AUTOIMMUNE BULLOUS DISORDERS - II

BULLOUS PEMPHIGOID

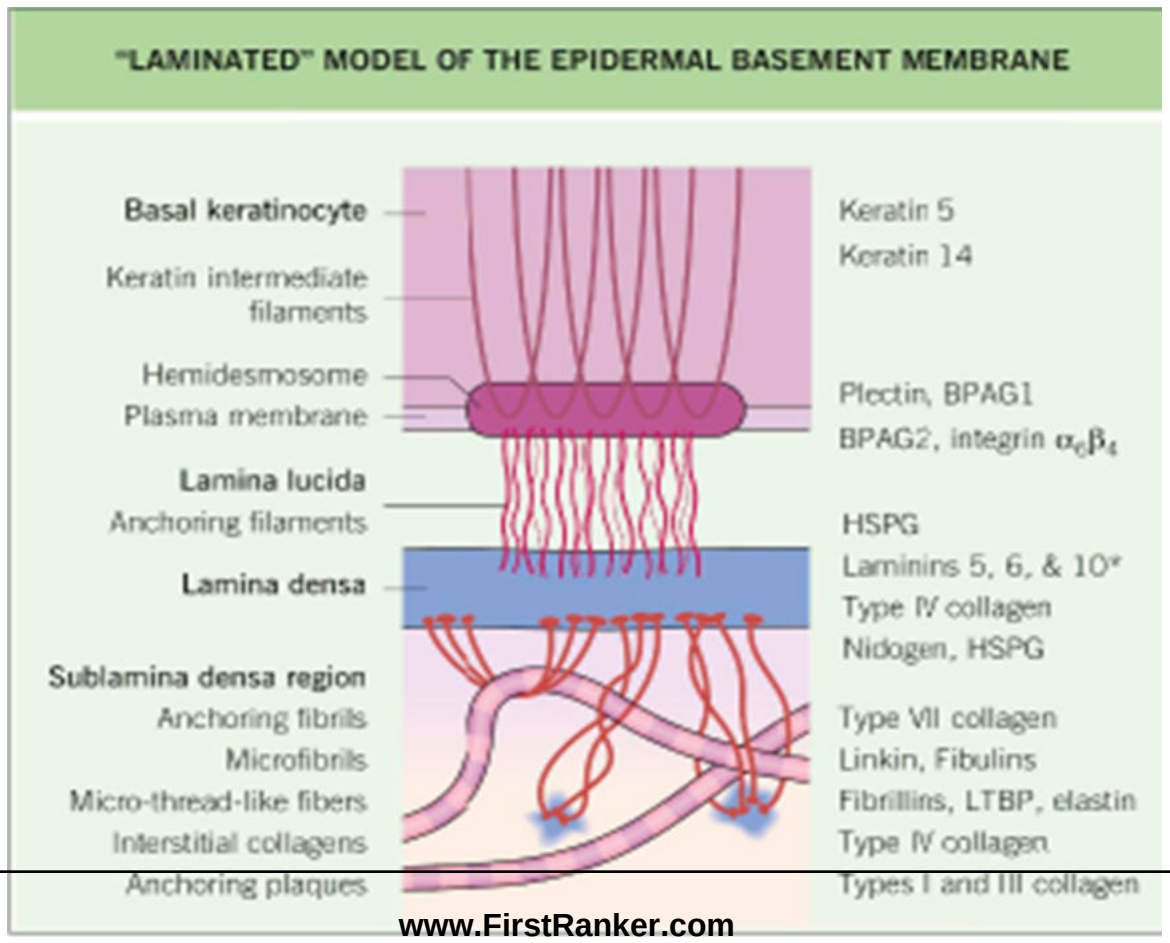
❖Acquired, non scarring, autoimmune, blistering disease

❖ Age – elderly

❖Histology – subepidermal bullae

❖ Immunopathologically – deposition of AutoAb and complement along basement membrane zone (BMZ)

• ANTIGENS - BPAg1 (230kDa) or BP 230
BPAg 2 (180kDa) or BP 180

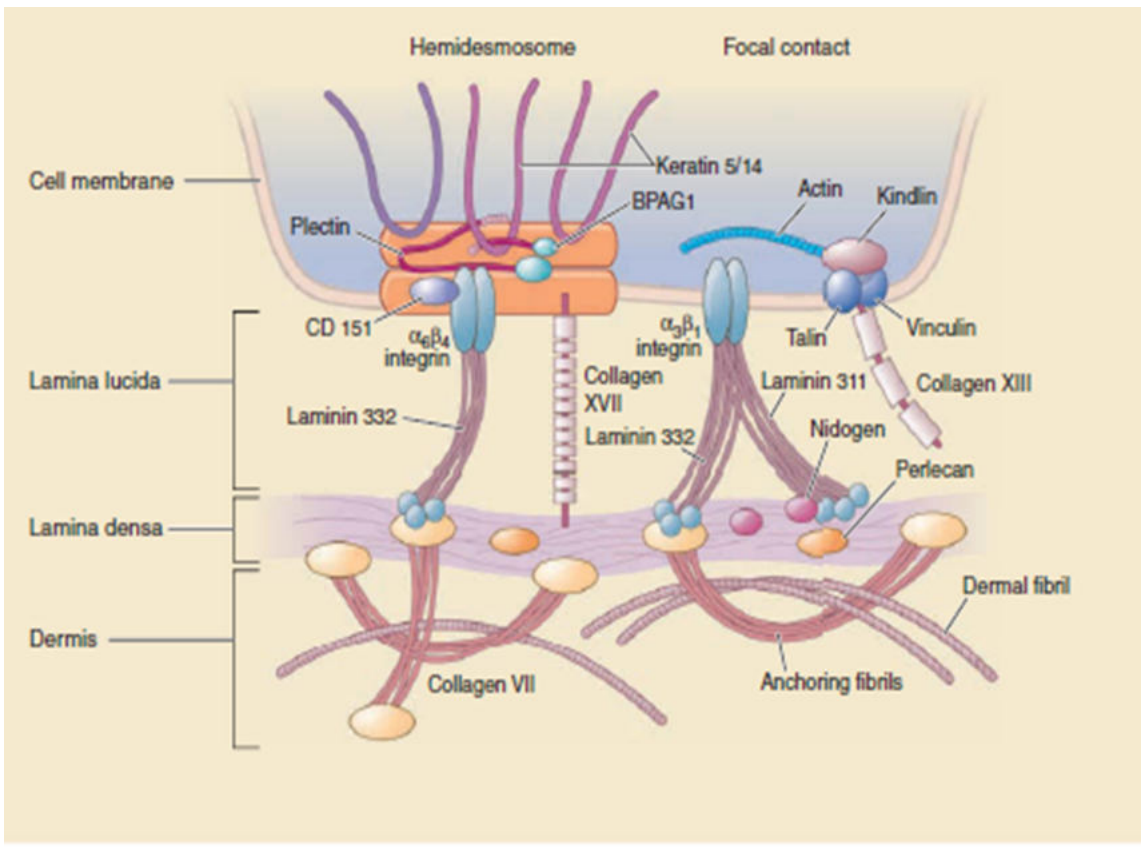


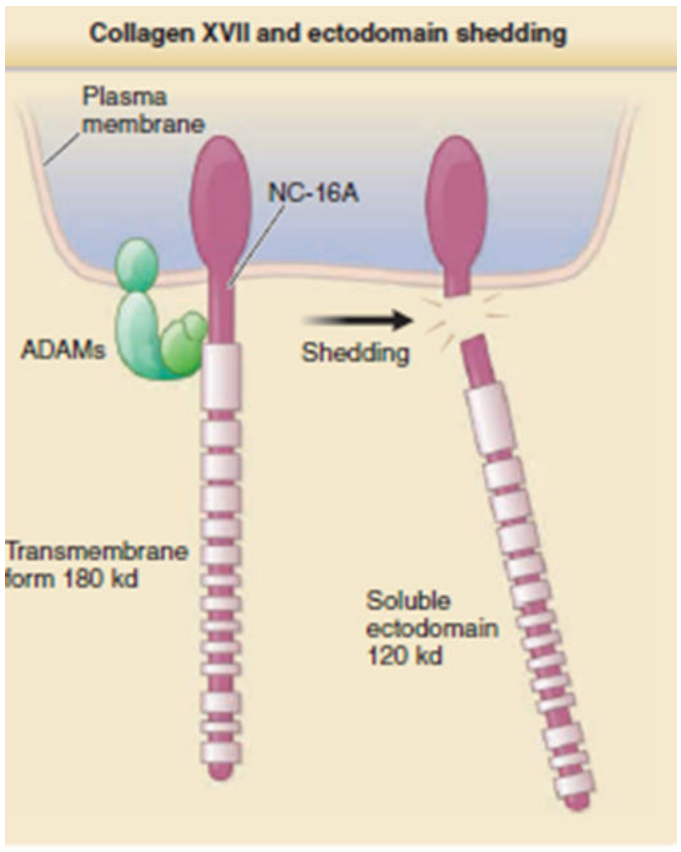
BP 230

- Intracellular protein synthesized by basal keratinocytes
- Component of cytoplasmic plaque of hemi-desmosome

BP 180

- Hemidesmosomal glycoprotein of basal keratinocytes
- Spans lamina lucida of dermoepidermal junction
- Has a short non collagenuous extracellular domain and a long non collagenuous ectodomain that interacts with anchoring filaments of the basement membrane
- Auto Ab directed against short NC 16A ectodomain



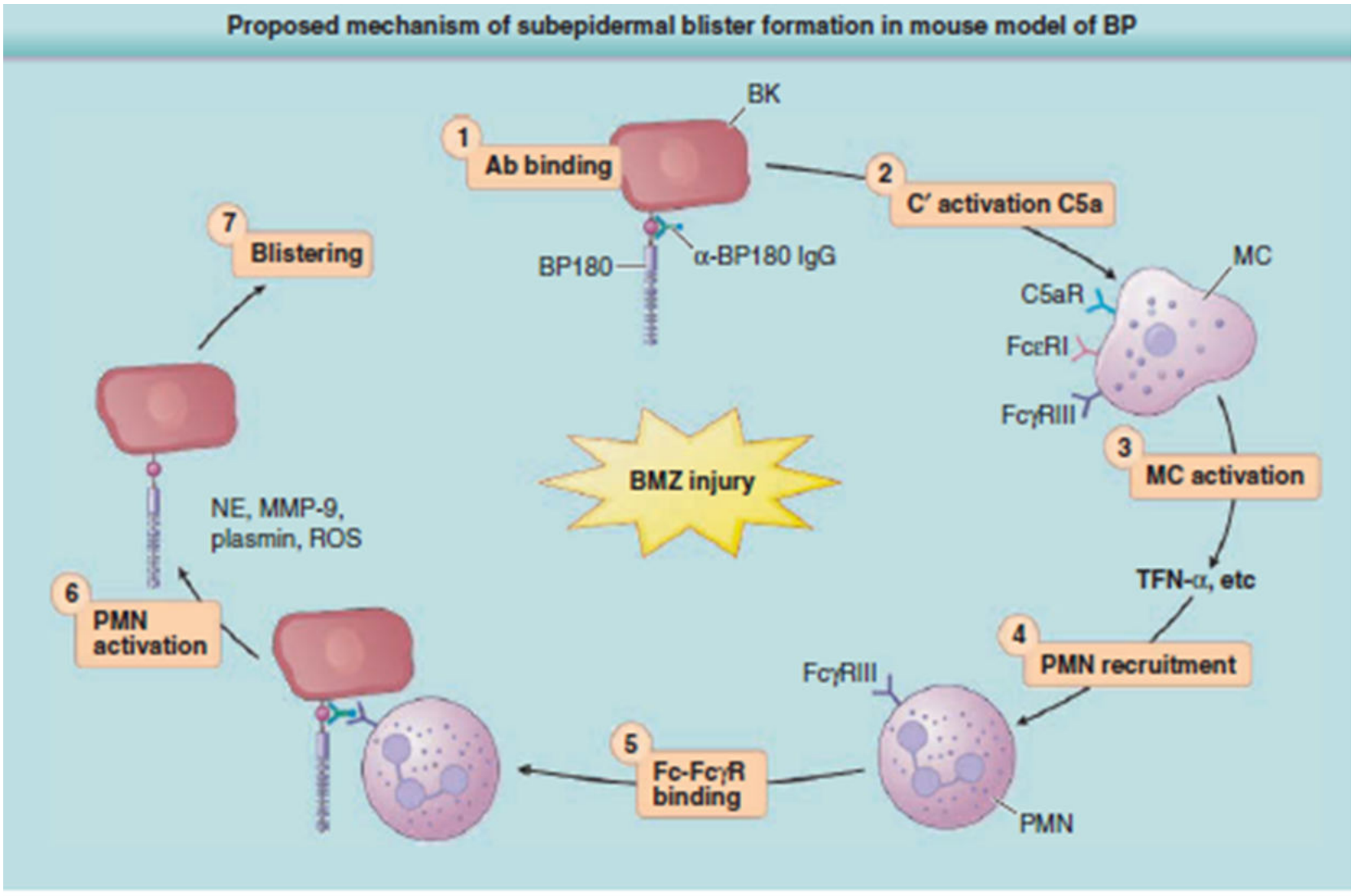


ANTIBODIES

- Anti BMZ antibodies in BP – IgG 1 and IgG 4
  Ig E (occasionally)

- IgG 4 and IgE target BP 180Ag in Bullous Pemphigoid

- Serum levels of IgG 4 and IgE reflect disease activity



CLINICAL FEATURES

- Age- elderly 60-75
- M>F

- Tense vesicles and bullae on urticated base/ normal skin
- Containing clear to turbid to haemorrhagic fliud
- Roof remain intact for several days as bullae is subepidermal.
- Sites – lower abdomen, inner thighs, groin, flexural aspects of limbs
- Palms and soles – occasional
- Nikolsky's sign –ve
- Asboe Hansen's sign –ve

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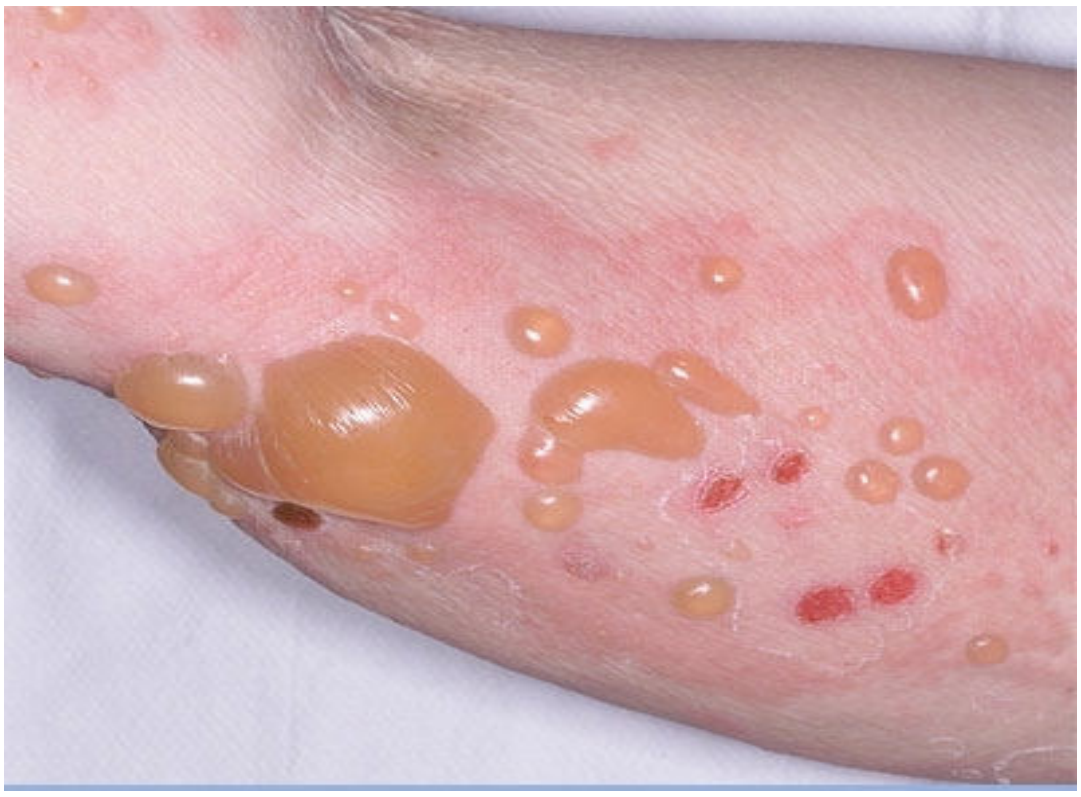
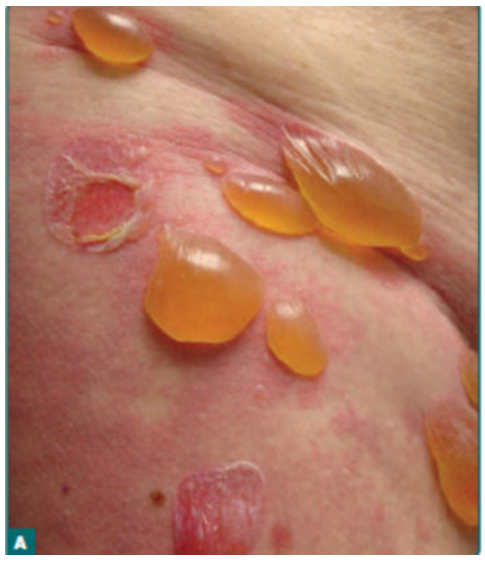




- Blister collapse and re-epithelialize
- For blisters that rupture, resulting erosions do not spread
- Erosions heal without scarring-post inflammatory pigmentary changes, milia

- Musosa- 10-40%

- Pruritus common; may precede several years

CLINICAL VARIANTS

1. Localised
2. Childhood
3. Vesicular
4. Vegetating
5. Nodular
6. Drug induced

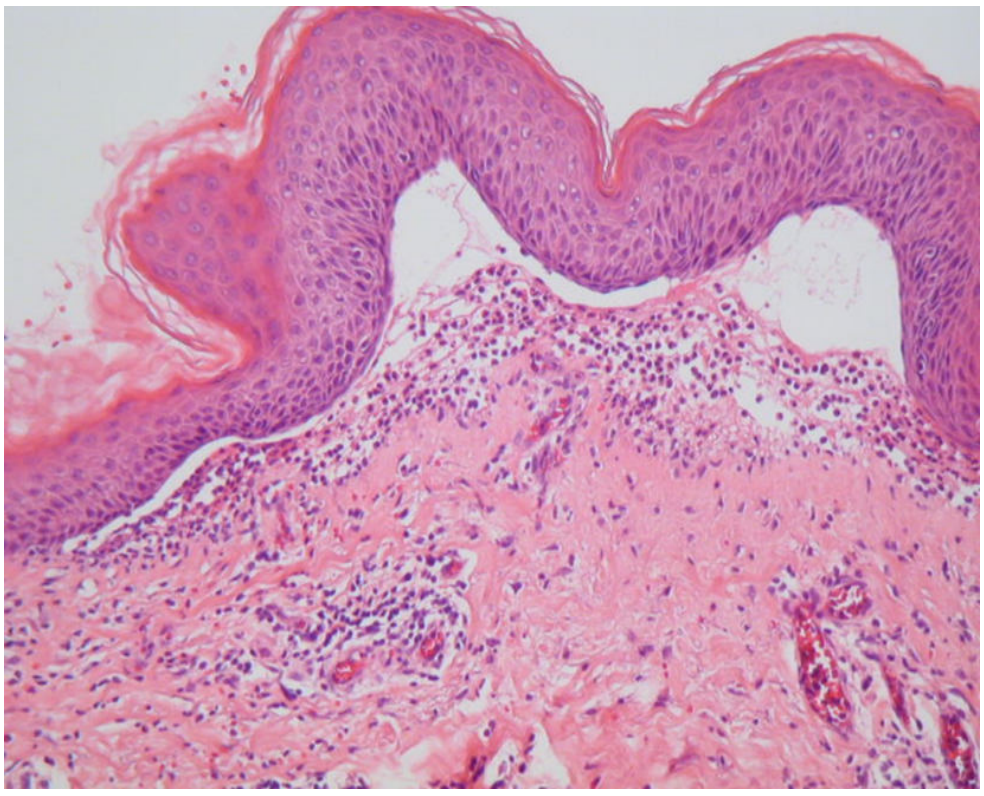
- Drug induced pemphigus

Oral drugs- penicillin, ampicillin, penicillamine, frusemide,PUVA therapy, anti diabetics, sulfonamides, clonidine, diclofenac, ibuprofen, practolol.

Topical – anthralin, 5-FU, benzoyl benzoate

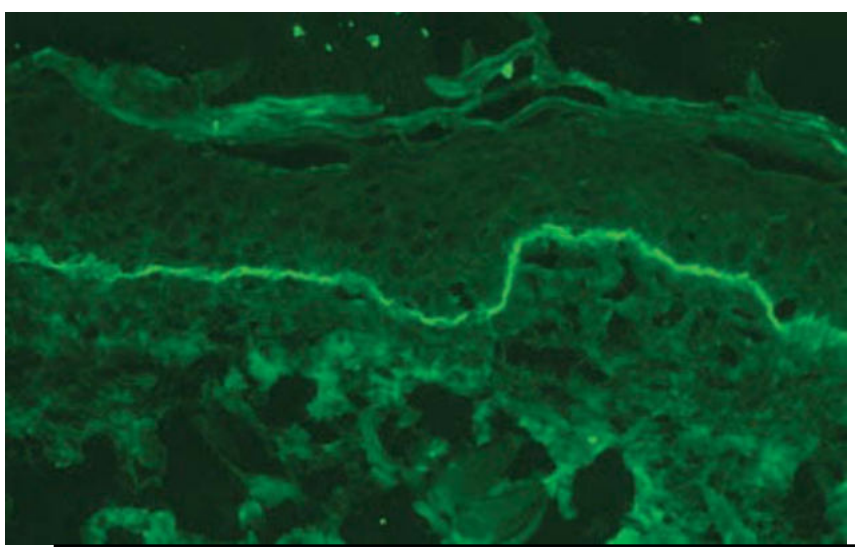
HISTOLOGY

- Subepidermal blister
- An intact epidermis as roof of bulla
- Blister cavity – neutrophils, eosiniphils, fibrin

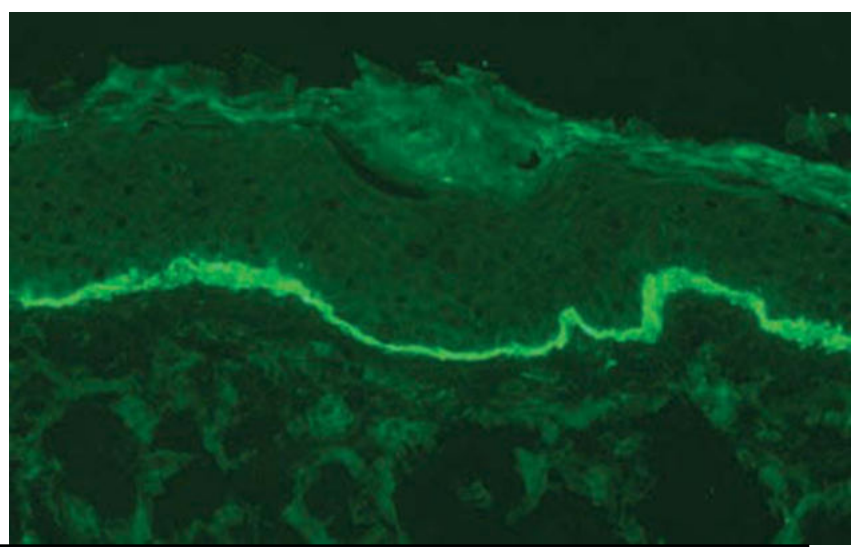


Direct immunono flourescense(DIF)

- Linear pattern of IgG, mainly IgG4 (90%), along BMZ
- C3 deposition in 100% cases

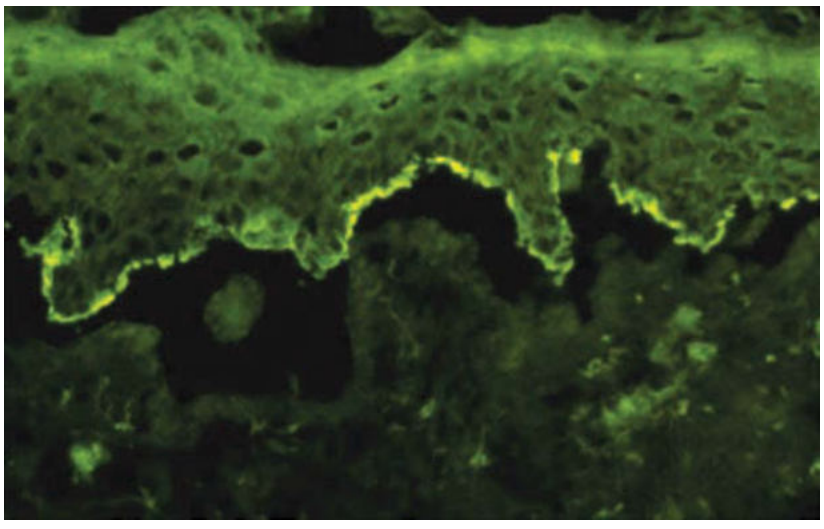


IgG



C3

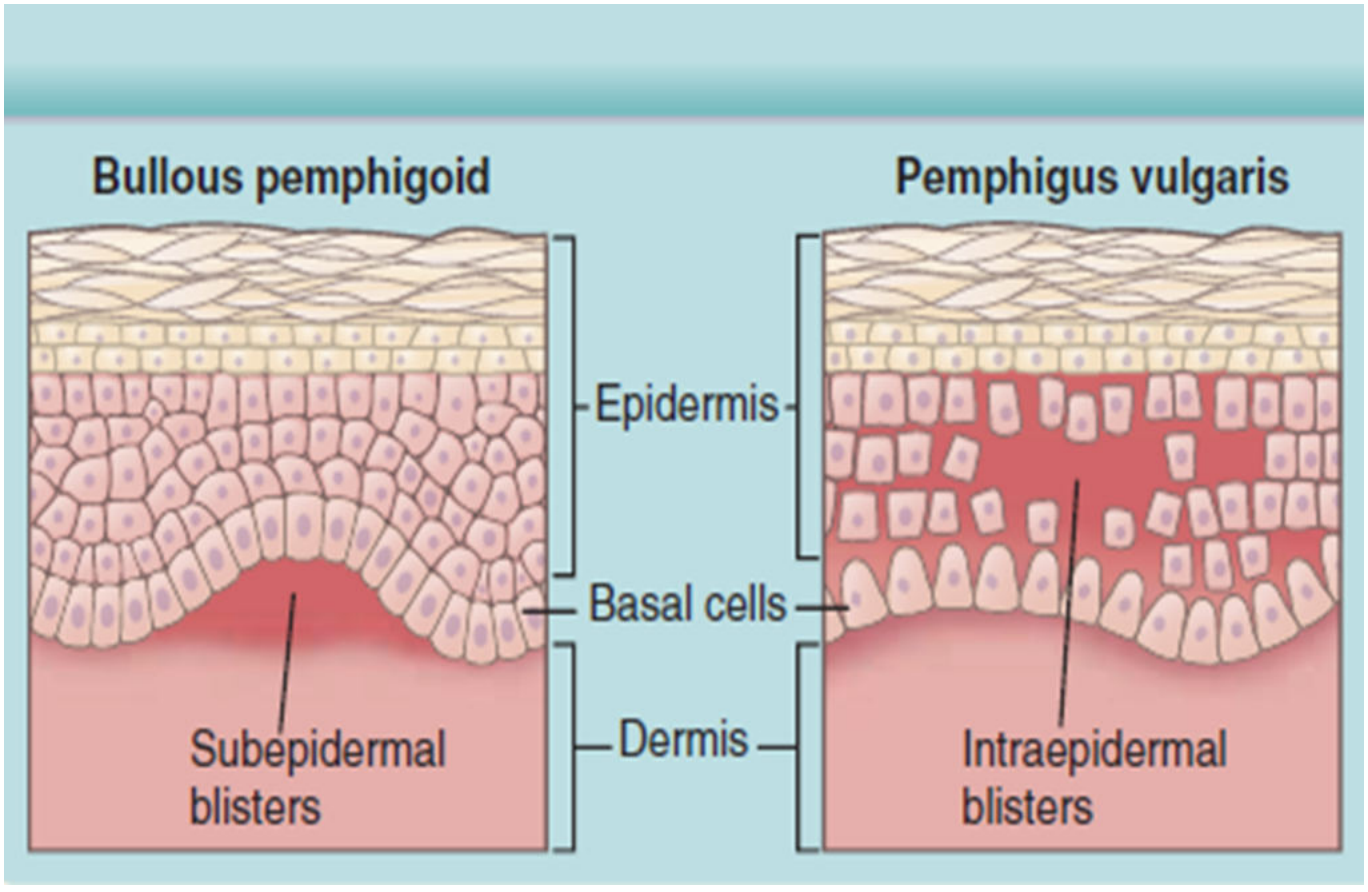
- Indirect immuno flourescence (IIF)
- Circulating anti BMZ IgG Ab (70%)



D/D

1. Pemphigus
2. Mucous membrane pemphigoid
3. Pemphigoid Gestationis
4. Linear IgA disease
5. Dermatitis herpetiformis
6. Bullous drug eruptions

Bullous pemphigoid vs Pemphigus



BULLOUS PEMPHIGOID	PEMPHIGUS VULGARIS
Subepidermal blister, eosinophil redominant inltrate, with neutrophils, lymphocytes, and monocytes and macrophages	Suprabasal blister with acantholysis; characteristic “row of tombstones”
Nikolsky sign (−)	Nikolsky sign (+)
Asboe-Hansen sign (−)	Asboe-Hansen sign (+)
Urticarial lesions precede tense bullae	Flaccid blister on any skin surface; erosions most commonly observed
Mucous membrane lesions present in 10%	Mucous membrane lesions presenting sign for majority of patients
BPAg1 (230-kDa) or BPAg2 (180-kDa) or type XVII collagen	Desmoglein 3 (130 kDa); desmoglein 1 (160 kDa)
DIF IgG in basement membrane	DIF IgG in intercellular pattern
Waxing and waning course, occasional spontaneous remission	Fatal if untreated

TREATMENT

1. Suppression Of Inflammation
   - ❖ Corticosteroids –oral daily doses (0.5-0.75/ kg/day) , potent topical steroids
   - ❖ tetracyclin, sulfones
2. Suppression Of Auto Ab Formation
   - ❖high dose corticosteroids – DCP pulse,
   - ❖azathioprine, Mtx, cyclosporin,
   - ❖ cyclophosphamide
3. Removal Of Antigens And Autoab-
   - ❖ Plasmapheresis
4. Immuno- Modulation – IV Ig

DERMATITIS HERPETIFORMIS

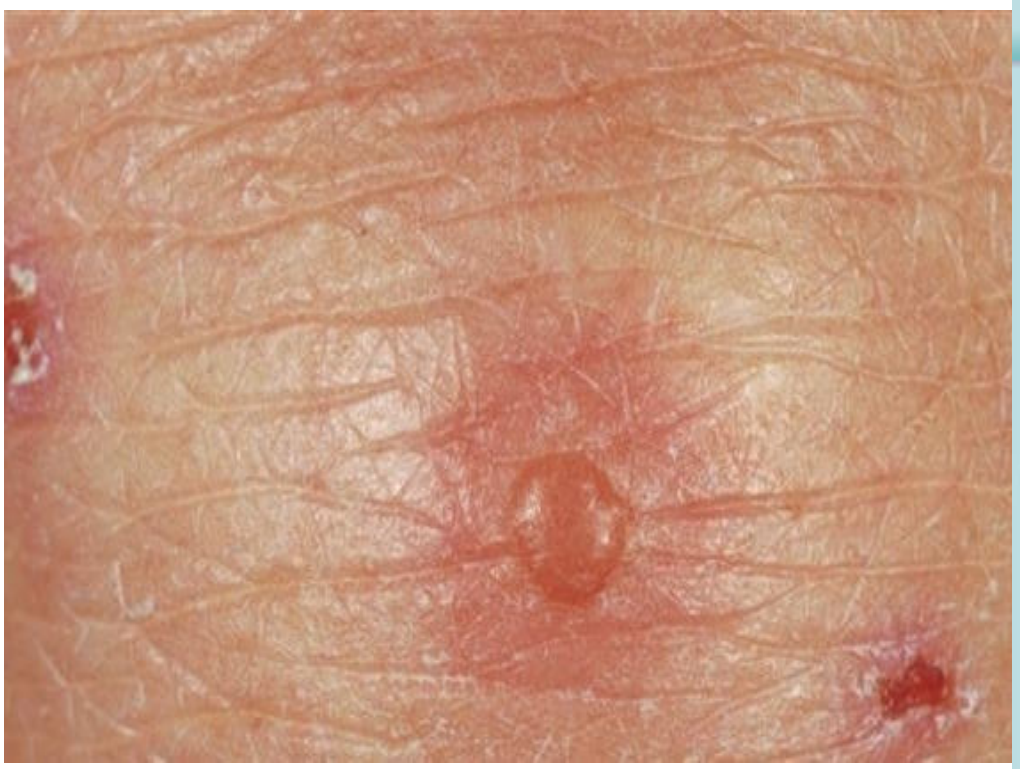
- Rare chronic blistering disorder
- Intensely pruritic grouped vesicles on an erythematous base
- DIF – granular deposits of Ig A in dermal papillae
- Associated with an gluten sensitive mostly asymptomatic enteropathy

PATHOGENESIS

- Predominant autoantigen in DH –epidermal transglutaminase (TGe)
- Predominant antibody in DH – IgA
- Pathological processes in skin are initiated when
- TGe - IgA immune complexes are deposit in papillary dermis and activate complement

CLINICAL FEATURES

- Age –(2-3)rd decade
- Classical lesion start as a vesicles on an erythematous, edematous base
- later new lesions arrange in groups
- intensely itchy
- most lesions excoriated; only crusts seen
- Site – elbows, knees, buttocks, sacrum, shoulders, posterior scalp,
- Symmetrical distribution
- Occasionally face



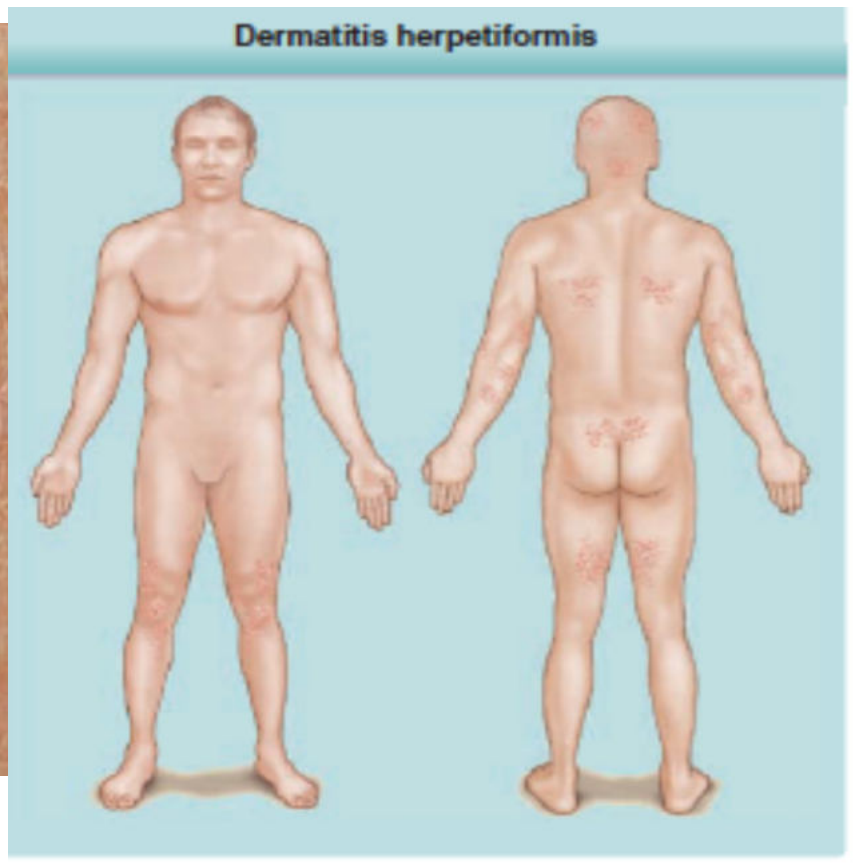
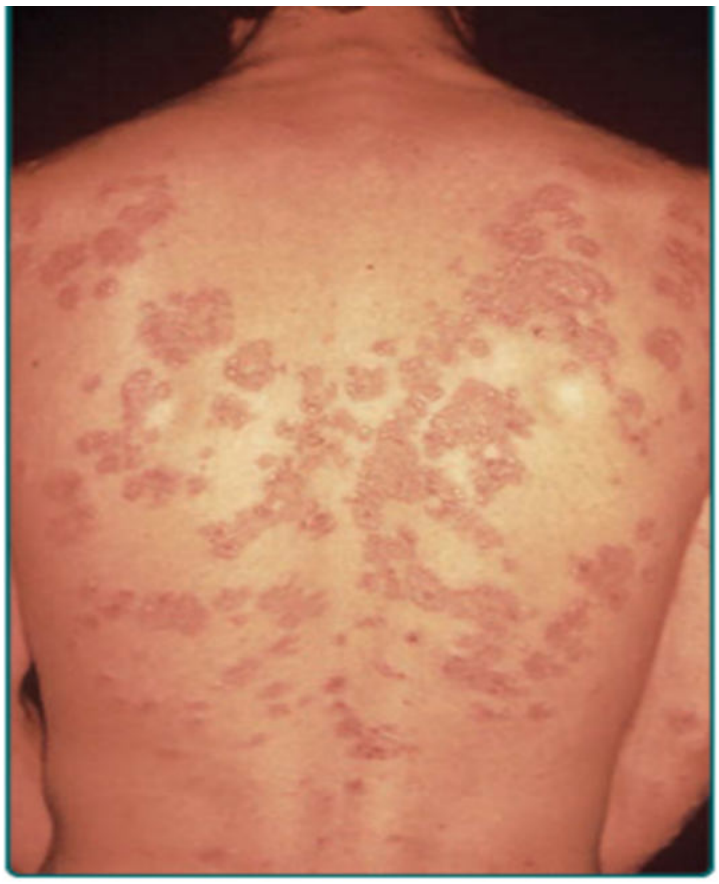
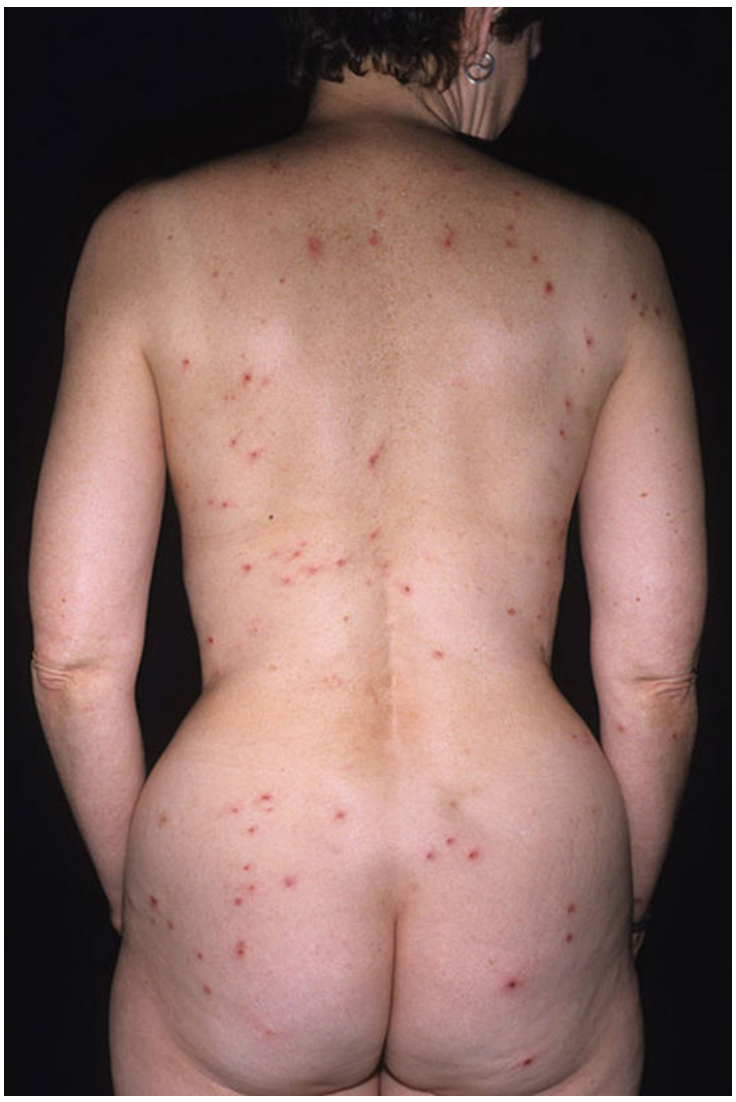
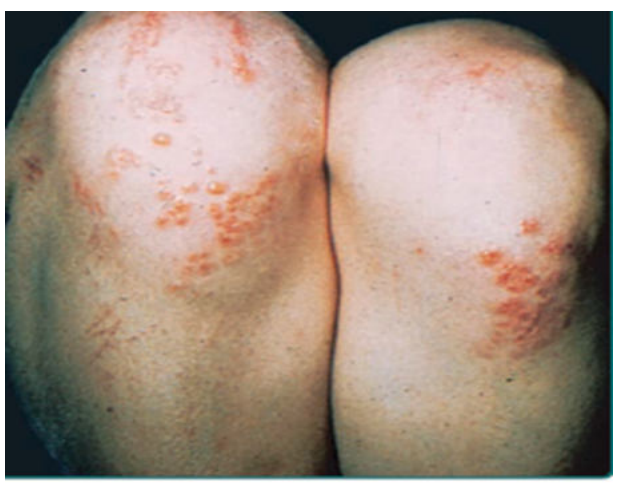


Figure 59-4 Pattern of distribution.







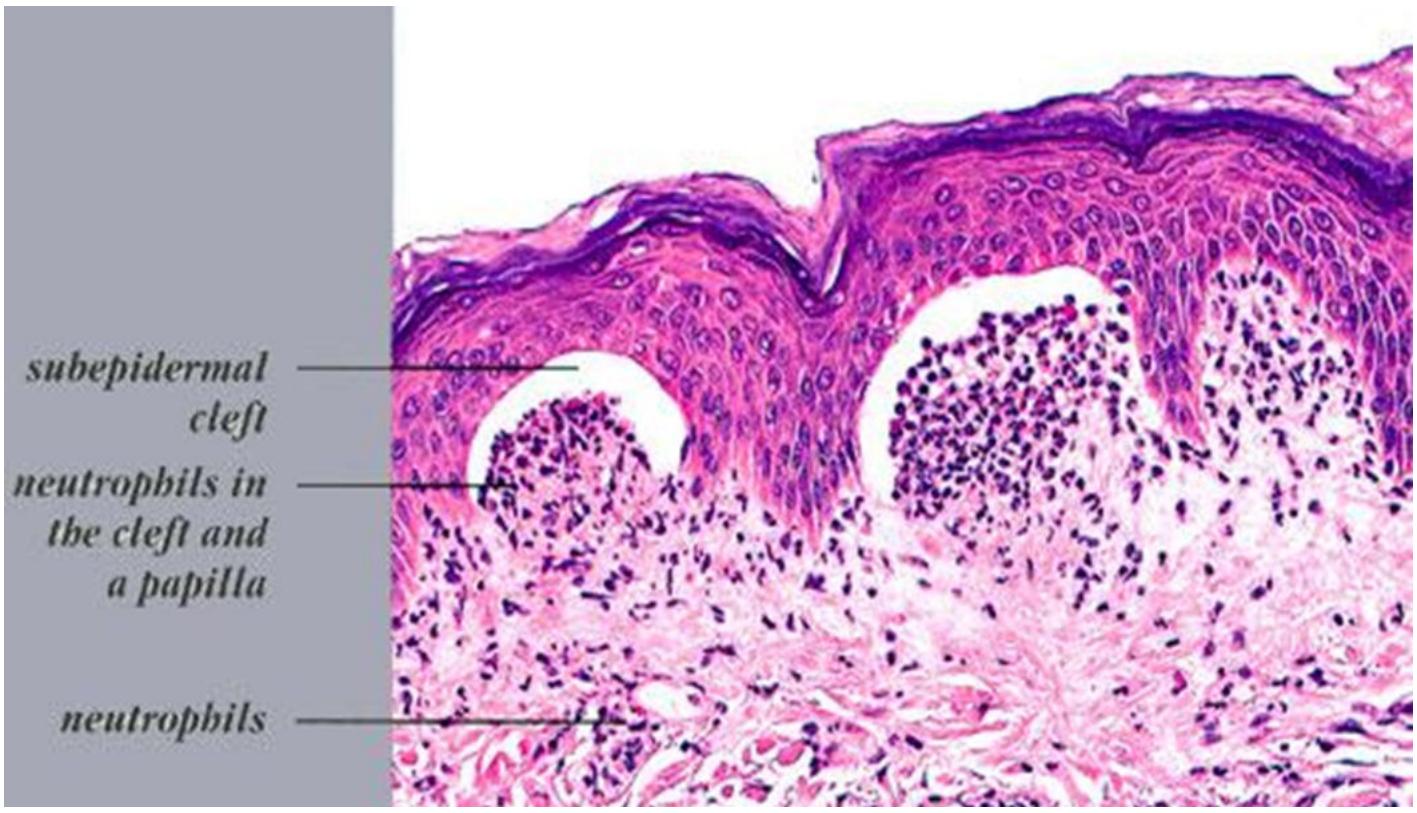
ASSOCIATIONS

Gluten Sensitive Enteropathy

- Gluten protein present in grasses of species Triticeae, eg. Wheat, rye, barley
- Due to non allergic sensitivity to gliadi fraction of gluten
- Usually asymptomatic
- Diarrhoea, steatorrhoea, abdominal distension, wt. loss

HISTOLOGY

- Neutrophillic microabscesses in tip of dermal papillae
- Slowly tips of dermal papillae separate from the epidermis
- Such cleft coalesce to form a subepidermal bullae



DIF

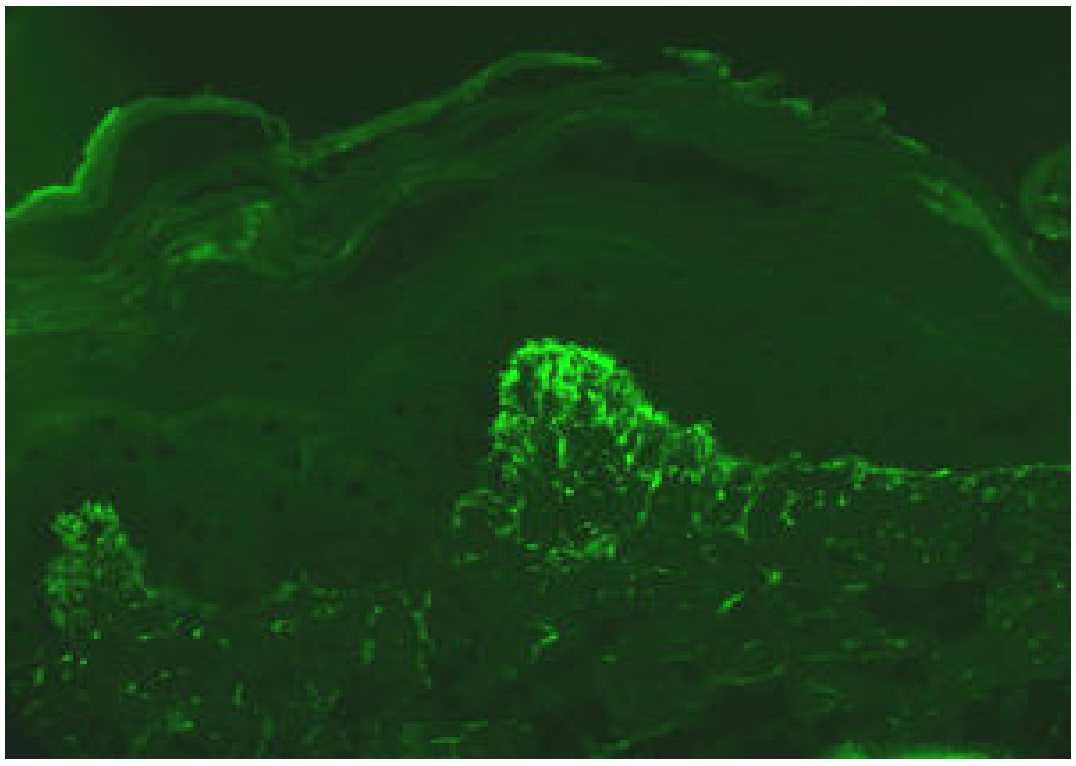
- Perilesional non involved skin – granular deposits of IgA in picket shaped appearance

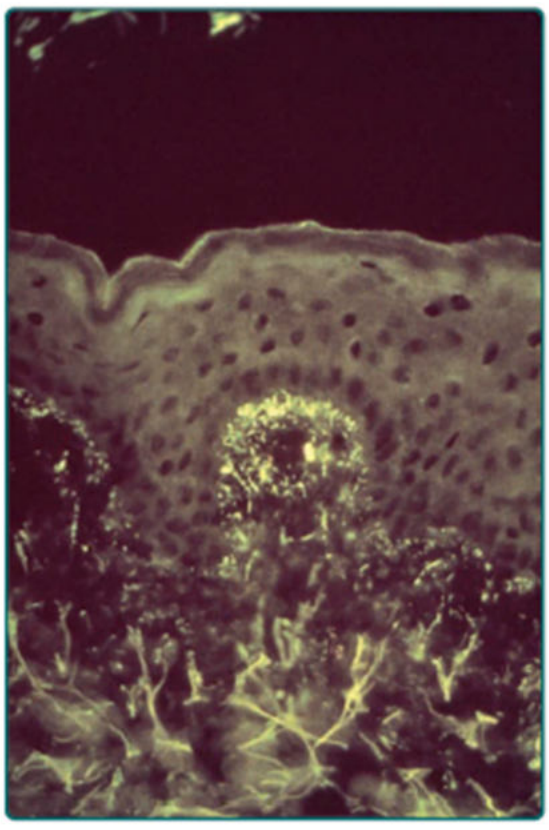
IIF-

- no circulating anti BMZ antibodies found

Immunoelectron Microscopy

- Amorphous grains of IgA deposits - DH bodies





D/D

- Papular urticaria
- Scabies
- Neurotic excoriations
- Erythema multiforme

TREATMENT

- Gluten free diet life long

- Dapsone 100-300mg daily
- Salfaslazine 0.5- 2g per day
- Colchicine 0.6 mg tid

THANK YOU