

Useful clues in assessing blistering disorders

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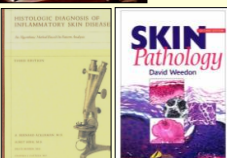
Inflammatory dermatoses!!



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

Location of bullae	Diseases
<p>Subcorneal bulla</p>	Bullous impetigo Miliaria crystallina Staphylococcal scalded skin syndrome
<p>Intra-epidermal bulla</p>	Acute eczema Viral vesicles Pemphigus Miliaria rubra Incontinentia pigmenti
<p>Sub-epidermal bulla</p>	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

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

The vesiculobullous reaction pattern

6

Introduction 109	Darier's disease 122	Subepidermal blisters with eosinophils 133
Epidemiological features 110	Genetic disease 122	Bullous pemphigoid 133
Classification of vesiculobullous diseases 111	Acute/chronic solar keratosis 122	Pemphigoid gestationis 135
Intraepidermal and subcorneal blisters 112	Subepidermal blisters - a classification 122	Arthropod bite 136
Impetigo 112	The epidermal keratinocyte membrane 122	Drug reactions 137
Subcorneal scalded skin syndrome 112	Subepidermal blisters with little inflammation 124	Subepidermal blisters with eosinophils 137
Dermatophytosis 112	Erythema multiforme 124	Dermatitis herpetiformis 137
Pemphigus foliaceus 113	Erythema nodosum 125	Linear IgA bullous dermatitis 139
Pemphigus erythematosus 114	Polypsiform scabies 125	Cicatricial pemphigoid 141
Subcorneal pustular dermatitis 114	Bullous pemphigoid (off-peak type) 130	Ocular cicatricial pemphigoid 142
IgA pemphigus 115	None 130	Localized cicatricial pemphigoid 142
Subacute cutaneous lupus erythematosus 116	Toxic epidermal necrolysis 130	Bullous scabies 142
Erythema multiforme major 116	Scarlet fever 131	Bullous scabies erythematosa 143
Toxicomania (acute paralytic rabies) 116	Measles (swelling) 131	Erythema 143
Acute generalized exanthematous pustulosis 116	Bullous scabies 131	Sawtooth syndrome 143
Miliaria crystallina 117	Bullous scabies 131	Epidermolysis bullosa acquisita 143
Intraepidermal blisters 117	Bullous drug reaction 131	Deep lamina lucida pemphigoid 143
Spongiform blistering diseases 117	Subepidermal blisters with lymphocytes 132	Bullous mucocystitis 143
Subacute cutaneous lupus 117	Erythema multiforme 131	Micelliferous blistering diseases 143
Viral blistering diseases 118	Paronychia pemphigoid 131	Drug-induced subcorneal bullae 144
Epidermolysis bullosa (Reiber-Cockayne type) 118	Lichen sclerosus et atrophicus 132	Miliaria (interdigital) bullae 144
Eosinophilic blisters 118	Lichen planus pemphigoides 132	Erythema nodosum bullae 144
Suprabullous blisters 118	Pemphigus (light response) 133	PUVA-induced bullae 144
Pemphigus vulgaris 118	Paronychia pemphigoid 133	Cancer-related bullae 144
Pemphigus vegetans 120	Dermatolysis (acute) dermatitis 133	Lymphatic bullae 145
Paronychia pemphigoid 121	Bullous lichen 133	References 145
Miliaria (blister) 121	Bullous systemic fungoides 133	

<p>Subepidermal blisters with little inflammation 124</p> <ul style="list-style-type: none"> Epidermolysis bullosa 124 Porphyria cutanea tarda 130 Bullous pemphigoid (cell-poor type) 130 Burns 130 Toxic epidermal necrolysis 130 Suction blisters 131 Blisters overlying scars 131 Bullous solar elastosis 131 Bullous amyloidosis 131 Bullous drug reaction 131 <p>Subepidermal blisters with lymphocytes 131</p> <ul style="list-style-type: none"> Erythema multiforme 131 Paraneoplastic pemphigus 131 Fixed drug eruptions 132 Lichen sclerosus et atrophicus 132 Lichen planus pemphigoides 132 Polymorphous light eruption 133 Fungal infections 133 Dermal allergic contact dermatitis 133 Bullous leprosy 133 Bullous mycosis fungoides 133 	<p>Subepidermal blisters with eosinophils 133</p> <ul style="list-style-type: none"> Bullous pemphigoid 133 Pemphigoid gestationis 135 Arthropod bites 136 Drug reactions 137 <p>Subepidermal blisters with neutrophils 137</p> <ul style="list-style-type: none"> Dermatitis herpetiformis 137 Linear IgA bullous dermatosis 139 Cicatricial pemphigoid 141 Ocular cicatricial pemphigoid 142 Localized cicatricial pemphigoid 142 Bullous urticaria 142 Bullous acute vasculitis 142 Bullous lupus erythematosus 143 Erysipelas 143 Sweet's syndrome 143 Epidermolysis bullosa acquisita 143 Deep lamina lucida pemphigoid 143
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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

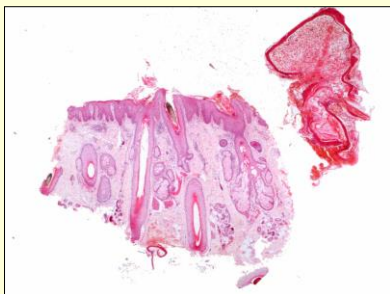
You can't see a blister: 'invisible dermatosis'

Consider:

- Dermatitis herpetiformis
- Pemphigus foliaceus
- Grover's disease
- **Additional levels often necessary**
 - Serial sections

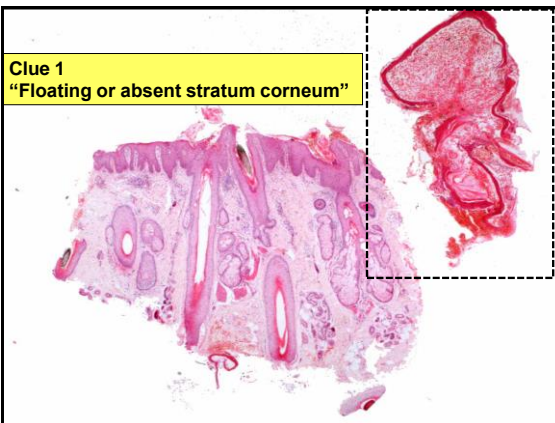
Case 1

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



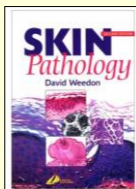
Clue 1

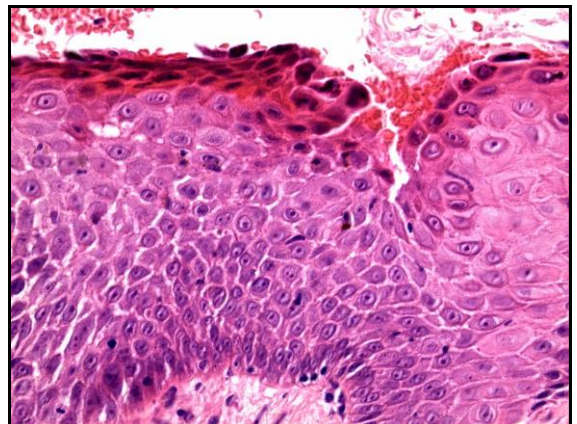
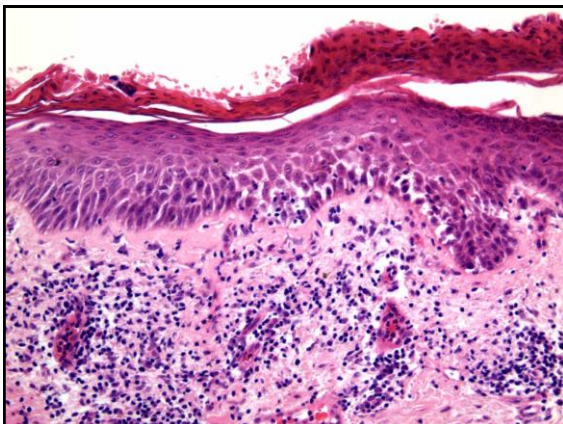
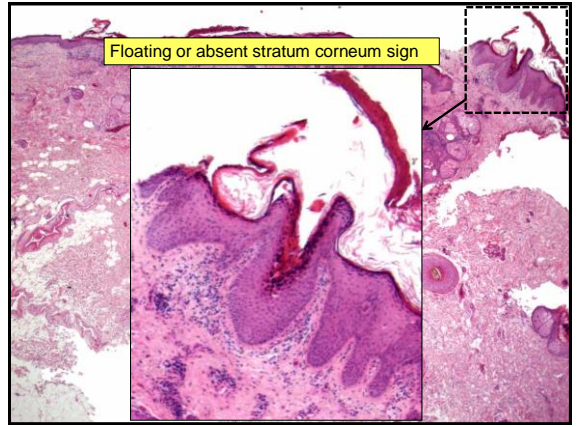
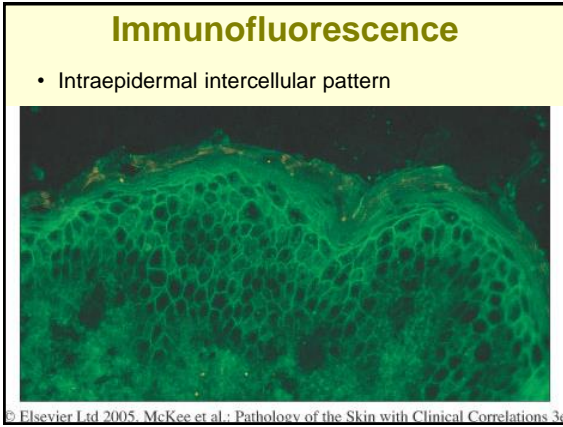
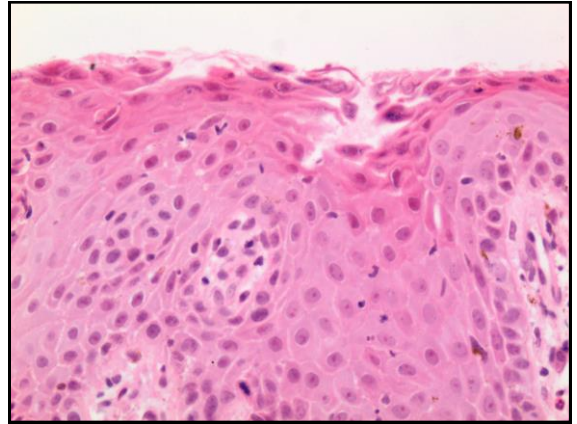
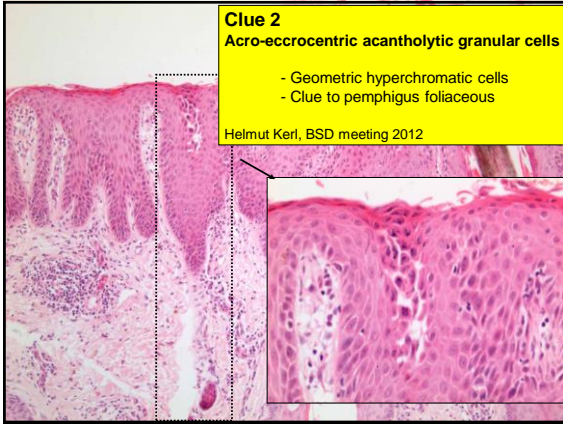
"Floating or absent stratum corneum"

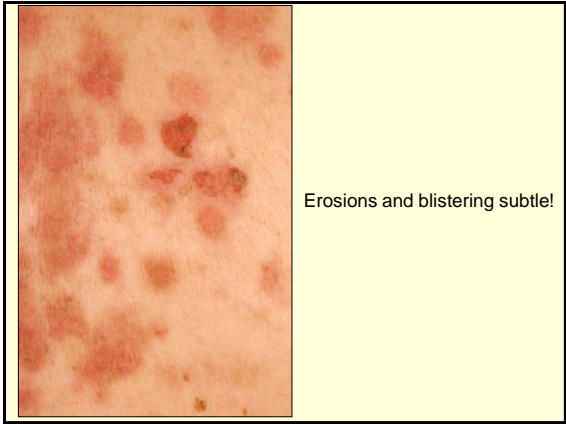
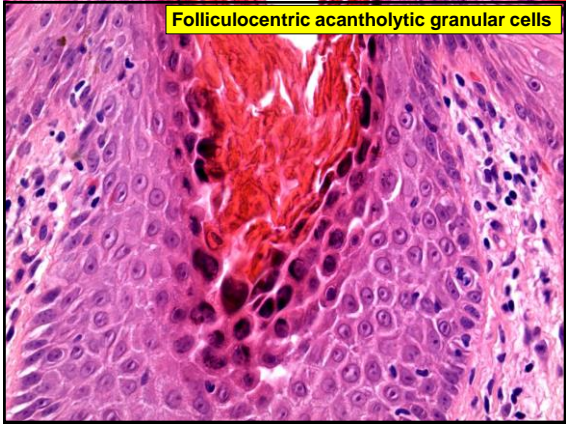


Floating or absent stratum corneum sign

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





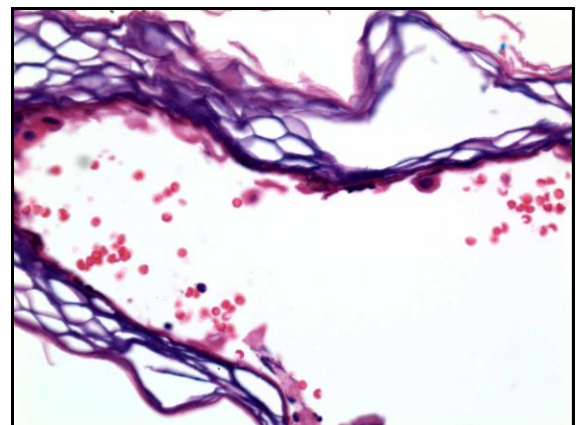
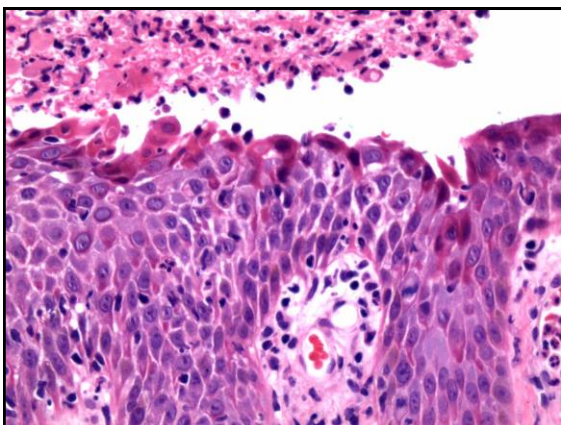
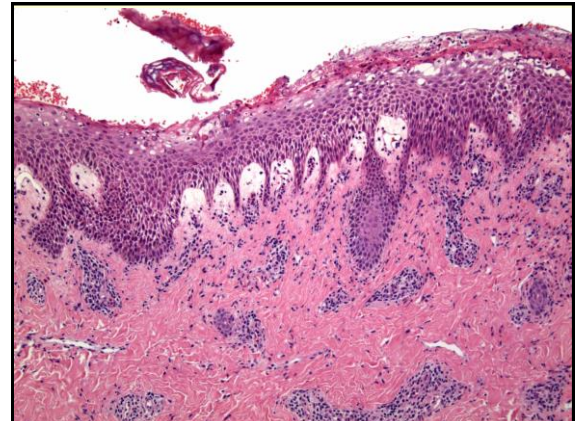
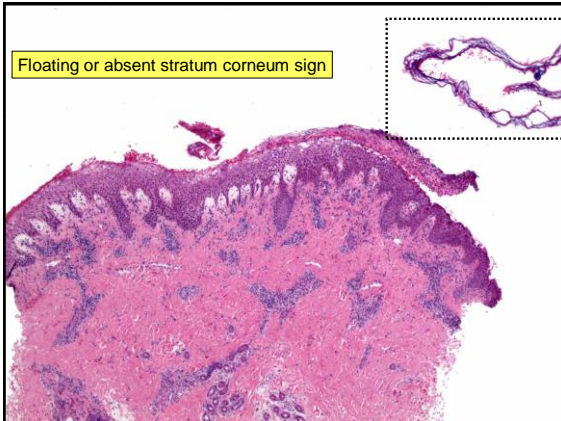


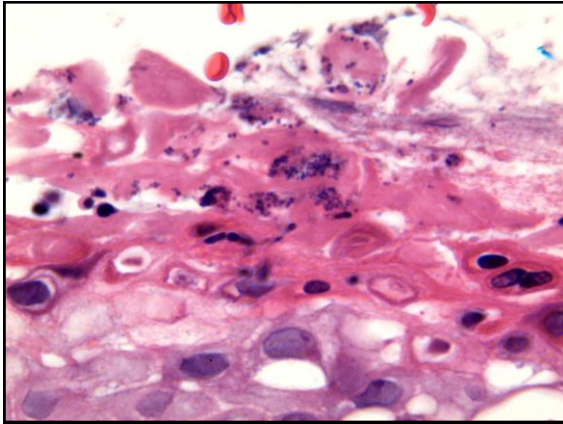
Pemphigus foliaceus vs vulgaris

	Pemphigus foliaceus	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





Bullous impetigo

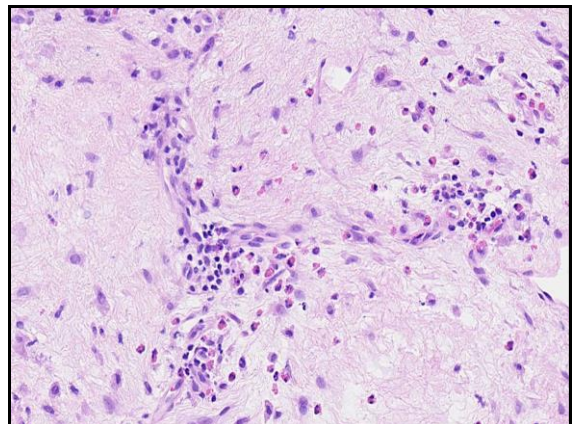
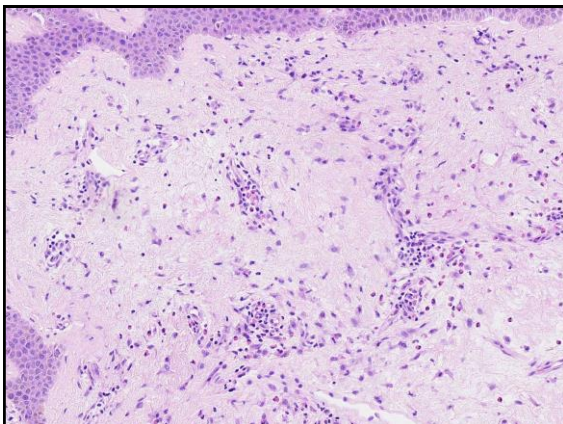
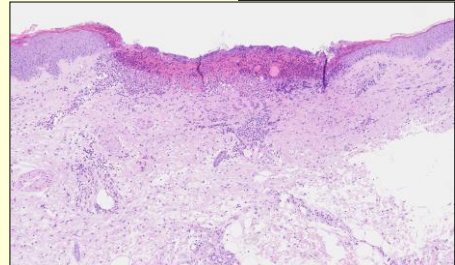
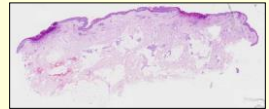
Staphylococcal Scalded Skin Syndrome

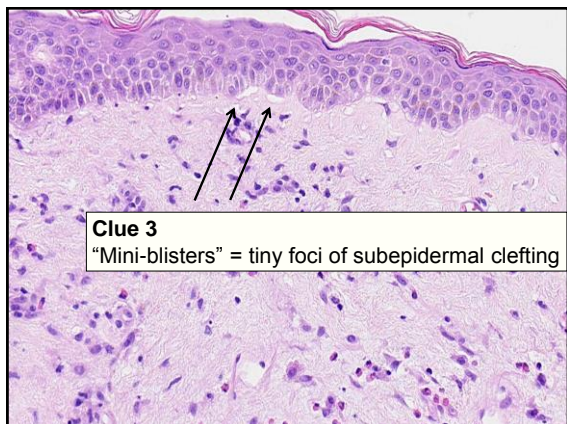


- Widespread blisters
- Exfoliative toxin produced by *Staphylococcus aureus*
- Organism **not** identifiable/cultured from affected skin

Case 3

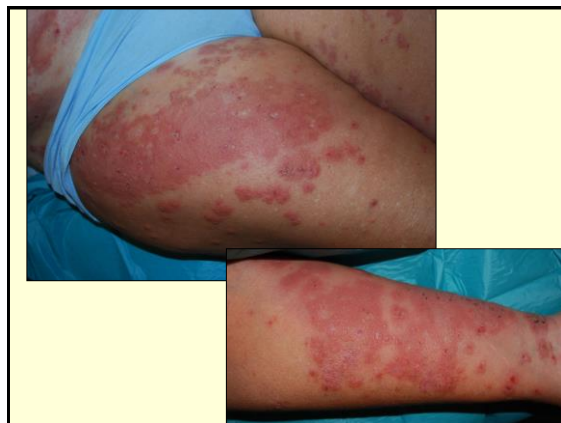
- Itchy rash
- ?scabies ?other





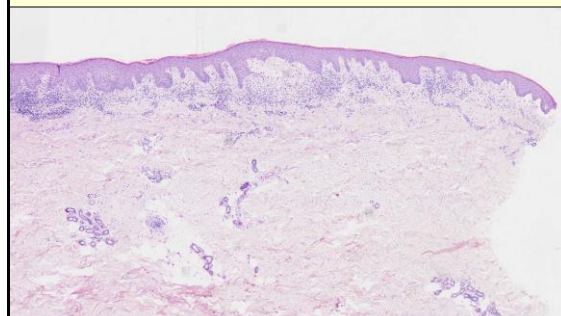
Prebullous pemphigoid

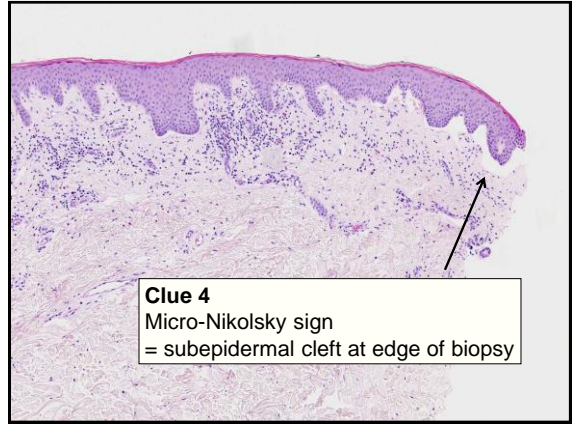
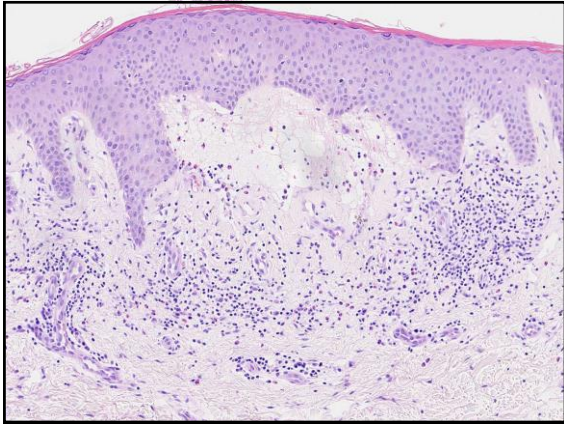
- Immunofluorescence:
Subepidermal IgG and C3 deposition
- Consider if:
Dermal eosinophils +/- spongiosis
'Mini-blisters'



Case 4

- Itchy urticated plaque on flank





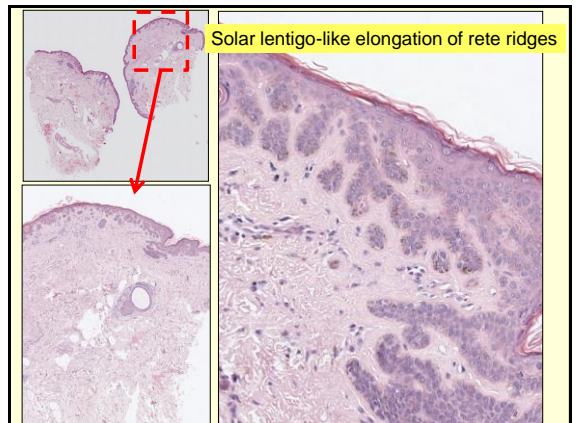
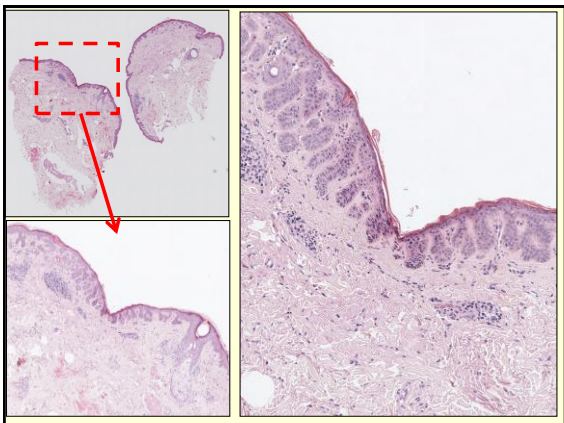
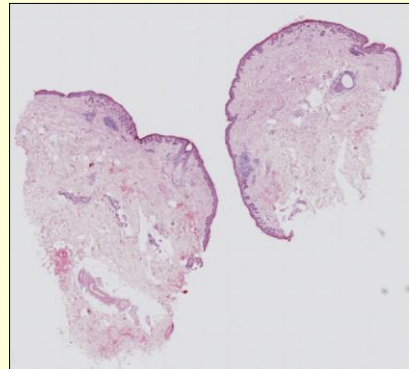
Clue 4
Micro-Nikolsky sign
= subepidermal cleft at edge of biopsy

Micro-Nikolsky sign:
D Metzger, ISDP Barcelona 2011



Shearing force of rotation of punch produces blister at edge

Case 5 • F78 - Itchy red papules



Solar lentigo-like elongation of rete ridges

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

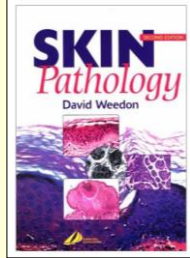
Grover's

Early Histopathologic Changes in Grover Disease
Priit 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
Maria-Teresa Fernández-Figueras, MD, Luis Puig, MD,† Pablo Canuteta, MD,‡*
Miriam Cuatrecasas, 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



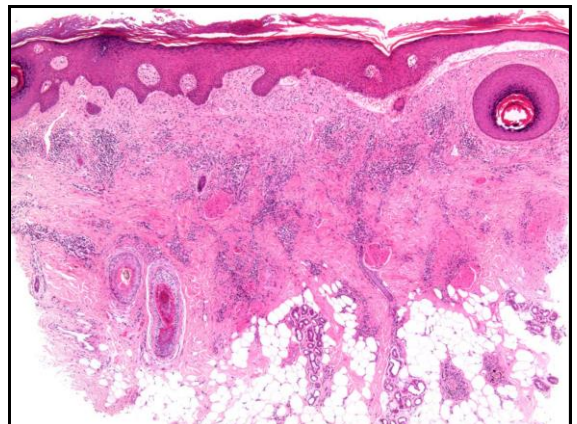
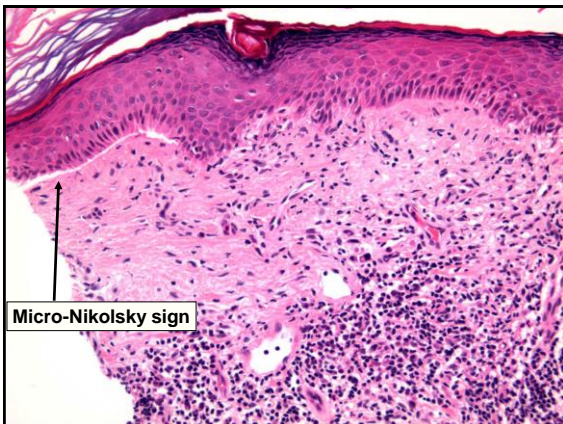
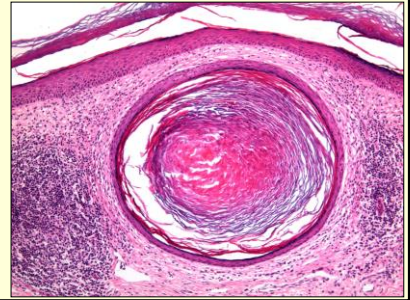
Case 6

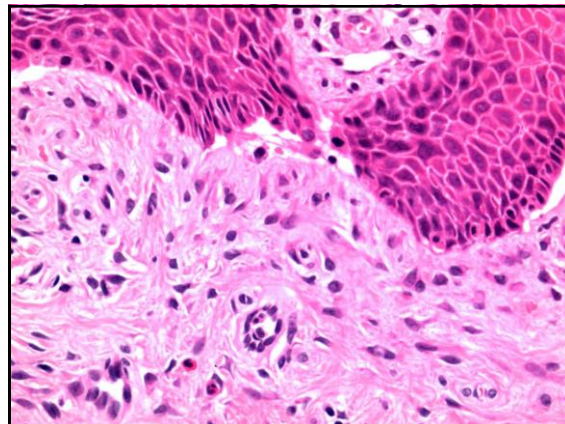
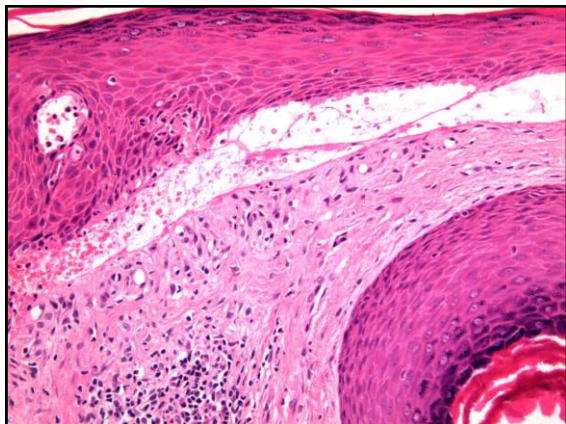
- F60. 5/12 erythematous scaly patch with scarring, alopecia and milia. ? BCC



Clue 6

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





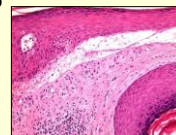
Be brave!



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

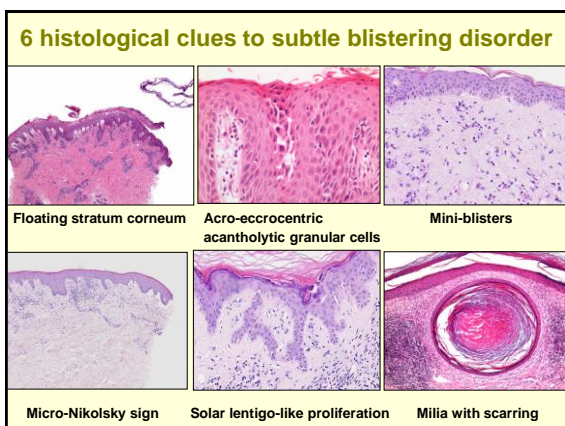
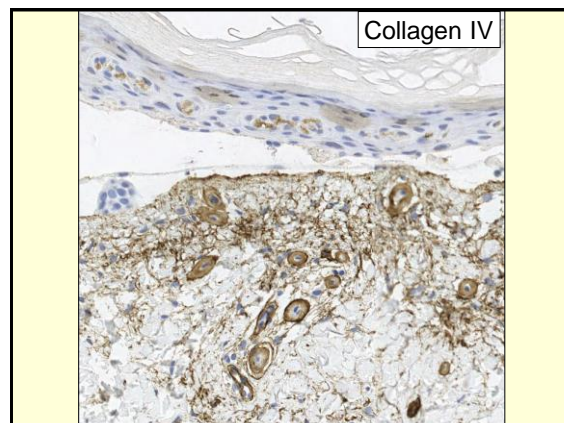
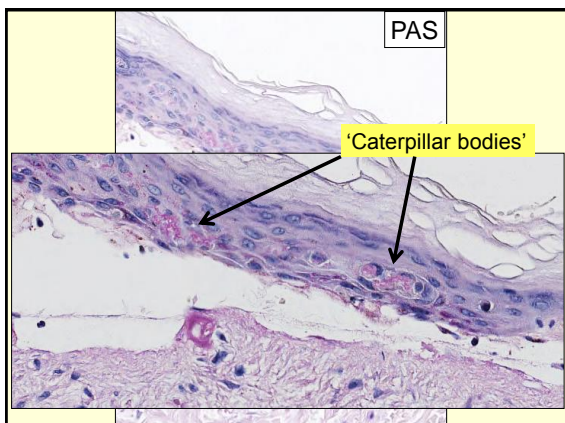
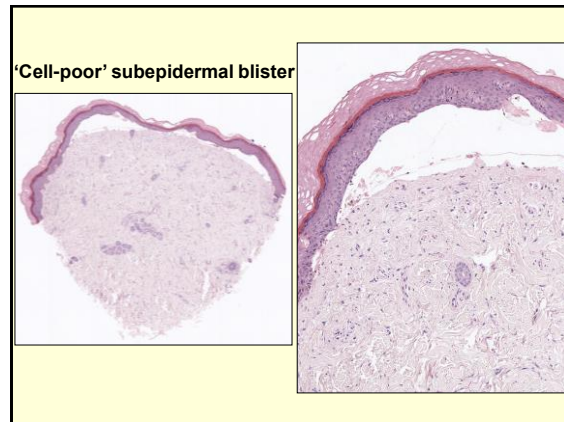


Milia with scarring =
 Clue to sub-epidermal blistering



Pseudoporphyria caused by naproxen





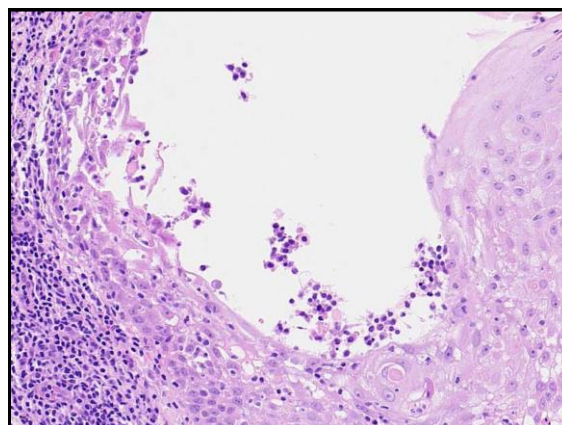
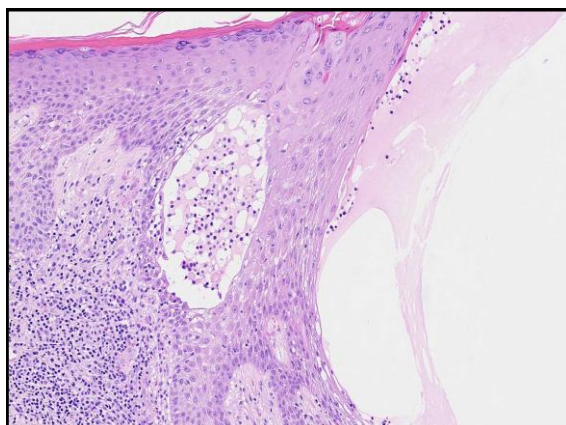
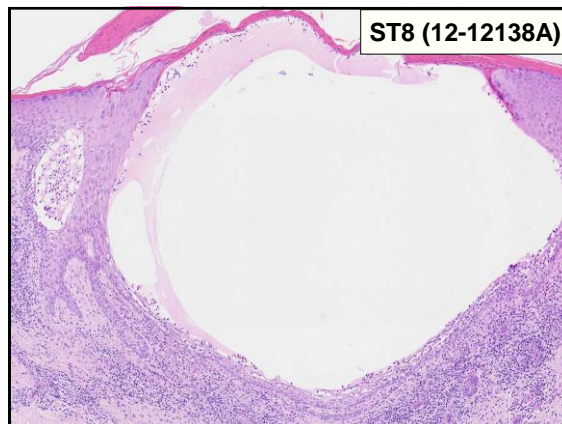
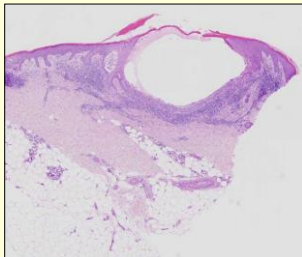
When you can see a blister, but doesn't seem to fit!

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

Diverse histology of common blistering disorders

Case 7

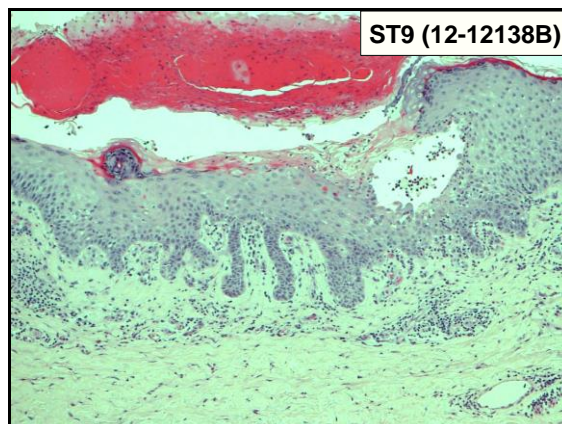
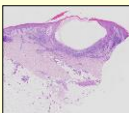
- Itchy rash trunk & legs

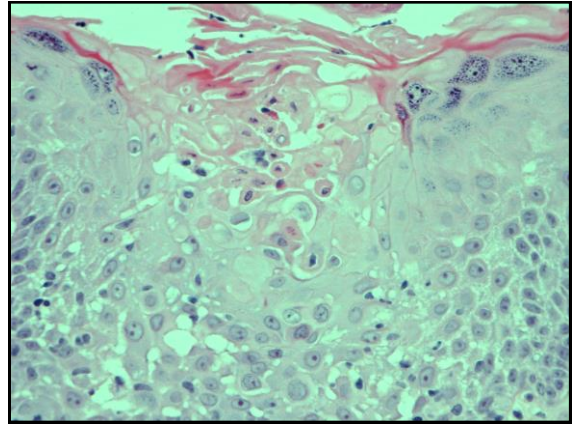
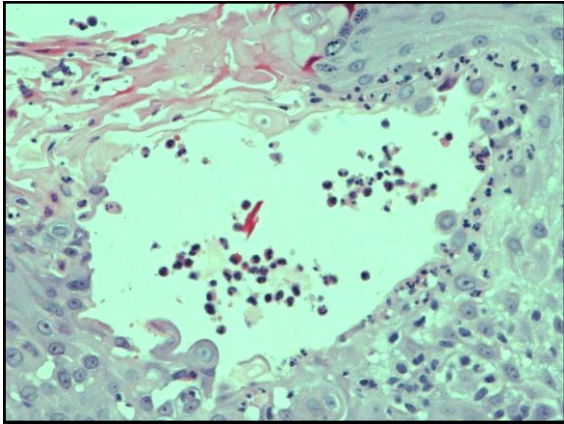


Grover's histology

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

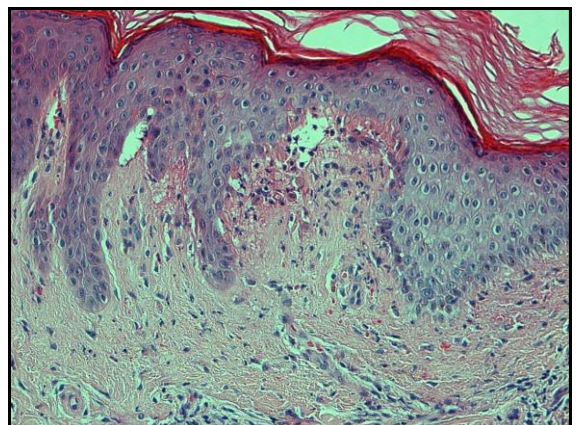
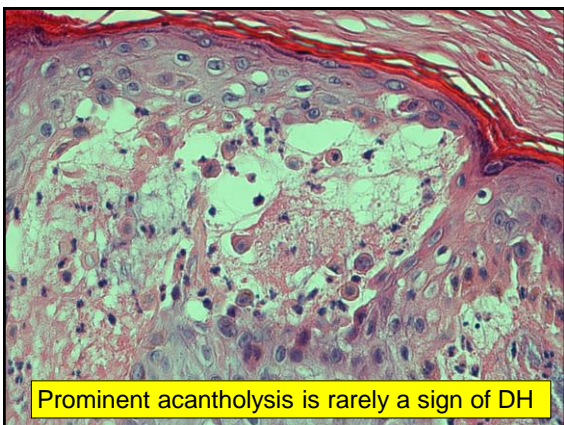
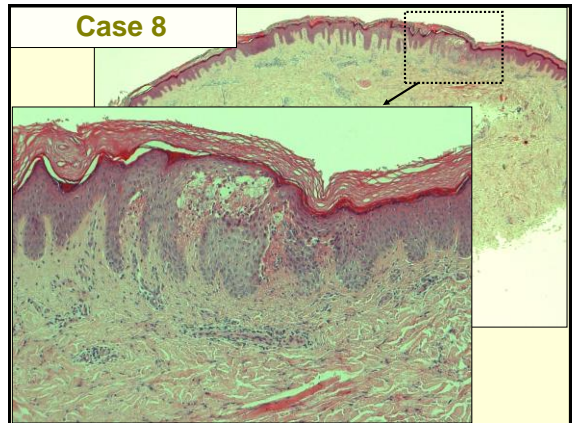


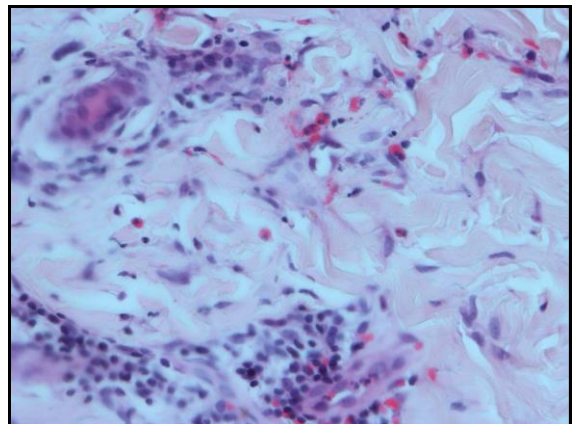
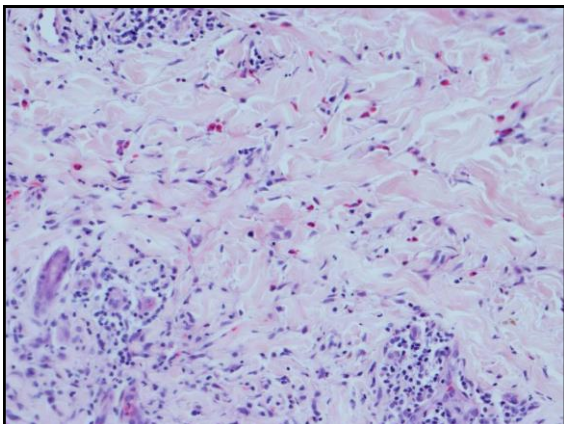
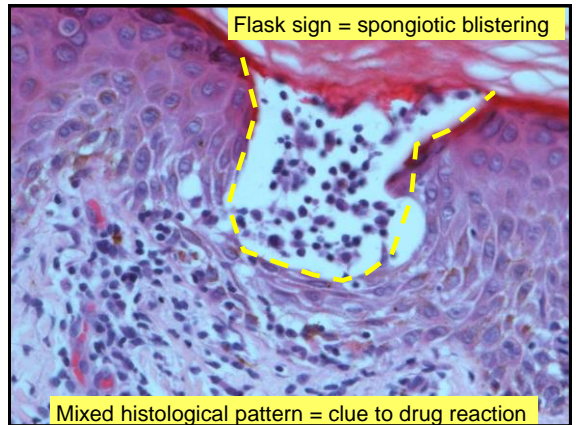
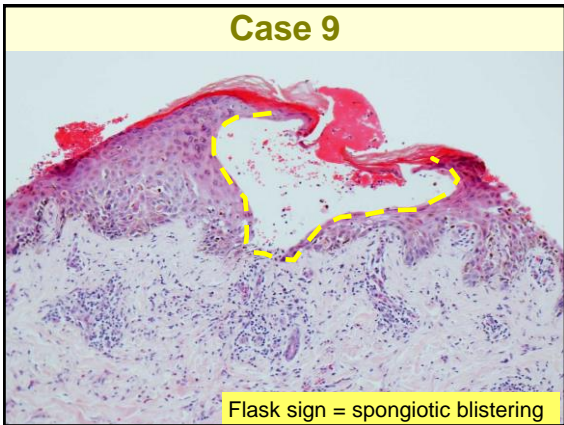
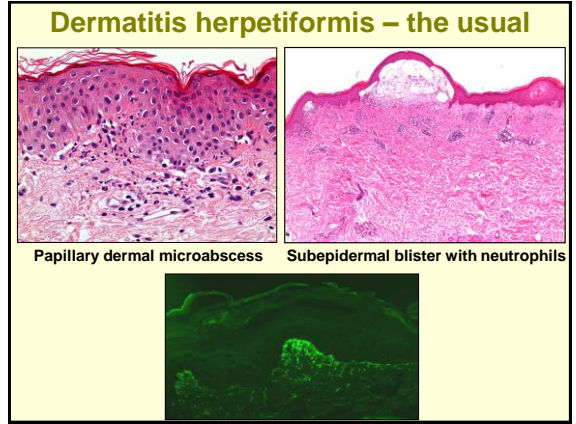
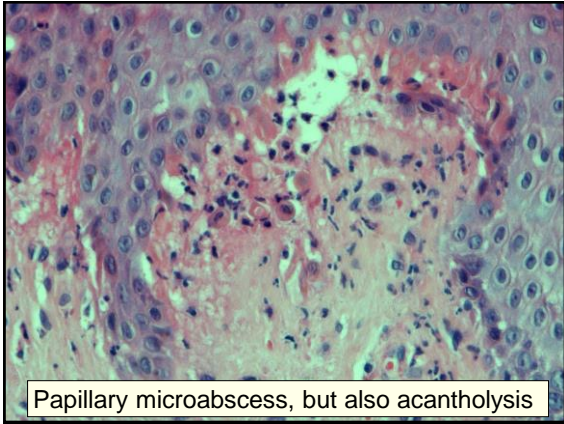


Diverse histology of common blistering disorders

Case 8

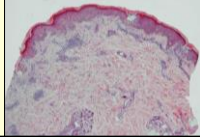
- Itchy vesicles knees & elbows

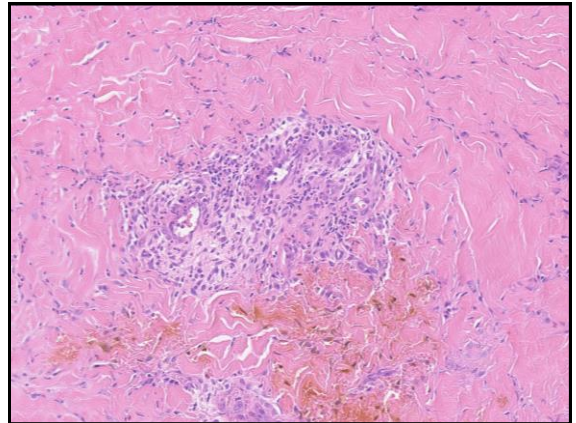
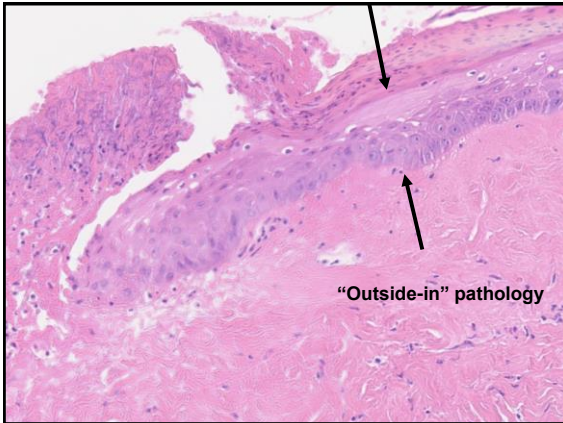
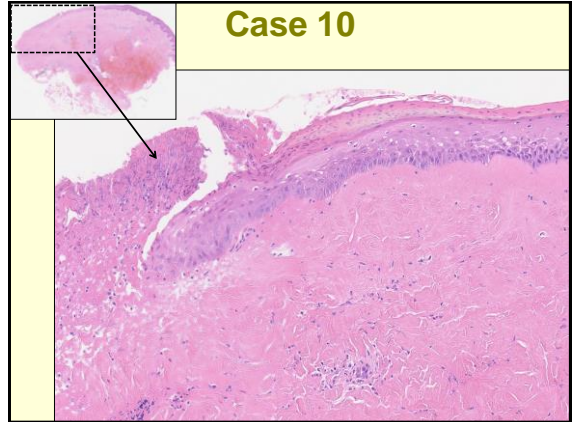


Case 9 - continued

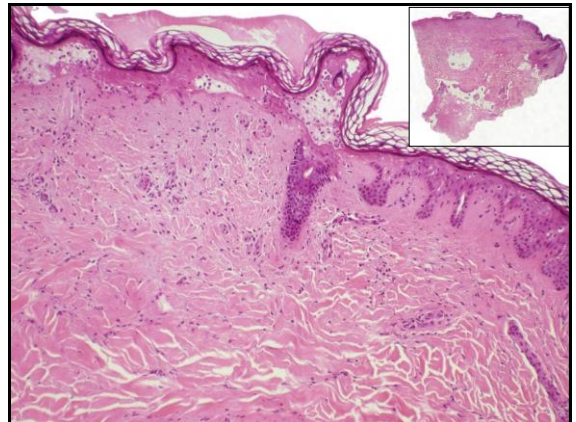
- 39 year old female, metastatic breast cancer
- Blistering dorsum right hand 6 days after first infusion of docetaxel, localised to infusion site
- Mixed inflammatory pattern - THINK DRUG REACTION

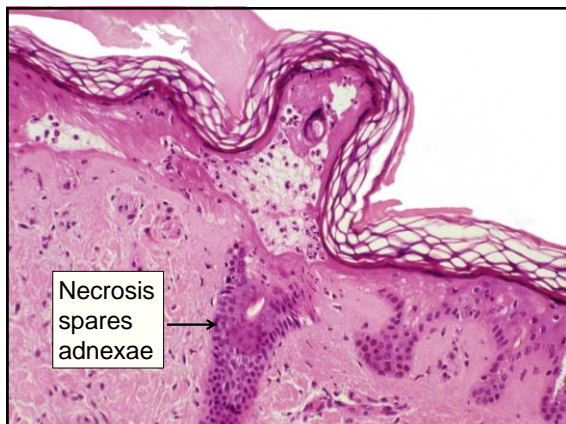


Case 10



Courtesy of Wolfgang Weyers





Histological clues to dermatitis artefacta

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

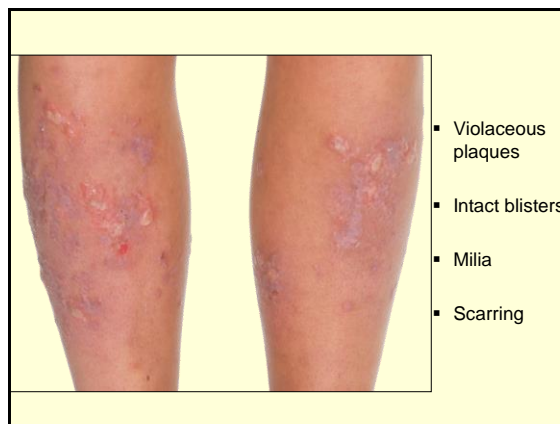
- Doesn't fit with known bullous disorder
- Sharply demarcated ulcer or blister
- Mummified pattern of epidermal necrosis sparing adnexal epithelium
- 'Outside-in' – spinous layer predilection
- Fibrin & superficial neutrophilic infiltrate
- Vessels show red cell extravasation and fibrin localised to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

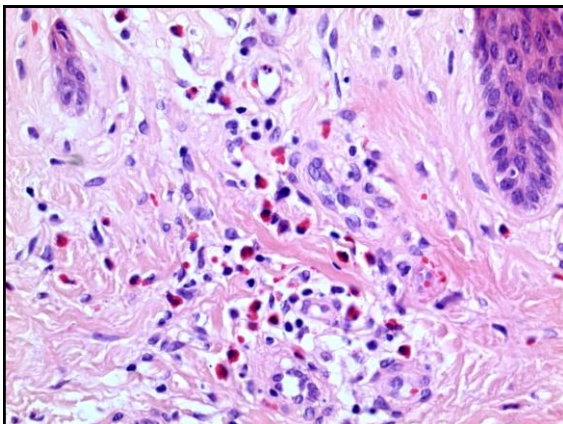
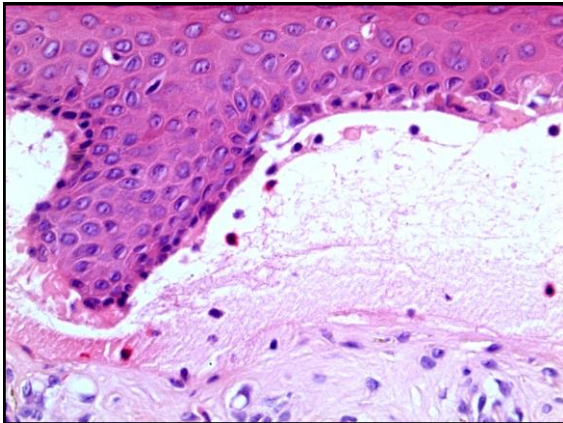
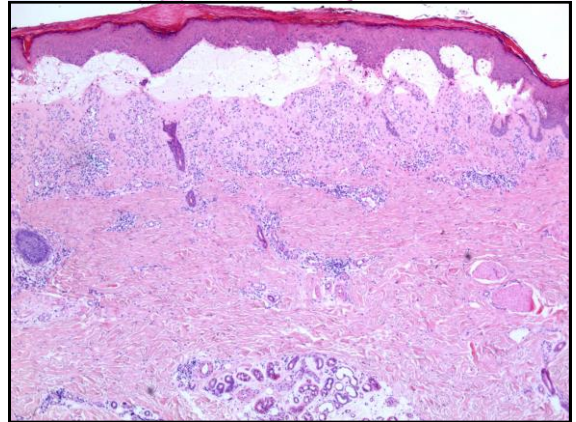
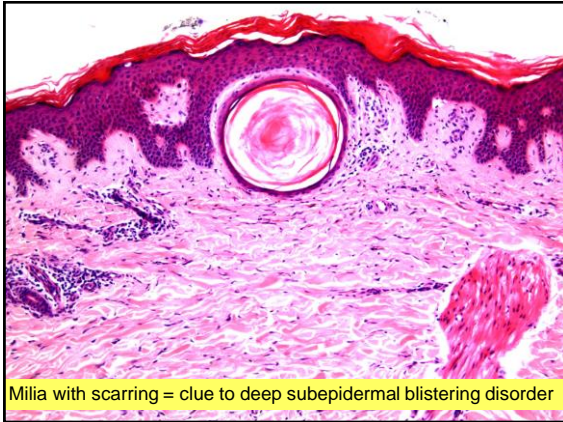
When you can see a blister, but doesn't seem to fit!

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

Case 11

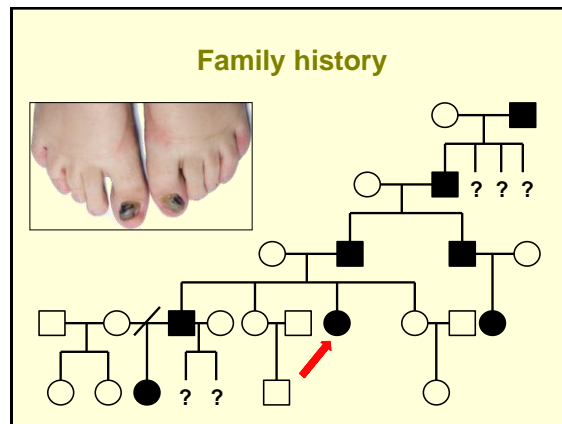
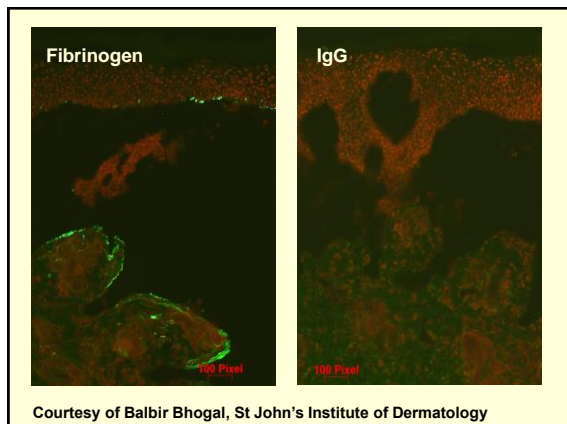
- Dystrophic nails
- Itchy plaques on shins





Histology summary

- Milia
- Scarring
- Subepidermal blister
- Lichenification
- Inflammation including eosinophils
- ?immunobullous disorder e.g. pemphigoid



Mutation analysis of COL7A1

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

→ Dominant dystrophic epidermolysis bullosa pruriginosa

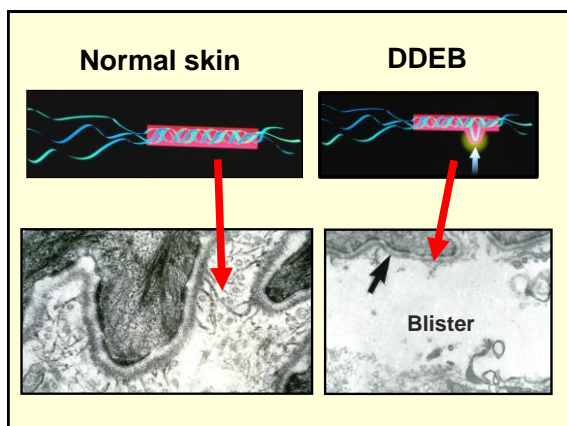
British Journal of Dermatology (1994) 130, 617-625.

Epidermolysis bullosa pruriginosa: dystrophic epidermolysis bullosa with distinctive clinicopathological features

J.A.McGRATH, O.M.V.SCHOFIELD AND R.A.J.EADY
 Department of Cell Pathology, St John's Institute of Dermatology, St Thomas' Hospital, London SE1 7EH, U.K.
 Accepted for publication 22 October 1993

- 1st described by Kuske in 1946¹
- Term EB 'pruriginosa' coined by McGrath et al in 1994²
- Rare subtype of DEB³
- 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

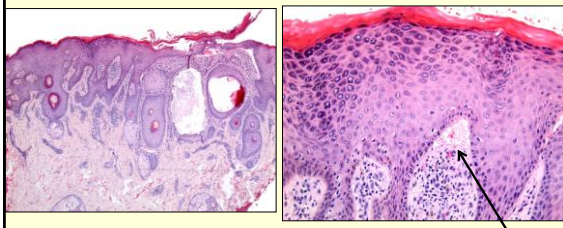


EB pruriginosa – learning points

- 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

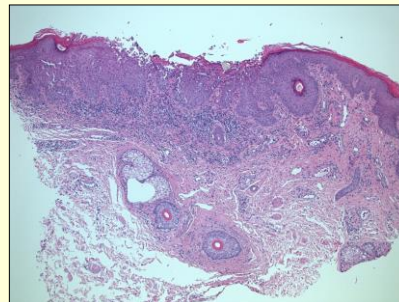
The sister

- Dystrophic nails
- Itchy blisters / papules neck

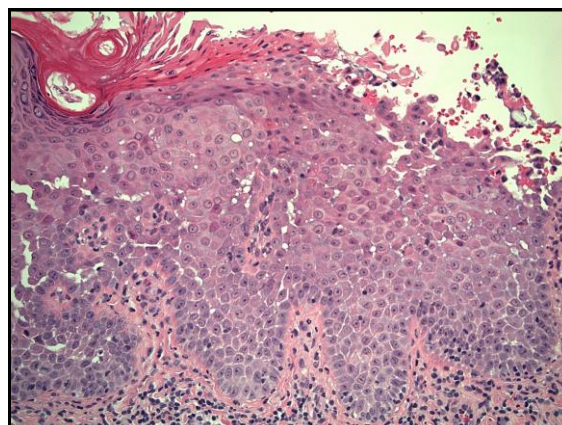
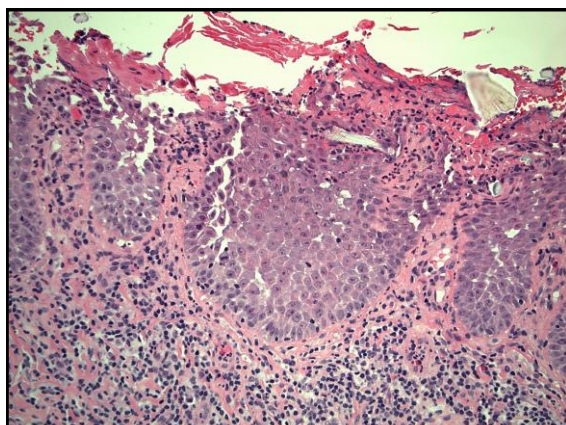


Case 12

Female with itchy papular rash in genital region



Courtesy of Luisa Motta



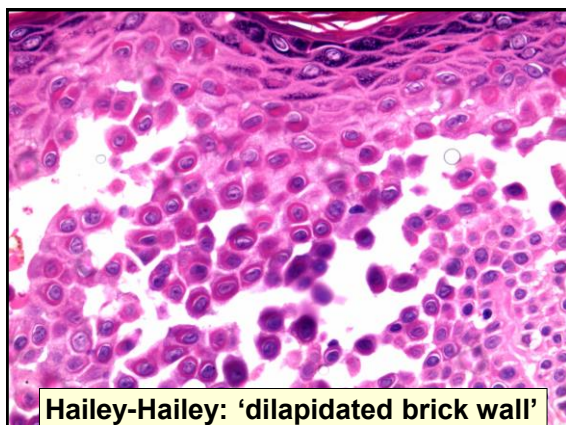
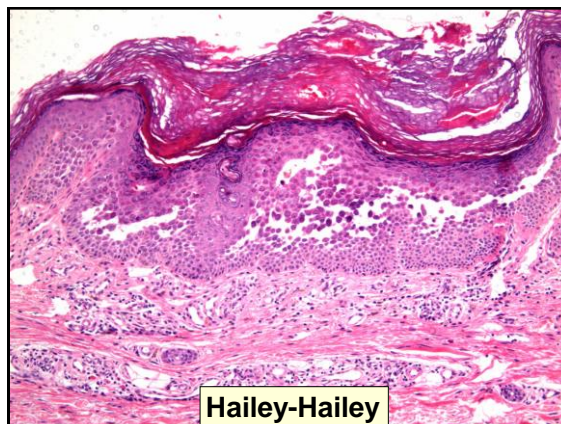
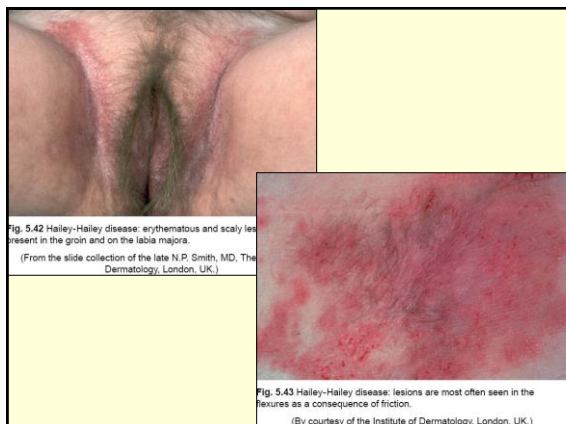
Acantholytic dermatosis of the genitocrural area



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



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.britisocdermpath.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

Acknowledgements

- Richard Carr
- Marie-Anne Brundler
- Jerry Marsden
- Luisa Molta
- Robert Charles Holmes
- Gwladys Wroblewska
- Andrew Ichyshyn
- Wolfgang Weyers
- Claudia Roberts

Thank you for listening!

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