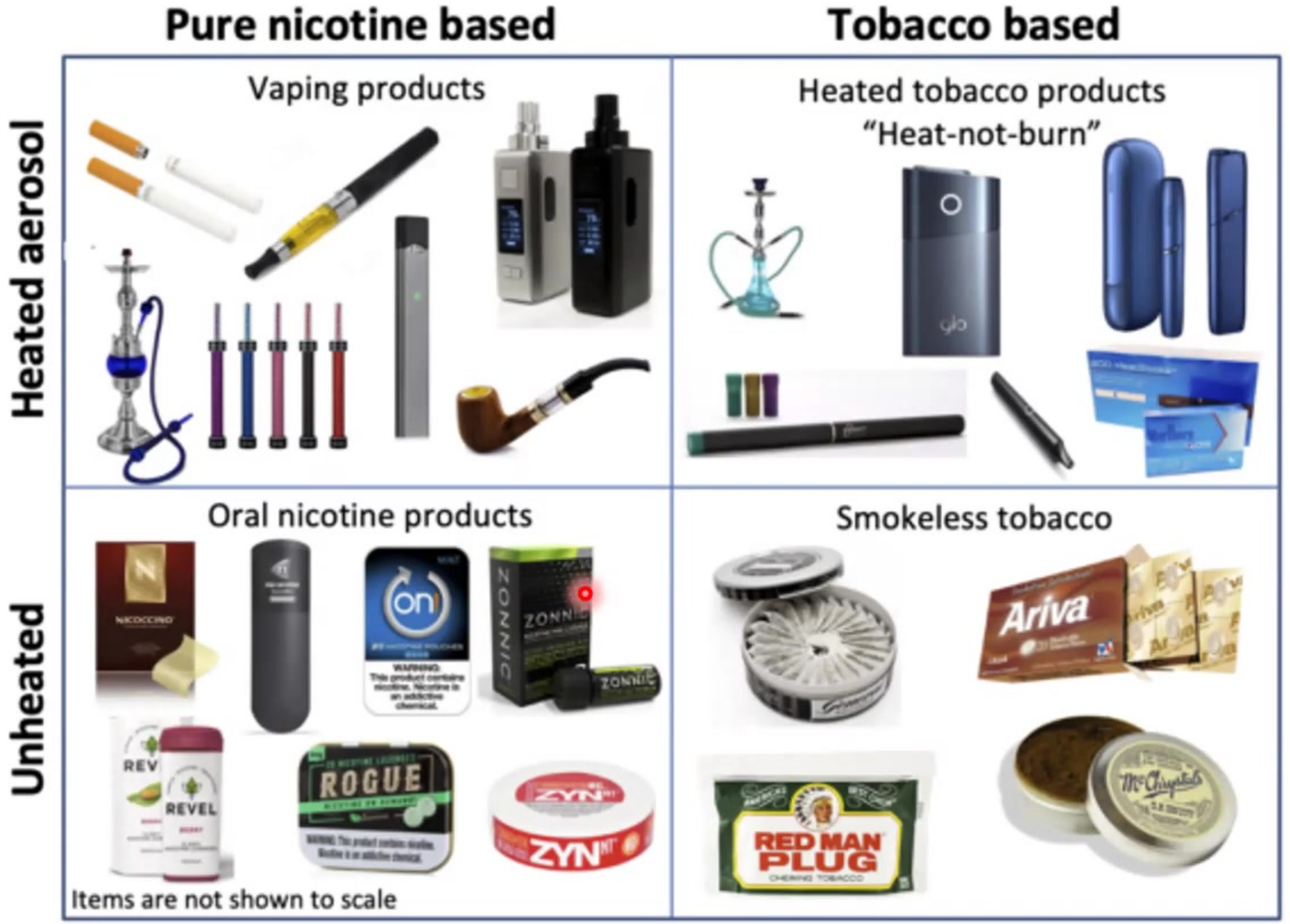

Kujan, O. (2017). Human Oral Cancer (Epidemiology and Characteristic). In: Al Moustafa, AE. (eds) Development of Oral Cancer. Springer, Cham. https://doi.org/10.1007/978-3-319-48054-1_1

Smokers are also at **10 times** higher risk for oral cancer compared to non-smokers.

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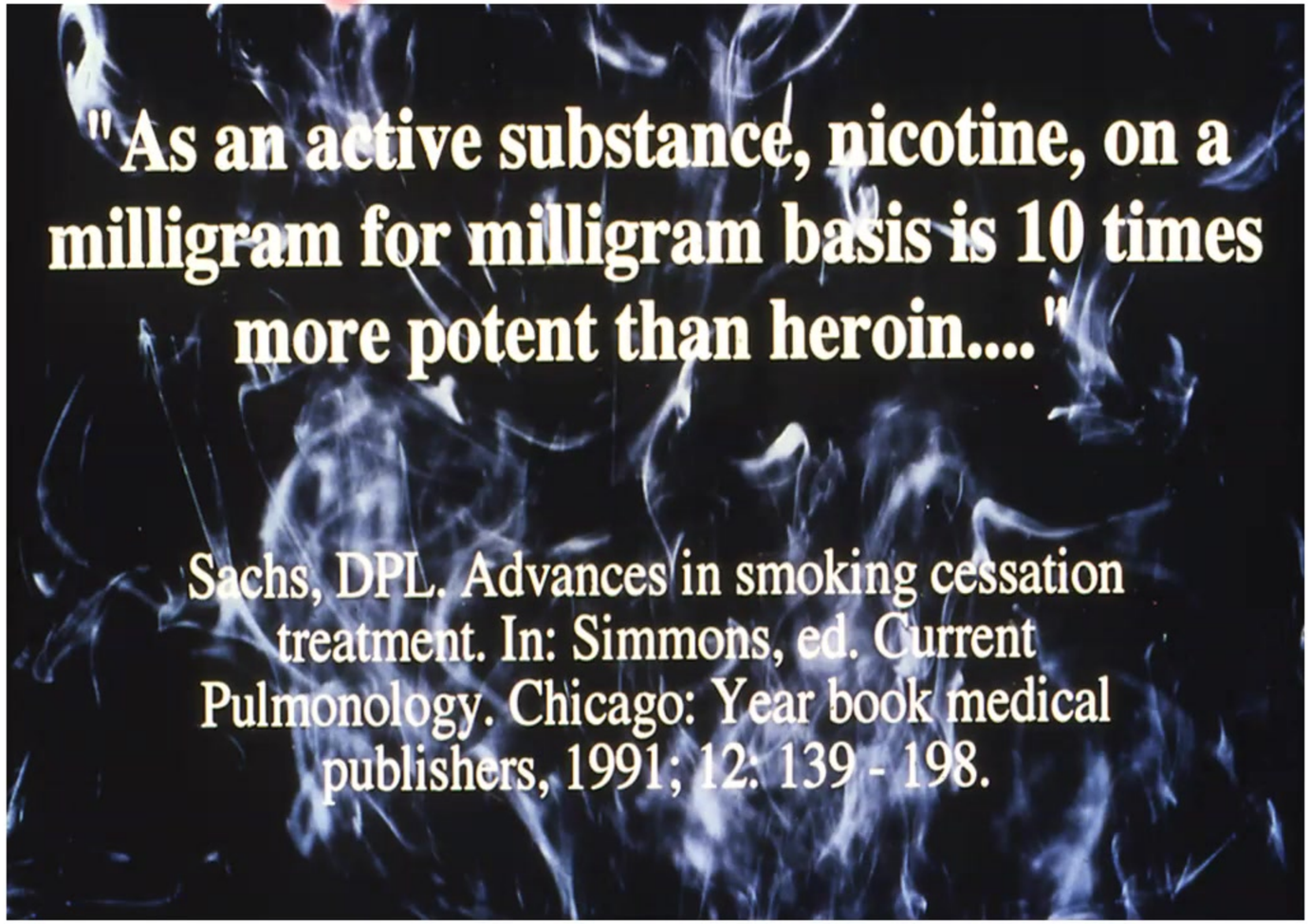


Risk factors

Moderate drinkers have 1.8-fold higher risks of oral cavity and pharynx cancers and 1.4-fold higher risks of larynx cancers than non-drinkers, and heavy drinkers have 5-fold higher risks of oral cavity and pharynx cancers and 2.6-fold higher risks of larynx cancers

Kujan, O. (2017). Human Oral Cancer (Epidemiology and Characteristic). In: Al Moustafa, AE. (eds) Development of Oral Cancer. Springer, Cham. https://doi.org/10.1007/978-3-319-48054-1_1

Risk factors

- **The combination of smoking and drinking is the most important aetiological factor for oral cancer and OPMDs**
- Many patients smoke and drink heavily (>5 standard drinks/day)
- Both of these account for up to 75% of all OPMD cases

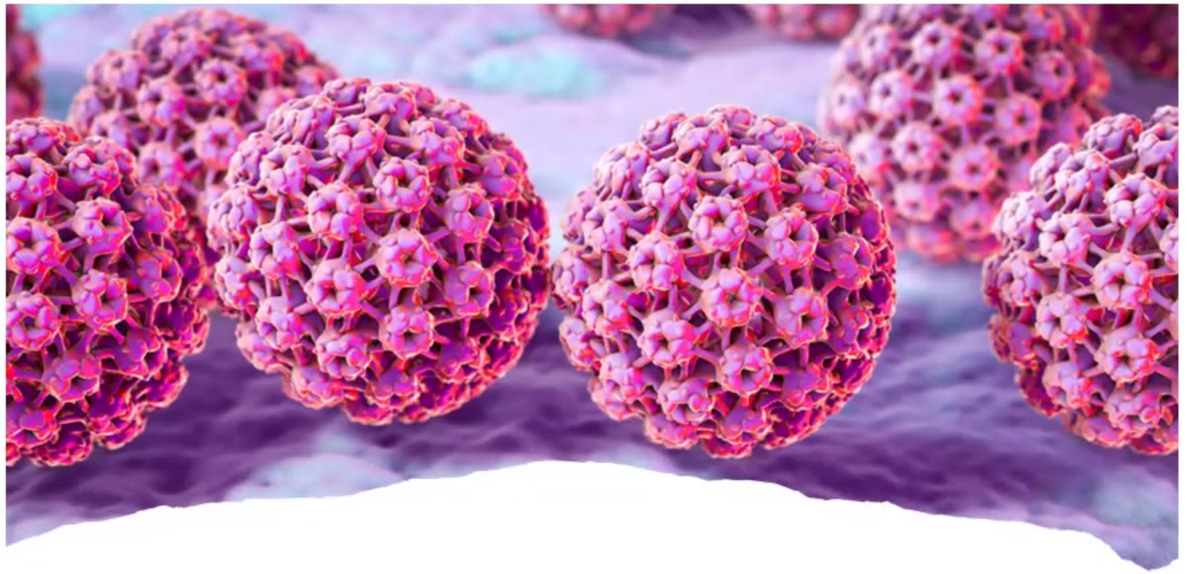
Oral potentially malignant disorders: A consensus report from an international seminar on nomenclature and classification, convened by the WHO Collaborating Centre for Oral Cancer. Oral Dis. 2021 Nov;27(8):1862-1880. doi: 10.1111/odi.13704.

Risk factors

Betel quid/Areca nut

- Areca nut
  - Abundant copper and flavonoids
    - Stabilize and enhance cross-linking of collagen
      - Fibrosis
  - Alkaloids (arecoline)
    - Stimulate collagen synthesis and reduce collagen degradation
    - Can be converted to carcinogenic nitrosamines
- Gutka
  - Powdered tobacco, slaked lime, and spices wrapped in *Piper betle* leaf, also referred to as "betel leaf"
    - more rapid development of oral lesions

Risk factors



HPV is thought to cause 70% of oropharyngeal cancers in the United States.

Oral potentially malignant disorders: A consensus report from an international seminar on nomenclature and classification, convened by the WHO Collaborating Centre for Oral Cancer. Oral Dis. 2021 Nov;27(8):1862-1880. doi: 10.1111/odi.13704.

Clinical types

Leukoplakia

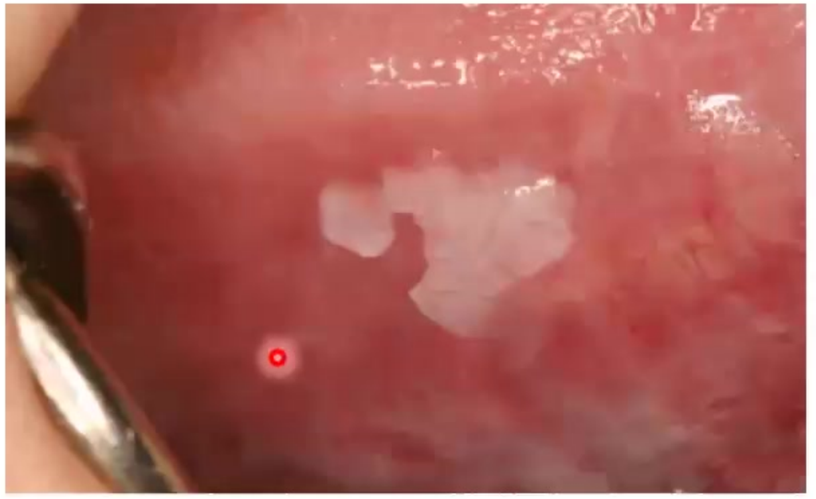
Persistent white patch that cannot be rubbed off. Generally asymptomatic

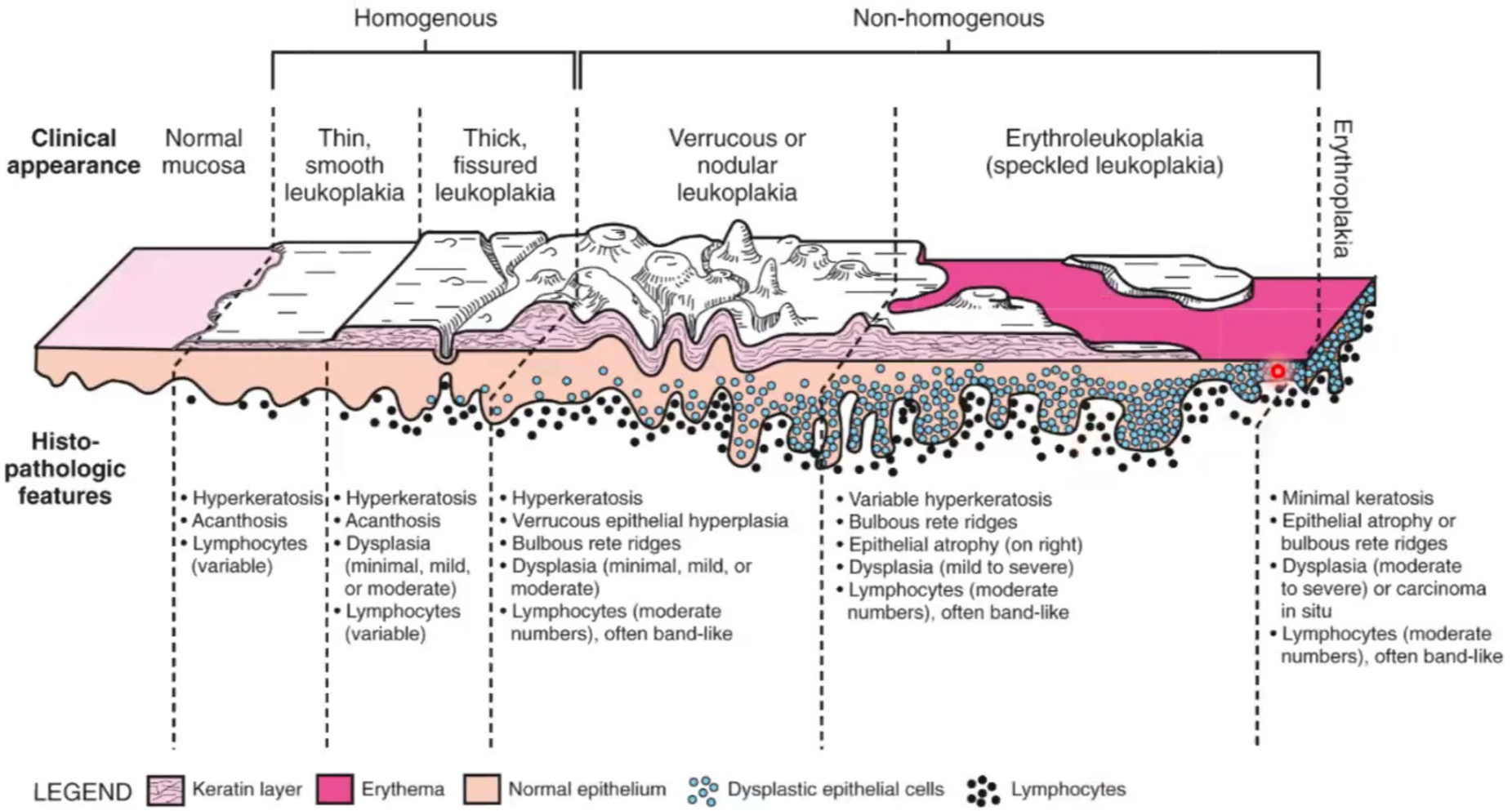
- 1-4% in Western countries
- Higher prevalence in SE Asia
- Global prevalence: 2-3%

Homogeneous leukoplakia : Uniformly white, flat and thin, have a smooth surface and may exhibit shallow cracks.

Nodular leukoplakia : Small polypoid or rounded outgrowths, red or white excrescences.

Verrucous leukoplakia : The surface is raised, exophytic, wrinkled or corrugated





Bouquot JE, Gnepp DR. Laryngeal precancer: a review of the literature, commentary, and comparison with oral leukoplakia. Head Neck. 1991;13:488–497.

Leukoplakia

Definition: “A predominantly white plaque of questionable risk having excluded (other) known diseases or disorders that carry no increased risk for cancer”

The following criteria should be considered when making a clinical diagnosis of oral leukoplakia:

- A predominantly white patch/plaque that cannot be rubbed off.
- Most homogeneous Leukoplakia affect a circumscribed area and have well-demarcated borders. A smaller subset can present with diffuse borders.
- Non-homogeneous Leukoplakia typically present with more diffuse borders and may have red or nodular components.
- No evidence of chronic traumatic irritation to the area (e.g., a sharp tooth rubbing on the tongue, a white patch on the alveolar ridge or retromolar pad from masticatory friction, a white patch on gingiva from overzealous toothbrushing).
- Is not reversible on elimination of apparent traumatic causes, that is demonstrates a persistence feature.
- Does not disappear or fade away on stretching (retracting) the tissue.
- By exclusion of other white or white/red lesions

Leukoplakia and Erythroplakia

Aetiology and pathogenesis

- Tobacco (smoking or chewing)
- Alcohol consumption
- Areca nut/betel quid with or without tobacco
- High-risk HPV infection is very rare in OPMDs

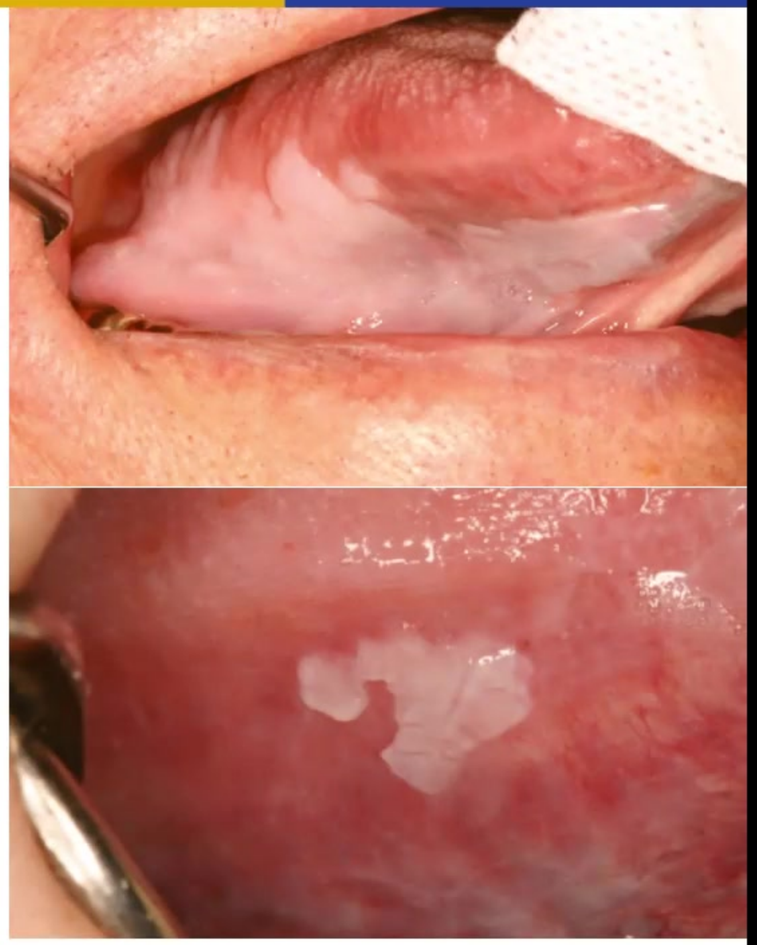
Epidemiology

- Leukoplakia
  - 1-4% in Western countries
  - Higher prevalence in SE Asia
  - Global prevalence: 2-3%

Leukoplakia

Clinical features

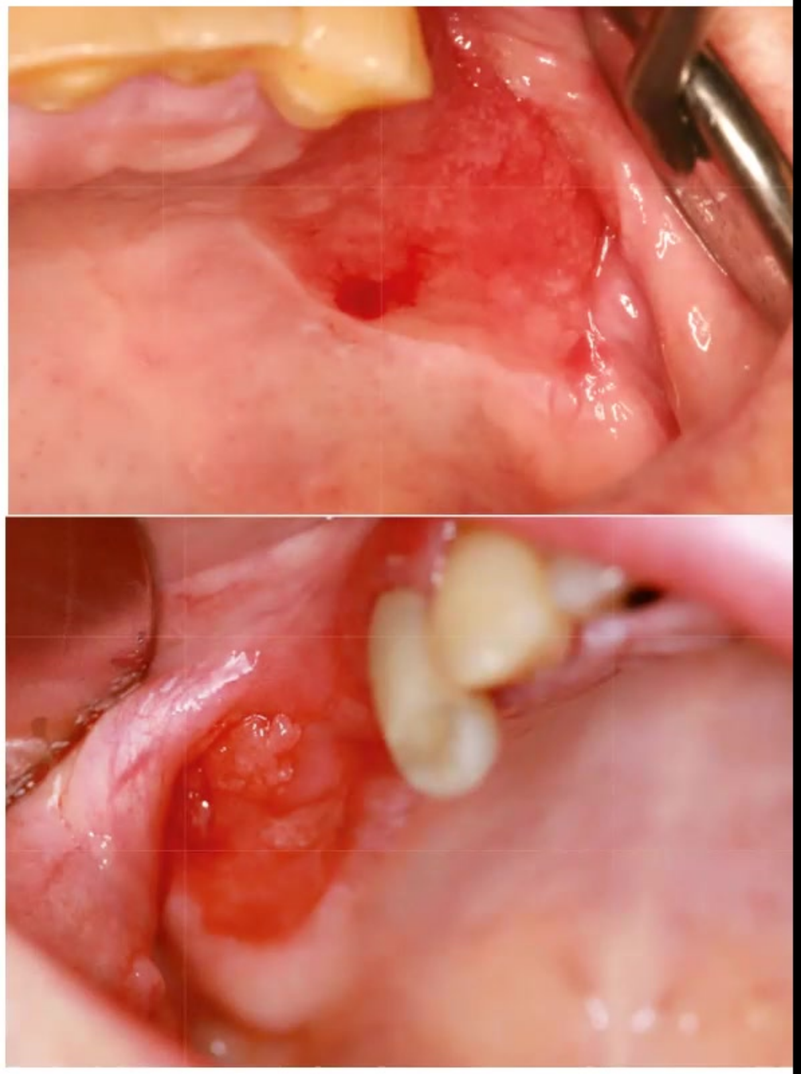
- This means:
  - It cannot be attributed to
    - Reactive, frictional, traumatic, or other causes
- Older individuals



Erythroplakia

Defined as “A predominantly fiery red patch that cannot be characterized clinically or pathologically as any other definable disease”

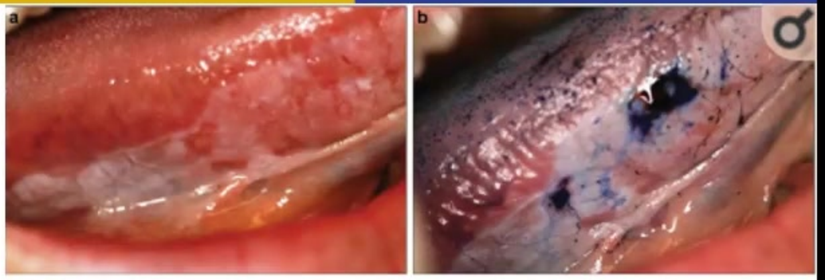
Clinical features



Leukoplakia and Erythroplakia

Diagnosis

- Diagnosis of exclusion
- Diagnostic aids
  - Tolonium chloride or toluidine blue dye
  - Oral CDx brush biopsy kits



Oral submucous fibrosis

Aetiology and pathogenesis

- Areca nut
  - Abundant copper and flavonoids
    - Stabilize and enhance cross-linking of collagen
      - Fibrosis
  - Alkaloids (arecoline)
    - Stimulate collagen synthesis and reduce collagen degradation
    - Can be converted to carcinogenic nitrosamines

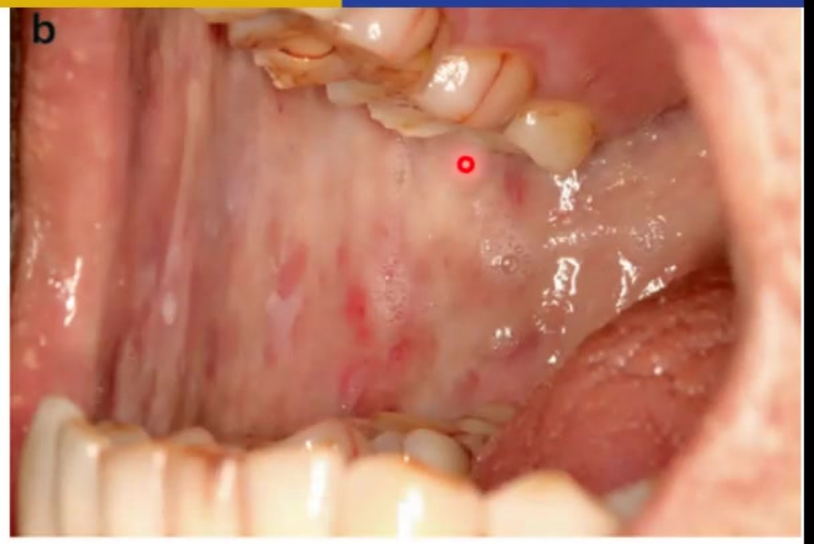
- Gutka
  - Powdered tobacco, slaked lime, and spices wrapped in *Piper betle* leaf, also referred to as "betel leaf"
    - more rapid development of oral lesions

Clinical features

Farah CS, balasubramanian R, McCollough M. Contemporary Oral Medicine: A Comprehensive Approach to Clinical Practice. First edition. China. Springer 2019.

Clinical features

- Diffuse, pale, marble-like, and keratotic areas
- Sites
  - Buccal mucosa
  - Soft palate
  - Tongue



Farah CS, balasubramanian R, McCollough M. Contemporary Oral Medicine: A Comprehensive Approach to Clinical Practice. First edition. China. Springer 2019.

Histopathologic features

Diagnosis and management

- History and clinical presntation
- Obtain good clinical images and write comprehensive clinical notes
- Obtain a biopsy if indicated
- Watchful monitoring
- Temporomandibular disorder management

Sadaksharam J, Mahalingam S. Evaluation of Oral Pentoxifylline in the Management of Oral Submucous Fibrosis - An Ultrasonographic Study. Contemp Clin Dent. 2017 Apr-Jun;8(2):200-204.

Palatal lesions in reverse smokers

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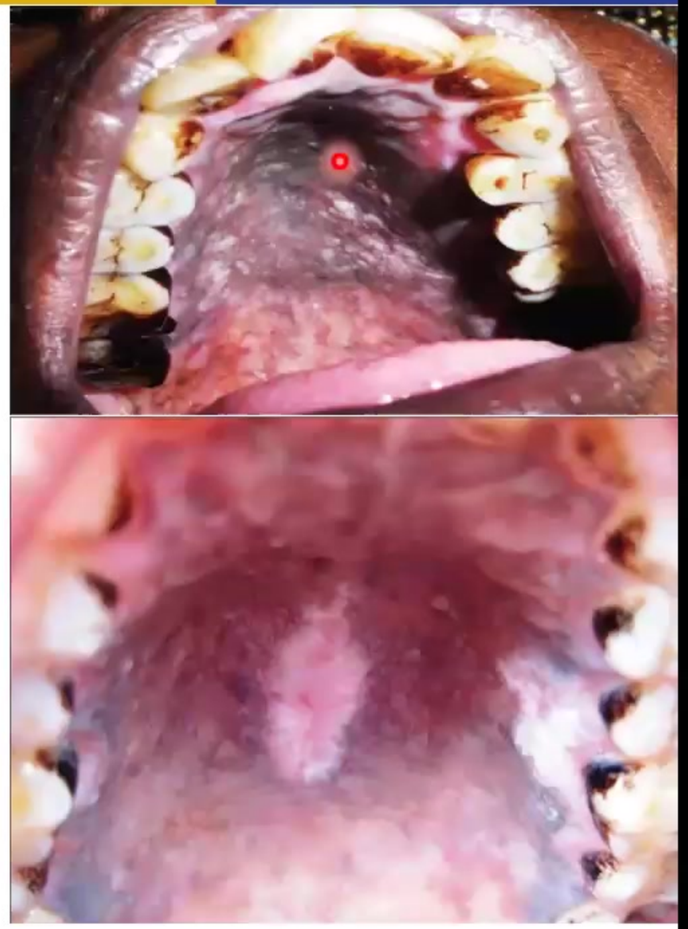
Clinical features



Bharath TS, Kumar NG, Nagaraja A, Saraswathi TR, Babu GS, Raju PR. Palatal changes of reverse smokers in a rural coastal Andhra population with review of literature. J Oral Maxillofac Pathol. 2015 May-Aug;19(2):182-7.

Actinic Cheilitis

Aetiolgy and pathogenesis

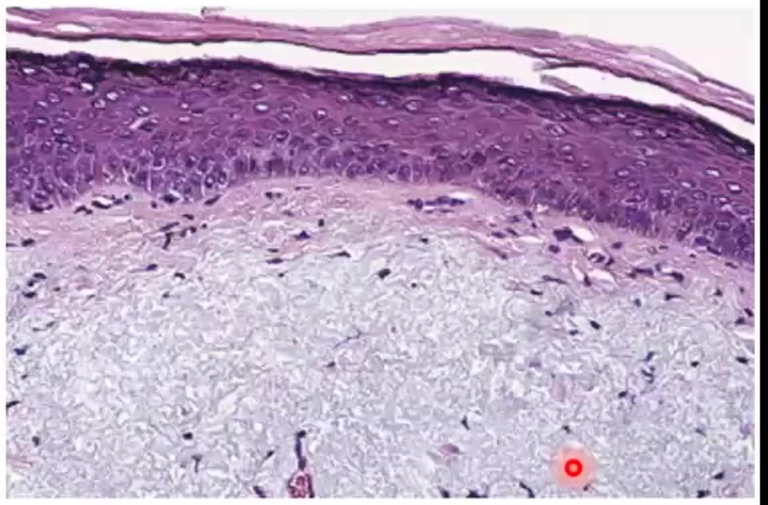
- UV light exposure
- Aetiopathogenesis similar to that of actinic keratosis of the skin
- Higher prevalence in
  - Closer to the equator
  - Middle-aged to elderly, fair complexioned men
  - Outdoor occupation
  - Certain genetic disorders
    - Xeroderma pigmentosum
    - Albinism
    - Porphyria cutanea tarda

Neville B, Allen C, Damm D. Oral and maxillofacial pathology. . Fourth edition.; Place of publication not identified Elsevier; 2016

Clinical features

Neville B, Allen C, Damm D. Oral and maxillofacial pathology. . Fourth edition.; Place of publication not identified Elsevier; 2016

Histopathologic features

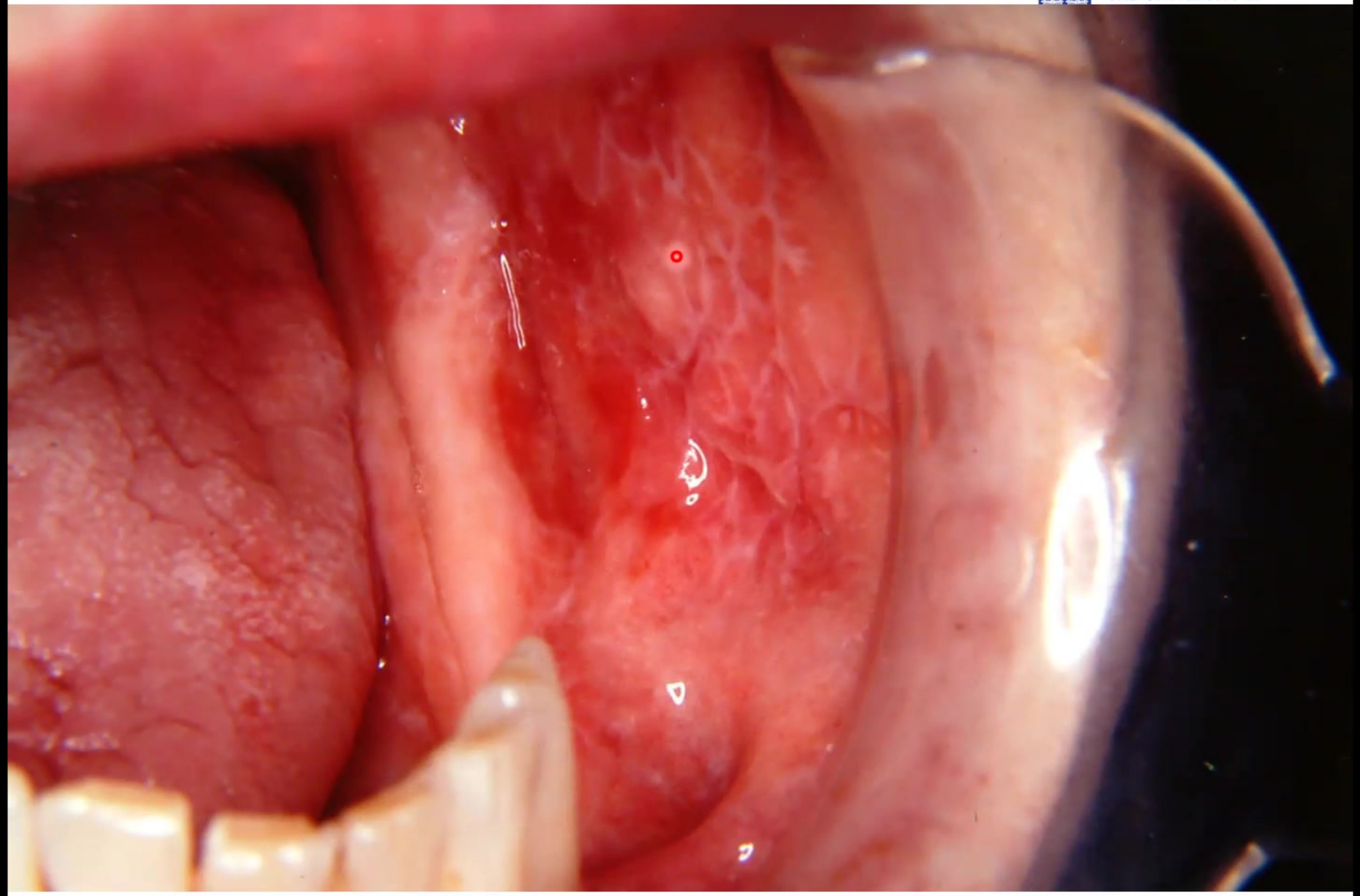


Neville B, Allen C, Damm D. Oral and maxillofacial pathology. . Fourth edition.; Place of publication not identified Elsevier; 2016

Lichen Planus

Aetiolgy and pathogenesis

- Immune mediated
  - T lymphocytes mainly
- Idiopathic vs drug induced
- Prevalence
  - 0.22-5% worldwide
  - 30-80 year olds
- Approximately 15% have cutaneous disease as well
- Females > Males



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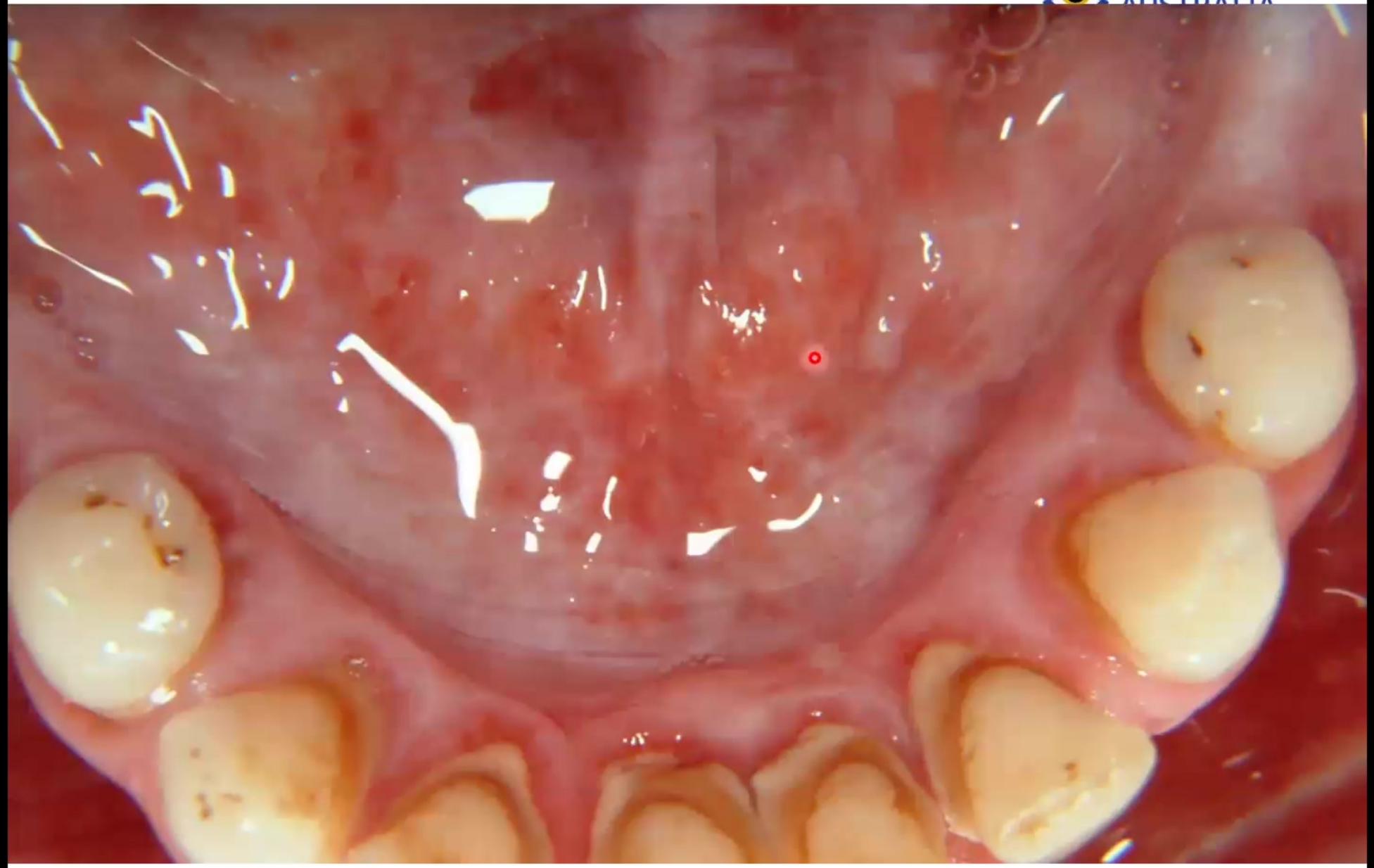

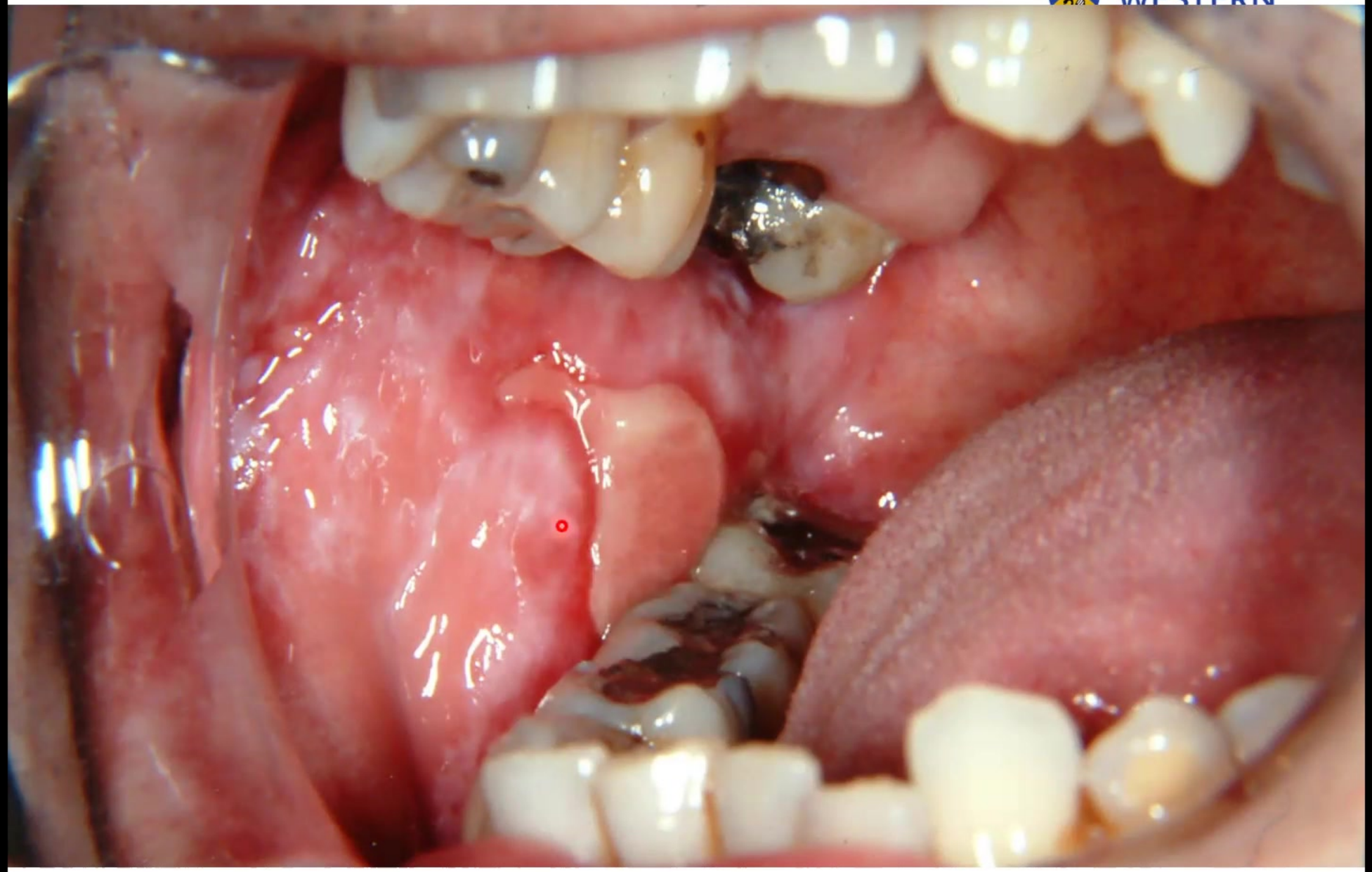

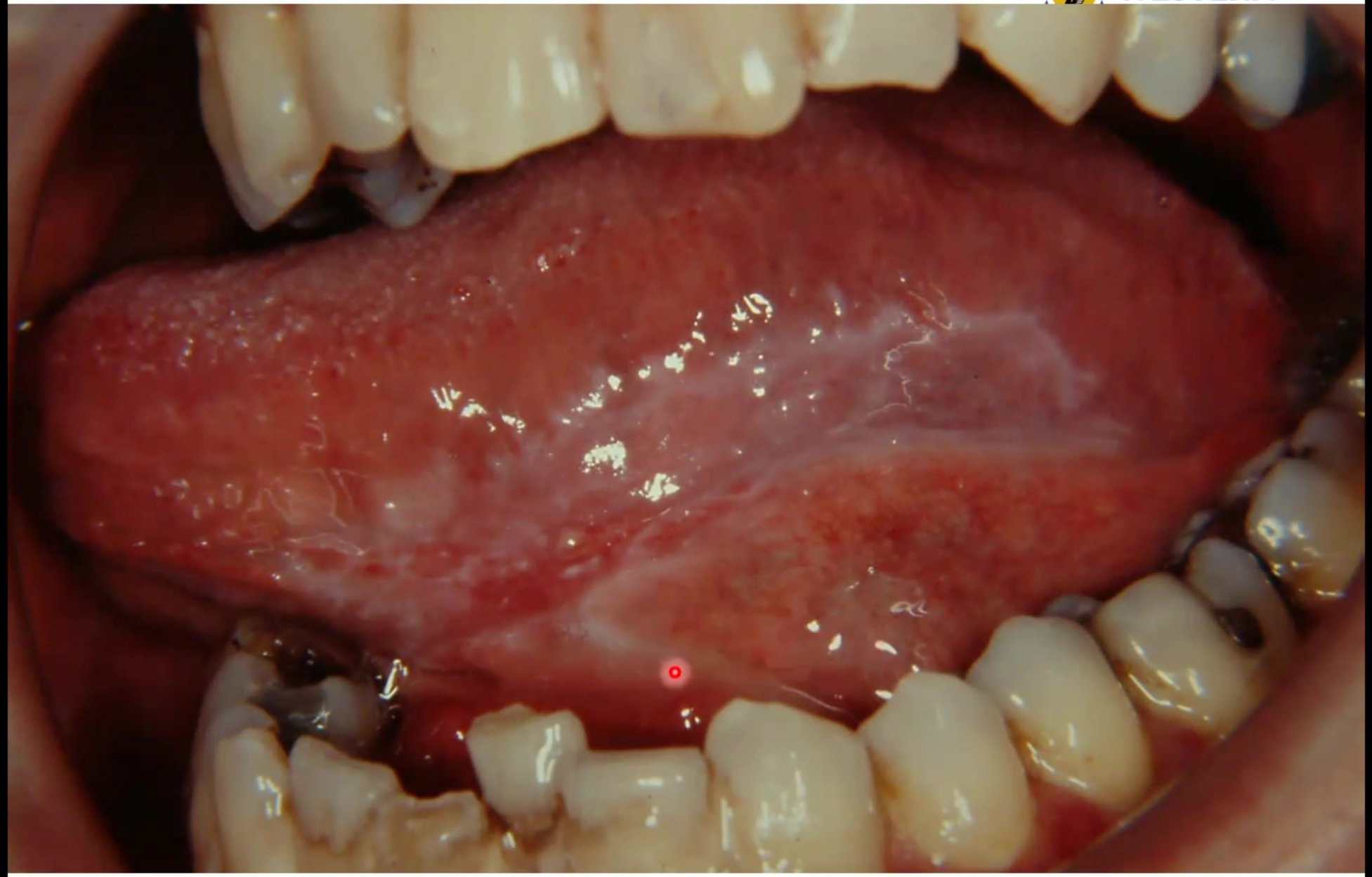

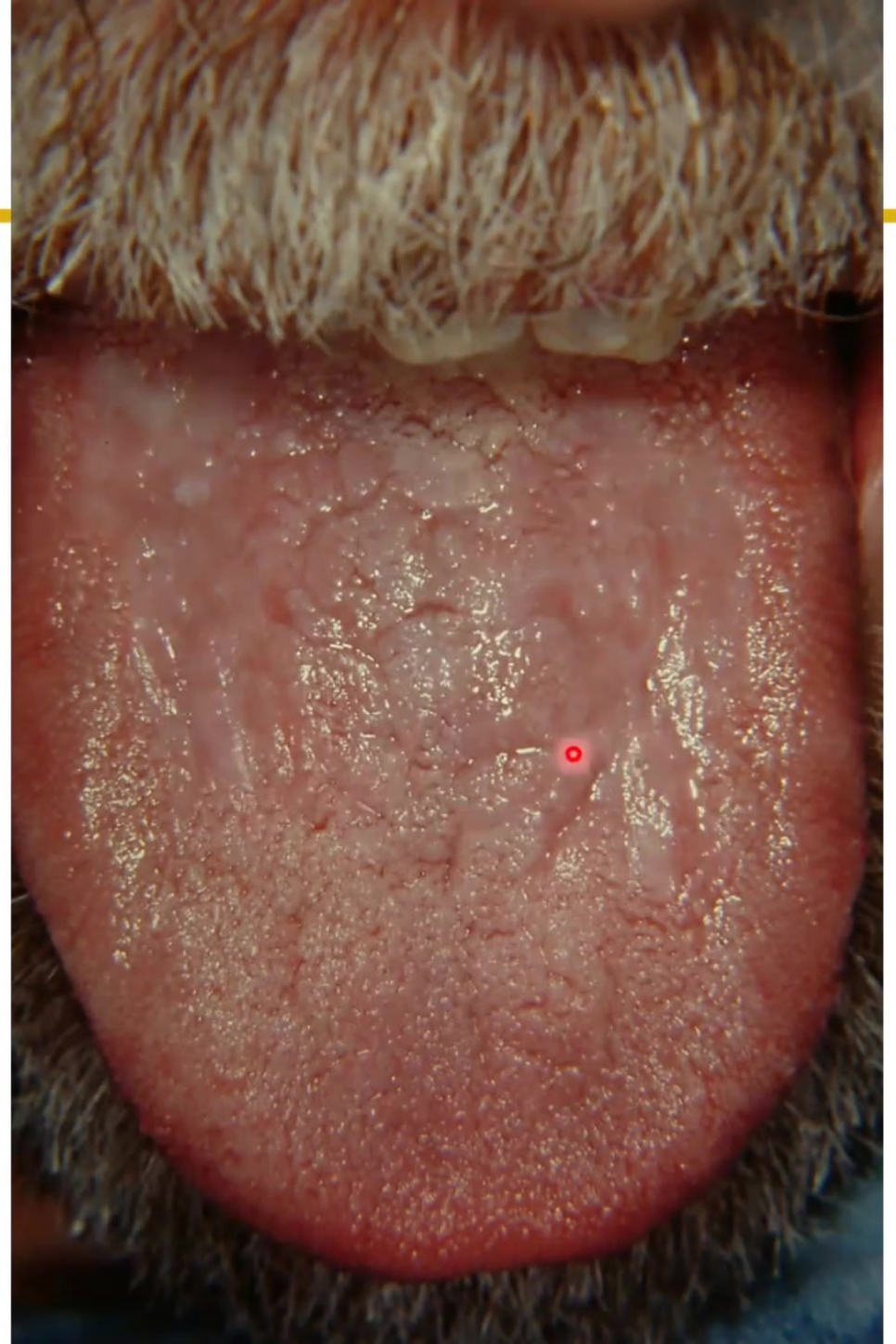

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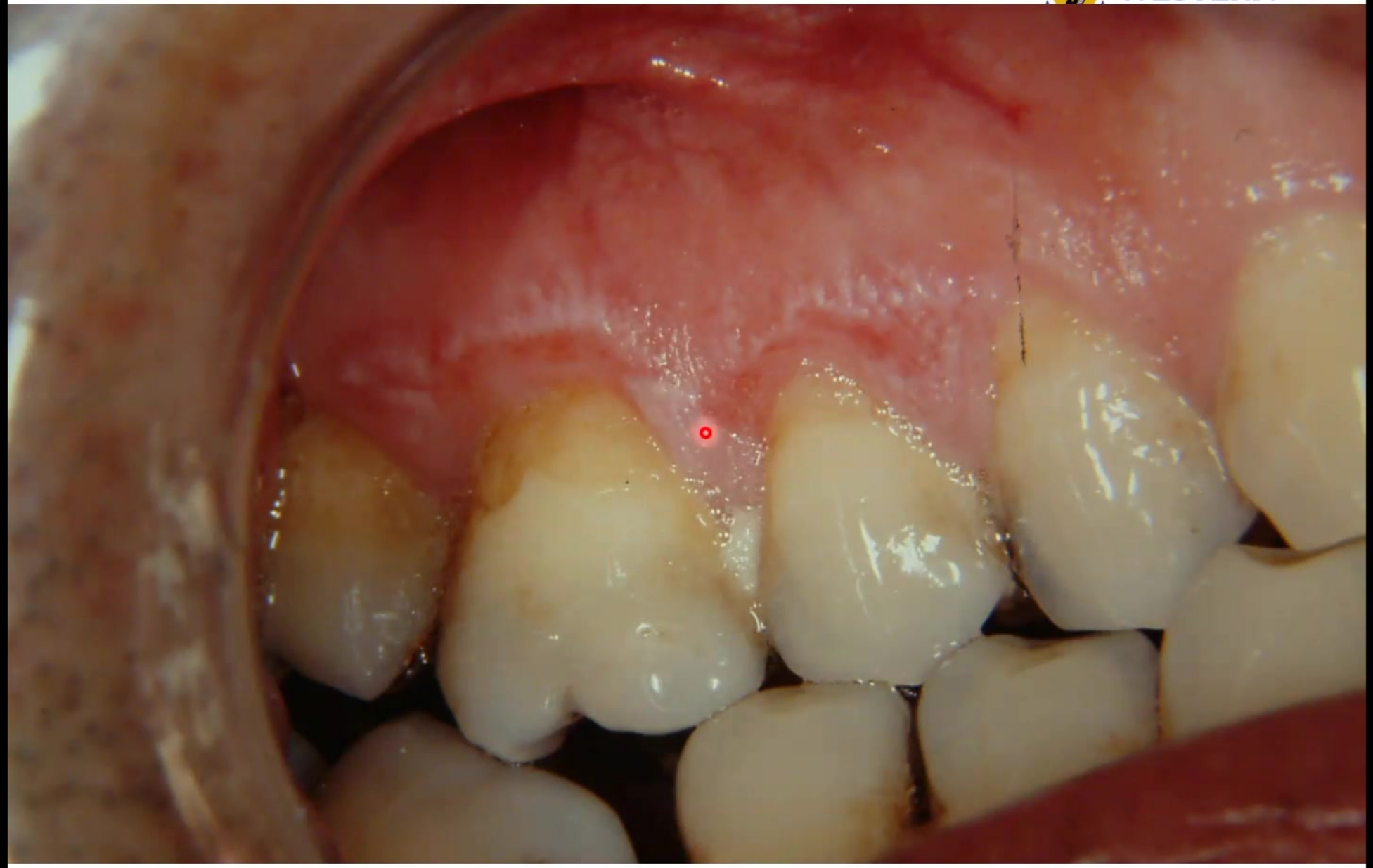


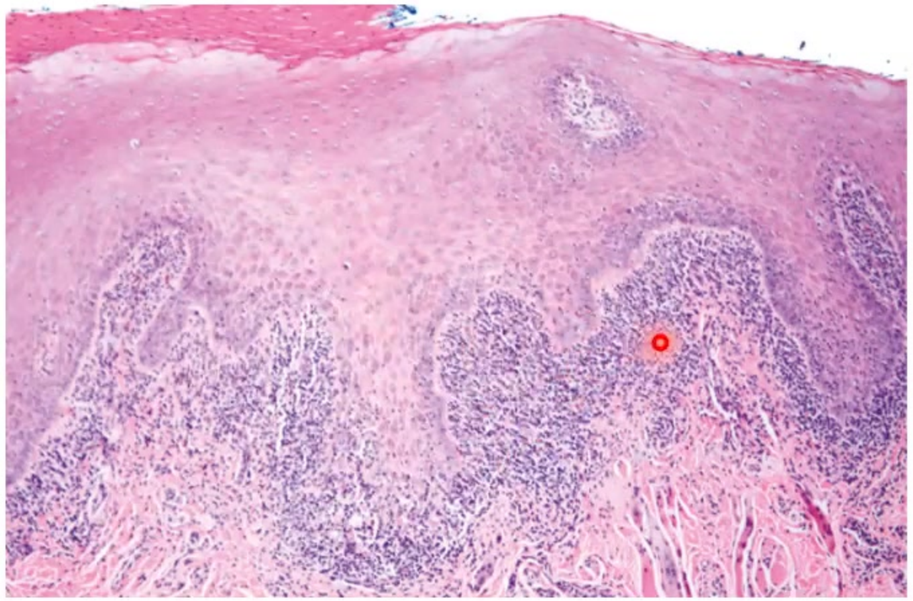
Histopathologic features

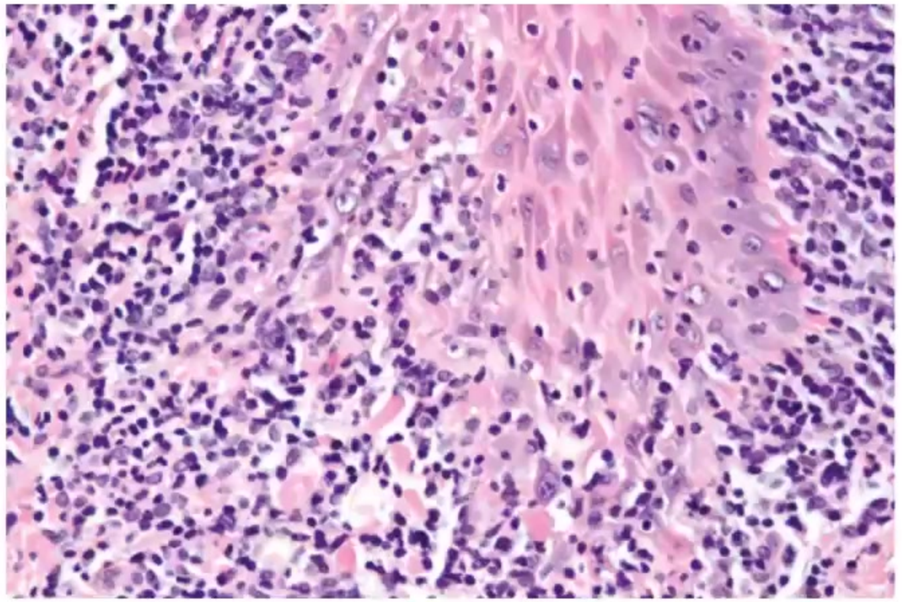
- Surface epithelial findings largely depends on clinical presentation
  - e.g., Hyperkeratosis in reticular, papular and plaque like and ulceration in atrophic

Cheng YS, Gould A, Kurago Z, Fantasia J, Muller S. Diagnosis of oral lichen planus: a position paper of the American Academy of Oral and Maxillofacial Pathology..

Histopathologic features

- Surface epithelial findings largely depends on clinical presentation
  - e.g., Hyperkeratosis in reticular, papular and plaque like and ulceration in atrophic
- Important criteria
  - Degeneration and loss (squamatization) of the basal cell layer
  - Lymphocytic band of variable thickness





Cheng YS, Gould A, Kurago Z, Fantasia J, Muller S. Diagnosis of oral lichen planus: a position paper of the American Academy of Oral and Maxillofacial Pathology..

Diagnosis and management

- Position paper from the American Academy of Oral and Maxillofacial Pathology recommends obtaining a biopsy from everyone.

- Most agree that oral lichen planus is treated
  - Symptomatically
  - With mainly topical and occasionally systemic anti-inflammatory therapy

Lupus erythematous

- LUPUS
  - Systemic (SLE)
  - Cutaneous
    - Acute cutaneous LE (ACLE)
    - Subacute cutaneous LE (SCLE)
    - Chronic cutaneous LE (CCLE)
      - Classic discoid LE (DLE)

- The most common form of chronic cutaneous LE
- Approximately 15-30% of SLE patients have DLE

Lupus erythematous

Clinical features

- Begins:
  - Red purples/macules, or small plaques and rapidly develop a hyperkeratotic surface

- Evolve into:
  - Sharply demarcated discoid plaques covered by an adherent scale that extends into the orifices of dilated hair follicles

Woo, S-B. Oral pathology : a comprehensive atlas and text. Second edition.; Philadelphia, PA : Elsevier; 2017

Lupus erythematous

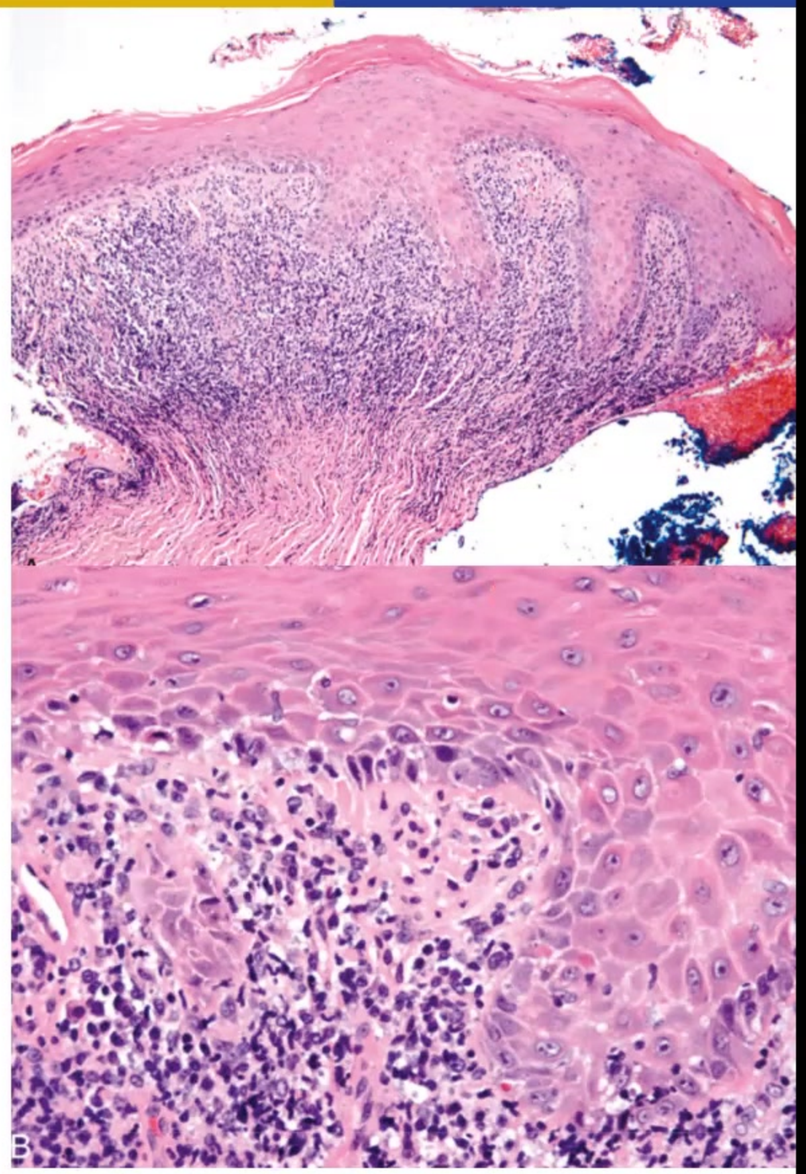
Clinical features

- Oral
  - Sharp margins
  - Irregular, scalloped white borders with radiating striae and telangectasia
  - Honeycomb appearance on the palatal lesion
  - Painful ulceration is common

Woo, S-B. Oral pathology : a comprehensive atlas and text. Second edition.; Philadelphia, PA : Elsevier; 2017

Histopathologic features

- Both acanthosis and atrophy of the epithelium
- Vacuolar degeneration of basal cells
- Bandlike lymph
  - deep perivascular and paravascular lymphocytic infiltratesocytic infiltrate at the interface



Woo, S-B. Oral pathology : a comprehensive atlas and text. Second edition.; Philadelphia, PA : Elsevier; 2017

Diagnosis and management

- Diagnosis based on clinical presentation and obtaining a biopsy
- Management
  - Unpredictable relapsing remitting course
  - Treatment with immunosuppression

Special Topic: Potentially premalignant oral epithelial lesions (PPOEL)

Vol. 125 No. 6 June 2018

Oral potentially malignant disorders: risk of progression to malignancy

Paul M. Speight, BDS, PhD, FDSRCPS, FDSRCS (Eng), FRCPath,[a]
Syed Ali Khurram, BDS, MSc, PhD, MFDSRCS, FDSRCS, FRCPath,[a] and
Omar Kujan, DDS, DipOPath, MSc, PhD[b]

Oral potentially malignant disorders (OPMDs) have a statistically increased risk of progressing to cancer, but the risk varies according to a range of patient- or lesion-related factors. It is difficult to predict the risk of progression in any individual patient, and the clinician must make a judgment based on assessment of each case. The most commonly encountered OPMD is leukoplakia, but others, including lichen planus, oral submucous fibrosis, and erythroplakia, may also be seen. Factors associated with an increased risk of malignant transformation include sex; site and type of lesion; habits, such as smoking and alcohol consumption; and the presence of epithelial dysplasia on histologic examination. In this review, we attempt to identify important risk factors and present a simple algorithm that can be used as a guide for risk assessment at each stage of the clinical evaluation of a patient. (Oral Surg Oral Med Oral Pathol Oral Radiol 2018;125:612–627)