

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 in diameter, and containing 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 striae*
- Asymptomatic but rough mucosa



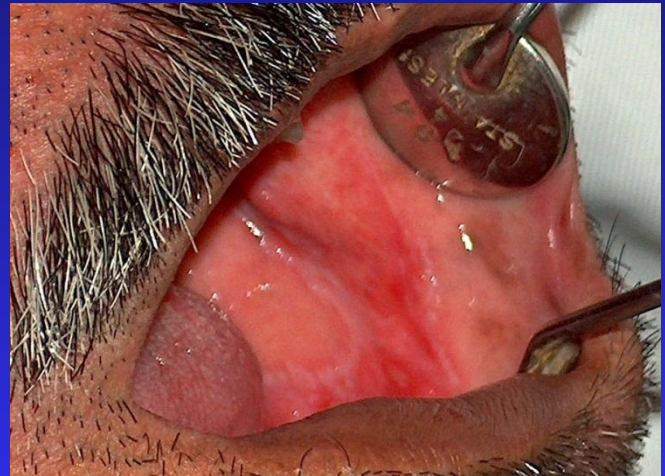
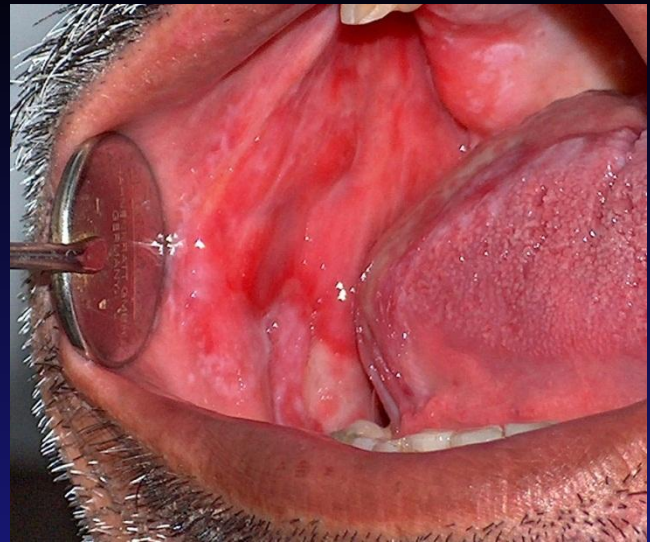
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Erosive LP.

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





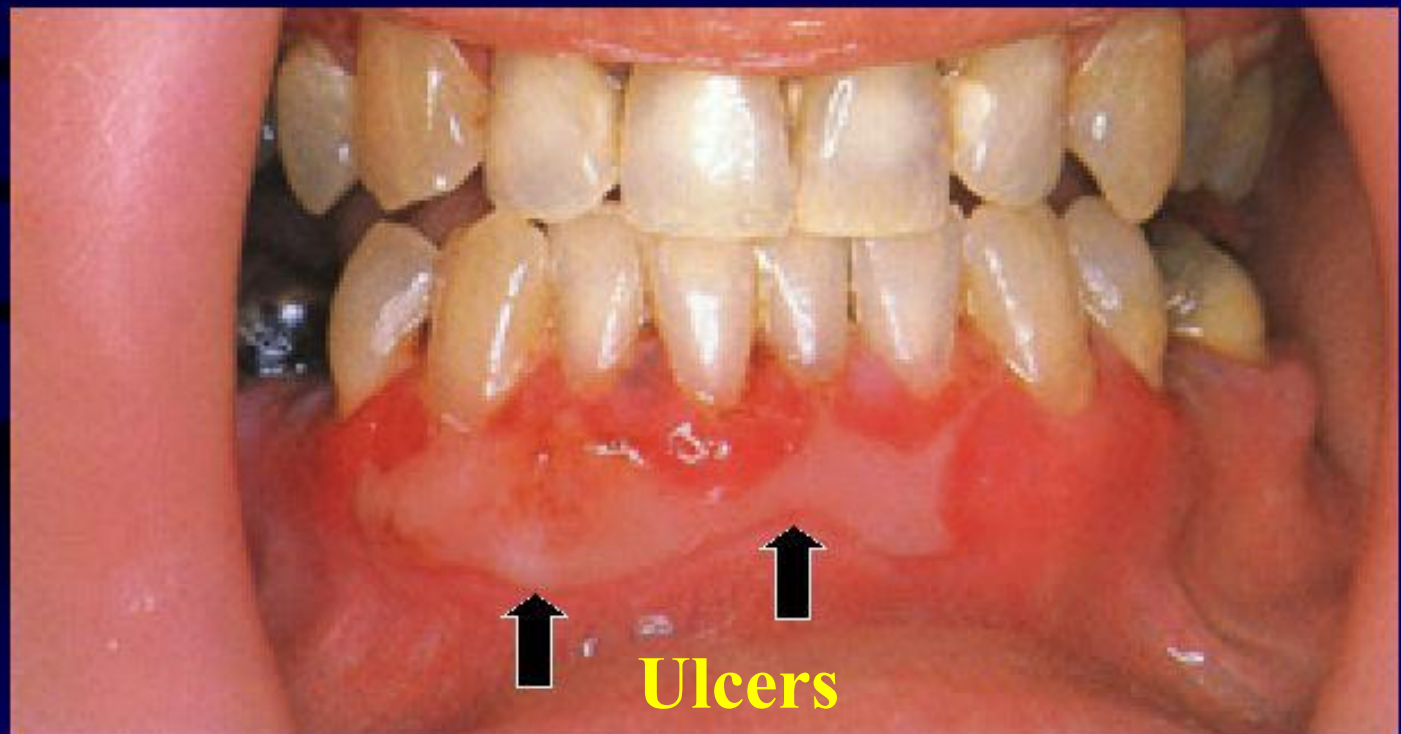
Non-erosive LP.
Plaque type



Desquamative gingivitis on attached gingiva

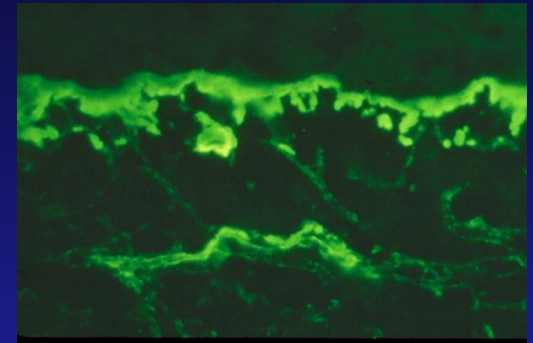
Is a clinical rather than a pathological entity

Desquamative Gingivitis in CP

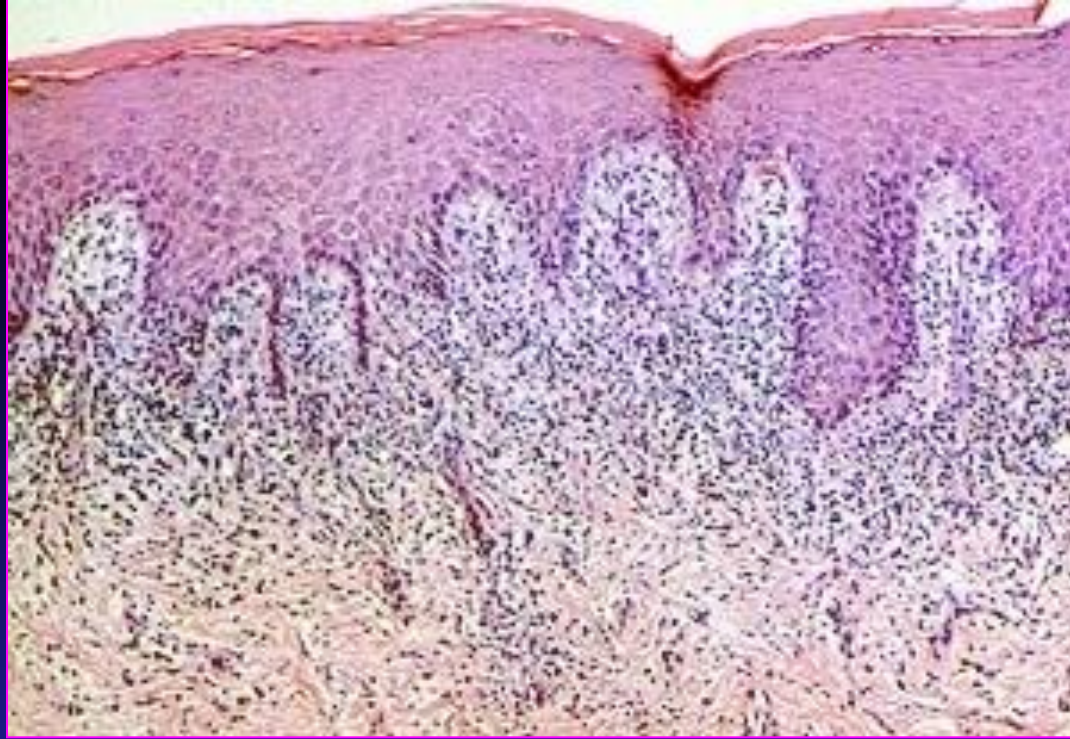


Oral Lichen Planus

- **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.

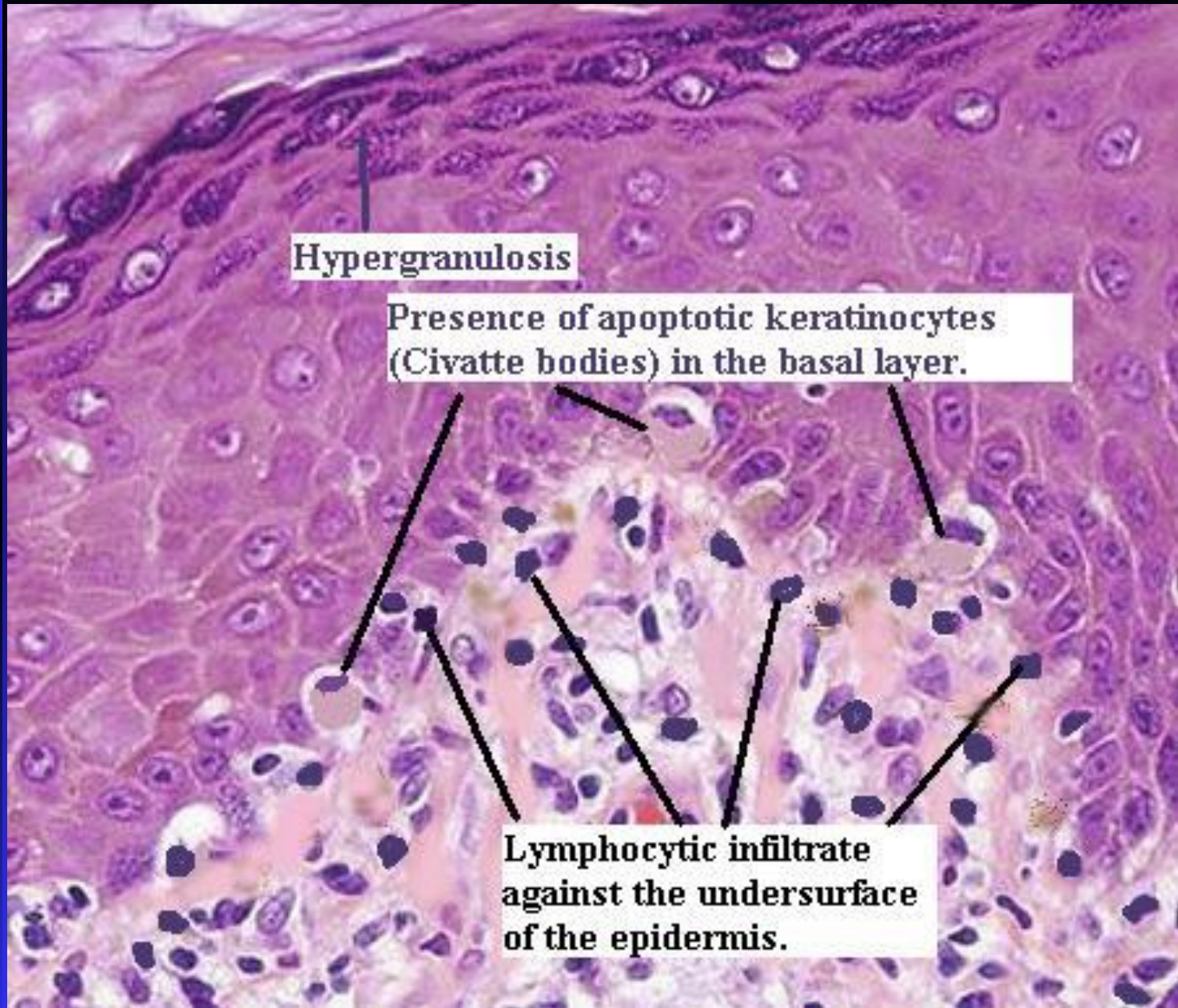


*Fibrinogen at BMZ
(non-specific)*



Histopathology of LP.

- Epithelial hyperplasia or atrophy
- Saw teeth appearance of rete ridges
- Liquifaction degeneration of the basement membrane
- Dense band of lymphocytic 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 adhesive paste,
 - ◆ Beclomethasone 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

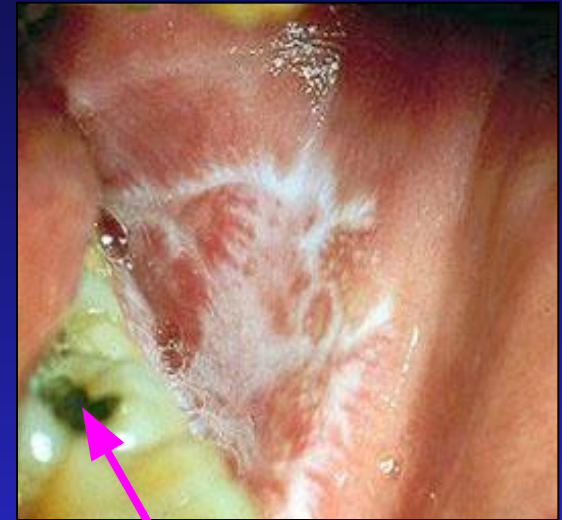
- **The expression or unmasking of the lichen planus antigen may be induced by:**
 - ◆ Drugs (lichenoid drug reaction)
 - ◆ Contact allergens in dental restorative materials or toothpastes (contact hypersensitivity reaction)
 - ◆ Mechanical trauma (Koebner phenomenon)
 - ◆ Viral infection
 - ◆ Other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

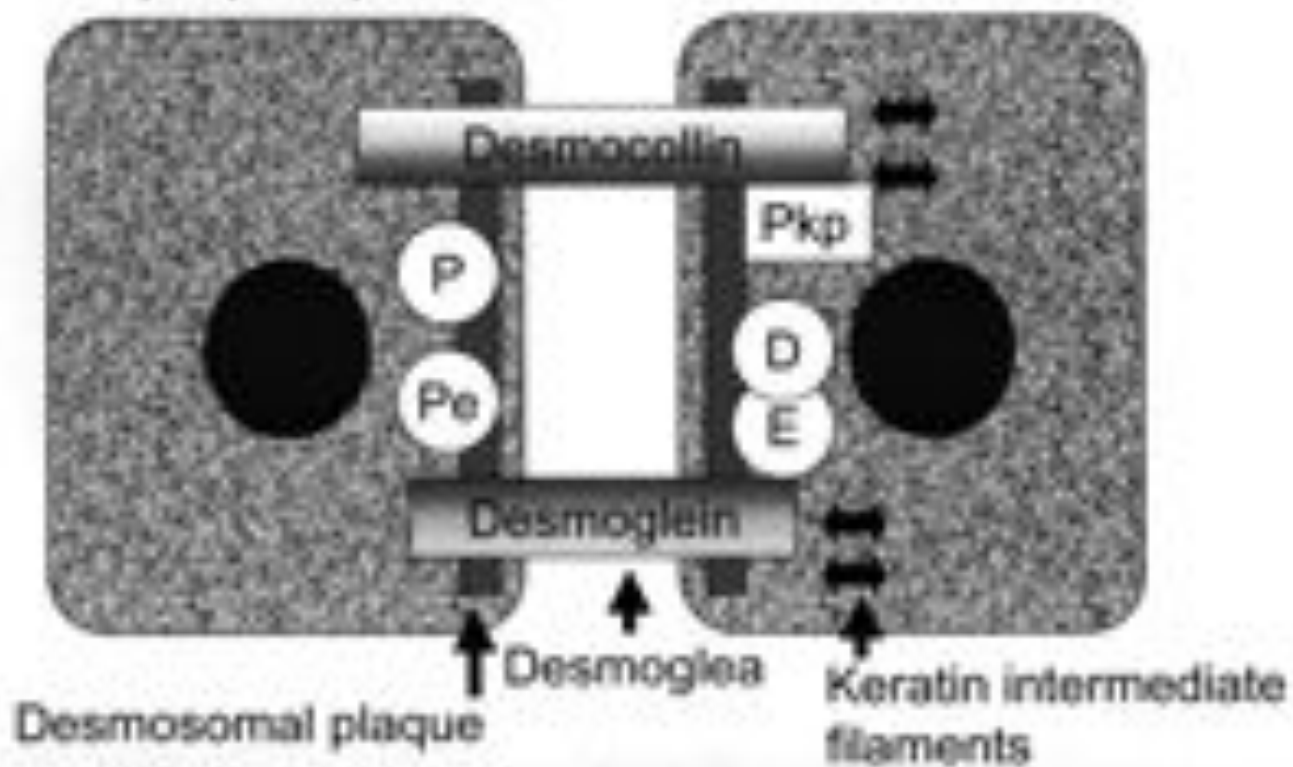


Pemphigus

- 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.

D = desmoplakin
E = envoplakin
P = plectin
Pe = periplakin
Pkp = plakophilin

Keratinocyte



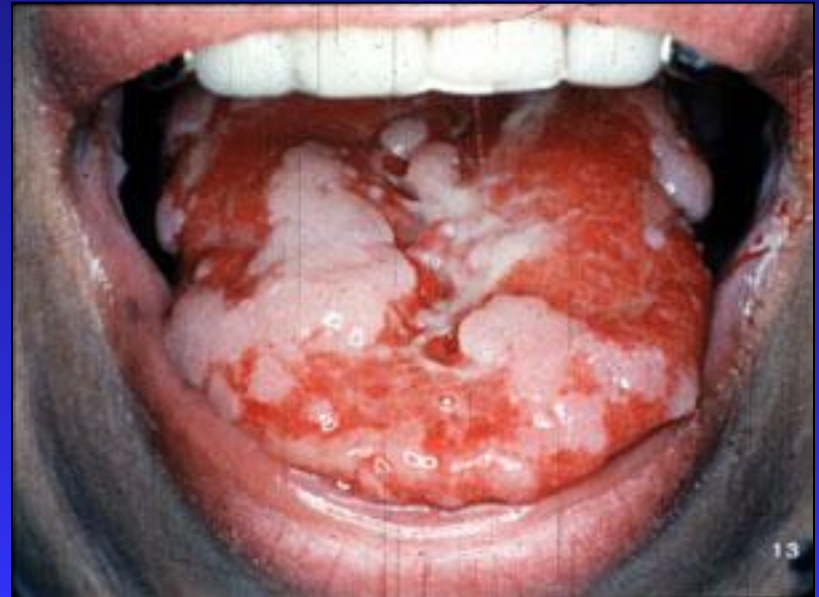
Pemphigus – Clinical picture

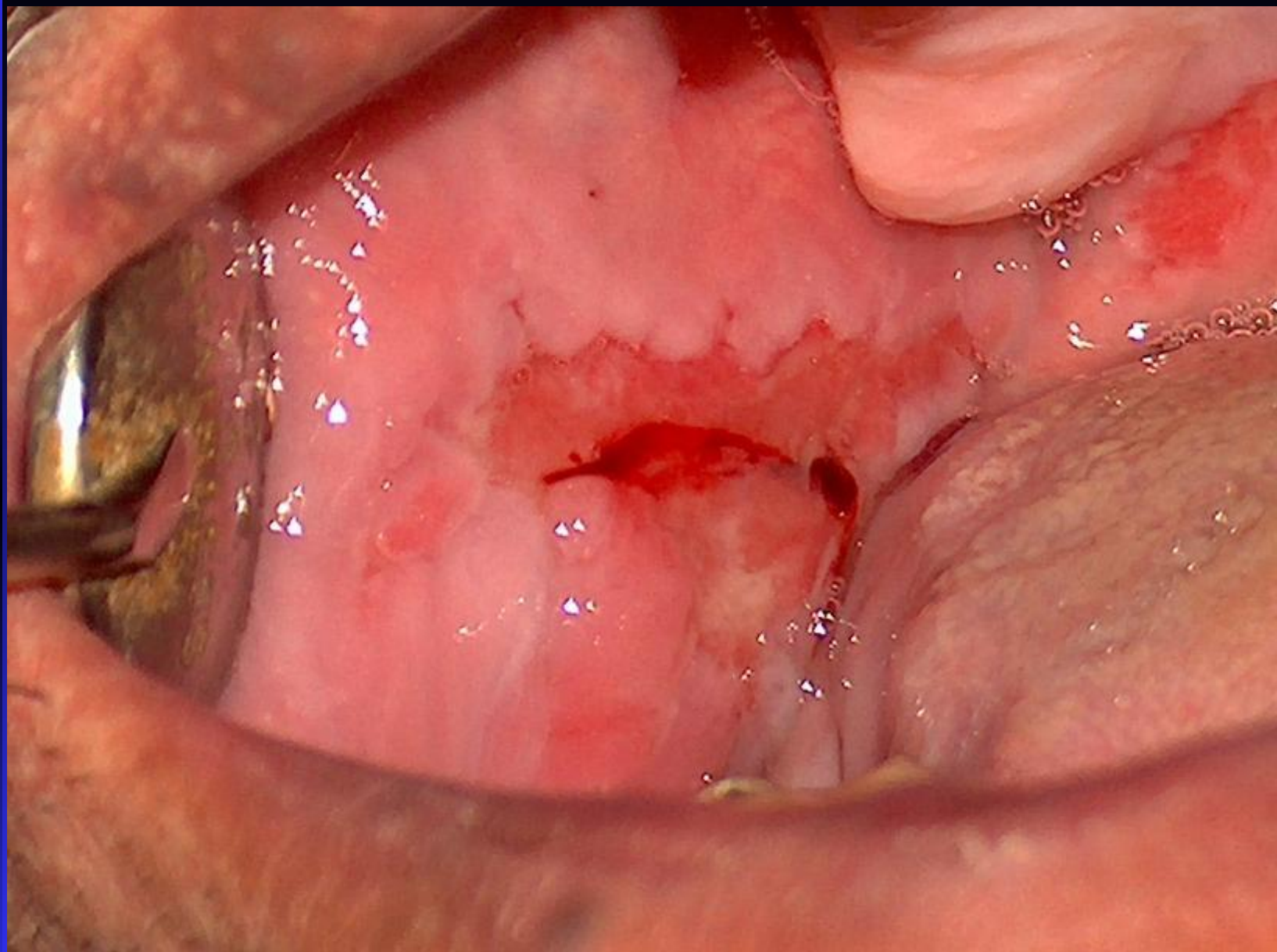
- Widespread fragile, clear fluid-filled, bullae affecting skin and mucosae
- Large irregular ulcerations
- Positive Nikolski sign.

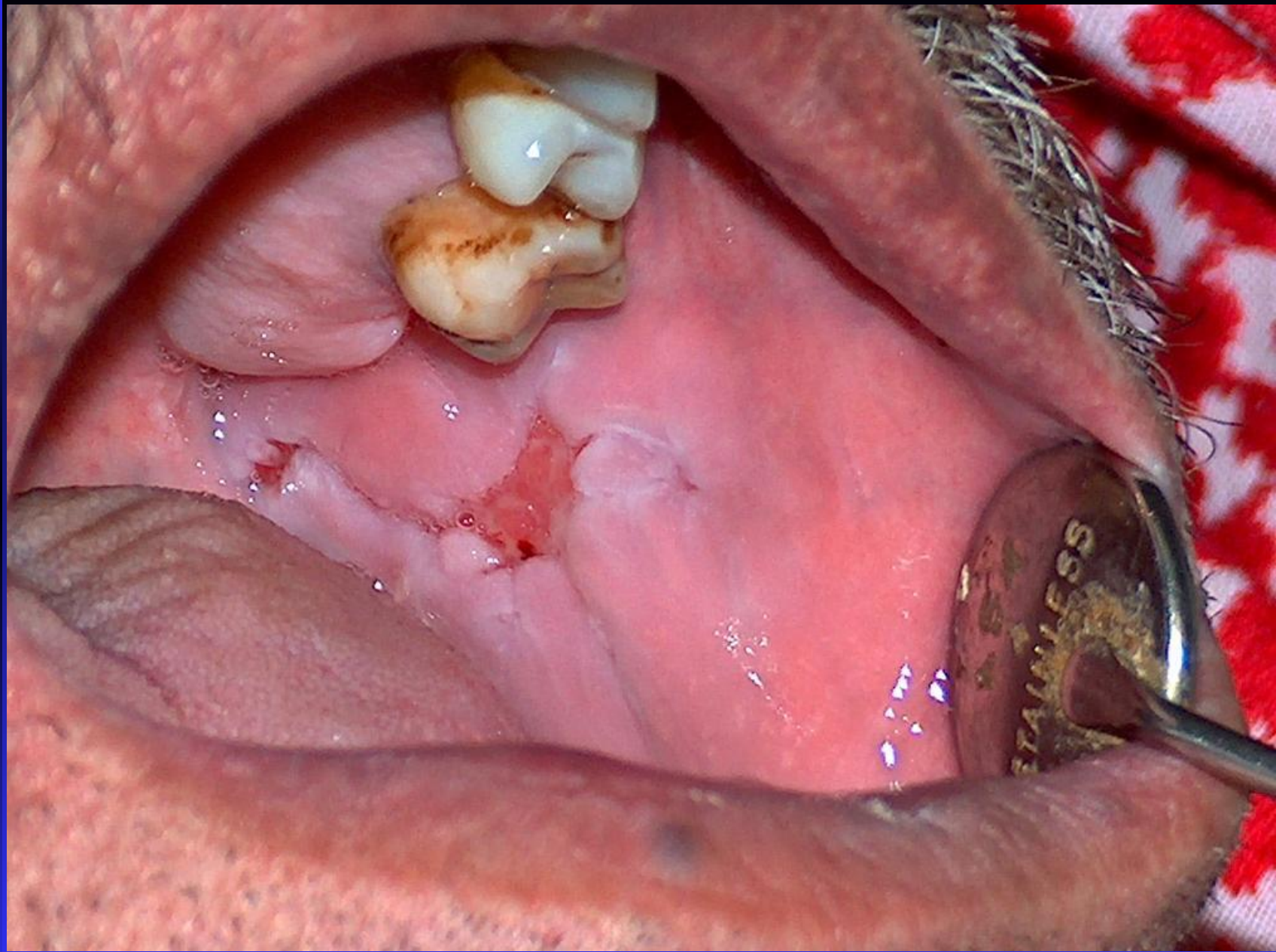


Pemphigus

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



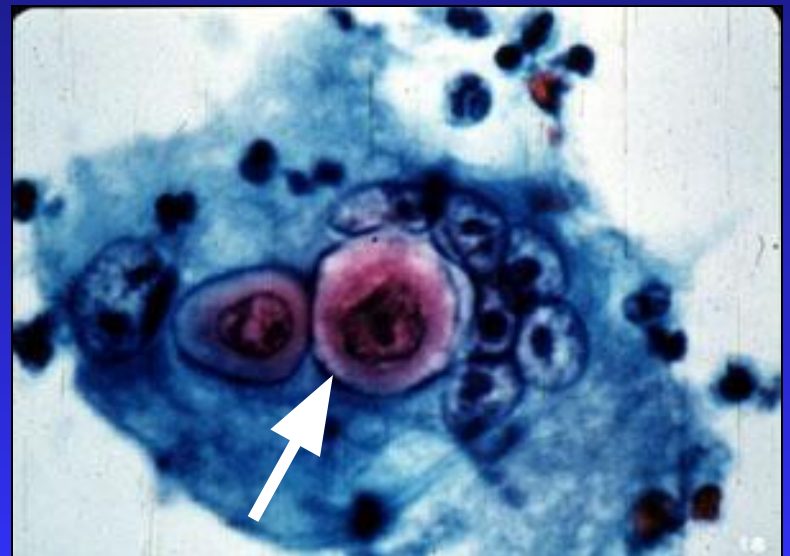
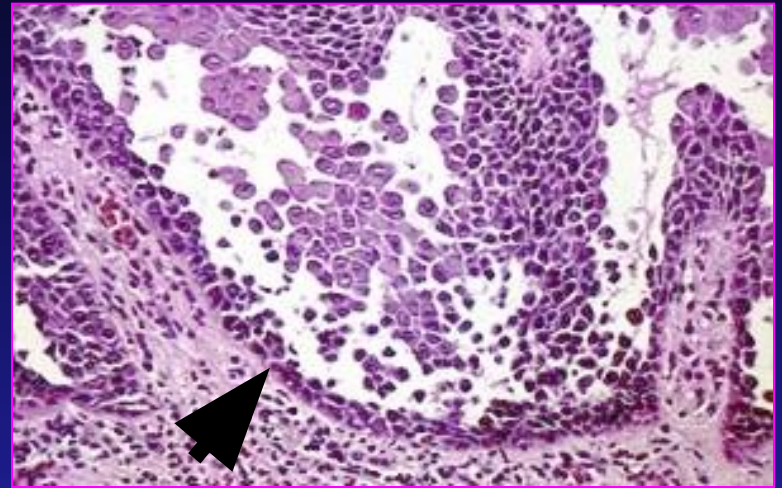






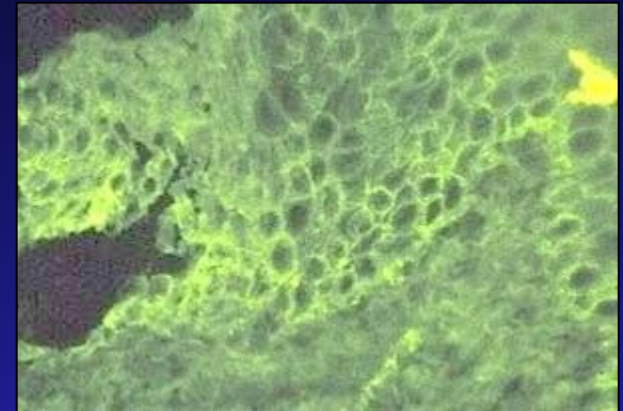
Pemphigus - Diagnosis

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

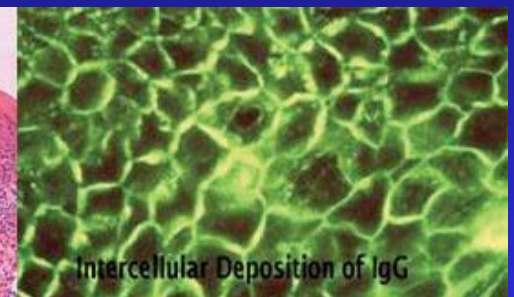
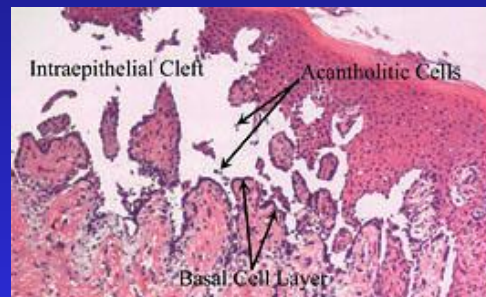


Pemphigus - Diagnosis

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

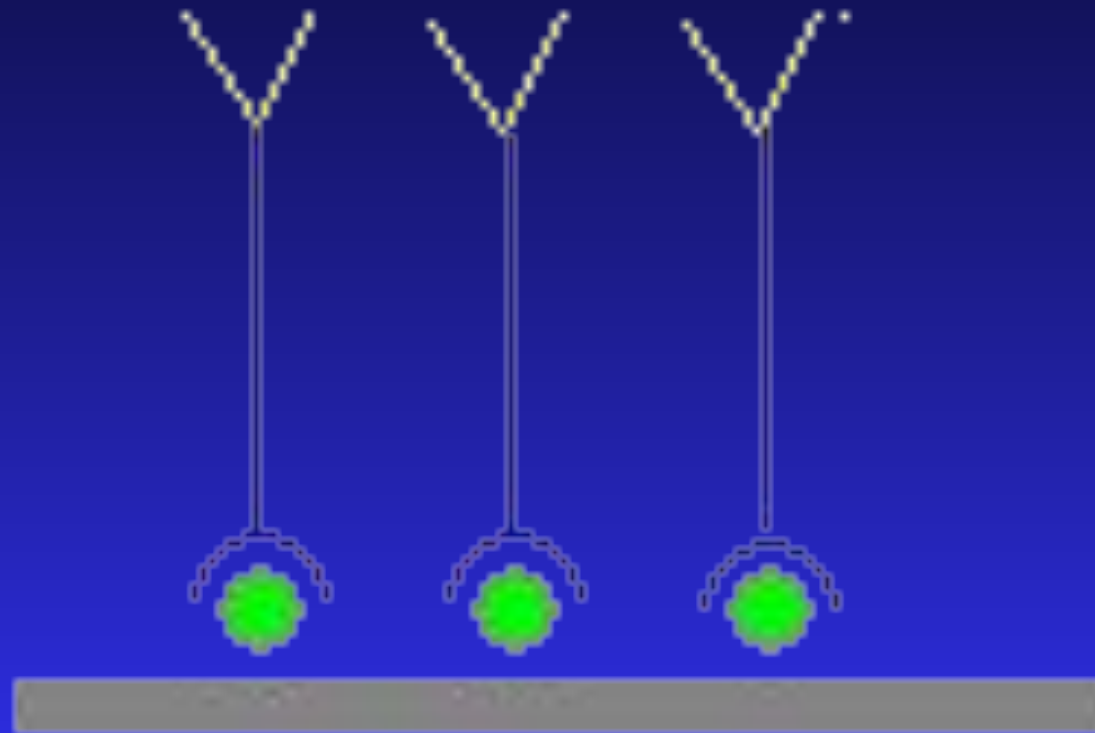


- **IIF** (correlate with the severity of the disease): +ve IgG auto-antibodies in 90% of patients



- **ELISA:** anti-desmoglein antibodies in serum

Direct & Indirect IF



Pemphigus - Treatment

- Multidisciplinary
- 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) pemphigoid**
 - ◆ **Mucousal (cicatricial) pemphigoid**

Generalized (bullous) pemphigoid

- Patients > 60 yrs. Old
- No racial or gender predominance
- **Skin:**
 - ◆ Starts as skin rash
 - ◆ tense, blood-tinged, bullae mainly on limbs
- **Oral:**
 - ◆ In about 20% of patients
 - ◆ Bullae may remain intact for some time

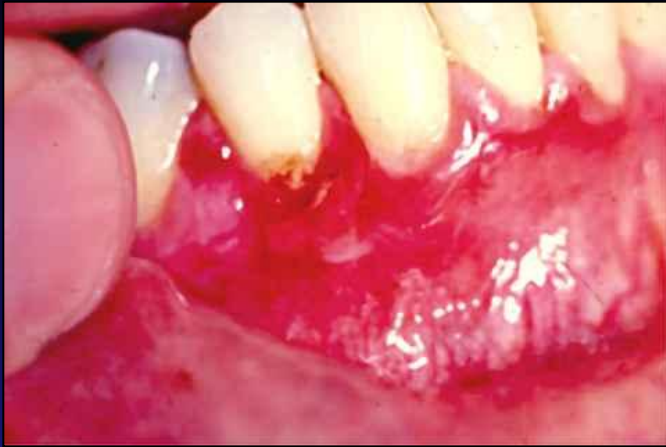


Mucosal (cicatricial) pemphigoid

- 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 scarring

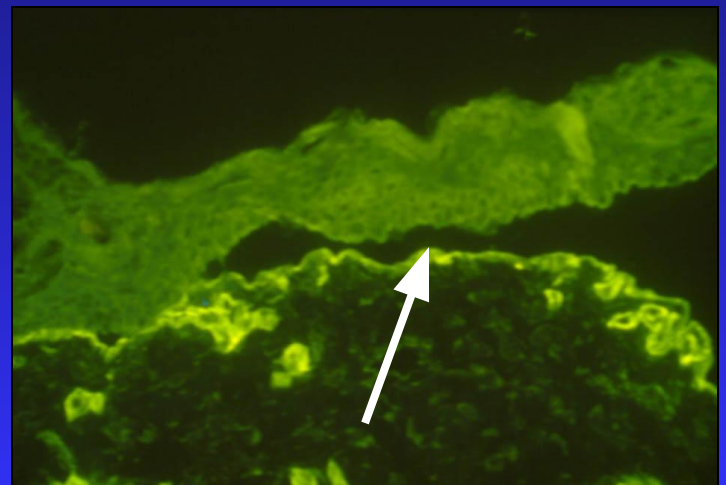


Opacification and blindness



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

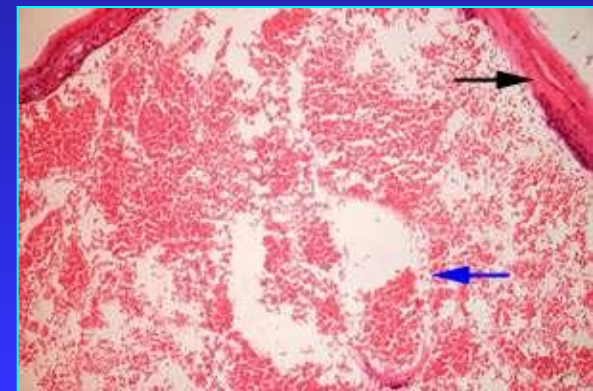
- ◆ Systemic steroids and / or steroid sparing immunosuppressive agents.
- ◆ Topical steroid may be used for oral lesions.

■ Mucosal pemphigoid

- ◆ Perforate the bullae if necessary
- ◆ Topical steroids: e.g.
 - ◆ Beclamethasone spray
 - ◆ Triamcinolone in orabase
- ◆ Antiseptic mouth wash.
- ◆ Multidisciplinary management e.g. ophthalmologist, dermatologist and internist 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

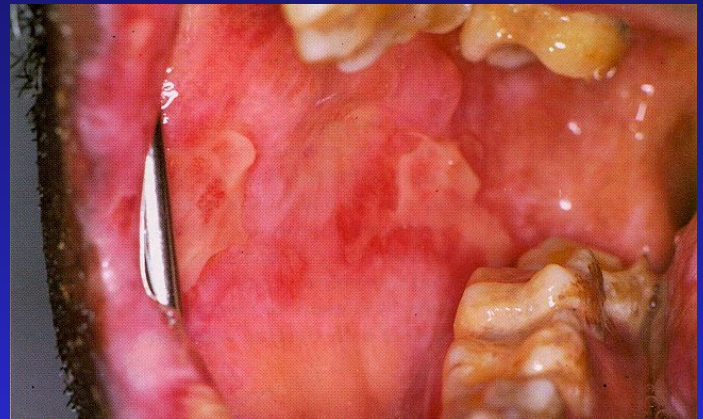


EM



General features:

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

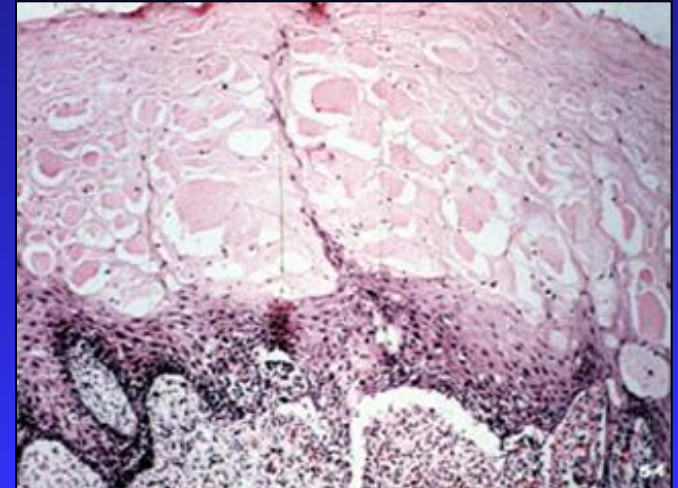




EM

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

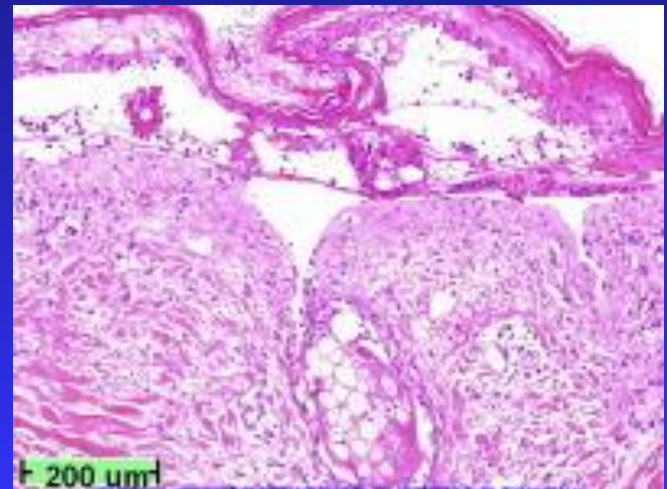
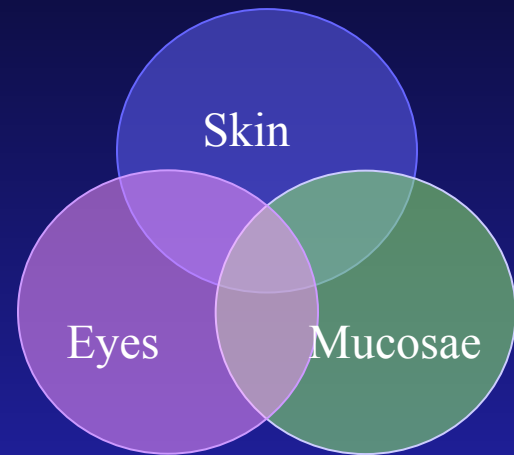
Treatment - Management

- ◆ 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 scarring
 - ◆ **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

