Mucocutaneous Diseases

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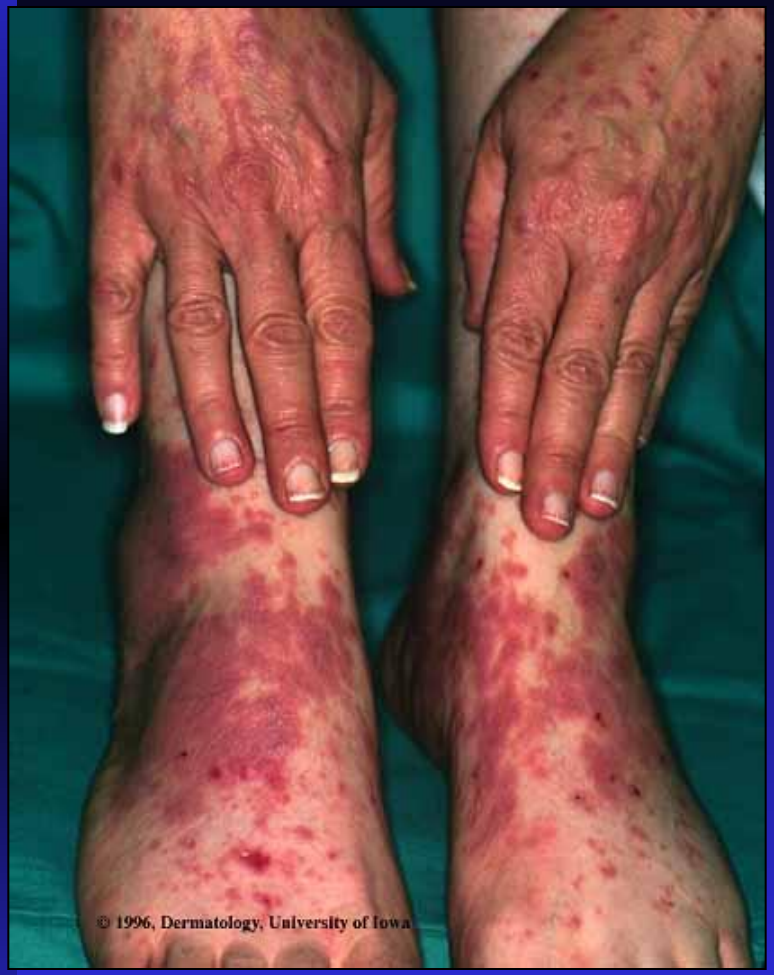
Terms used to describe skin / oral lesions

Macule	Small flat area of altered colour or texture
Papule	Small solid elevation of skin, < 0.5cm in diameter
Nodule	Solid mass usually > 0.5cm in diameter
Plaque	Elevated area > 2cm in diameter but without substantial depth
Vesicle	Circumscribed elevation < 0.5cm in diameter, and containing fluid
Bulla	Circumscribed elevation > 0.5cm indiameter, and containg fluid
Pustule	A visible accumulation of pus in the skin
Abscess	A localized collection of pus in a cavity, > 1cm in diameter
Weal	An elevated, white, compressible, evanescent area produced by dermal oedema
Papilloma	A nipple-like mass projecting from the surface

Petechiae	Pinhead-size macule of blood in the skin / mucosa
Purpura	A large macule or papule of blood
Ecchymosis	A large extravasation of blood into skin / mucosa
Haematoma	A swelling from gross bleeding
Telangiectasia	The visible dilatation of small blood vessels

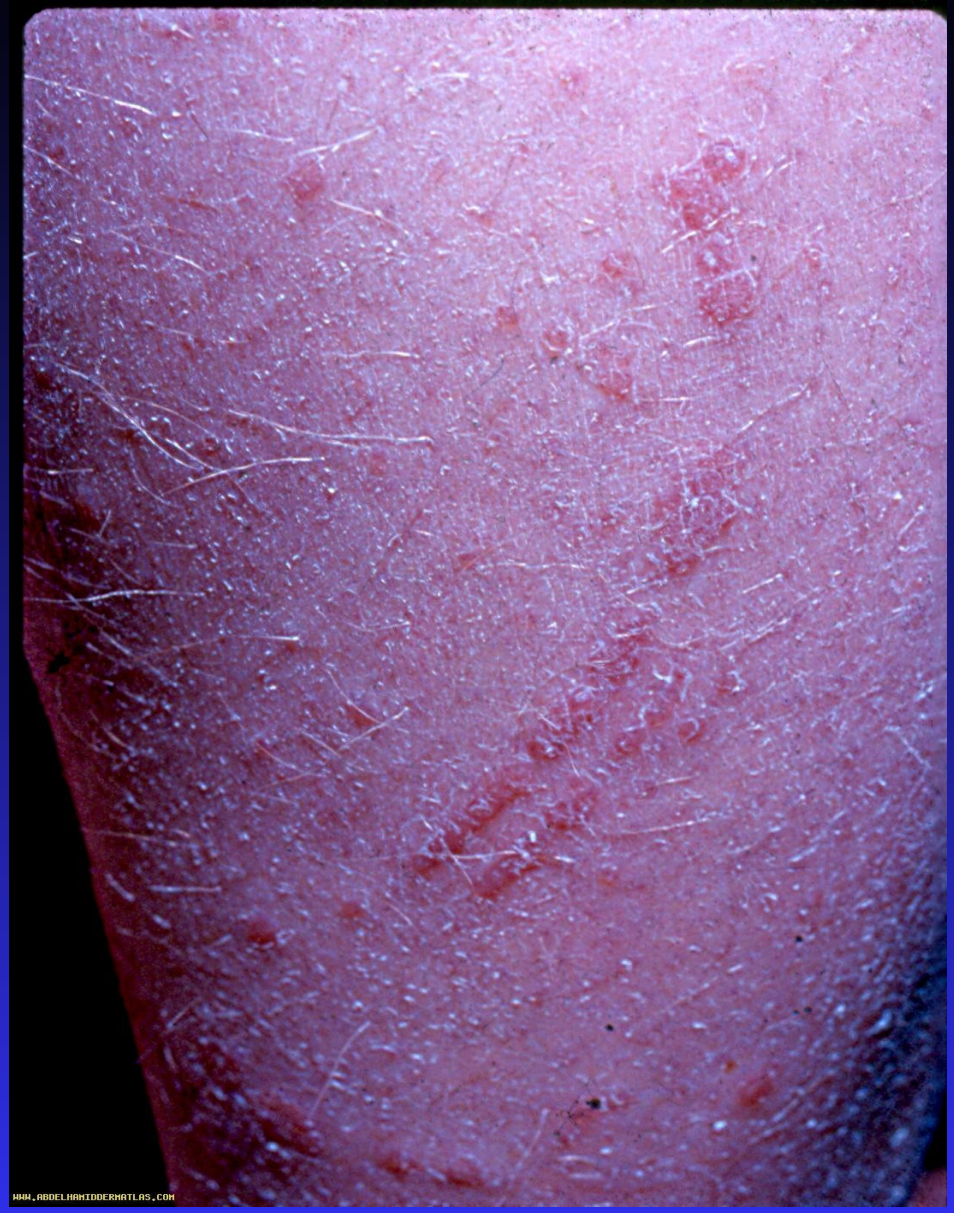
Lichen Planus

- Aetiology: not clear yet
  - Viral aetiology (HPV-6, 11, 16, 18; HHV 6)
  - Autoimmune disease
  - Autocytotoxic CD8+ T cells trigger the apoptosis of oral epithelial cells
- Sites affected in the body:
  - Skin
  - Scalp
  - Mucosa
  - Nails
- Associated Diseases: ……*may be coincidental*
  - Hepatitis C virus
  - HPV and HHV
  - Primary biliary cirrhosis
  - Autoimmune chronic active hepatitis
  - Exacerbation have been linked to psychological stress and anxiety
  - Myasthenia gravis
  - Ulcerative colitis



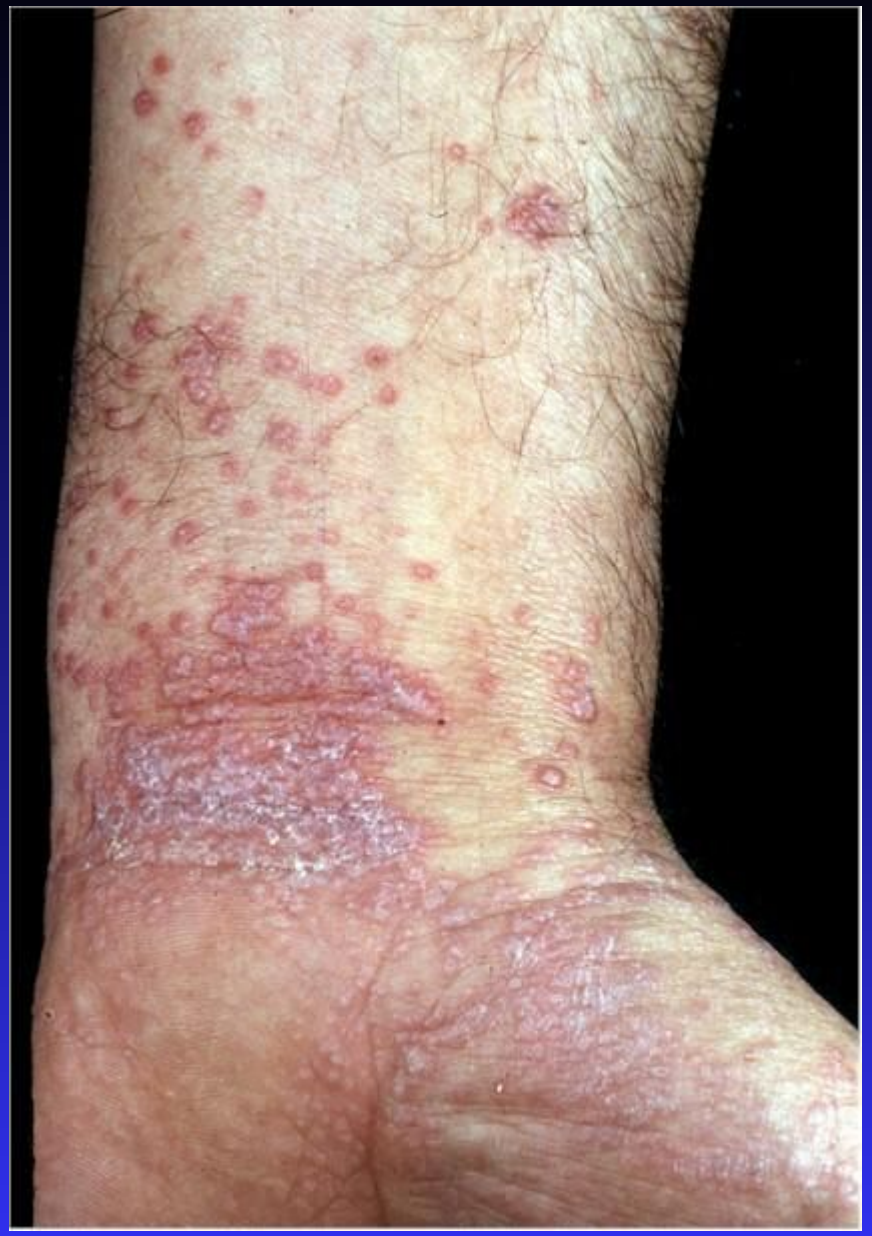
Skin lesions:

- Pink papules overlaid by fine white striations (Wickham's striations).
- Itchy and bilateral
- Last for 9-12 months, but subjected to recurrency
- Mainly on
  - front surfaces of wrists,
  - genitalia
  - abdomen
  - lumbar region



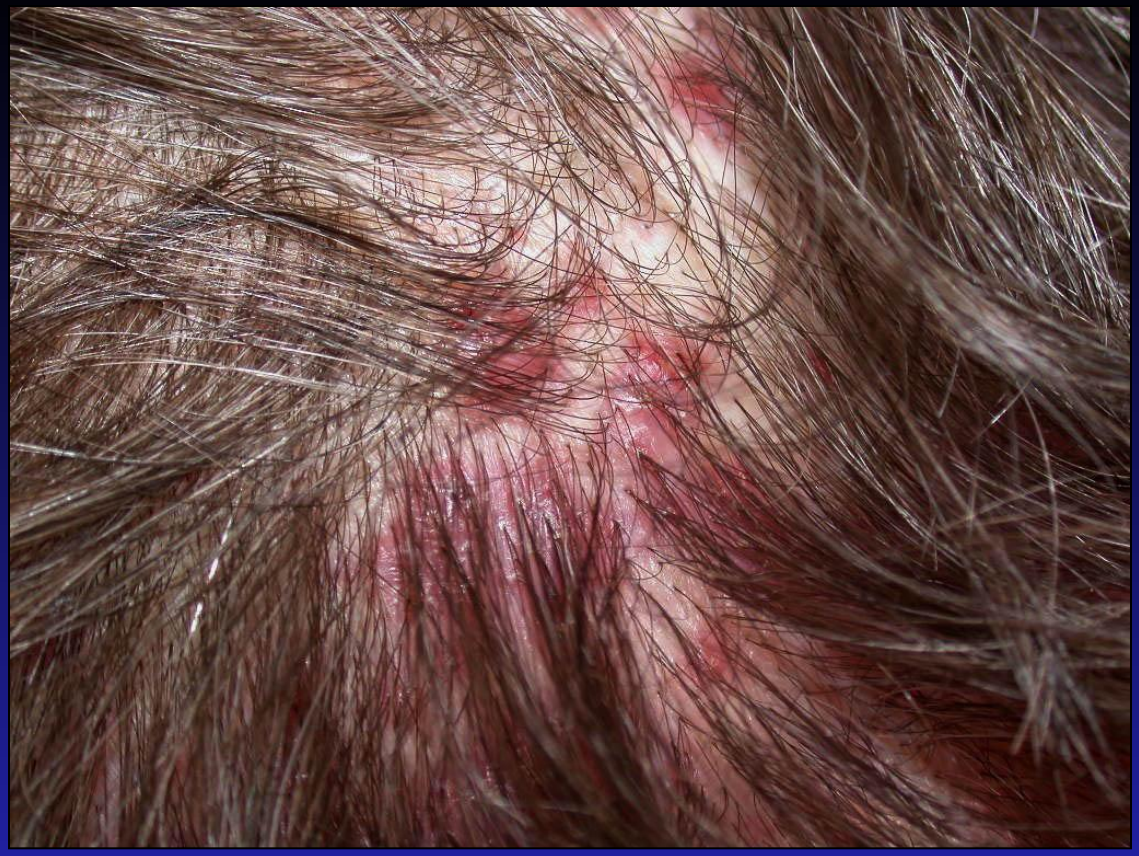
Kobner phenomenon

Bilateral, itchy papules with scaly surface



Nail lesions:

Vertical grooving and destruction of the nails (*nails dystrophy*).

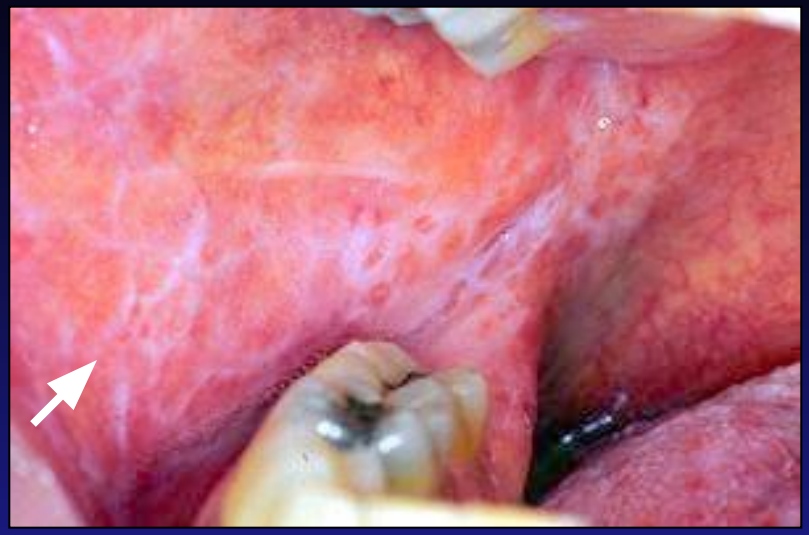


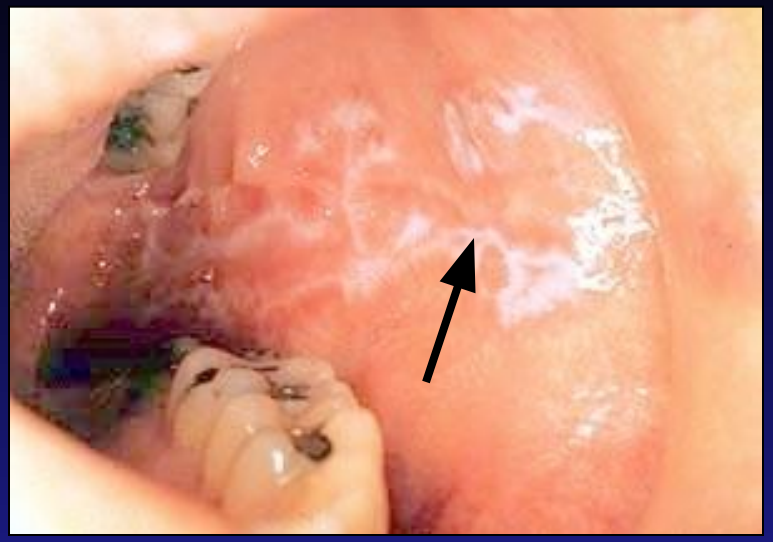
Scalp lesions (*lichen planopilaris*)

Patches of alopecia in few patients, usually in females

Oral Lichen Planus

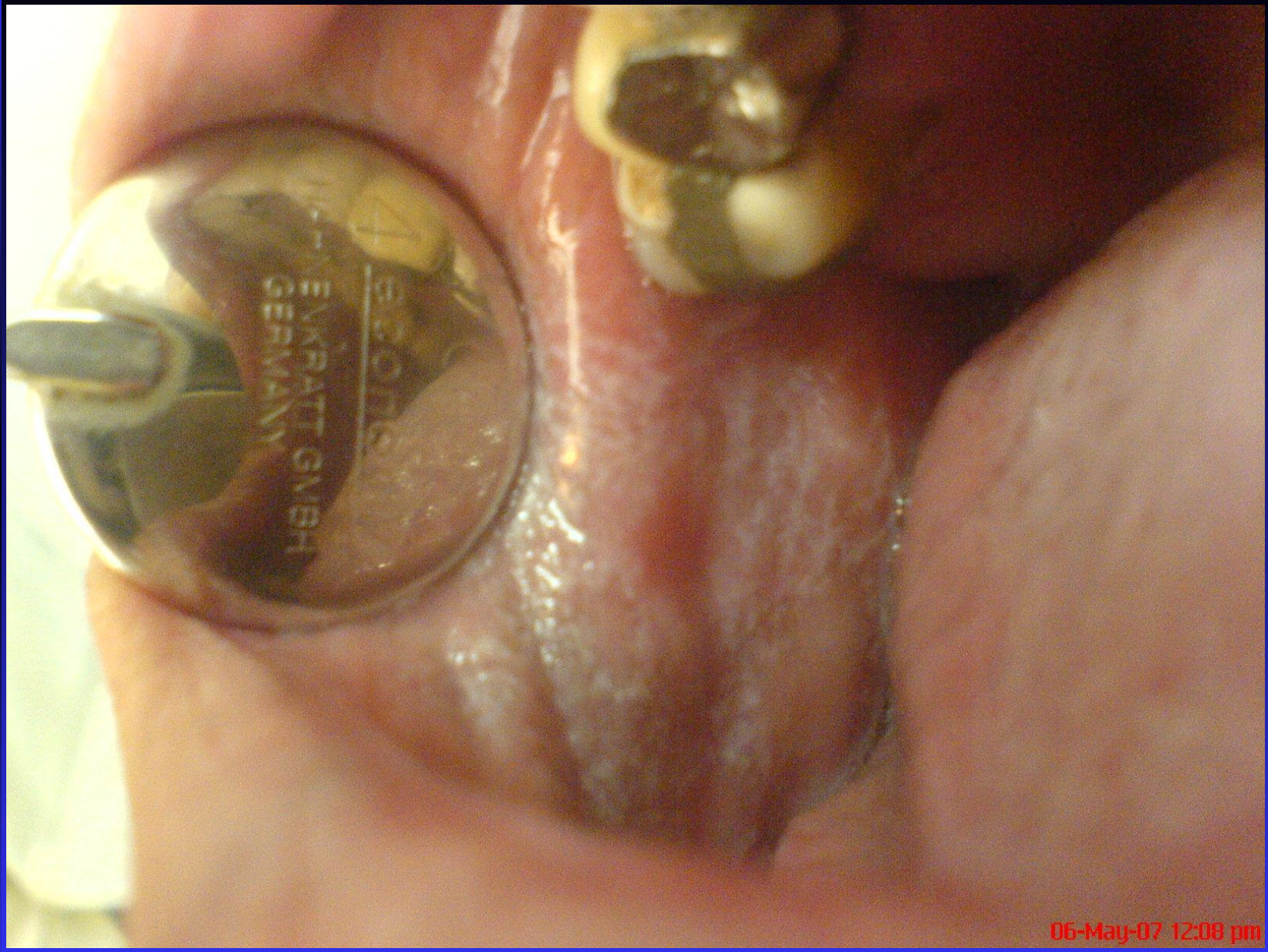
- Non-erosive
  - Papular
  - Linear
  - Reticular
  - Annular
  - Plaque type
- Erosive
  - Atrophic
  - Bullous
  - Ulcerative





Non-erosive LP.

- Notice the bilateral *Wickham's striations*
- Asymptomatic but rough mucosa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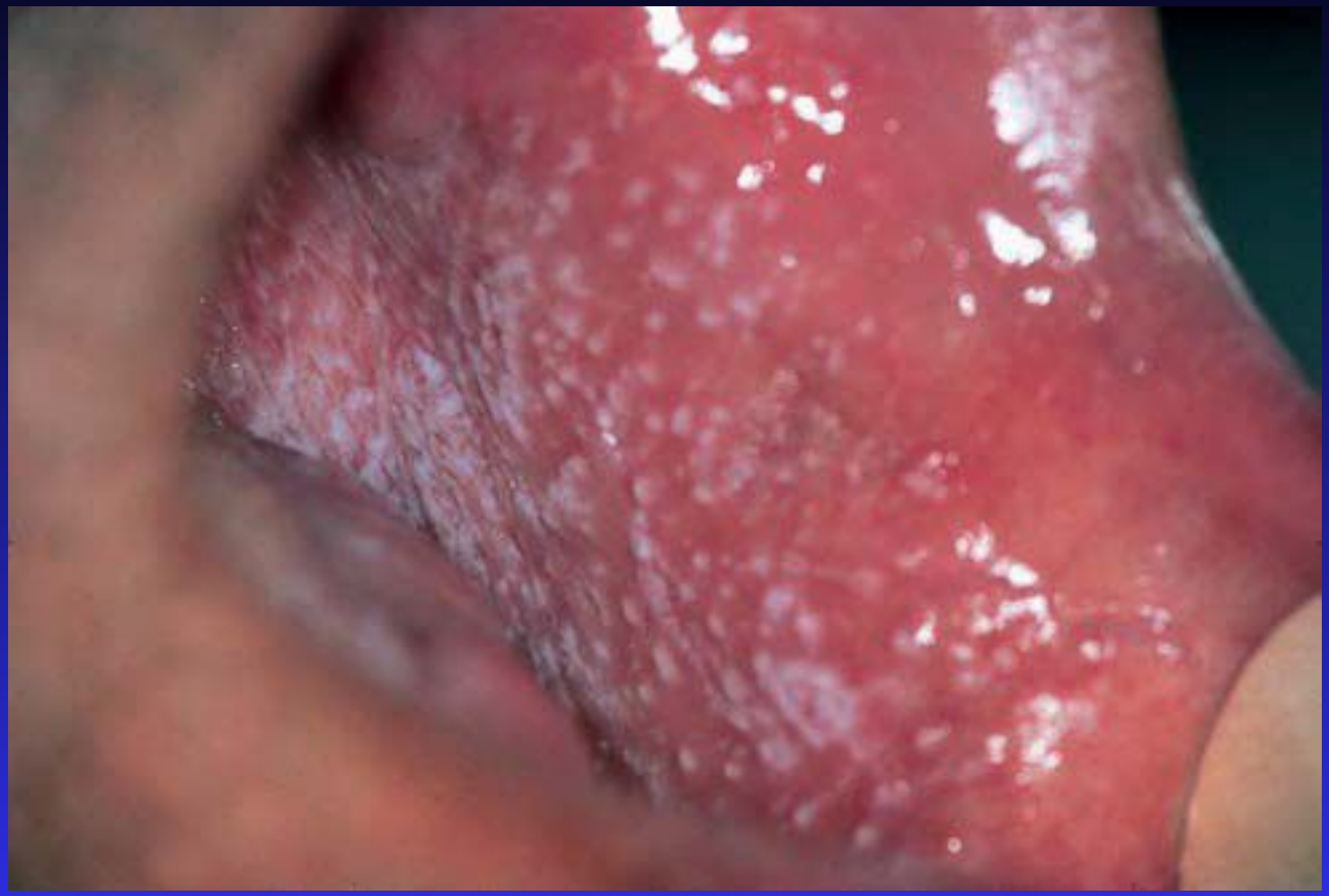
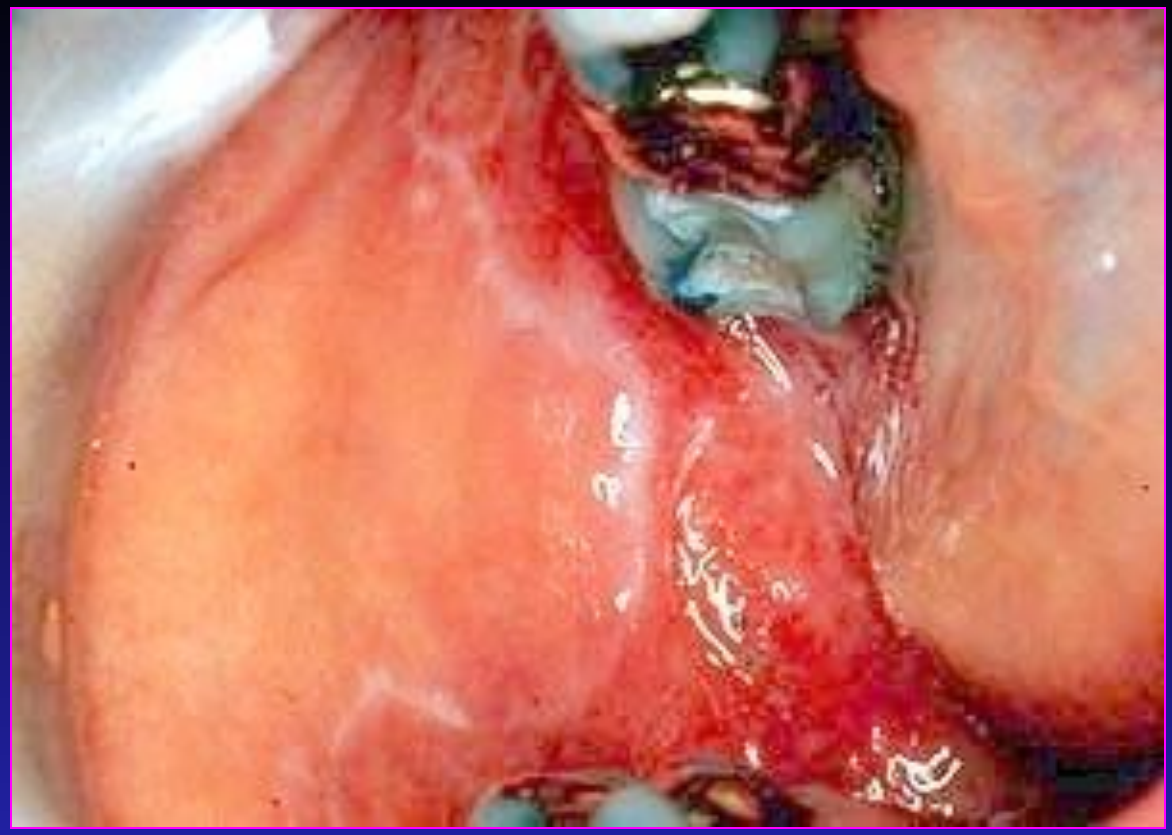
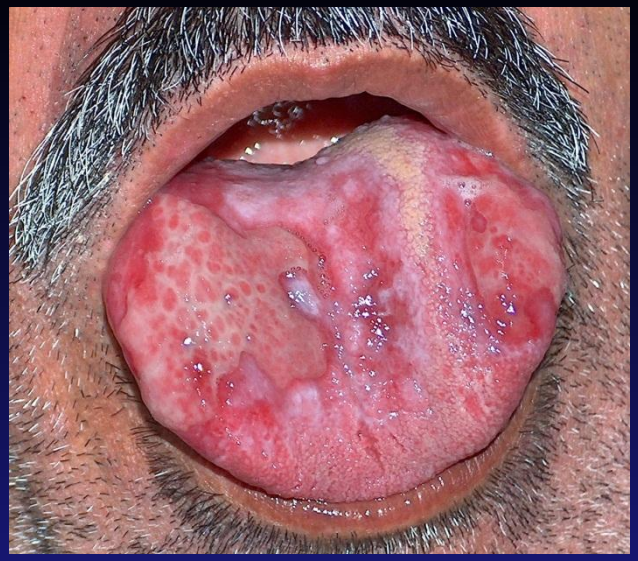
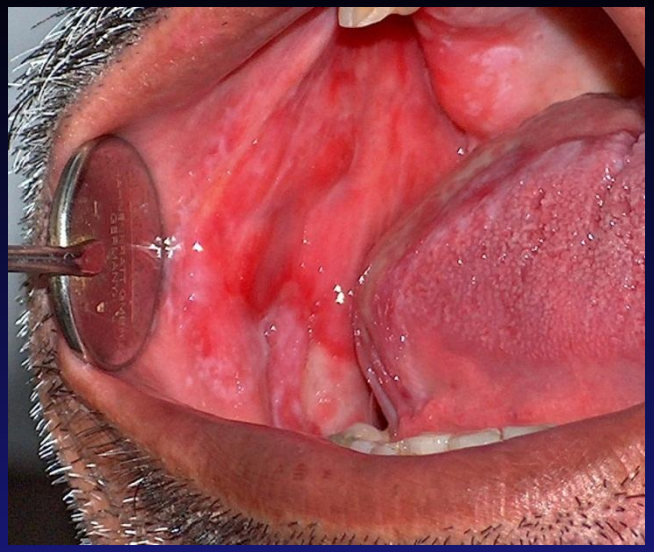


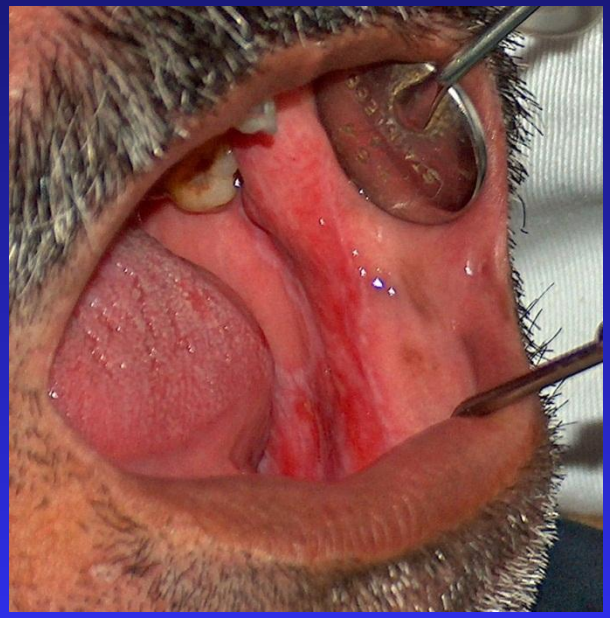


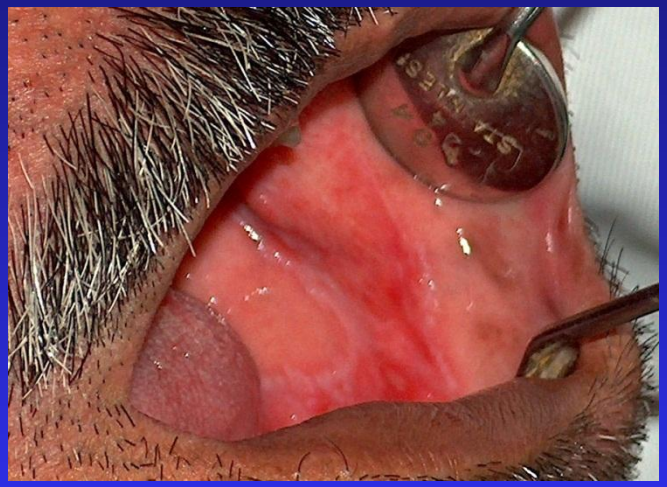
Erosive LP.

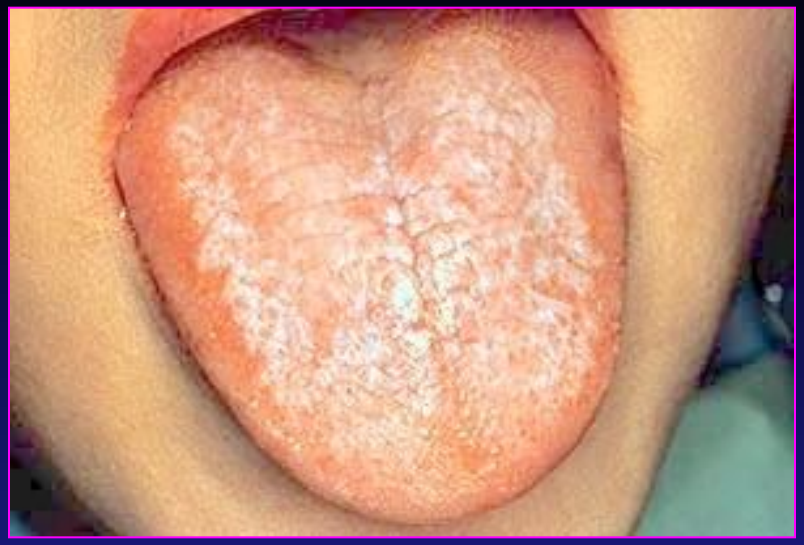
- White striations on erythematous or ulcerative base
- Painful, specially with hot drink or spicy food.

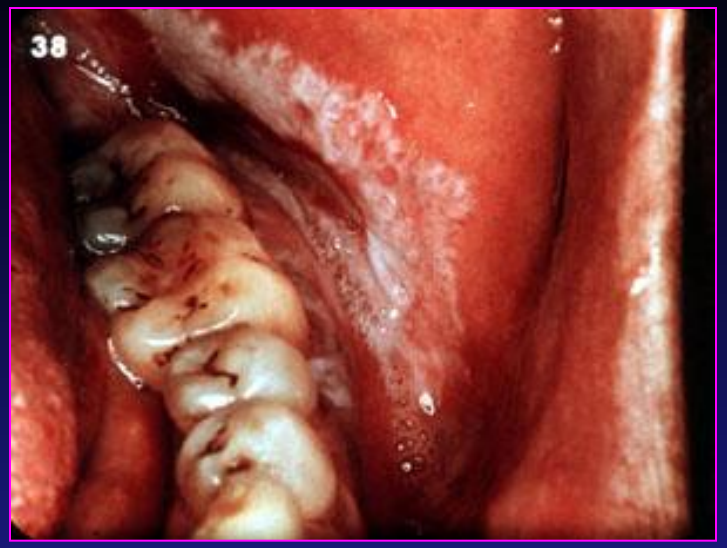






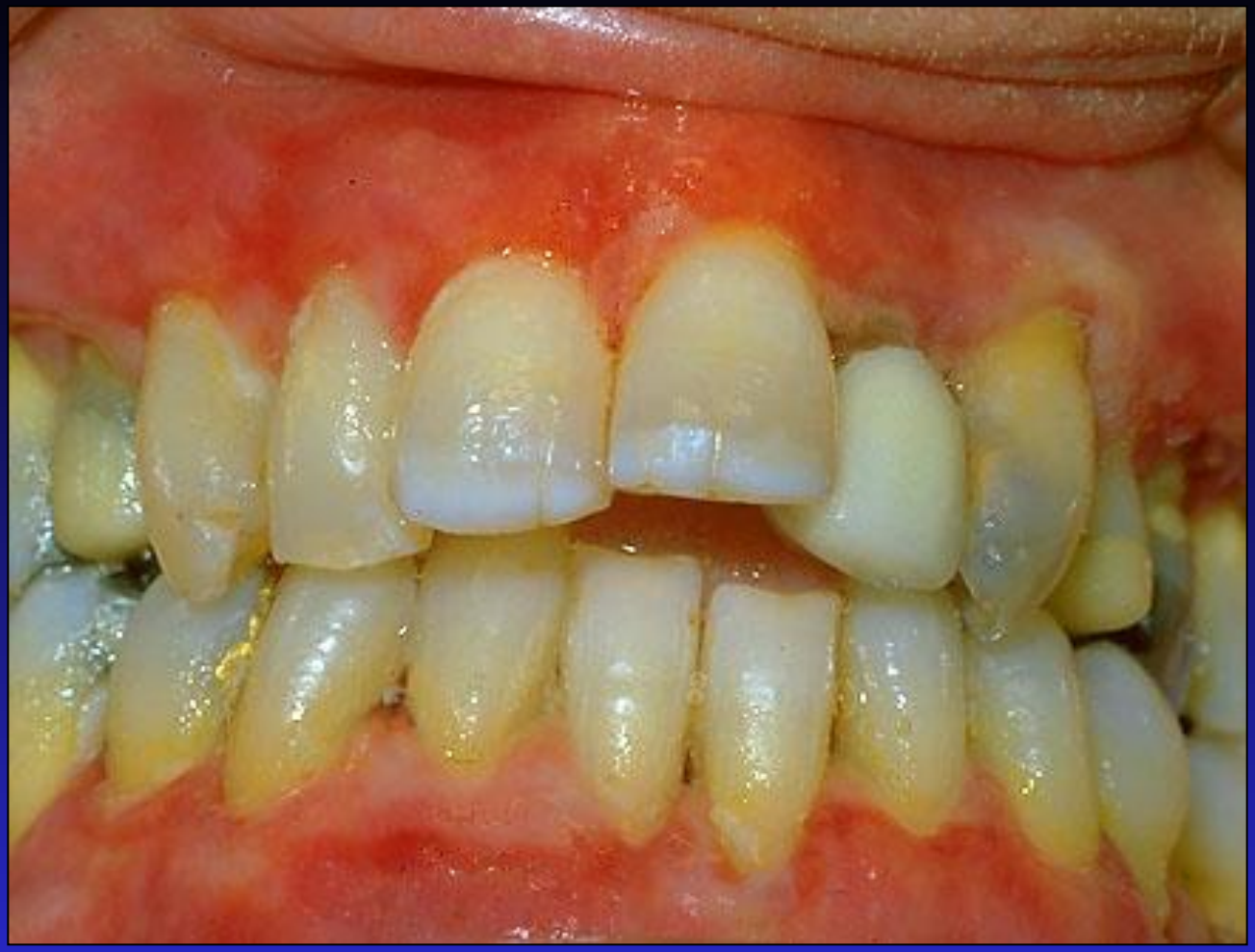






Non-erosive LP.

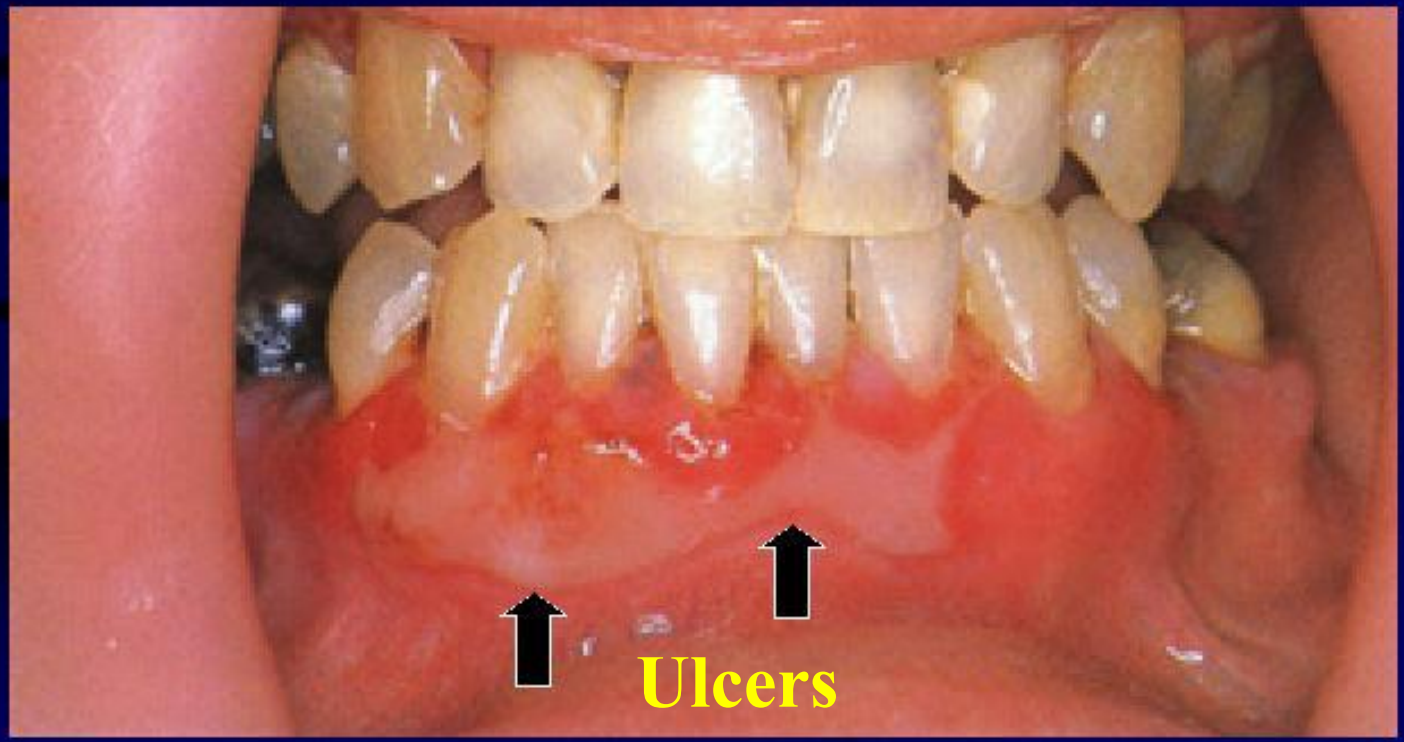
Plaque type



Desquamative gingivitis on attached gingiva

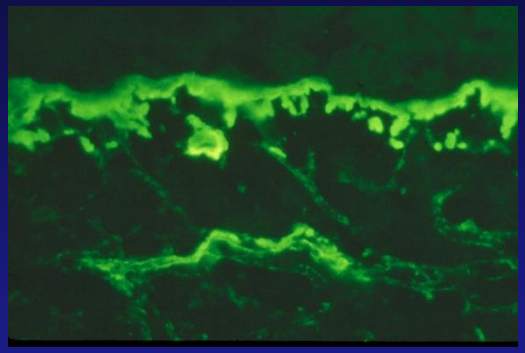
Is a clinical rather than a pathological entity

Desquamative Gingivitis in CP

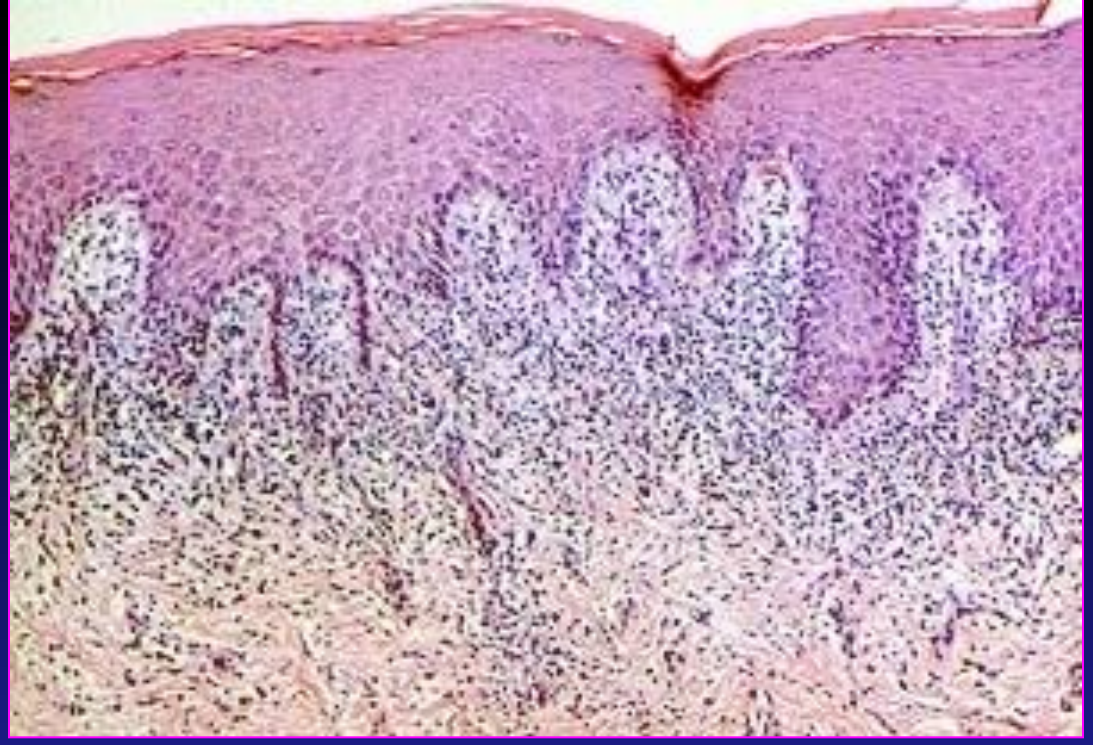


Oral Lichen Planus

- Diagnosis:
  - Clinical picture
  - Incisional biopsy
  - DIF & IIF to exclude other diseases
- Prognosis:
  - Oral lesions are more reluctant than skin lesions
  - Malignant transformation rate (?) is < 1%, hence repeated biopsy may be needed.

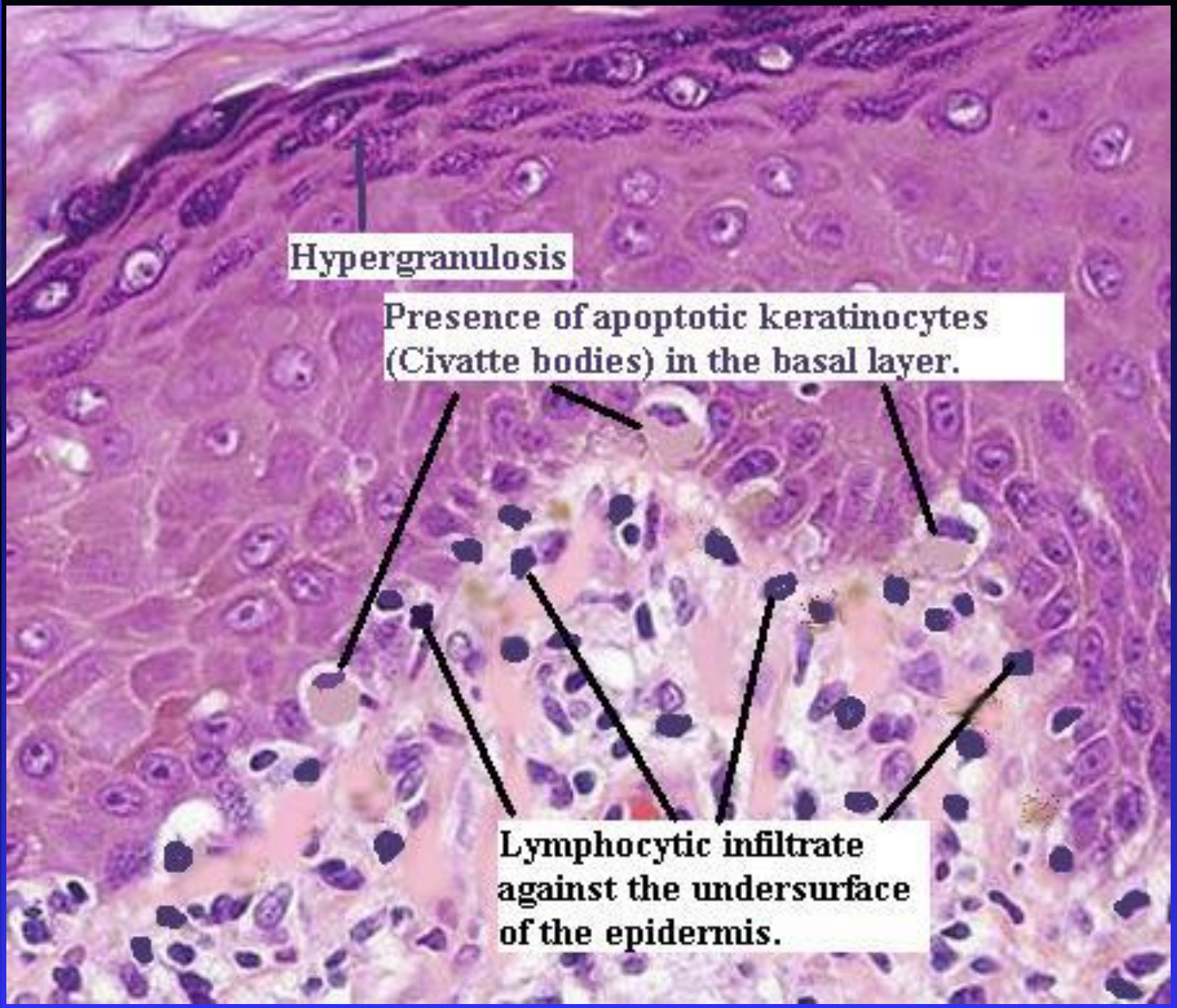


Fibrinogen at BMZ (non-specific)



Histopathology of LP.

- Epithelial hyperplasia or atrophy
- Saw teeth appearance of rete ridges
- Liquifaction degeneration of the basement membrane
- Dense band of lyphocytic infiltration in the lamina propria
- Hyaline (Civatte) bodies


Hypergranulosis
Presence of apoptotic keratinocytes (Civatte bodies) in the basal layer.
Lymphocytic infiltrate against the undersurface of the epidermis.

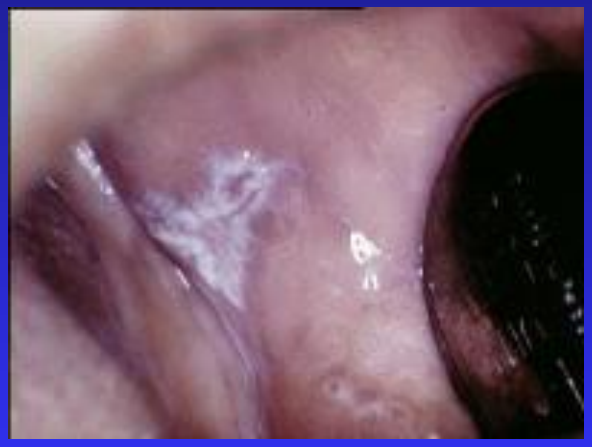
Treatment of OLP

Aims of treatment

- Resolution of oral painful symptoms
- Resolution of oral mucosal lesions
- Reducing the risk of oral cancer
- Maintenance of good oral hygiene
- Prolongation of symptom-free intervals

Concerns

- No treatment is curative
- Local and systemic adverse effects of therapy
- Recurrence after treatment withdrawal



Treatment of OLP.

- Skin lesions
  - Steroid cream
  - Systemic steroids
- Oral lesions: Minor erosive type
  - Remove trauma
  - Antiseptic mouth wash
  - Local steroids
    - Betamethasone valerate aerosol,
    - Beclomethasone dipropionate,
    - 0.1% triamcinolone acetonide in adhesoive paste,
    - Beclometasone dipropionate
    - 0.05% Flucinonide ointment in an orabase paste
    - 0.025% clobetasol propionate
  - Meconazole oral gel or chlorhexidine mouth wash

Treatment of OLP.

- Oral lesions: Major erosive type
  - High concentration steroid mouth wash
  - Triamcinolone intra-lesional injections (0.2 to 0.4 ml of 10 mg/mL)
  - Topical tacrolimus
  - Systemic steroids: 40-80 mg/day prednisolone for <2 weeks
  - Azathioprine (50 to 100 mg/day)
  - Levamisole (150 mg/day)

?Potentially malignant condition

- 0.4%-2% per five years observation

OLP – Patient's follow up

- Follow up:
  - Every month till resolution of symptoms
  - Every 6-12 month afterward

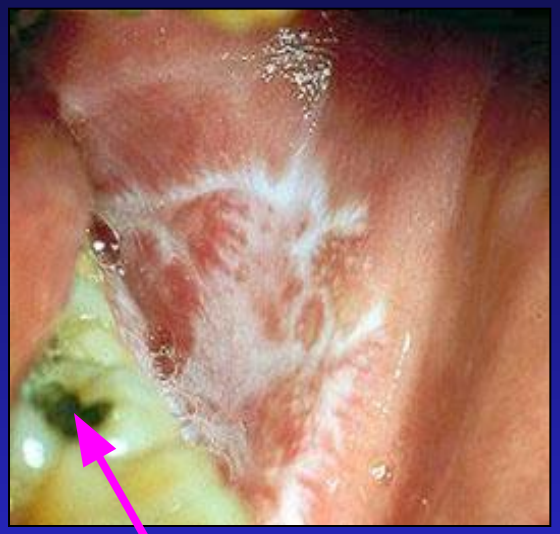
- The risk of oral cancer in patients with OLP may be reduced by means of the following:
  - Elimination of smoking and alcohol consumption
  - Effective treatment of atrophic, erosive, and plaque oral lichen planus lesions
  - Consumption of a nutritious diet including fresh fruit and vegetables
  - Elimination of *C albicans* super-infection
  - Regular clinical examination and repeat biopsy as required. Oral brush biopsy can be used to limit the number of scalpel biopsies

Lichenoid eruption

- **The expression or unmasking of the lichen planus antigen may be induced by:**
  - Drugs (lichenoid drug reaction)
  - Contact allergens in dental restorative materials or toothpastes (contact hypersensitivity reaction)
  - Mechanical trauma (Koebner phenomenon)
  - Viral infection
  - Other unidentified agents

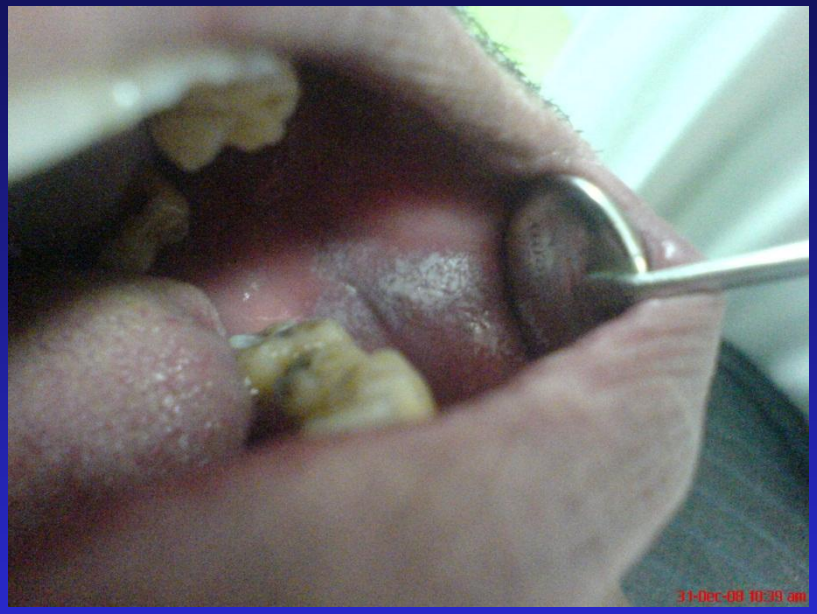
Lichenoid eruption

- Precipitated by:
  - Non-steroidal anti-inflammatory
  - Antihypertensive drugs (beta-blockers, ACE inhibitors)
  - Oral hypoglycaemic agents (e.g. sulphonylurea)
  - Lithium
  - Gold injections
  - Antimalarial drugs
  - Some antibiotics
  - Chronic graft versus host disease
  - *Amalgam*
  - *Coposite resine*
  - *Tooth paste (cinnamon flavored)*
- Management: remove the cause



Amalgam filling

- **Oral lichenoid lesions may be triggered by mechanical trauma (*Koebner phenomenon*) due to**
  - **Calculus deposits**
  - **Sharp teeth**
  - **Rough surfaces of dental restorations or prostheses**
  - **Cheek or tongue biting**
  - **Oral surgical procedures**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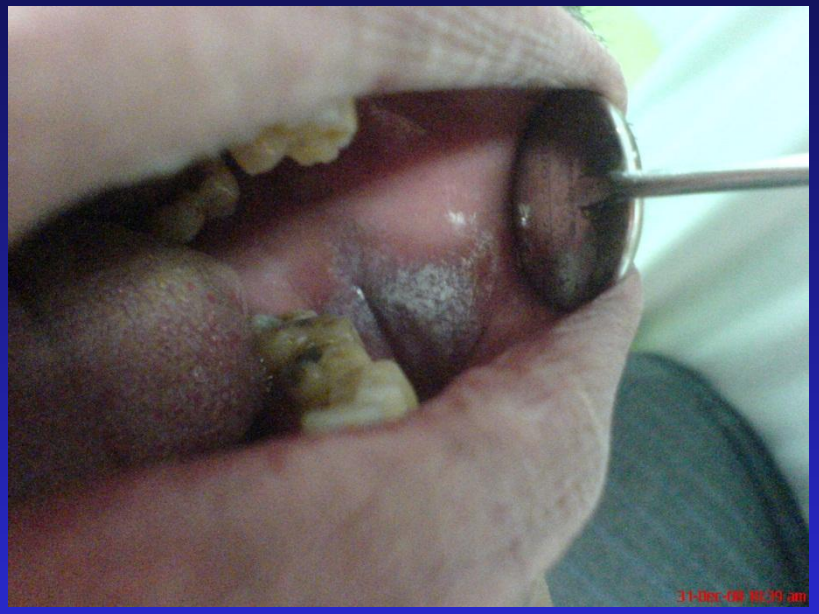
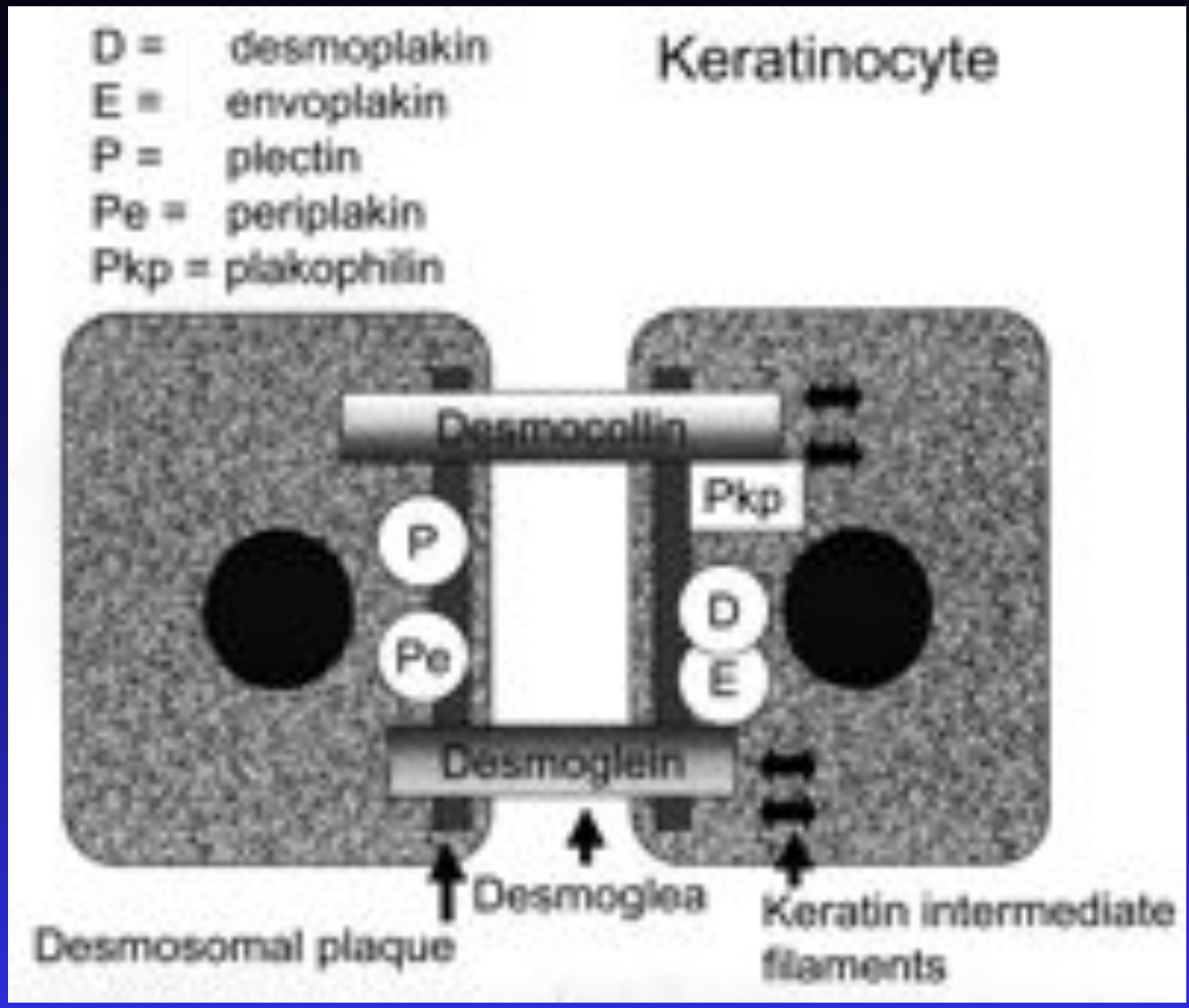


Pemphigus

- Auto-immune disease
- The patients usually between 40-60 years old
- Racial difference in incidence
- Most of the patients have oral lesions which may be the initial presentation.
- The prognosis used to be very poor.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Keratinocyte
Desmocollin
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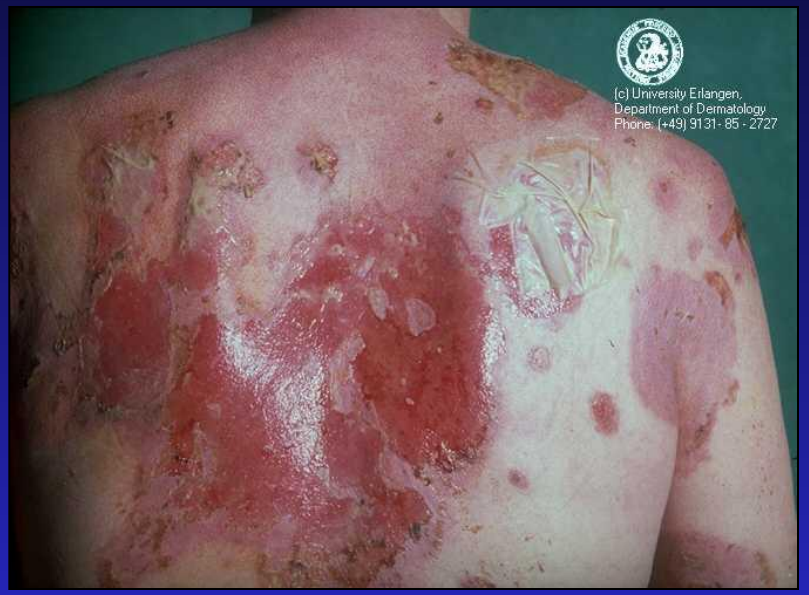
Desmoglein
Desmosomal plaque
Desmoglea
Keratin intermediate filaments

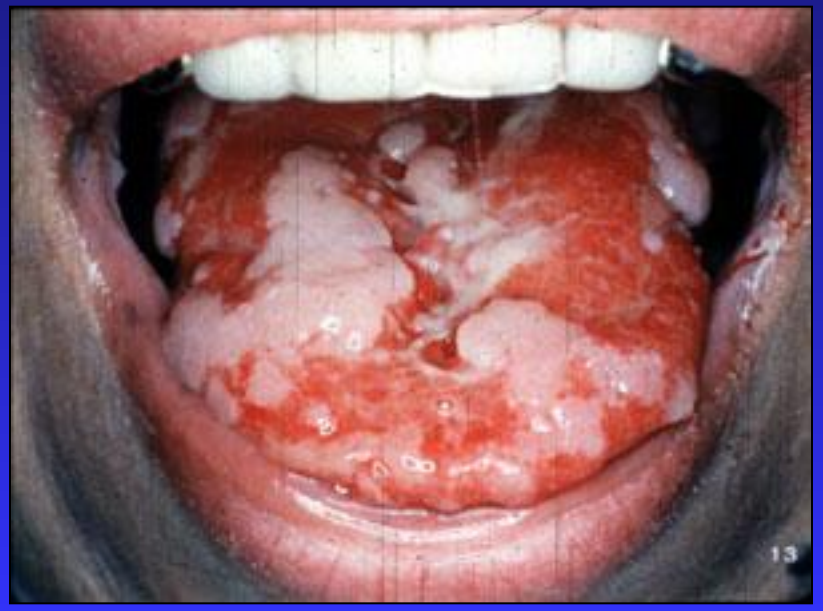
Pemphigus – Clinical picture

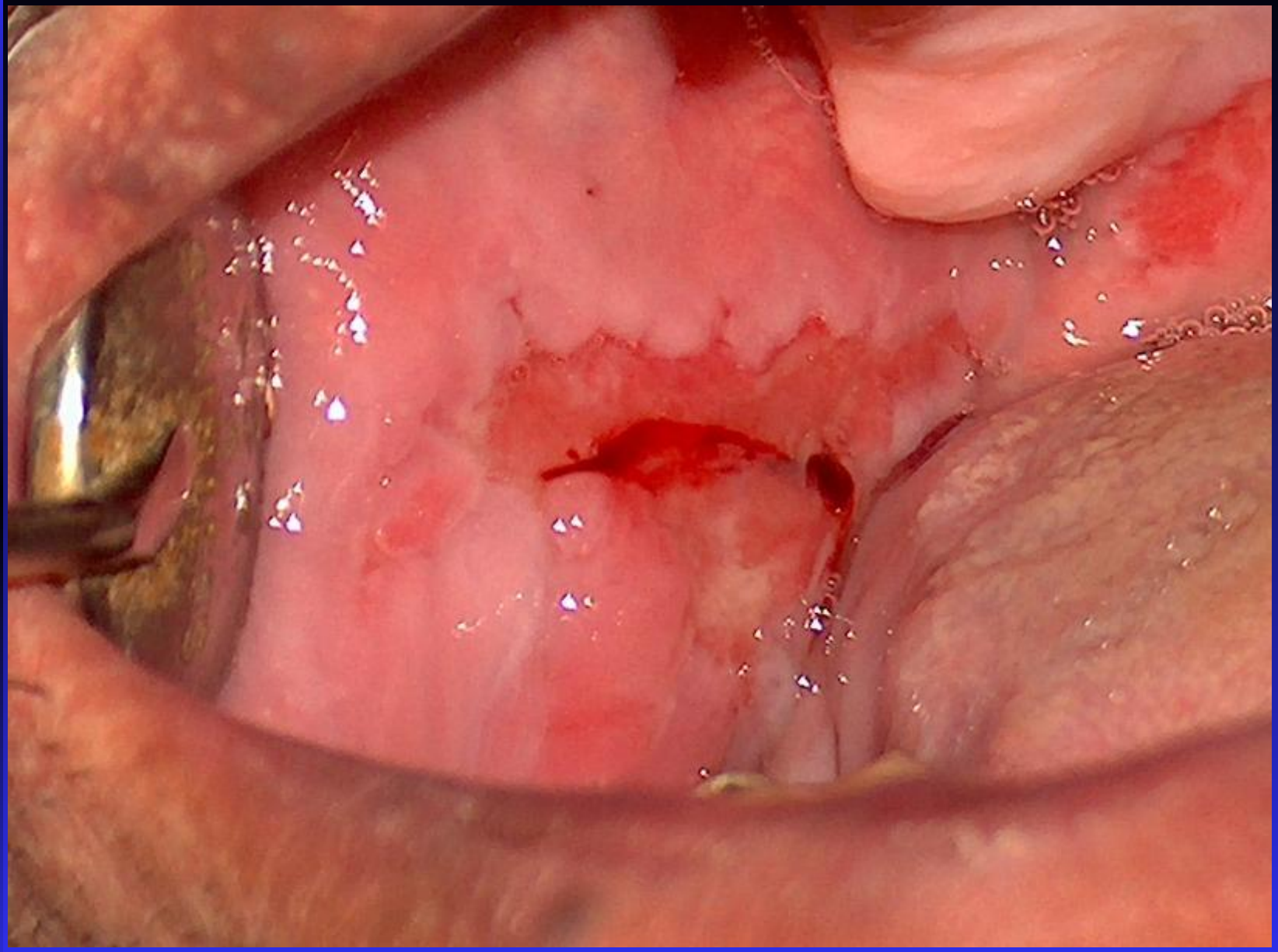
- Widespread fragile, clear fluid-filled, bullae affecting skin and mucosae
- Large irregular ulcerations
- Positive Nikolski sign.

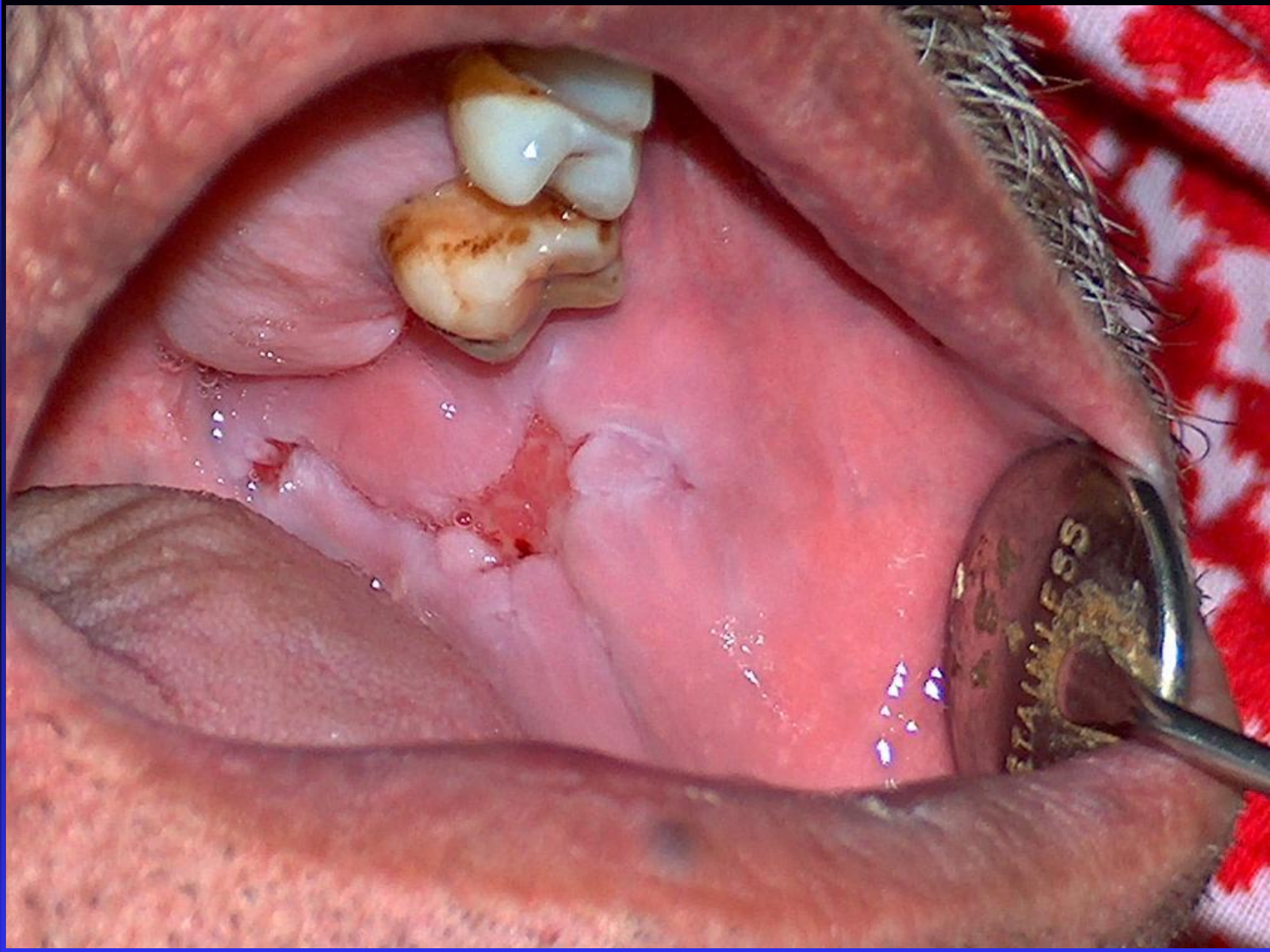


Pemphigus

- Oral lesions may be associated with other mucosal lesions
- Bullae are more fragile
- Spreading and enlarging ulcers
- Clinical types
  - Pemphigus vulgaris
  - Pemphigus vegitans
  - Pemphigus erythematosus
  - Pemphigus foliaciois
  - Paraneoplastic pemphigus



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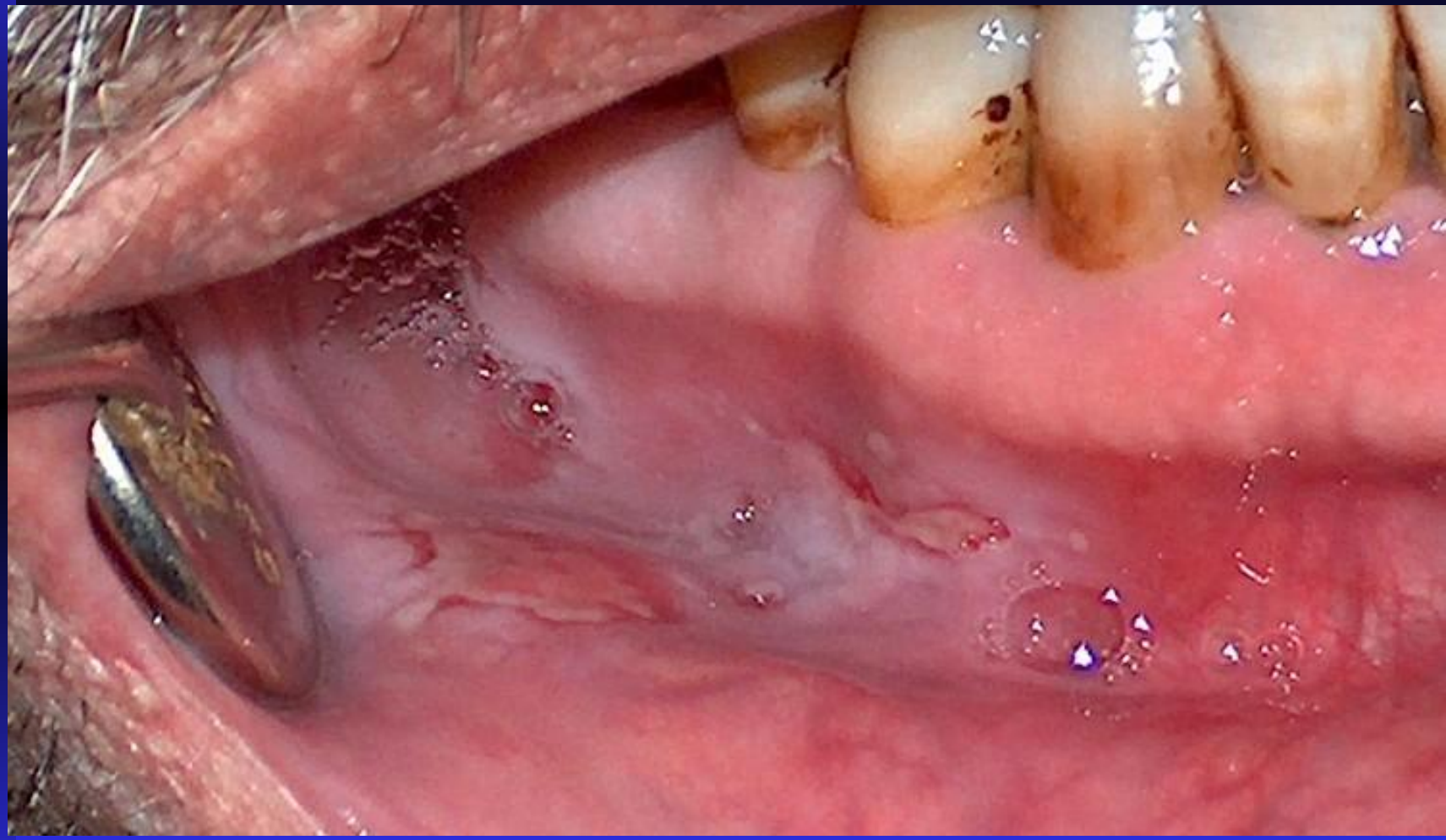
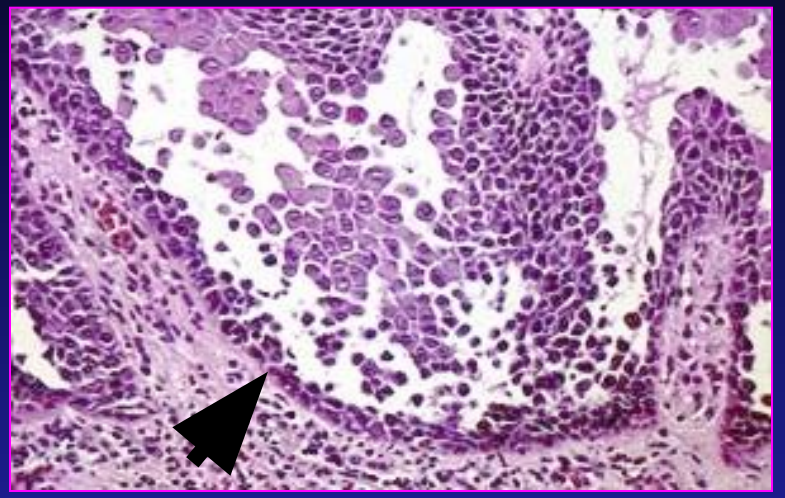
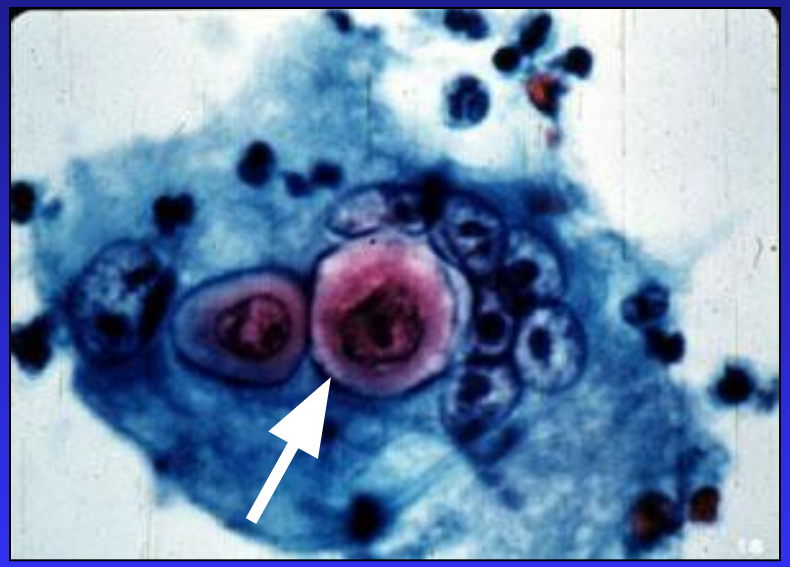


Pemphigus - Diagnosis

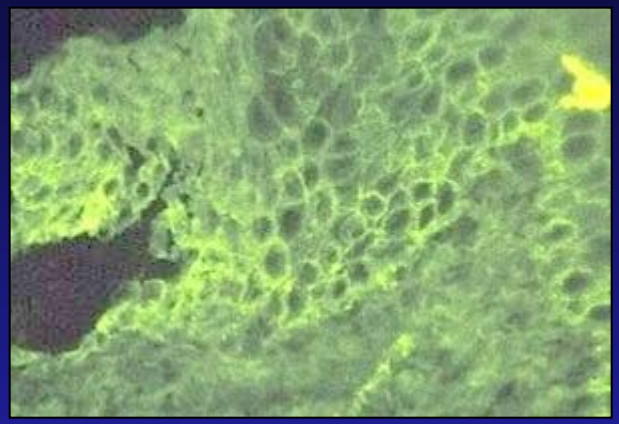
- Positive Nikolski sign on *clinical examination*
- *Incisional biopsy*: intra-epithelial vesicle or bulla
- *Smear* from bulla fluid to see Tzank cells



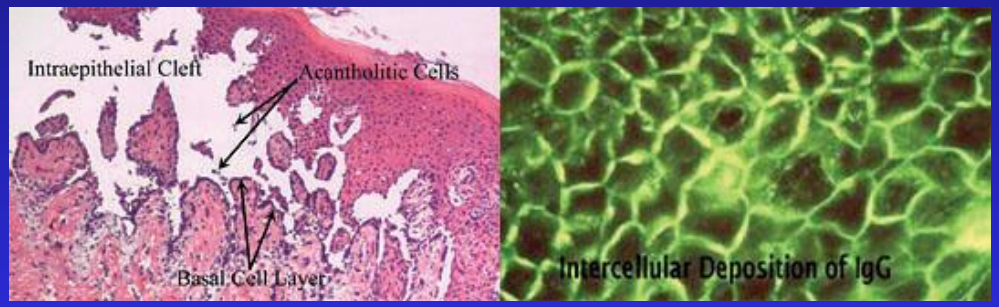


Pemphigus - Diagnosis

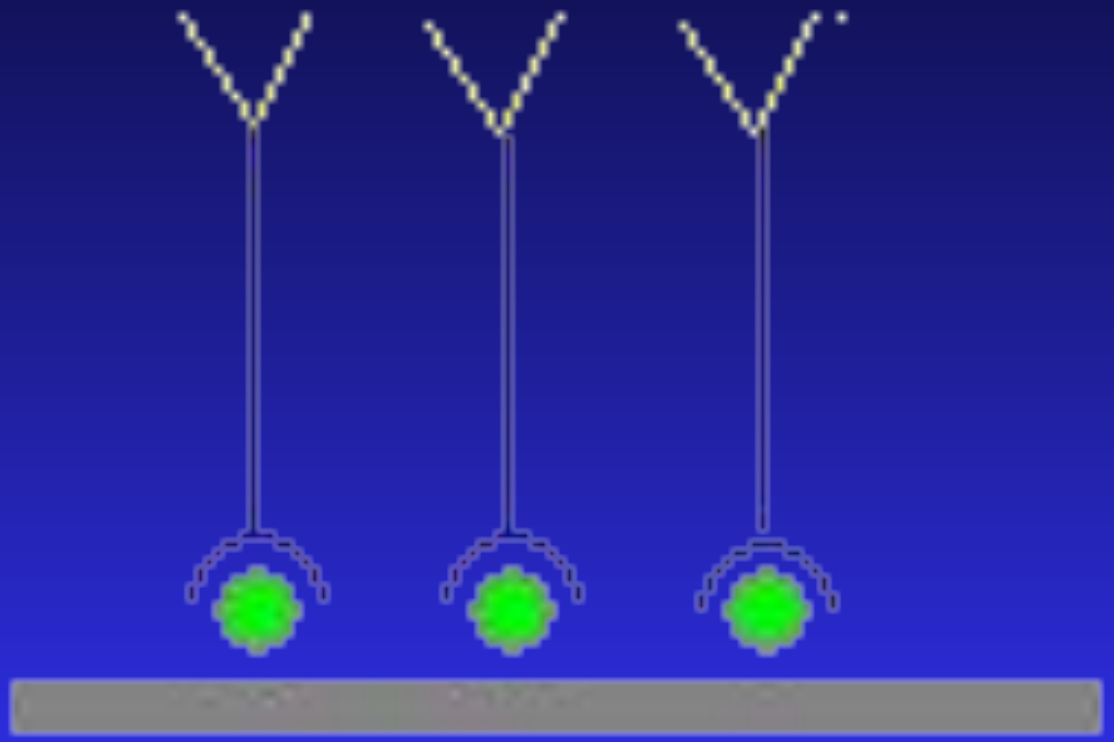
- **DIF**: IgG auto-antibodies (also IgM and C3) on the intercellular substances (against the adhesion molecule desmoglein-3 and ? 1)



- **IIF** (correlate with the severity of the disease): +ve IgG auto-antibodies in 90% of patients
- **ELISA**: anti-desmoglien antibodies in serum



Direct & Indirect IF



Pemphigus - Treatment

- Multidisplinary
- Initial treatment with high doses of steroid (100mg prednisolone / day)
- Patients are maintained on steroids and/or steroid sparing drugs (e.g. azathioprine)
- High-concentration steroid mouth wash.
- Antifungal therapy may be needed.
- Dental considerations

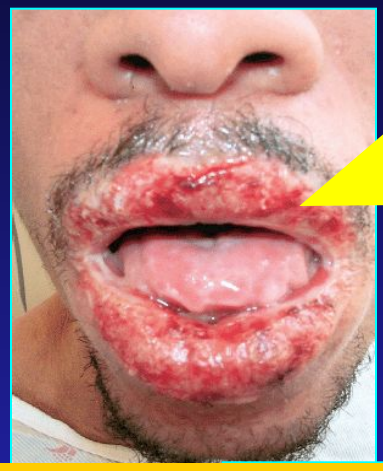
Paraneoplastic pemphigus

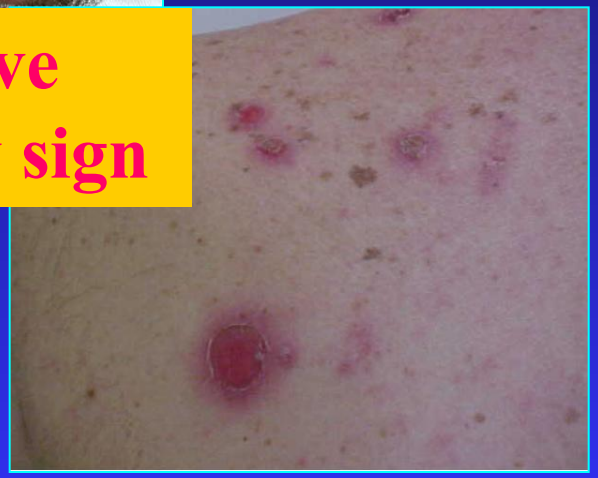
http://emedicine.medscape.com/article/1064452-overview

- Anhalt GJ, *et al*. Paraneoplastic pemphigus. An autoimmune mucocutaneous disease associated with neoplasia. *N Engl J Med*. Dec 20 1990;323(25):1729-35.

- Autoimmune disease
- Anti-plakin antibodies
- 90% mortality rate
- Pemphigus + neoplasm commonly lymphoproliferative neoplasm (most commonly non-Hodgkin's lymphoma)
- No race or gender predilection
- Age >60 yrs.
- The only type affects epithelia other than squamous !!!

- Mucosal lesions
  - Oral
    - Erosions and mucositis
    - Resembling SJS
  - Genital
  - Nasal: epistaxis
- Skin lesions
  - Diffuse erythema
  - Vesiculobullous
  - Papules
  - Scaly plaques
  - Exfoliative erythroderma
  - Erosions
  - Ulcerations





Positive Nikolsky sign

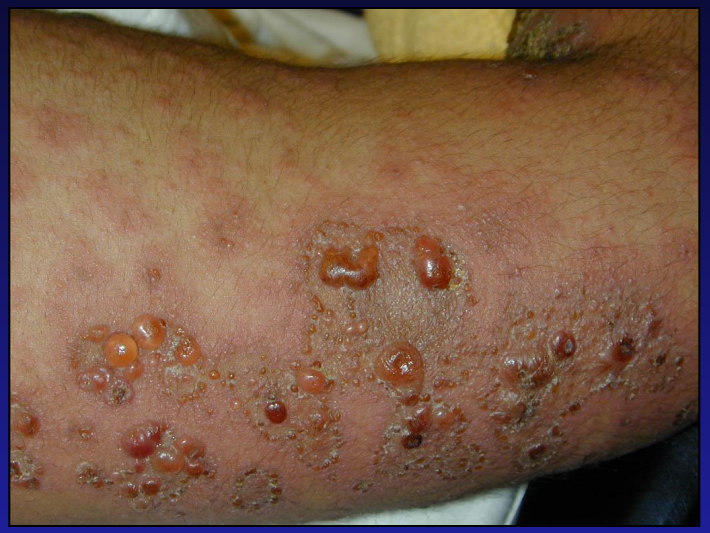
Pemphigoid

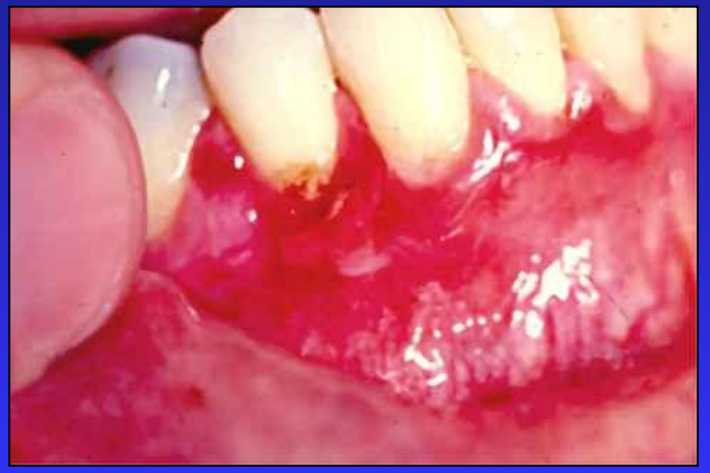
- Auto-immune disease
- No racial predominance
- Two basic clinical types:
  - **Bullous (generalized) pemhigoid**
  - **Mucousal (cicatricial) pemhigoid**

Generalized (bullous) pemphigoid

- Patients > 60 yrs. Old
- No racial or gender predominance

- **Skin:**
  - Starts as skin rash
  - tense, blood-tenged, bullae mainly on limps
- **Oral:**
  - In about 20% of patients
  - Bullae may remain intact for some time

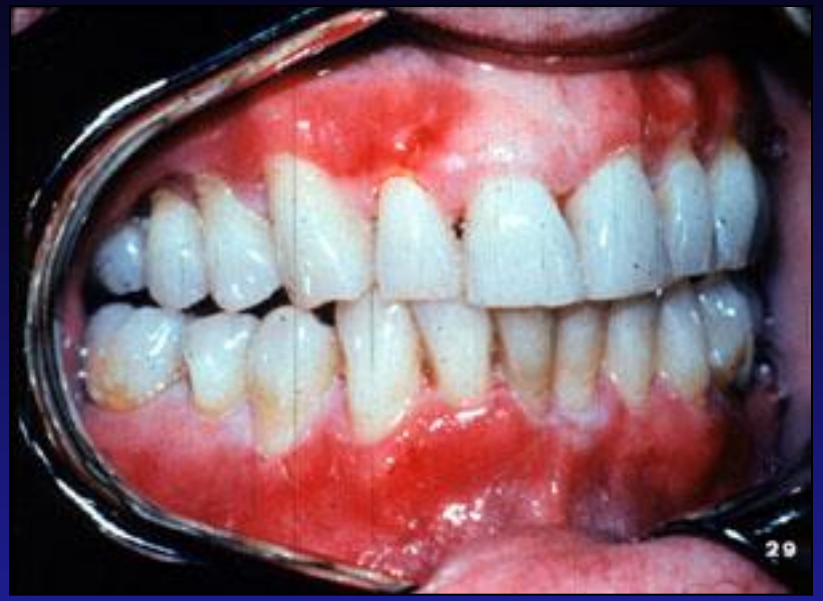


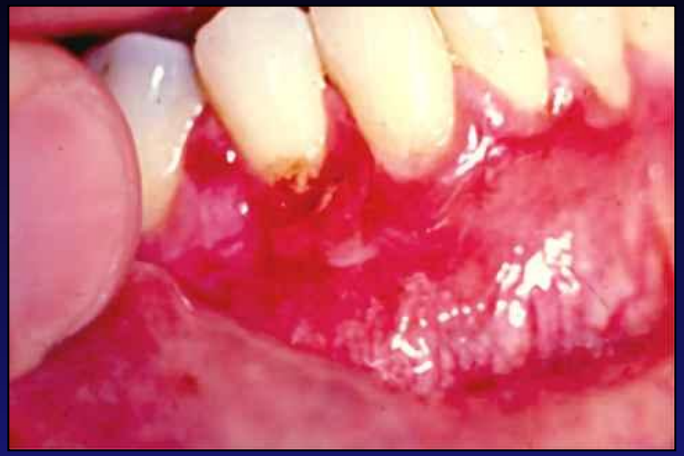


Mucosal (cicatricial) pemphigoid

- Patients age: 50-70 yrs.
- M/F = ~ 1/4

- **Oral lesions**
  - Almost always present, and mainly in the soft palate
  - Desquamative gingivitis is the most common lesion
- Other mucosae may be affected
  - Conjunctiva
  - Nasal
  - Genital
- Starts as bullae or erosions
- Heals by scaring

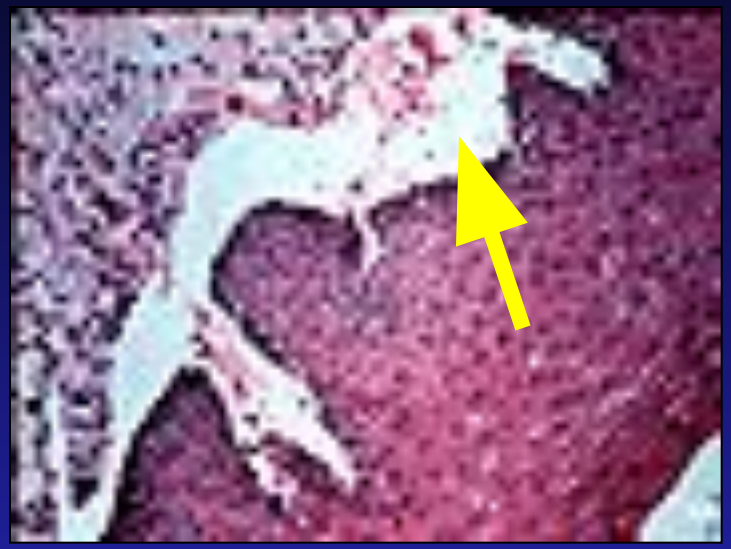


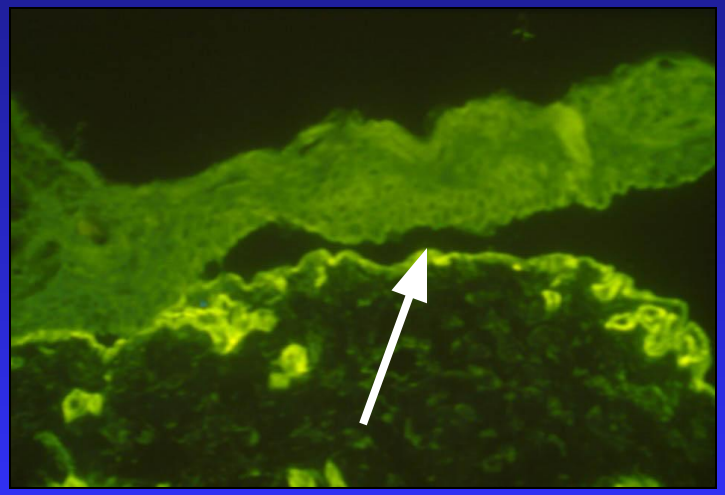



SFS

Mucosal pemphigoid - Diagnosis

- Incisional biopsy: sub-epithelial bulla
- DIF: *on perilesional mucosa*
  - +ve in 75% of patients.
  - Auto-antibodies (mainly IgG) in a linear distribution at the basement membrane zone. IgA and complement may be detected
- IIF
  - Chemically separated normal human epithelium as substrate
  - Salt-split human skin
  - IgG in 20% of patients
  - Low titre





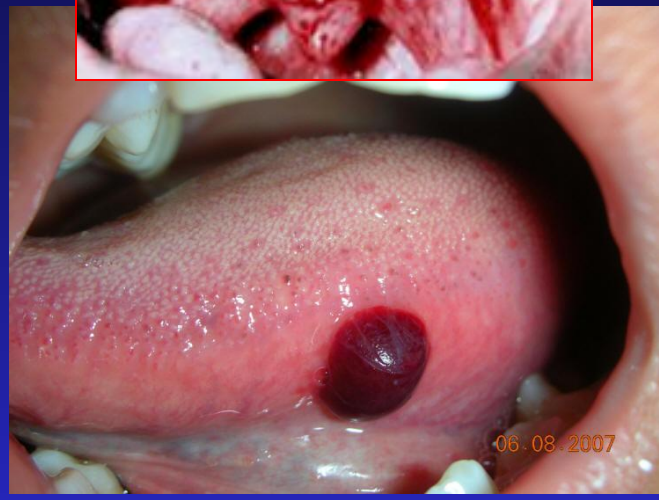
Pemphigoid – Treatment

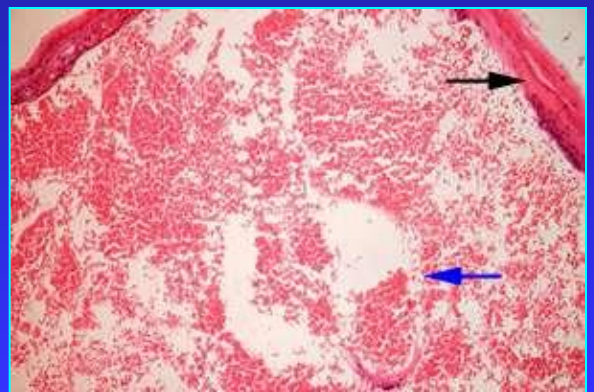
This disorder is extremely difficult to treat. Even with optimum control, blisters may continue to develop in some patients

- Generalized pemphigoid
  - Systemic steroids and / or steroid sparing immunosuppressive agents.
  - Topical steroid may be used for oral lesions.
- Mucosal pemphigoid
  - Perforate the bullae if necessary
  - Topical steroids: e.g.
    - Beclamethasone spray
    - Triamcinolone in orabase
  - Antiseptic mouth wash.
  - Multidisplinary management e.g. ophthalmologist, dermatologist and internest opinion is mandatory
  - High-dose intravenous immune globulin in refractory cases

Oral Blood Blisters (angina bullosa haemorrhagica)

- Unknown etiology
- Sudden development of blood-filled blister on the oral mucosa
- Possibility of airway obstruction
- Blood clotting mechanism is normal
- Platelets count is normal
- Management:
  - Perforating the blister
  - No known preventive measures



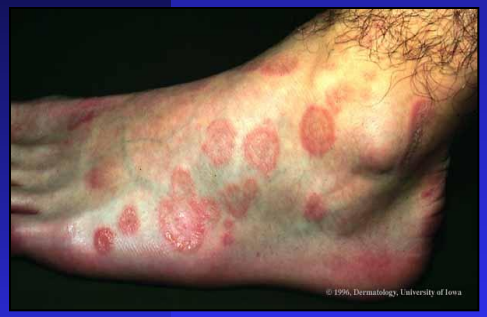


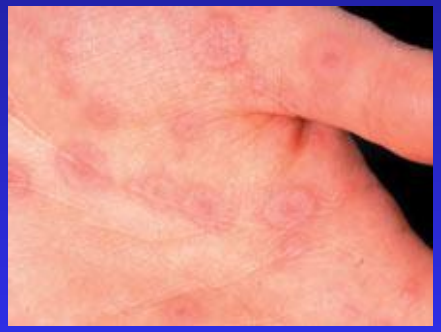
Erythema multiforme

- **Precipitating factors:** *Type IV hypersensitivity reaction*
  - Viral infections (e.g herpes simplex, mycoplasma)
  - Bacterial infections
  - Internal malignancy or its treatment with radiotherapy
  - Pregnancy
  - Drugs (e.g. sulphonamides, penicillins, phenylbutazone, barbiturates)
  - Excessive exposure to UV light
  - Unknown factors
- More in males
- More in young people

Erythema multiforme – Clinical features

- **Oral mucosal lesions:**
  - Sudden development of widespread erosions
  - Crusting and bleeding lip lesions
  - Self-limiting
  - Recurrent
- **Skin lesions:**
  - Target appearance
  - Symmetrical





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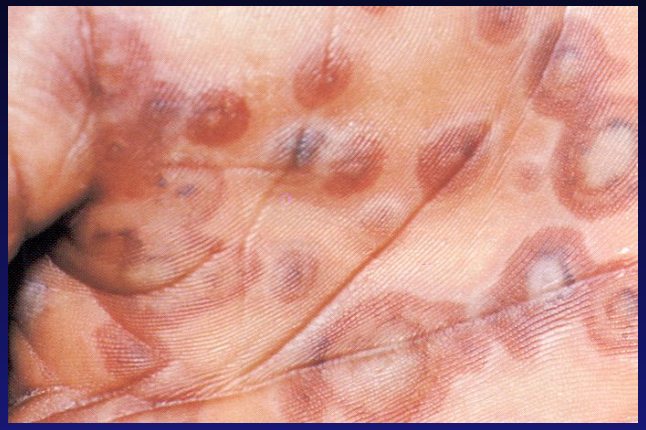
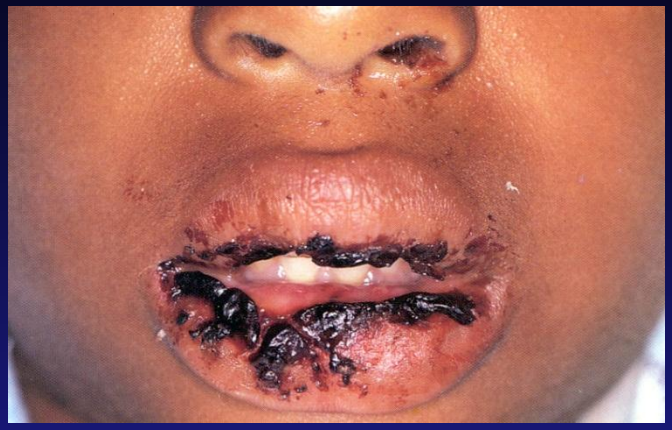
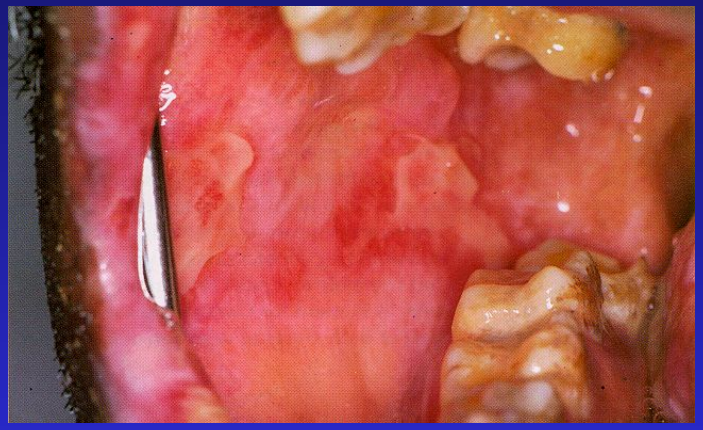
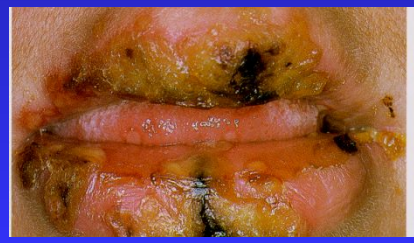


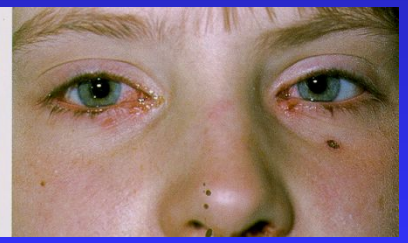


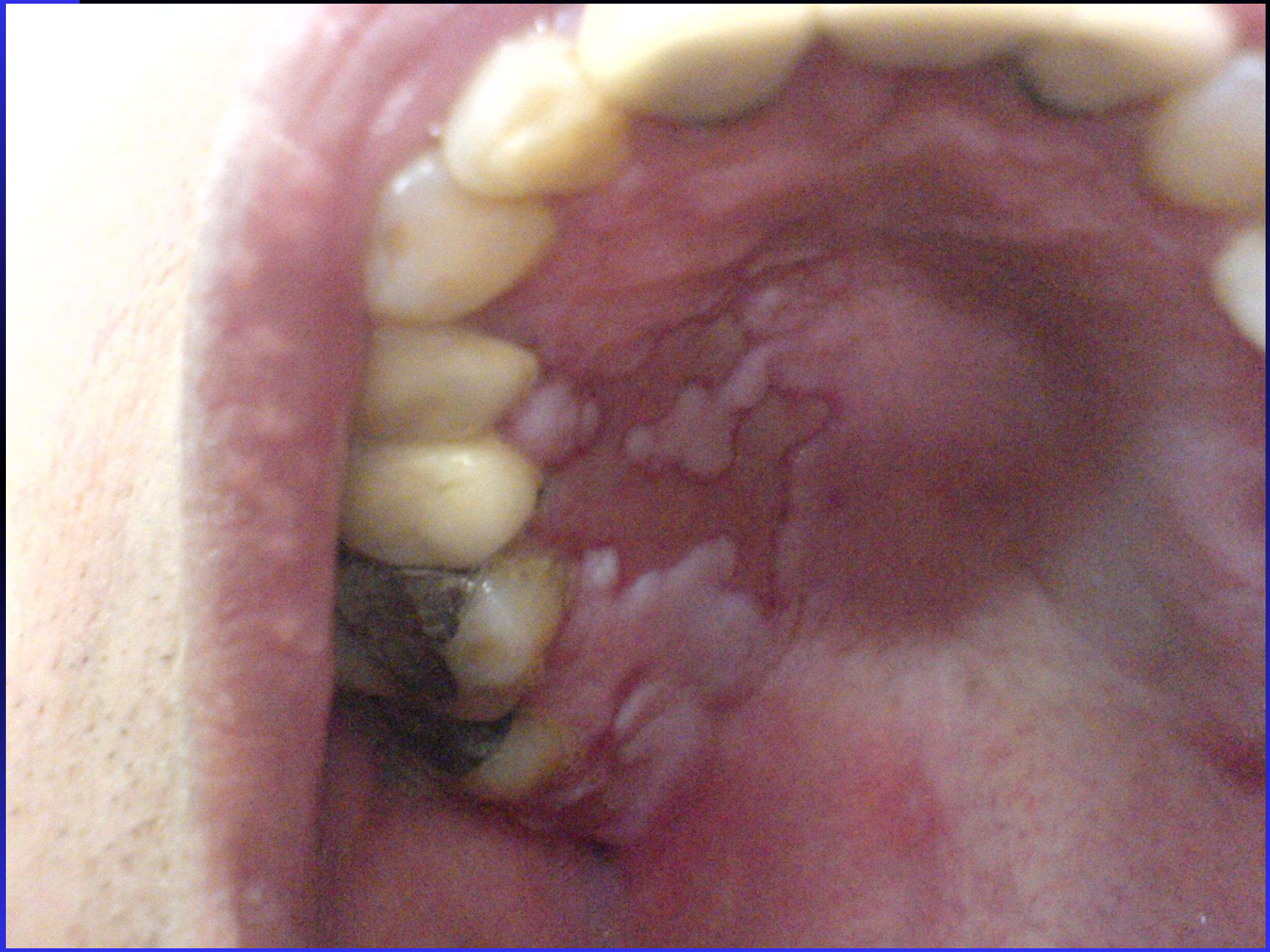


General features:

- Cervical lymphadenitis
- Pyrexia
- Subside in 10 days
- Subjected to recurrence
- > in young patients

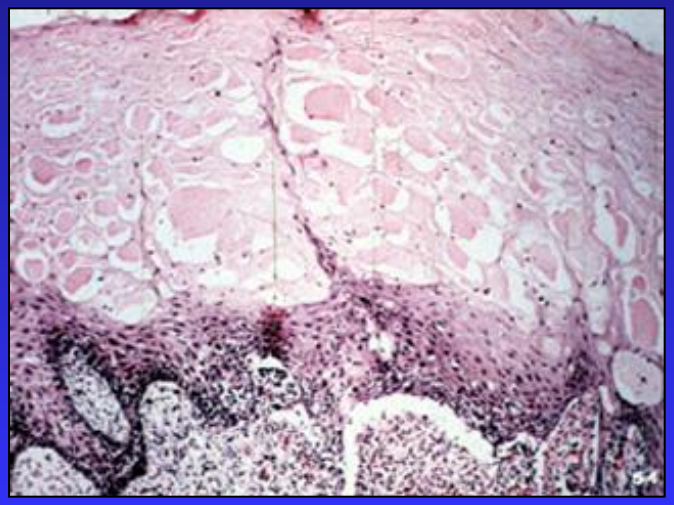






EM
Diagnosis and work-out

- Clinical picture (lip lesions, target lesions and recurrence)
- CBC: leukocytosis
- Electrolytes
- BUN
- ESR: elevated
- Liver function test: mildly elevated liver transaminase
- Culture (sputum, erosion, blood) in severe cases
- Biopsy: non-specific (to rule out differential diagnosis)
  - Sub-epidermal split
  - Lymphocytic infiltration
  - Hydropic changes in basal cells
  - Epithelial necrosis



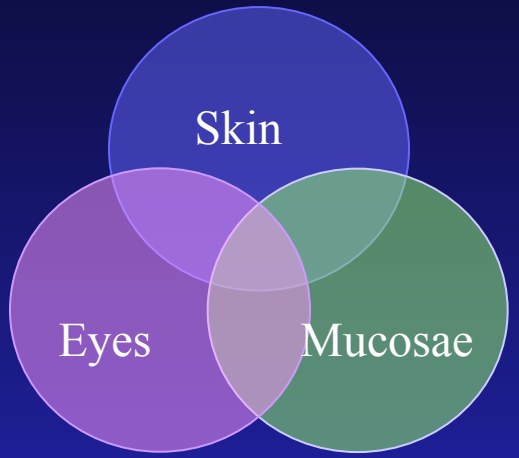
EM
Treatment - Management

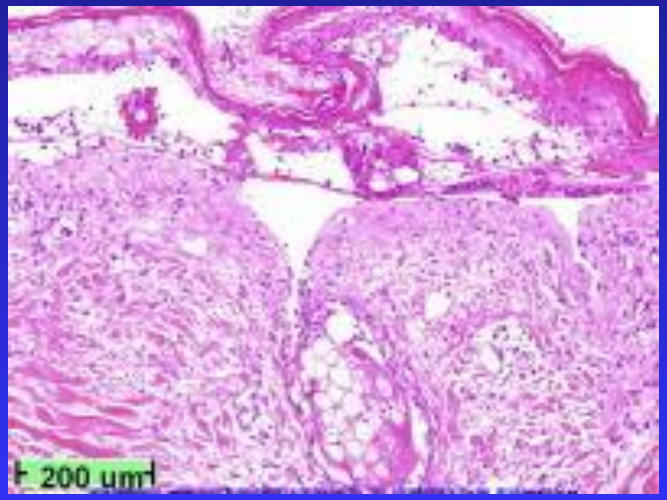
- Remove the cause if possible
- Treat infections
- Fluid intake and soft diet; possibly IV line is needed
- Oral antihistamines
- Antiseptic mouth wash
- Topical steroids
- ?? Systemic steroids
- Acyclovir as a prophylaxis

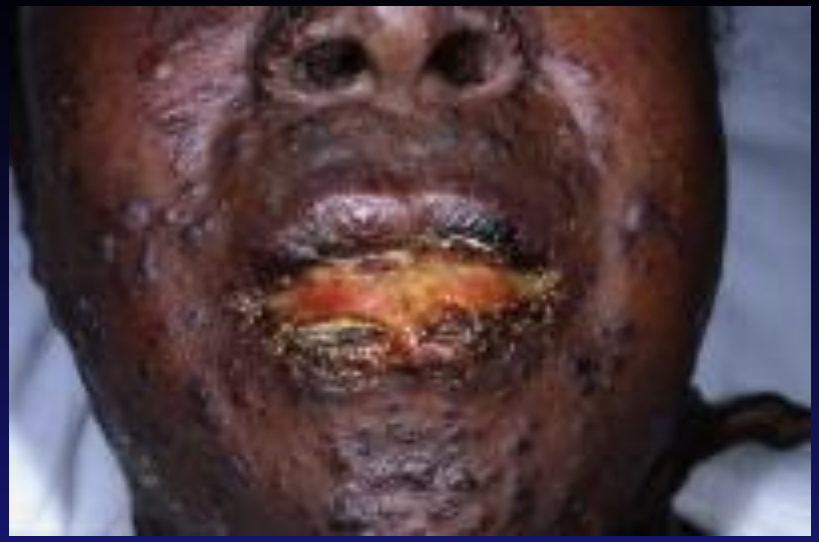
- Consultations:
  - Dermatologist
  - Ophthalmologist
  - Internal medicine specialist

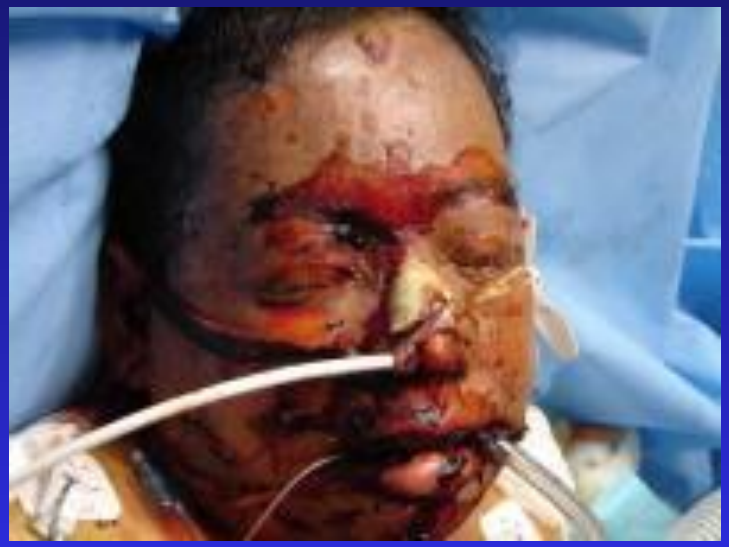
Steven-Johnson Syndrome
Toxic epidermal necrosis

- Mortality
  - 5% SJS
  - 40% TEN
- Management
  - Fluid replacement
  - Sterile techniques
  - Wound care
  - Medical consultation
  - Systemic corticosteroid therapy is controversial
  - Cyclosporin therapy







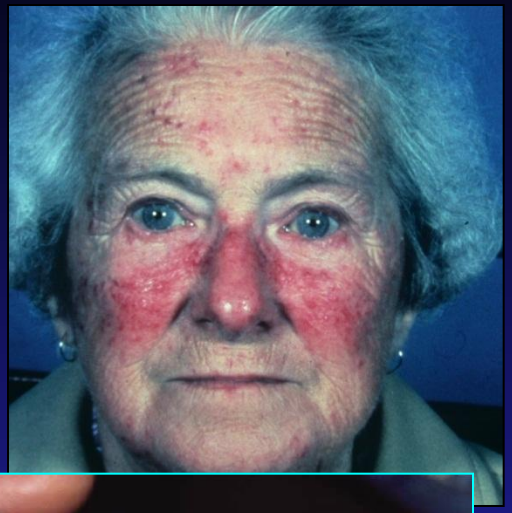


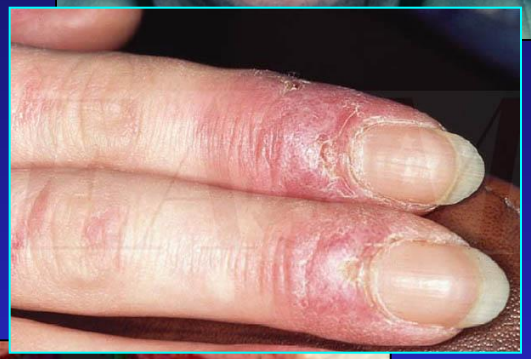
Lupus Erythematosus

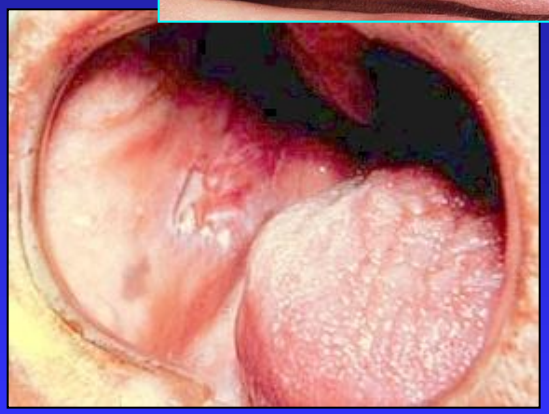
- Autoimmune disease
- Two main clinical divisions:
  - Discoid lupus erythematosus (DLE)
  - Systemic lupus erythematosus (SLE)
- M:F = 9:1 (18-65 years; peak 25-45 years)
- DLE & SLE may represent different ends of the spectrum of the disease activity
- SLE may be precipitated by some drugs e.g. Hydralazine (lupoid reaction).
- Oral mucosal lesions in 25-75% of the cases

Lupus Erythematosus – Clinical Features

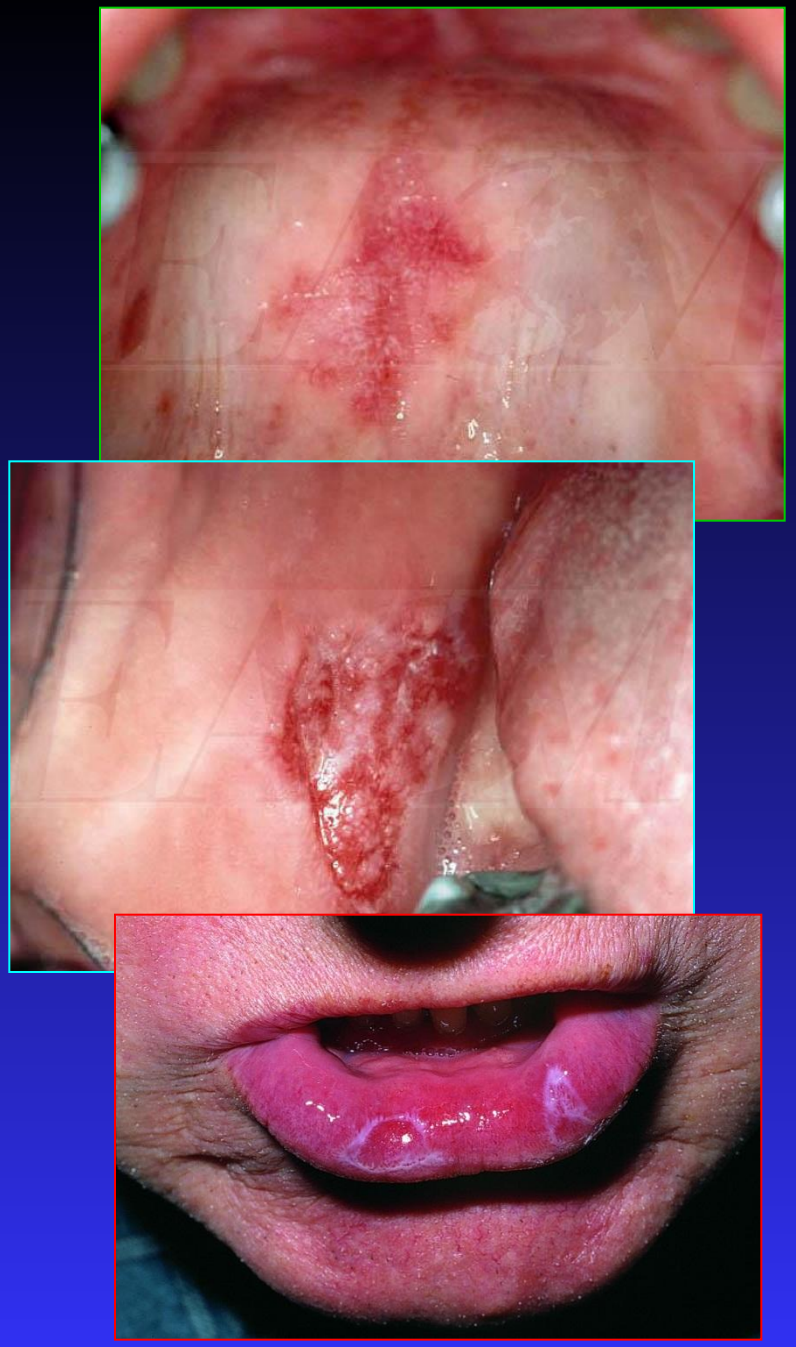
- **SLE:**
  - **Skin:** erythematous itchy rash (butter fly appearance)
  - **Systemic manifestations:** arthritis, kidney, heart, lung, brain, depression, alopecia, Raynouds phenomena
  - **Mucosa:** superficial erosions and erythematous patches
    - SLE is similar to DLE
  - Oral symptoms:
    - Dryness
    - Soreness
    - Burning







- **DLE:** mainly cutaneous lesions
  - **Skin:** resemble SLE, symmetrical, heals with scaring
  - **Mucosa:** superficial erosions and erythematous patches with peripheral white striations
- DD: Oral lichen planus



Lupus Erythematosus

- Diagnosis:
  - IMF: antinuclear antibodies (ANA) +ve in 90% of patients.
  - DMF
  - Biopsy and histopathological examination: resembles OLP

- Prognosis
  - No cure
  - Renal disease is the main morbidity and mortality
  - Thrombocytopenia and hemolytic anemia in 85% of patients
  - Oral lesions are considered potentially malignant

- Treatment: antifungal agents may be required for oral lesions

- **SLE:**
  - High doses systemic steroids + steroid sparing drugs.
  - High concentration steroid mouth wash
- **DLE:**
  - Topical steroids to reduce symptoms
  - Antimalarial drug (chloroquine) may be useful (? Retinopathy)
  - ? Potentially malignant condition

Conclusion