18th Summer Academy of Dermatopathology, July, 2026

The epidermis decoded: New patterns, incidental findings, and clues

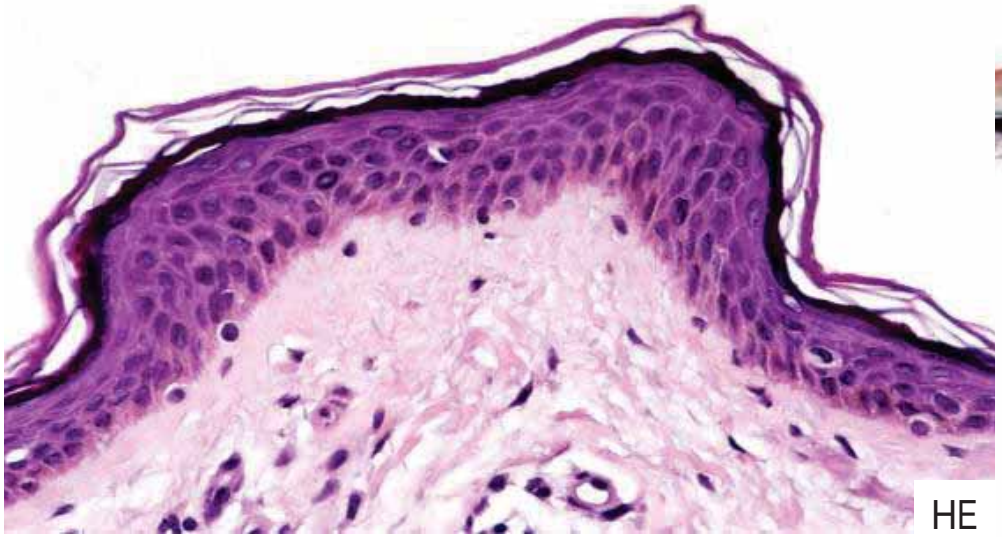
Dieter Metze

SPECIALTY TRAINING CENTRE IN DERMATOPATHOLOGY

DERMATOHISTOLOGY UNIT
DEPARTMENT OF DERMATOLOGY, UNIVERSITY OF MÜNSTER

40 Minuten

Epidermis decoded



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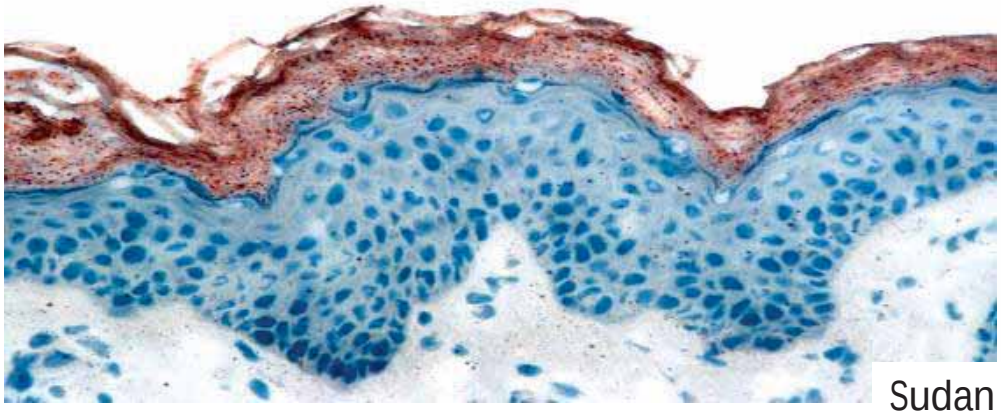
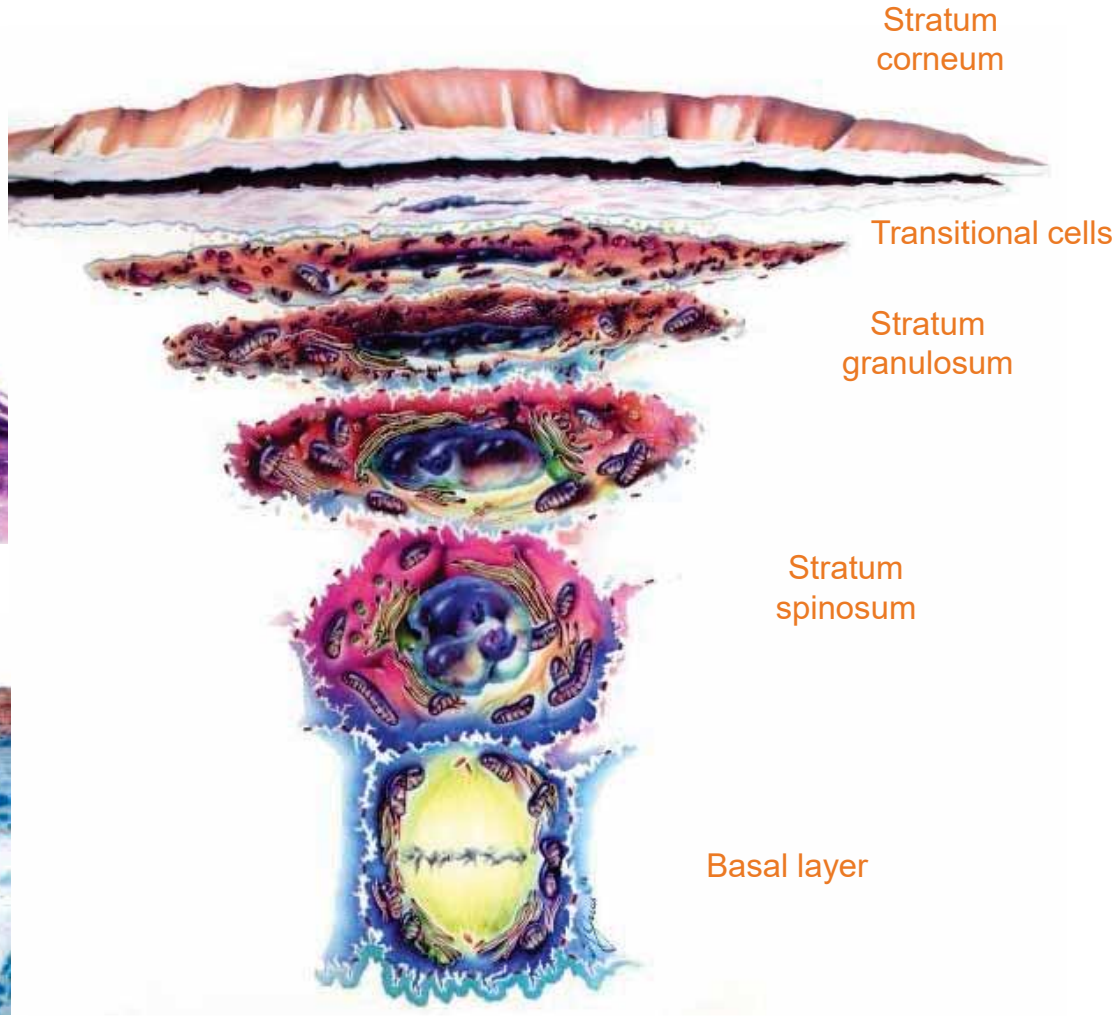
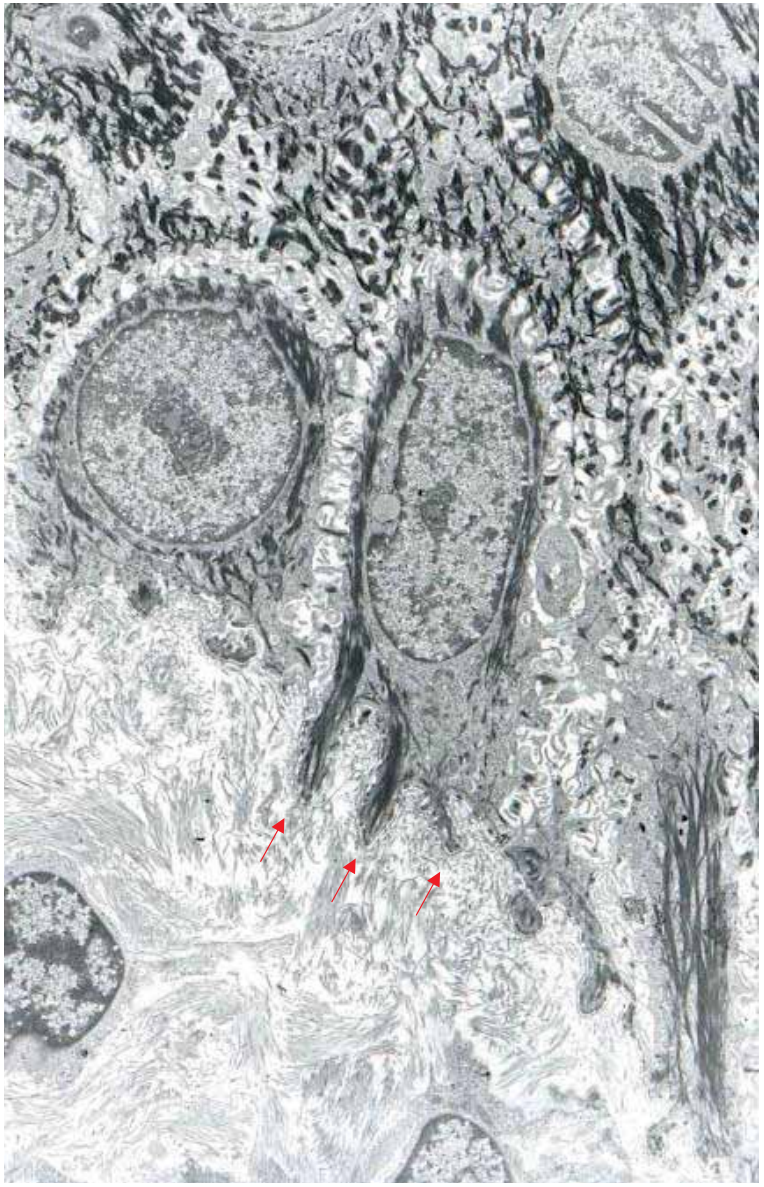


Sudan



A. Geras, Sandoz Medical publications



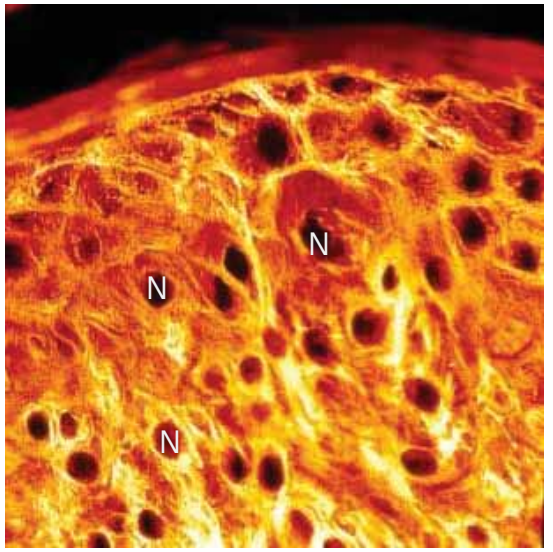
Suprabasal K.

Stratum spinosum

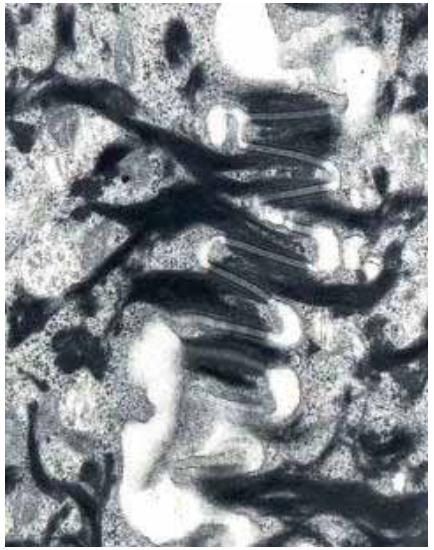
Stratum basale
(Stem cells,
differentiating K.)

Wurzelfüßchen
(anchoring
foot processes)

Basement membrane

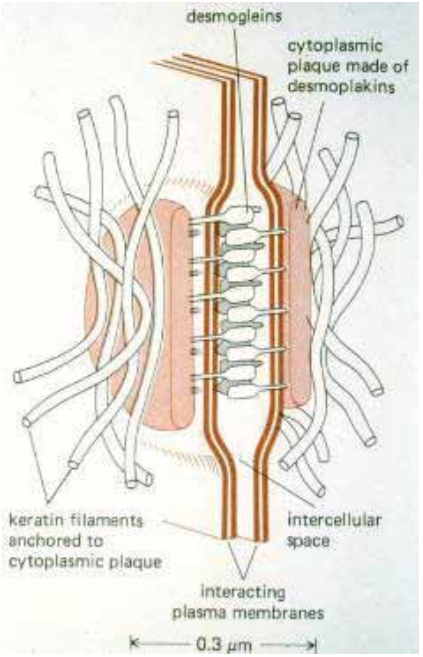


Keratin cytoskeleton: transcellular gothic arch pattern and flexibility demonstrated by immunofluorescence



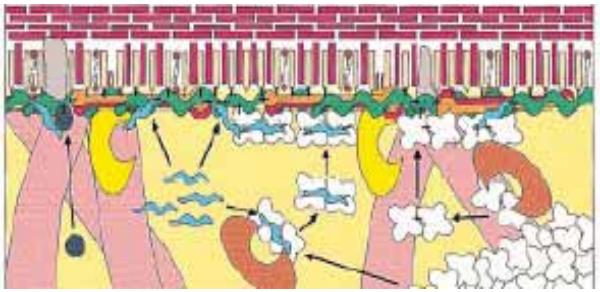
Keratin filaments

Desmosomes



Stratum Corneum: via Transitional cells, loss of nuclei, compact keratin structure with thickened cell membrane (cornified envelope), intercellular lipids from Odland bodies (O);corneodesmosomes (c), shedding of the uppermost corneocytes ↑

Stratum granulosum: Keratinocytes flat, keratohyalin granules
(absent in inflammatory dermatoses, ichthyoses)



IEM: filaggrin, keratin glue, apoptosis

Epidermal reaction patterns
in genodermatoses, epidermal nevi, acquired skin diseases or as an incidental finding

Pattern	Dermatosis	Mosaicism	Solitary lesion	Incidental finding
Epidermolytic hyperkeratosis	Keratinopathic Ichthyosis, Palmoplantar Keratoderma	+	Epidermolytic acanthoma	+
Focal acantholytic dyskeratosis	M. Darier	+	Acantholytic dyskeratotic acanthoma	+
Hailey–Hailey–type acantholysis	M. Hailey–Hailey	+	Hailey–Hailey–type acanthoma	+
Desmosomal-type acantholysis	Genetic diseases with desmosome related mutations	?	Acantholytic acanthoma (Hyaline inclusion acanthoma)	+
Epidermolysis bullosa simplex-type vacuolization	Epidermolysis bullosa simplex	+	?	+
Granular Parakeratosis	Granular parakeratosis	-	Granular parakeratotic acanthoma	+
.....				

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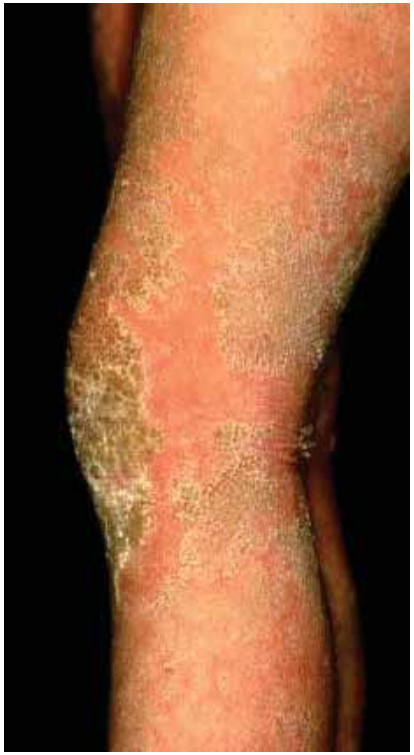
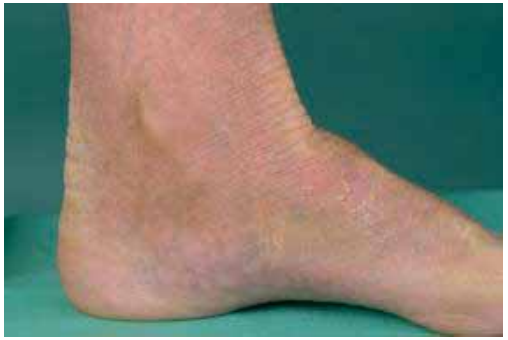
Granular Parakeratosis	Granular parakeratosis	-	Granular parakeratotic acanthoma	+
.....				

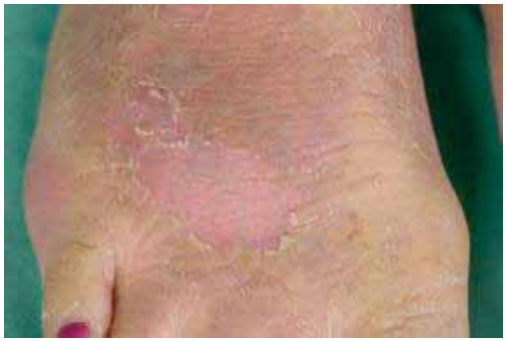
Keratinopathic Ichthyoses

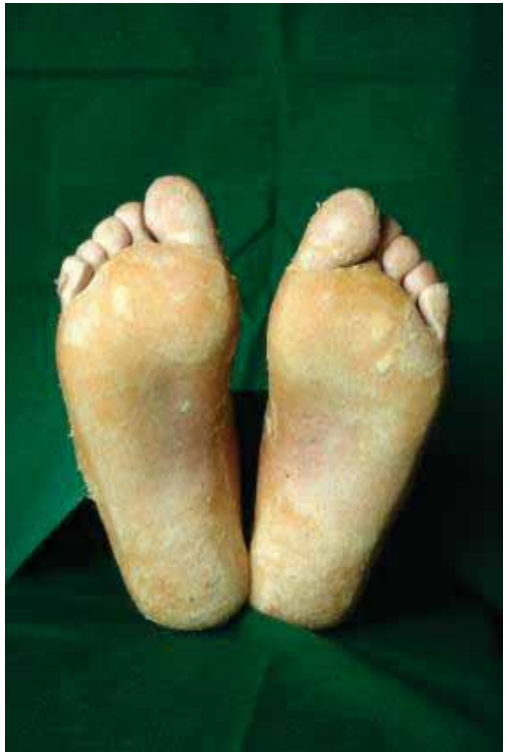
- Epidermolytic ichthyosis (*Ichthyosis Brocq*, KRT1/10-nEDD)
- Superficial epidermolytic ichthyosis (*Ichthyosis Siemens*, KRT2-nEDD)

Epidermolytic palmoplantar Keratoses (KRT1/9-pEDD)

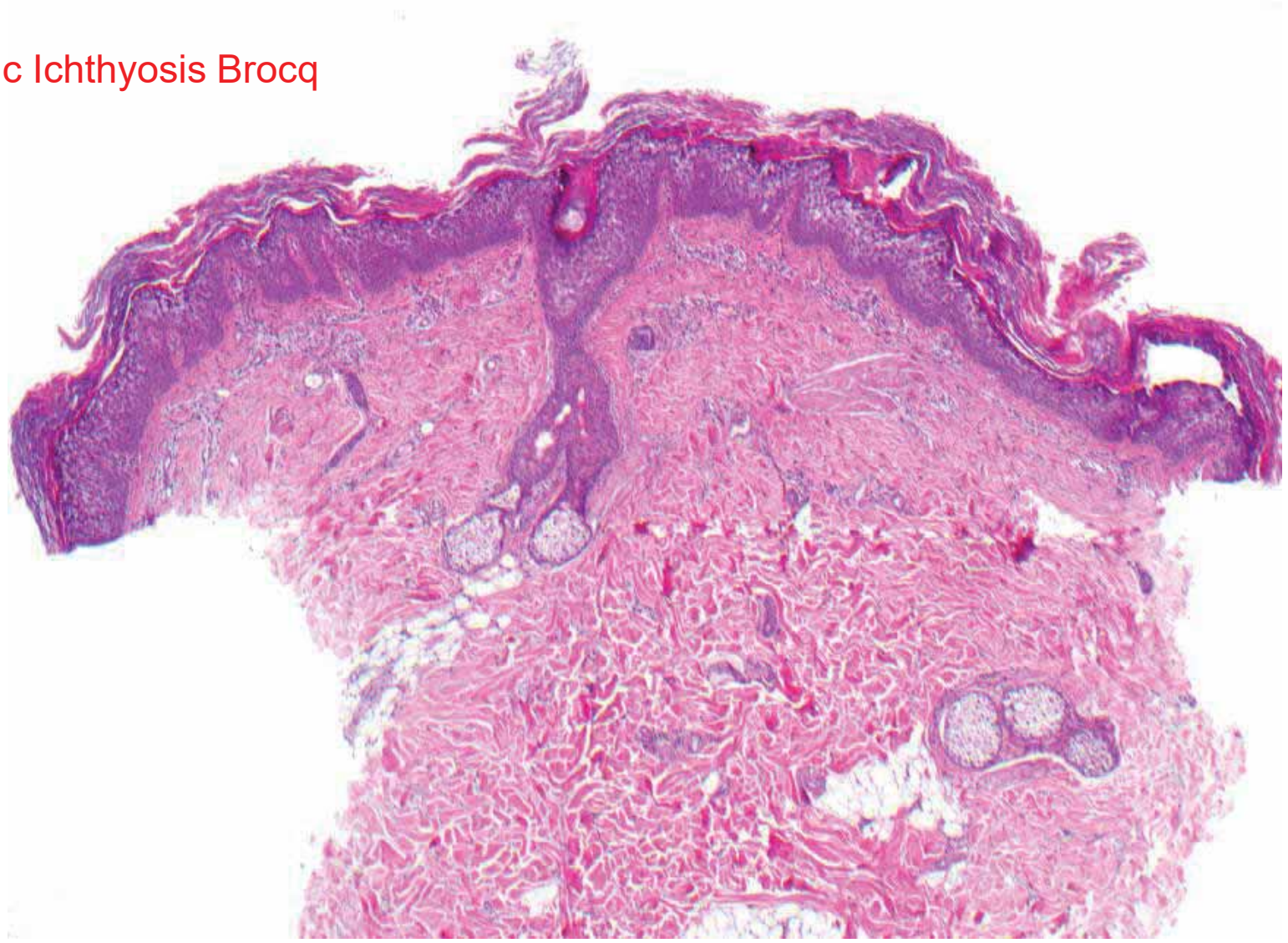




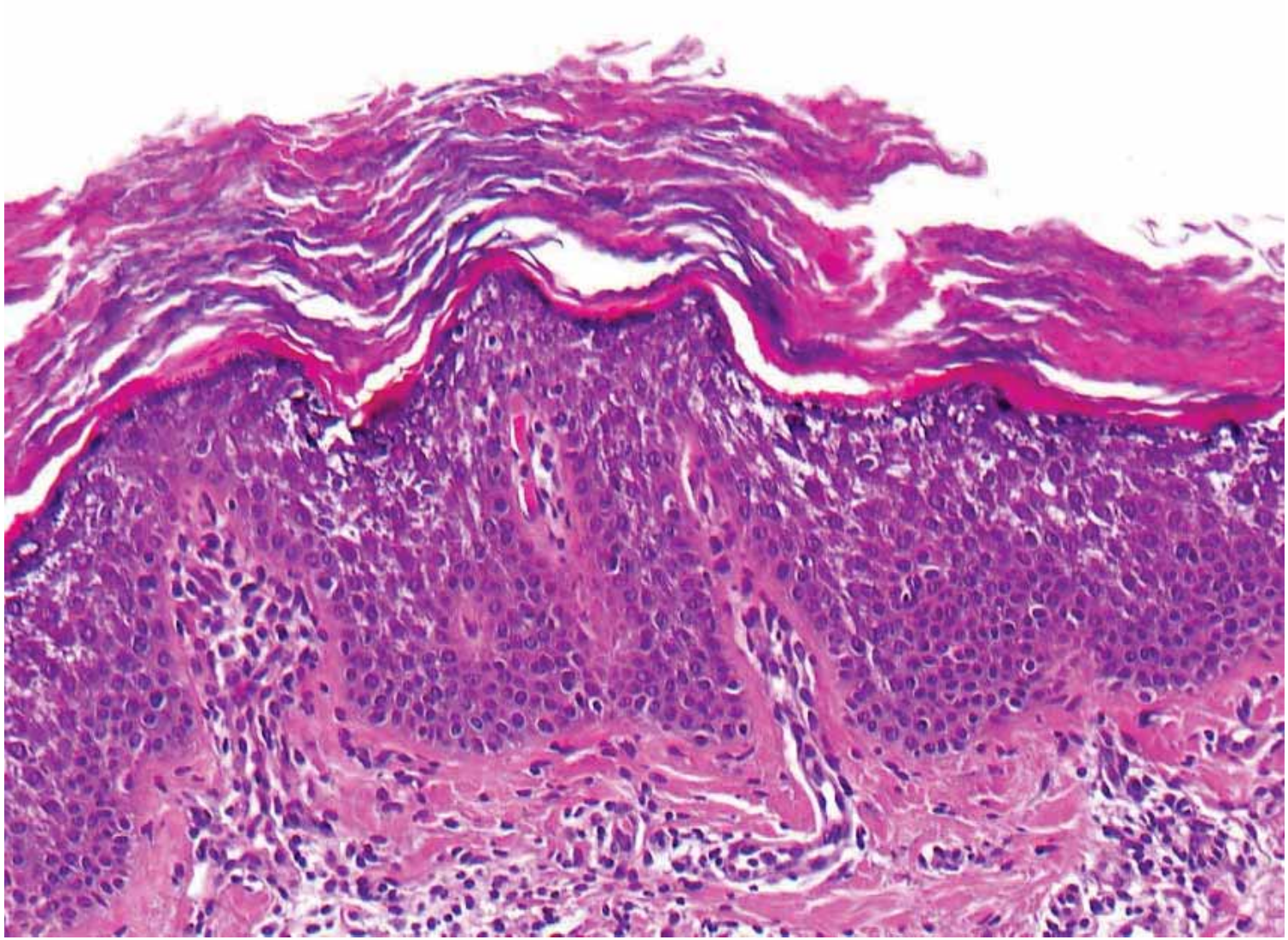




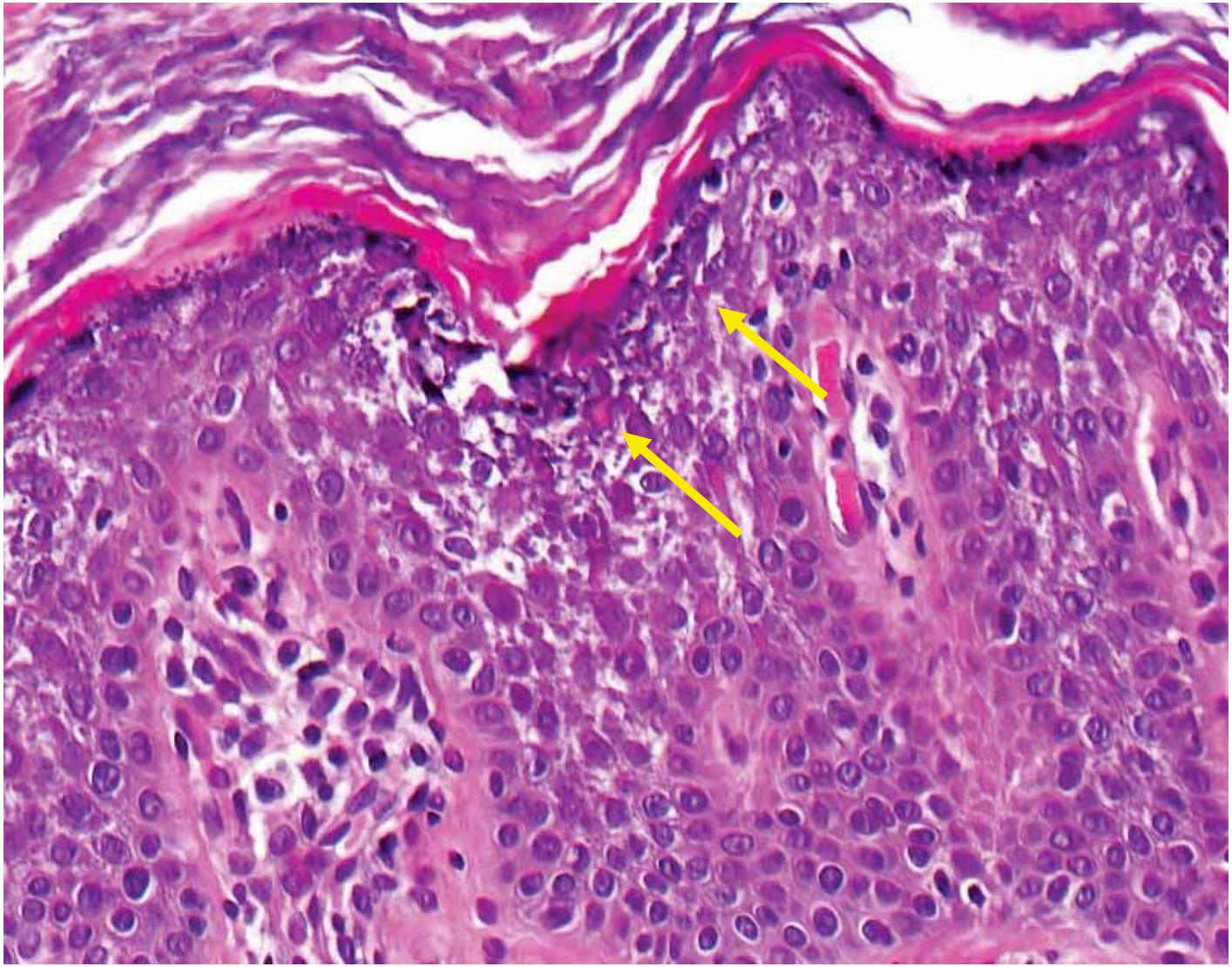
Epidermolytic Ichthyosis Brocq



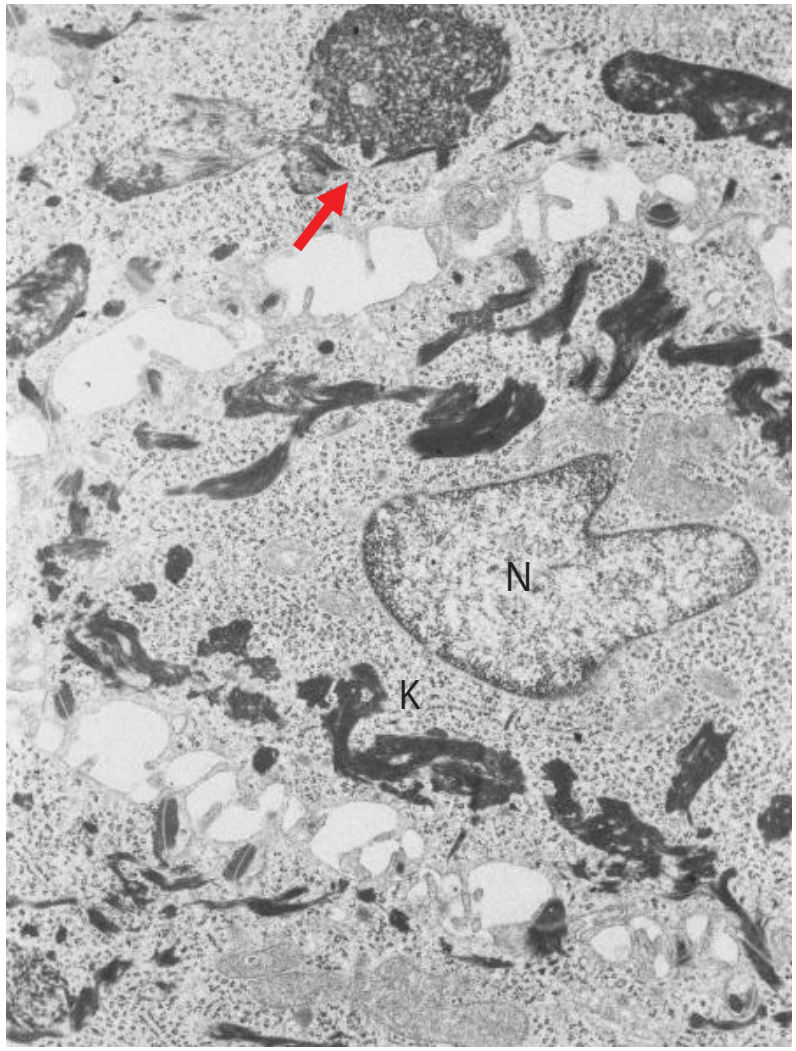
Mostly non-inflammatory, epidermal hyperplasia, pale keratinocytes, orthohyperkeratosis

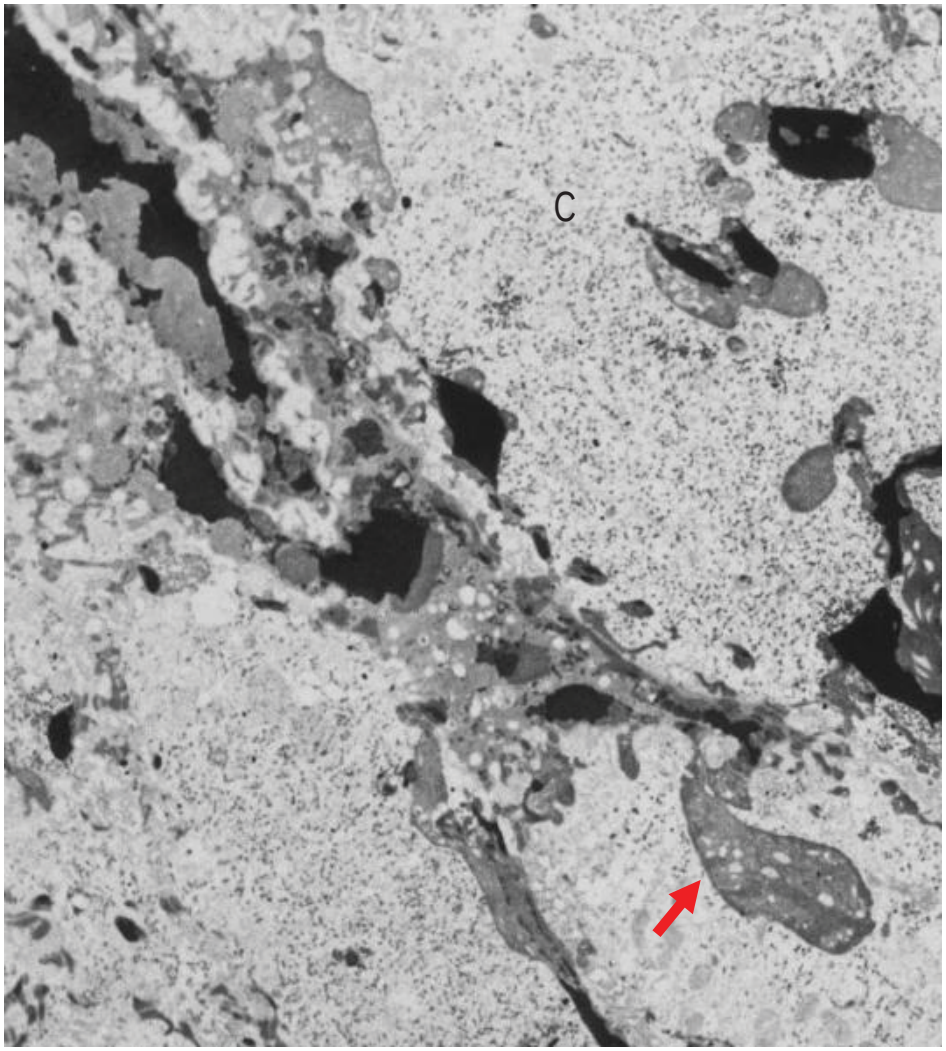


Keratinocytes ill-defined cell borders, clear spaces



Keratohyaline granules coarse, variably sized, eosinophilic granules

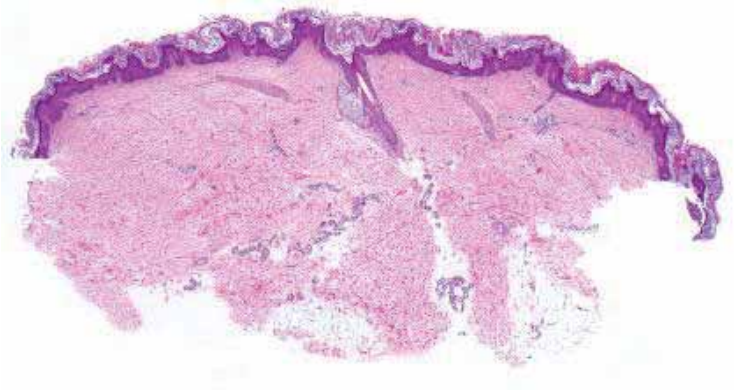


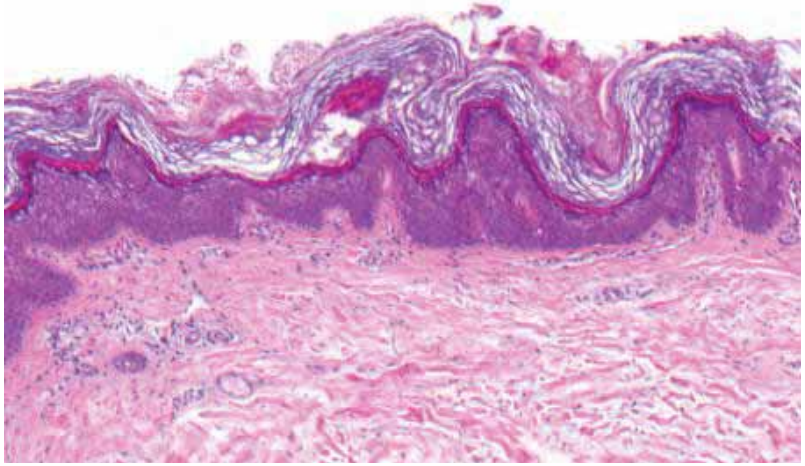


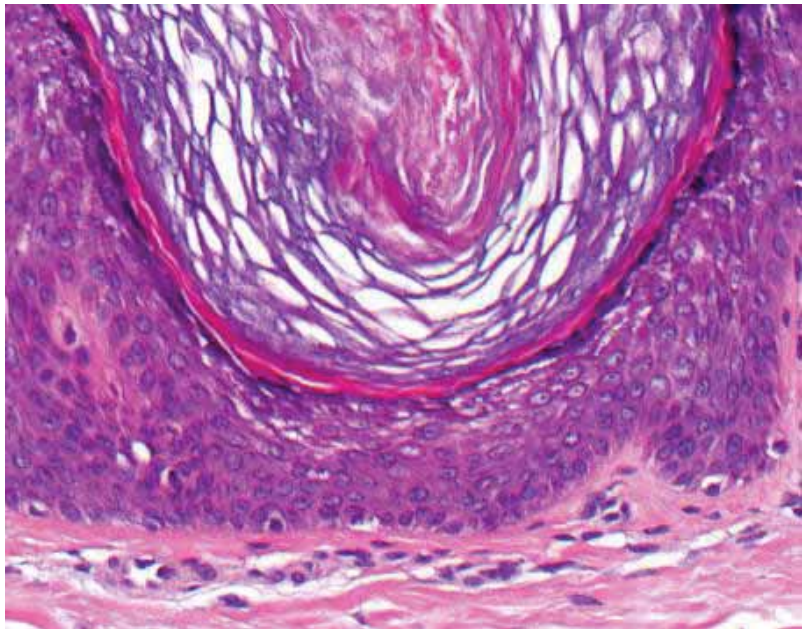
Mutation of keratin 1, 2, 9 or 10: clumping of keratin skeleton and irregular KHG

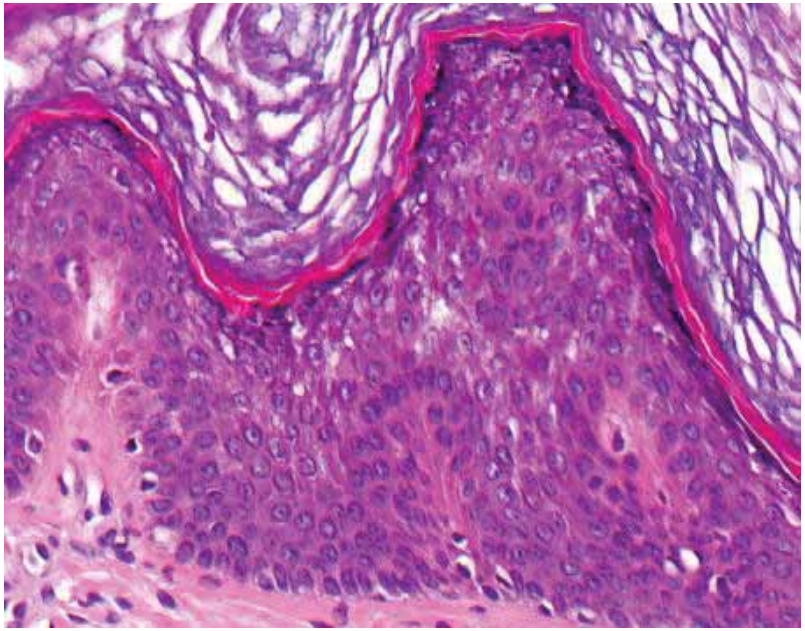
Epidermolytic Ichthyosis Brocq

Note: discrete epidermolysis

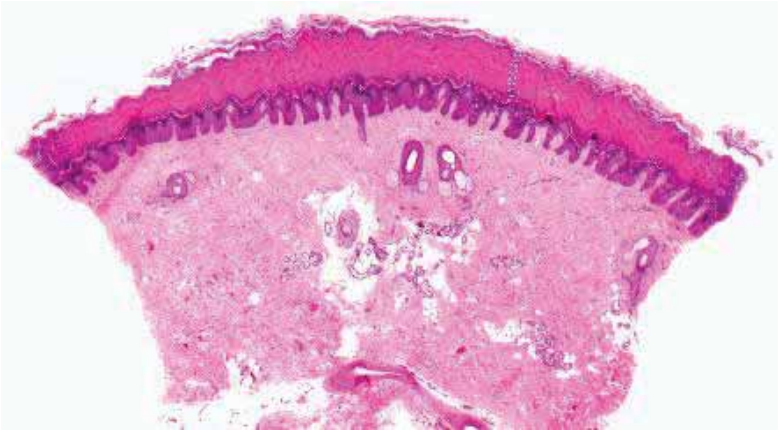


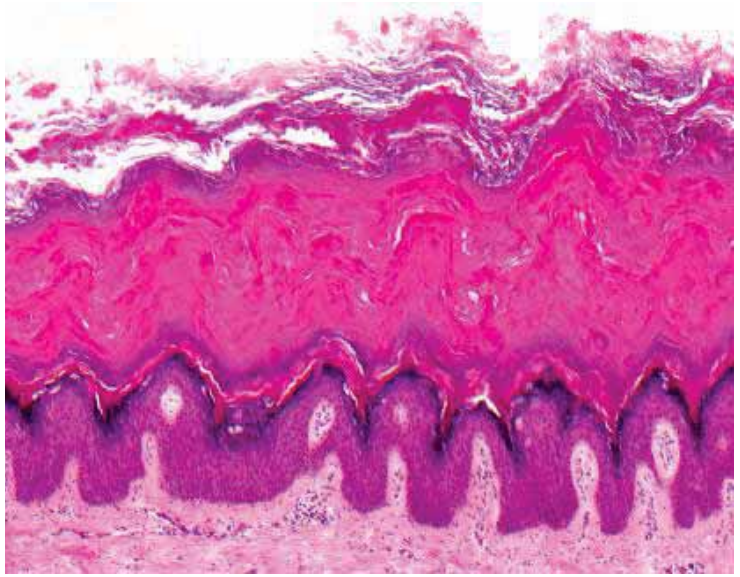




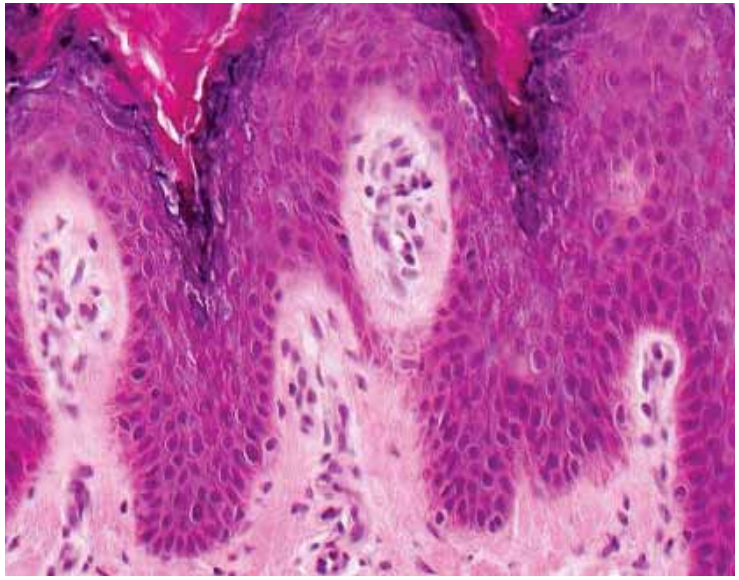


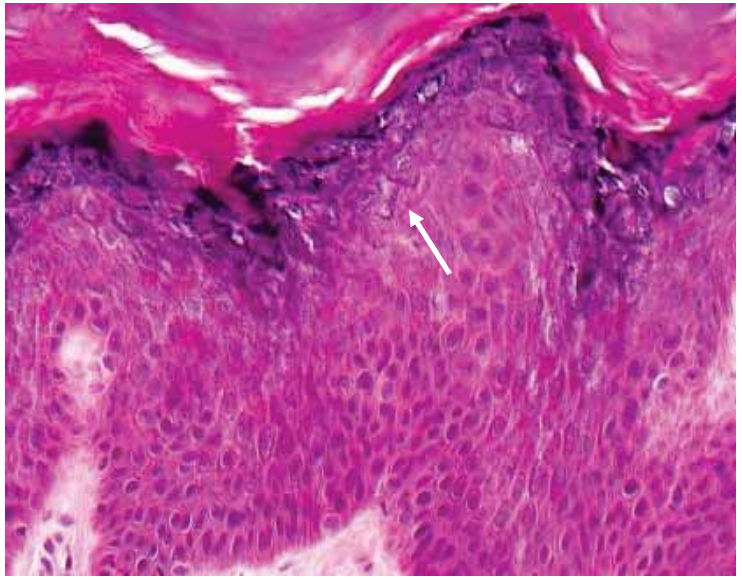
Ichthyosis bullosa of Siemens





Massive
Ortho-
hyperkeratosis



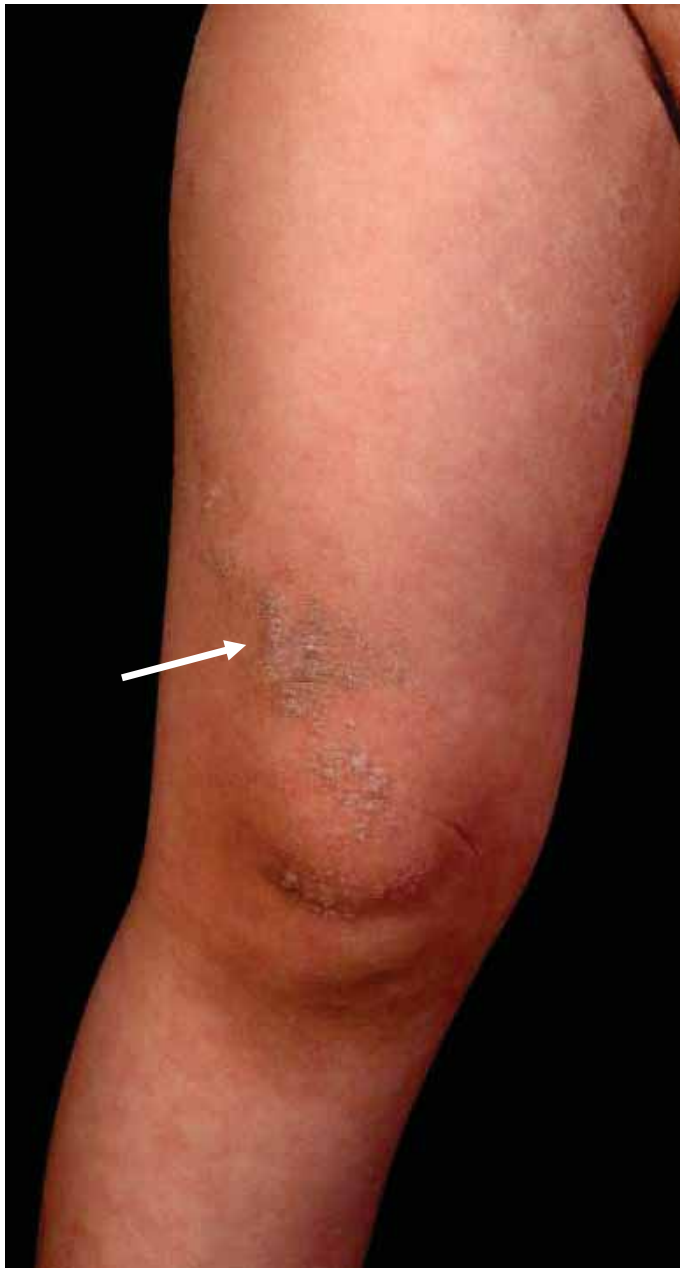


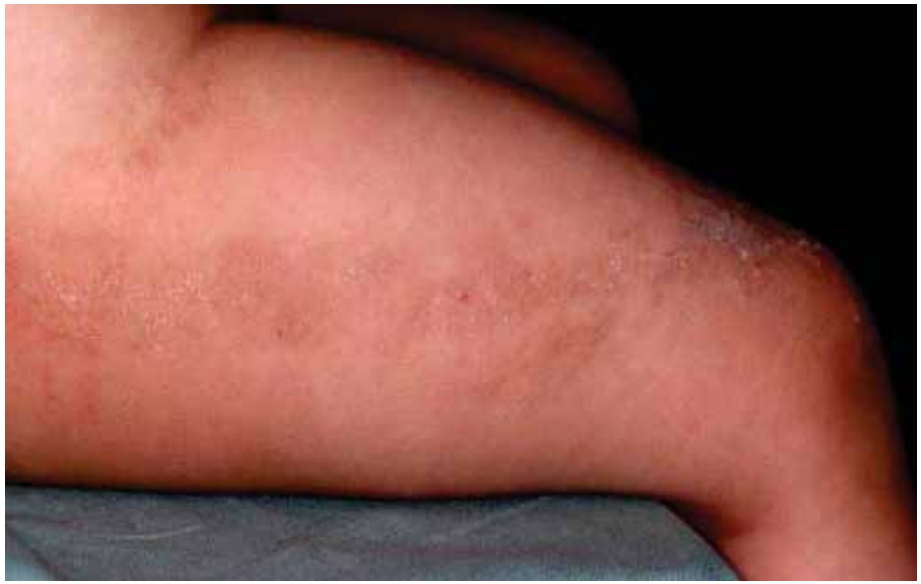
Discrete changes

Mutation of keratin 2

irregular KHG

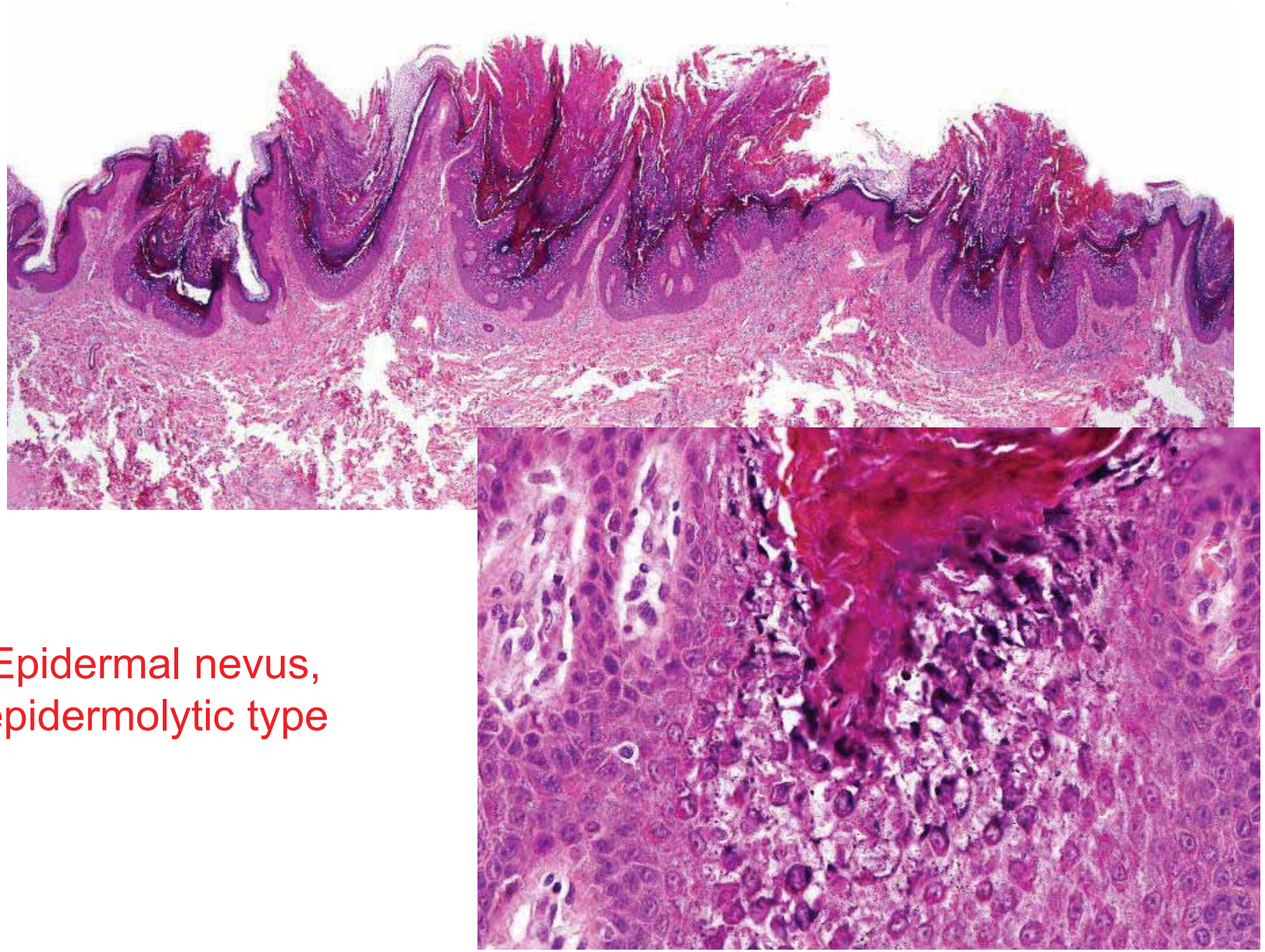
few clear spaces



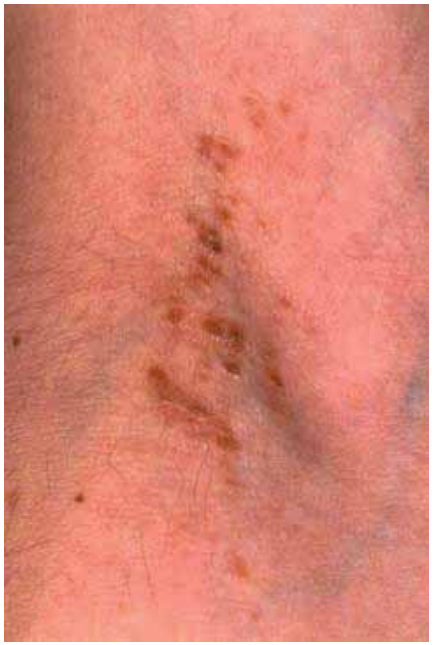


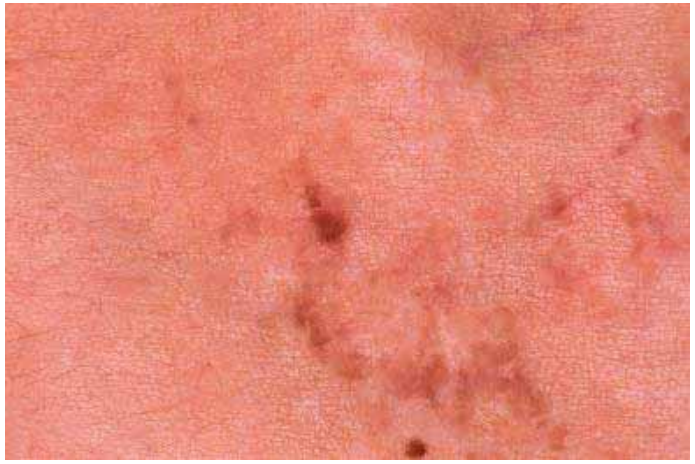
Epidermal Nevus with epidermolytic hyperkeratosis

(somatic mutations in *KRT1* or *KRT10*, postzygotic mosaicism)

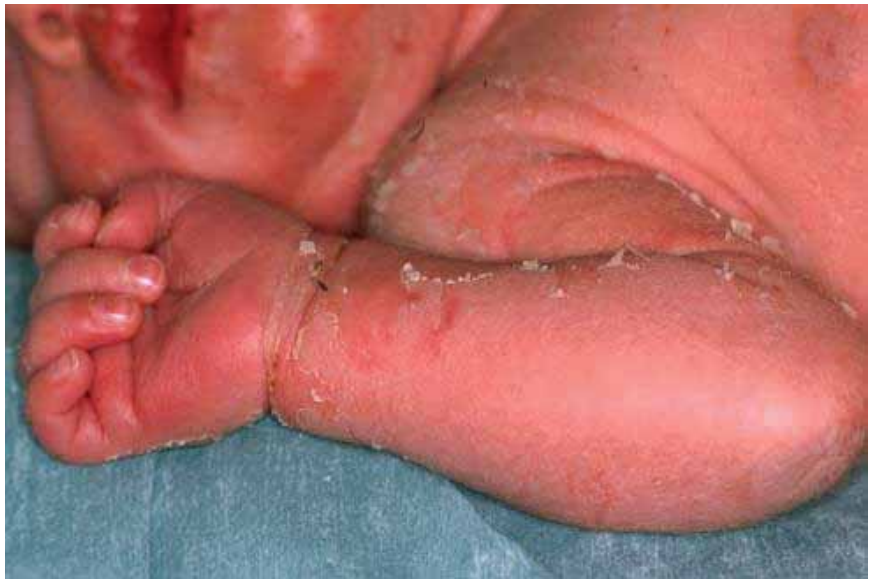


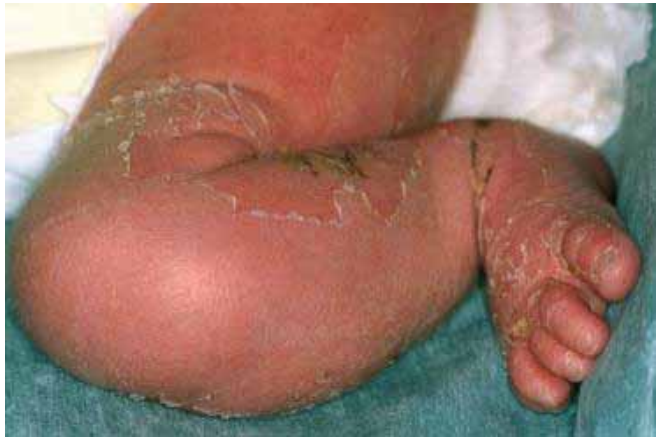
Epidermal nevus,
epidermolytic type





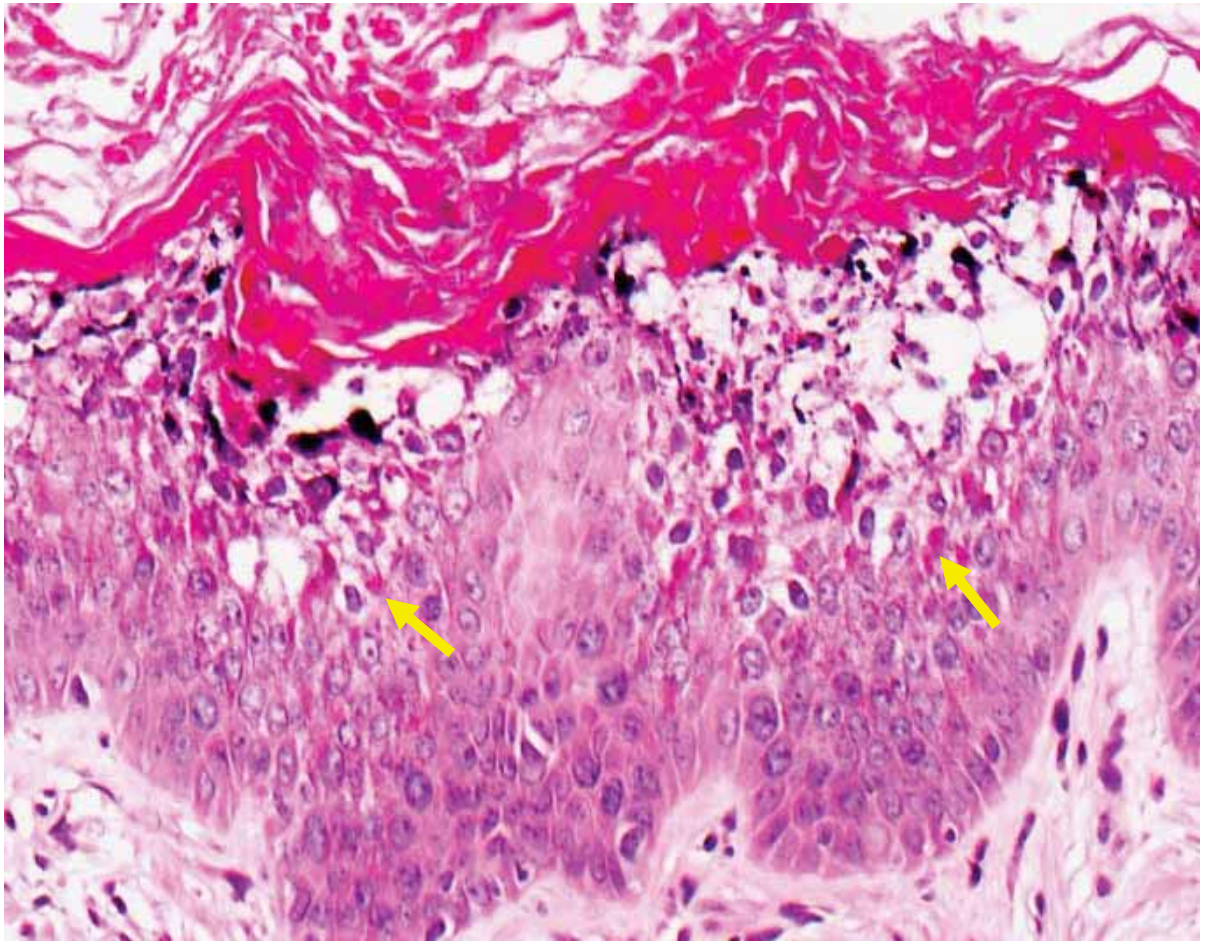
Father, epidermal nevus on the arm





Son, newborn, Bullous congenital ichthyotic erythroderma Brocq

Pattern Epidermolytic Hyperkeratosis (EHK)



- Orthohyperkeratosis

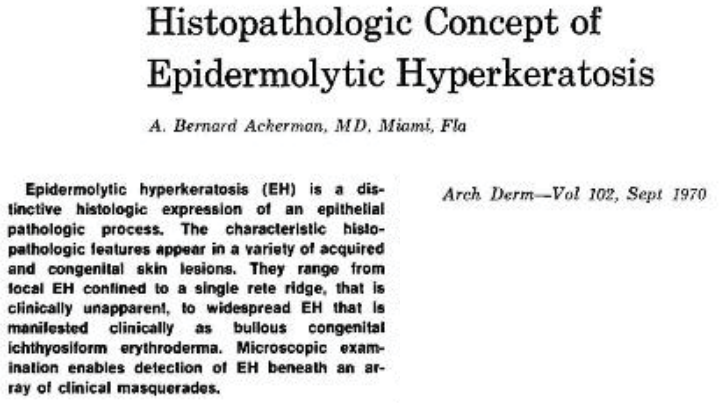
Acanthosis and papillomatosis

Cell borders ill-defined
Vesicles

- Keratohyaline granules coarse, variably sized
- Eosinophilic granules

Thin sections, strong eosin !

Pattern
Epidermolytic Hyperkeratosis (EHK)



Histopathologic Concept of
Epidermolytic Hyperkeratosis

A. Bernard Ackerman, MD, Miami, Fla

Epidermolytic hyperkeratosis (EH) is a distinctive histologic expression of an epithelial pathologic process. The characteristic histopathologic features appear in a variety of acquired and congenital skin lesions. They range from focal EH confined to a single rete ridge, that is clinically unapparent, to widespread EH that is manifested clinically as bullous congenital ichthyosiform erythroderma. Microscopic examination enables detection of EH beneath an array of clinical masquerades.

Arch Derm—Vol 102, Sept 1970

- Epidermolytic palmoplantar keratoses
  (KRT1/9-pEDD)
- Keratinopathic Ichthyoses
  (KRT1/10-nEDD, KRT2-nEDD)
- Epidermal nevi (Mosaicism)
- Nevoid follicular EHK, persistent actinic epidermolytic hyperkeratosis

➢Epidermolytic acanthoma (isolated, disseminated)

➢Epidermolytic leukoplakia

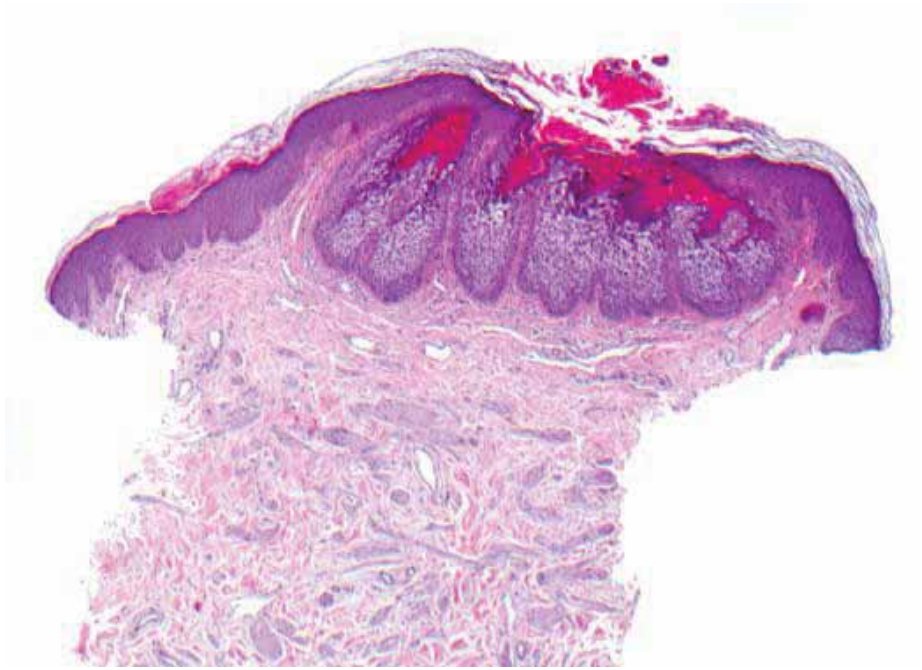
➢Epidermoid (Infundibular) Cyst

➢Incidental finding

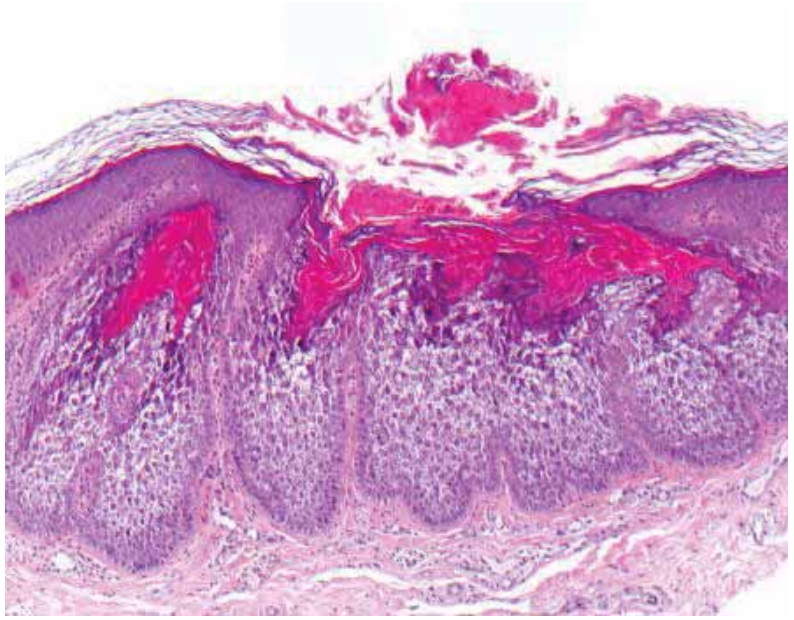
- Grover disease

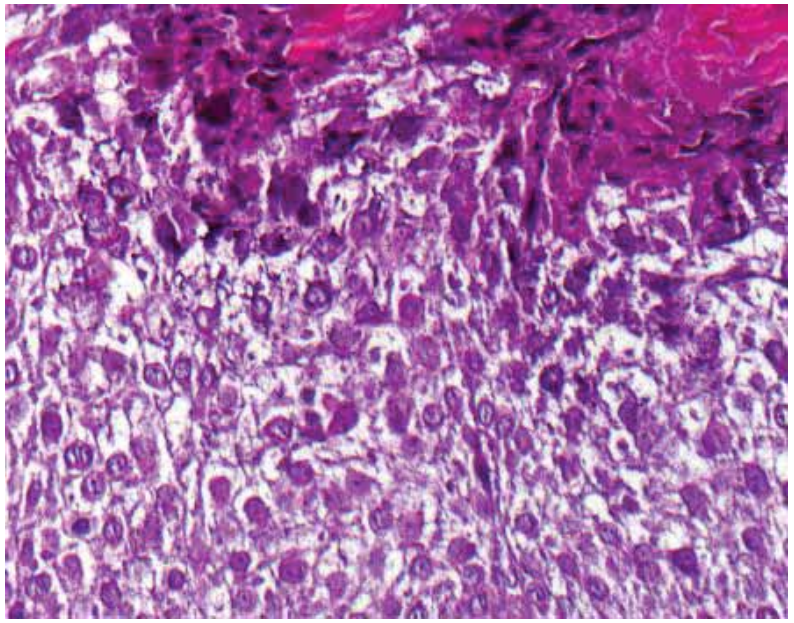
Epidermolytic Acanthoma

solitary, multiple, genital and extragenital



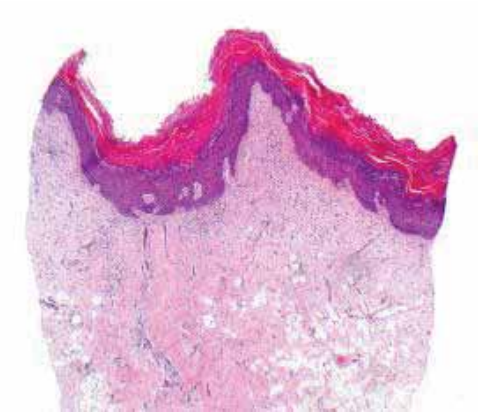
Mutations in KRT10 in epidermolytic acanthoma.
Cheraghlou S, et al. J Cutan Pathol., 2020

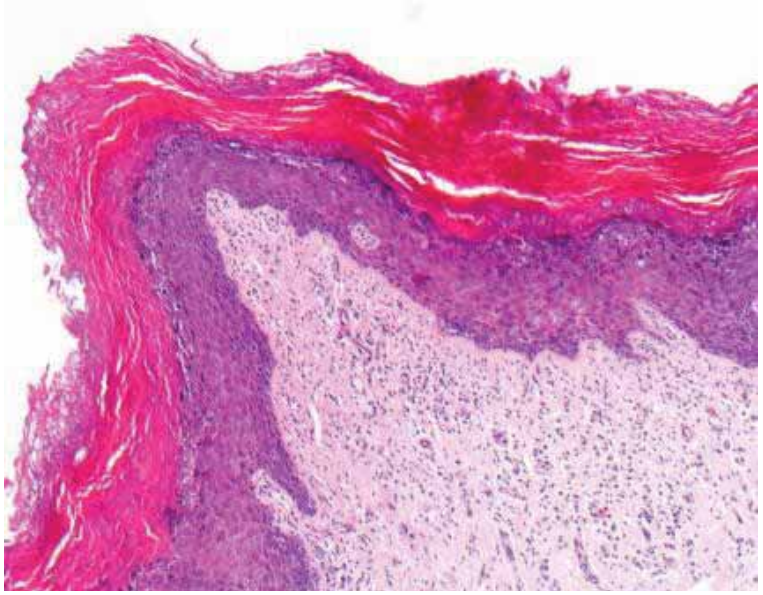


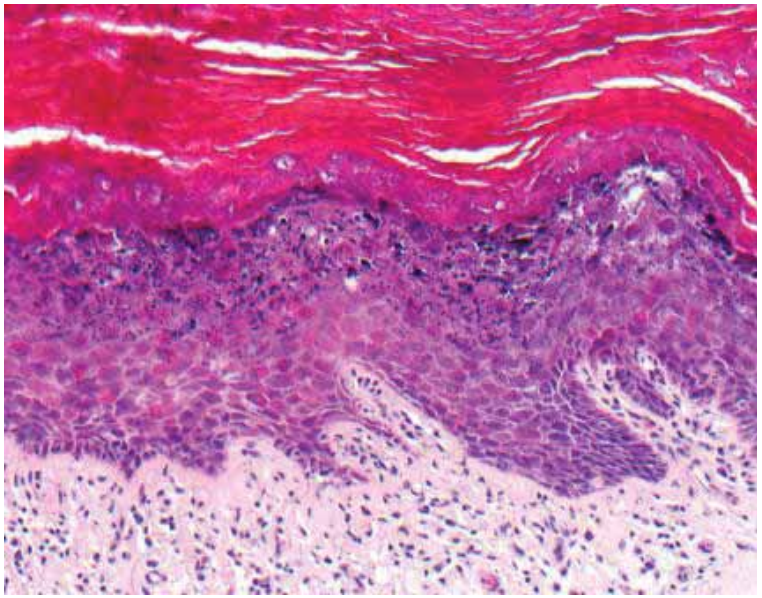


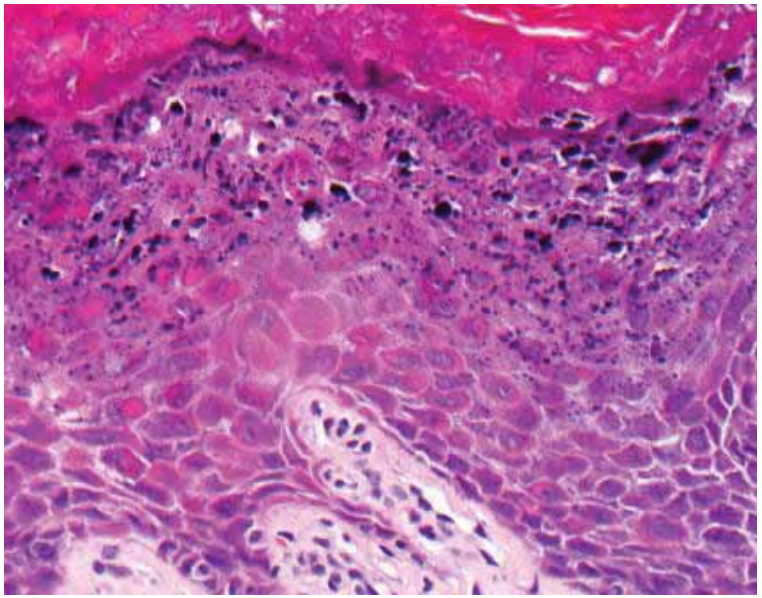
Epidermolytic Leukoplakia

oral, genital mucosa, w/o PPK, SSC



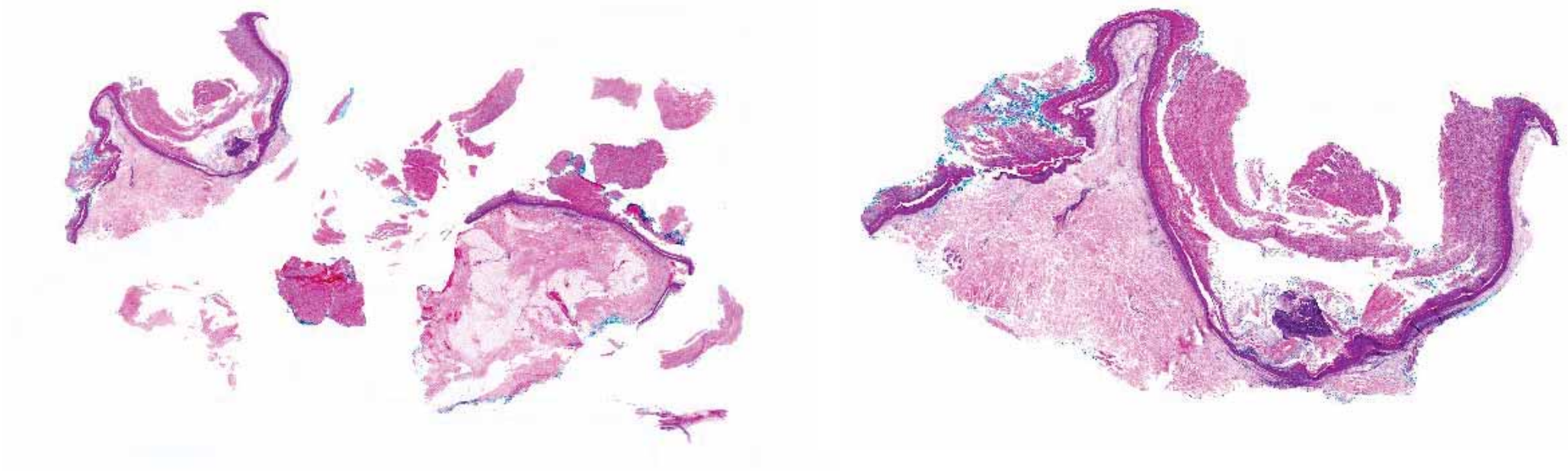






Epidermoid (Infundibular) Cyst with epidermolytic hyperkeratosis

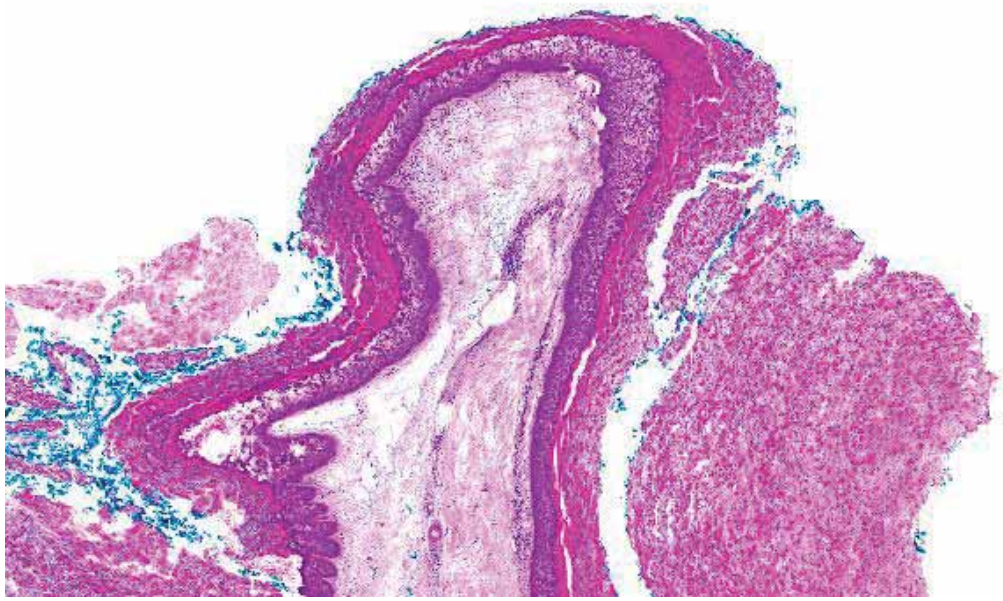
rare, 4 cases published

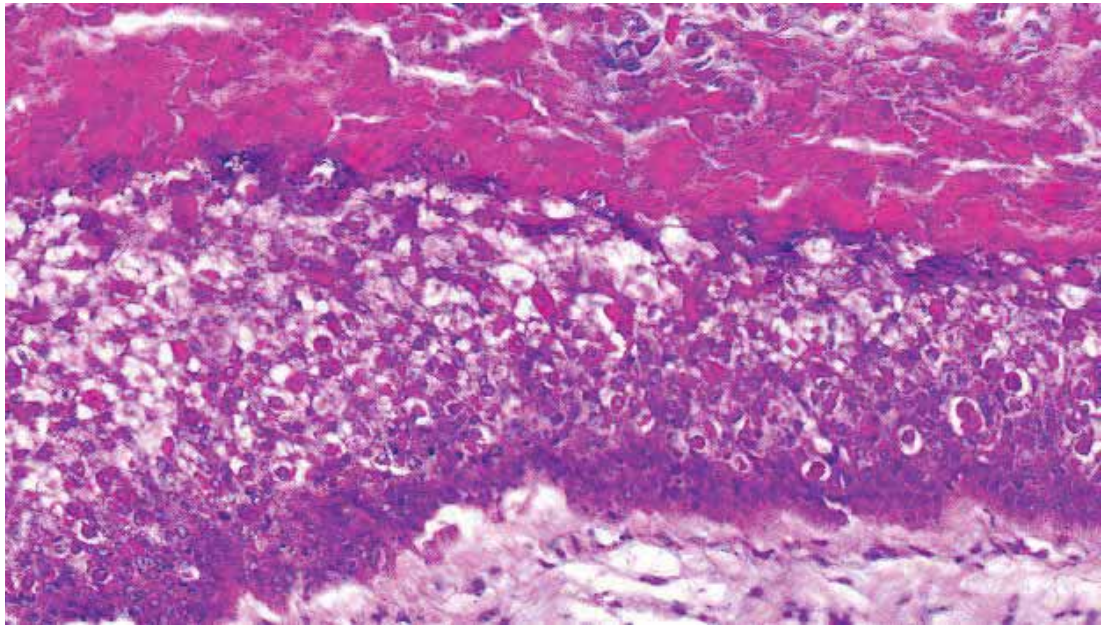


Consultant Case, M. Fülle,
Dermatohistologisches Labor, Münster

Prestwood, C, Vandergriff, T. Epidermolytic Hyperkeratosis in an Epidermoid (Infundibular) Cyst. Am J Dermatopathol, 44:215-217, 2022, review including incidental findings

Epidermoid (Infundibular) Cyst with epidermolytic hyperkeratosis





Clue: Keratin more compact than in conventional epidermoid cysts

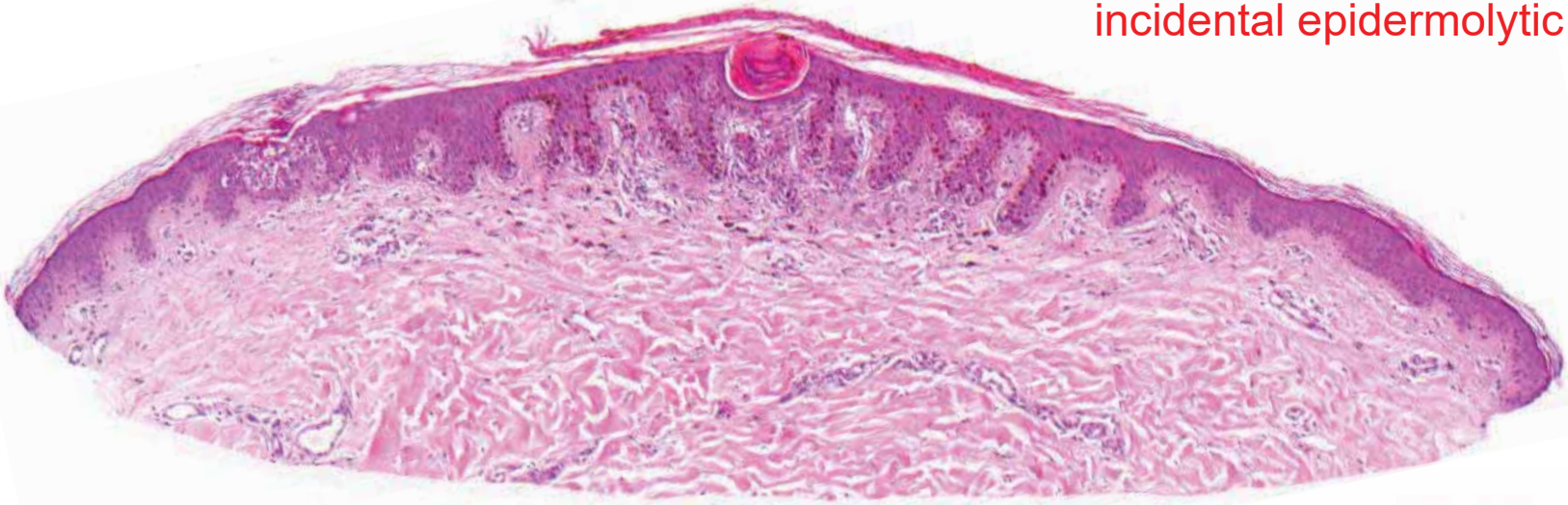
Pattern: EHK

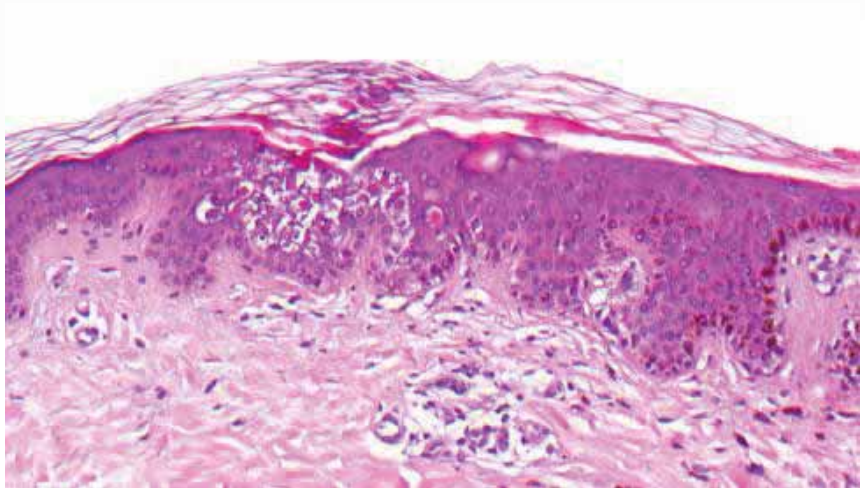
Pattern
Epidermolytic Hyperkeratosis

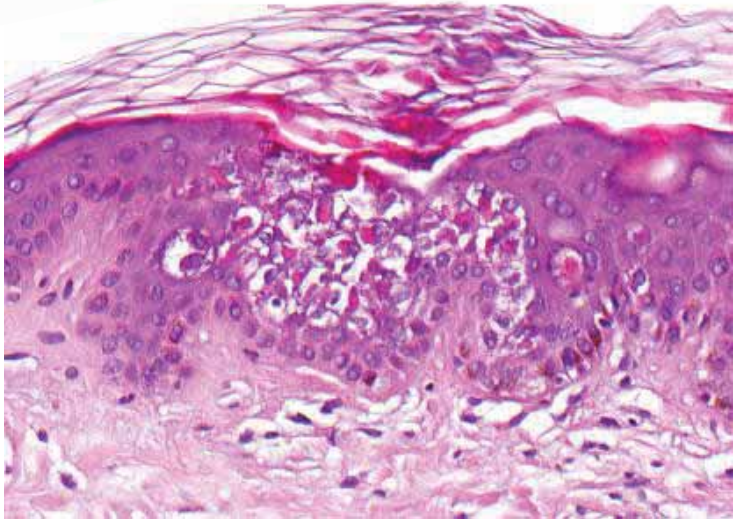
incidental finding

in normal or actinically damaged skin, in melanocytic nevi, seborrheic keratosis, actinic keratosis, invasive squamous cell carcinoma, BCC, overlying scars and dermatofibroma, epidermal and pilar cysts, inflammatory diseases (Lichen planus, nummular dermatitis, Pityriasis versicolor, Grover disease, granuloma annulare, ...)

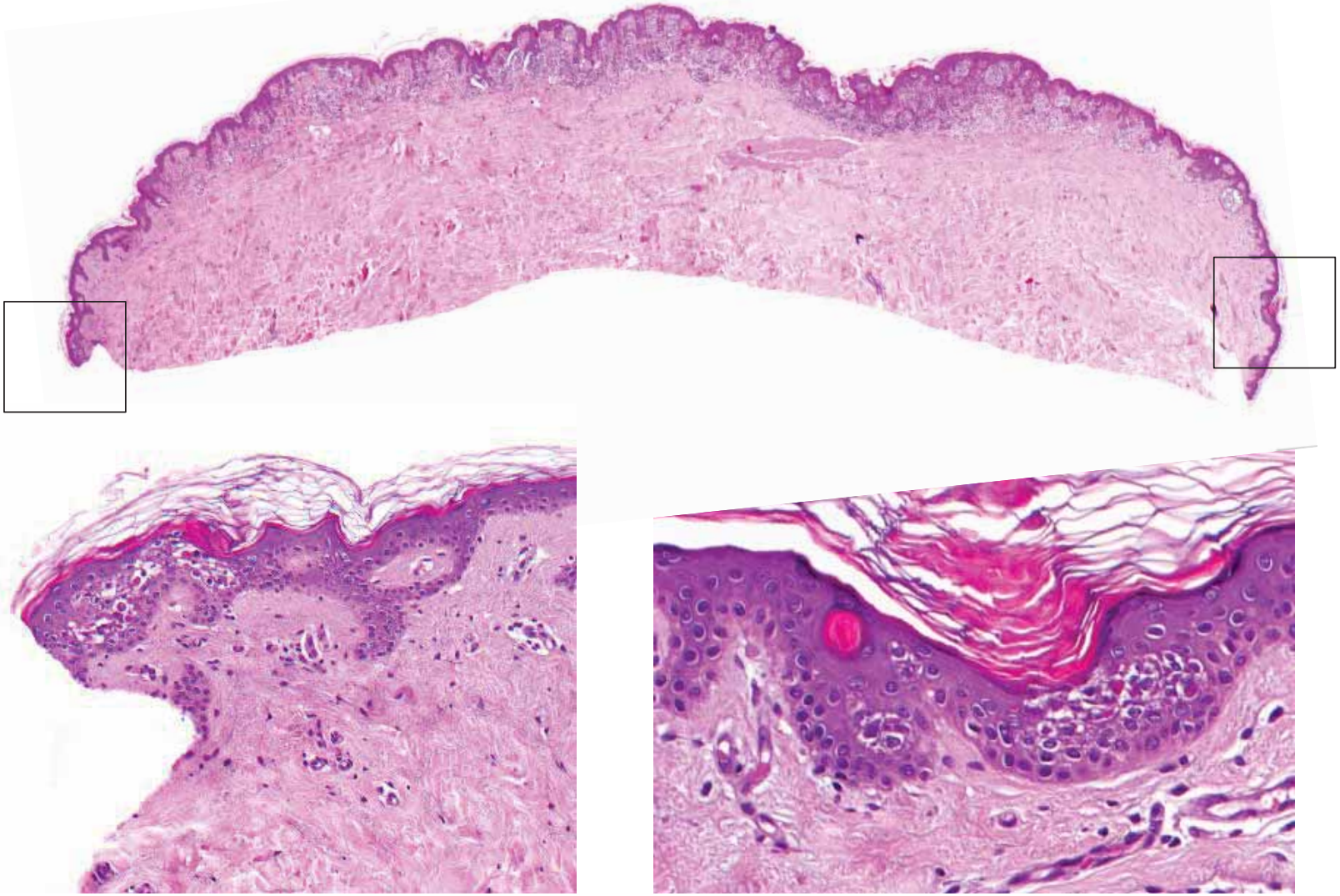
Melanocytic nevus with
incidental epidermolytic hyperkeratosis



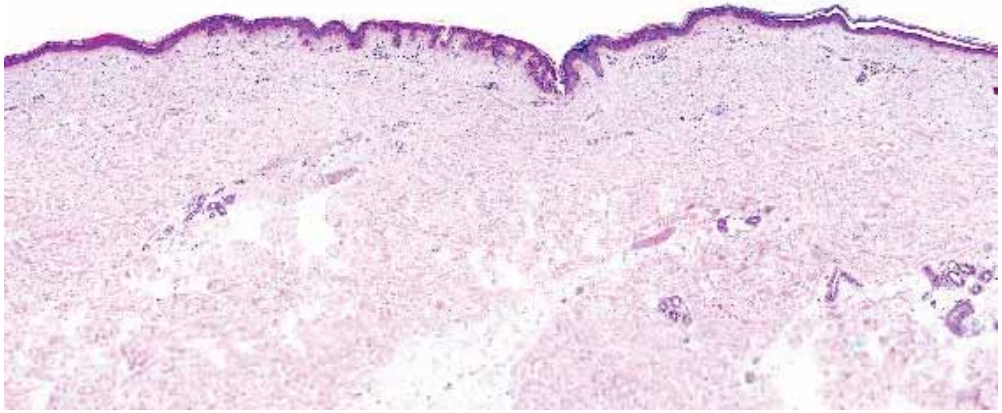


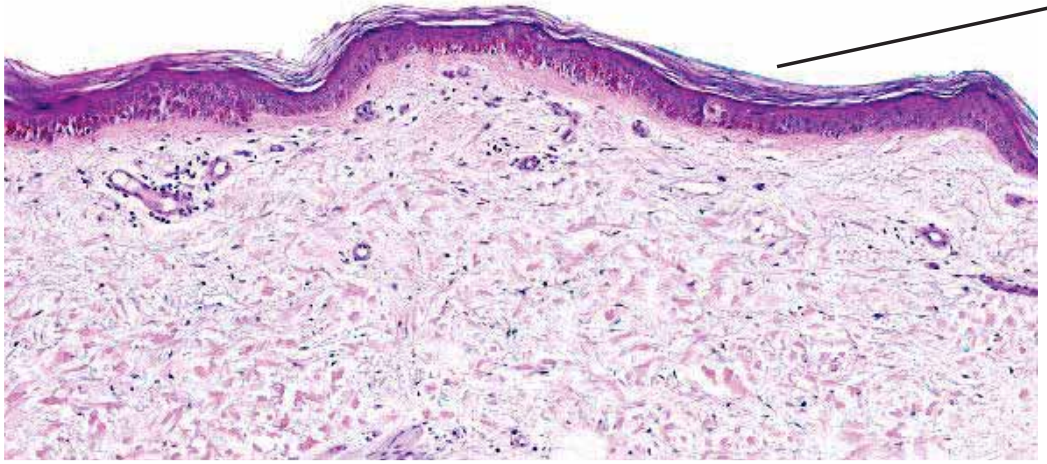


Melanocytic nevus, incidental epidermolytic hyperkeratosis, both sides

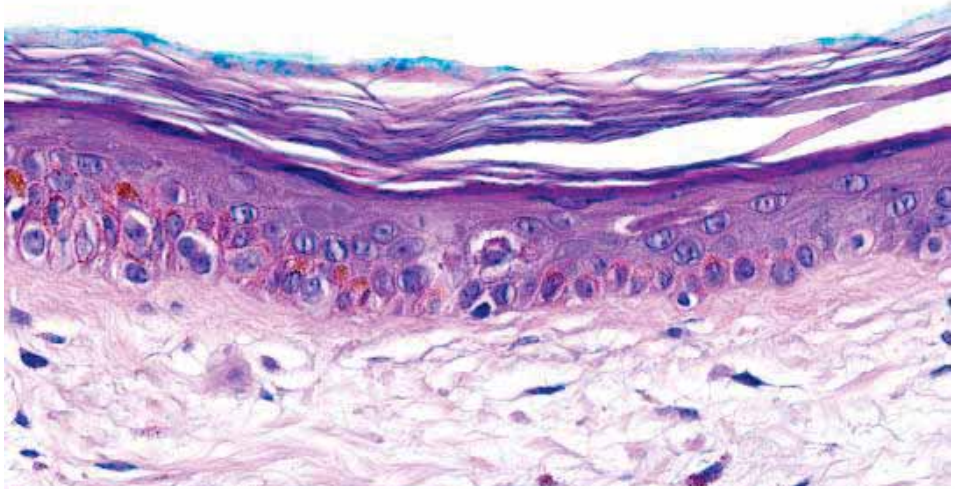


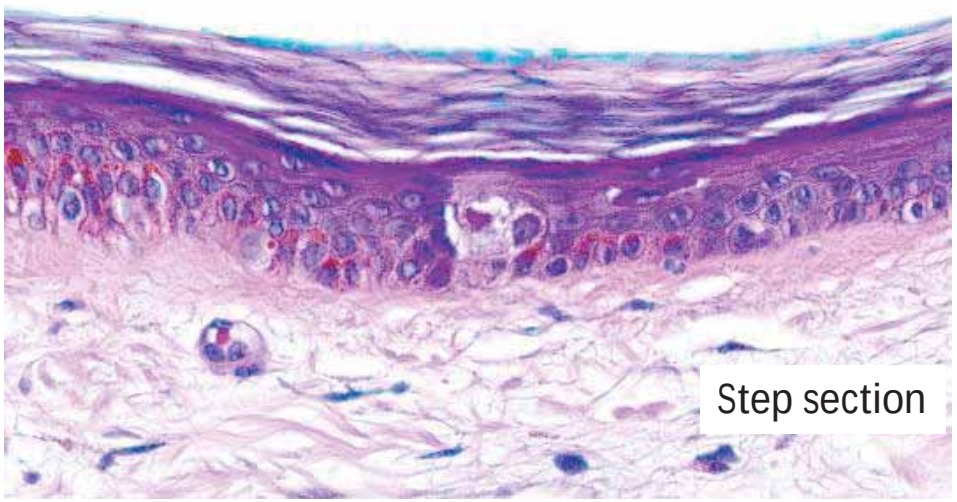
Melanocytic nevus with incidental epidermolytic hyperkeratosis



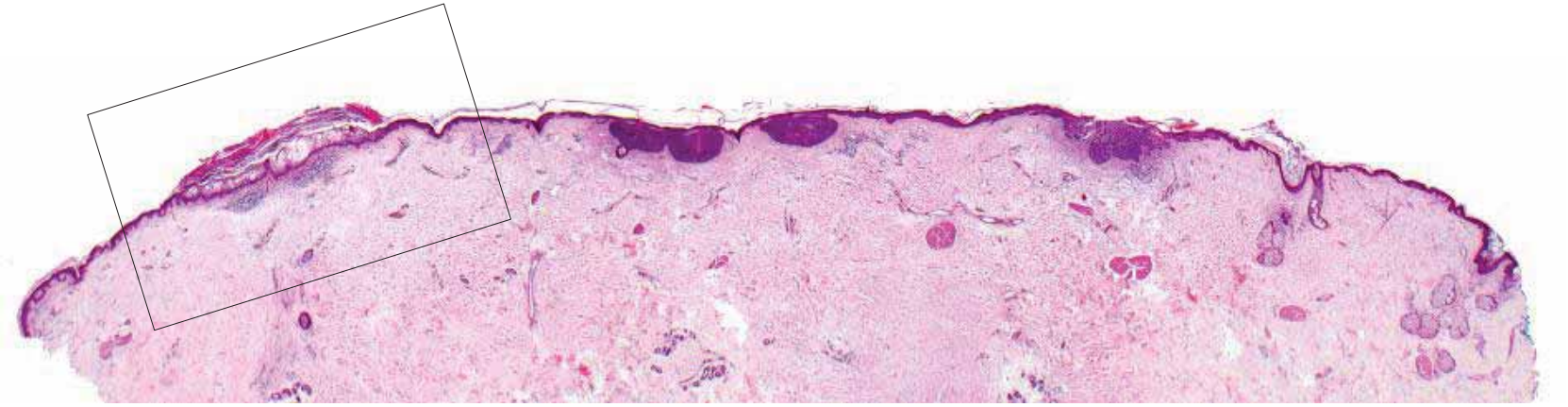


single cell level

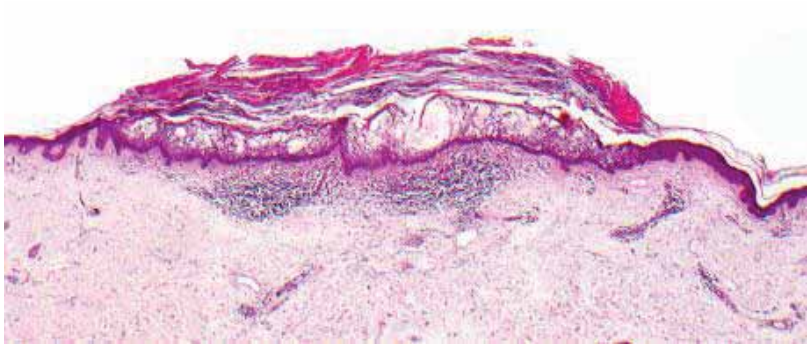


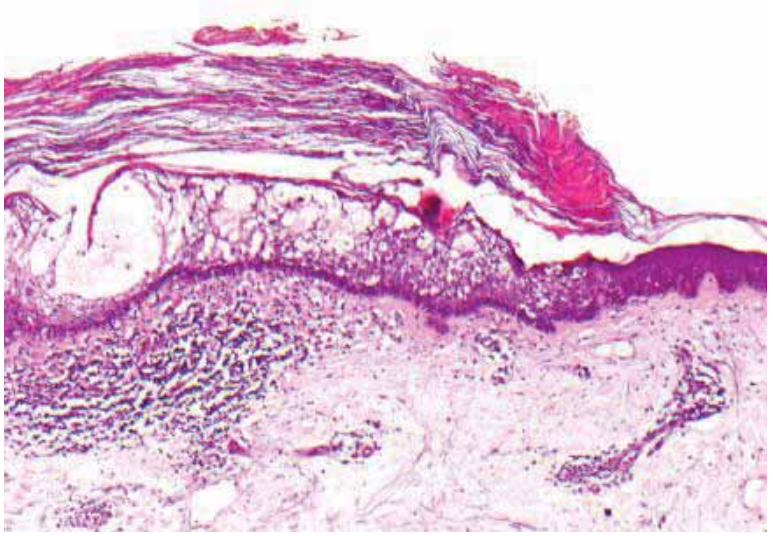


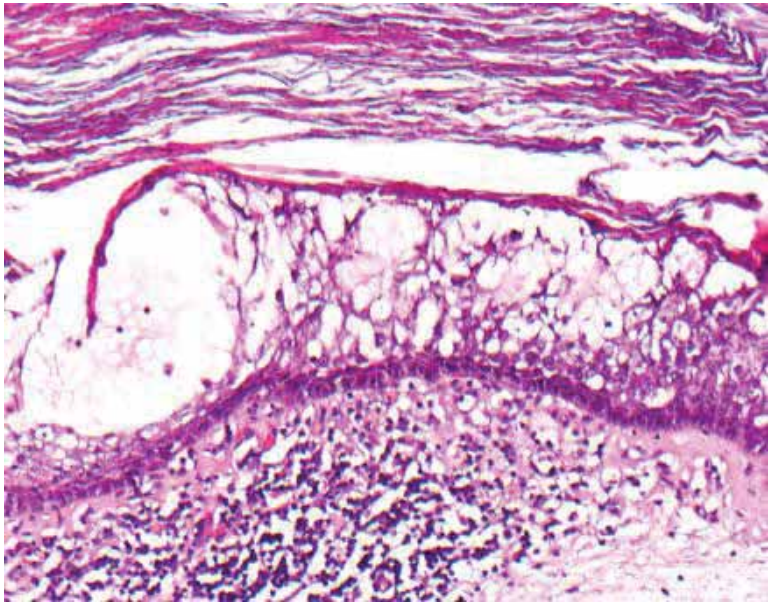
Basalcell carcinoma
Incidental epidermolytic hyperkeratosis

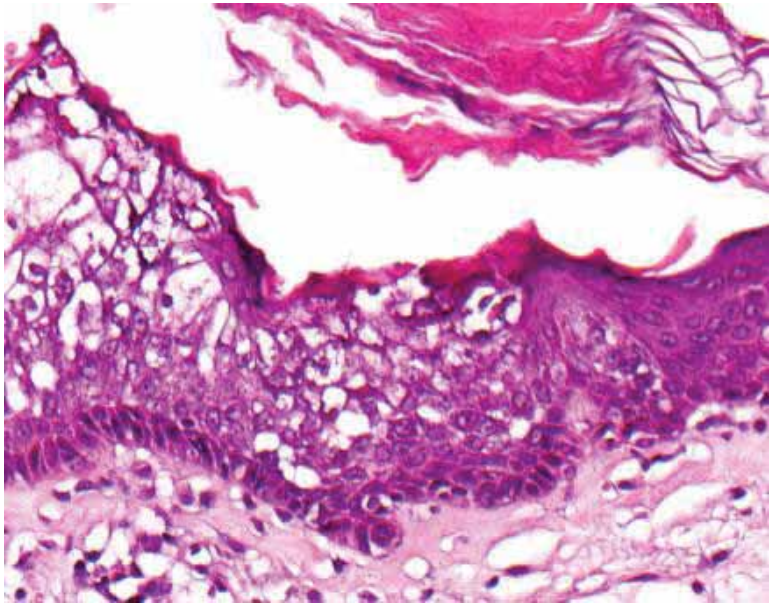


Prominent EHK

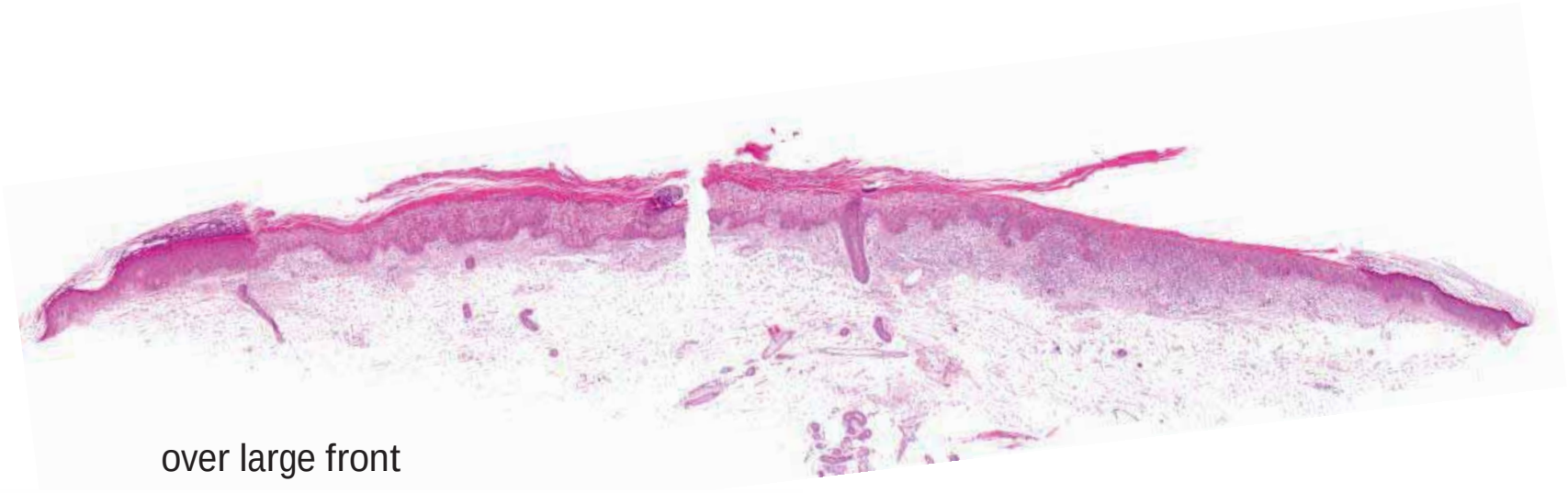




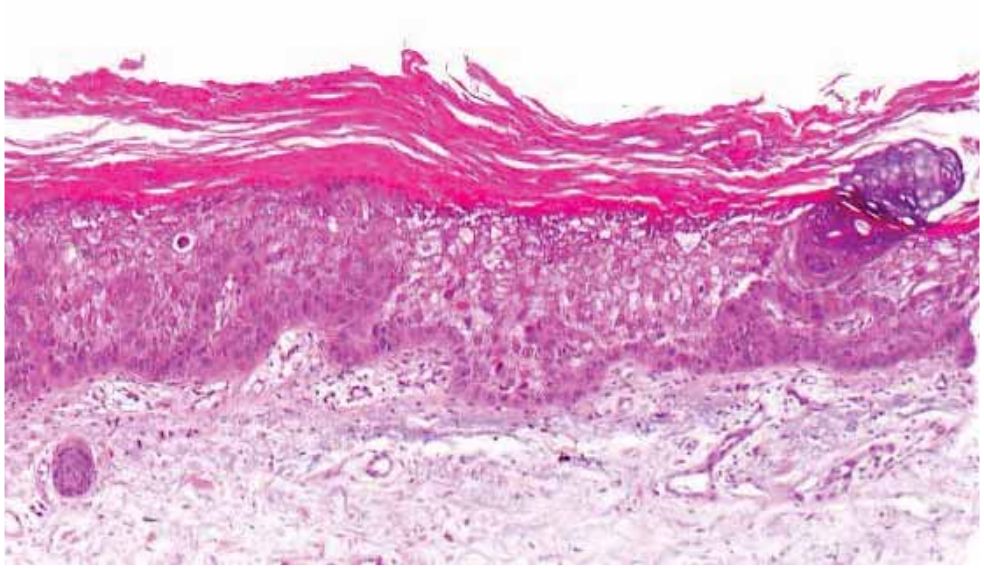


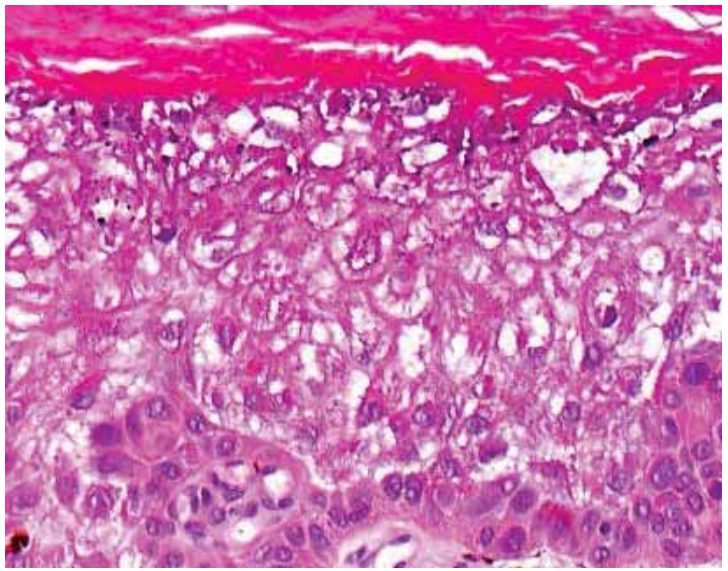


Actinic keratosis with incidental epidermolytic hyperkeratosis

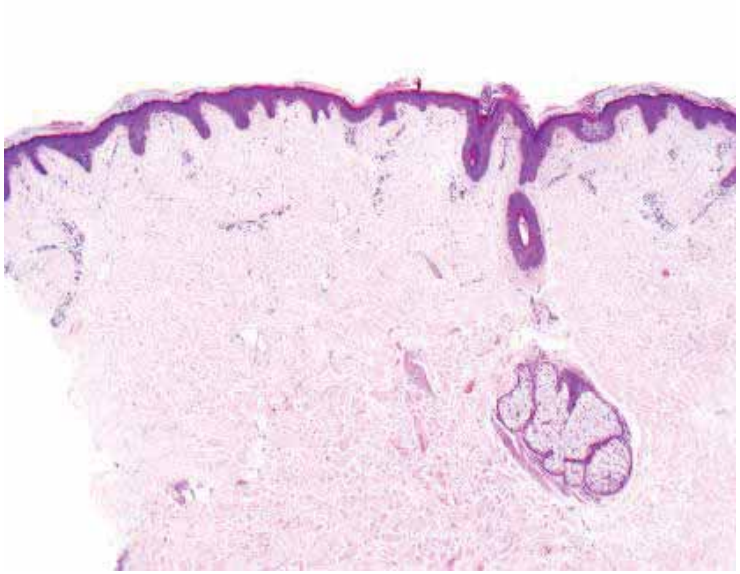


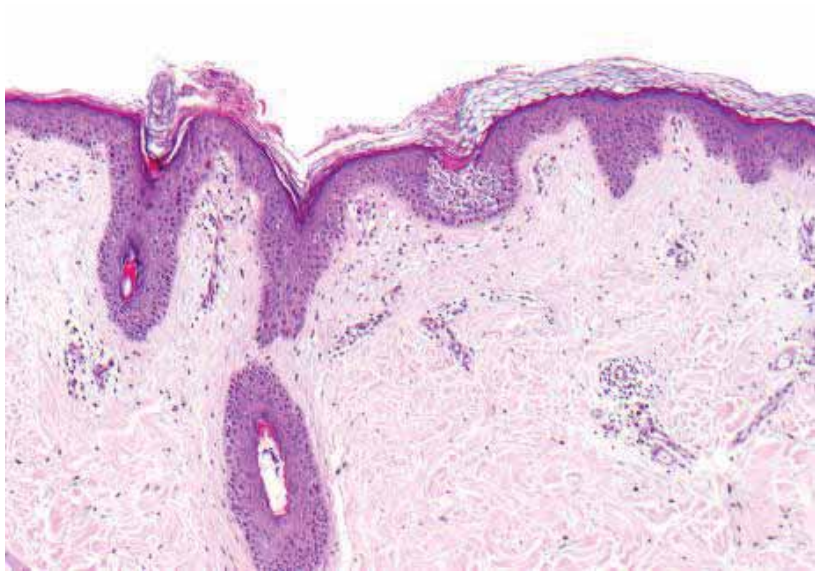
over large front

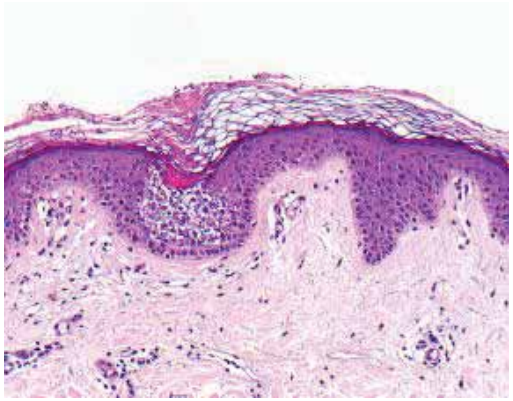


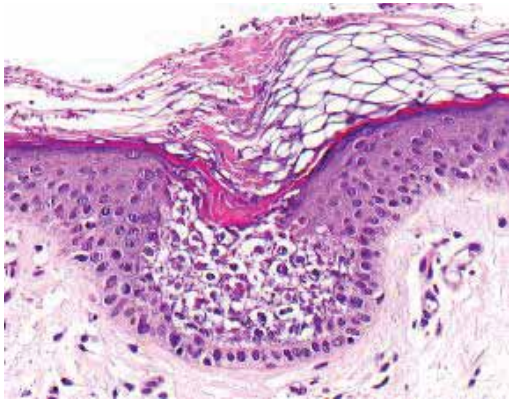


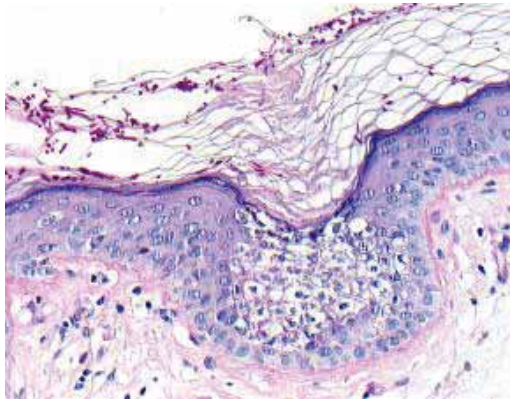
Pityriasis versicolor
Incidental epidermolytic hyperkeratosis



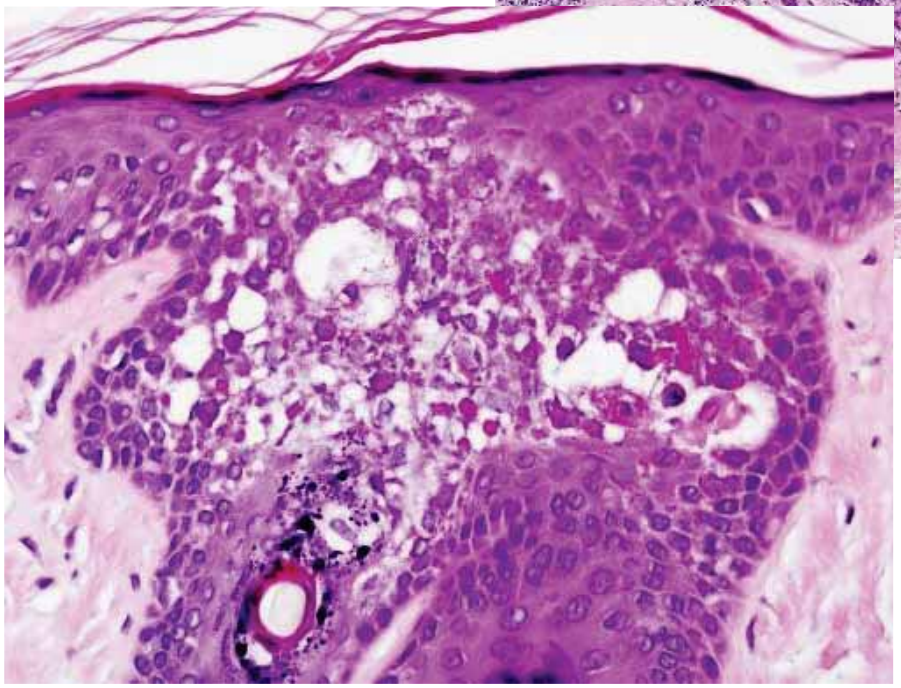


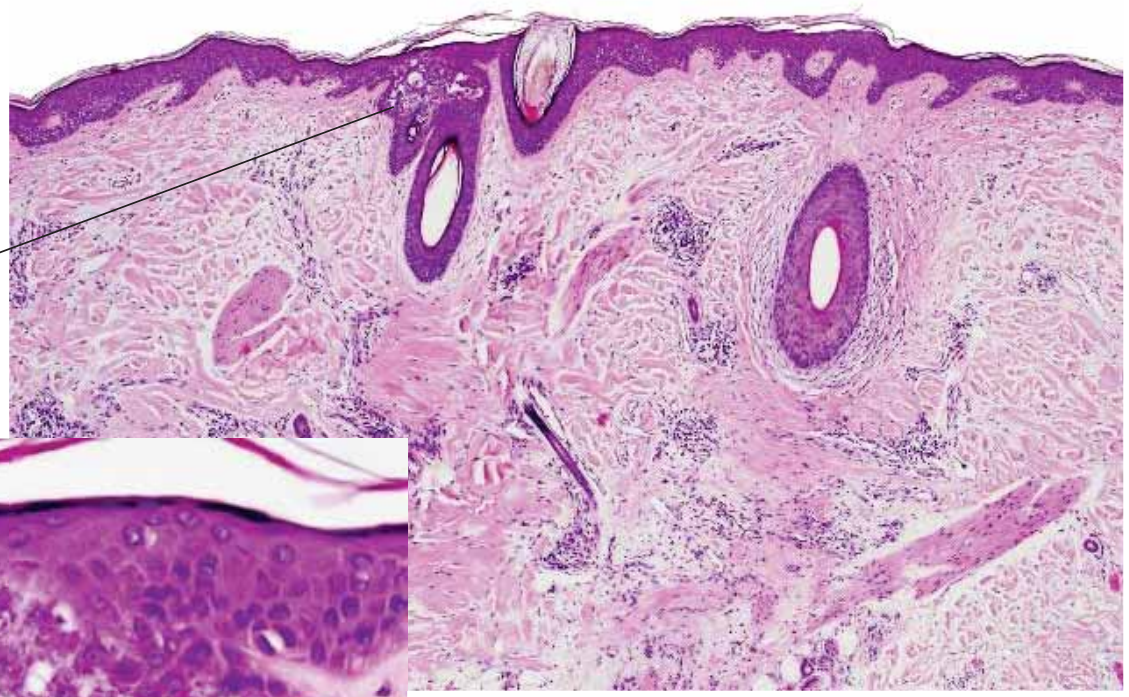






Lichen planopilaris



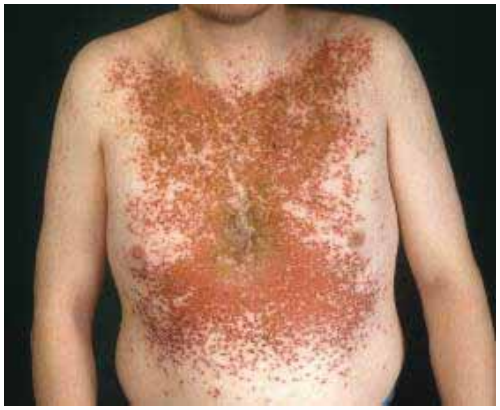


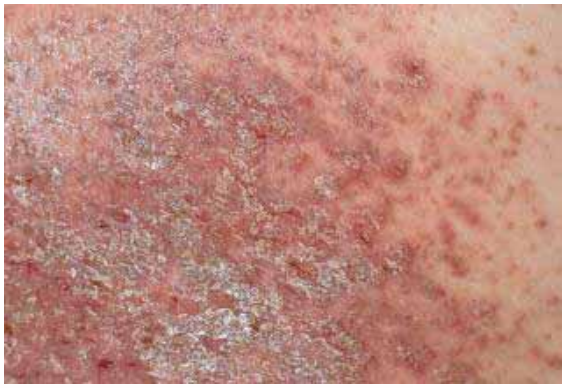
Incidental epidermolytic hyperkeratosis

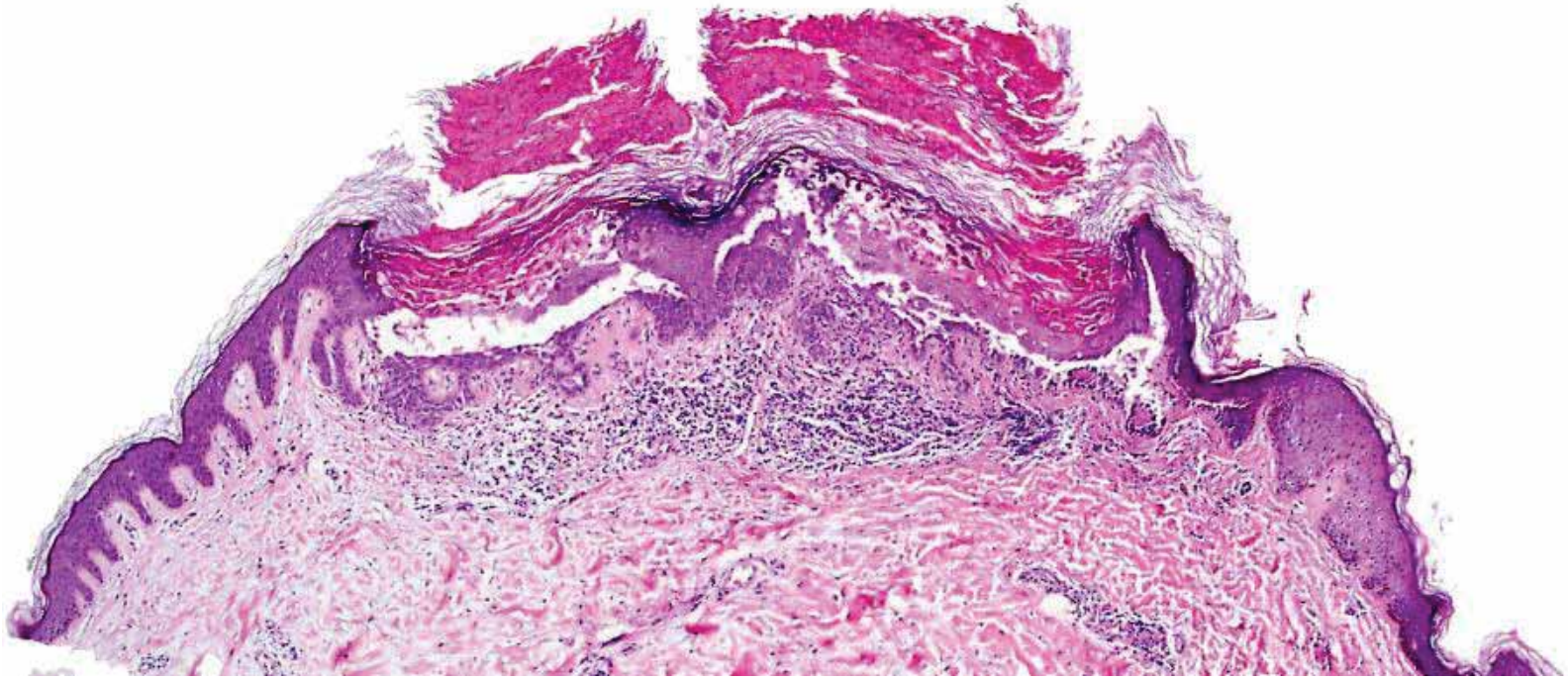
Epidermal reaction patterns
in genodermatoses, epidermal nevi, acquired skin diseases or as an incidental finding

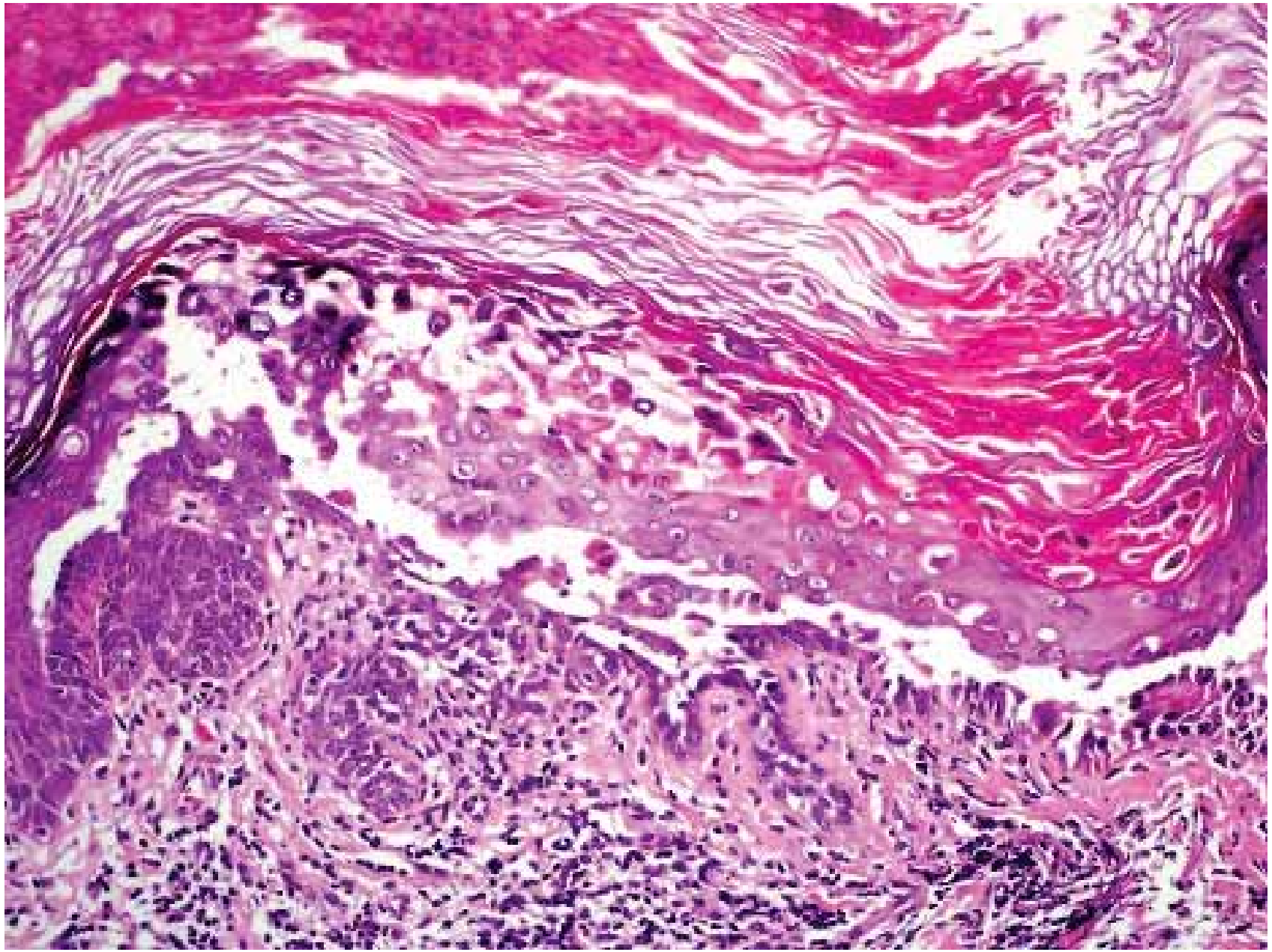
Pattern	Dermatosis	Mosaicism	Solitary lesion	Incidental finding
Epidermolytic hyperkeratosis	Keratinopathic Ichthyosis, Palmoplantar keratoderma	+	Epidermolytic acanthoma	+
Focal acantholytic dyskeratosis	M. Darier	+	Acantholytic dyskeratotic acanthoma	+
Hailey–Hailey–type acantholysis	M. Hailey–Hailey	+	Hailey–Hailey–type acanthoma	+
Desmosomal-type acantholysis	Genetic diseases with desmsosome related mutations	?	Acantholytic acanthoma (Hyaline inclusion acanthoma)	+
Epidermolysis bullosa simplex-type vacuolization	Epidermolysis bullosa simplex	+	?	+
Granular Parakeratosis	Granular parakeratosis	-	Granular parakeratotic acanthoma	+
.....				

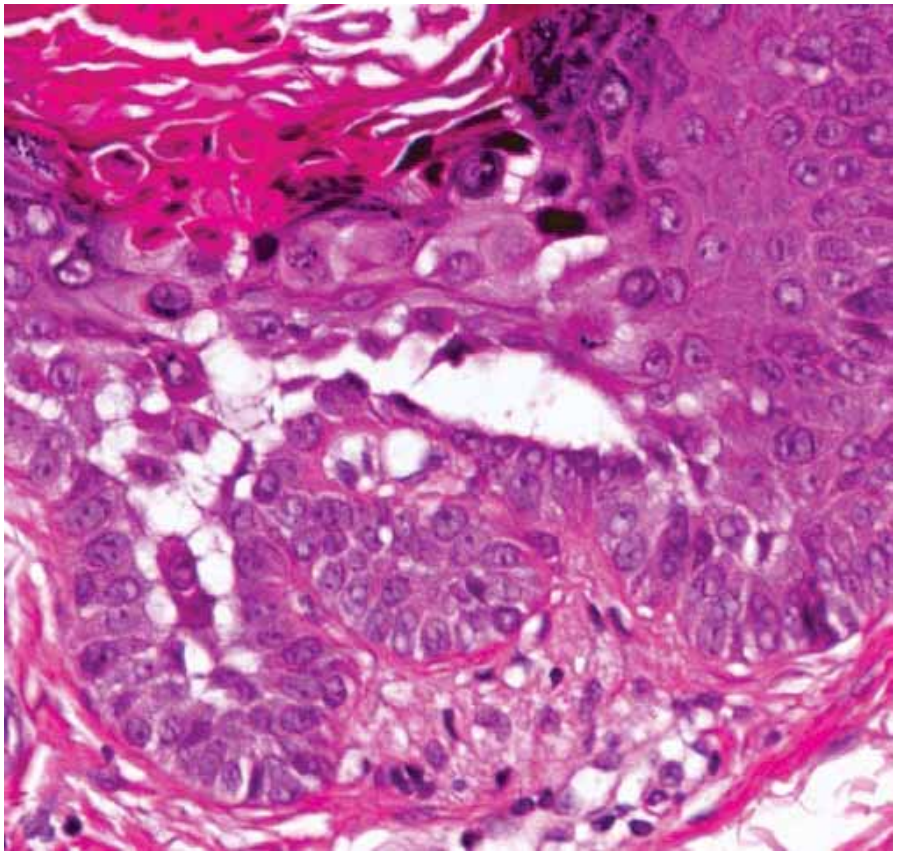
Darier-White disease







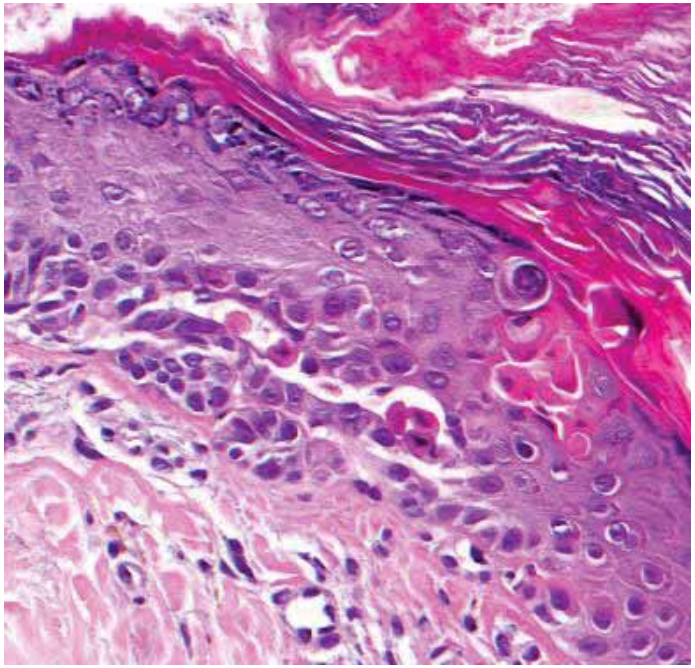




Darier-White Disease

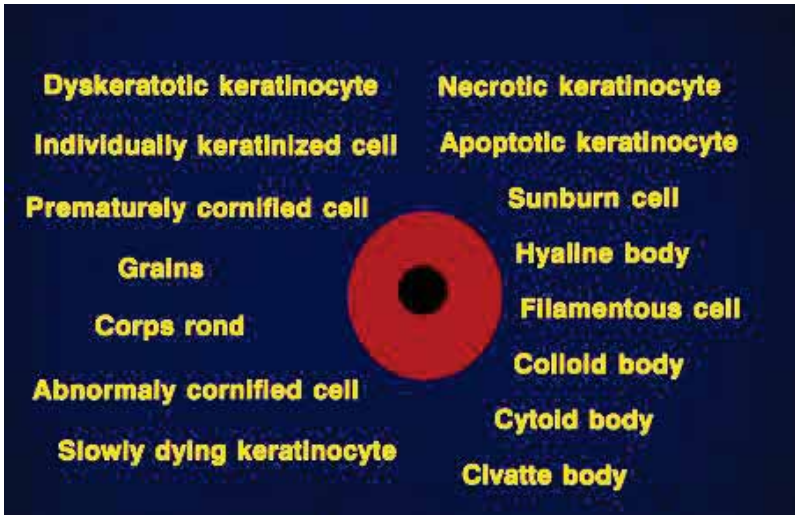
Focal Acantholytic Dyskeratosis (FAD)

- Suprabasal acantholysis
- Proliferation of basal keratinocytes
- Dyskeratotic cells with pyknotic nuclei in all layers („Corps rond and grains“)
- Thick parakeratotic plug
- Granular layer (if present) composed of plump keratinocytes

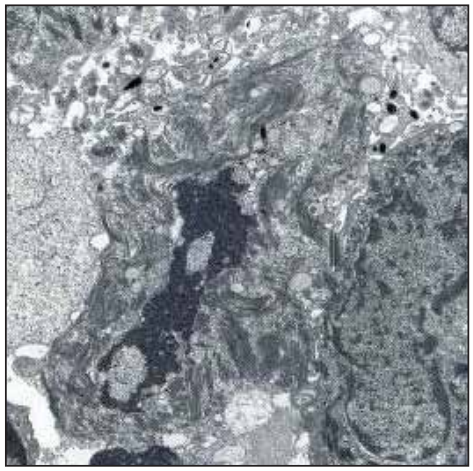


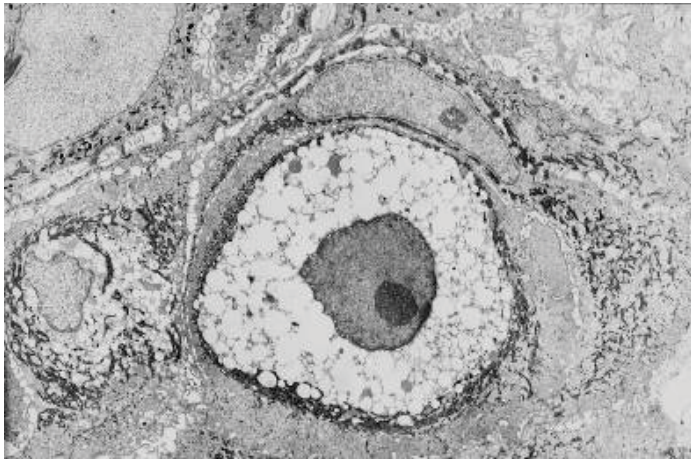
Dyskeratosis and Apoptosis

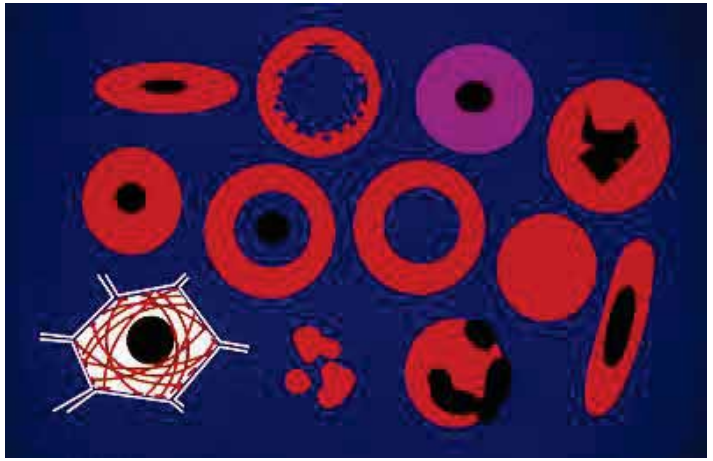
Many terms
and interpretations



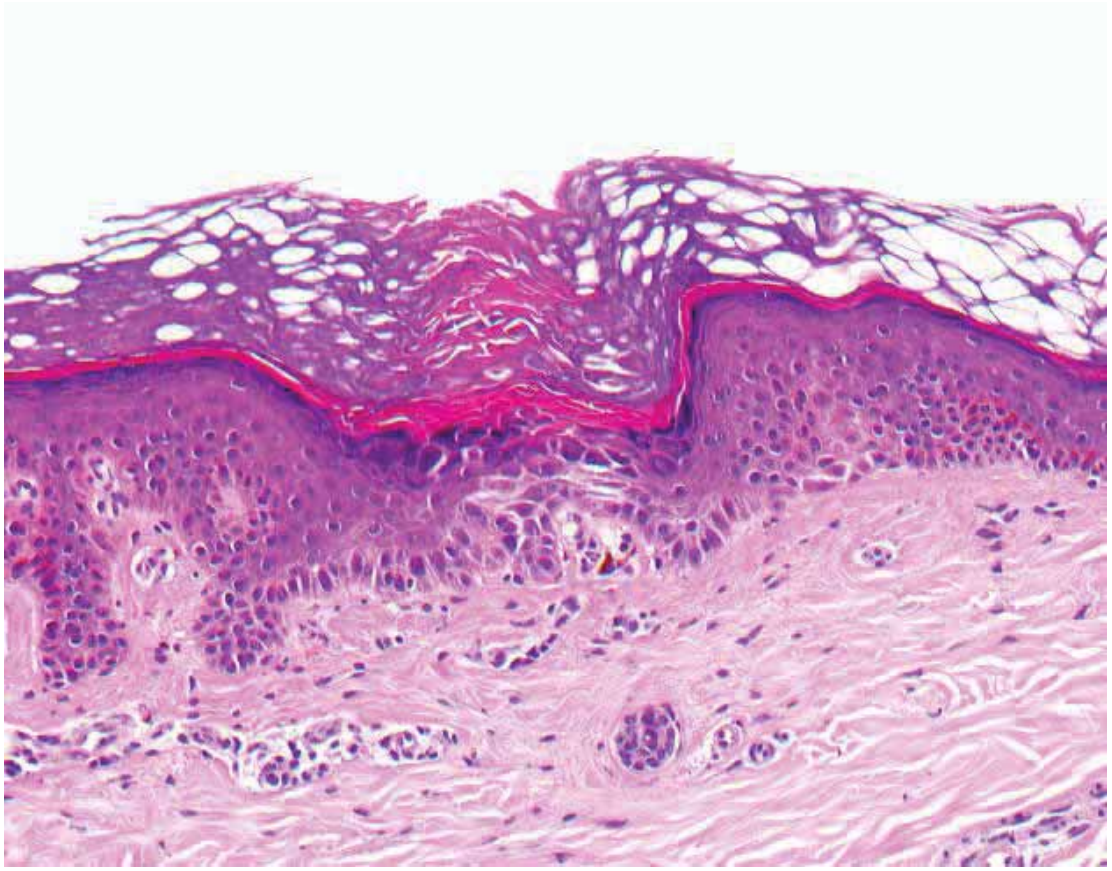
A Medley of Ideas about Dermatopathology, Giorgio Annessi, Giorgio Annessi, Rome, October,1995



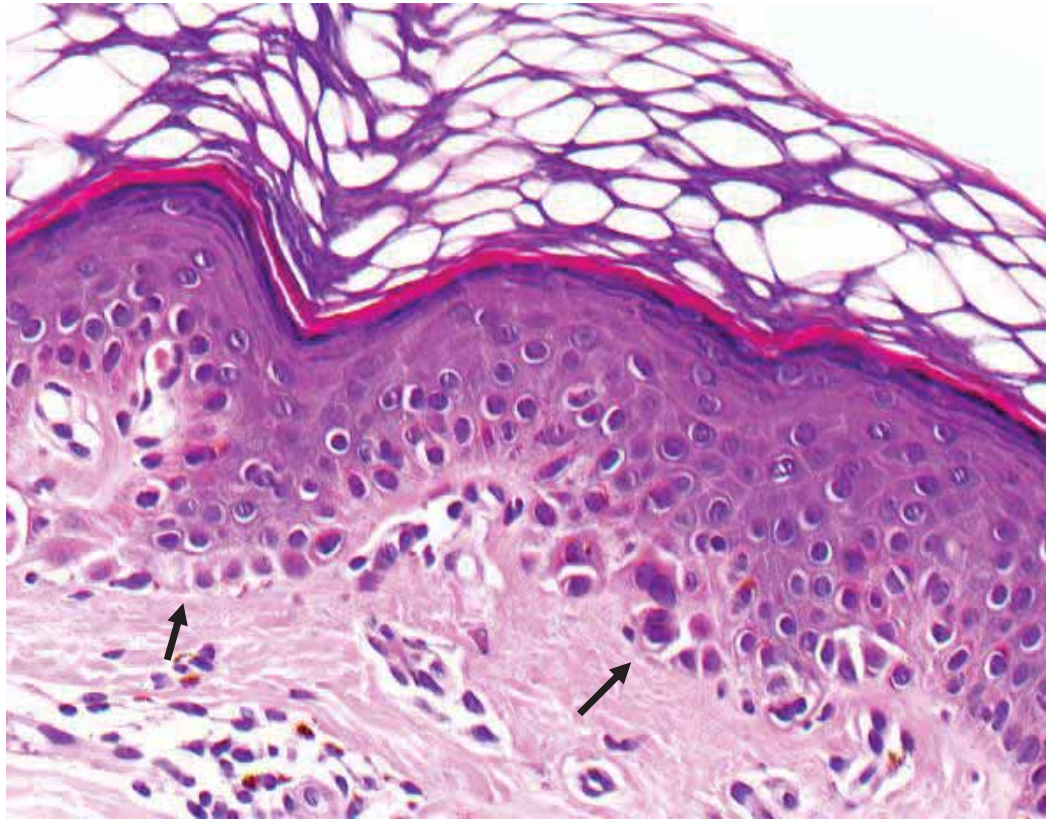




Darier-White disease, life of lesions

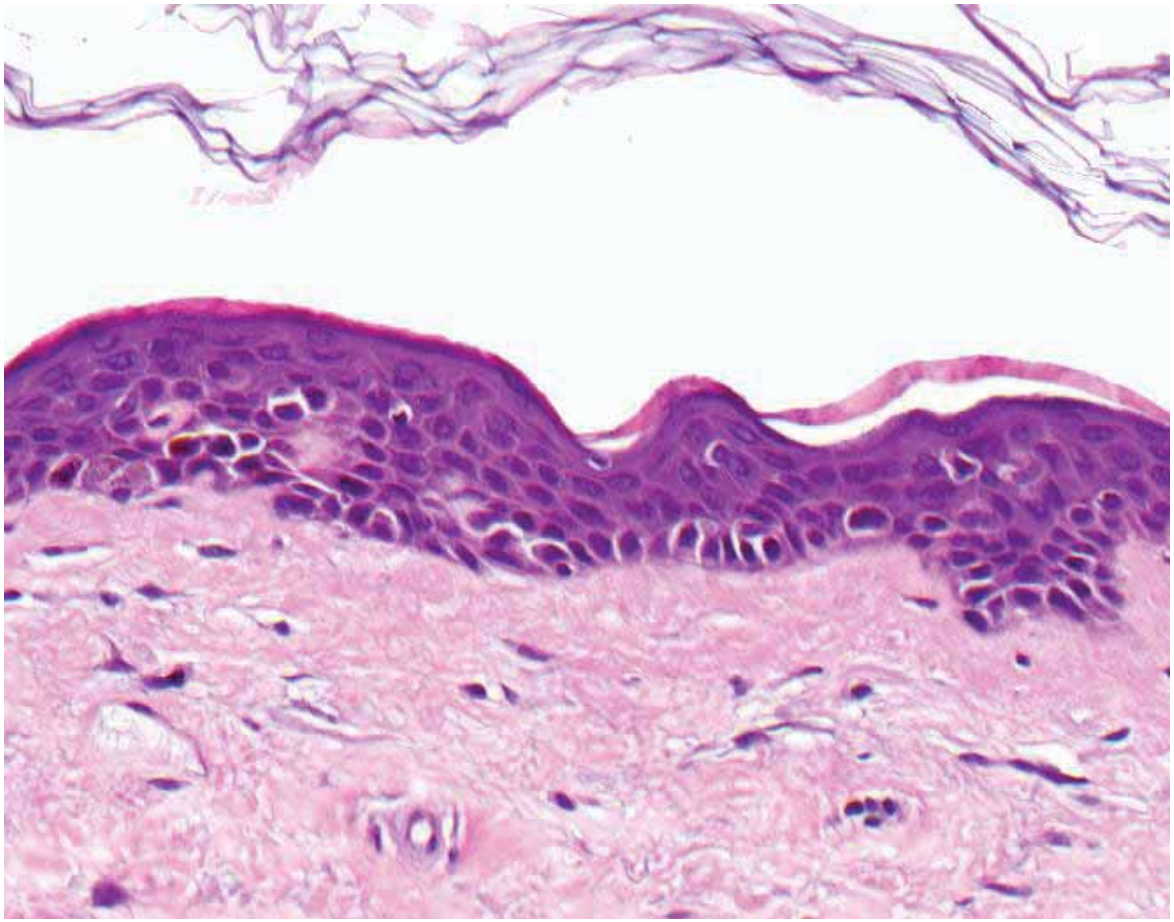


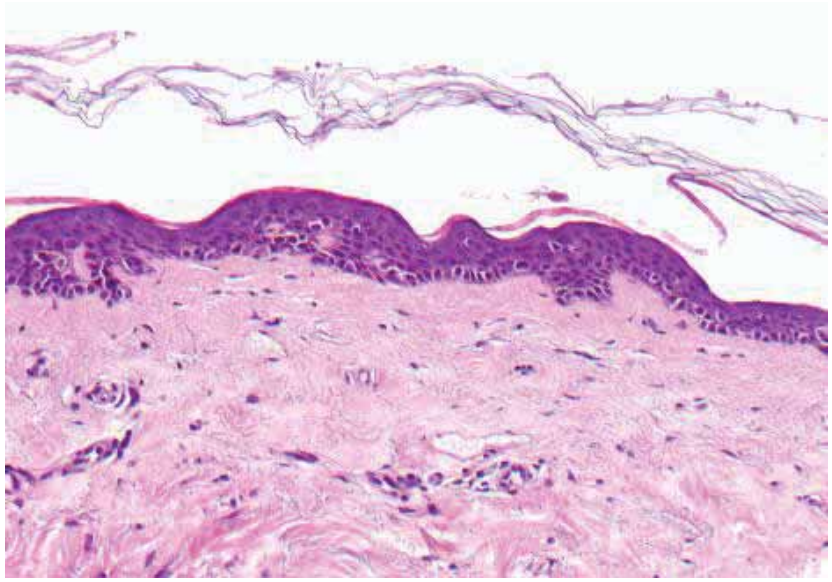
Suprabasal acantholysis Str. granulosum plump

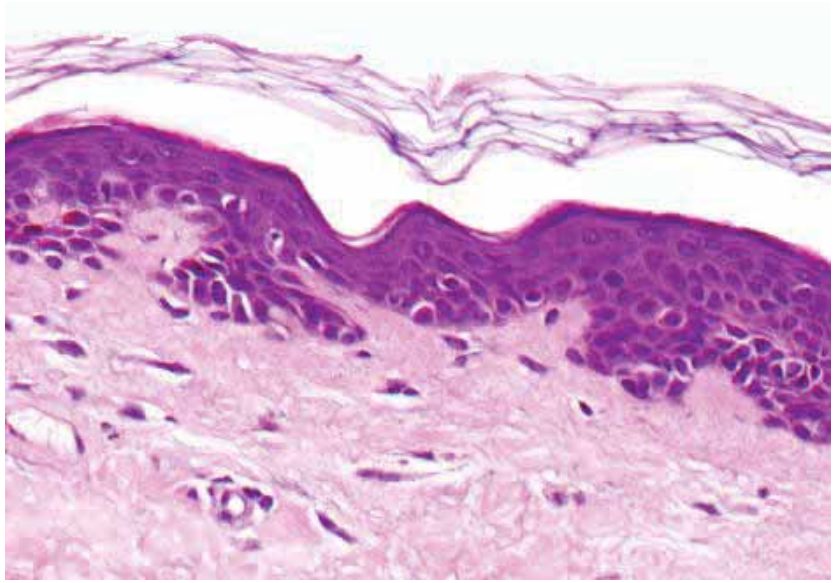


Suprabasal acantholysis and dyskeratosis

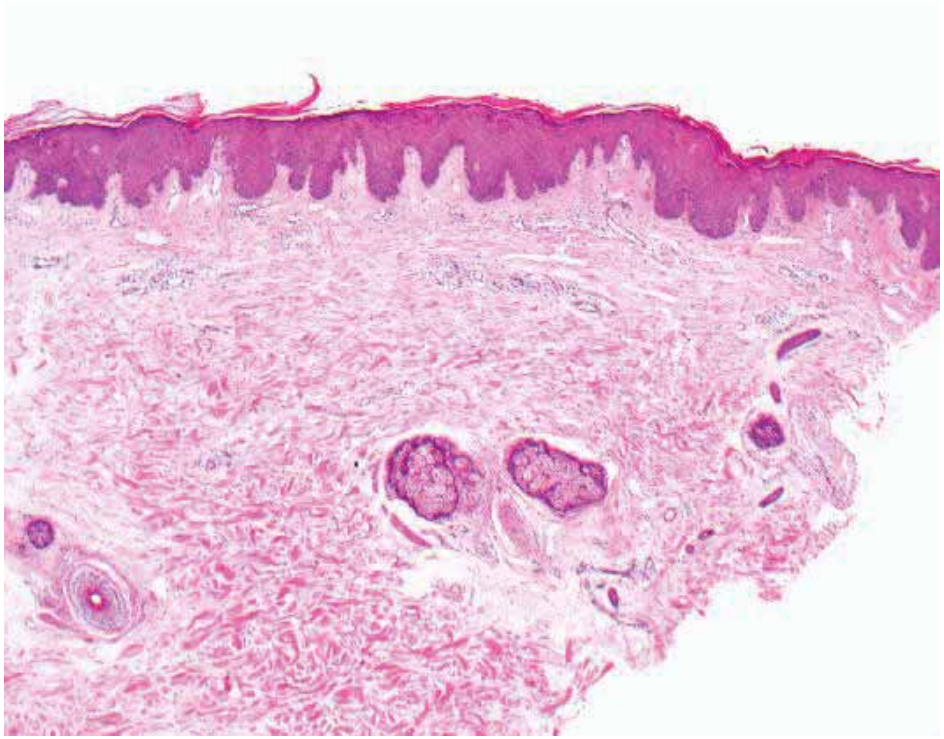
Darier-White disease, early stage



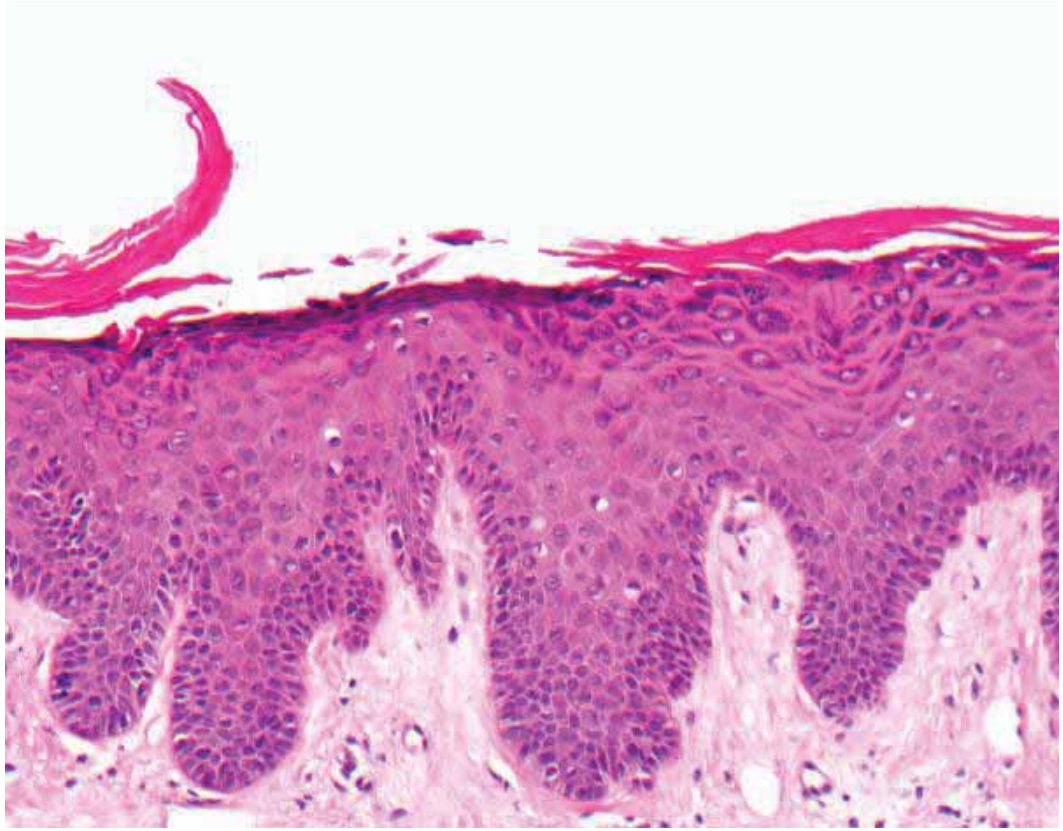




Darier-White disease, after retinoid therapy

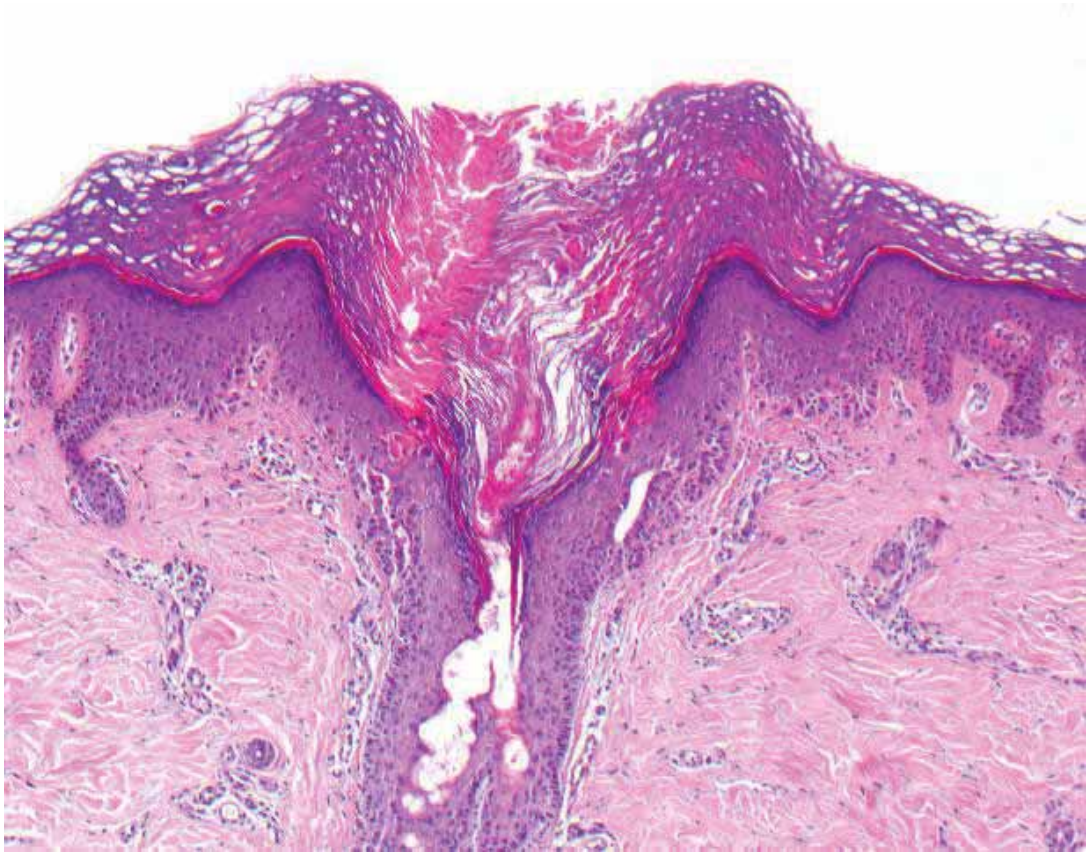


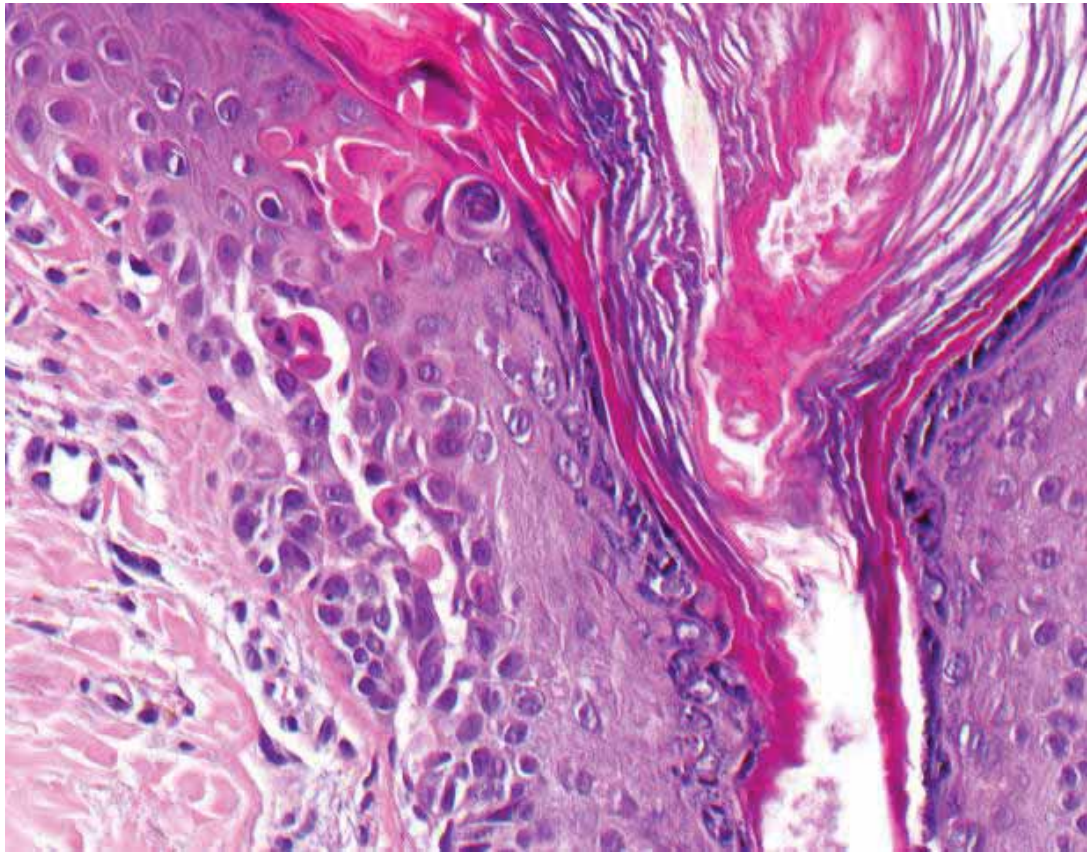
Hyperplasia, orthohyperkeratosis



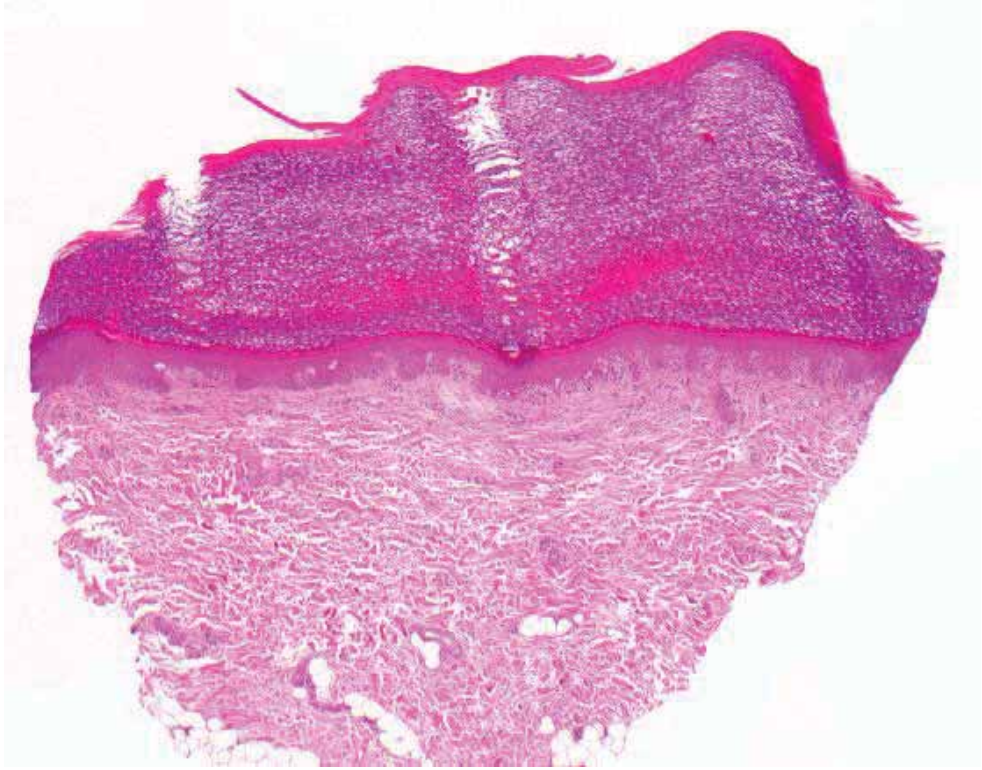
Hypergranulosis and plump keratinocytes

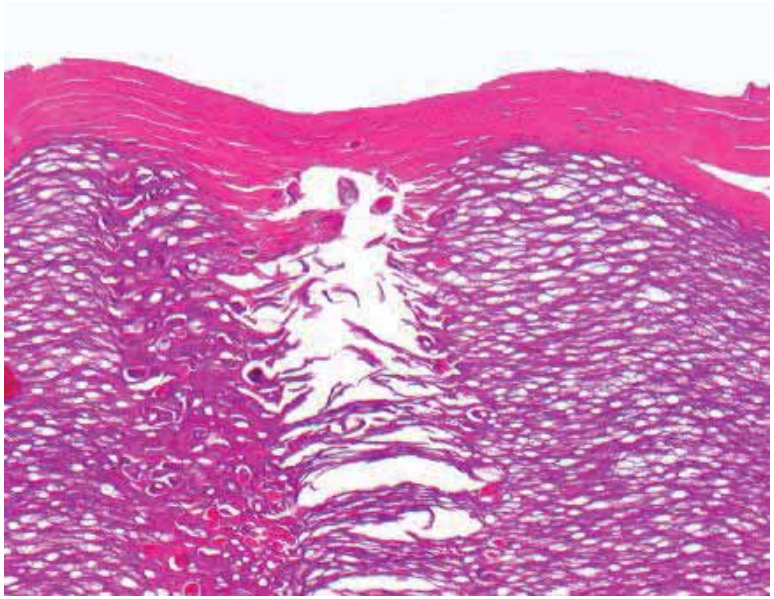
Darier-White, comedo variant

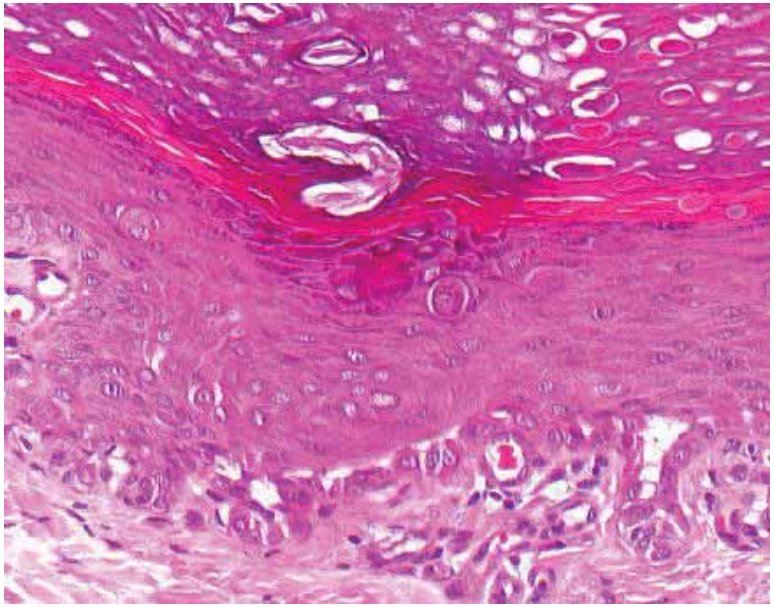




Darier-White disease, palmar pits







Focal Acantholytic Dyskeratosis

A. Bernard Ackerman, MD, Miami, Fla

The histologic features traditionally associated with Darier's disease were found in a variety of other conditions. These histologic changes occurred in (1) single lesions that were (*a*) clinically inapparent, (*b*) papular, or (*c*) nodular, and in (2) multiple lesions that were (a) persistent or (*b*) evanescent. The term "focal acantholytic dyskeratosis" describes the dominant histologic features and, like the designation "epidermolytic hyperkeratosis," denotes a distinctive histologic pattern with numerous clinical expressions.

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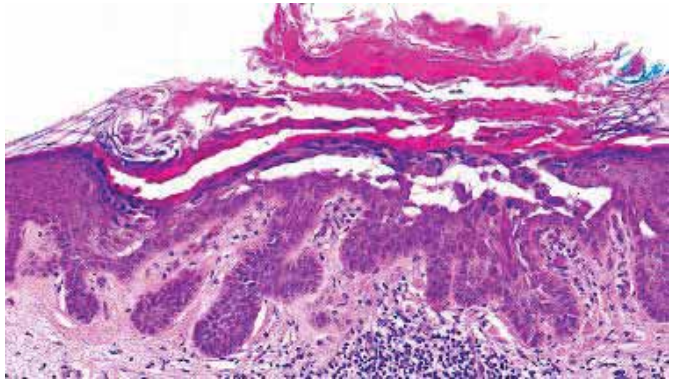
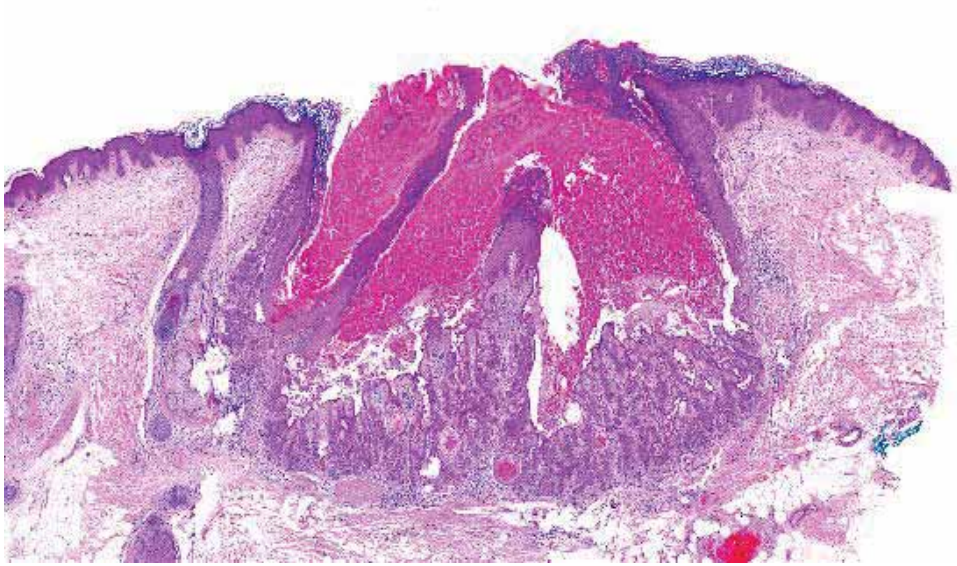


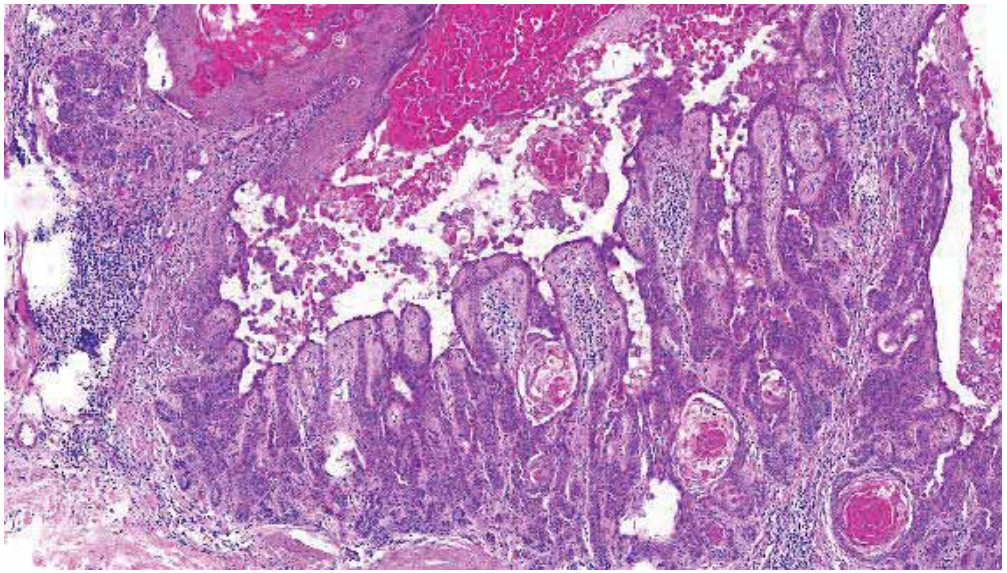
Epidermal reaction pattern

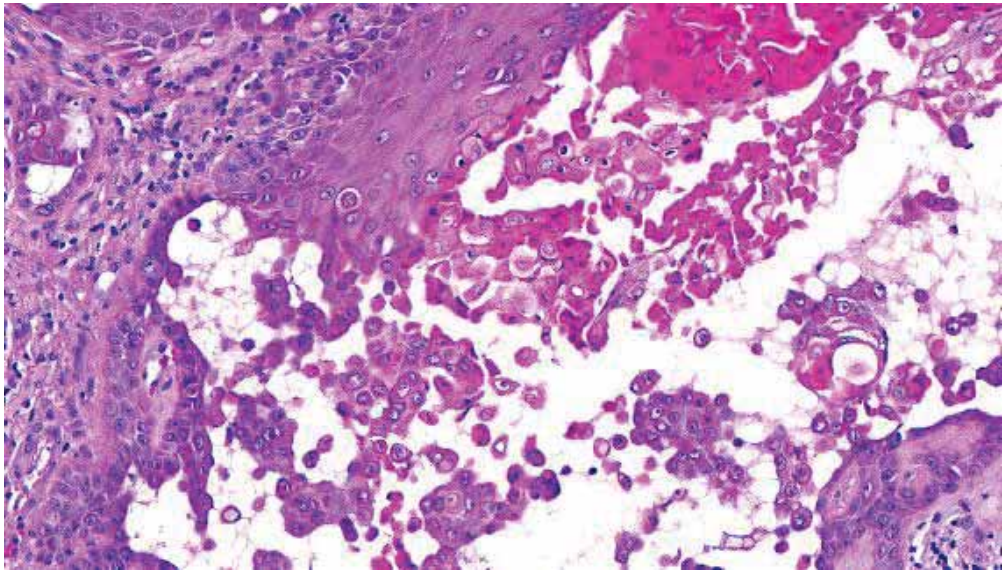
Focal Acantholytic Dyskeratosis (FAD)

- M. Darier
- Epidermal Naevi
- ➢ Warty Dyskeratoma
- ➢ Akantholytic Dyskeratotic Akanthoma
- ➢ Leukoplakia
- ➢ Inzidental: Normal skin, melanocytic nevi, melanoma, seborrheic keratosis, actinic keratosis, SCC, BCC, …
- ➢ Grover disease

Warty dyskeratoma

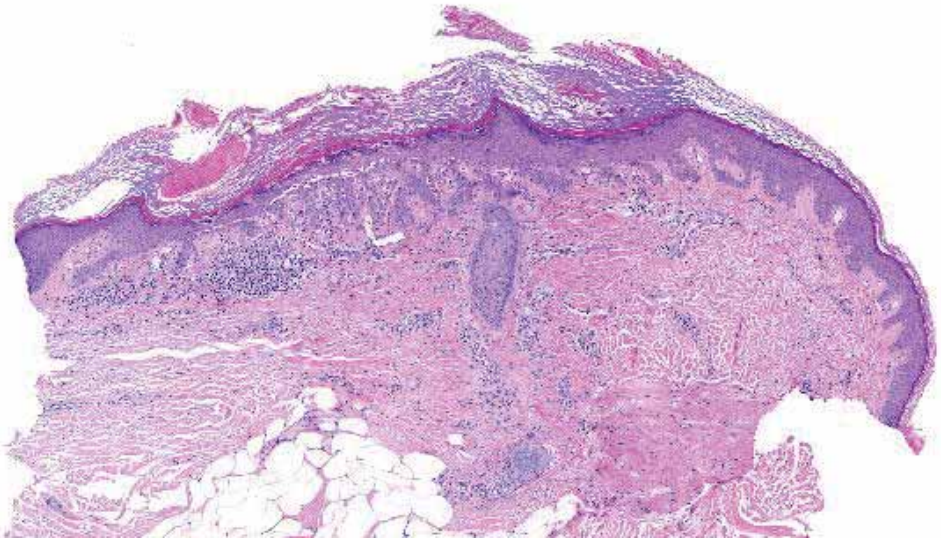


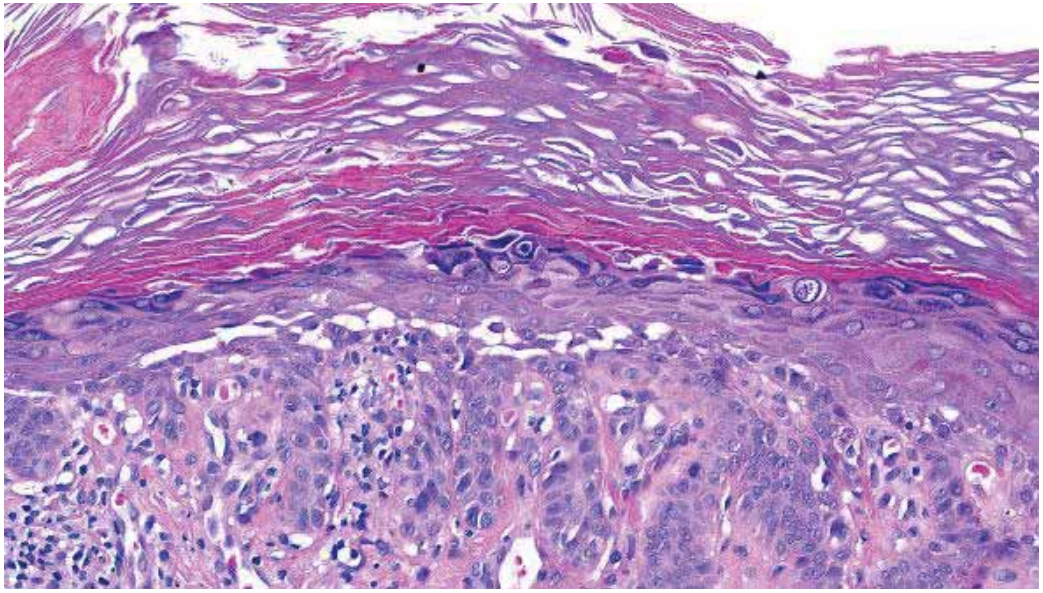


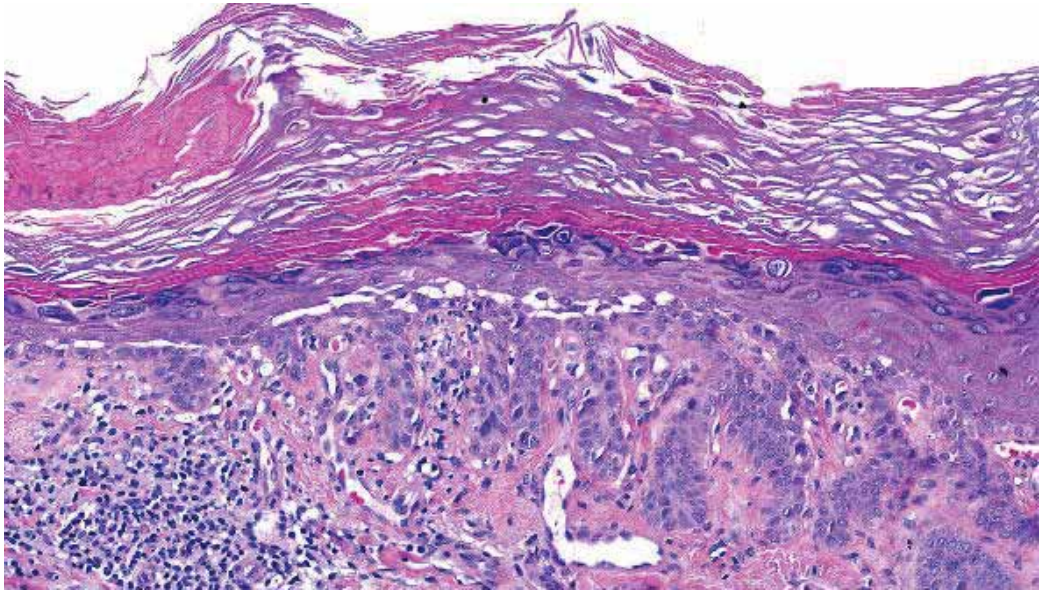


Cup-shaped invagination, verrucous architecture and acantholytic dyskeratosis

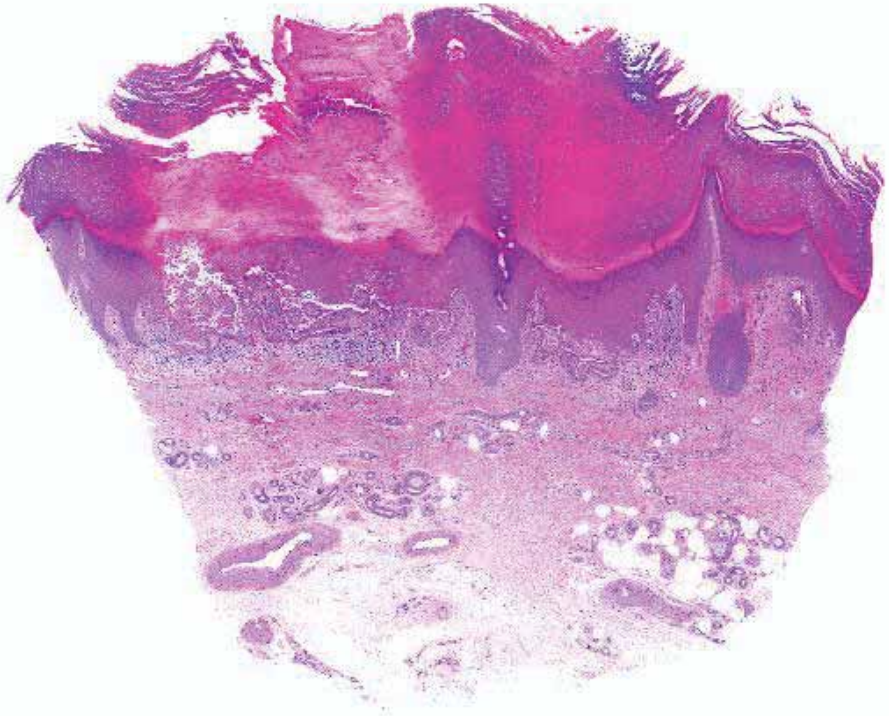
Akantholytic dyskeratotic acanthoma

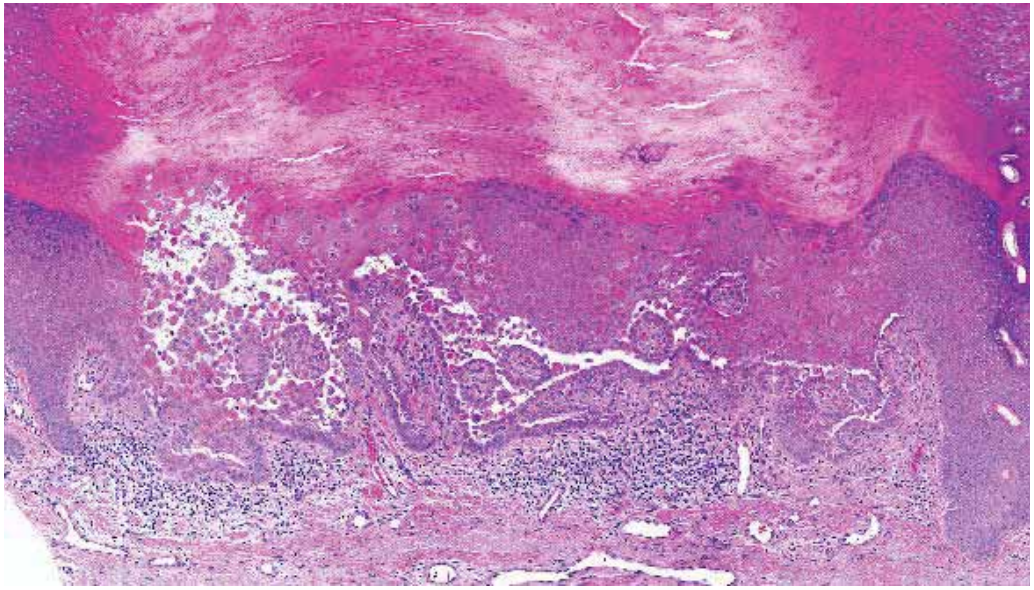


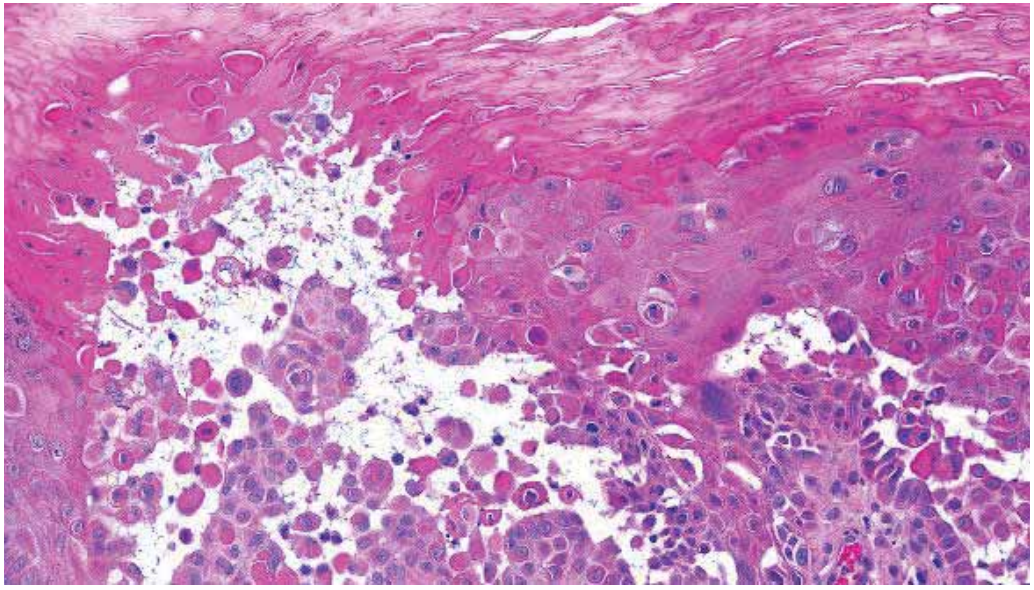




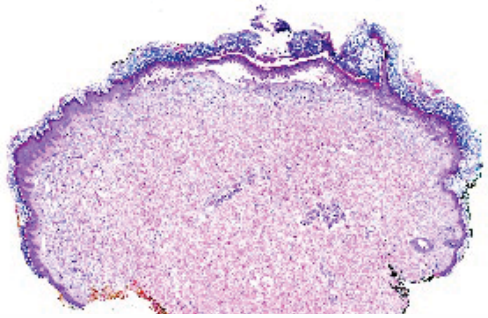
Akantholytic dyskeratotic akanthoma, palmar

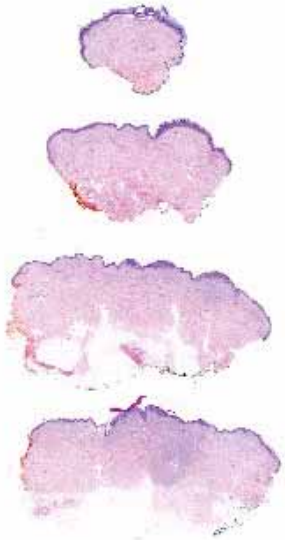


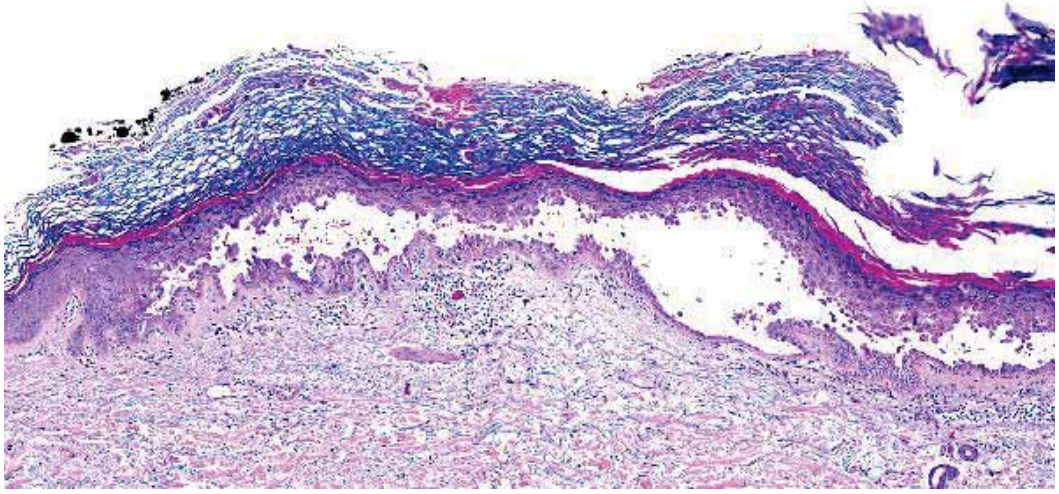


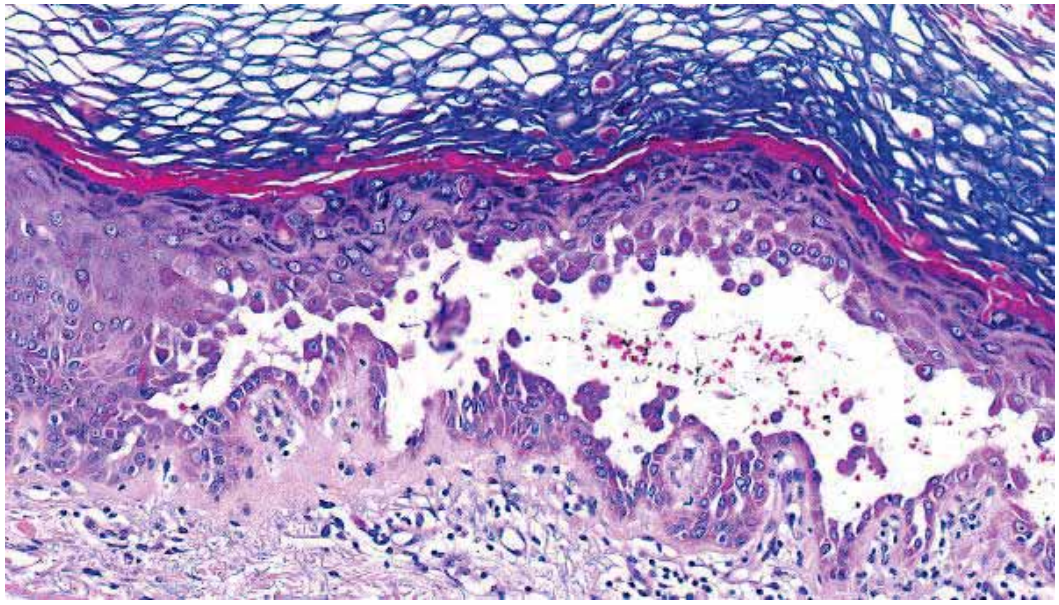


Akantholytic dyskeratotic akanthoma, Bowen disease and incidental EHK

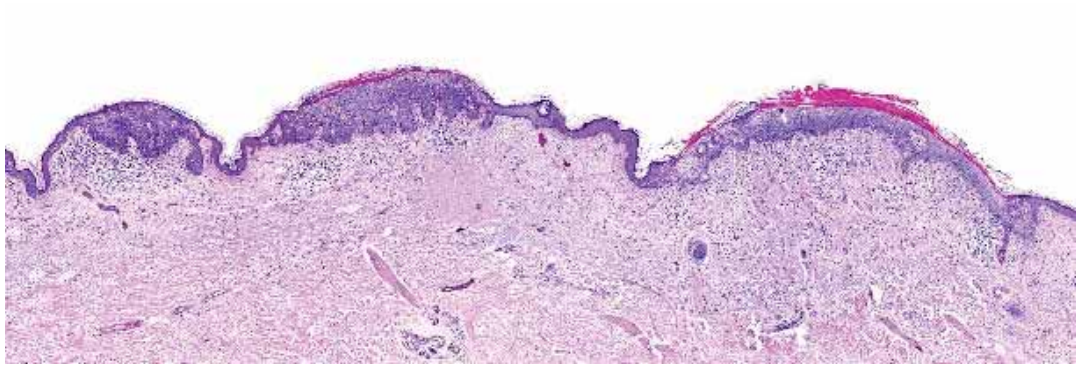


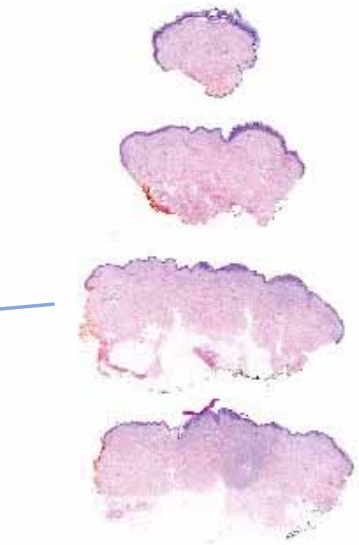


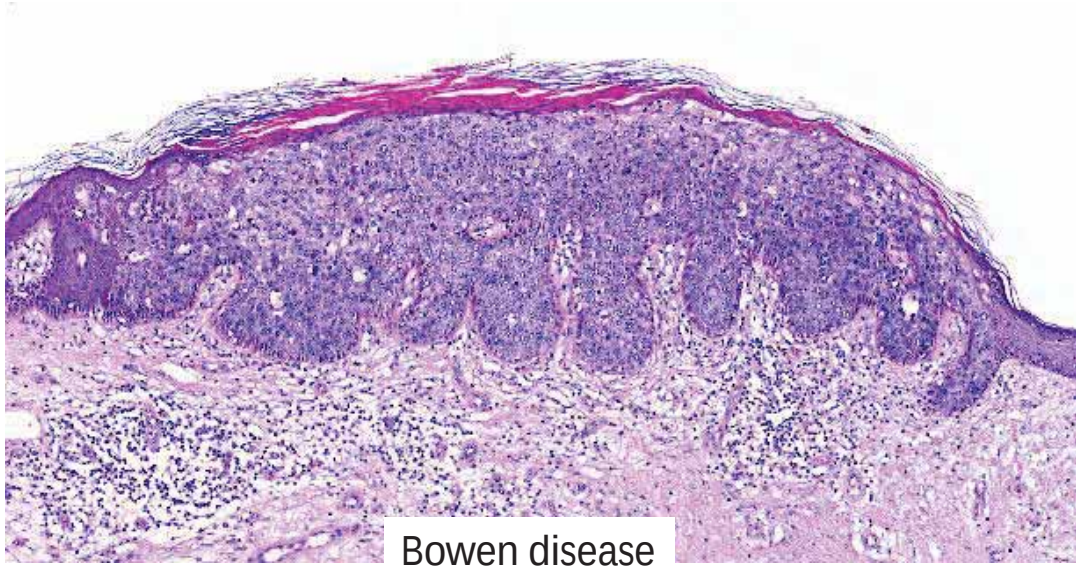




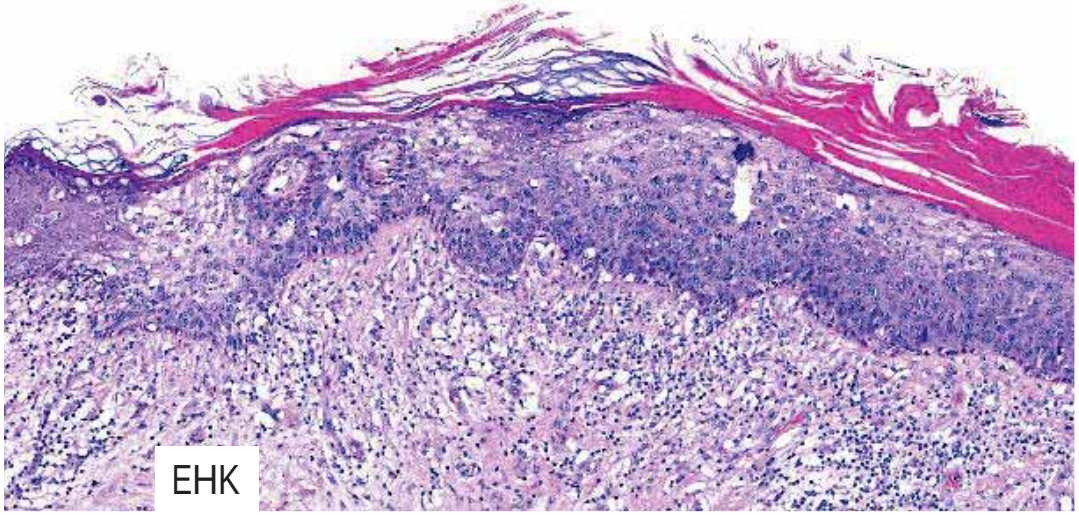
Akantholytic dyskeratotic akanthoma, Bowen disease and incidental EHK





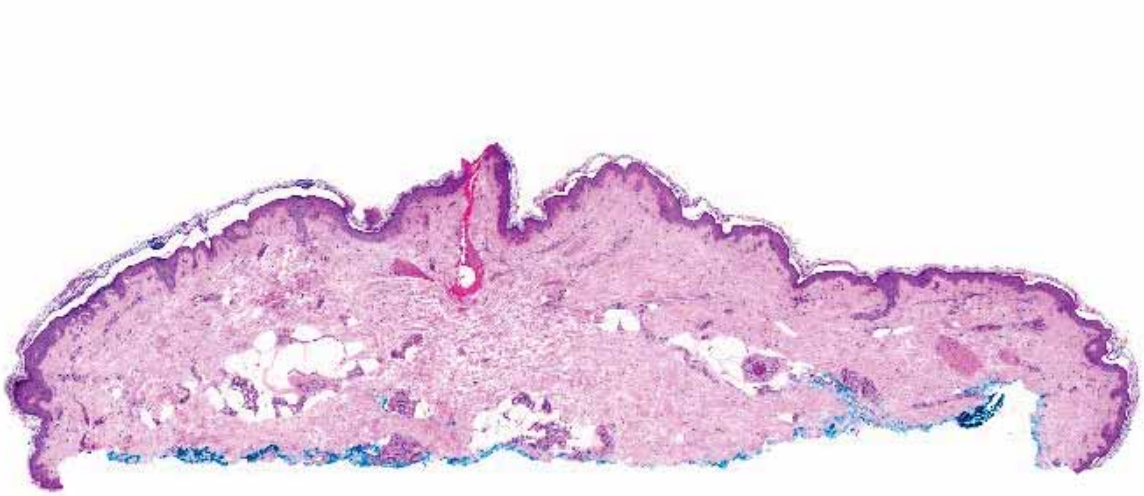


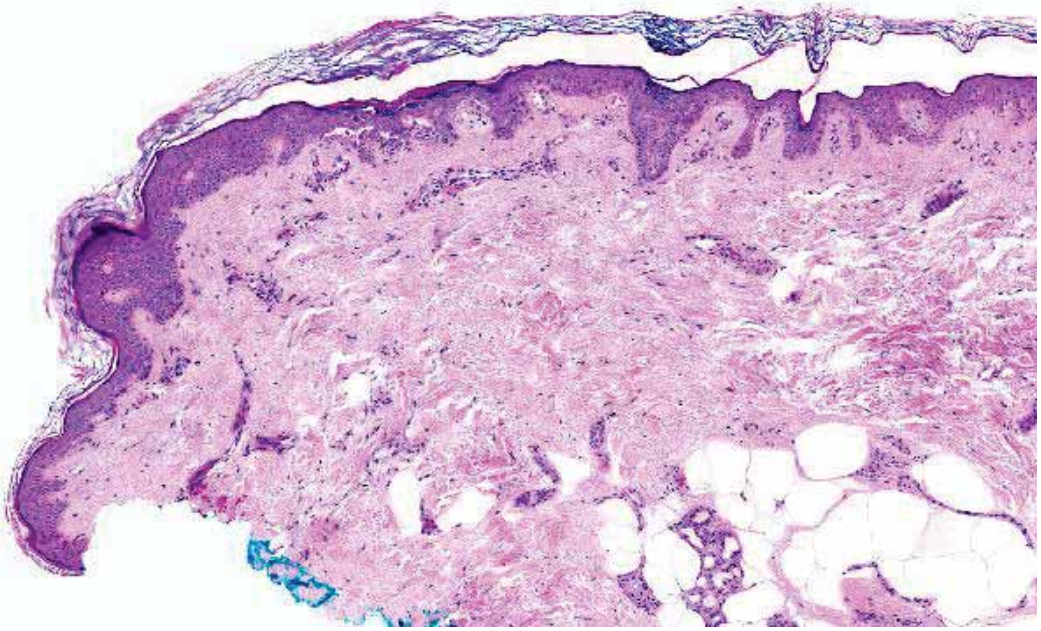
Bowen disease

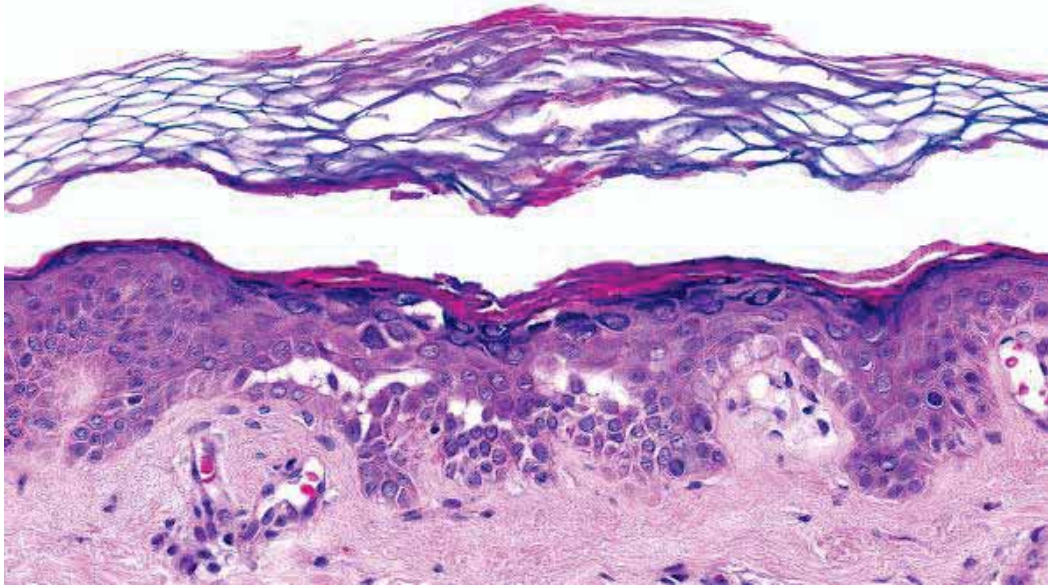


EHK

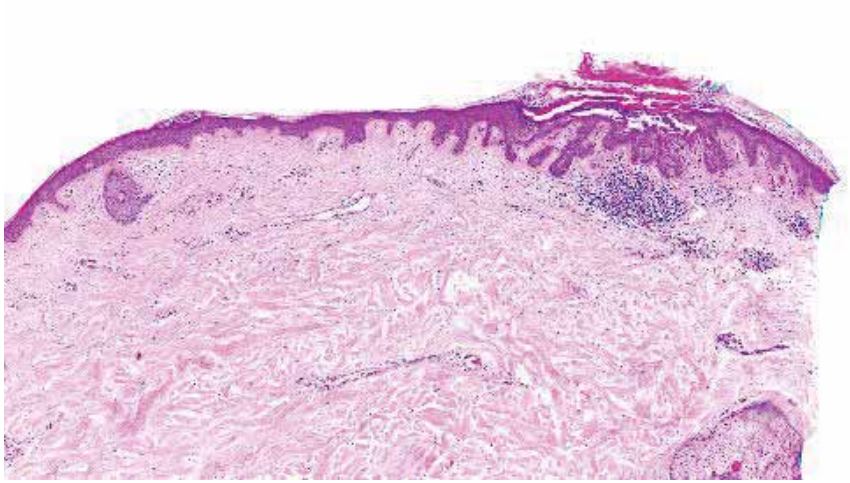
FAD, incidental in a melanocytic nevus

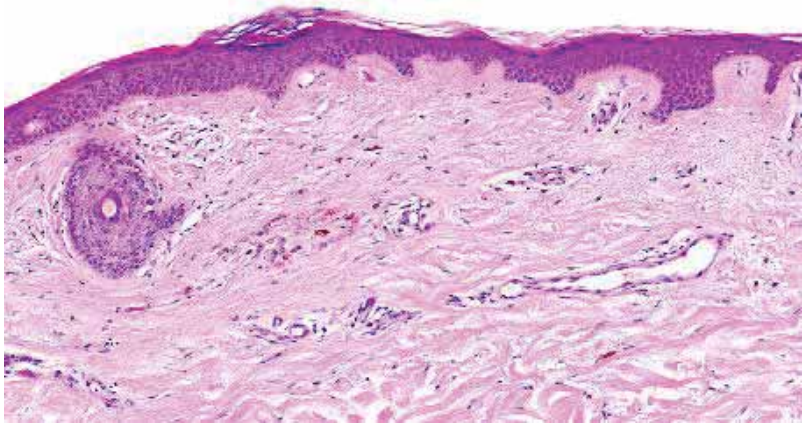


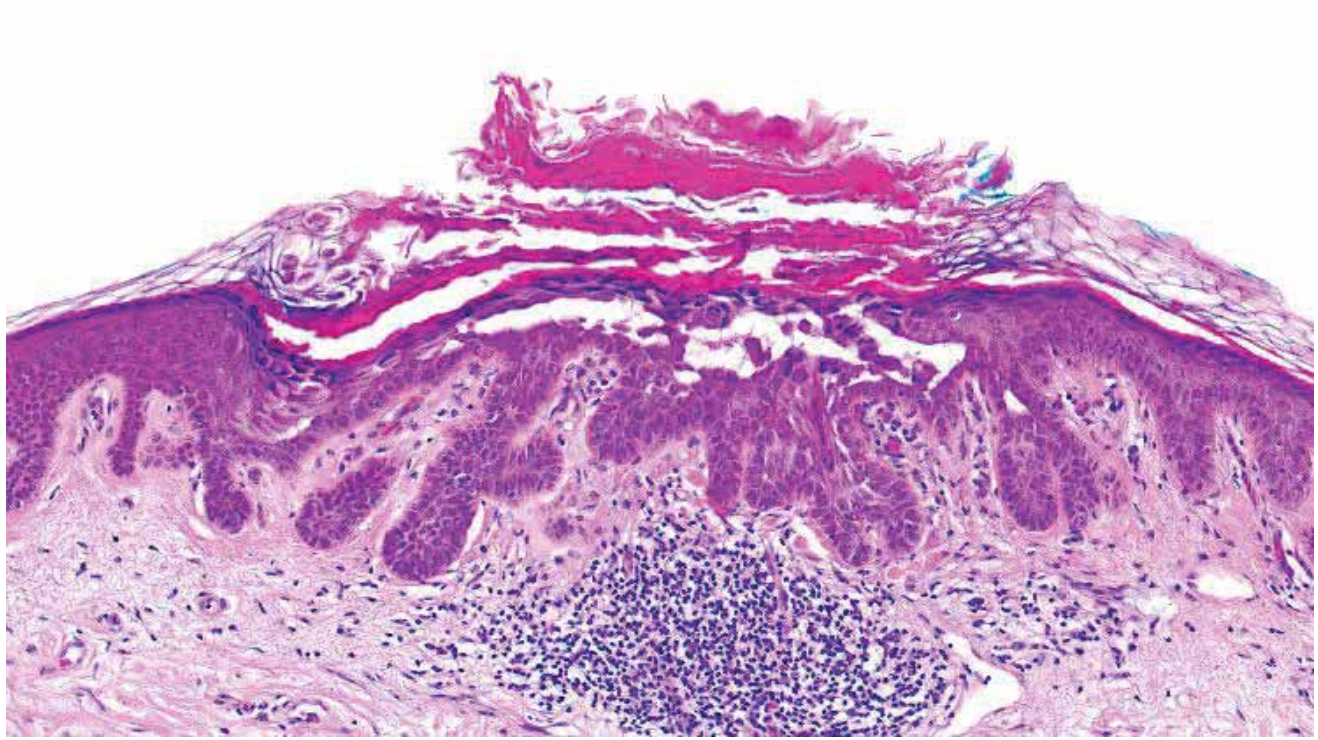




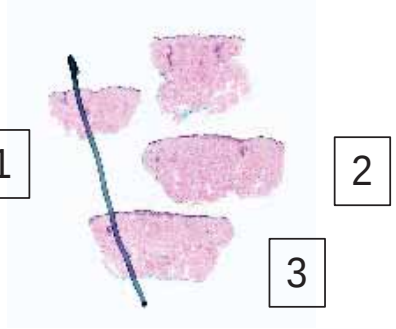
FAD, incidental, blues nevus

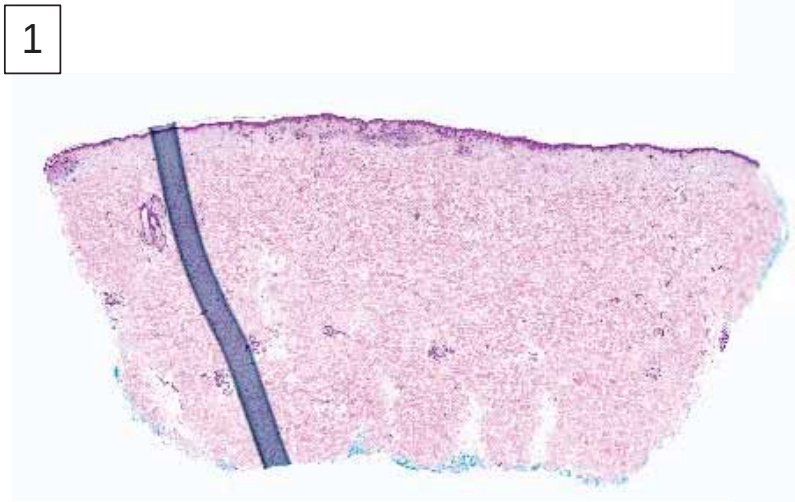


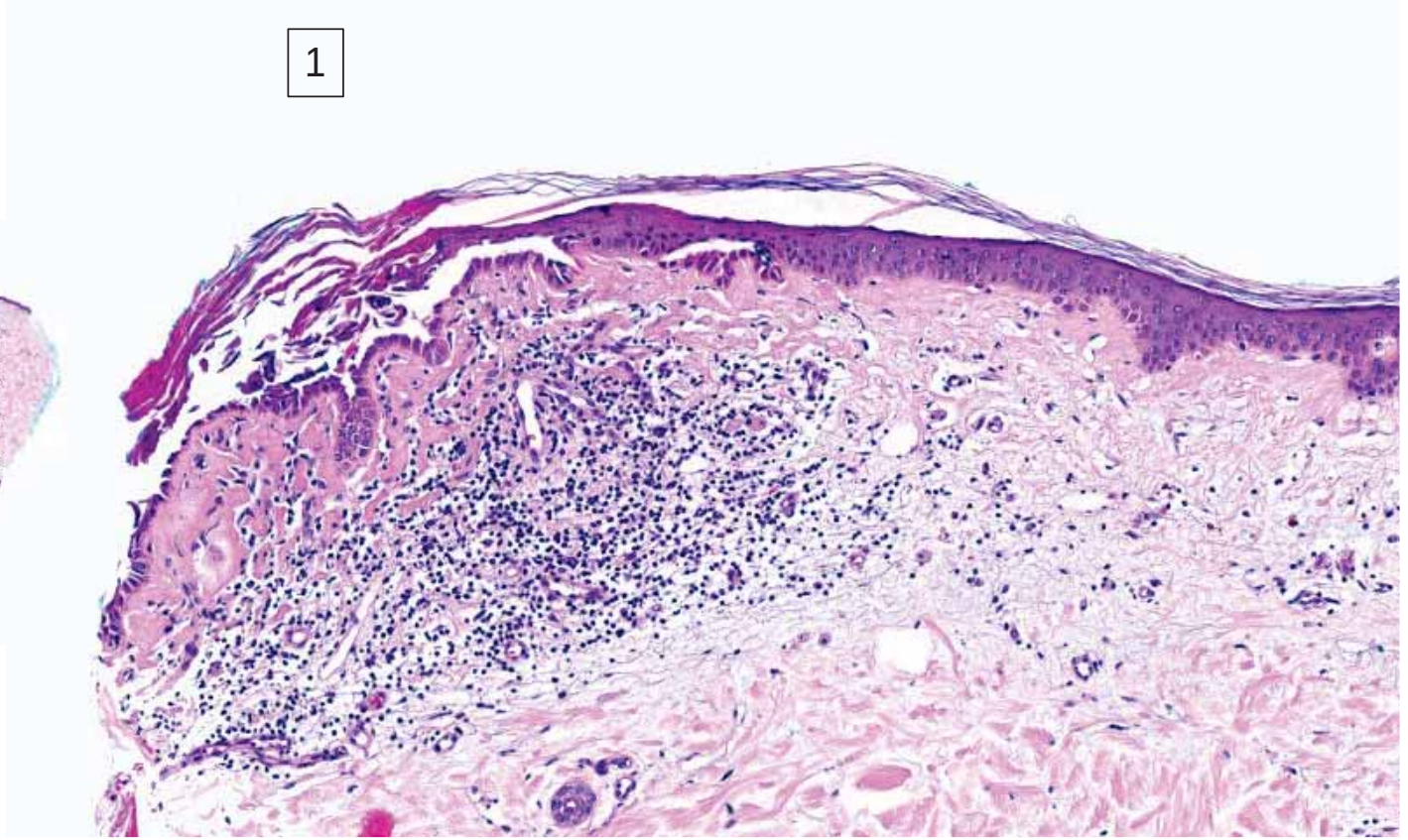


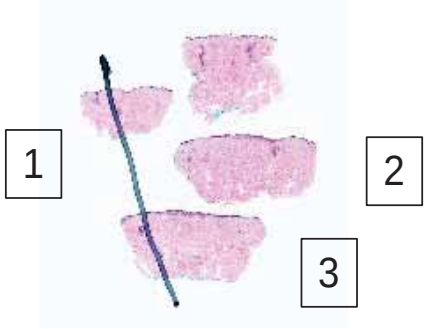


FAD, incidental, melanocytic nevus



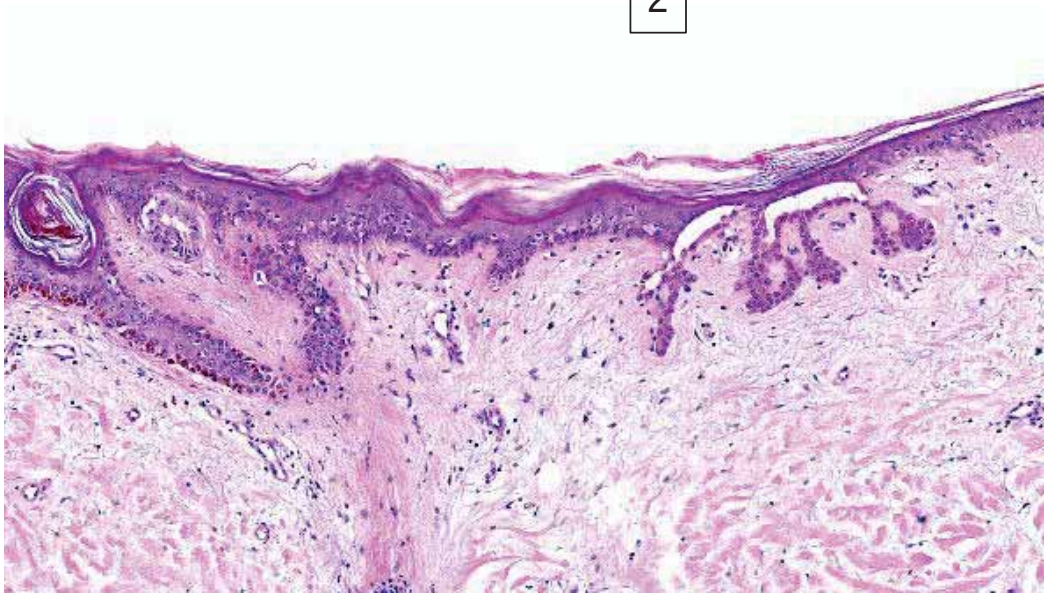






FAD, incidental, melanocytic Naevus

2



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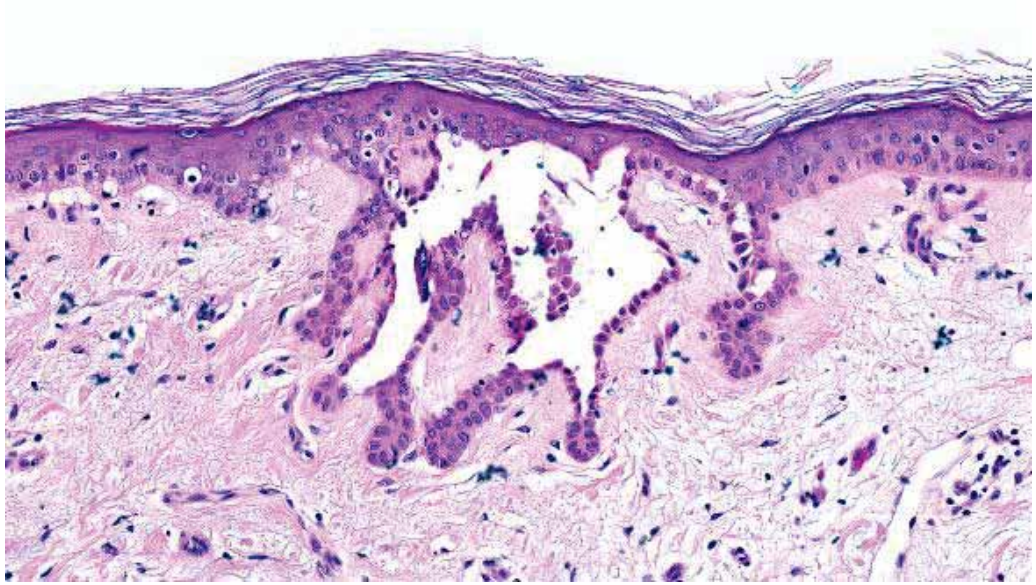
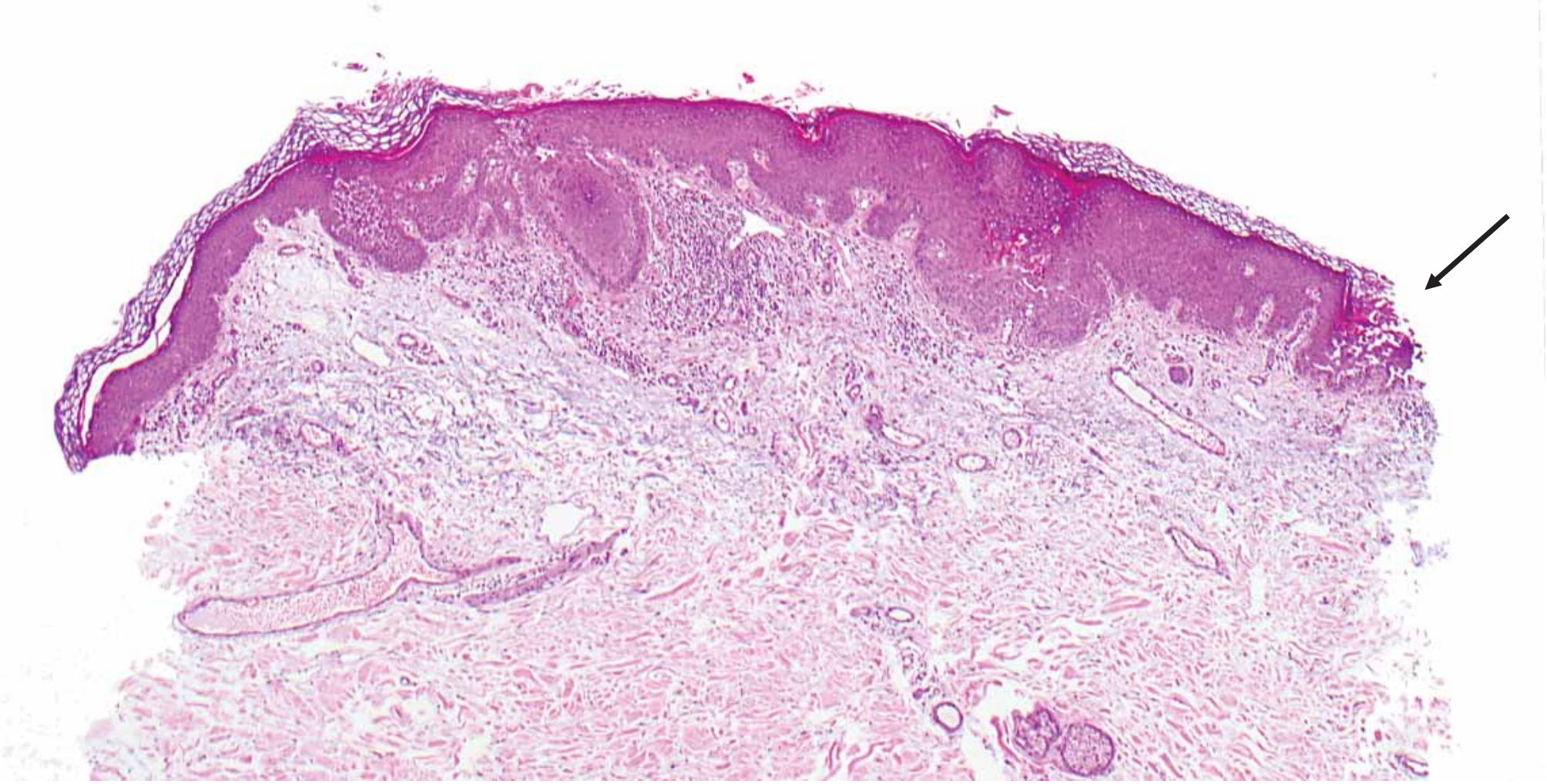
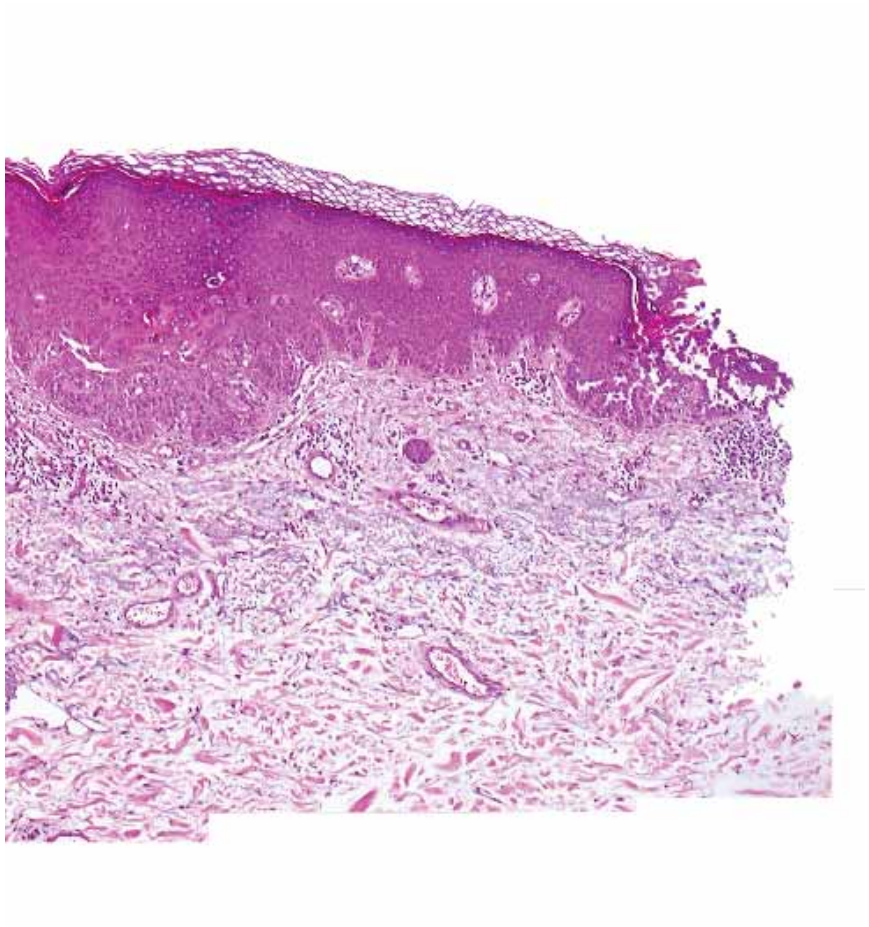


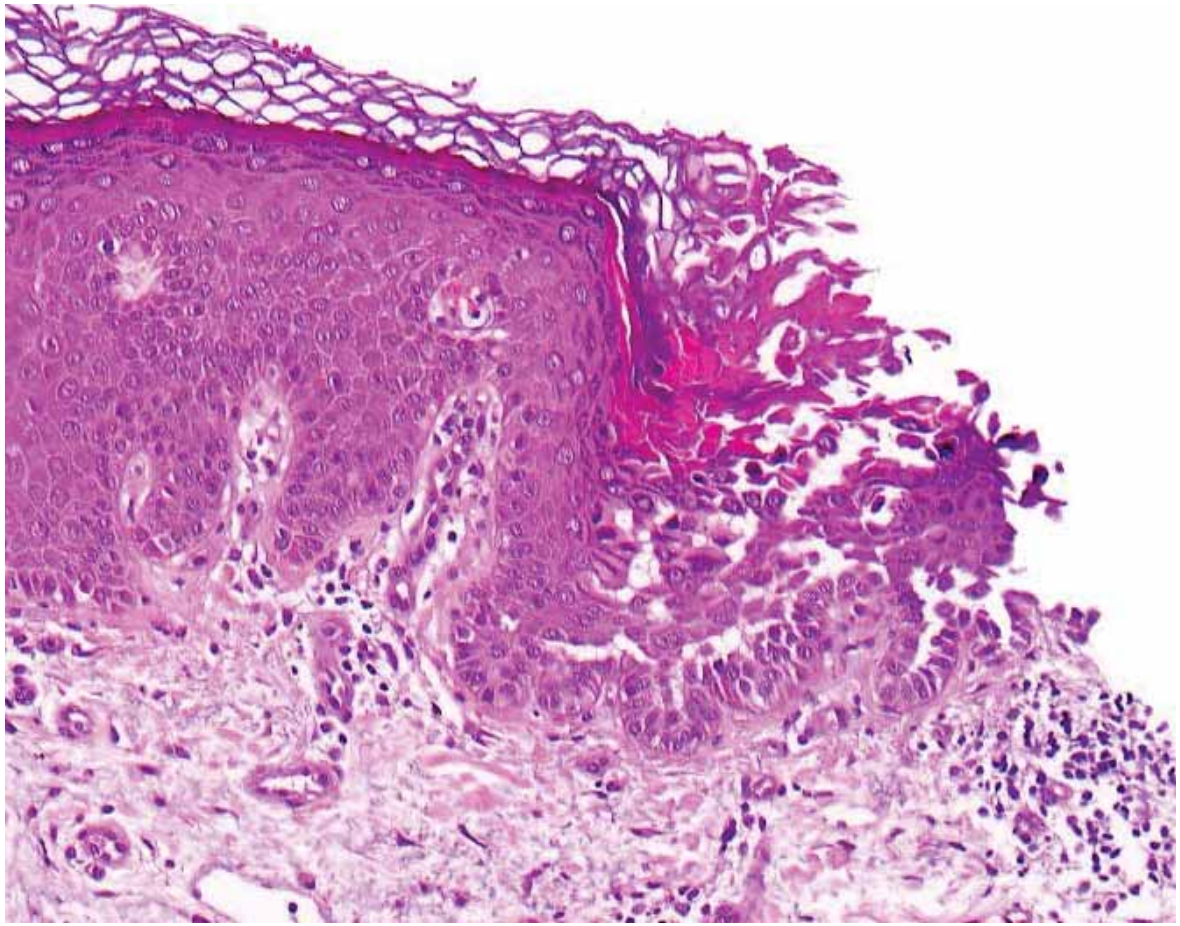
Grover disease with focal acantholytic hyperkeratosis and epidermolytic hyperkeratosis



Grover disease, focal acantholytic hyperkeratosis I

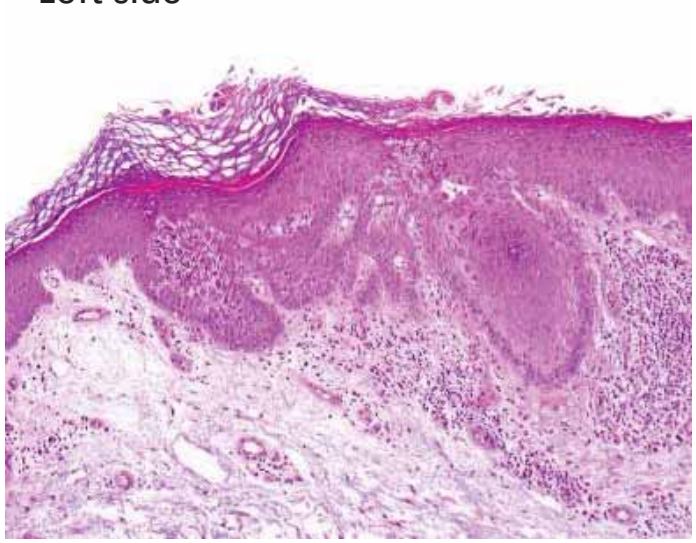
Right side

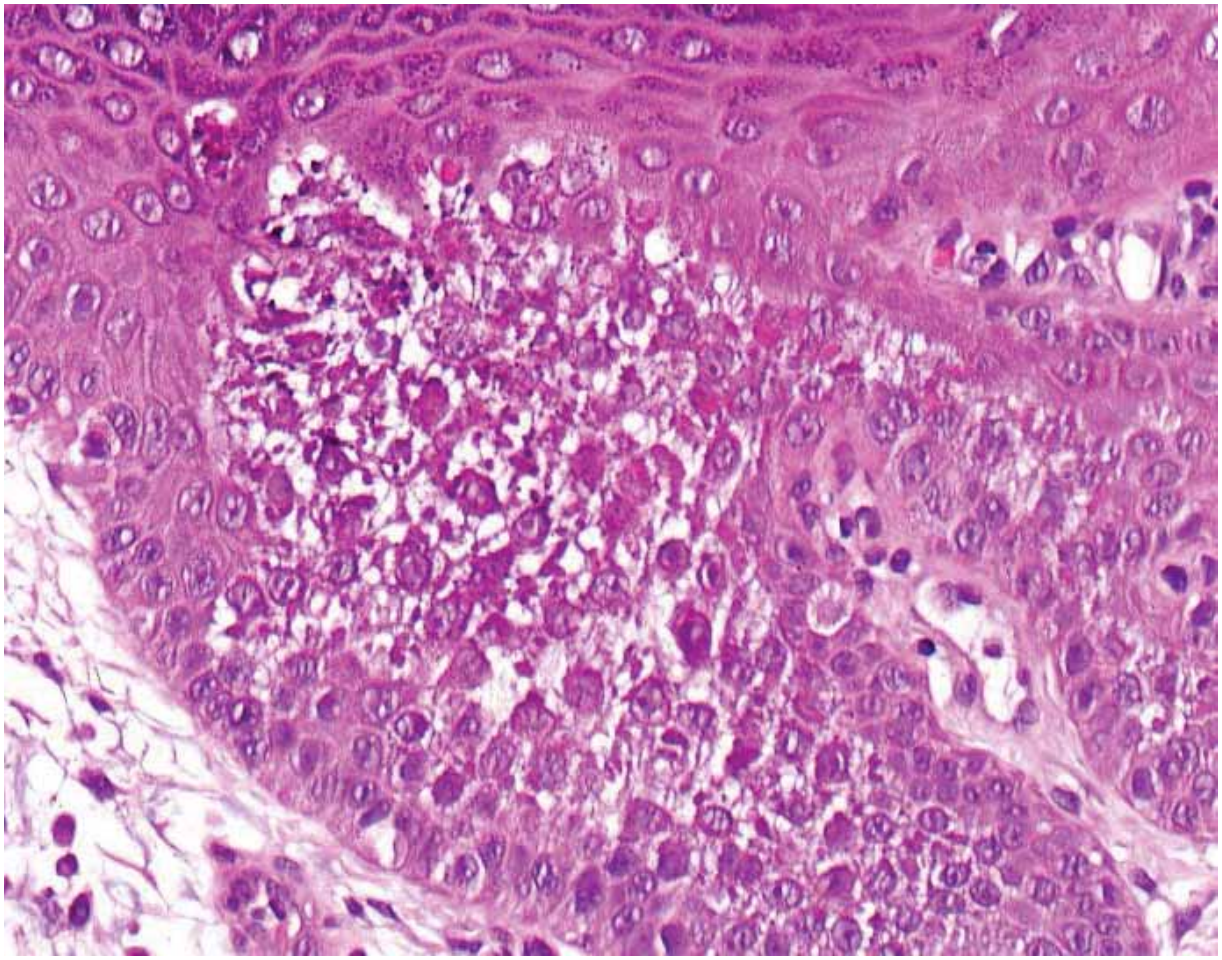




Grover disease, epidermolytic hyperkeratosis II

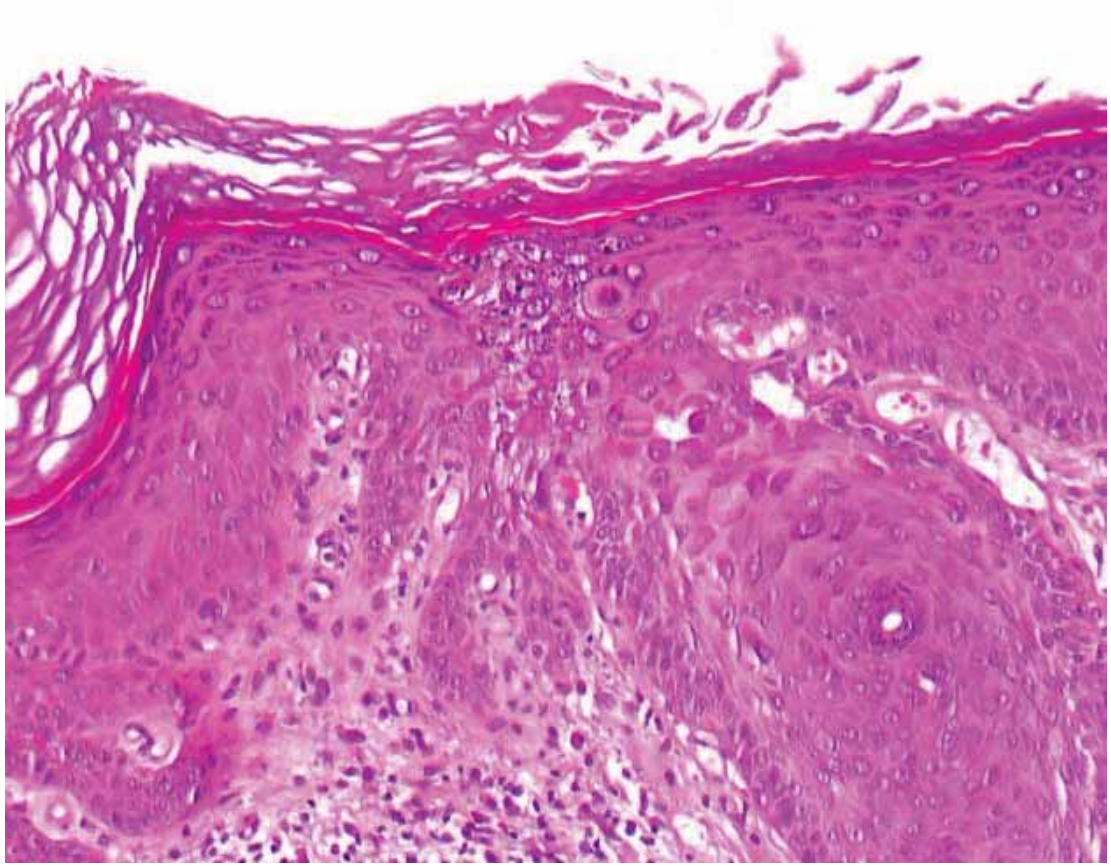
Left side

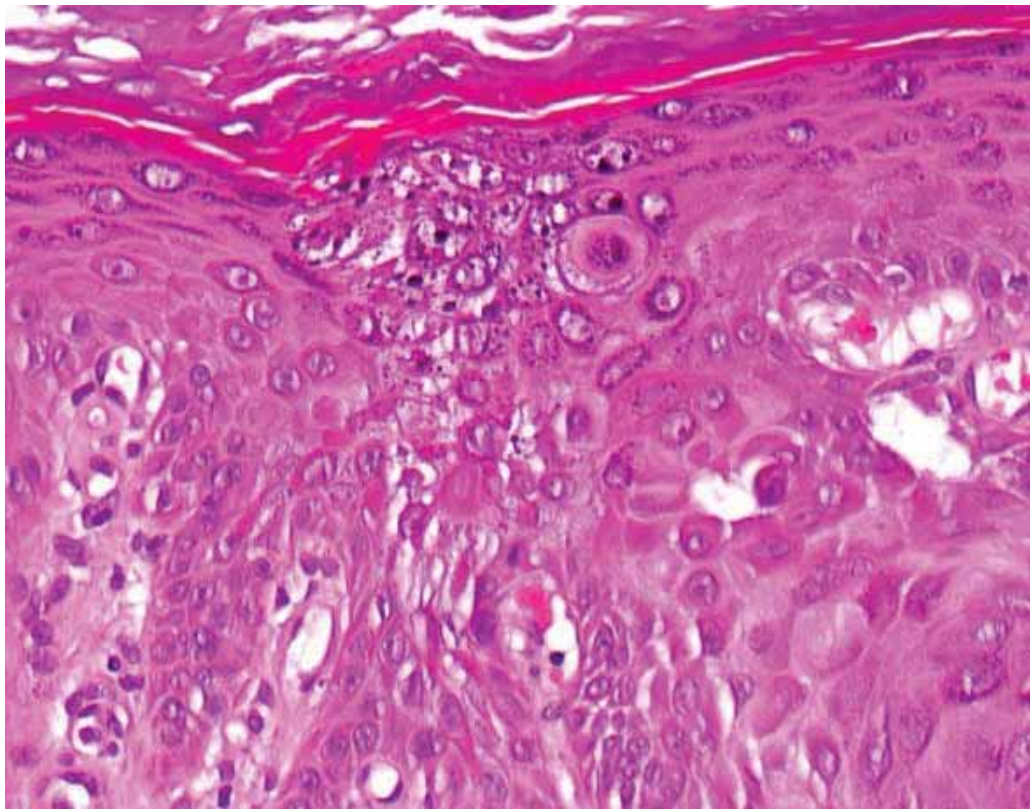




Grover disease with epidermolytic hyperkeratosis and focal acantholytic hyperkeratosis III

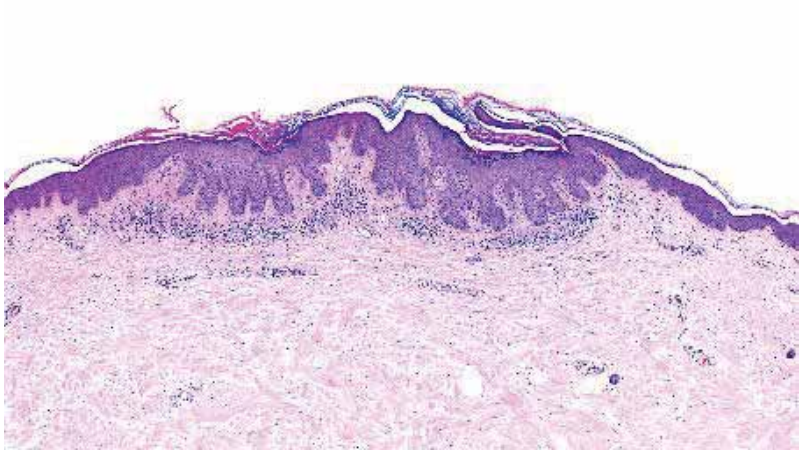
Center



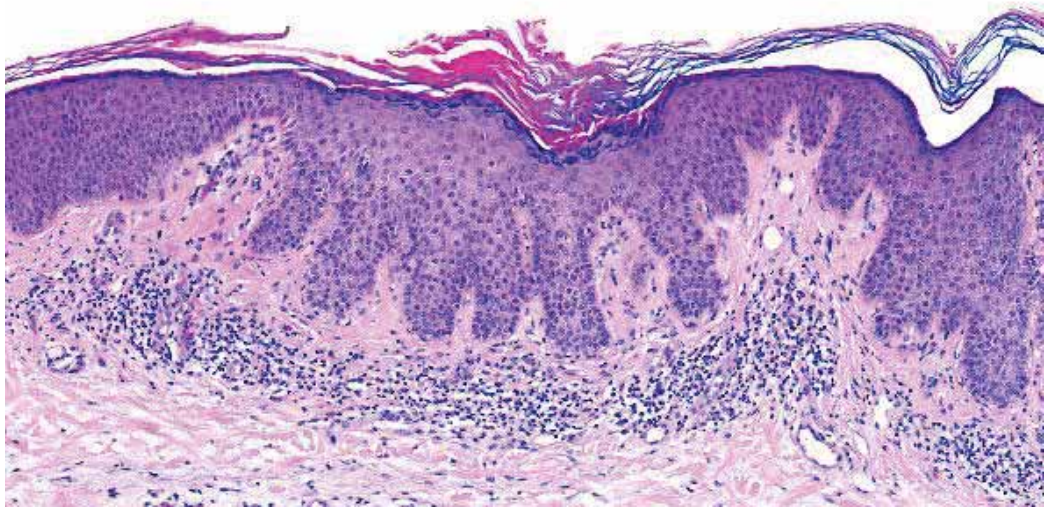


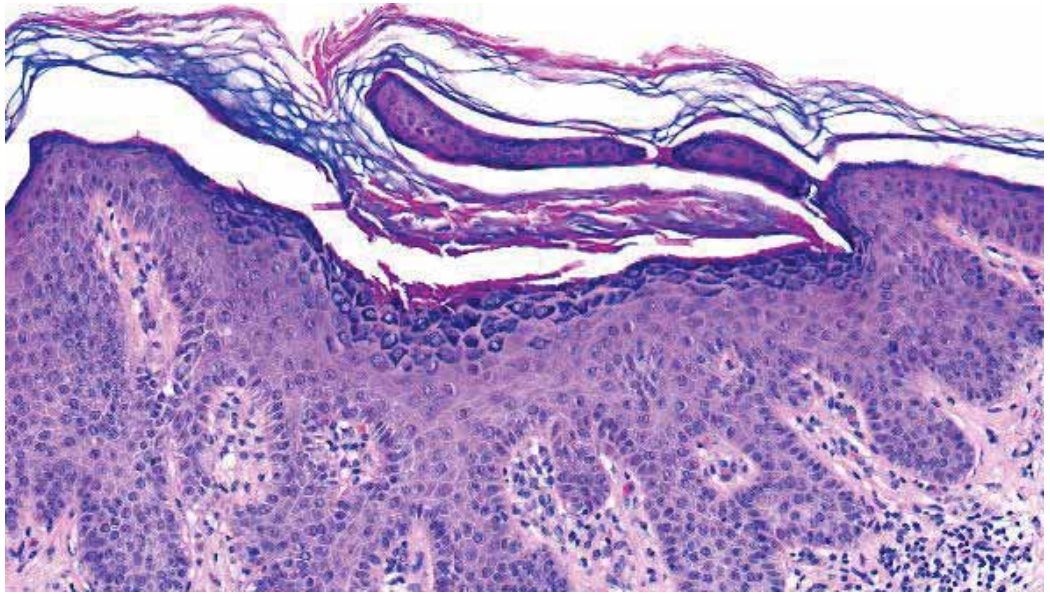
Grover disease with plump keratinocytes in the stratum granulosum

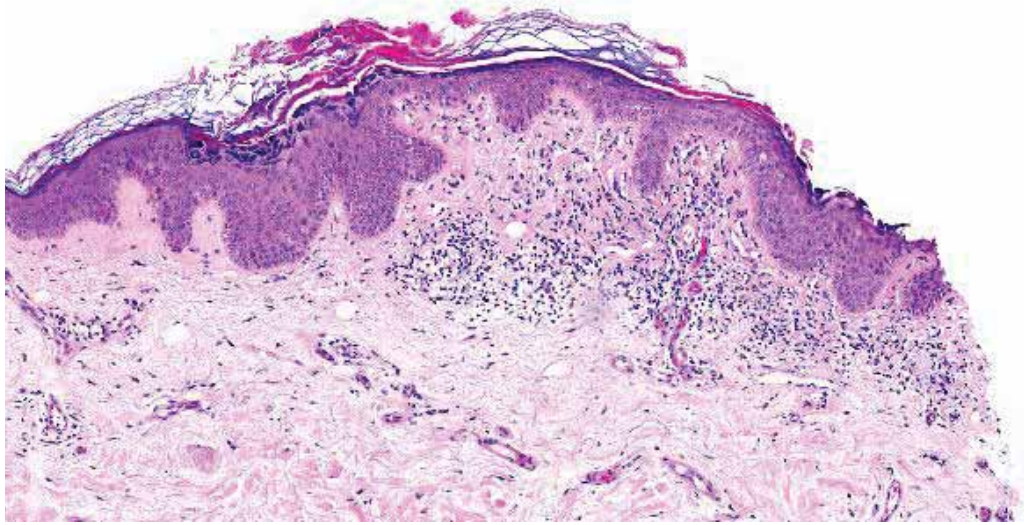
(Clue for Grover disease)



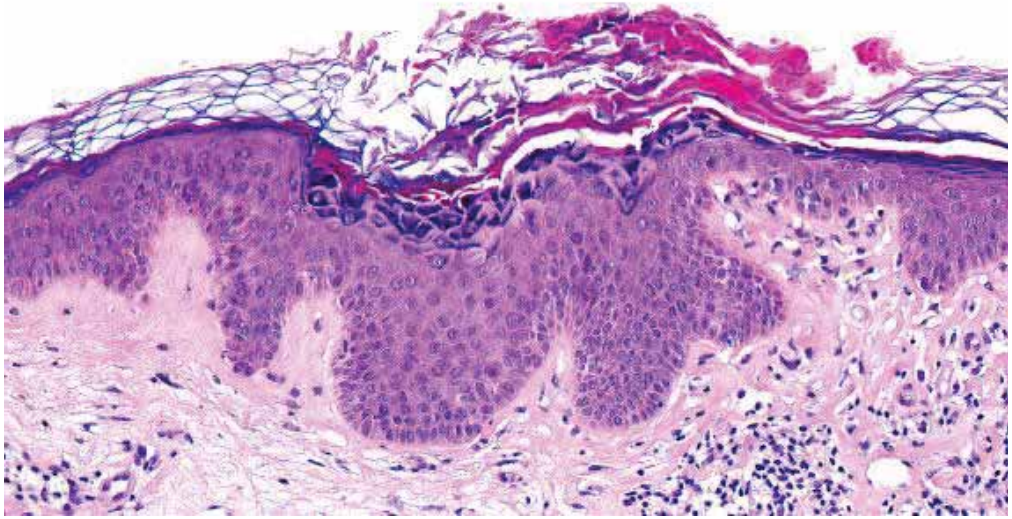
Residual of focal acantholytic dyskeratosis in an older lesion?

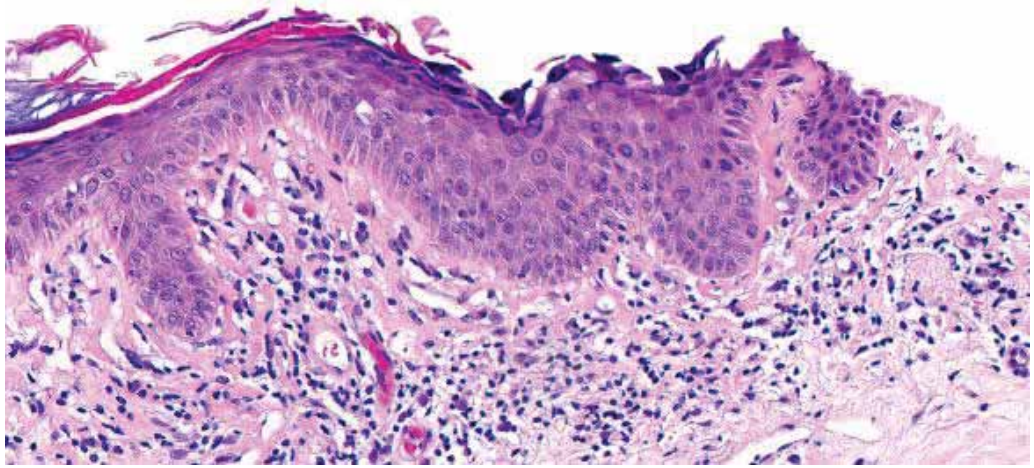






Grover disease, focal acantholytic dyskeratosis (P. foliaceus-like)





Grover disease
Patterns

- Darier disease, Epidermolytic Ichthyosis, Hailey-Hailey disease
- Nevoid or lentiginous silhouette (Dowling-Degos)
- Porokeratosis
- Dysmaturation (IEN-like)
- Pemphigus
- Spongiotic dermatitis
- Lichenoid dermatitis with basal vacuolization and dyskeratosis

AB Ackerman, Clues to Diagnosis in Dermatopathology, 1991
Fernández-Figueras, et al. Am J Dermatopathol. 2010
Melwani P, et al. Am J Dermatpatol., 2010
Bearden et al, Am J Dermatopathol. 2014

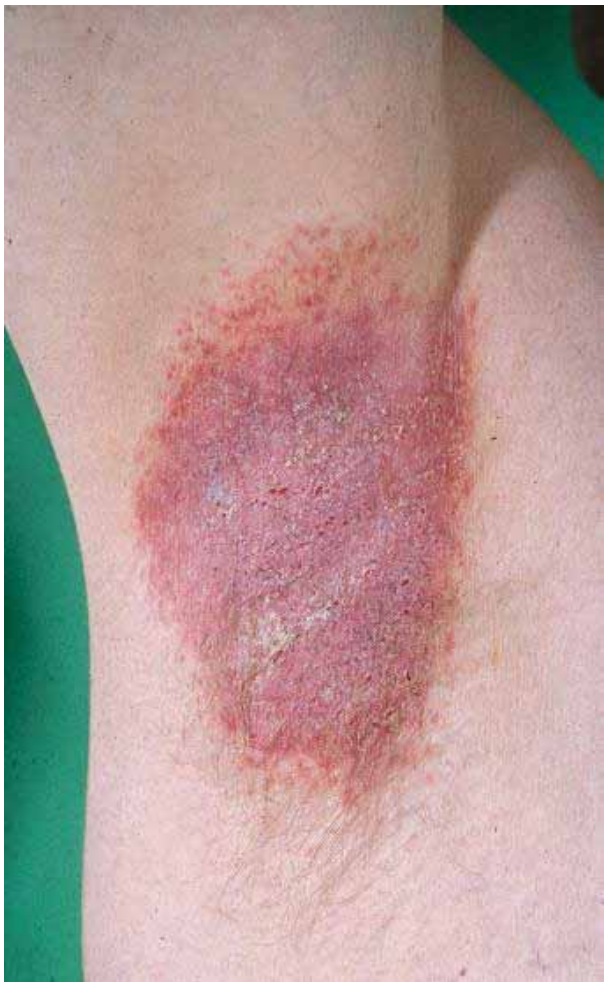
Grover disease
Clues

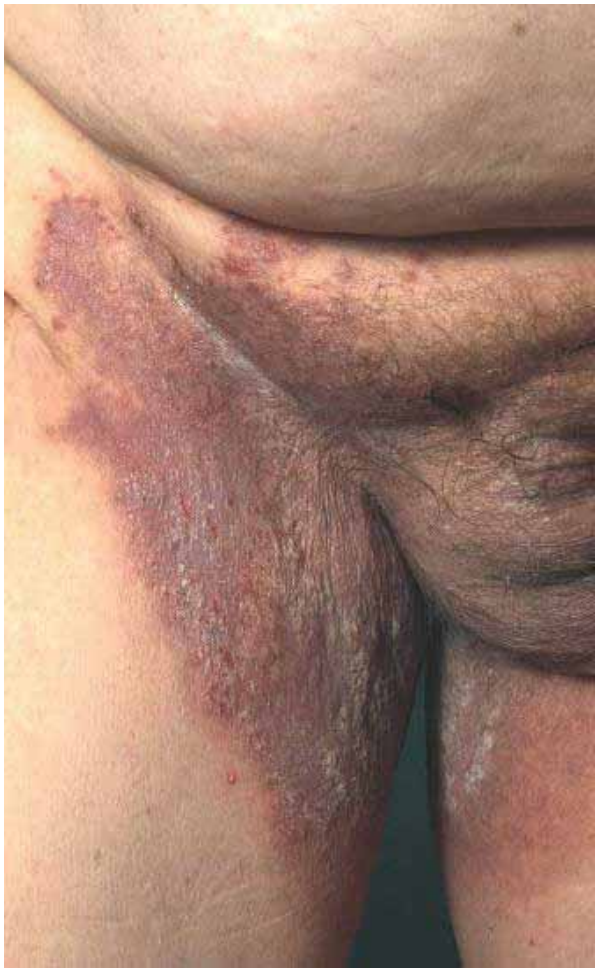
- Two and more patterns in one punch biopsy (step sections!)
- Elongation of rete ridges with acantholysis (early lesion)
- Plump keratinocytes in the str. granulosum (older lesion)
- Variably dense, patchy infiltrate in the papillary dermis: lymphocytes, eosinophils, (neutrophils, plasma cells, melanophages)
- Signs of scratching: excoriation, keratinocyte necrosis, fibrin, erythrocytes, fibrosis, ...

AB Ackerman, Clues to Diagnosis in Dermatopathology, 1991
Fernández-Figueras, et al. Am J Dermatopathol. 2010
Melwani P, et al. Am J Dermatpatol., 2010
Bearden et al, Am J Dermatopathol. 2014
A Böer, Clues, 2025

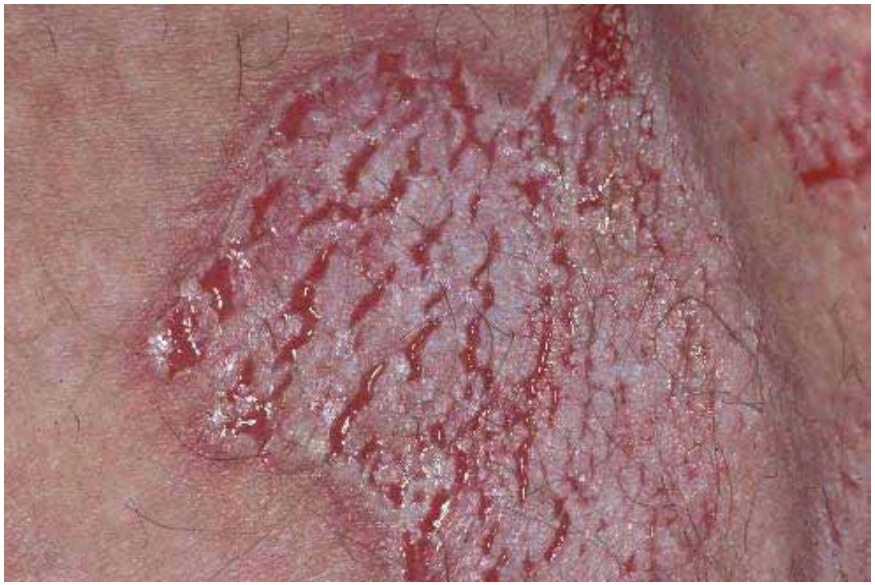
Epidermal reaction patterns
in genodermatoses, epidermal nevi, acquired skin diseases or as an incidental finding

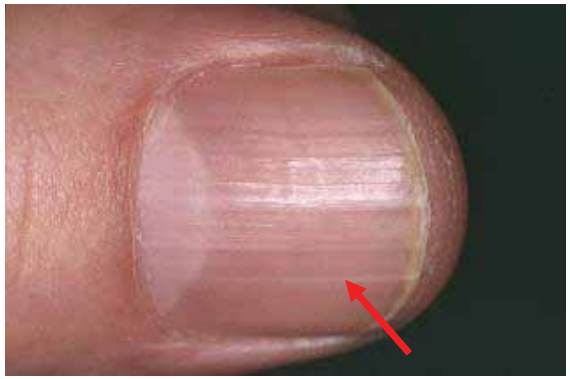
Pattern	Dermatosis	Mosaicism	Solitary lesion	Incidental finding
Epidermolytic hyperkeratosis	Keratinopathic Ichthyosis, Palmoplantarkeratoderma	+	Epidermolytic acanthoma	+
Focal acantholytic dyskeratosis	M. Darier	+	Acantholytic dyskeratotic acanthoma	+
Hailey–Hailey–type acantholysis	M. Hailey–Hailey	+	Hailey–Hailey–type acanthoma	+
Desmosomal-type acantholysis	Genetic diseases with desmsosome related mutations	?	Acantholytic acanthoma (Hyaline inclusion acanthoma)	+
Epidermolysis bullosa simplex-type vacuolization	Epidermolysis bullosa simplex	+	?	+
Granular Parakeratosis	Granular parakeratosis	-	Granular parakeratotic acanthoma	+
.....				





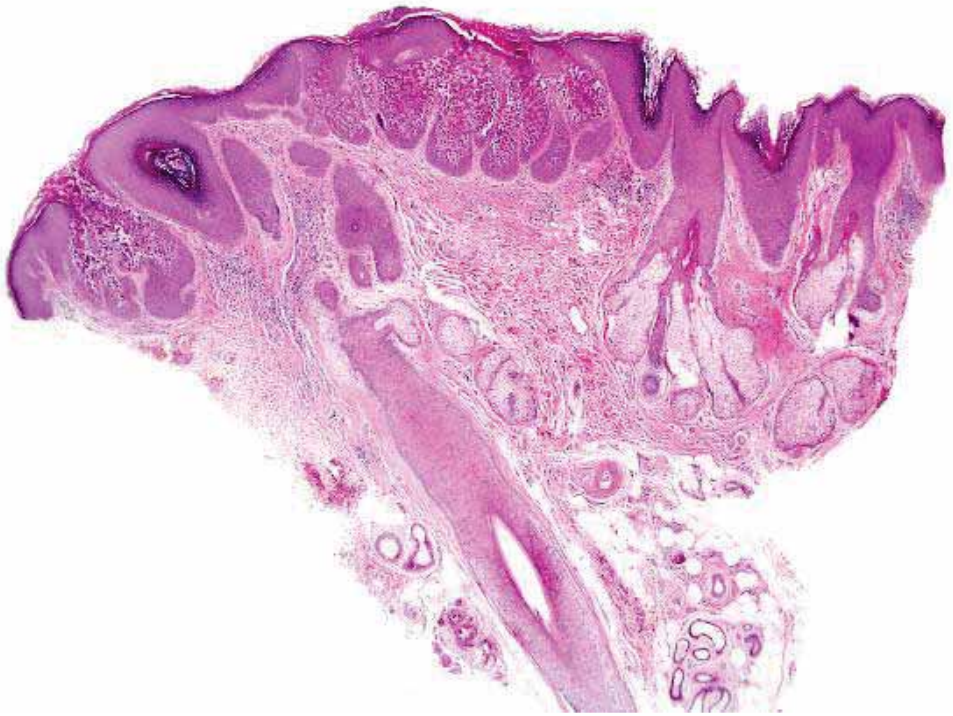
Hailey-Hailey disease

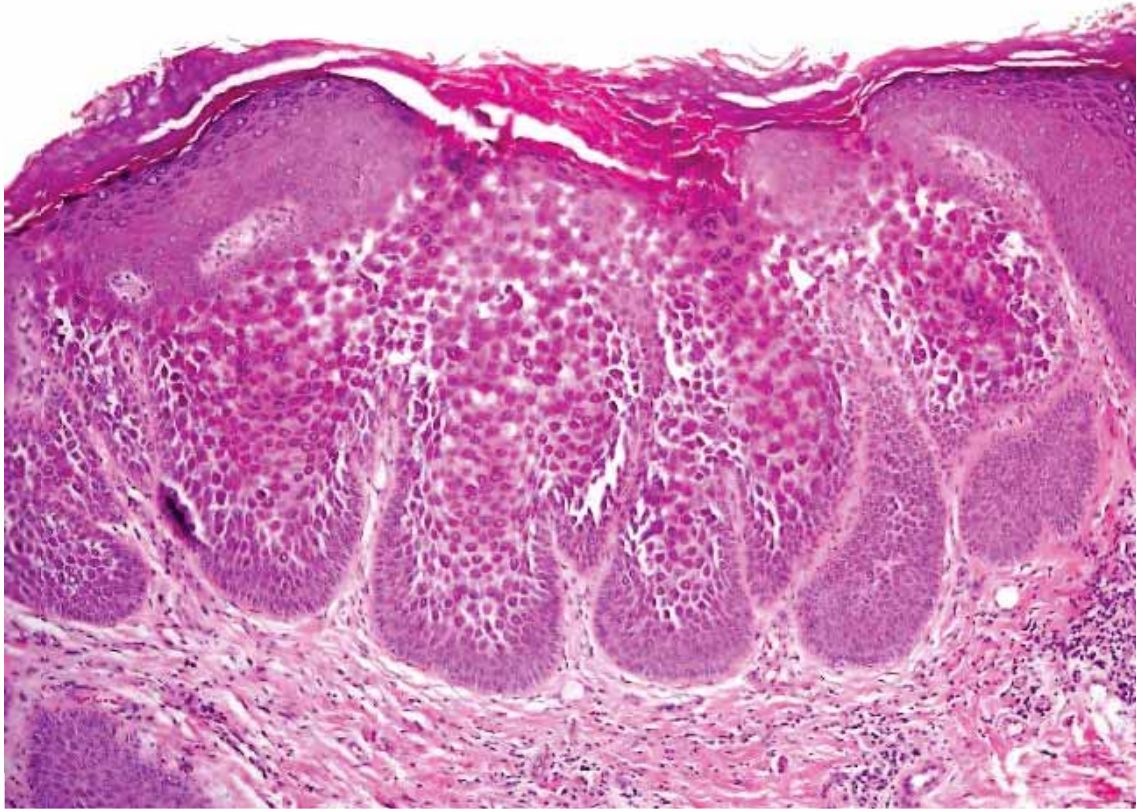


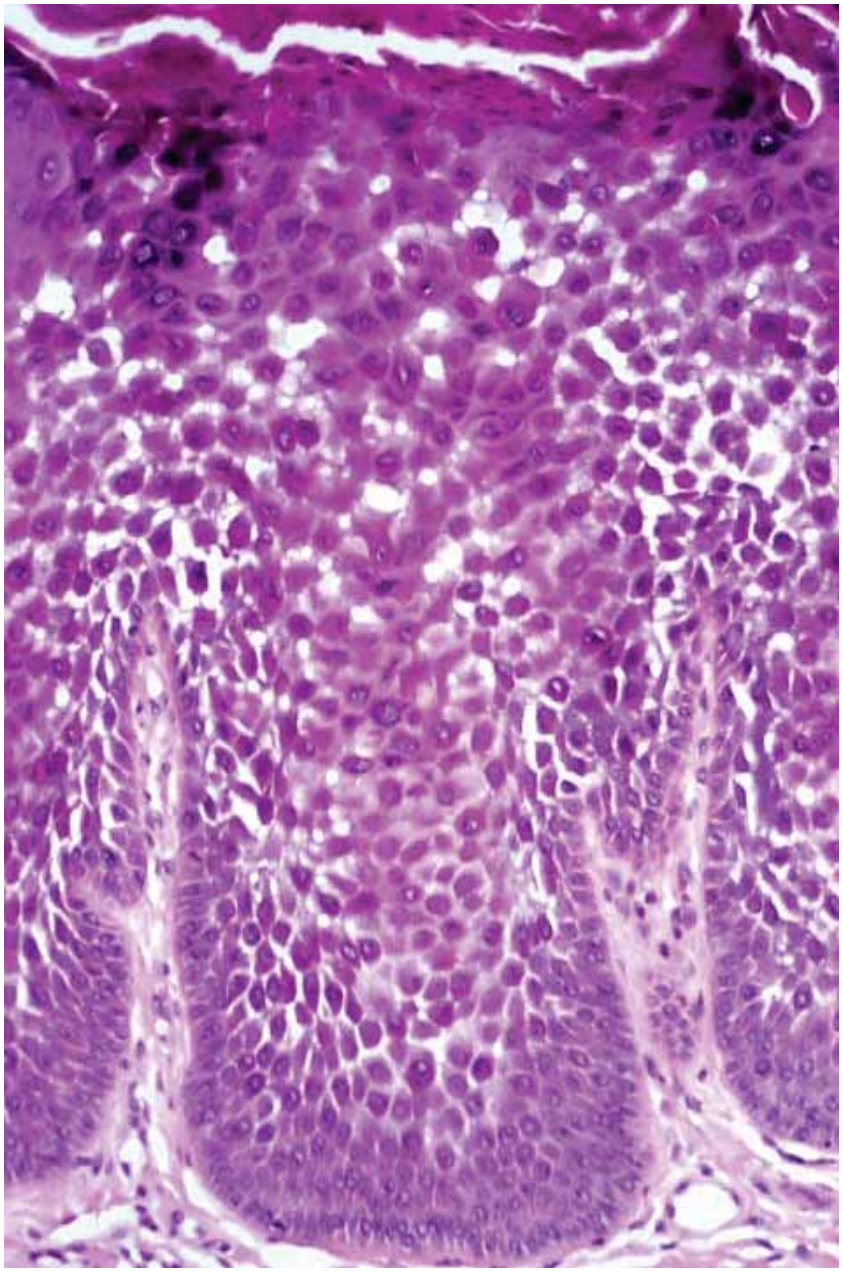


Recurrent erosive, oozing, erythematous plaques, no blisters, painful, unpleasant smell

Hailey-Hailey disease







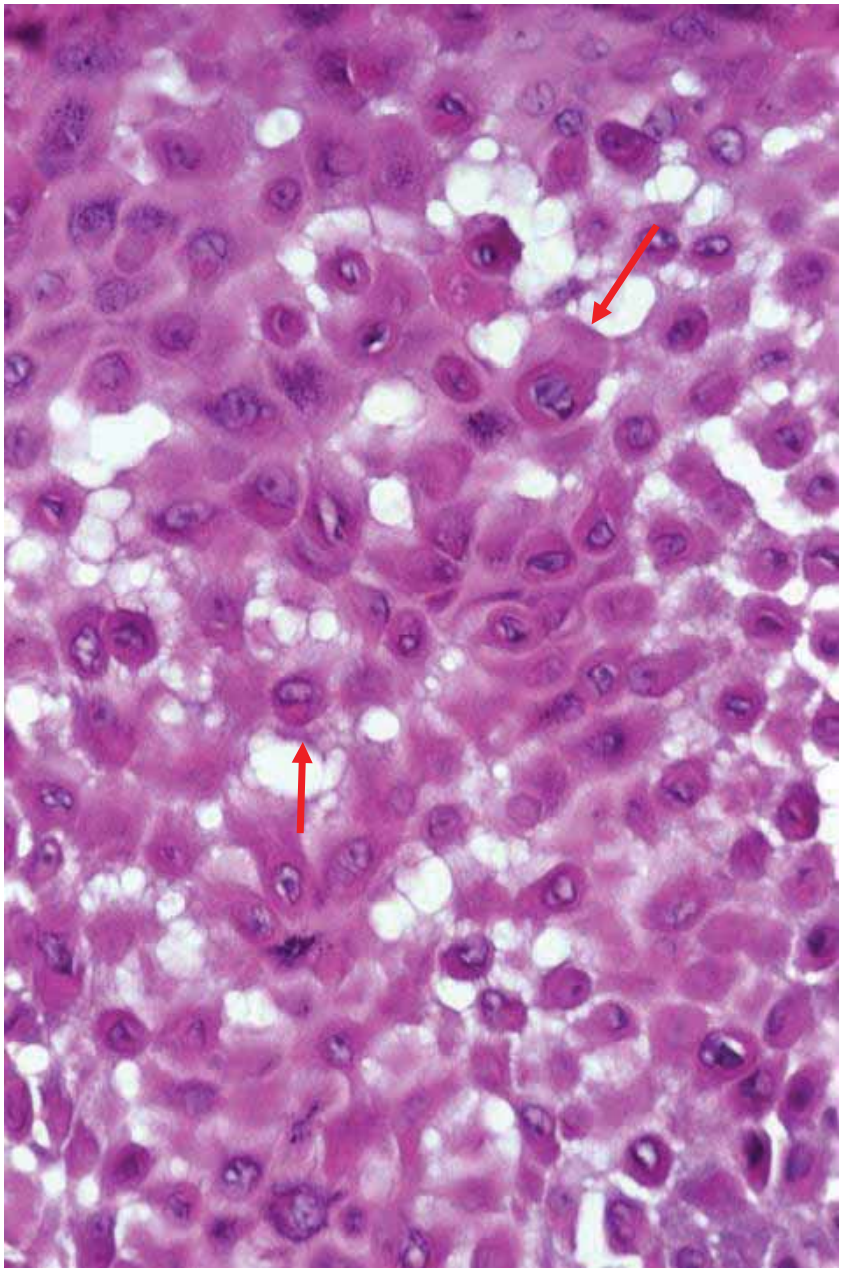
Hailey-Hailey-type acantholysis

Poor descriptions in textbooks

Focal acantholytic dyskeratosis throughout the epidermis

Dilapidated brick wall

Incomplete acantholysis

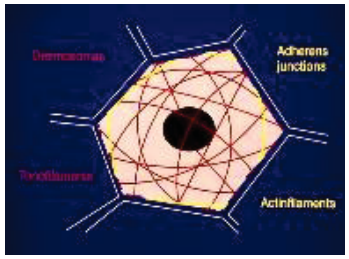


Hailey-Hailey-type acantholysis

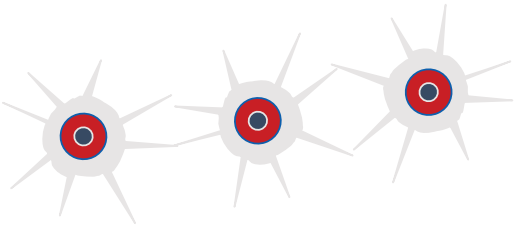
Keratinocytes polygonal with elongated microvilli bridging adjacent cells

Perinuclear hypereosinophilia and pale peripheral cytoplasm

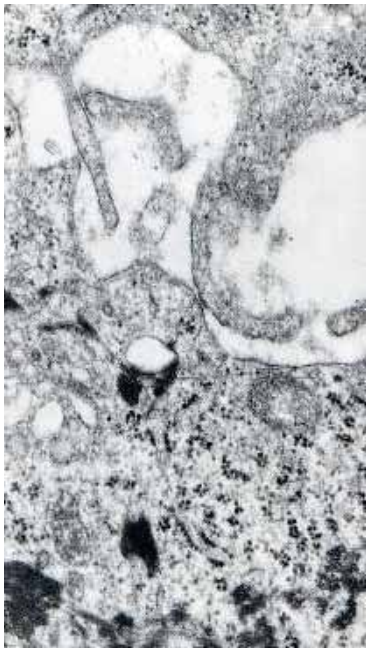
Intact nuclei with mitotic activity; no pyknosis



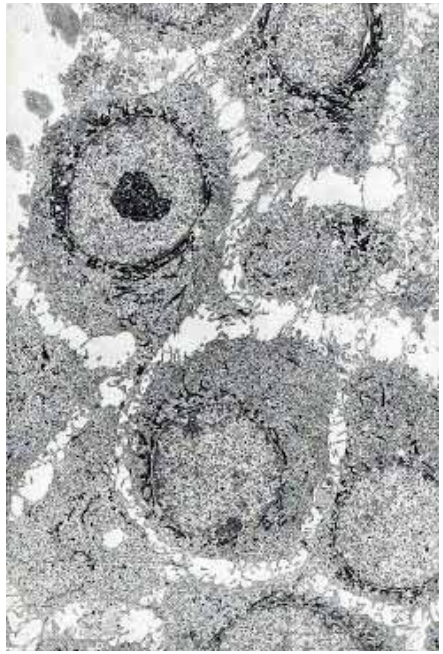
M. Hailey-Hailey: Mutation of ATP2C1 gene (3q) ->
ATP-dependent Ca^{2+} Pumpe ->
Dysregulation of cell junctions
following physical stress



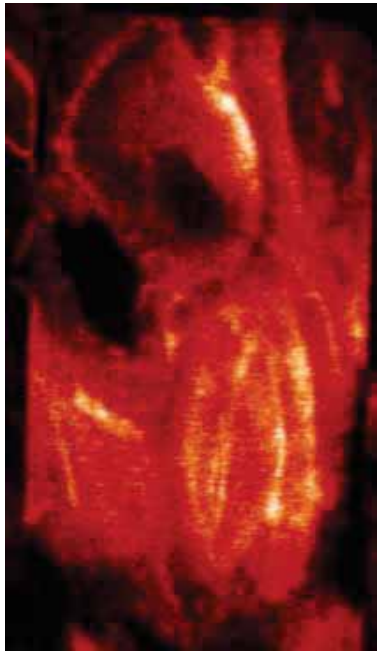
Metze D, et al. J Cutan Pathol. 1996



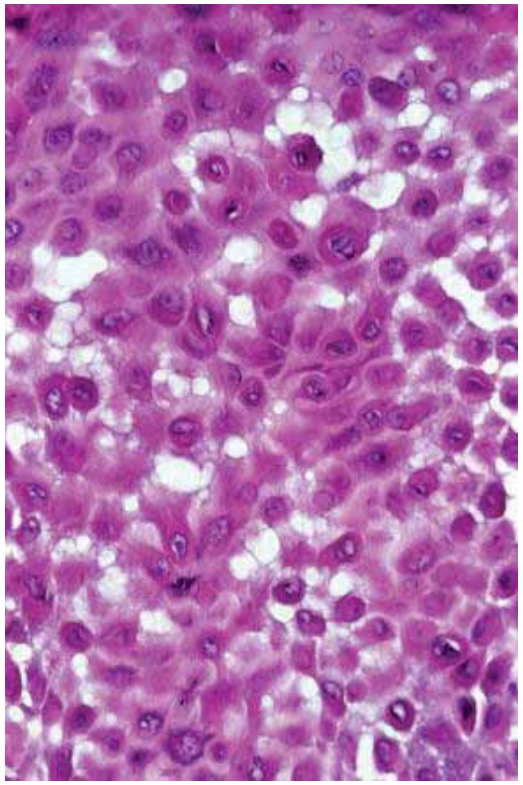
Dissolution/Internalisation
of Desmosomes



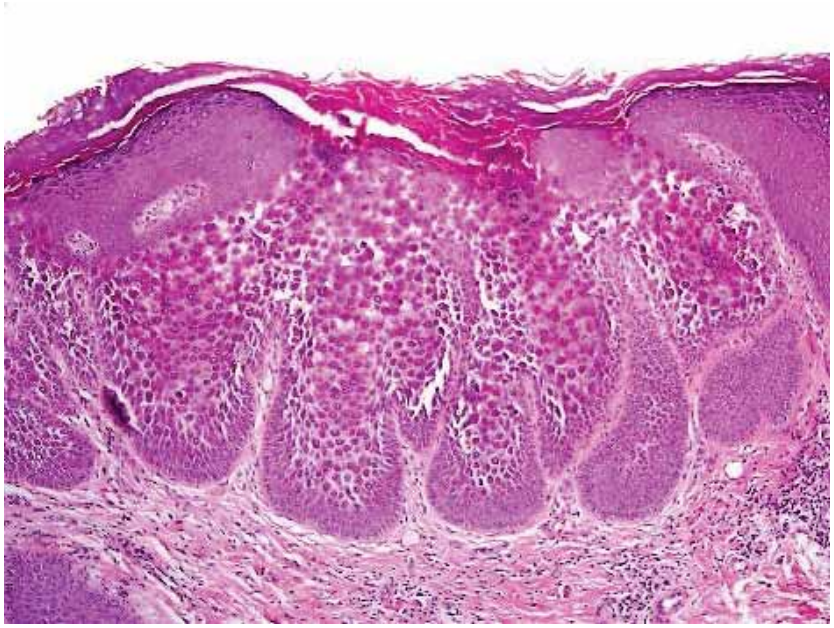
Collapse of
the keratin skeleton

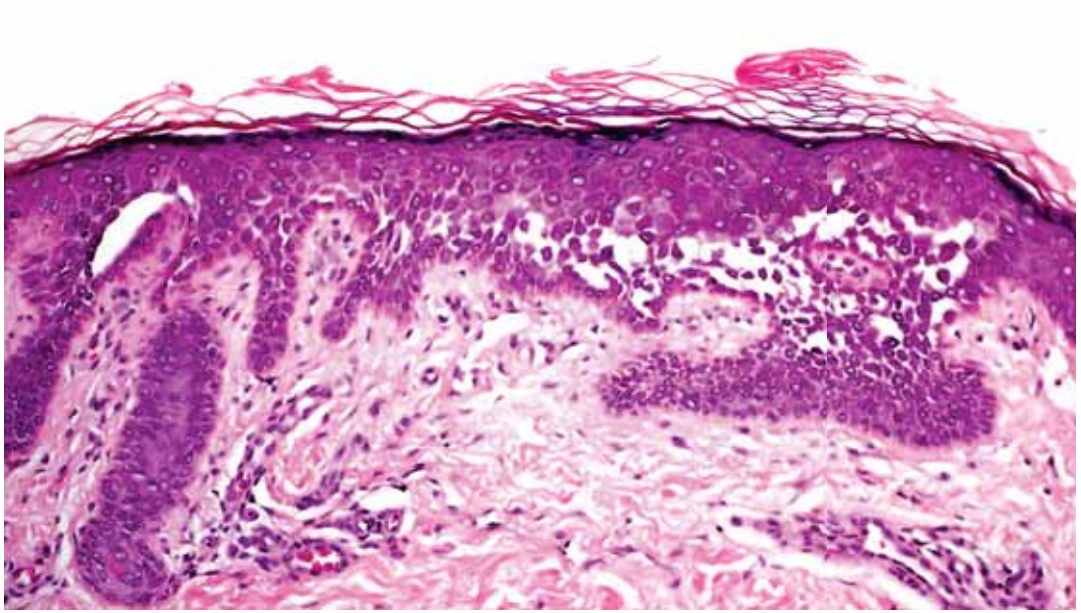


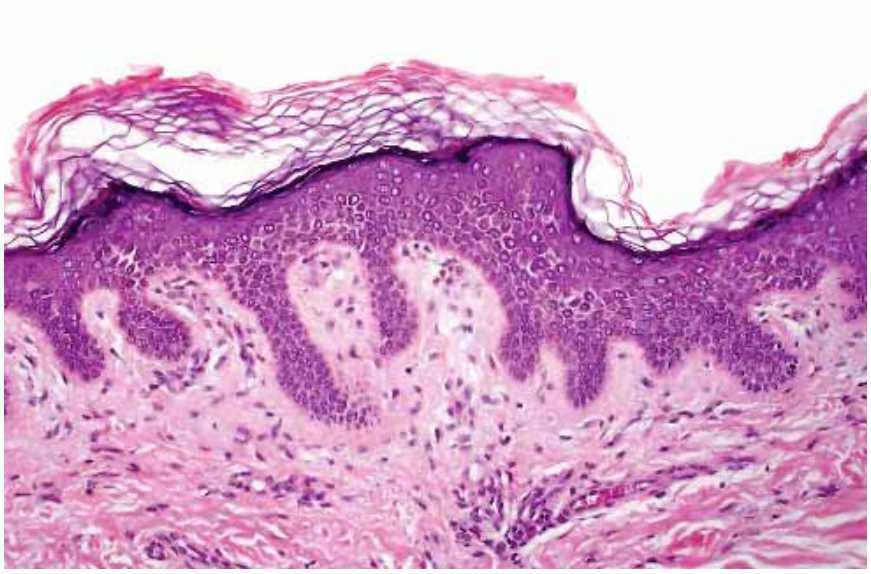
Overexpression
of actin skeleton



„Incomplete“ acantholysis

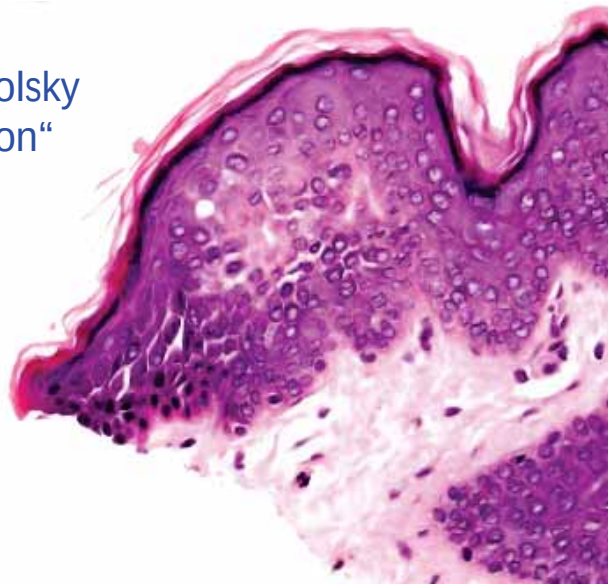




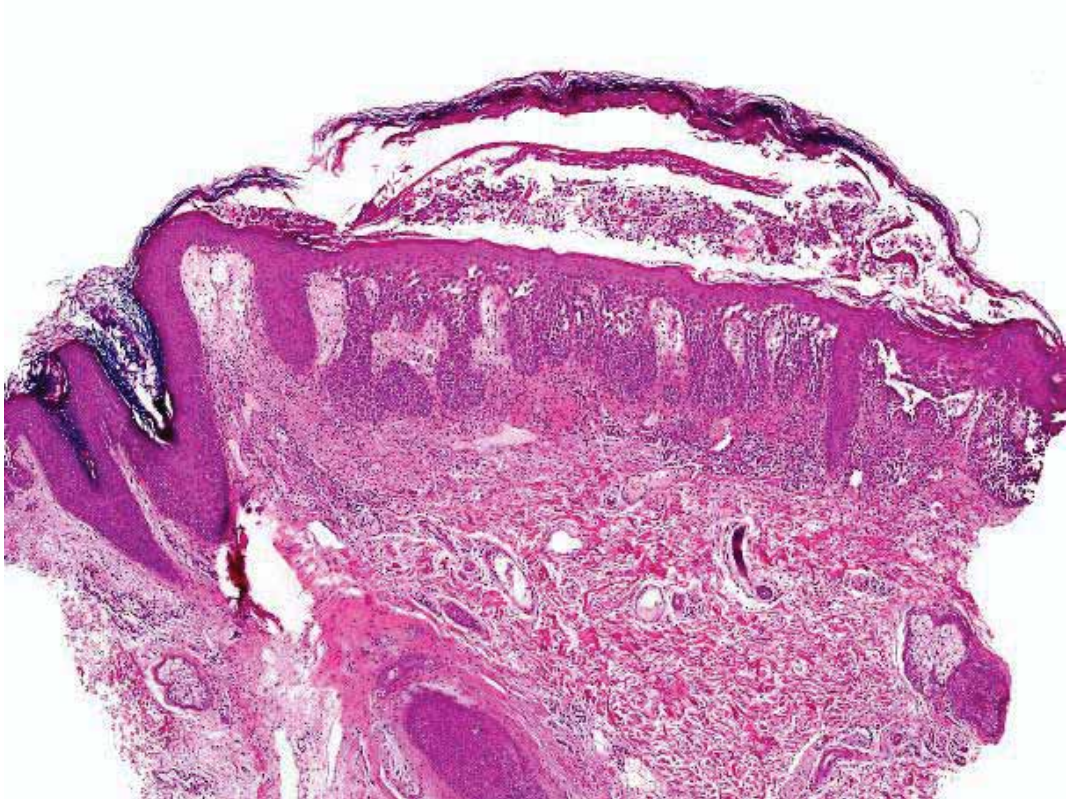


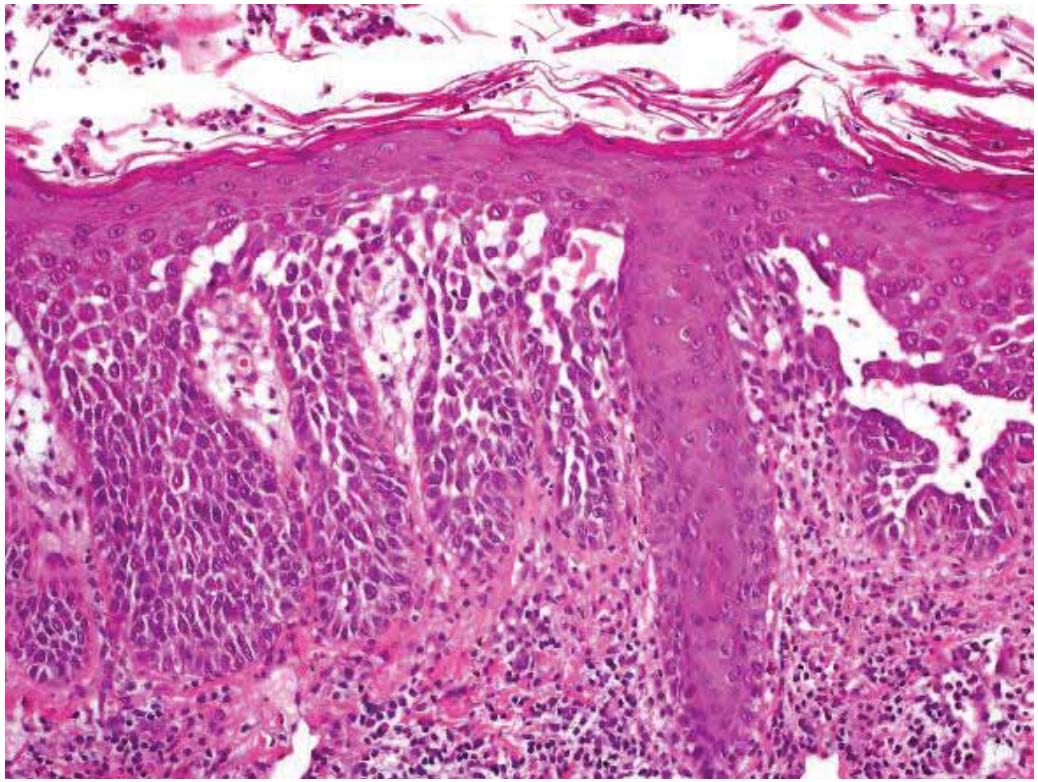
"Mikro-Nikolsky Phenomenon"

Biopsy margin

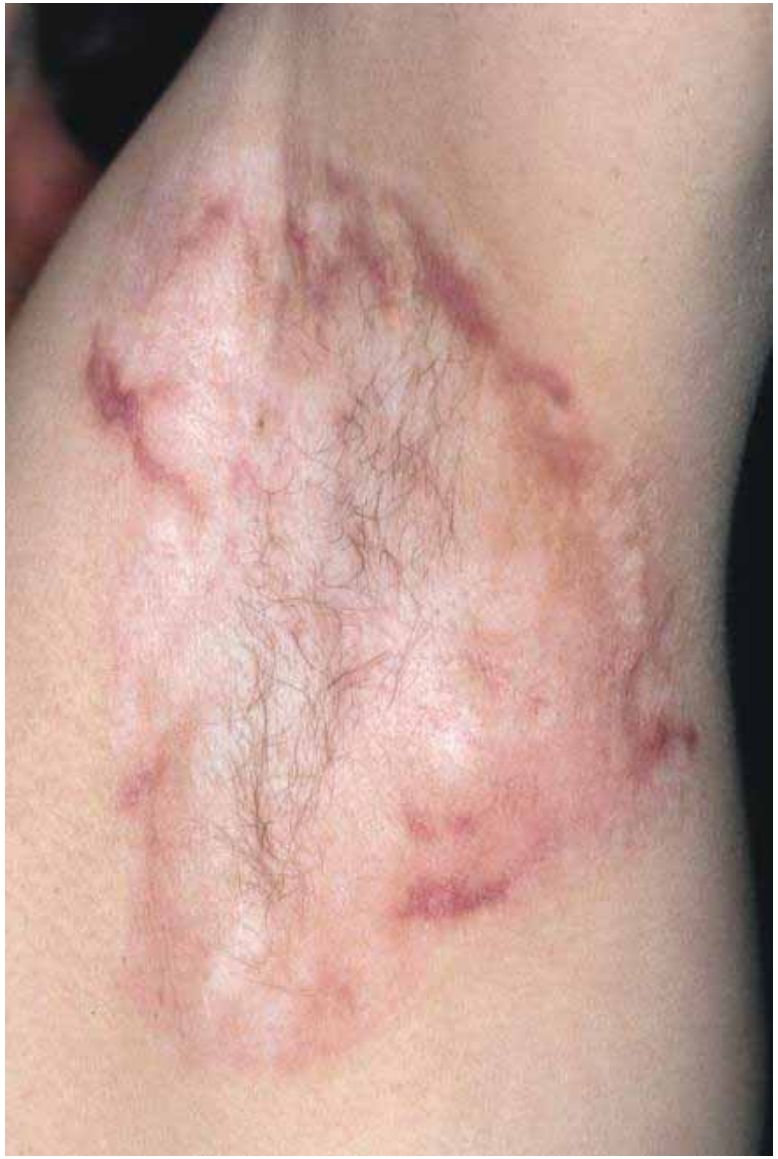


Hailey-Hailey disease, fully developed

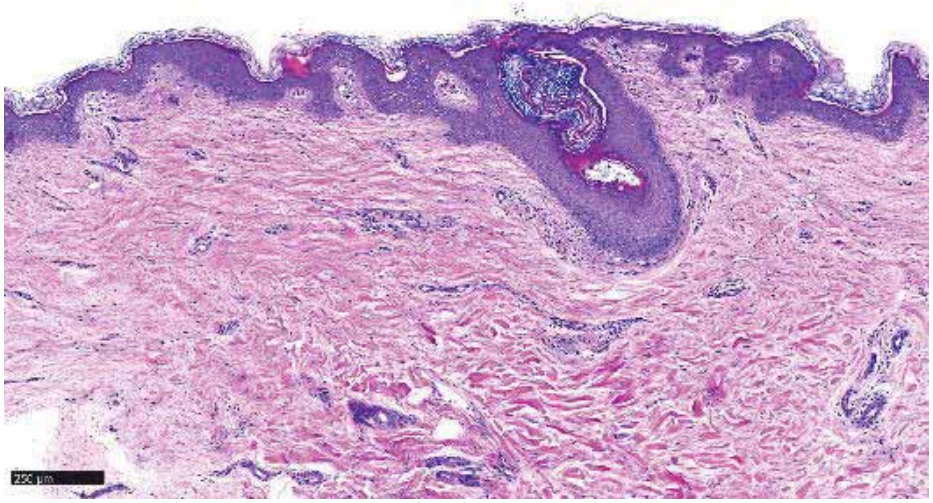


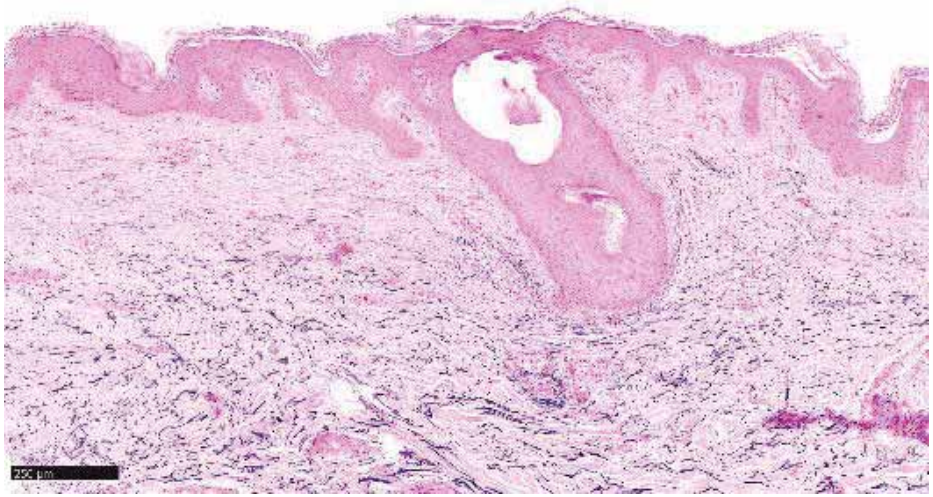


Hyperplasia, parakeratosis, crusts, mixed inflammatory infiltrate

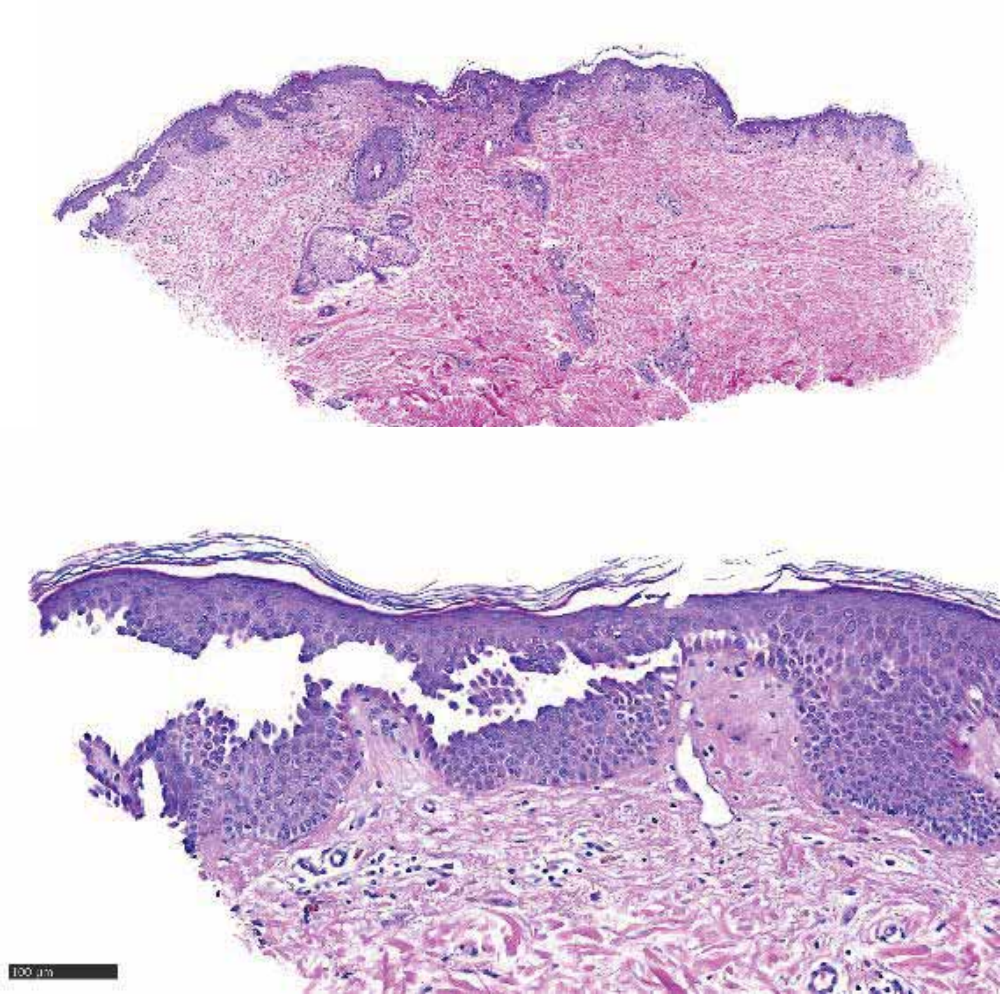


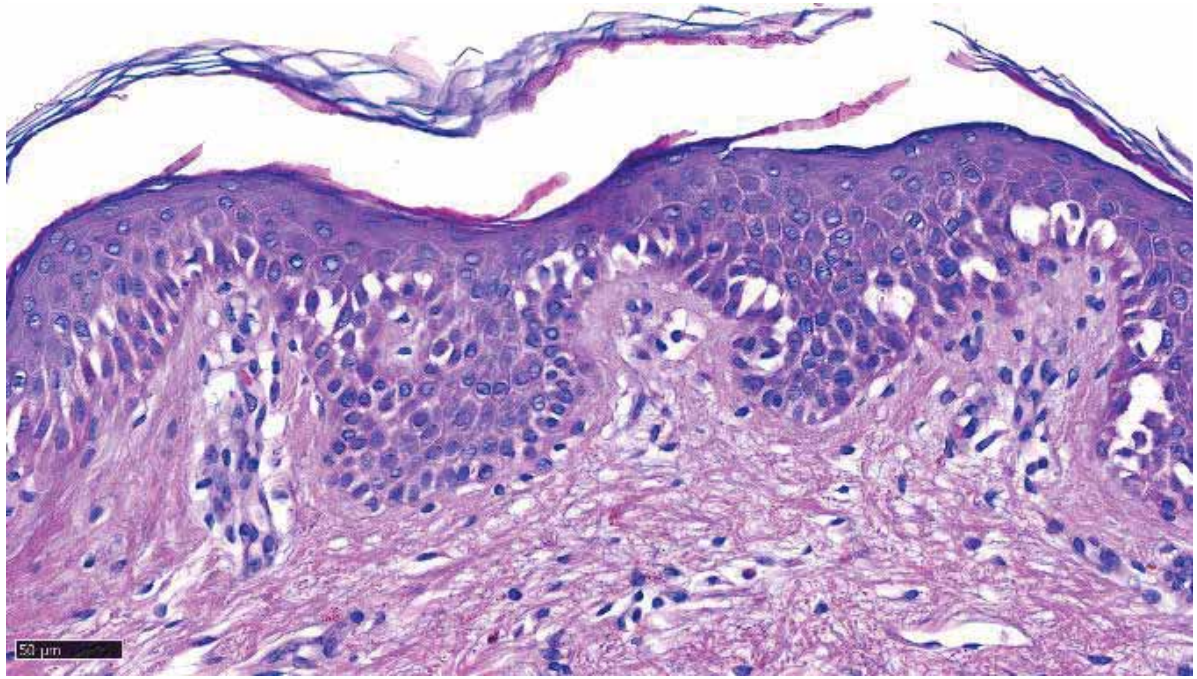
Status post ablative therapy (dermabrasion, laser)





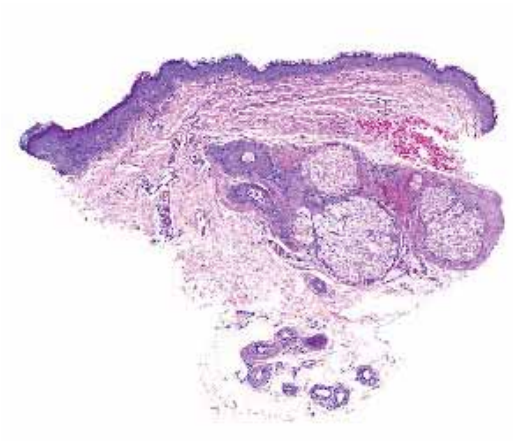
Status post ablative therapy, recurrence, periphery

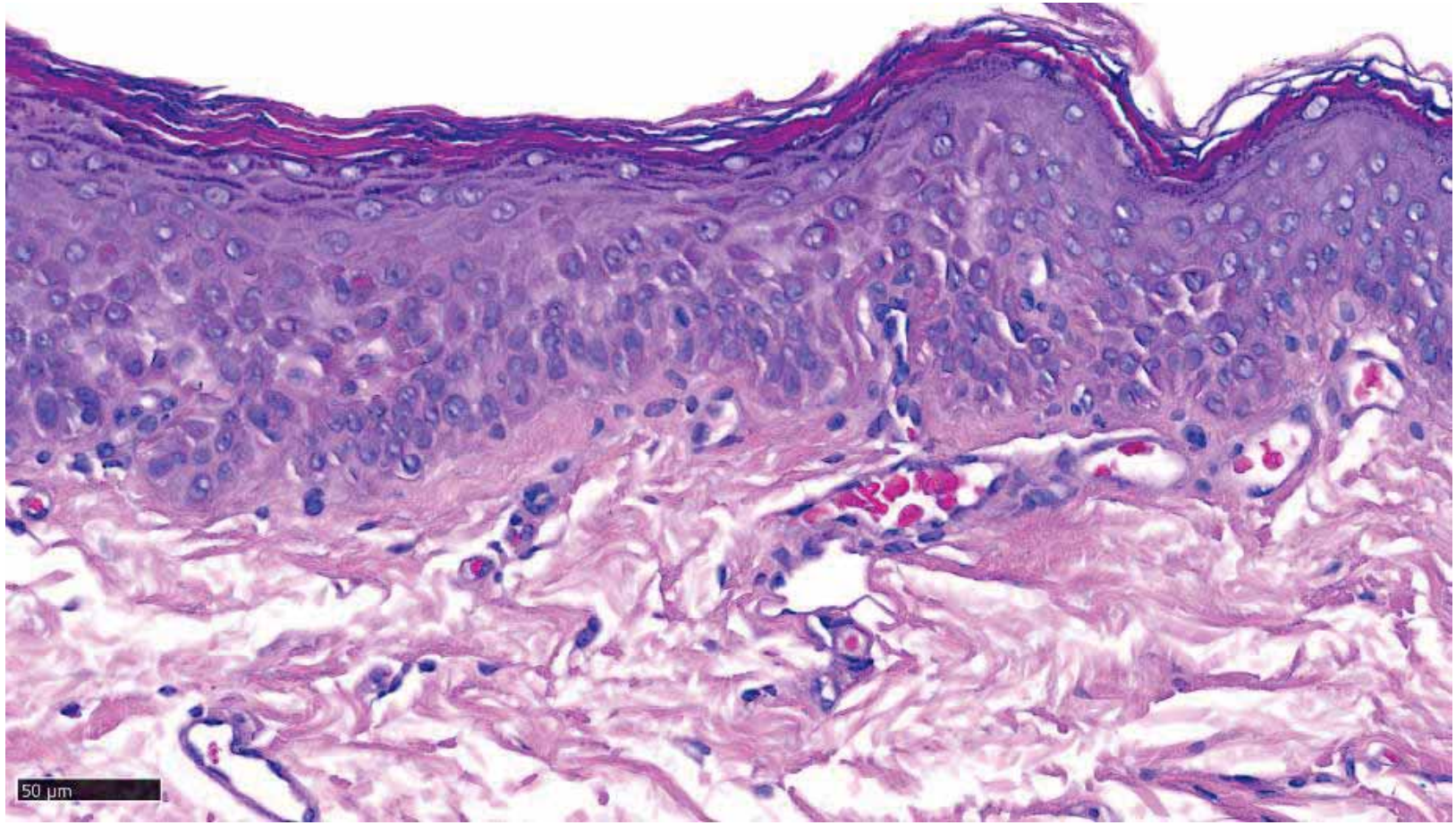




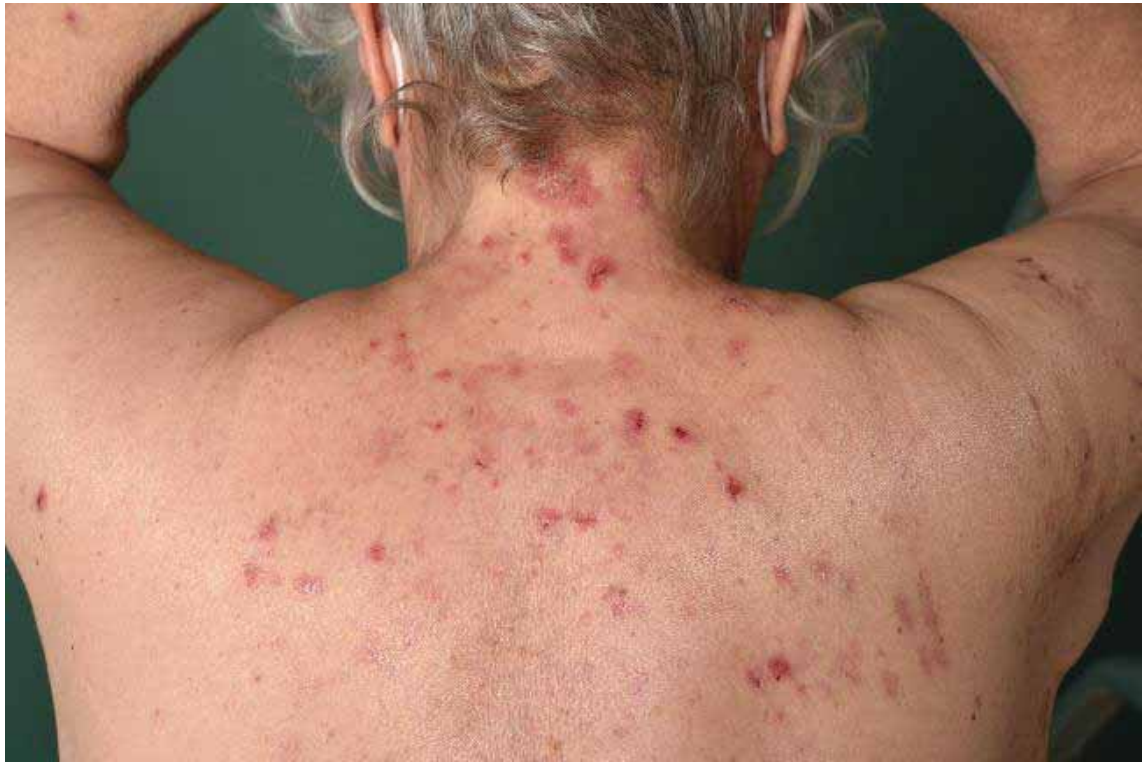
Würzburg, L. Streikiene, H. Hamm, G. Weyandt, Thesis

Status post ablative therapy, recurrence, periphery

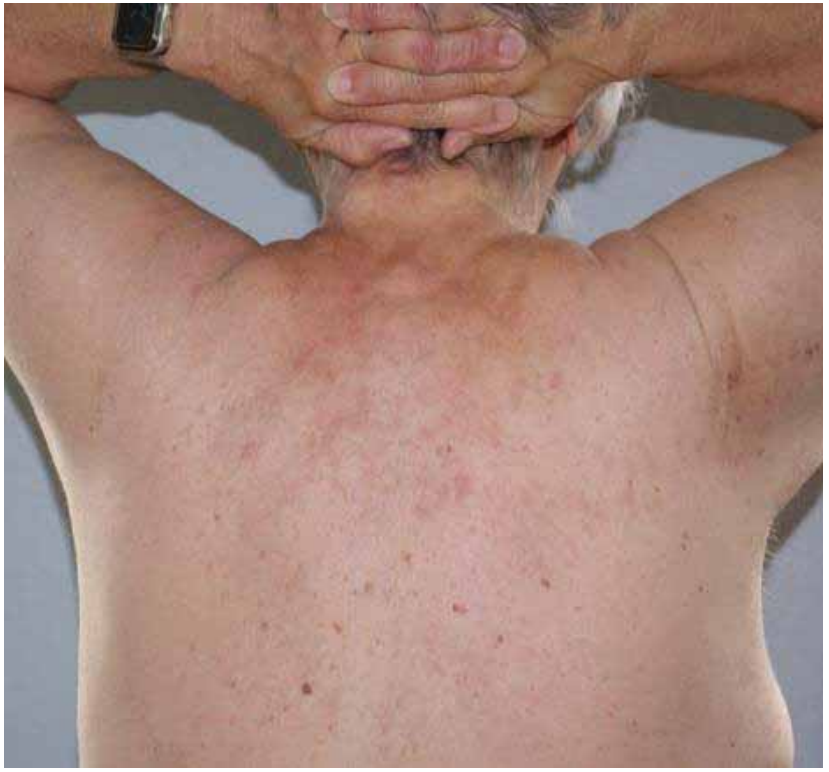




Würzburg, L. Streikiene, H. Hamm, G. Weyandt, Thesis

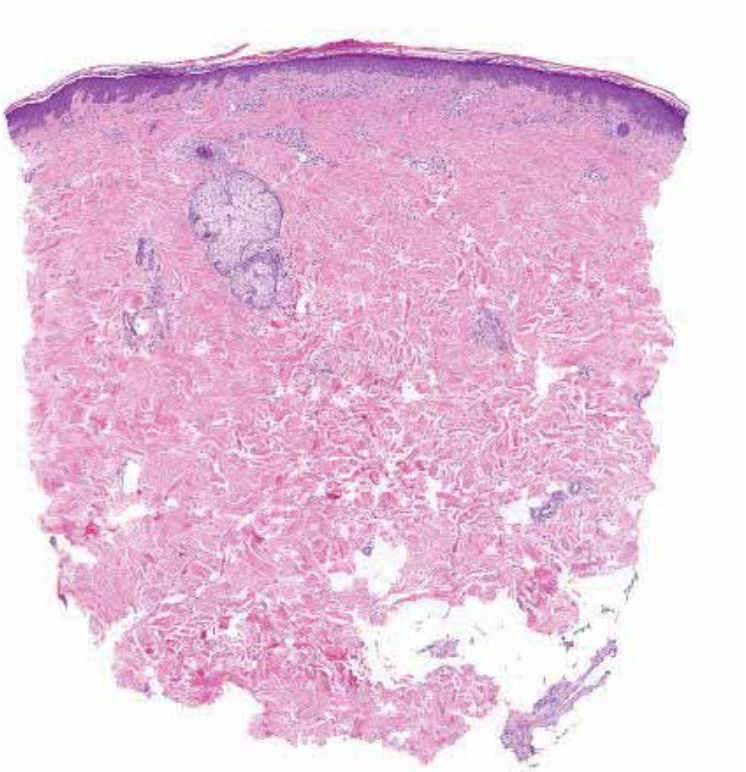


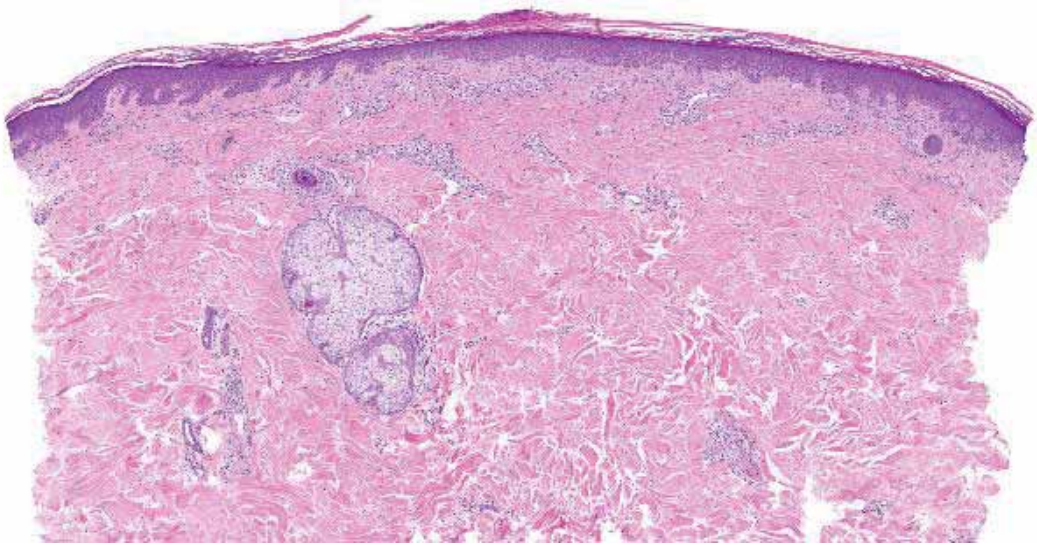
Patient with Hailey-Hailey disease with generalized pruritus

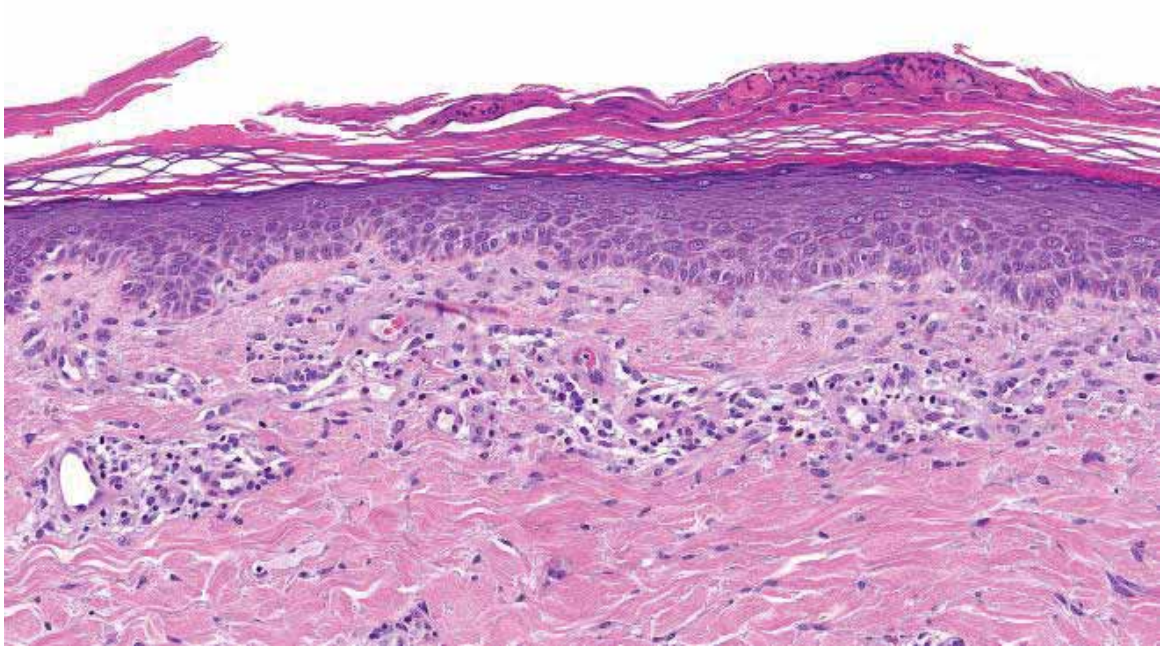


Remission after treatment with opioid antagonists

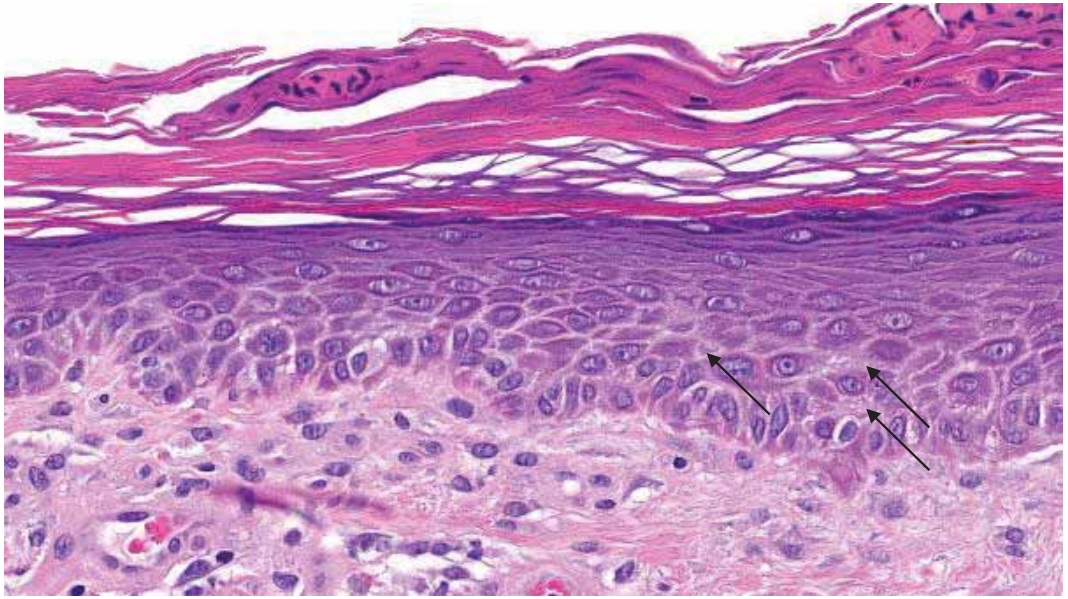
Witte F, Metze D, Ständer S, Zeidler C. JEADV Clin Pract., 2024

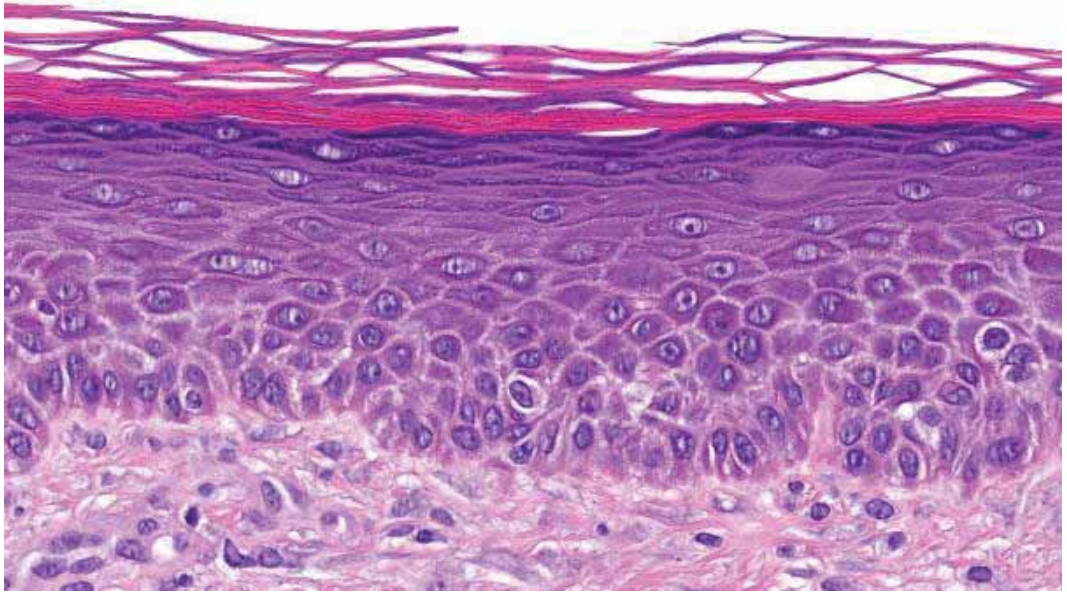


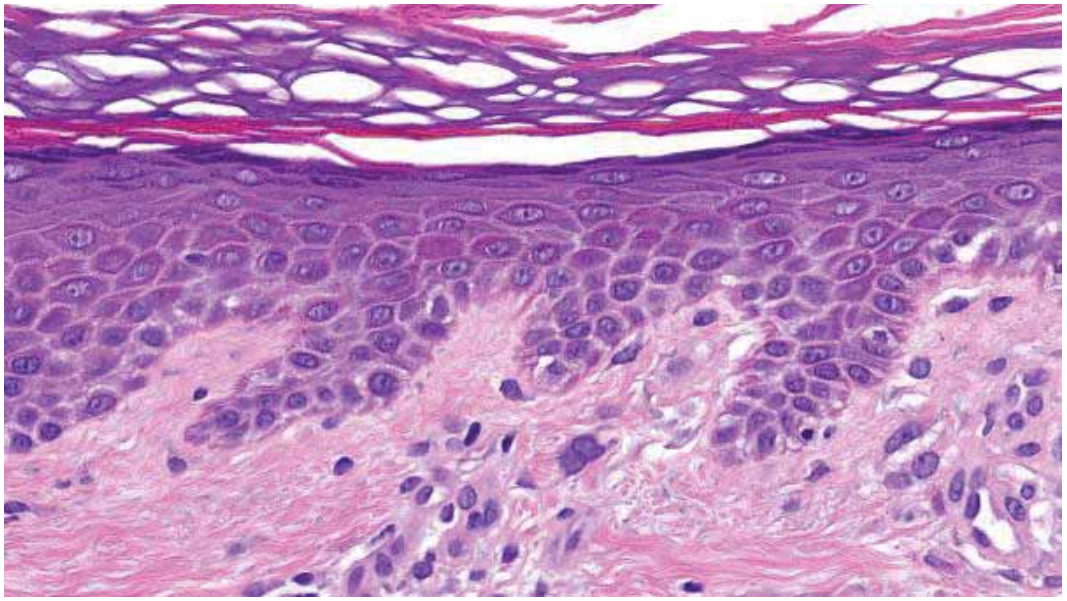




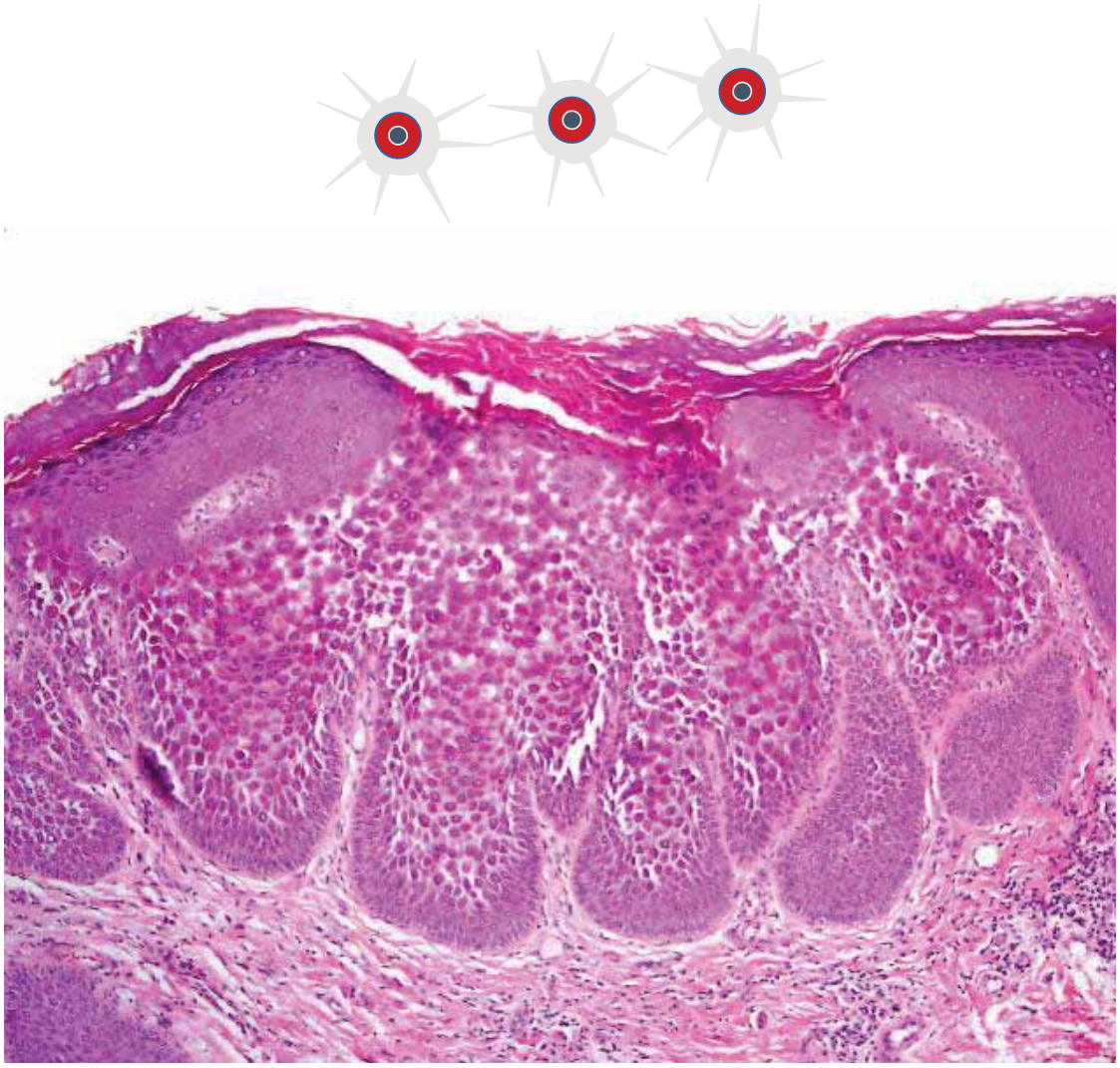
Signs of scratching/friction:
hyperkeratotic, hyperplastic epidermis;
inflammatory fibrosis of the papillary dermis







Hailey–Hailey-like changes: incomplete acantholysis, peripheral cytoplasmic pallor, and perinuclear hypereosinophilia of keratinocytes



Epidermal reaction patterns

Hailey-Hailey-type acantholysis

- Hailey-Hailey disease (Relapsing linear acantholytic dermatosis, papular acantholytic dyskeratosis of the genitalia)
- Nevus corniculatus

➢Familial dyskeratotic comedones

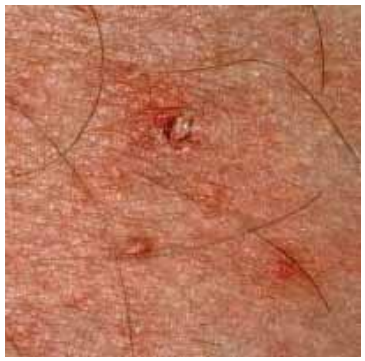
➢Acantholytic acanthoma

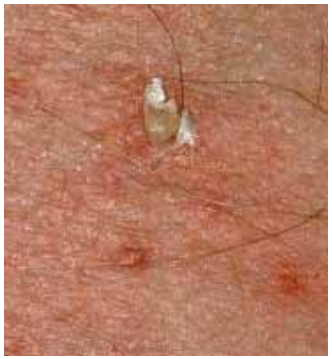
➢Incidental finding

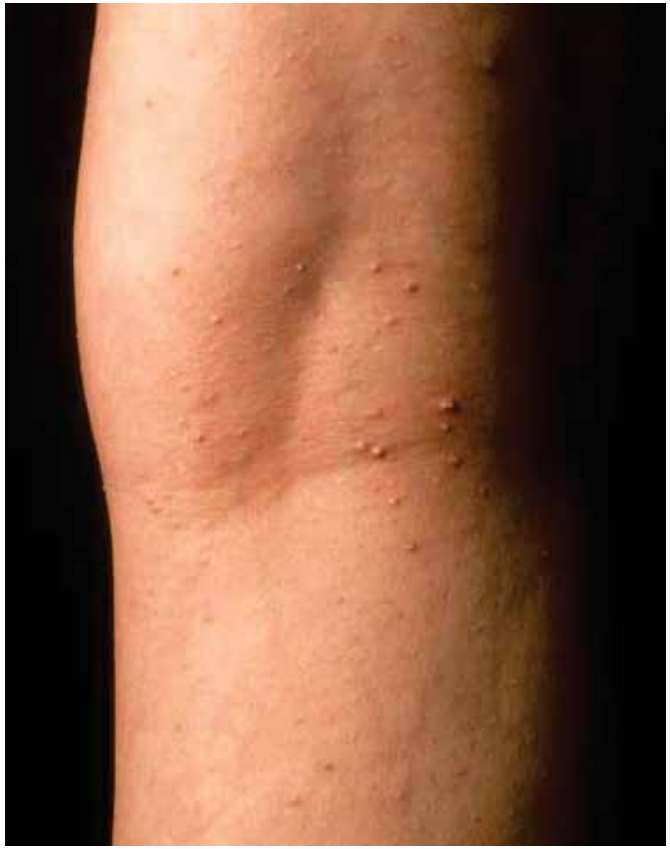
➢Grover disease

Familial Dyskeratotic Comedones

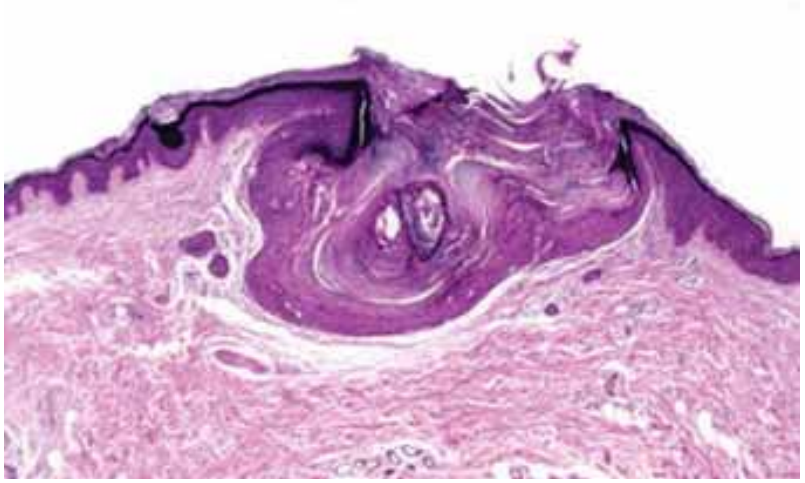
- Rare genodermatosis (autosomal-dominant)
- early onset
- disseminated papules with keratotic plug
- extremities > trunk > face

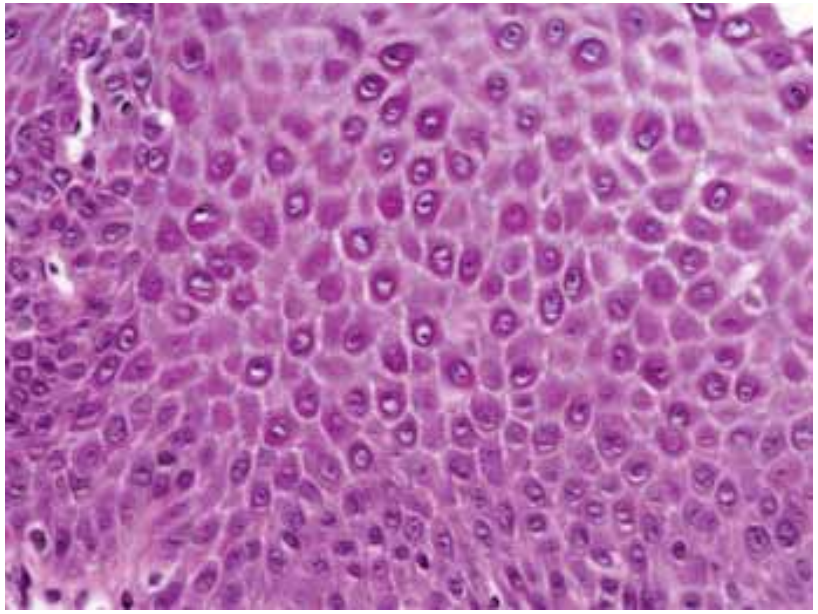


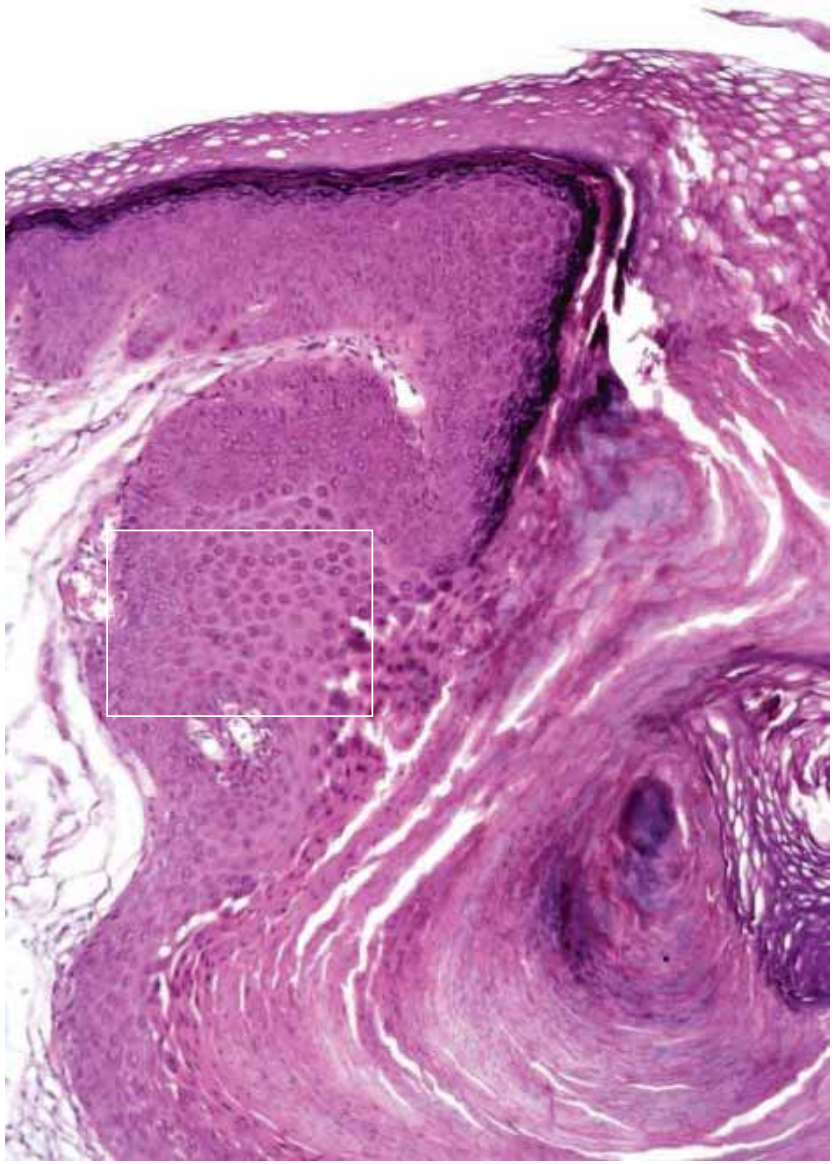


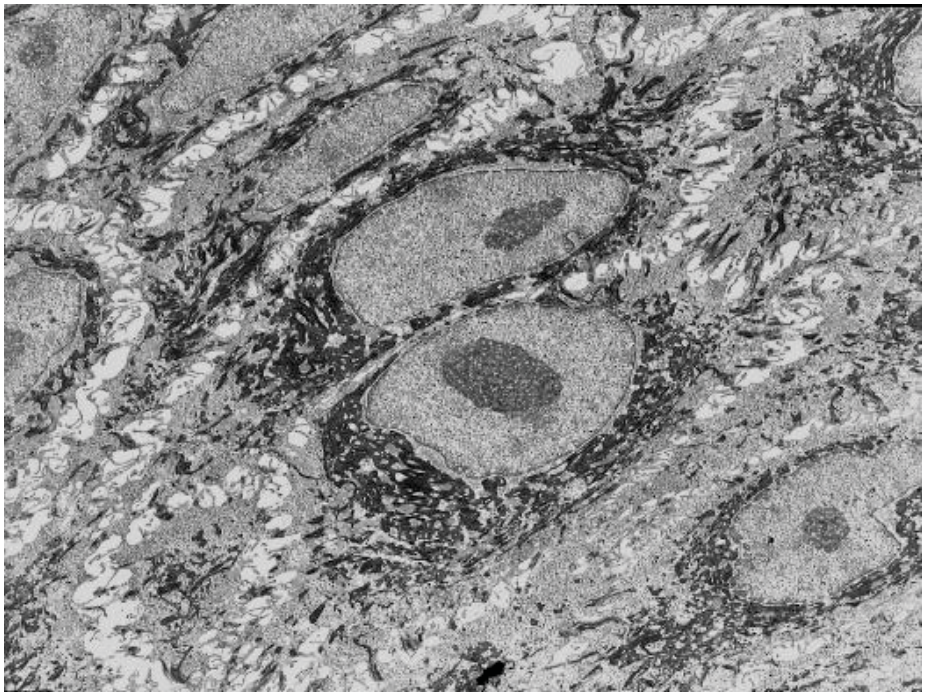


Reimann et al, Am J Dermatopathol, 1997



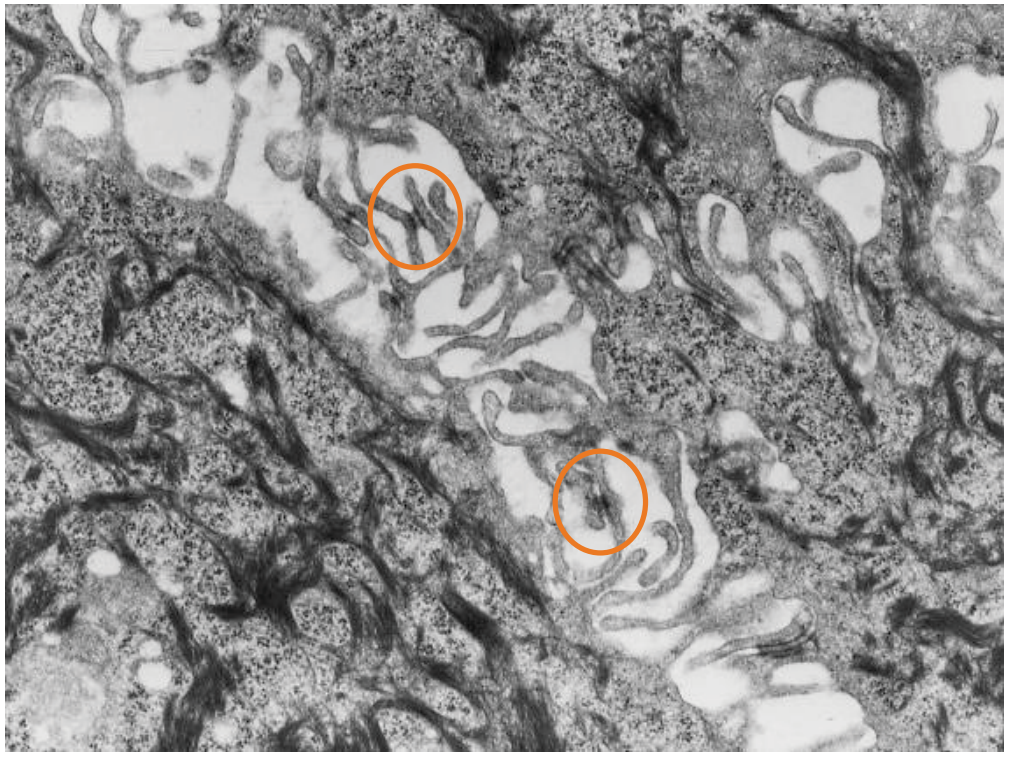






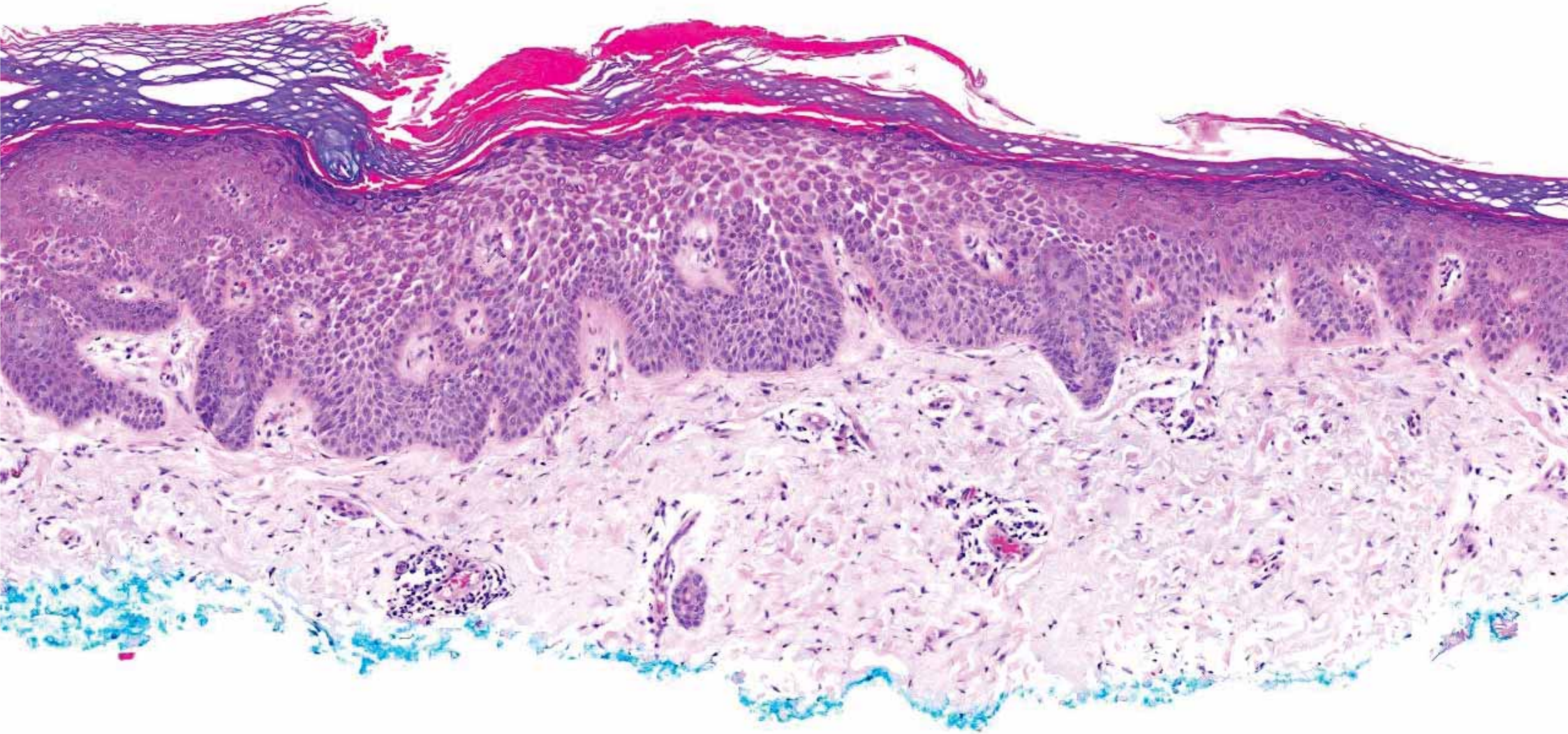
Preservation of adherens junctions-actin skeleton

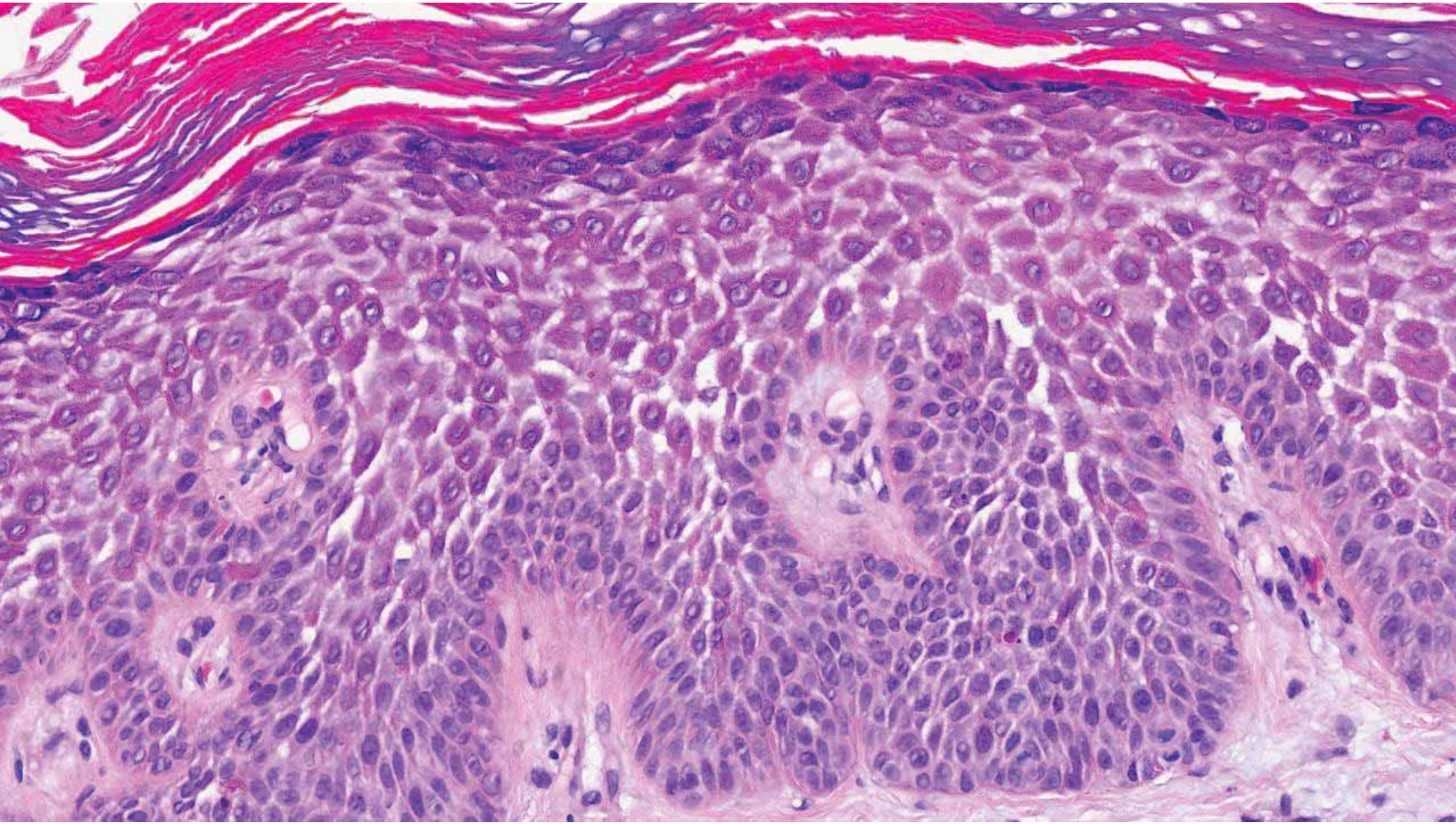
Dissolution of desmosomes
Collapse of keratins keleton



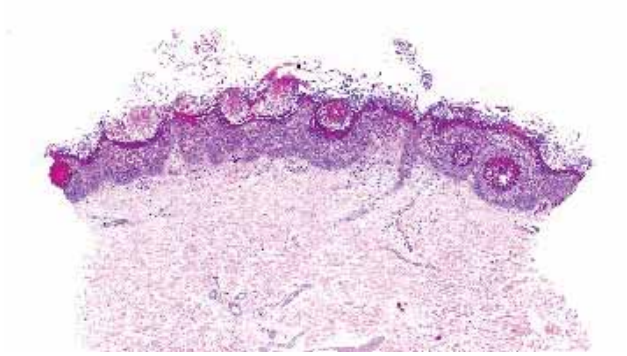
Acanthoma with Hailey-Hailey-type of acantholysis

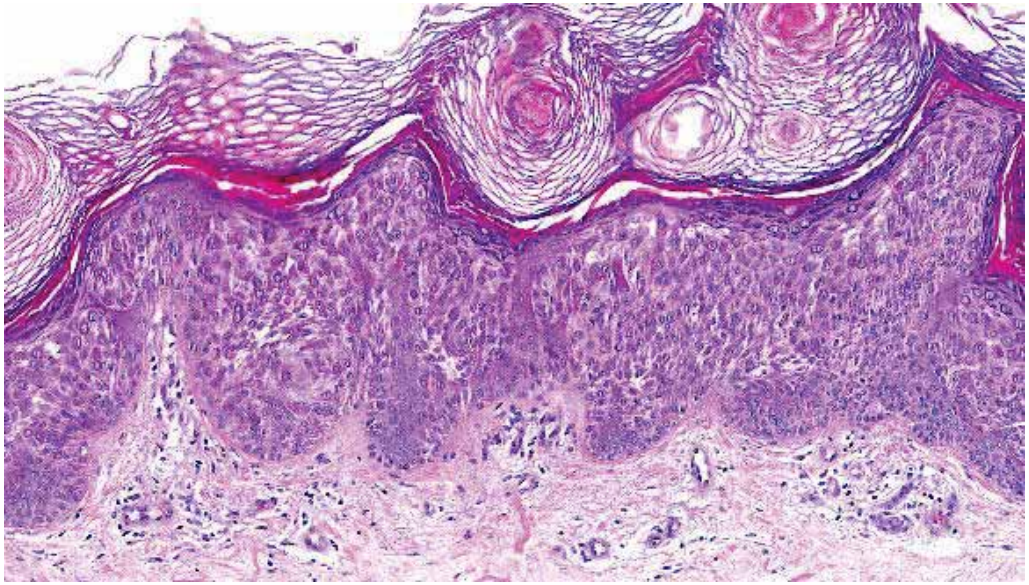
Back of the hand, 35-year-old-man

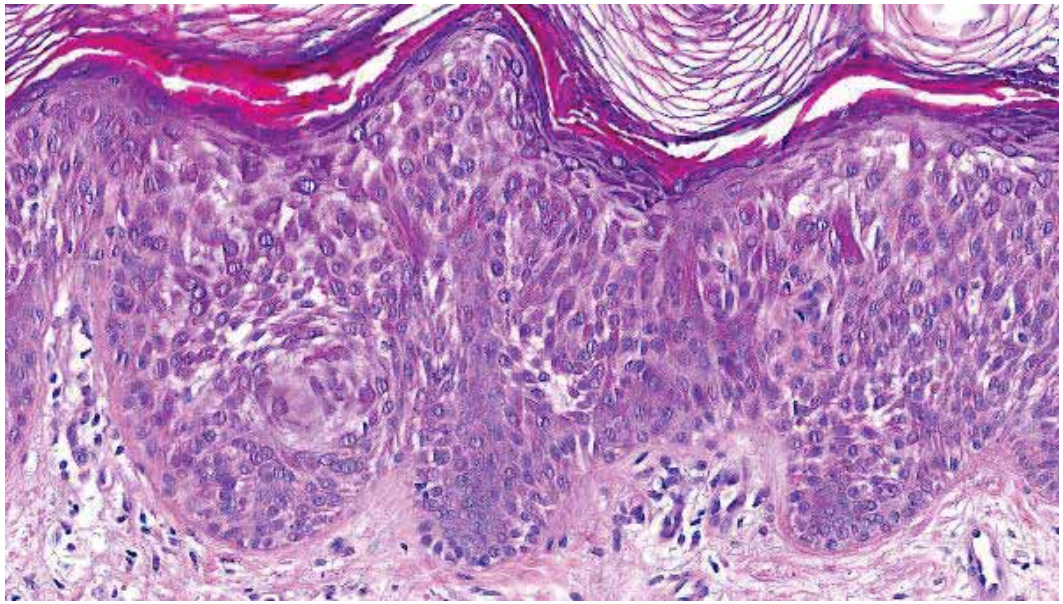




Acanthoma with Hailey-Hailey-type of acantholysis







Acanthoma with Hailey-Hailey-type of acantholysis
(solitary acantholytic acanthoma)

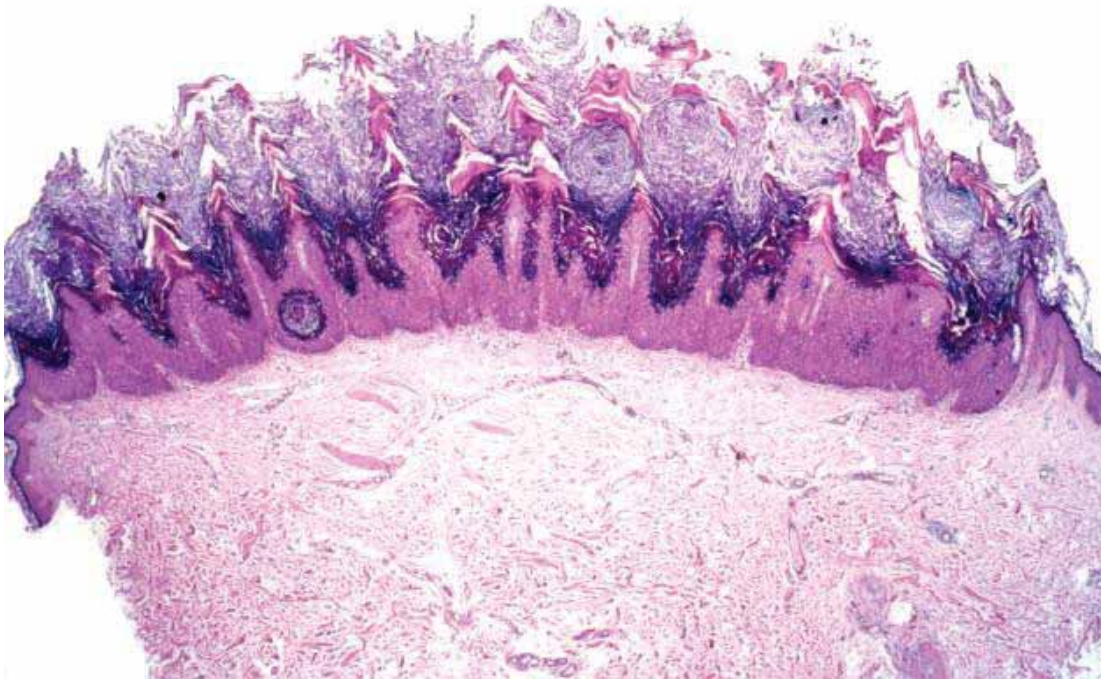
Degree of hypergranulosis

Hypergranulotic dyskeratotic acanthoma
(Hypergranulotic dyscornification,
benign hypergranulotic keratosis with dyscornification)

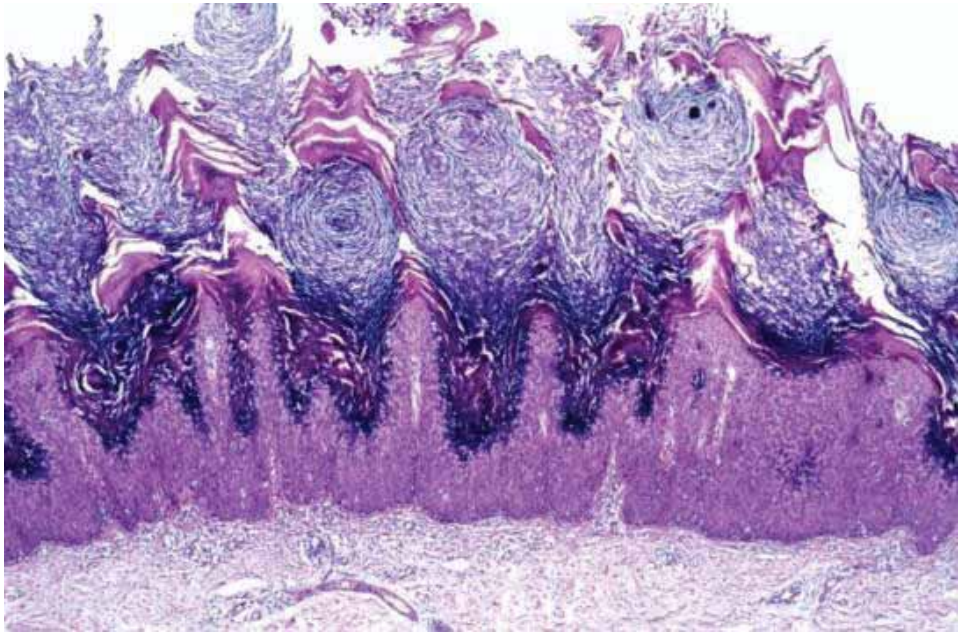
Lee SH , et al. Am J Dermatopathol, 2021
Roy S, et al, J Cutan Pathol, 2019
Reichelt M. Am J Dermatopathol, 1999
DohseL, et al. J Am Acad Dermatol, 2010

Hypergranulotic dyskeratotic acanthoma

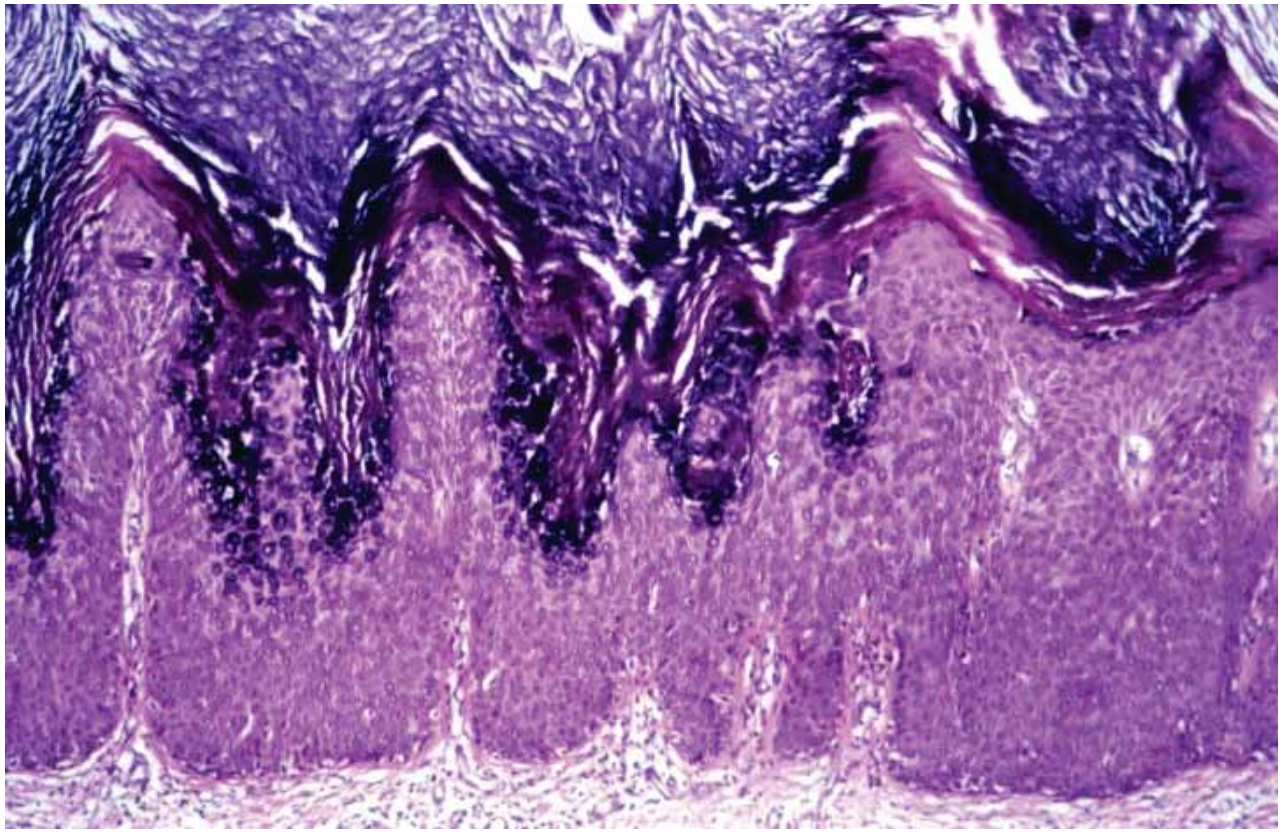
A variant of acanthoma with Hailey-Hailey-type of acantholysis ?



Acanthoma, orthohyperkeratosis, Hailey-Hailey-type of acantholysis

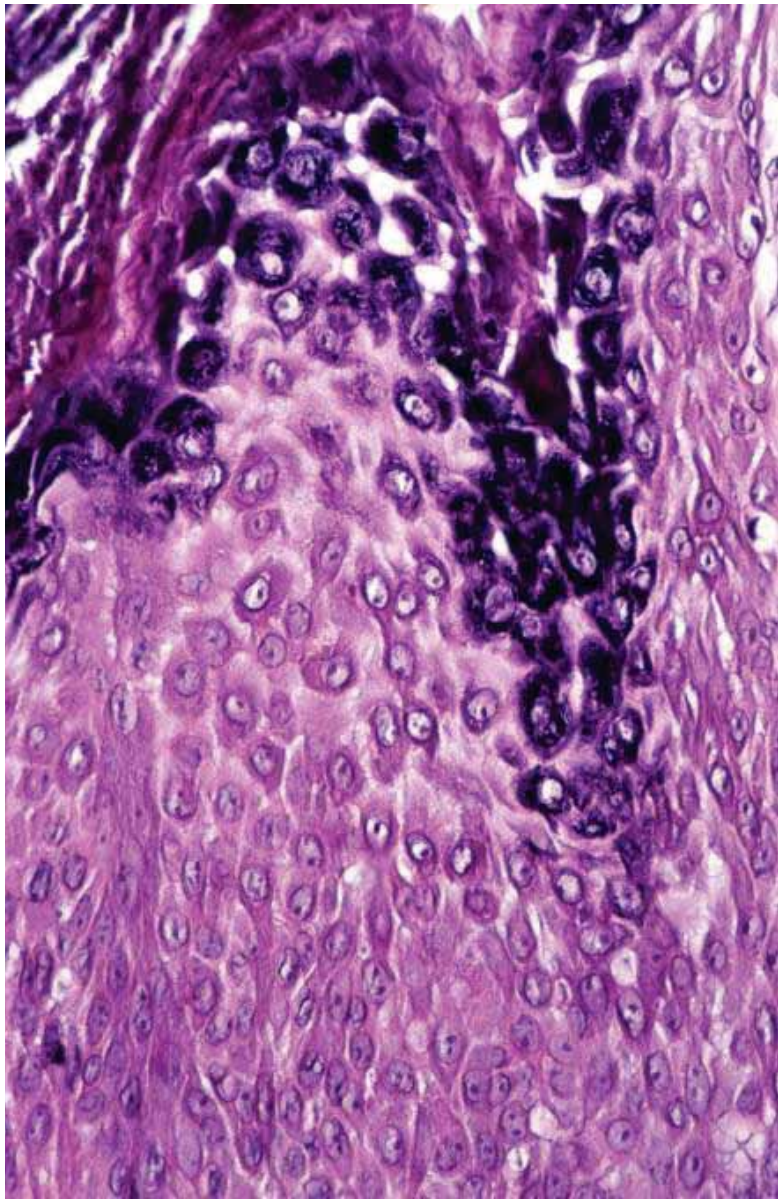


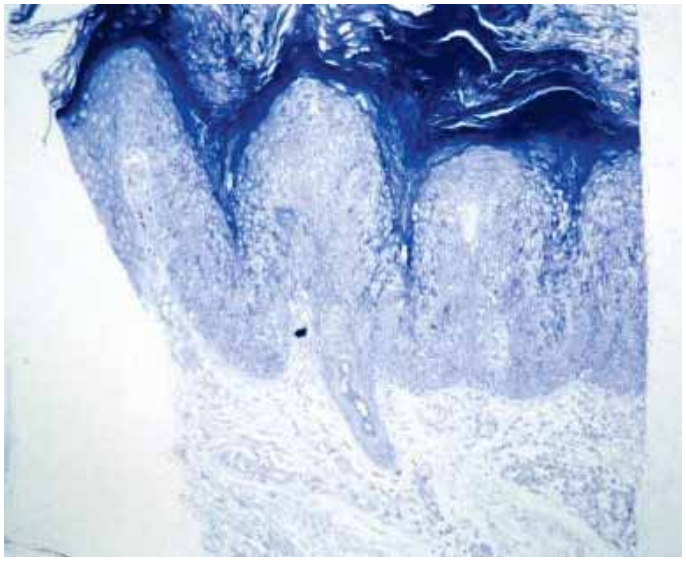
plus Hypergranulosis

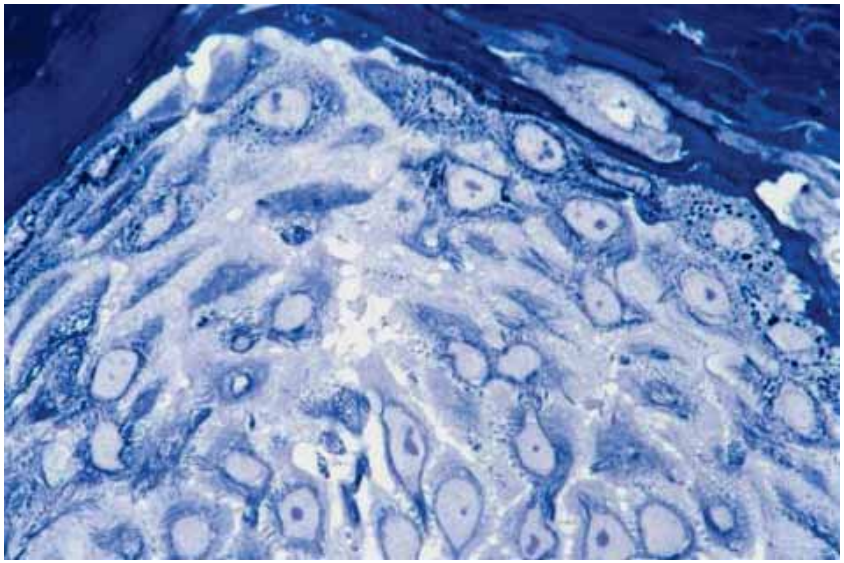


Hailey-Hailey-type
of acantholysis

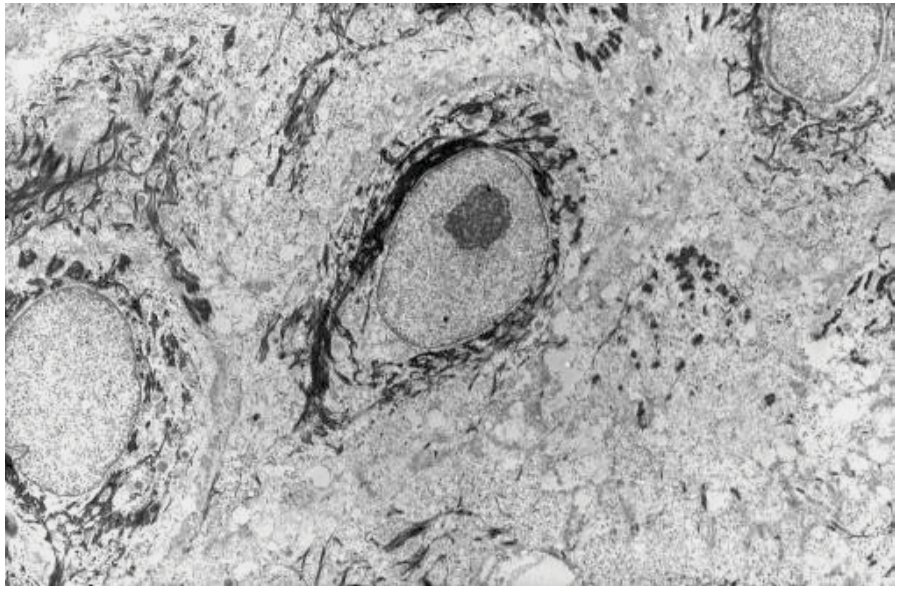
plus Hypergranulosis





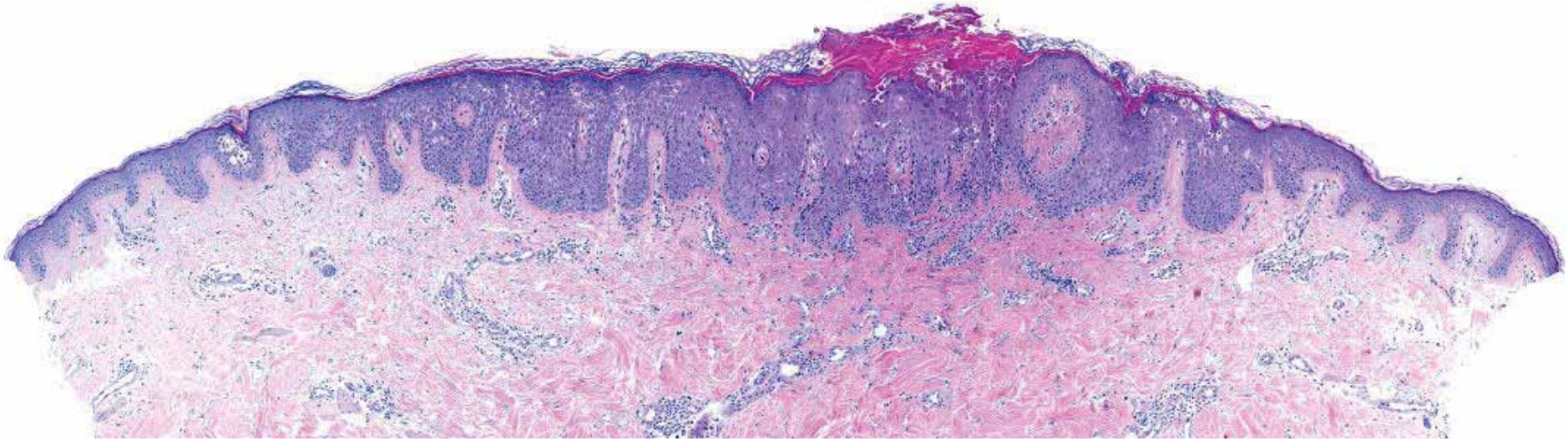


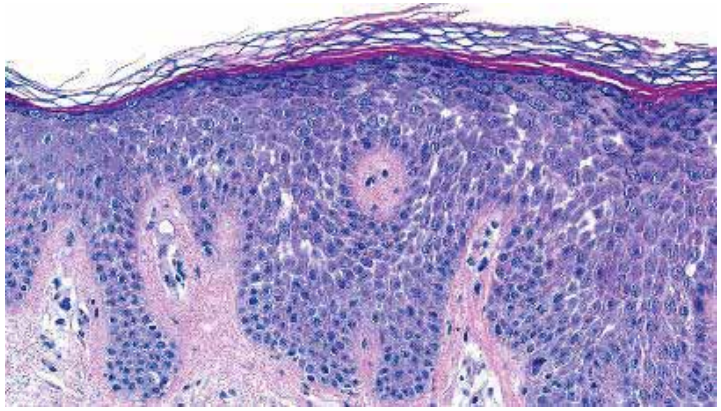
Epon re-embedding
Semithinsection, EM

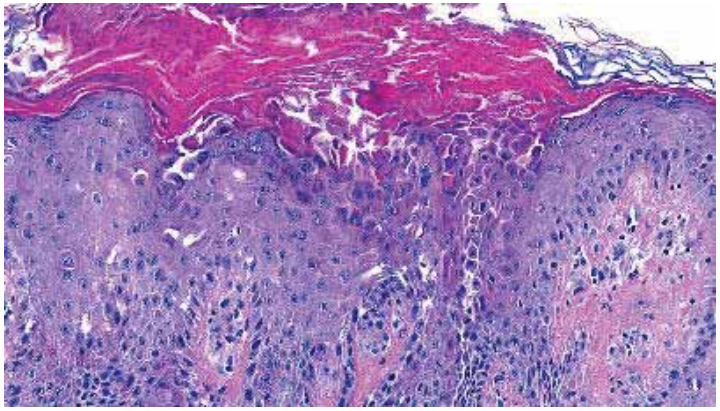


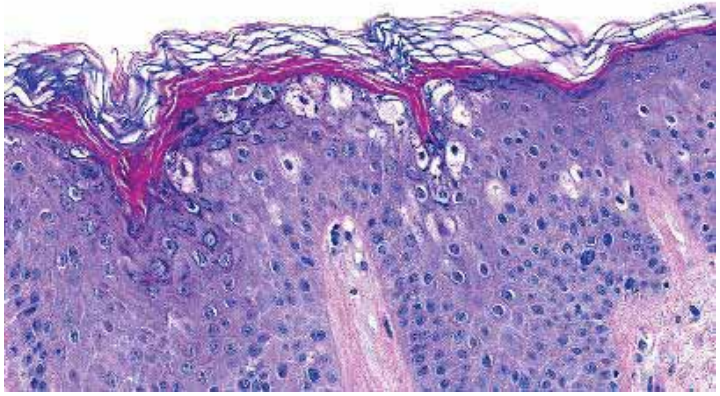
Hailey-Hailey pattern
of acantholysis

Acanthoma with Hailey-Hailey-type acantholysis, FAD, EHK



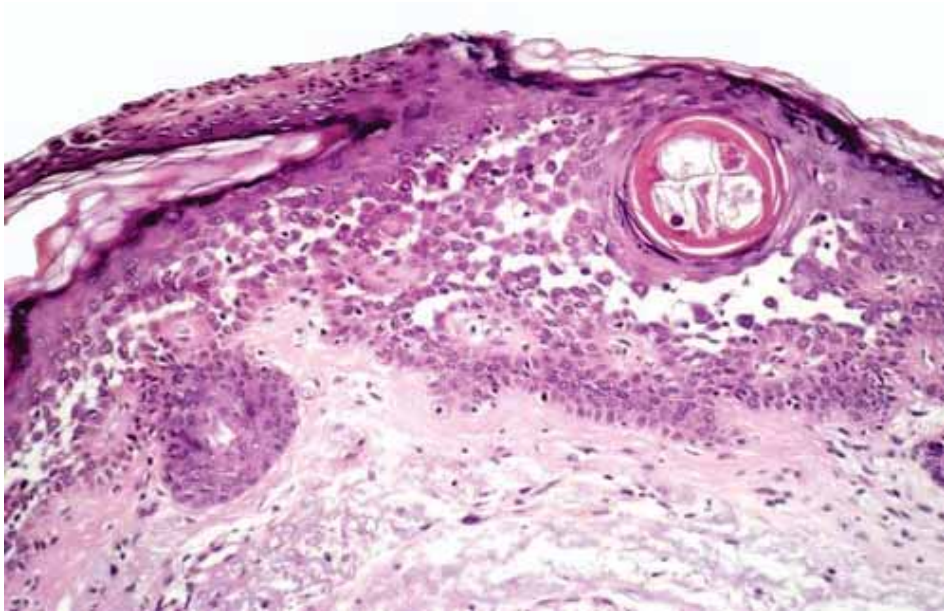


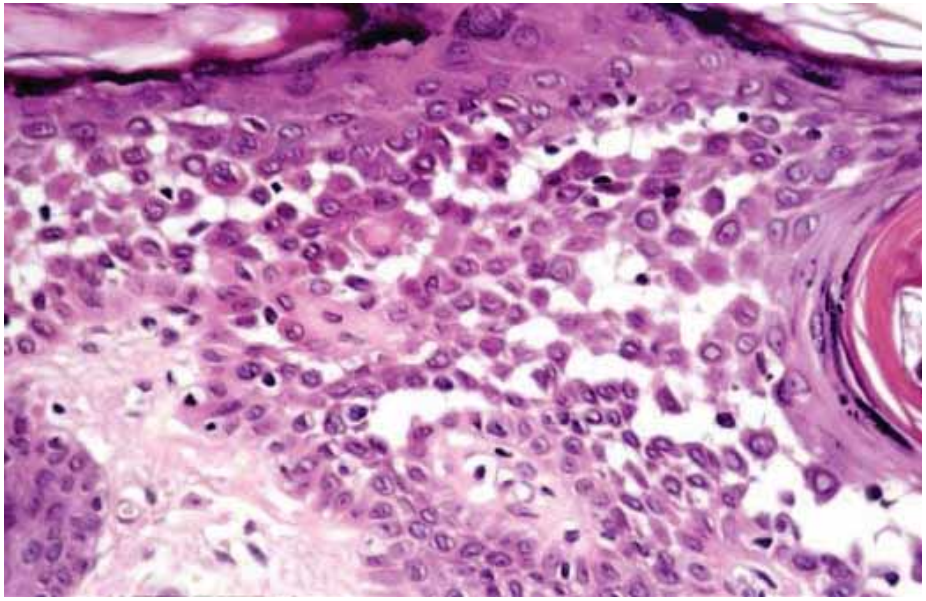




Incidental Hailey-Hailey-type acantholysis in seborrheic keratosis

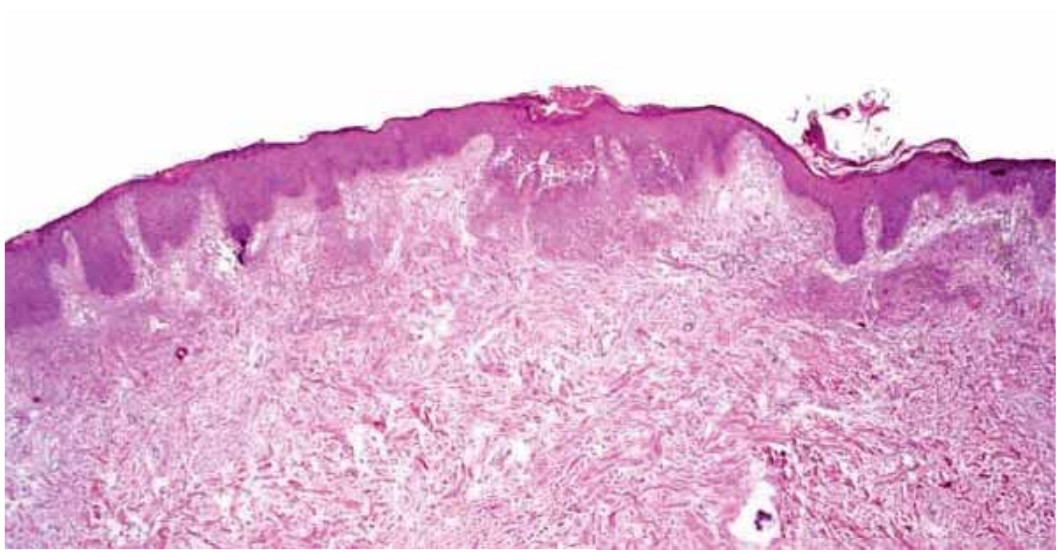
Normal skin, marginal control,
no history of Hailey-Hailey disease

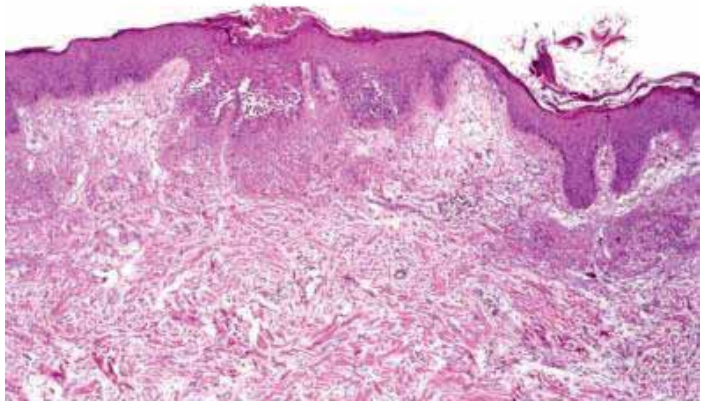


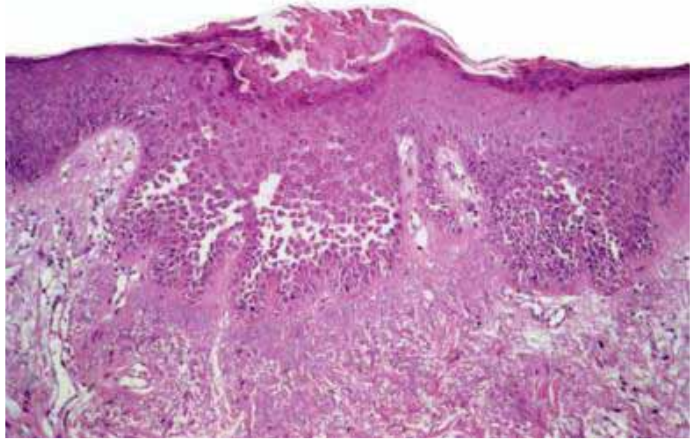


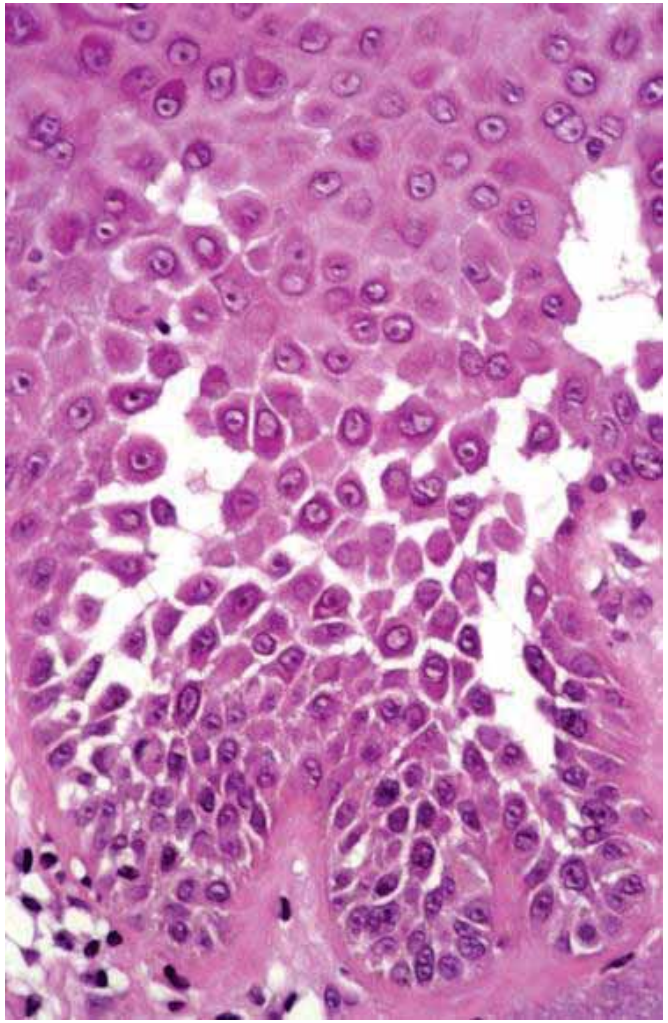
Incidental Hailey-Hailey-type acantholysis in Lichen simplex

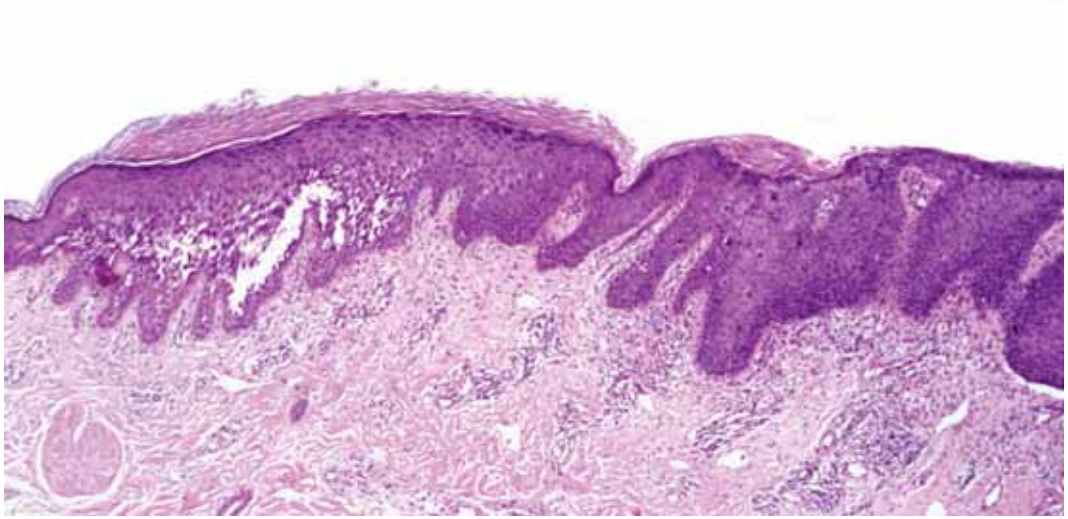
no history of Hailey-Hailey disease

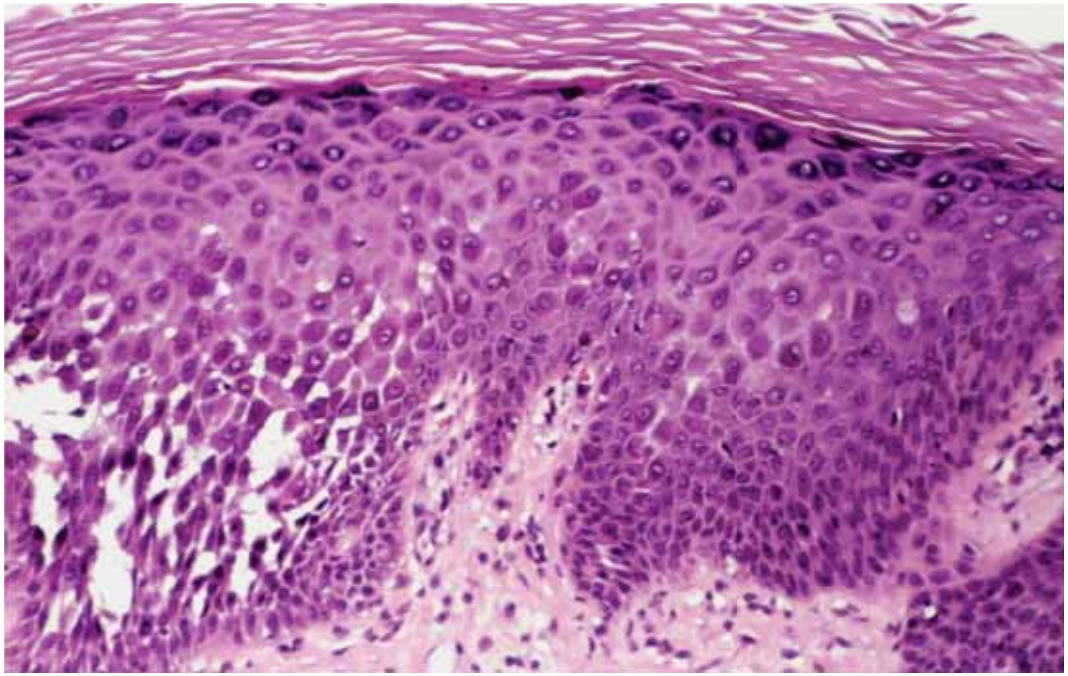






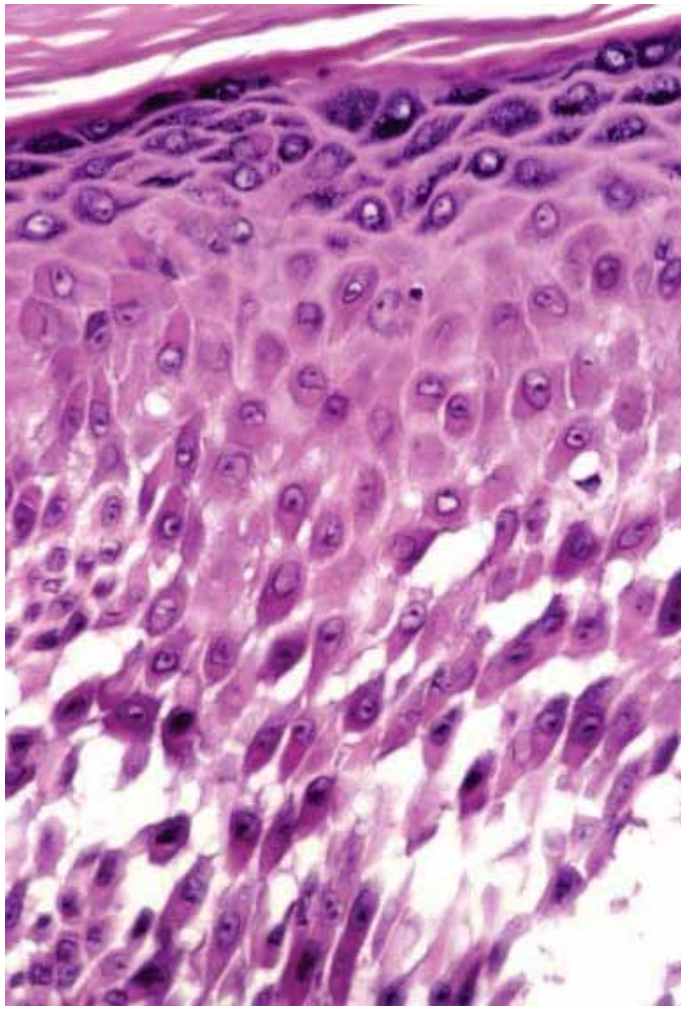




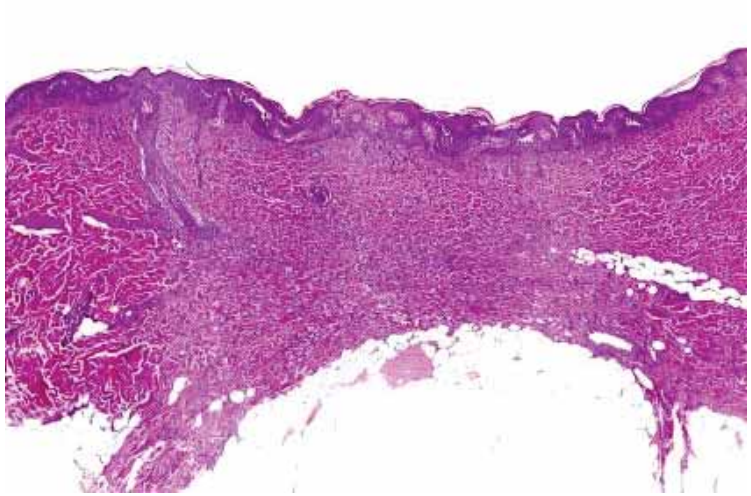


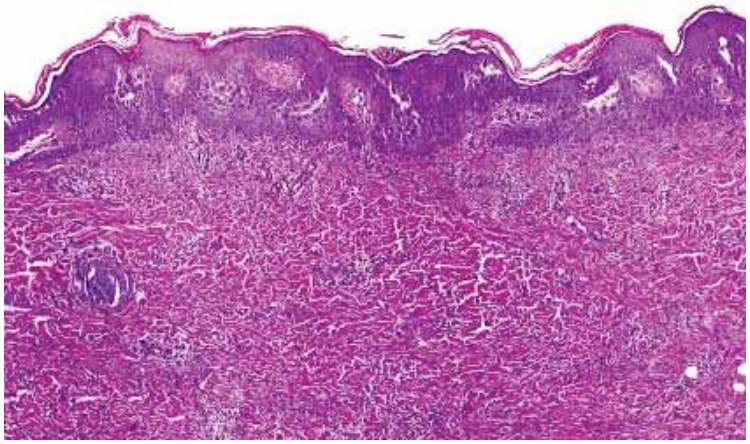
Bowen‘s disease

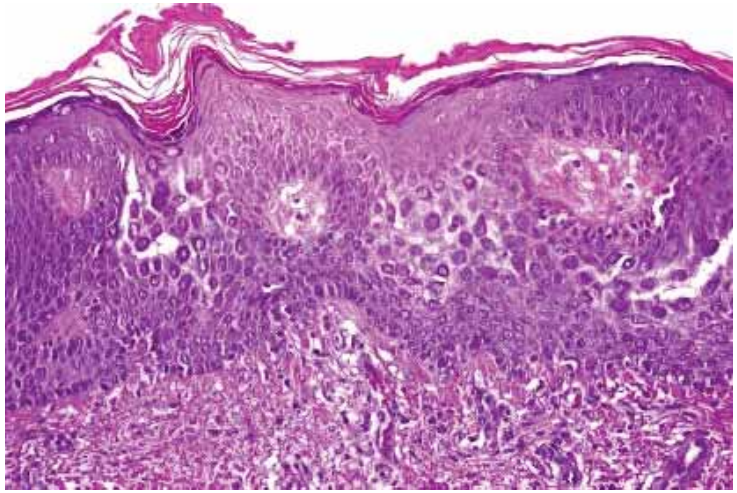
no history of Hailey-Hailey disease

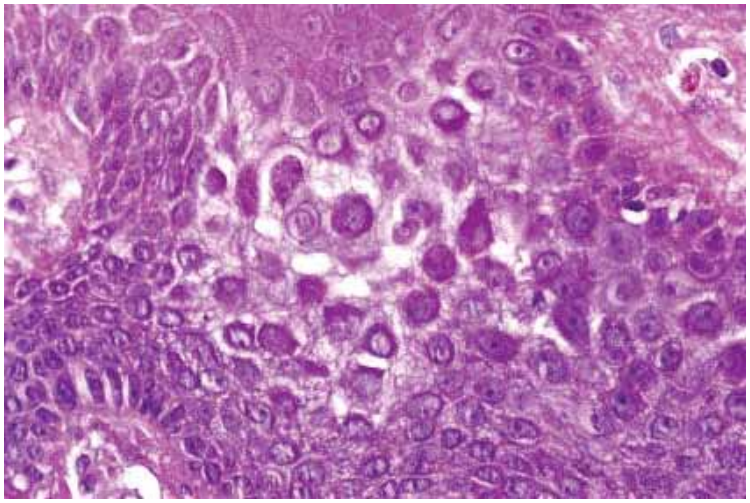


Incidental Hailey-Hailey-type acantholysis in Dermatofibroma

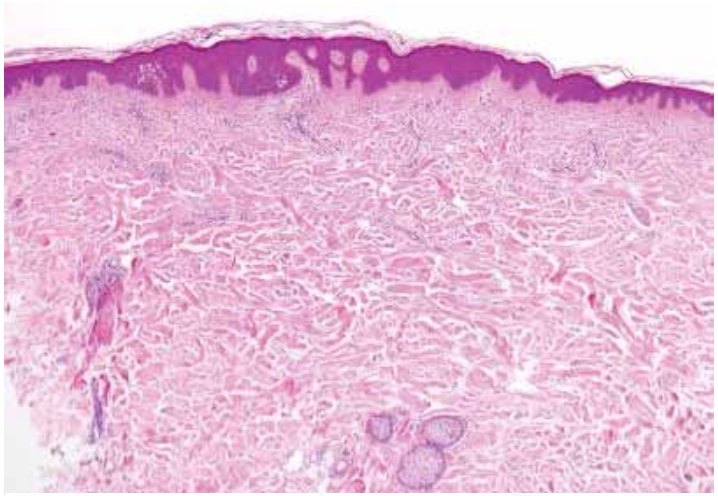


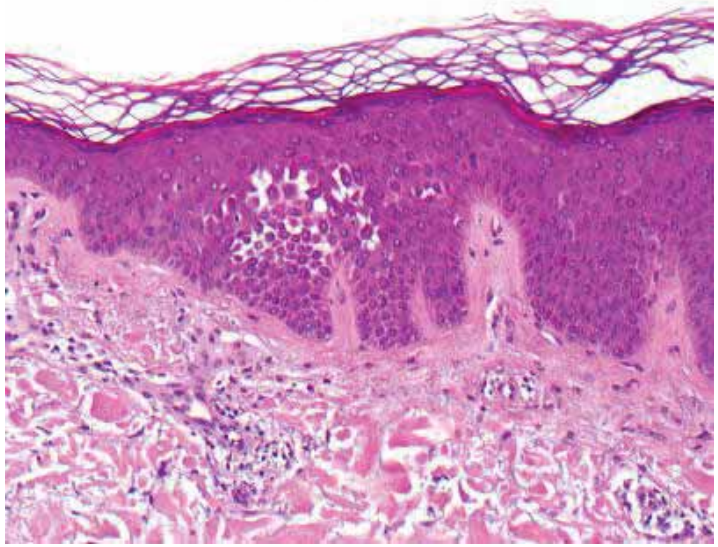


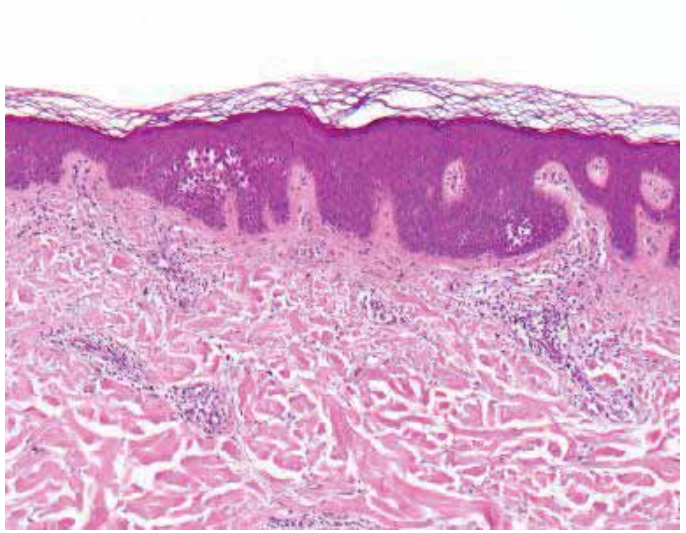


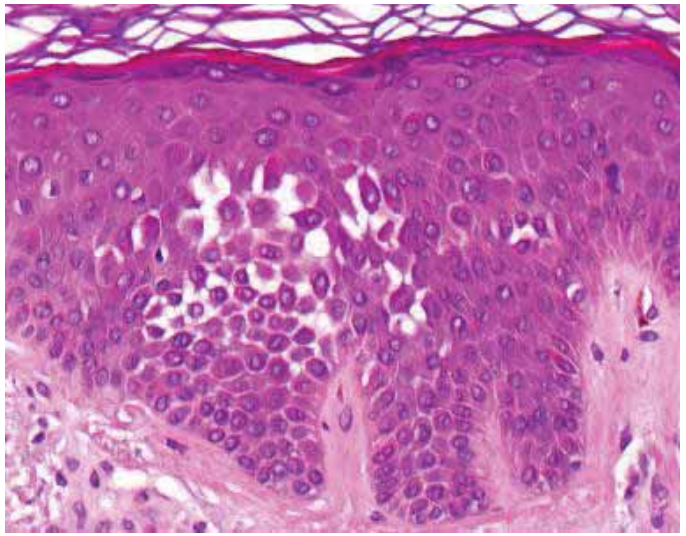


Grover disease with Hailey-Hailey-type acantholysis





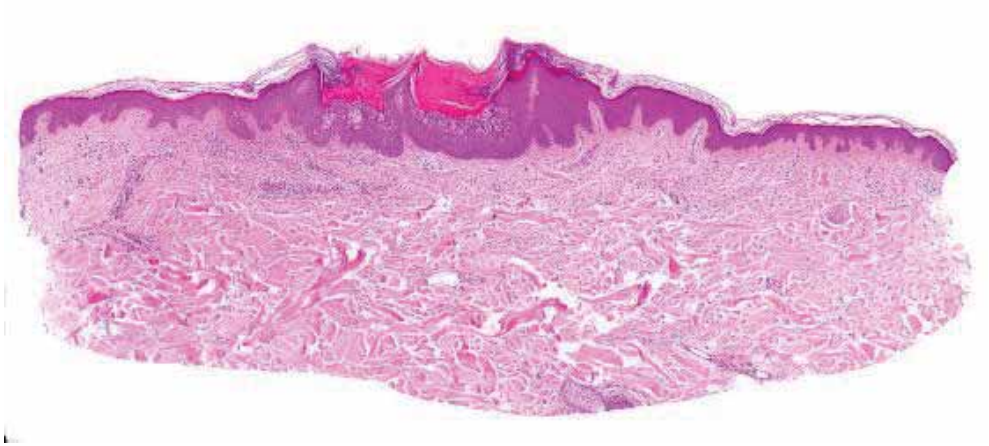


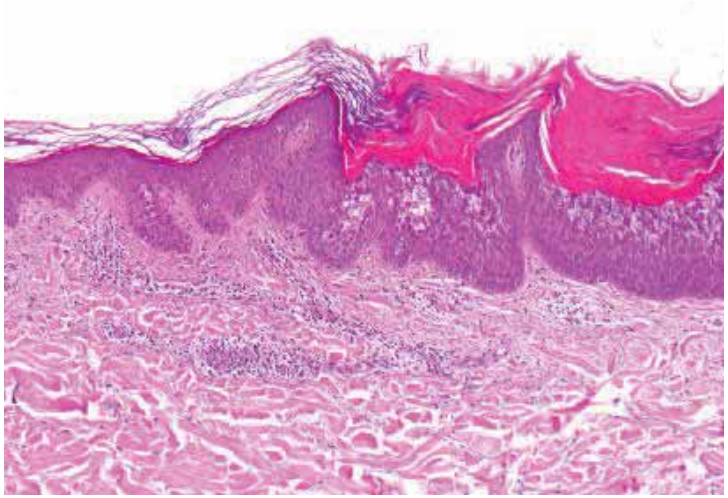


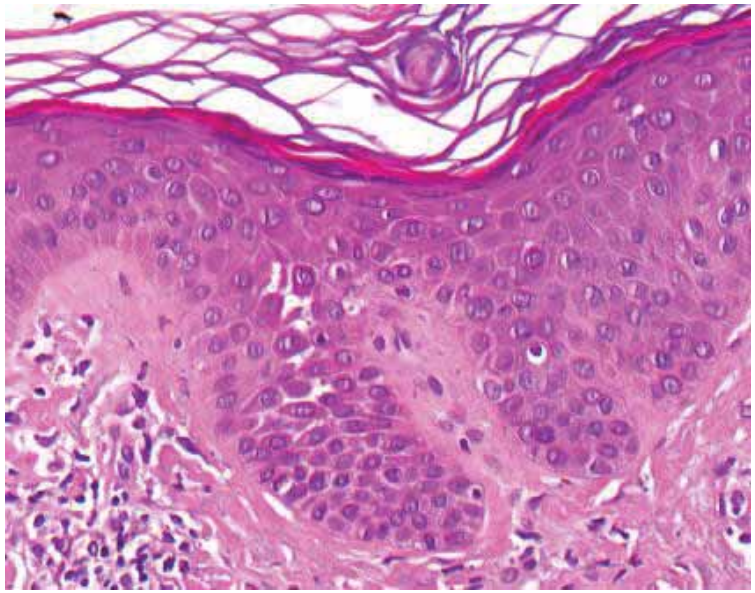
Step section 1

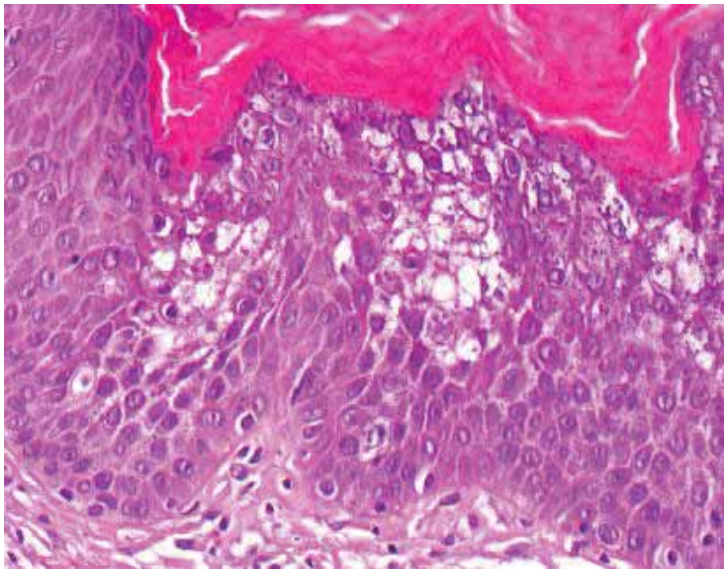
Grover disease with Hailey-Hailey-type acantholysis and EHK

Step section 2





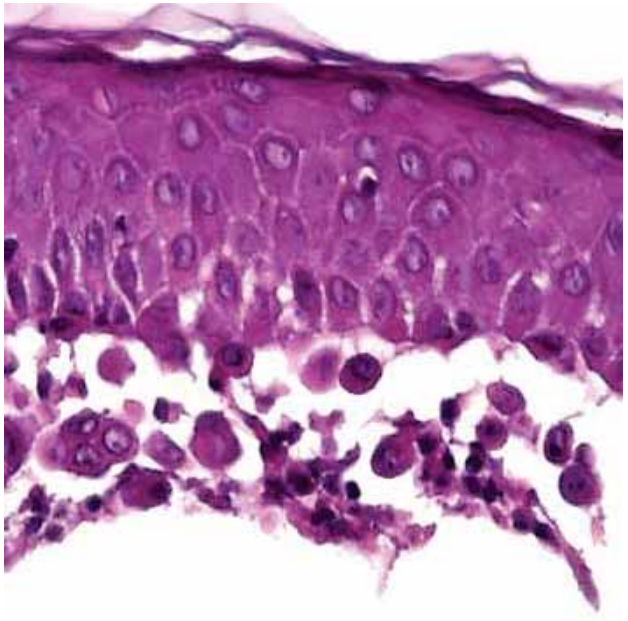


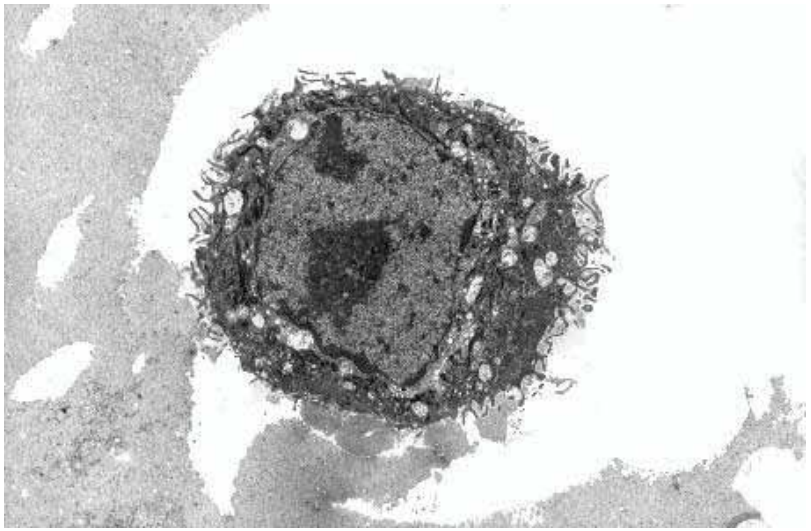


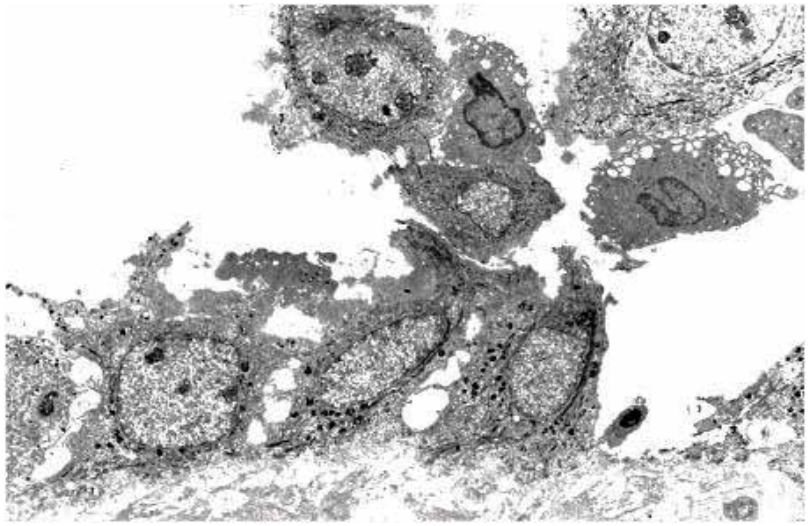
Epidermal reaction patterns
in genodermatoses, epidermal nevi, acquired skin diseases or as an incidental finding

Pattern	Dermatosis	Mosaicism	Solitary lesion	Incidental finding
Epidermolytic hyperkeratosis	Keratinopathic Ichthyosis, Palmoplantar keratoderma	+	Epidermolytic acanthoma	+
Focal acantholytic dyskeratosis	M. Darier	+	Acantholytic dyskeratotic acanthoma	+
Hailey–Hailey–type acantholysis	M. Hailey–Hailey	+	Hailey–Hailey–type acanthoma	+
Desmosomal-type acantholysis	Genetic diseases with desmosome related mutations	?	Acantholytic acanthoma (Hyaline inclusion acanthoma)	+
Epidermolysis bullosa simplex-type vacuolization	Epidermolysis bullosa simplex	+	?	+
Granular Parakeratosis	Granular parakeratosis	-	Granular parakeratotic acanthoma	+
.....				

Acantholytic keratinocyte



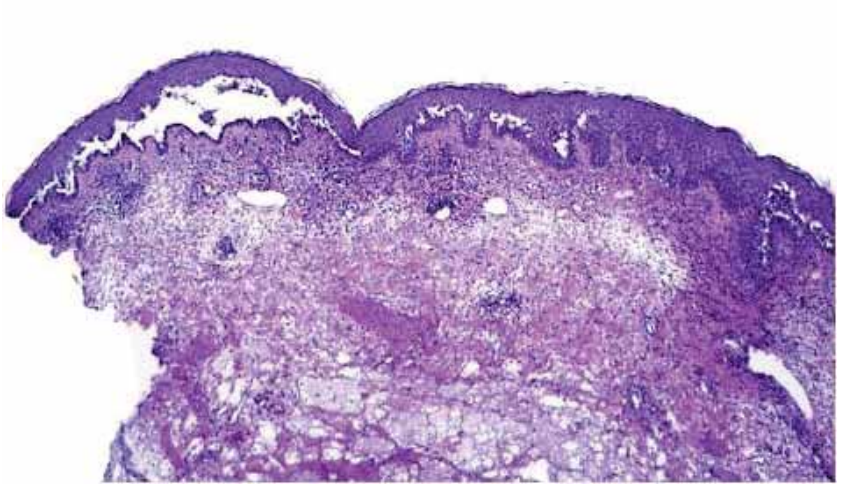


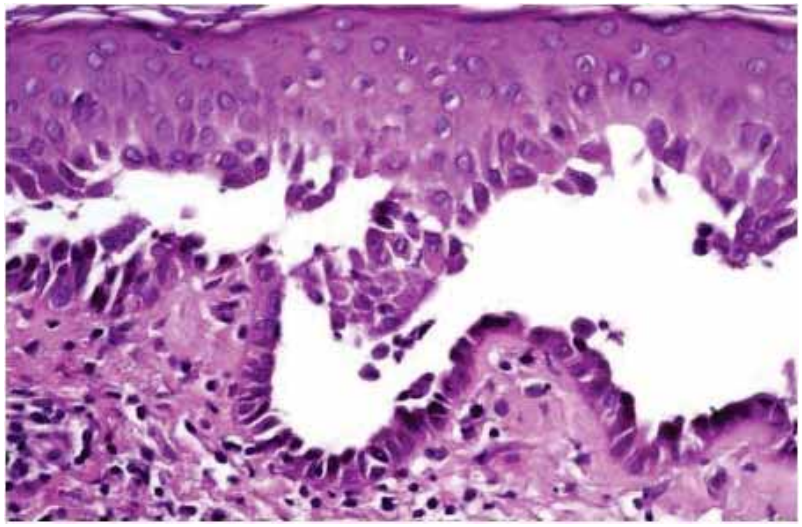


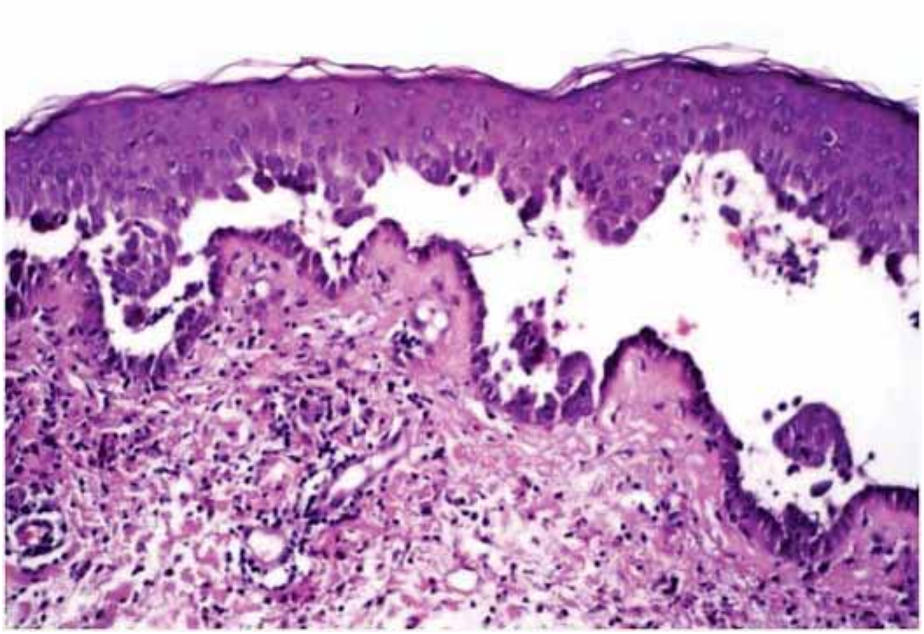
Fully acantholytic keratinocyte:

- roundish,
- hypereosinophilic cytoplasm
- pyknotic nucleus

Pemphigus vulgaris







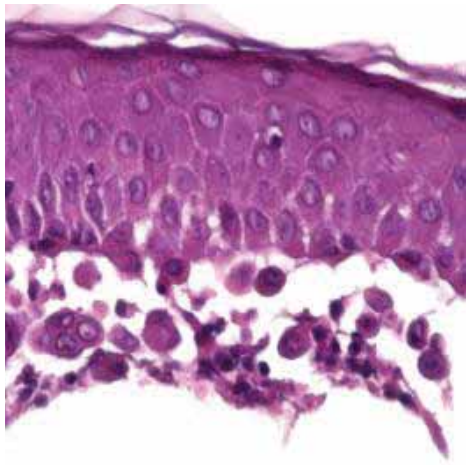
Mostly suprabasal separation, focal or over a broader front

Fully acantholytic keratinocytes

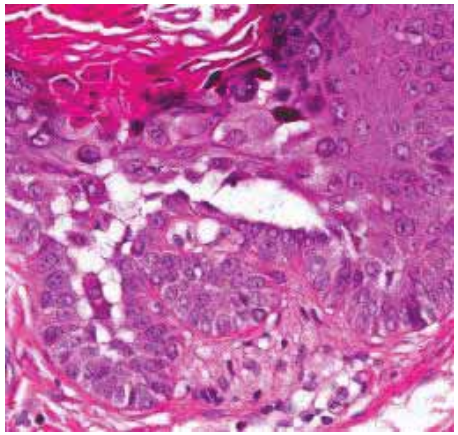
Epidermis above the blister cohesive and regular horny layer

Diseases with Acantholysis

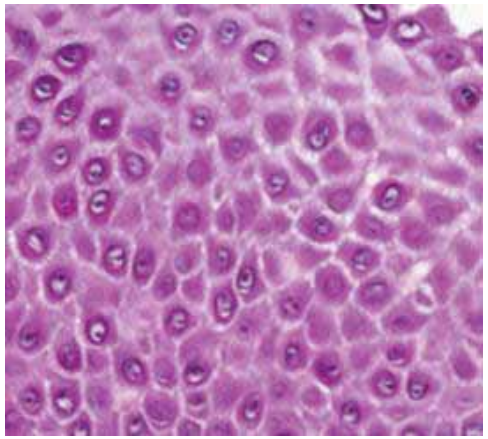
- Pemphigus: blistering with intact roof, roundish keratinocytes (fully acantholytic cells)
- Darier: pyknotic nuclei and hypereosinophilic cytoplasm throughout the epidermis
- Hailey-Hailey: regular nuclei, perinuclear hypereosinophilia and pale periphery throught the epidermis
- Herpes and other viral infections: ballooning (intracellular edema)



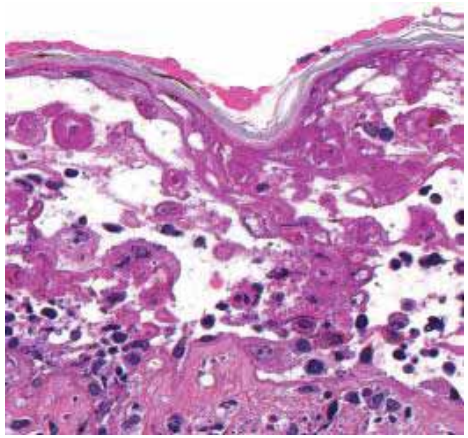
Pemphigus



M. Darier



M. Hailey-Hailey

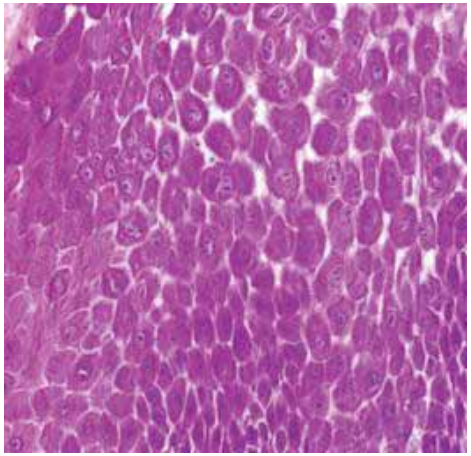


Herpes

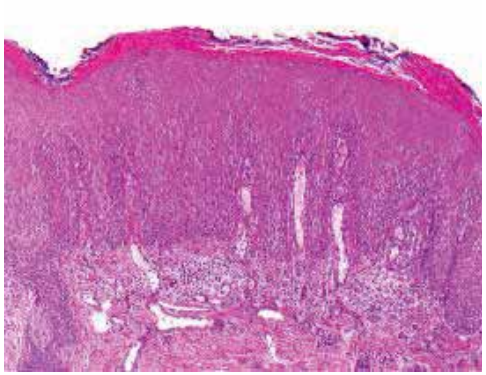
Acantholysis of the Desmosomal Type

(Acantholysis related to mutations of desmosomal proteins)

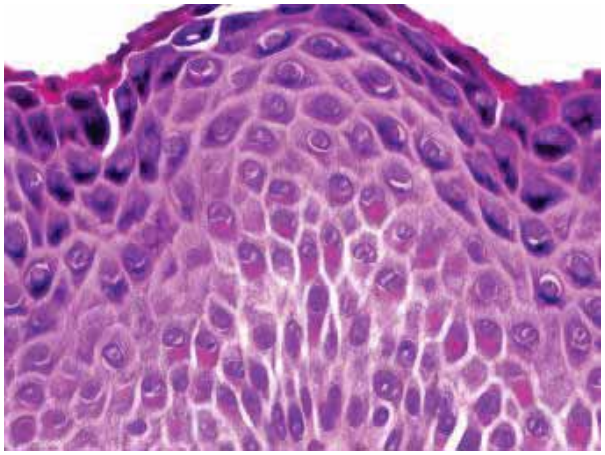
- Widening of intercellular spaces and partial dehiscence of hypereosinophilic keratinocytes with regular nuclei (Striate PPK or PPK areata and striata)
- See above plus hyperkeratosis and hypergranulosis, psoriasiform hyperplasia (SAM Syndrome)
- Eosinophilic clumping of the cytoplasm (McGrath syndrome)
- Subcorneal variant (Peeling skin disease)



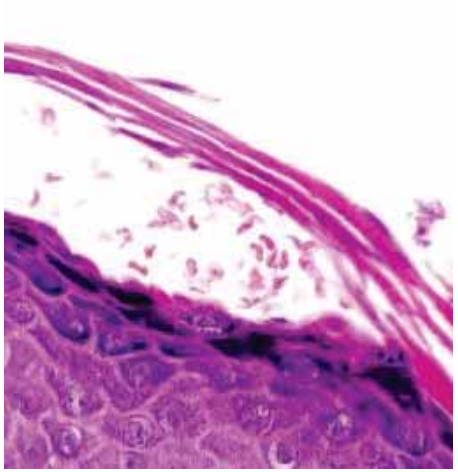
Striate PPK



SAM syndrome



McGrath syndrome



Peeling skin disease

Acantholysis of the Desmosomal Type syndromic, non-syndromic

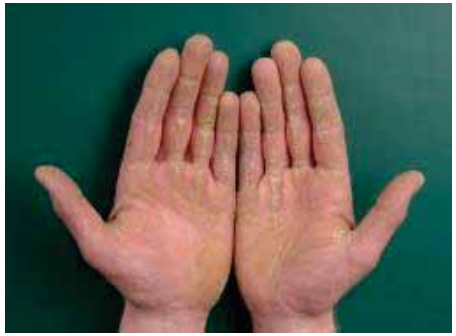
Keratosis palmoplantaris areata et striata,
Carvajal-Huerta-, Naxos-Syndrome,
SAM-, McGrath, Peeling skin-syndrome, ……

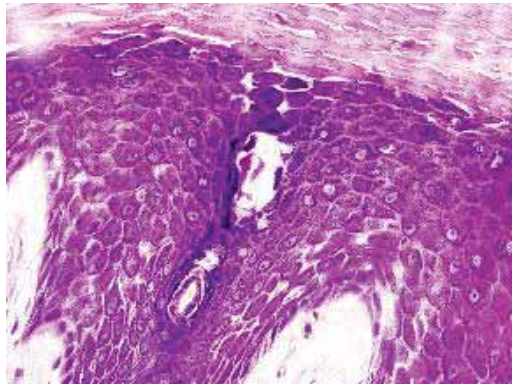
Article

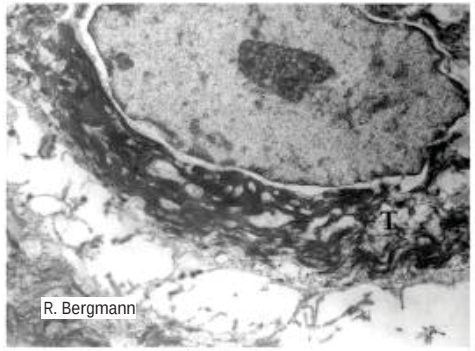
Desmosomal-Type Acantholysis - A New Histologic Pattern Related to Mutations of Genes for Desmosomal Proteins

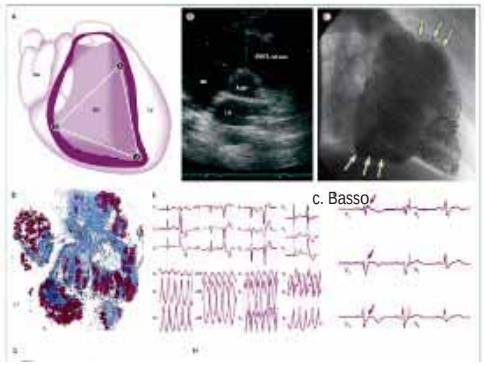
Dieter Metze, Kira Süßmuth, Clemens Metze, Vinzenz Oji and Heiko Traupe

Dermatopathology, 2026, 13(2), 17









Pattern
Acantholysis of the Desmosomal Type

- Hereditary, syndromic and non-syndromic diseases
- Acantholytic acanthoma
- Incidental finding

Article

Desmosomal-Type Acantholysis - A New Histologic Pattern Related to Mutations of Genes for Desmosomal Proteins

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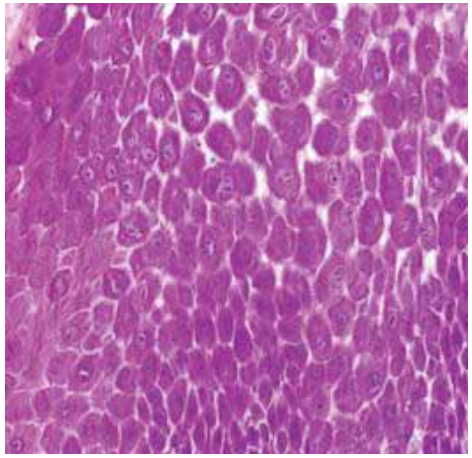
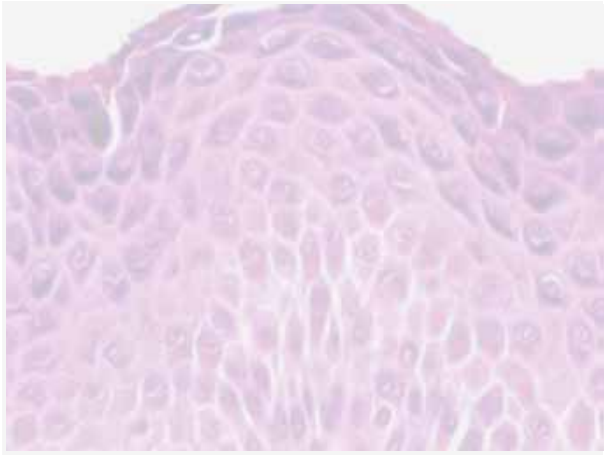


Striate PPK

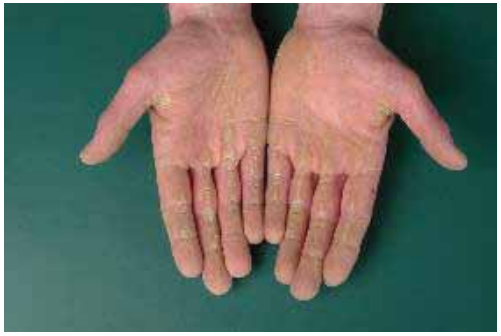


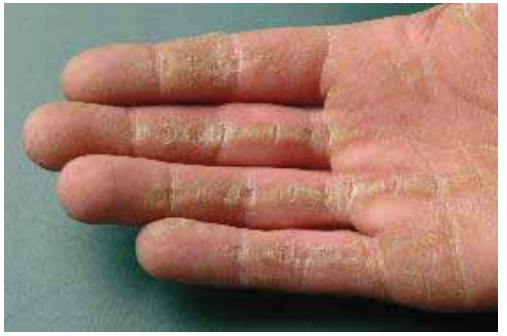
McGrath syndrome

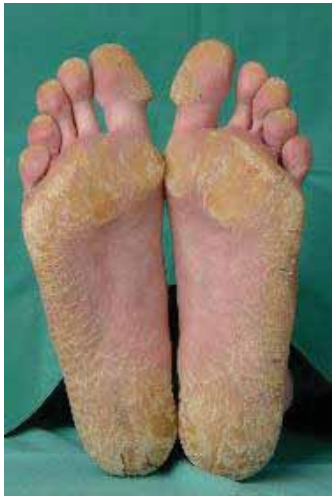
Keratosis palmoplantaris areata et striata

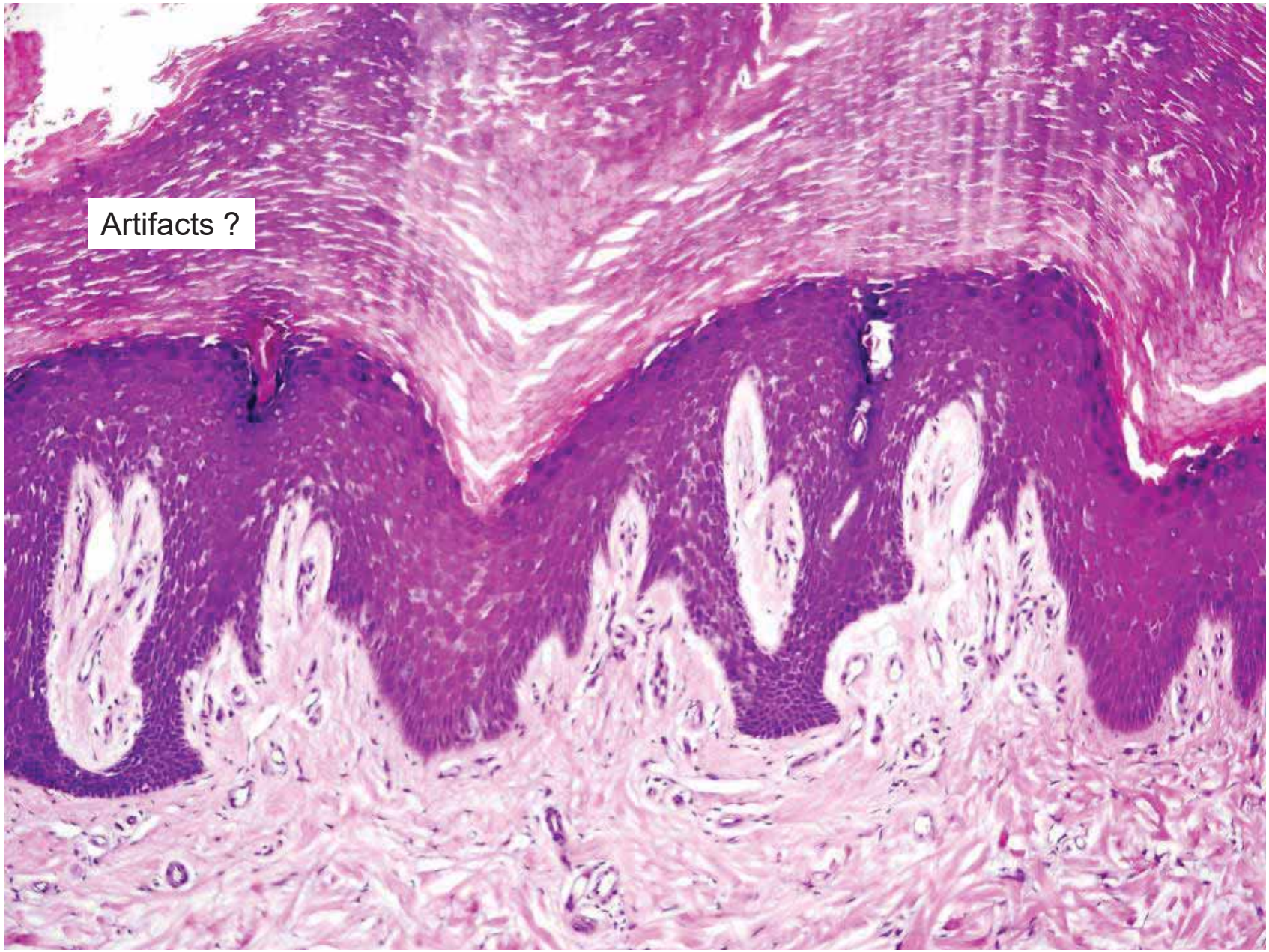
(Striate Palmoplantar Keratoderma-type I, SPPK type I,
Brünauer-Fuchs-Siemens syndrome, acral keratoderma)

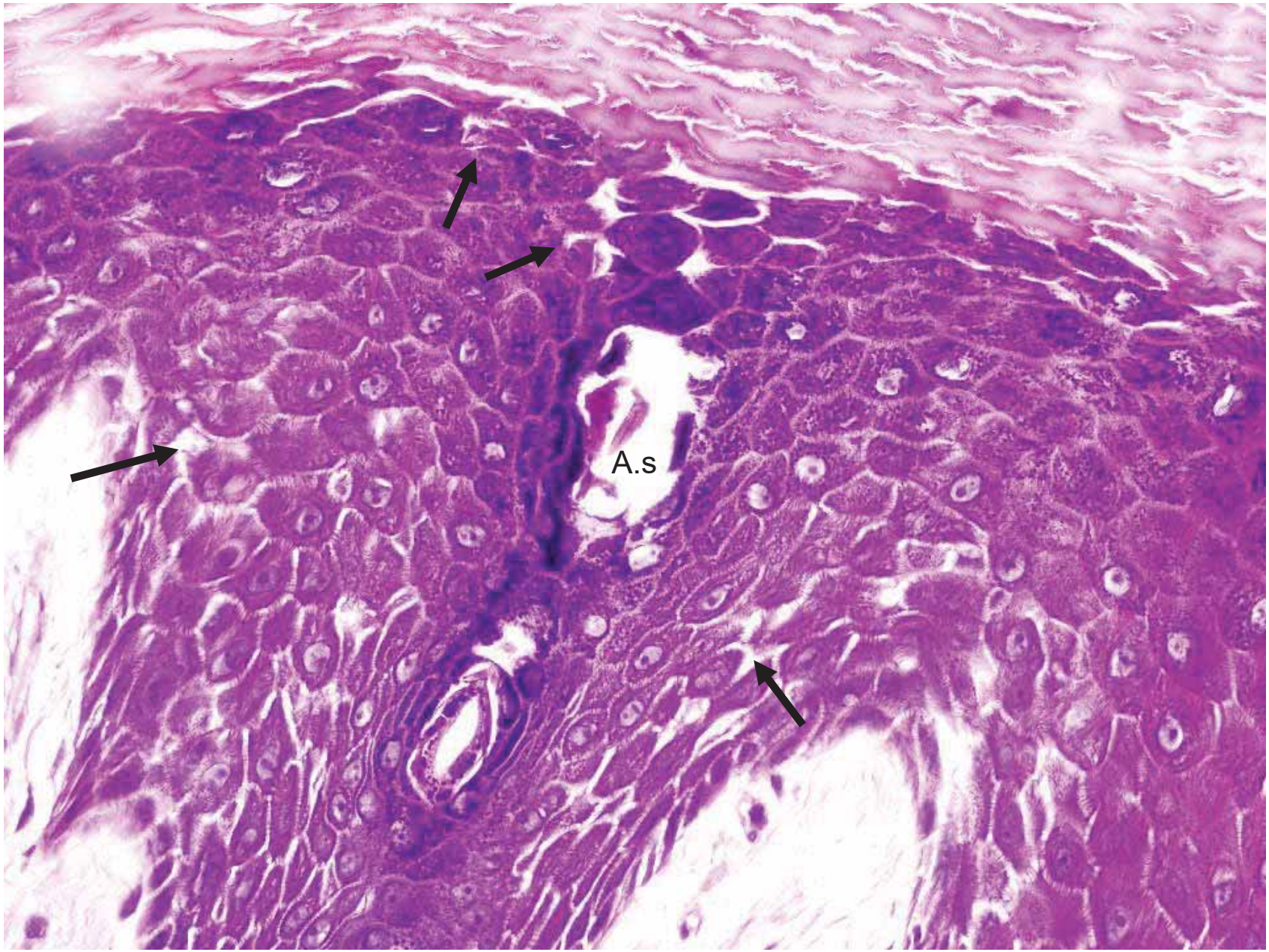
- Autosomal dominant, #148700
- Mutation of Desmoglein 1
- Linear keratotic bands on palms and fingers, island-like areas of hyperkeratosis on the soles
- Late manifestation (adolescence)
- Exacerbation by manual labor; painful
- Hyperhidrosis, intermittent blistering possible
- No associated diseases (non-syndromic)







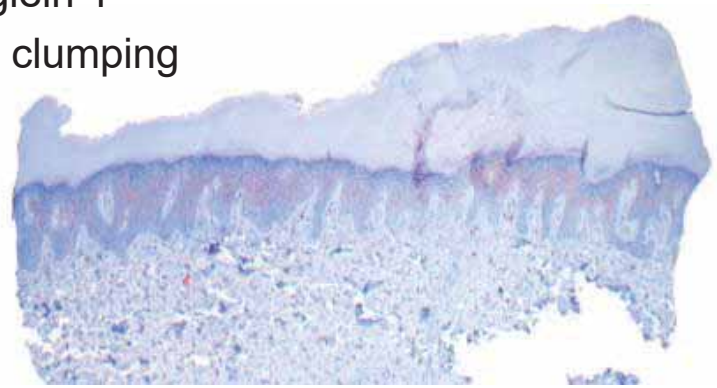

Artifacts ?

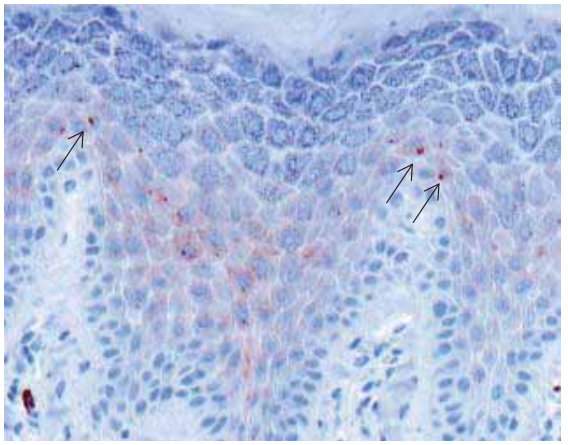

A.s

Striate Palmoplantar Keratoderma-type I

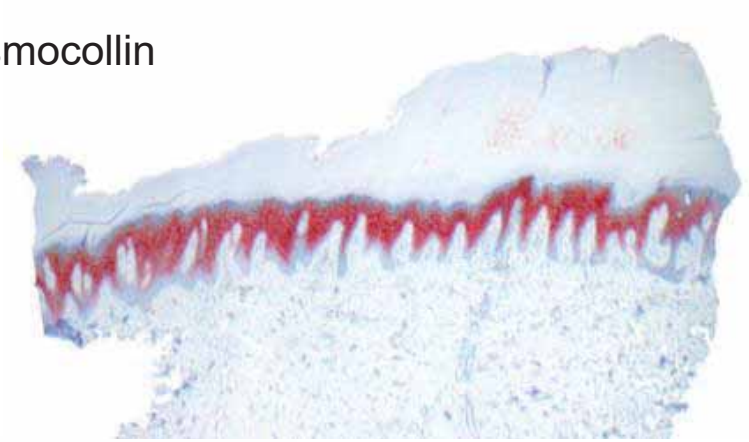
Desmoglein 1

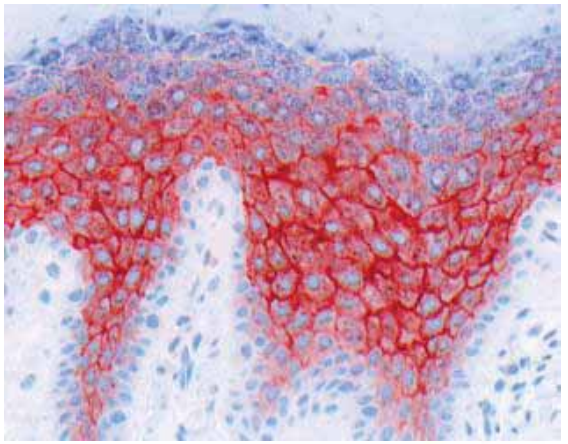
Loss and clumping



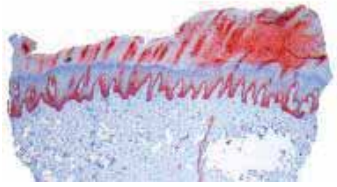


Desmocollin

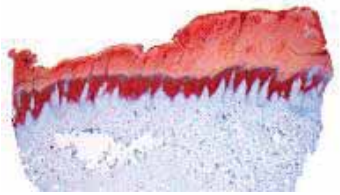




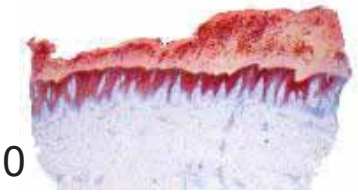
CK5

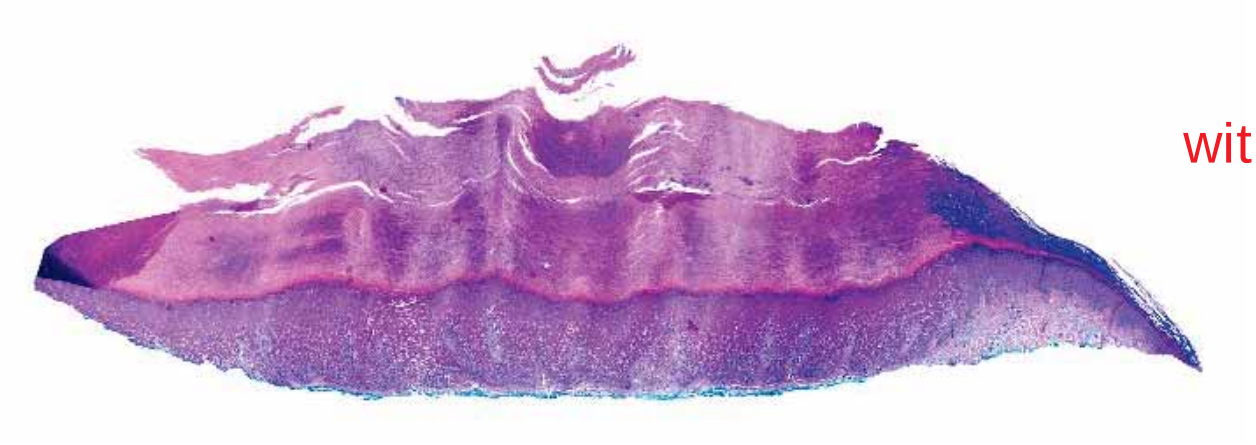


CK2



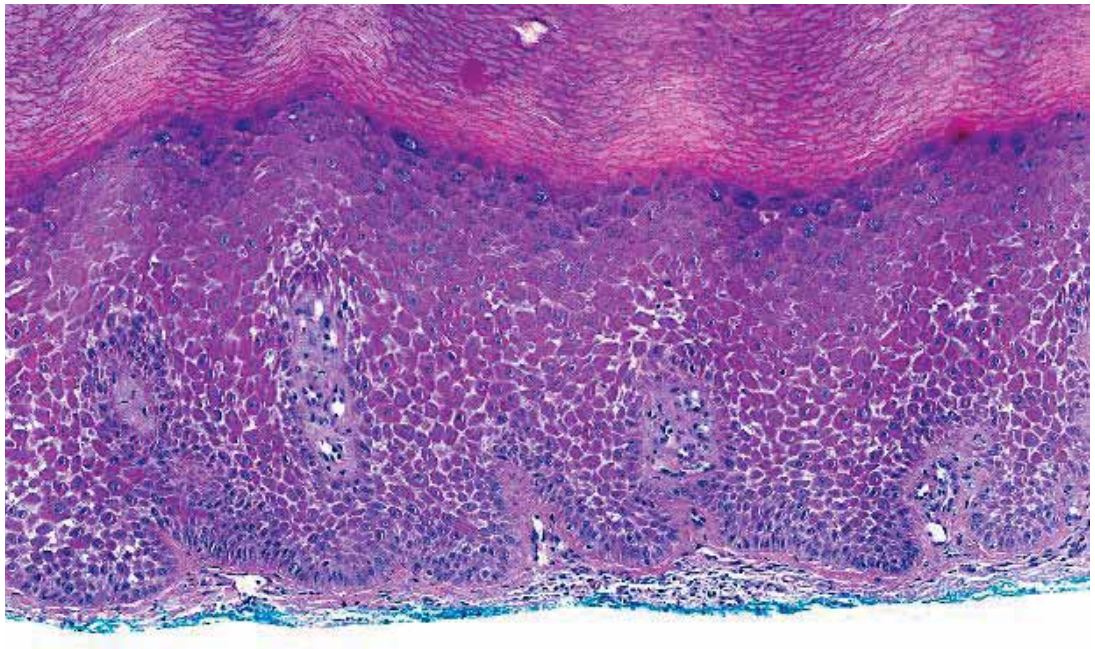
CK10

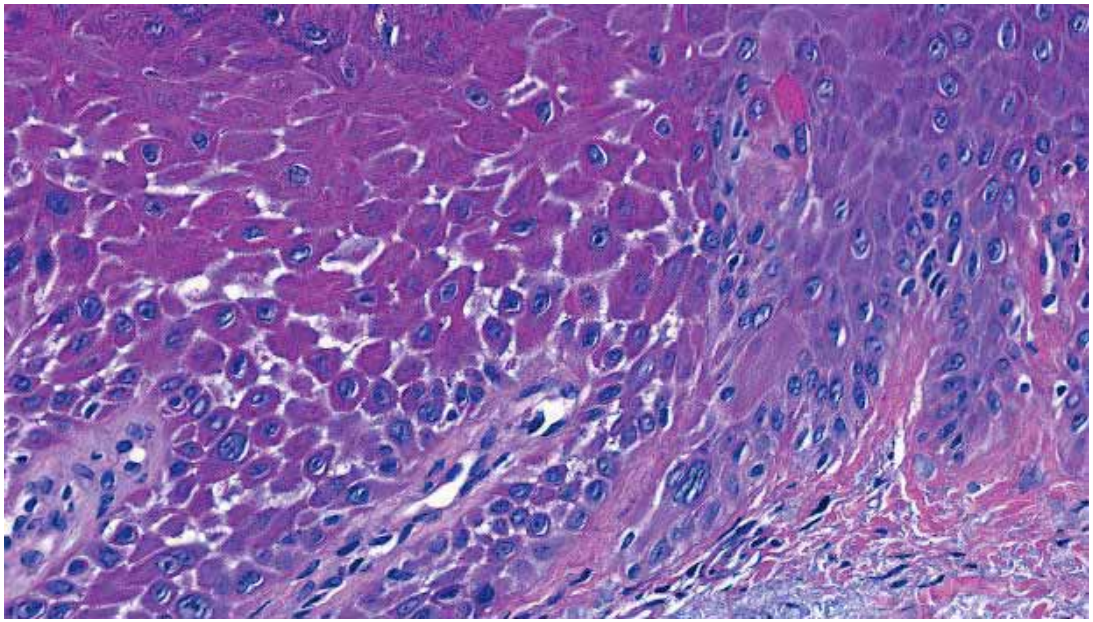




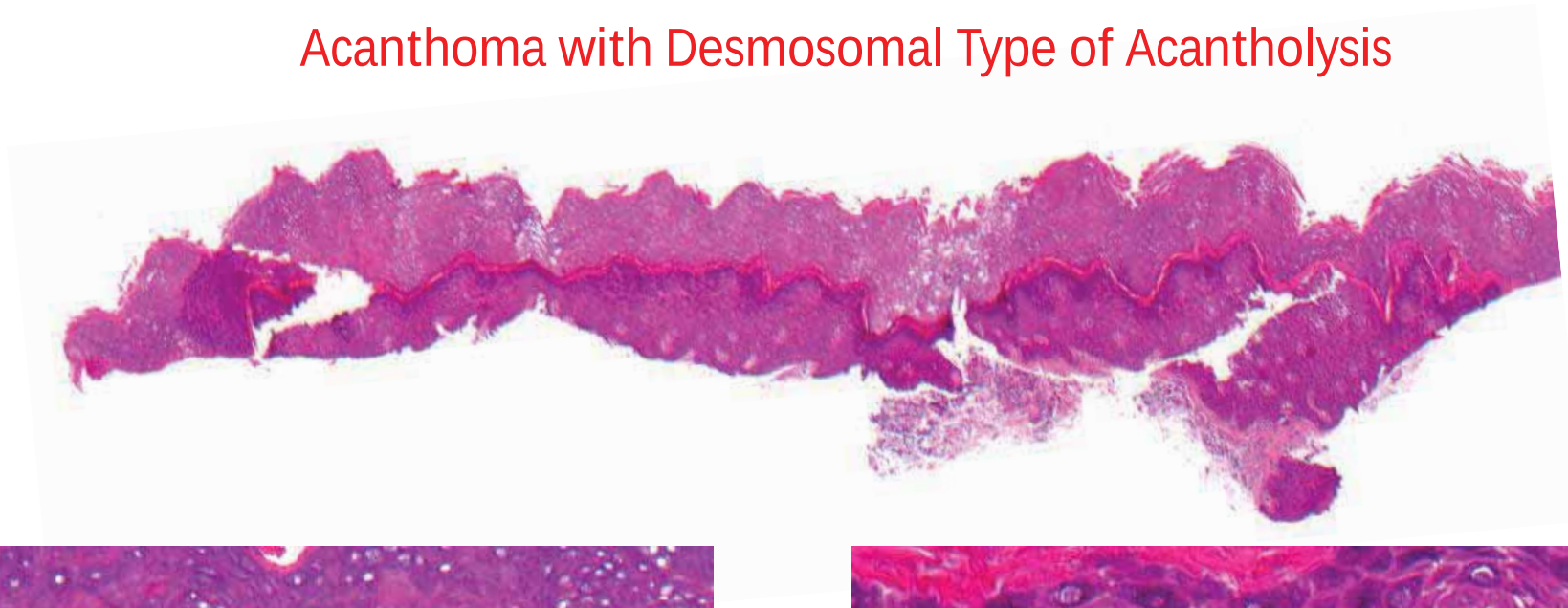
Solitary Acanthoma with Desmosomal Type of Acantholysis

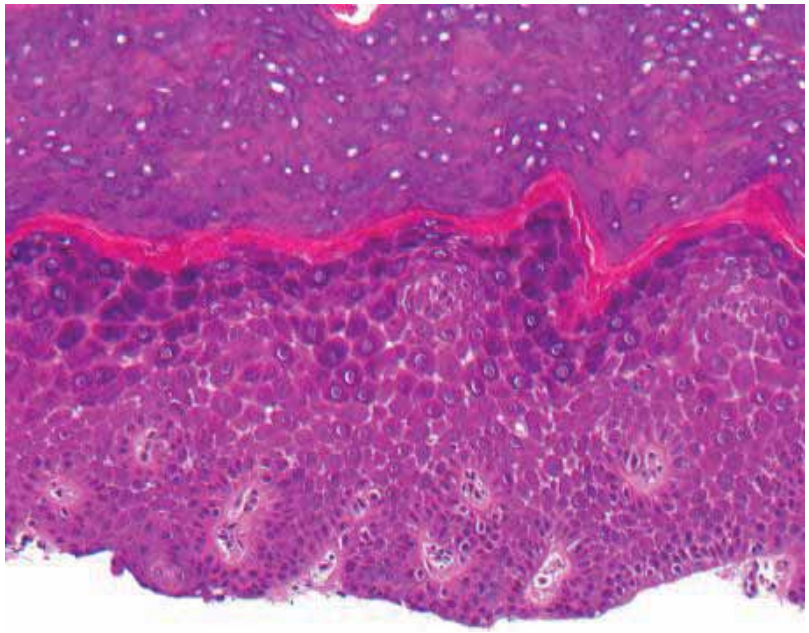
Widening of the intercellular spaces,
Keratinocytes hypereosinophilic, regular nuclei
No blistering, no spongiosis,
no vesicles, no serous exudate

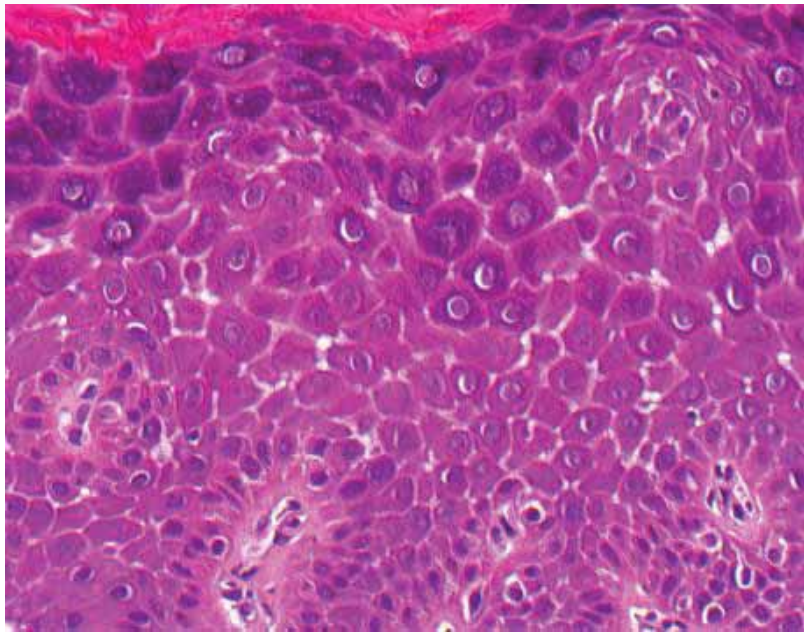




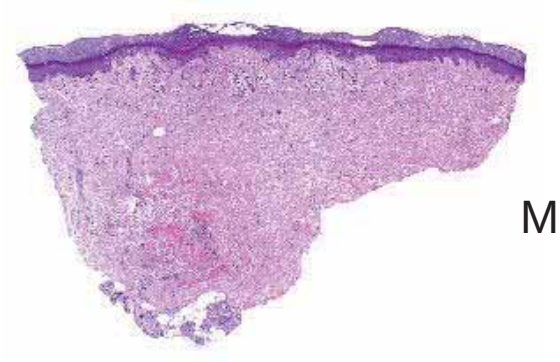
Acanthoma with Desmosomal Type of Acantholysis



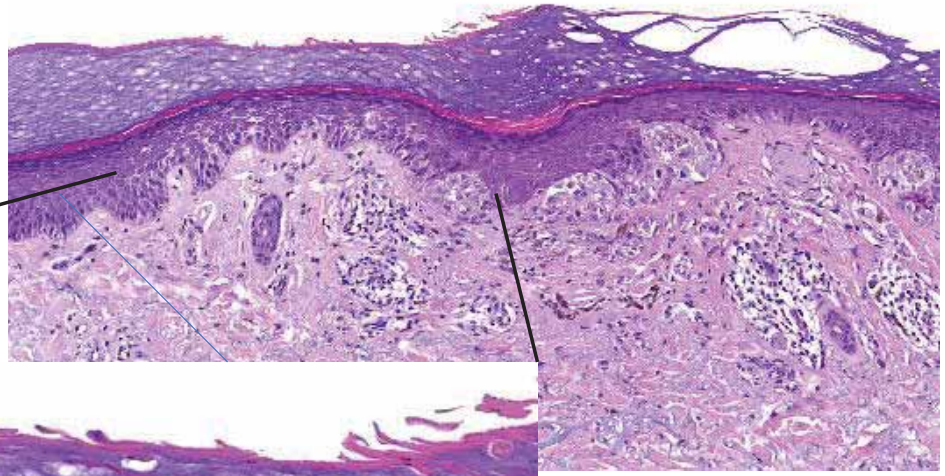


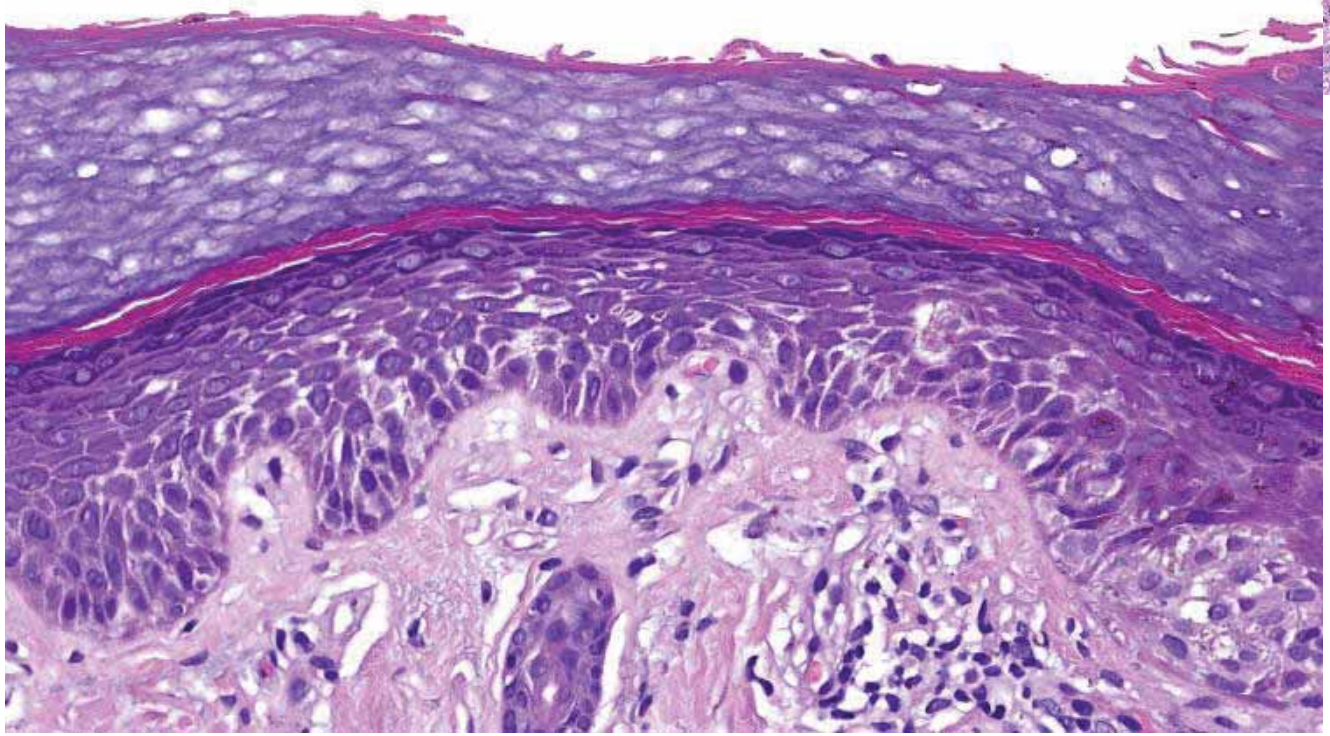


Acantholysis of the Desmosomal Type, incidental



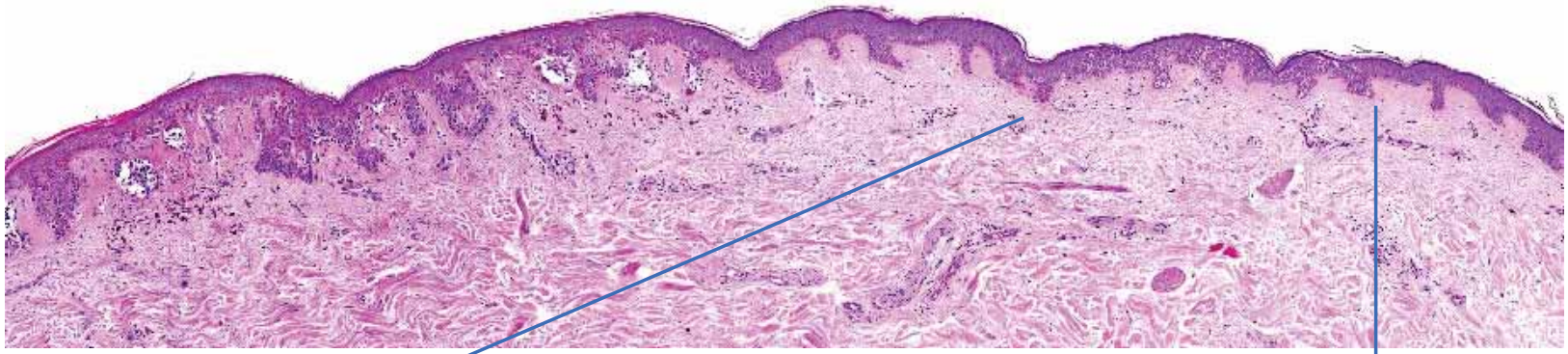
Melanocytic nevus

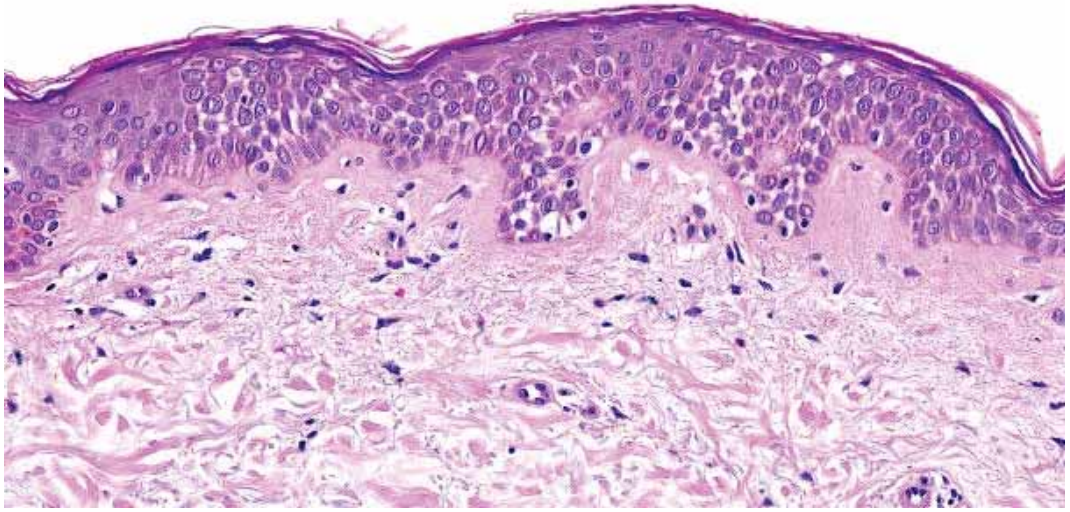


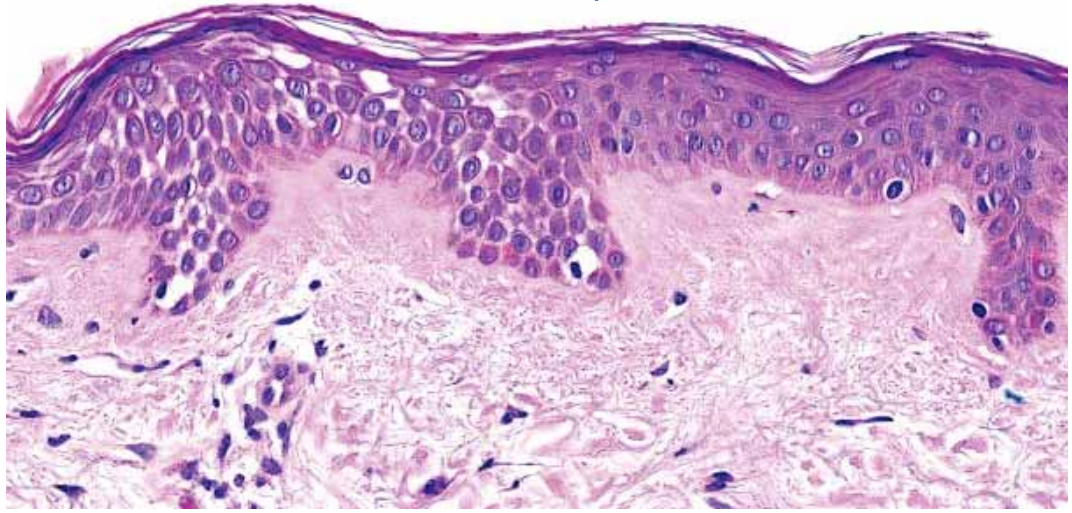


Acantholysis of the Desmosomal Type, incidental

Melanocytic nevus







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- Incidental finding

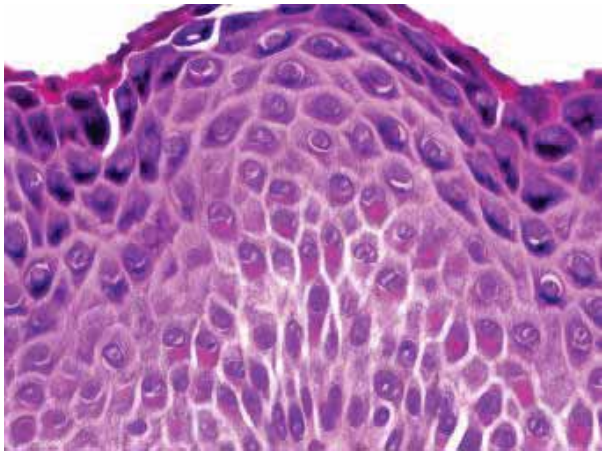
Article

Desmosomal-Type Acantholysis - A New Histologic Pattern Related to Mutations of Genes for Desmosomal Proteins

Dieter Metze, Kira Süßmuth, Clemens Metze, Vinzenz Oji and Heiko Traupe

Dermatopathology, 2026, 13(2), 17

Striate PPK



McGrath syndrome

McGrath Syndrome

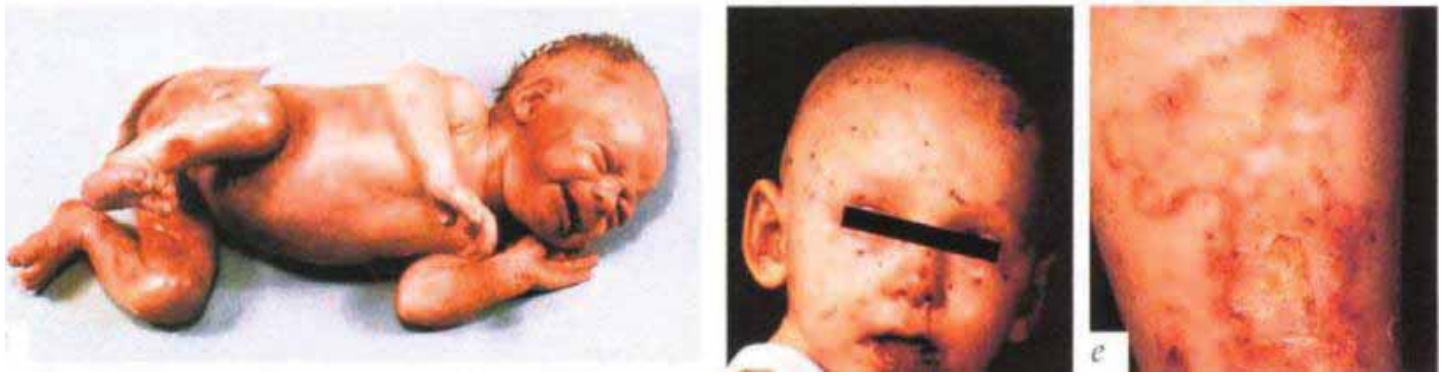
letter

Mutations in the plakophilin 1 gene result in ectodermal dysplasia/skin fragility syndrome

John A. McGrath[1], James R. McMillan[1], Carrie S. Shemanko[2], Sarah K. Runswick[3], Irene M. Leigh[4], E. Birgitte Lane[2], David R. Garrod[3] & Robin A.J. Eady[1]

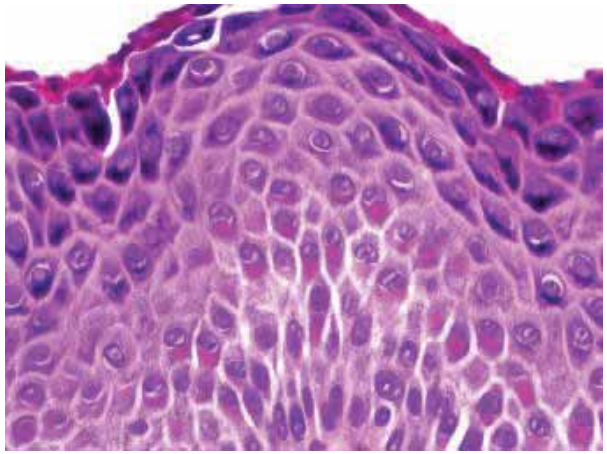
- AR mutations in Plakophilin 1
  - nuclear protein for transcription/signaling (hair cycle, ...)
  - adhesive protein for desmosomal keratin binding

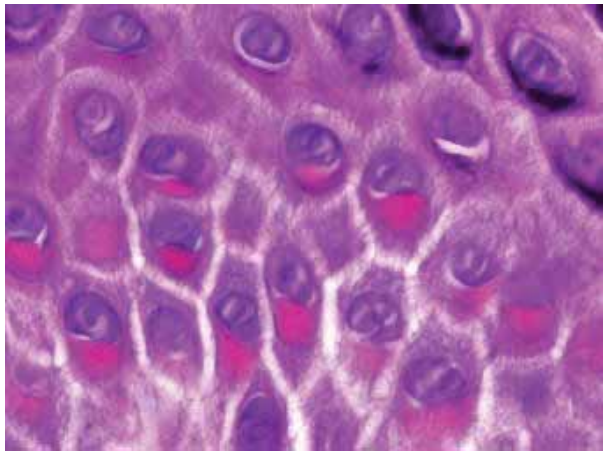
- Newborns: Peeling, reddish skin and blisters on the soles
- Focal palmoplantar hyperkeratosis with painful cracking, skin erosions, perioral fissures
- Hypotrichosis or alopecia, nail dystrophy, and hypohidrosis
- Growth delay, no cardiac complications



Ectodermal dysplasia–skin fragility syndrome: a novel mutation in the PKP1 gene. A. Hernández-Martín, et al, Clinical and Experimental Dermatology, Volume 38, 2013

Courtesy Isabel Colmenero

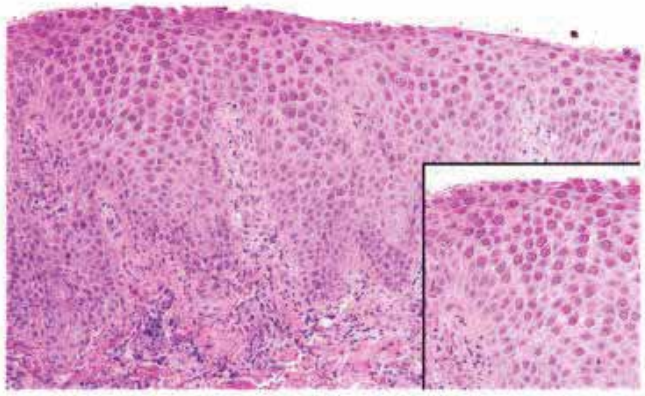


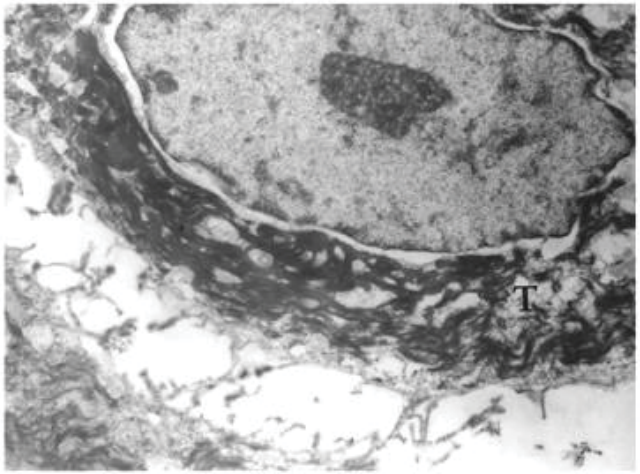


Histopathological and Ultrastructural Study of Ectodermal Dysplasia/Skin Fragility Syndrome

Reuven Bergman, MD and Eli Sprecher, MD, PhD

(*Am J Dermatopathol* 2005;27:333–338)





Plakophilin mutation

Am J Dermatopathol • Volume 43, Number 7, July 2021

Hyaline Inclusion Acanthoma

Tien Anh N. Tran, MD, Ourania Parra, MD,† and Konstantinos Linos, MD†‡*

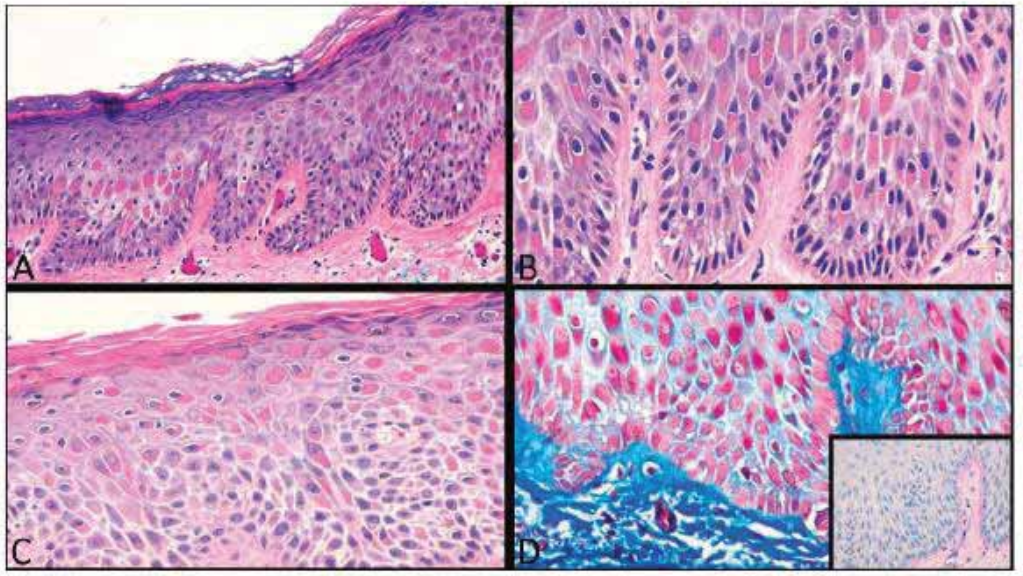
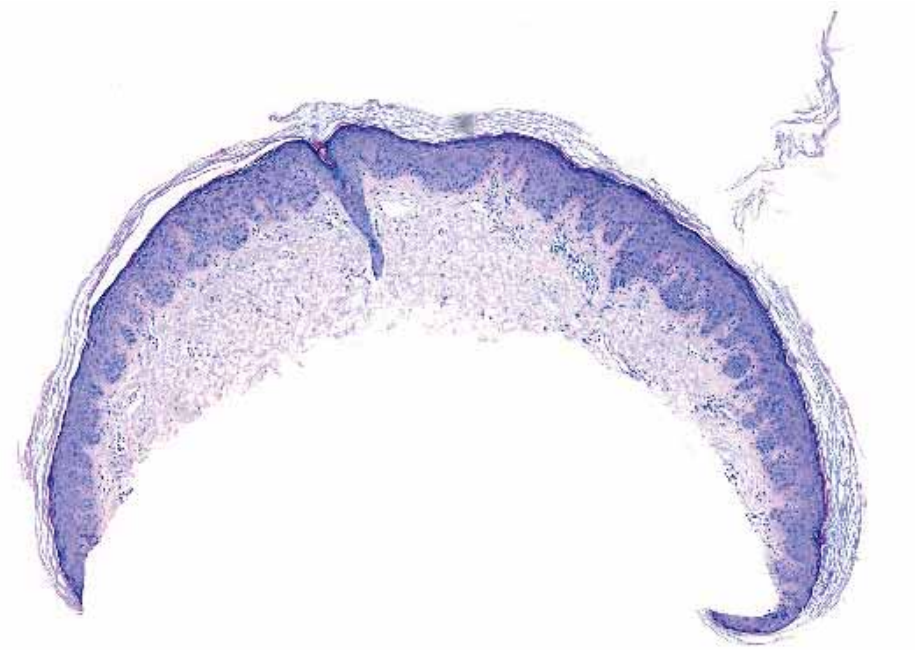
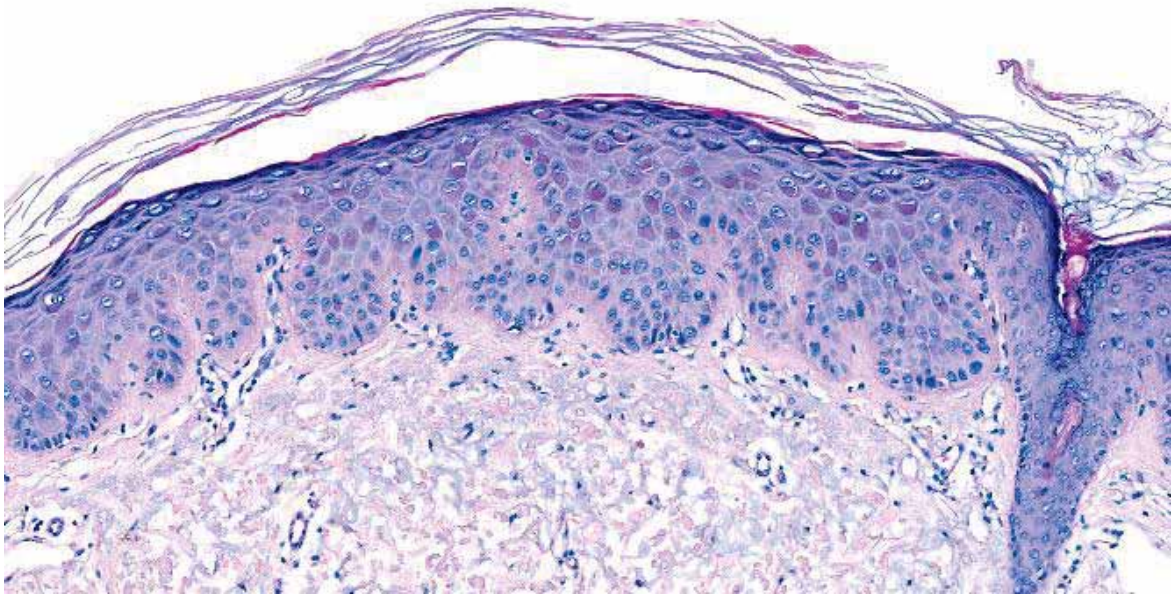


FIGURE 3. Medium-power view showing hypergranulosis and hyperkeratosis as well as the pale appearance of the lesional cells compared with the adjacent normal keratinocytes (A, ×200). A high-power view highlighting the palisading arrangement of the columnar basal keratinocytes on the basement membrane, the suprabasal confinement of the lesional keratinocytes (B, ×400), and the gradual transition of the lesional cells into the granular layer (C, ×400). Note scattered keratinocytes with intracytoplasmic eosinophilic hyaline globules in the granular layer. The intracytoplasmic hyaline inclusions stain red with Masson's trichrome (D, ×400) and are negative for PAS stain (inset, ×400).

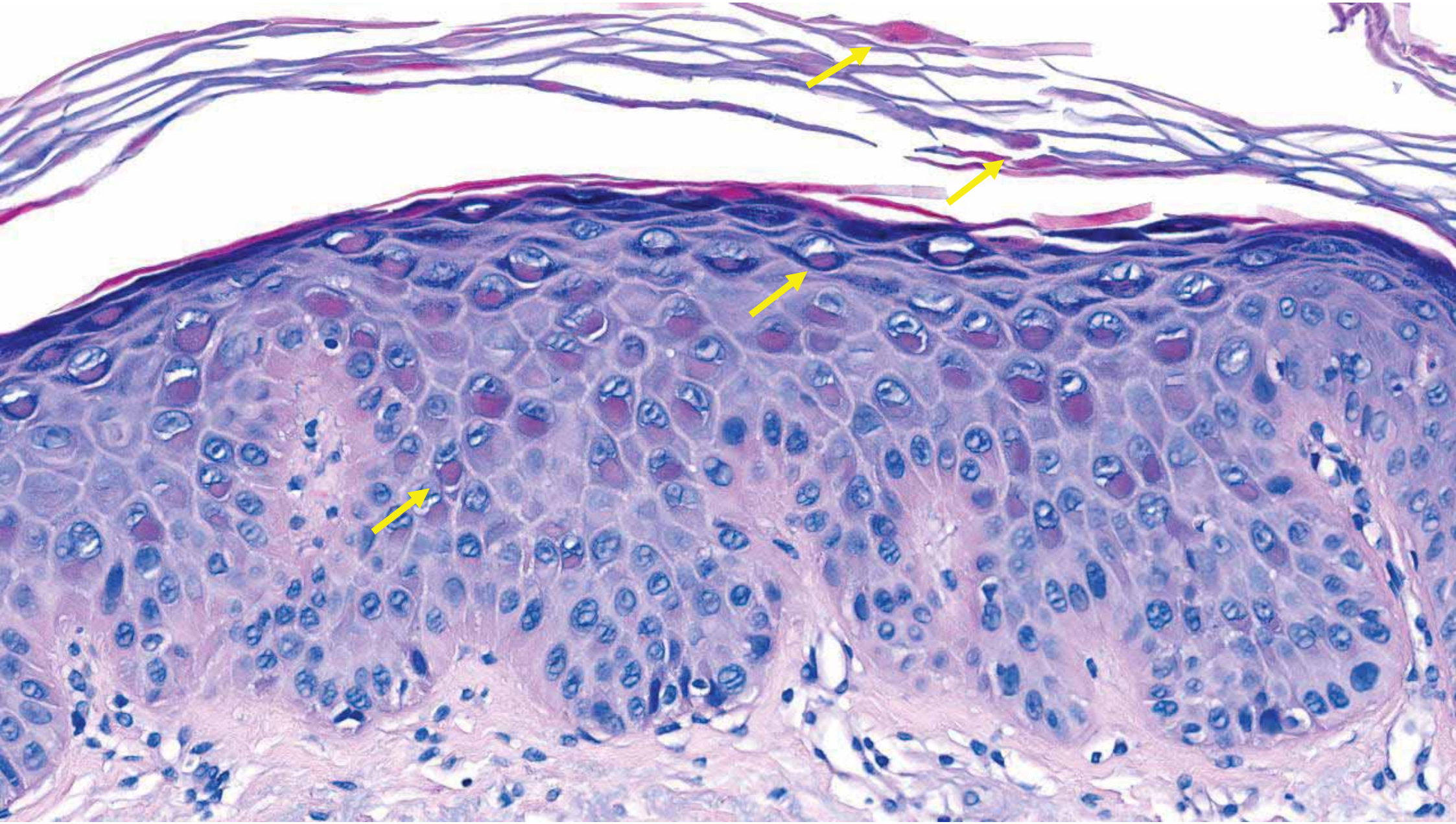
Hyaline inclusion Acanthoma

(Variant of Acanthoma with Desmosomal-Type of Acantholysis)





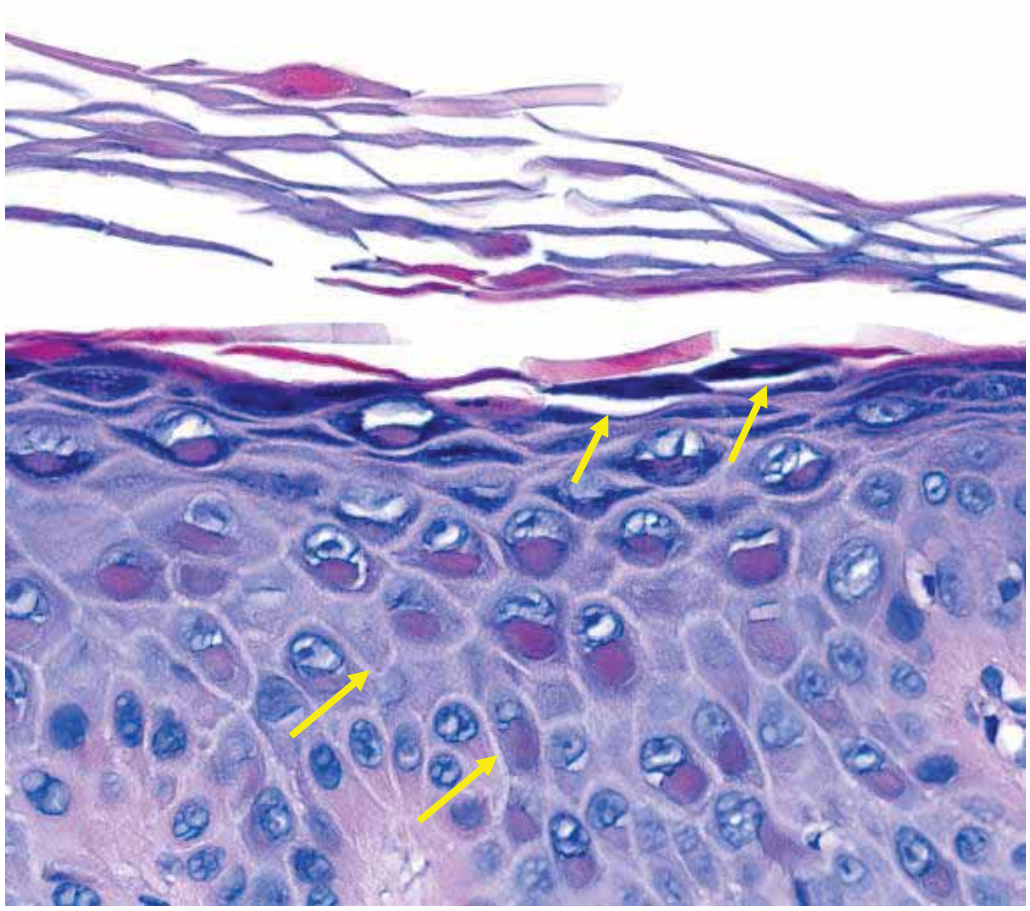
57-year-old male, reddish plaque on the thigh
(Consulant Case, U. Hillen, Duisburg-Essen)

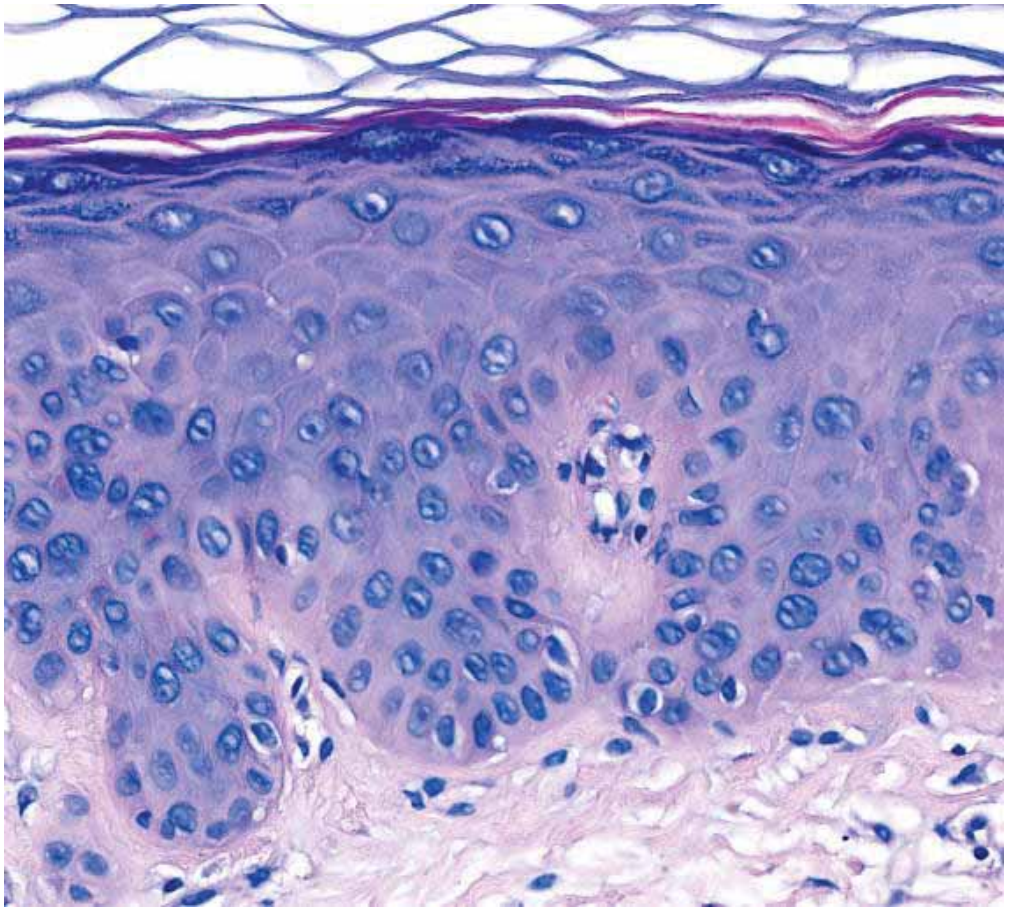


Center

Periphery

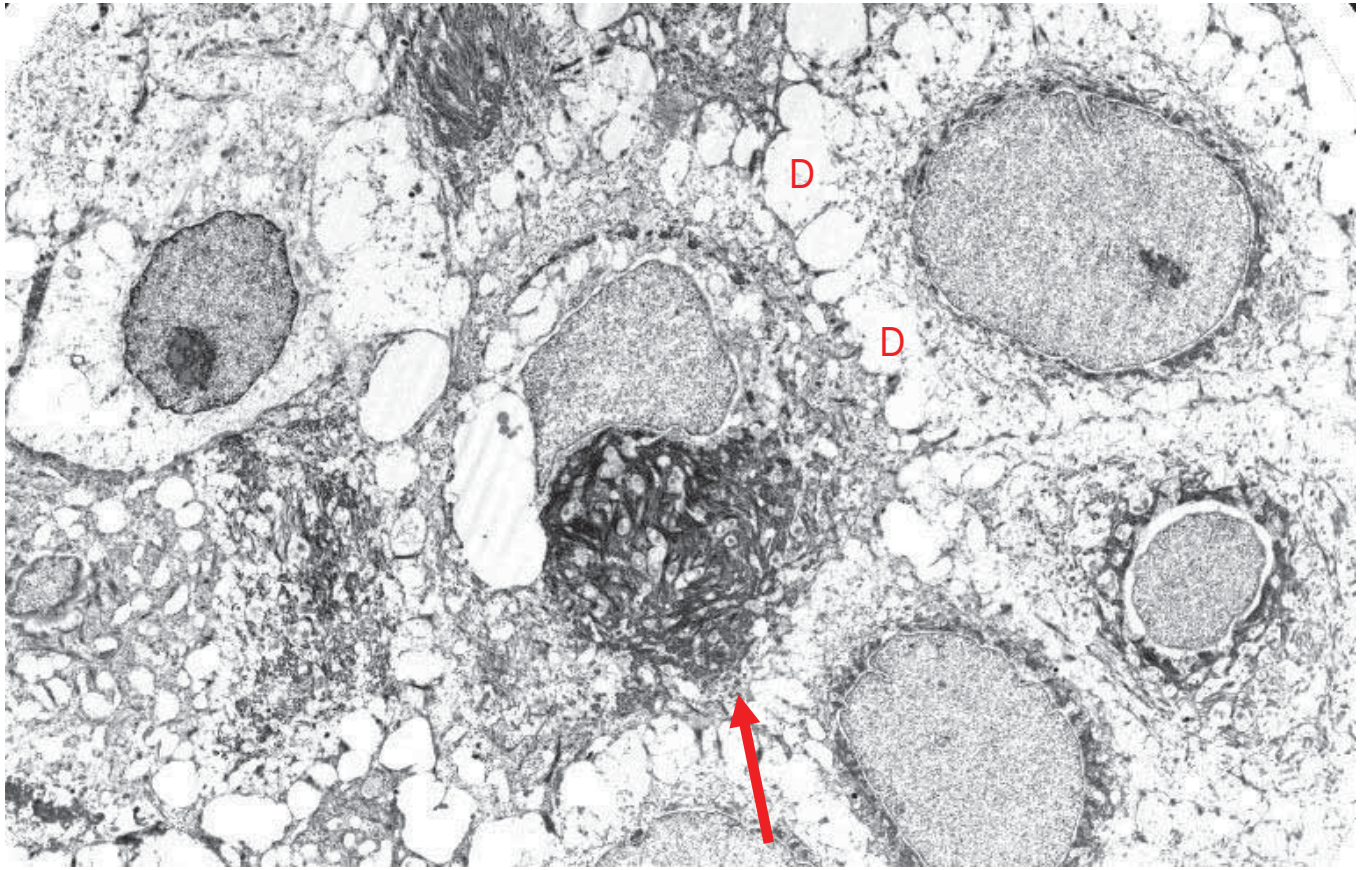
In addition to intracellular inclusions…..



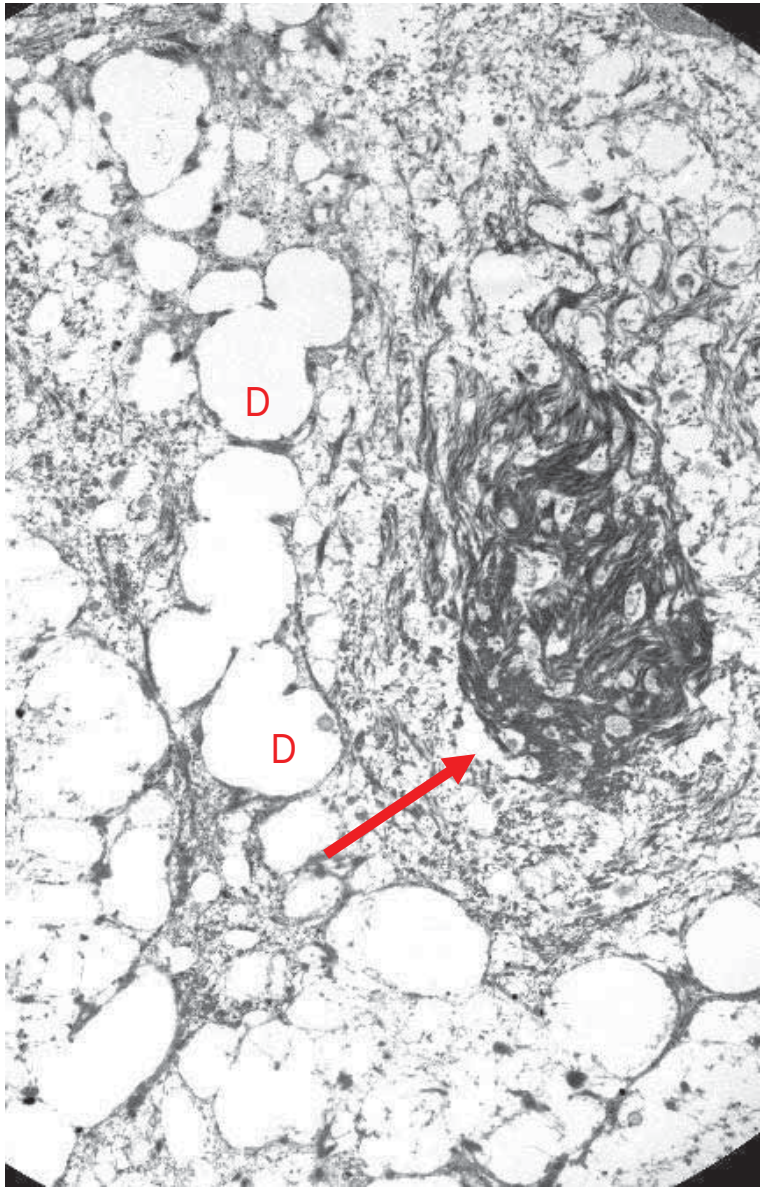


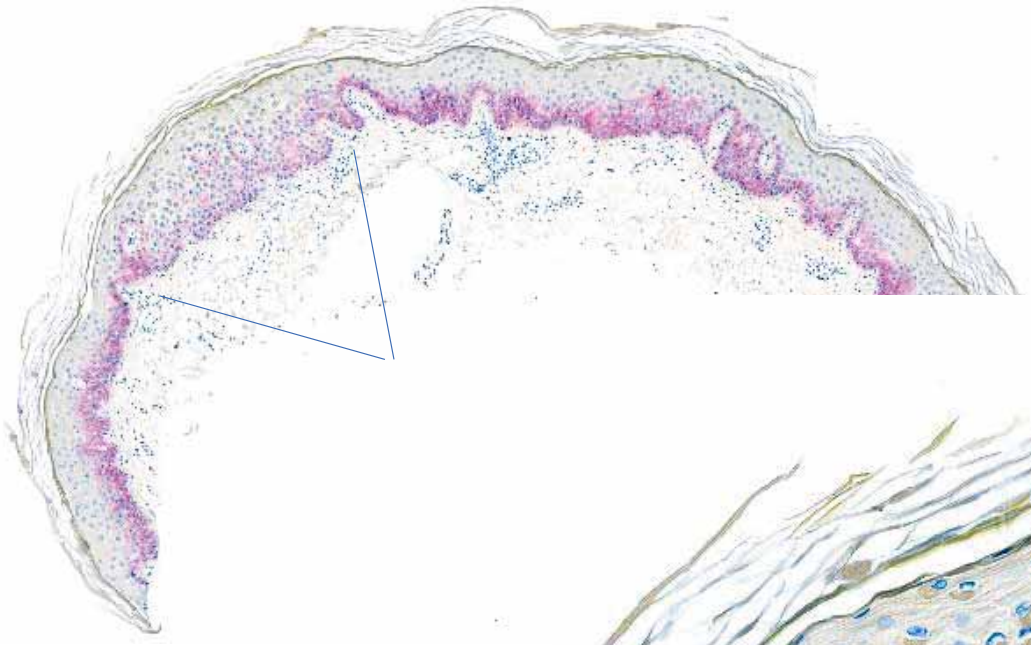
Widening of the intercellular spaces and subcorneal acantholysis

Center of the Acanthoma

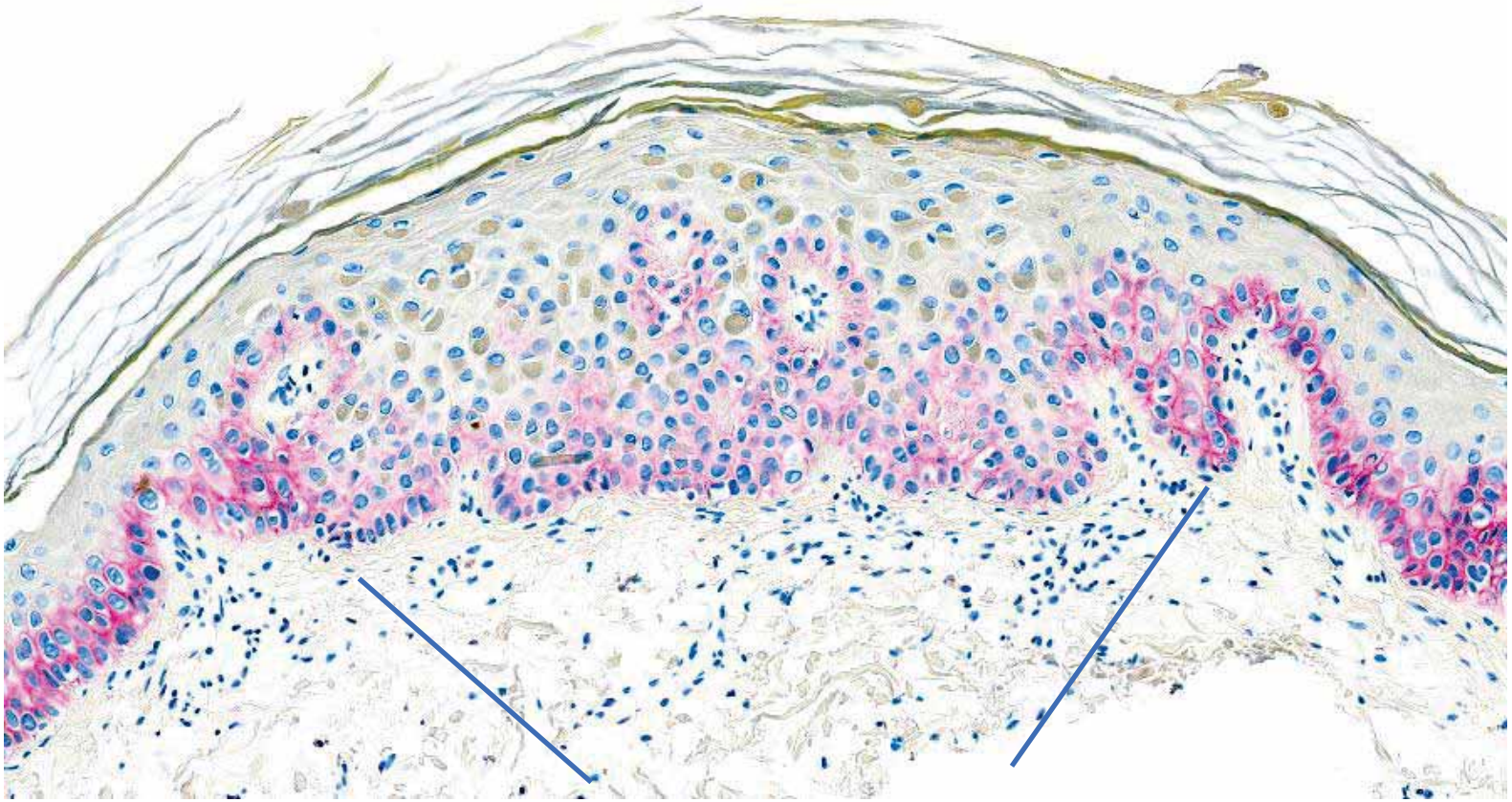


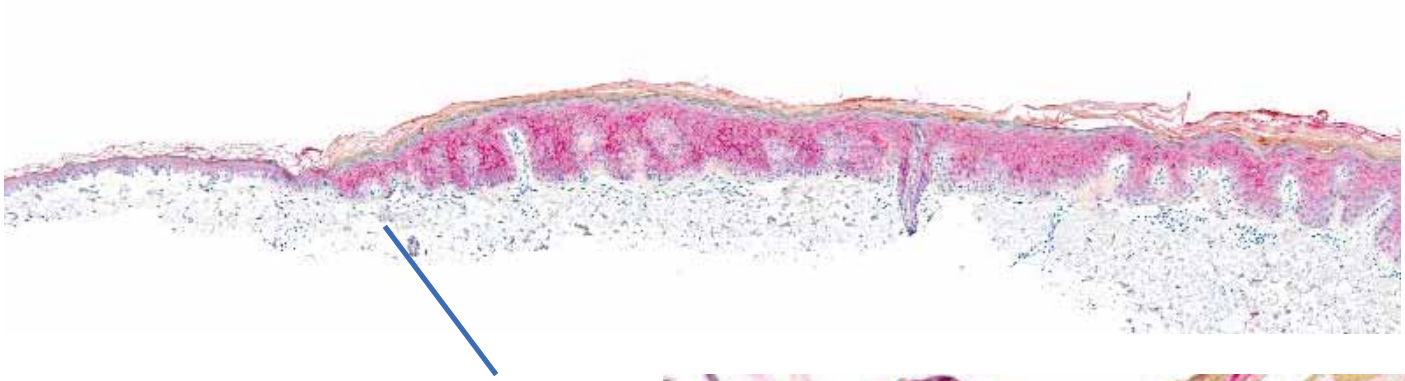
Collapse of the keratin skeleton and cytoplasmic clumping of keratin, ↗ widening of the intercellular spaces and reduction of desmosomes (D)



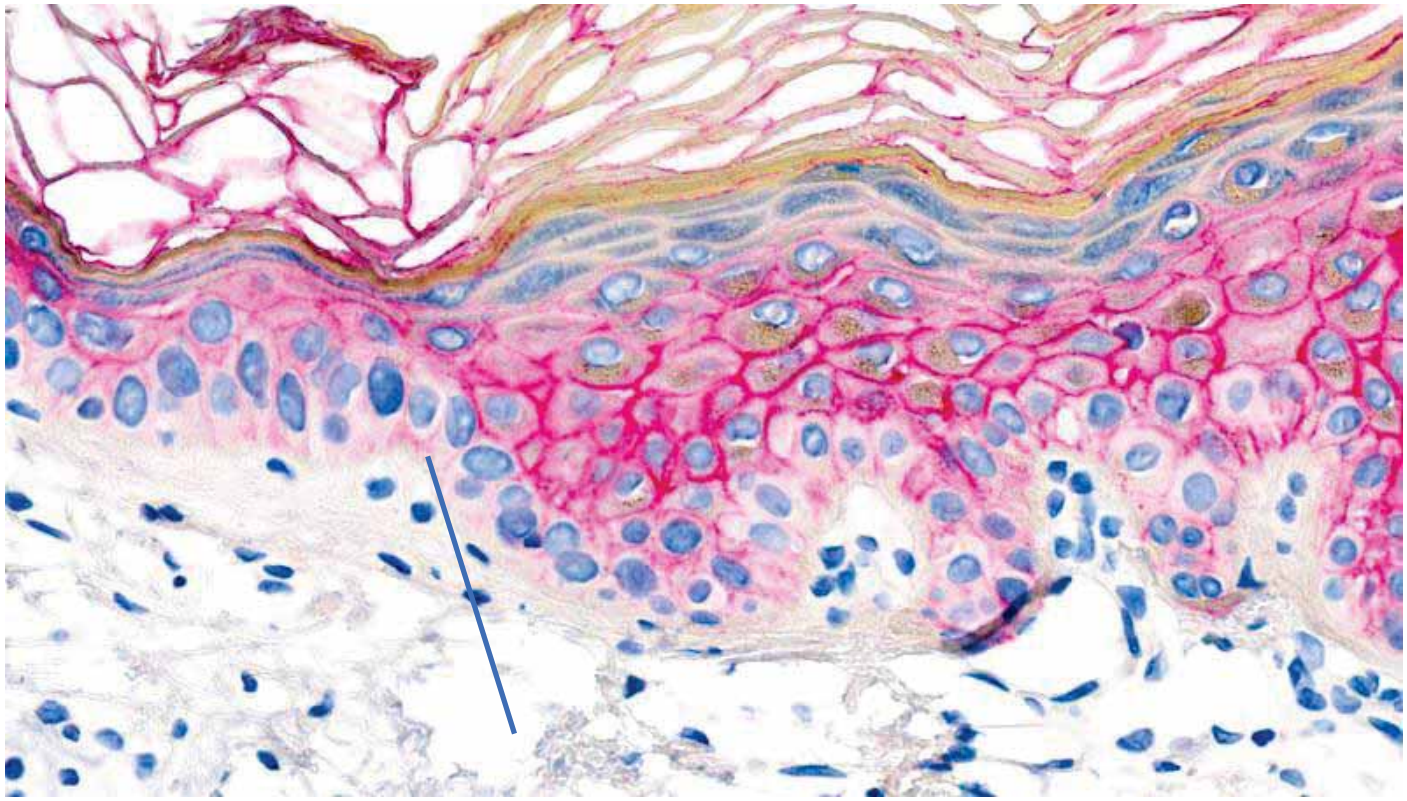


Desmoglein 3, reduced expression





Desmoglein 1, overexpression

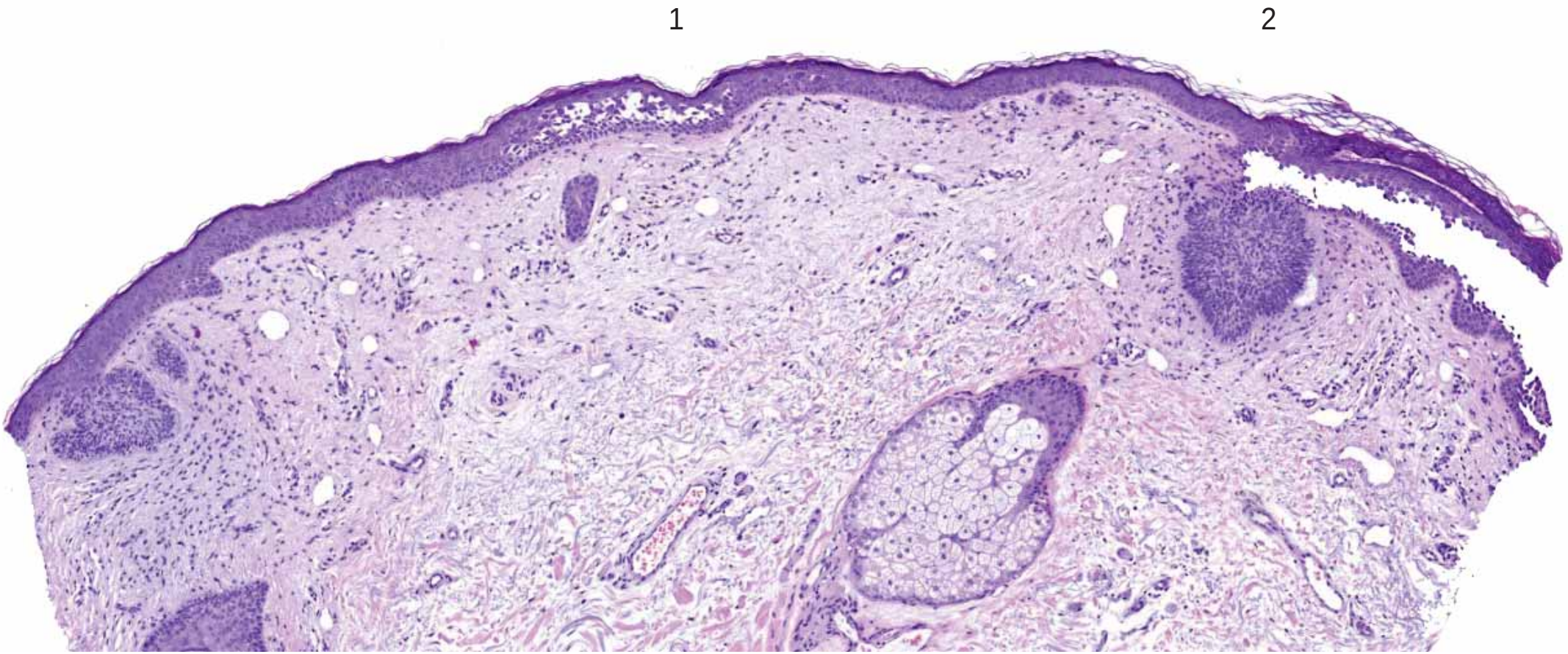


Benign Acanthoma

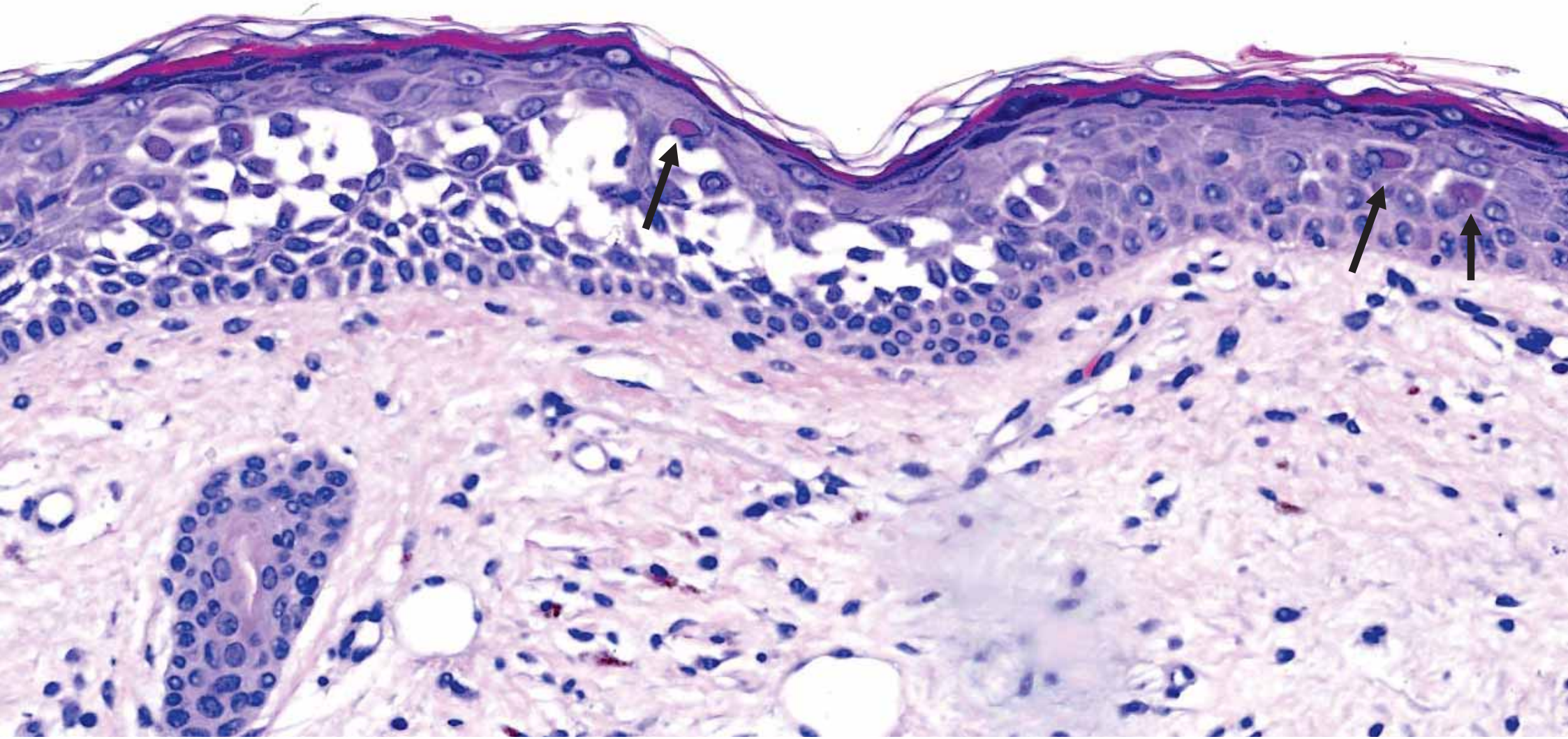
- Seborrheic keratosis
- Dermatosis papulosa nigra
- Lichen planus-like keratosis
- Pale cell acanthoma
- Large cell acanthoma
- Clear cell papulosis
- Porokeratoma
- .....

- Epidermolytic acanthoma
- Acantholytic dyskeratotic acanthoma
- Acanthoma with H.-H.-type acantholysis
  <-> Hypergranulotic dyskeratotic acanthoma
- Acanthoma with Desmosomal-type acantholysis
- Hyalin inclusion acanthoma
- Granular parakeratotic acanthoma
- .....

Incidental hyaline inclusions in a case of BCC



1



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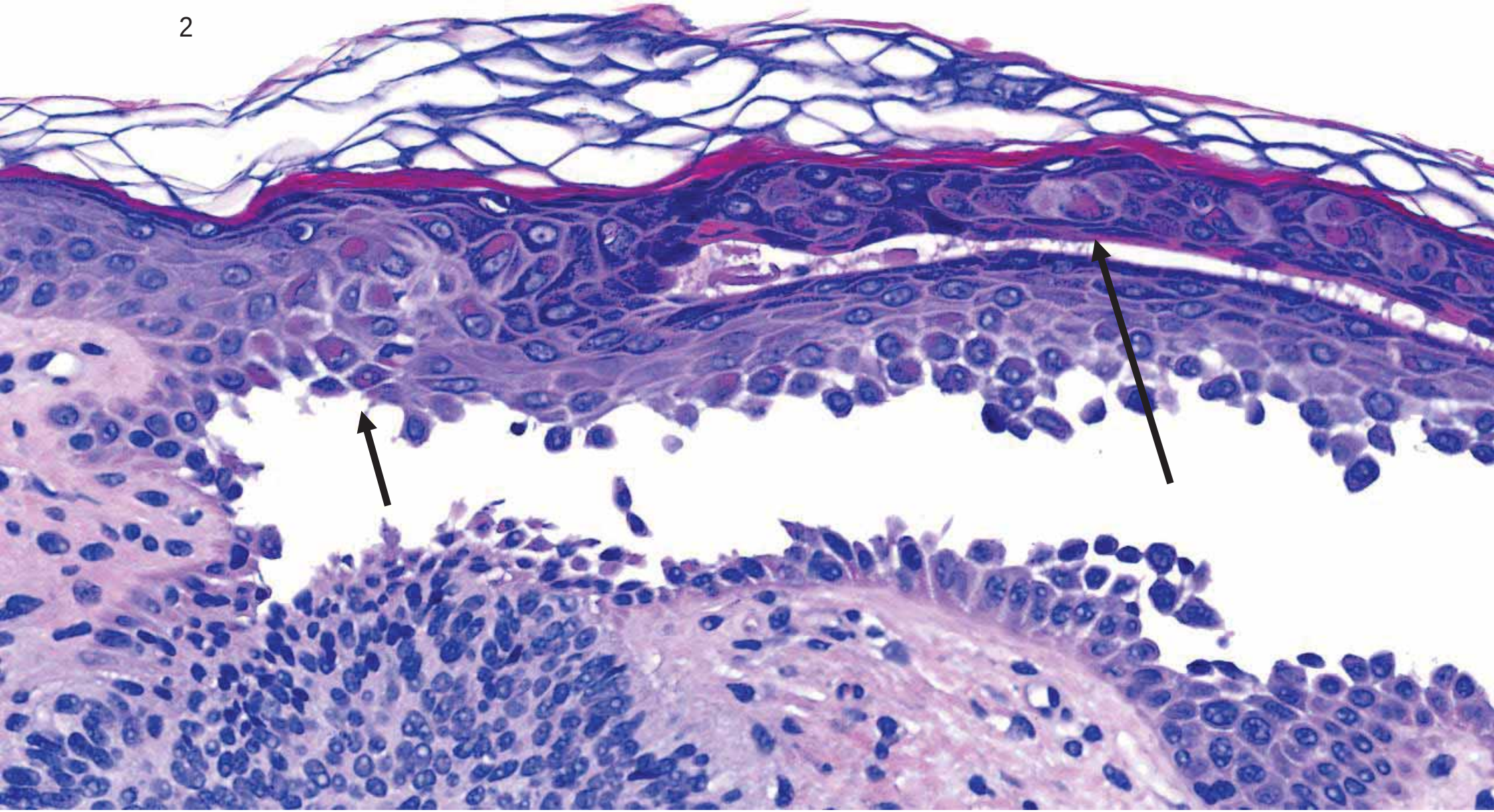
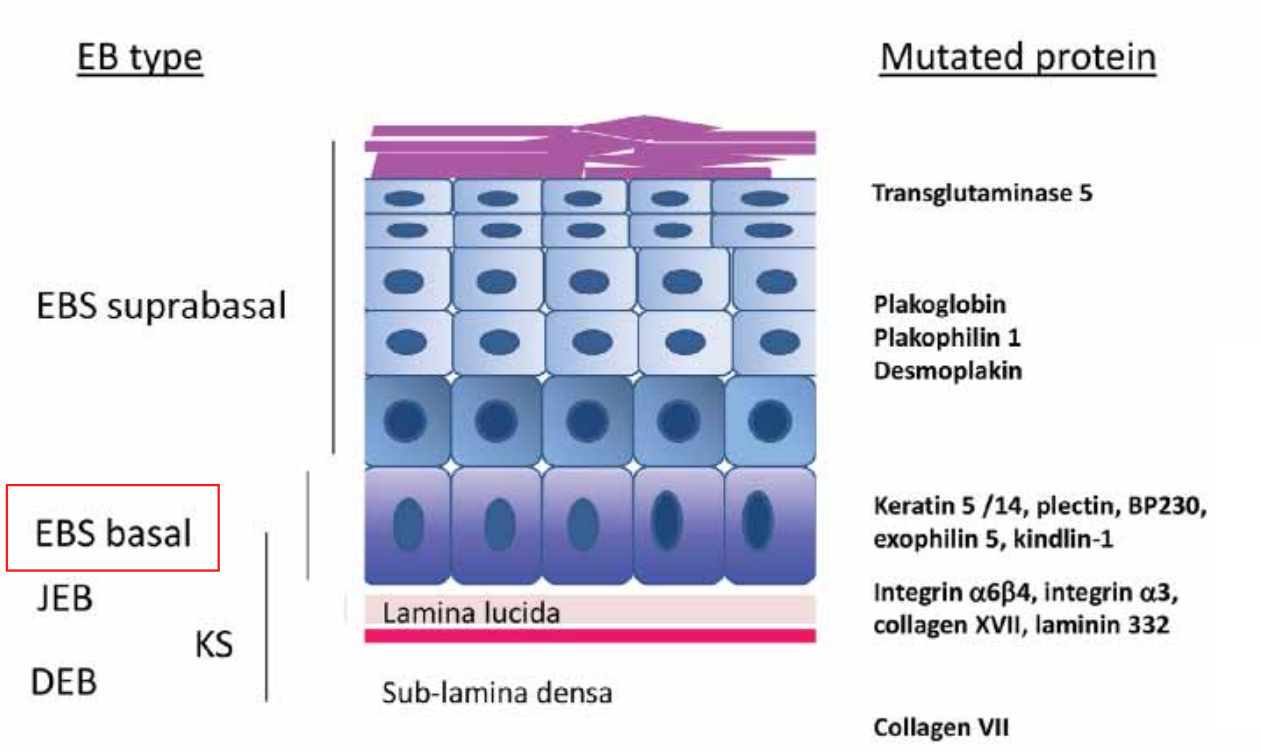


Epidermal reaction patterns
in genodermatoses, epidermal nevi, acquired skin diseases or as an incidental finding

Pattern	Dermatosis	Mosaicism	Solitary lesion	Incidental finding
Epidermolytic hyperkeratosis	Keratinopathic Ichthyosis, Palmoplantar Keratoderma	+	Epidermolytic acanthoma	+
Focal acantholytic dyskeratosis	M. Darier	+	Acantholytic dyskeratotic acanthoma	+
Hailey–Hailey–type acantholysis	M. Hailey–Hailey	+	Hailey–Hailey–type acanthoma	+
Desmosomal-type acantholysis	Genetic diseases with desmsosome related mutations	?	Desmosomal-type acanthoma (Hyaline inclusion acanthoma)	+
Epidermolysis bullosa simplex-type vacuolization	Epidermolysis bullosa simplex	+	?	+
Granular Parakeratosis	Granular parakeratosis	-	Granular parakeratotic acanthoma	+
.....				

Epidermolysis bullosa hereditaria



Fine et al, JAAD, 2014

Onion-skin approach and classification (instead of eponyms):

Level of blistering (EB type) – phenotype
– mode of inheritance
– protein level (IFM)
– mutation – type of mutation

REVIEW

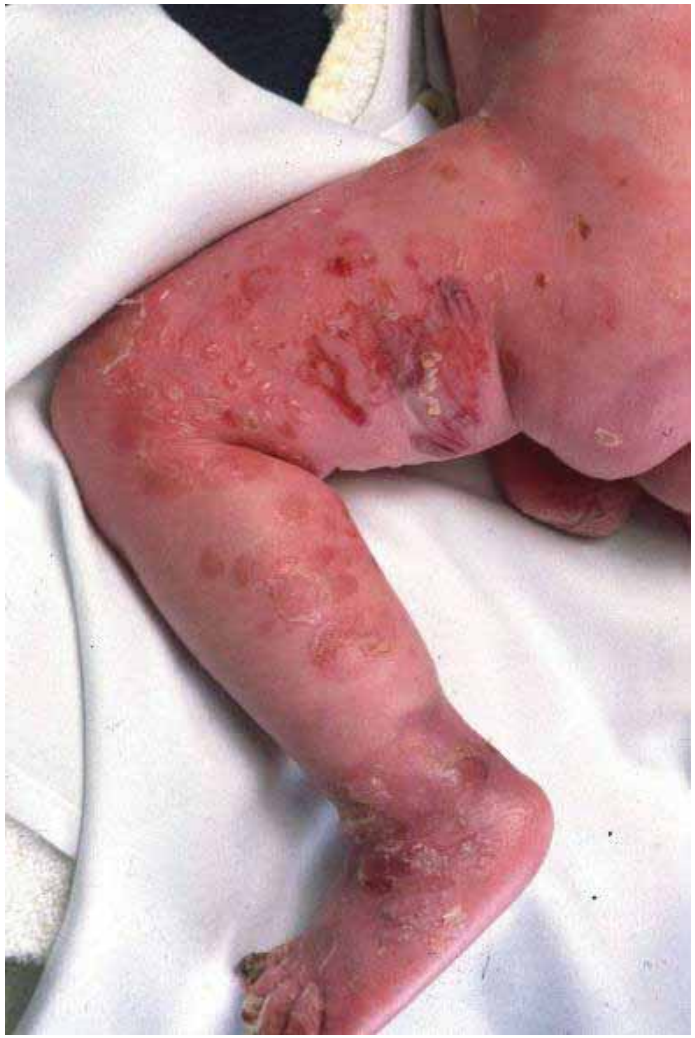
Inherited epidermolysis bullosa: Updated recommendations on diagnosis and classification

Jo-David Fine, MD, MPH, FRCP,[a,b] Leena Bruckner-Tuderman, MD, PhD,[c] Robin A. J. Eady, DSc, FRCP, FMedSci,[d] Eugene A. Bauer, MD,[e] Johann W. Bauer, MD,[f] Cristina Has, MD,[c] Adrian Heagerty, MD, FRCP,[g] Helmut Hintner, MD,[f] Alain Hovnanian, MD, PhD,[h] Marcel F. Jonkman, MD, PhD,[i] Irene Leigh, CBE, DSc, FRCP, FRSE, FMedSci,[j] M. Peter Marinkovich, MD,[e,k] Anna E. Martinez, FRCPCH,[l] John A. McGrath, MD, FRCP, FMedSci,[d] Jemima E. Mellerio, MD, FRCP,[d,l] Celia Moss, DM, FRCP, MRCPCH,[m] Dedee F. Murrell, MD, FACD,[n] Hiroshi Shimizu, MD, PhD,[o] Jouni Uitto, MD, PhD,[p] David Woodley, MD,[q] and Giovanna Zambruno, MD[r]

Nashville, Tennessee; Freiburg, Germany; London and Birmingham, England; Stanford, Palo Alto, and Los Angeles, California; Salzburg, Austria; Toulouse, France; Groningen, The Netherlands; Dundee, Scotland; Sydney, Australia; Sapporo, Japan; Philadelphia, Pennsylvania; and Rome, Italy

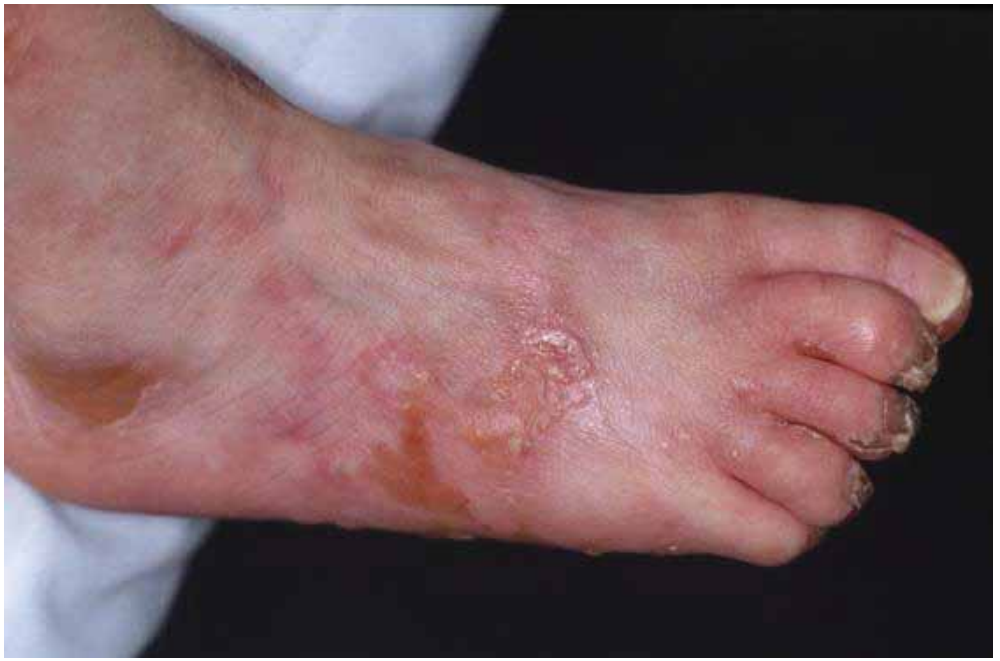
J Am Acad Dermatol. 70:1103-26, 2014

Epidermolysis bullosa (EB) simplex

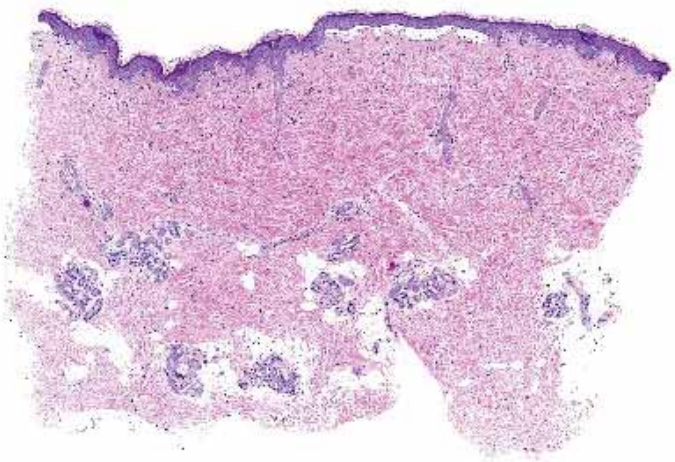


Blisters localised, herpetiform-grouped
or generalised, hyperpigmentation
Inducible by heat, trauma, …
Acral skin, and other sites, oral cavity

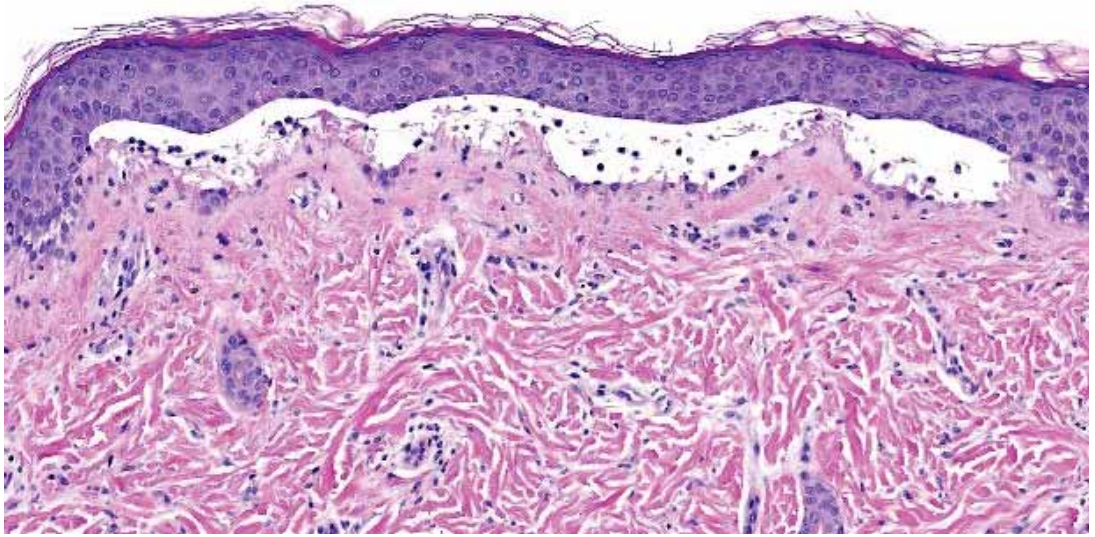
Palmoplantar Keratosis, Nail Dystrophy

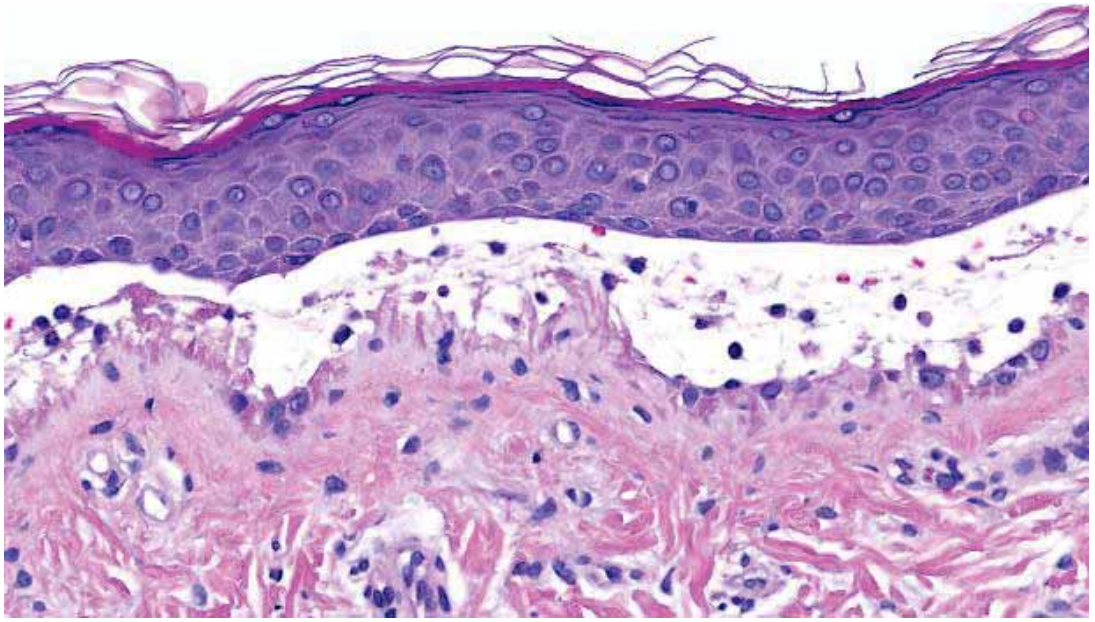


EB simplex (Keratin 5 Mutation)

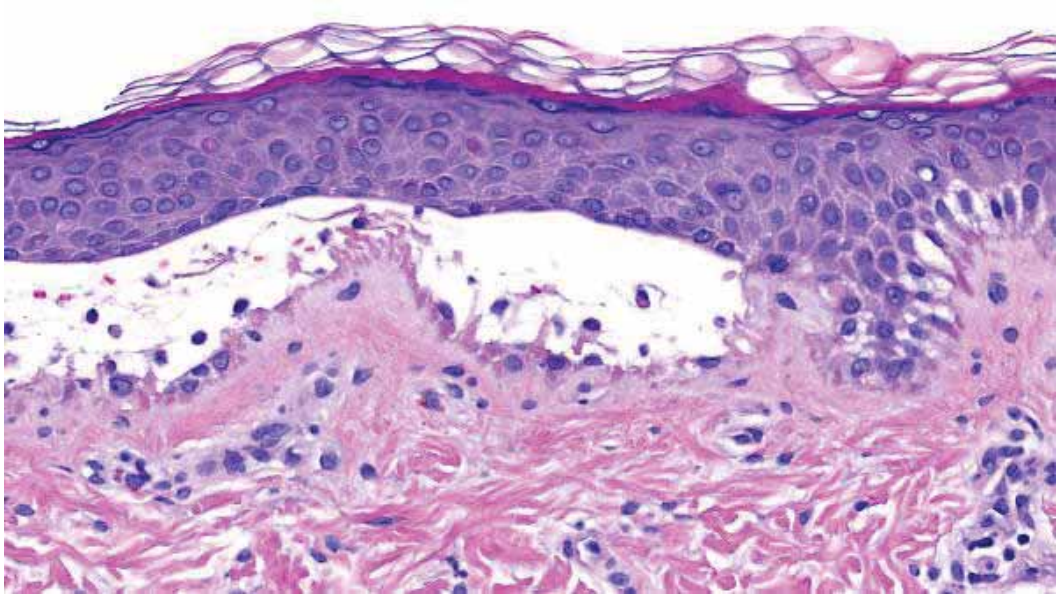


Intraepidermal clefting and blistering

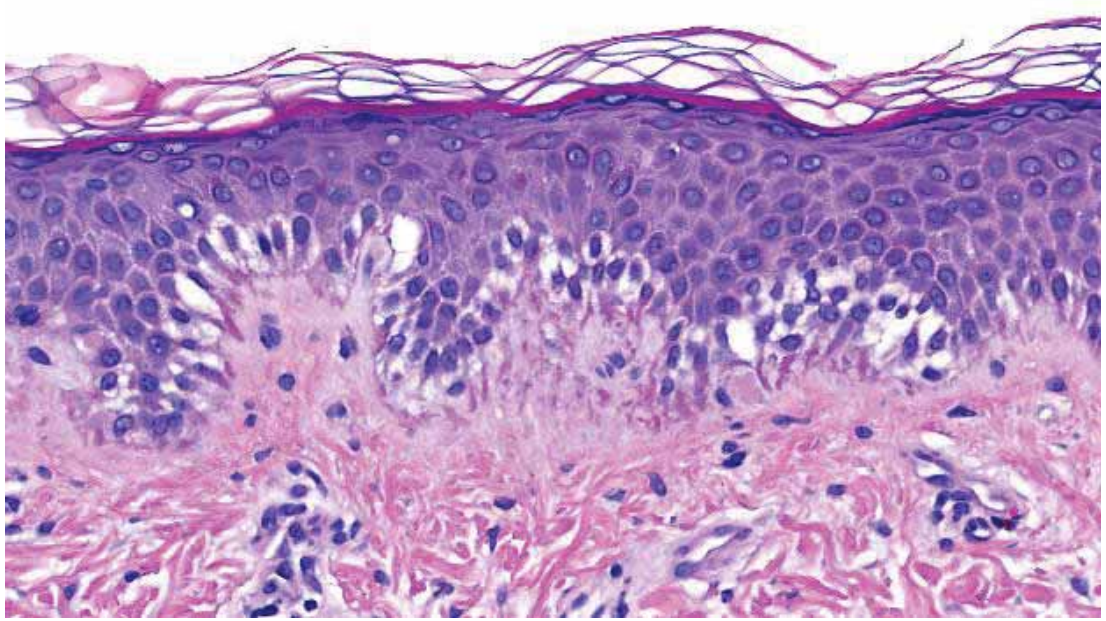




EB simplex (Keratin 5 Mutation)



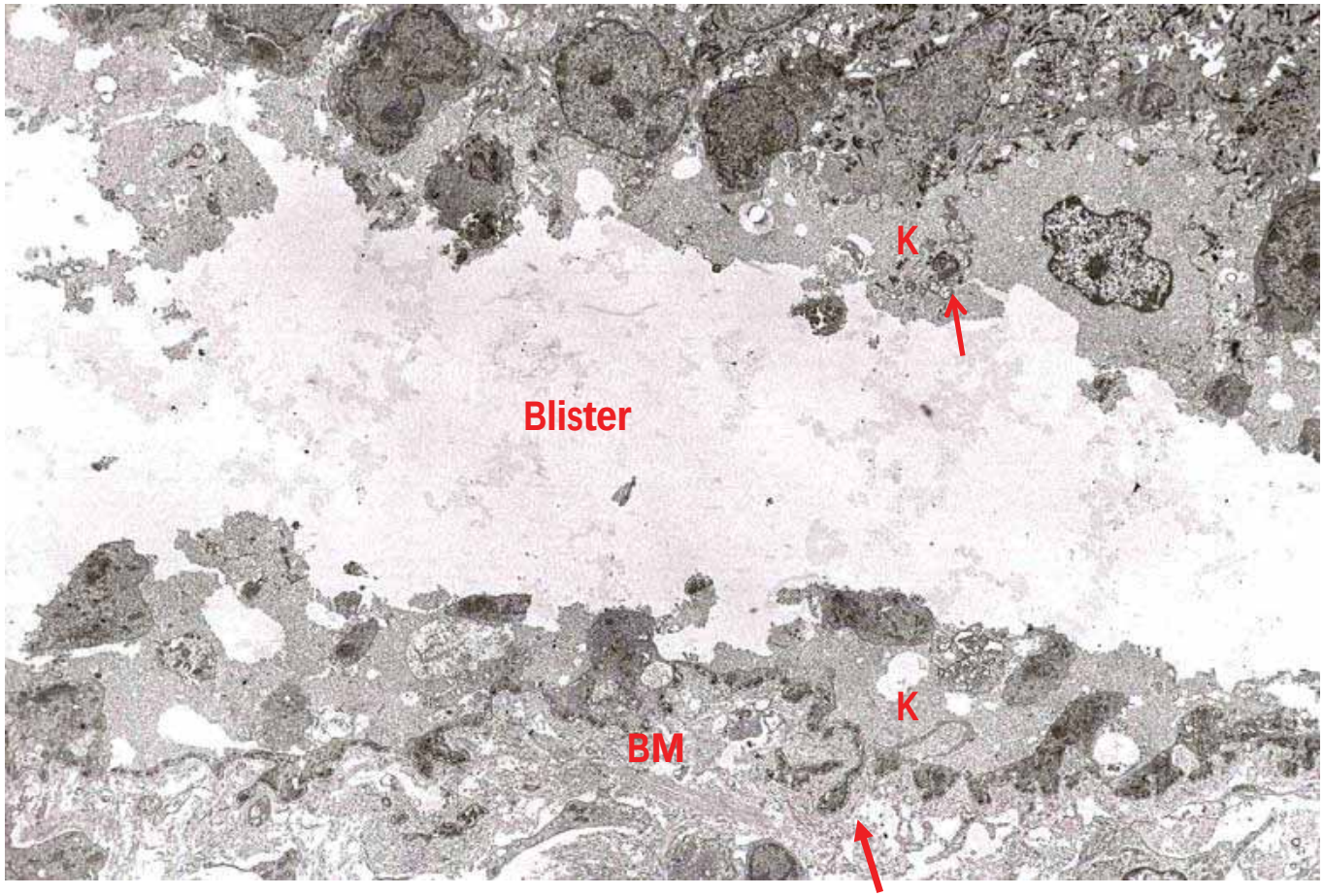
Intracellular clefting in the basal layer,
baseline of the basal keratinocytes remains intact



Periphery-early stage of EBS:
vacuolization of basal keratinocytes,
baseline appears fringe-like and hypereosinophilic

EB simplex (Keratin 5 Mutation)

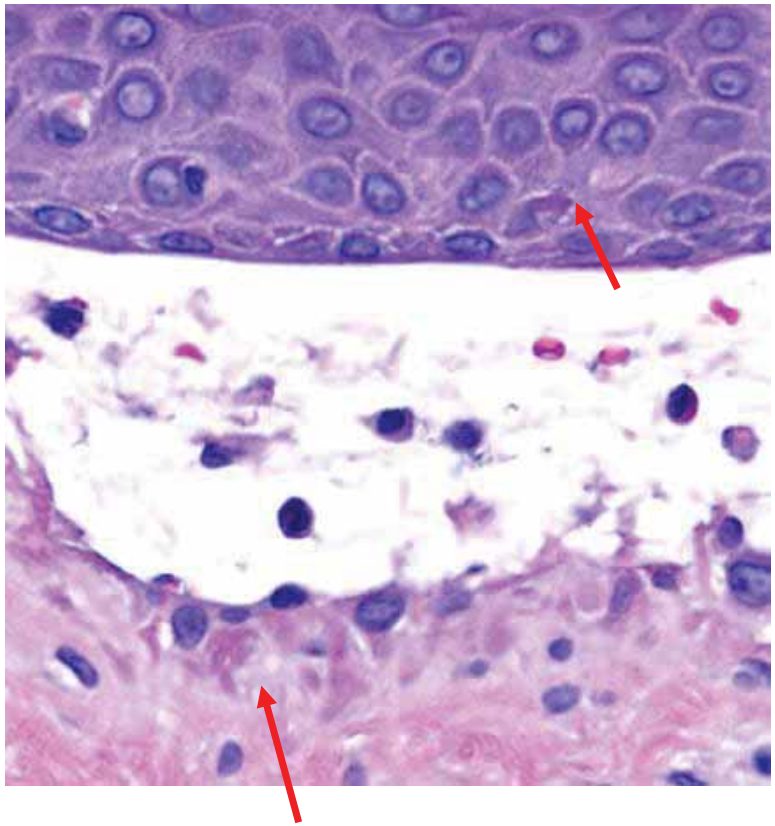
Electron microscopy and HE



Baseline remains intact

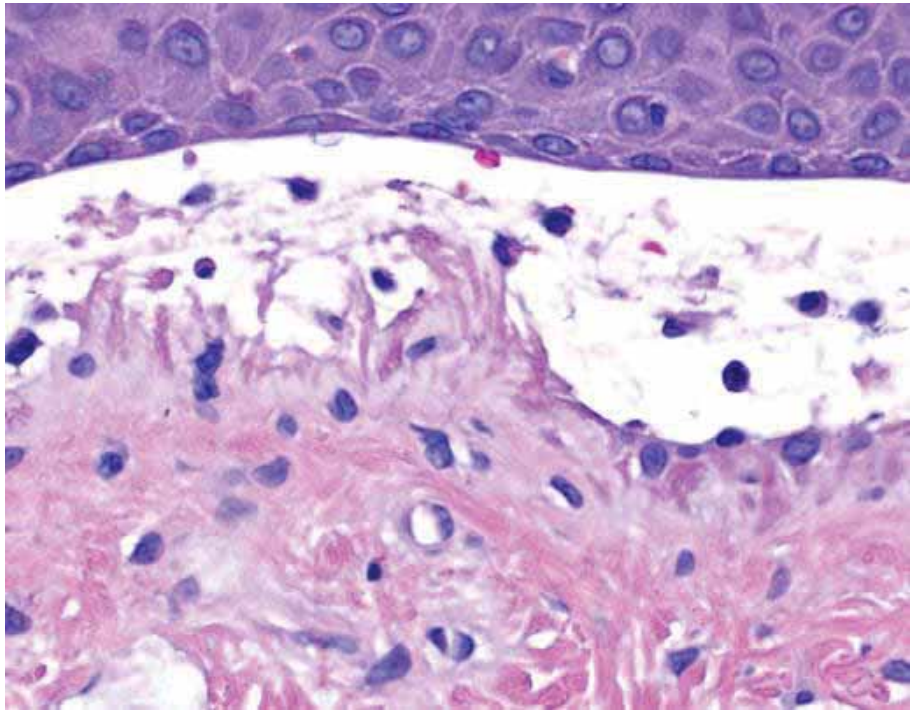
Anchoring foot processes (Wurzelfüsschen)

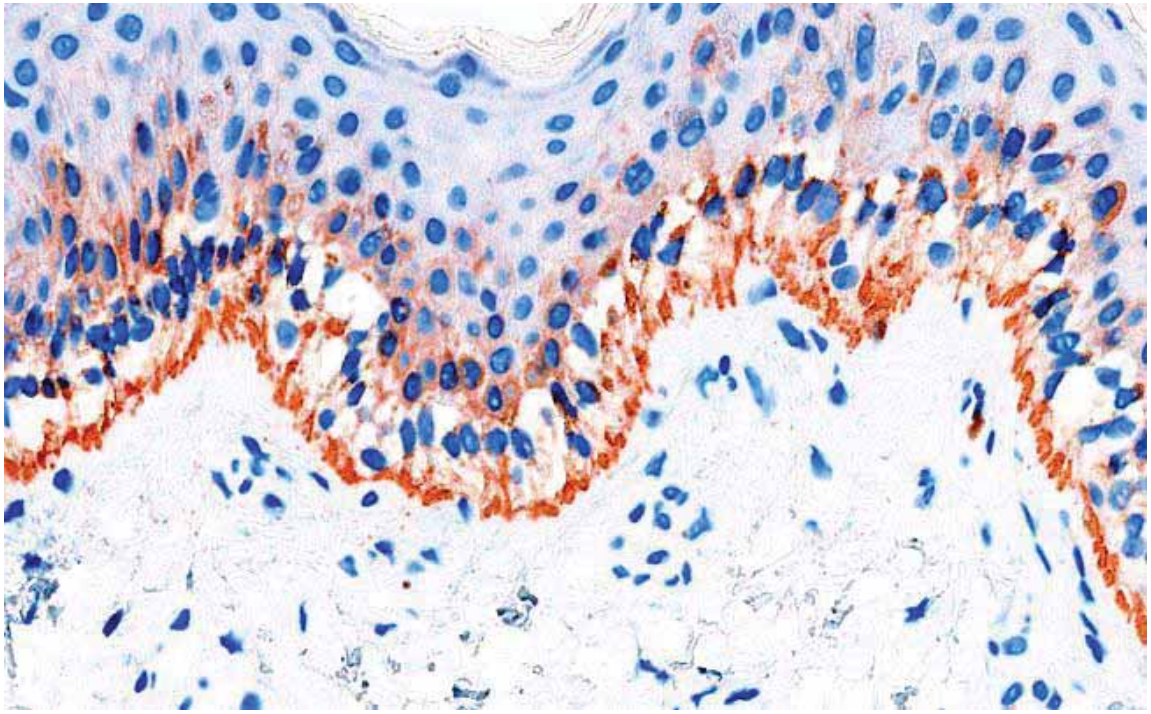
Intracellular splitting



Fringe-like projections

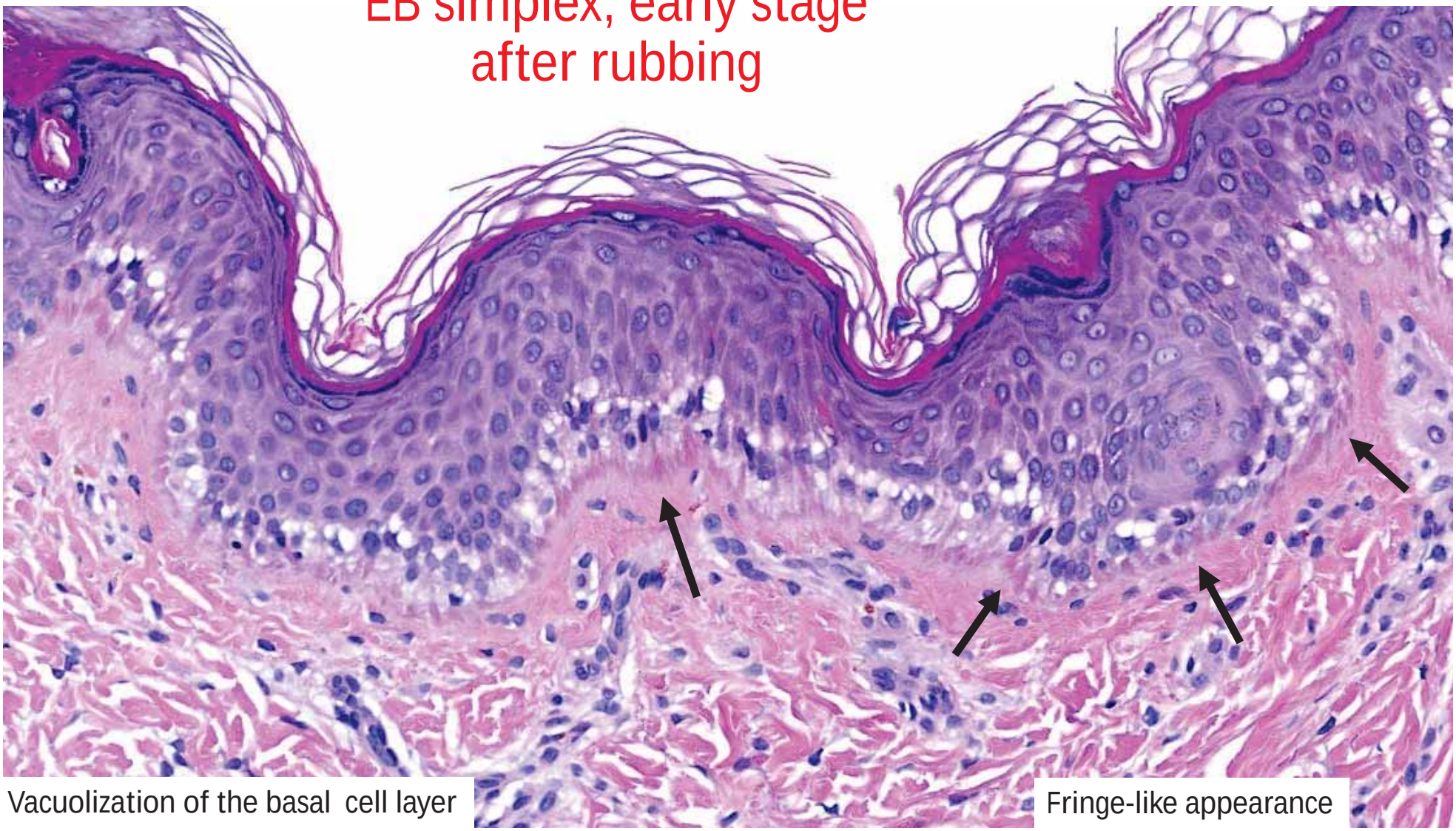
Epidermolysis bullosa simplex





Keratin 14 immunostaining

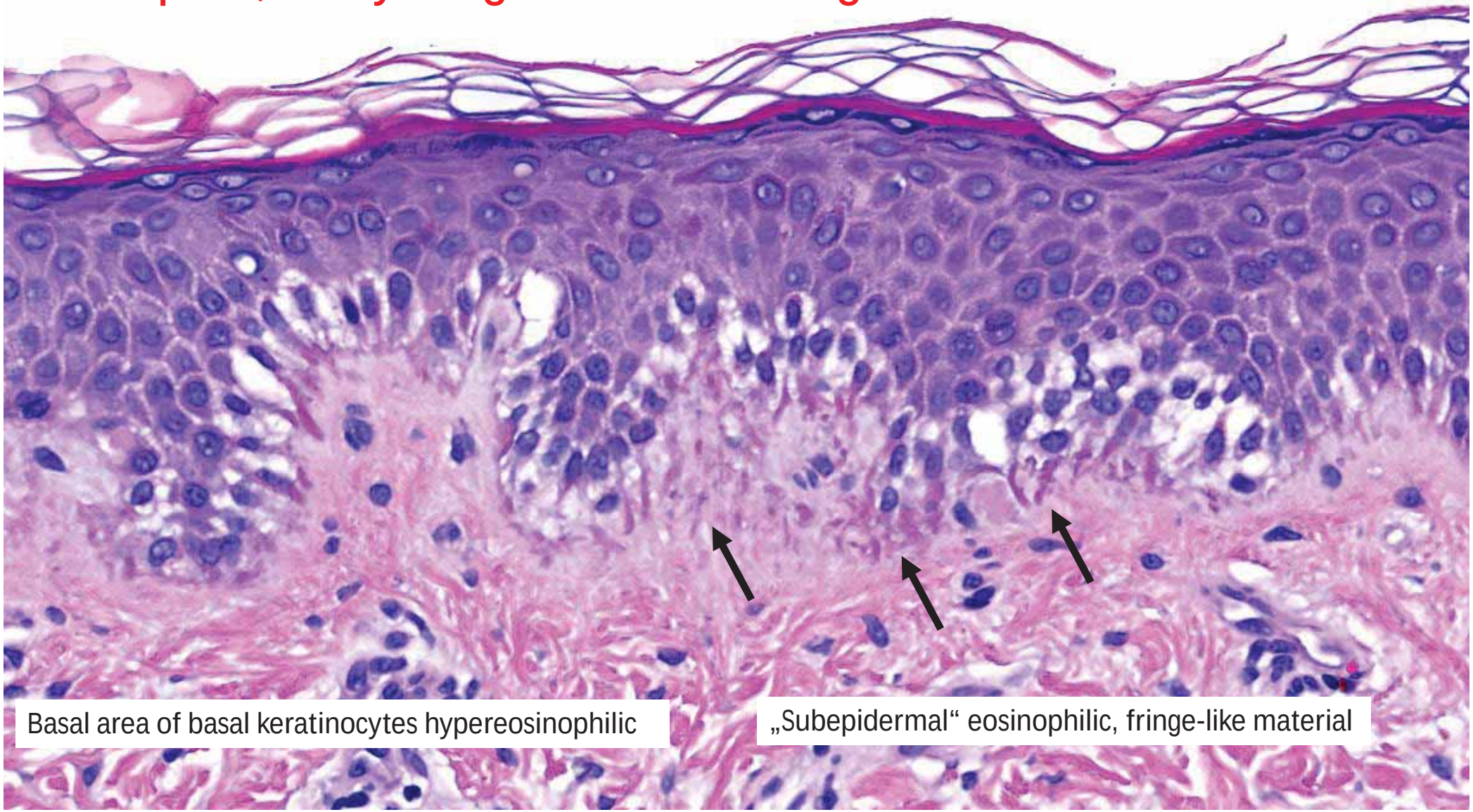
EB simplex, early stage after rubbing



Vacuolization of the basal cell layer

Fringe-like appearance

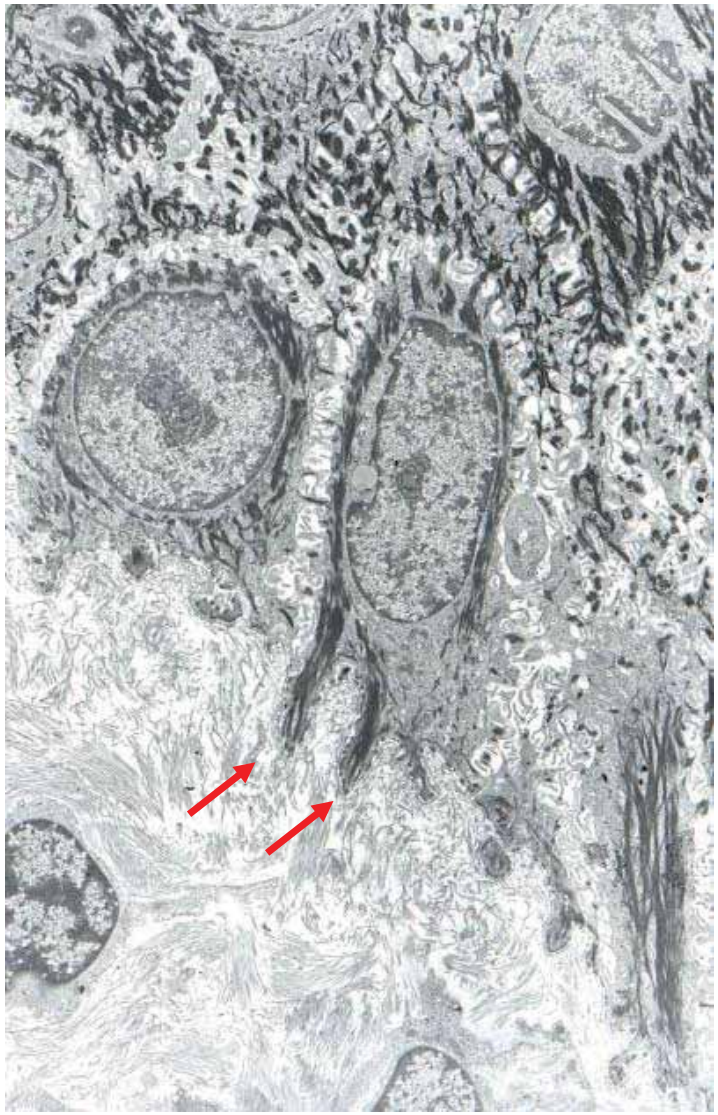
EB simplex, early stage after rubbing



Basal keratinocytes

Basement membrane

Wurzelfüßchen (anchoring foot processes)



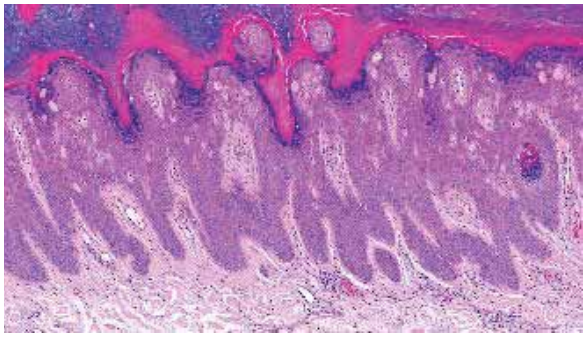
Suprabasal Keratinocytes

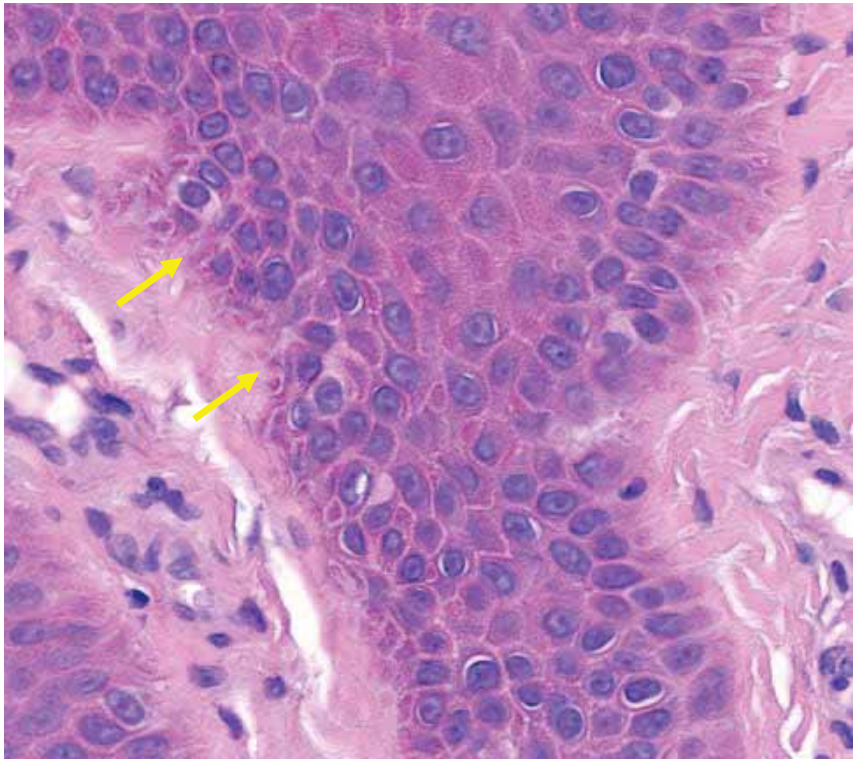
Dermal-epidermal junction

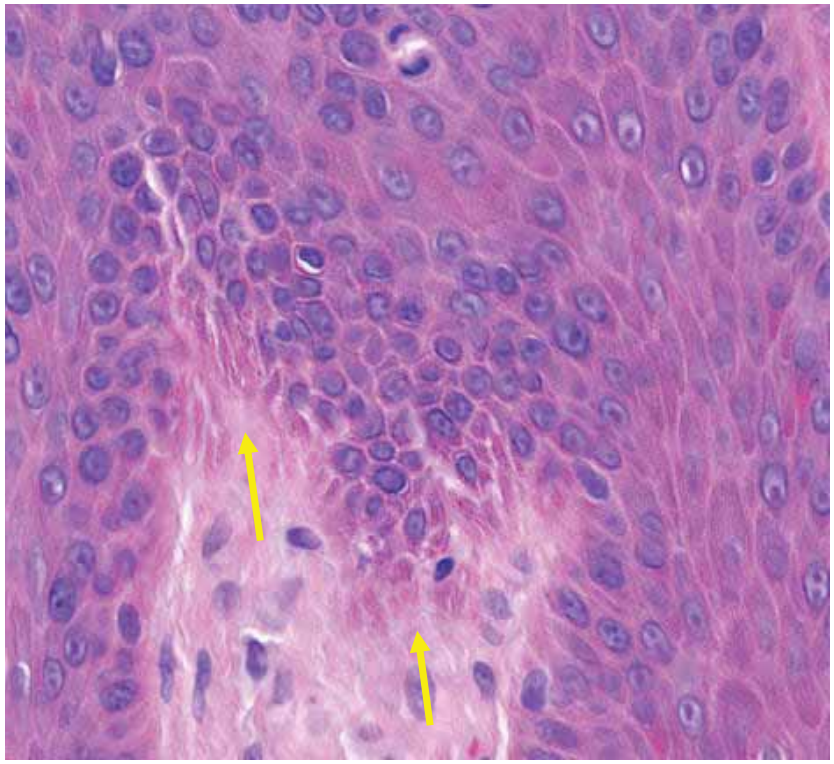
Verruca vulgaris

Wurzelfüßchen
(anchoring foot processes)

Note: no vacuolization and clefting

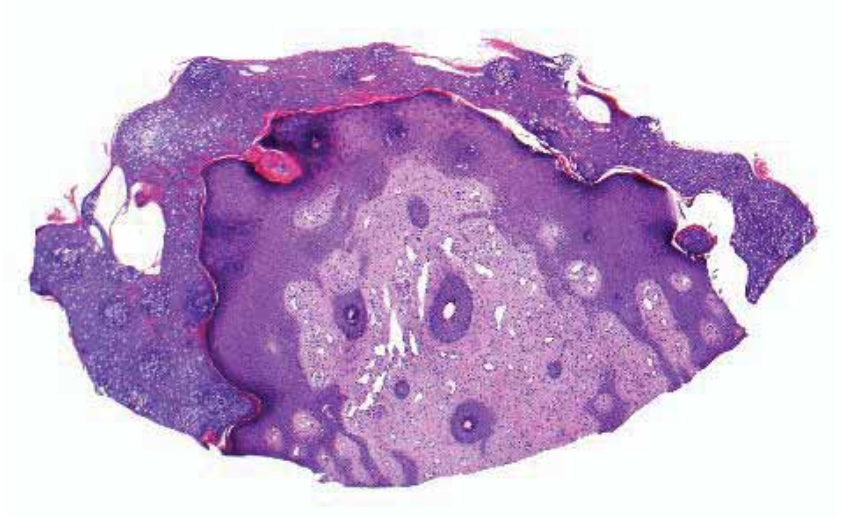






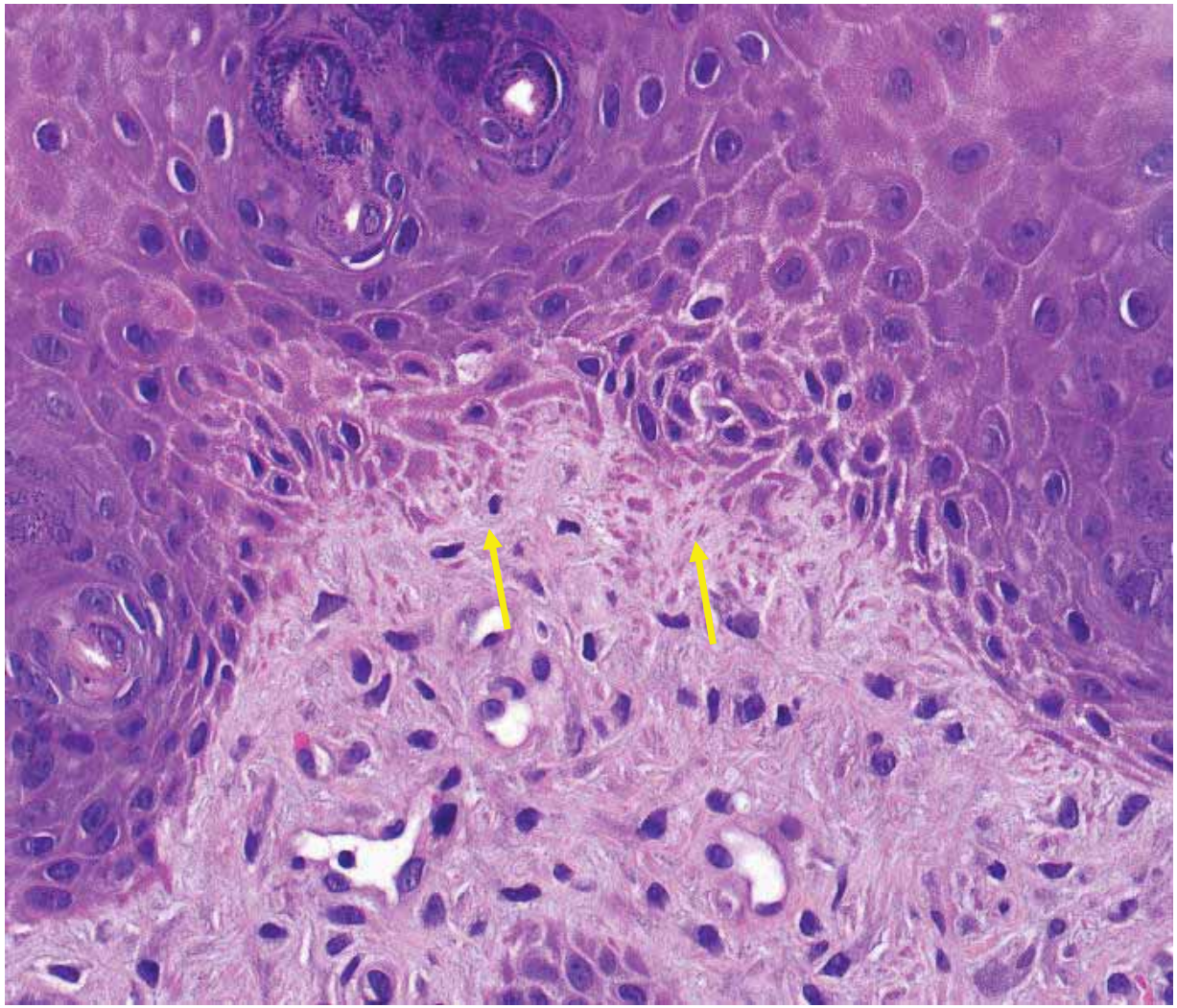
Prurigo nodularis

Oblique section



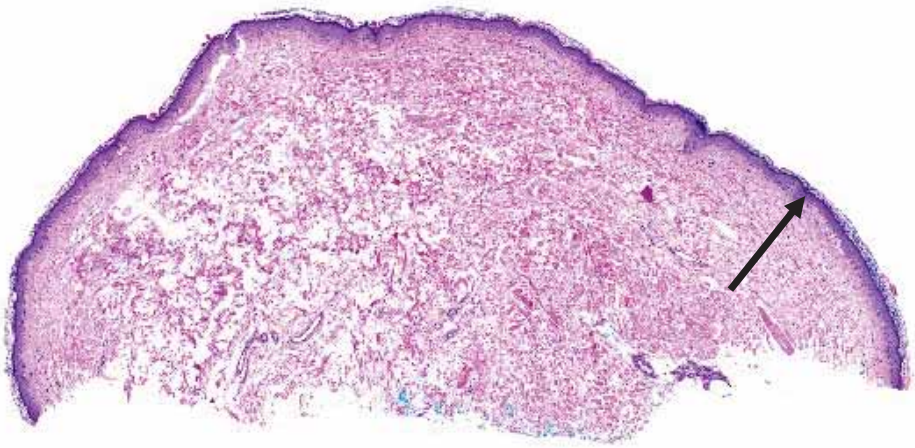
Wurzelfüßchen
(anchoring foot processes)

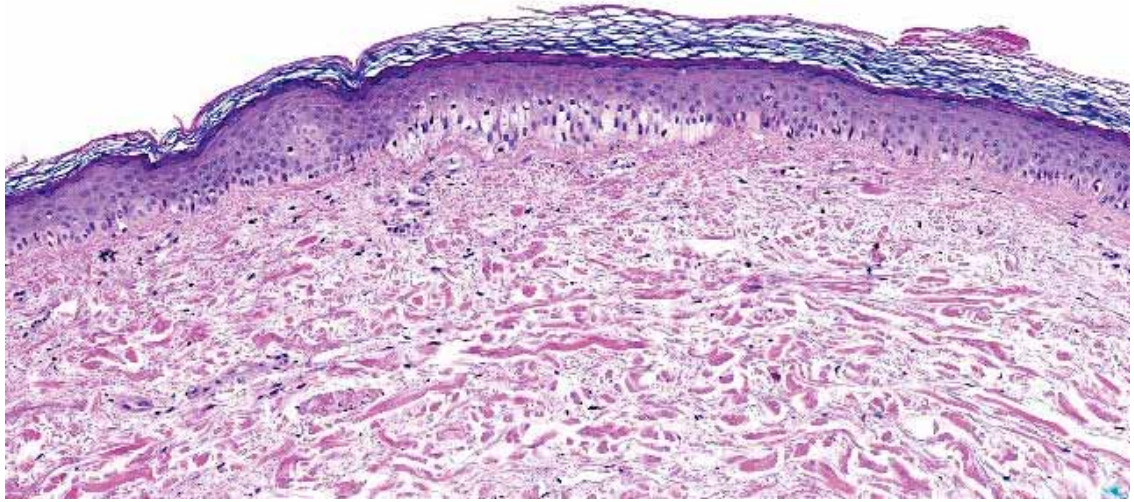
No vacuolization and clefting



Incidental finding:
Epidermolysis bullosa simplex-type vacuolization

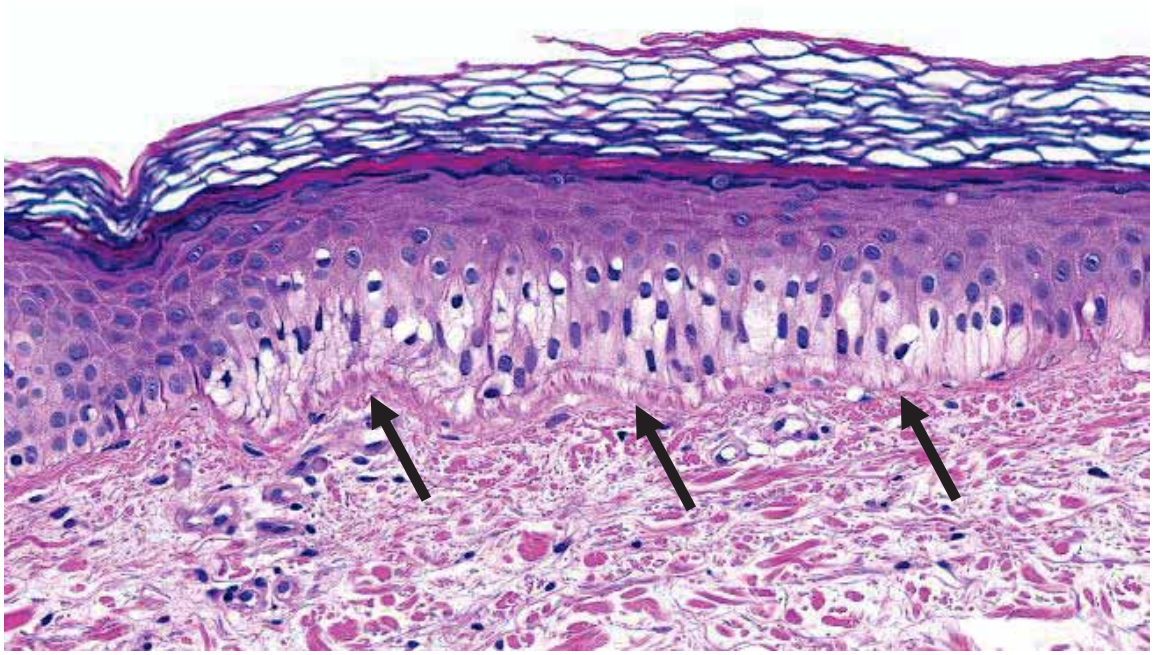
Lentiginous nevus, lower leg, 60-year-old man, no history of EB



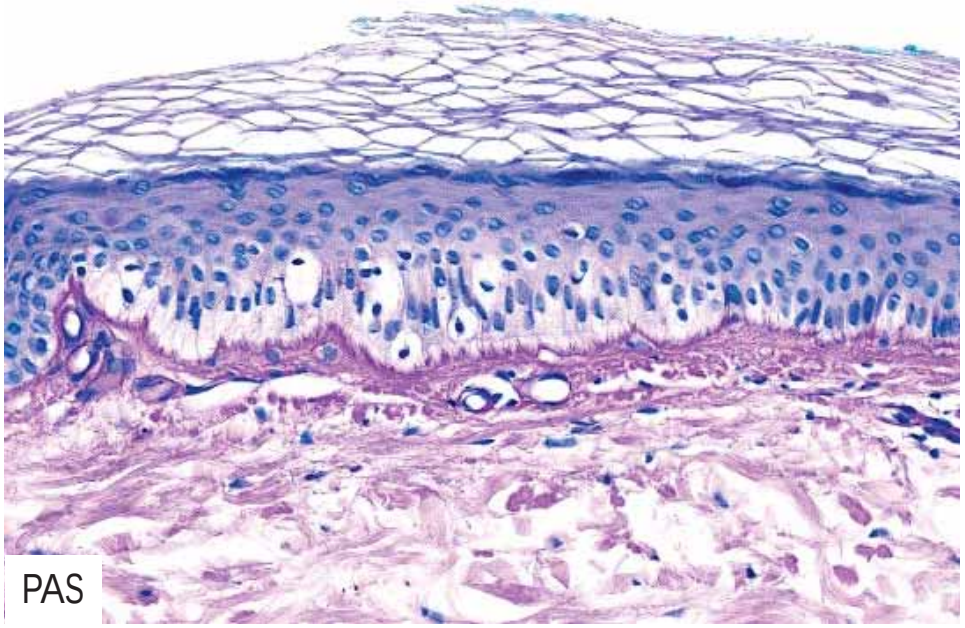


Cluster of clear cells in the basal epidermis
adjacent to a melanocytic nevus

Incidental finding:
Epidermolysis bullosa simplex-type vacuolization

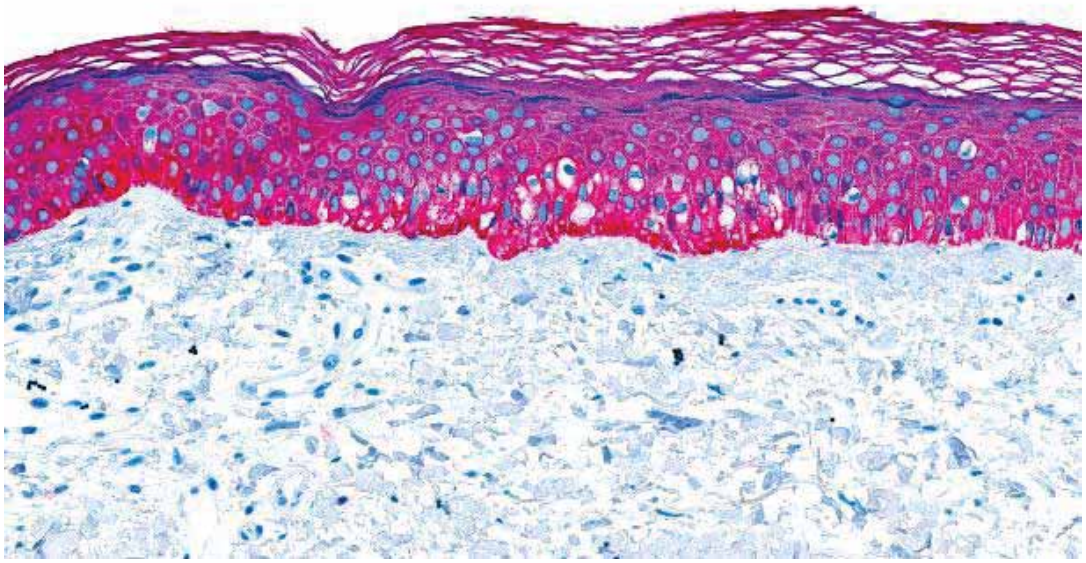


Vacuolization of basal keratinocytes,
baseline remains hypereosinophilic, fringe-like appearance

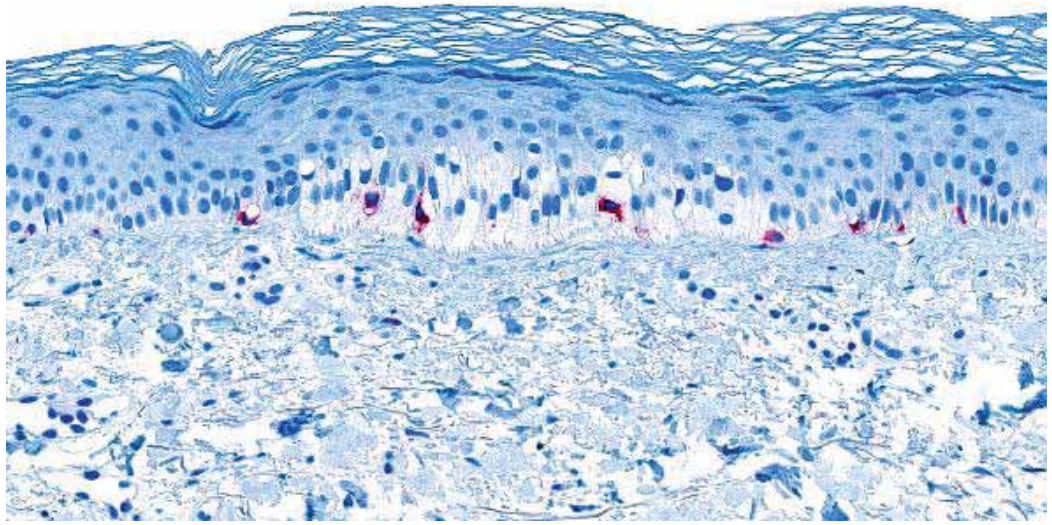


Intact basement membrane

Incidental finding:
Epidermolysis bullosa simplex-type vacuolization

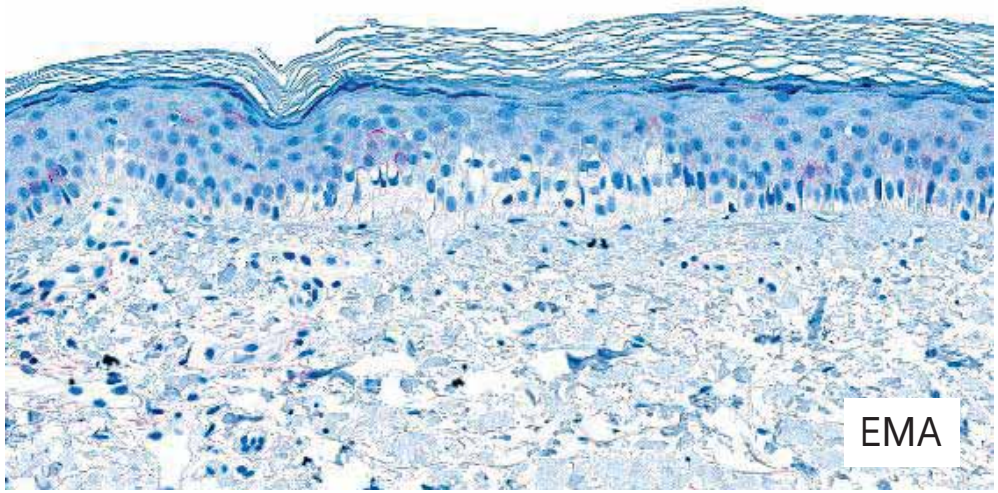


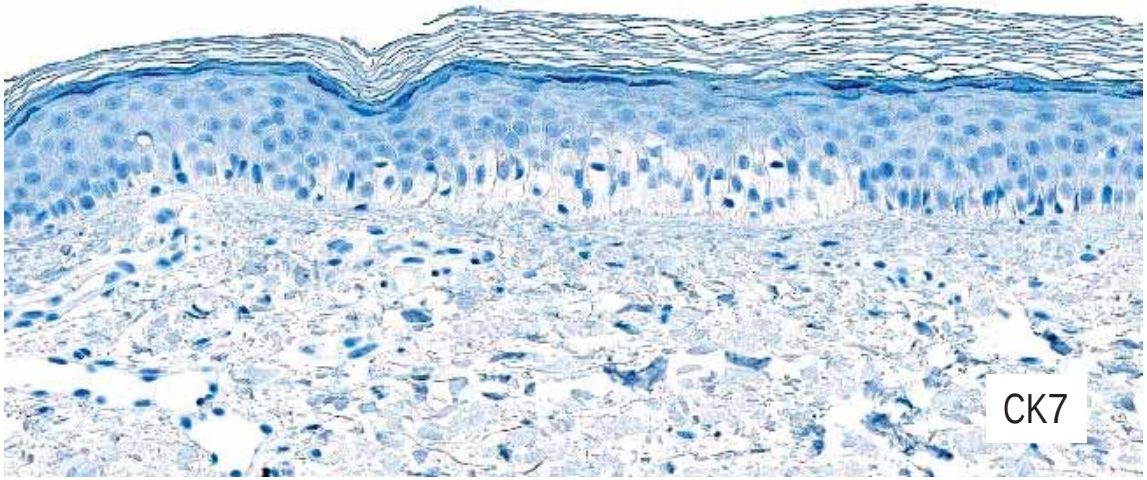
Pankeratin Immunostaining



MelanA immunostaining

Incidental finding:
Epidermolysis bullosa simplex-type vacuolization

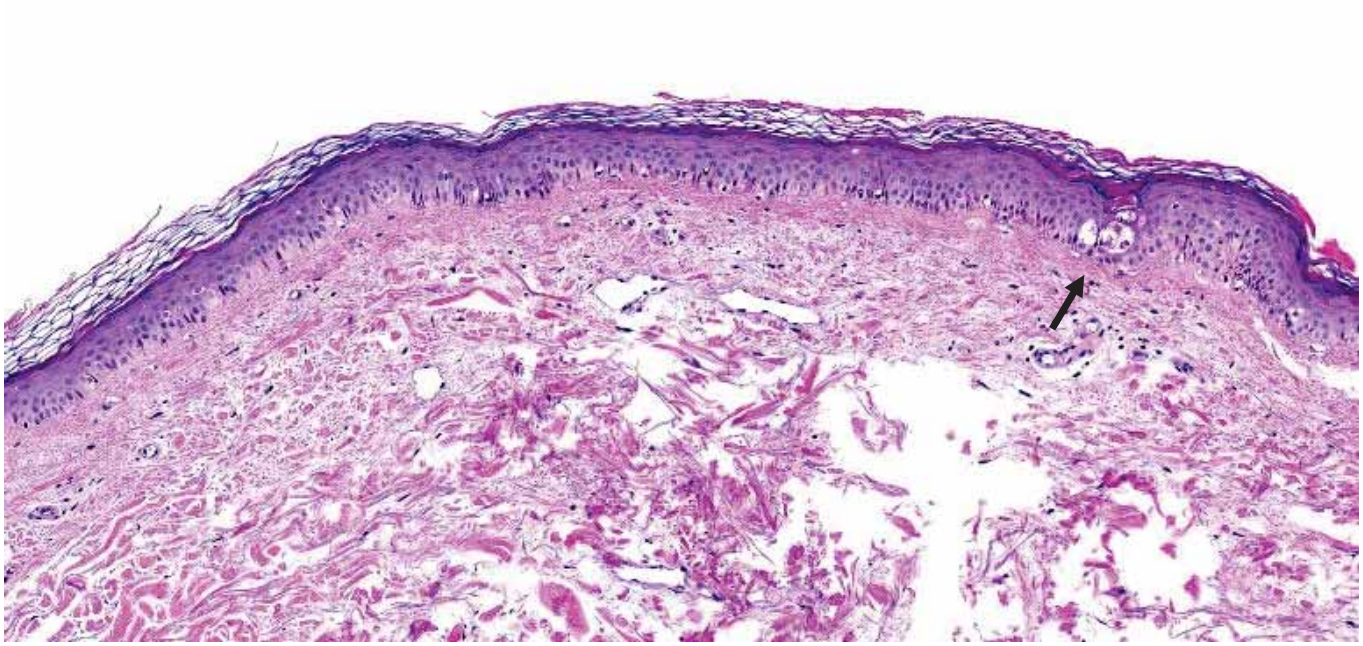


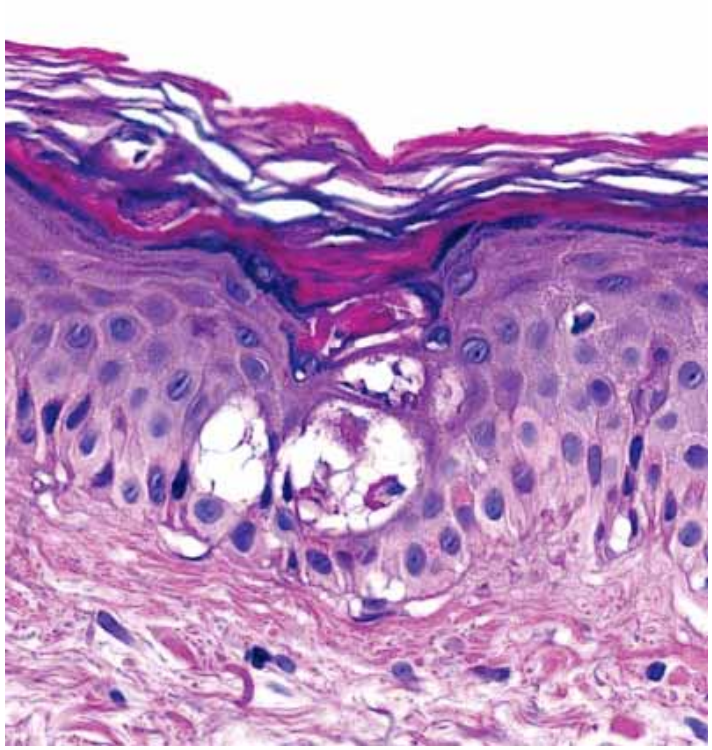


Negative: EMA, CEA, CK7, CK20

Incidental Epidermolytic Hyperkeratosis

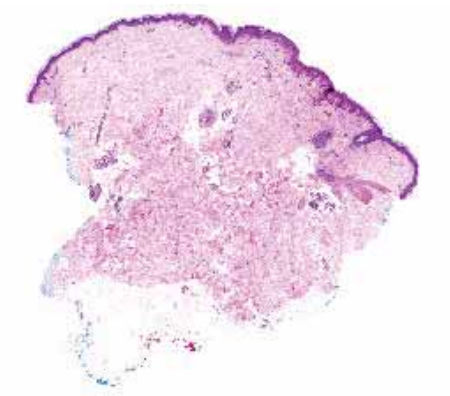
same lentiginous nevus, lower leg II

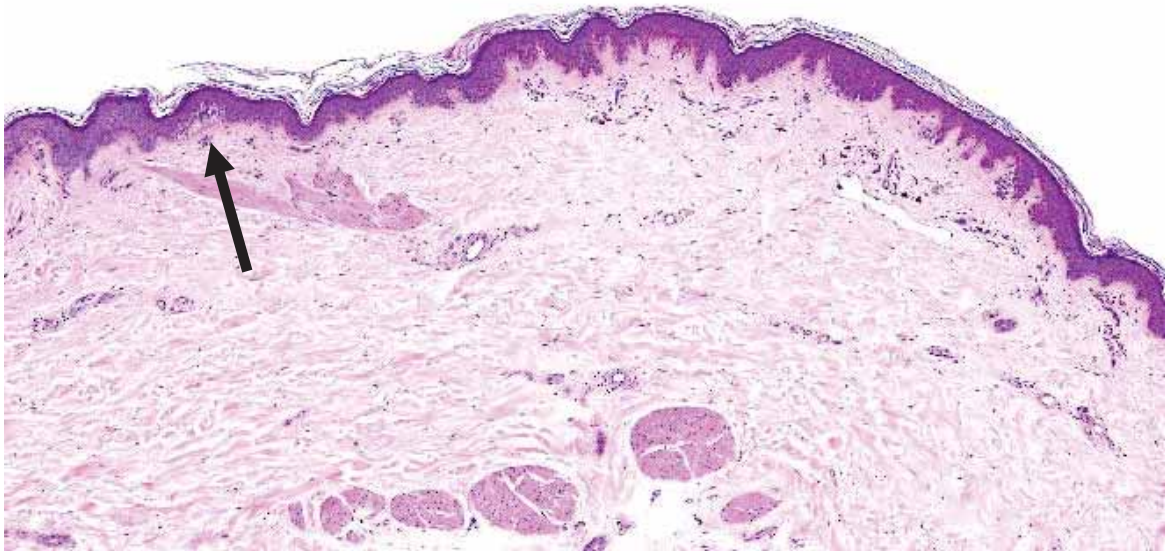


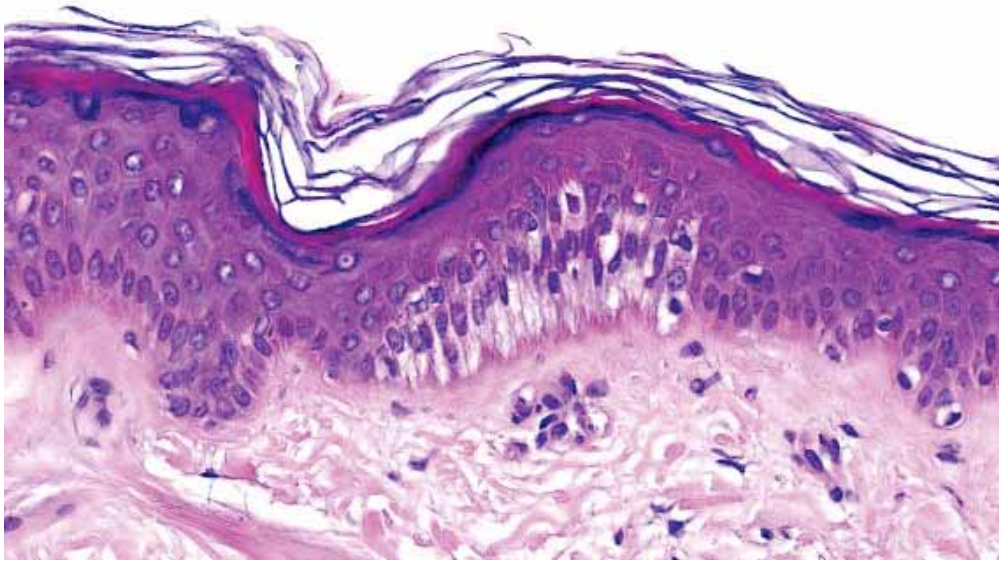


Incidental EB simplex-type vacuolization

Melanocytic nevus

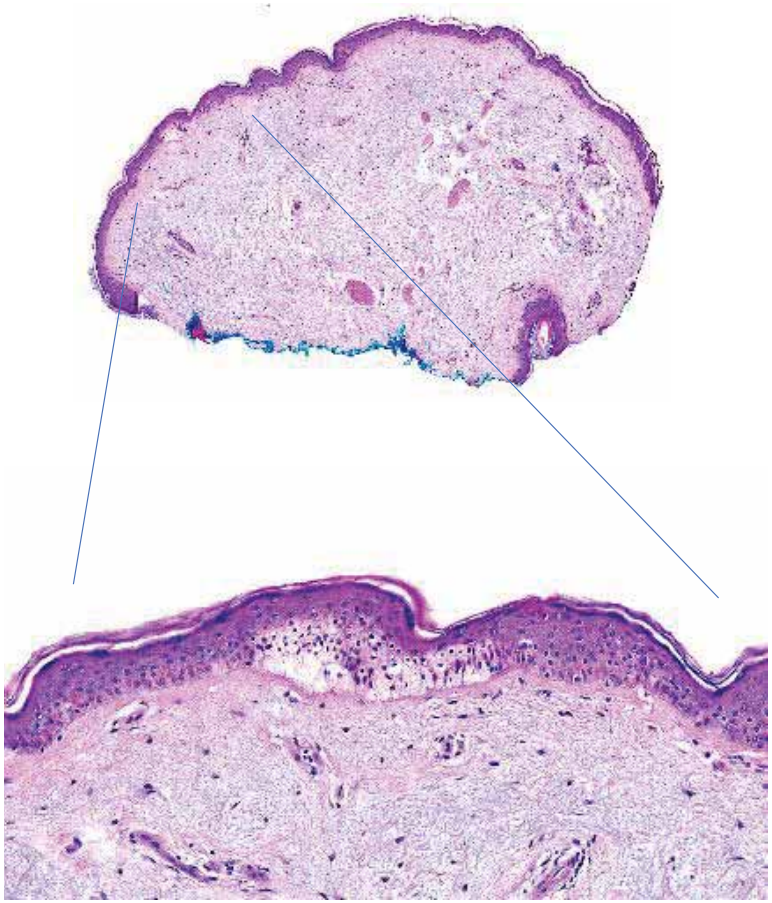


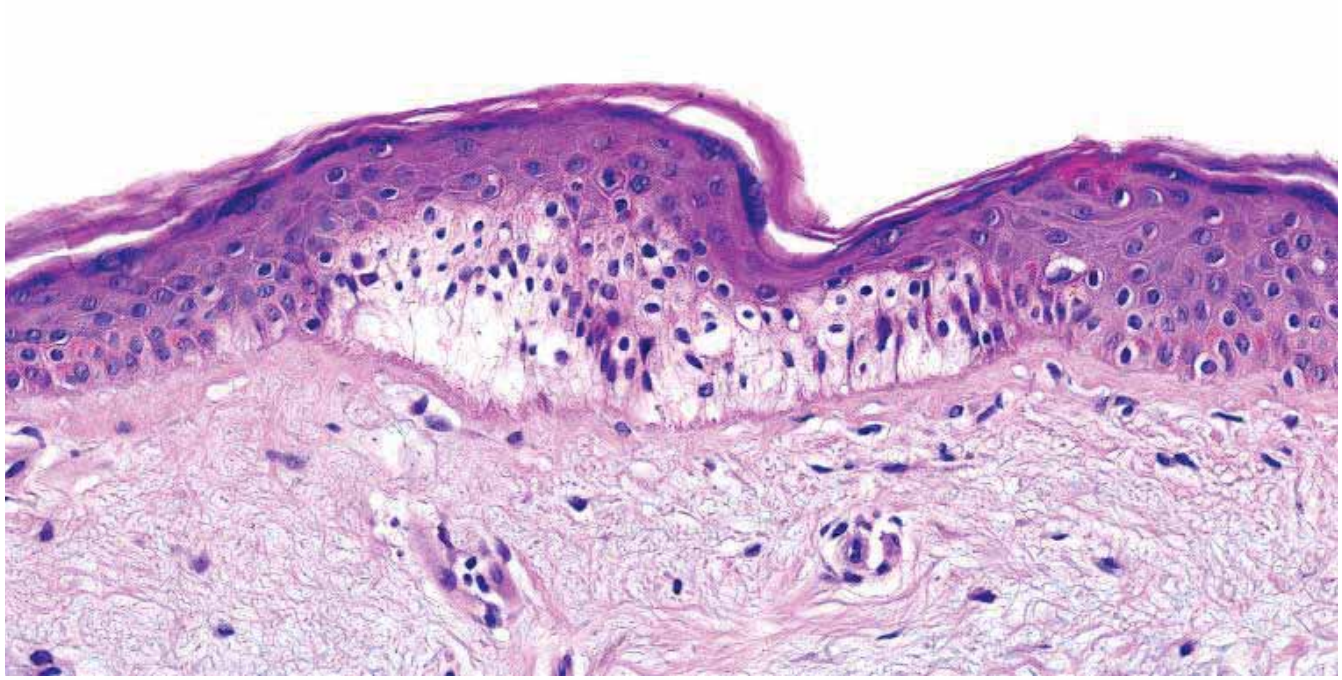




Incidental EB simplex-type vacuolization

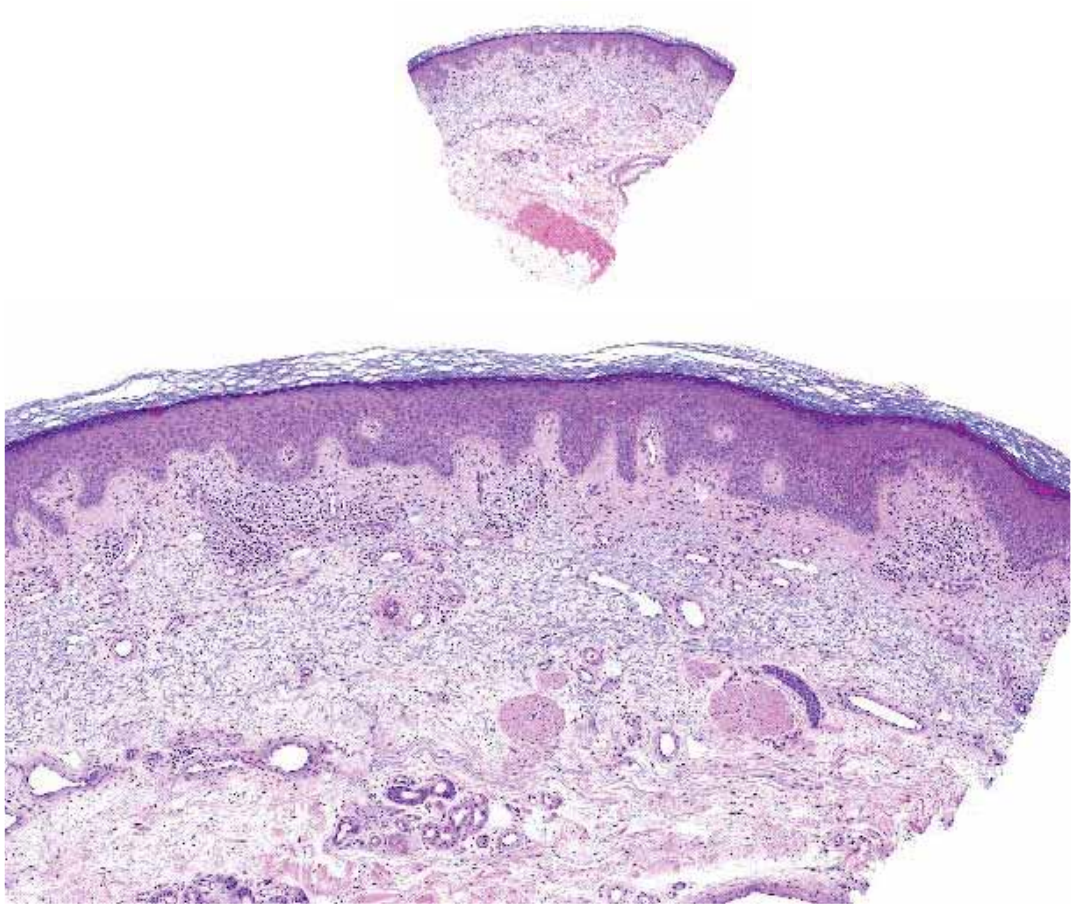
periphery of SCC



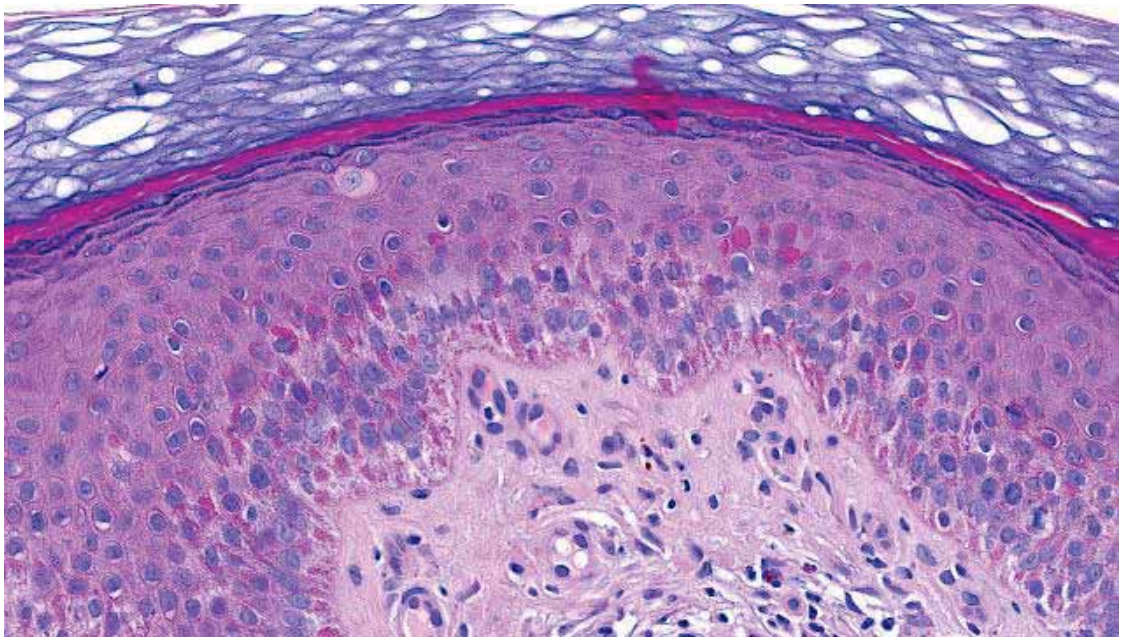


Incidental EB simplex-“suprabasal“ type vacuolization

Lichen simplex chronicus



Oblique section

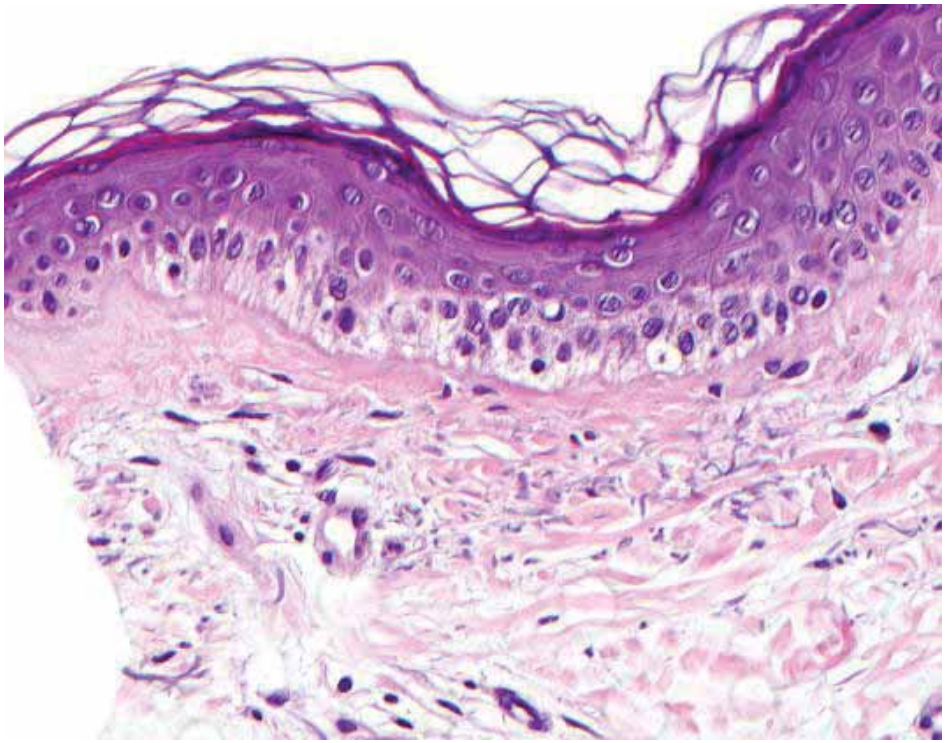


Incidental finding:
Epidermolysis bullosa simplex-type vacuolization

12 Cases
Melanocytic nevi (n=8), SCC (1), Bowen (1),
Angiosarcoma (1), Lichen simplex (1)

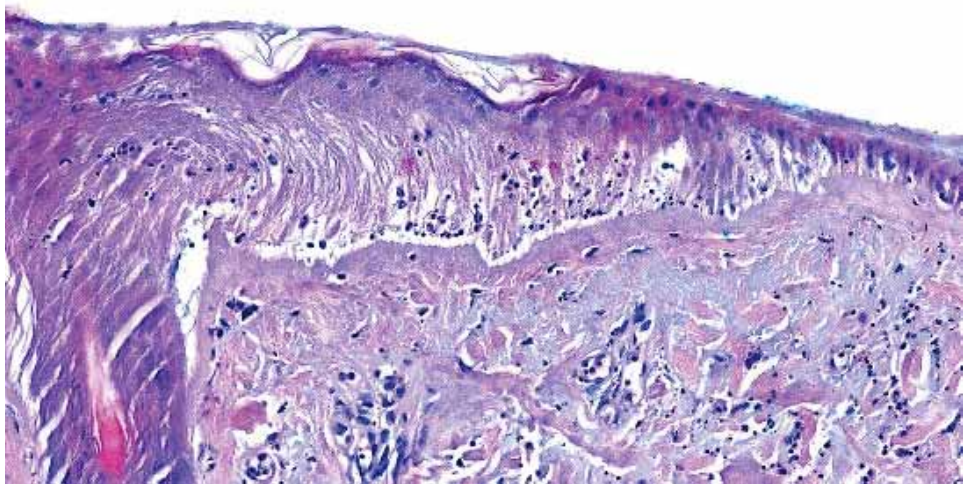
3 Laboratories
Processing artifacts unlikely (shrinkage artifacts, ...)

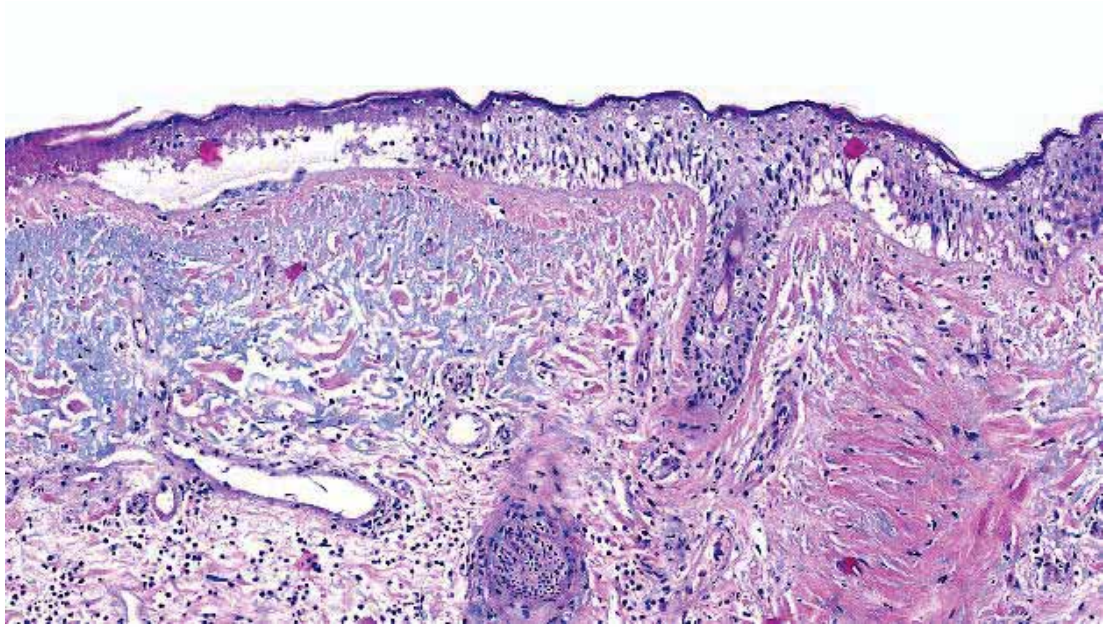
Dermatopathologie der Univ.-Hautklinik Münster (S. Braun)
Dermatohistologisches Labor Münster (M. Fülle)
MVZ Dermatopathologie Duisburg Essen (U. Hillen)



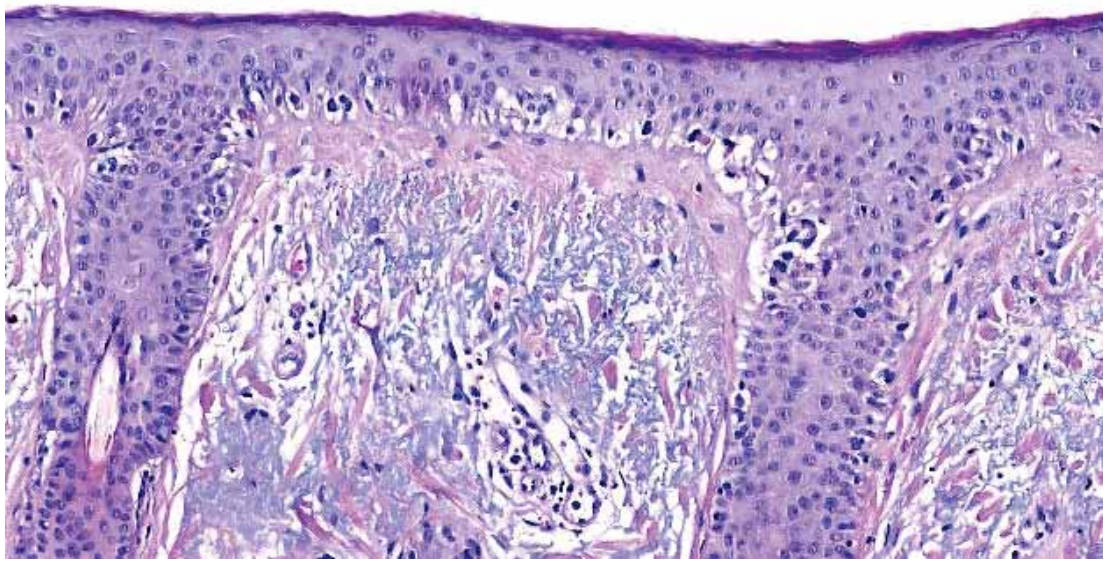
DDx
Electrocautery artifacts

Streaming of spindled hyperchromatic keratinocytes



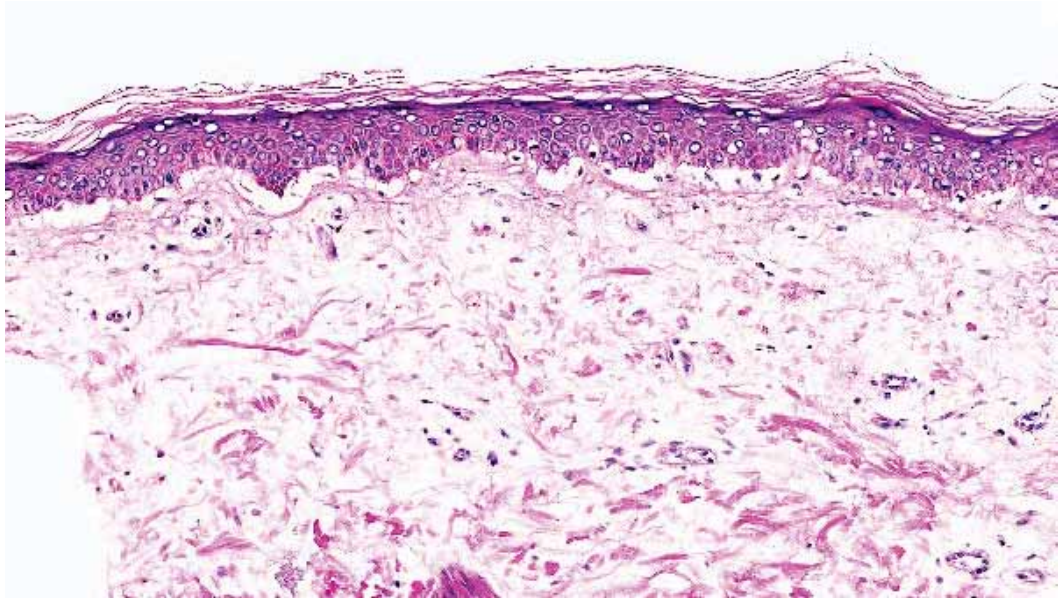


Clear cells and clefting in basal epidermis
without fringe-like appearance

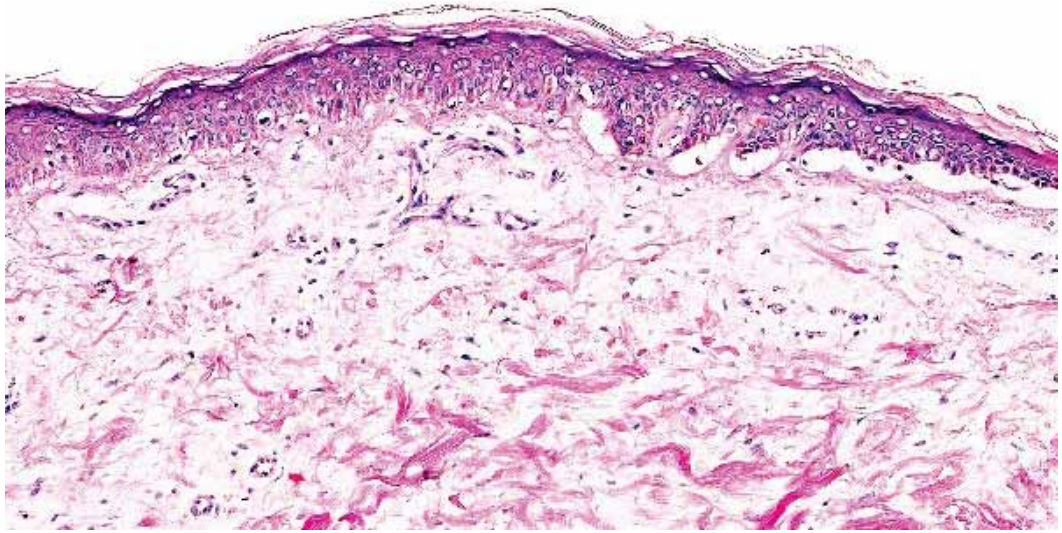


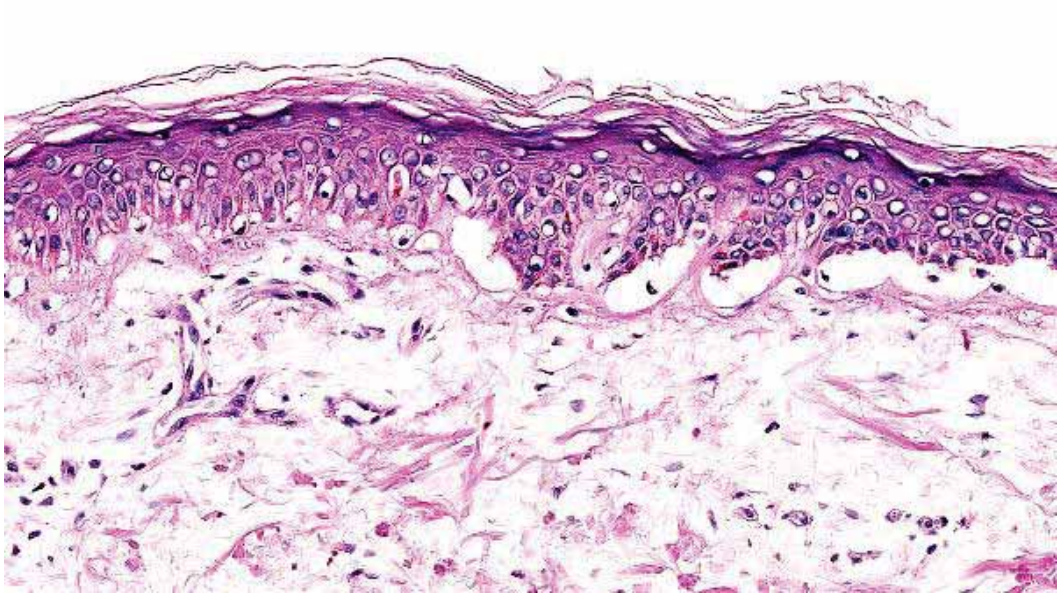
Split-skin

(re-embedding of
cryo section -> paraffin)

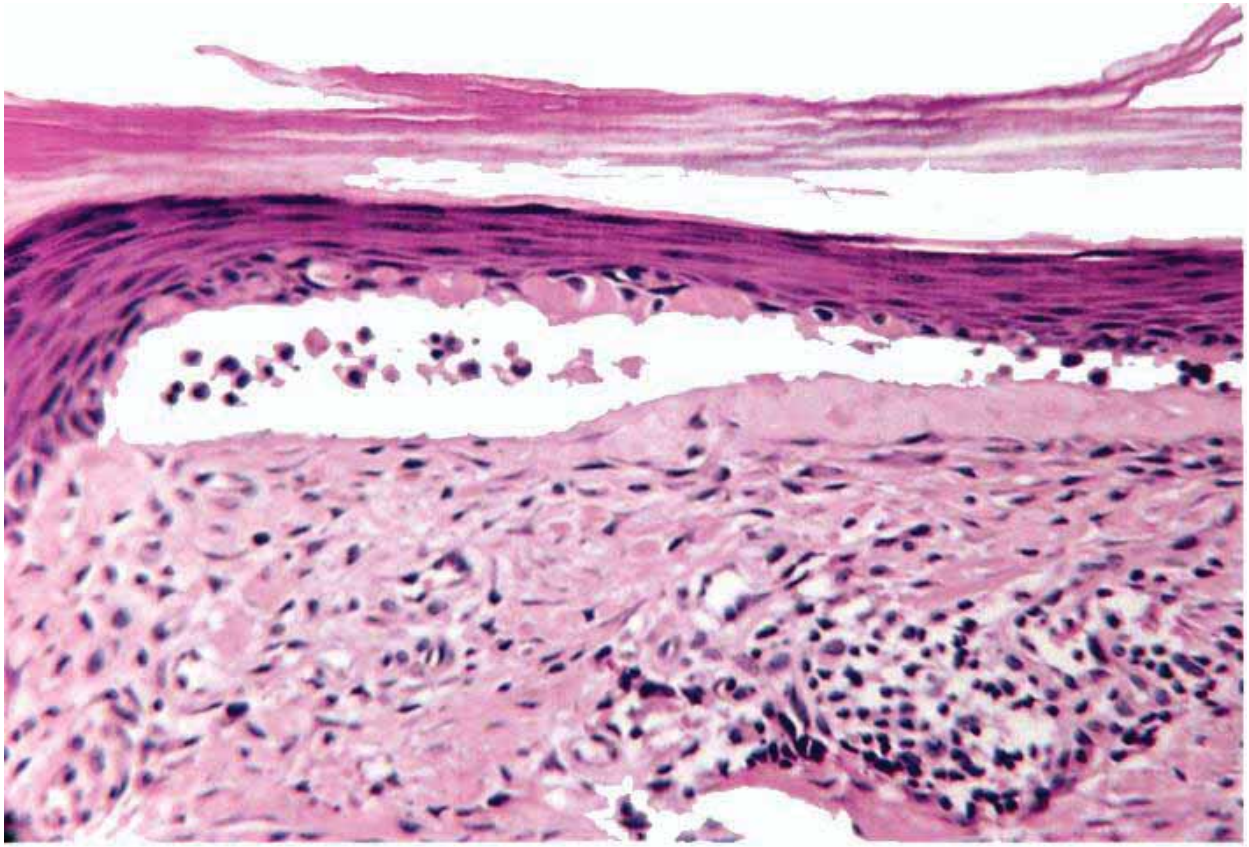


Subepidermal clefting





Blisters/subclinical clefting overlying scars



Subepidermal clefting overlying scar tissue. (H&E)

Subepidermal clefting without hypereosinophilic fringe-like appearance

dermal scar

Weddon´s Skin Pathology, 2026

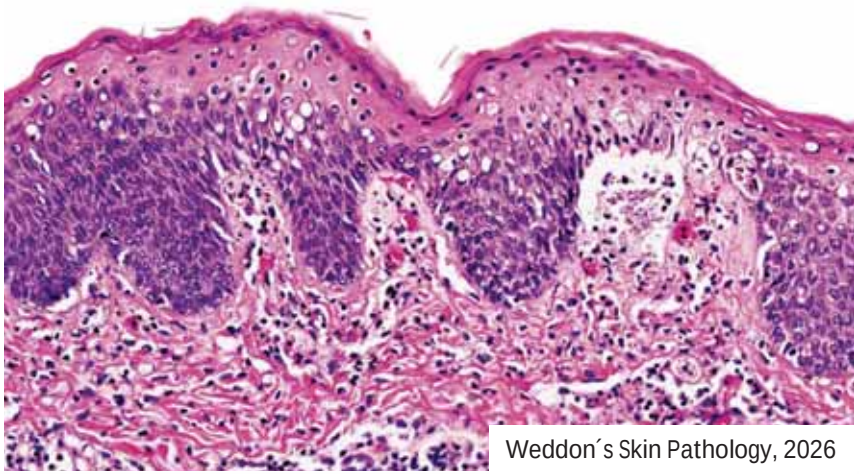
DDx
Clear cells in the epidermis

- Artefacts
- Clear cells in normal skin
- Pagetoid dyskeratosis
- Clear cell papulosis
- Seb keratoses, BCC, Bowen, ...

Irritant contact dermatitis

(EMLA© cream)

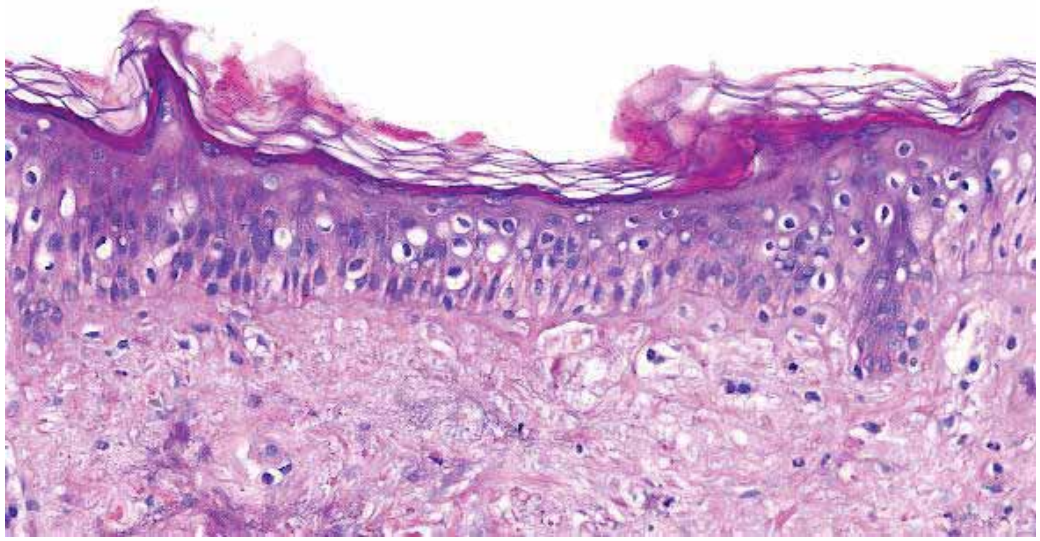
Pallor and necrosis in the upper epidermal layer

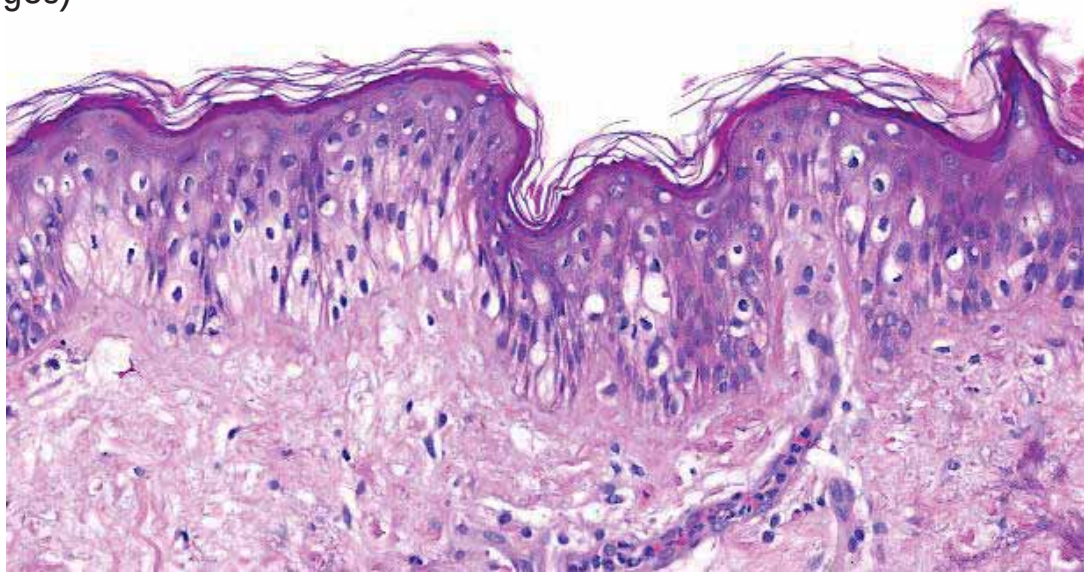


Weddon´s Skin Pathology, 2026

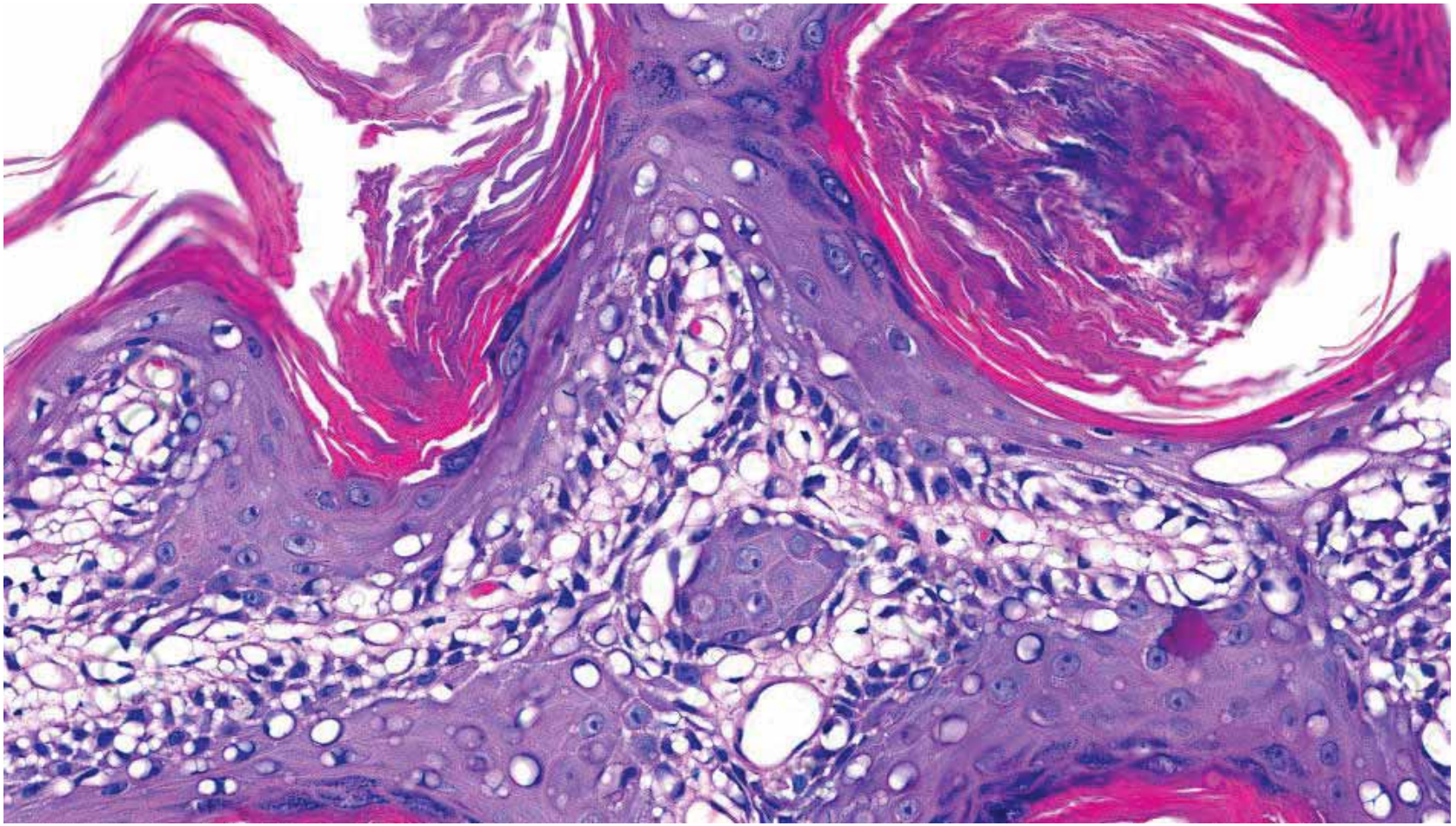
Vacuolization of keratinocytes

Vacuolar alteration DEJ
(no fringe-like changes)



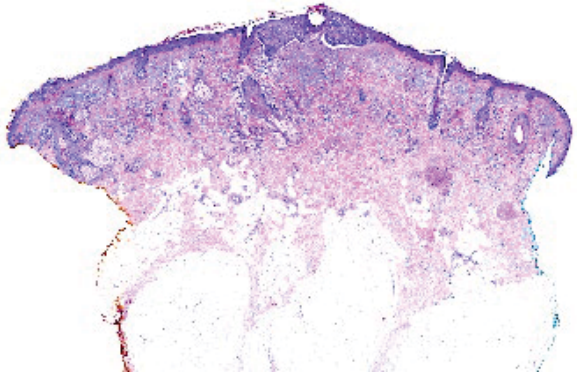


Freezing artifact (Winter Conditions during mailing)

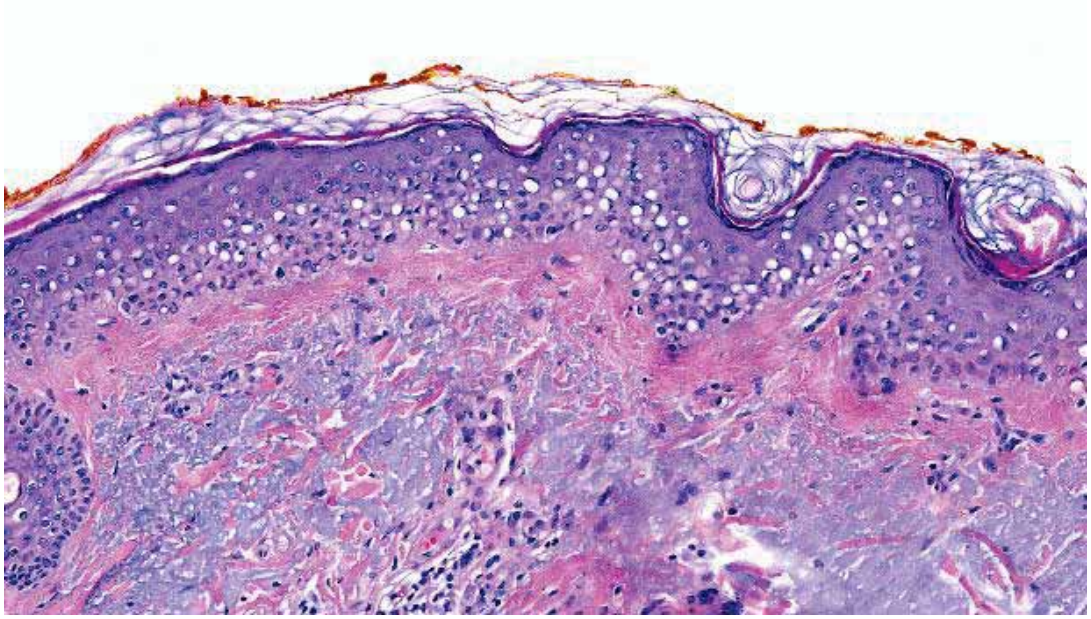


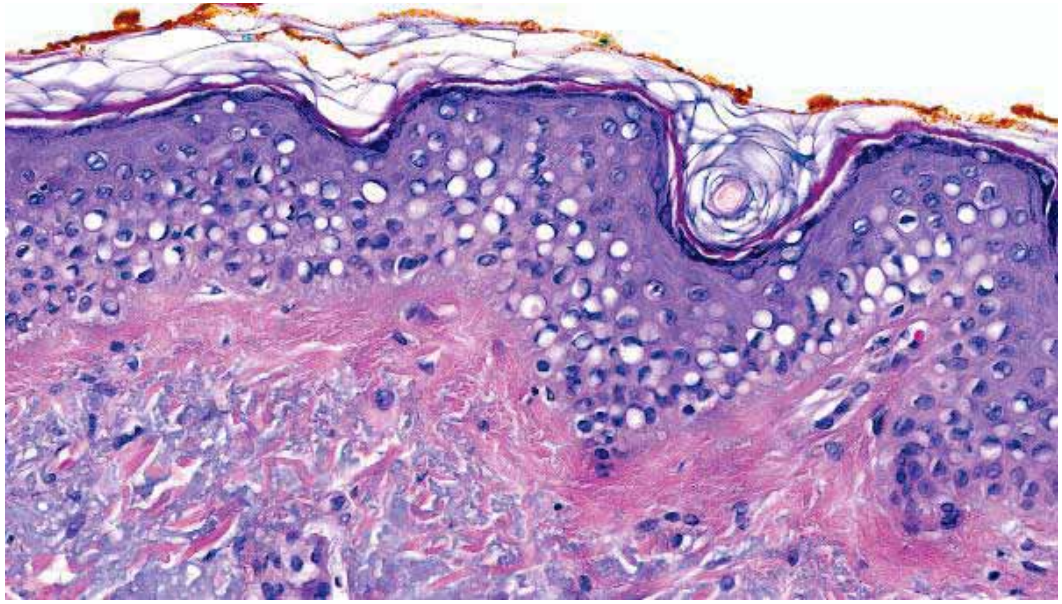
Formation of vacuoles, eccentric pyknotic nuclei, keratinocytes and dermal cells

Local anesthesia



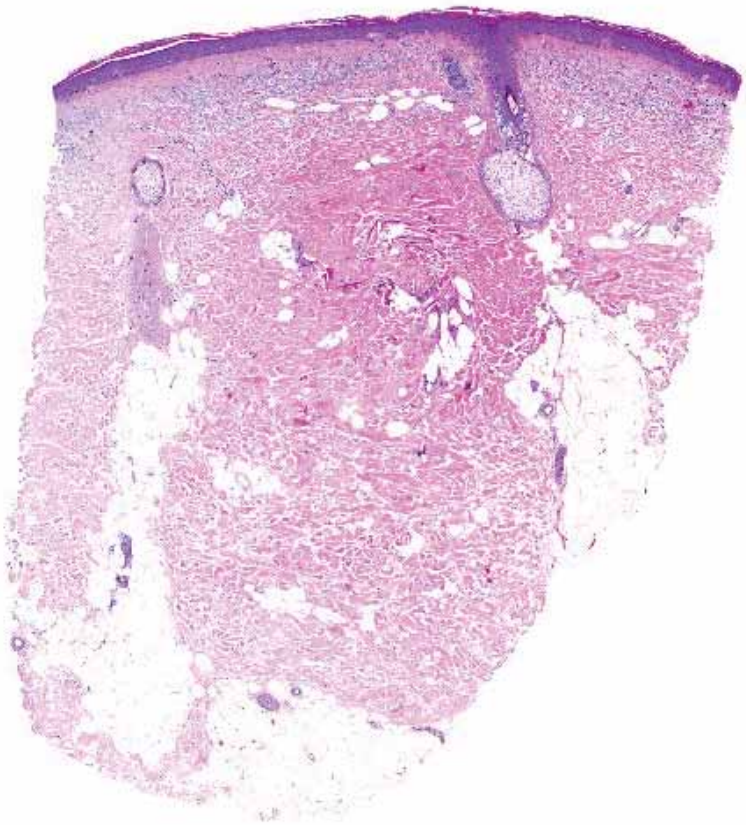
Keratinocytes with signet ring cell-like appearance

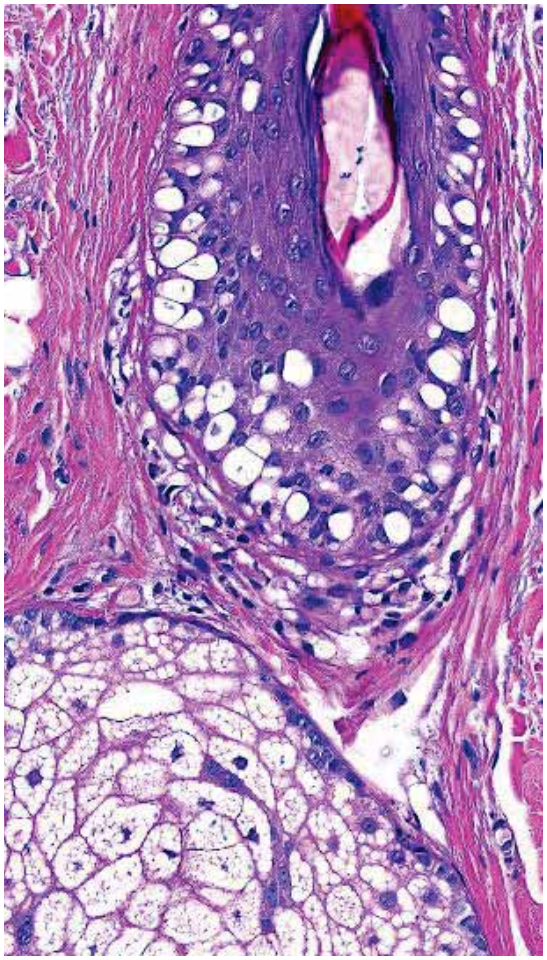




Hair infundibula with clear cells

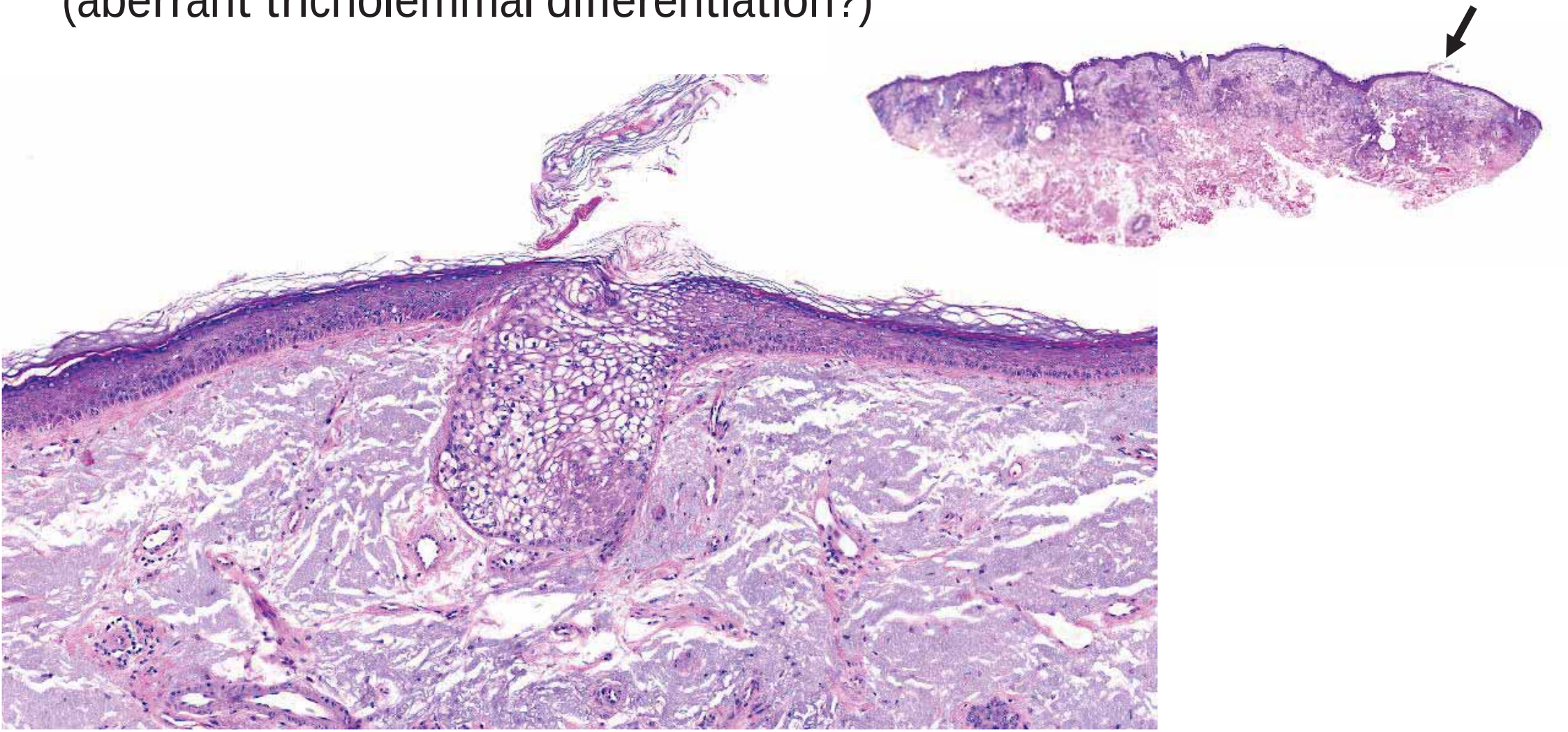
(aberrant tricholemmal differentiation?)





Hair infundibula with clear cells

(aberrant tricholemmal differentiation?)



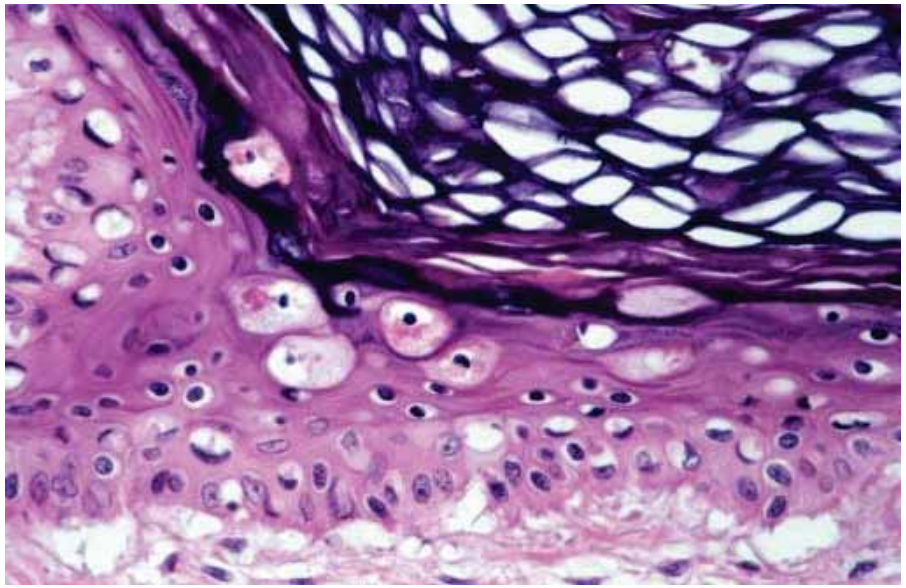
Pagetoid Dyskeratosis

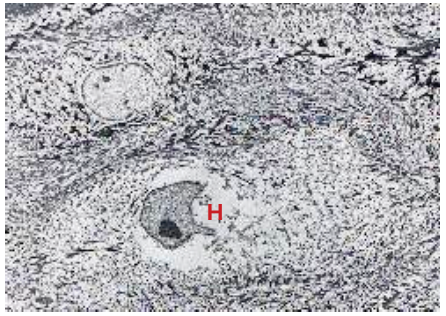
Incidental histologic finding with no clinical relevance due to friction and maceration

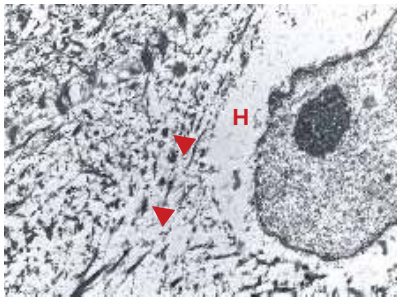
- Large body folds
- Exophytic skin tumors
- Volar skin (clinically pigmented lesions !)
- Mucous membranes

DDx Toker cells, clear cell papulosis, Paget's disease (Cytology, IHC)

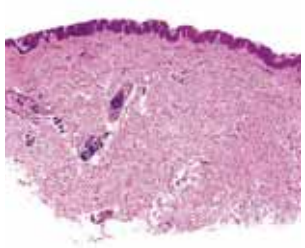
Mehregan, 1980 Tschen, 1988 Val-Bernal et al, 2000



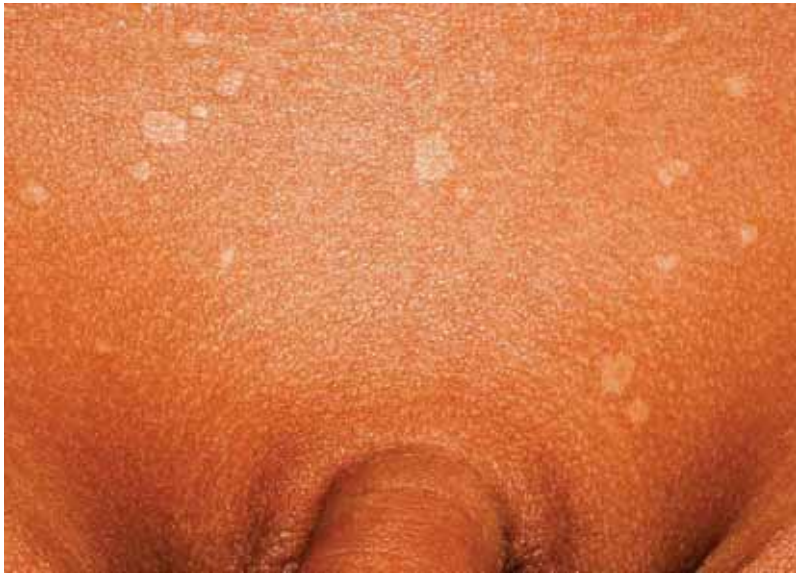


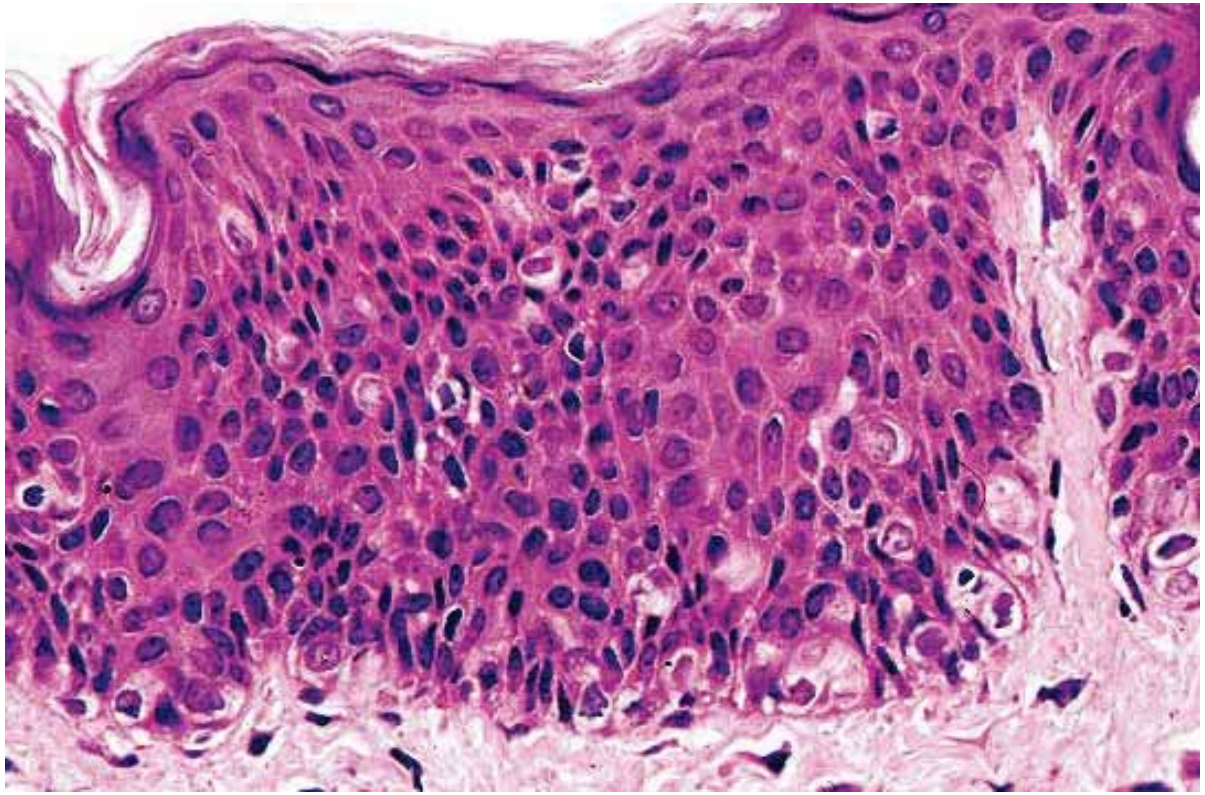


Clear cell papulosis



H. Kerl

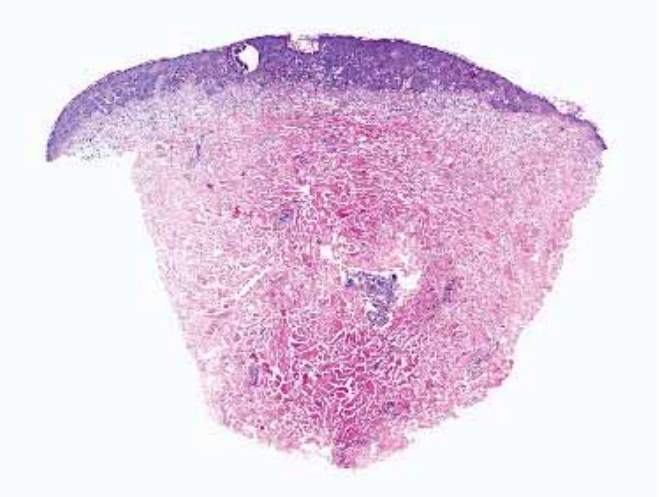


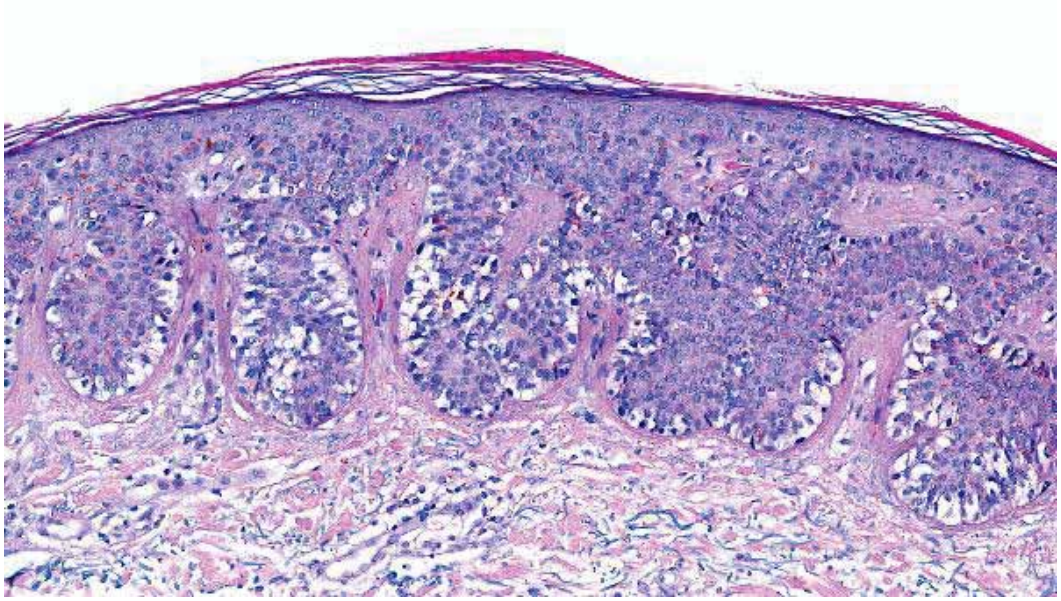


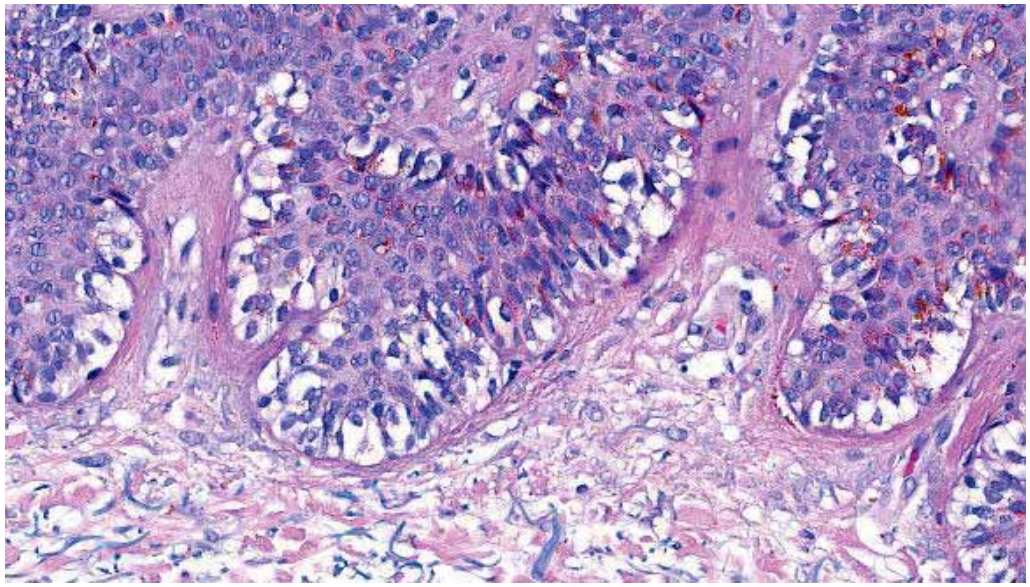
Hypopigmented macules or flat papules, lower abdomen and along the milkline, young children

Toker cell hyperplasia ?

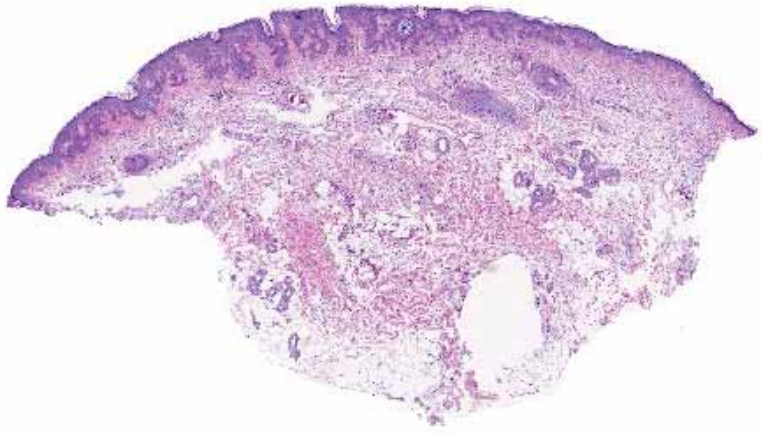
Seborrheic keratosis with basal, pigmented clear cells

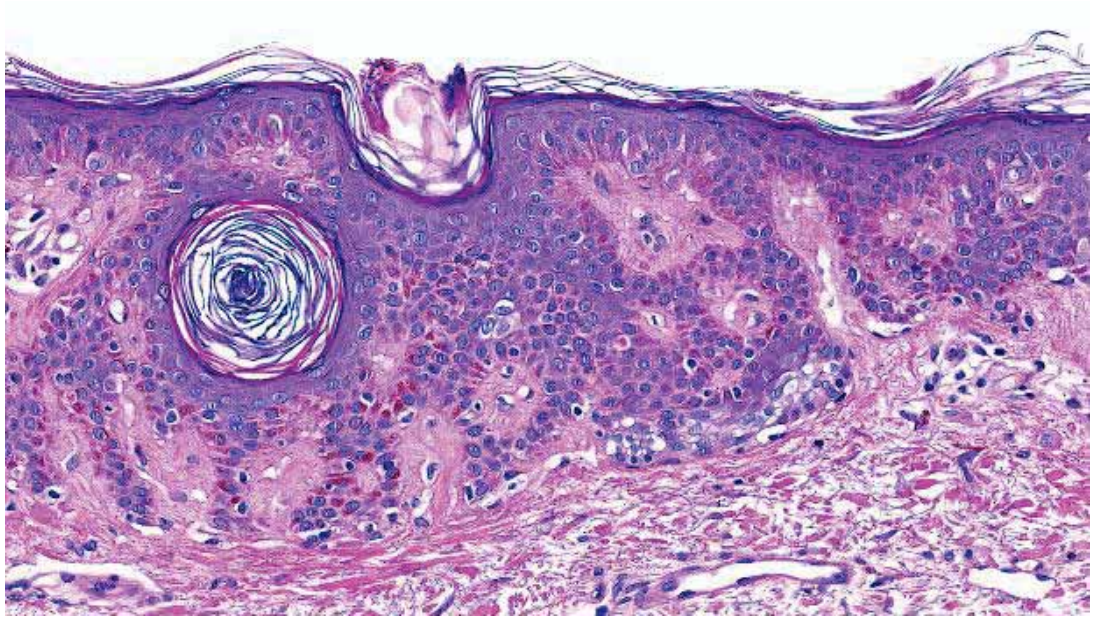


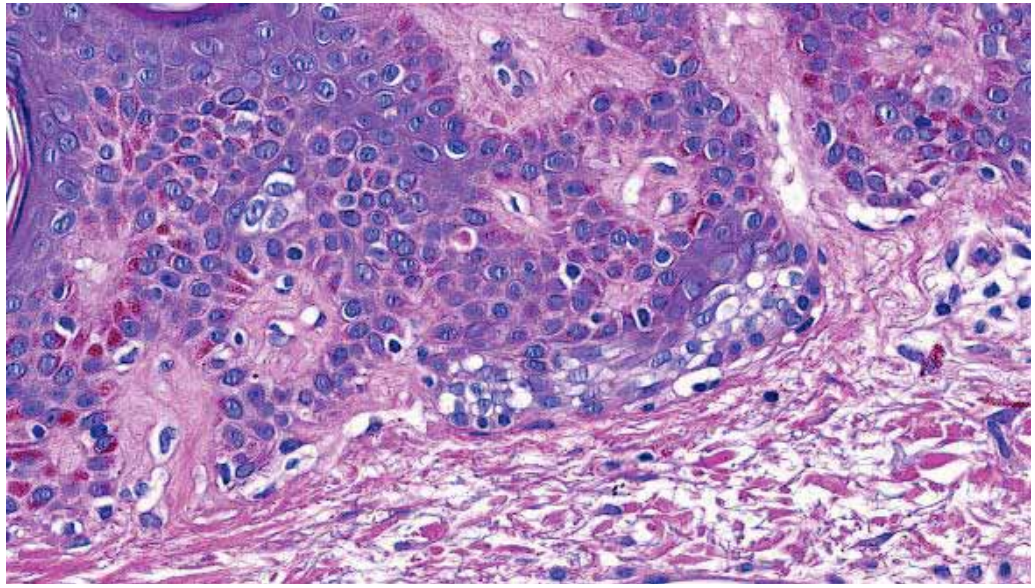




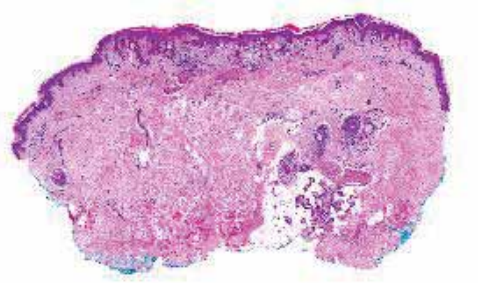
Seborrheic keratosis with basal, pigmented clear cells

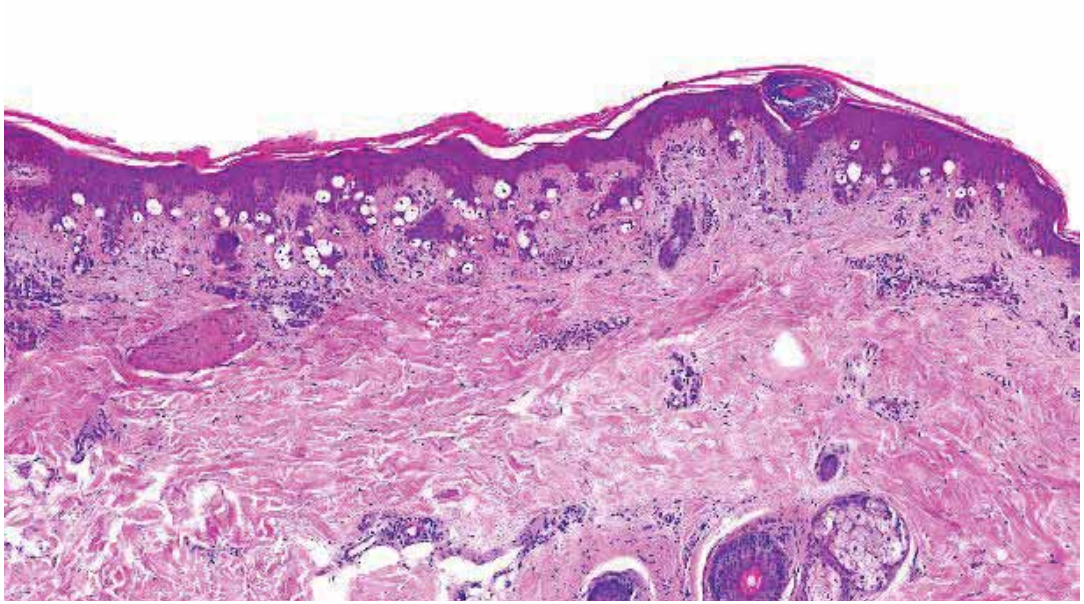


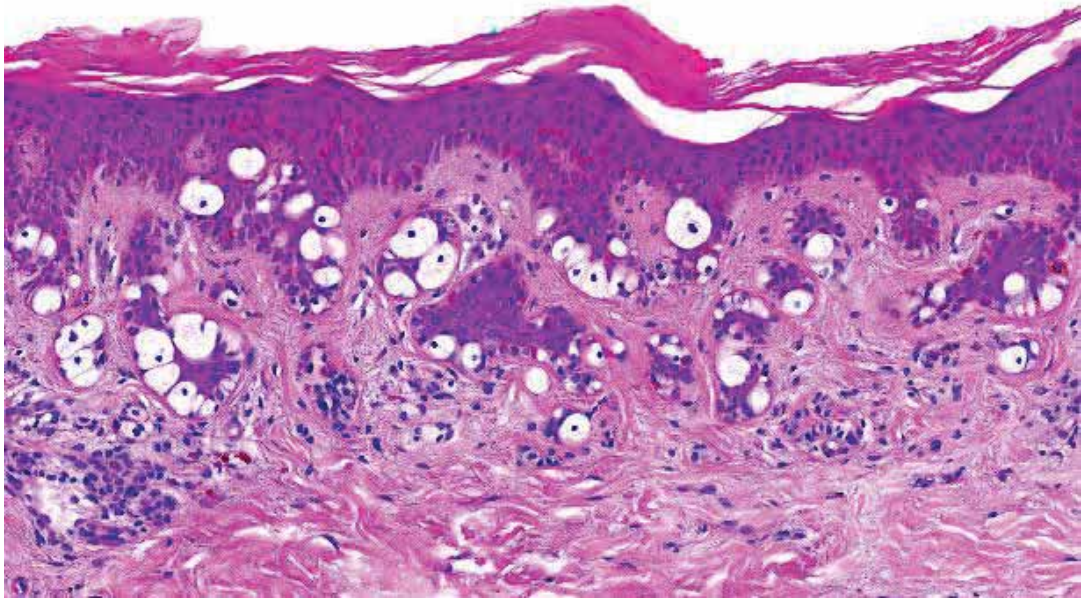


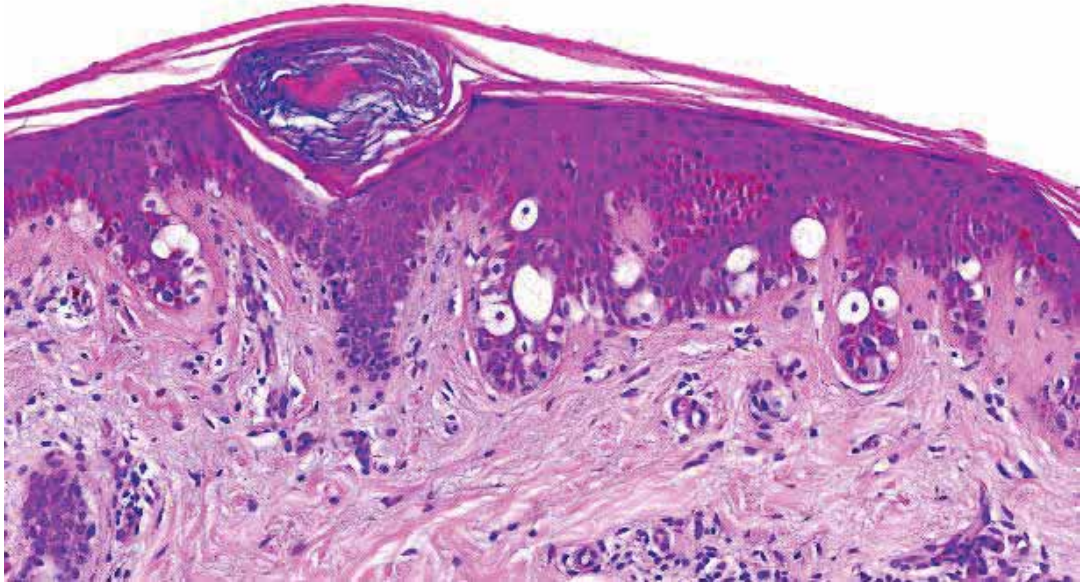


Melanocytic nevus with clear melanocytes

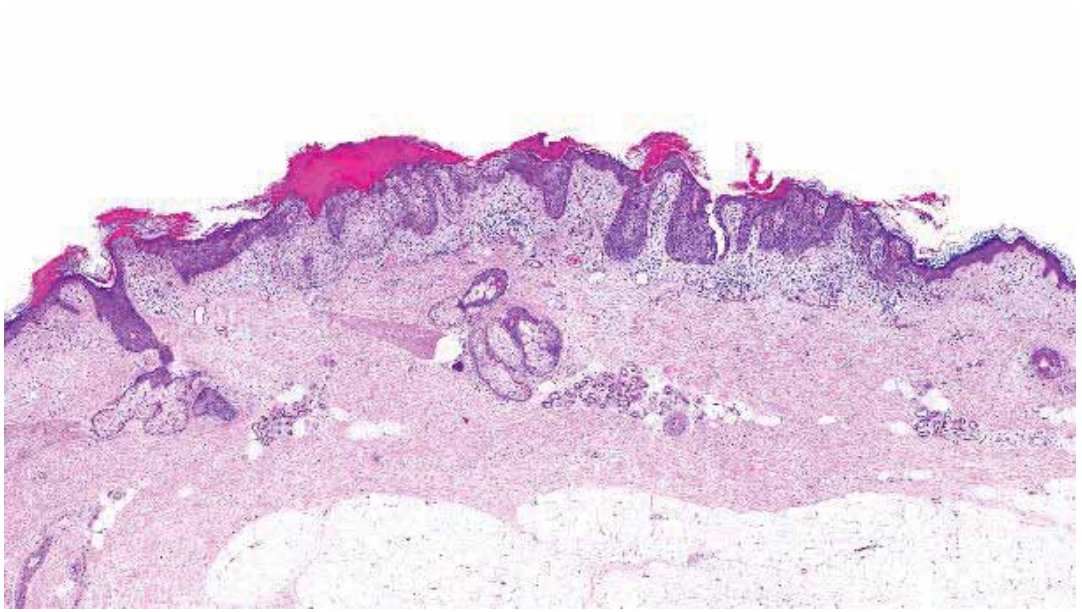


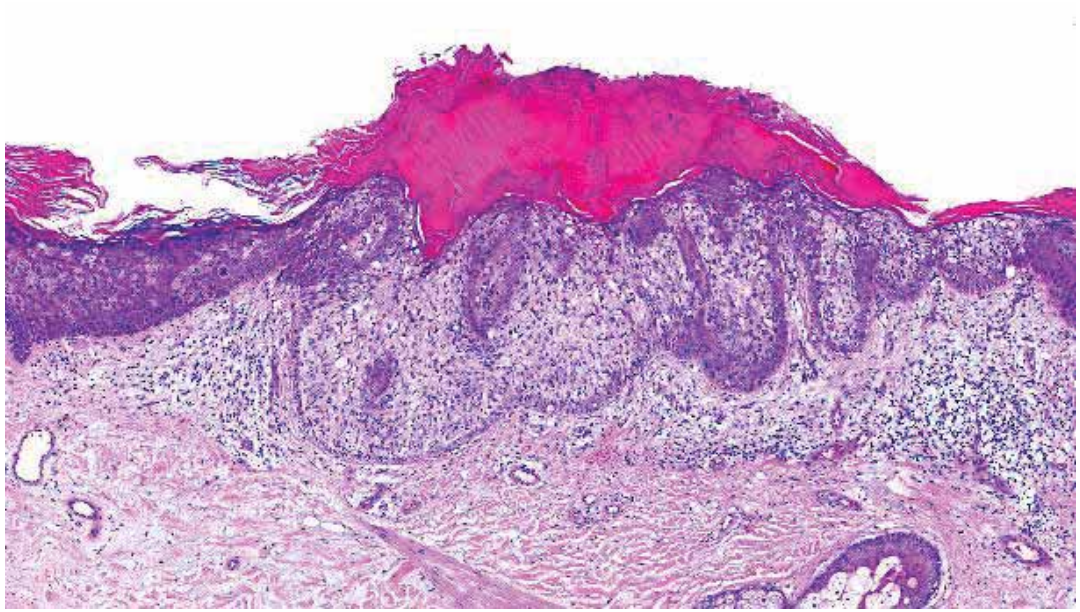


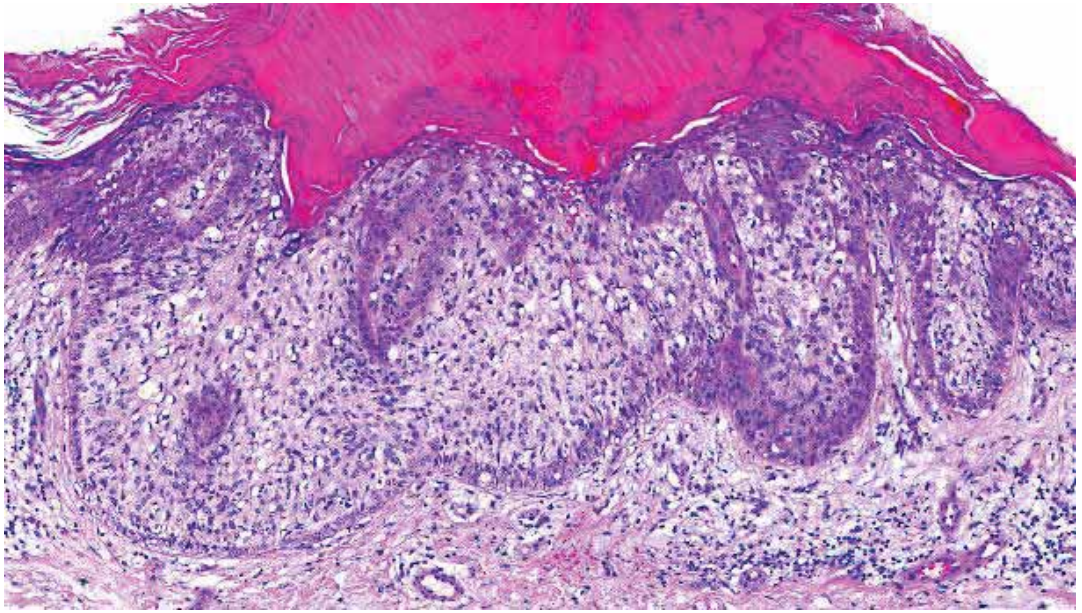




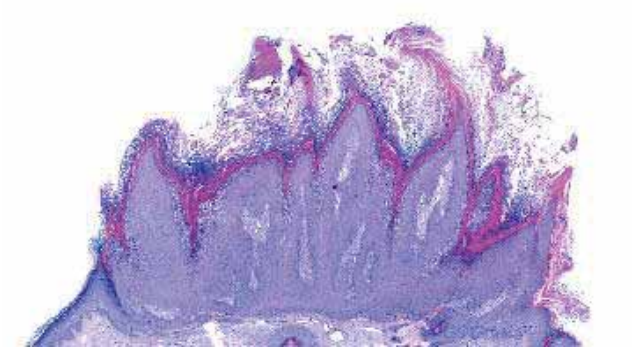
Bowen disease with clear cells

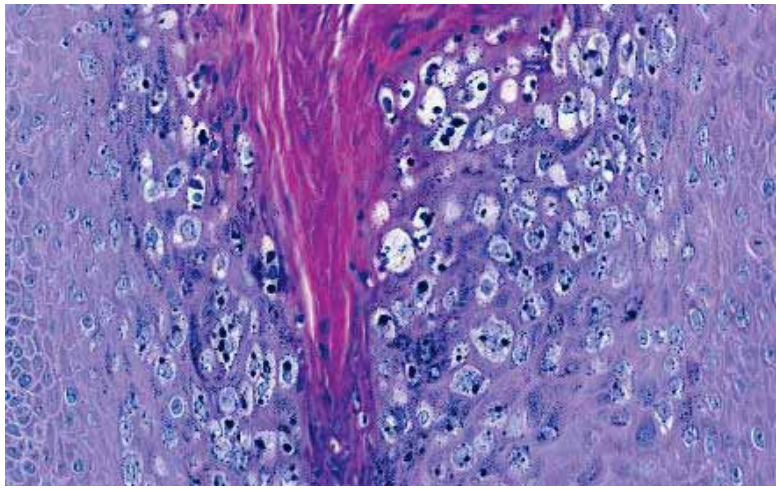


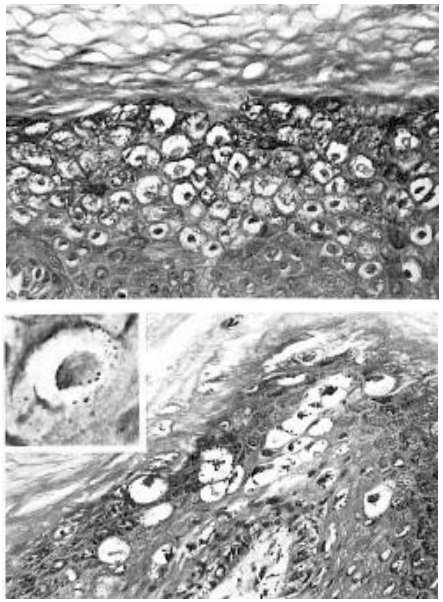


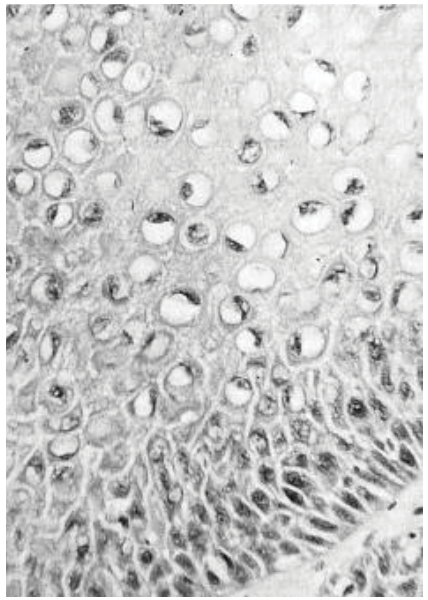


Cytopathic changes in HPV









#4
Vacuolized cells with fine granules /„bird eyes“

#5
Vacuoliced cells with marginal sickle-shaped nuclei

Stephan A. Braun, *Joint Meeting of the ISDP, Orlando, 2025*

Gross et al., J Invest Dermatol 1982

Epidermal reaction patterns
in genodermatoses, epidermal nevi, acquired skin diseases or as an incidental finding

Pattern	Dermatosis	Mosaicism	Solitary lesion	Incidental finding
Epidermolytic hyperkeratosis	Keratinopathic Ichthyosis, Palmoplantar Keratoderma	+	Epidermolytic acanthoma	+
Focal acantholytic dyskeratosis	M. Darier	+	Acantholytic dyskeratotic acanthoma	+
Hailey–Hailey–type acantholysis	M. Hailey–Hailey	+	Hailey–Hailey–type acanthoma	+
Desmosomal-type acantholysis	Genetic diseases with desmosome related mutations	?	Desmosomal-type acanthoma (Hyaline inclusion acanthoma)	+
Epidermolysis bullosa simplex-type vacuolization	Epidermolysis bullosa simplex	+	?	+
Granular Parakeratosis	Granular parakeratosis	-	Granular parakeratotic acanthoma	+
.....				

Catherine Stefanato

www.intsocdermpath.org

Interactive Online Course: Basics in Dermatopathology

10/11 and 17/18 November 2027

D. Metze, S. Braun

Thank you
For your
attention

Warm regards

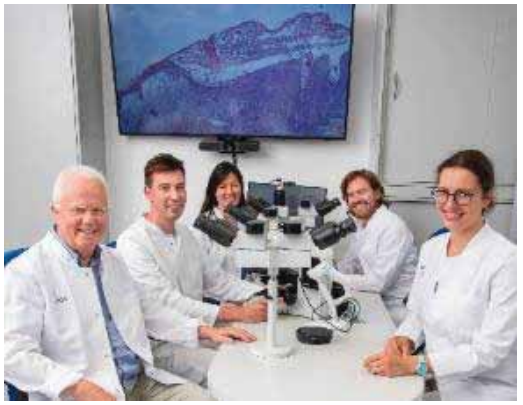
from Münster

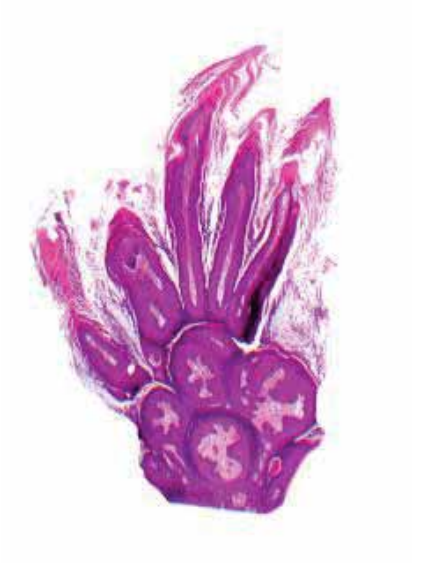
EUROPEAN SOCIETY OF DERMATOPATHOLOGY

2st European Joint Meeting of the International Society of Dermatopathology (ISDP): A Pre-Congress Event of ESP

12 September 2026, Stockholm

Maite Fernández-Figueras, D. Metze





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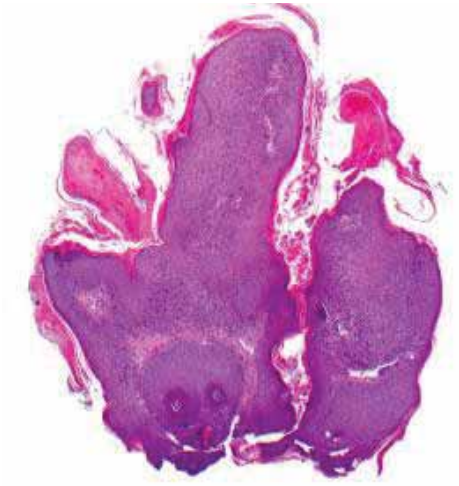

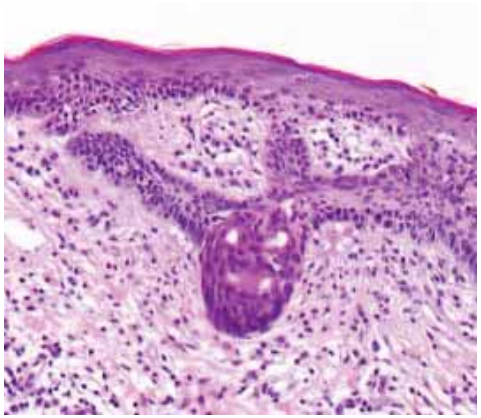

The Epidermis – a Mystery