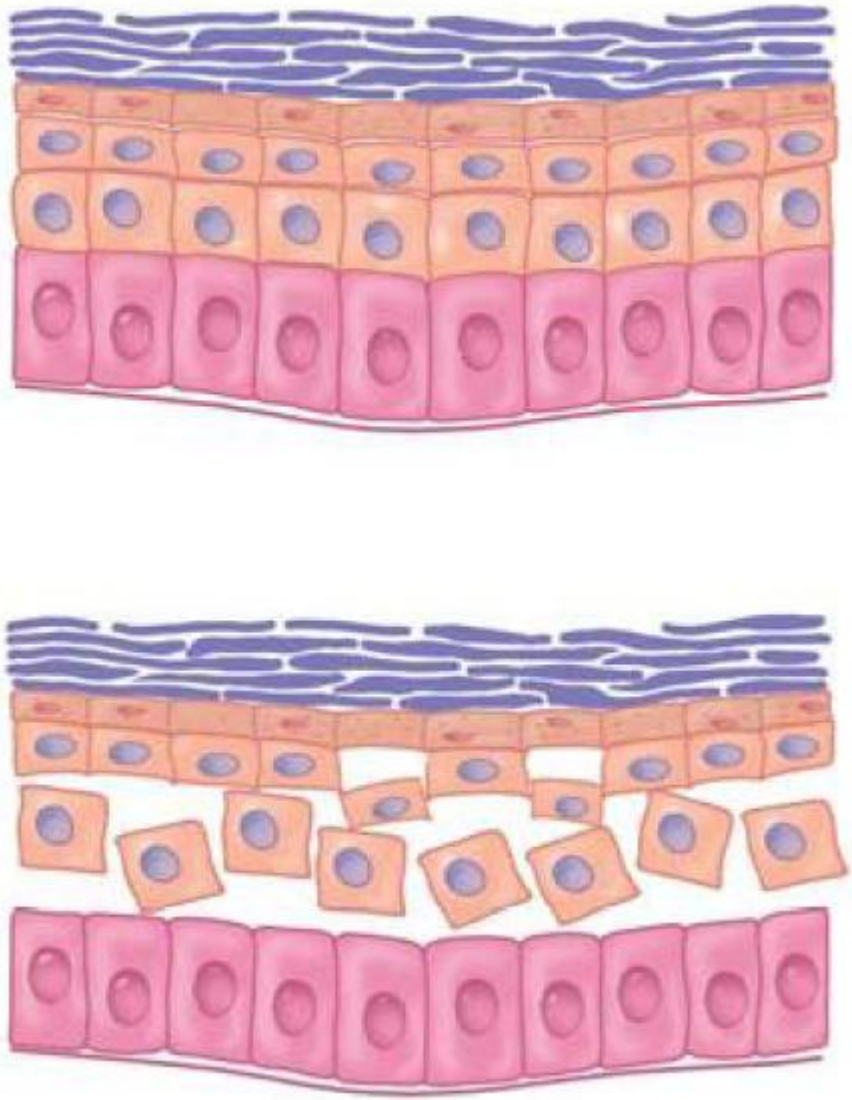
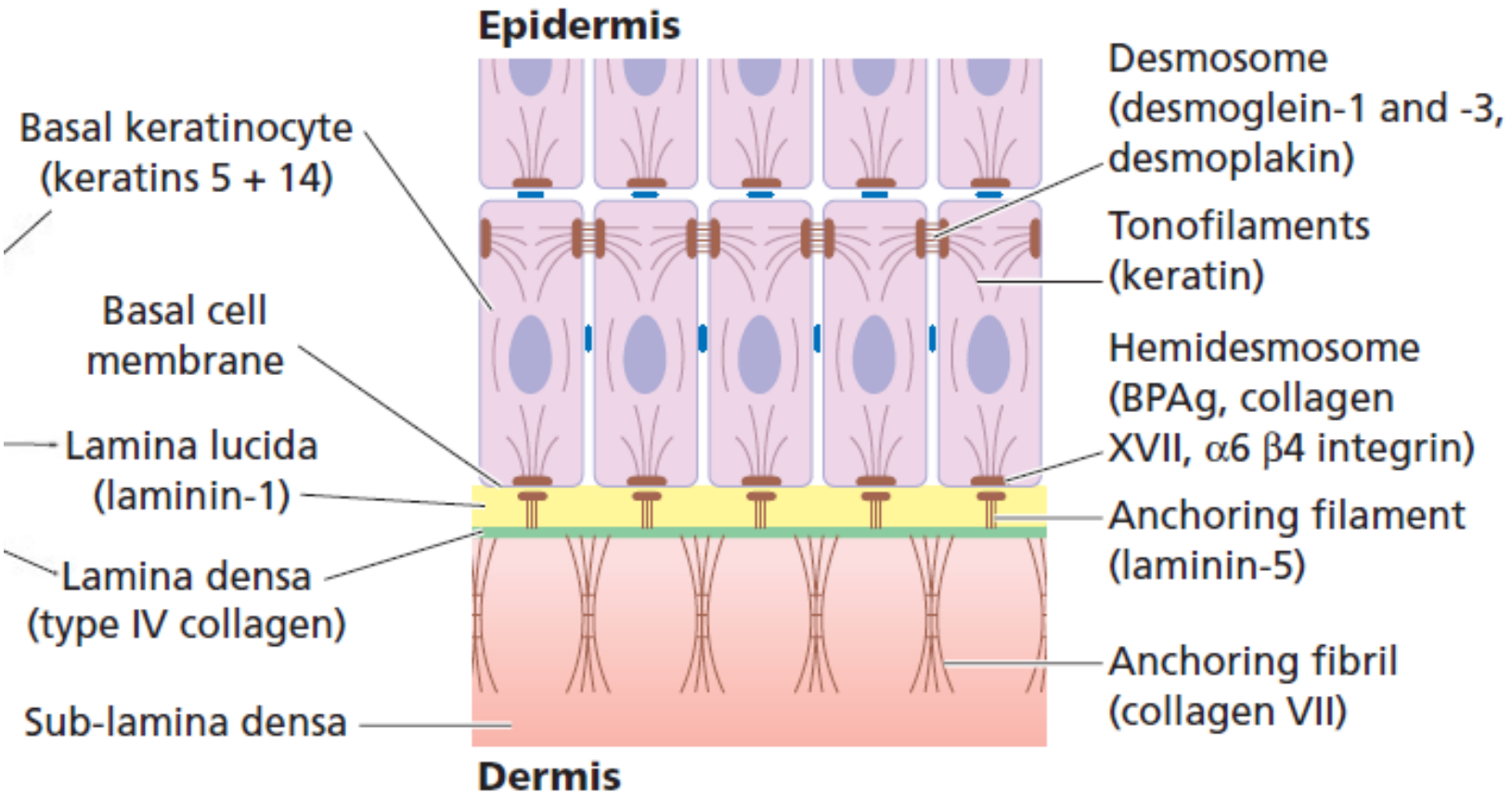
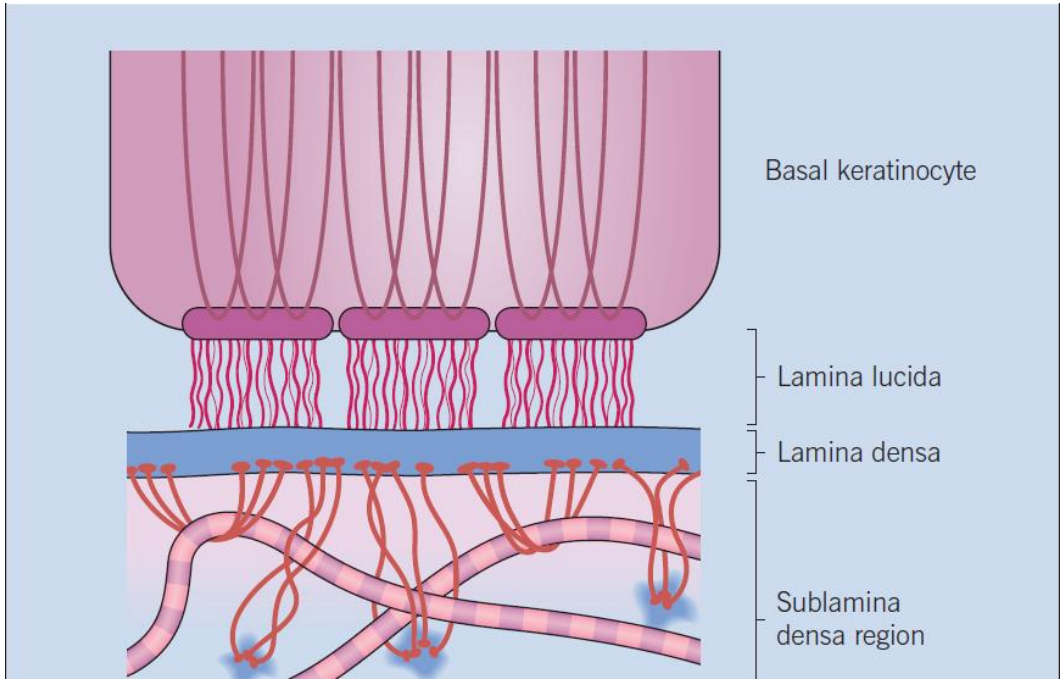
Blistering Diseases

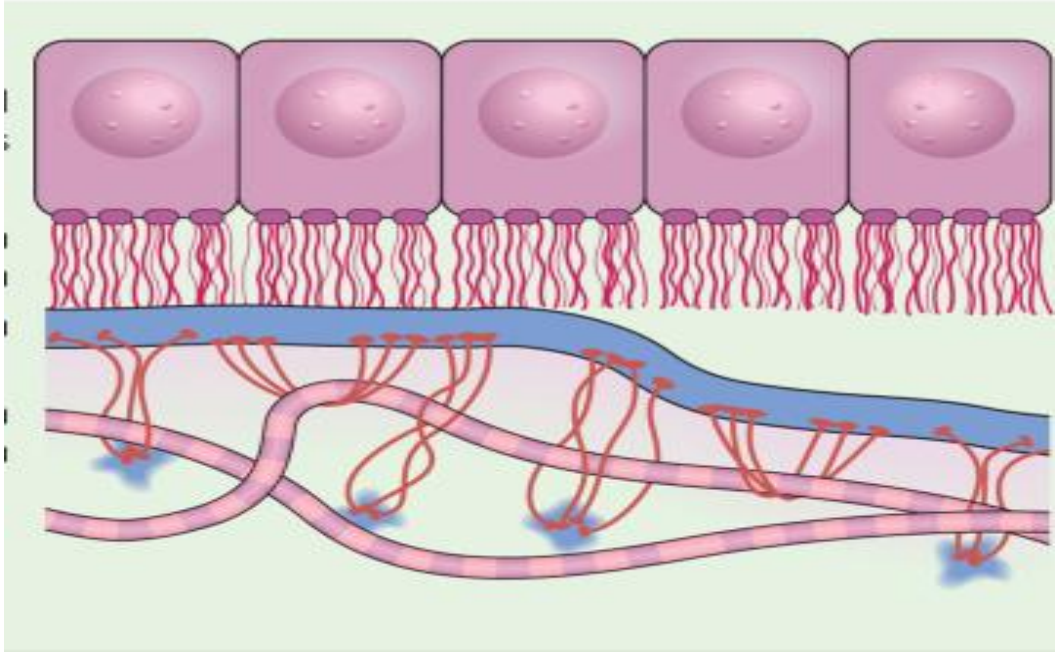
Skin

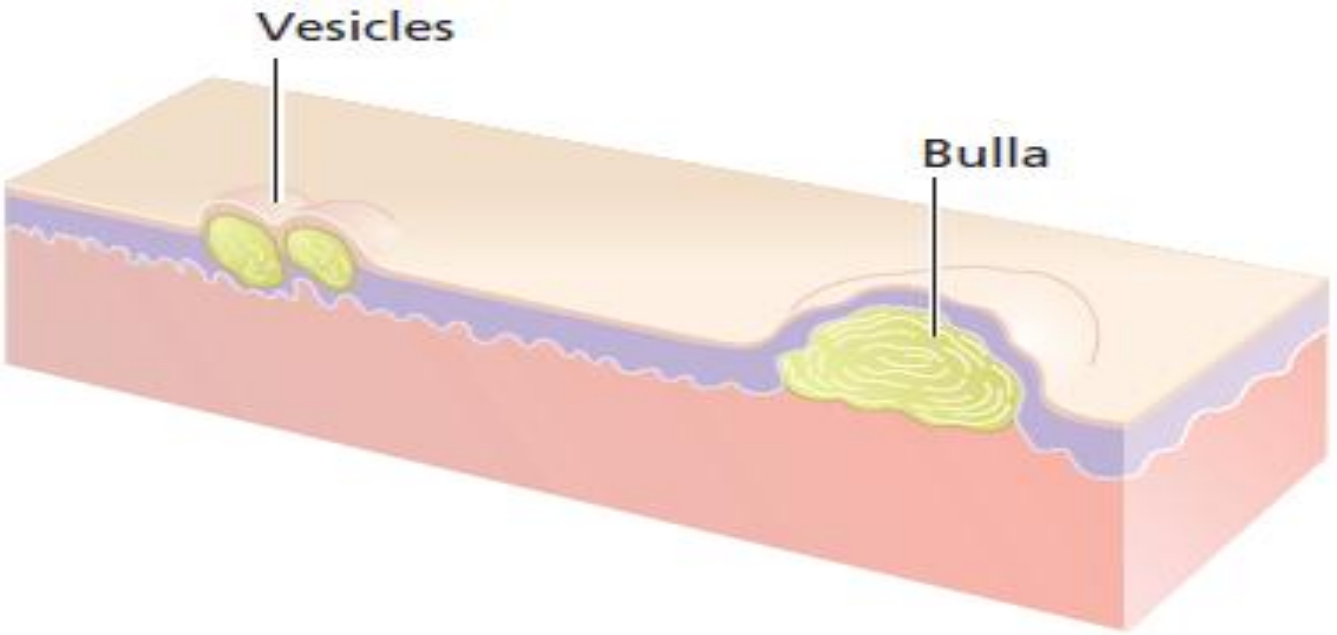




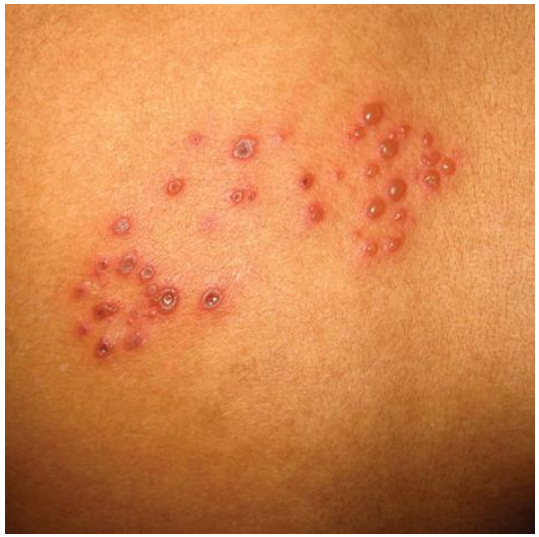
Dermo-edidermal junction

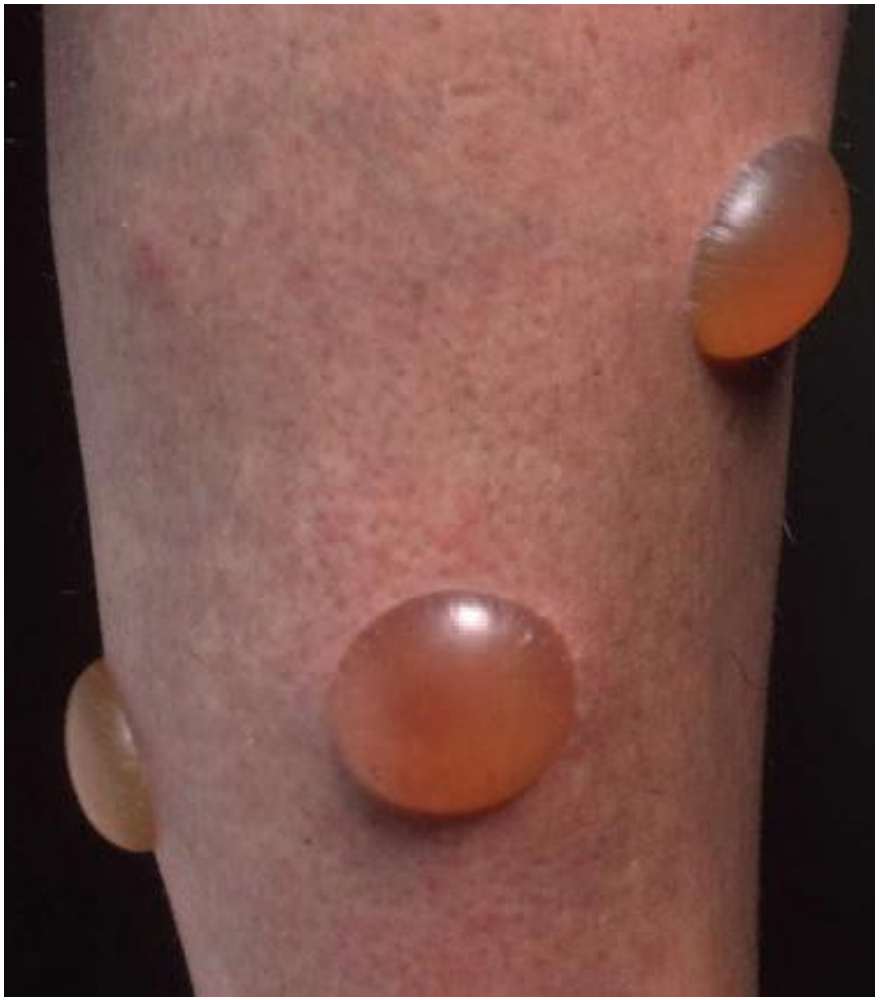

Basal keratinocyte
Lamina lucida
Lamina densa
Sublamina
densa region

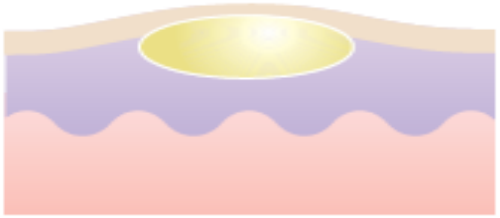
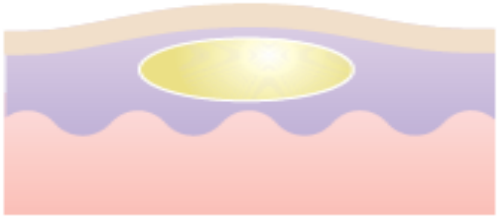
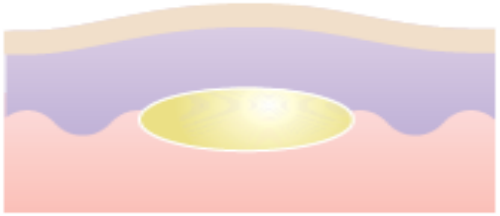




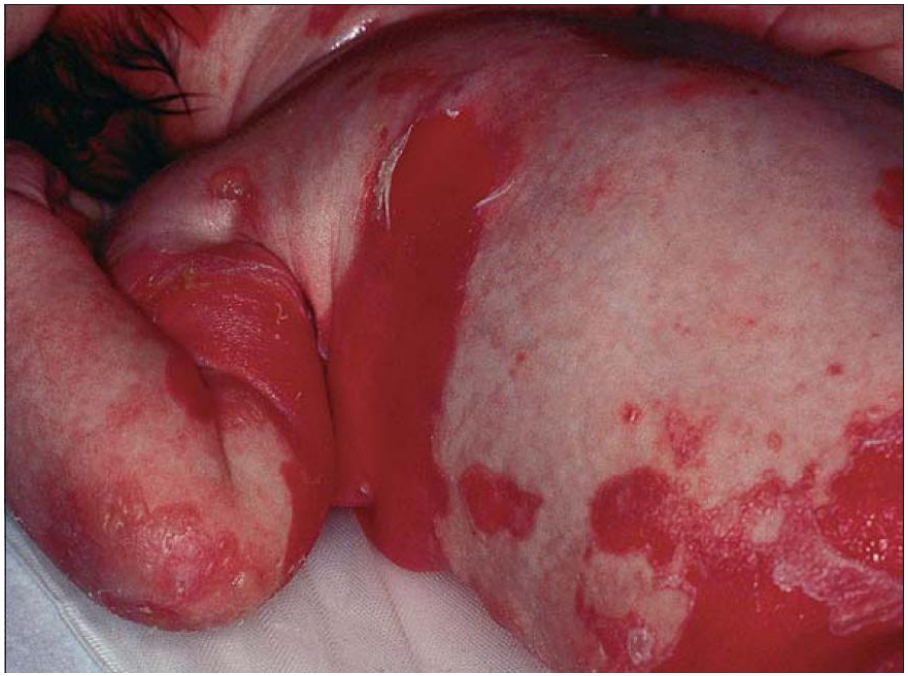
- Vesicles and bullae are raised lesions that contain fluid.
- A vesicle is less than 0.5 cm in diameter.
- A bulla is larger than 0.5 cm in diameter.

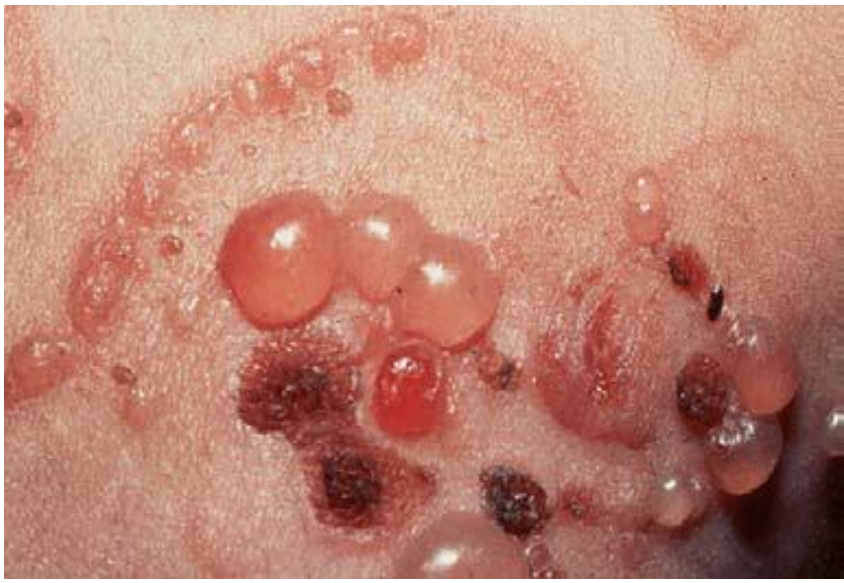




Location of bullae	Diseases
 Subcorneal bulla	Bullous impetigo Miliaria crystallina Staphylococcal scalded skin syndrome
 Intra-epidermal bulla	Acute eczema Viral vesicles Pemphigus Miliaria rubra Incontinentia pigmenti
 Subepidermal bulla	Bullous pemphigoid Cicatricial pemphigoid Pemphigoid gestationis Dermatitis herpetiformis Linear IgA disease Bullous erythema multiforme Bullous lichen planus Bullous lupus erythematosus Porphyria cutanea tarda Toxic epidermal necrolysis Cold or thermal injury Epidermolysis bullosa

- In adults: the main group of blistering problems is associated with auto antibody formation.
- In children :genodermatoses, epidermolysis bullosa associated mainly with mechanical defects in and around the basement membrane zone.

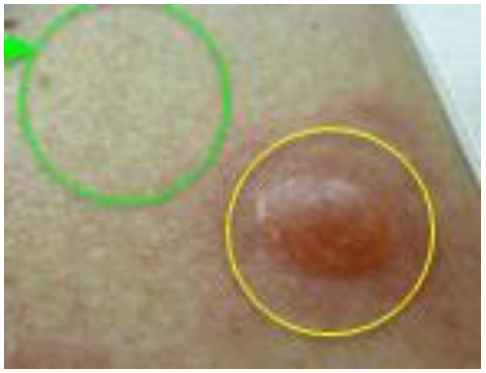




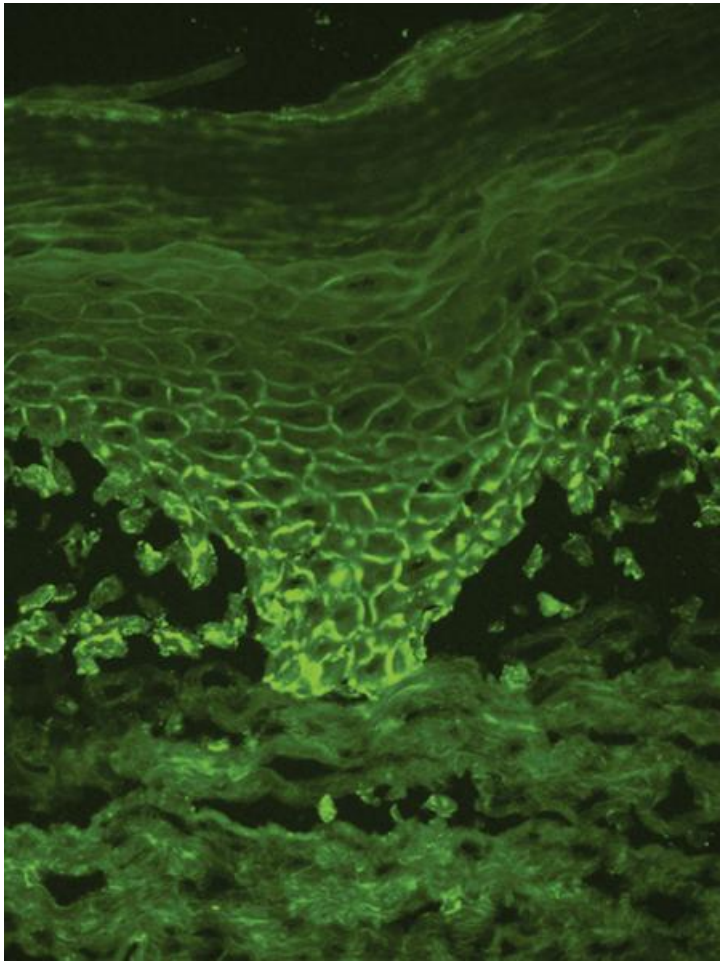
- Accurate pathological diagnosis requires a biopsy of a small newly formed lesion and of perilesional skin for immunopathological studies.
- In the case of blisters in children electron microscopy may be required.

Diagnostic tests

1. **Routine histology**
   - Lesional sample in formalin –small bulla or edge of large one.
2. **Direct immunofluorescence**
   - Perilesional sample
3. **Indirect immunofluorescence**
   - Patient's serum is added to specific substrates that express antigen of interest.
4. **Electron microscopy.**



Direct immunofluorescence

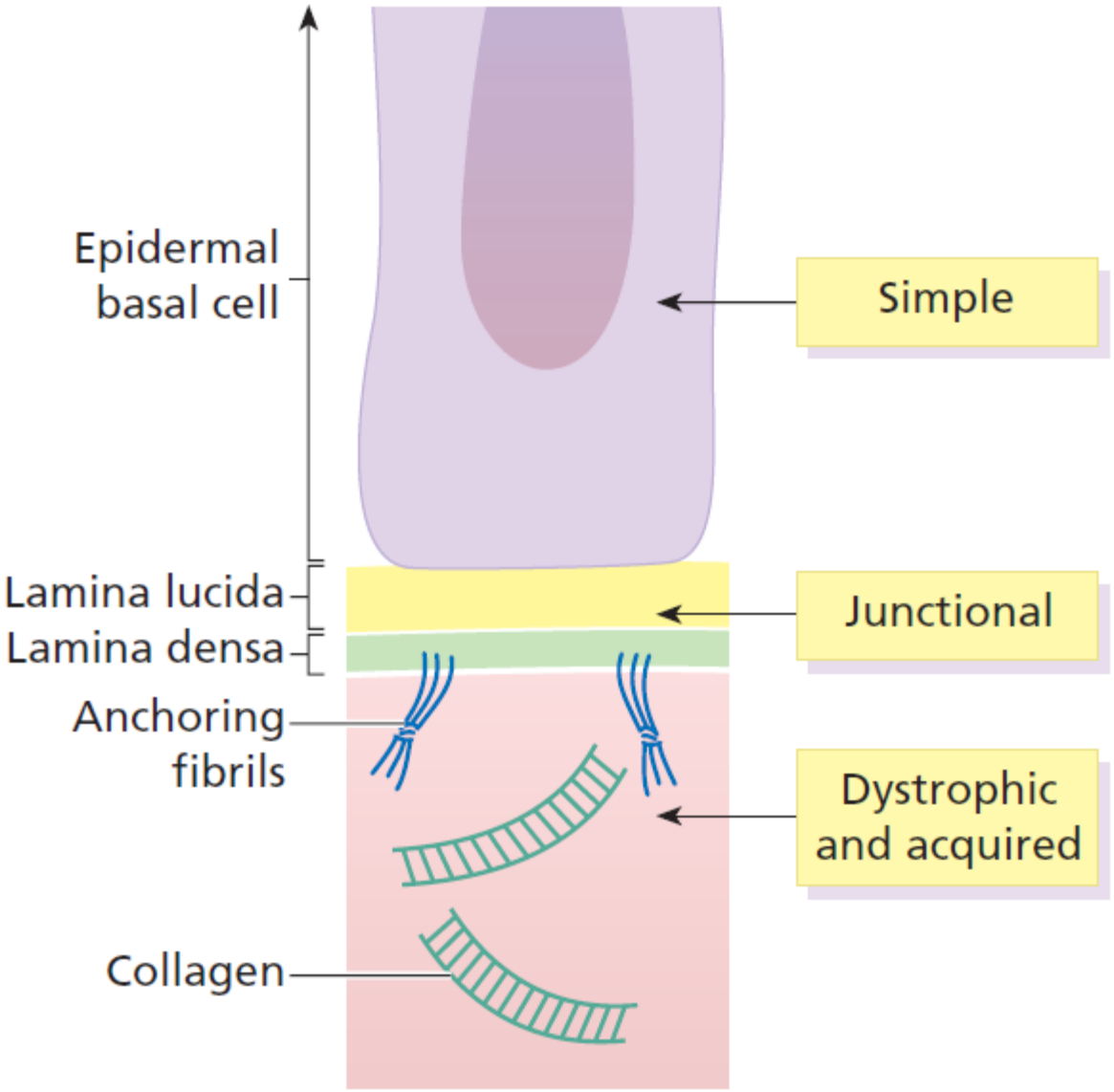


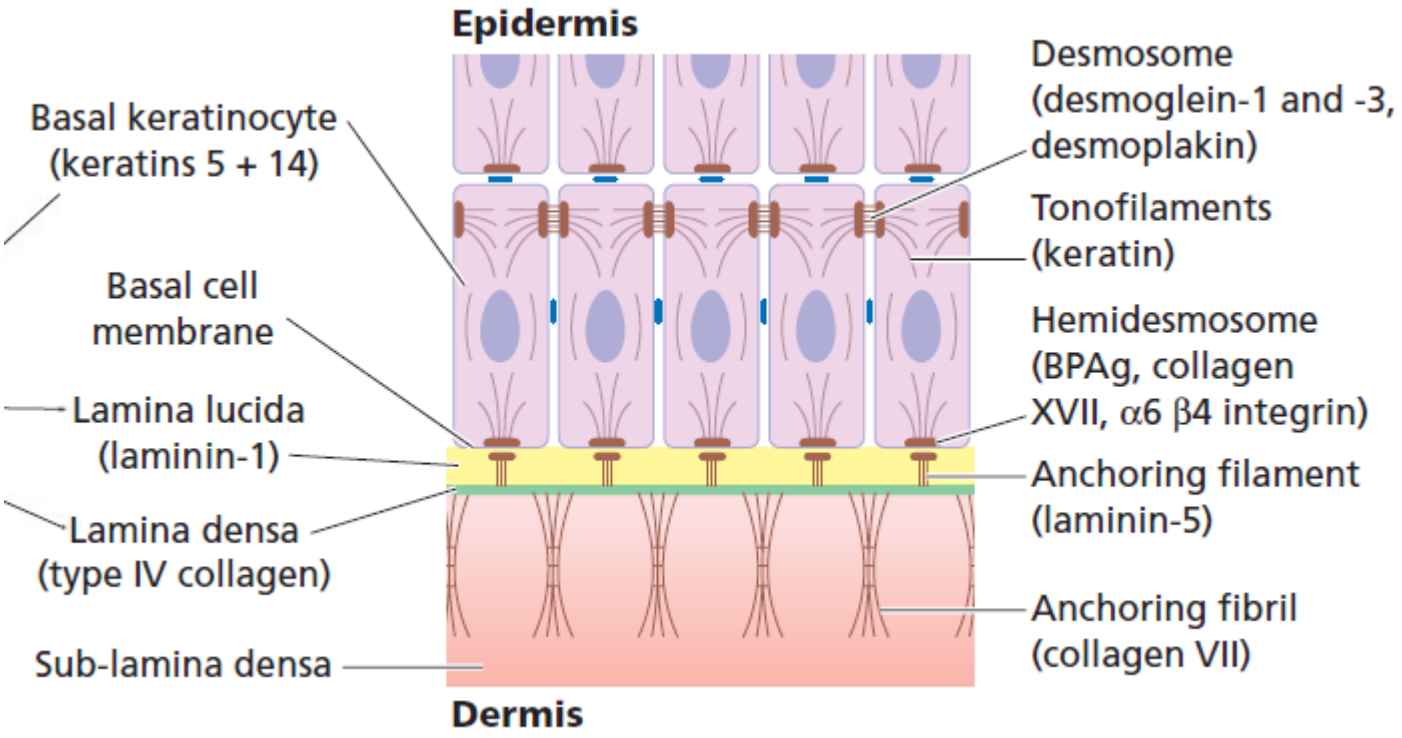
The epidermolysis bullosa group of blistering disorders

- This group of blistering genodermatoses is rare.
- mechanobullous disorders.
- usually present at birth or in infancy.
- range from localized relatively mild with trauma induced blisters to life threatening and life ruining conditions.

- diagnosis can be made on the basis of a family history, clinical examination, and light microscopic examination of a skin biopsy and the use of electron microscopy

- The main subsets are:
  - epidermolysis bullosa simplex-mainly autosomal dominant
  - junctional epidermolysis bullosa autosomal recessive .
  - dystrophic epidermolysis bullosa-both autosomal dominant, and autosomal recessive varieties.

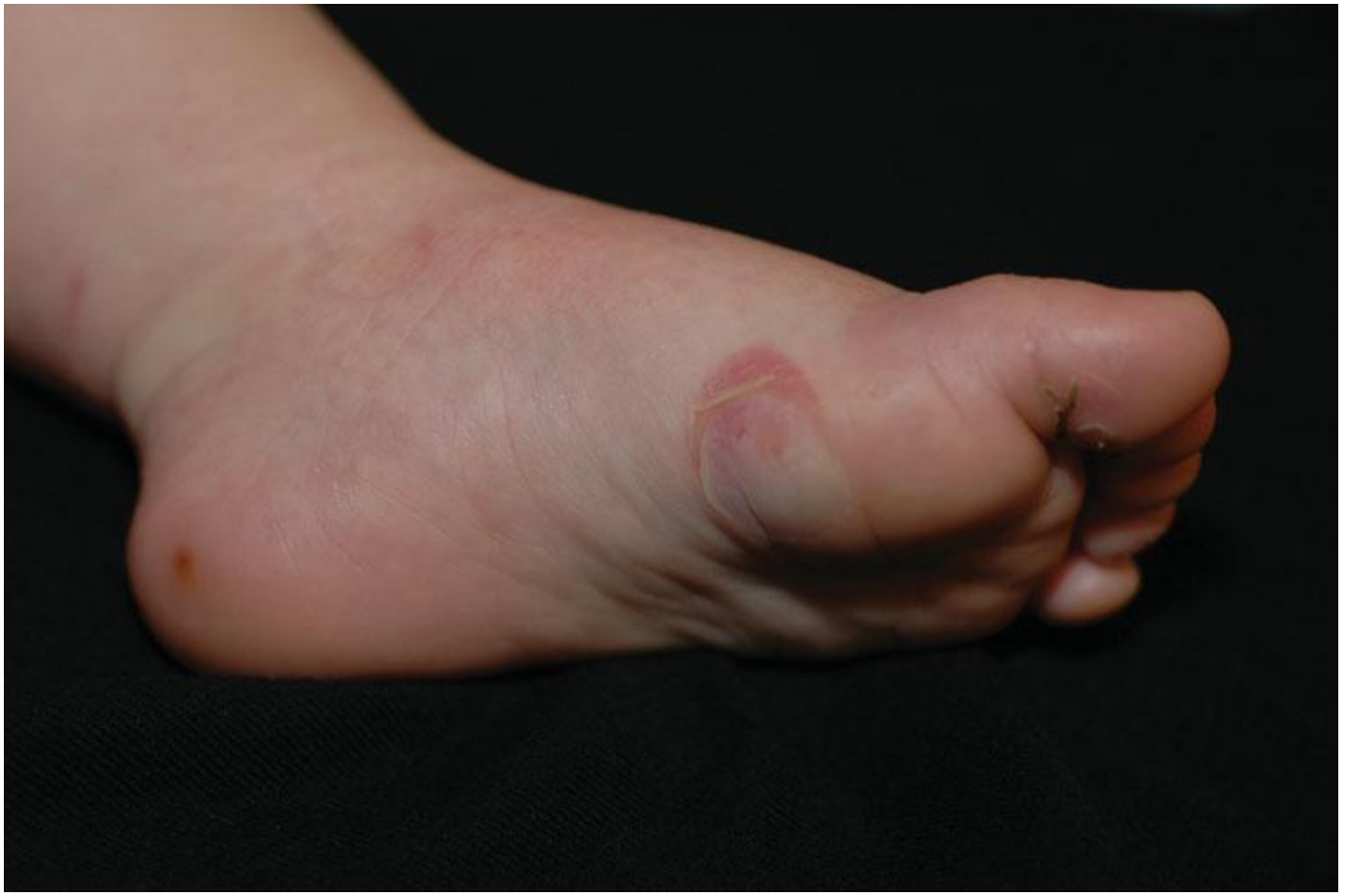

Epidermal basal cell
Lamina lucida
Lamina densa
Anchoring fibrils
Collagen
Simple
Junctional
Dystrophic and acquired


Epidermis
Basal keratinocyte (keratins 5 + 14)
Basal cell membrane
Lamina lucida (laminin-1)
Lamina densa (type IV collagen)
Sub-lamina densa
Desmosome (desmoglein-1 and -3, desmoplakin)
Tonofilaments (keratin)
Hemidesmosome (BPAg, collagen XVII, α6 β4 integrin)
Anchoring filament (laminin-5)
Anchoring fibril (collagen VII)
Dermis

Epidermolysis bullosa simplex

- Majority are autosomal dominant transmission.
- The pathological damage lies within the epidermis.
- main defect lies in defective genes coding for keratins 5 and 14 in the basal layer.

- Blisters may be present at birth, or when the child starts to walk or crawl, and develops mild blistering on knees, hands, feet, and other sires of friction
- These blisters quickly rupture and heal with no scarring.

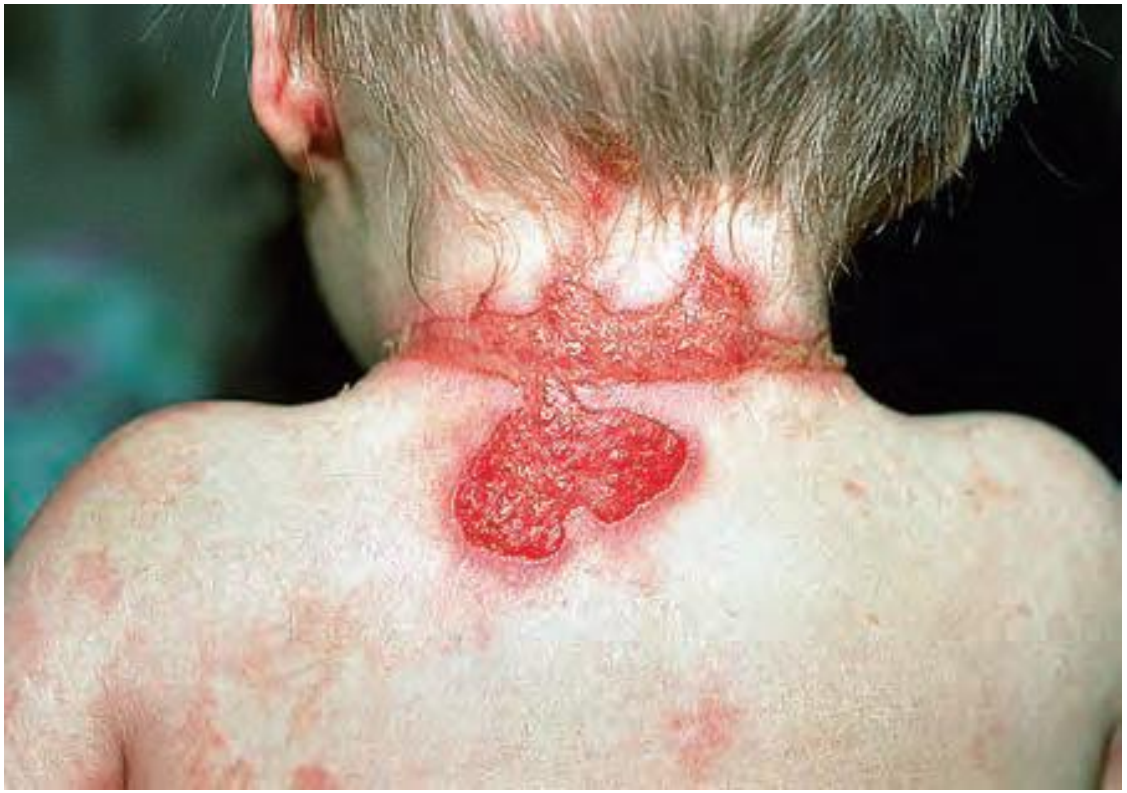


Epidermolysis bullosa simplex Localized flaccid bullae on the foot of an infant.

Junctional epidermolysis bullosa

- autosomal recessive transmission.
- The protein/gene which is abnormal, is larninin 5 in two types of junctional EB, and alpha 6 beta 4 inregrin in the third.
- Split at the level of the lamina lucida.

- Clinical features may be present at birth either as blisters, often around the nails, or raw denuded areas.
- Mucous membranes may be severely involved .
- teeth are commonly abnormal.



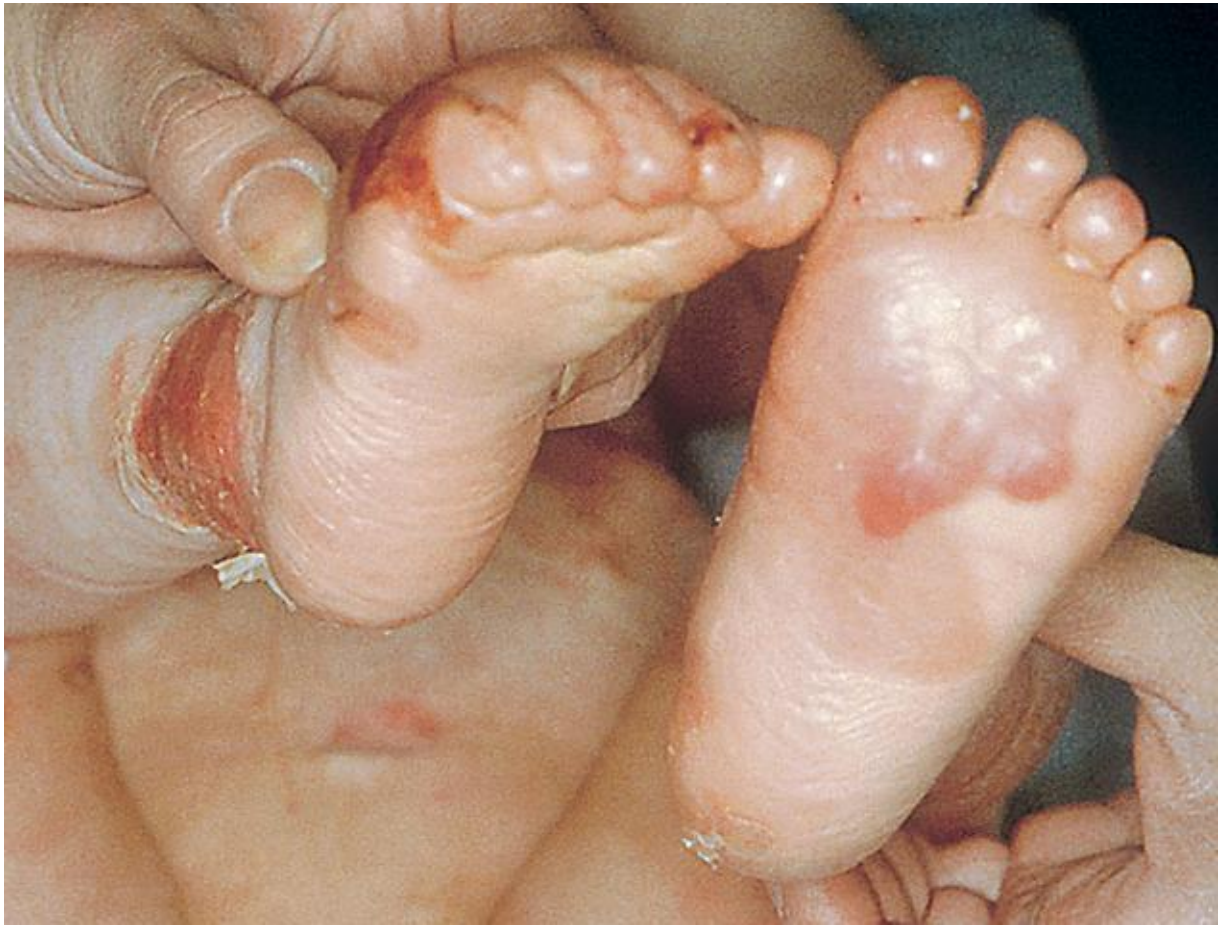
Junctional epidermolysis bullosa –
chronic nonhealing granulation tissue around the neck

Dystrophic epidermolysis bullosa

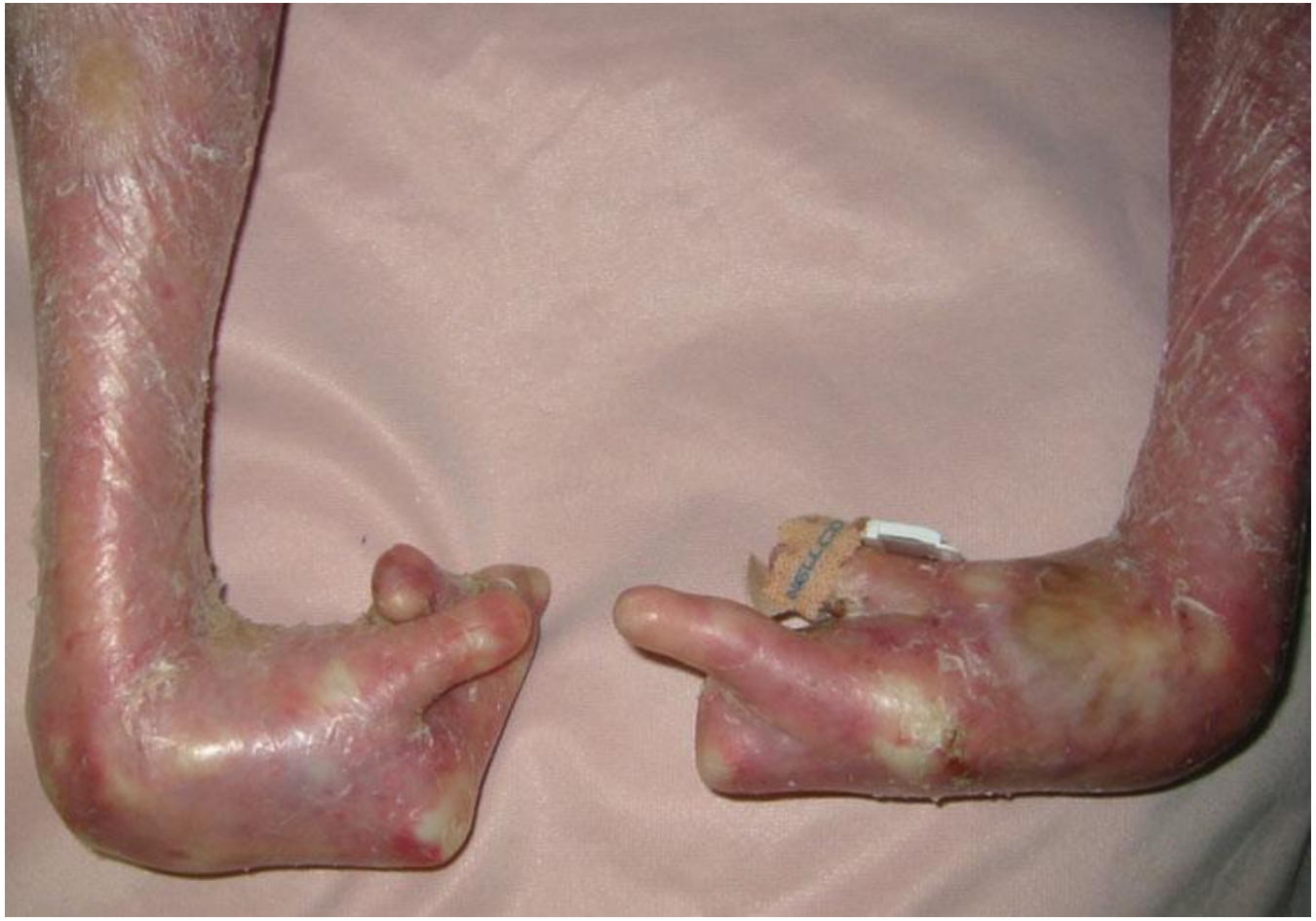
- Autosomal dominant or autosomal recessive.
- all are associated with defects in the type 7 collagen gene which causes defective anchoring fibrils.
- Squamous carcinoma may develop on the scar sites.

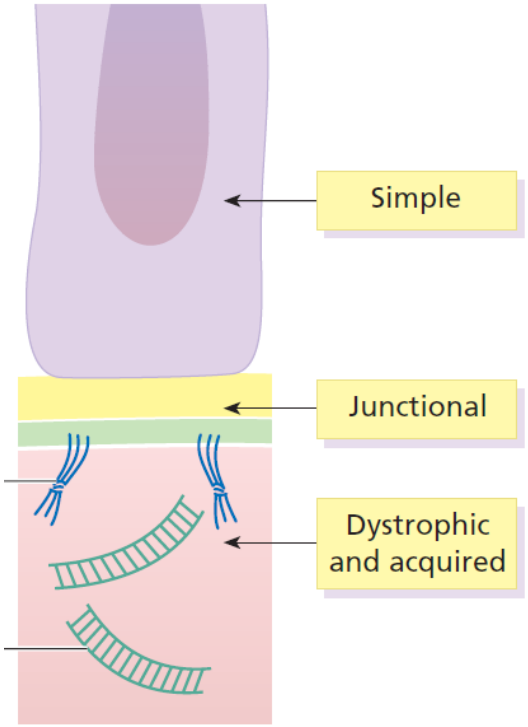
- The dominant varieties: blisters develop in later infancy or early childhood on friction sites and heal with scarring.
- Hair and teeth develop normally.

- Recessive types: Large bullae are present at birth, and they heal with scarring.
- Mucous membranes, hair, nails and teeth may be abnormal.



Recessive dystrophic epidermolysis bullosa in a newborn





Recessive dystrophic epidermolysis bullosa in a child

Treatment

- Team management.
- biopsy and ultrastructural studies.
- prevent friction bullae .
- Occupational therapy.
- dental care.
- Skilled nursing care.

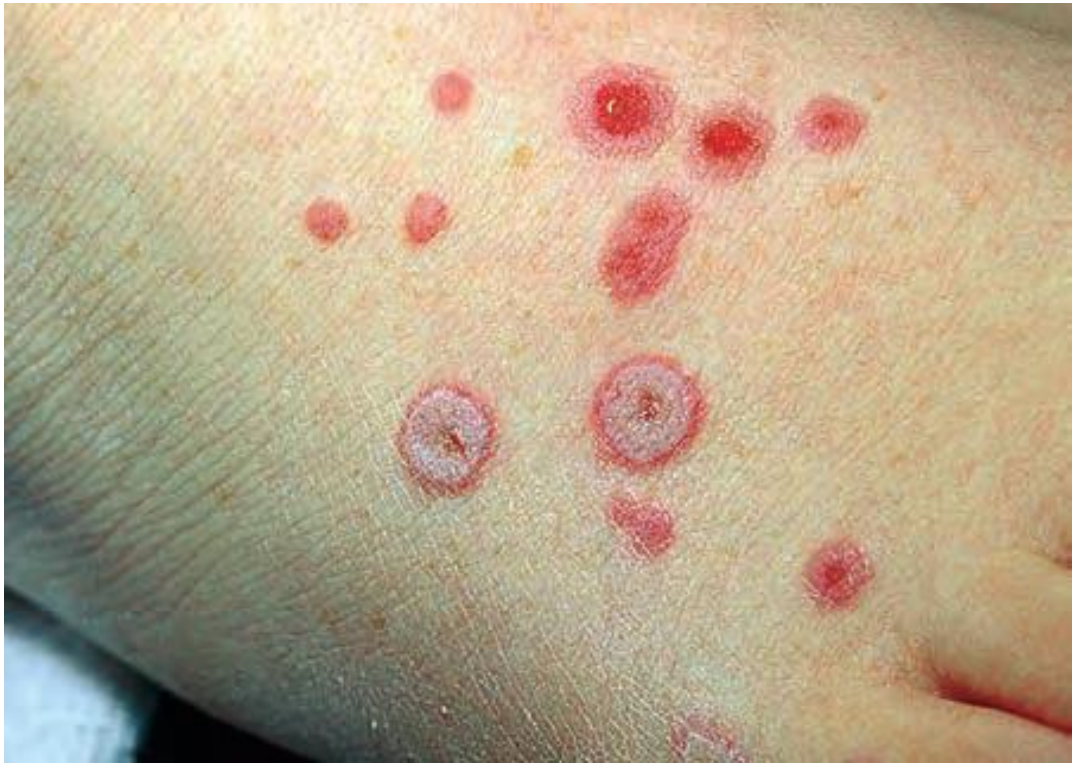
Erythema multiforme

- An eryrhernarous disorder characterized by annular target lesions which may develop into frank blisters.
- may be provoked by many stimuli like viral infection commonly herpes simplex, bacterial infection, and adverse drug reactions.

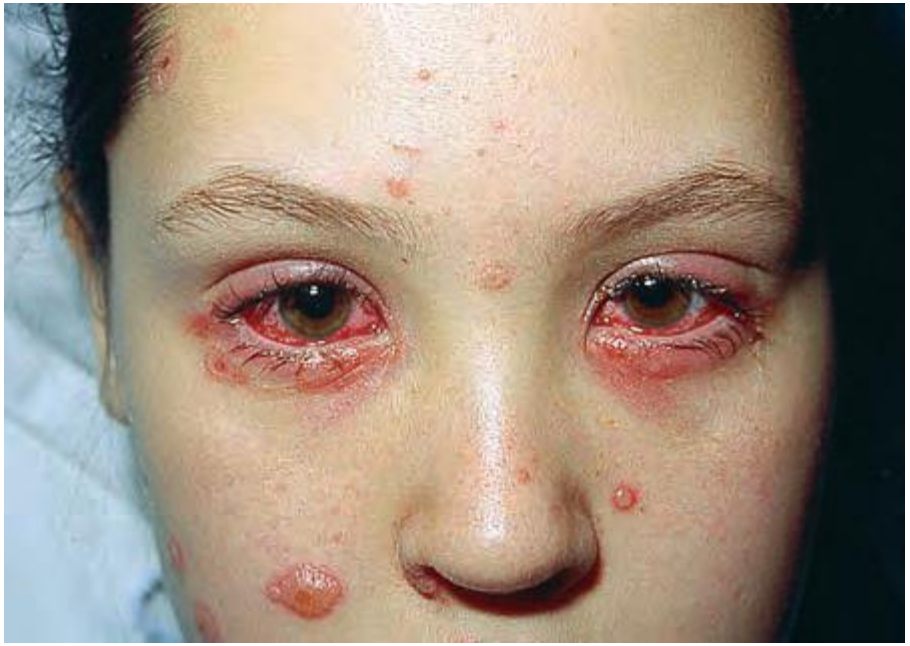
- In many cases no precipitating factor can be identified.
- In bullous lesions the blister forms at the dermo-epidermal junction, and there is necrosis and destruction of the overlying epidermis.

Clinical features

- Iris lesion or trarget lesions appearance.
- most commonly seen on the hands and feet.
- Severe involvement of the eyes and mucosal surfaces is termed Stevens-Johnson syndrome.

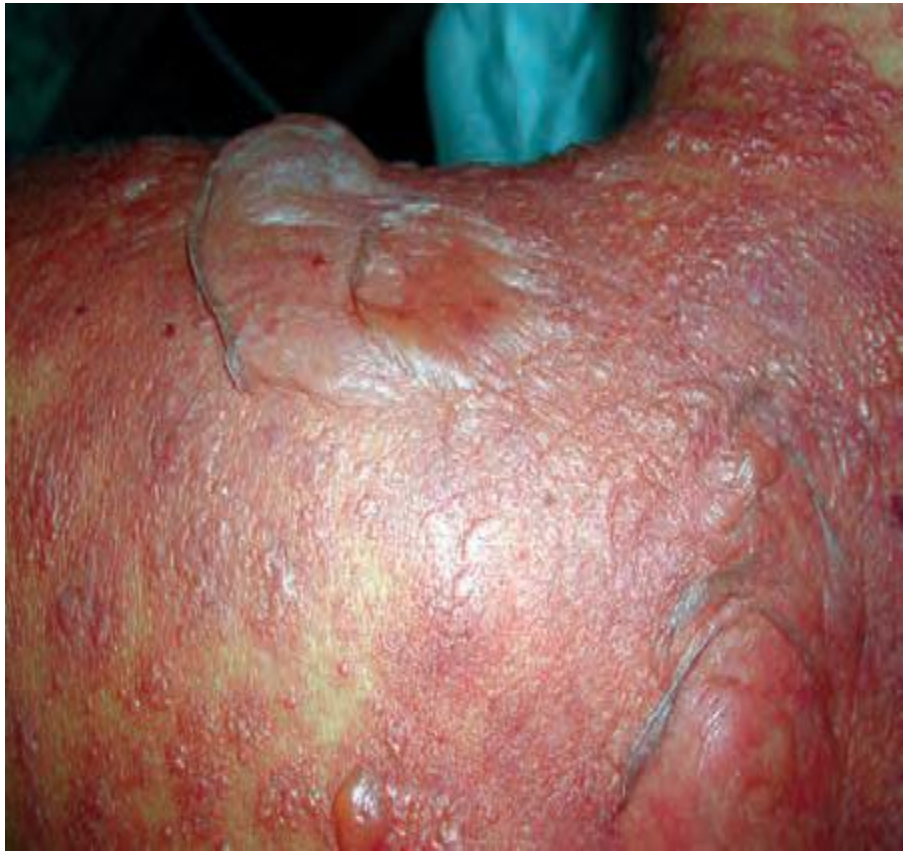


Erythema multiforme – target lesions with bullous component



Stevens–Johnson syndrome – marked eye involvement

- Toxic epidermal necrolysis (TEN) is a severe variant with extensive shedding of the epidermis.
- Identification and removal of the cause is important, and all suspect drugs should be withdrawn.

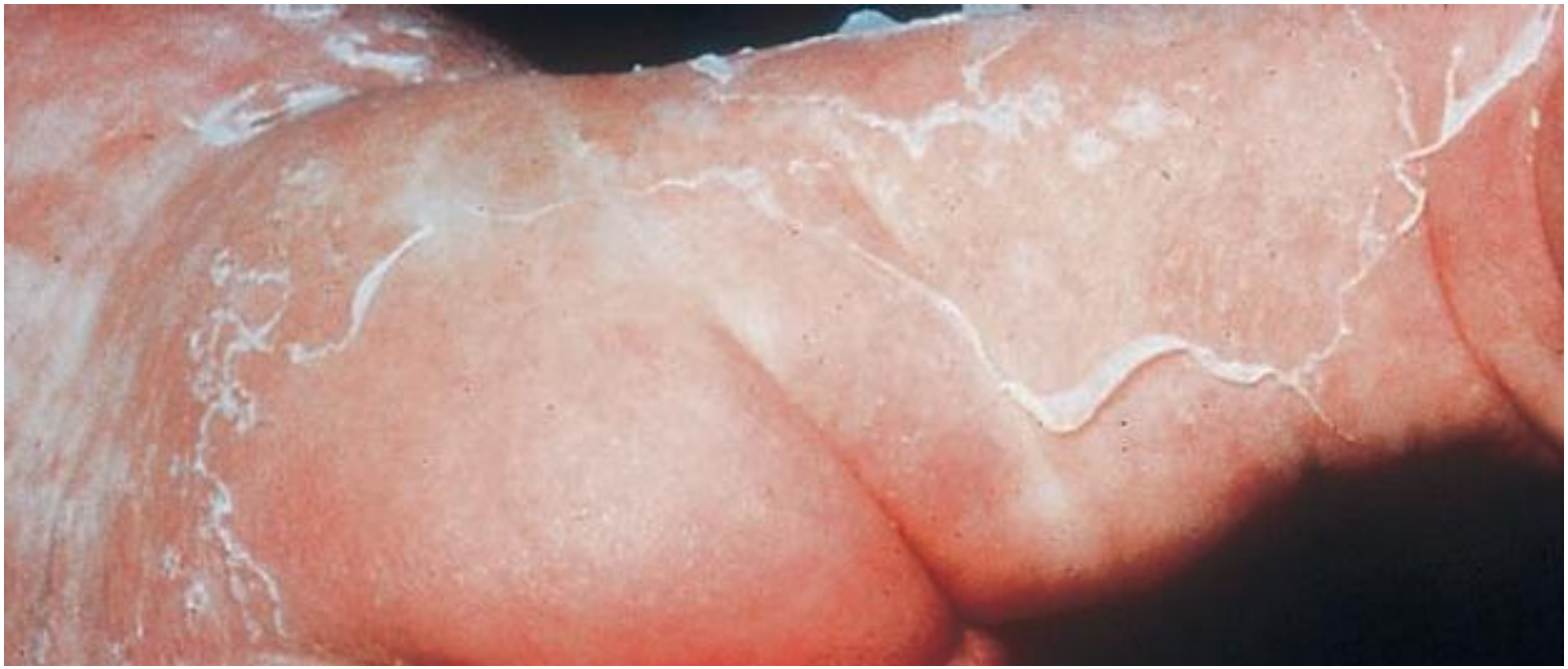


Treatment

- A search should be made for the precipitating factor, which should be withdrawn in the case of a suspected drug or treated in the case of a suspected infection.
- Dressings.
- Systemic treatment ?.

Staphylococcal scalded skin syndrome

- caused by an epidermolytic toxin of certain phage types of Staph.*aureus* which splits the epidermis at the level of the granular layer by cleaving desmoglein 1.
- commoner in children.



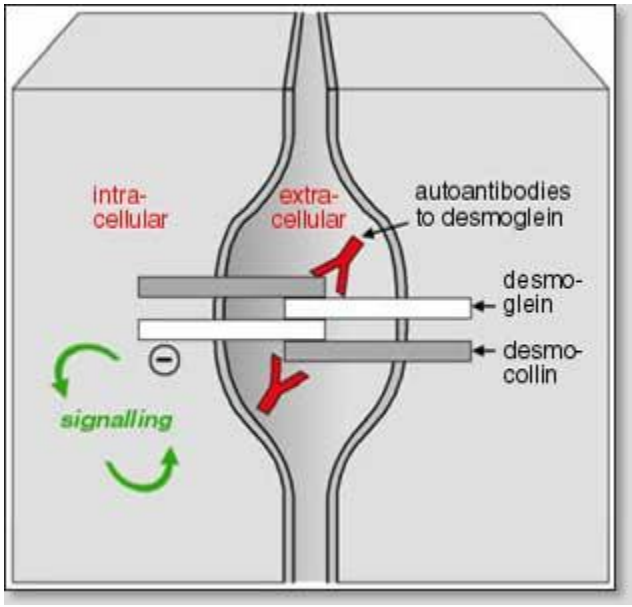
Staphylococcal scalded skin syndrome

- Rapidly expanding shallow blisters which quickly rupture leaving painful raw areas .
- patients should have bacteriological study.
- Treatment with systemic anti staphylococcal antibiotics.
- Dressing.
- healing without scarring.

Blistering Diseases
(2)
Pemphigus Vulgaris and Bullous pemphigoid

Pemphigus

- Pemphigus is a group characterized by blistering of the skin and mucous membranes.
- Auto-antibodies against desmogleins and desmocollins in epidermis and mucosal surface.



Four main clinical varient :

1-Pemphigus Vulgaris: is the most common Pemphigus variant, and the form usually responsible for oral lesions.

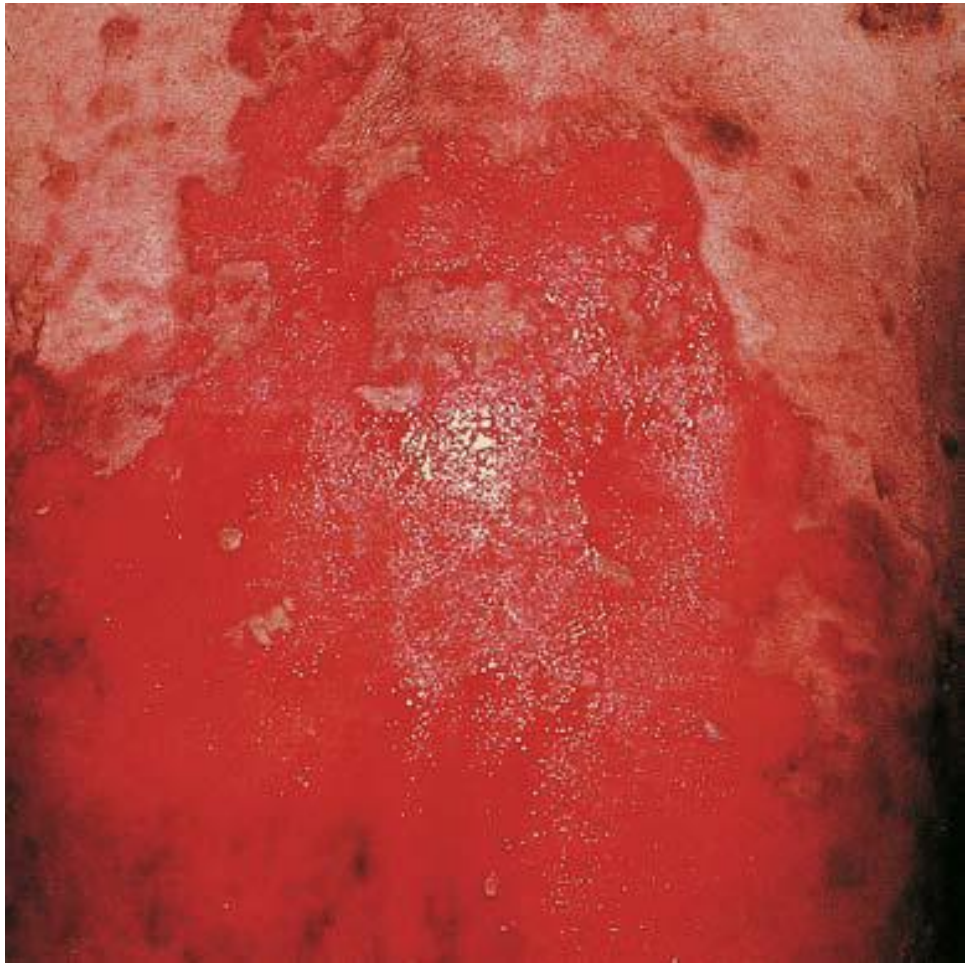
2-Pemphigus vegetans :cahracraized by papillomatous proliferation of the flexures.

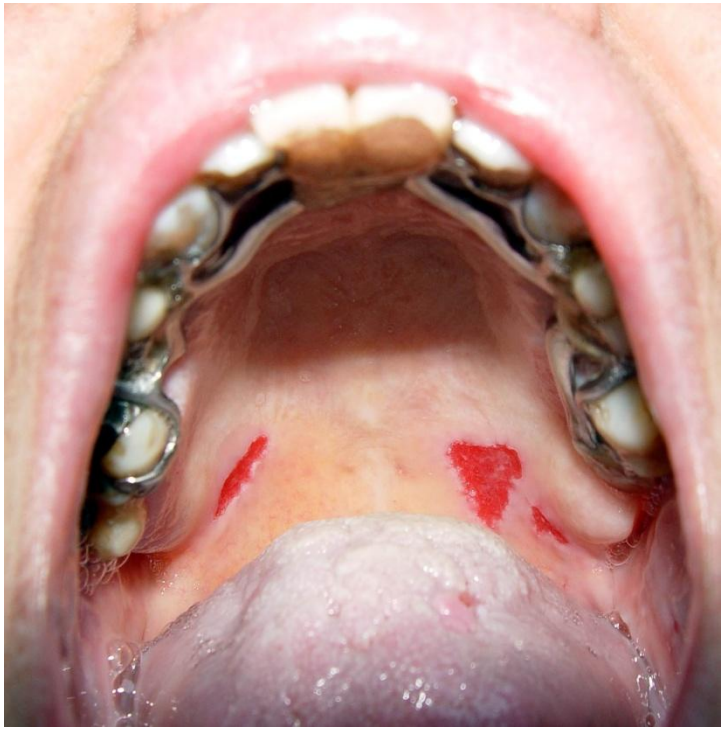
3-Pemphigus foliaceus :mild superficial varient.

4- Pemphigus erythematosus :share some features of lupus blisters on sun exposed sites .

Pemphigus Vulgaris

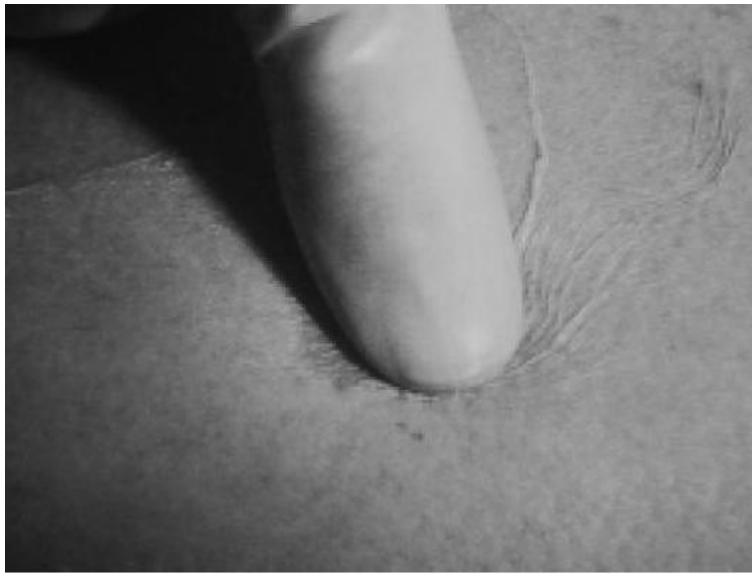
- Begins with erosions on mucous membrane then other skin areas.
- Very painful.
- +ve Nikolsky's sign.
- Age: middle-age .
- Secondary infection and disturbance of fluid and electrolyte balance are common complications .

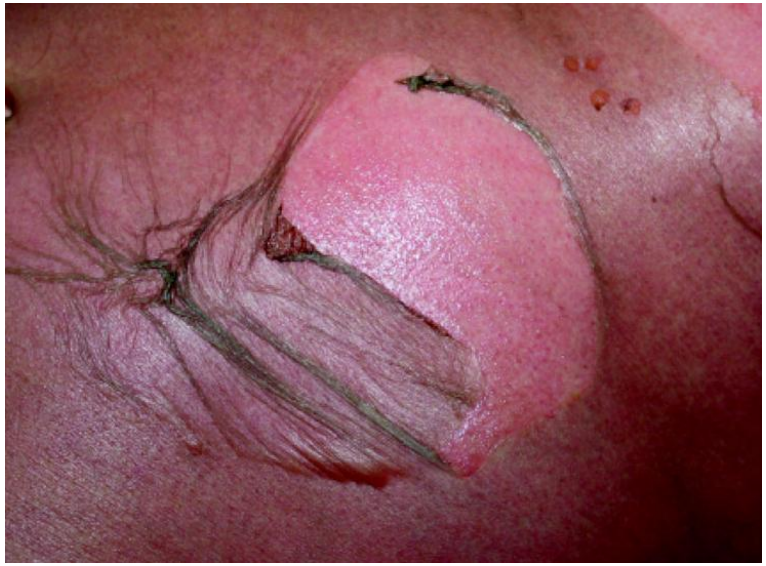




+ve Nicholsky sign

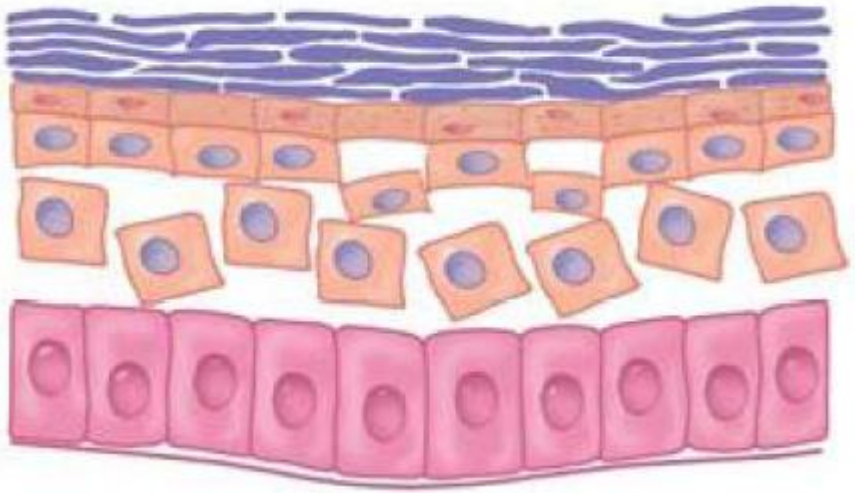
- Twisting pressure on normal skin shears skin.

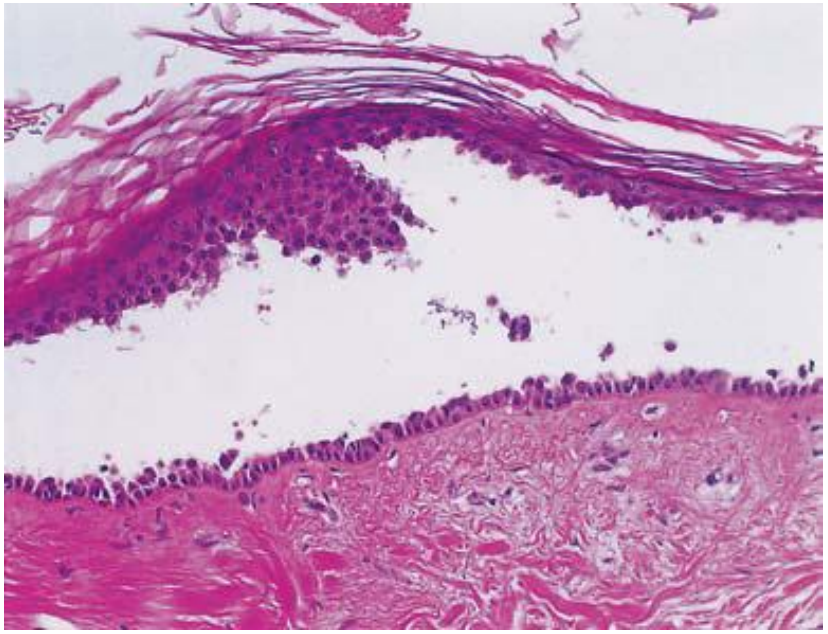


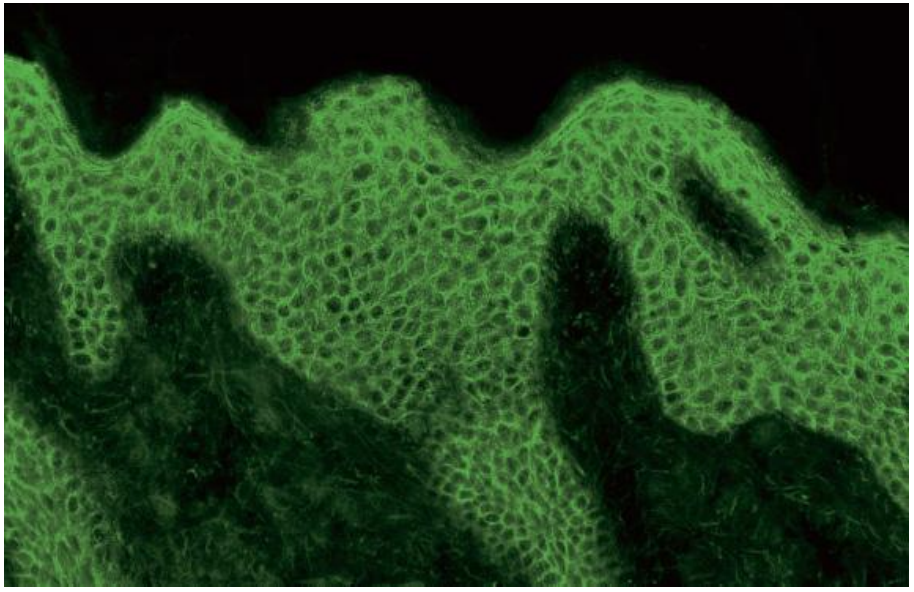


Pathology and immunopathology

- Acantholysis:Individual keratinocytes detach from their neighbours and float free in the blister.
- Immunopathology shows the presence of auto-antibodies directed against the epidermal intercellular.
- Usually IgG .
- In pemphigus vulgaris the main circulating auto-antibody is desmoglein 3, while in the more superficial forms of pemphigus the main form is desmoglein 1.



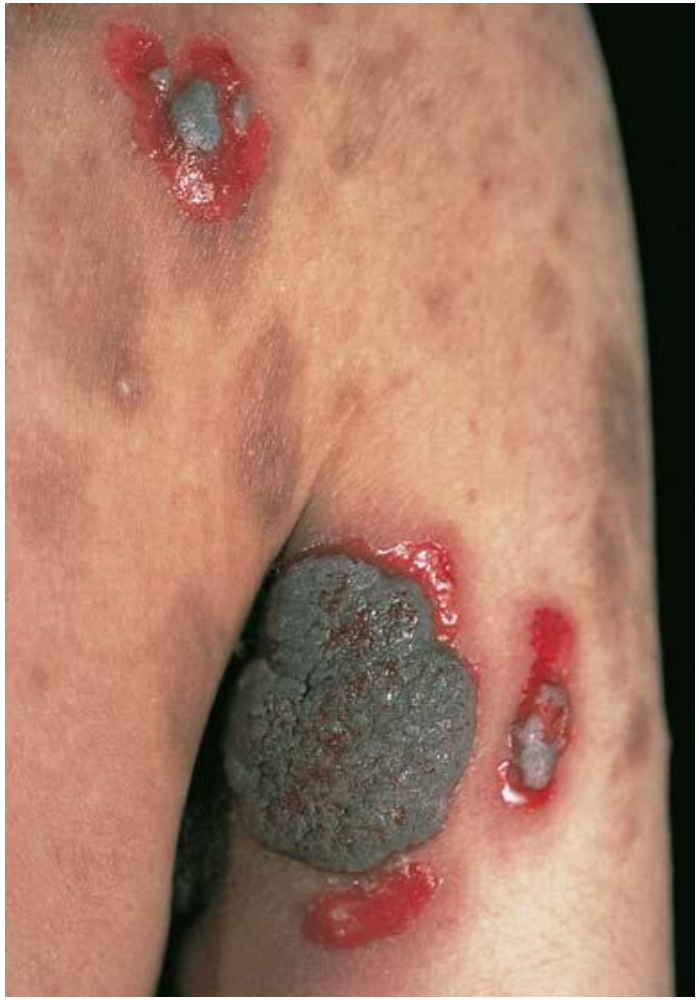




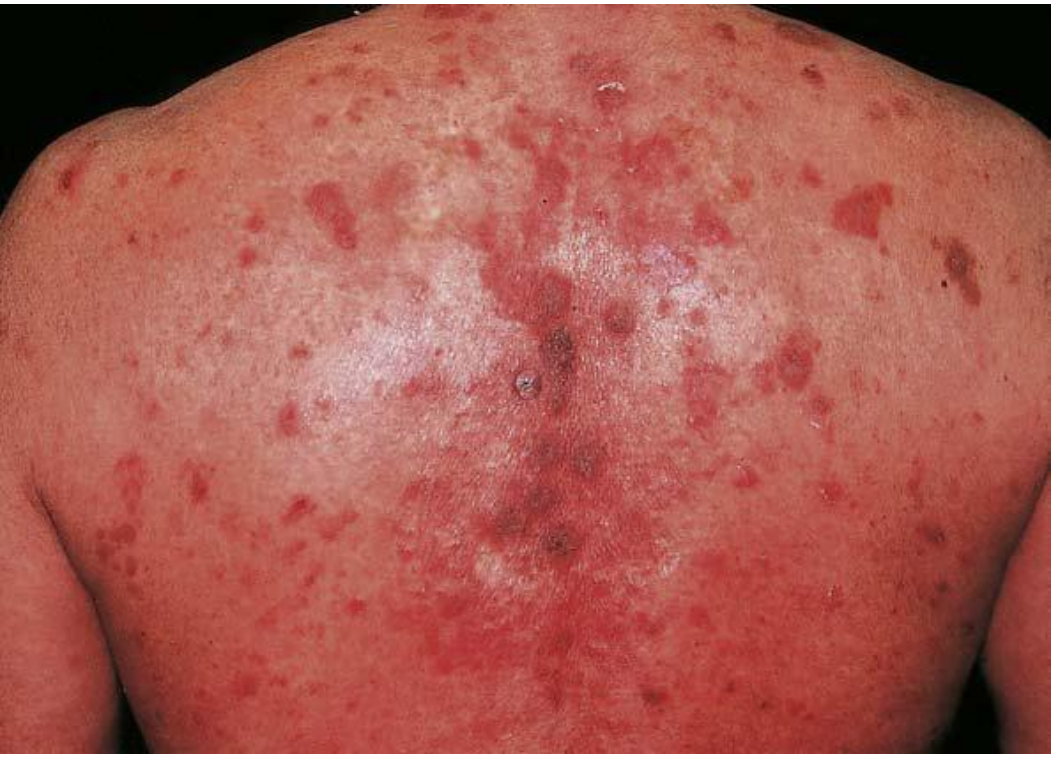
Treatment

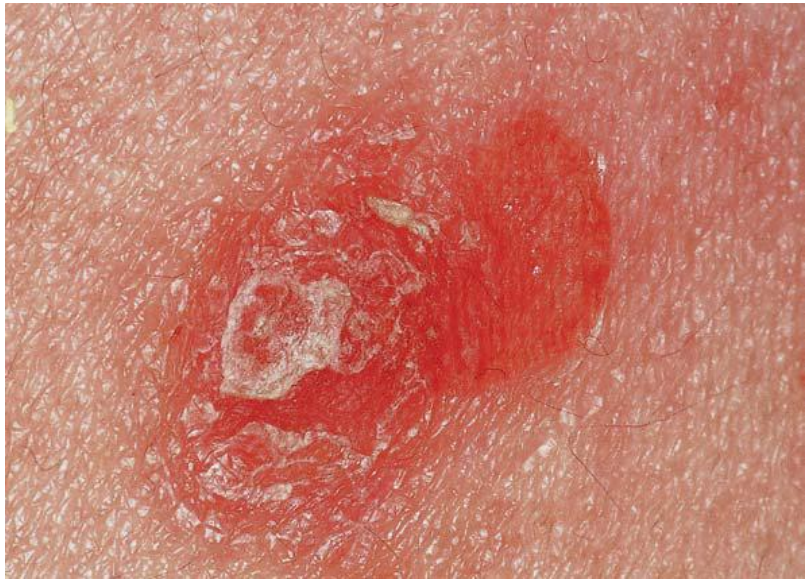
- High dose systemic steroids 60-100 mg of prednisolone.
- Immunosuppressive agent such as azathioprine cyclophosphamide or mycophenolate mofetil will allow further reduction of steroid dose.
- Topical therapy is mainly symptomatic.
- Patient will probably have to remain on systemic steroids for life.
- Careful surveillance for steroid-induced side effects.

Pemphigus vegetans



Pemphigus foliaceus



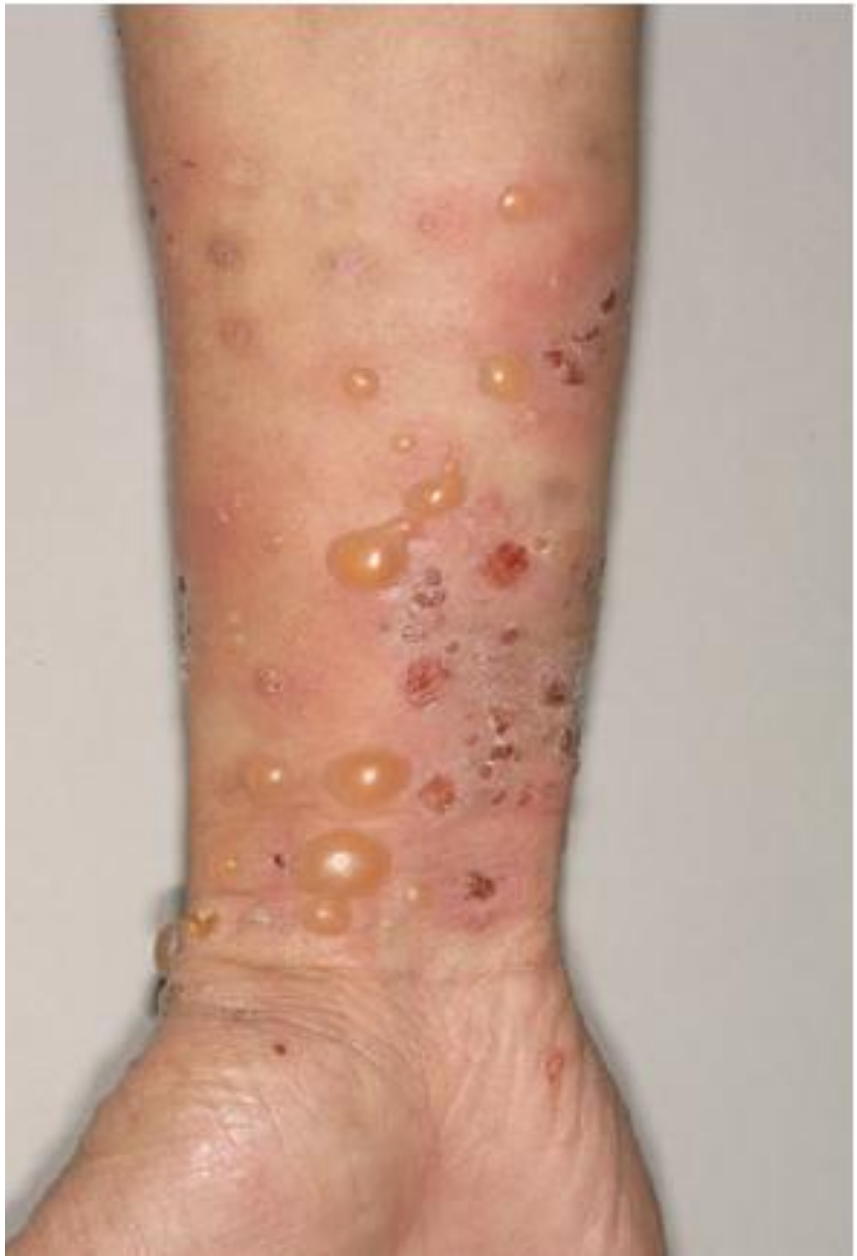


Bullous pemphigoid

- Characterized by large blisters on an erythematous base.
- Mainly in older age group more than 60 y.
- The prognosis is usually good.

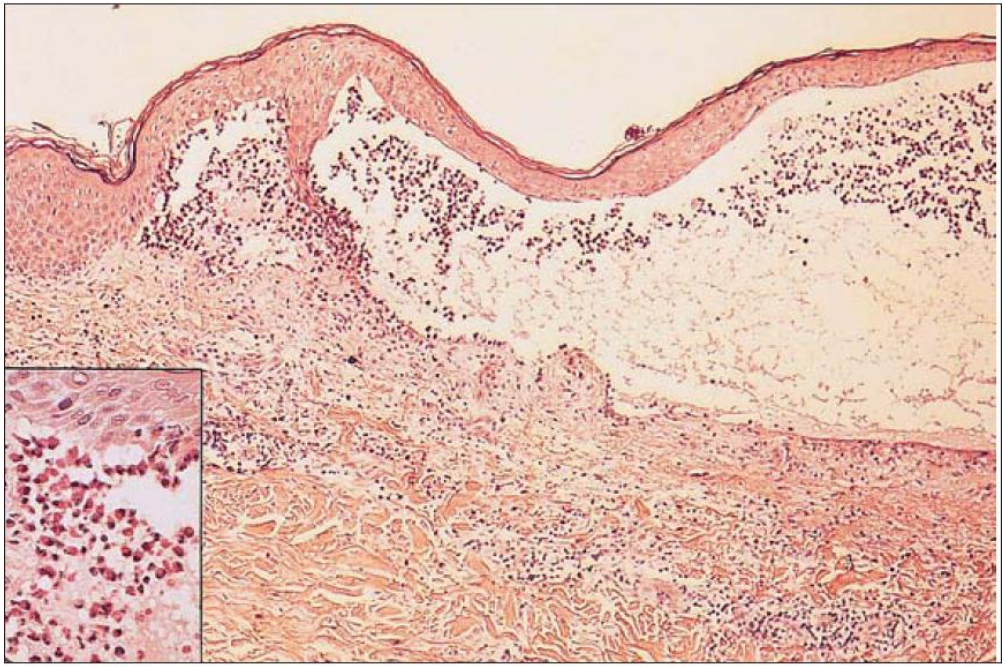
Clinical features

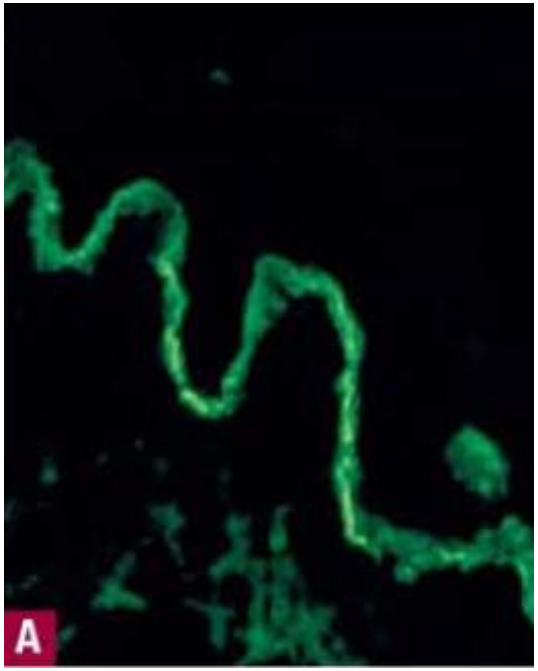
- Elderly patents.
- Large tense blisters on upper arms and thighs.
- Eczematous base .
- Itch rather than pain.
- Oral lesions are less frequent than pemphigus.



Pathology

- Sub epidermal between epidermis and dermis the epidermis forms the roof of the blister.
- Antigens identified are BP 1 and BP 2.
- Immunoglobulin and complement are deposited in the lamina lucida of the basement membrane in a linear band.

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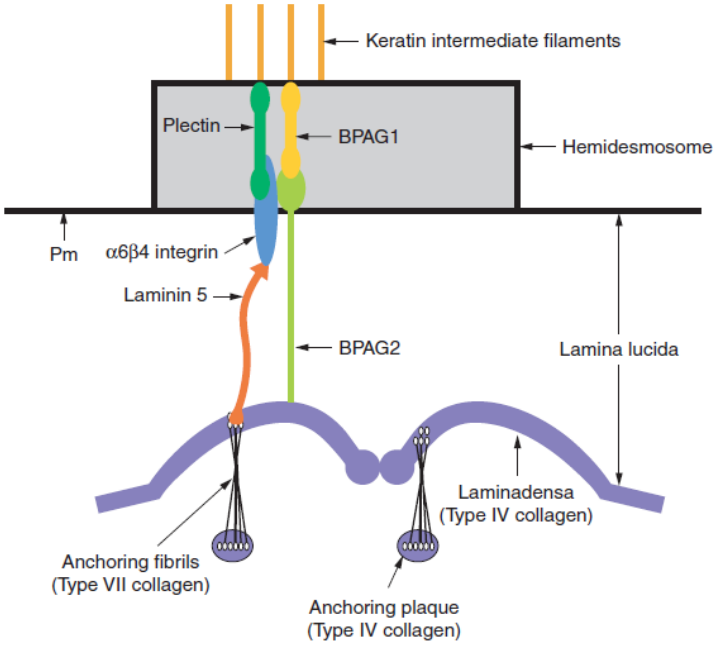

Keratin intermediate filaments
Plectin
BPAG1
Hemidesmosome
Pm
α6β4 integrin
Laminin 5
BPAG2
Lamina lucida
Laminadensa
(Type IV collagen)
Anchoring fibrils
(Type VII collagen)
Anchoring plaque
(Type IV collagen)

Treatment

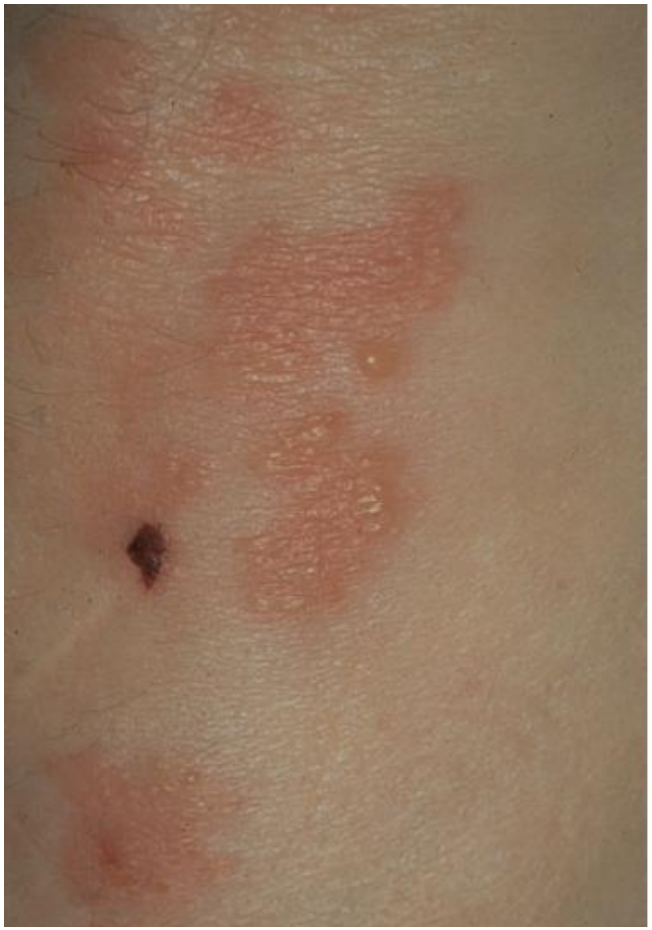
- Severe pemphigoid :Systemic steroids , but unlike pemphigus, it may be possible to discontinue.
- The addition of either azathioprine enable the oral steroid dose to be reduced more rapidly.
- Milder may also respond very well to potent or moderately potent topical steroids alone.

Dermatitis Herpetiformis

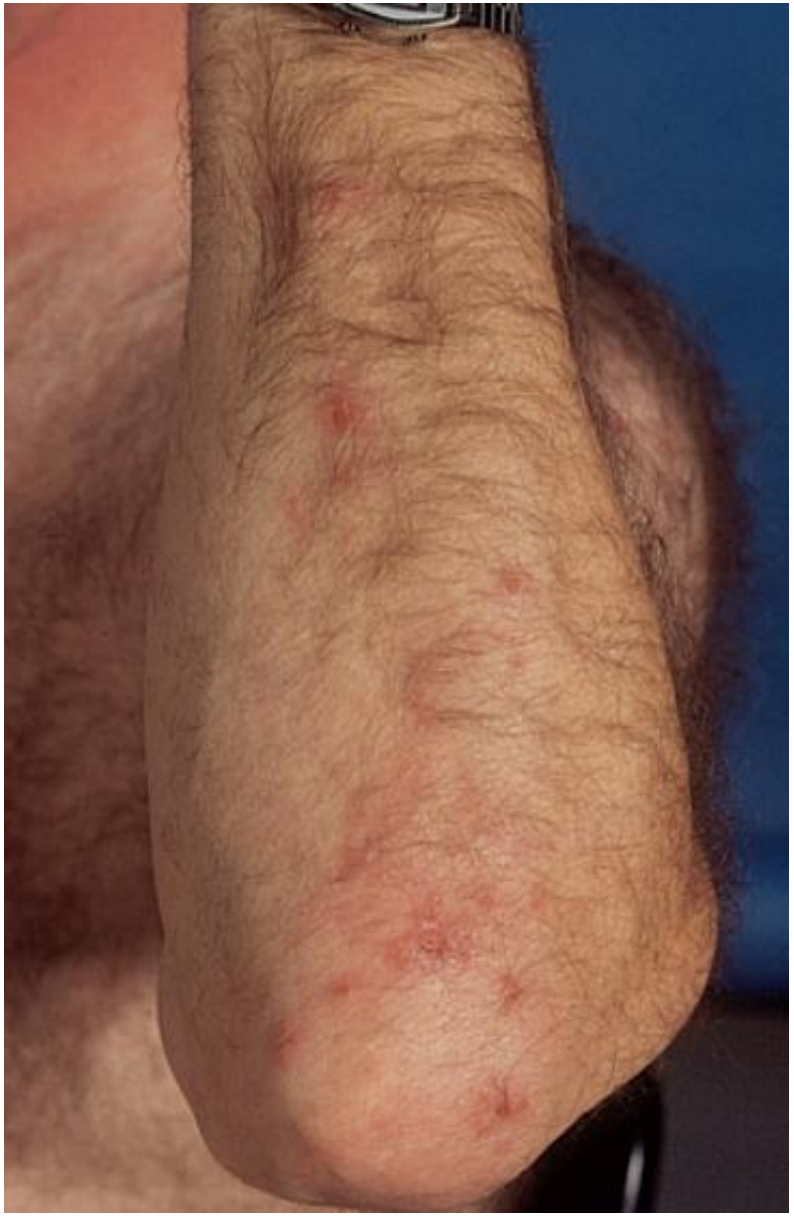
- Causes severe itching.
- Affect younger age group than BP and PV.
- Association with gluten-sensitive enteropathy.

Clinical features :

- grouped erythematous papules and vesicles found most typically on the elbows and extensor surfaces of the forearms, knees and shins, buttocks, shoulders and scalp.
- Most patients do not report any bowel symptoms.

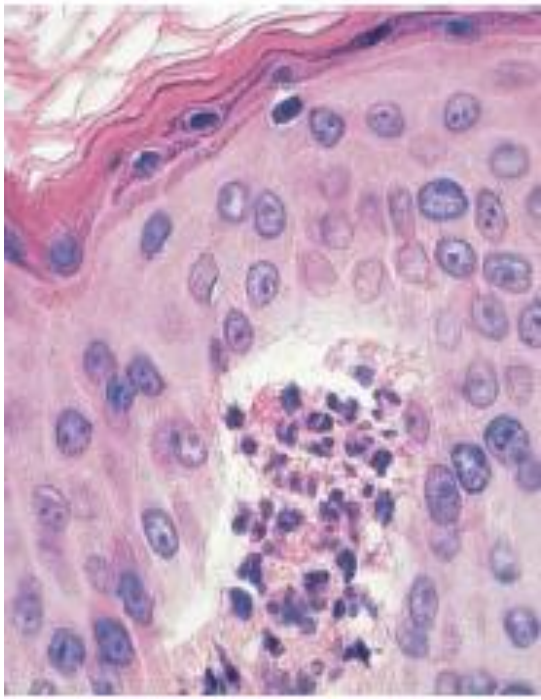


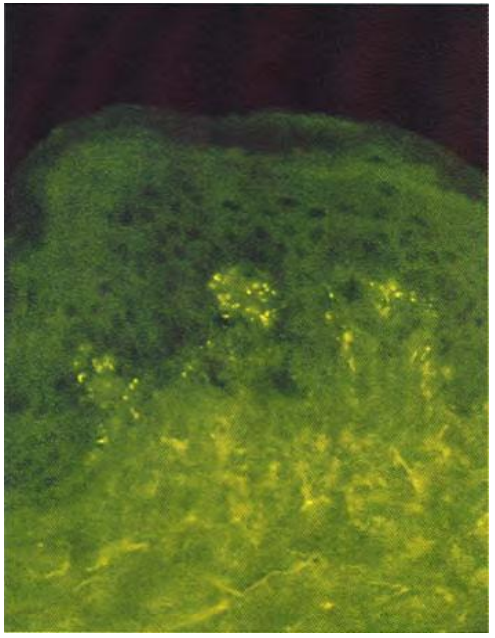
- Intense pruritus leads to excoriation of the small vesicles.



Pathology

- Dermal papillary collections of neutrophils (micro-abscesses).
- DIF :shows granular IgA deposits in dermal papillae.





Treatment

- Gluten-free diet (6 months– 1 yr to see effect)
- Dapsone
  - G6PD
  - initial dose 50-150mg.
- Topical :steroid and antibiotics.
- Life long treatment .

	Age	Site of blisters	General health	Blisters in mouth	Nature of blisters
Pemphigus	Middle age	Trunk, flexures and scalp	Poor	Common	Superficial and flaccid
Bullous pemphigoid	Old	Often flexural	Good	Rare	Tense and blood-filled
Dermatitis herpetiformis	Primarily adults	Elbows, knees, upper back, buttocks	Itchy	Rare	Small, excoriated and grouped

Thank you