

Porokeratosis



D. Metze

SPECIALTY TRAINING CENTRE IN DERMATOPATHOLOGY

DERMATOLOGY UNIT

DEPARTMENT OF DERMATOLOGY, UNIVERSITY OF MÜNSTER



Porokeratosis

History (“Poro-”) and Definition (“Cornoid Lamella”)

Histology and Clinical Aspects

Genetic Background and Pathophysiology

Classical and Rare Variants

Differential Diagnoses



Review

Porokeratoses—A Comprehensive Review on the Genetics and Metabolomics, Imaging Methods and Management of Common Clinical Variants

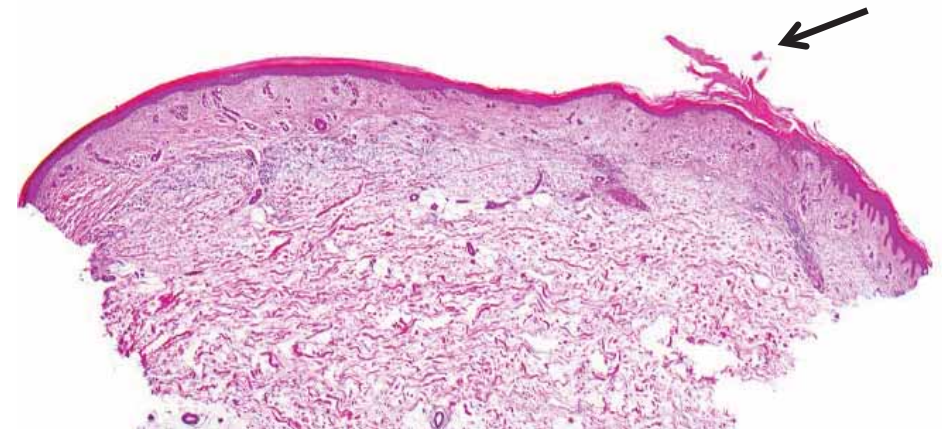
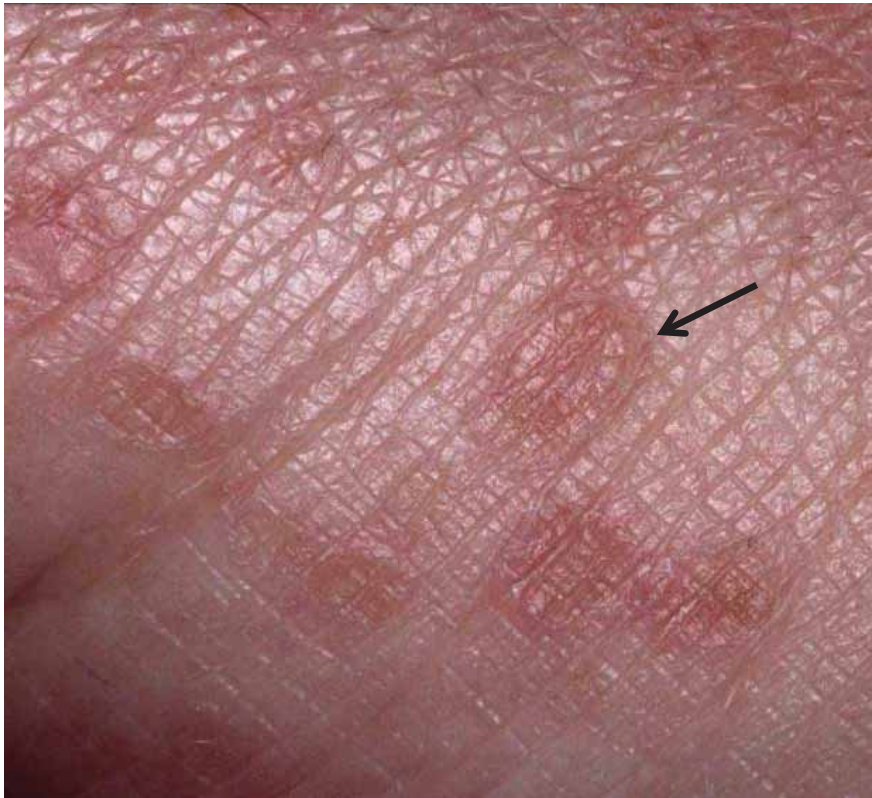
Pawel Pietkiewicz ^{1,2,*}, Katarzyna Korecka ^{2,3}, Natalia Salwowska ^{2,4}, Ihor Kohut ⁵, Adarsha Adhikari ⁶, Monika Bowszyc-Dmochowska ⁷, Anna Pogorzelska-Antkowiak ⁸ and Cristian Navarrete-Dechent ⁹

Download lecture

Porokeratosis

„Poro“, ostia sweat glands

Cornoid Lamella



Mibelli V. Contributo allo studio della ipercheratosi dei canali sudoriferi. G Ital Mal Ven, 1893

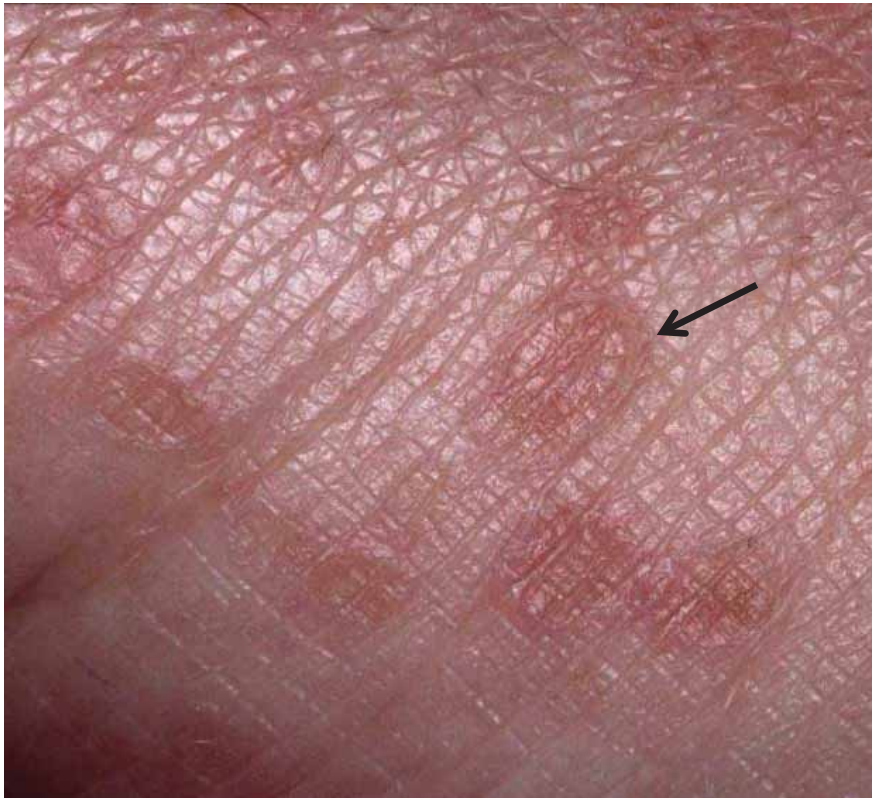
Mibelli, V. Ueber einen Fall von Porokeratosis mit Localisation im Munde und an der Glans. Arch. Dermat. Syph. 1899

Neumann, I. Uber Eine noch wenig bekannte Hautkrankheit (Dermatitis Circumscripta Herpetiformis). Vierteljahrsschr. Dermatol.Syph. 1875.

Respighi, E. Di Une Ipercheratosi Non Ancora Descritta. G. Ital. Dermatol. Venereol., 1893

Porokeratosis

Cornoid Lamella



Strong light (spotlight)

Lens



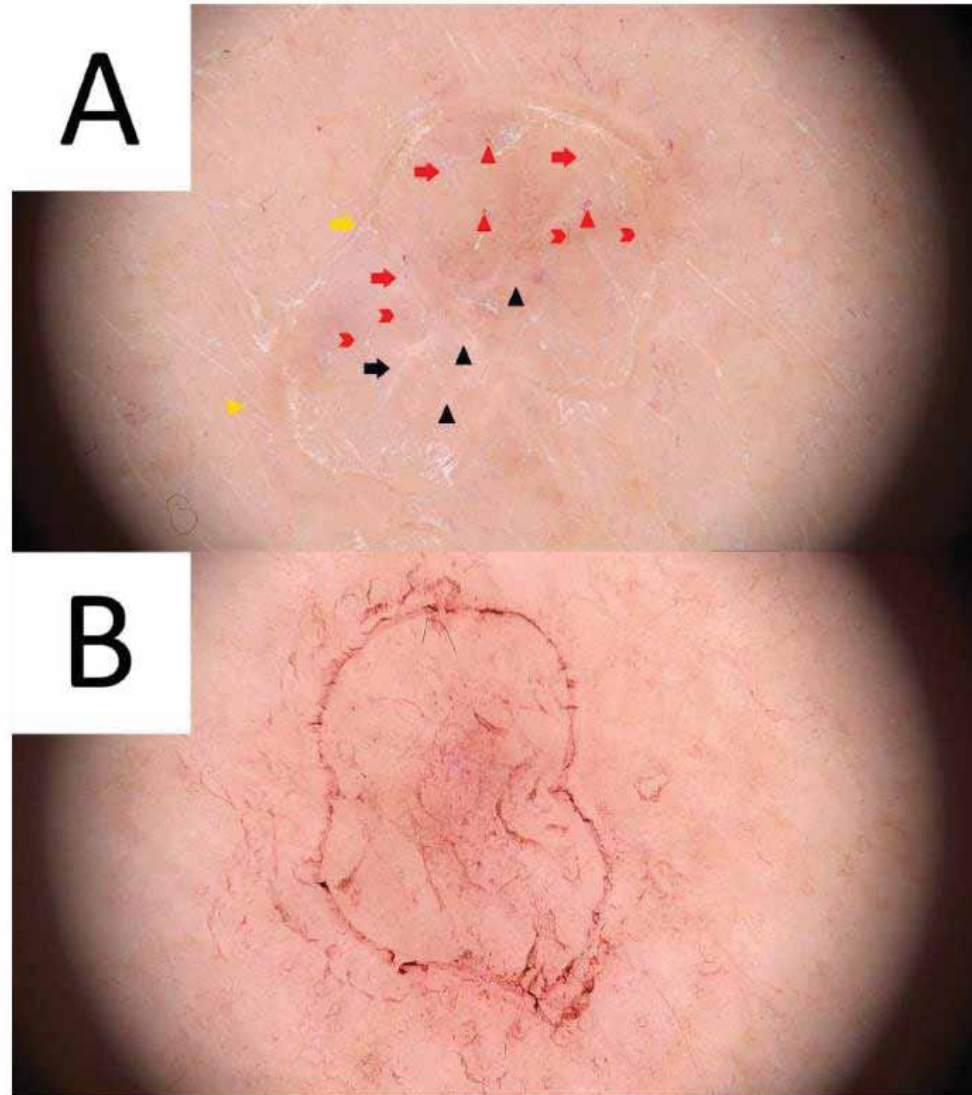


Figure 2. Dermatoscopy of disseminated superficial actinic porokeratosis (magnification 20×): central atrophic pink-tan area with polarising-specific white lines (black arrow), small white areas (black arrowheads) and vascular polymorphism (dots, linear serpentine and linear glomerular vessels; red arrows, red arrowheads and red V-shaped arrows, respectively), surrounded by a continuous yellowish double-edged keratin rim (yellow arrow). Radially arranged peripheral scaling (yellow arrowhead) can be observed on both sides of cornoid lamella (A). “Ink test”: Colouring the lesion and wiping out excessive pigment enhances the visibility of the keratotic rim, especially in non-obvious cases (B). In this case, brown pen ink was used, yet whiteboard marker or gentian violet can also be used.

Dermatoscopy

UV-light, polarized light
(Diamond-necklace sign)

Colouring
(ink, fake tan lotion,
iodine, ...)

*Pietkiewicz P et al. Porokeratosis –
A comprehensive review. Metabolites, 2023
Thatte S et al, Diamond-necklace sign. JAAD, 2014*

In vivo konfokale Reflexionsmikroskopie

Ahlgrimm-Siess V, Kerl H et al, JDDG, 7:591, 2008

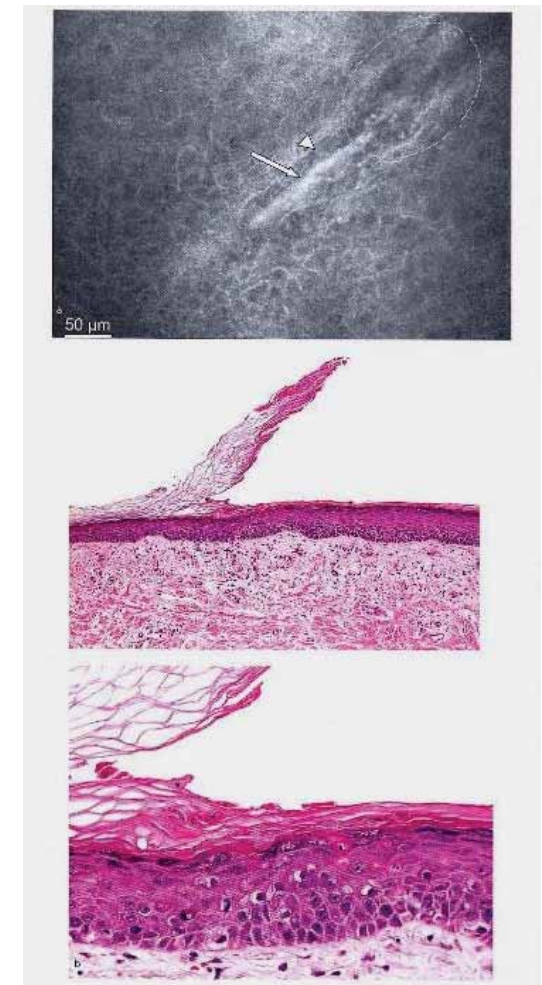
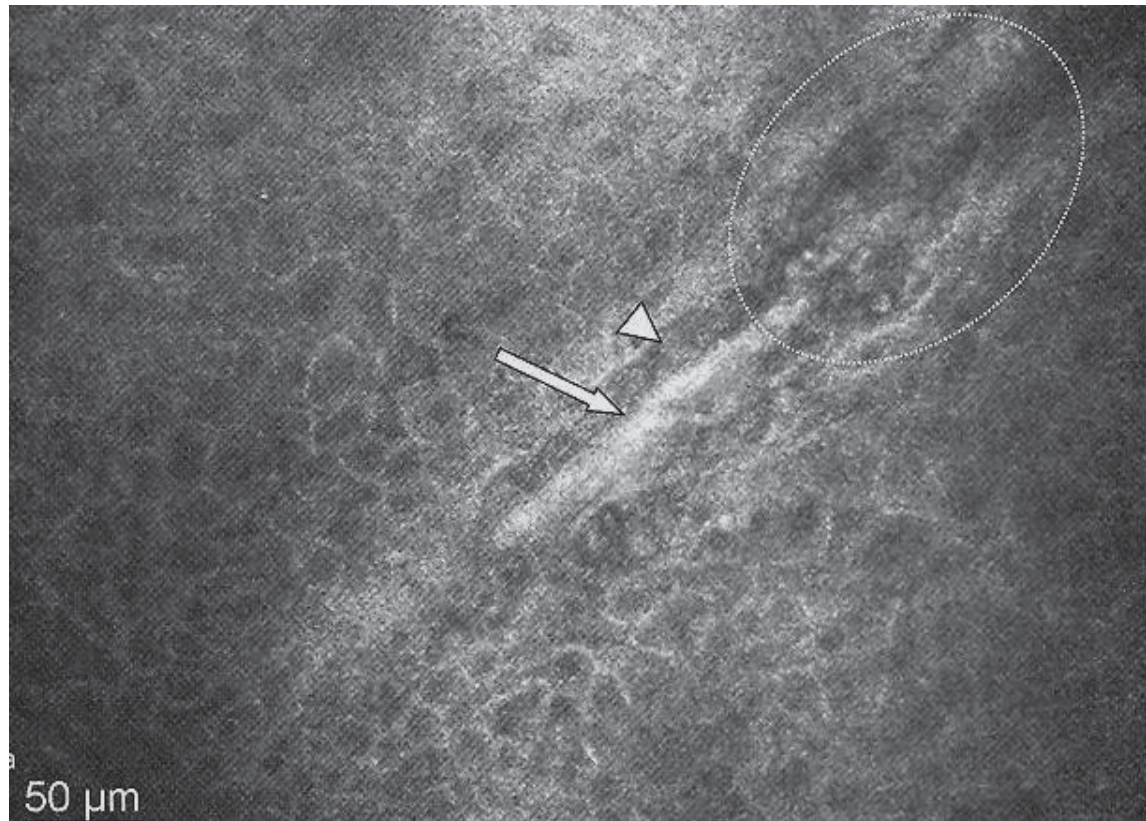
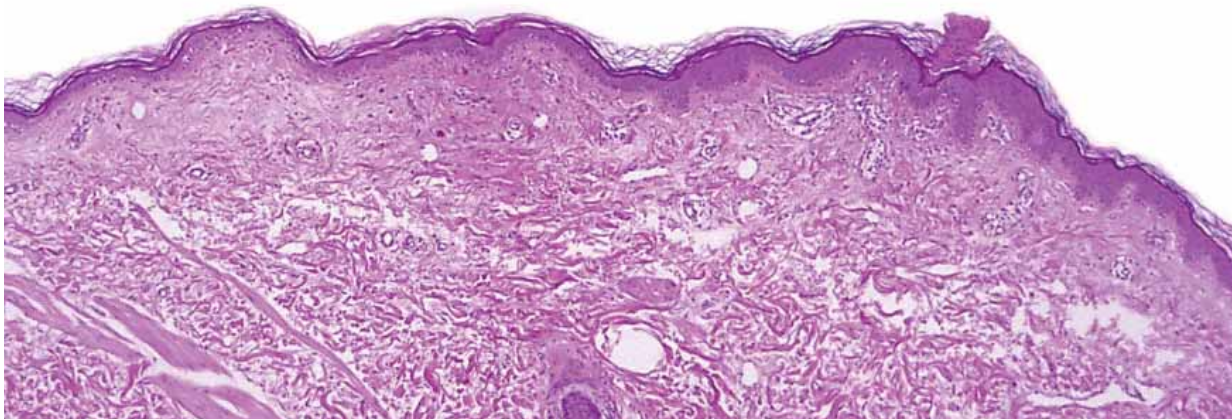


Abbildung 2: (a) Konfokale Reflexionsmikroskopie. Homogene, helle, lineare Struktur (Pfeil) mit angrenzender Hyporeflektivität entsprechend einer epidermalen Differenzierungsstörung im Randbereich (Pfeilspitze). Aufhebung der regulären epidermalen Schichtung (Kreis). In der Umgebung gelangt das typische „Honigwabem“-Muster zur Ansicht. (b) Biopsie II: Porokeratosis. Kornoide Lamelle (parakeratotische Säule). Beachte vakuolisierte und vereinzelt dyskeratotische Zellen.



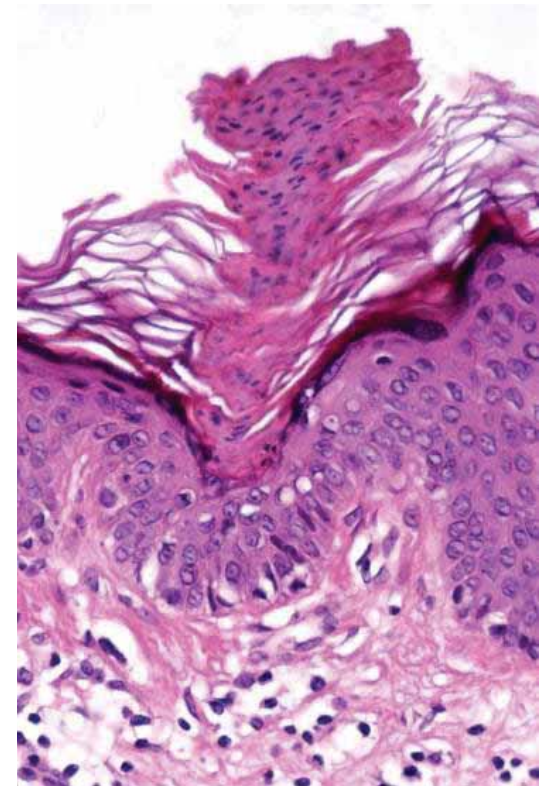
Regressive atrophic center

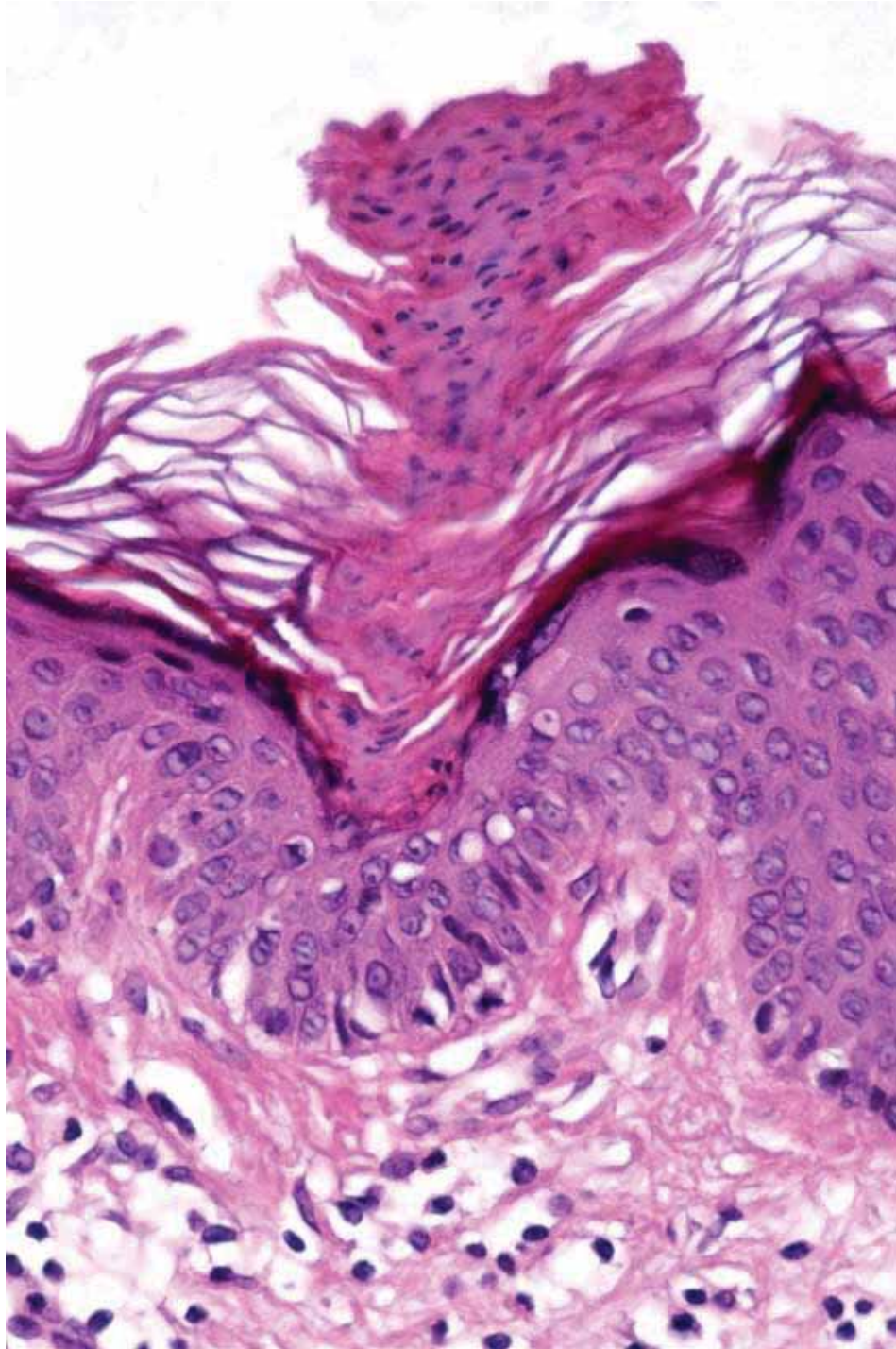


Porokeratosis (classical form)

Cornoid Lamella

Parakeratotic column above
epidermal invagination



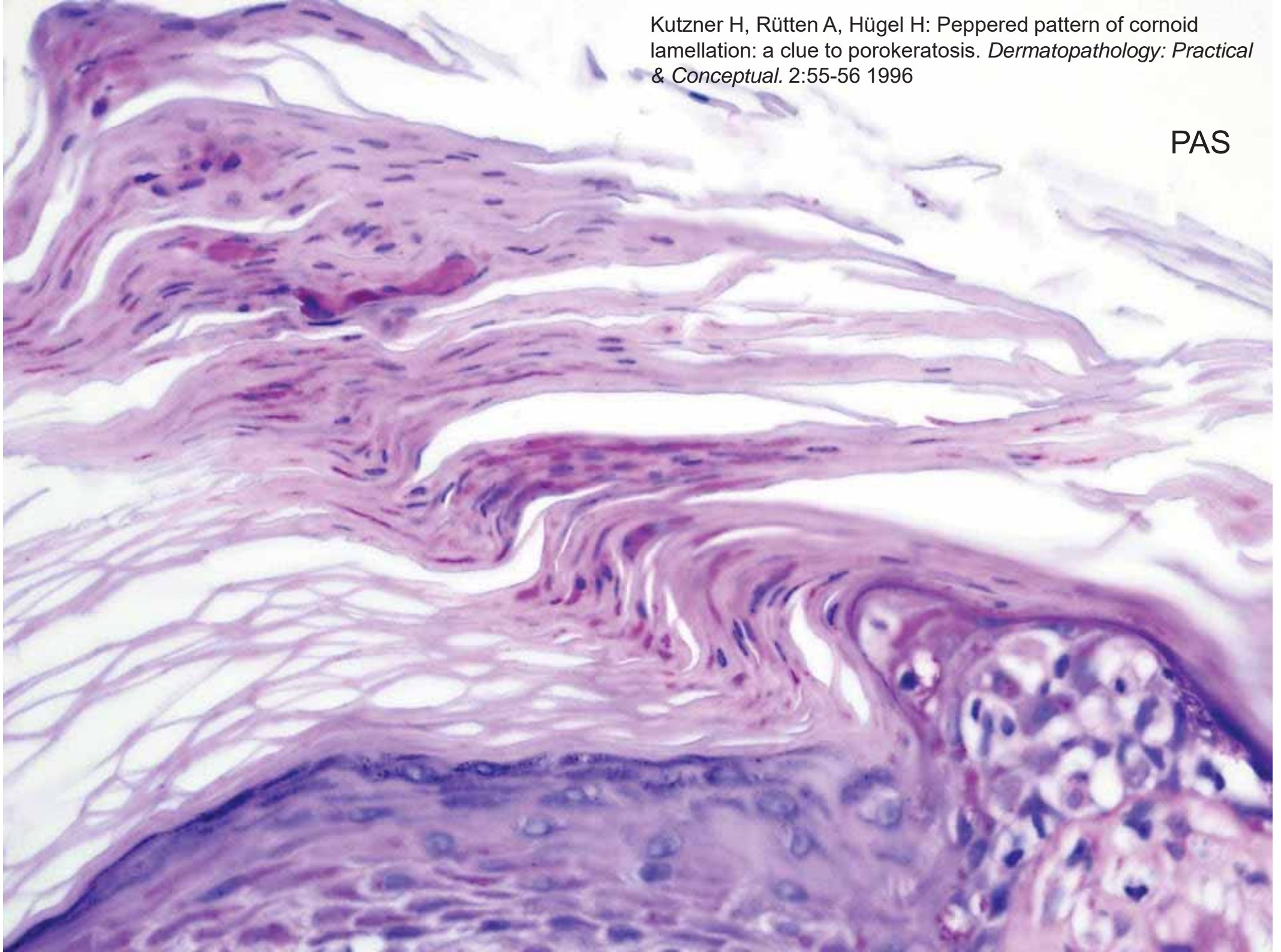


Cornoid Lamella in Porokeratosis

Parakeratotic column
&
Hyperplastic epidermis with
invagination
&
Absence of granular layer
&
Dysmaturation: Vacuolated,
larger keratocytes with pyknotic
nuclei, dyskeratotic cells
&
Variable lymphoid infiltrate,
Interface-Dermatitis possible

Kutzner H, Rütten A, Hügel H: Peppered pattern of cornoid lamellation: a clue to porokeratosis. *Dermatopathology: Practical & Conceptual*. 2:55-56 1996

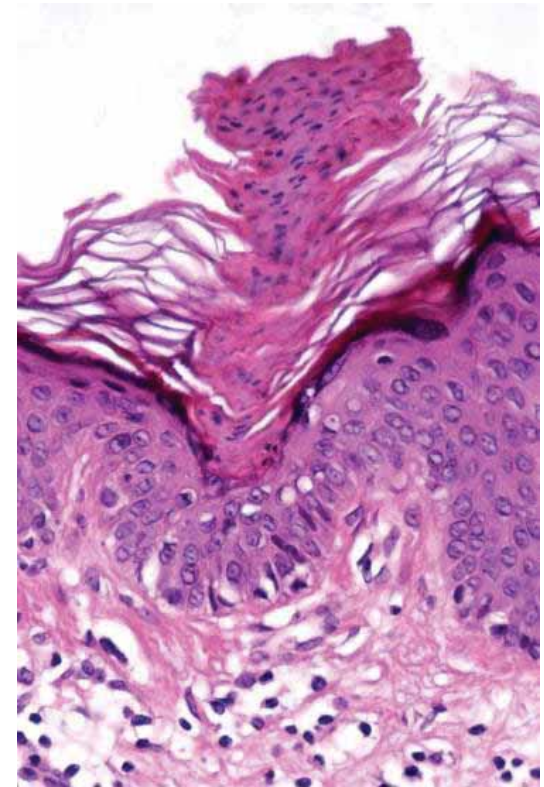
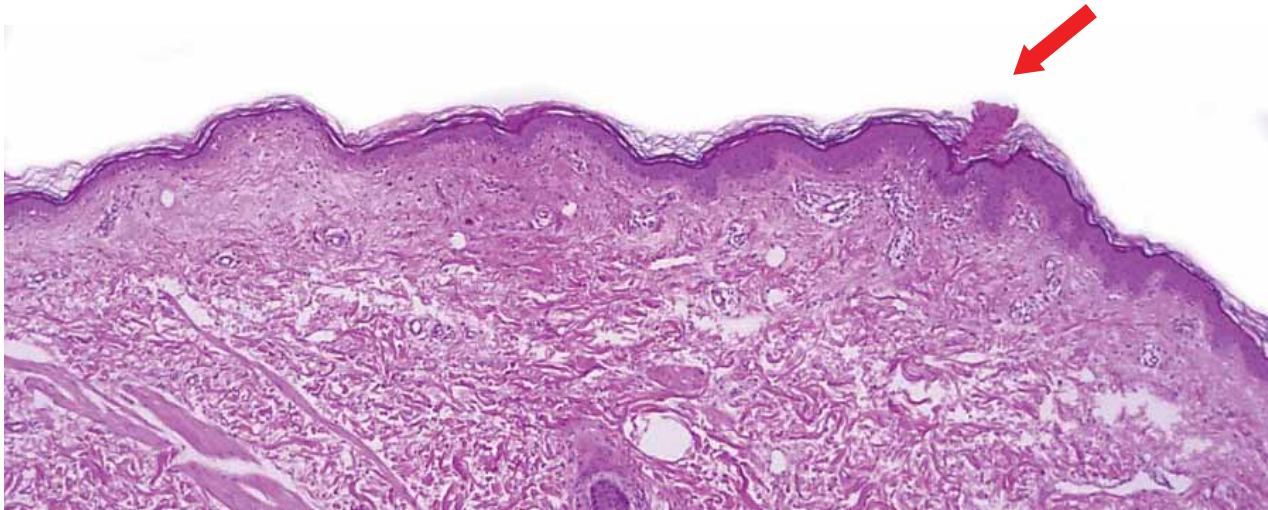
PAS





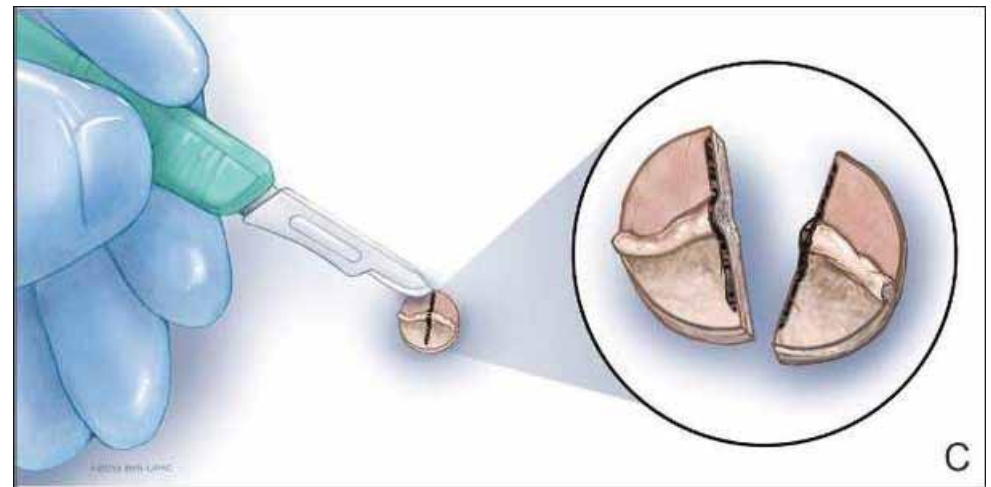
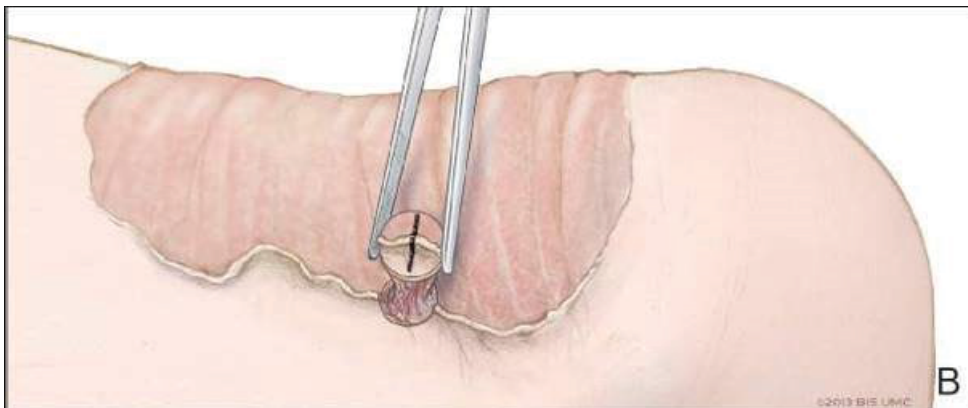
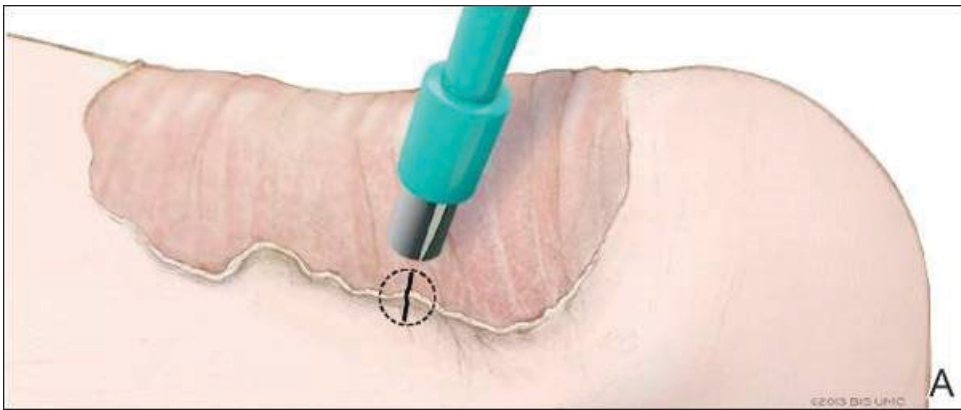
Processing perpendicular
to the keratotic rim
Cave: punch biopsy

Cornoid Lamella



Diagnosing Porokeratosis

Simple ideas are the best



Caitlyn Reed C et al, Diagnosing Porokeratosis of Mibelli Every Time: A Novel Biopsy Technique to Maximize Histopathologic Confirmation. Cutis, 97:188-190, 2016

Cornoid lamellation

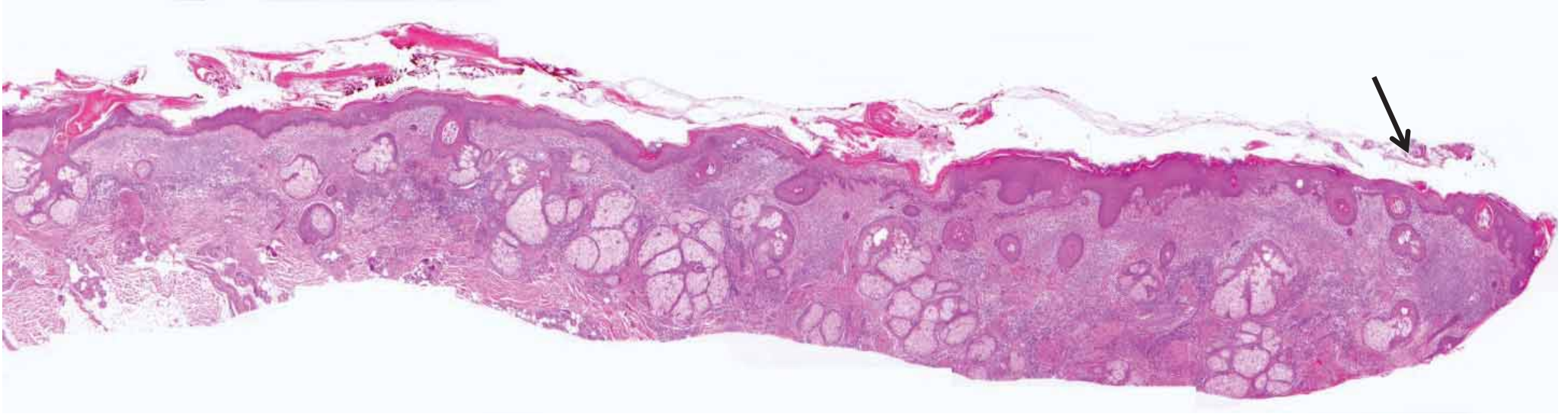
A histologic reaction pattern

- **Porokeratosis**
- **Coexistence** of Porokeratosis with other dermatoses (collision)
- **Incidental** finding in inflammatory (Grover disease, Psoriasis vulgaris, Lichen planus, Dermatomyositis, M. Fox-Fordyce...), hyperplastic (Verrucae), and neoplastic diseases (Seborrheic keratosis, LPLK, AK, SCC, BCC, NZN), scar, or epidermal nevi (Nevus sebaceous)

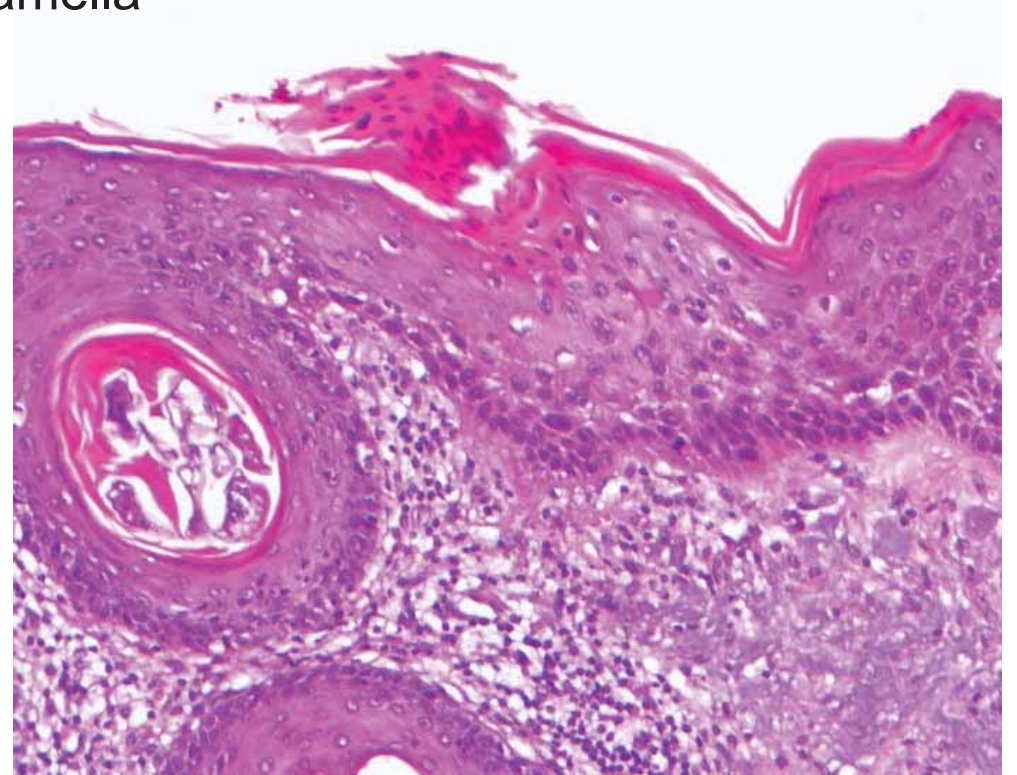
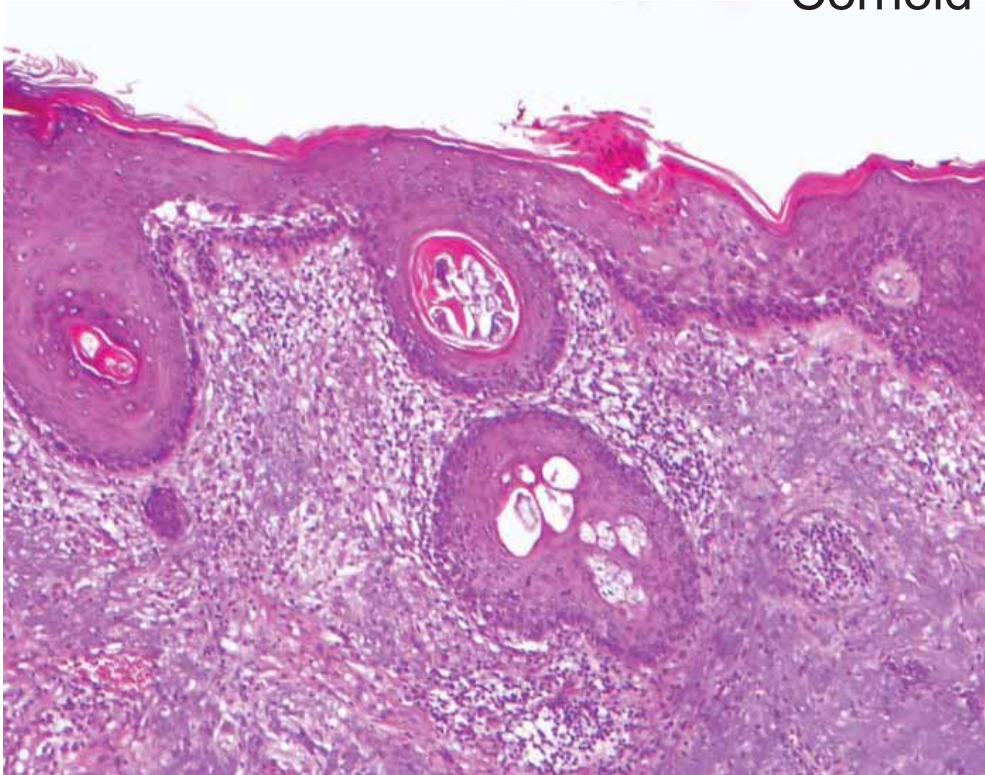
DDx: Column of parakeratotic cells (cornoid lamella-like structures) without typical dysmaturation

Incidental finding

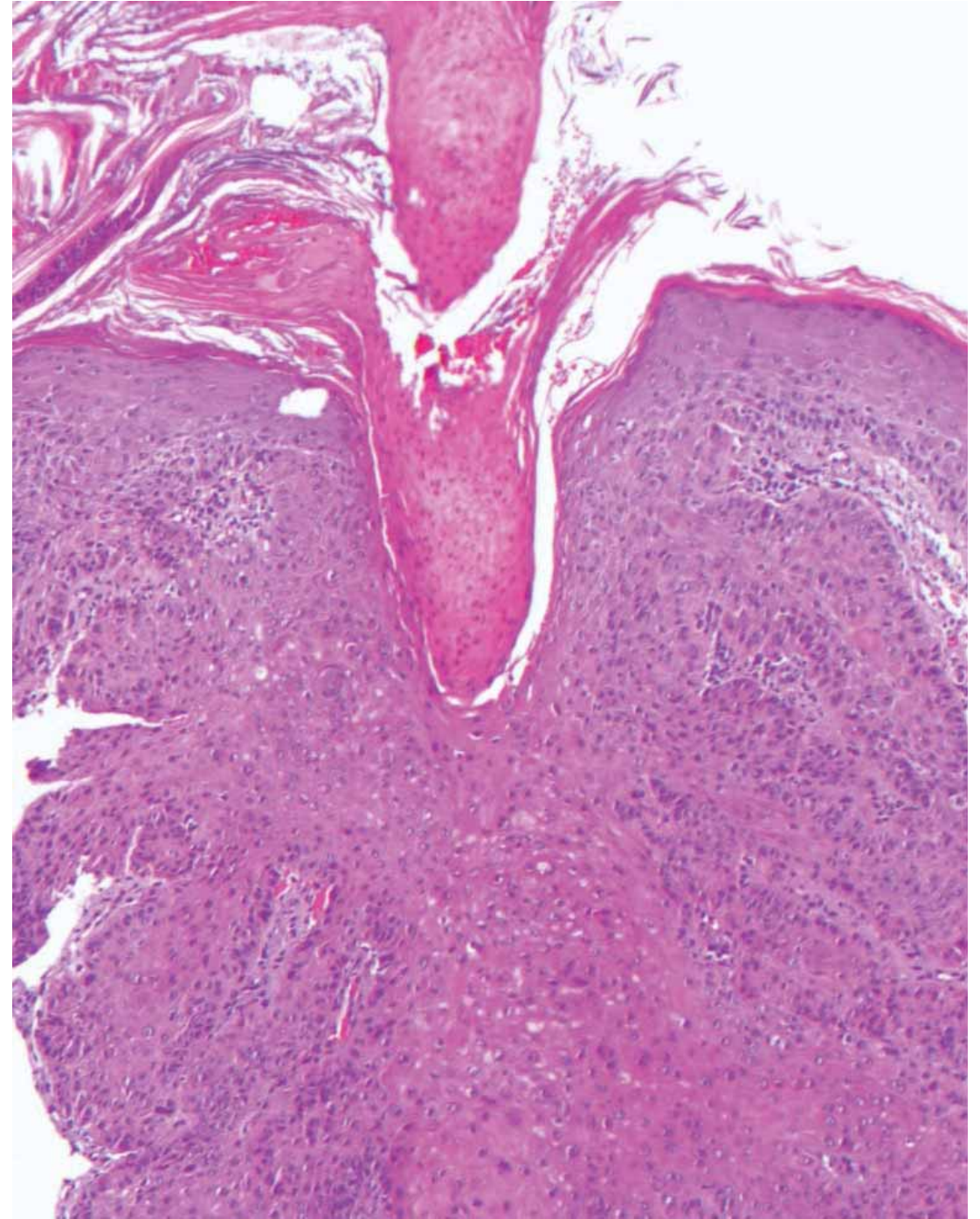
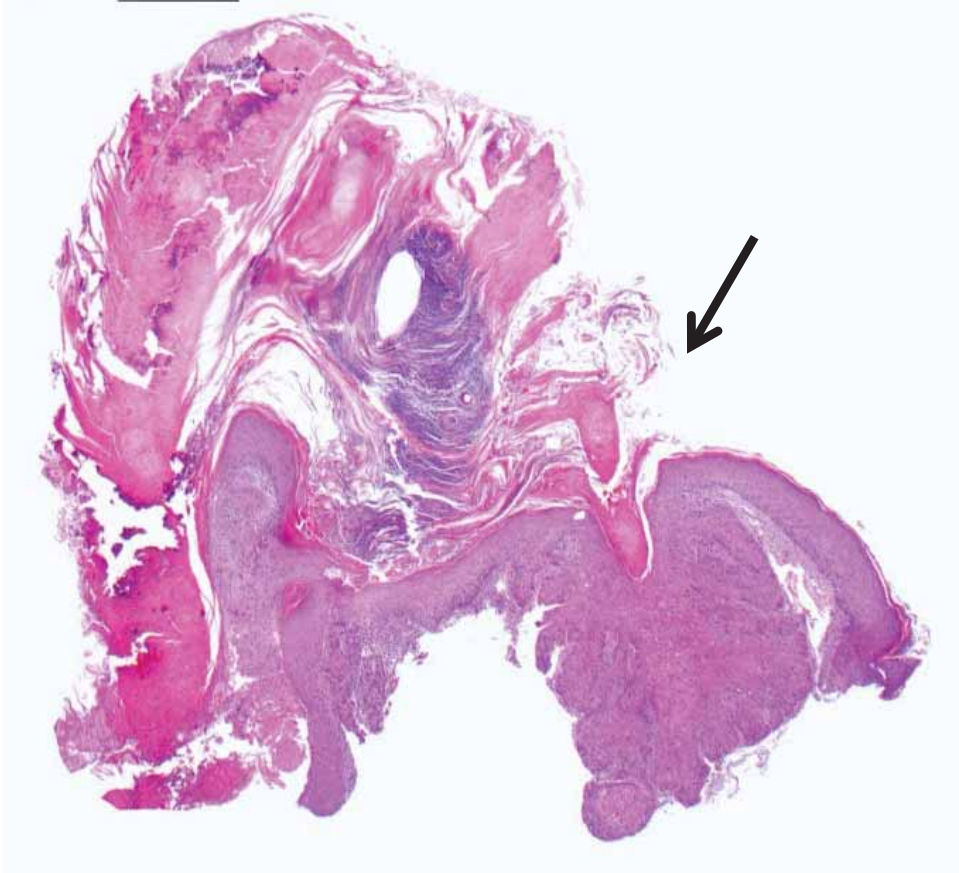
Actinic keratosis

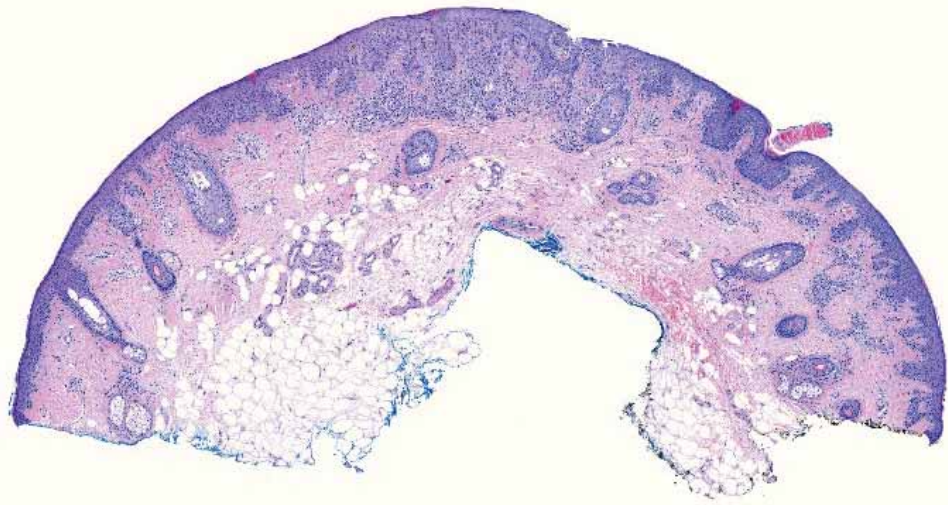


Cornoid lamella



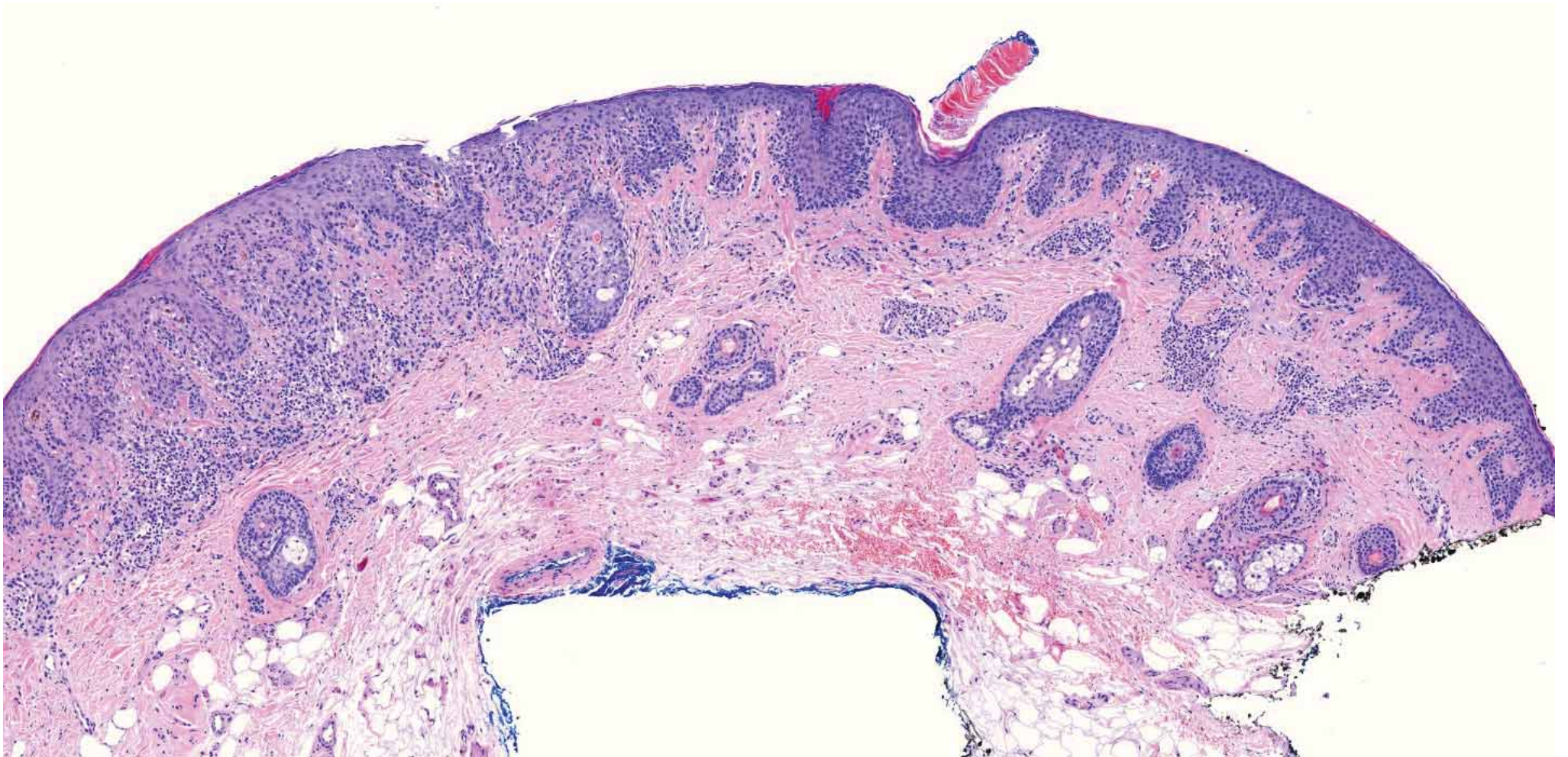
SCC, Porokeratosis ?

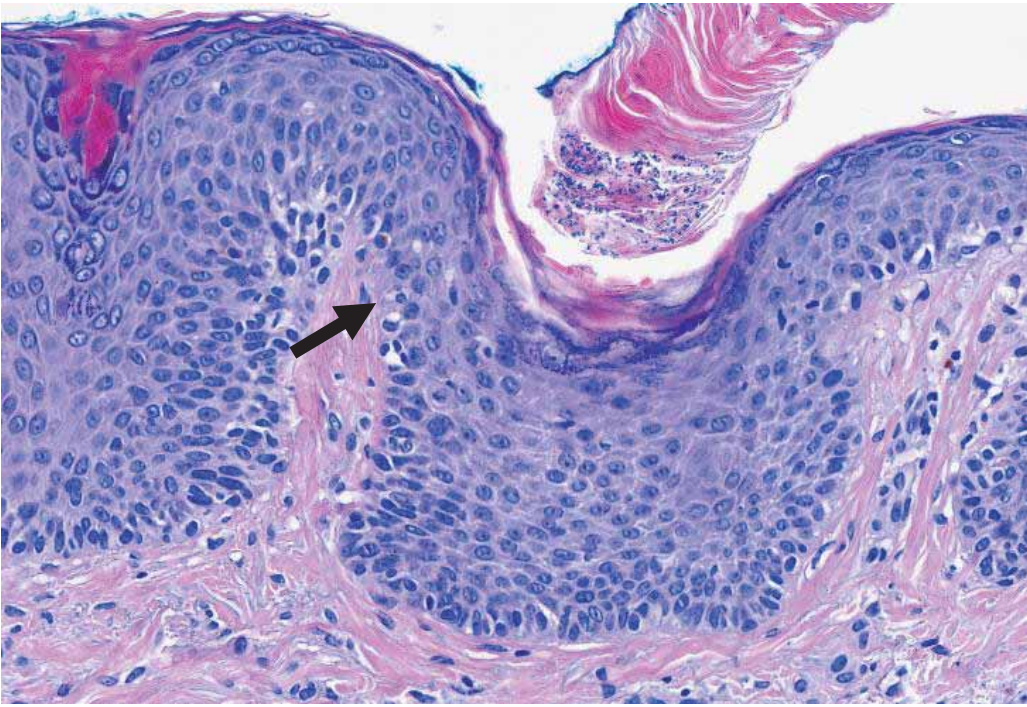




Melanocytic Naevus,
inflamed

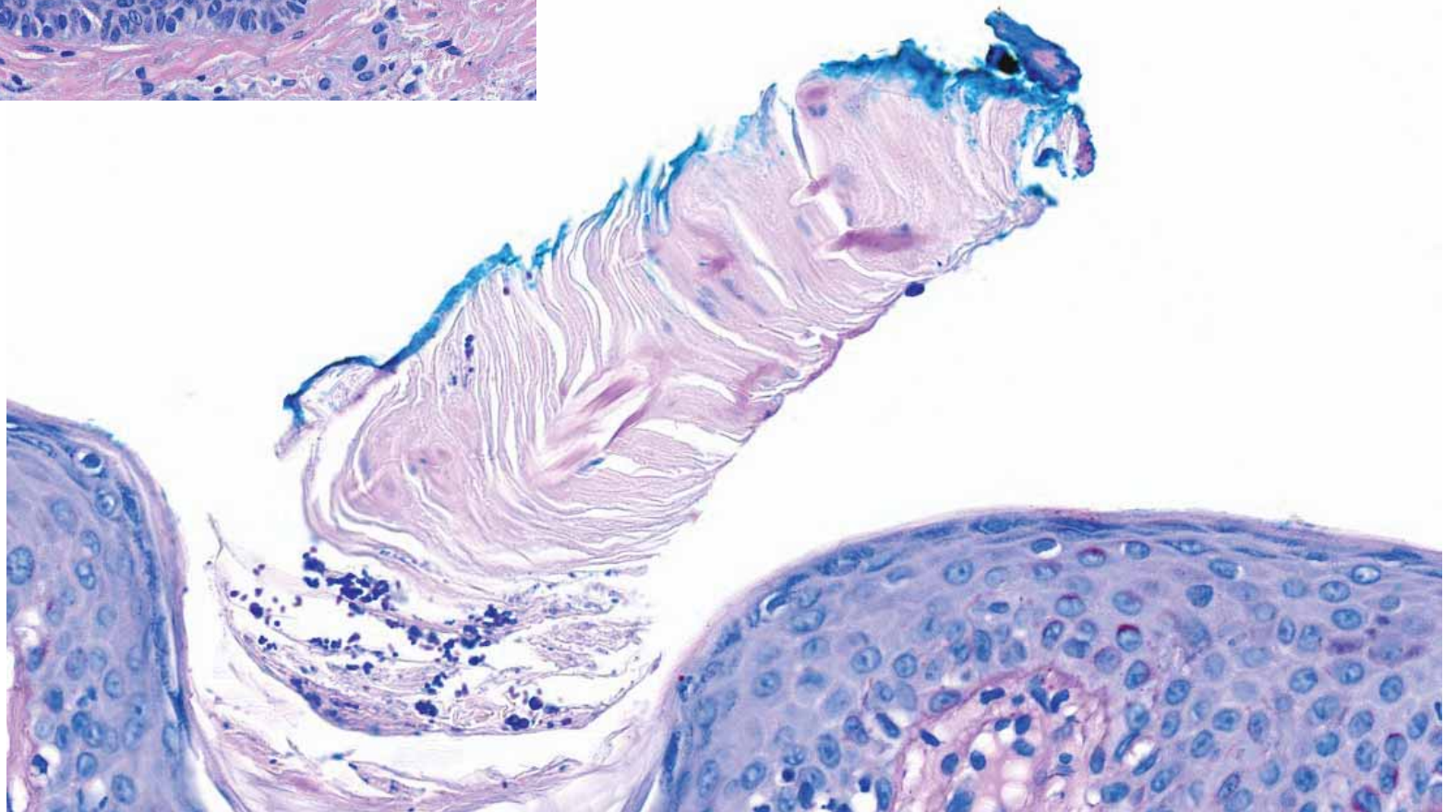
Cornoid Lamella





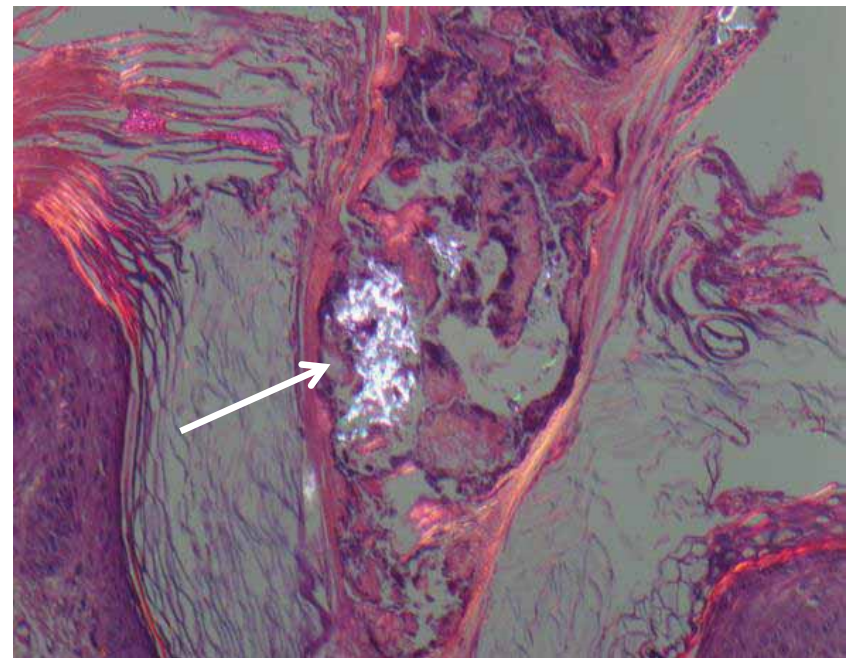
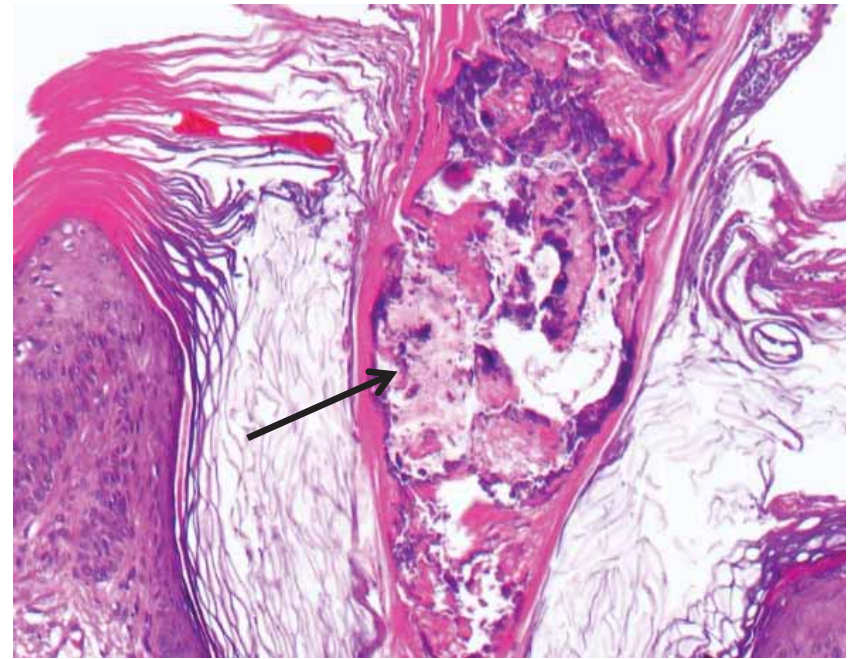
DDx Porokeratosis

no PAS pos granules



Open Comedo

No Cornoid Lamella

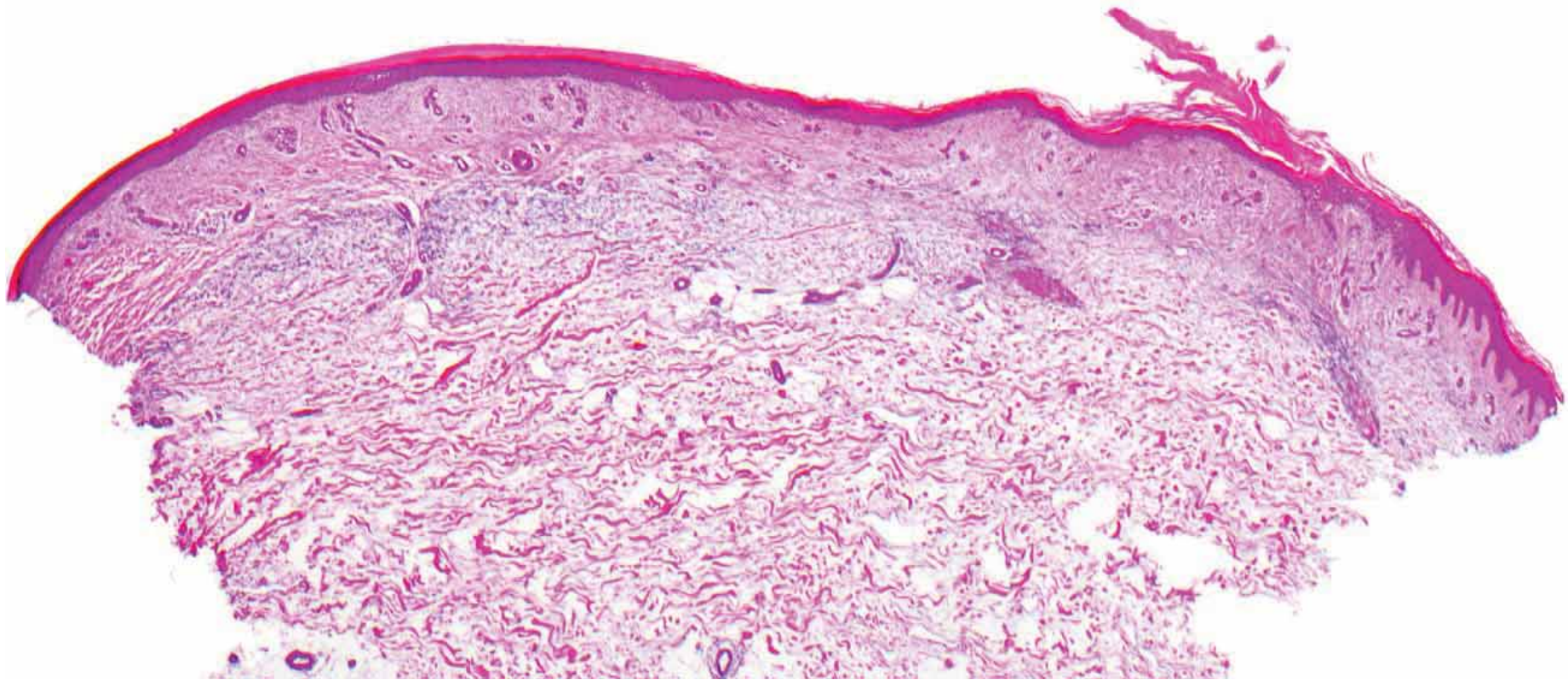


Polarisation - sebum

Histology of Classical Porokeratosis

Center

Periphery

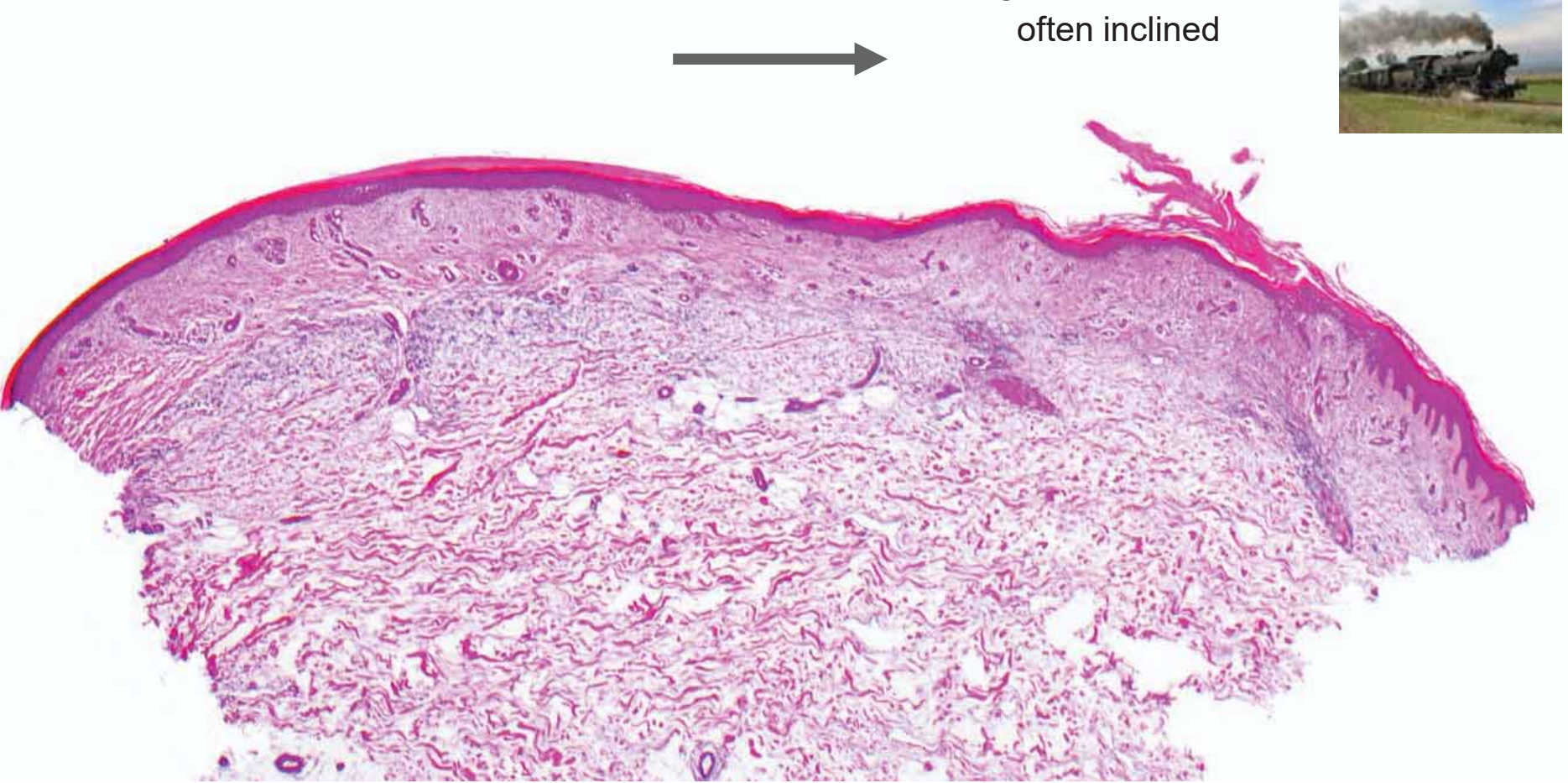


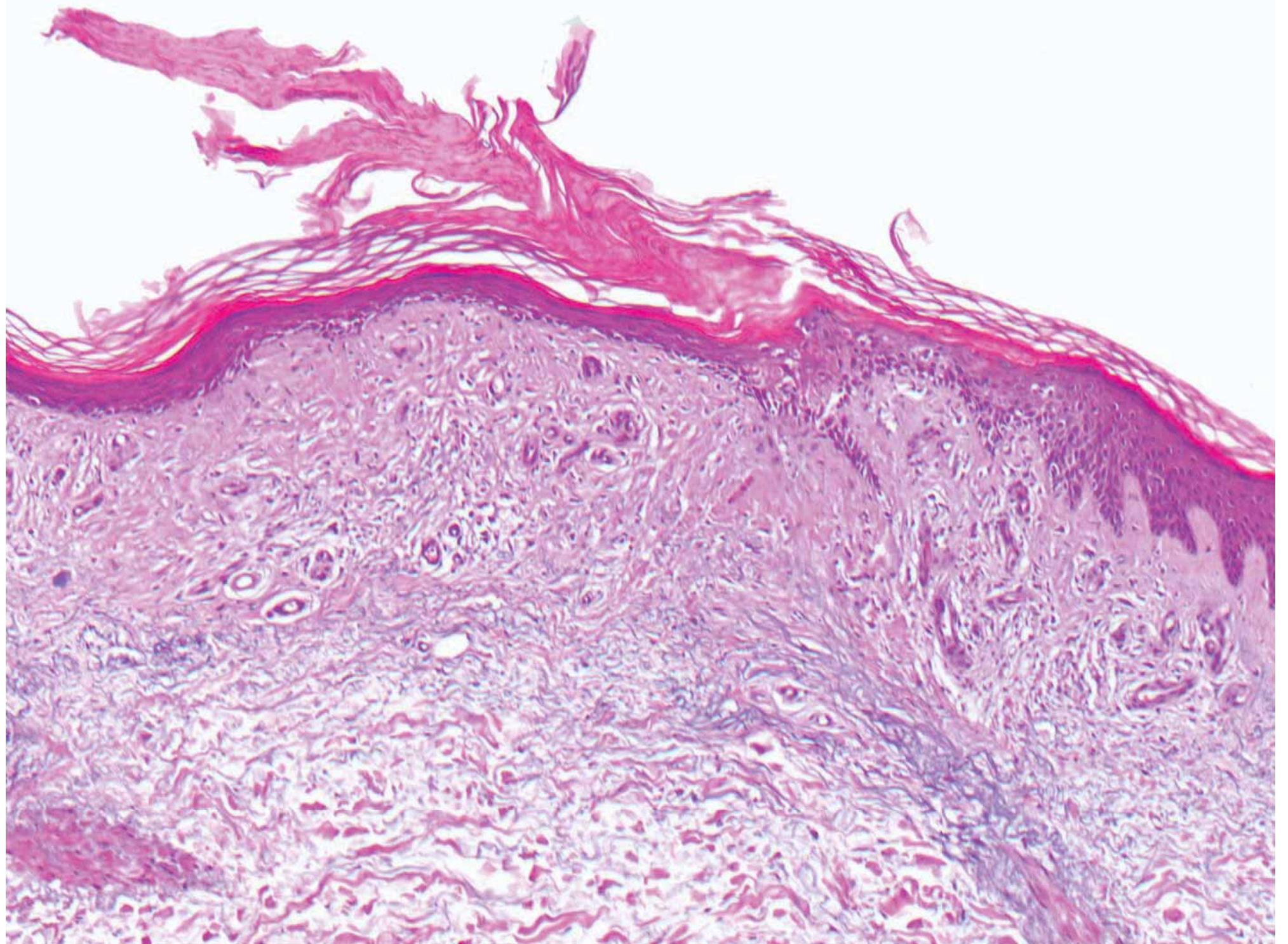
Porokeratosis

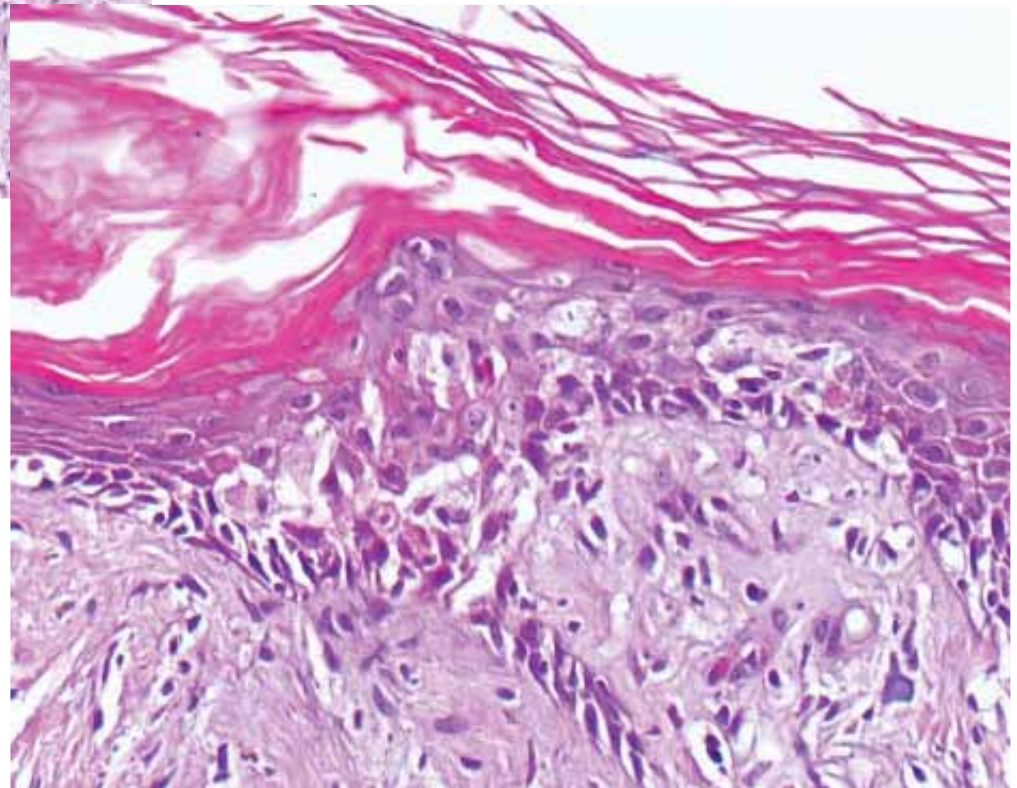
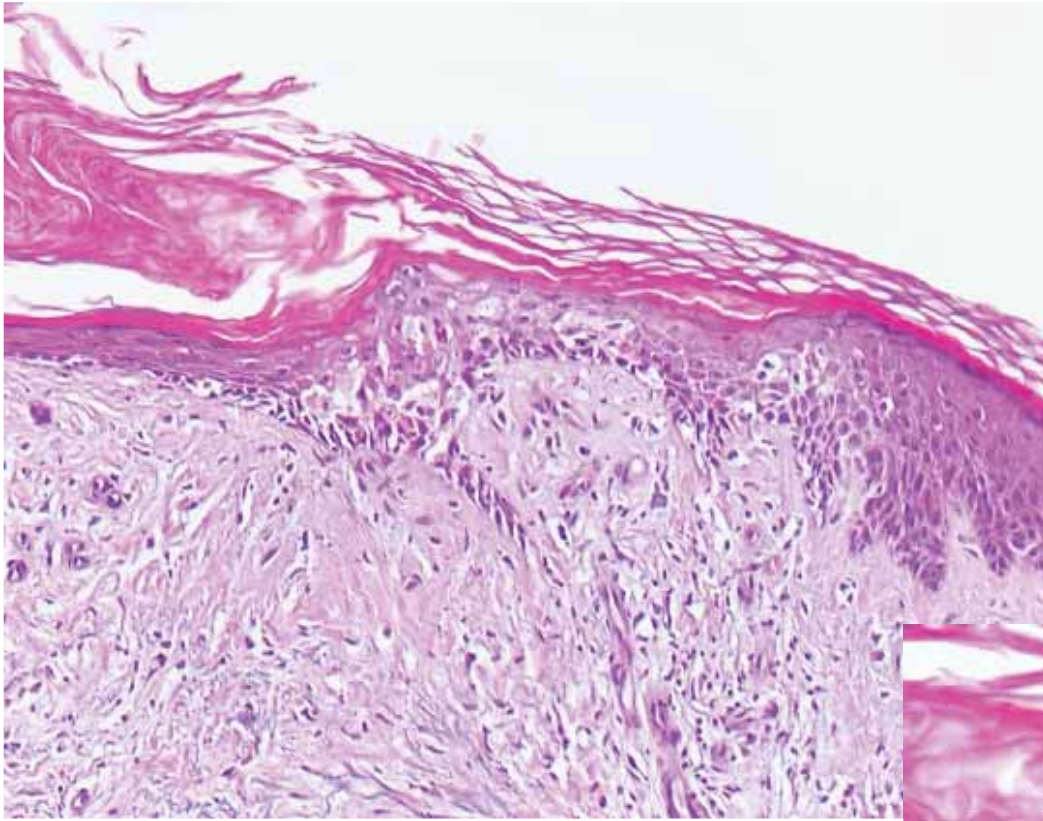
Centrifugal growth



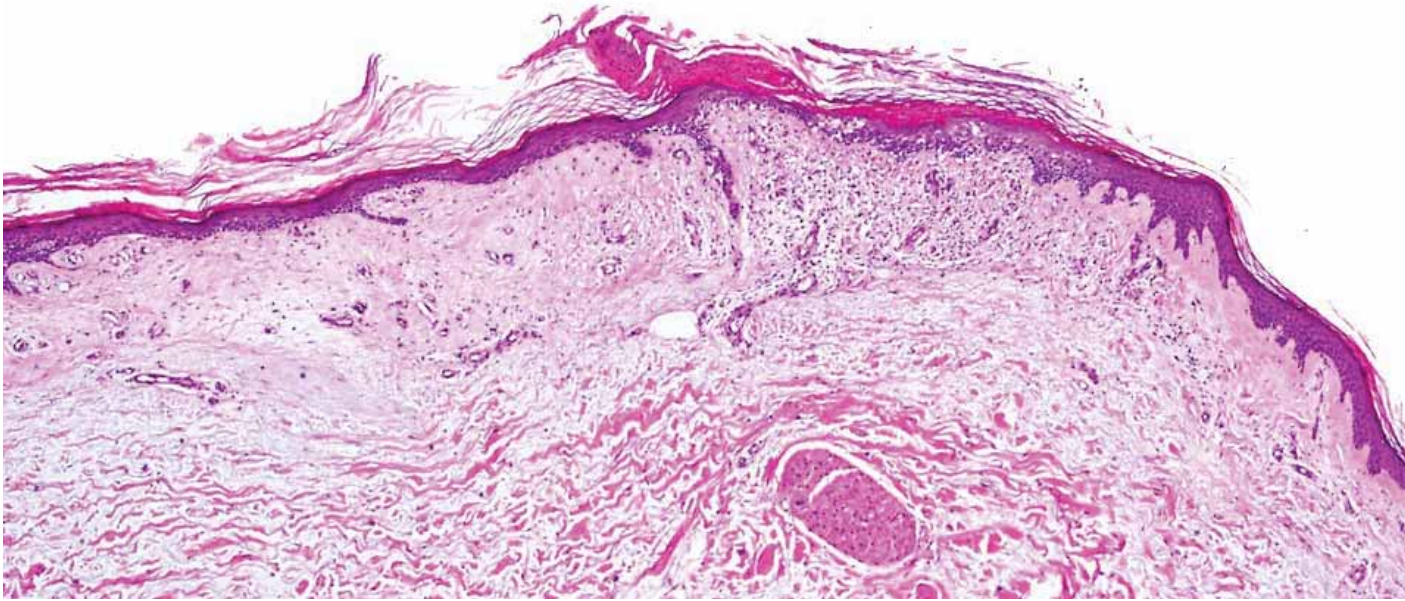
Cornoid Lamella
often inclined



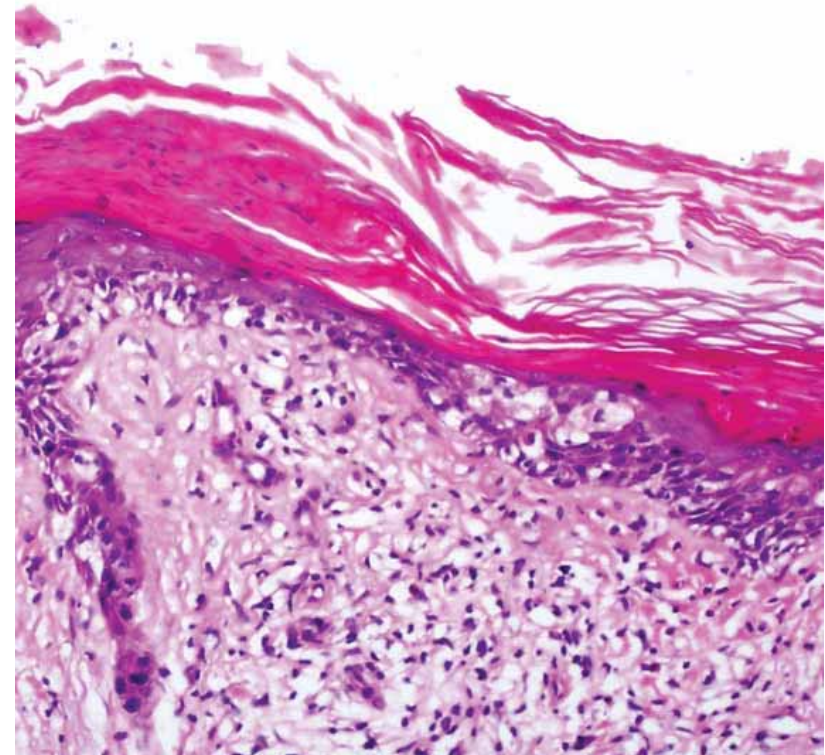
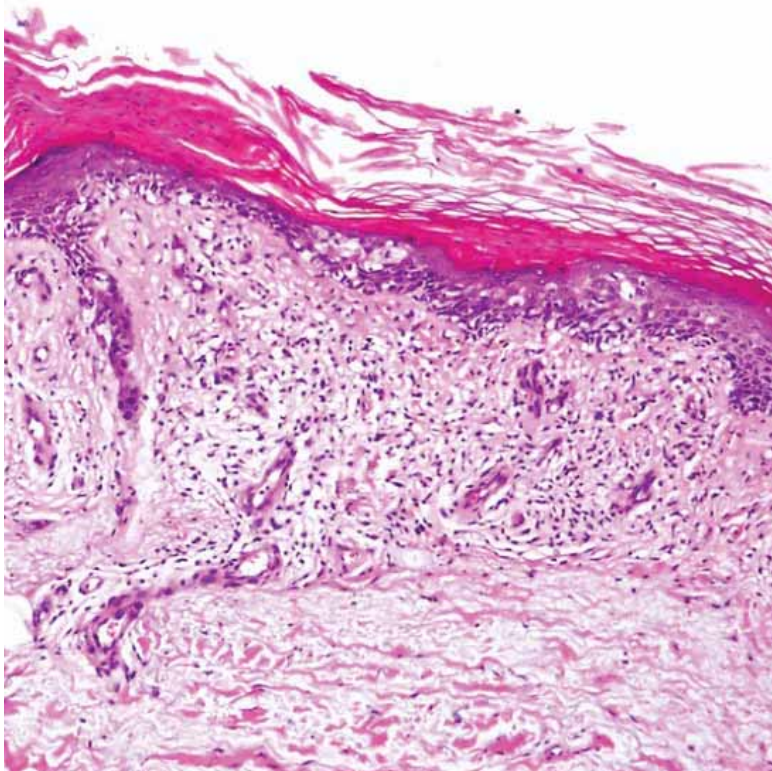


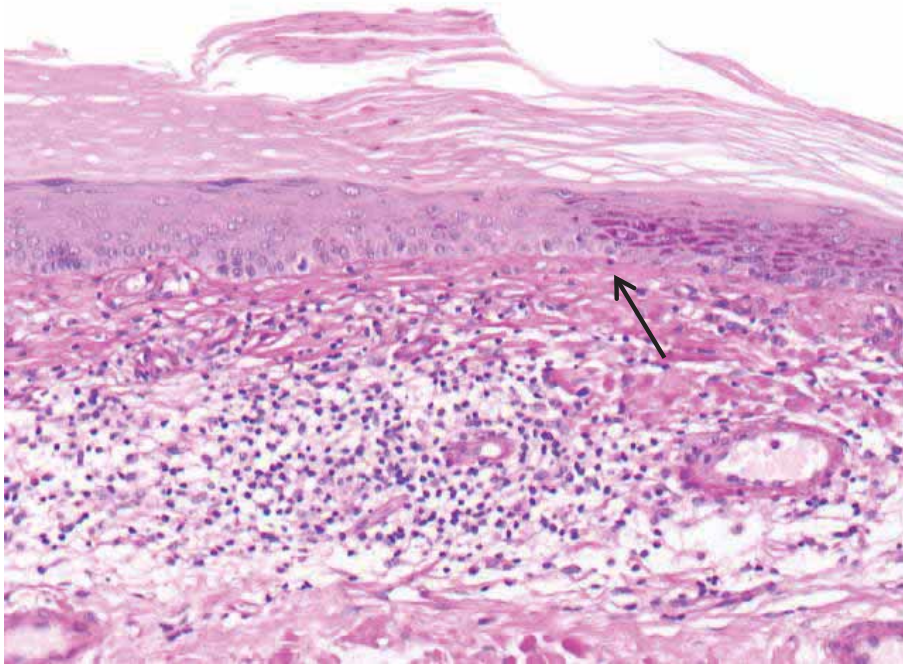


Step section



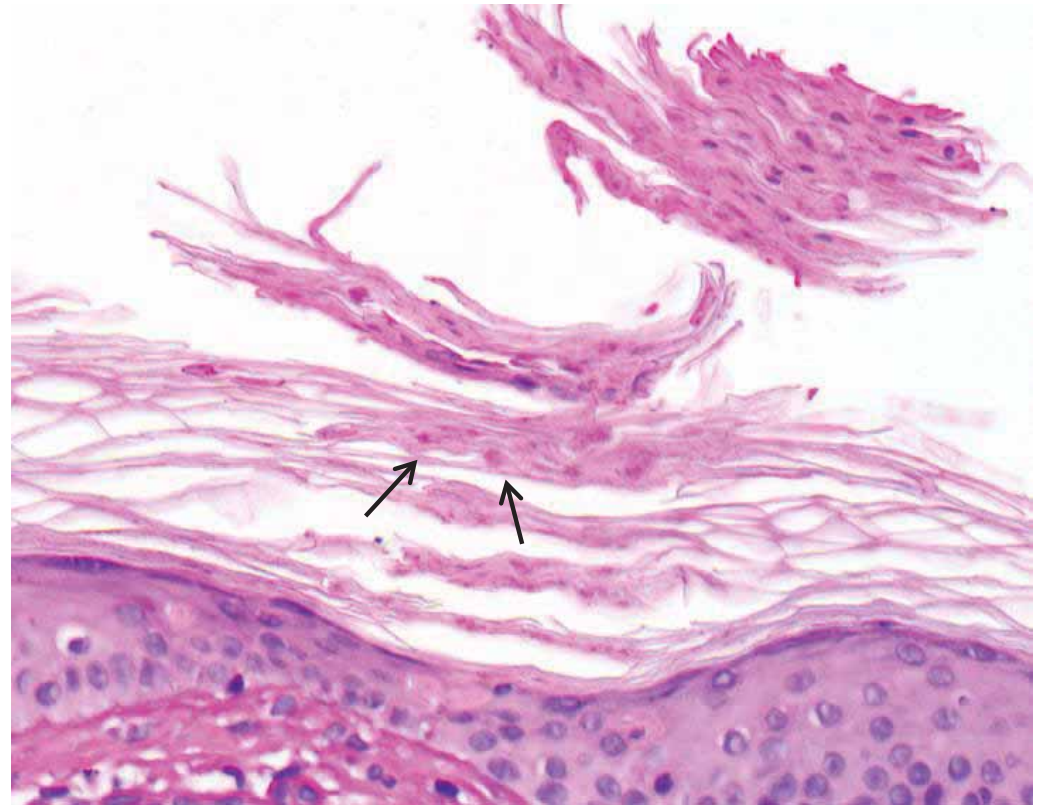
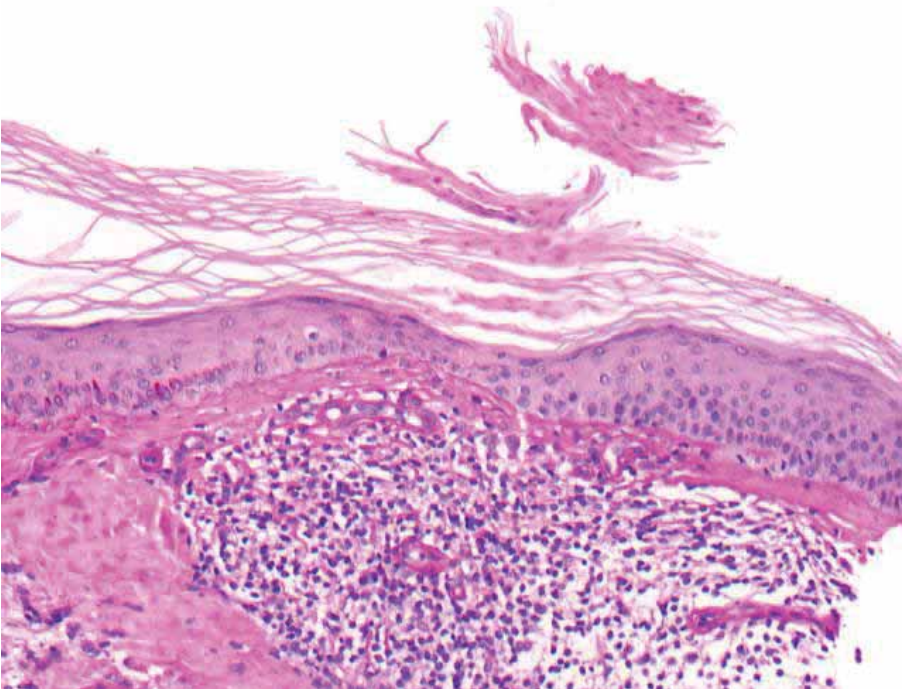
Cave oblique section:
cornoid lamella
can be overlooked,
DDx
Interface-dermatitides

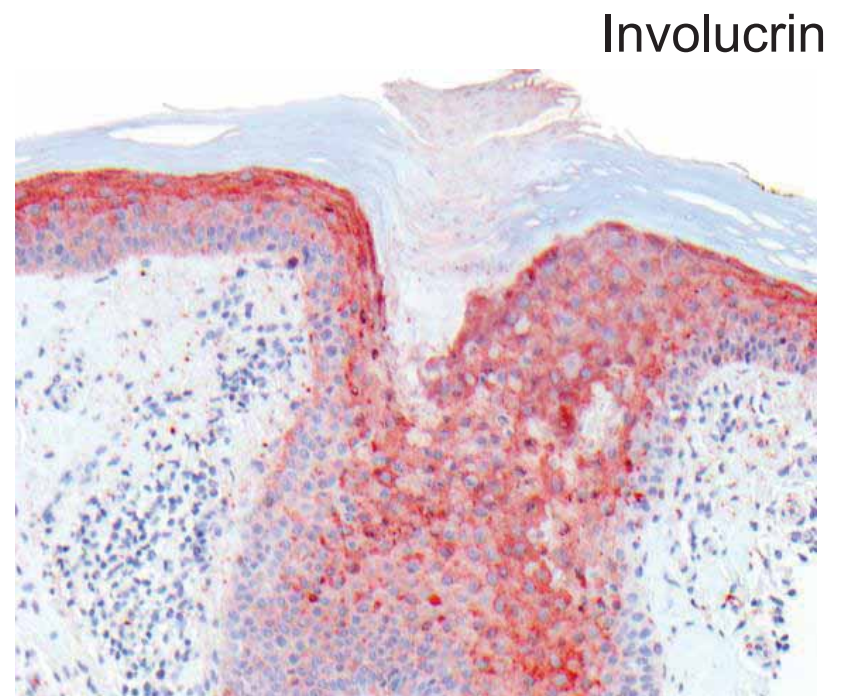
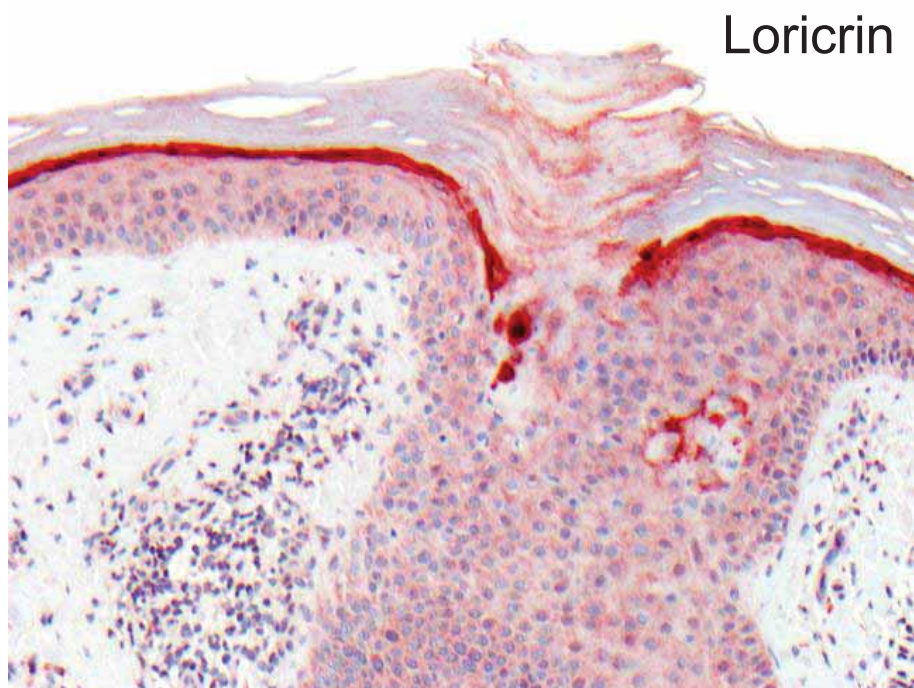
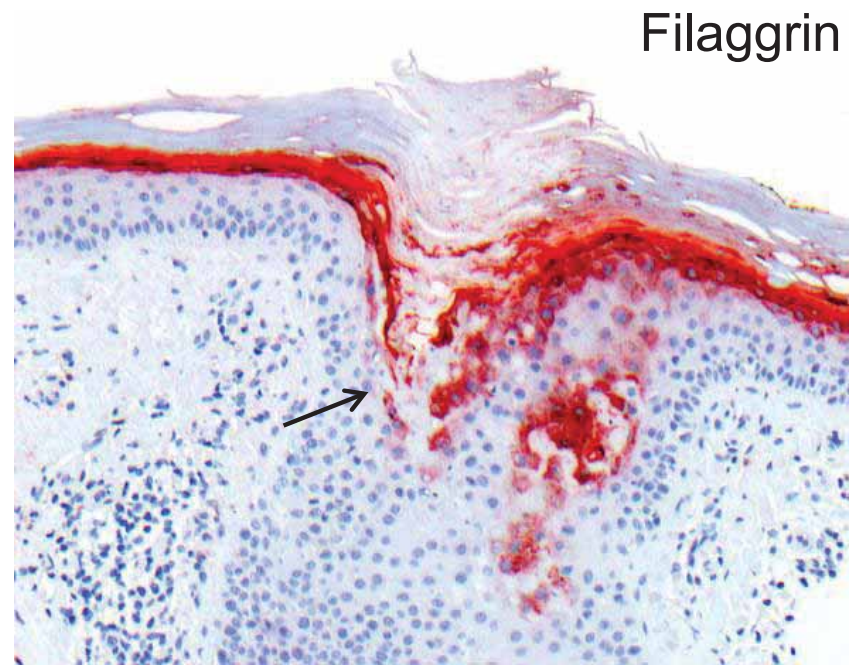
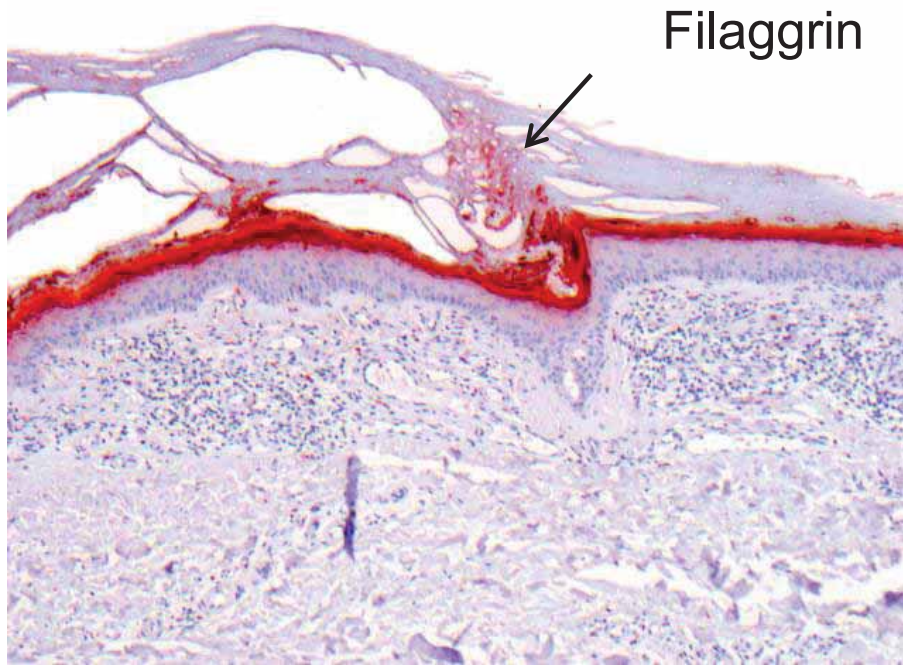




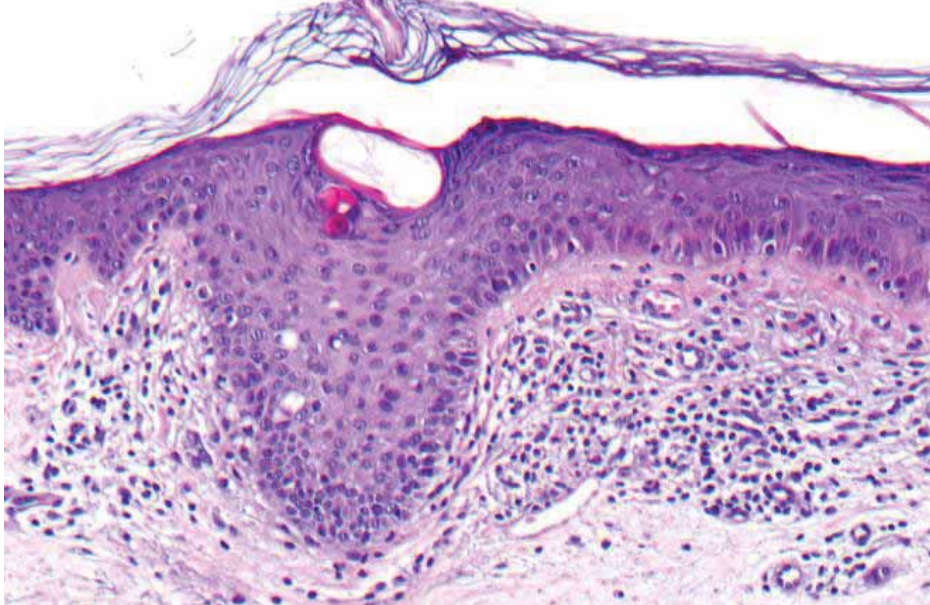
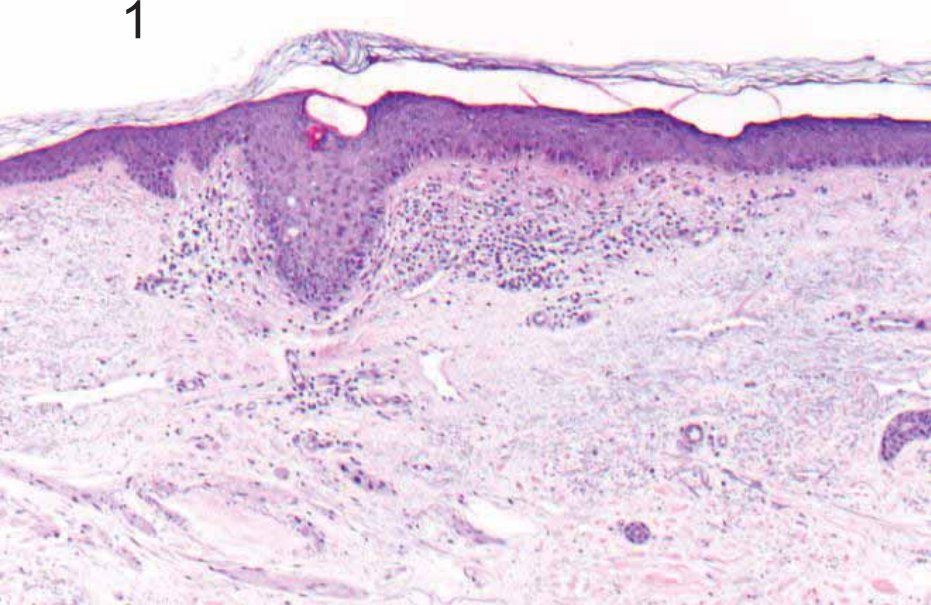
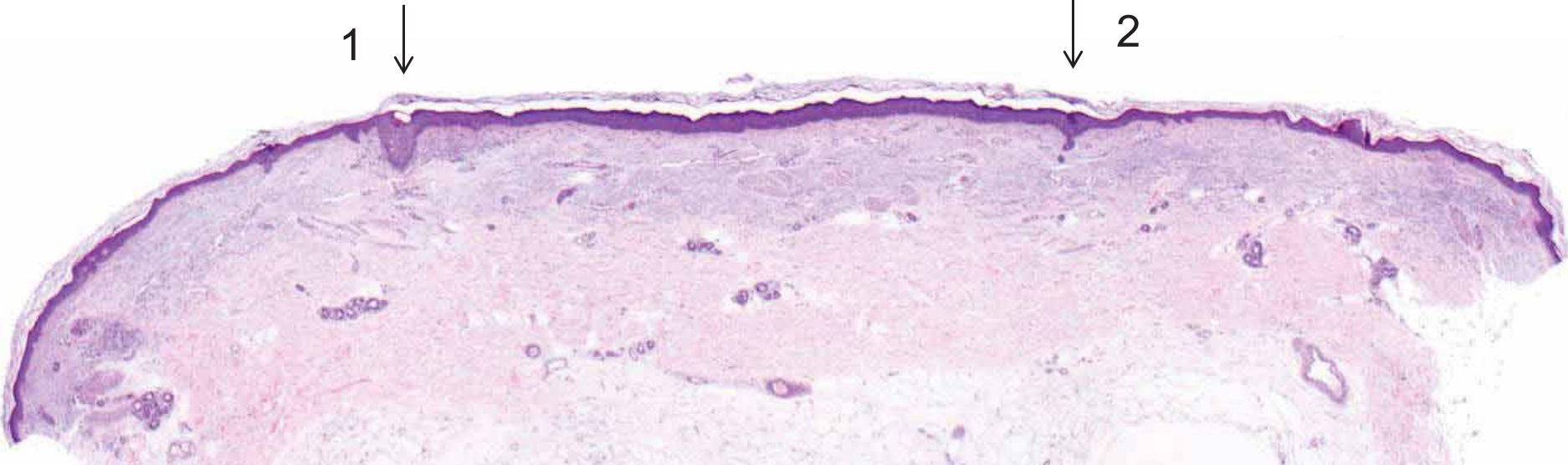
Cornoid lamella, PAS

DSAP

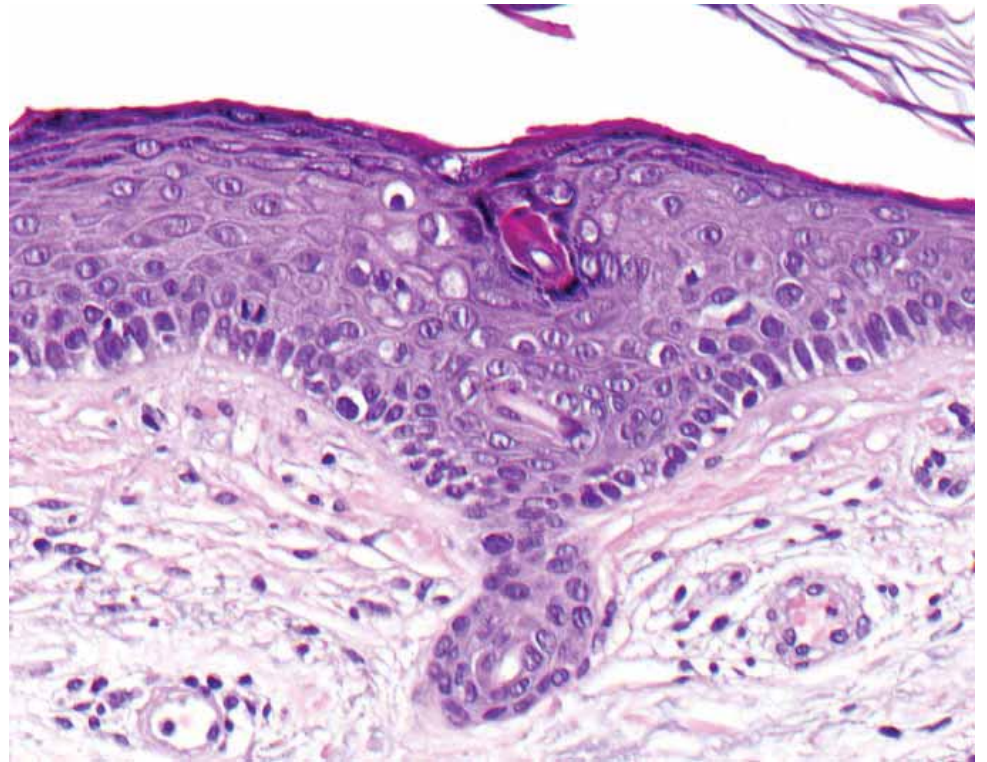
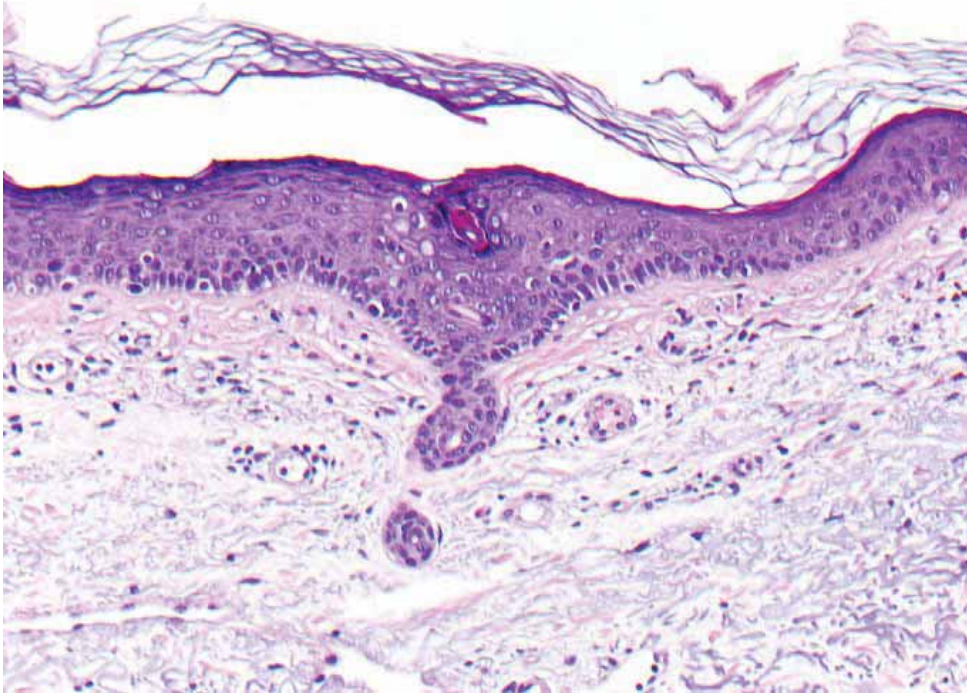




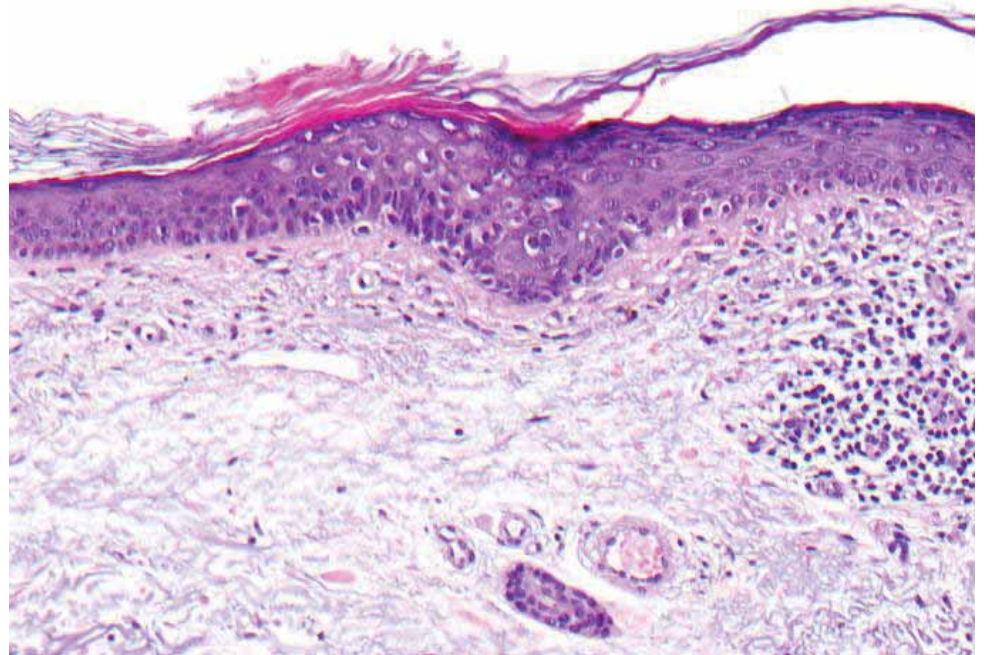
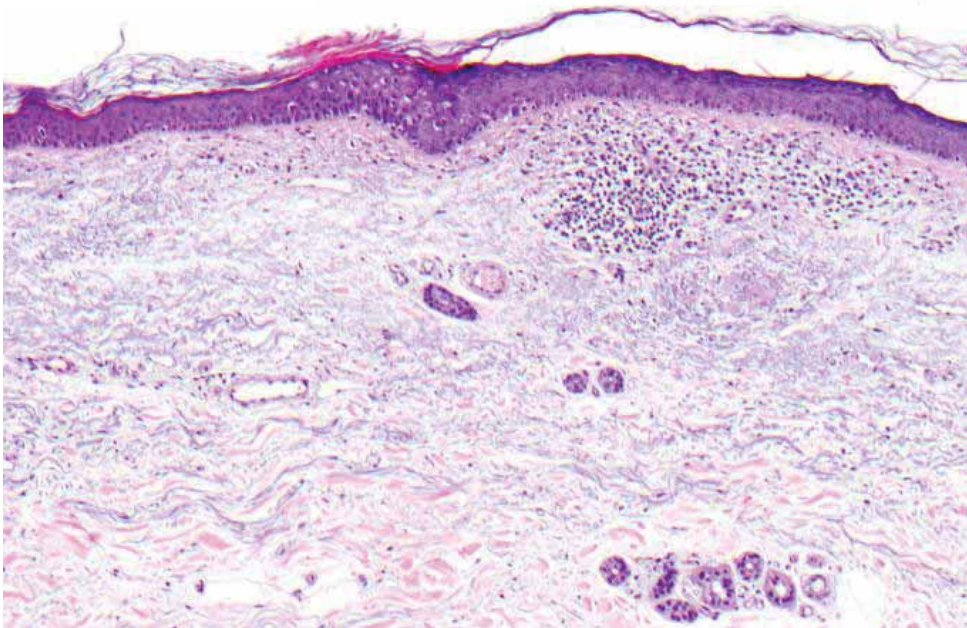
Porokeratosis, acrosyringal (Poro-)



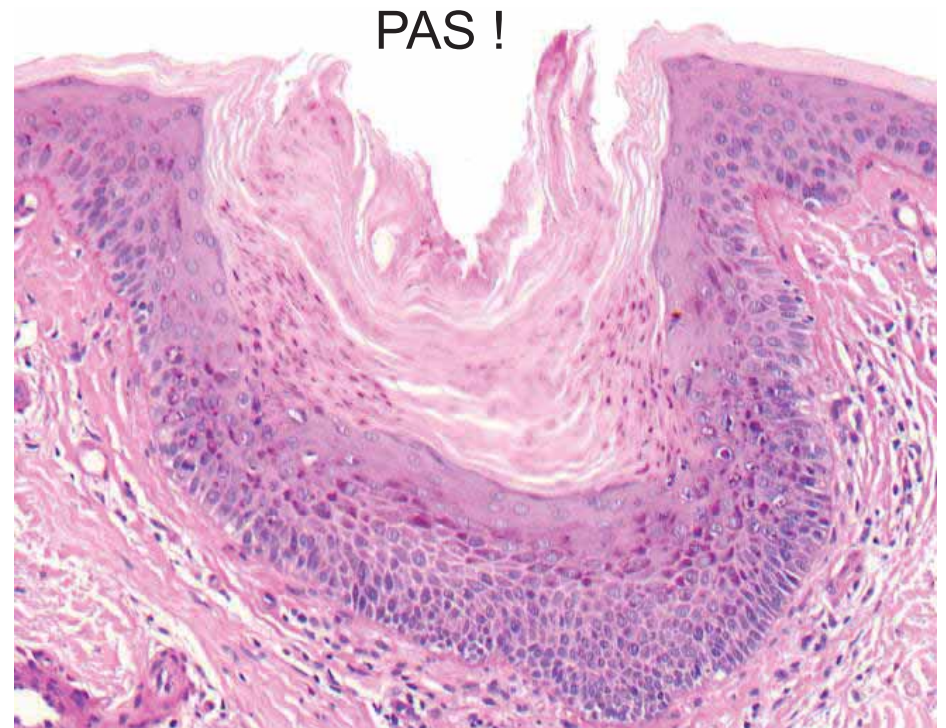
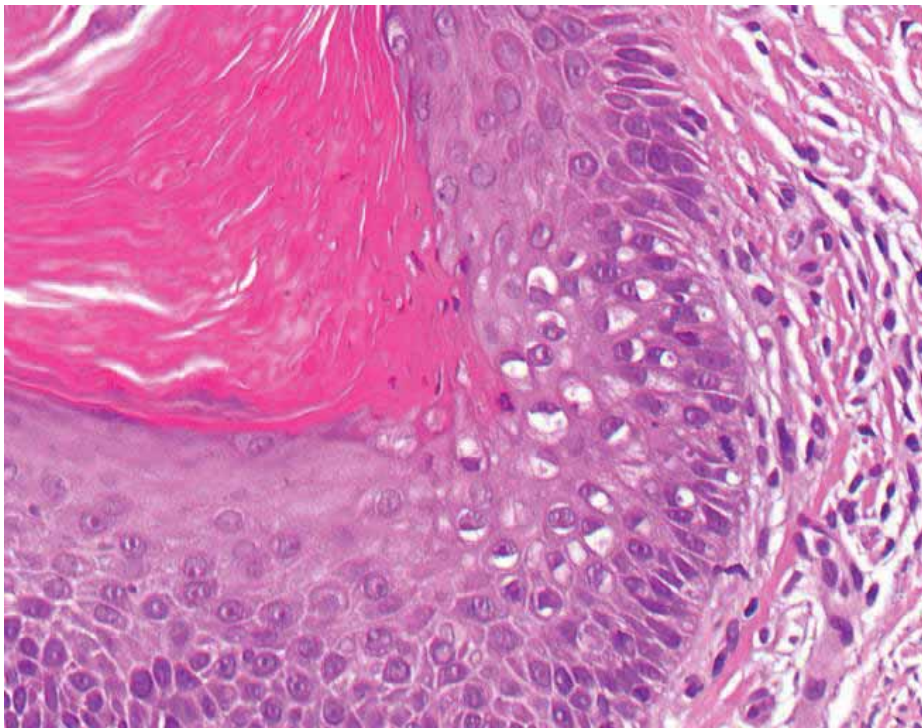
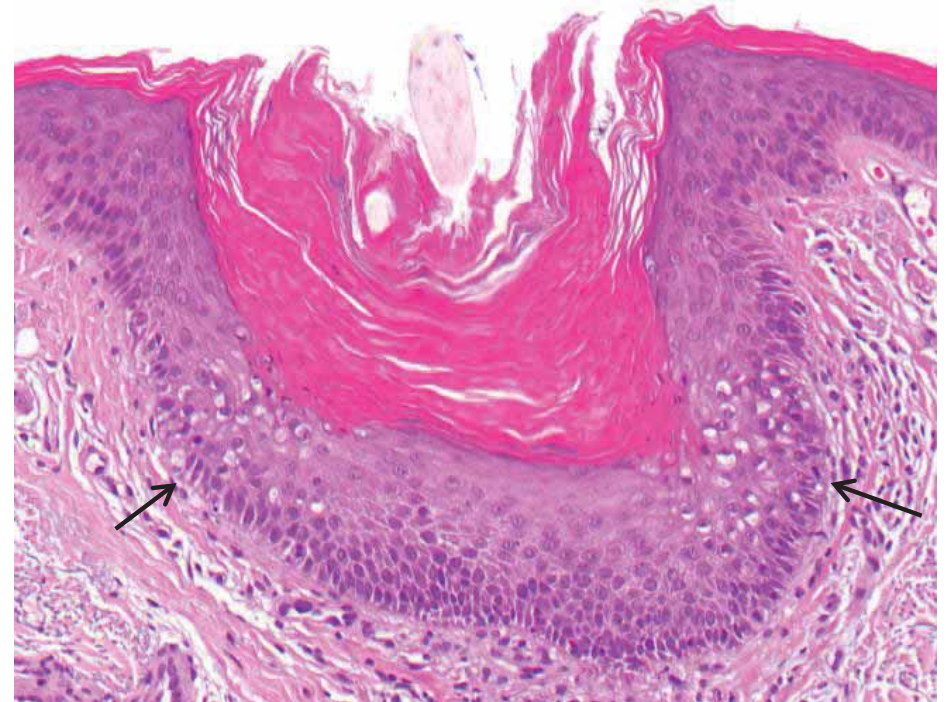
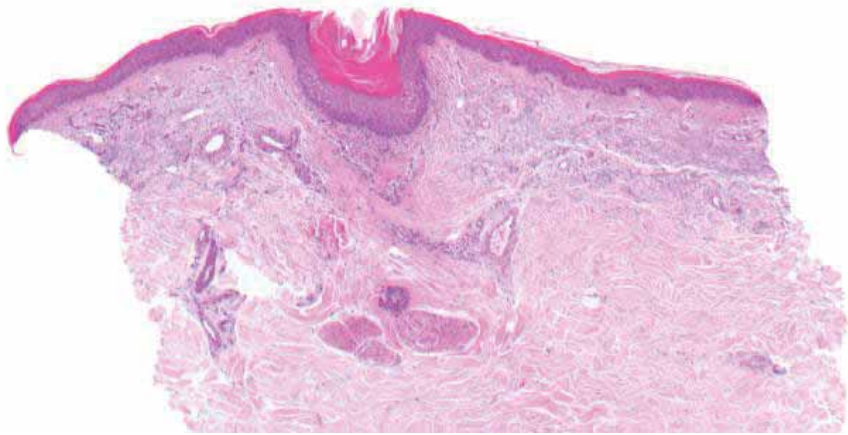
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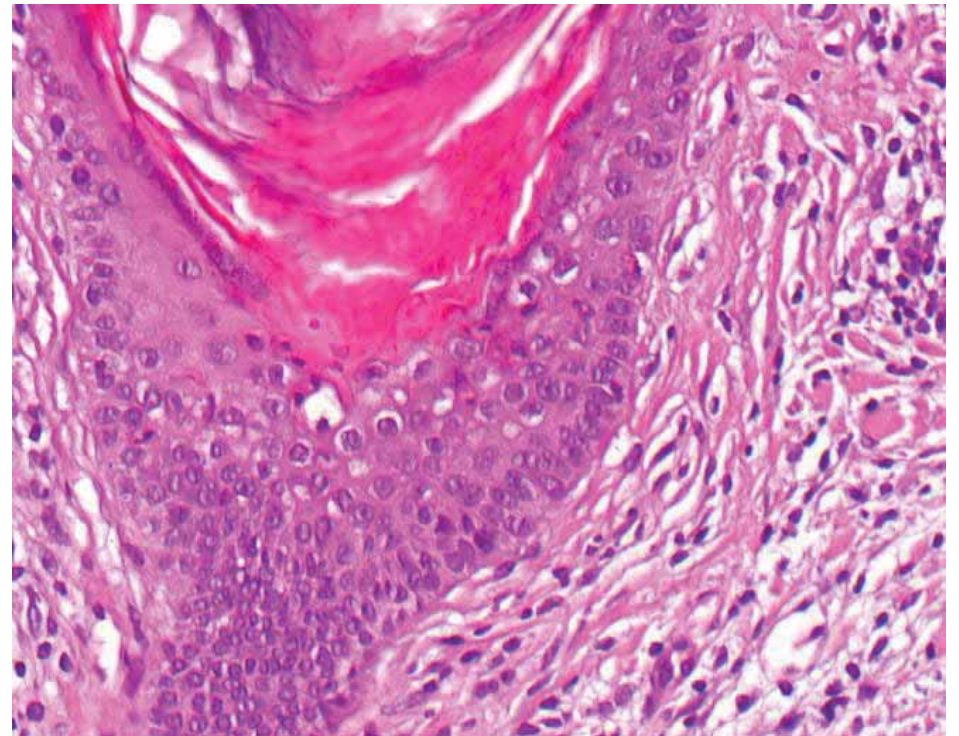
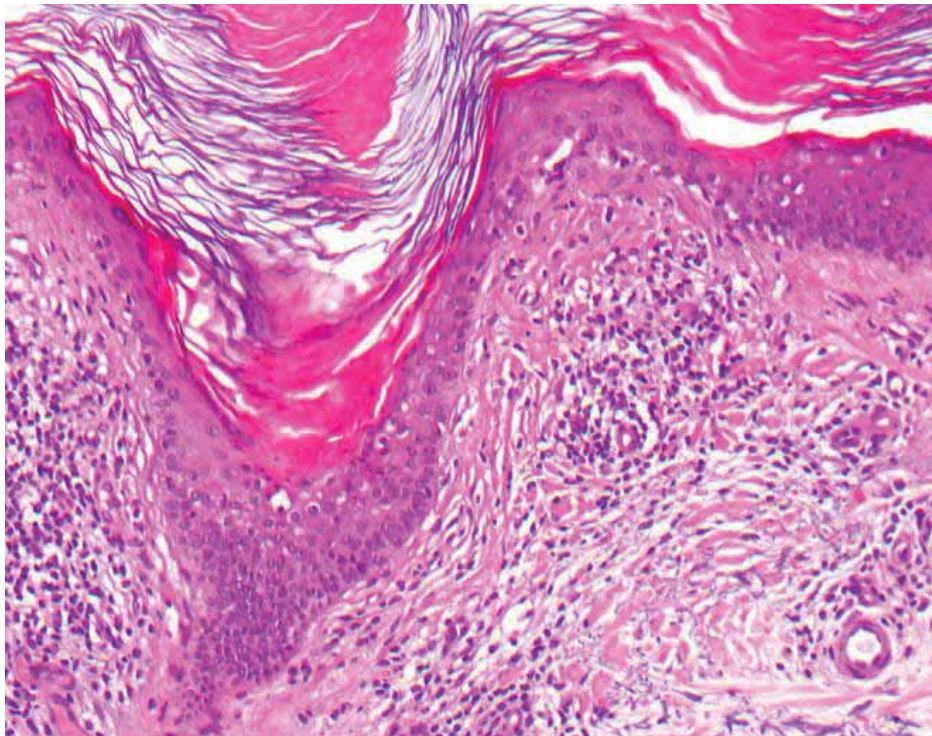
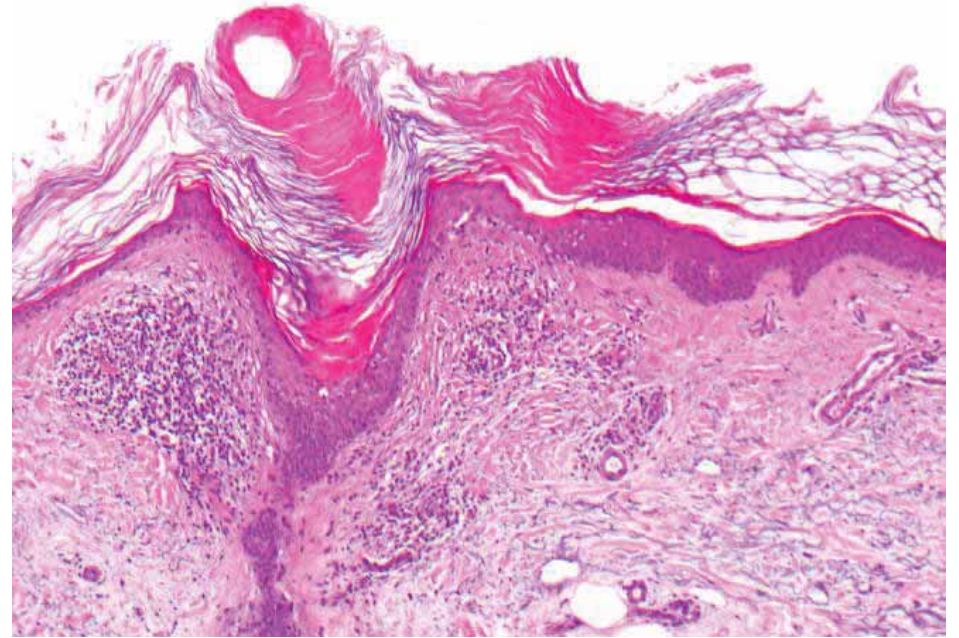
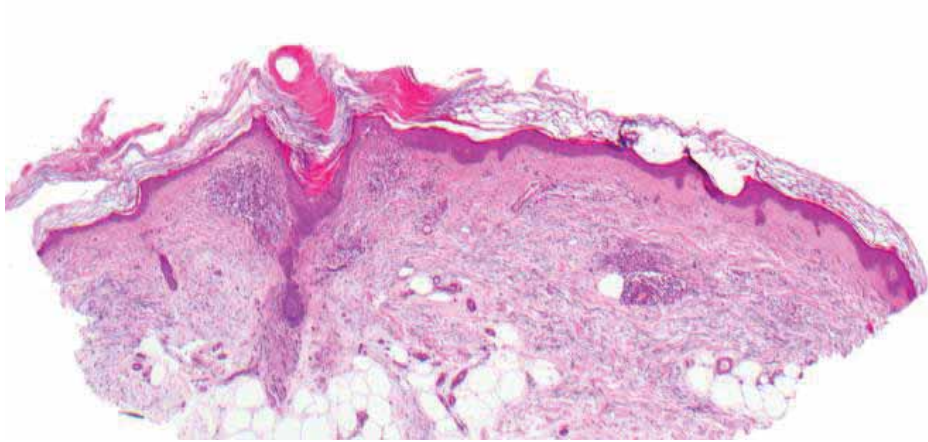
Step section

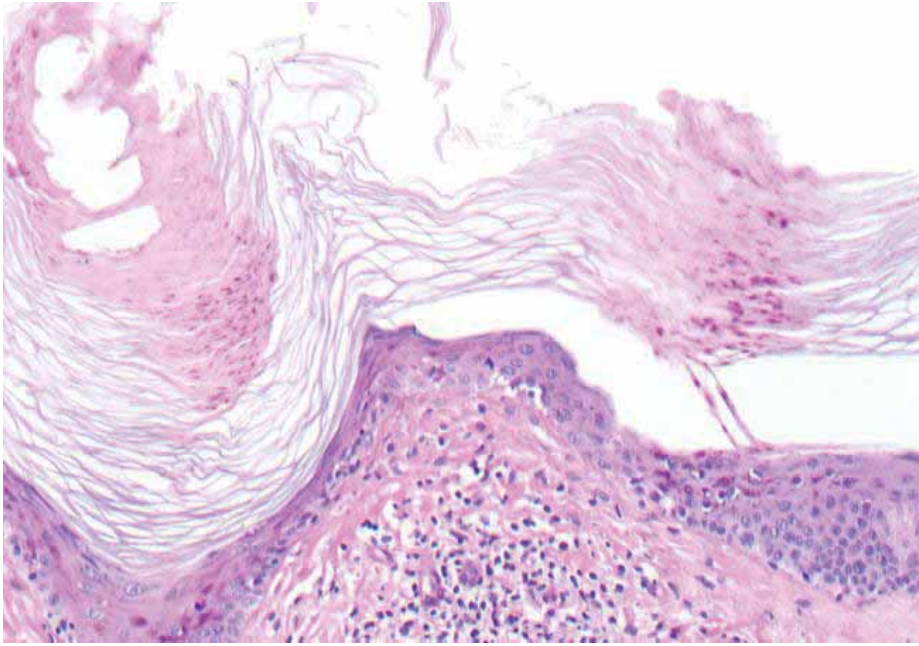


Porokeratosis, follicular



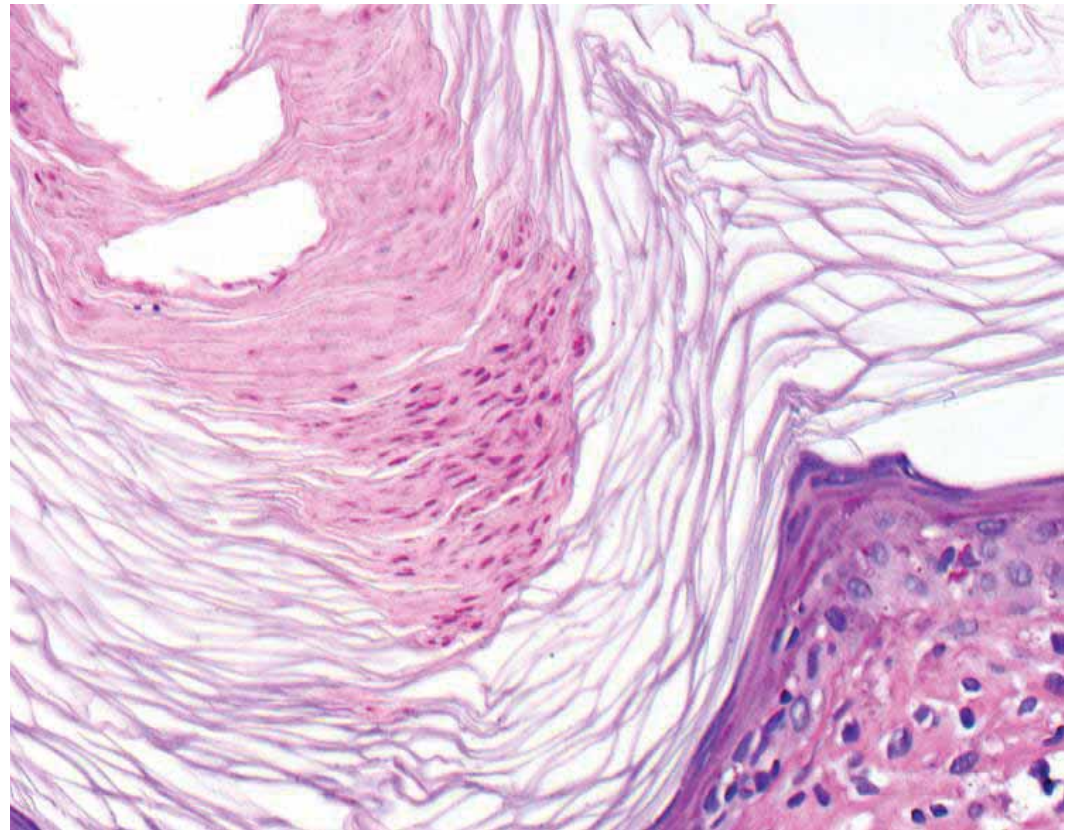
Porokeratosis, follicular



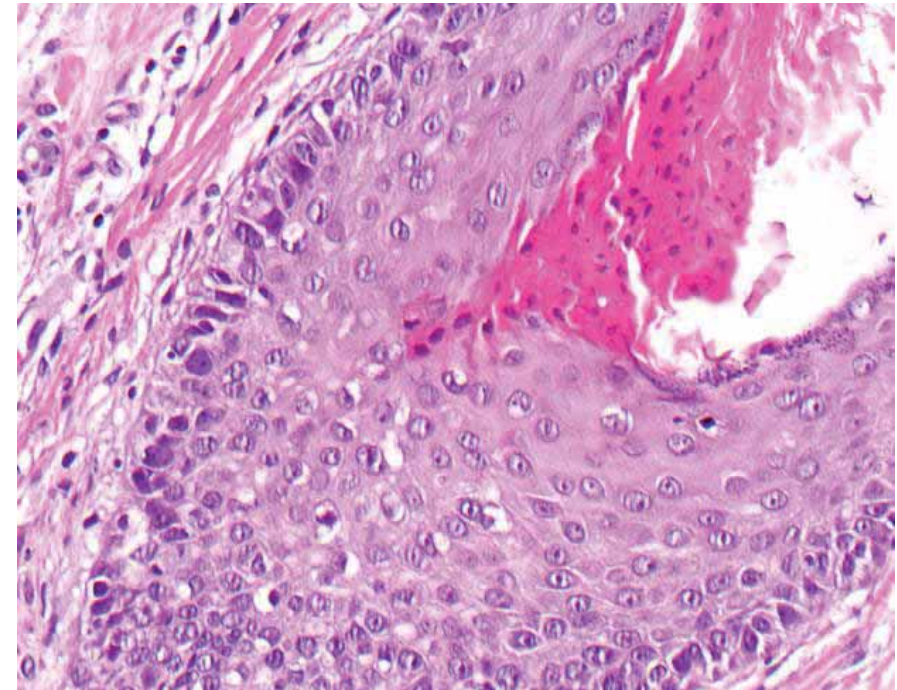
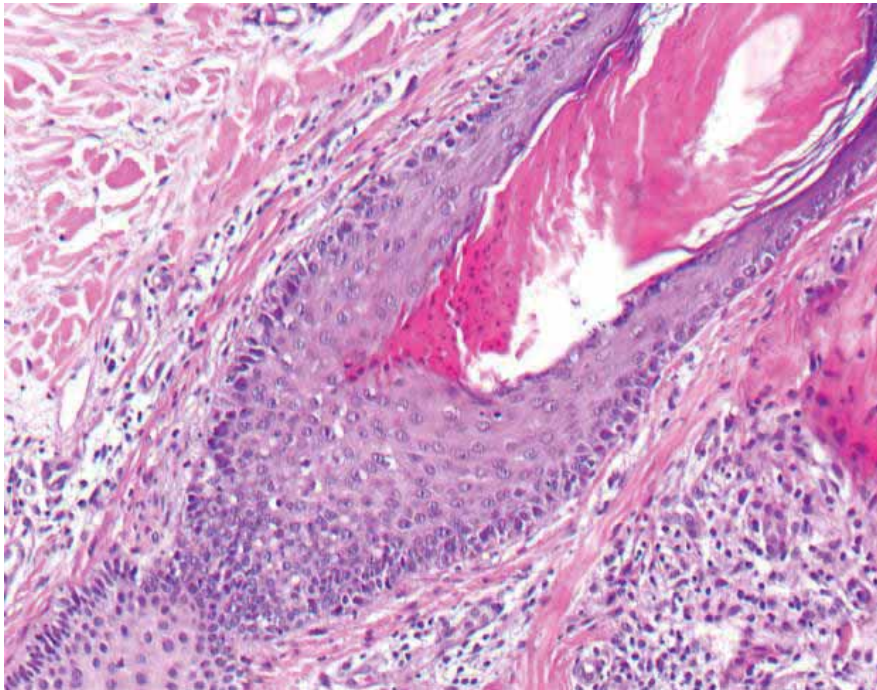
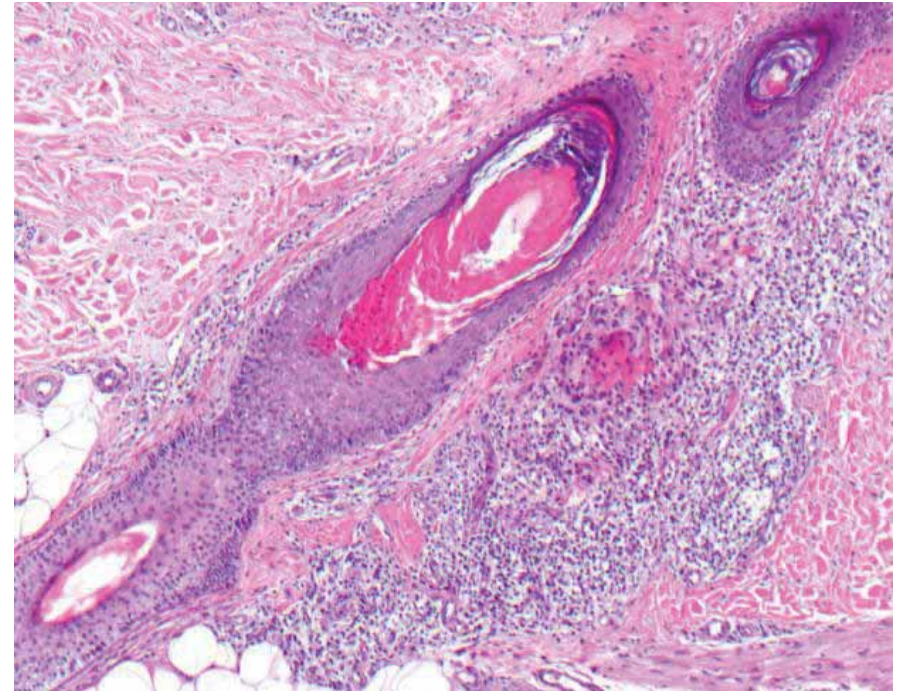


Porokeratosis, follicular

If you are not sure:
PAS staining !

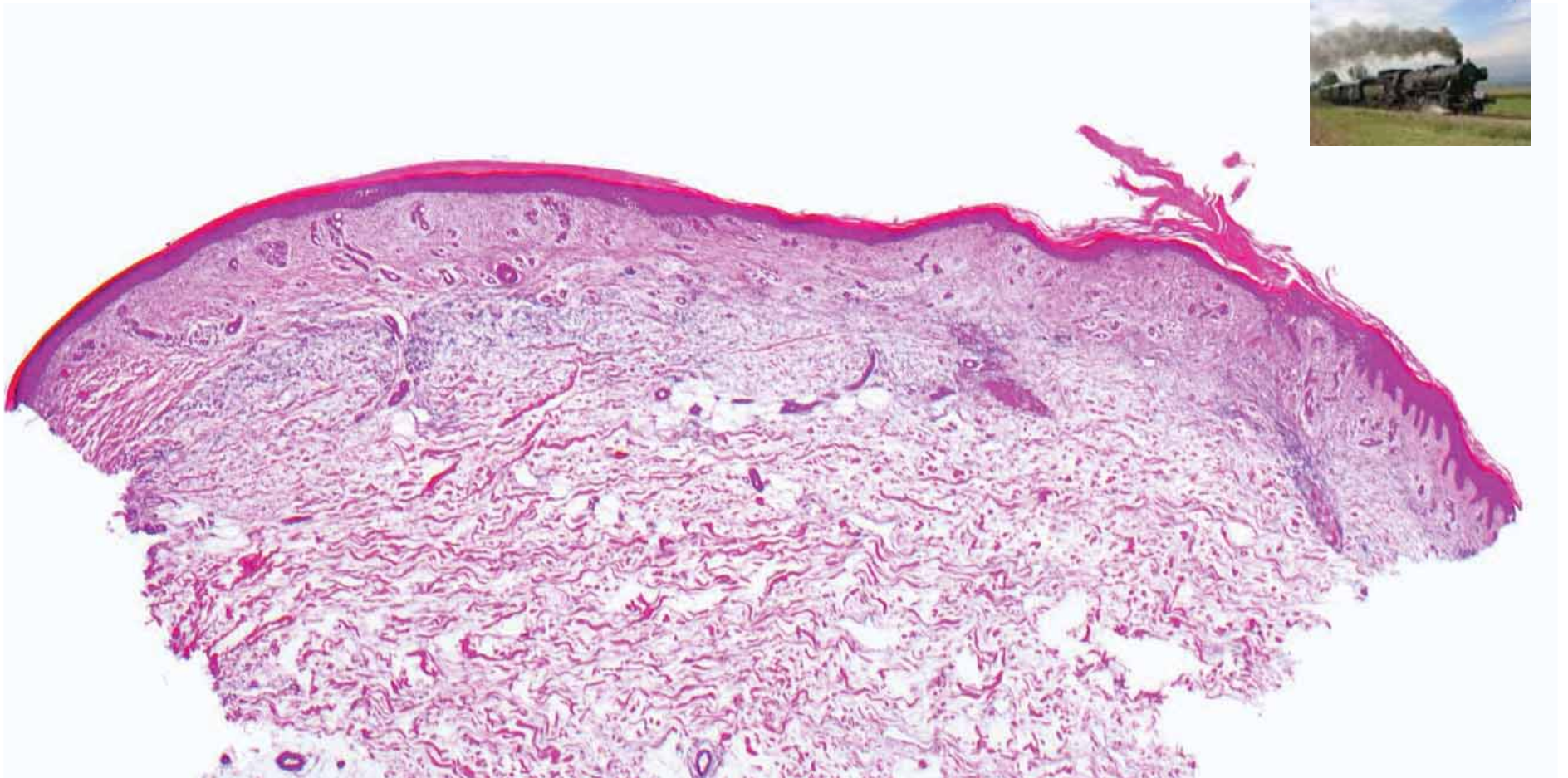


Porokeratosis, deep follicular

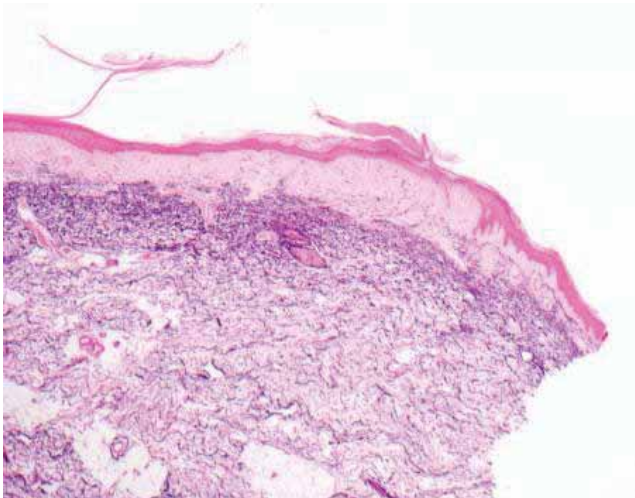
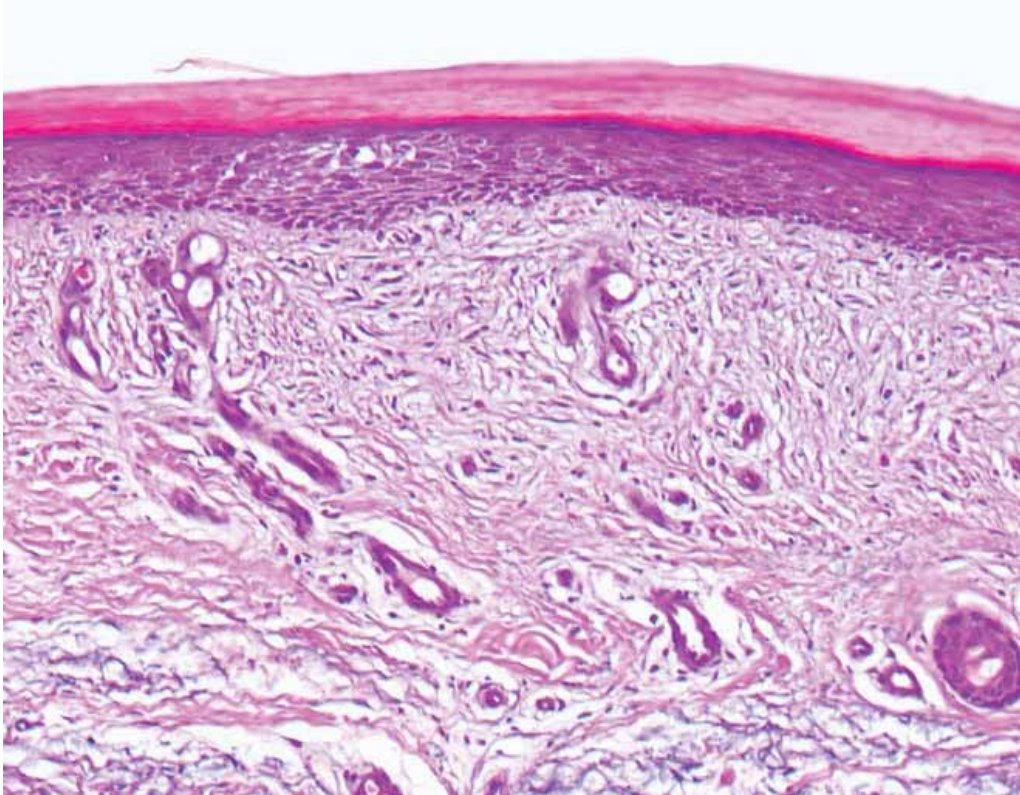
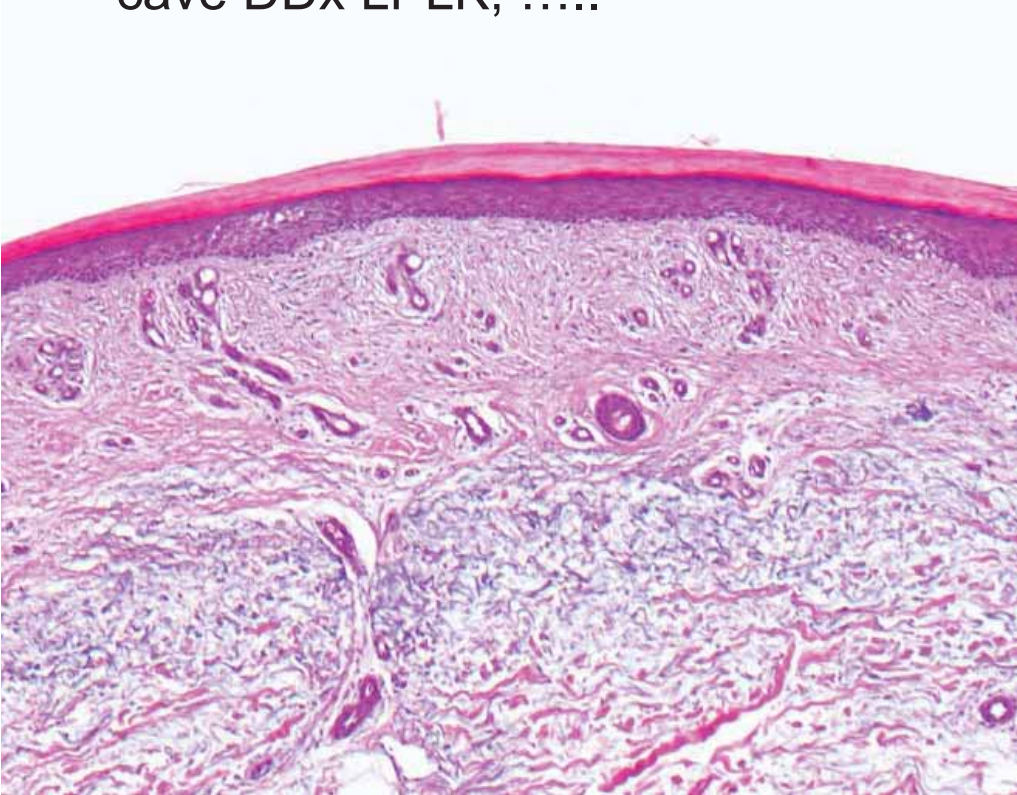


Porokeratosis

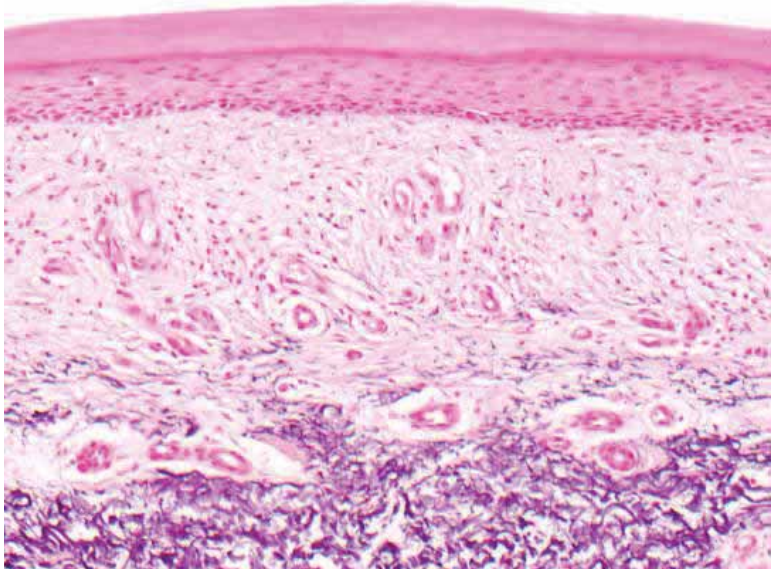
The center



Porokeratosis, signs of regression
- cave DDx LPLK,

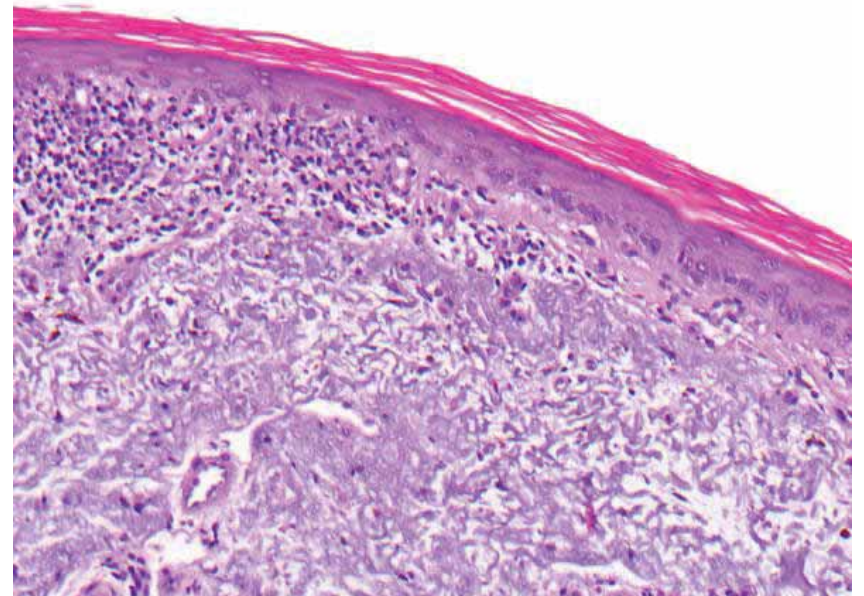
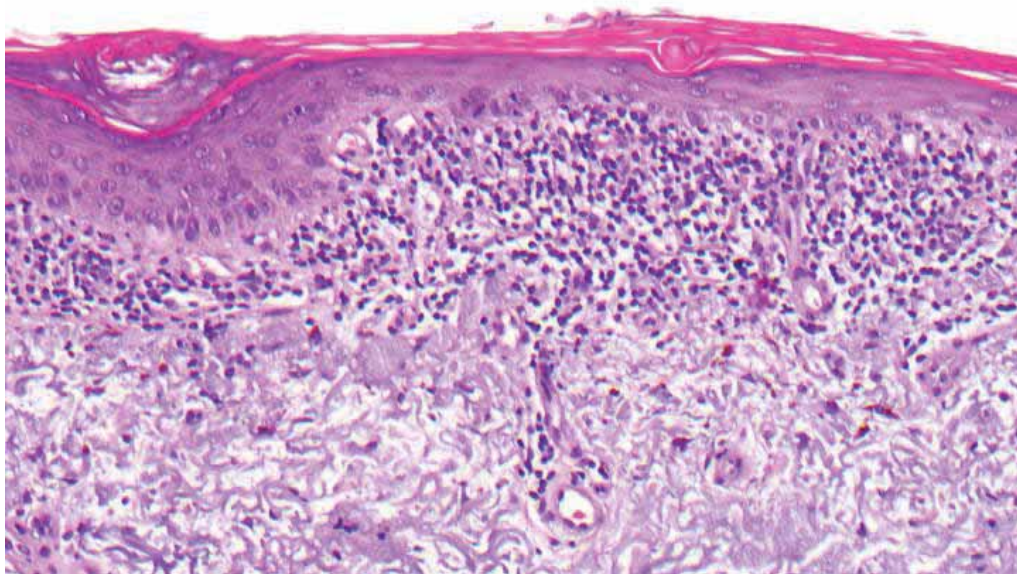
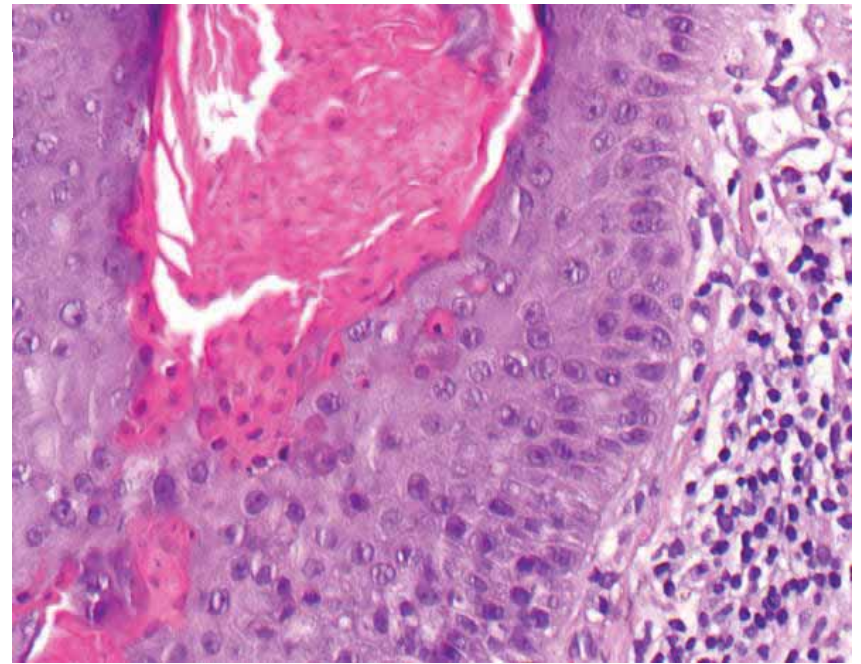
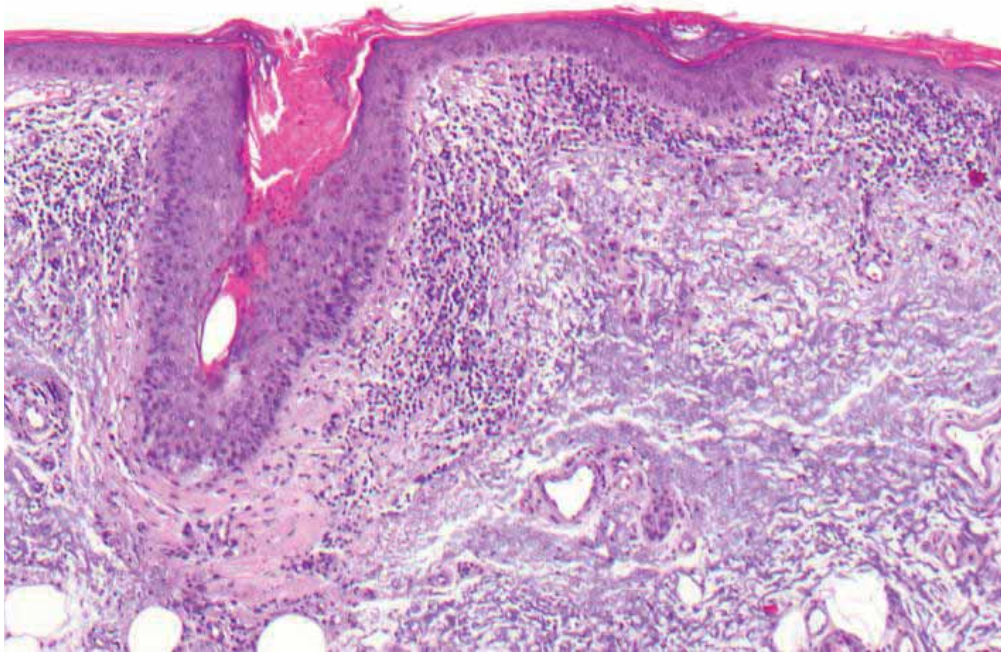


Elastica stain

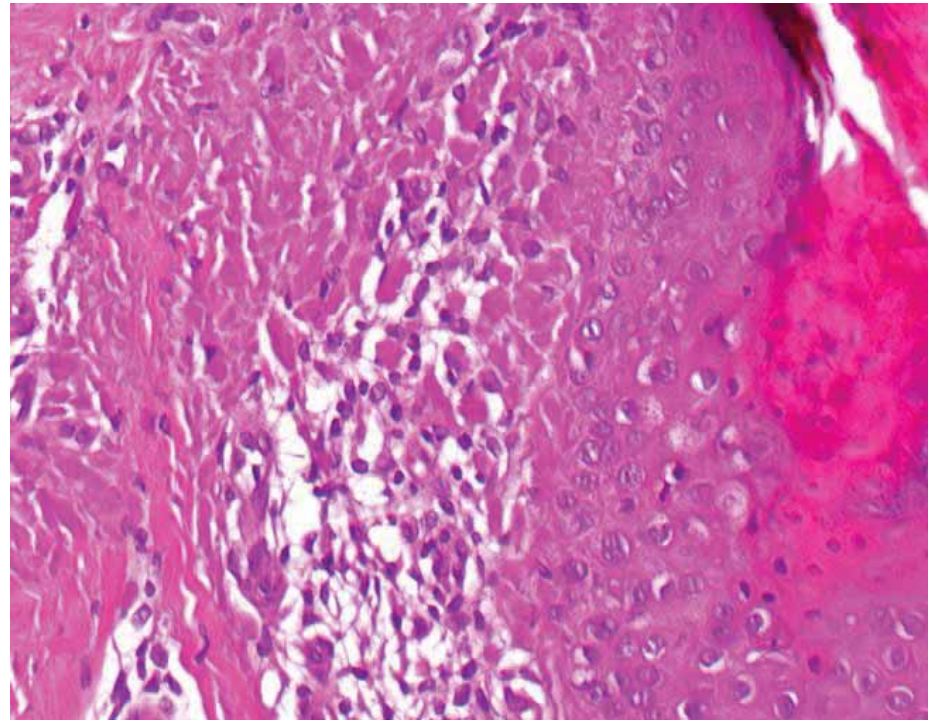
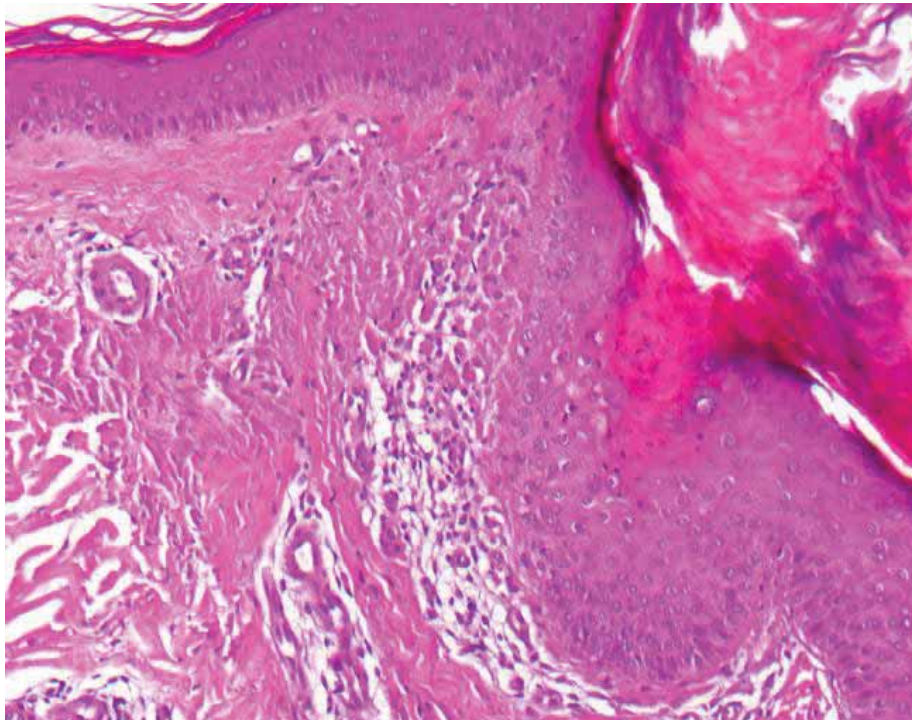
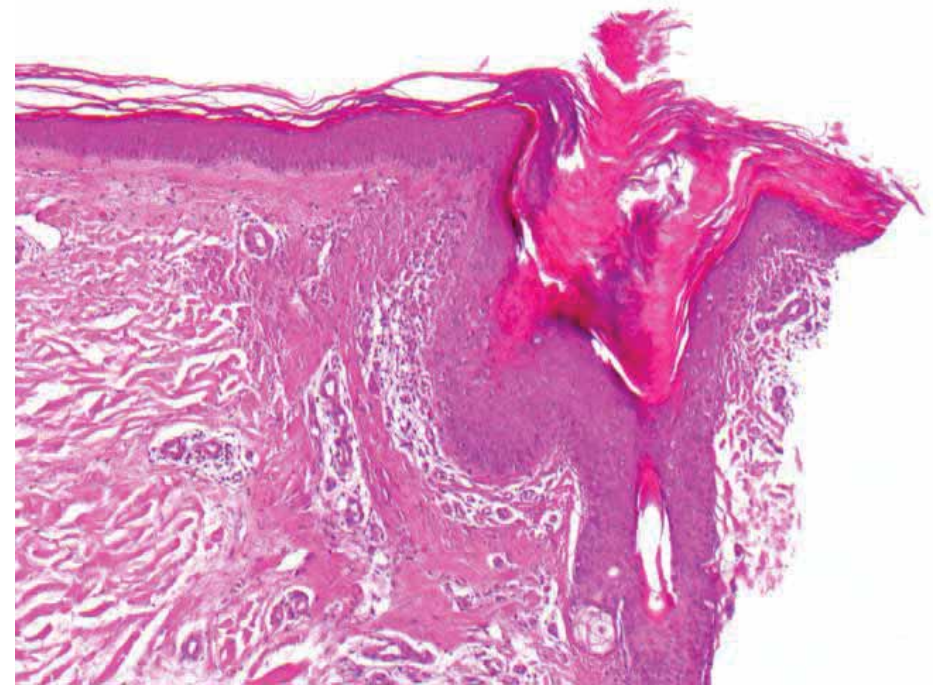
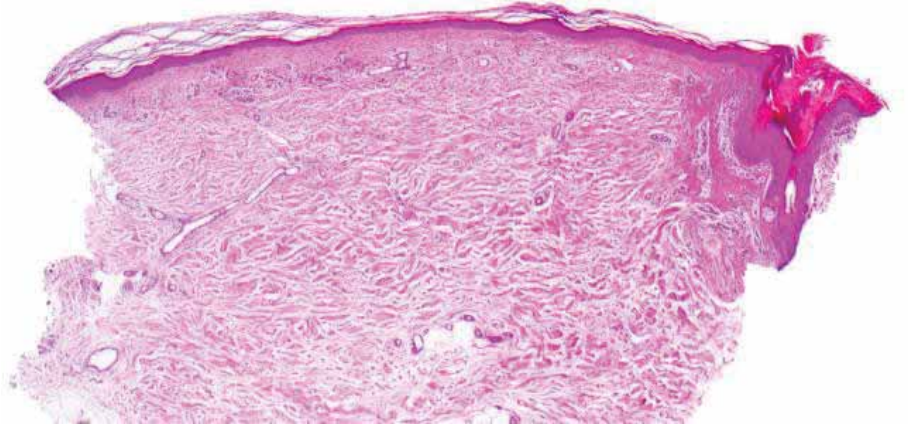


Porokeratosis, follicular

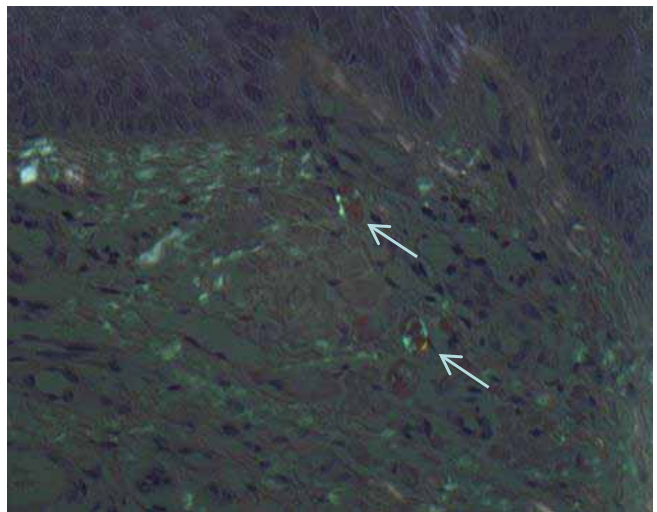
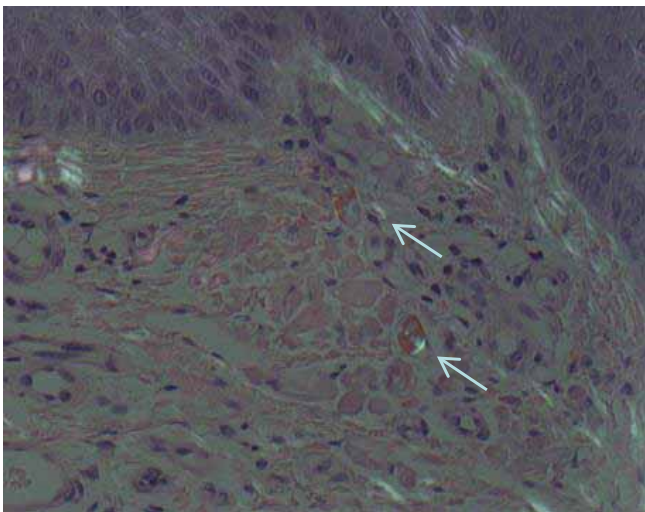
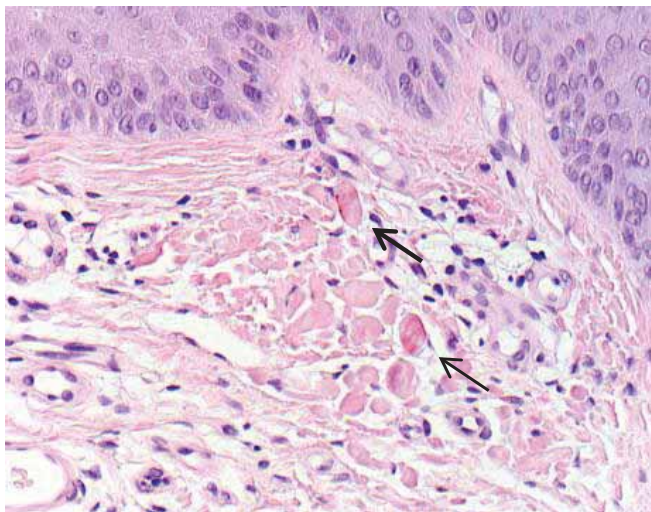
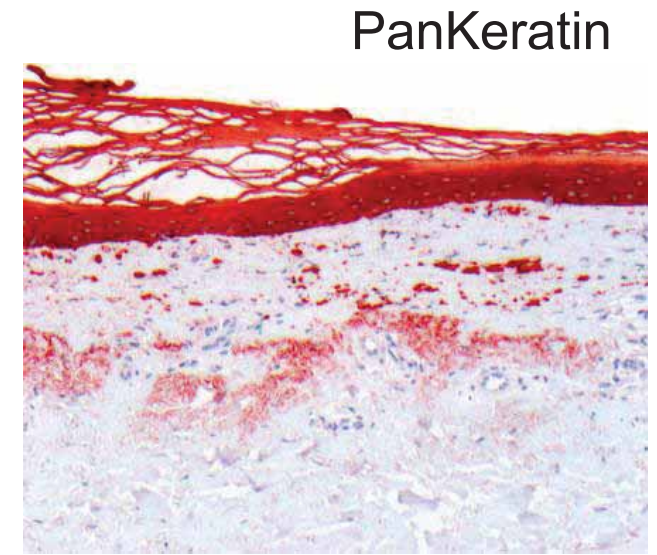
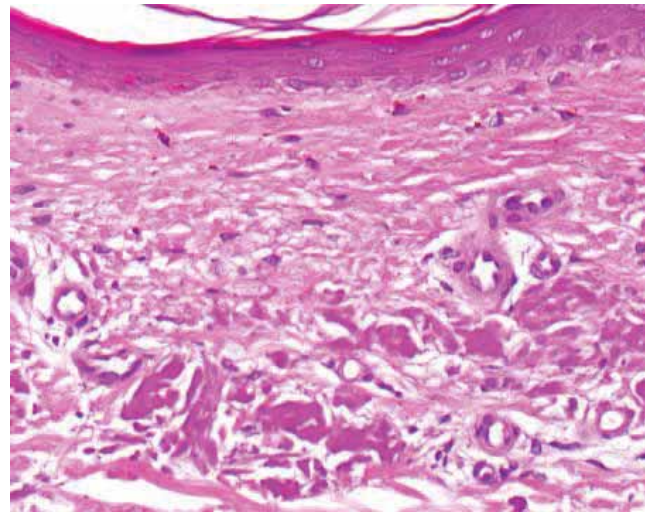
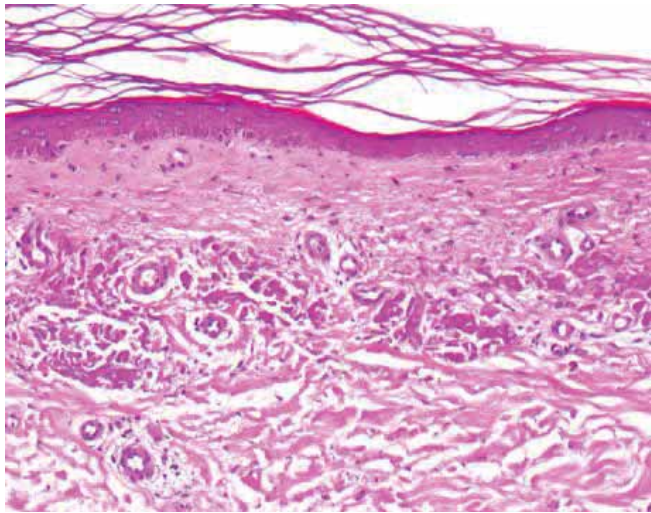
Signs of interface dermatitis – DDx LPLK,



Porokeratosis, DSAP, colloid bodies, amyloid



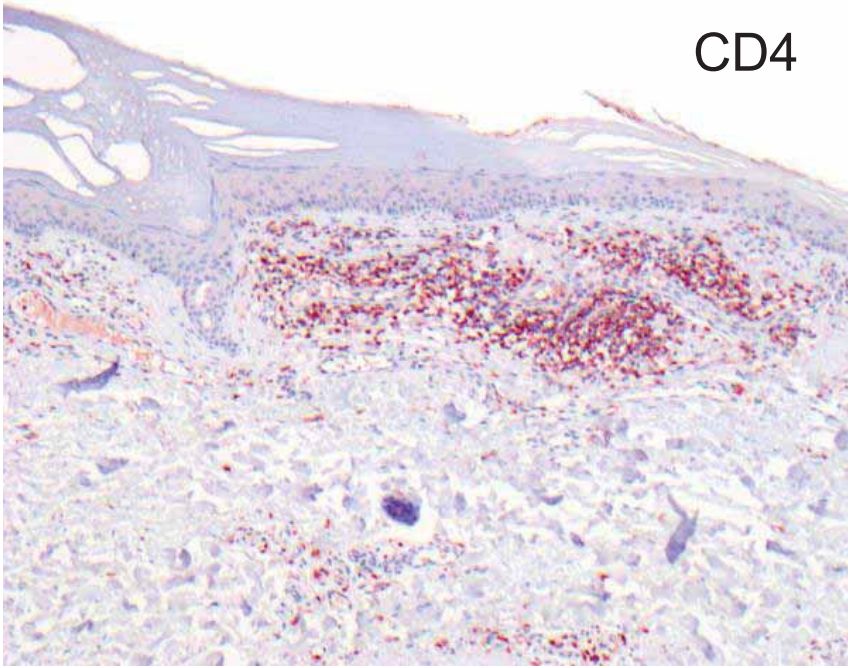
Porokeratosis, DSAP, colloid bodies, amyloid



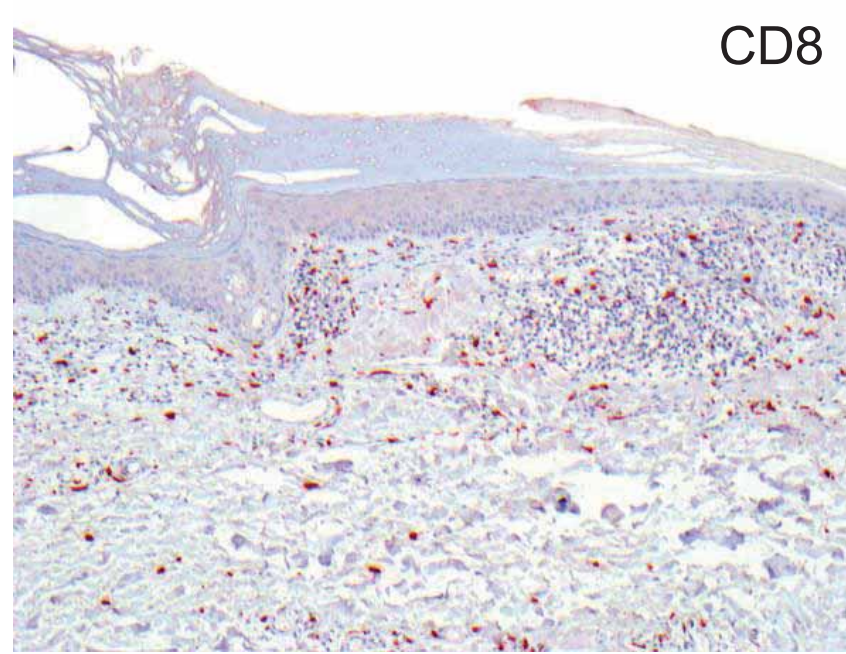
Kongo red

Polarisation (+/- 90°)

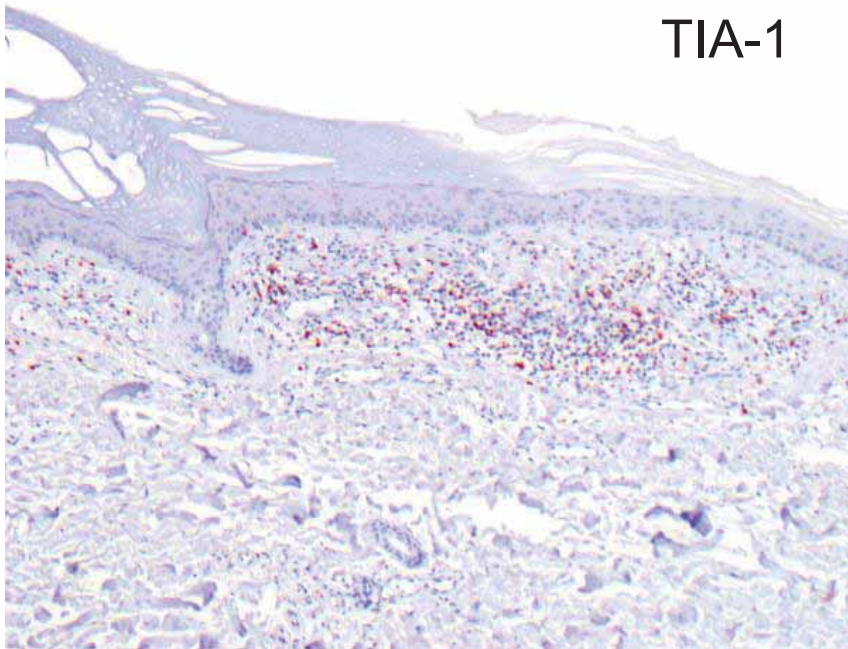
CD4



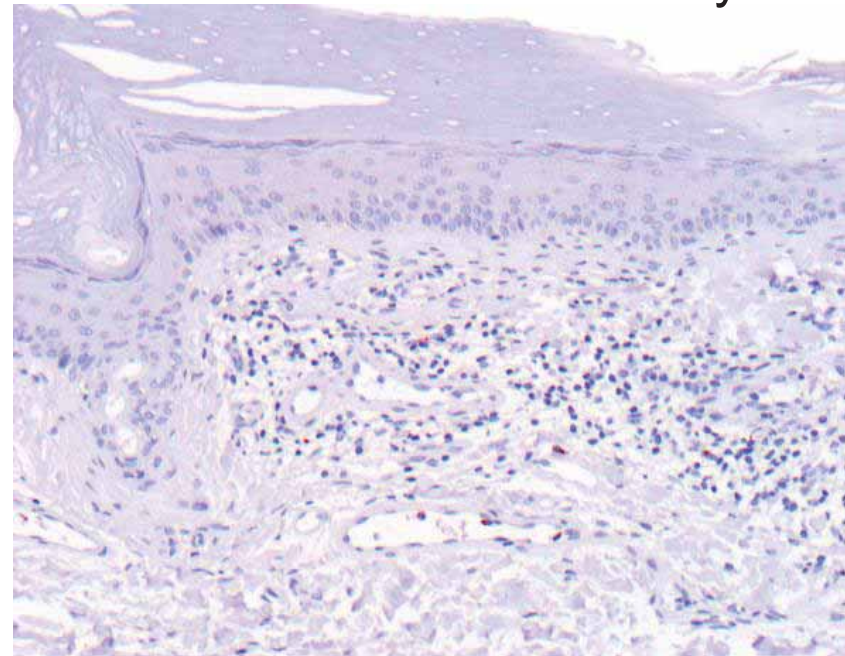
CD8



TIA-1



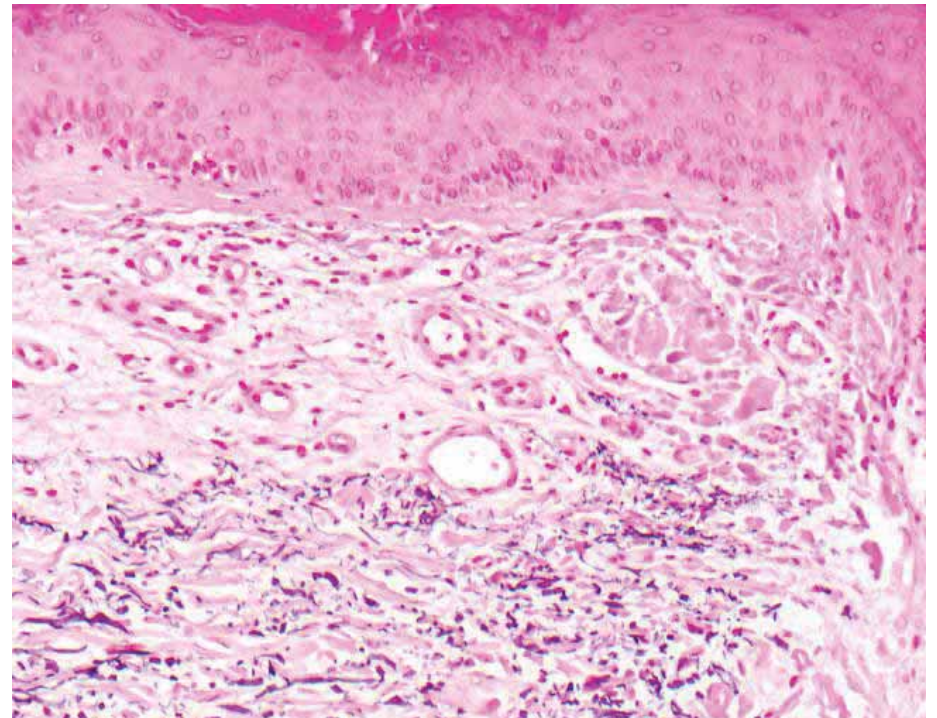
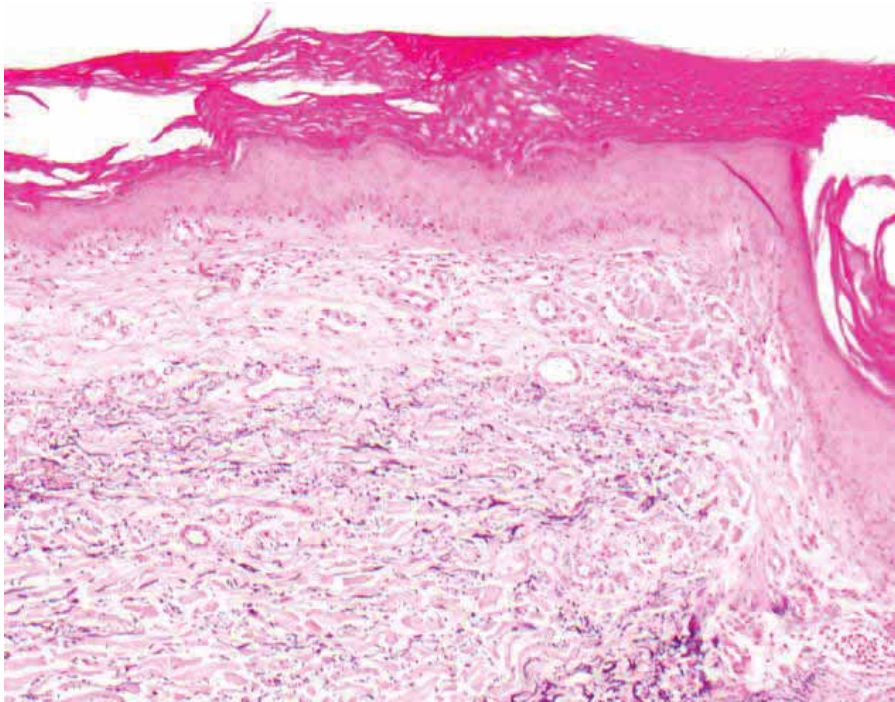
Granzyme B





DSAP

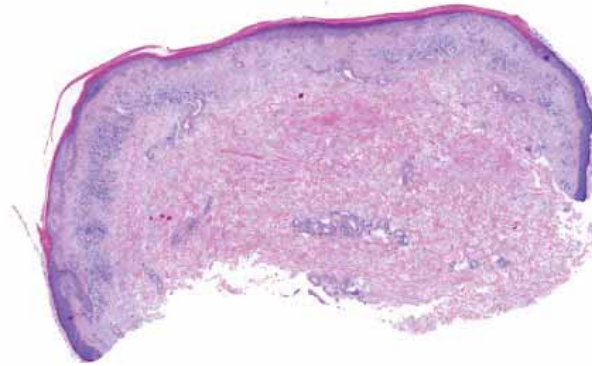
Elastica



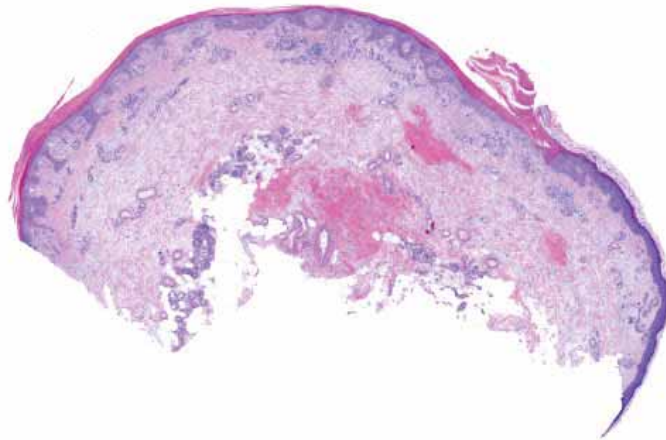
Porokeratosis, DSAP, center: atrophic -> hyperplastic

with compact orthokeratosis !

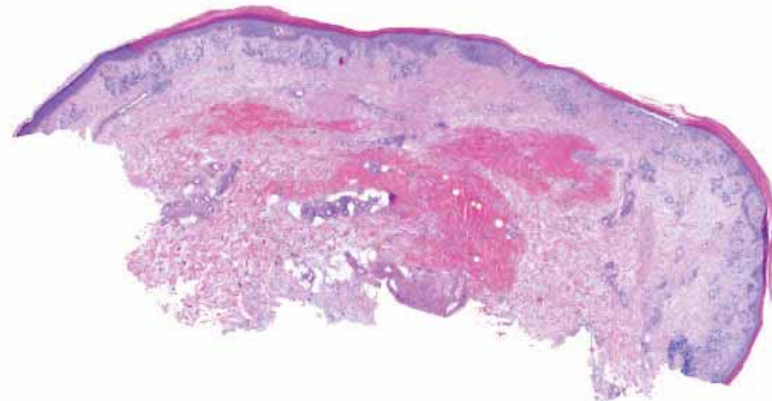
One Excision biopsy



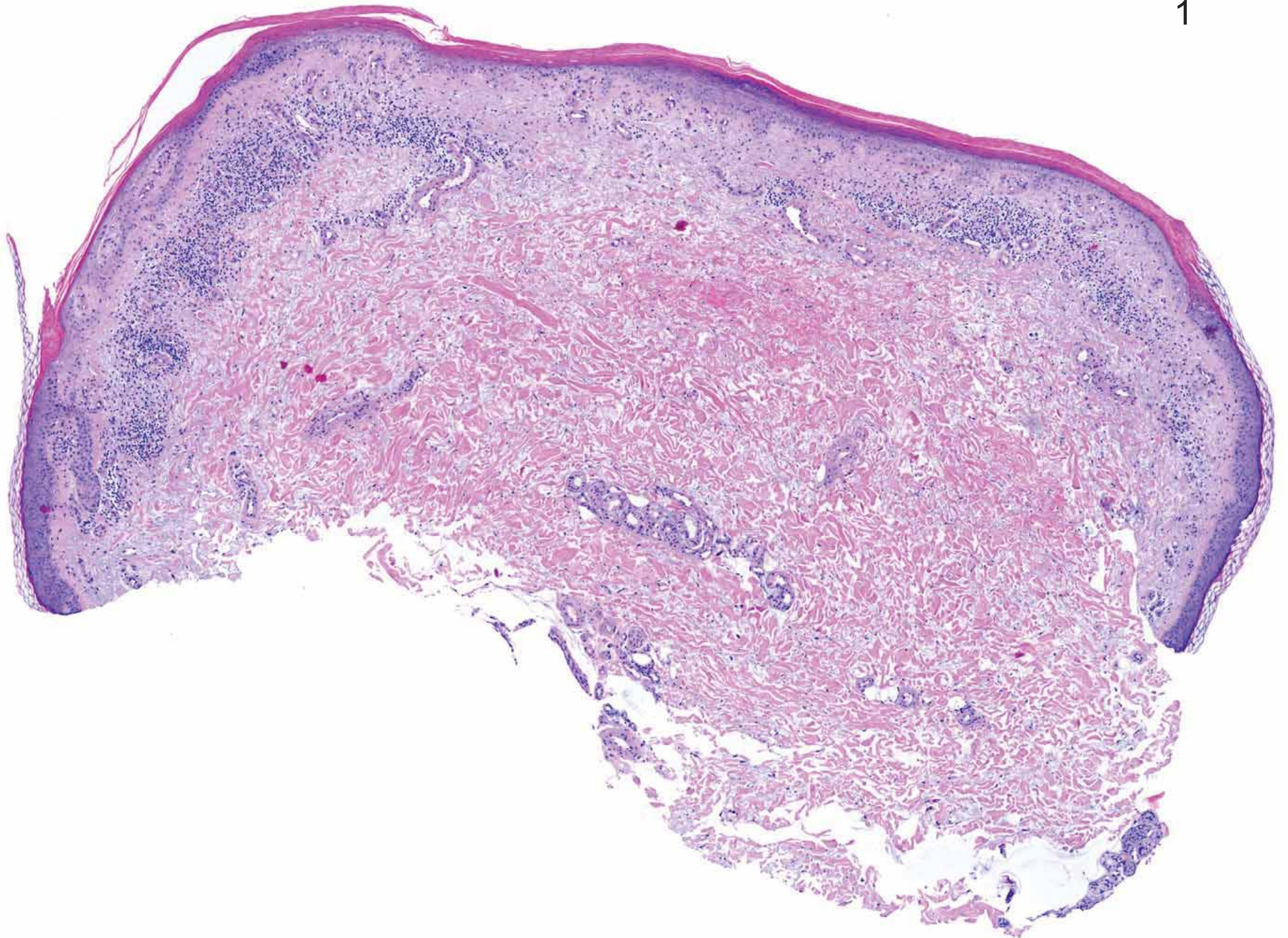
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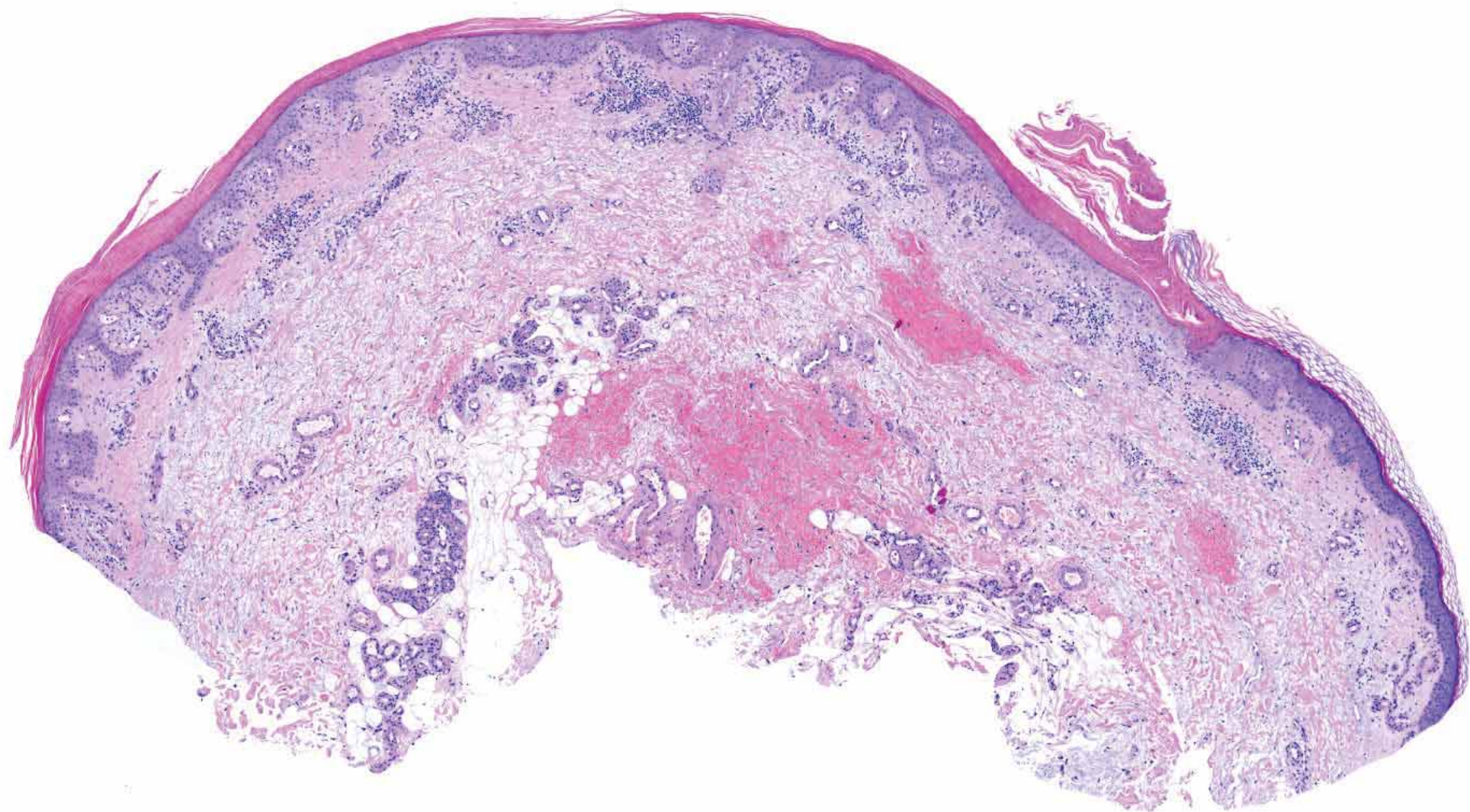


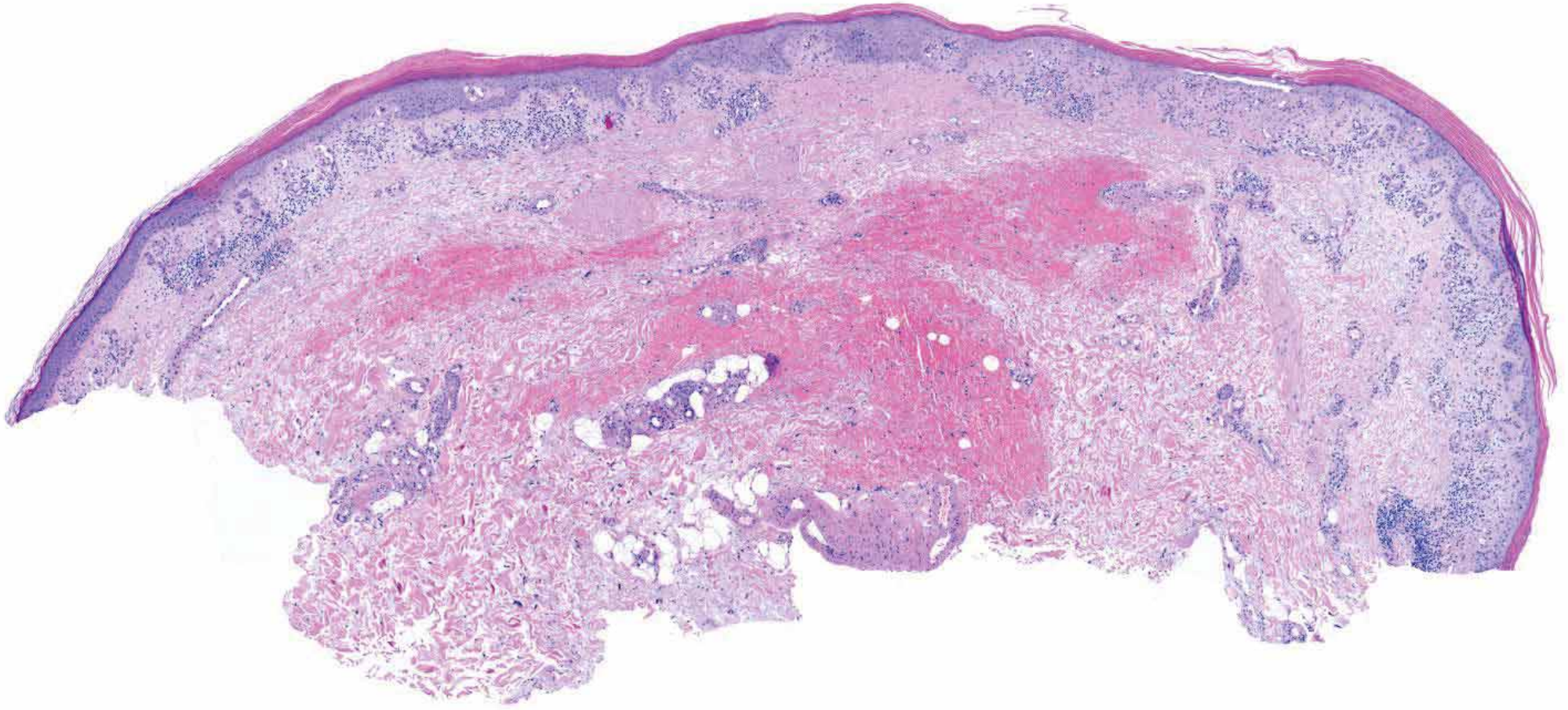
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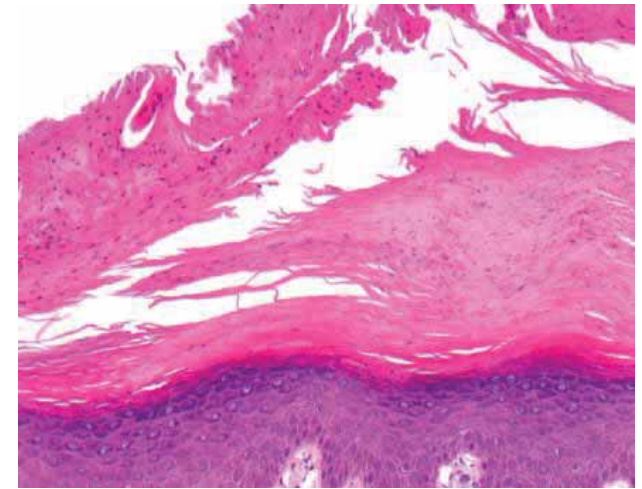
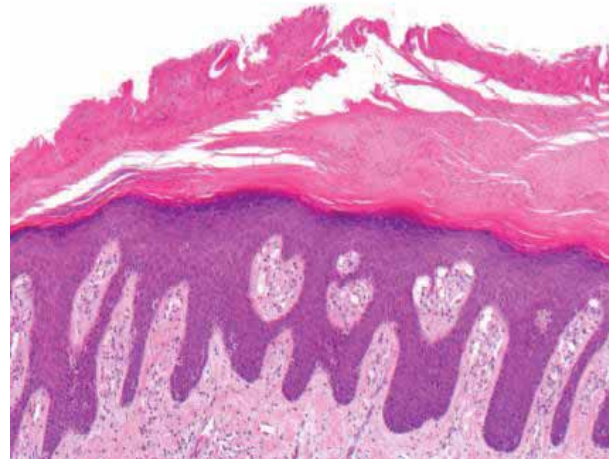
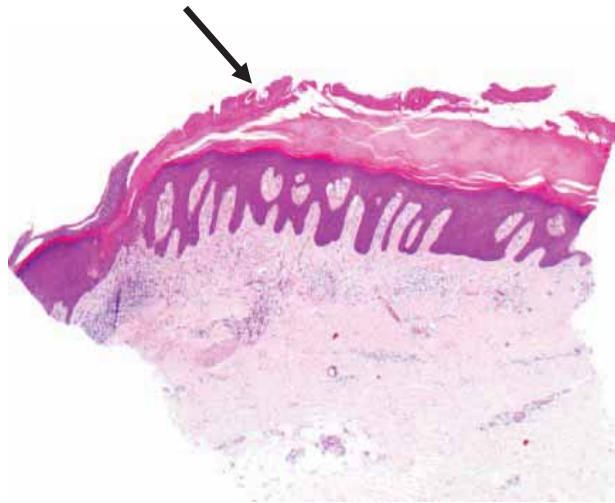
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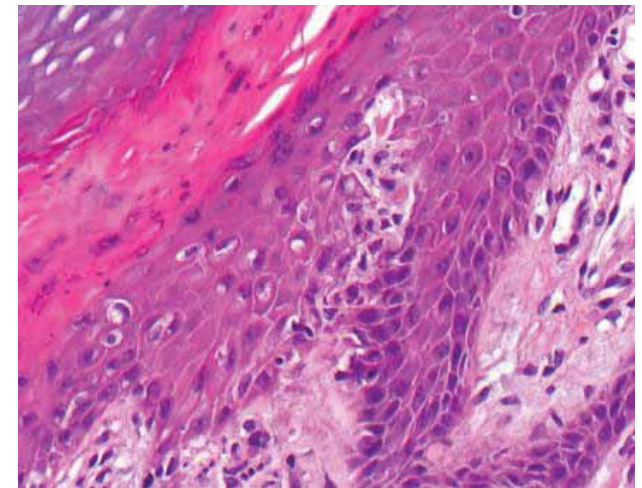
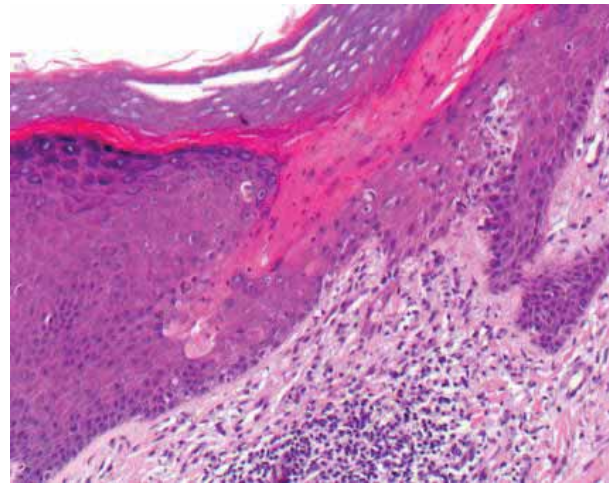
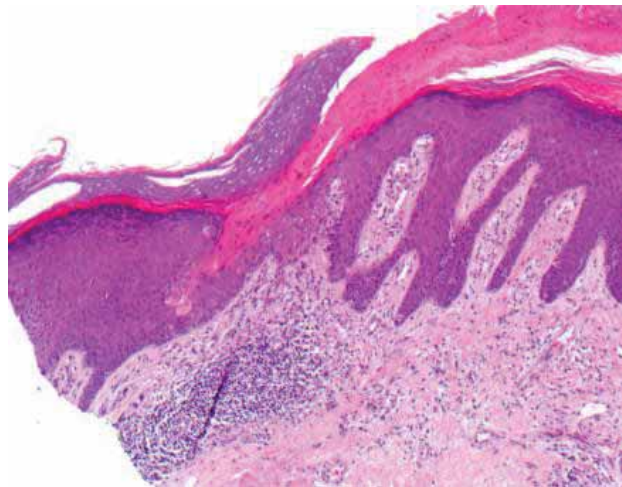




Porokeratosis, center: psoriasiform and hyperkeratotic



↘ Cornoid lamella on top of central orthohyperkeratosis



Interface-colloid bodies

Summary - Histology of Porokeratosis

Periphery of the lesion

- Vertical column of parakeratotic cells with PAS positive inclusions (cornoid lamella; varies in extent and distribution, can be overlooked !)
- Invagination of the underlying epidermis, absence of granular layer
- Dysmaturation with large, vacuolated or dyskeratotic keratocytes
- Signs of interface-dermatitis possible (cave DDx when cornoid lamella lacking), subepidermal clefting possible
- Variable infiltrate, sparse superficial perivascular or lichenoid with lymphocytes and few melanophages, rarely eosinophils

Center of the lesion (absent in punctate forms)

- Atrophic or acanthotic epidermis with hyperkeratosis (compact > basket-weave), ulceration possible
- Melanocytic hyperplasia reported
- Thick, fibrotic papillary dermis with numerous blood vessels, loss of elastic fibrils, colloid bodies, amyloid-deposits of keratin origin possible
- Variable lymphocytes (few, patchy or lichenoid), melanophages

Clinical aspects of Porokeratosis

- Inherited (AD) and spontaneous forms/variants with various mutations, different age of manifestation
- Trigger factors: UV, immunosuppression, ...
- Lesions solitary or numerous, small or large
- Extremities > trunk > face > anogenital > oral
- Atrophic or hyperkeratotic, pigmented or reddish macules, papules and plaques, clue: elevated keratotic rim
- Course: slowly progressive, rarely remission
- Development of SCC, Bowen and BCC (7-11%,
P. gigantea > P. linearis > P. disseminata)

Porokeratosis, classical type: continuous cornoid lamella

(combinations and variations possible)

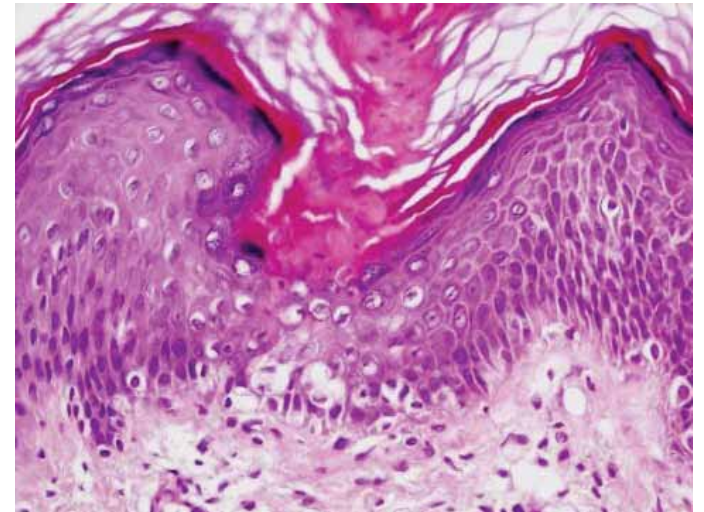
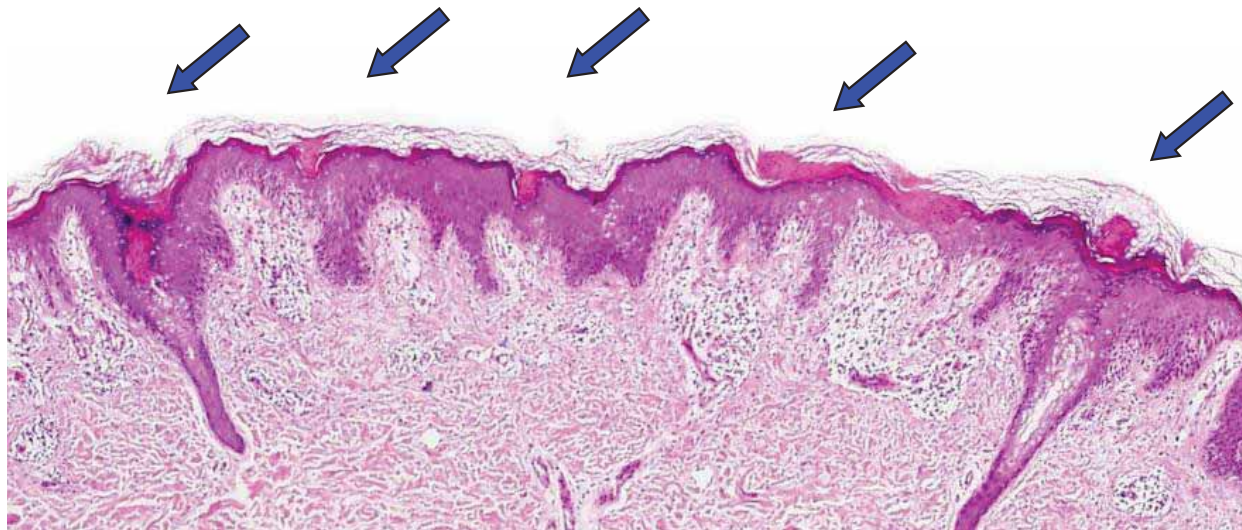
- Porokeratosis of Mibelli, *P. gigantea*
- Disseminated superficial actinic Porokeratosis (DSAP)
- Disseminated superficial Porokeratosis (DSP)
- Eruptive papular pruritic Porokeratosis
- Porokeratosis linearis
- Porokeratosis palmaris et plantaris disseminata

(CAP syndrome: Craniosynostosis, genitourinary and anal Anomalies, Porokeratosis, RNU12 gene)



Porokeratosis, punctate type

Multifokal
Cornoid Lamella



Porokeratosis, punctata type:

Multiple, reticulated or focal „cornoid lamellae“

(combinations and variations possible)

- Porokeratosis linearis
- Eruptive pruritic papular Porokeratosis
- Porokeratosis ptychotropica
- Follicular porokeratosis
- Reticulated Porokeratosis (Kossard)
- Porokeratoma

(Porokeratosis palmoplantaris punctata = PPKP2)

(Porokeratotic adnexal ostial Naevus, PAON)

Porokeratosis – variants, some combined in one patient:
linear P., reticulated P., Mibelli-like P.





Genetic Background and Pathophysiology

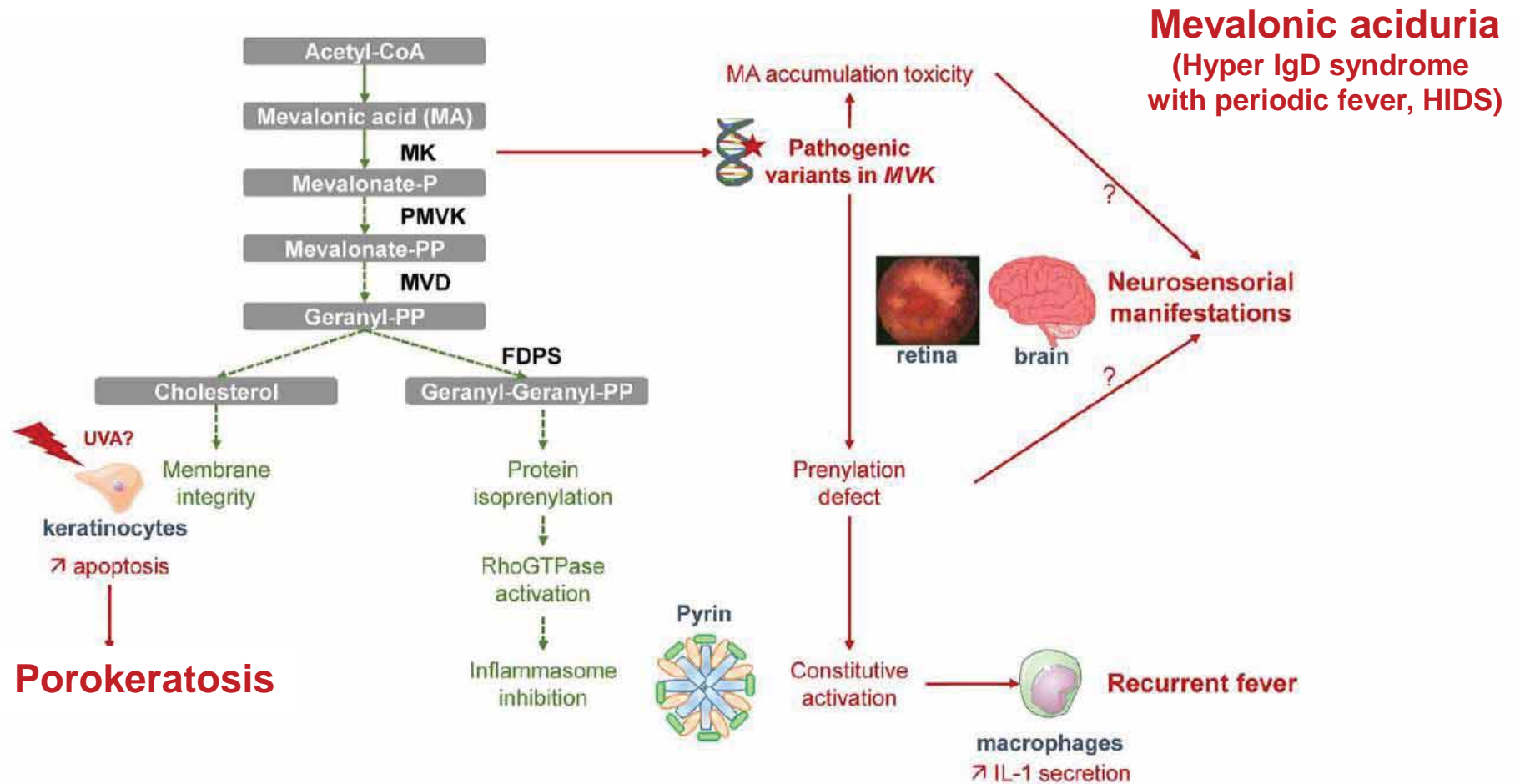
- Chromosomes 12q (DSAP1), 15q (DSAP2), 1p (DSAP3), 16q (DSAP4)
 - Heterozygous mutations of genes encoding enzymes in the mevalonate pathway (**MVK** > **MVD**, **PMVK**, **FDPS**): biosynthesis of cholesterol and isoprenoid affecting keratocyte differentiation and protection from UVA induced apoptosis
 - Rare mutations **SART341** (regulation of messenger RNA splicing), **SSH142**, **ARPC343** (polymerization and dynamics of actin filaments); **SLC17A9** (vesicular nucleotide transporter, Ca/ATP release), **EMILIN2** (pro-apoptotic gene)
-
- Disturbed epidermal differentiation with cornoid lamella and premature apoptosis (Filaggrin↓, Loricicrin↓, involucrin↑)
 - DNA-polyploidy, overexpression of p16, p53, and pRb, reduction of mdm2 and p21, mutation of p53 in cases of porokeratosis with malignant transformation
 - Centrifugal migration of a clone of abnormal cells with regression in the center

Twists and turns of the genetic story of mevalonate kinase-associated diseases: A review

Isabelle Touitou ^{a,b}

Genes & Diseases (2022) 9, 1000–1007

Mevalonate–isoprenoid pathway



Dominant inheritance with recessive somatic expression (second mutation of the wild-type allele -> late manifestation)

Recessive inheritance

Trigger Factors/Associations

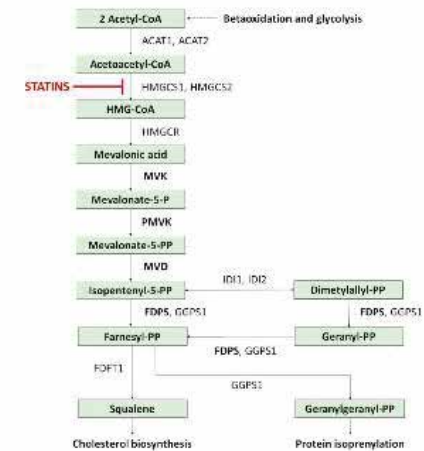
- **Immunosuppression, UV, radiation therapy, chronic GvHD**
- **Scar** (Burn, access region of hemodialysis), **lymphedema**
- **Drugs:** Furosemid, antibiotics, TNF α inhibitor, hydroxyurea, systemic and topical steroids, AZT,
- **Infections:** HPV, HIV, HVC, HSV, SARS-CoV-2
- **Autoimmune and other diseases:** SLE, DM, Psoriasis, Vitiligo, Alopecia areata, Lichen planus, LSA, Pemphigus, Diabetes, rheumatoid arthritis, Crohn's disease, liver or renal dysfunction, pancreatitis,...
- **Neoplasms:** Hepatocellular-, cholangiocarcinoma, hereditary non-polyposis colorectal carcinoma, lymphoma, leukemia, myeloma, Mycosis fungoides, ...
- **Hereditary Immunodeficiencies and Genetic diseases:** CAP syndrome, Agammaglobulinaemia, Werner-syndrome, Rothmund-Thompson syndrome, cystic fibrosis, trisomy 16, erythropoietic protoporphyria, pseudoxanthoma elasticum

Treatment

- Topical 5-fluorouracil, retinoids in combination with 5-FU, imiquimod, tacrolimus, corticosteroids, ingenol mebutate, vitamin D3 analogs, retinoids, diclofenac 3% gel

Lovastatin/cholesterol cream or lovastatin alone, twice daily

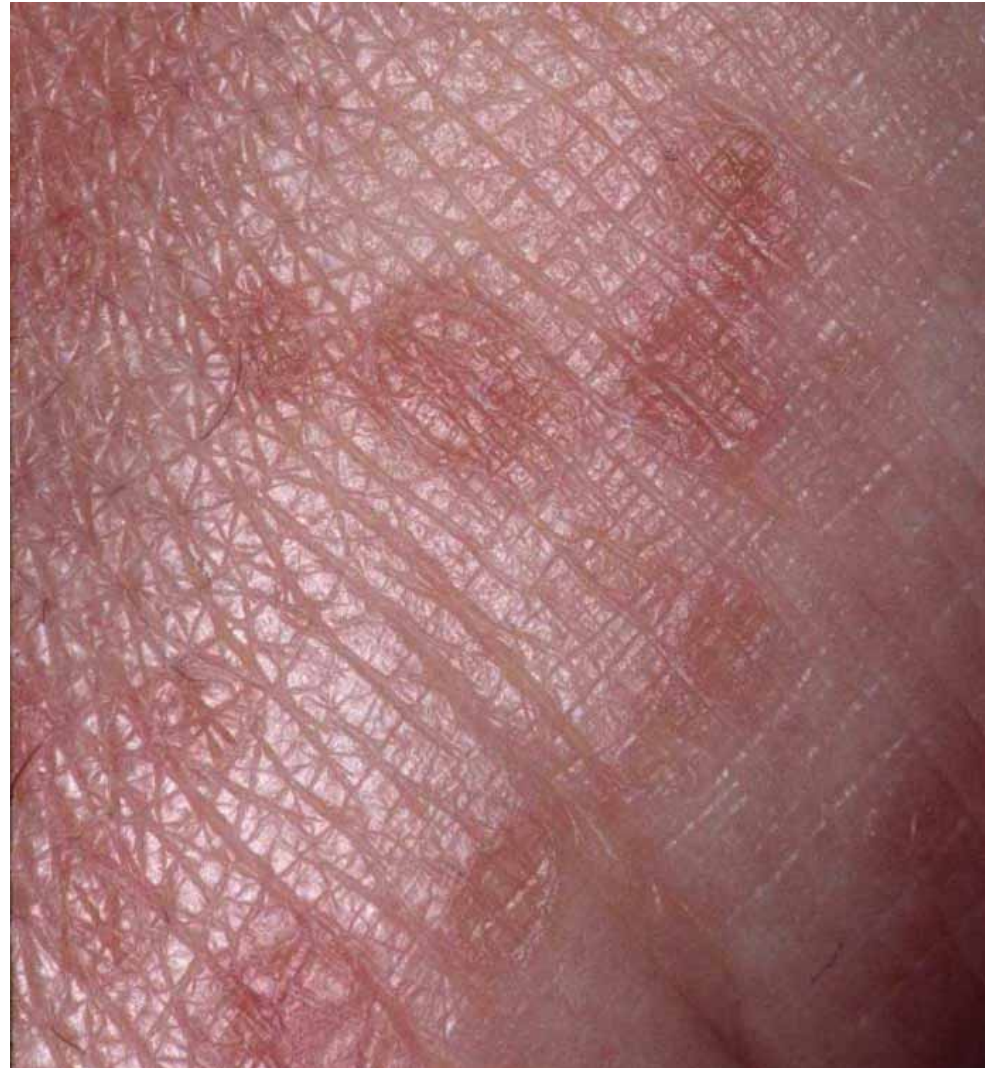
- Systemic retinoids in widespread or refractory lesions
- Chemical peeling, photodynamic therapy, radiotherapy, laser therapy, cryotherapy, shave excision, curettage, excision, dermabrasion
- **Porokeratosis is very difficult to treat or eradicate !**



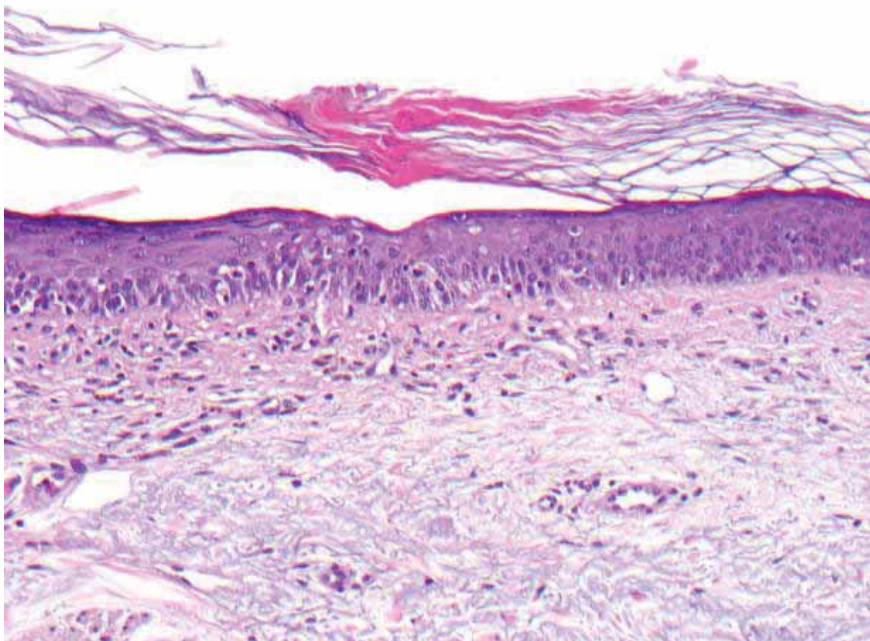
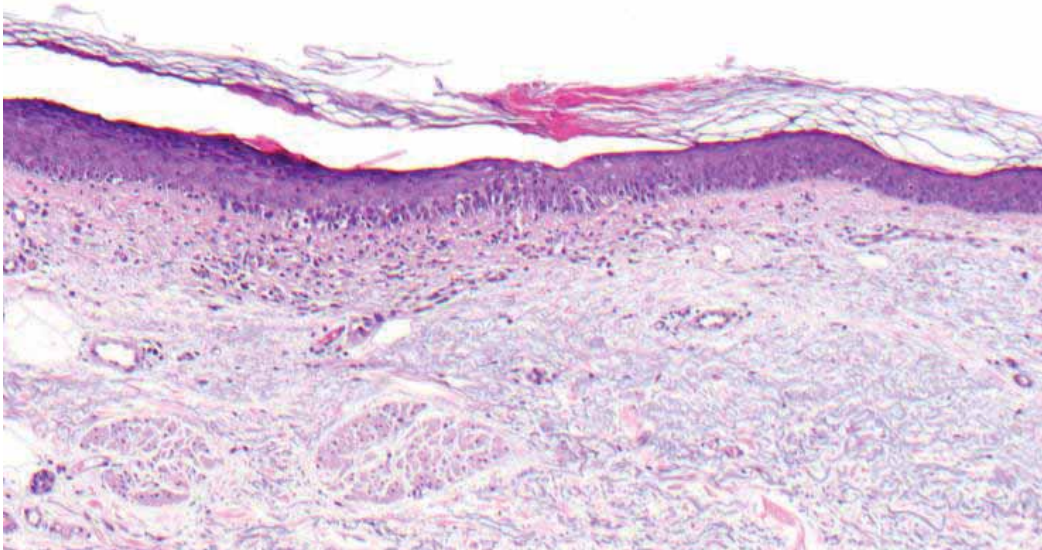
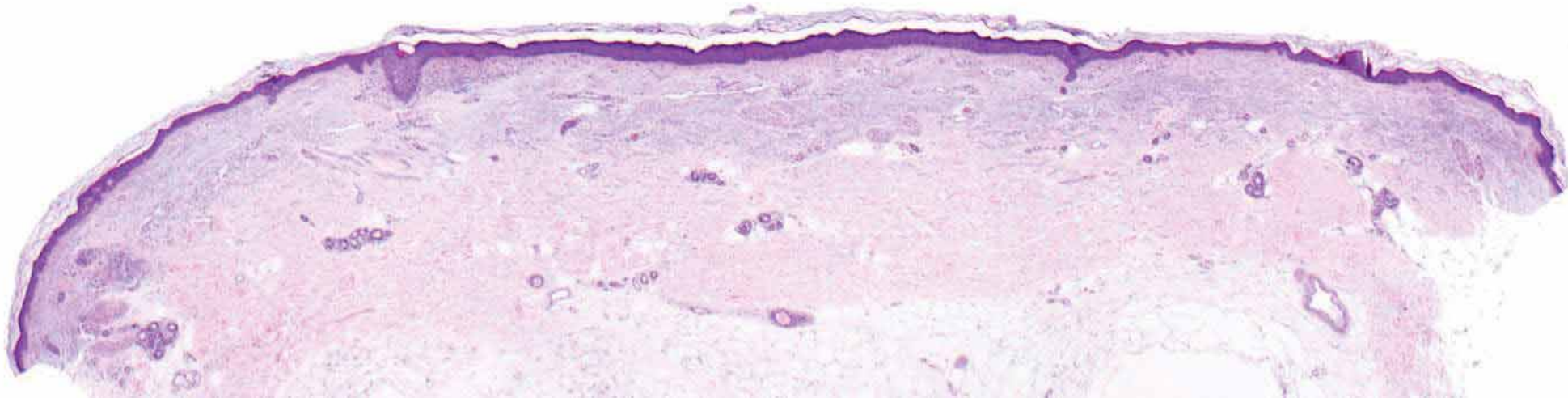
Porokeratosis Mibelli

- Archetype of Porokeratosis, rare, males > female
- AD inherited with onset in childhood [MIM 175800], sporadic with later onset
- Single or small number of annular lesions, roundish, skin-colored, red, or brownish, fine keratotic ridge, may itch
- Centrifugal growth, several centimetres in diameter up to 20cm (*P. gigantea*, high risk for malignant degeneration)
- Mostly limbs, rare face, scalp, volar, nail (pterygium), genitalia, oral mucosa
- Associations: Immunosuppression, diabetes, hepatitis, renal insufficiency,

Porokeratosis Mibelli



Porokeratosis Mibelli

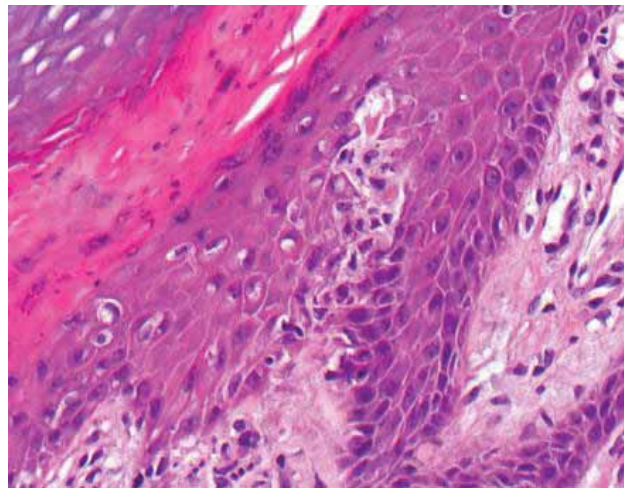
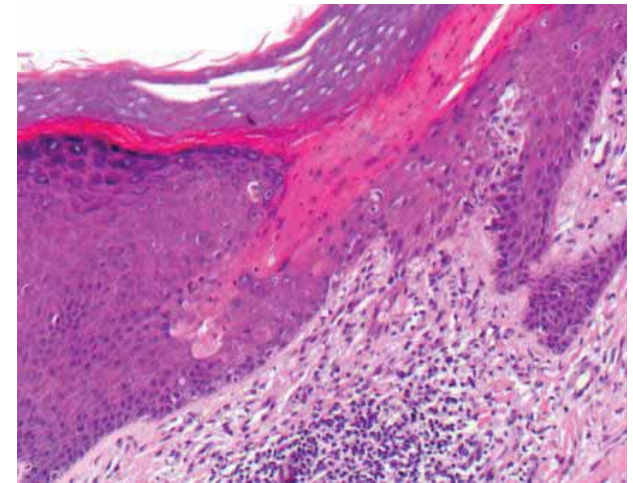
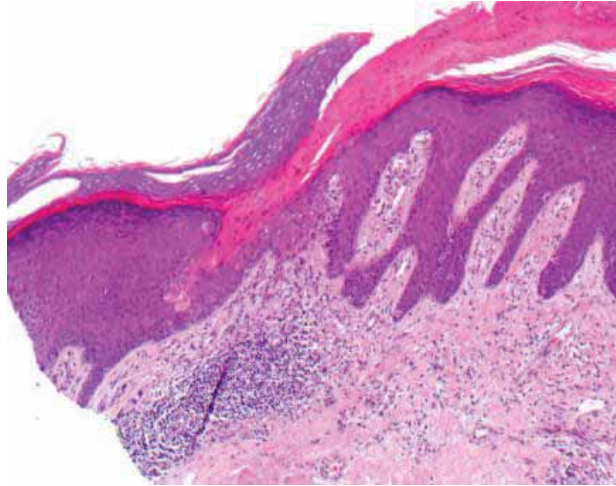
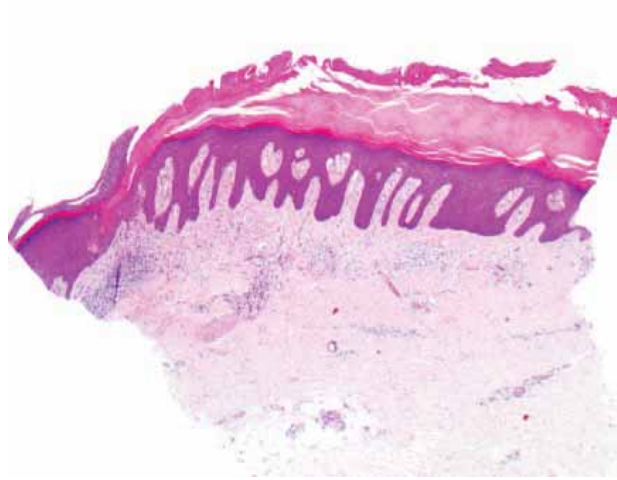


Porokeratosis gigantea

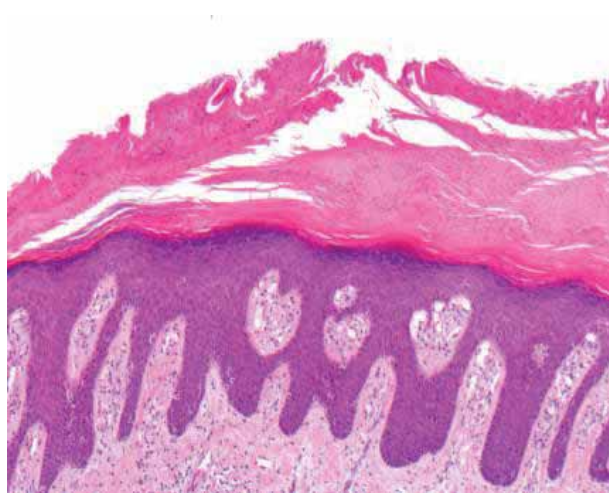
hyperkeratotic, erosive plaques



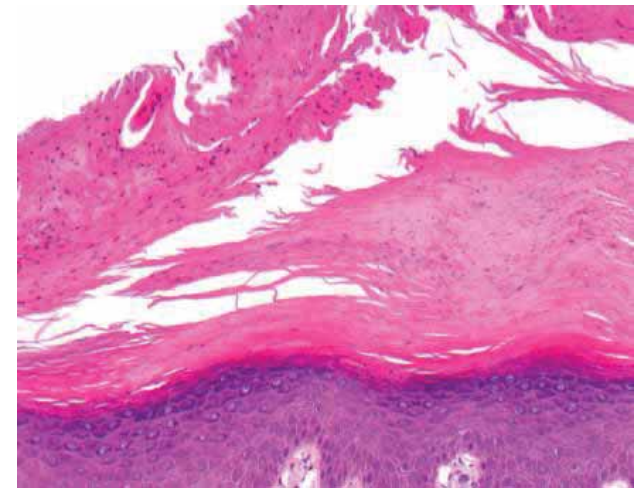
Porokeratosis gigantea, hyperkeratotic



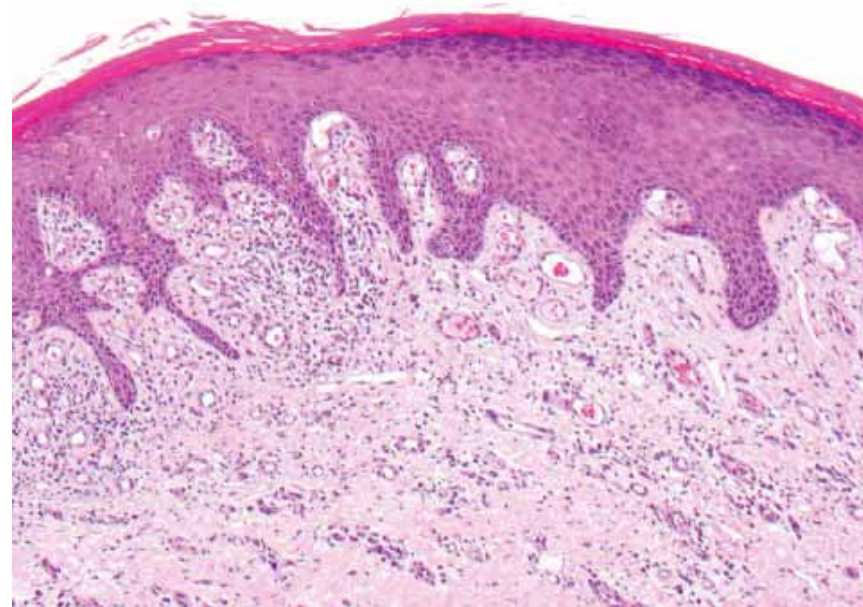
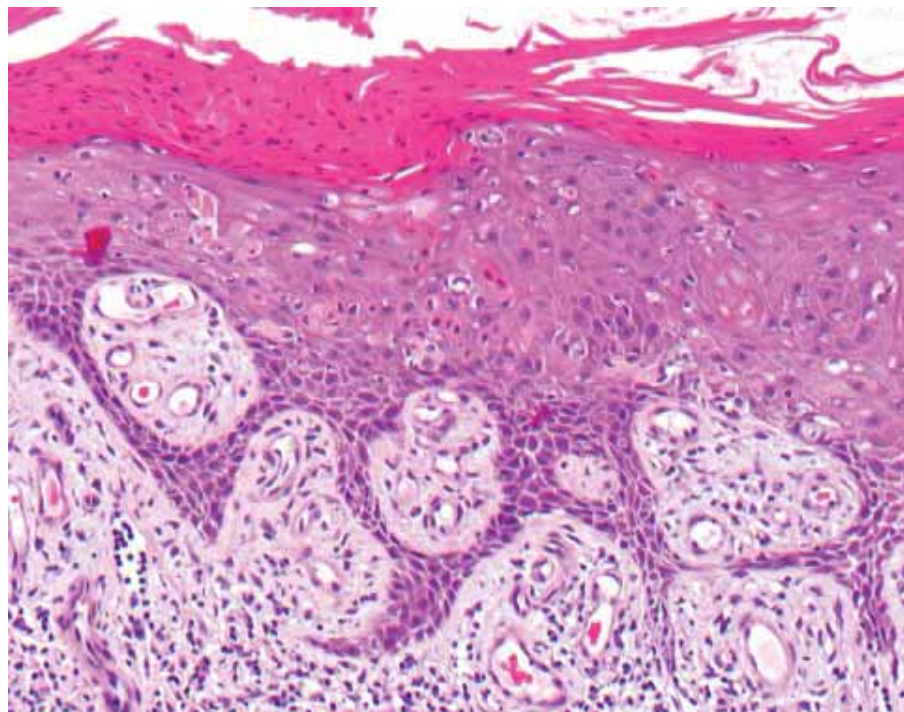
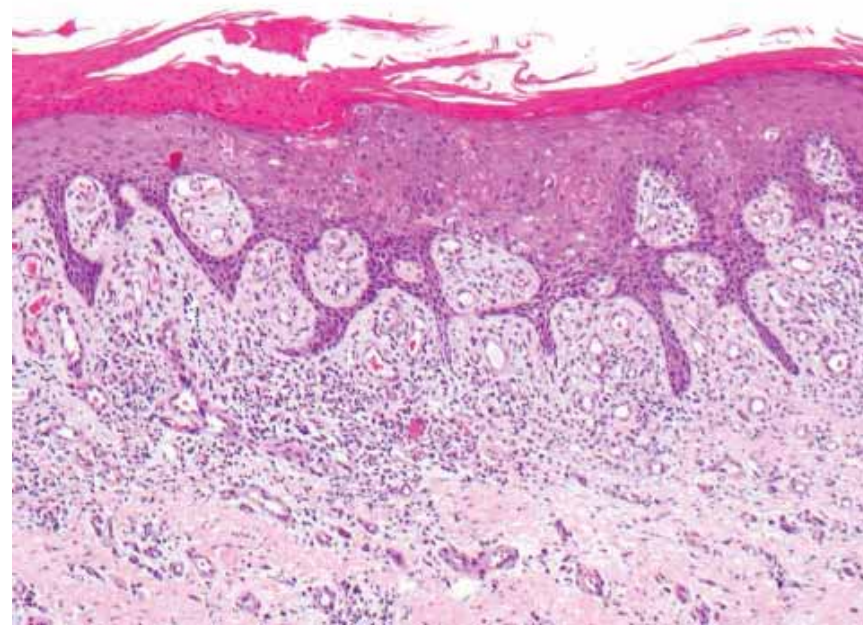
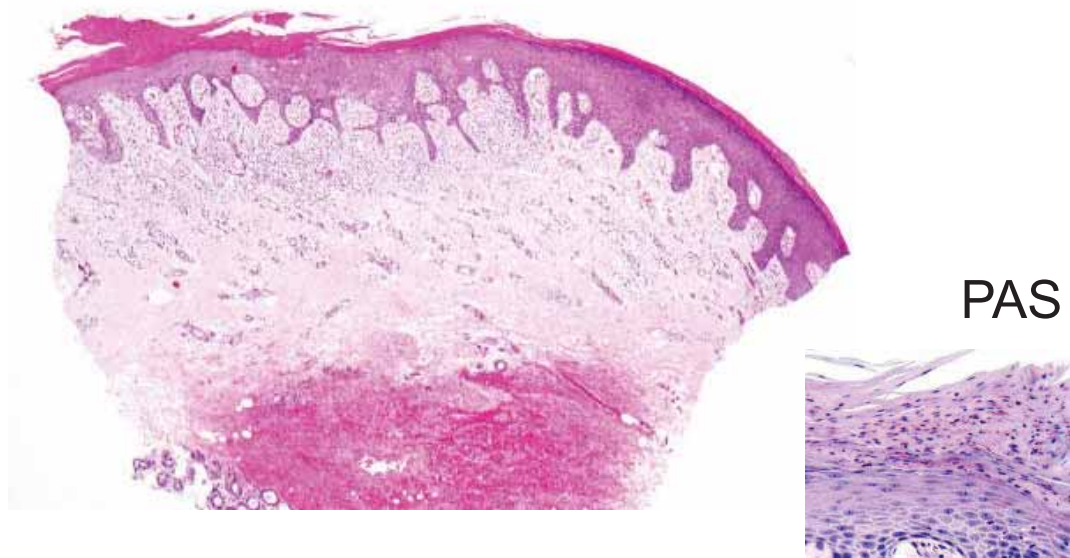
Interface-colloid bodies



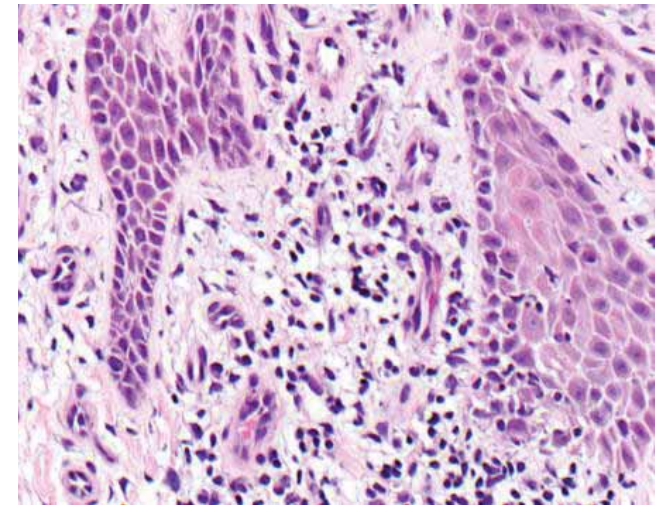
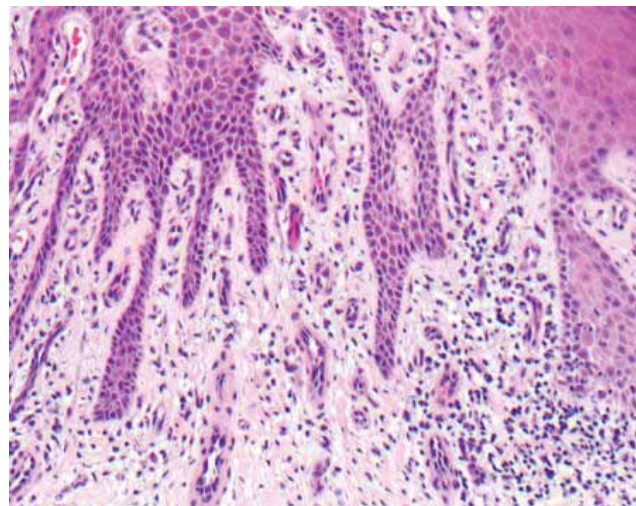
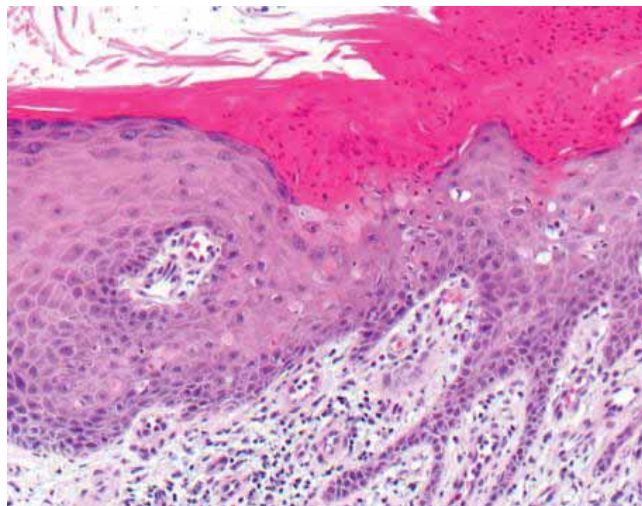
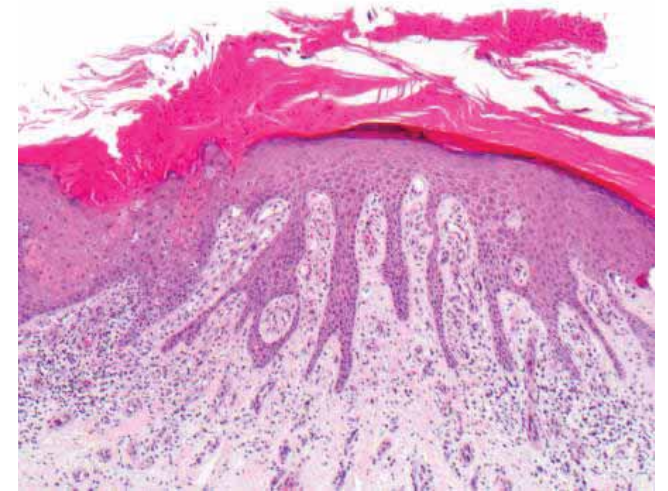
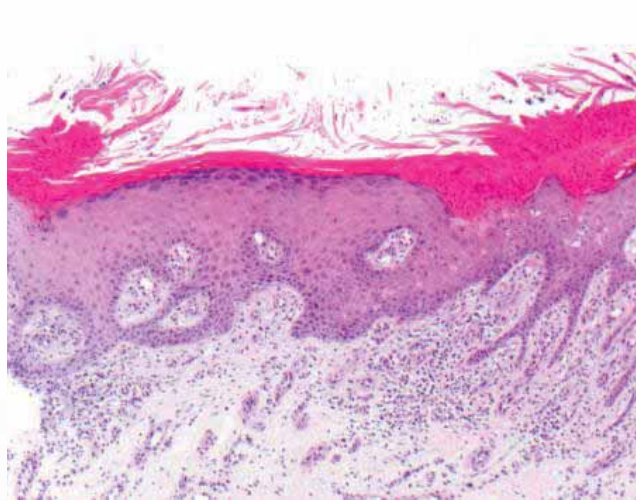
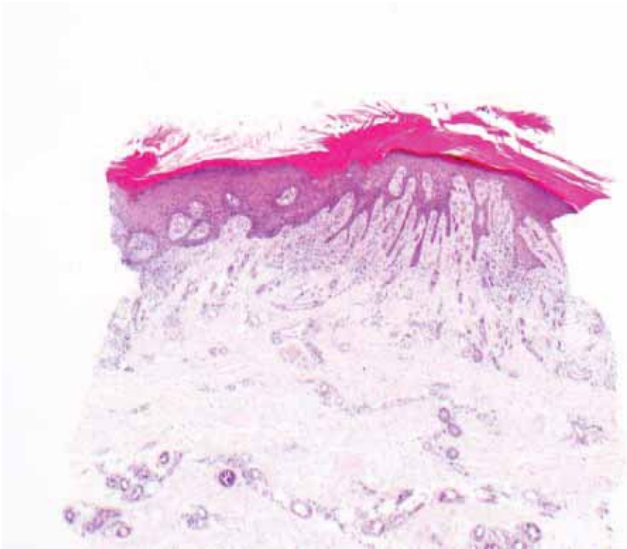
Cornoid lamella on top of central orthohyperkeratosis



Porokeratosis gigantea, hyperproliferative



Porokeratosis gigantea, early SCC ?



Disseminated superficial actinic Porokeratosis (DSAP)

- Most common type [MIM 175900], AD inherited or sporadic
- Women > men, 3rd-4th decade, rare in blacks
- Extensor aspect of extremities, shoulder, rarely face
- Multiple, confluent, skin-colored, red, or brownish annular lesions, hyperkeratotic or with a fine keratotic ridge , up to 1 cm, may itch
- Triggers: Sun, PUVA, radiation therapy, ...
- DDx actinic keratosis

Disseminated superficial Porokeratosis

- Same clinical aspect but no association with UV light
- Sun and non-sun exposed skin, also genital, palmoplantar
- Immunosuppression: organ and bone marrow transplantation, AIDS, ...

Porokeratosis superficialis disseminata actinica (DSAP)



Porokeratosis superficialis disseminata actinica (DSAP)



Porokeratosis superficialis
disseminata actinica (DSAP)



DSAP, progressive



2008



2012



2015

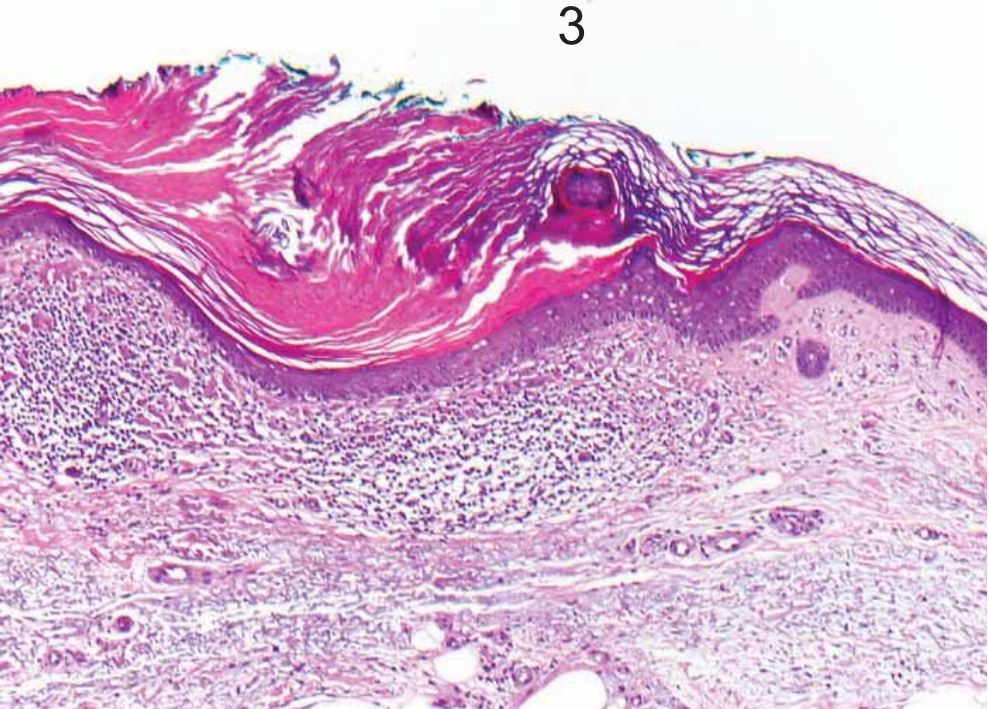
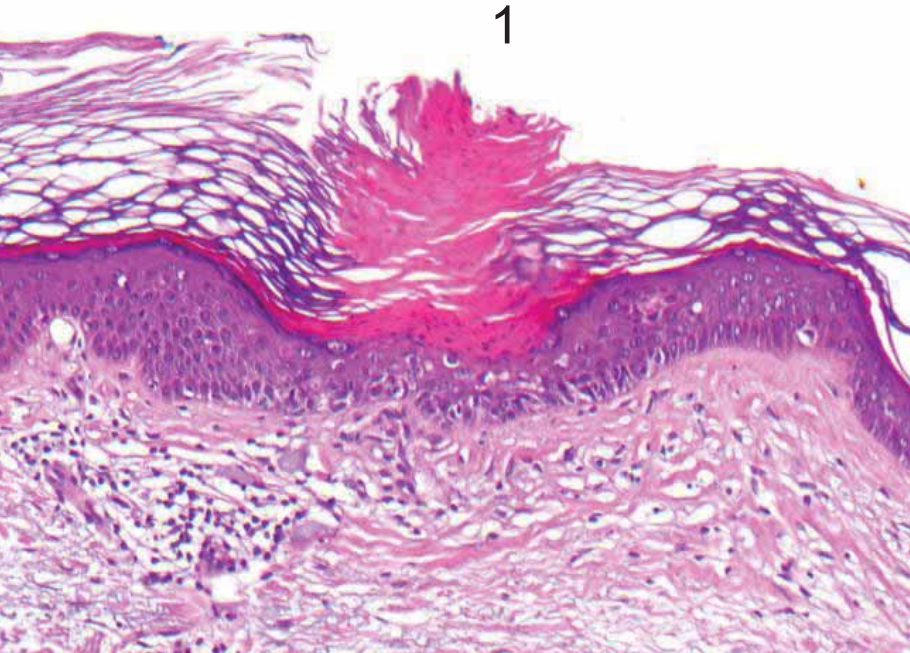
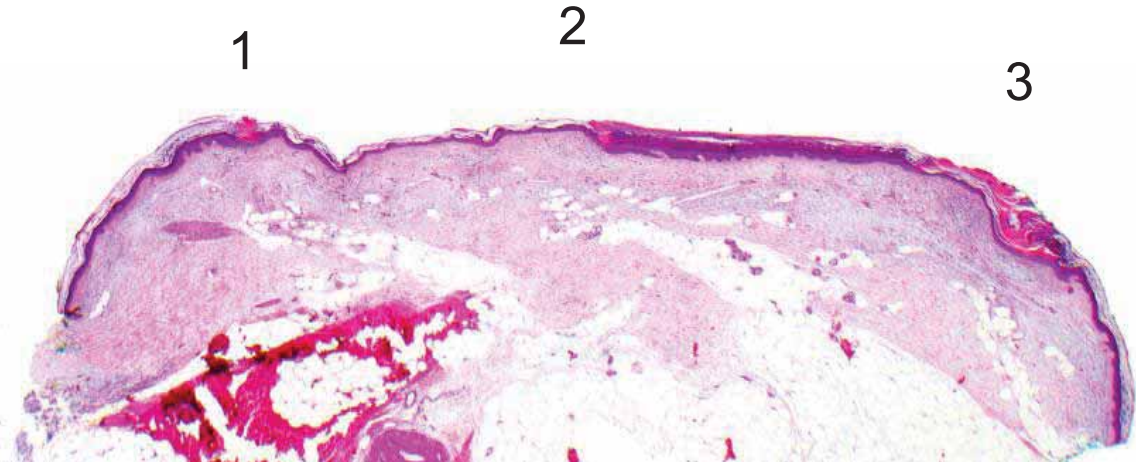
P. superficialis disseminata actinica (DSAP), erosive, hyperkeratotic



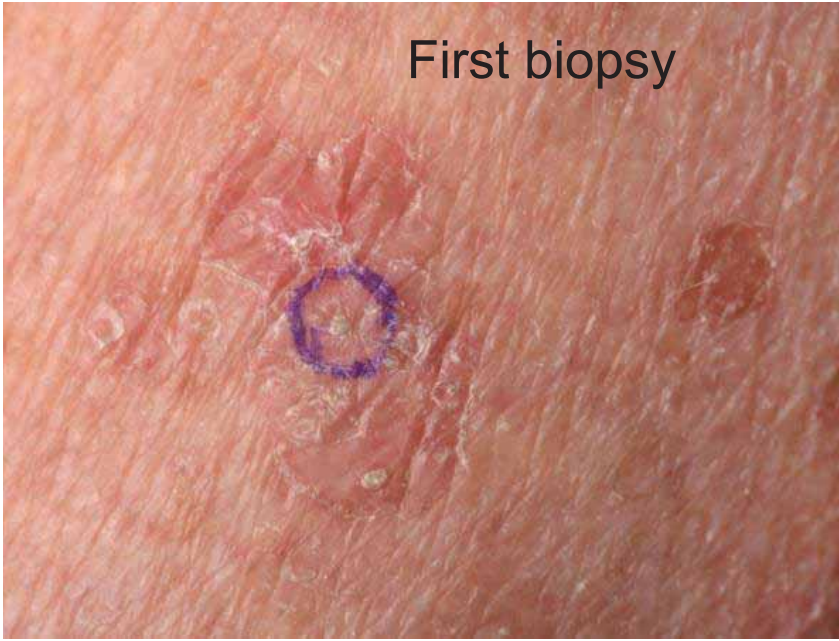
Porokeratosis superficialis disseminata actinica (DSAP), pustular



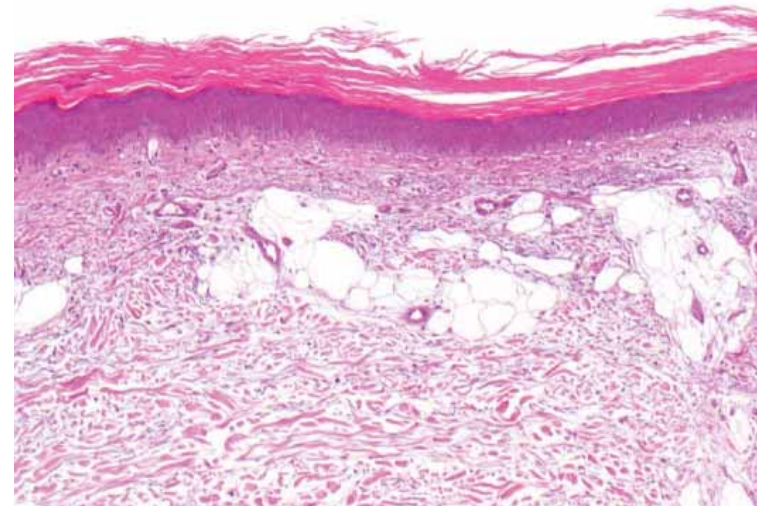
Disseminated superficial actinic
Porokeratosis (DSAP)



First biopsy

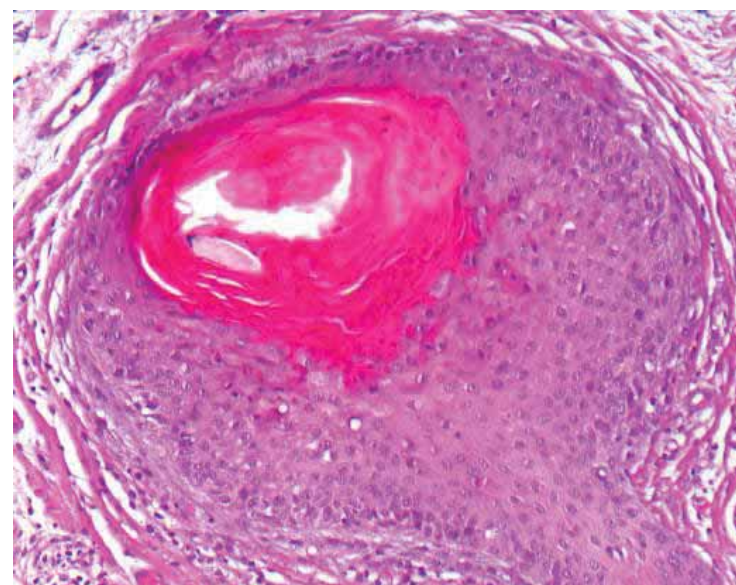
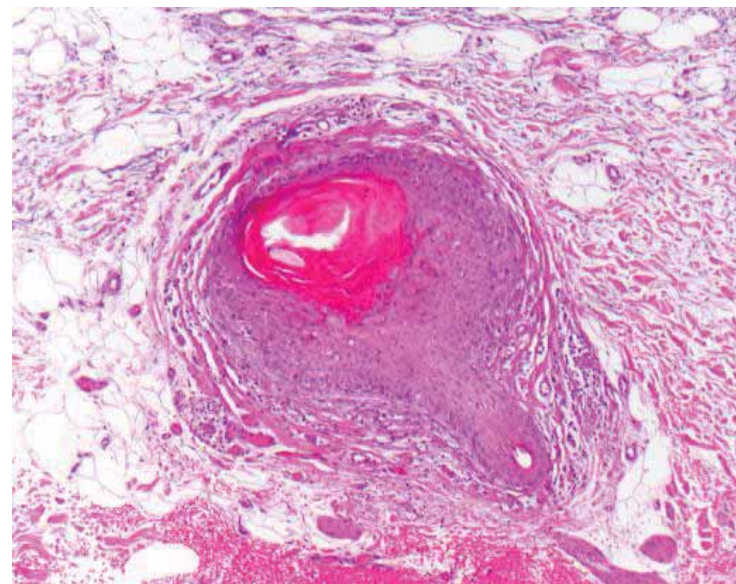
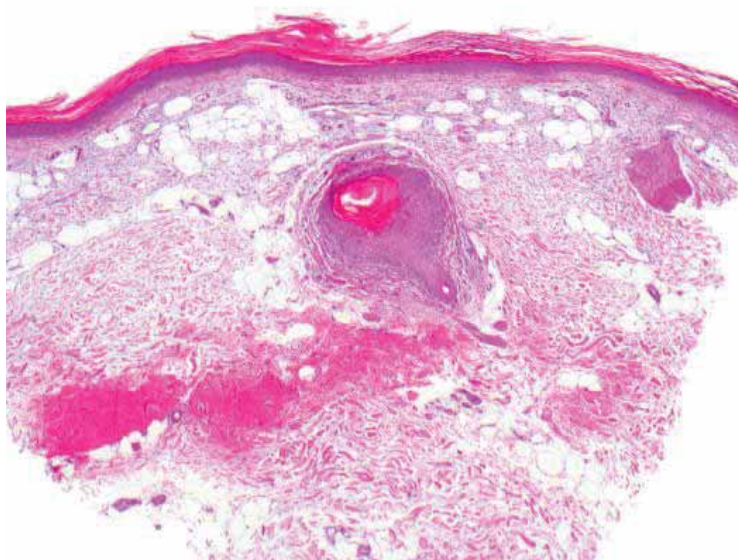


Porokeratose, DSAP, follicular



Step section

deep infundibular



Porokeratose, DSAP, follicular



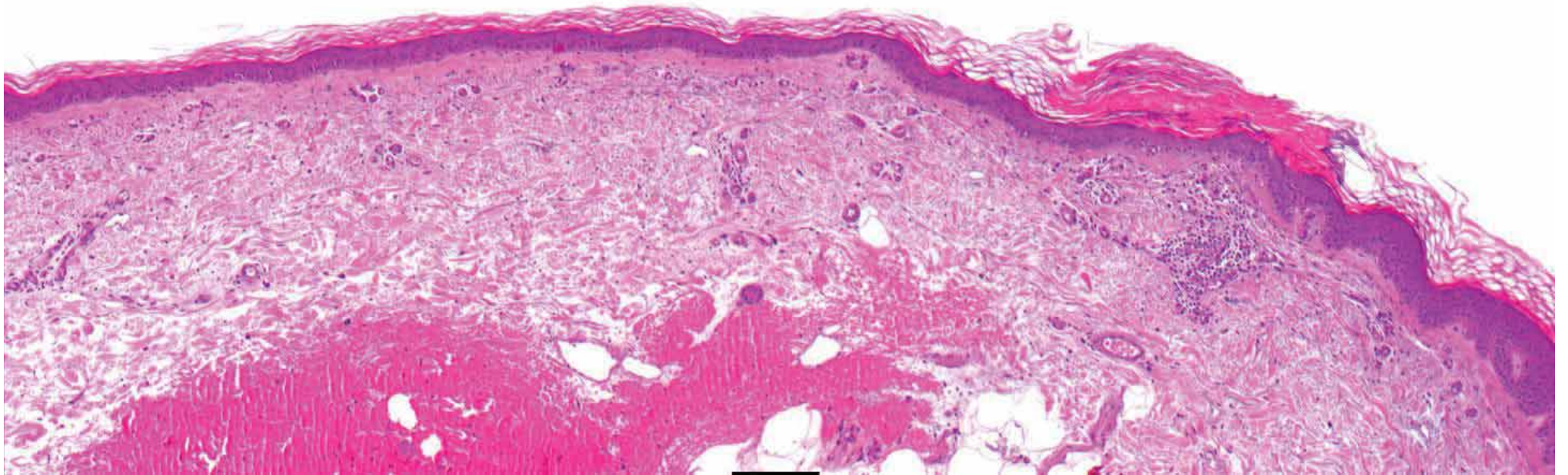
Second biopsy



2nd biopsy

Regular cornoid lamella

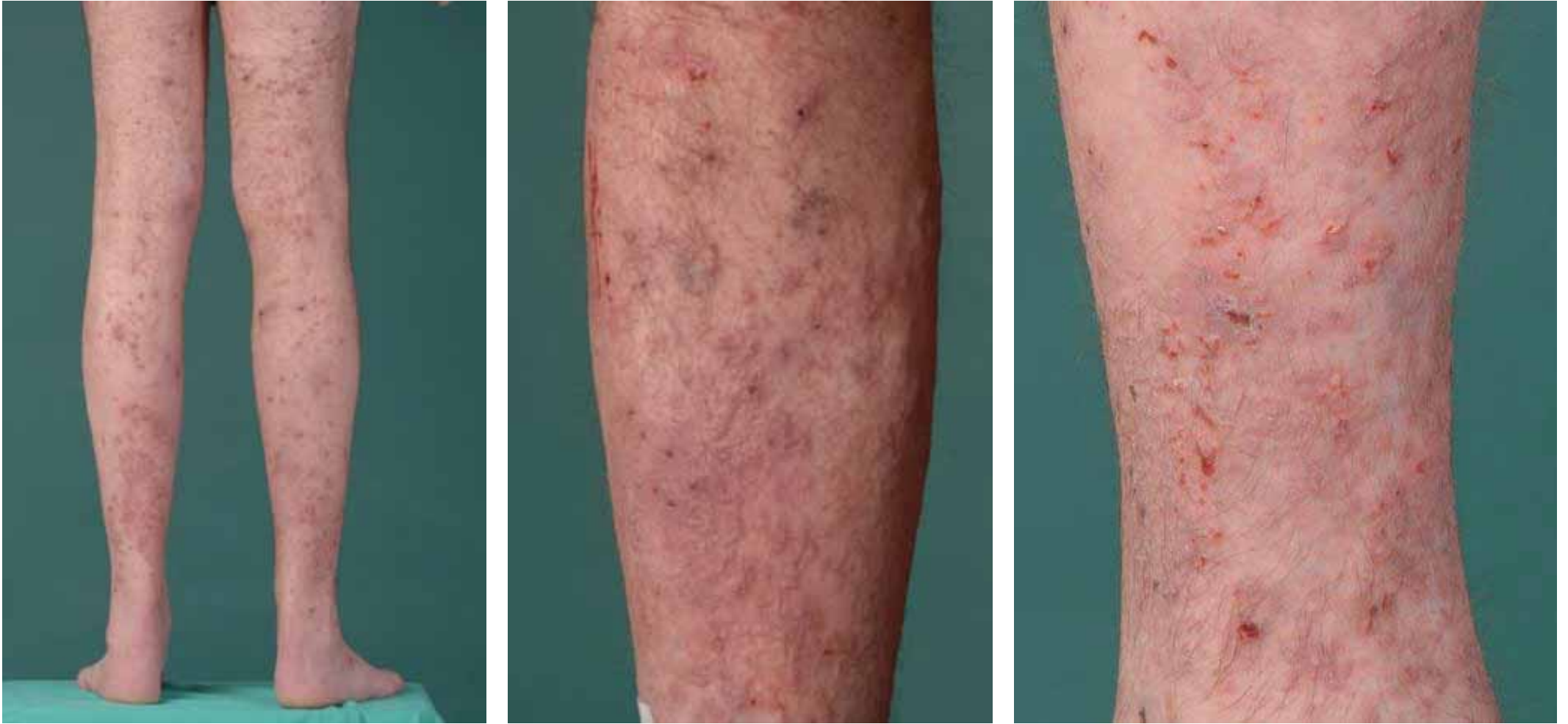
Atrophic center



Eruptive papular pruritic Porokeratosis

- Pruritic variant of disseminated superficial Porokeratosis (DSP) or disseminated superficial actinic Porokeratosis (DSAP)
- Papular porokeratotic lesions, with time pruritic and inflamed
- Histologic features of Porokeratosis, and, eventually, Prurigo nodularis/Lichen simplex chronicus, inflammatory infiltrate with eosinophils, spongiosis, subepidermal blister formation
- Spontaneous remission with postinflammatory hyperpigmentation reported
- Systemic treatment of pruritus

54-y-old man, disseminated highly itchy papules



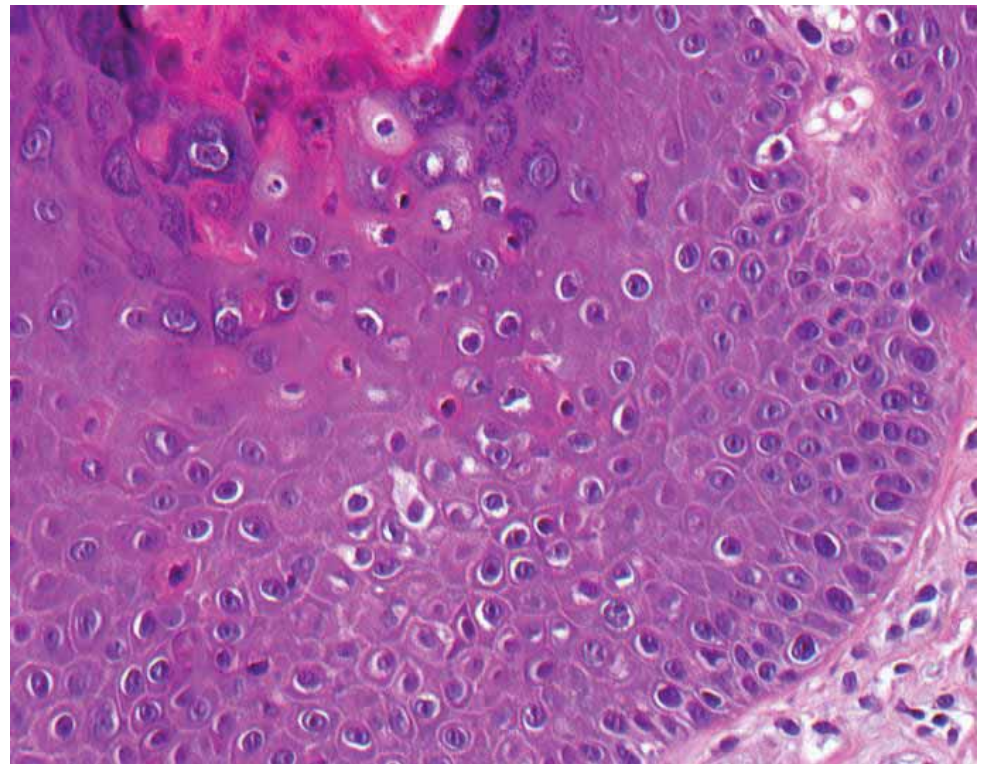
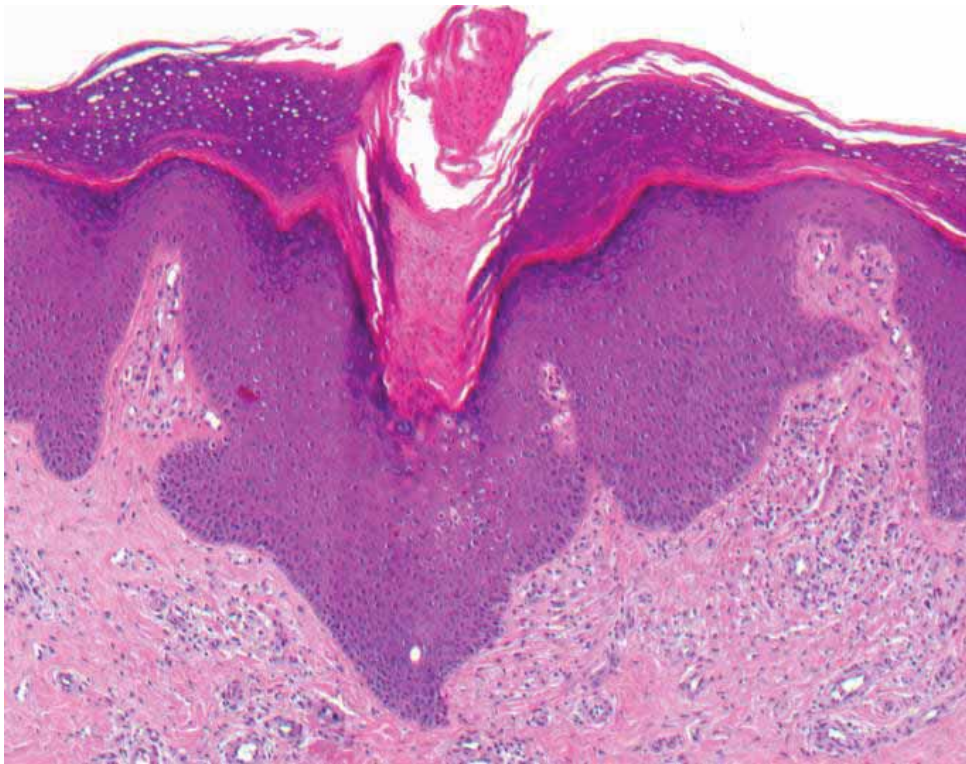
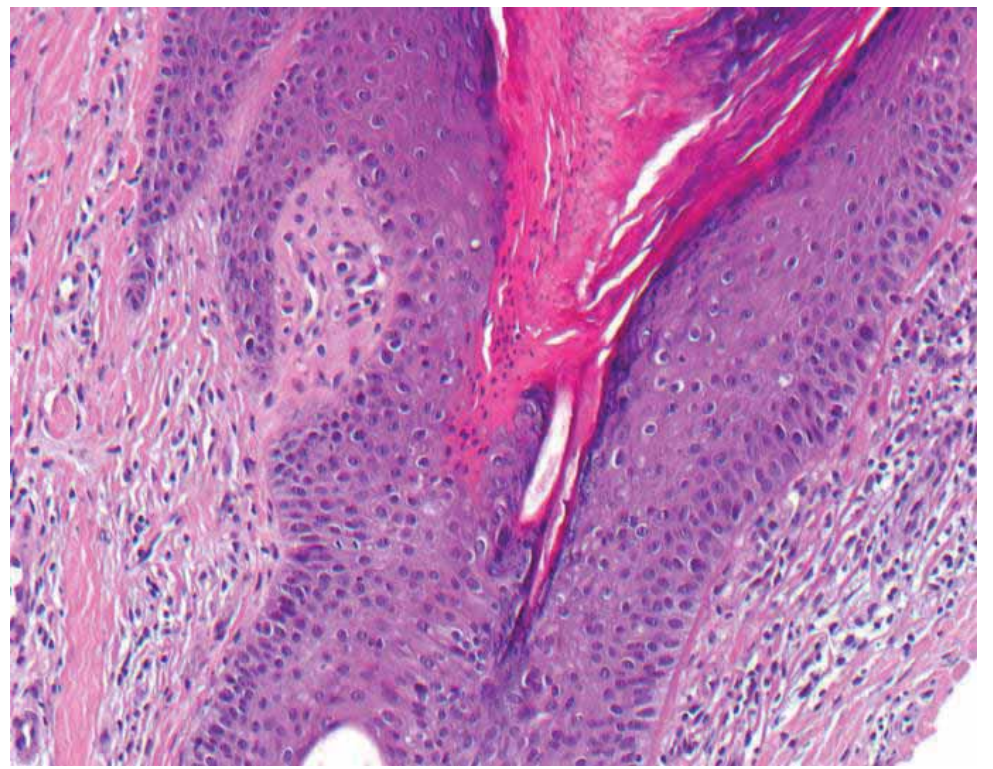
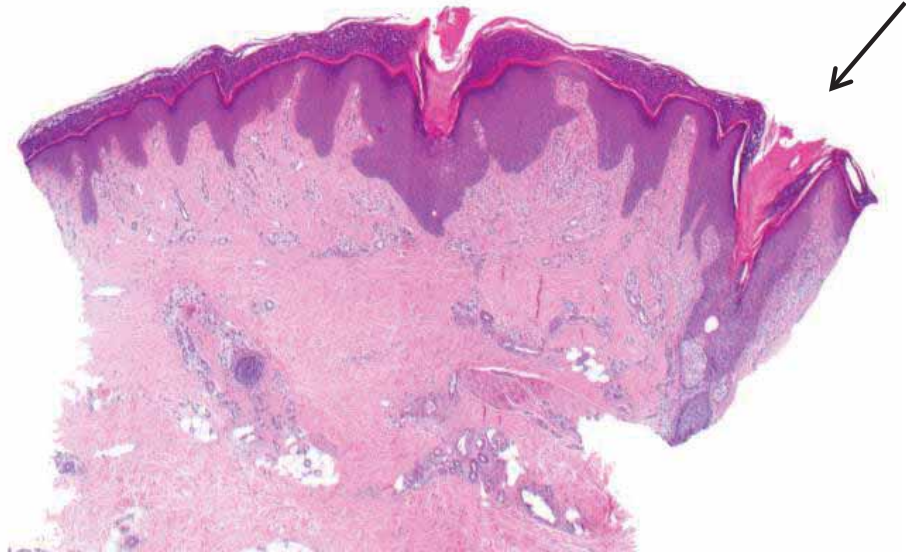
Highly pruritic nodules with excoriations



Closer inspection !

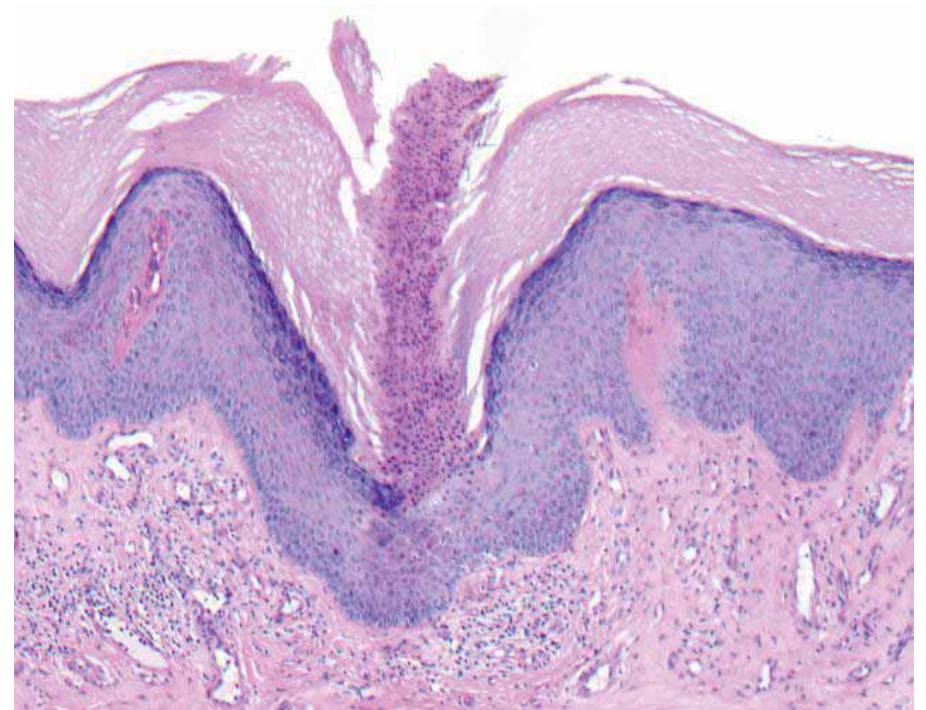
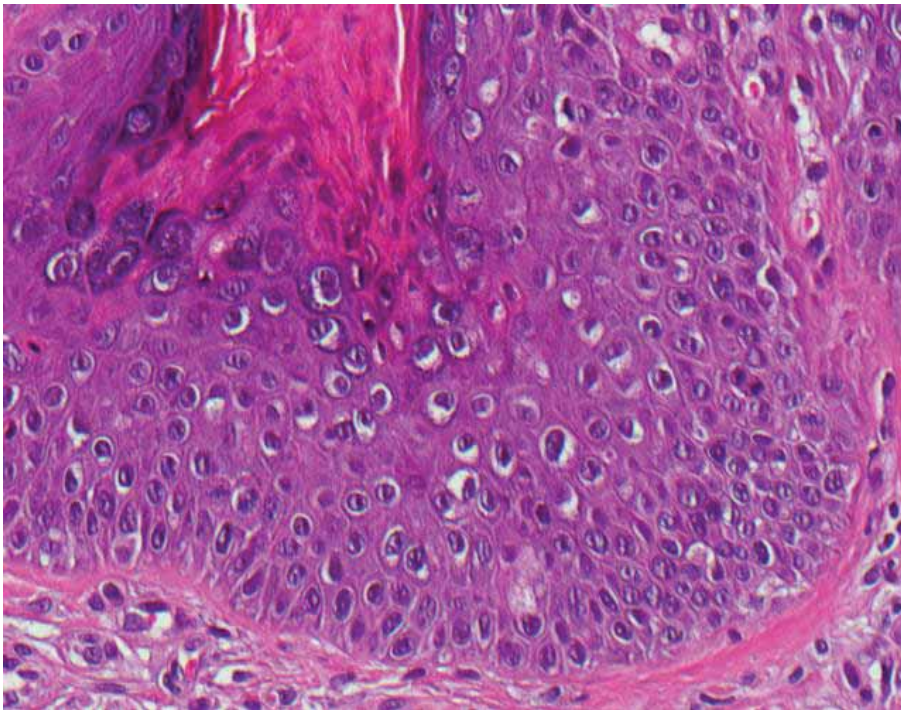
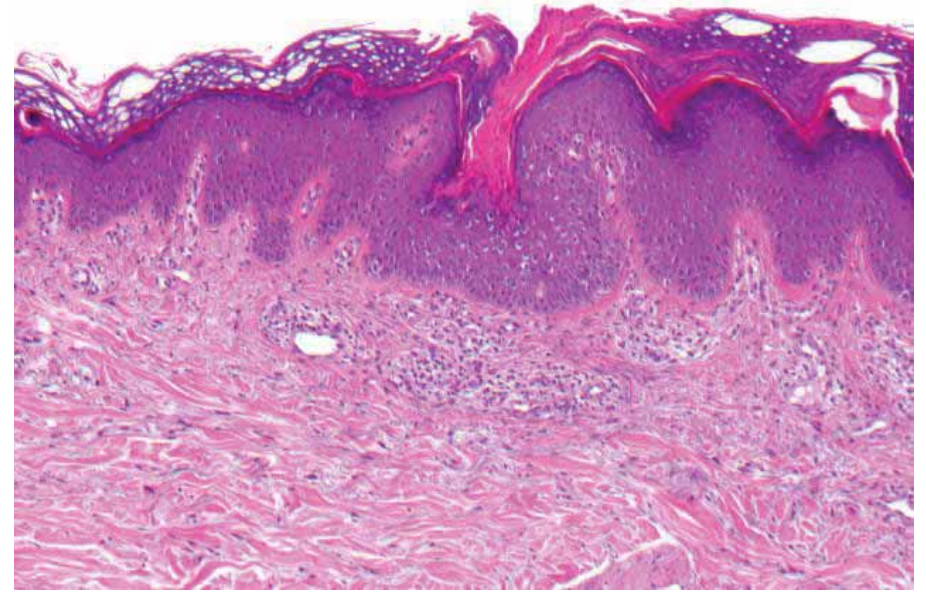
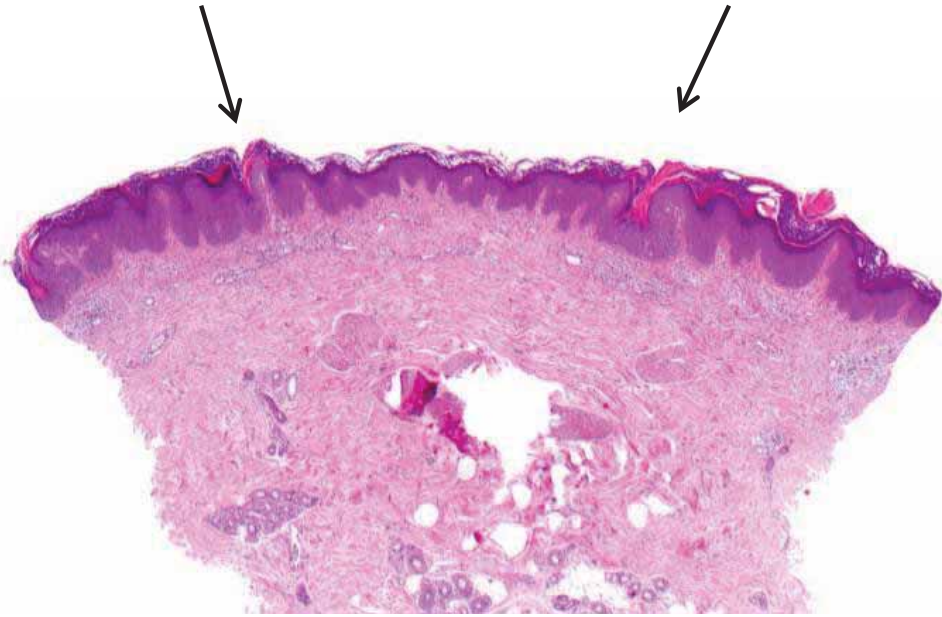
1st Biopsy

Prurigo +
Porokeratosis



2nd Biopsy

Lichen simplex + Porokeratosis



Porokeratosis linearis

- Mosaic form of DSAP: Type 2 of segmental distribution of AD disorder (Happle): loss of heterozygosity early in life/congenital
- Grouped macules, papules or plaques, localized or generalized, Blaschko distribution or zosteriform, extremities > facial, genital
- Nail fissures, pterygium, pseudoainhum
- Histology: Two or multiple cornoid lamellae (classical or punctata type), hyperkeratotic
- Risk for malignancies

Porokeratosis linearis



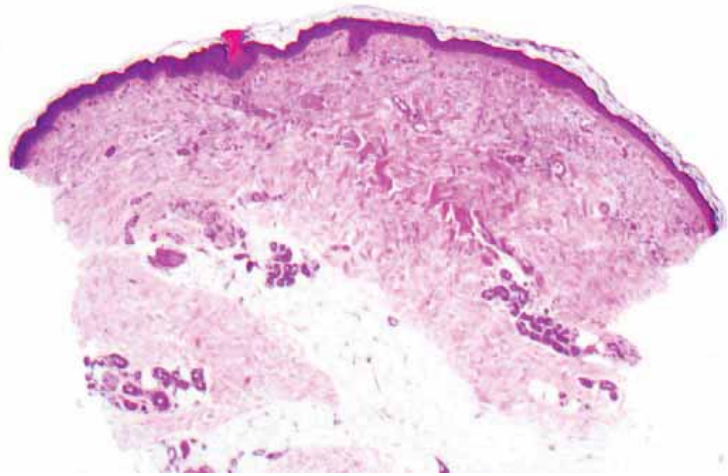




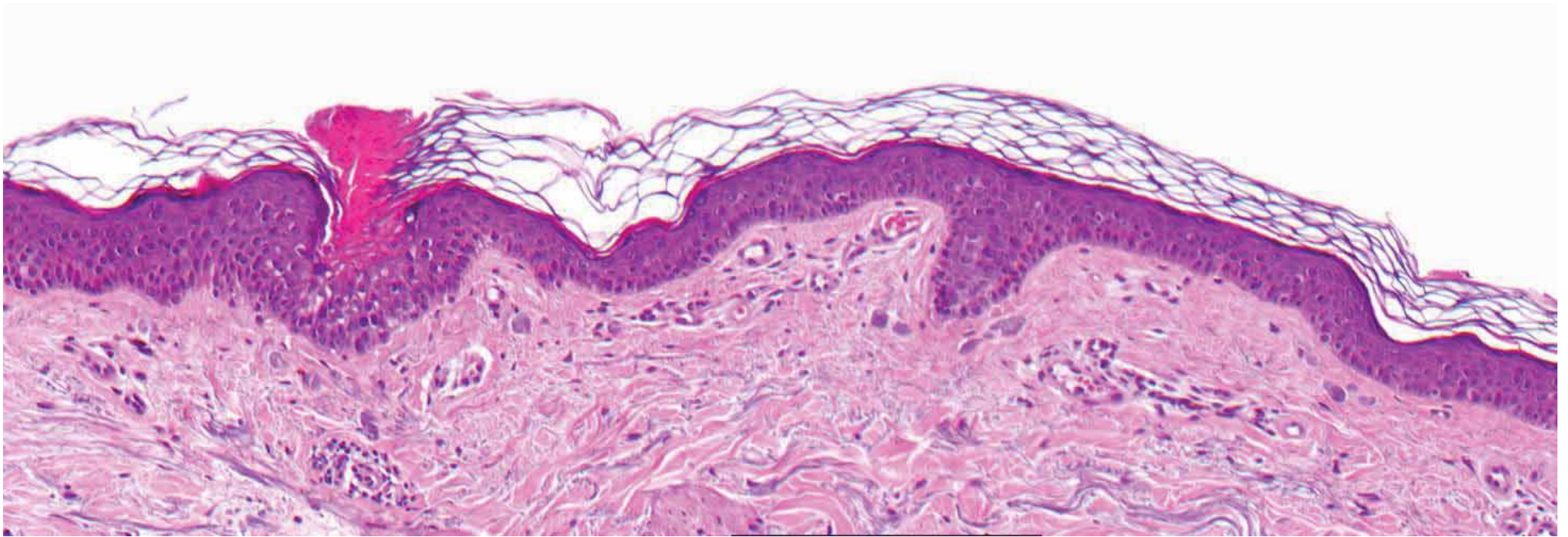
DDx
Disseminated superficial
Porokeratosis (DSP)

triggered by herpes zoster
(Isotope reaction, Wolf's phenomenon)

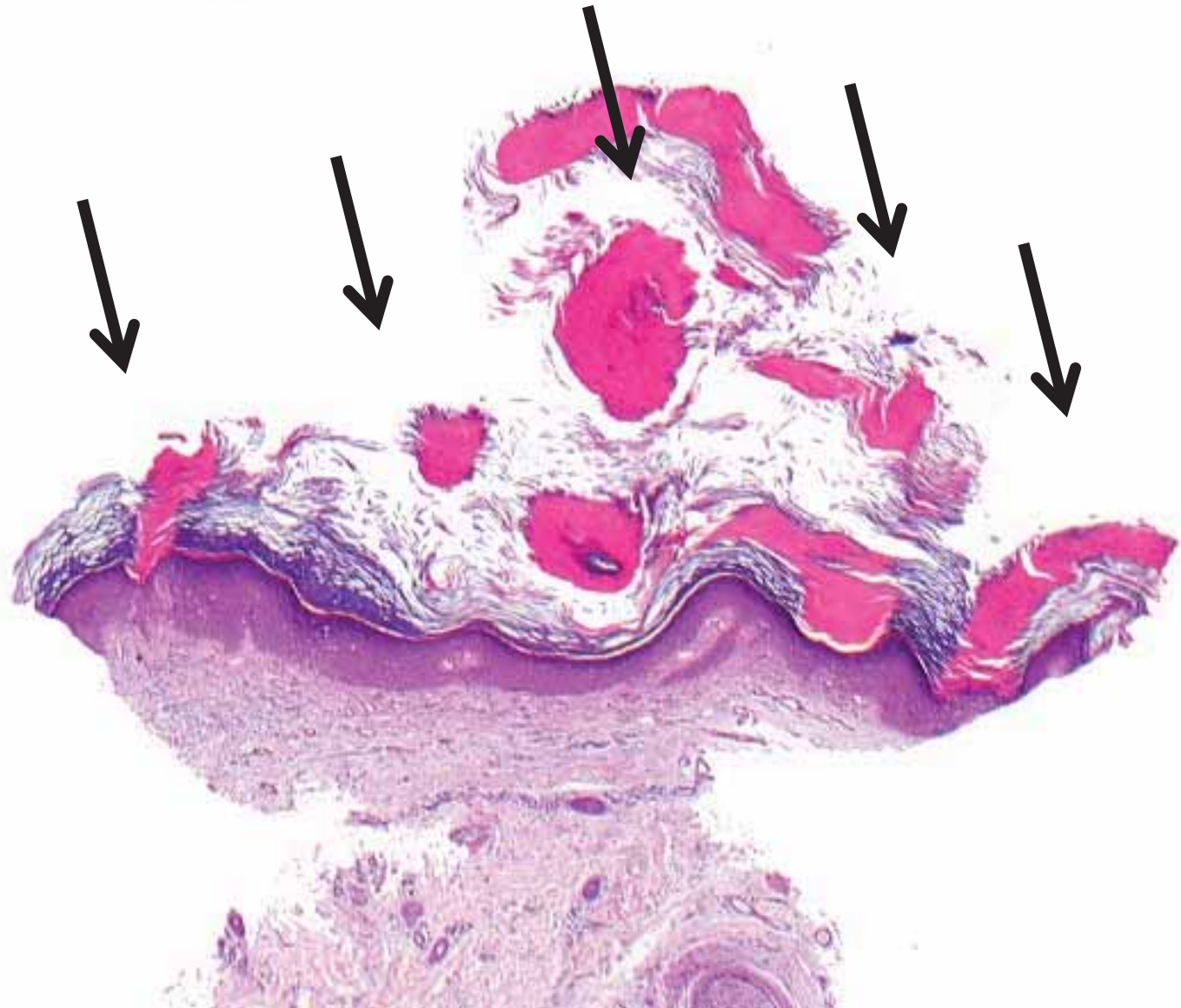


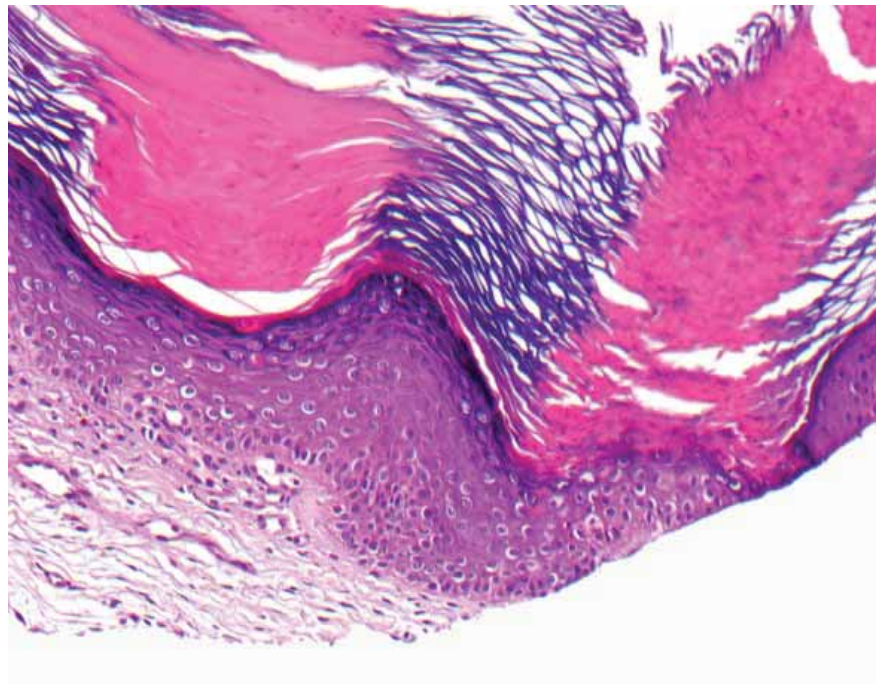
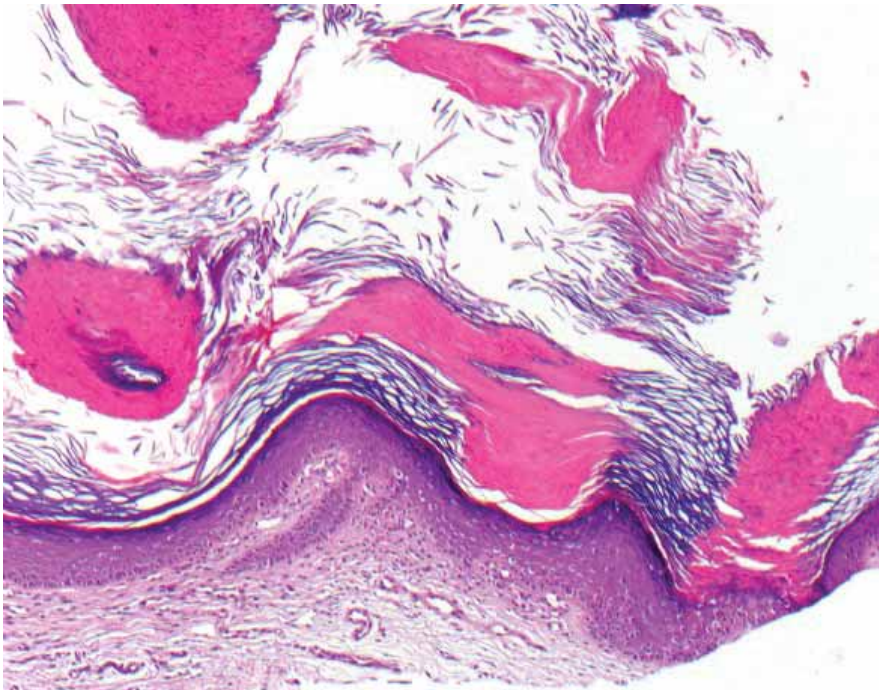
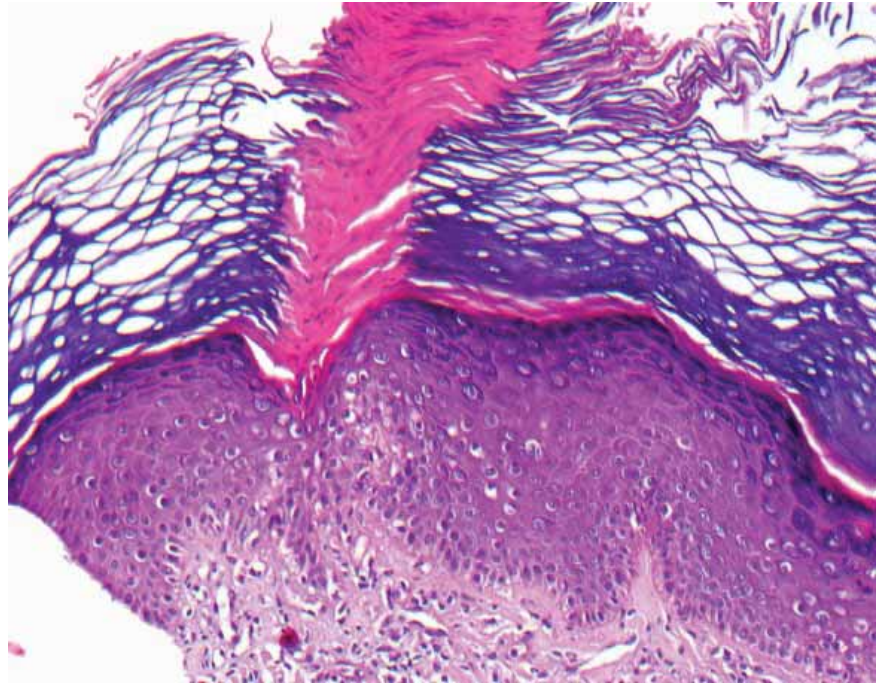


Linear Porokeratosis,
continuous cornoid lamella

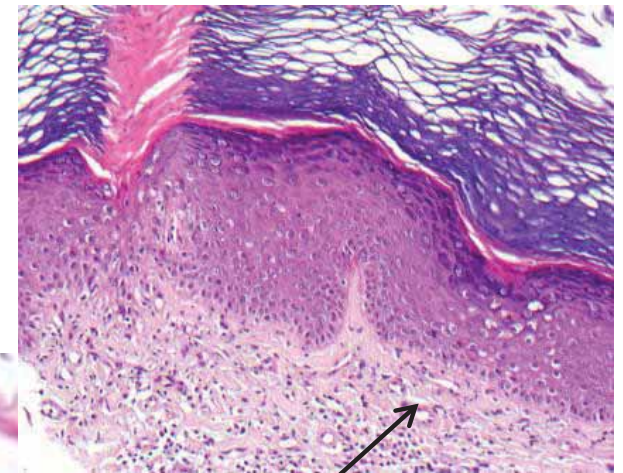
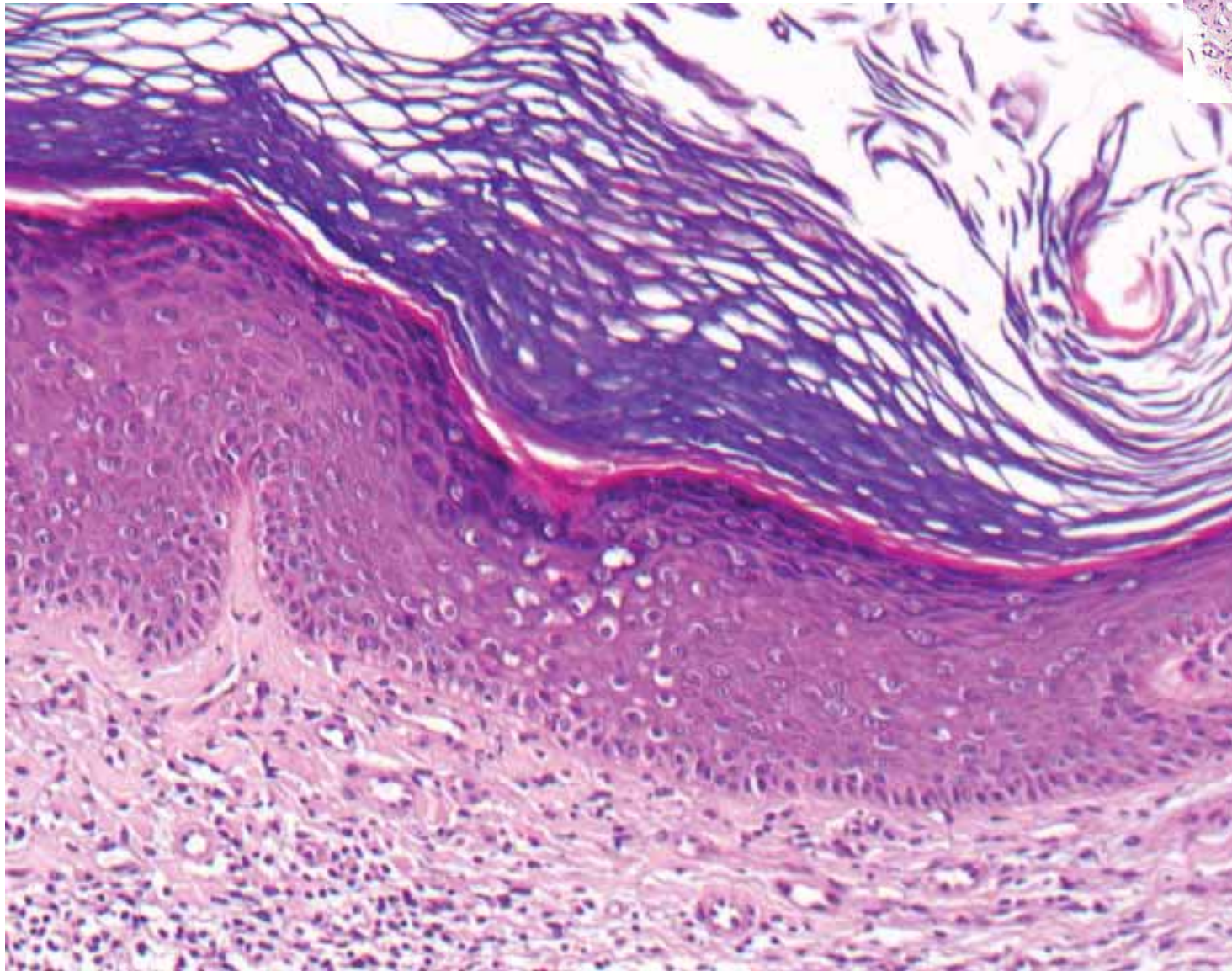


Linear Porokeratosis, punctate type





Punctate type “without” cornoid lamella





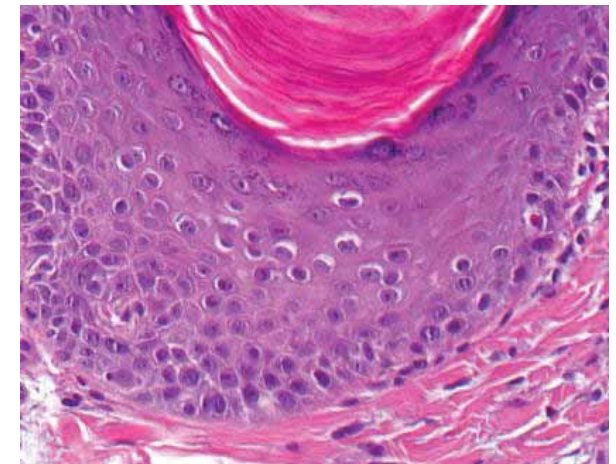
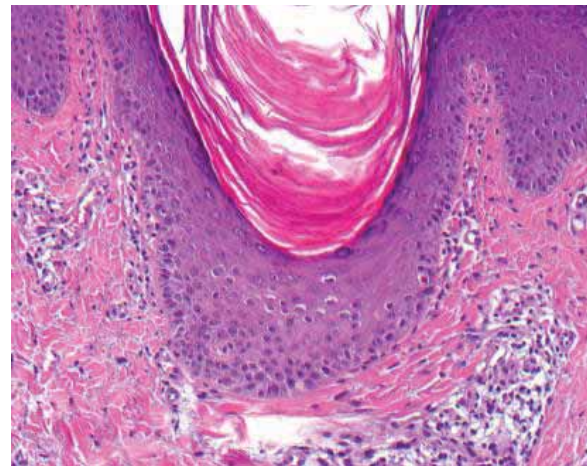
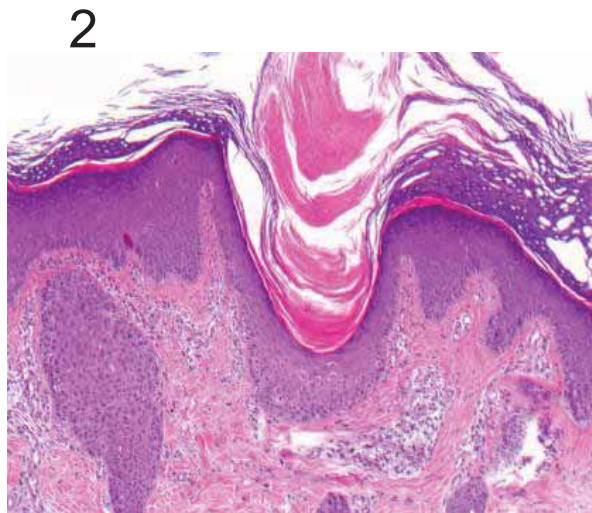
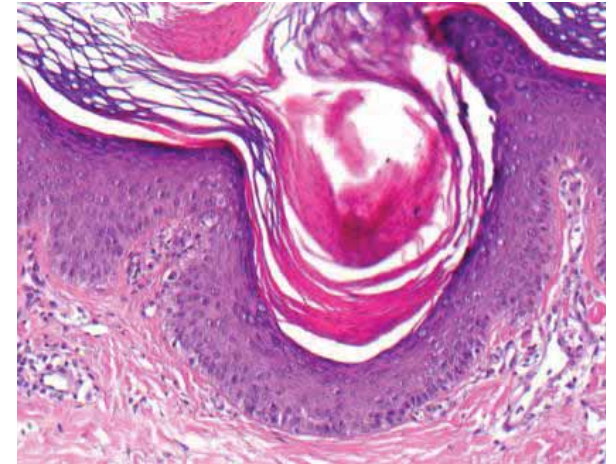
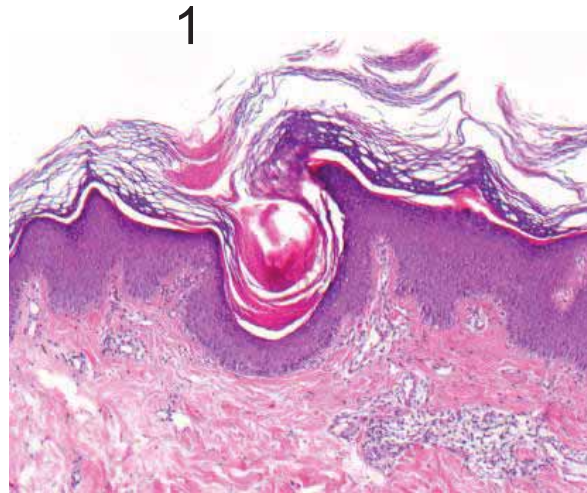
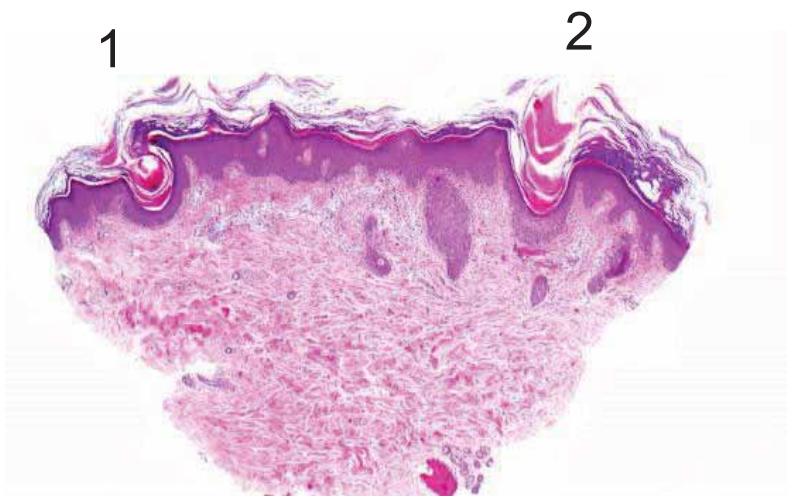
Porokeratosis linearis



Verrucous surface

DDx Epidermal naevus

Porokeratosis linearis, comedo-like



DDx ILVEN, systematized, left-sided



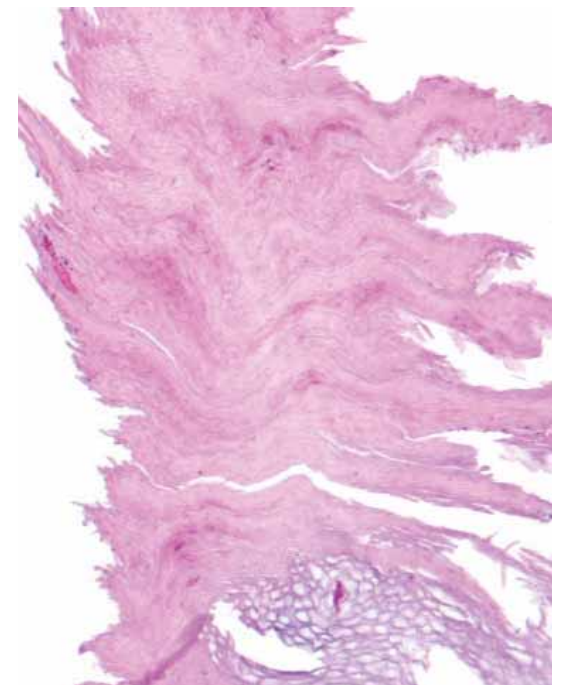
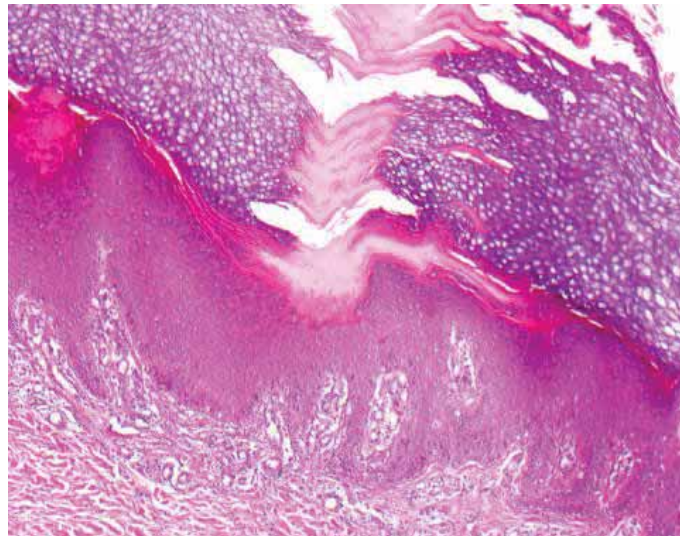
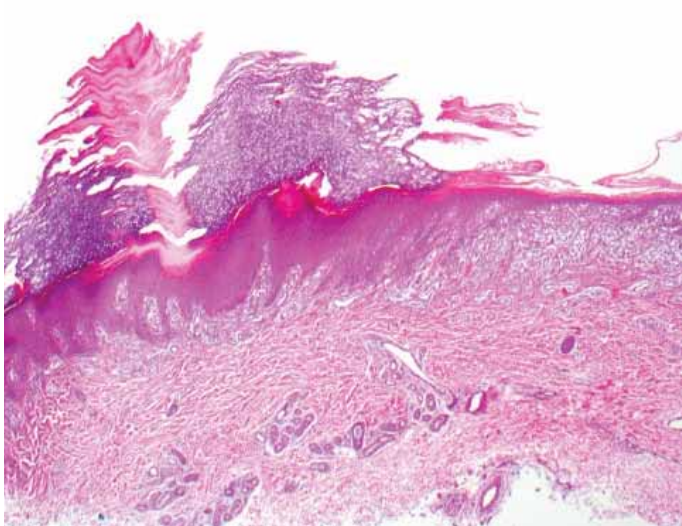
ILVEN

First biopsy
bi-sected, I

Courtesy
Hornheide



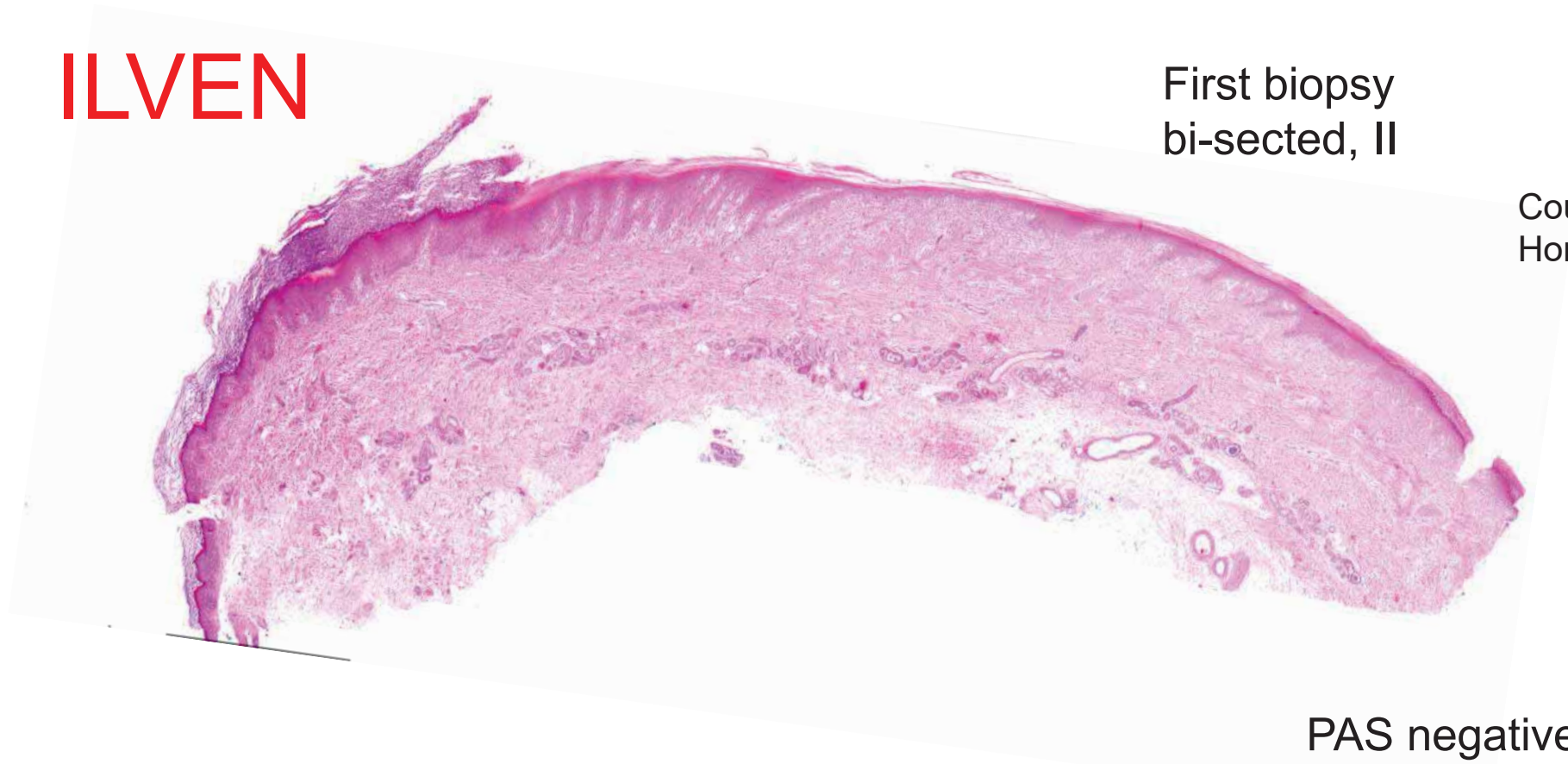
PAS negative



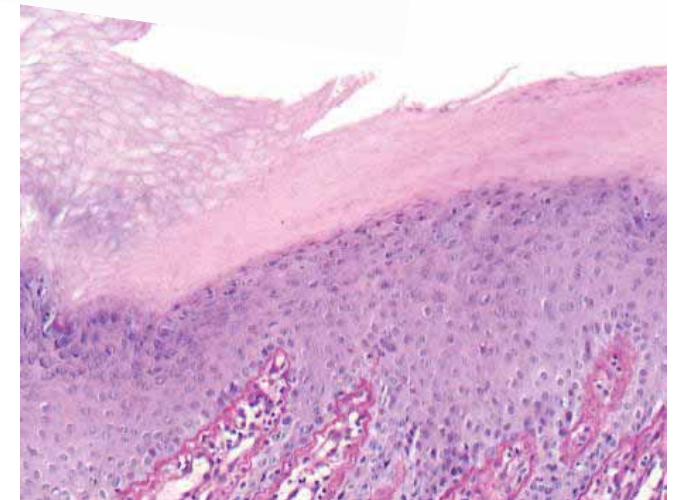
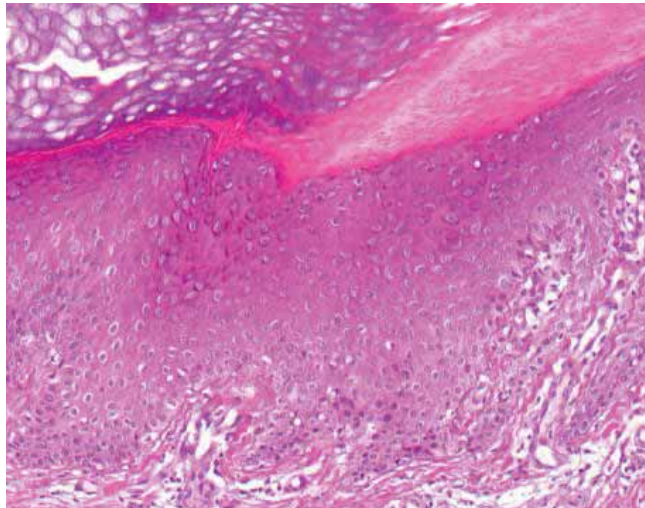
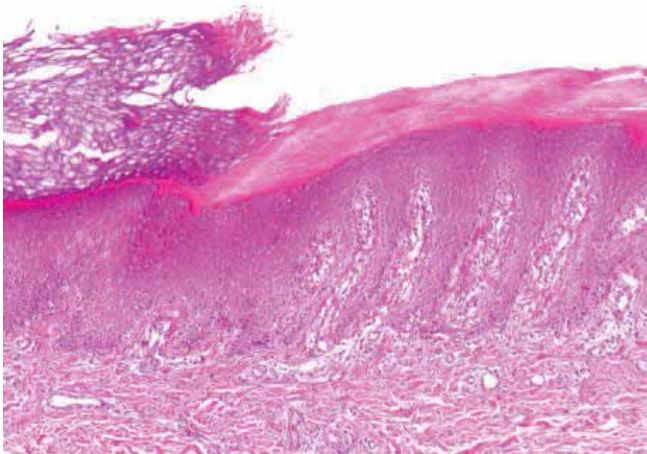
ILVEN

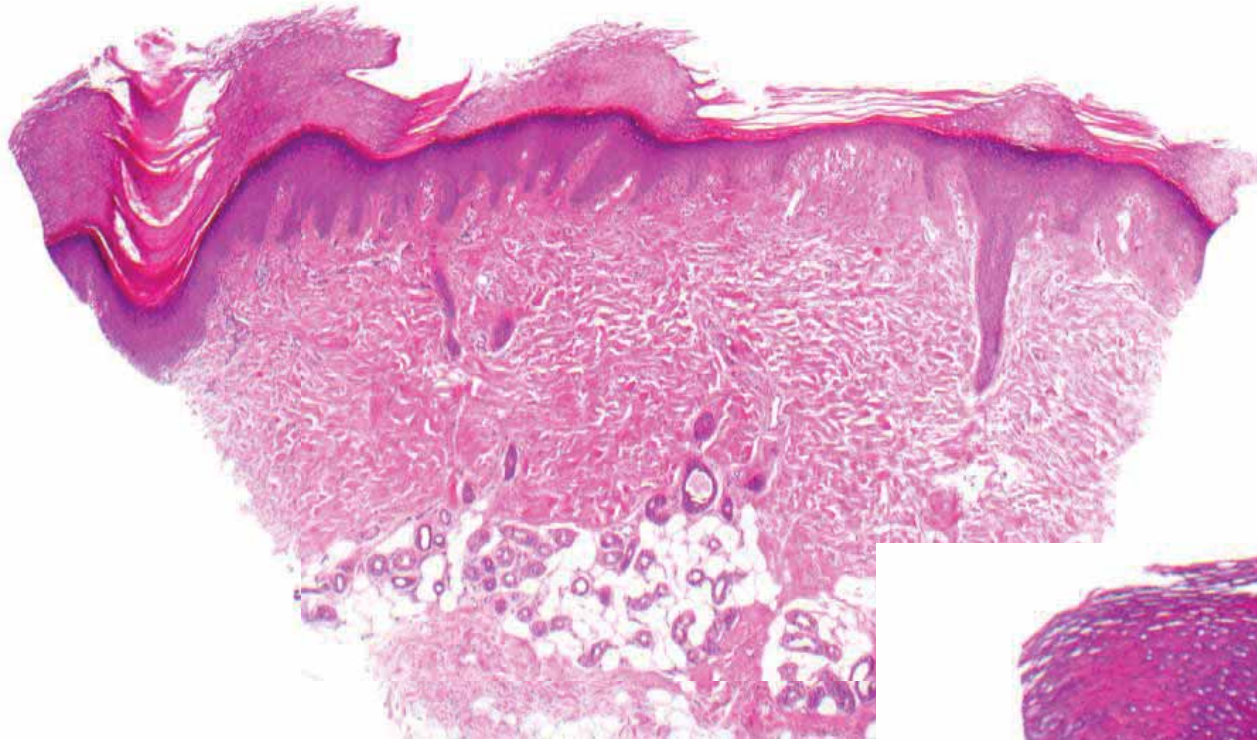
First biopsy
bi-sected, II

Courtesy
Hornheide

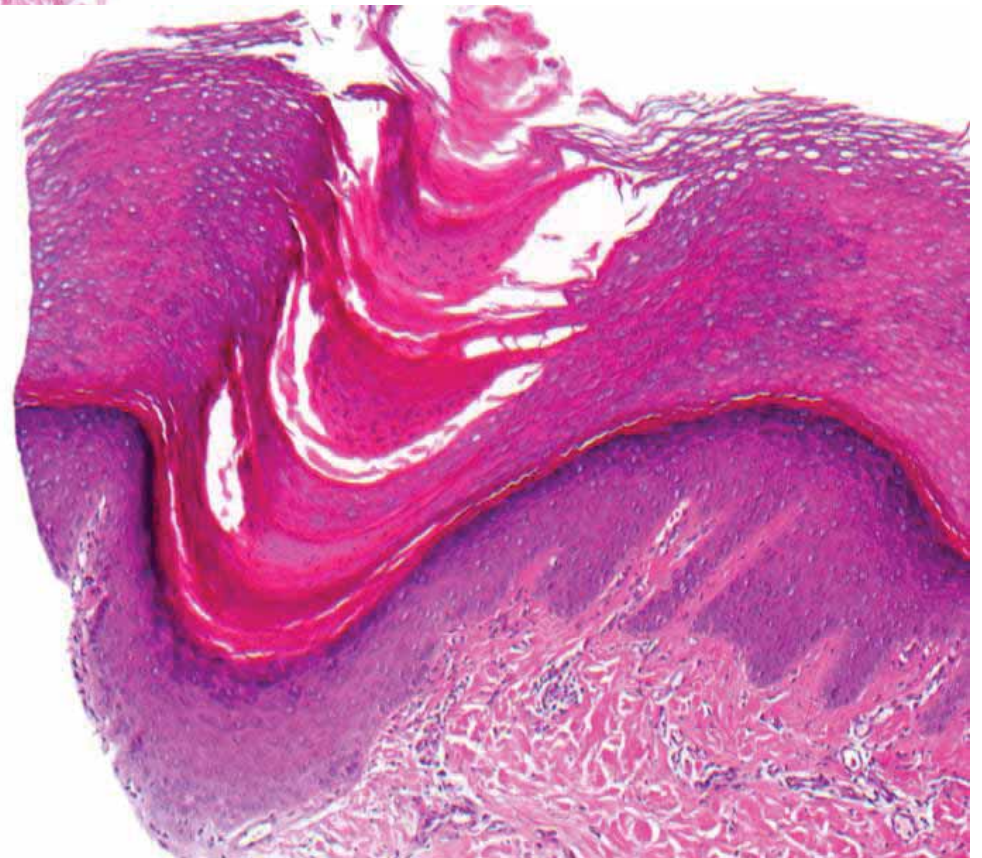


PAS negative



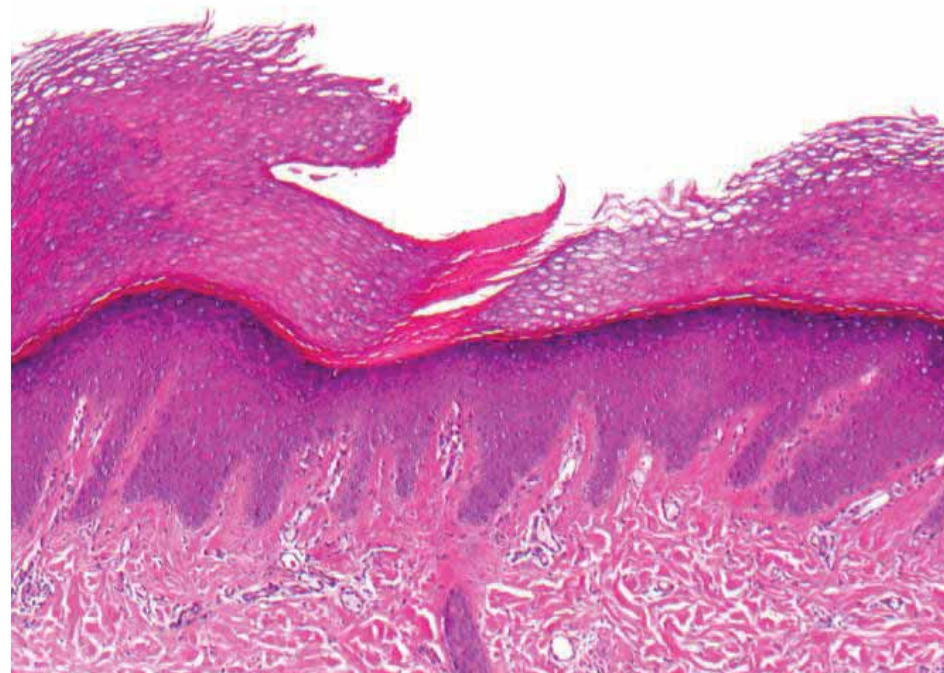
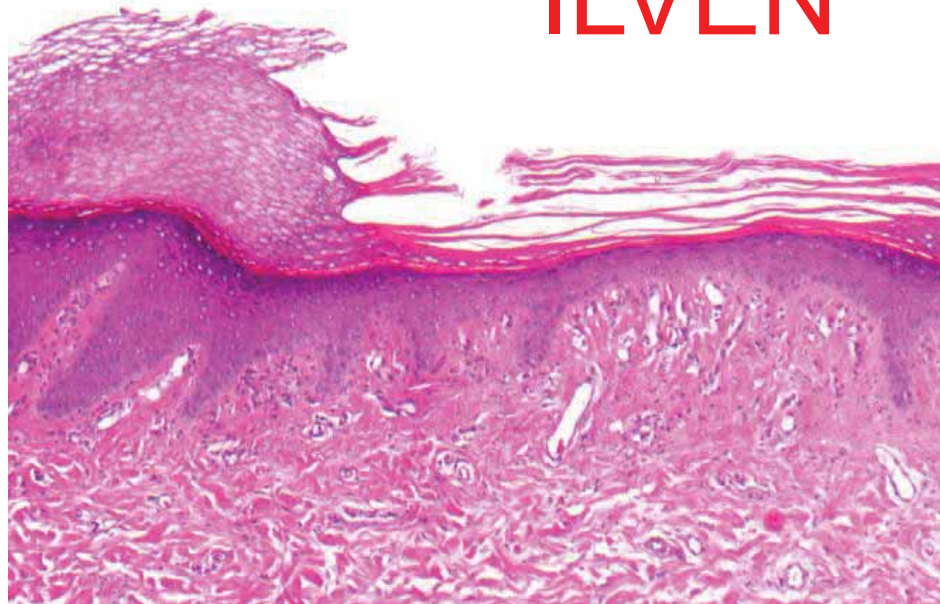


ILVEN

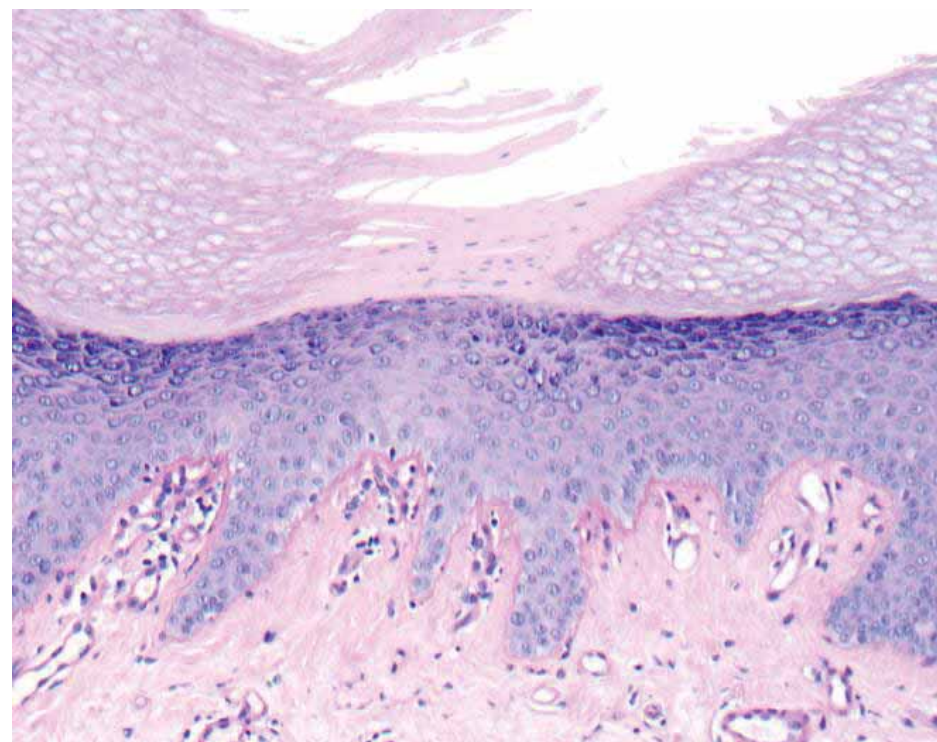
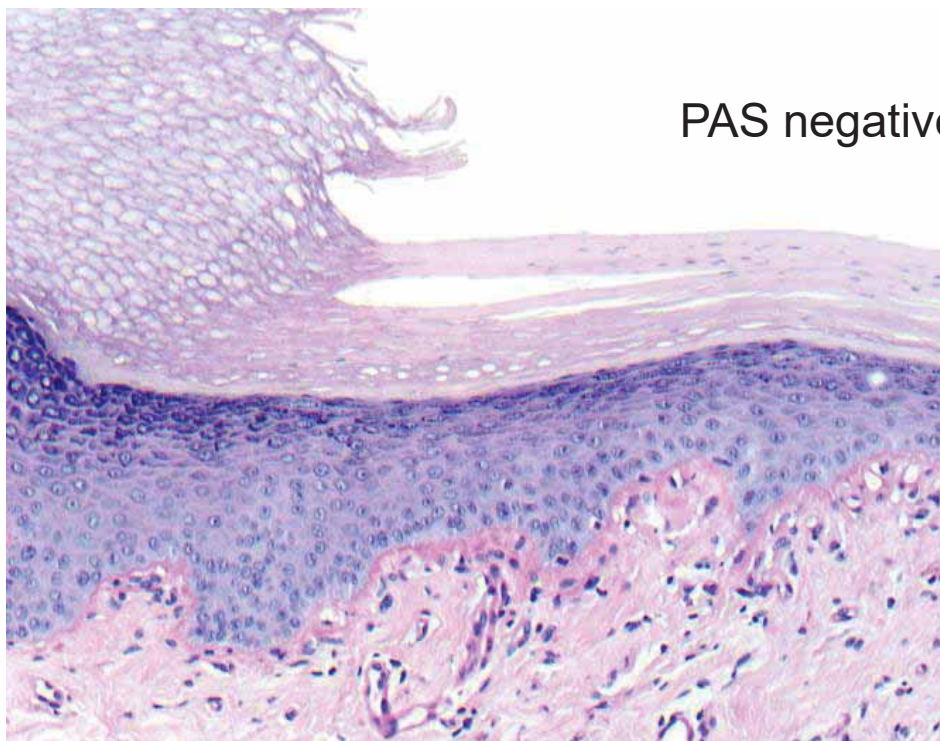


Second biopsy,
Münster

ILVEN



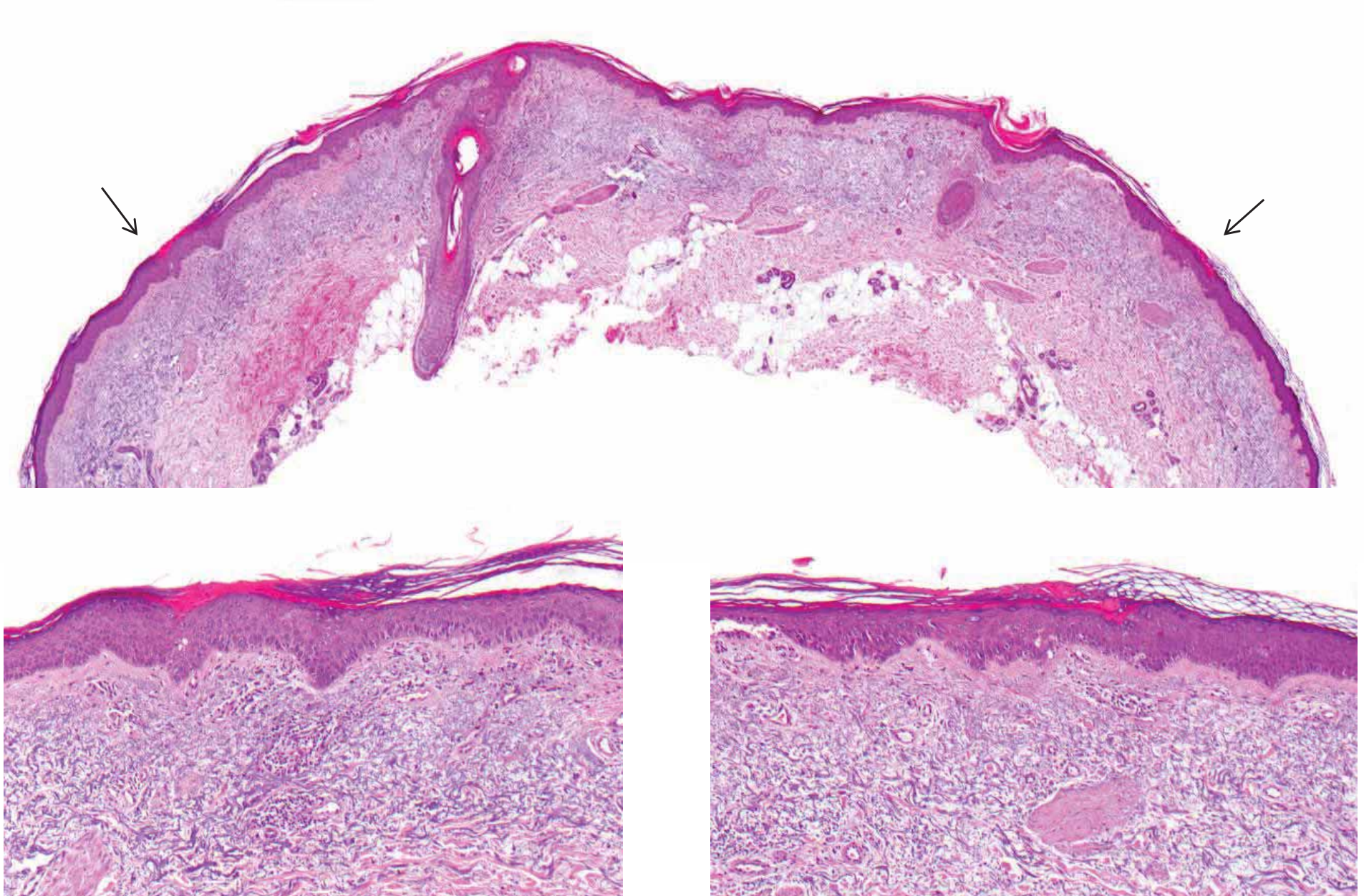
PAS negative



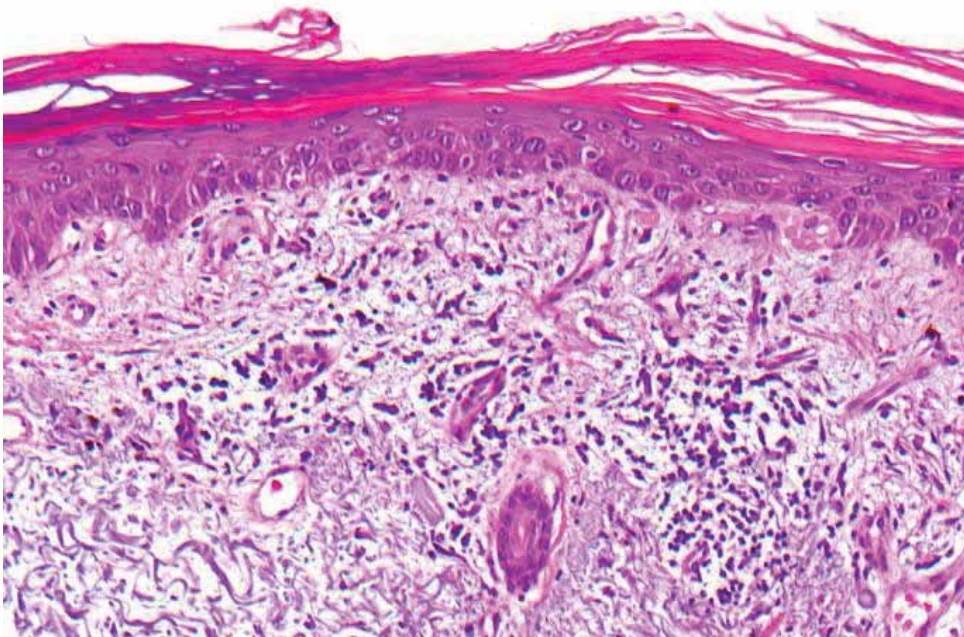
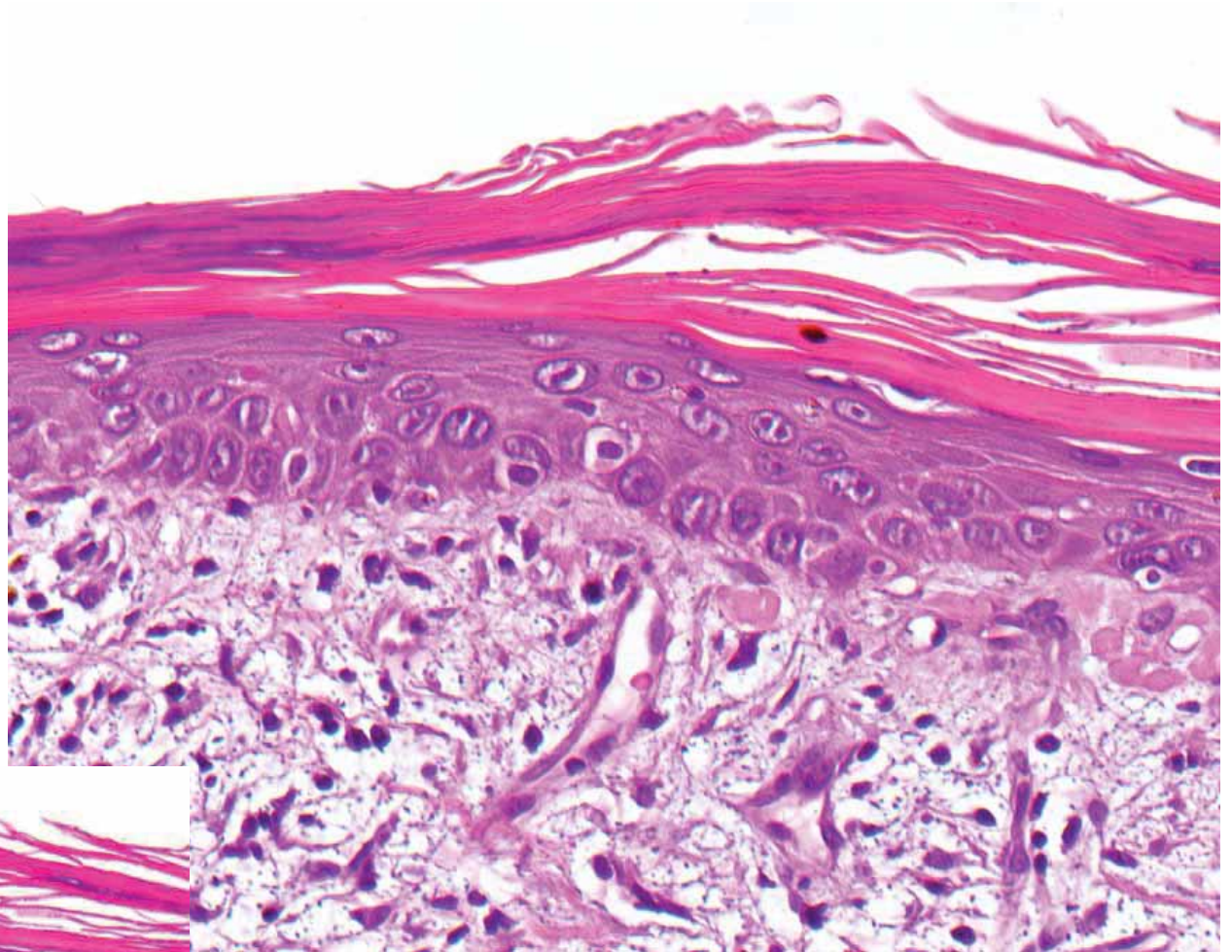
Porokeratosis – Risk of malignancies

- Development of SCC, Bowen, BCC, KA in 7-12%, only slightly increased risk for Melanoma
- Risk factors: size, duration, acral site, age of patient, irradiation, immune status, and type
- P. linearis (19%) > P. Mibelli (7,6%) > P. disseminate (3,4%)

Porokeratosis, DSAP, with in situ carcinoma

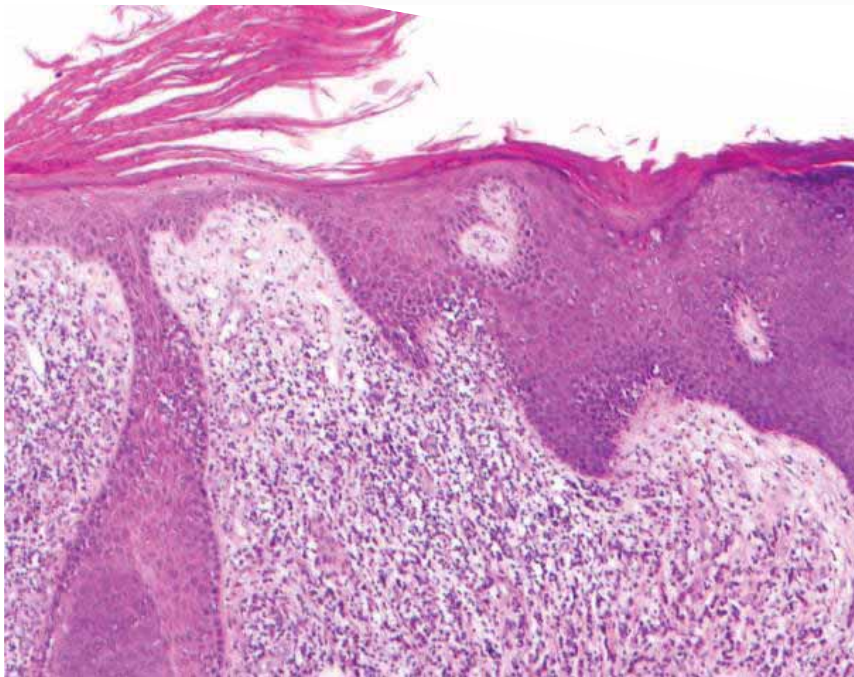


Porokeratosis,
DSAP, with
in situ carcinoma

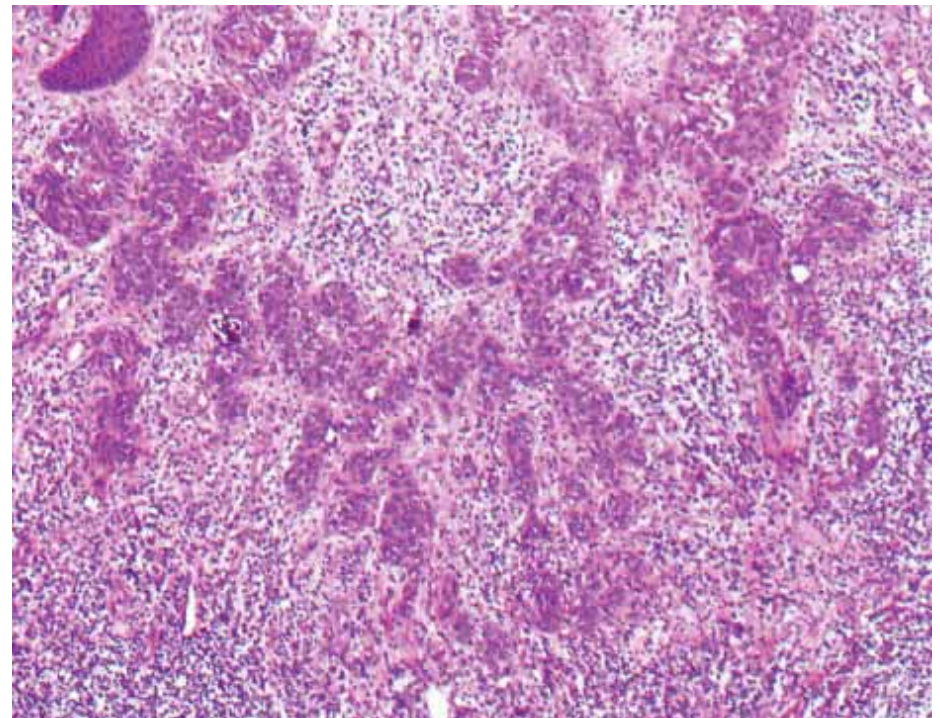
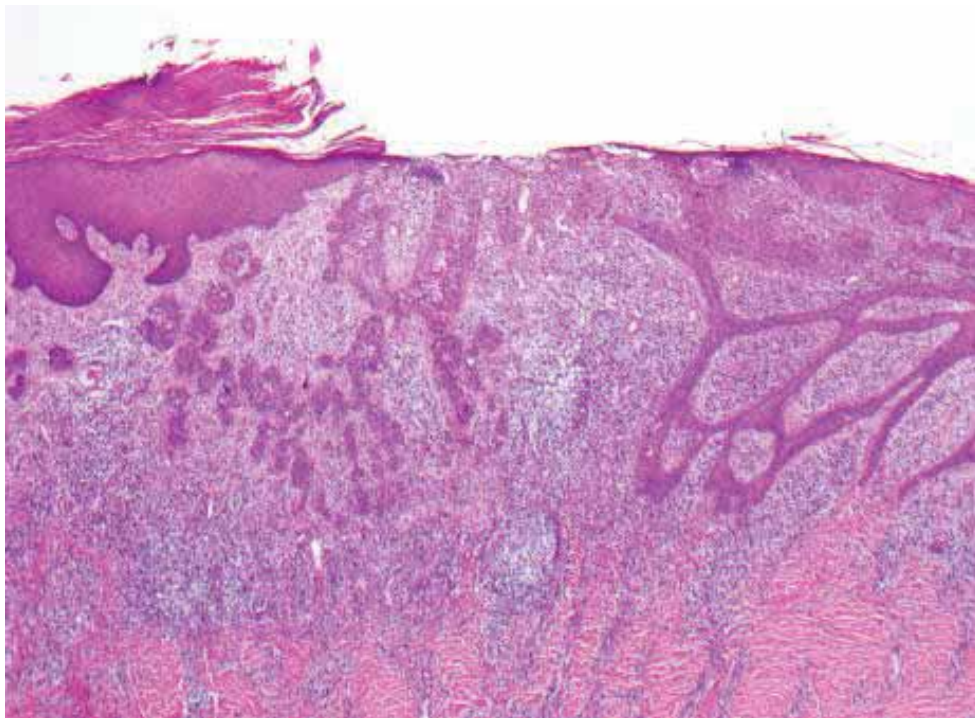
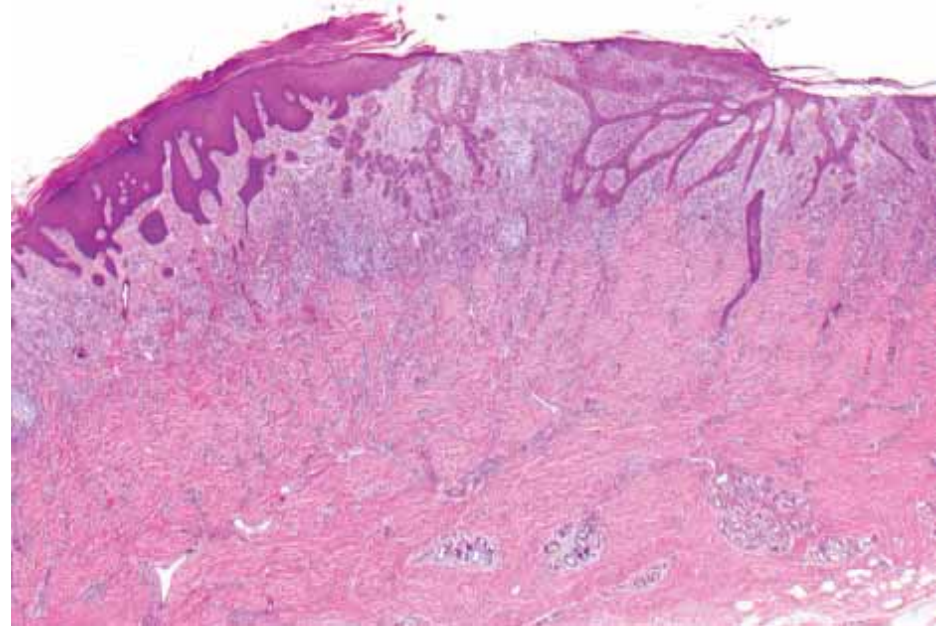


Porokeratosis,
DSAP, with SCC

Cornoid lamella



Porokeratosis, DSAP



Porokeratosis ptychotropica

(Perianal verrucous porokeratosis, reticulated porokeratosis)

(*ptyche*, Greek for fold)

- Mostly non-hereditary, males, peak 3rd- 4th decade
- Symmetric on buttocks and natal cleft, scrotum, rarely penis
highly pruritic, brownish, confluent hyperkeratotic papules and plaques, keratotic rim difficult to detect
- Associated classical porokeratosis on other body sites (DSAP, Porokeratosis linearis, P. Mibelli)
- Almost no malignant degeneration
- No spontaneous remission
- Radical surgical removal (Excision, Dermatome, CO2 Laser)

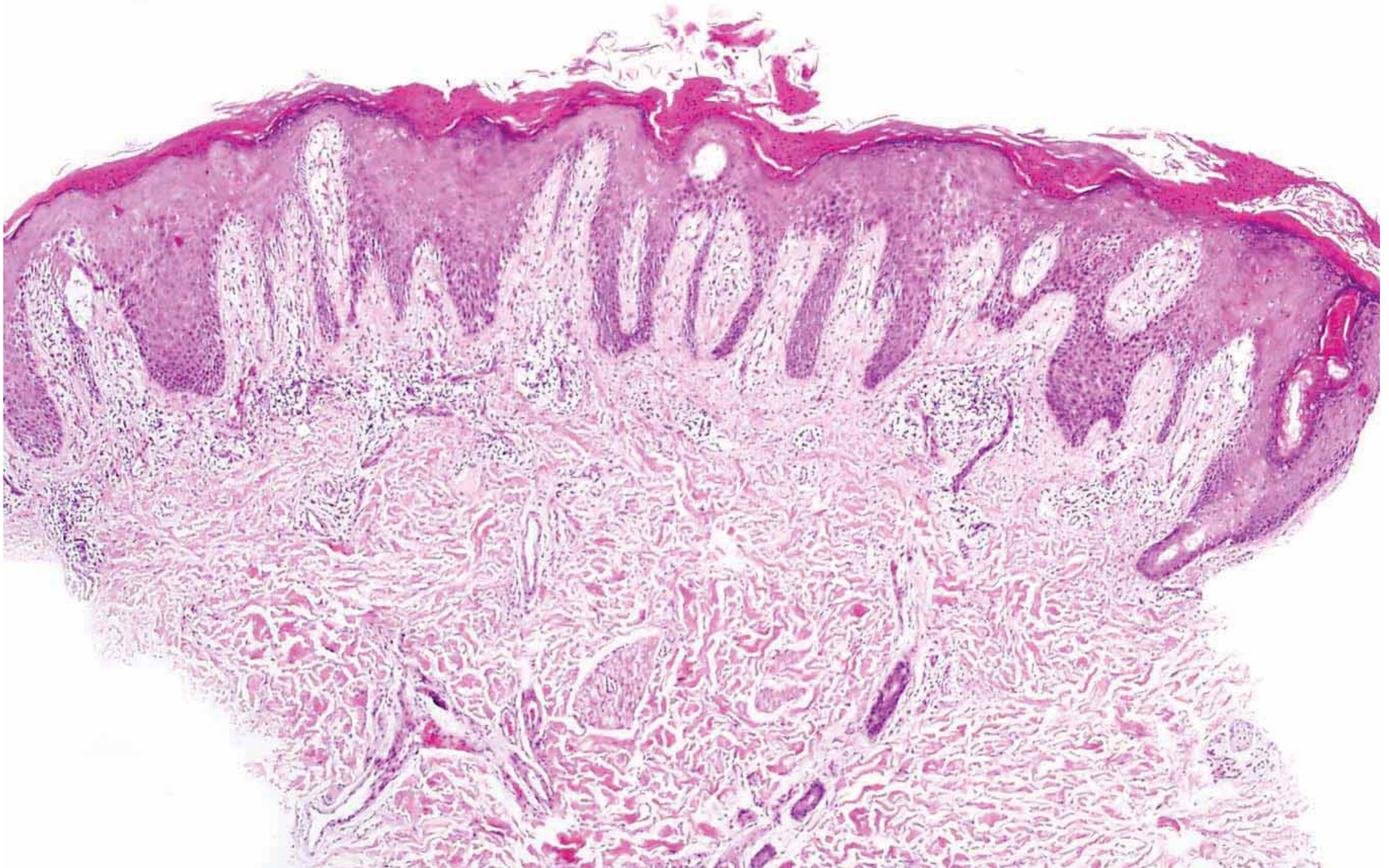
26-year-old man, since 1 year development of pruritic hyperpigmented macules and scaly plaques in the natal cleft extending bilaterally onto the buttocks.

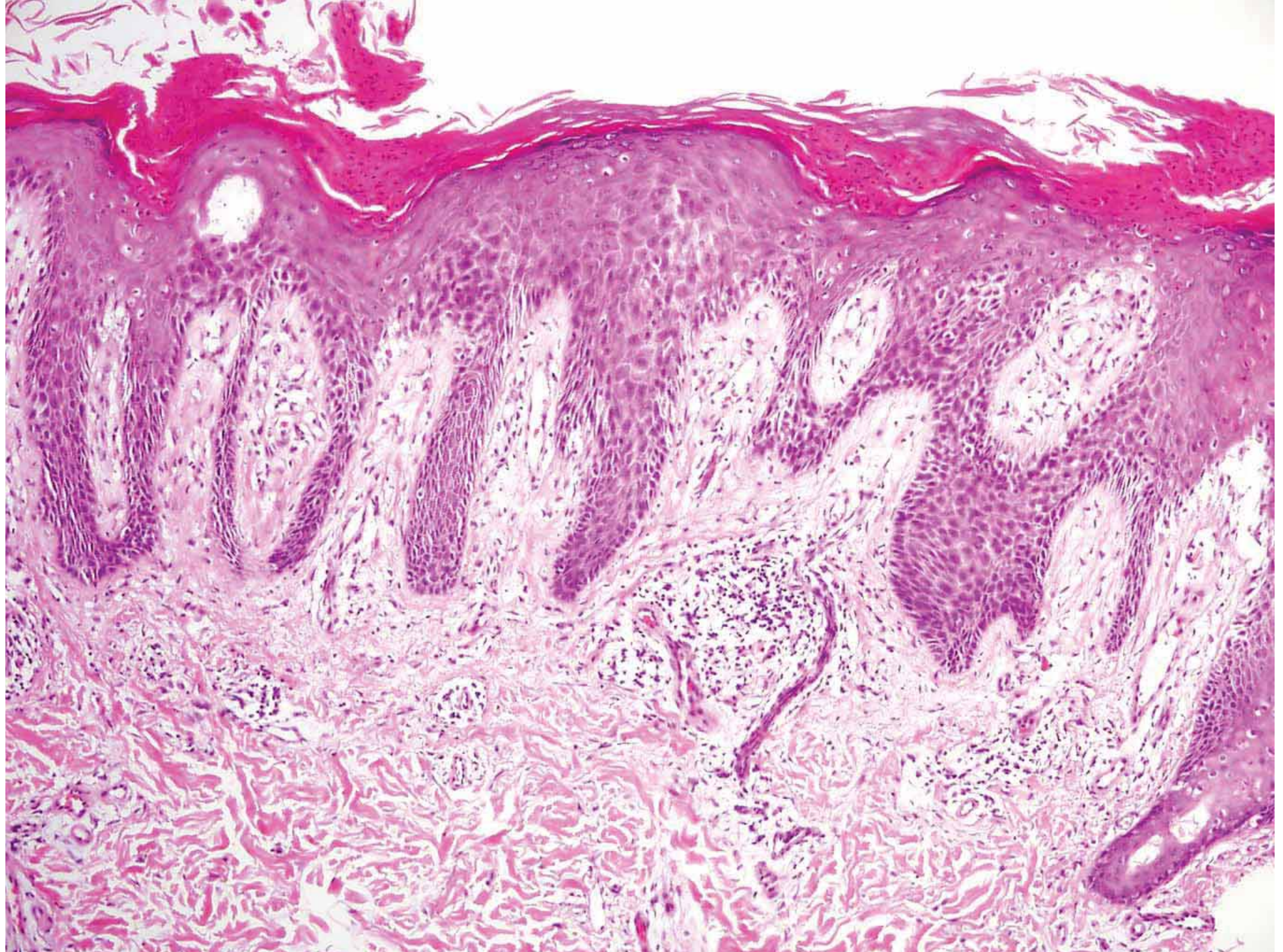


Prof. Steigleder, Köln

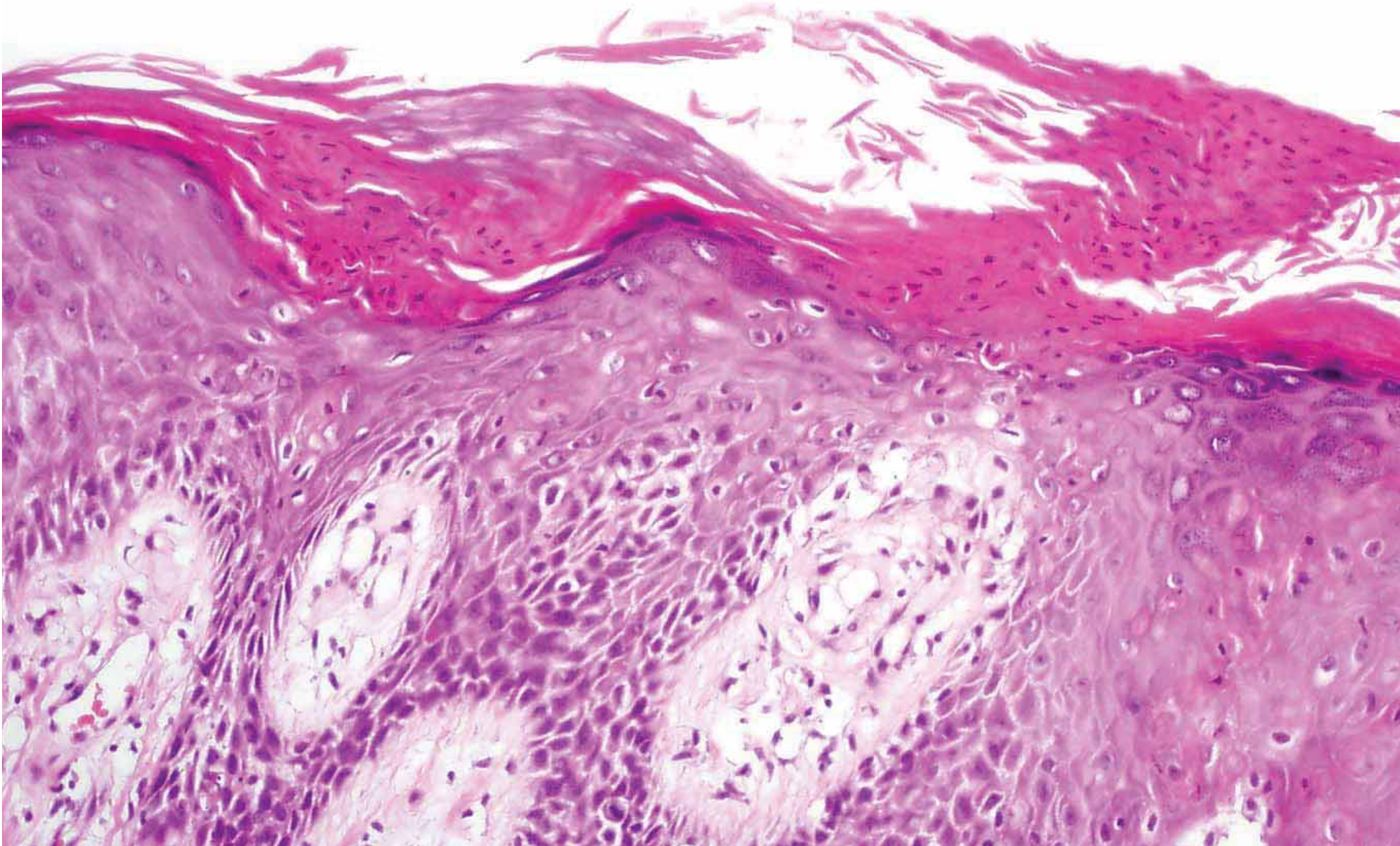
1st Biopsy
Plaque

Pattern:
Superficial perivascular psoriasiform Dermatitis

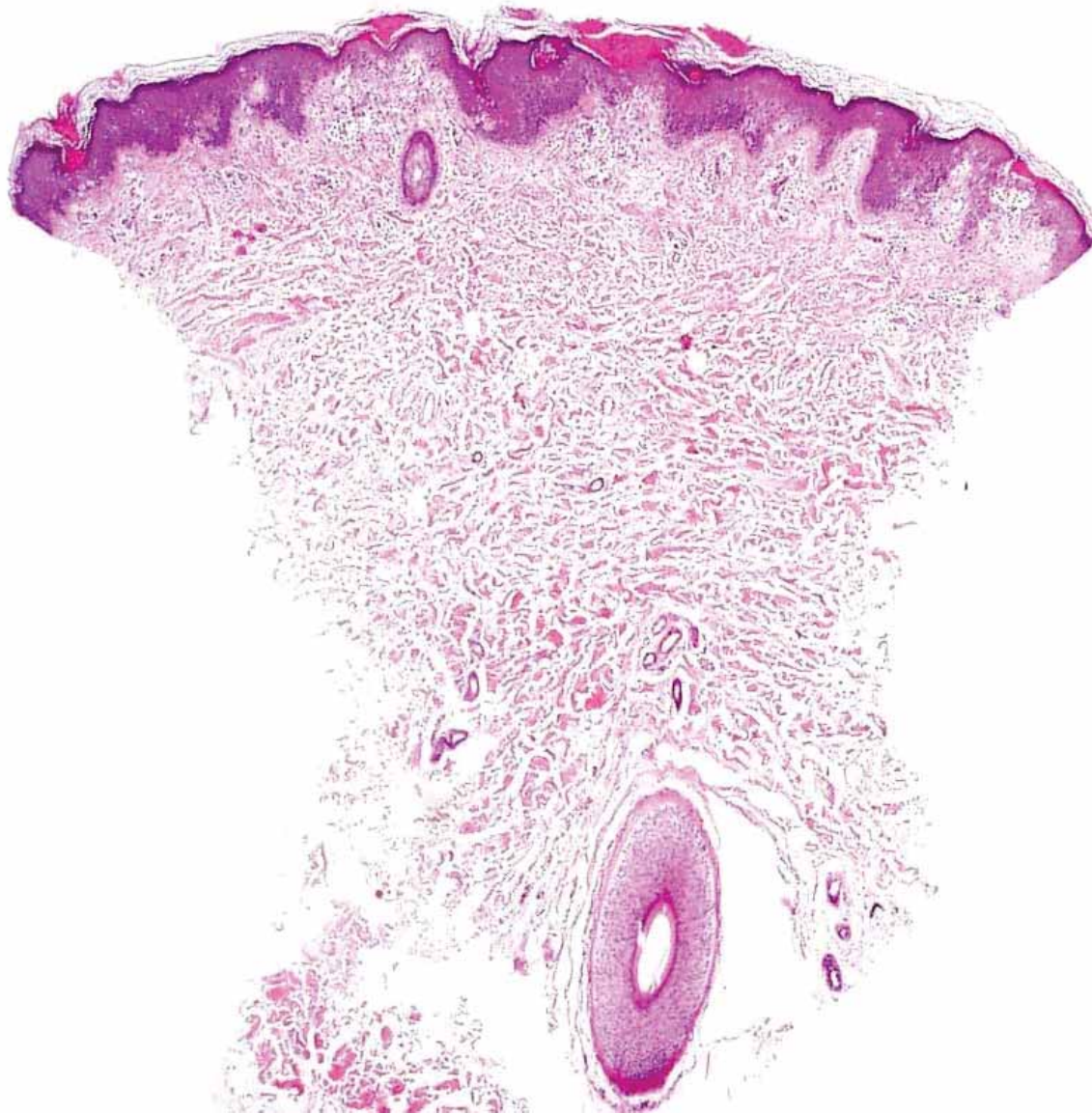




Focal Parakeratosis

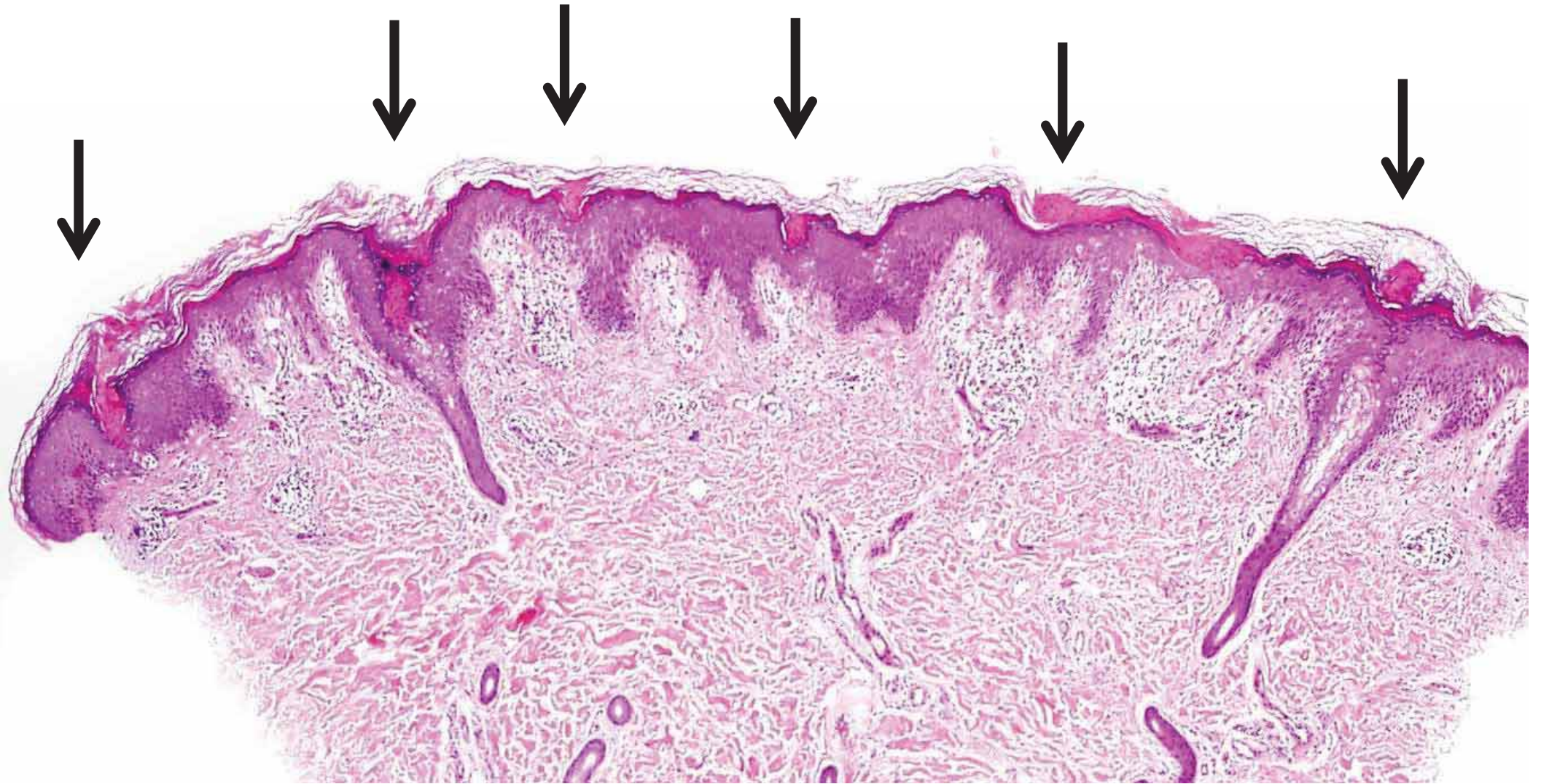


2nd Biopsy
Macula

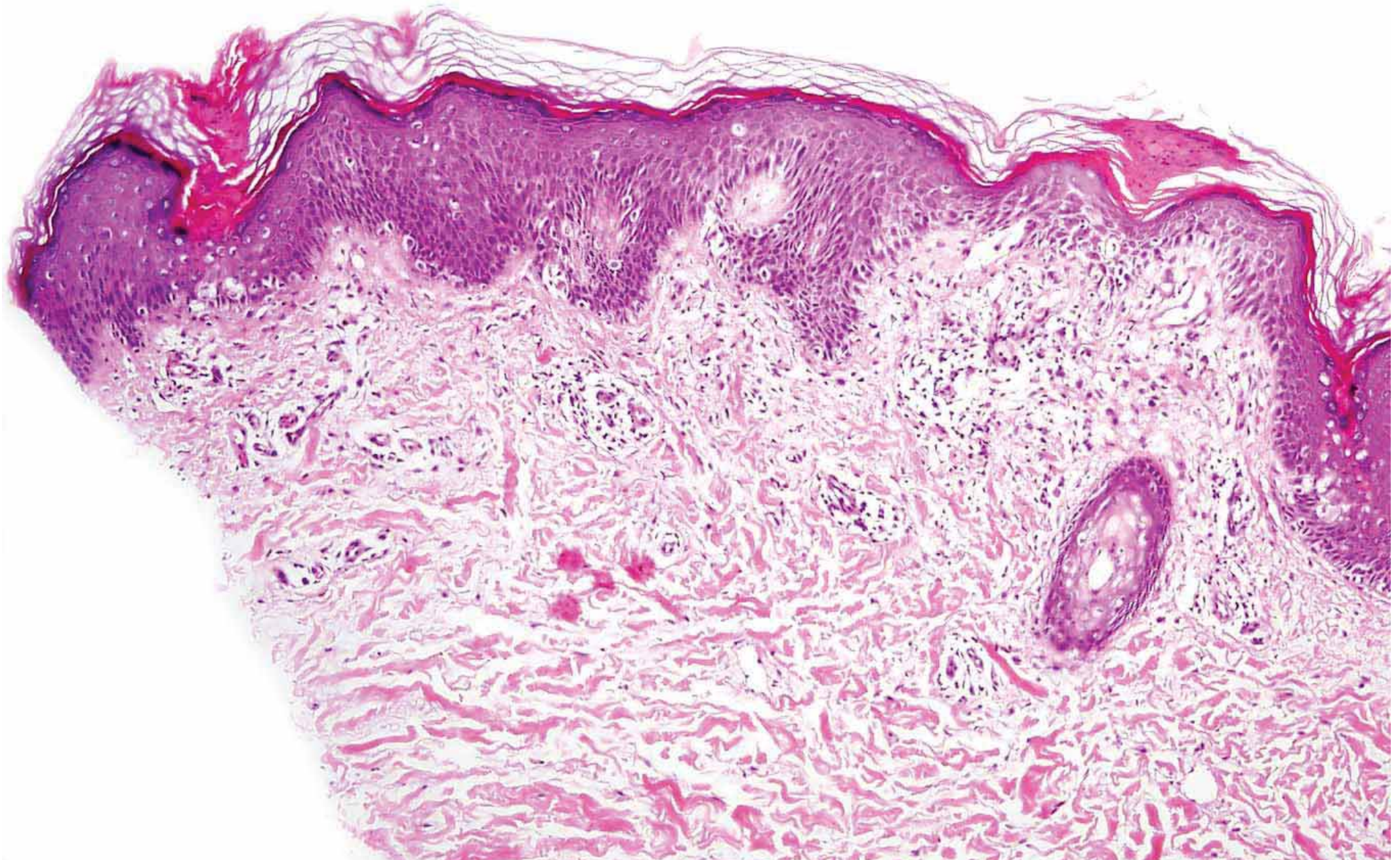


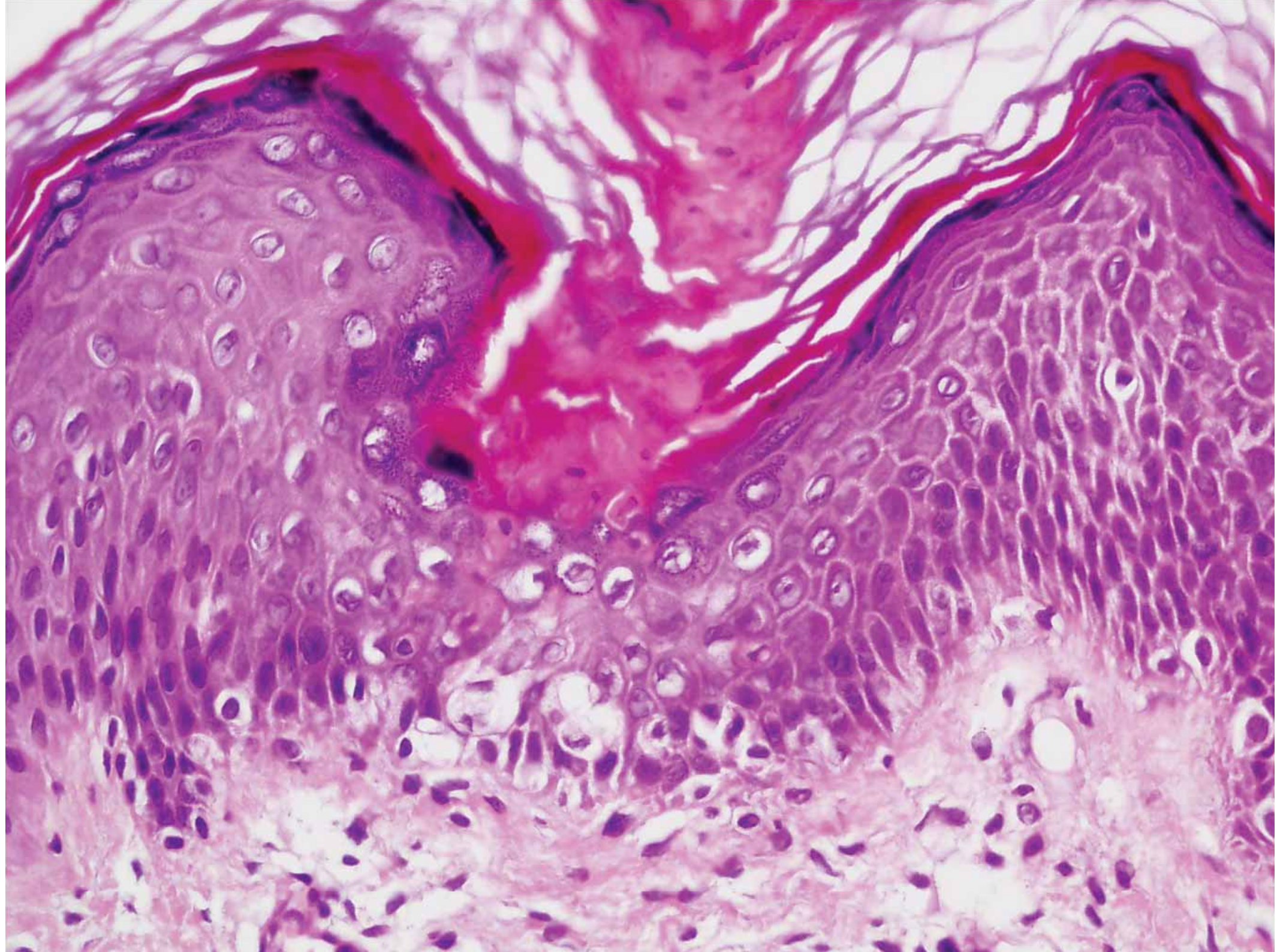
Pattern:
Superficial perivascular
psoriasiform Dermatitis

Porokeratosis punctata



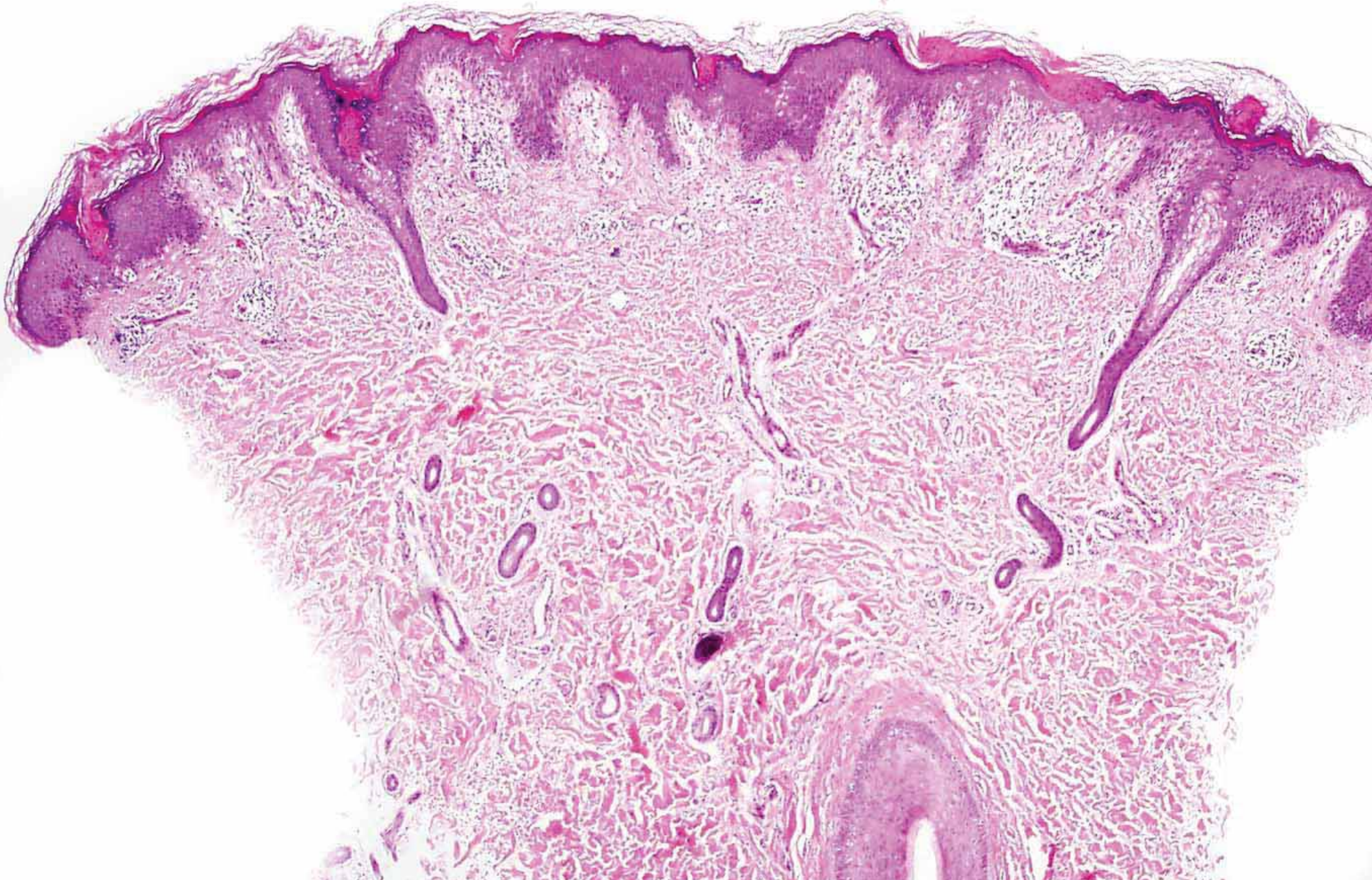
Cornoid Lamella





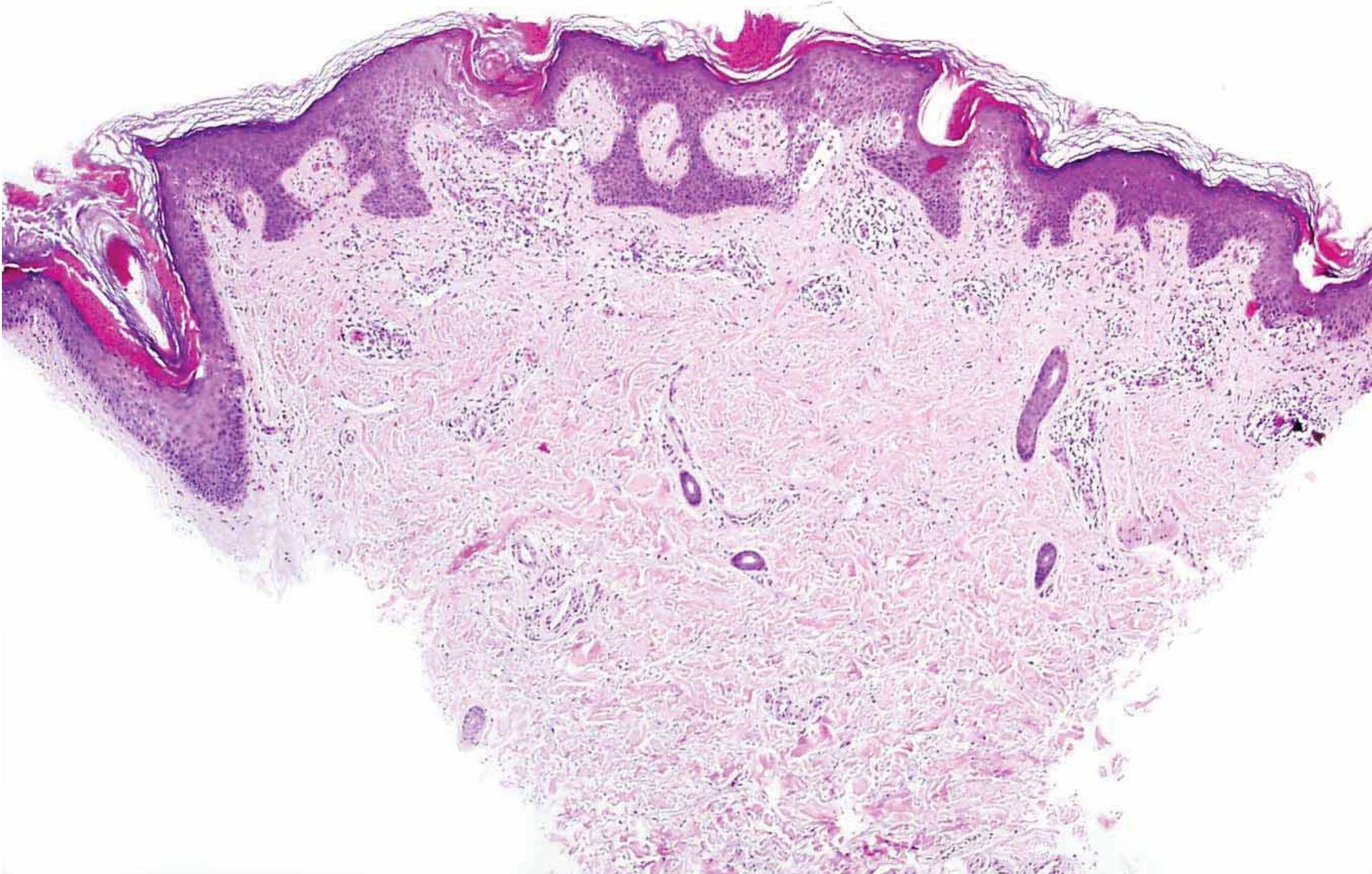
Sweat gland involvement

step section



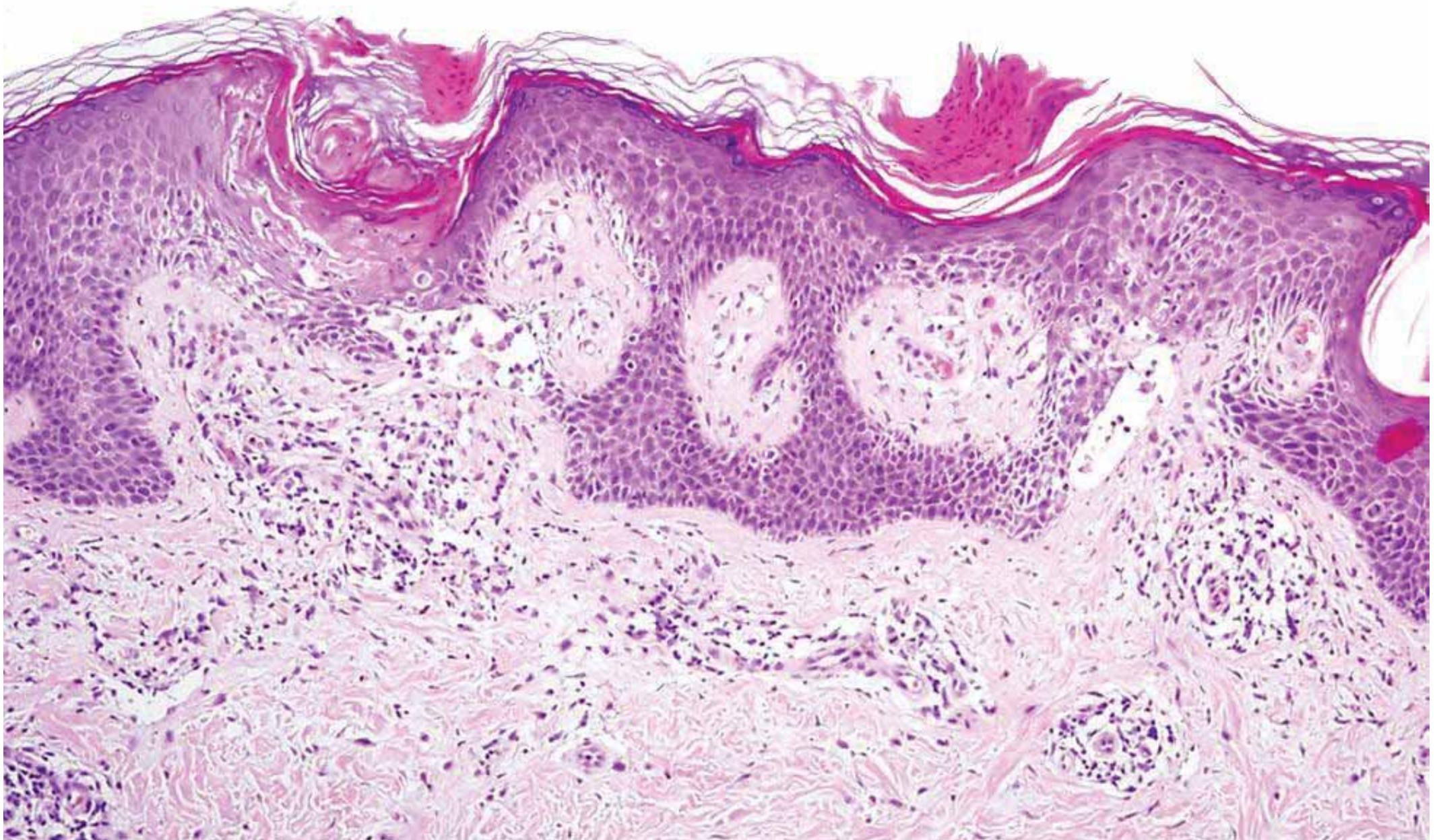
Hair follicle involvement

step section



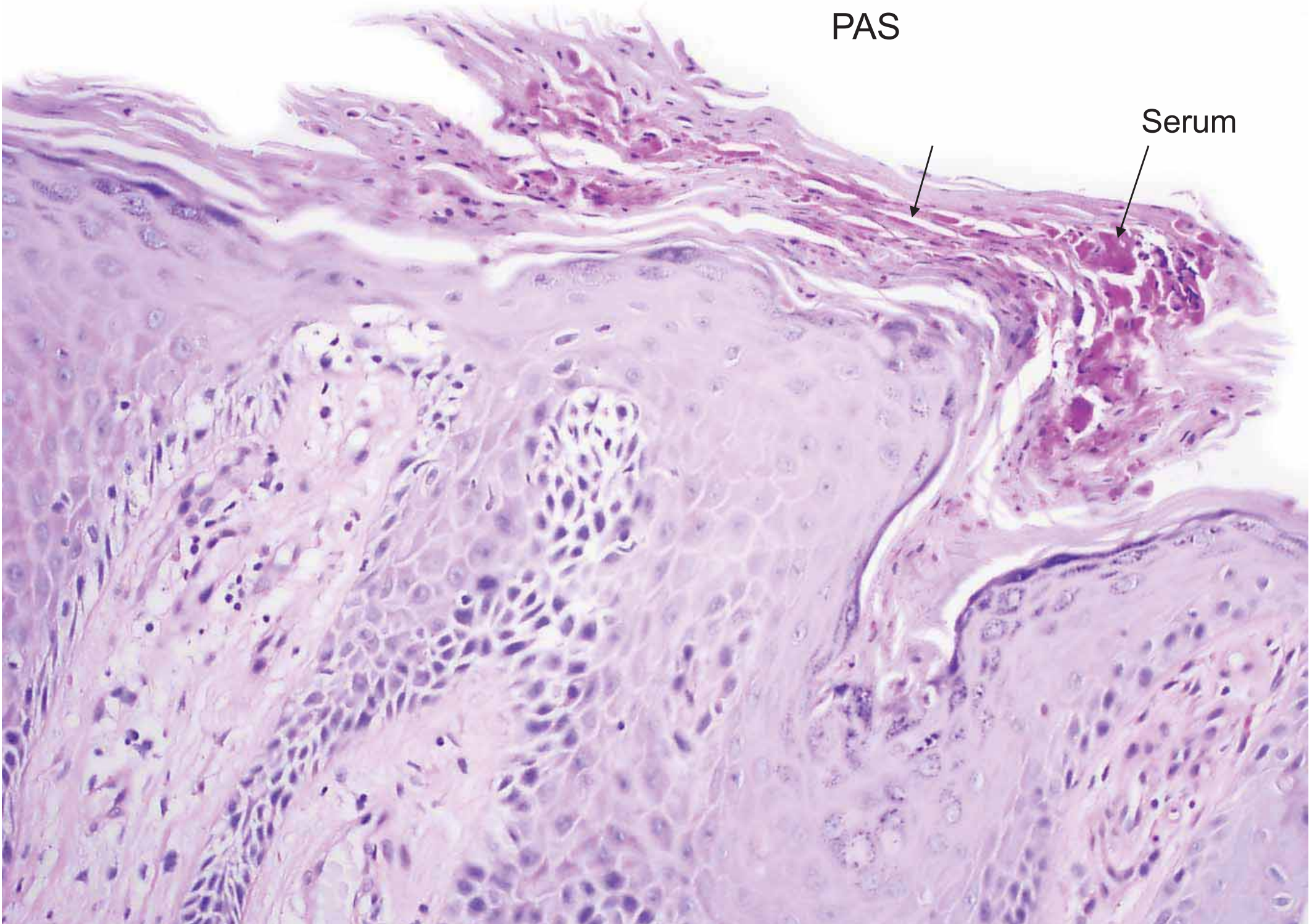
+ Epidermis psoriasiform and spongiotic, cave DDx

step section



PAS

Serum

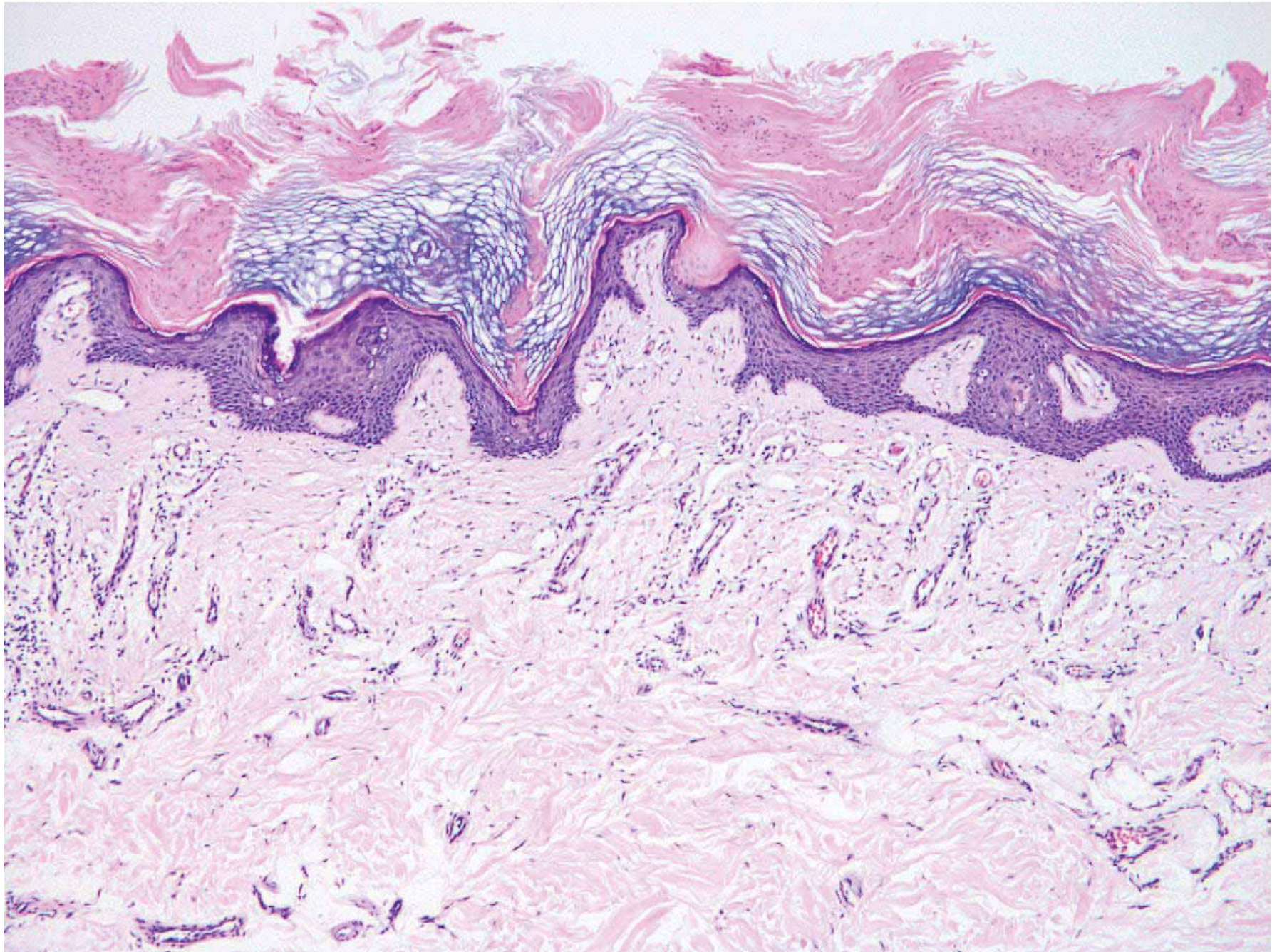


Porokeratosis ptychotropica



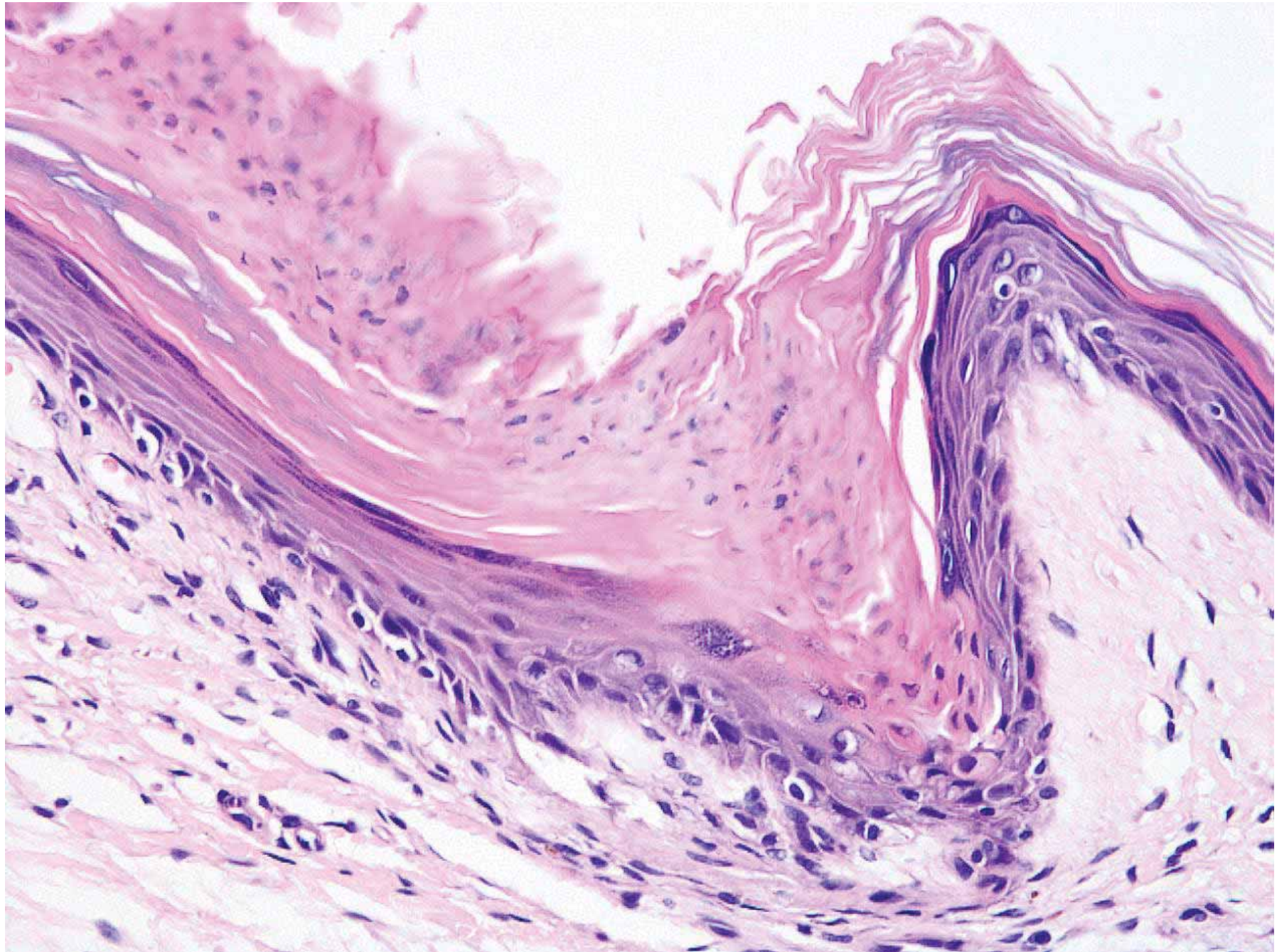
59-year-old man

Courtesy A. von Köckritz, Duisburg



Broad, fibrotic papillary dermis

Courtesy A. von Köckritz, Duisburg



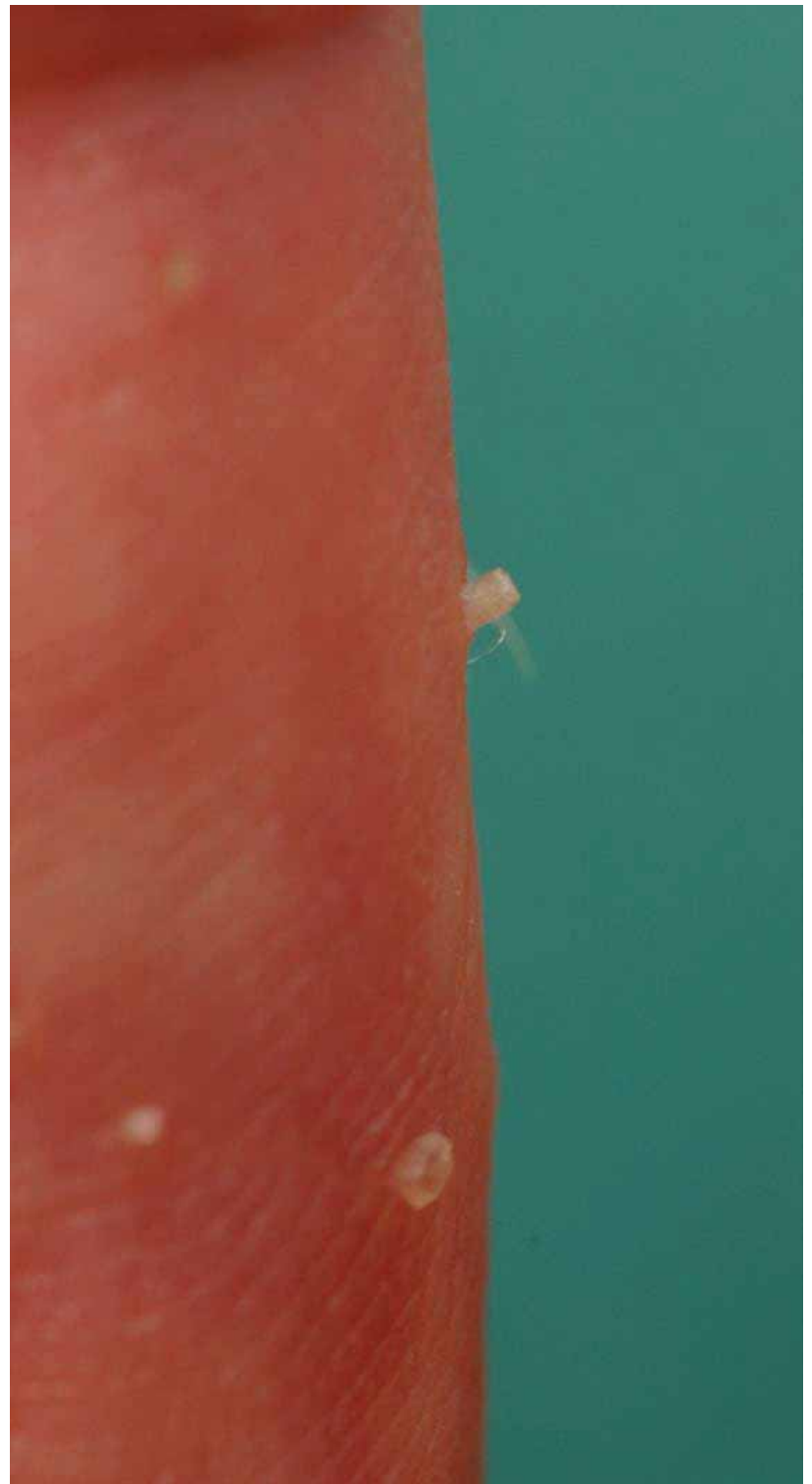
Courtesy A. von Köckritz, Duisburg

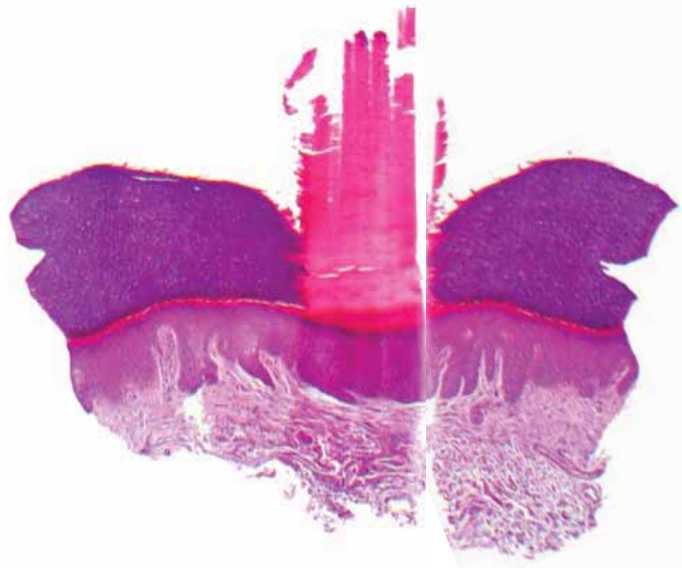
Porokeratosis on palms and soles

- **Classical forms of Porokeratosis:** annular lesions with a peripheral cornoid lamella reported
- **Porokeratosis palmaris et plantaris disseminata (MIM 175850):** Porokeratosis on palms and soles, very hyperkeratotic, nails involvement possible, starts in the 2nd-3rd decade, with subsequent extension to extremities and trunk – no personal experience
- **„Porokeratosis punctata palmoplantaris“ (MIM 175860):** multiple keratotic papules and spines with focal „cornoid lamellae“ = *PPK punctata, type 2* (also MIM 175860)

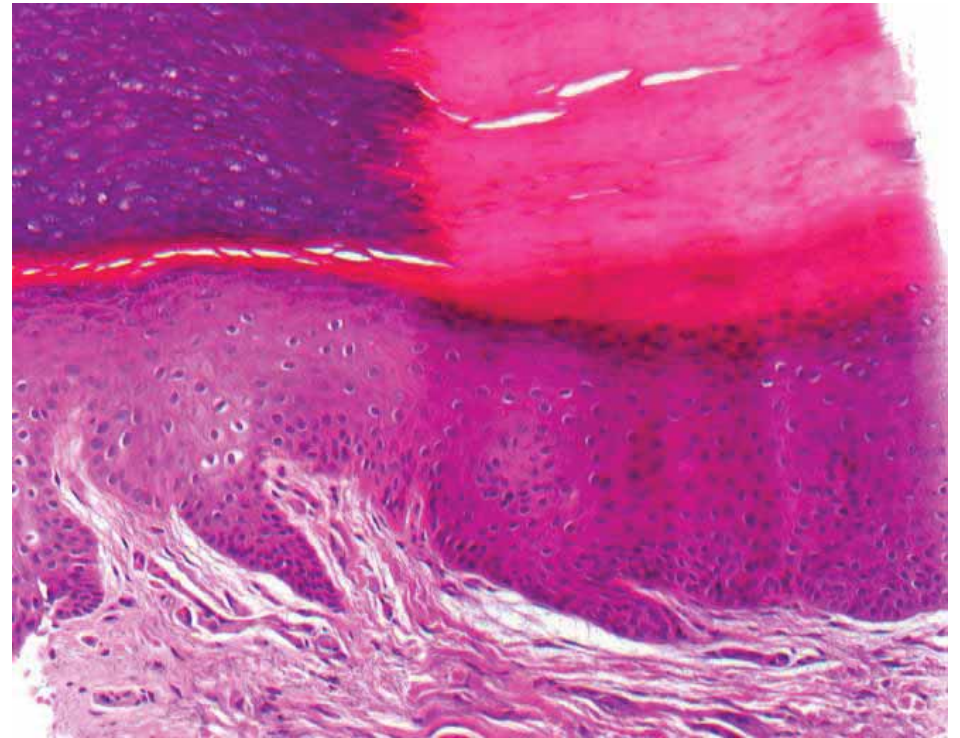
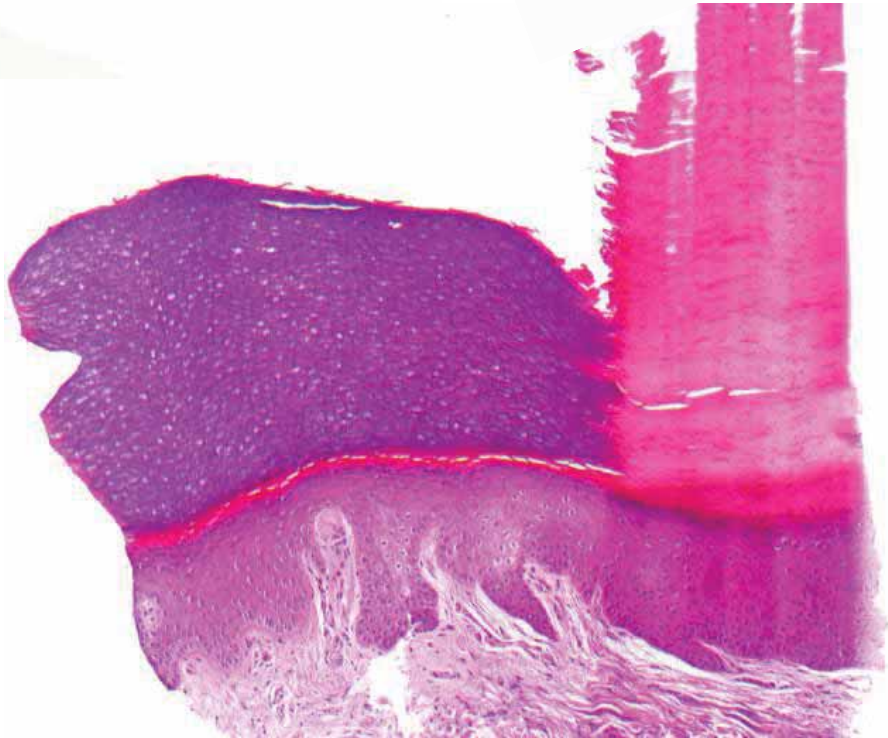
Palmoplantar keratoderma punctata, type II (spiny PPK, „porokeratotic PPK“, „Porokeratosis punctata palmaris et plantaris“)

- Autosomal dominant, MIM175860
- Multiple tiny keratotic spines on palms and soles
- Nails, teeth, and sweating normal
- Late onset 2nd or 3rd decade
- Histology: Epidermal depression with spiny hyperkeratosis, focal parakeratosis, attenuated stratum granulosum
- Acquired forms (after 50y): paraneoplastic (visceral carcinoma, melanoma, leukemia) or internal diseases (hyperlipidemia type IV, asthma, renal insufficiency, polycystic kidney with liver cysts), CoVID-19





PAS negativ



Follicular Porokeratosis

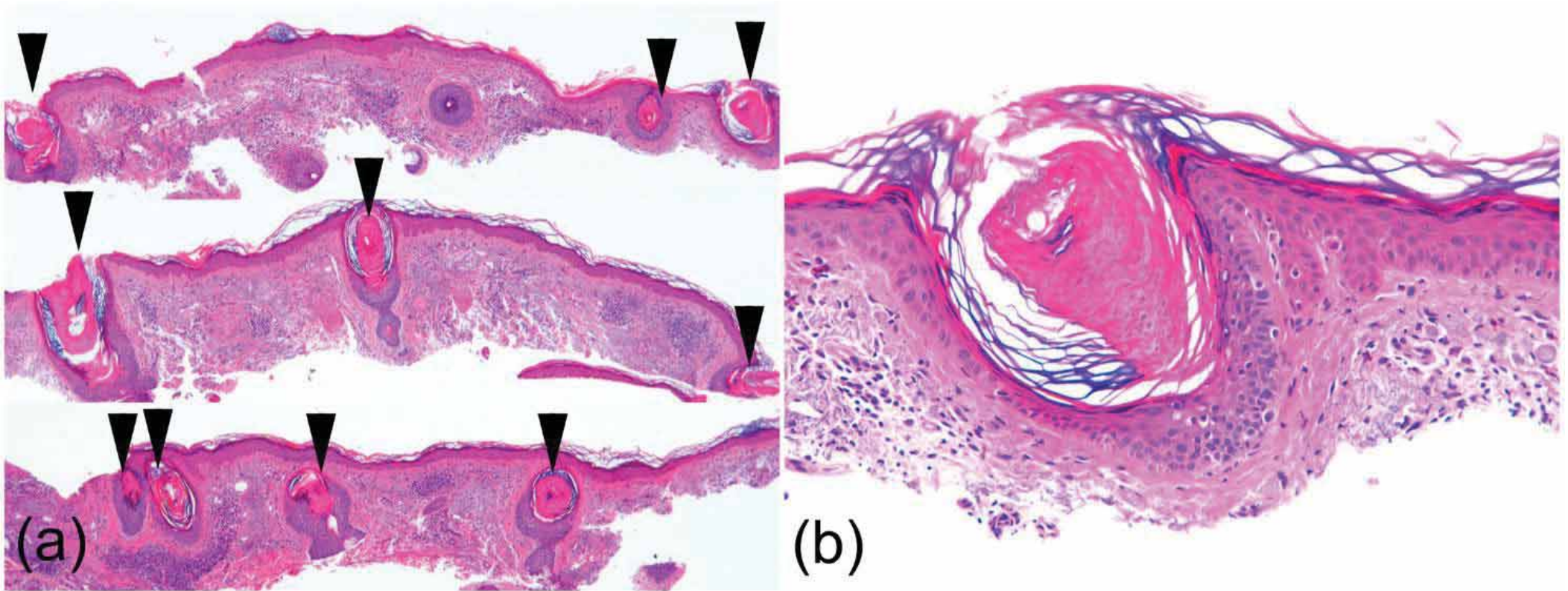
- Distinct clinicopathologic entity or follicular involvement in other types of porokeratosis (in 14% follicular involvement) ?
- Solitary or multiple, small (< 1cm) lesion with persistent follicle-centred aggregated papules or erythematous to brown-coloured annular plaques with a peripheral keratotic ridge.
- Trunk, limbs, genitogluteal, face; sun- and non-sun exposed areas
- Histology: Cornoid lamella limited to follicular ostia
- Association with other subtypes of porokeratosis, porokeratoma, solar lentigo

*Pongpudpunth, M et al. Follicular Porokeratosis: Distinct Clinical Entity or Histologic Variant?
J Cutan Pathol, 2009*

*Minami-Hori, M et al. Cornoid Lamellae Associated with Follicular Infundibulum and Acrosyringium
in Porokeratosis. J Dermatol. 2009*

Sud, A et al. Follicular Porokeratosis: Four New Cases. Clin. Exp. Dermatol. 2017

Follicular porokeratosis arising within a solar lentigo



Courtesy Richard A Carr

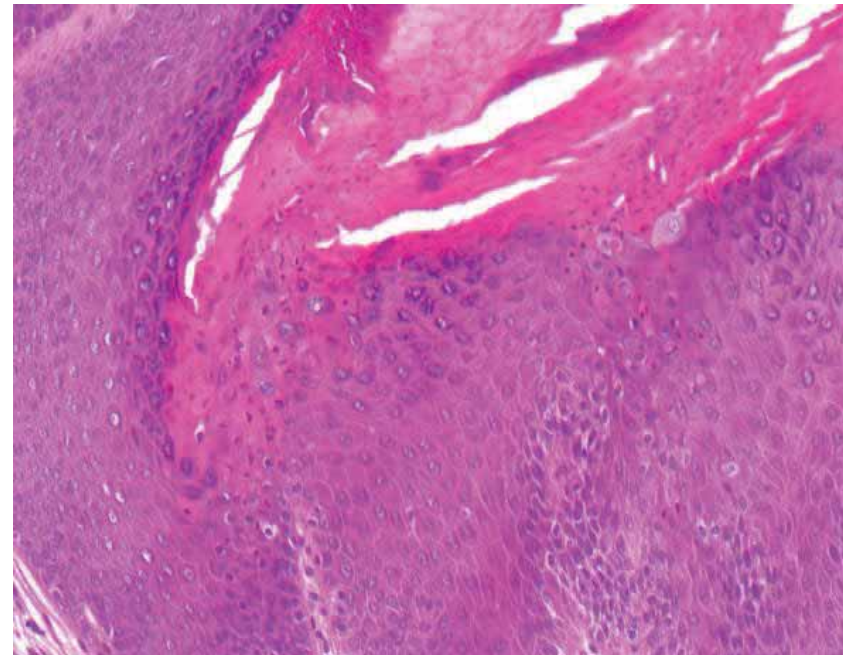
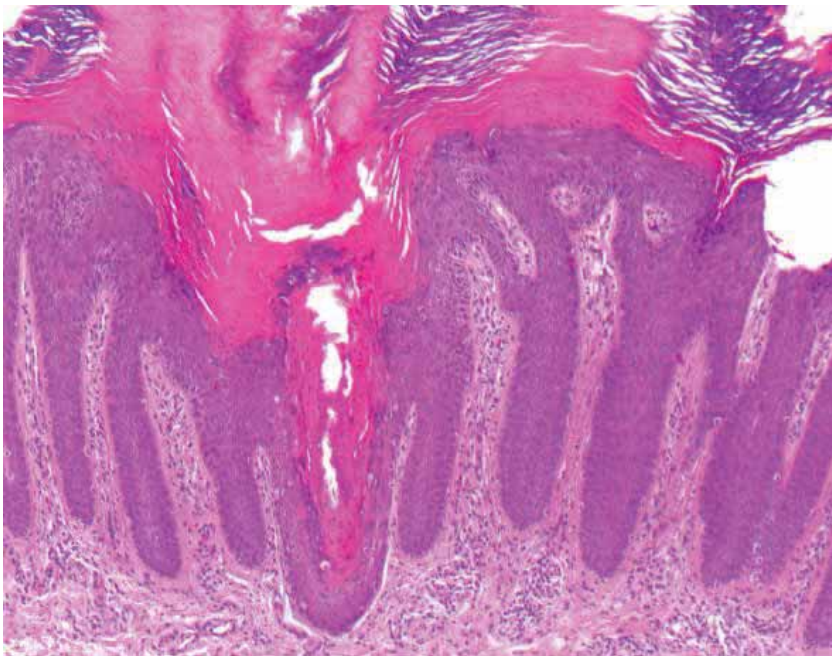
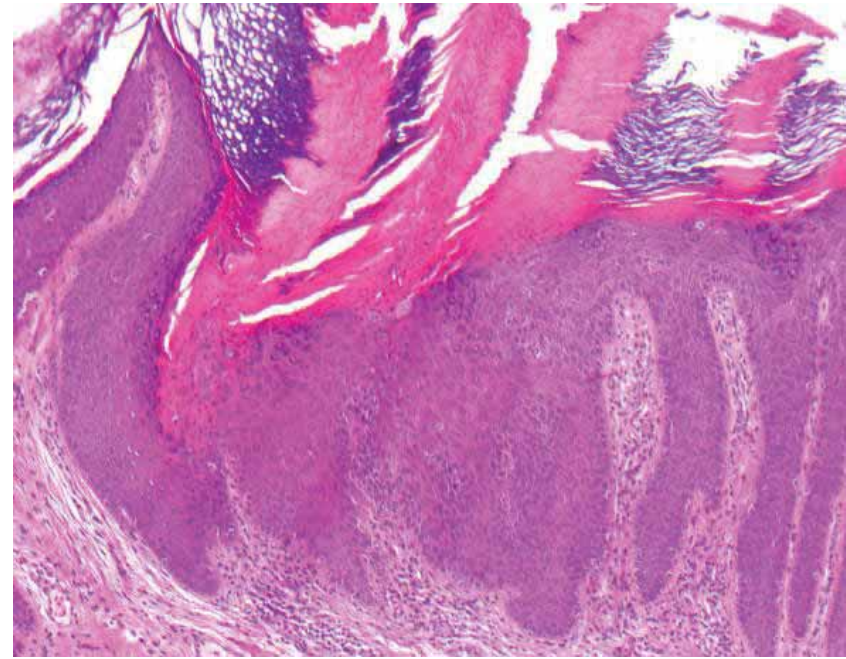
Porokeratoma (Porokeratotic Acanthoma)

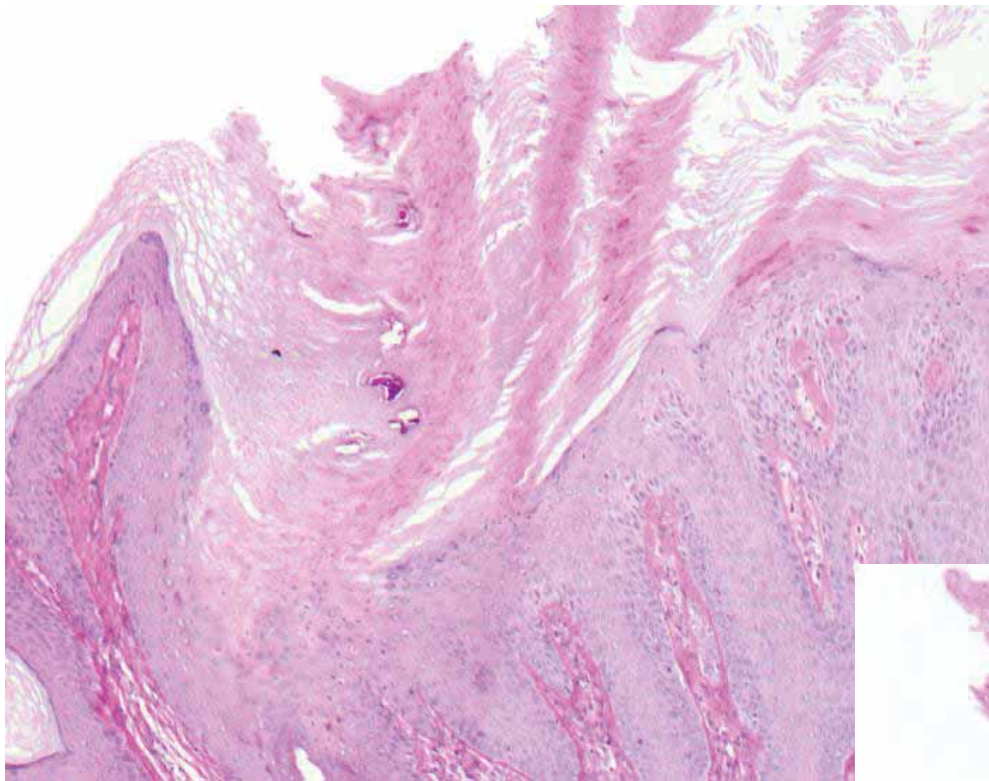
- Middle aged patients, male >> woman
- Hyperkeratotic nodule or plaque without a keratotic rim, solitary or multiple
- Distal limbs >> face, trunk, gluteal folds
- Rare association with ankylosing spondylarthritis
- No other manifestation of Porokeratosis
- Histology: well demarcated verrucous epidermal hyperplasia with multiple broad cornoid lamellae
- Relationship to other forms of Porokeratosis controversial: MVK mutation demonstrated, Verruca vulgaris with incidental cornoid lamella, HPV16 ?
- DDx: Verruca vulgaris, Bowen Carcinoma, Verrucous carcinoma

Walsh et al. Porokeratoma. Am J Surg Pathology, 2007

Kanitakis et al. Porokeratotic Acanthoma, J Cutan Pathol, 2009

Porokeratoma

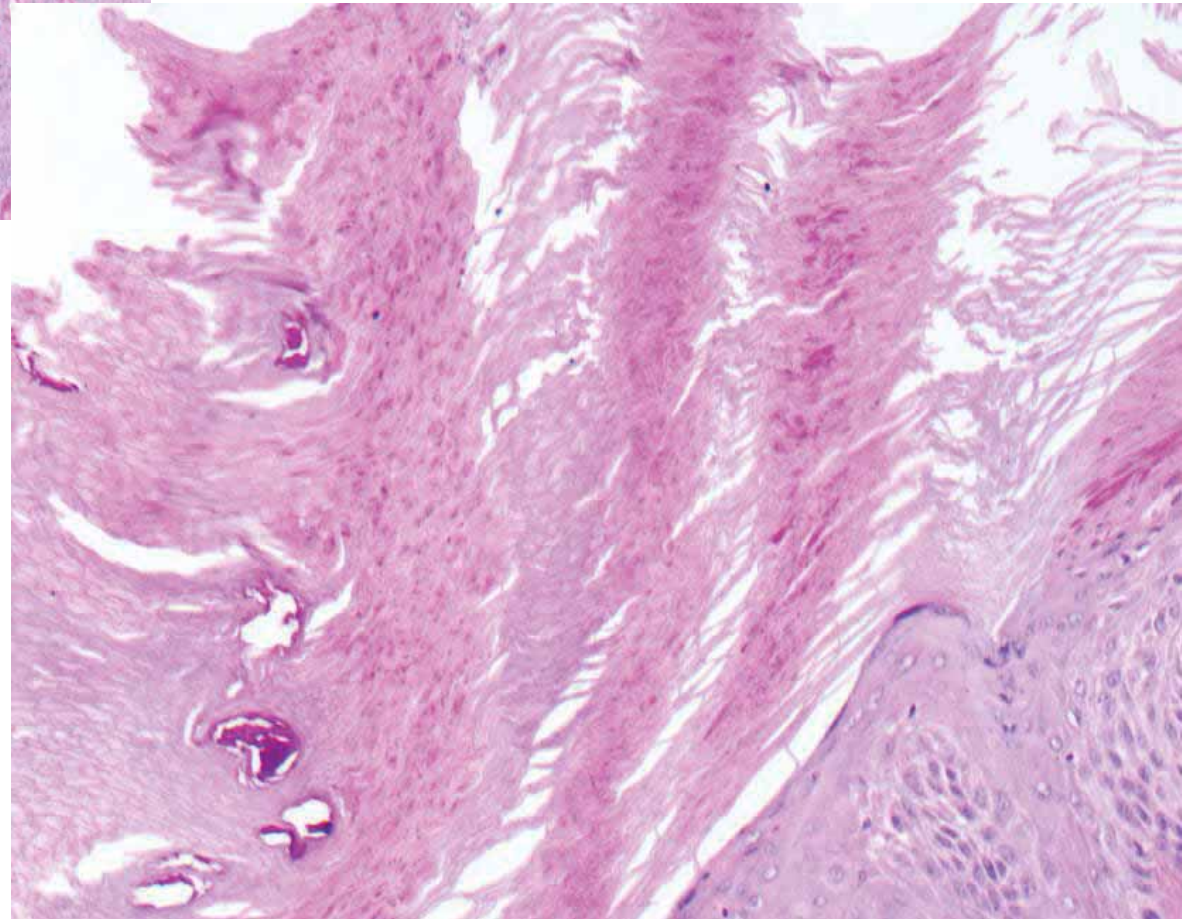




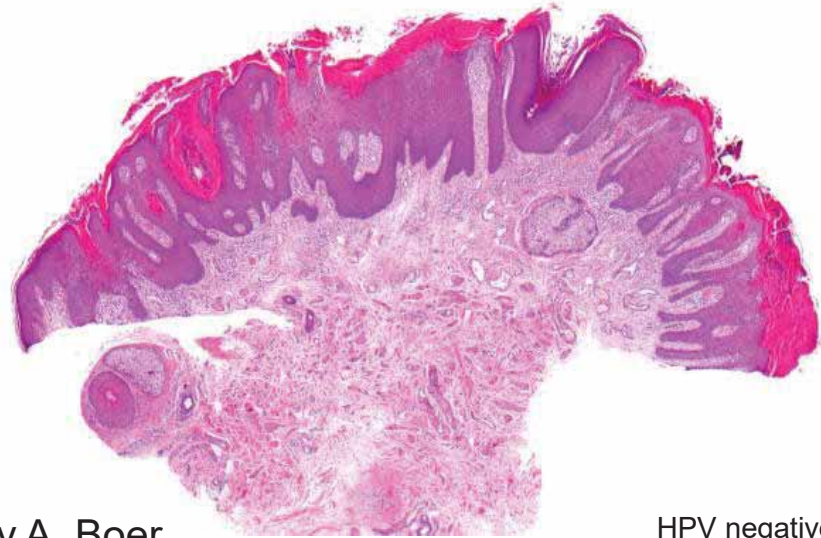
Porokeratoma

granular PAS positivity of
corneocytes in the
cornuoid lamella

HPV: IHC and PCR negative
(Dermatologikum, Hamburg)

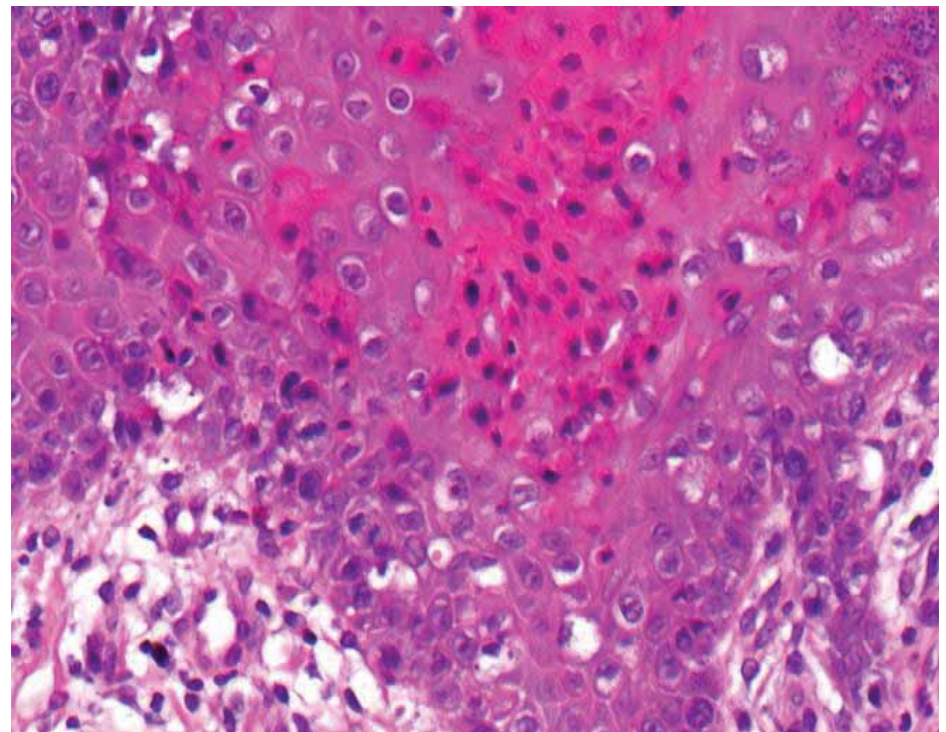
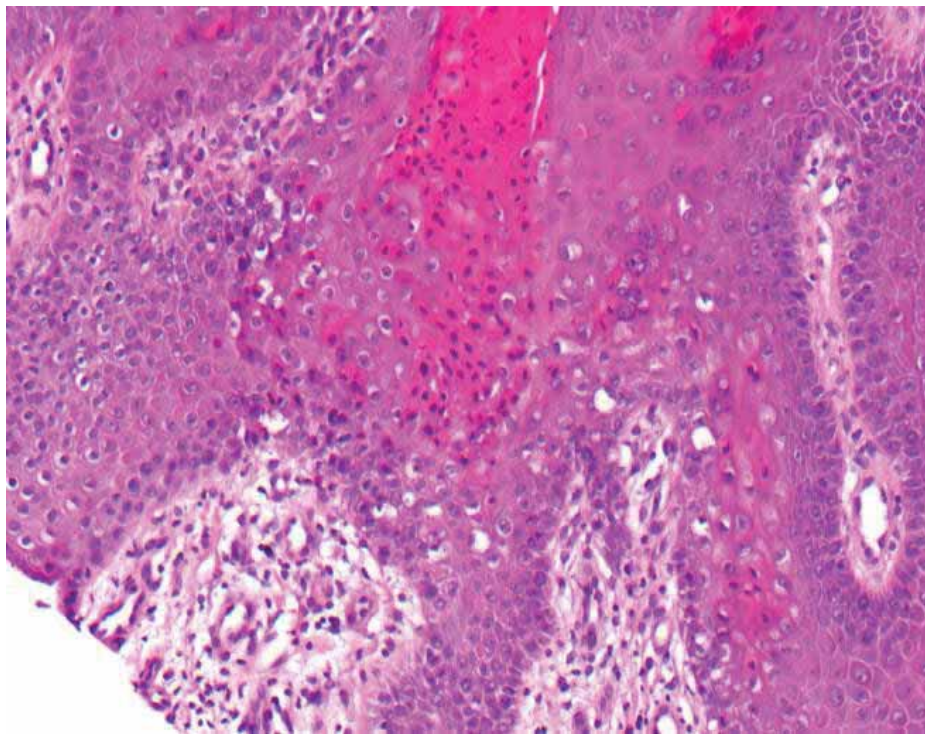
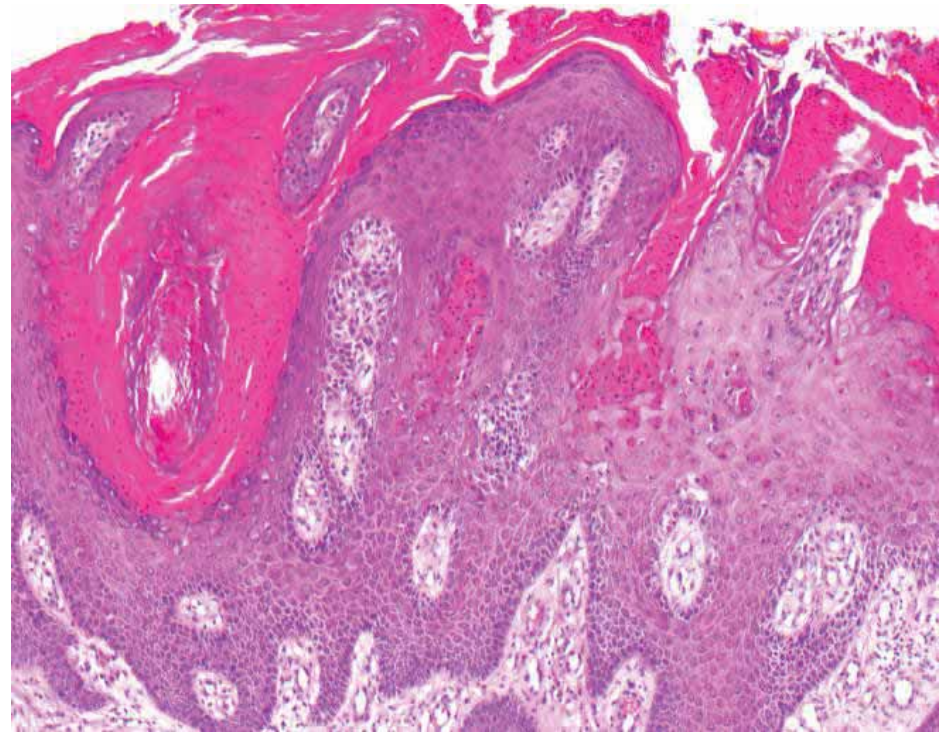


Porokeratoma



Courtesy A. Boer

HPV negative



Porokeratosis - DDx



PAON

Flegel's disease

Keratosis lichenoides chronica

Multiple minute digitate hyperkeratosis

Hystrix-like Keratosis

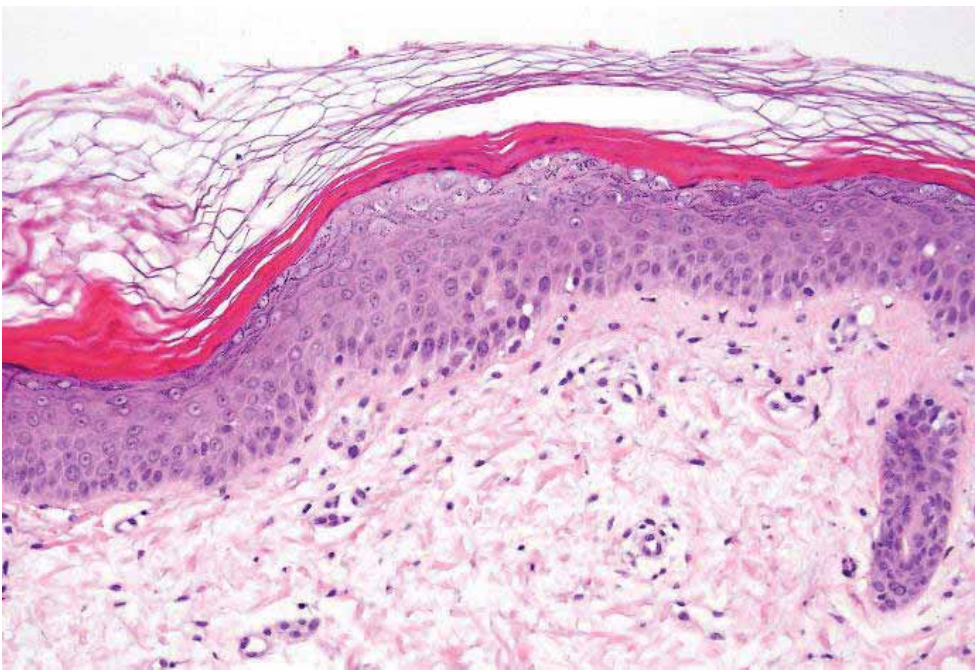
I. Porokeratotic Adnexal Ostial Naevus (PAON)

Syn.: Porokeratotic eccrine nevus (PEN), Porokeratotic eccrine ostial and dermal duct nevus, Porokeratotic eccrine and hair follicle nevus

- Postzygotic mutations of *GJB2* encoding connexin 26: Mosaicism
Germline mutation in *GJB2*: generalized manifestation (KID syndrome)
- No sex predilection
- Manifestation: connatal or at younger age, late onset possible
- Associated diseases: deafness, developmental delay, skoliosis, unilateral breast hypoplasia, seizures, hemiparesis, polyneuropathy, palmoplantar keratoderma

KID syndrome (Keratitis-Ichthyosis-Deafness)

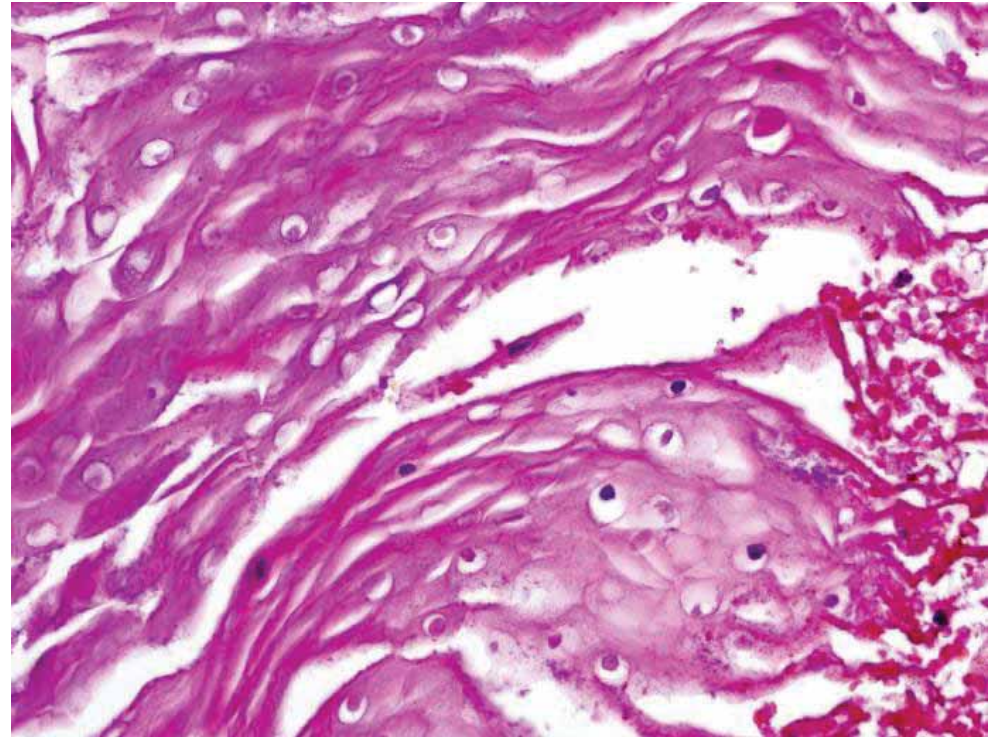
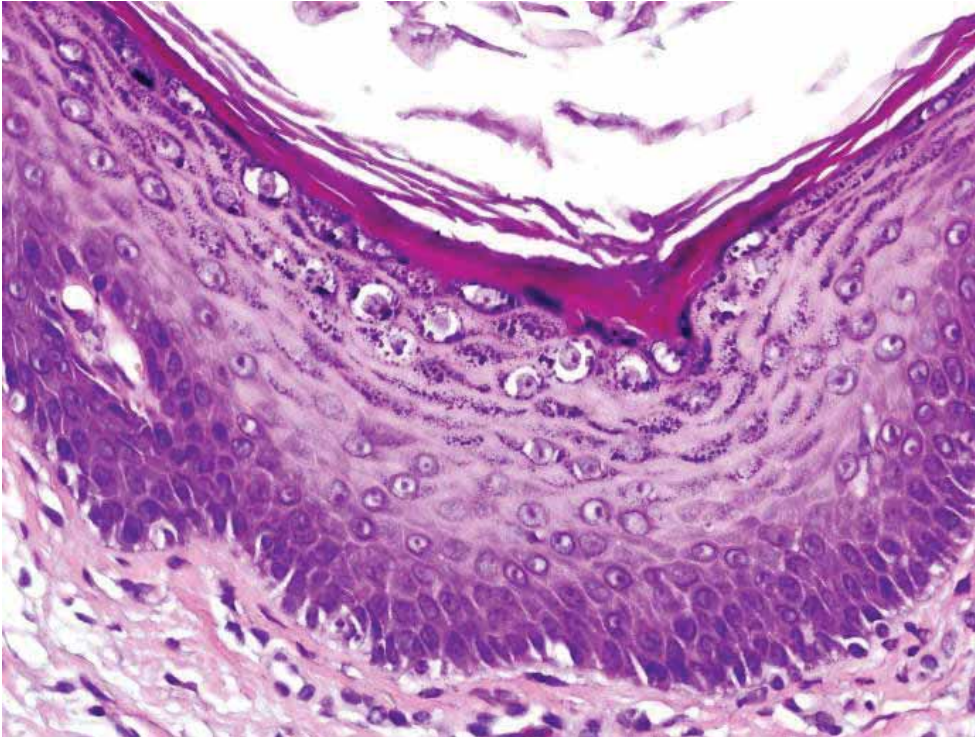




Keratitis-ichthyosis-deafness syndrome (KID) /

Connexin 26 Mutation

Psoriasiform hyperplasia with hyperkeratosis
Keratinocytes: perinuclear vacuoles (“bird’s eye”)
Corneocytes: roundish nuclear remnants or shadow nuclei



II. Porokeratotic Adnexal Ostial Naevus (PAON)

- In Blaschko-lines comedo-like papules and keratotic, verrucous plaques, filiform keratosis, keratotic pits on palms and soles
- Erosions at birth reported
- Unilateral > bilateral > widespread
- Extremities including palms and soles, rarely trunk, face
- Histology: epidermis acanthotic with papillomatosis, orthohyperkeratosis, parakeratotic columns in ostia of hyperplastic and dilated sweat glands and hair follicles, loss of granular layer, vacuolated cells with pyknotic nuclei but no dysmaturation, inflammatory infiltrate sparse or lichenoid but without interface dermatitis;
- Focal anhidrosis, hair loss, onychodysplasia, pruritus possible
- Squamous cell carcinoma, Bowen disease
- Therapy: Laser ablation

Porokeratotic Adnexal Ostial Naevus (PAON)



Porokeratotic Adnexal Ostial Naevus (PAON)

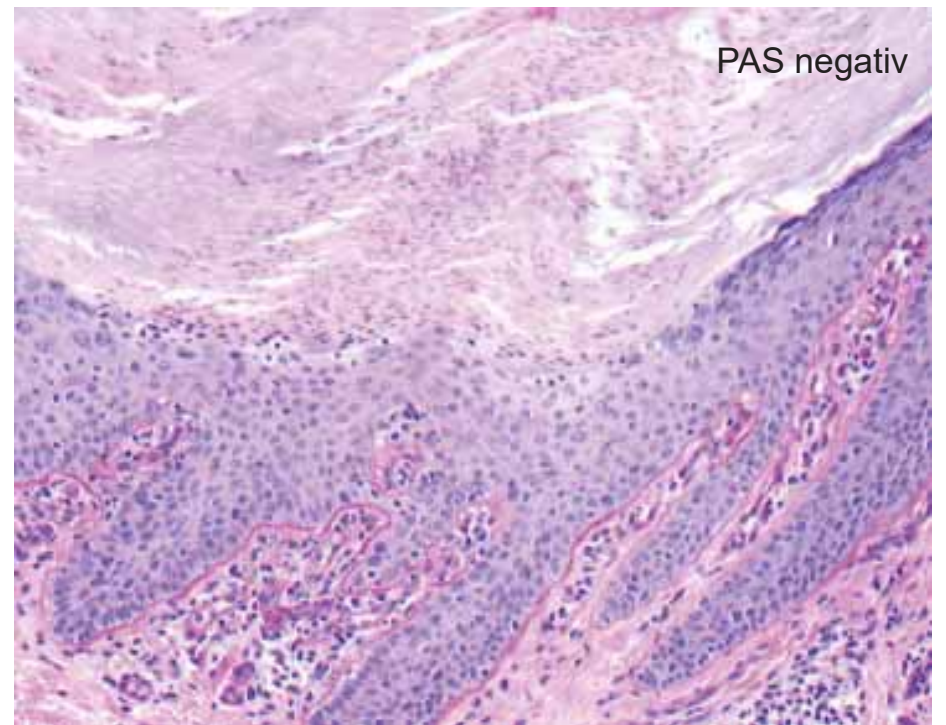
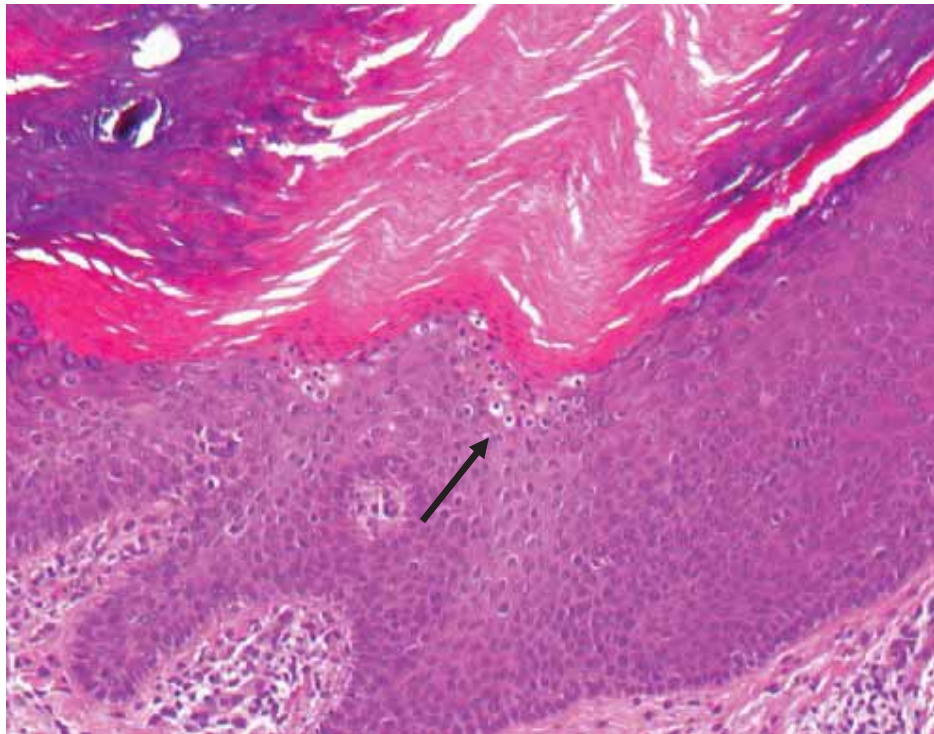
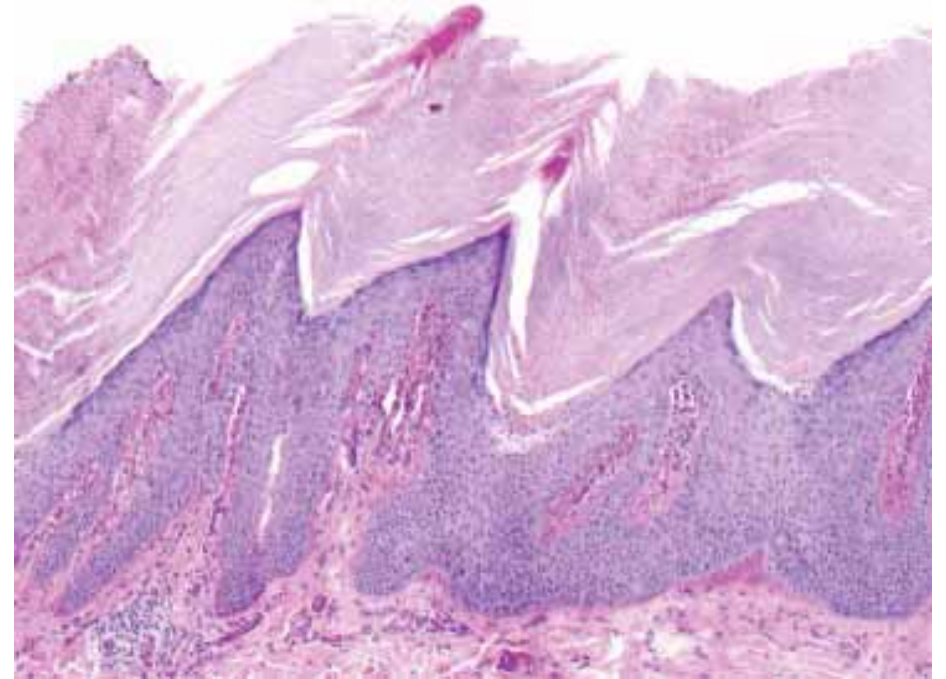
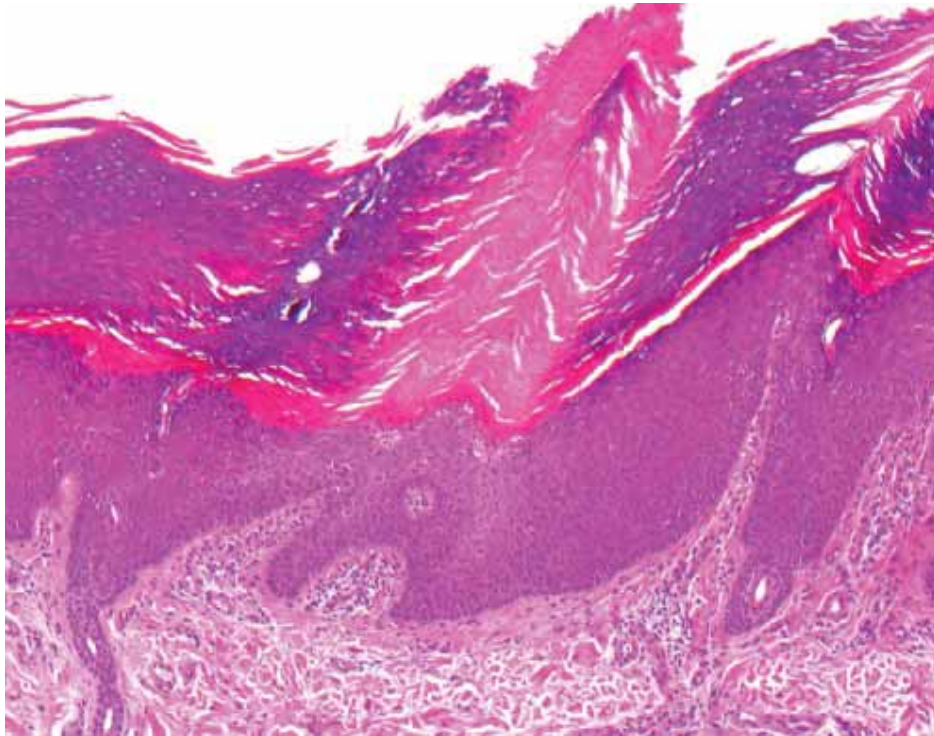


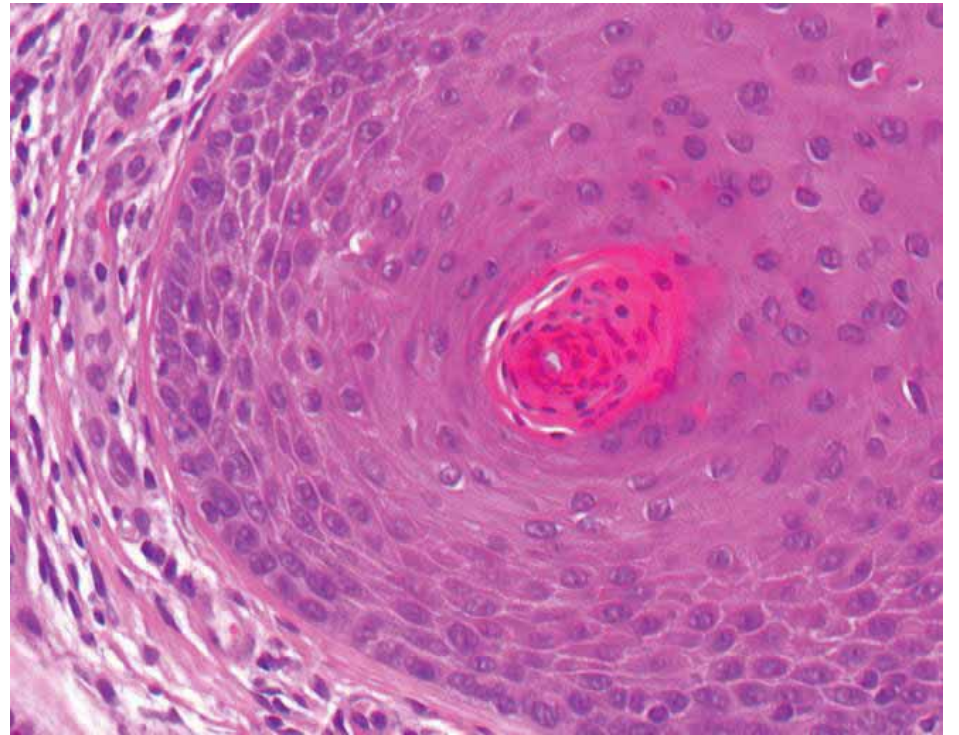
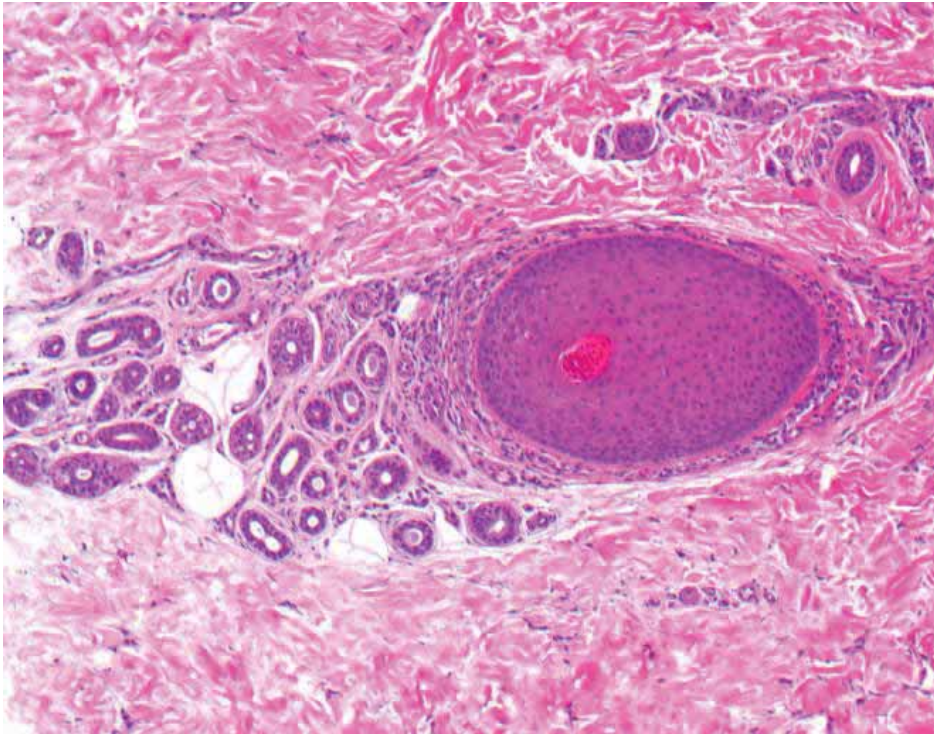
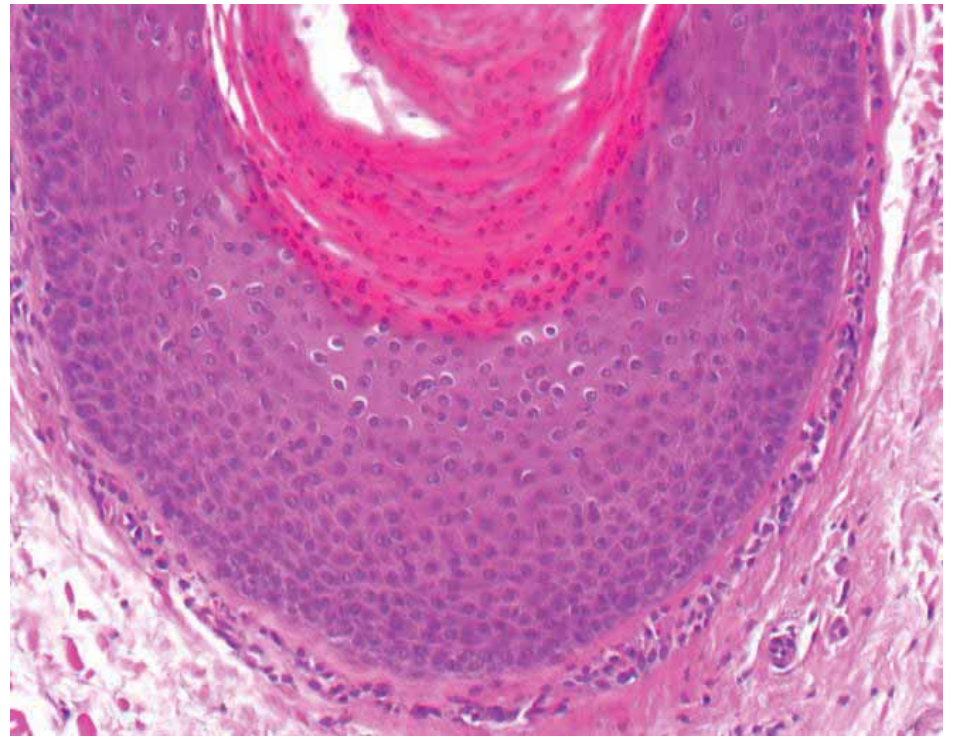
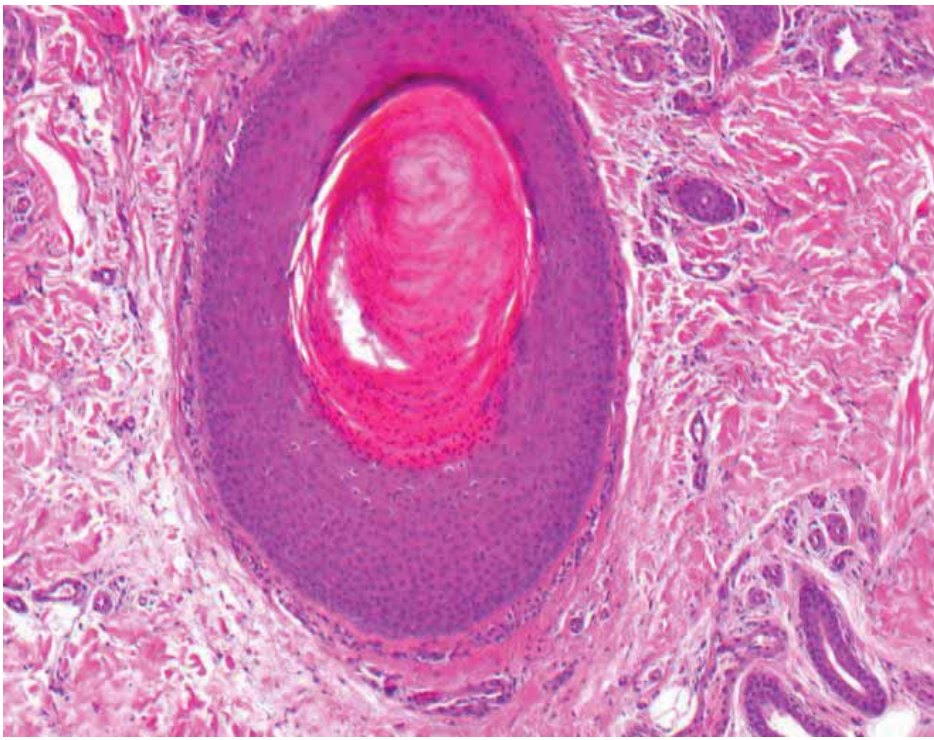
Porokeratotic Adnexal Ostial Naevus (PAON)



Ortho- and
parakeratotic
columns ↗

Vacuolated keratocytes
without underlying
dysmaturation

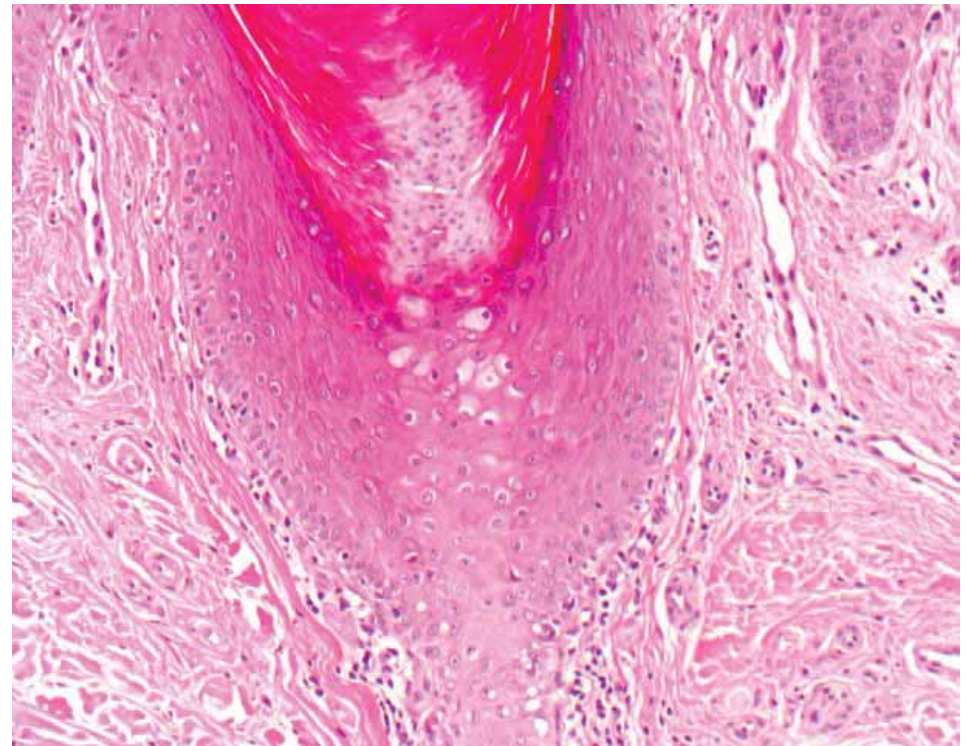
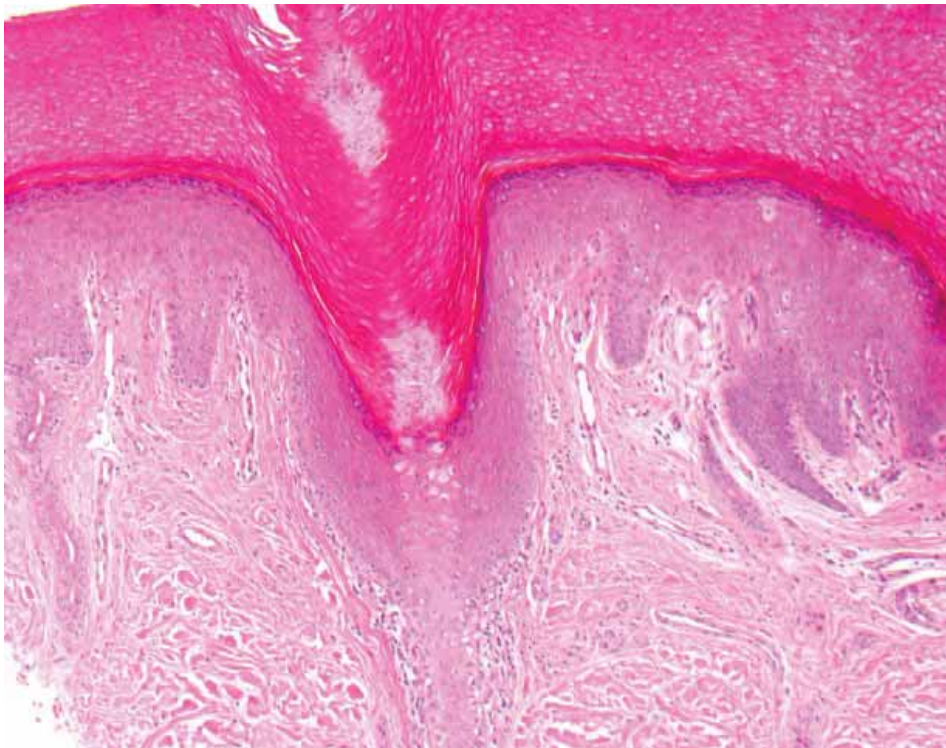




Porokeratotic adnexal ostial Naevus (PAON)

(Courtesy, H. Hamm, Würzburg)

82-y-o-woman, filiform hyperkeratoses, striated, left palms and left sole

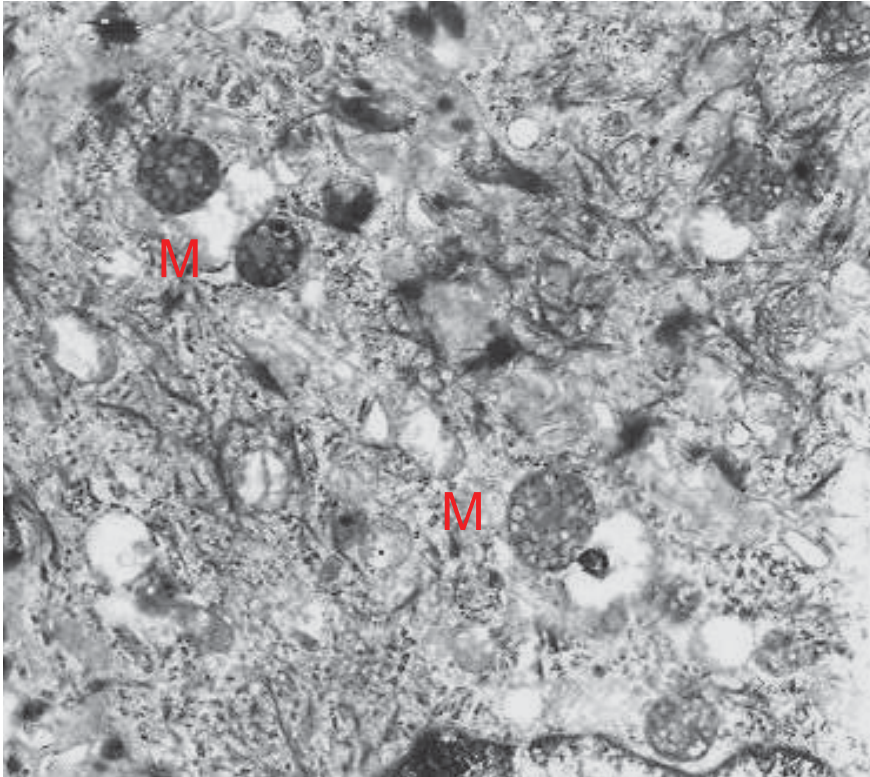
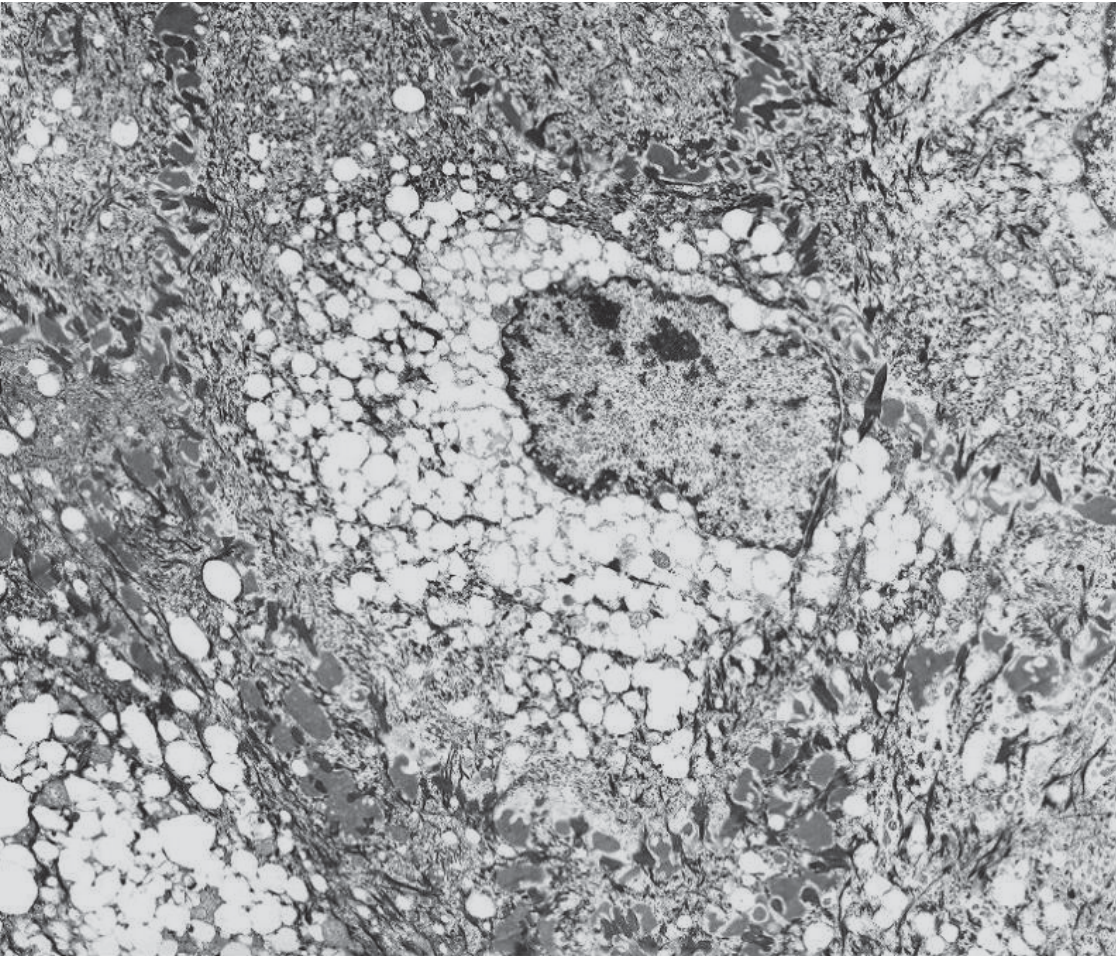
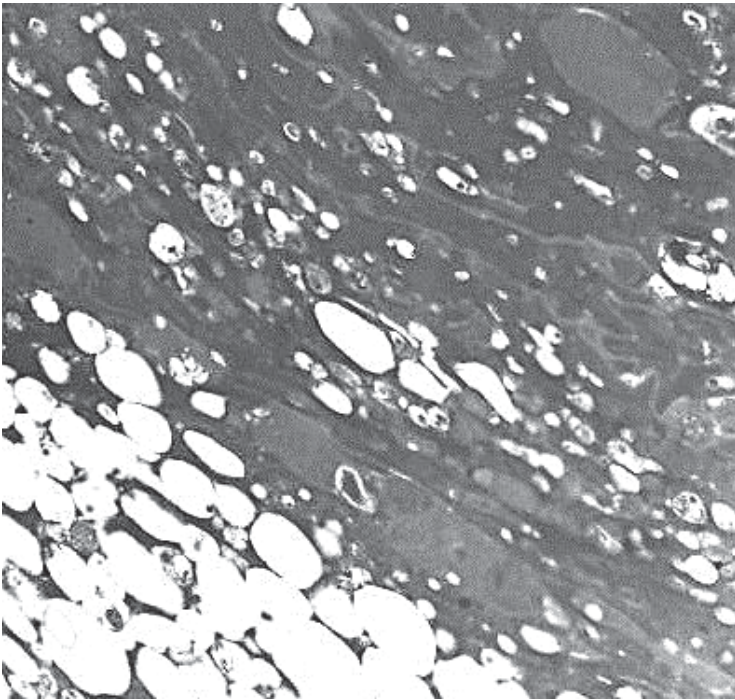




Keratocytes with vacuoles but
without dyskeratosis, dysmaturation,
and interface dermatitis !

Electron microscopy:
Acrosyringal differentiation
with signs of degeneration

Multivesicular bodies (M)



Porokeratosis

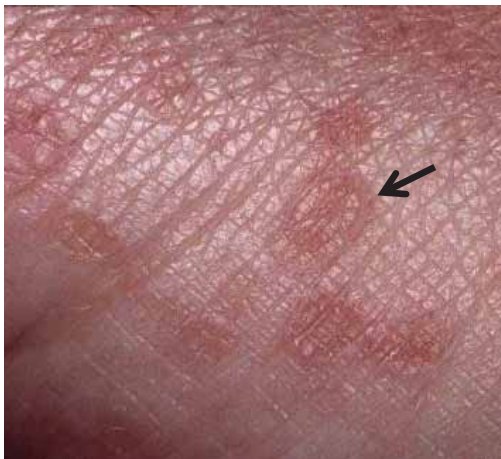
History and Definition (“Poro-” and the cornoid lamella)

Histology and Clinics of Porokeratosis

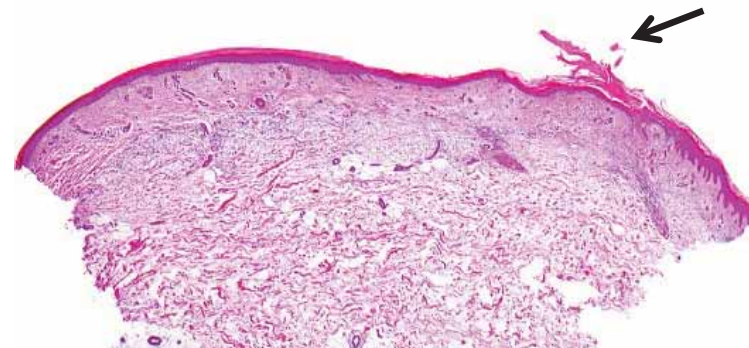
Genetic Background and Pathophysiology

Classical and rare variants

Differential diagnoses



Cornoid lamella

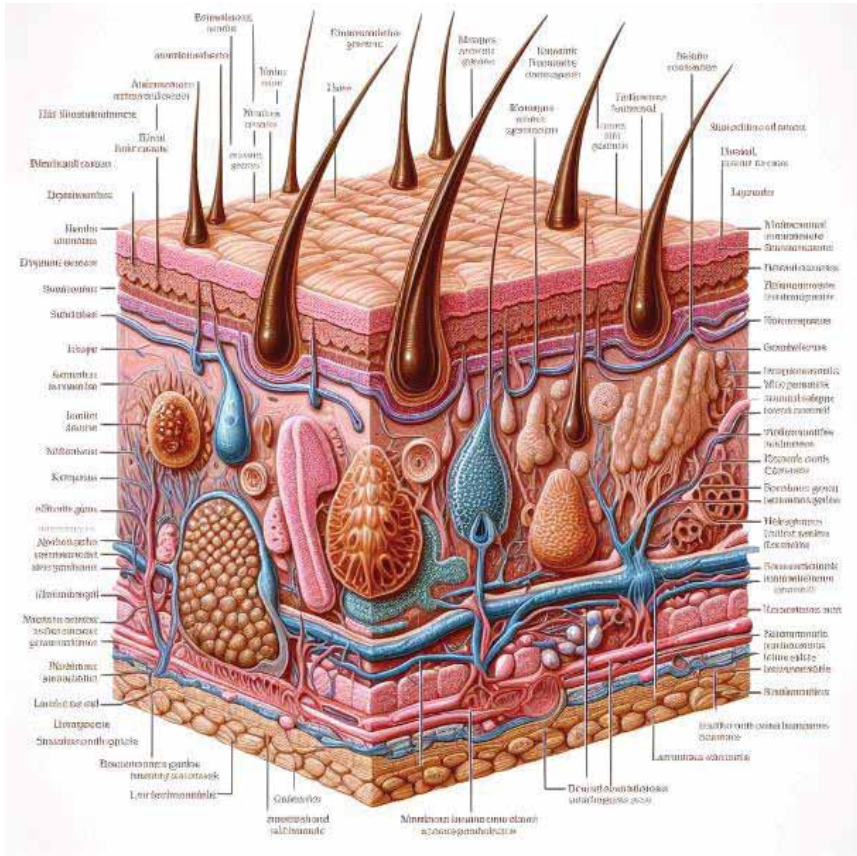




Recognize the morphology

Understand the pathophysiology

The Future



„Anatomy of the skin“
AI, Image Generator, 2023



„Santa Clause uses the microscope“
AI, Image Generator, 2023

International Society of Dermatopathology



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Make friends from around the world



Nice places to visit

XLIII Symposium of the ISDP, Queenstown, New Zealand

September 5-7, 2024

International Board Certification in Dermatopathology, Frankfurt

October 5, 2024



28th Joint Meeting of the ISDP

Orlando, USA

March 5-6, 2025