

# Mucocutaneous Diseases

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# Terms used to describe skin / oral lesions

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



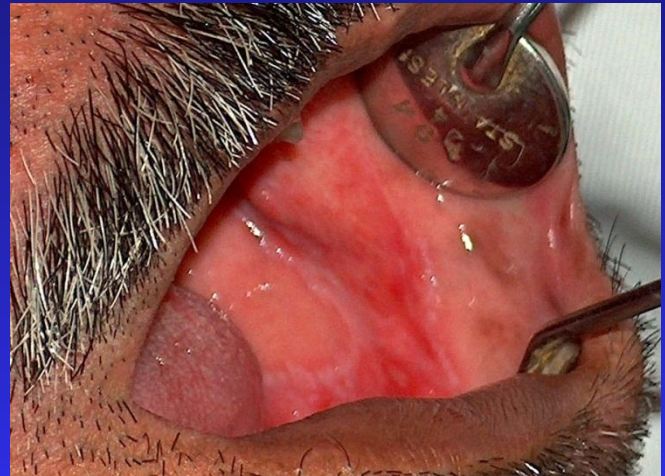
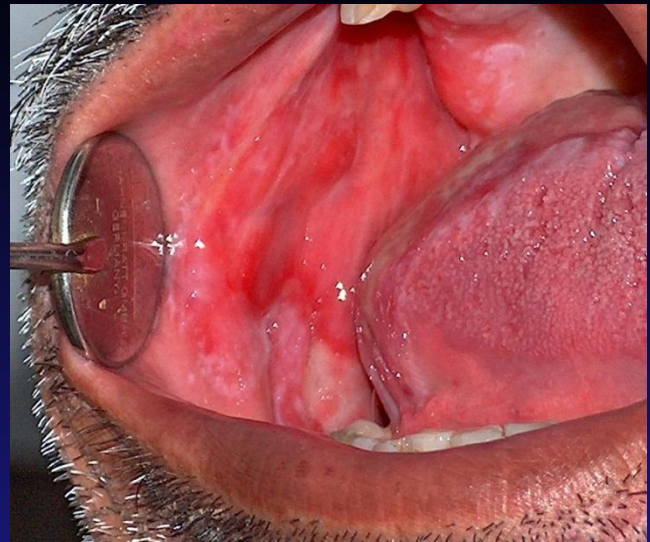
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## **Erosive LP.**

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





Non-erosive LP.  
Plaque type

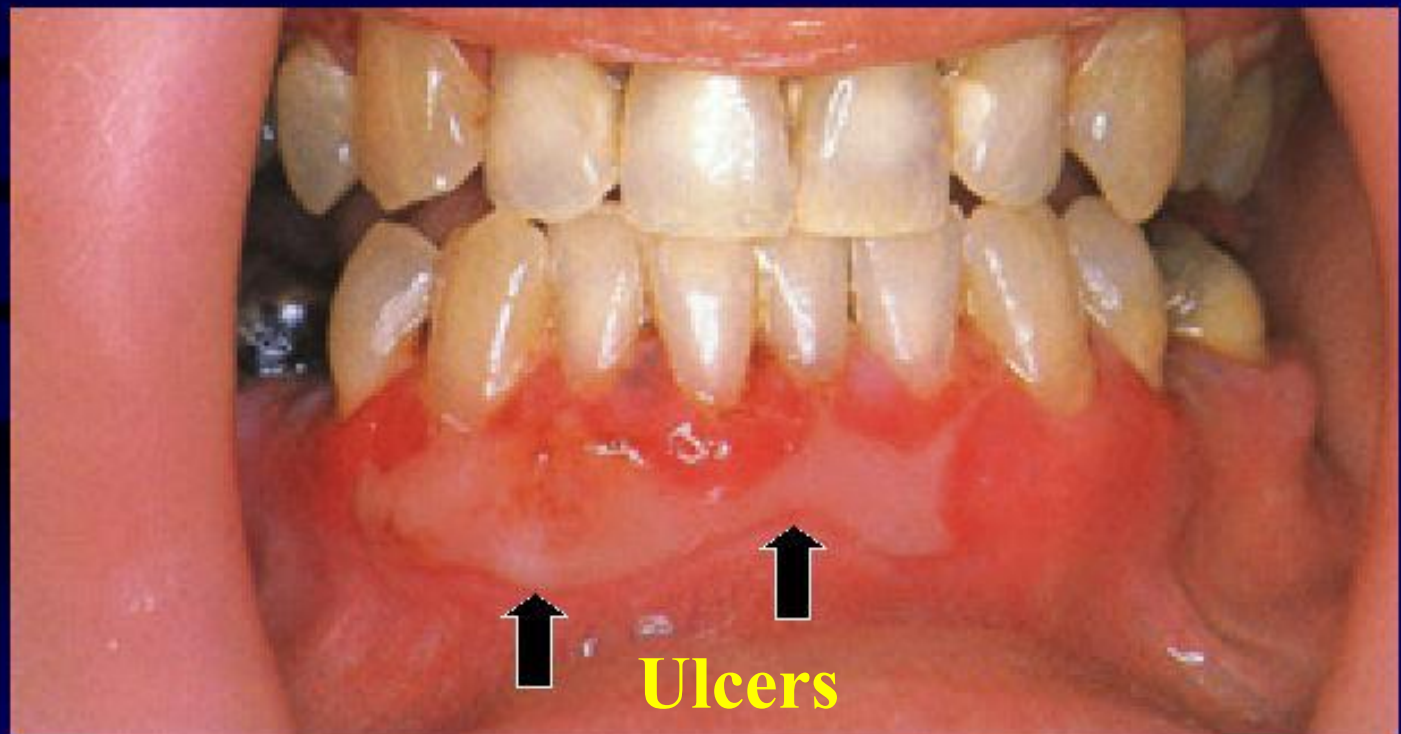




Desquamative gingivitis on attached gingiva

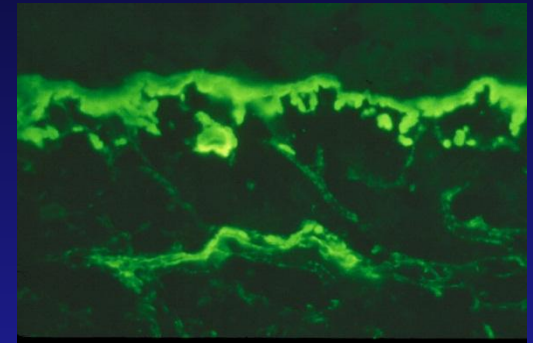
*Is a clinical rather than a pathological entity*

## Desquamative Gingivitis in CP

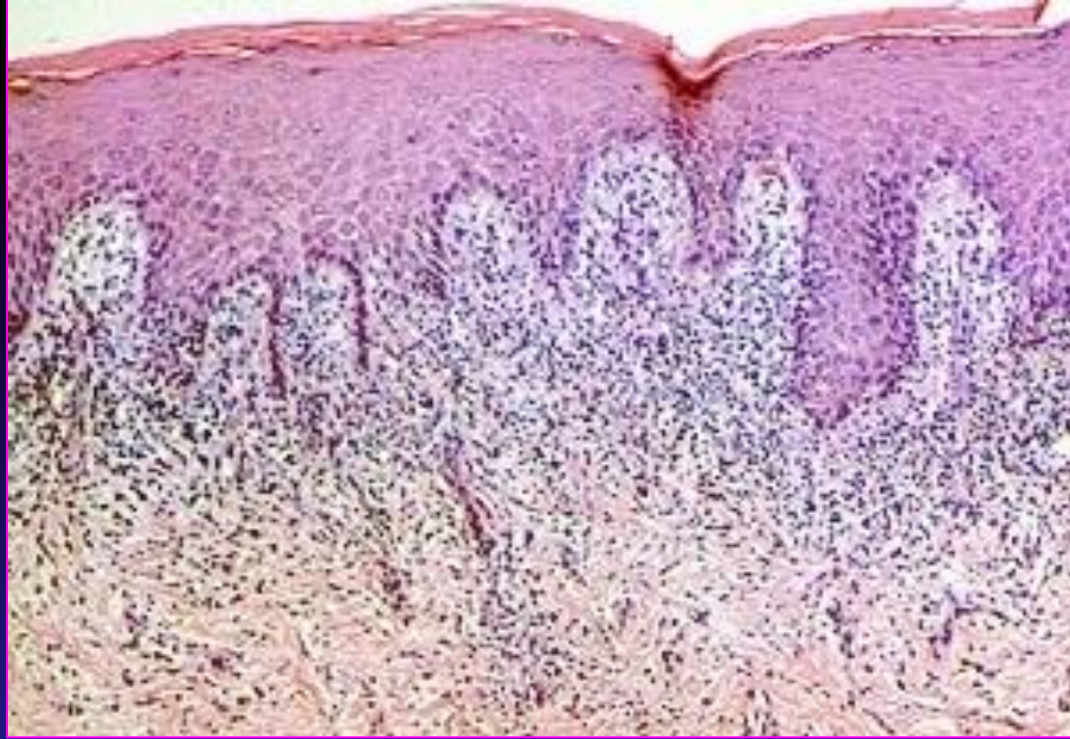


# Oral Lichen Planus

- **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.

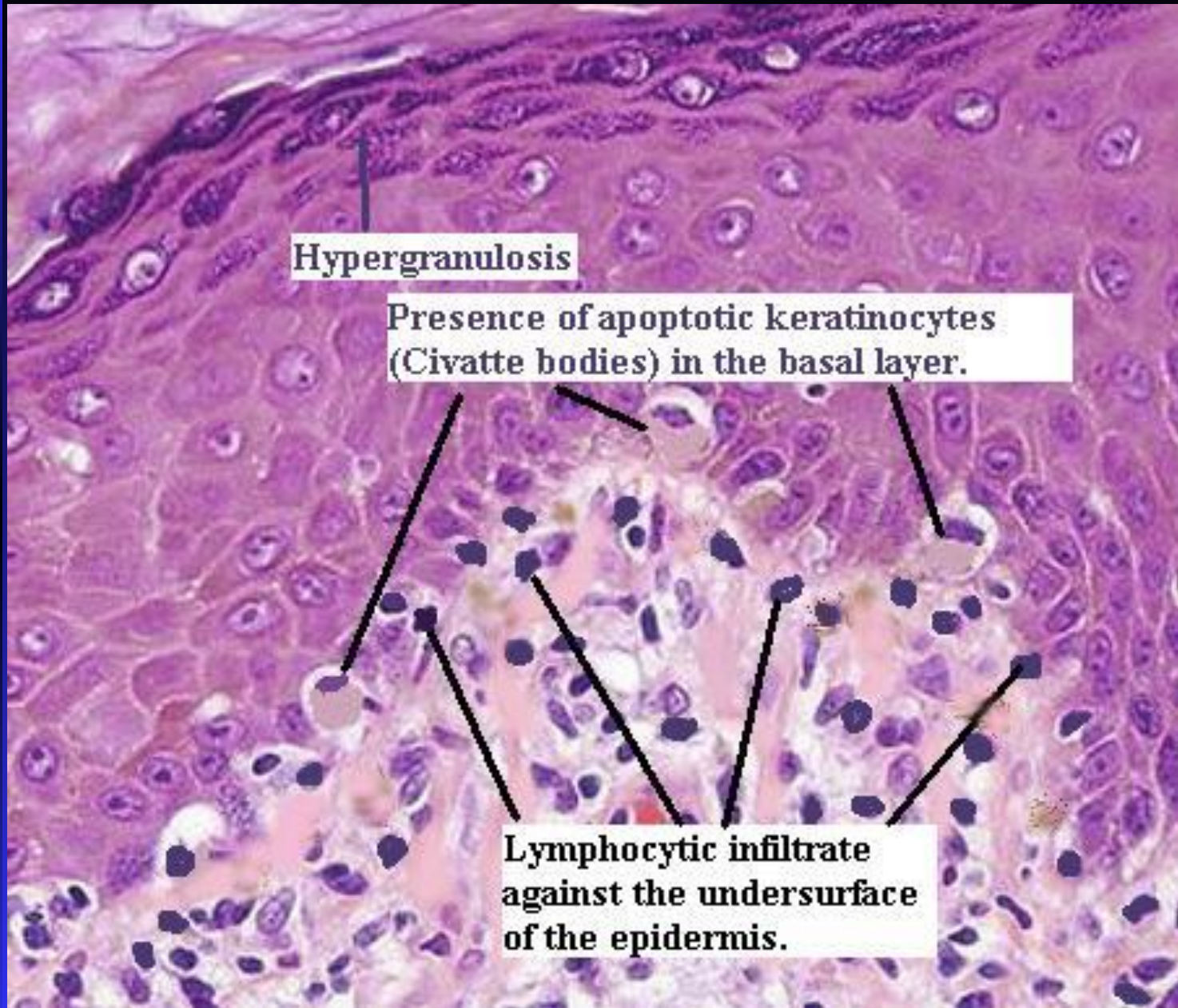


*Fibrinogen at BMZ  
(non-specific)*



## 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

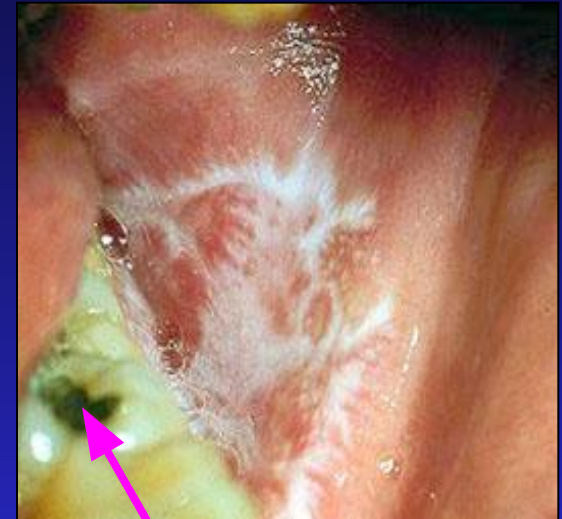
- **The expression or unmasking of the lichen planus antigen may be induced by:**
  - ◆ Drugs (lichenoid drug reaction)
  - ◆ Contact allergens in dental restorative materials or toothpastes (contact hypersensitivity reaction)
  - ◆ Mechanical trauma (Koebner phenomenon)
  - ◆ Viral infection
  - ◆ Other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

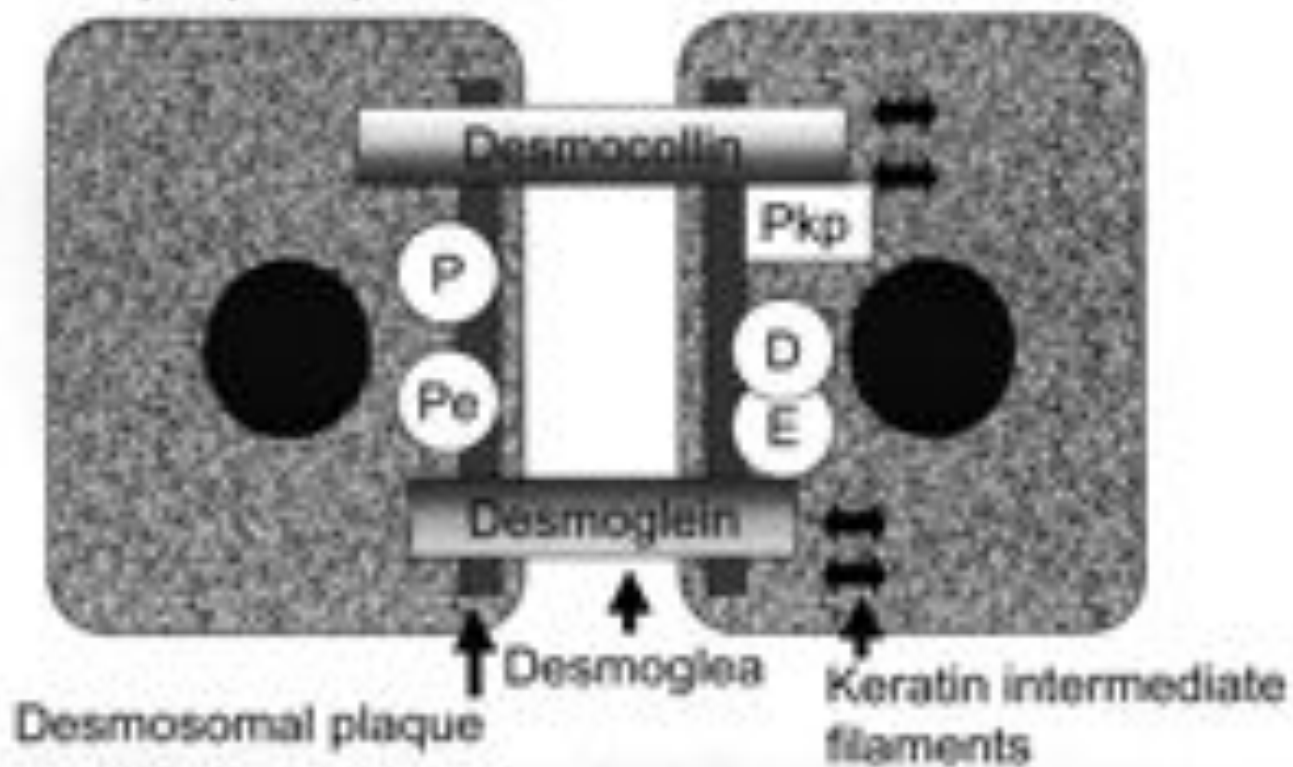


# Pemphigus

- 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

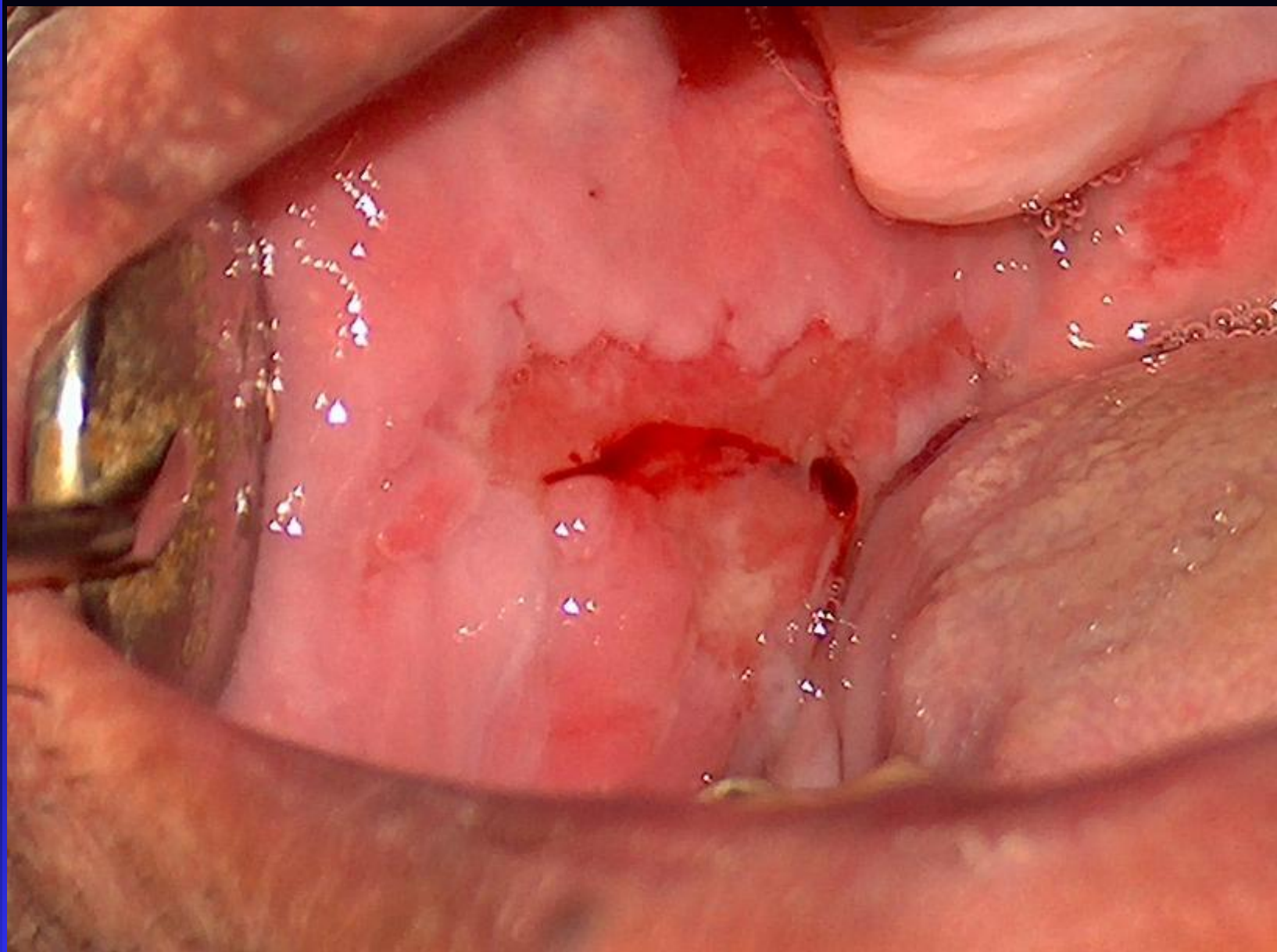
- Widespread fragile, clear fluid-filled, bullae affecting skin and mucosae
- Large irregular ulcerations
- Positive Nikolski sign.

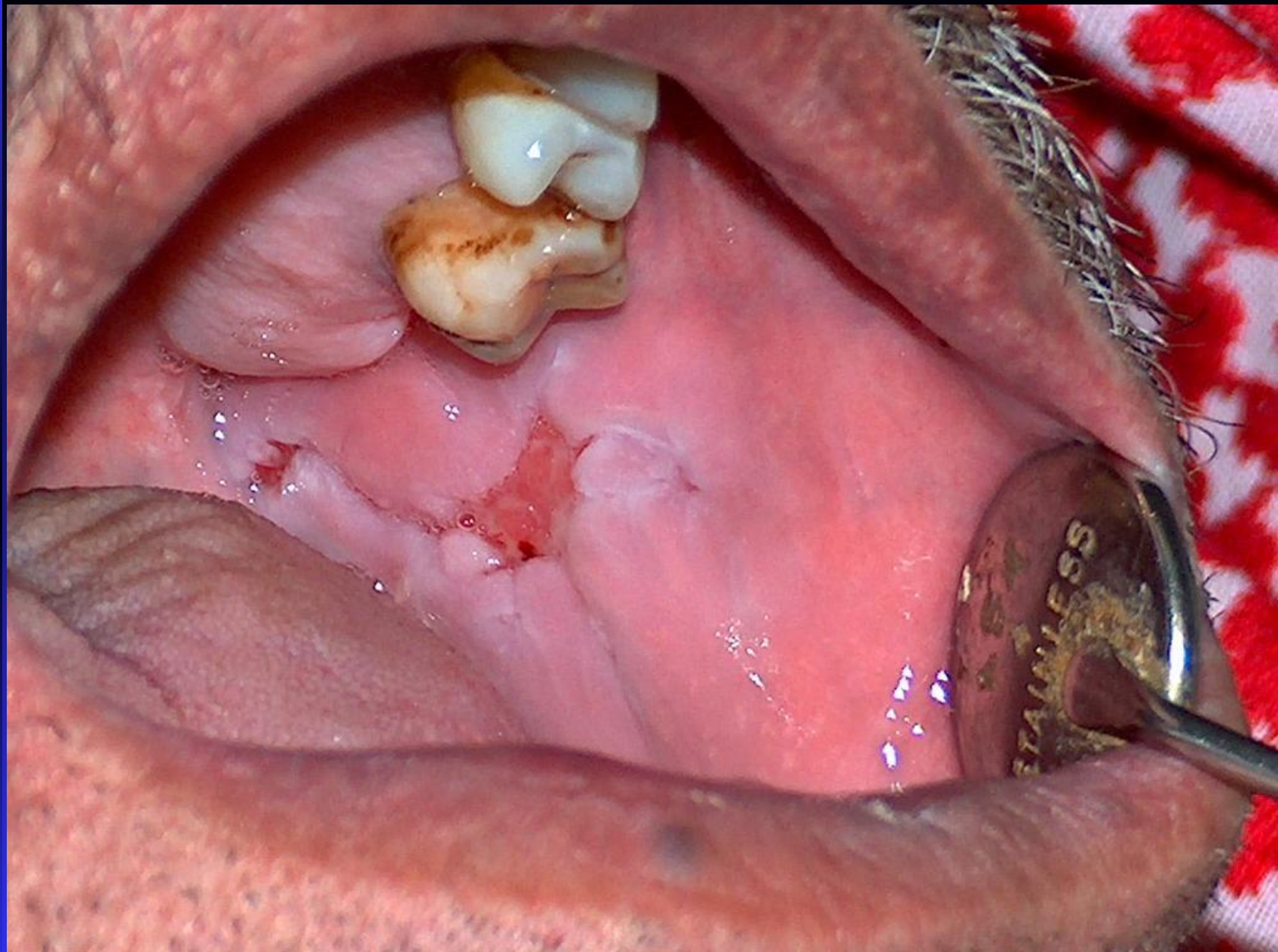


# Pemphigus

- 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



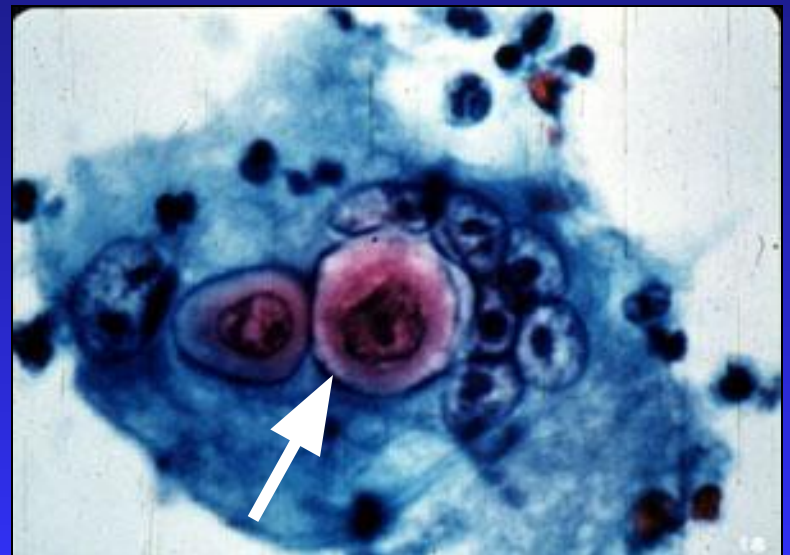
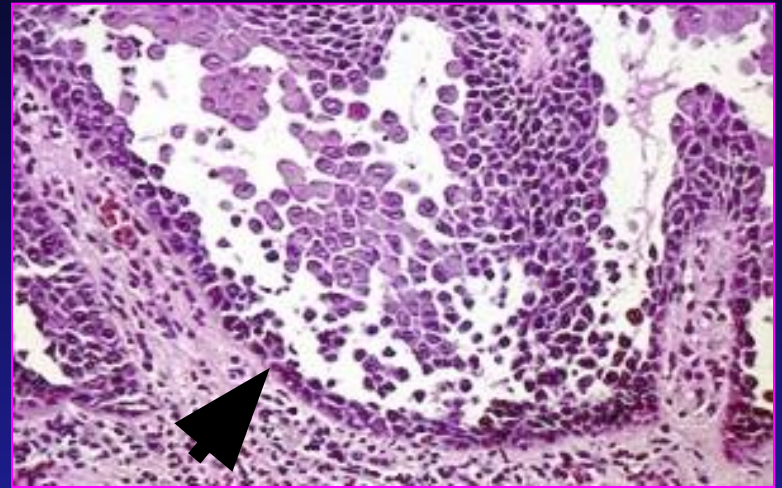






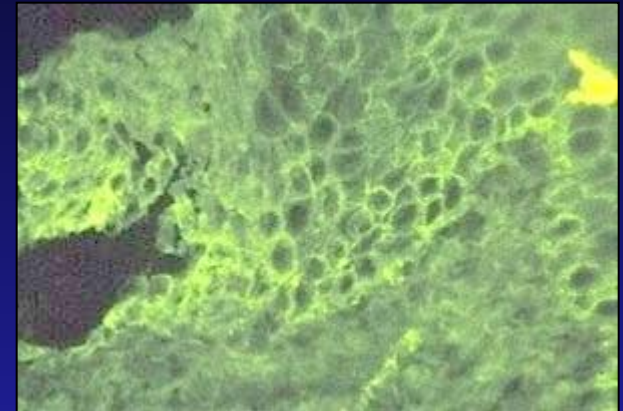
# Pemphigus - Diagnosis

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

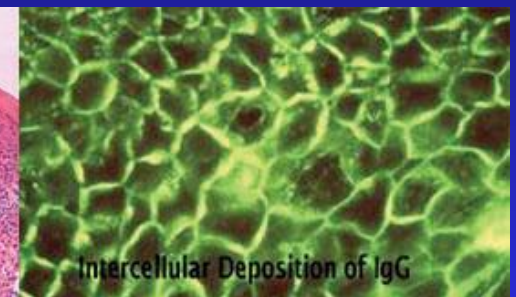
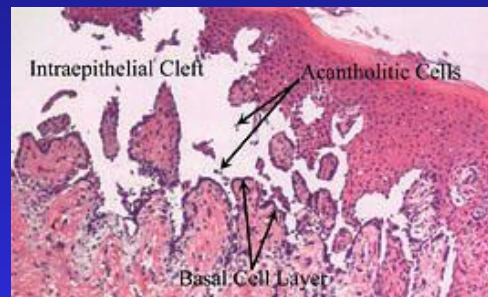


# Pemphigus - Diagnosis

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

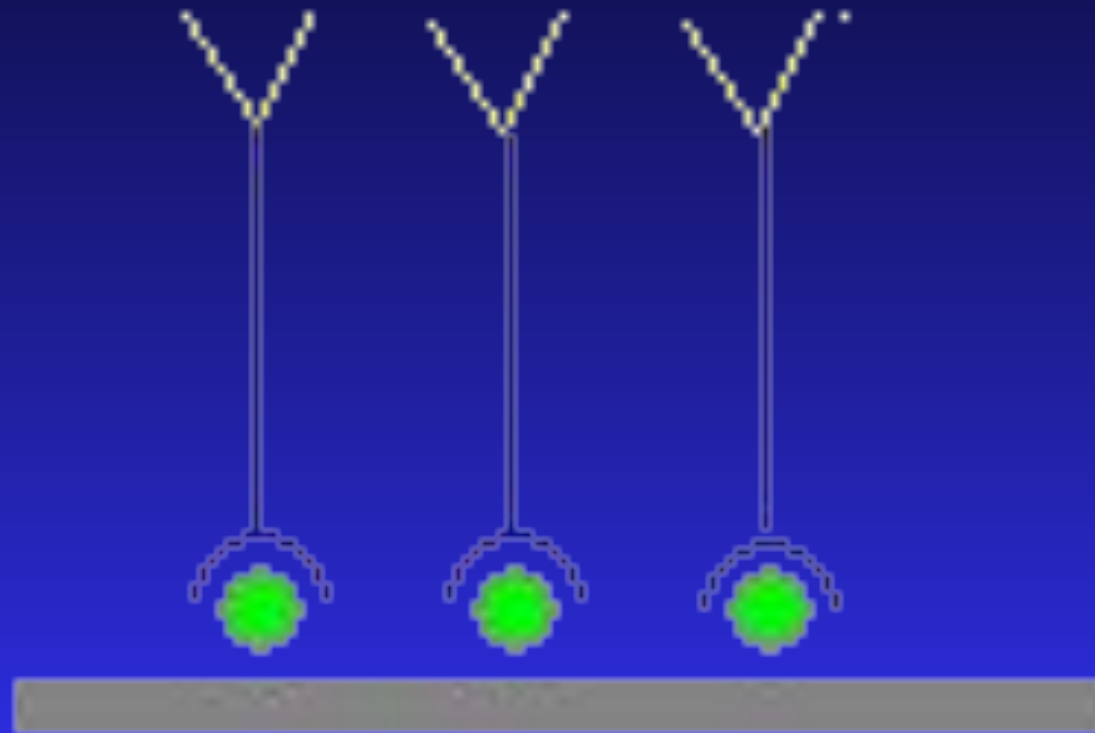


- **IIF** (correlate with the severity of the disease): +ve IgG auto-antibodies in 90% of patients



- **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

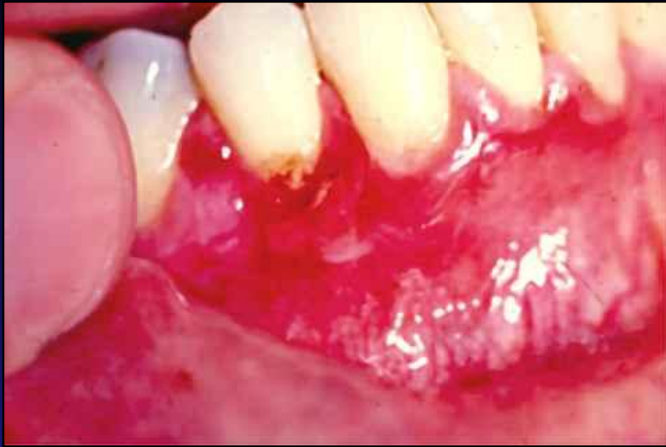


# Mucosal (cicatricial) pemphigoid

- 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

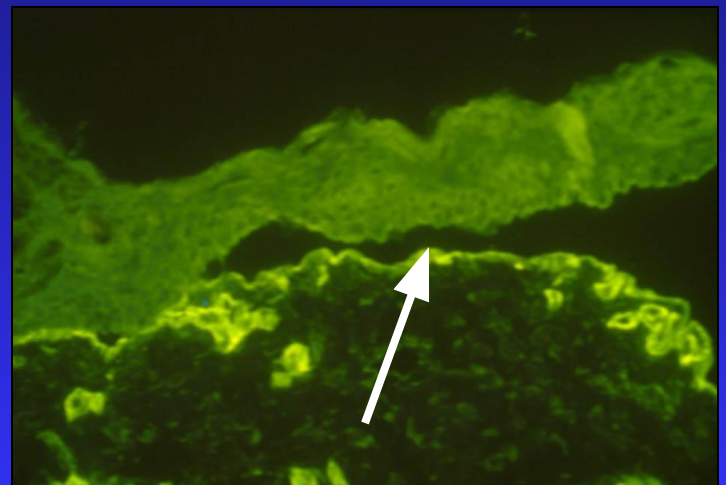


Opacification and blindness



# 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

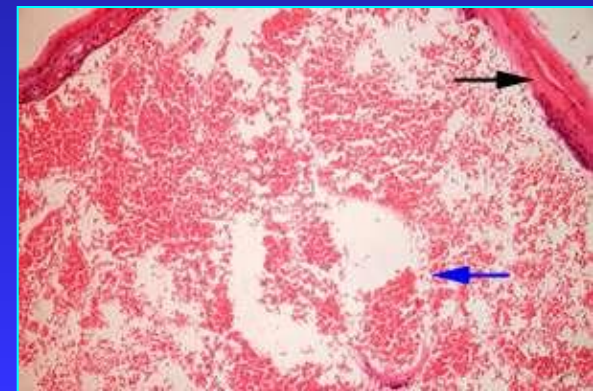
- ◆ Systemic steroids and / or steroid sparing immunosuppressive agents.
- ◆ Topical steroid may be used for oral lesions.

## ■ 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

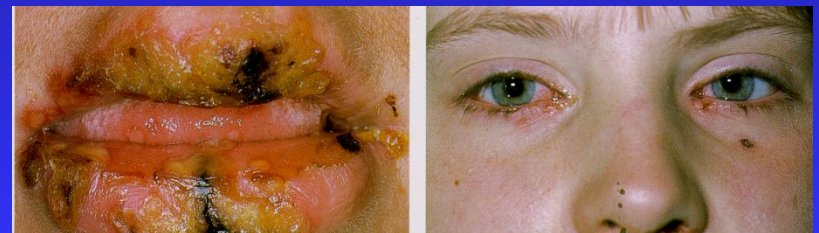


# EM



## General features:

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

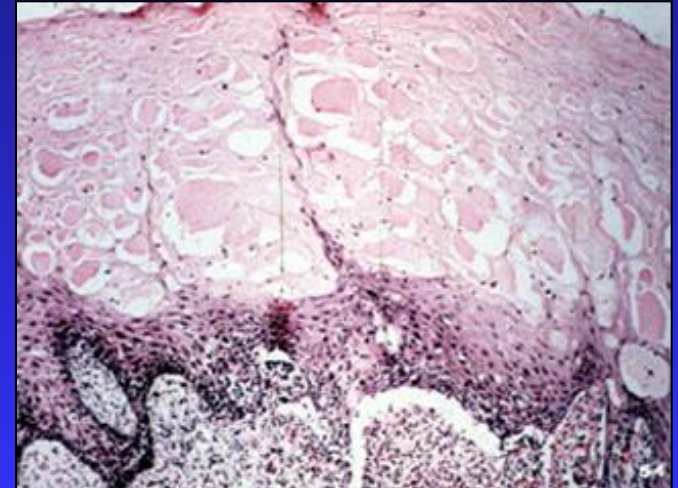




# EM

## 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

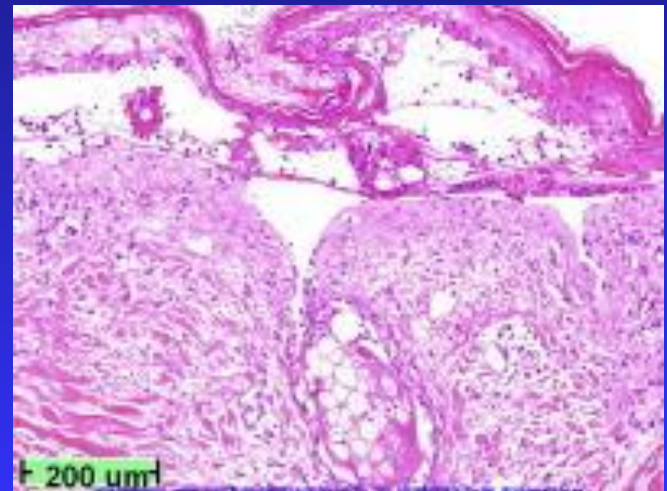
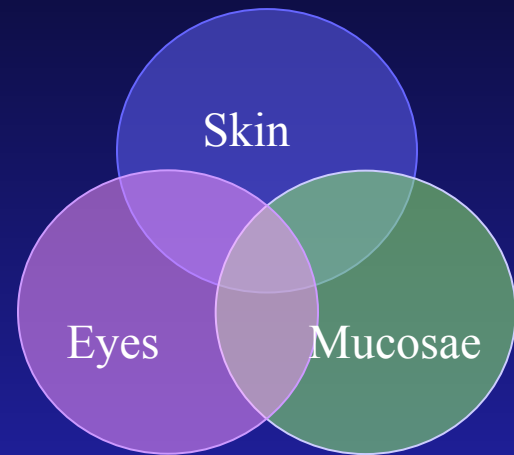
- ◆ Remove the cause if possible
  - ◆ Treat infections
  - ◆ Fluid intake and soft diet; possibly IV line is needed
  - ◆ Oral antihistamines
  - ◆ Antiseptic mouth wash
  - ◆ Topical steroids
  - ◆ ?? Systemic steroids
  - ◆ Acyclovir as a prophylaxis
- Consultations:
    - ◆ Dermatologist
    - ◆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

