

Keratoses and precancerous (or premalignant) lesions and conditions.

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Keratoses

- Increase and/or abnormal keratin production
- Not removed by scraping
- Classified on basis of aetiology

Leukoplakia

- WHO definition: white patch or plaque that cannot be characterized clinically or histopathologically as any other disease
- Dysplastic or non-dysplastic

Histopathological terms

- Orthokeratosis
- Parakeratosis
- Hyperkeratosis
- Hyperparakeratosis
- Acanthosis
- Epithelial atrophy
- Cellular atypie
- Epithelial dysplasia

Aetiological classification of white lesions of the oral mucosa

- **Hereditary**
 - oral epithelial naevus (white sponge nevus); AD, genes encoding CK 4 and 13 mutated
 - oral manifestation of other rare genodermatoses
 - Leukoedema (in persons with racial pigmentation; whiteness of slightly folded mucosa)
- **Traumatic** (mechanical – frictional keratosis, chemical, thermal injury, nicotinic stomatitis)
- **Infective**
 - Candidosis
 - Syphilitic leukoplakia
 - Hairy leukoplakia
- **Idiopathic (leukoplakia)**
- **Dermatological**
 - Lichen planus
 - Lupus erythematosus
- **Neoplastic**
 - Carcinoma *in situ*
 - SCC

Genodermatoses

■ Pachyonychia congenita

- AD, thickening of nail, oral white lesions

■ Dyskeratosis congenita

- ?, M, skin pigmentation, dystrophic nails, mucosal hyperkeratosis, gingivitis/periodontal destruction, premalignant hyperkeratotic lesions

■ Tylosis

- AD, hyperkeratosis palms/soles; predisposes to oesophageal ca, oral hyperkeratosis

■ Hereditary benign intraepithelial dyskeratosis

- AD, US, oral epithelial naevus-like lesion, premature keratinisation-dyskeratosis

■ Follicular keratosis (Darier's disease)

- AD, keratotic coalescing papules skin (e.g. forehead, scalp, oral lesions in 50 % - hard palate and gingiva)
- intraepithelial acantholytic clefts with dyskeratotic cells

Leukoplakia

- The diagnosis of leukoplakia is one of the exclusion
- It is a clinical diagnosis
- It has no histological connotation
- Epithelial dysplasia may or may not be present (may be precancerous)
- The severity of dysplasia is assessed subjectively

Clinical features of leukoplakia

■ Homogeneous

- flat, uniform, predominantly white plaques
- may show shallow cracks/fissures

■ Non-homogeneous

- irregular nodular/thickened surface
- often speckled with areas of erythroplakia

■ Non-homogeneous lesions have a worse prognosis (more likely to be dysplastic, precancerous)

- **Erythroplakia:** a bright red velvety plaque on oral mucosa, homogeneous and well defined or intermingled with leukoplakia (erythroleukoplakia), may represent carcinoma *in situ*

Aetiological factors – multifactorial aetiology

- Tobacco
- Alcohol
- Candida (superimposed infection?)
- Viruses
- Oral epithelial atrophy (in iron deficiency, tertiary syphilis, submucous fibrosis, in vitamin deficiencies, sideropenic dysphagia)
- Inactivation of tumor suppressor genes

Epithelial dysplasia – reflects abnormalities in proliferation, maturation and differentiation of cells

- Increased and abnormal mitoses
- Basal cell hyperplasia
- Drop-shaped rete ridges (wider at their deepest part)
- Disturbed polarity of cells, loss of cellular orientation
- Increased N/C ratio
- Nuclear hyperchromatism
- Prominent and enlarged nucleoli
- Irregular epithelial stratification and disturbed maturation
- Nuclear and cellular pleomorphism
- Abnormal keratinization
- Loss or reduction of intercellular adhesion (or cohesion)

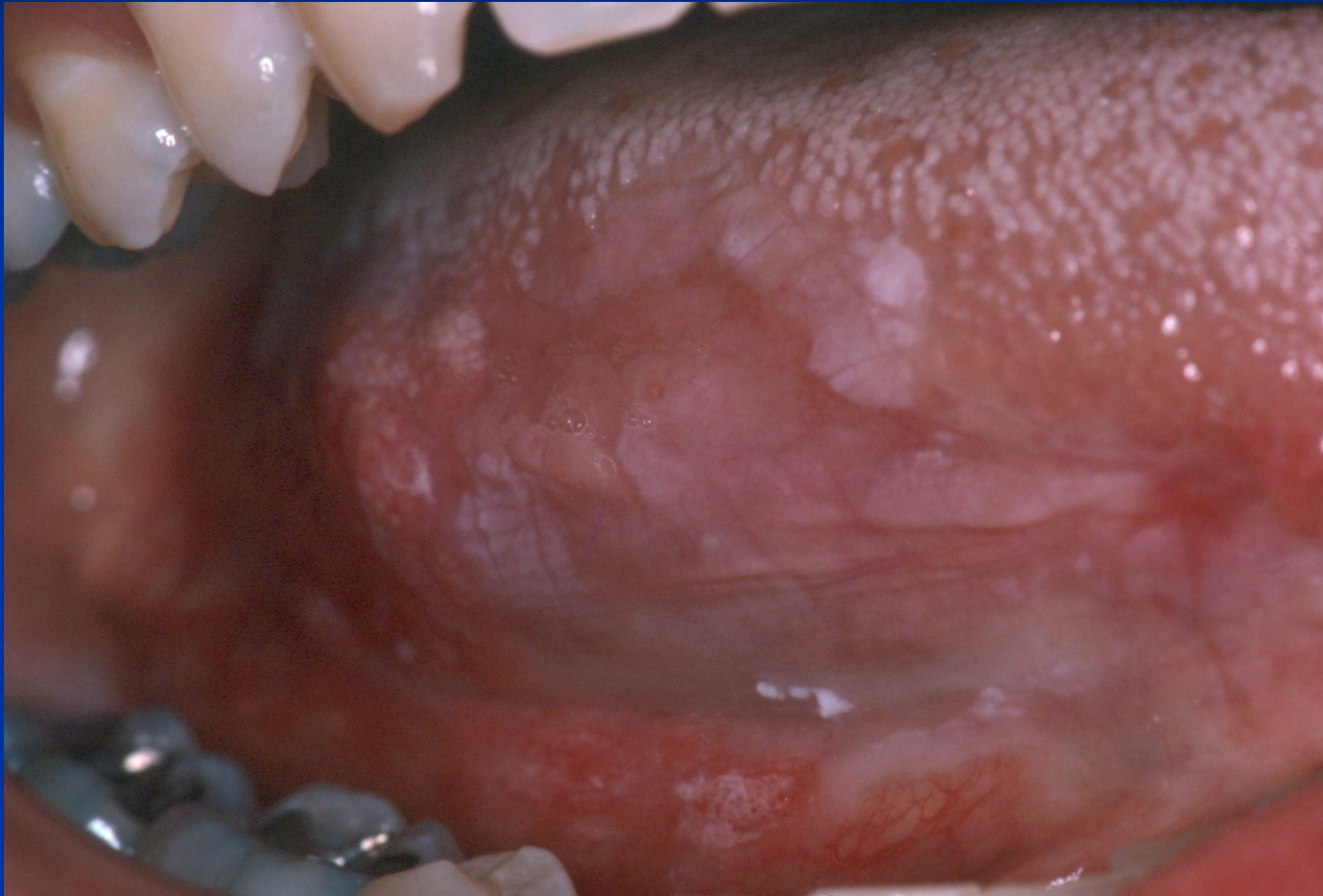
Prognosis of oral leukoplakia

- A proportion undergo malignant transformation
- Transformation times vary from one to several years
- Dysplastic lesions carry the risk of malignant transformation
- Malignant transformation likely to be due to progressive accumulation of genetic abnormalities over the time
- The potential for malignant transformation greater in high-risk sites (ventral tongue, floor of the mouth, lingual aspect of the lower alveolar mucosa)
- Lesions with abnormal DNA content (e.g. aneuploid – abnormal number of chromosomes) likely to progress to carcinoma

**Elevated keratotic lesion of lateral part of the tongue –
biopsy: focal benign keratosis.**



Patchy, focally thickened, keratotic lesions over the right lateral and ventral tongue surfaces – biopsy: focal moderate dysplasia



A mixed red and white lesion on the right ventral part of the tongue with atypical brush biopsy results and corresponding severe dysplasia by scalpel biopsy.



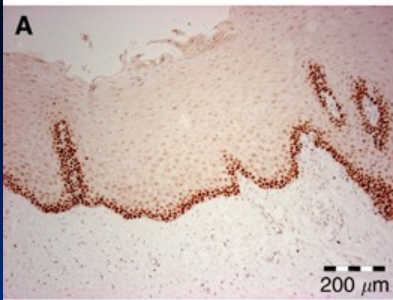
**Well-defined velvety patch of the maxillary alveolar ridge – biopsy:
carcinoma in situ.**



During a routine postradiation therapy examination, a focal red granular surface lesion was detected – biopsy: identification of recurrent invasive squamous cell carcinoma

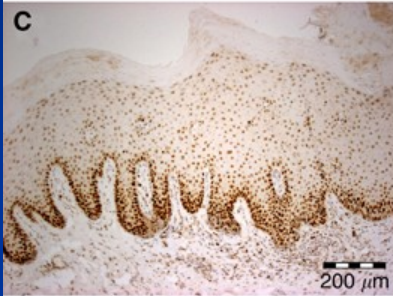
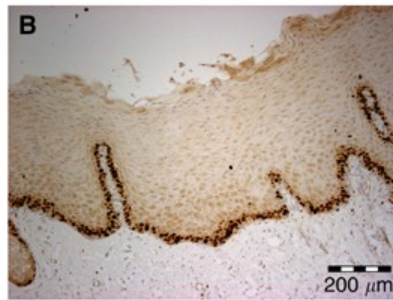


Mcm-2

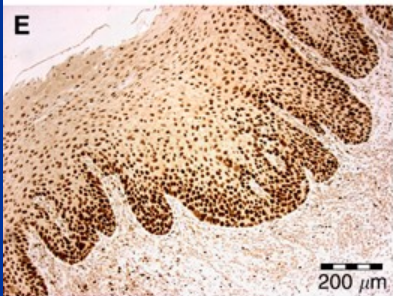
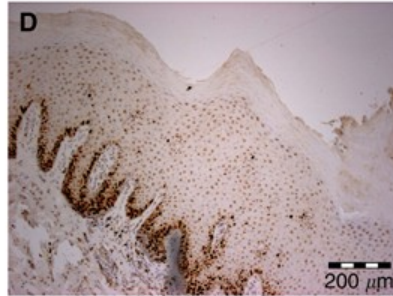


Oral keratosis

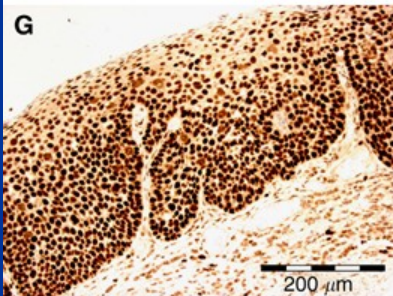
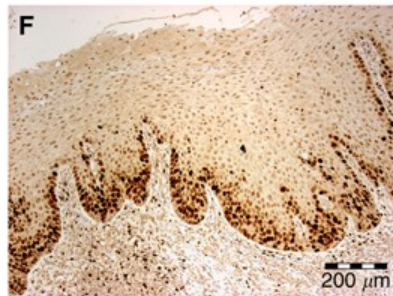
Ki67



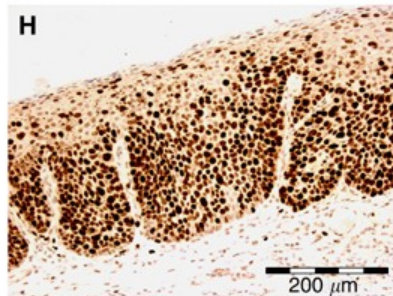
Mild dysplasia



Moderate dysplasia

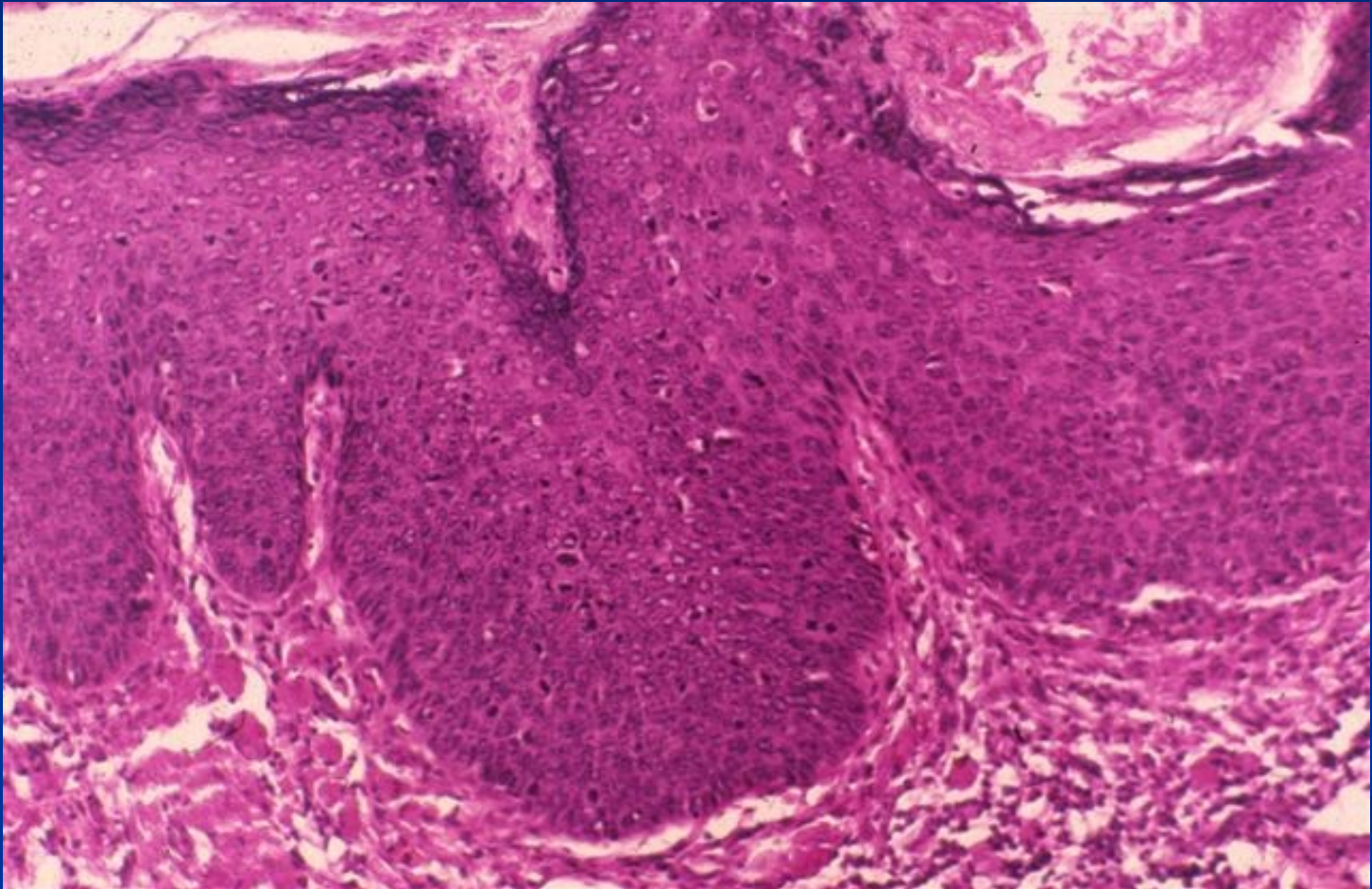


Severe dysplasia



Proliferative activity in benign and dysplastic oral lesions.

Carcinoma in situ



Oral lichen planus

- Alone or associated with skin lesions
- F>M; adults 3rd-5th decade
- Usually bilateral mucosal oral lesions
- Non-erosive forms symptomless
- Buccal mucosa mostly affected
- Gingival lesions presented as desquamative gingivitis

Aetiology of lichen planus

- Aetiology not fully understood – cell-mediated immune responses to an external antigen, or to internal antigenic changes in the epithelial cells (T-cell mediated, resembles type IV hypersensitivity reaction, CD8+ T cells damage basal epithelium)
- Often associated with other systemic disease
- May be associated HCV
- May be a part of GVHD (graft versus host reaction in recipients of transplants)
- Differential diagnosis: lichenoid reactions – hypersensitivity to drugs or dental materials

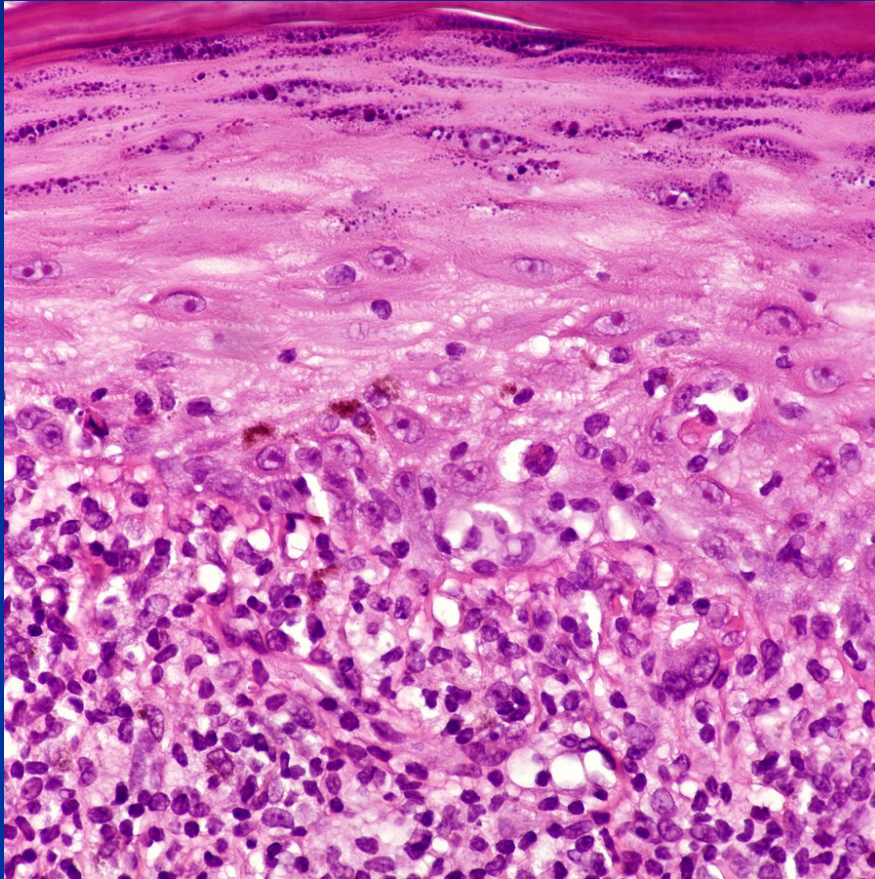
Clinical type of lichen planus

- Reticular (lace-like striae)
- Atrophic (resemble erythroplakia)
- Plaque-like (resemble leukoplakia)
- Papular
- Erosive
- Bullous

Lichen planus morphology and histopathology

- Violaceous, itchy papule with white streaks on the surface (Wickham's striae)
- Papules have a variable pattern (discrete, annular, linear, widespread rash,...)
- Typically flexor surface of the wrists affected, fingernail also affected (10 %); skin LP – 85 % resolve in 18 months; oral LP more chronic
- Ortho- or parakeratinized surface
- Acanthotic or atrophic epithelium
- Subepithelial band of T lymphocytes
- Liquefactive degeneration of basal cells

Oral lichen planus



Lupus erythematosus (LE)

■ **Chronic discoid LE (localized LE)**

- Facial skin may be involved (butterfly pattern)
- Cheeks commonest oral site
- Discoid area of erythema with keratotic borders

■ **Systemic LE (disseminated disease)**

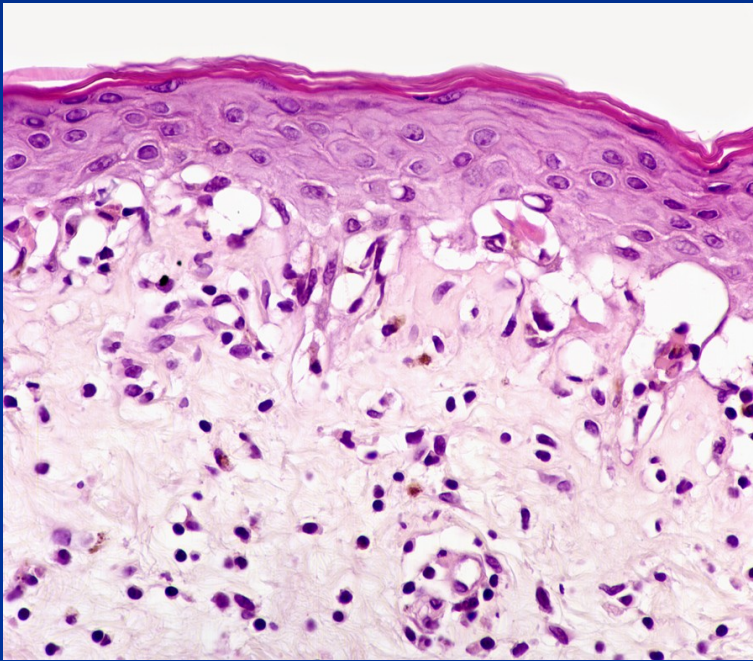
- Skin rashes and systemic involvement
- Oral lesion variable

■ **F>M**

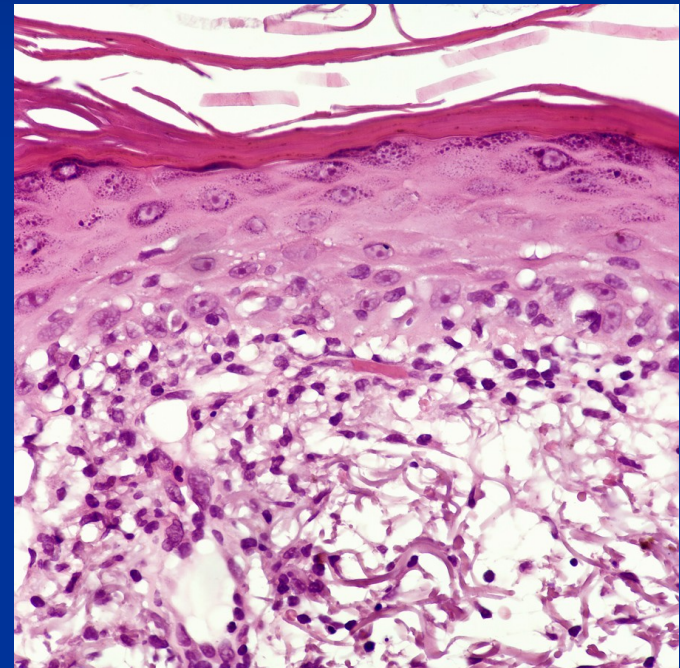
■ **Autoimmune disease** (a variety of autoantibodies (ANA))

- **Histology** of oral lesion often nonspecific (lymphocytic infiltration – perivascular, in connective tissue, may be liquefactive degeneration of basal cells; abundant deposits of Ig (IgG) and complement in the basement membrane zone forming a prominent „lupus band“

Lupus erythematosus (LE)

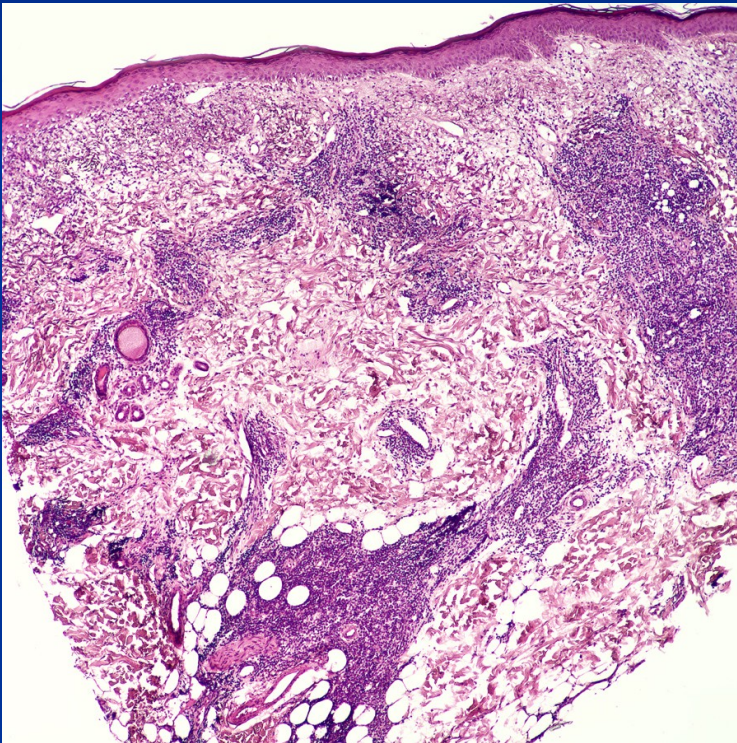


Lupus erythematosus subacuteus

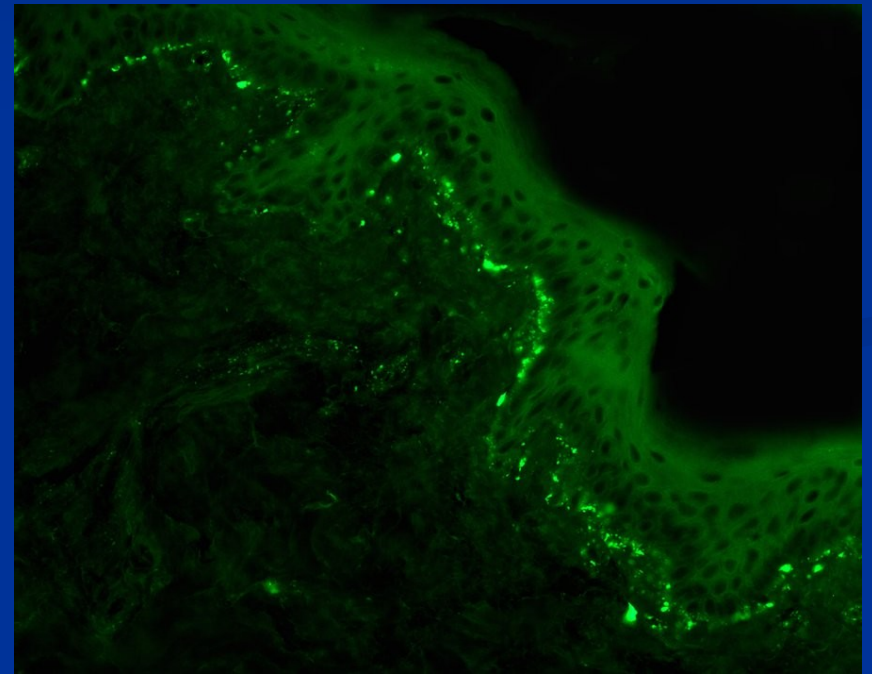


Lupus erythematosus chronicus

Lupus erythematosus (LE)



Lupus erythematosus chronicus



Direct immunofluorescence: granular deposits subepidermally

Precancerous (or premalignant) lesions and conditions

■ Precancerous lesions

- Leukoplakia
- Erythroplakia
- Carcinoma *in situ*

■ Precancerous conditions

- Oral submucous fibrosis
- Lichen planus
- Actinic keratosis (lips)
- Conditions assoc. with epithelial atrophy (e.g. siderophenic dysphagia)

