Useful clues in assessing blistering disorders

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Inflammatory dermatoses!!

Temptation =

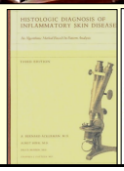
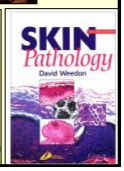
Look at clinical request form

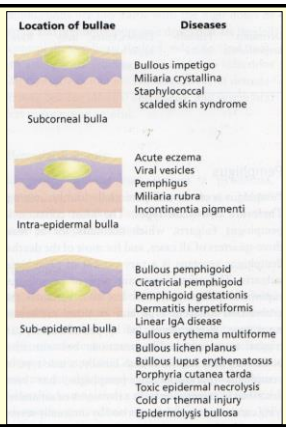
and agree / try to fit
with clinical suggestion

‘Blind’ reporting

- Look at slide ‘blind’ first without looking at request form

Inflammatory algorithms in textbooks



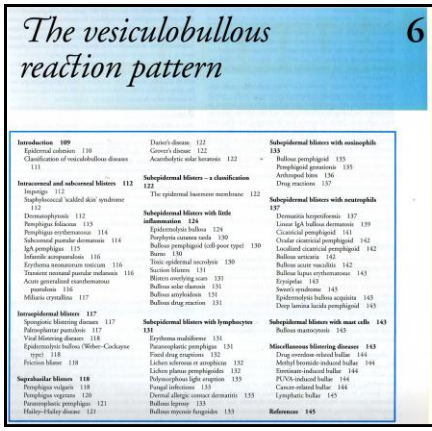
Intra-epidermal blistering

3 major mechanisms (Weedon)

- 1. Intercellular oedema (spongiosis) - eczema
- 2. Intracellular oedema (ballooning) - viral
- 3. Acantholysis - pemphigus

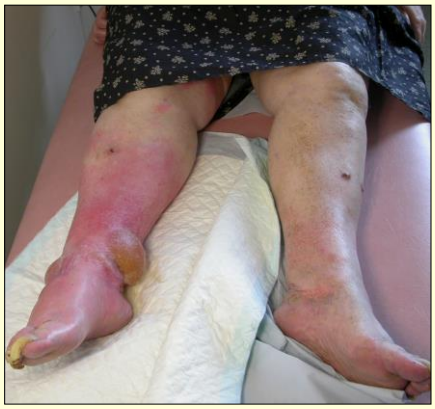
- (4. Individual cell necrosis – EM/SJS/TEN)

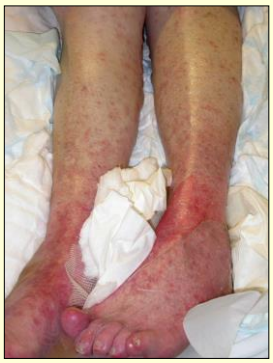
In some diseases more than one mechanism

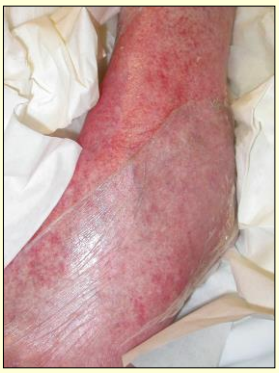


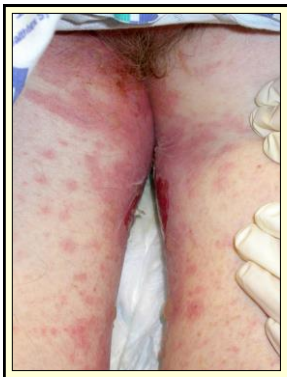
Blistering – clinical pitfalls

- Blistering is often a secondary event
  - e.g. cellulitis, vasculitis
- It can be difficult to determine the clinical level of the split
- Blistering maybe absent or subtle in true blistering disorders

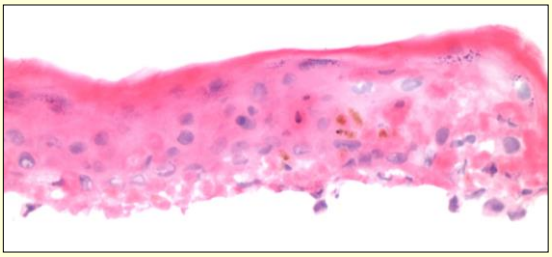








Frozen Section



This talk: Blistering – histological pitfalls

- 1. You can't see a blister!
  - Additional levels
  - 6 histological clues
- 2. You can see a blister, but doesn't seem to fit!
  - Diverse histological patterns in blistering disorders
  - Drug reaction
  - Dermatitis artefacta
  - Rarer condition

You can't see a blister: 'invisible dermatosis'

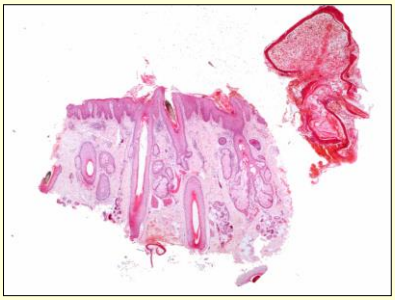
Consider:

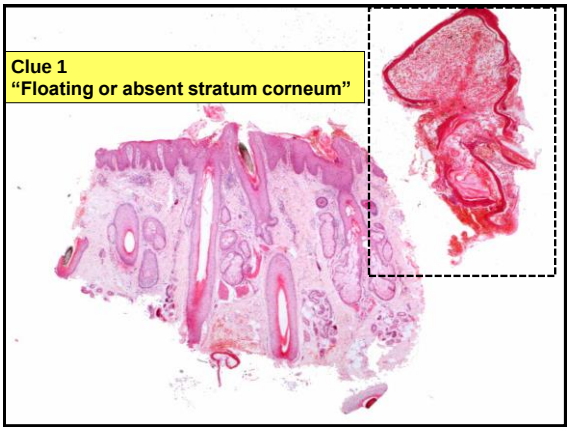
- Dermatitis herpetiformis
- Pemphigus foliaceous
- Grover's disease

- **Additional levels often necessary**
  - **Serial sections**

Case 1

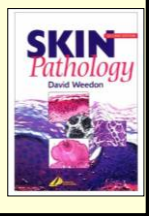
- 5 month history of erythematosquamous eruption with erosions on face, scalp, forehead and neck

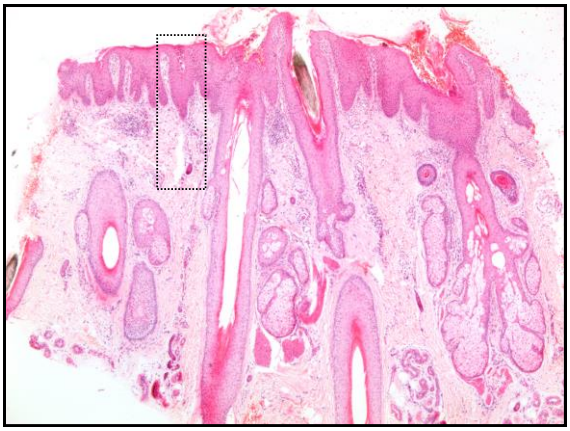


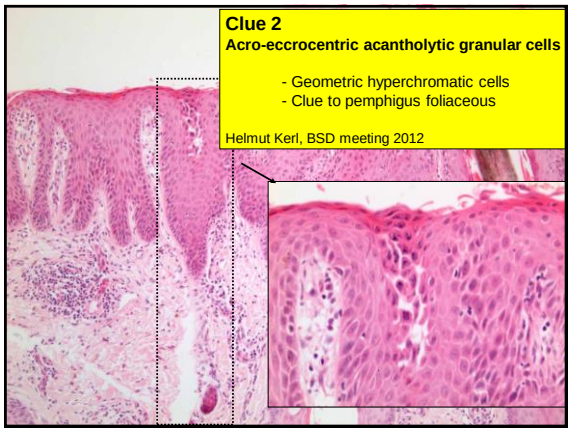


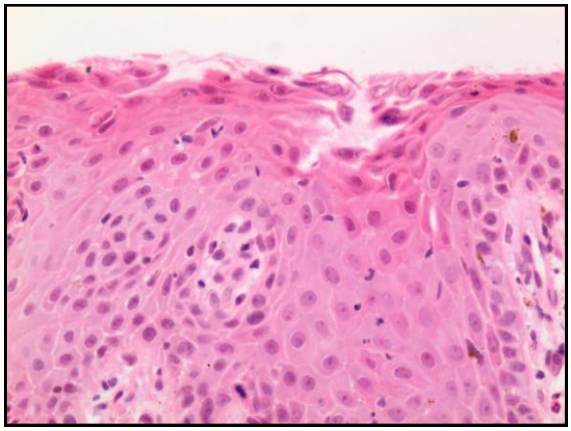
Floating or absent stratum corneum sign

- Clue to superficial (subcorneal) acantholytic blistering
  - **Pemphigus foliaceous**
  - **Bullous impetigo**
  - **Staphylococcal scalded skin syndrome**
  - Peeling skin syndrome
  - Psoriatic erythroderma
  - Artefact



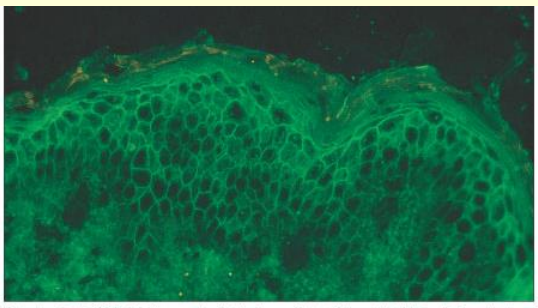


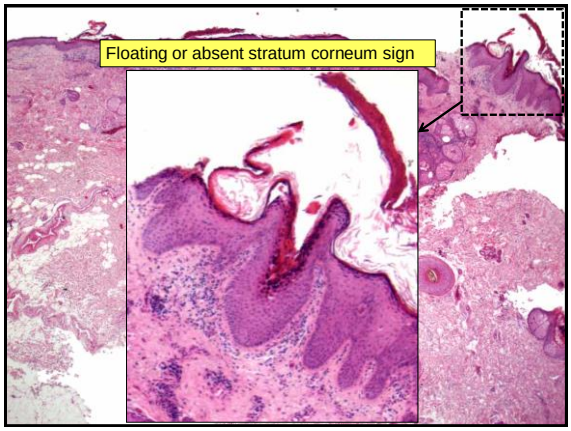


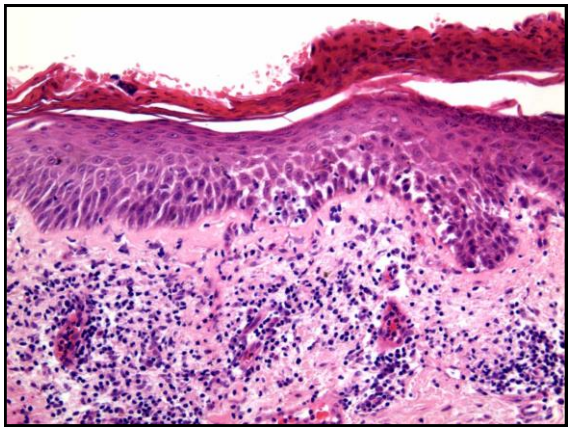


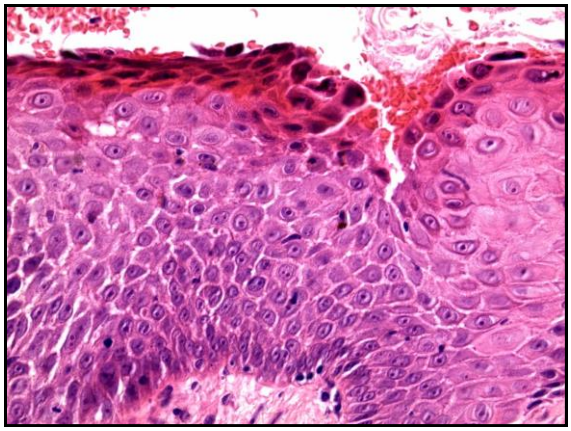
Immunofluorescence

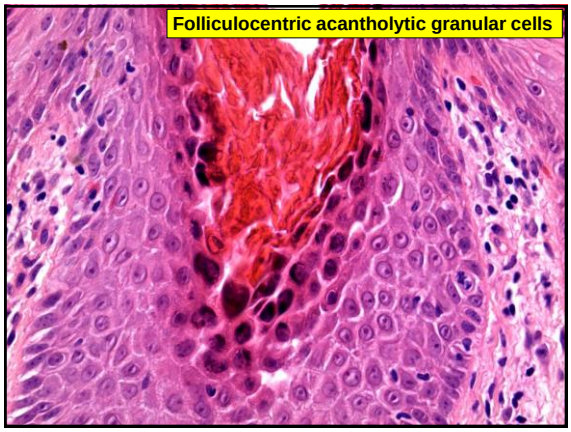
- Intraepidermal intercellular pattern

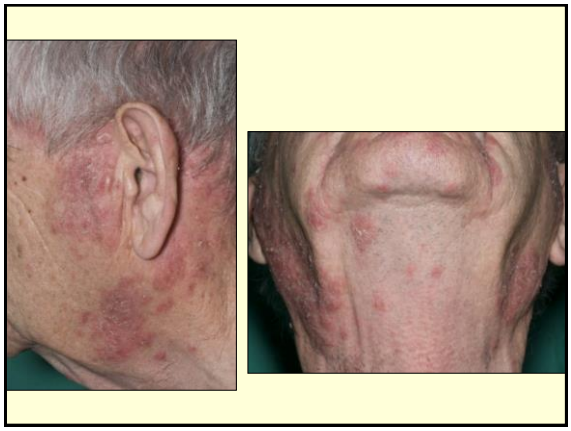


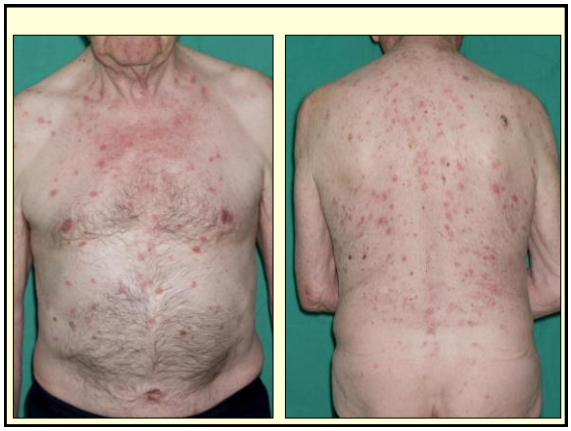


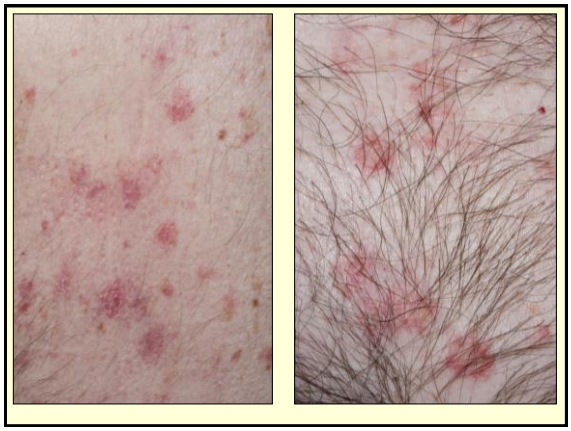


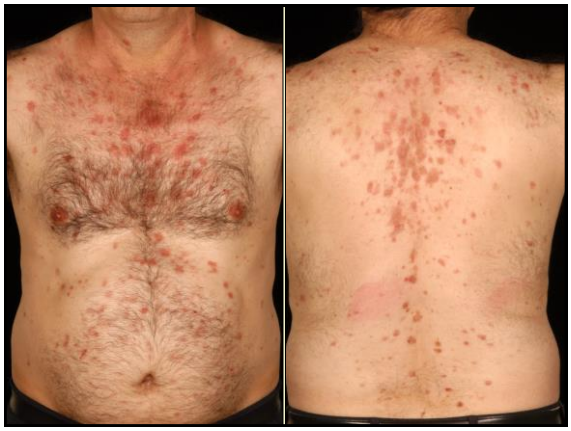


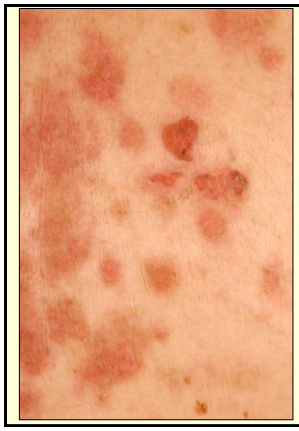












Erosions and blistering subtle!

Pemphigus foliaceous vs vulgaris

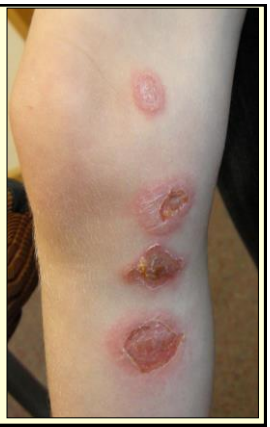
	Pemphigus foliaceous	Pemphigus vulgaris
Clinical morphology	Blisters and erosions subtle	Painful flaccid blistering
Mucosal involvement	Uncommon	Usual
Histology	Subcorneal acantholysis, may be subtle	Suprabasal acantholysis with adnexal involvement
Indirect immunofluorescence	Stains human skin strongly	Stains monkey oesophagus strongly
ELISA	Dsg-1 ++, Dsg-3 -	Dsg-1 +/-, Dsg-3 ++

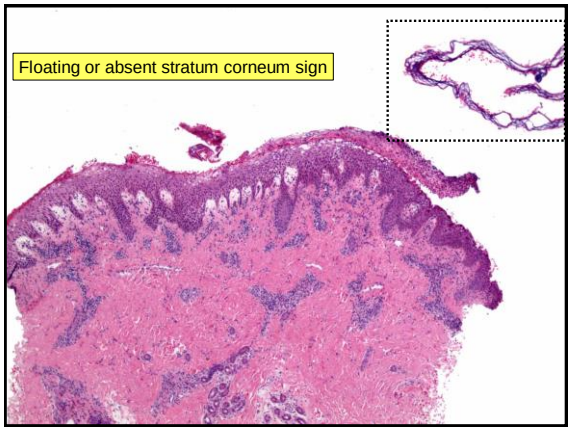
Case 2

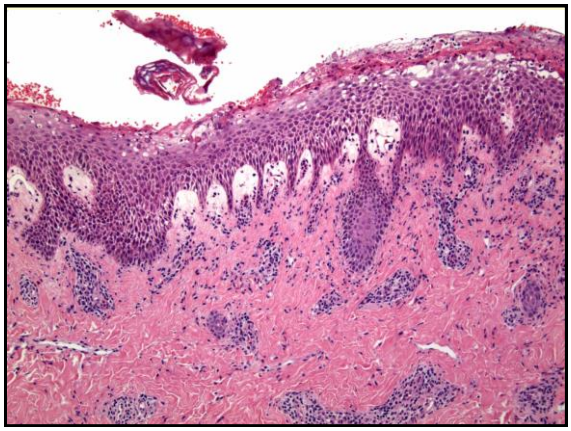
- 6-year-old child
  - 7 days history of bullous lesions right leg

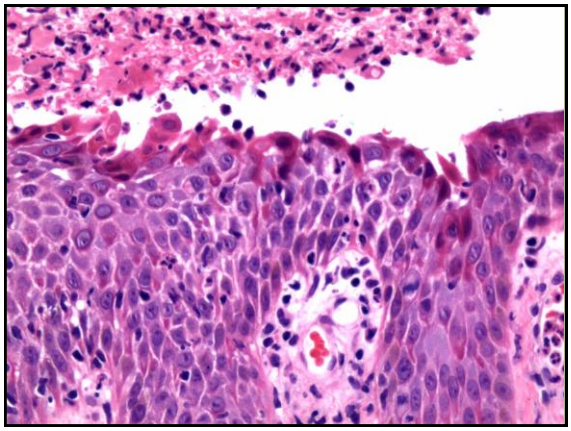
?Exaggerated response to insect bites

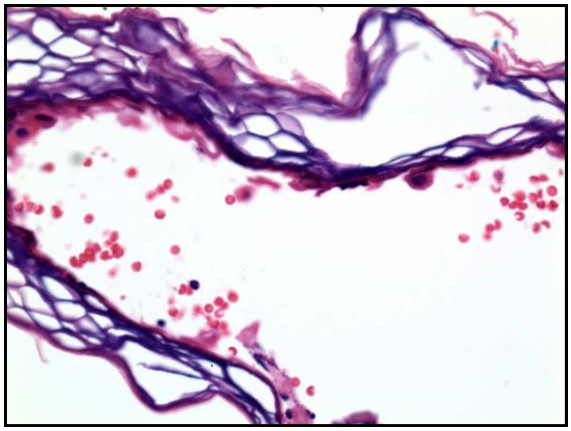
?Bullous disease of childhood

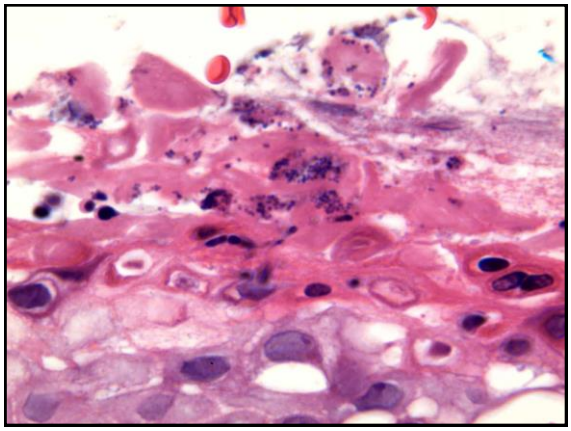


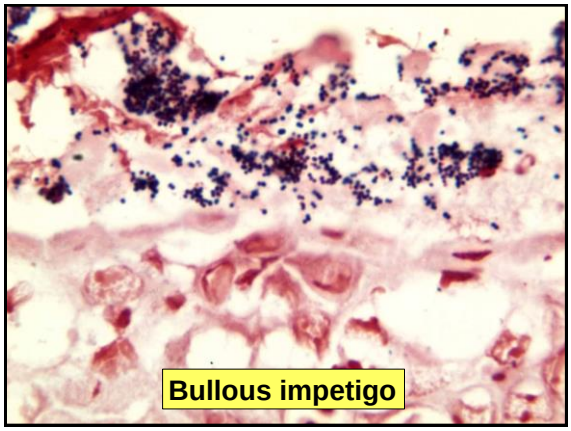




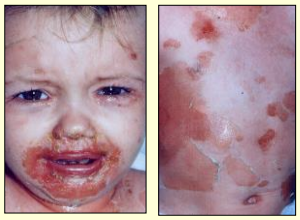








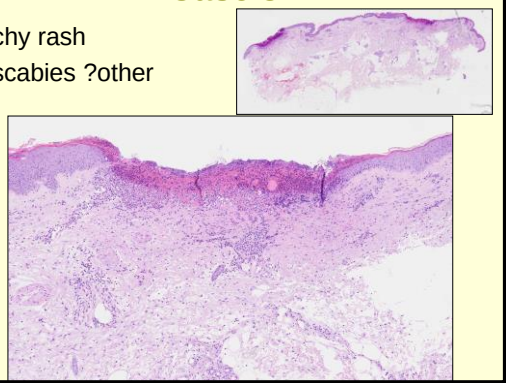
Staphylococcal Scalded Skin Syndrome

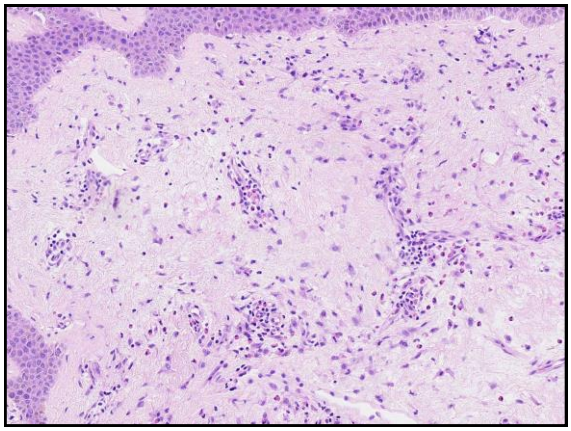


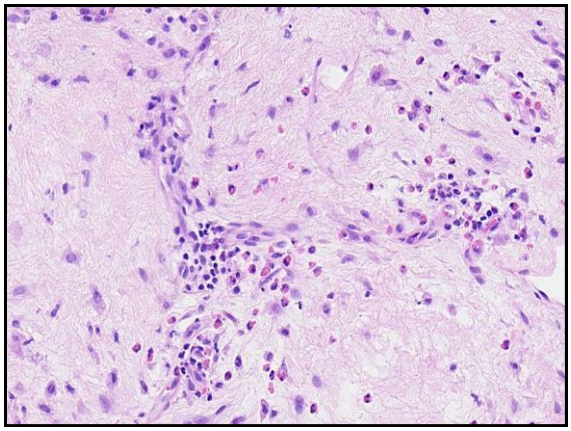
- Widespread blisters
- Exfoliative toxin produced by *Staphylococcus aureus*
- Organism **not** identifiable/cultured from affected skin

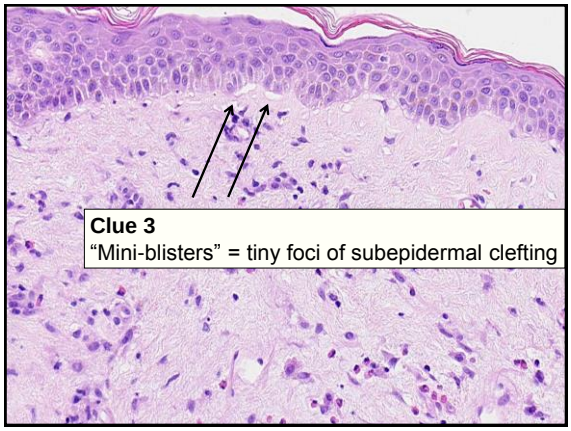
Case 3

- Itchy rash
  ?scabies ?other



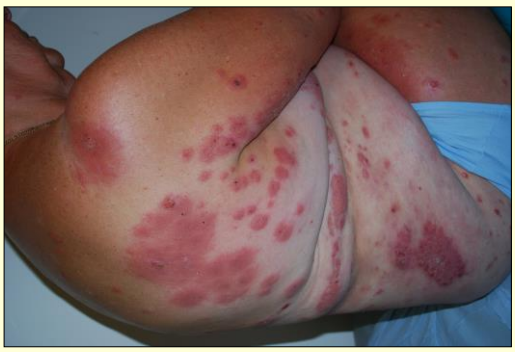




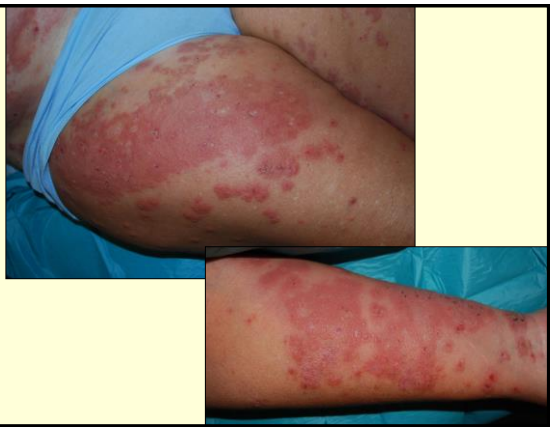


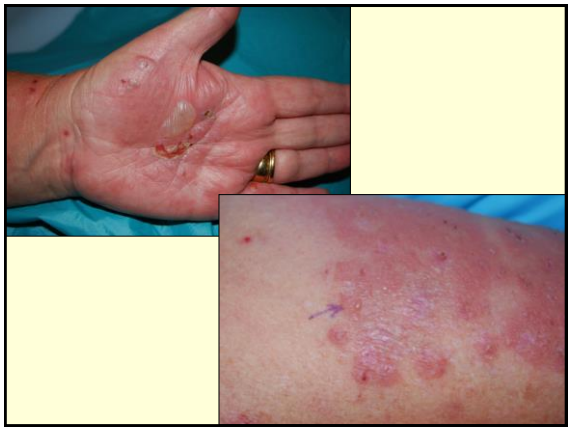
Prebullous pemphigoid

- Immunofluorescence:
  Subepidermal IgG and C3 deposition
- Consider if:
  Dermal eosinophils +/- spongiosis
  ‘Mini-blisters’



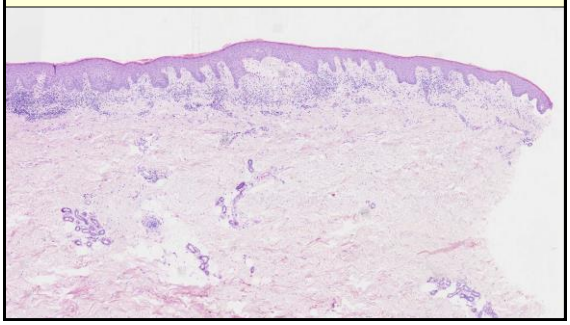
Courtesy of Dr Robert Charles-Holmes

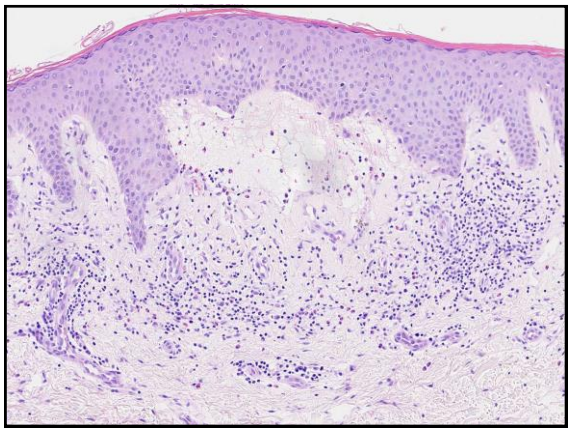


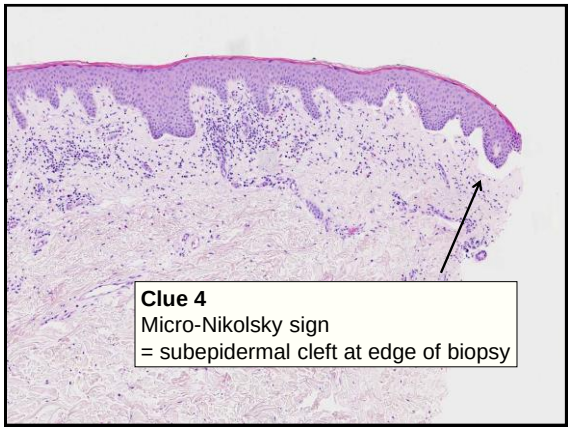


Case 4

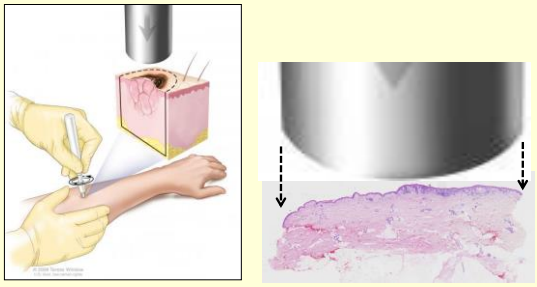
- Itchy urticated plaque on flank





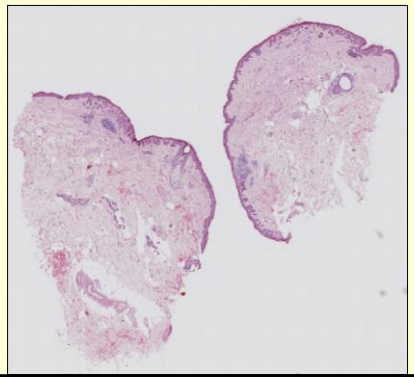


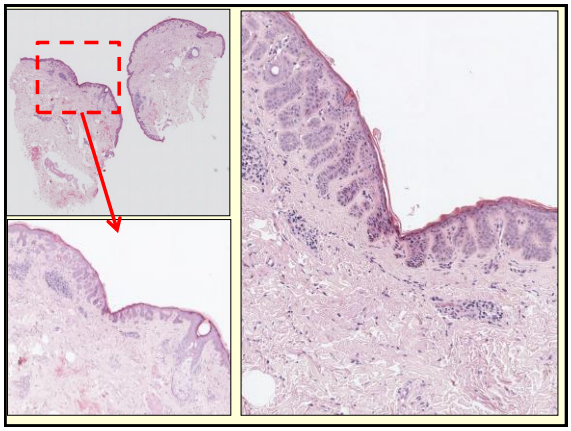
Micro-Nikolsky sign:
D Metze, ISDP Barcelona 2011

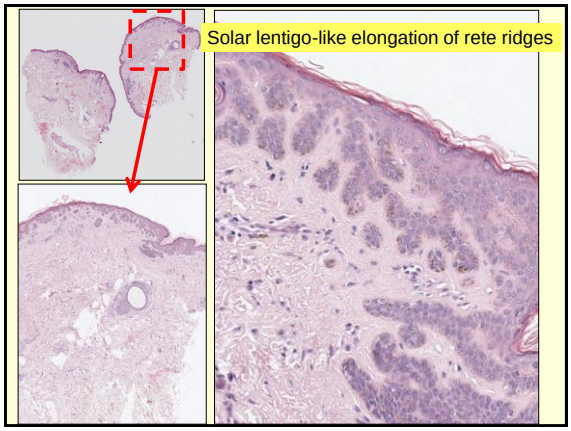


Shearing force of rotation of punch produces blister at edge

Case 5
• F78 - Itchy red papules

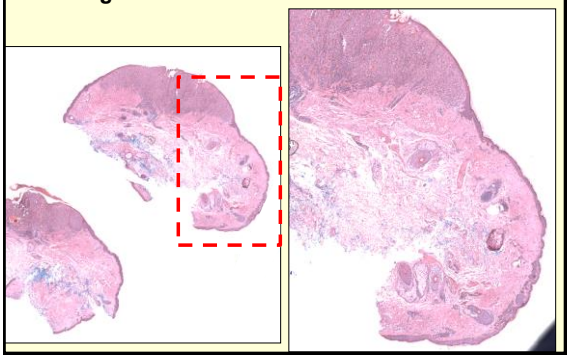


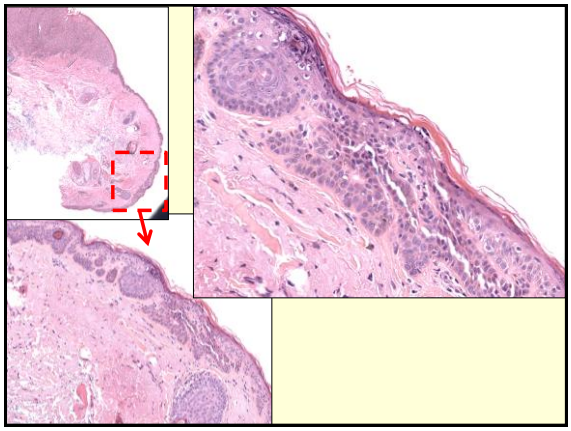




Same patient – Pigmented lesion neck

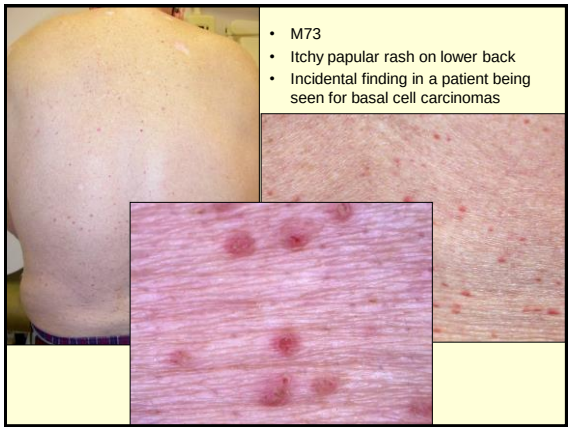
Malignant melanoma …….. and ……..?





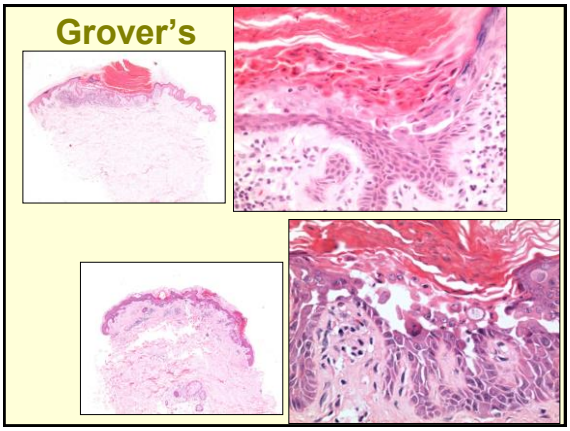
Grover's Disease

- Transient acantholytic dermatosis
- Middle aged/elderly
- Widespread itchy lesions, especially trunk
- Discrete pink papules & papulovesicles
- Often persists for months or years



- M73
- Itchy papular rash on lower back
- Incidental finding in a patient being seen for basal cell carcinomas

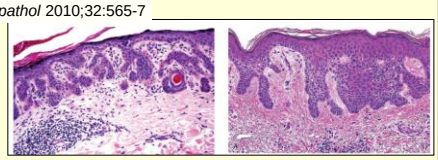
Grover's



Early Histopathologic Changes in Grover Disease

Priti M. Melwani, MD, Amy C. Parsons, MD,† and Omar P. Sangueza, MD‡*

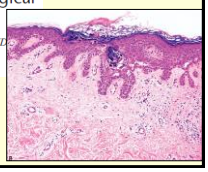
Am J Dermatopathol 2010;32:565-7



Grover Disease: A Reappraisal of Histopathological Diagnostic Criteria in 120 Cases

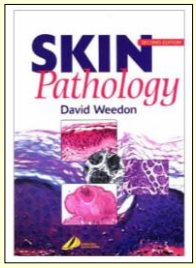
María-Teresa Fernández-Figueras, MD, Luis Puig, MD,‡ Pablo Cannata, MD,§ Miriam Cuatrecases, MD,§ Ariadna Quer, MD,* Carlos Ferrándiz, MD,† and Aurelio Ariza, MD**

Am J Dermatopathol 2010;32:541-9



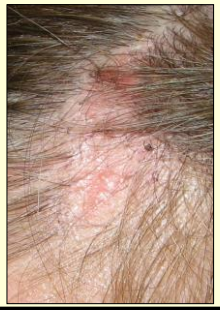
Clue to Grover's disease

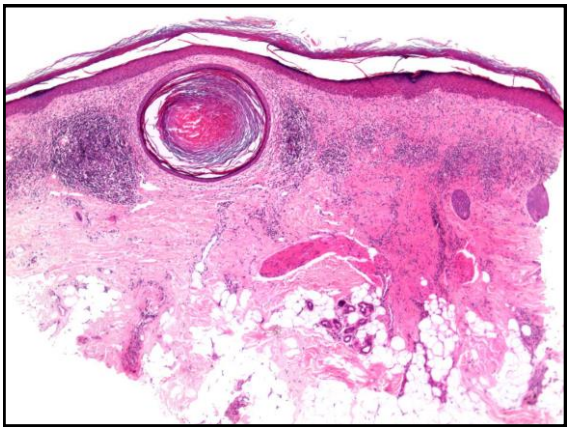
- **Late lesions have elongated rete ridges and may resemble solar lentigo**



Case 6

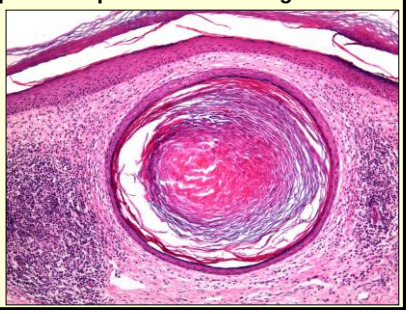
- F60. 5/12 erythematous scaly patch with scarring, alopecia and milia. ? BCC

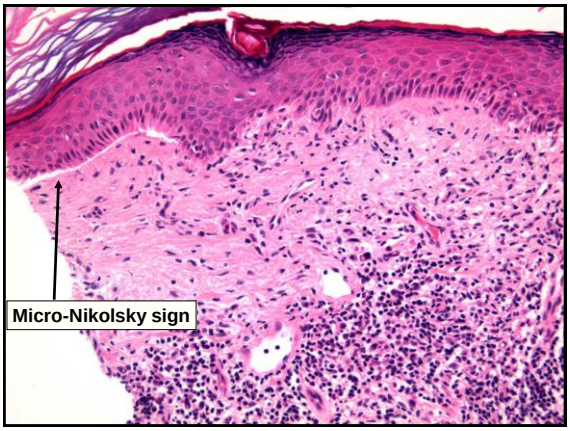


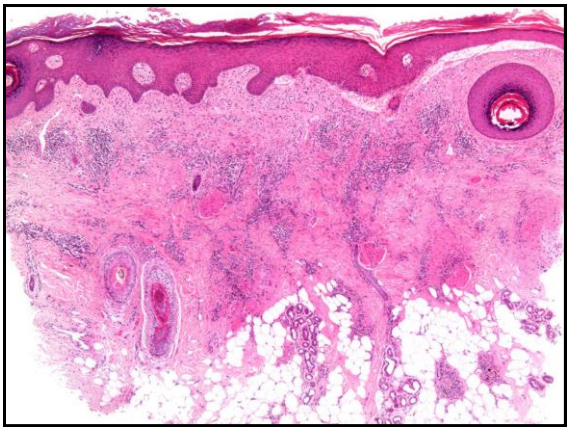


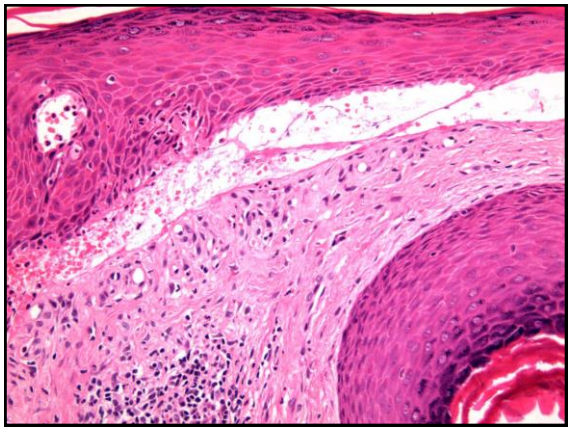
Clue 6

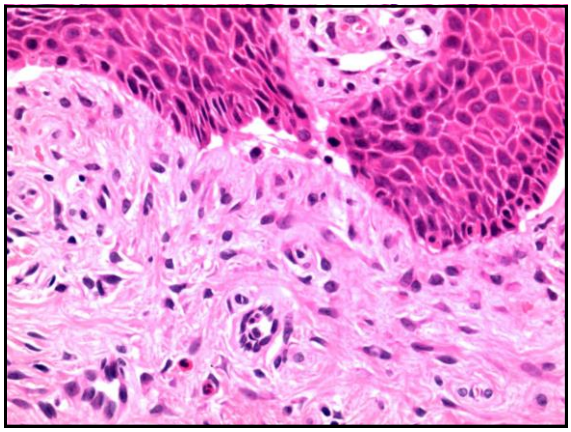
- **Milia with scarring = Clue to deeper sub-epidermal blistering disorder**











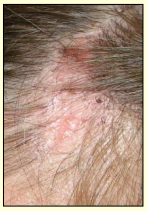
Be brave!

Richard Carr's report (summary):

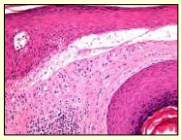
Dense lymphoplasmacytic infiltrate with vascular proliferation and papillary dermal fibrosis. Occasional eosinophils. Subepidermal clefting over a wide area, especially in specimen B.

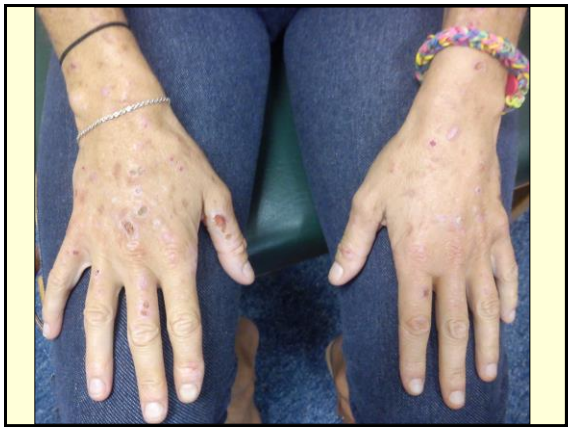
Although regression of tumour is a possibility we have also considered cicatricial pemphigoid.

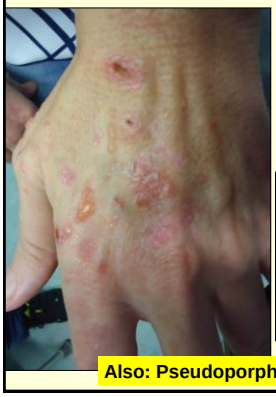
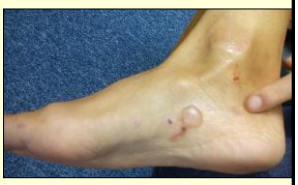
Brunstig-Perry pemphigoid



- **Immunofluorescence: Linear IgG deposition along basement membrane zone**
- **Variant of cicatricial pemphigoid**
  - **Lesions limited to forehead & scalp**

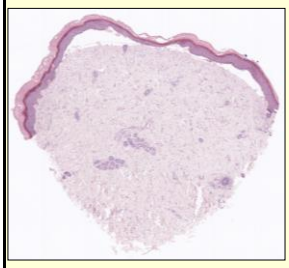
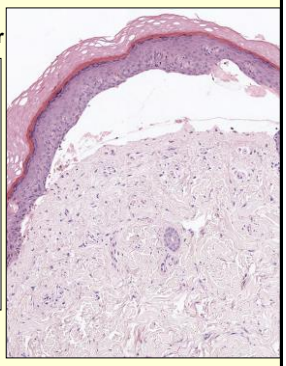


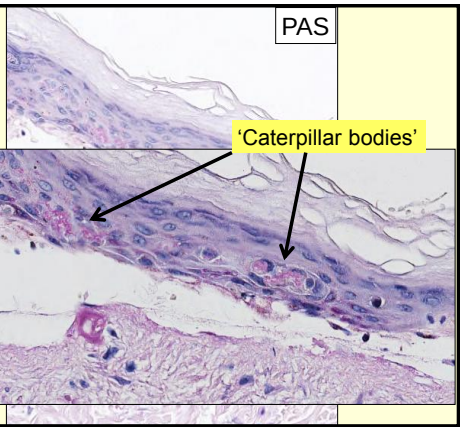


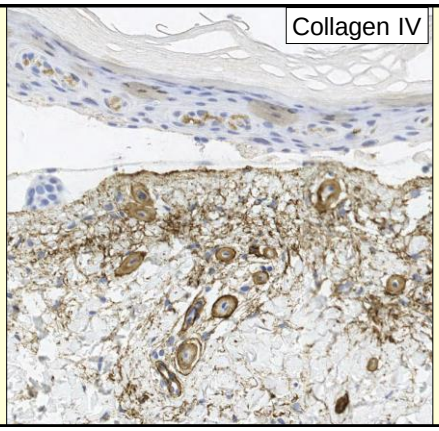



Also: Pseudoporphyria caused by naproxen

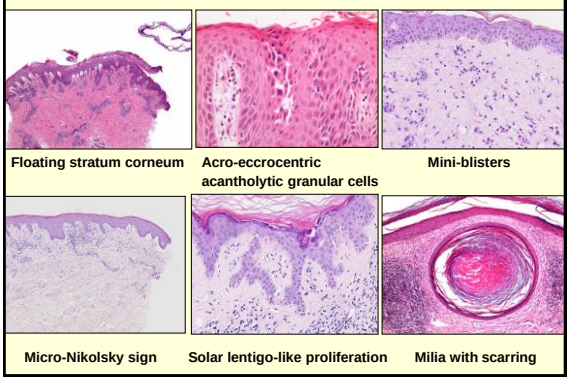
'Cell-poor' subepidermal blister





6 histological clues to subtle blistering disorder



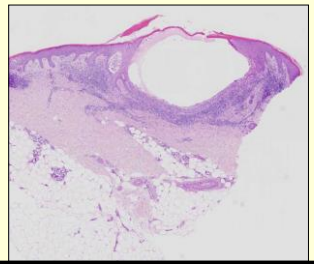
When you can see a blister, but doesn't seem to fit!

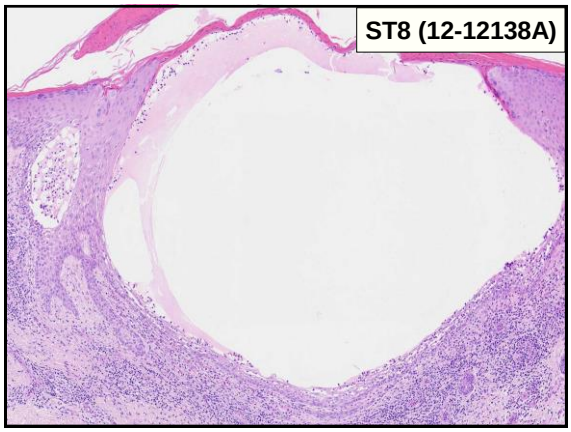
- Diverse histology of common blistering disorders
- Drugs
- Dermatitis artefacta
- Rarer entities

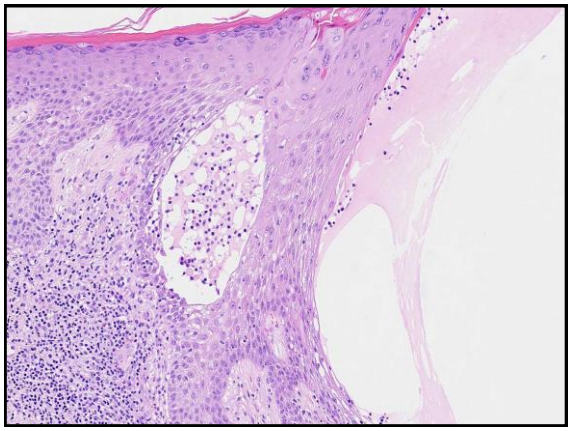
Diverse histology of common blistering disorders

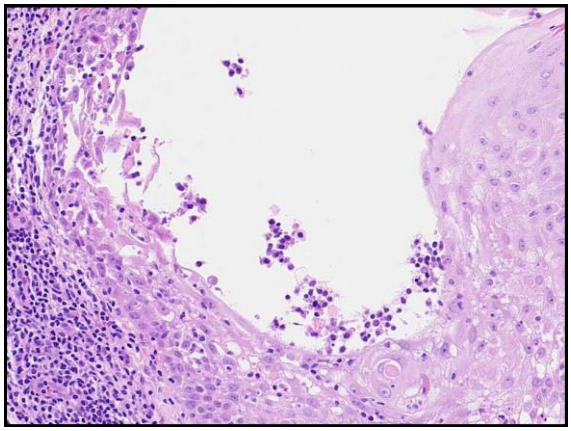
Case 7

- Itchy rash trunk & legs





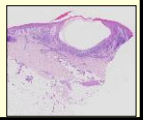


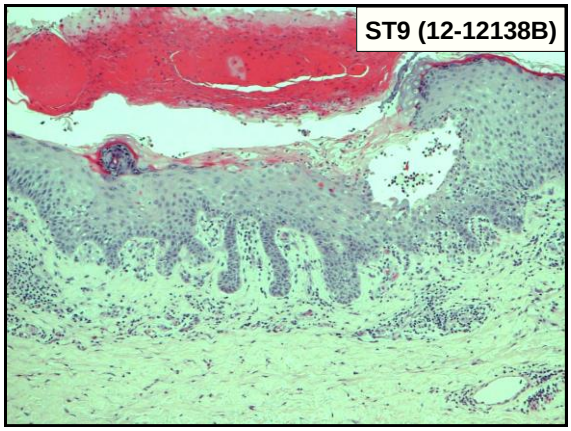


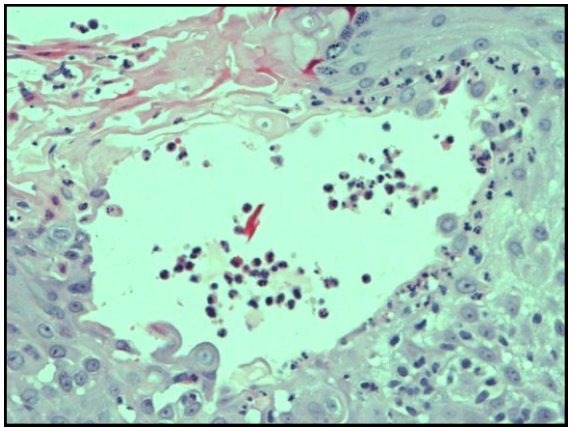
Grover's histology

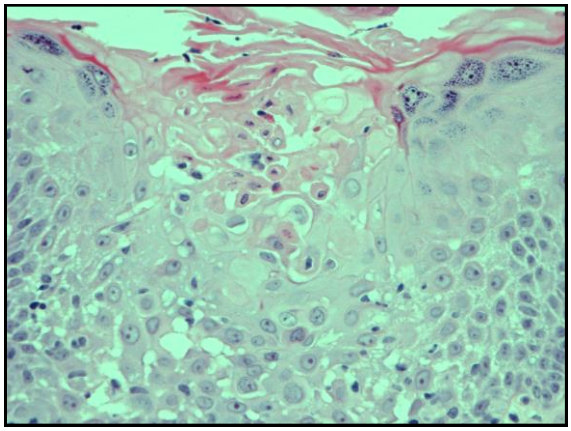
Patterns:

- DARIER-like
  - Acantholytic dyskeratosis
- HAILEY-HAILEY-like
  - Prominent acantholysis throughout epidermis
- PEMPHIGUS VULGARIS-like
  - Suprabasal clefting with sparse acantholytic dyskeratosis
- **SPONGIOTIC**
  - **Acantholytic cells within spongiotic foci**





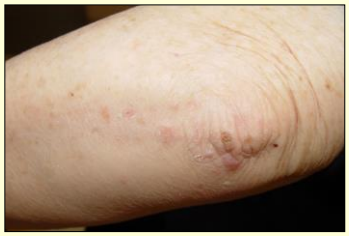


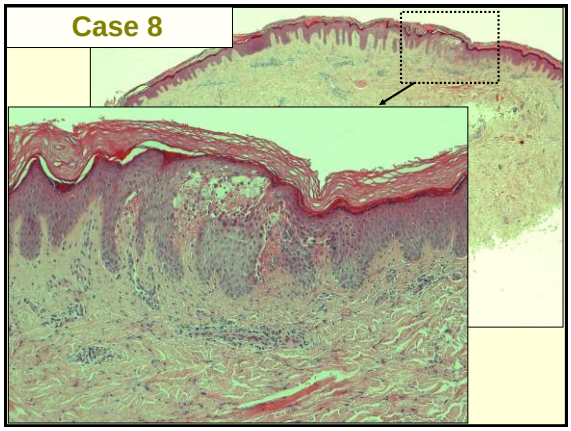


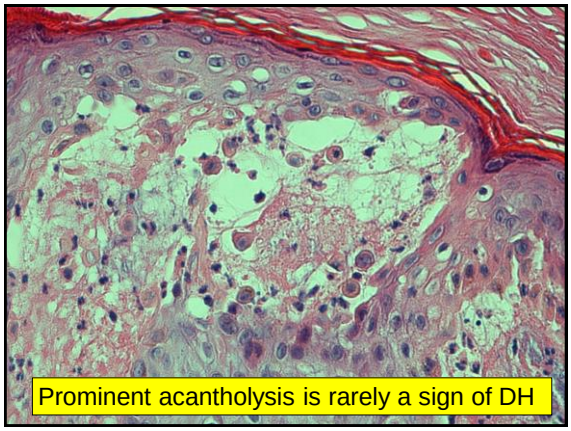
Diverse histology of common blistering disorders

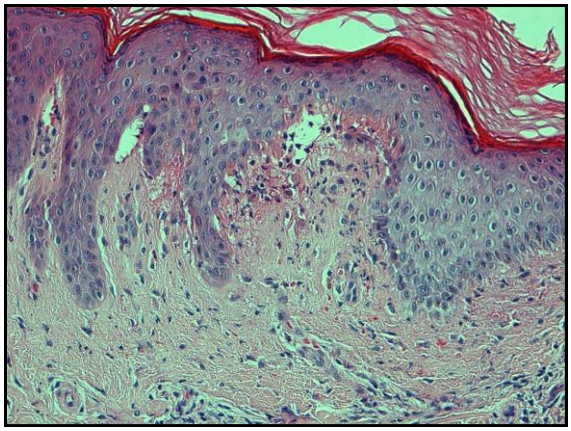
Case 8

- Itchy vesicles knees & elbows

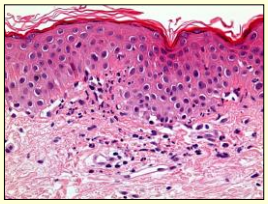




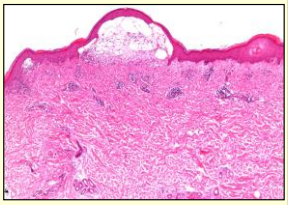




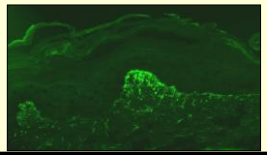
Dermatitis herpetiformis – the usual



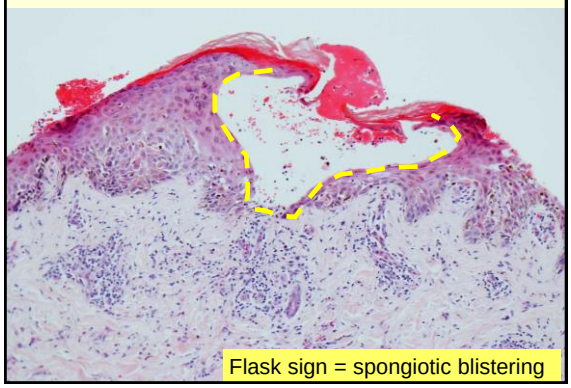
Papillary dermal microabscess

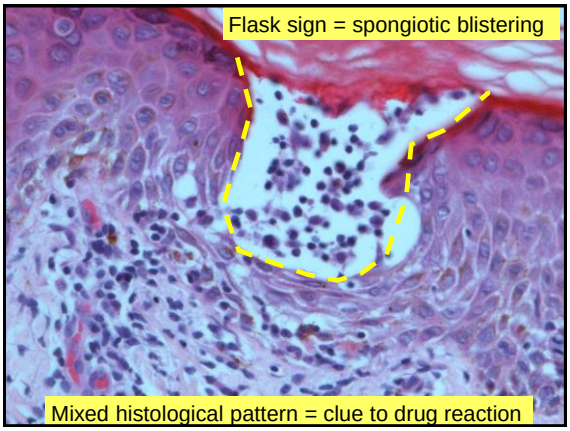


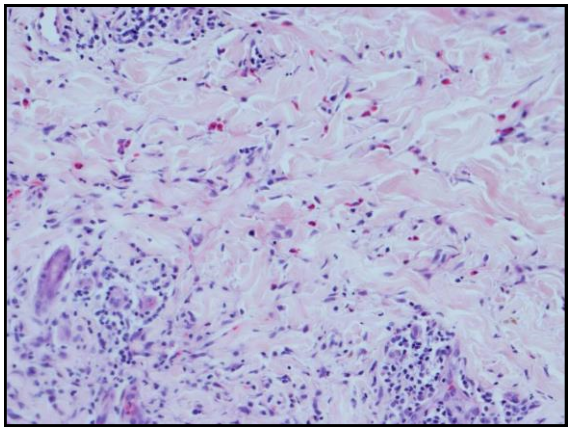
Subepidermal blister with neutrophils

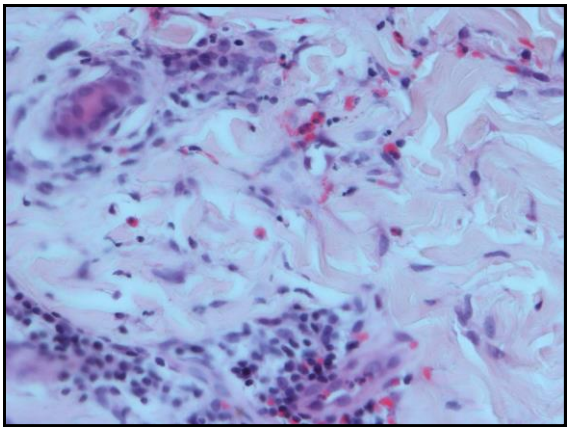


Case 9



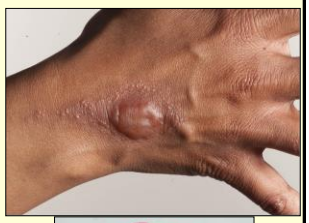


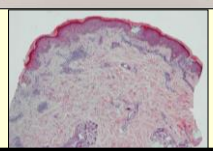




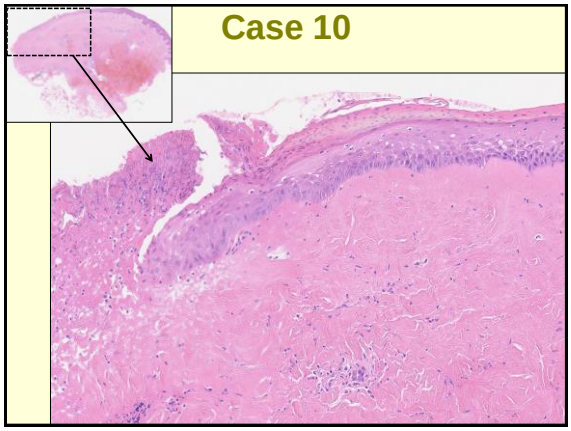
Case 9 - continued

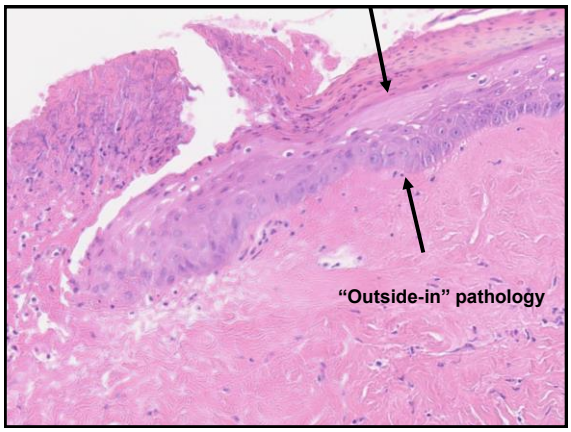
- 39 year old female, metastatic breast cancer
- Blistering dorsum right hand 6 days after first infusion of docetaxel, localised to infusion site
- Mixed inflammatory pattern
  - THINK DRUG REACTION

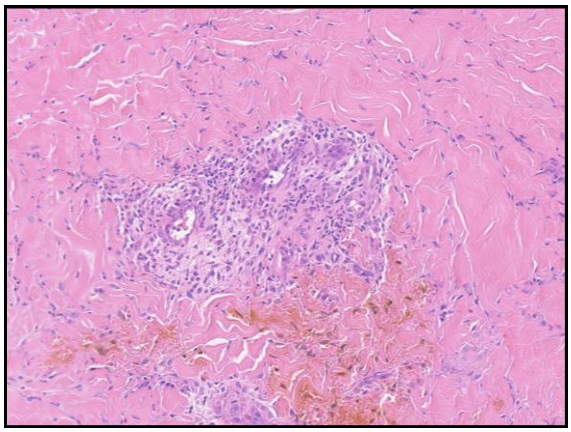




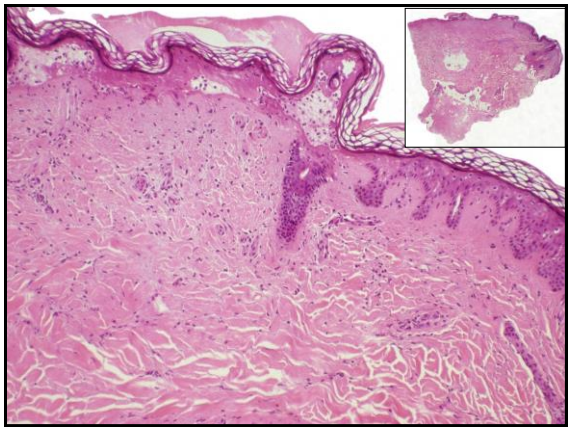
Case 10

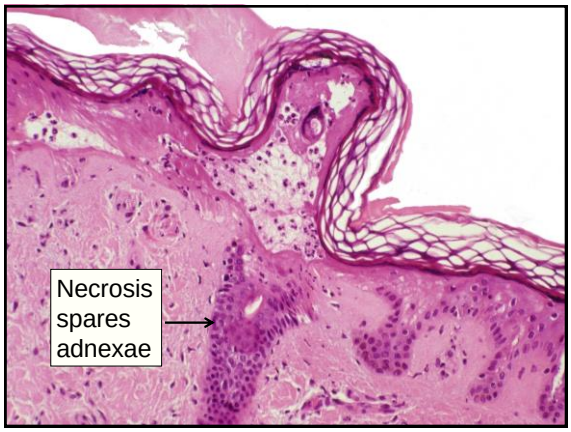


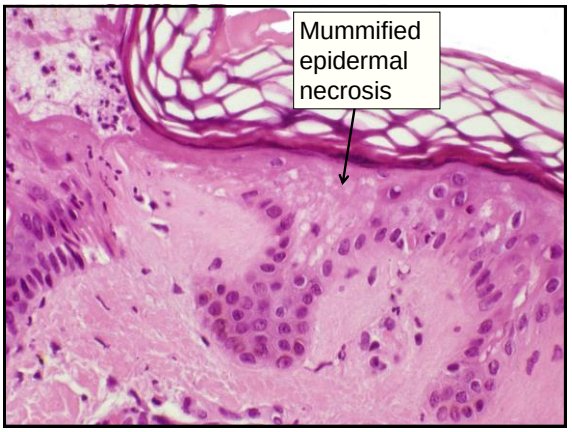




Courtesy of Wolfgang Weyers







Histological clues to dermatitis artefacta

Joe EK et al. Cutis 1999;63:209-14

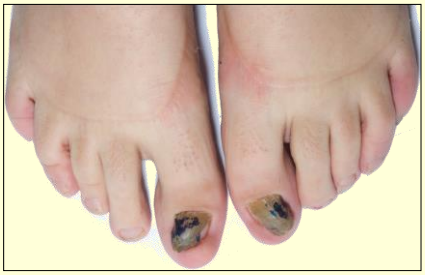
- Doesn't fit with known bullous disorder
- Sharply demarcated ulcer or blister
- Mummified pattern of epidermal necrosis sparing adnexal epithelium
- 'Outside-in' – spinous layer predilection
- Fibrin & superficial neutrophilic infiltrate
- Vessels show red cell extravasation and fibrin localised to area of epidermal injury

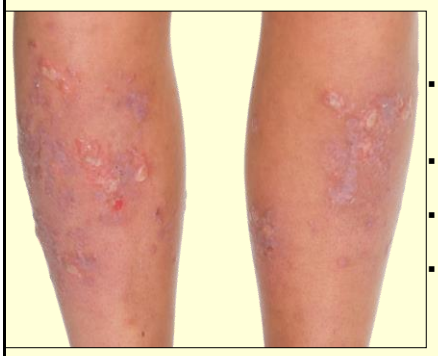
When you can see a blister, but doesn't seem to fit!

- Diverse histology of common blistering disorders
- Drugs
- Dermatitis artefacta
- **Rarer entities**

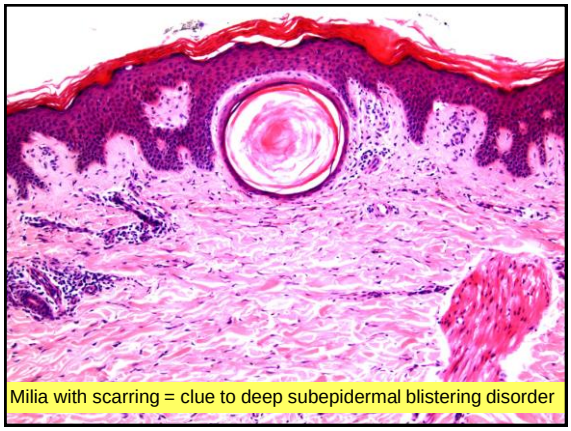
Case 11

- Dystrophic nails
- Itchy plaques on shins

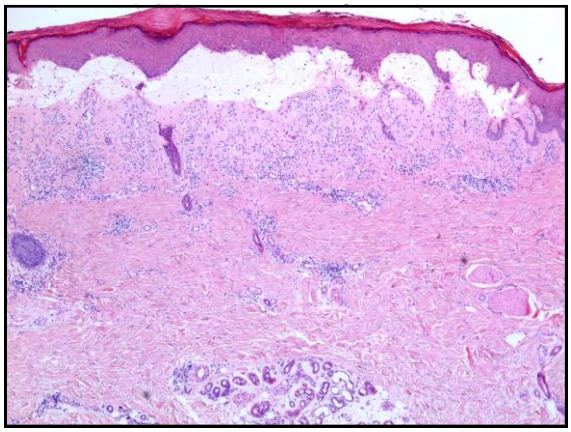


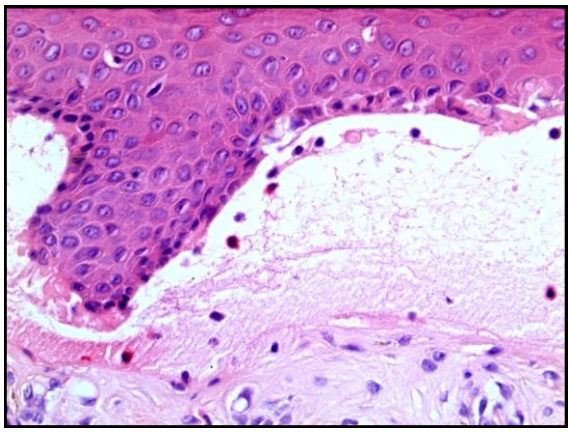


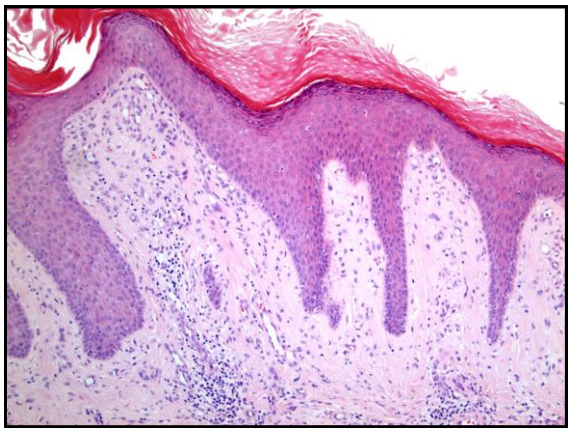
- Violaceous plaques
- Intact blisters
- Milia
- Scarring

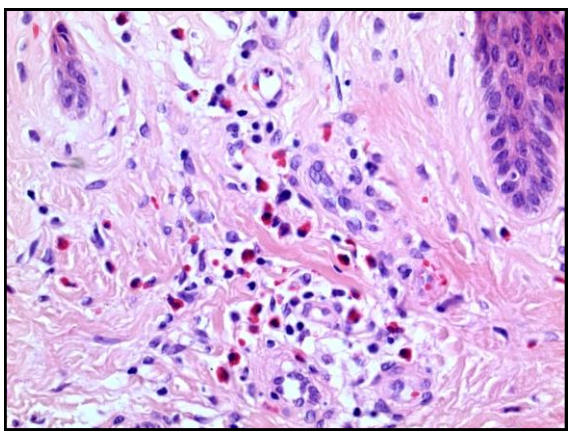


Milia with scarring = clue to deep subepidermal blistering disorder





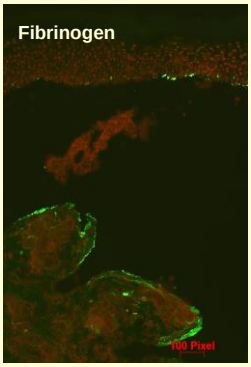


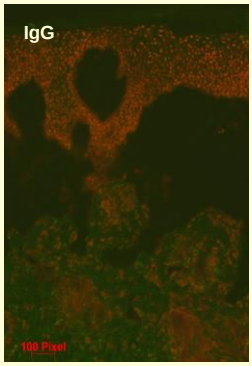


Histology summary

- Milia
- Scarring
- Subepidermal blister
- Lichenification
- Inflammation including eosinophils

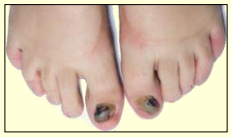
- ?immunobullous disorder e.g. pemphigoid





Courtesy of Balbir Bhogal, St John's Institute of Dermatology

Family history



Mutation analysis of *COL7A1*

(+/-) c.6215A>G,p.Gln2072Arg, exon 74

→ Dominant dystrophic epidermolysis bullosa pruriginosa

British Journal of Dermatology (1994) 130, 617–625.

Epidermolysis bullosa pruriginosa: dystrophic epidermolysis bullosa with distinctive clinicopathological features

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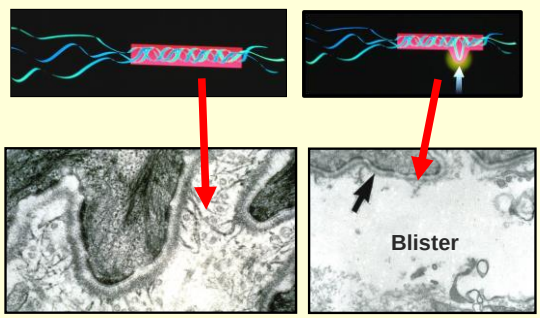
Accepted for publication 22 October 1993

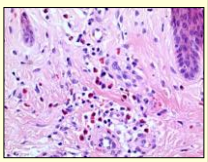
- 1st described by Kuske in 1946[1]
- Term EB 'pruriginosa' coined by McGrath et al in 1994[2]
- Rare subtype of DEB[3]
- Autosomal dominant / autosomal recessive / sporadic
- Late onset disease not uncommon

1. Kuske H. *Dermatologica* 1946; 91: 304–5
2. McGrath et al. *Br J Dermatol* 1994; 130: 617–25
3. Schumann H et al. *Br J Dermatol* 2008;159:464-469



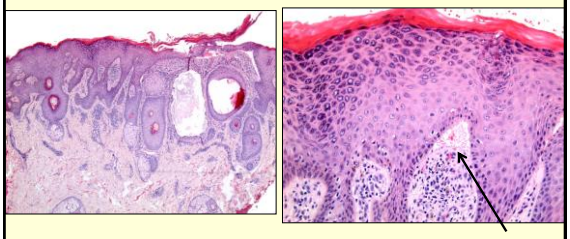
EB pruriginosa – learning points

- Hereditary condition BUT……..
  - Late onset
  - Significant intra-familial variability
- Unusual clinical features
  - Pruritic
  - May lack blisters
- Histological features
  - Milia with scarring +/- blister
  - Inflammation including eosinophils



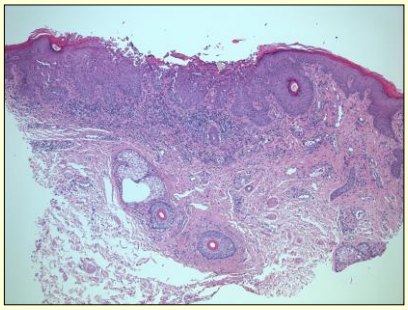
The sister

- Dystrophic nails
- Itchy blisters / papules neck

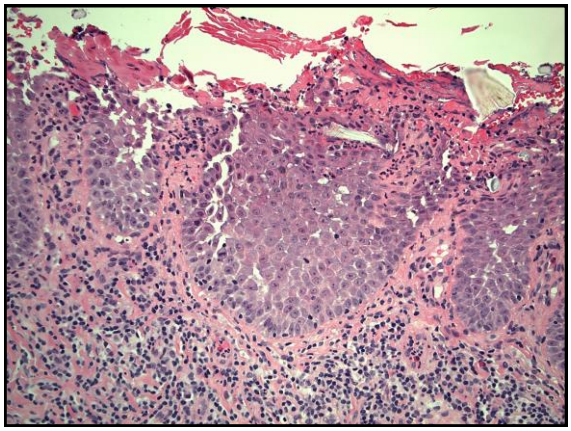


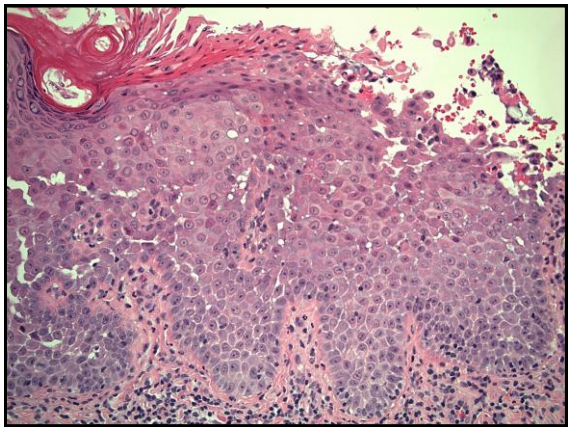
Case 12

Female with itchy papular rash in genital region

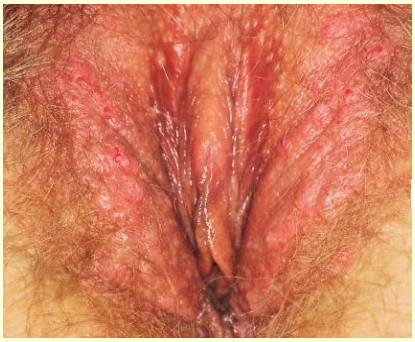


Courtesy of Luisa Motta





Acantholytic dermatosis of the genitocrural area



c/o Dr F Plantier

Acantholytic dermatosis of the genitocrural area

- Papular acantholytic dermatosis
- Confined to vulvocrural region (thigh and perineum) in middle-aged females
- Pruritic, keratotic papules, nodules or plaques
- Family history is negative c.f. Hailey-Hailey
- Pathogenesis unknown.
  - Moist environment – Infection ?
- IMF negative

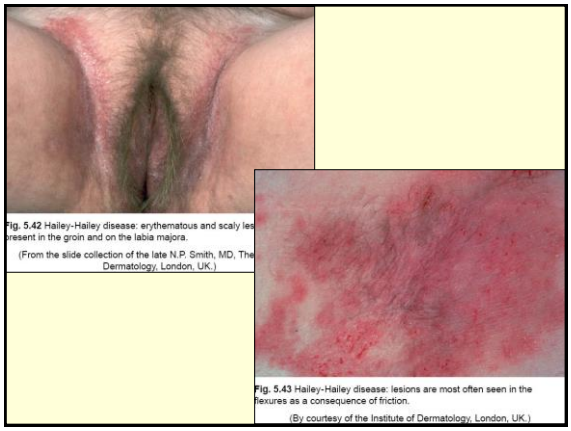
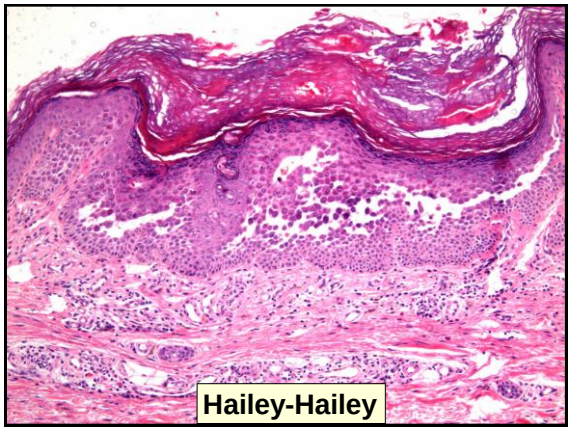
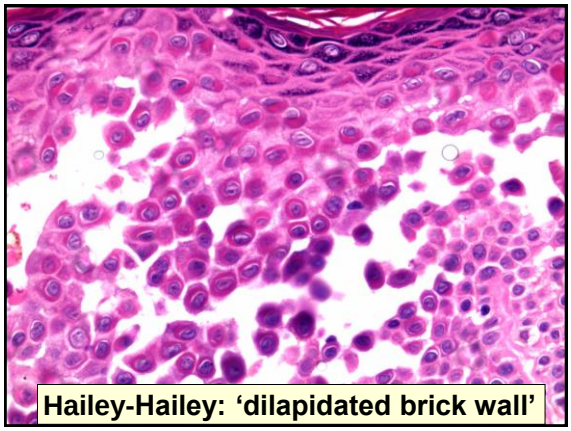


Fig. 5.42 Hailey-Hailey disease: erythematous and scaly les present in the groin and on the labia majora.
(From the slide collection of the late N.P. Smith, MD, The Dermatology, London, UK.)

Fig. 5.43 Hailey-Hailey disease: lesions are most often seen in the flexures as a consequence of friction.
(By courtesy of the Institute of Dermatology, London, UK.)





Summary

Blind reporting

When you can't see a blister!
- Serial sections / levels
- 6 histological clues

When you can see a blister, but doesn't seem to fit!
- Diverse histology of common blistering disorders
- Drug reactions
- Dermatitis artefacta
- Rarer entities

British Society for Dermatopathology

http://www.britsocdermpath.co.uk

President: Dr Paul Craig

British Society for Dermatopathology Annual Meeting on Tues 5 July 2016 at the ICC Birmingham
Closing date for abstracts is 8 Feb 2016
Abstract submission via BAD website at www.bad.org.uk/events/annualmeeting

The BSD Self-assessment meeting is Mon 4 July at same venue

6th British Society for Dermatopathology Annual Trainees' Workshop
3 September 2015 in Bristol


Thank you for listening!
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