Puzzling Cases in Dermatology

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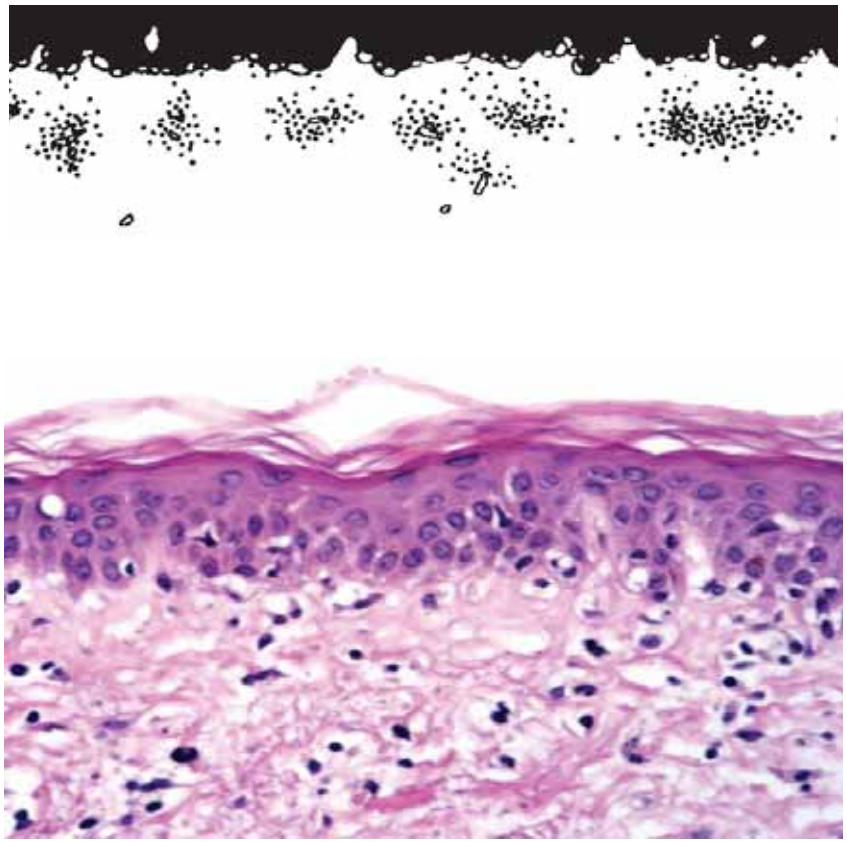
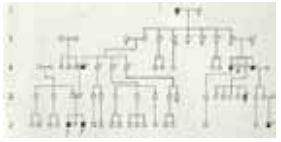
Histological puzzle

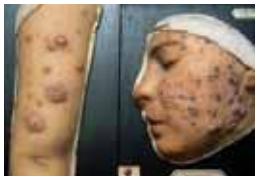
Analysis – "blinded fashion"

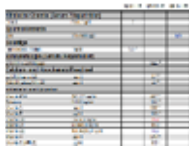


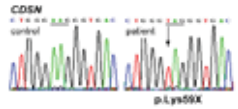
Recognize the patterns and criteria,
conclude on the diagnosis

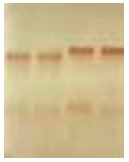
Clinical puzzle

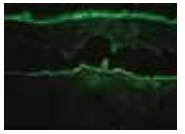


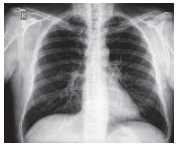








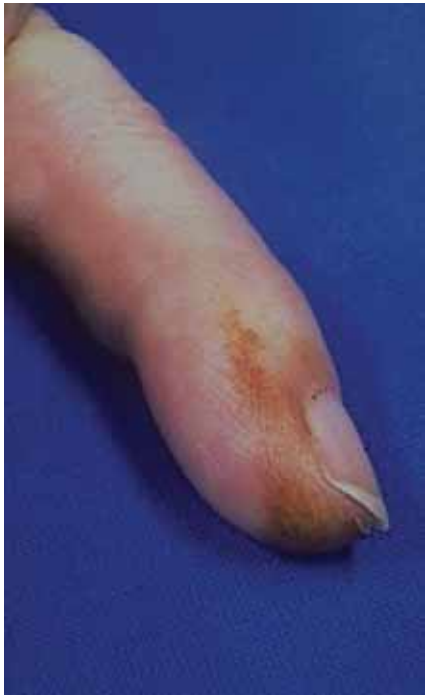


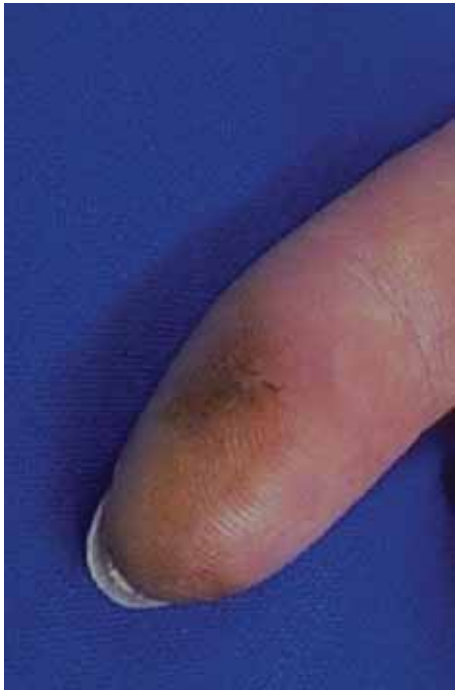


Final Diagnosis is made by the clinician

H. Kutzner, A. Rütten, Nineties

Macular Hyperpigmentation on the finger tips, digitus V, female
rule out Melanoma





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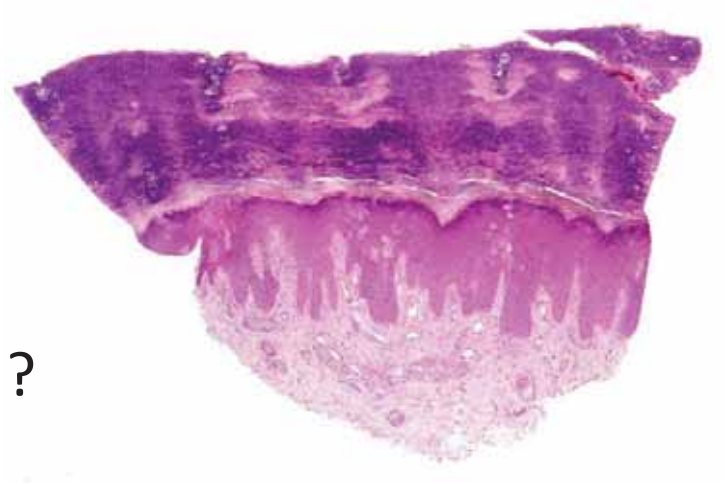
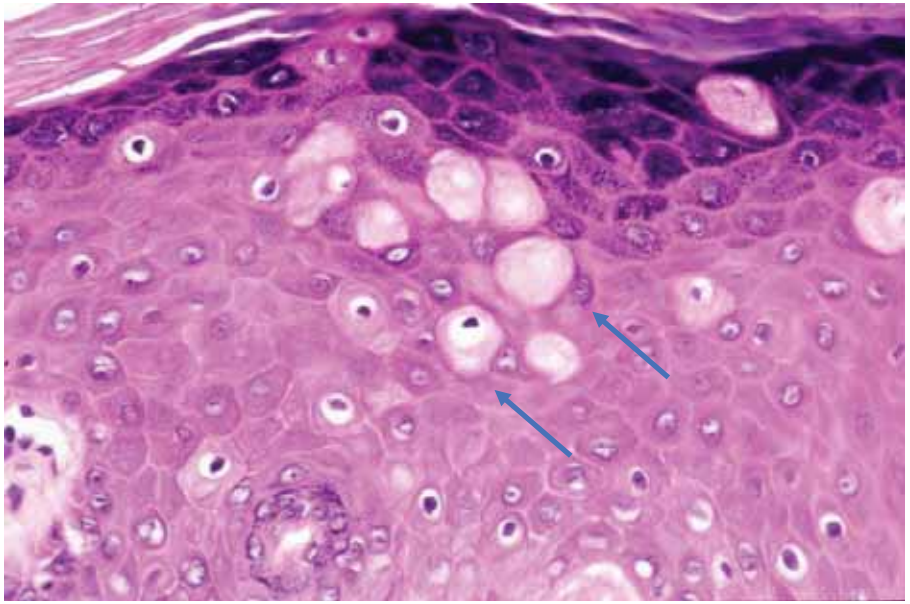
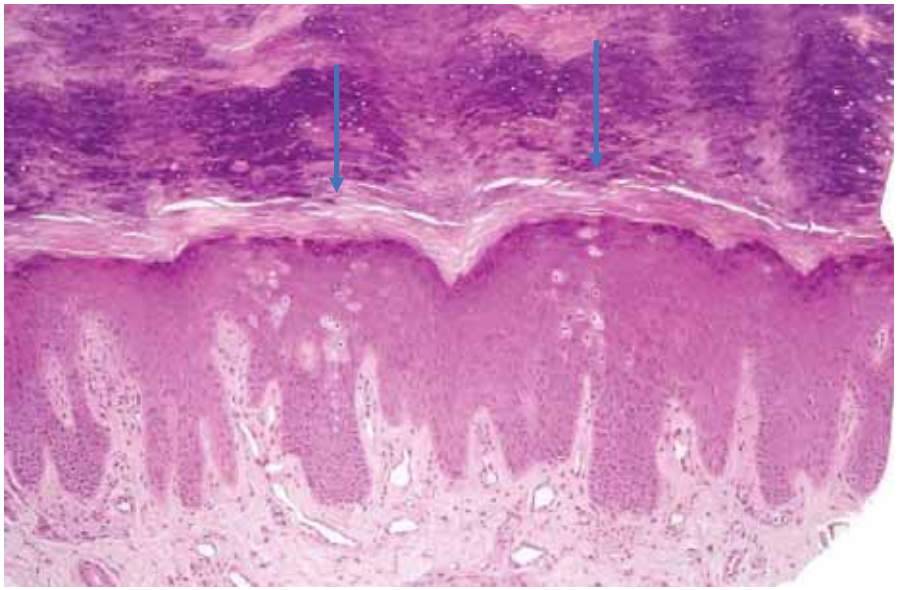
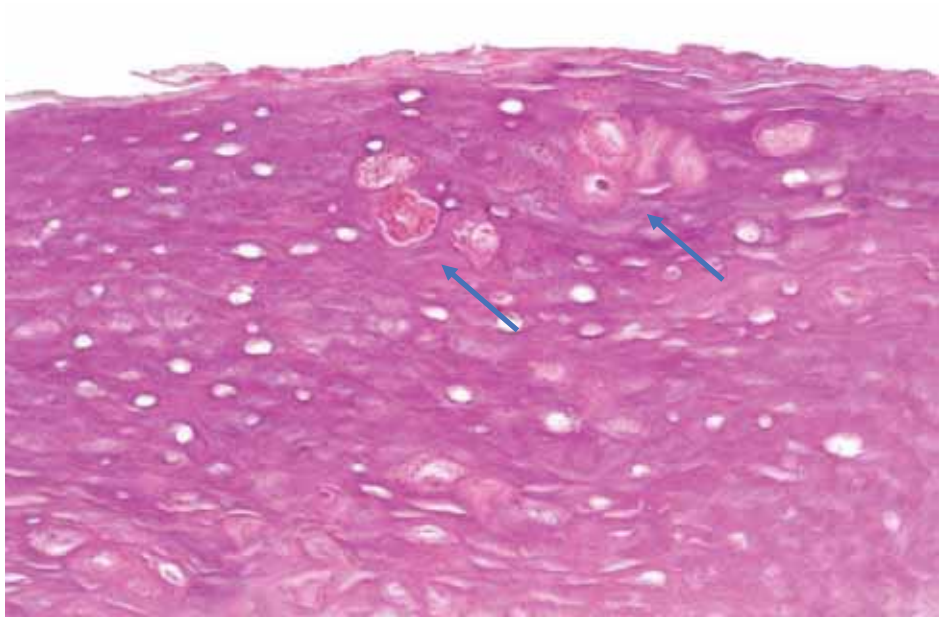






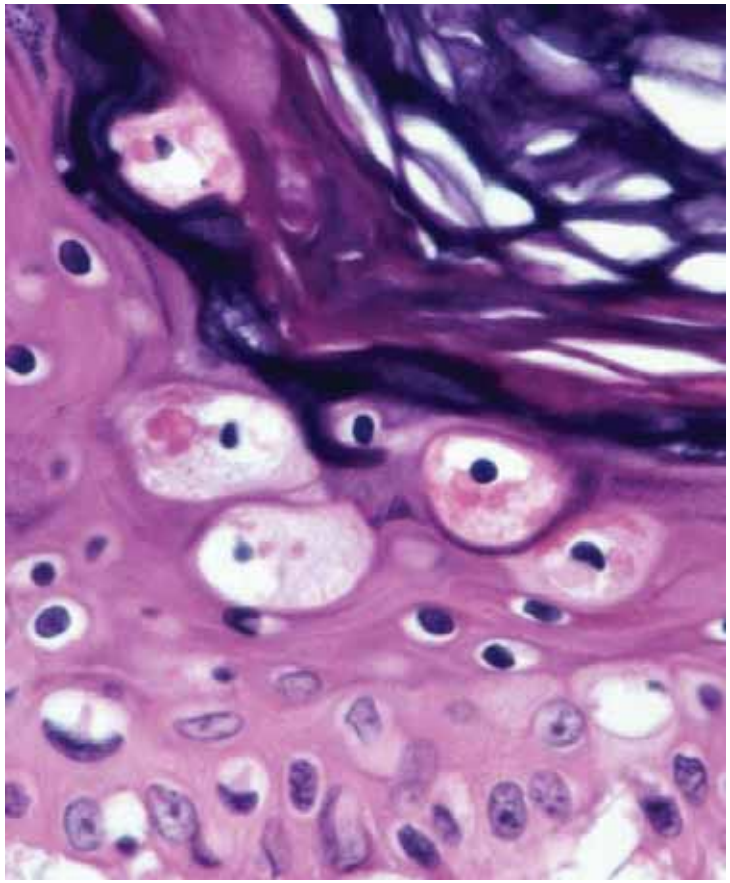



Pagetoid Dyskeratosis

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

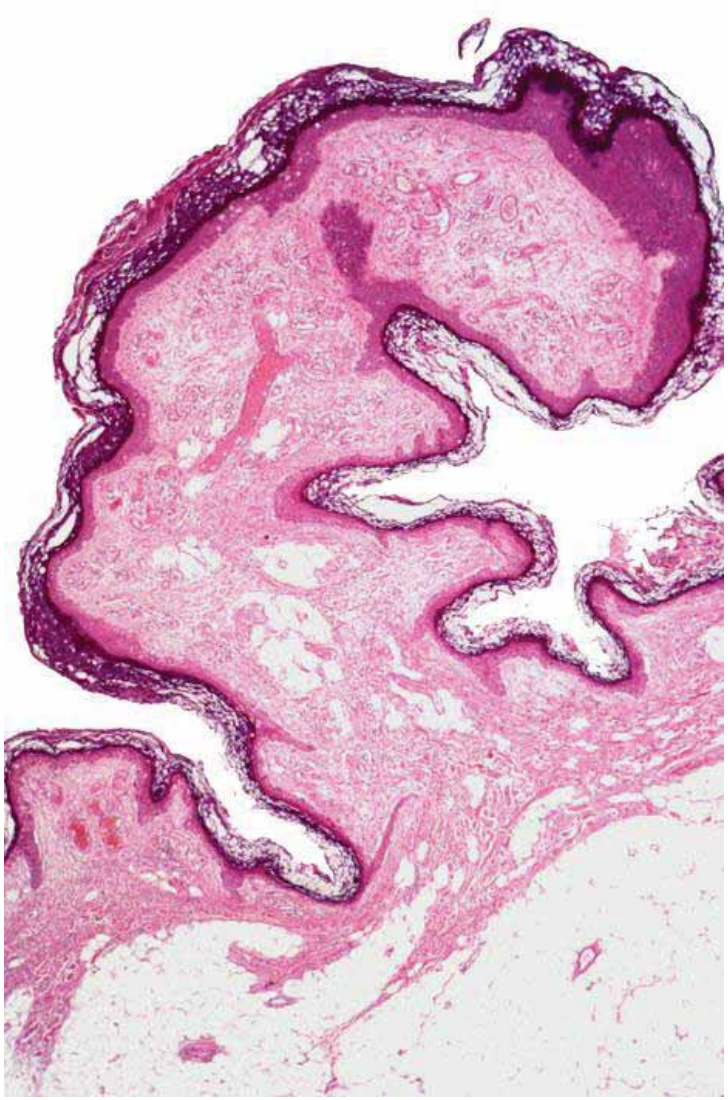
- Large body folds
- Exophytic skin tumors
- Mucous membranes
- Wound dressing
- Volar skin

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

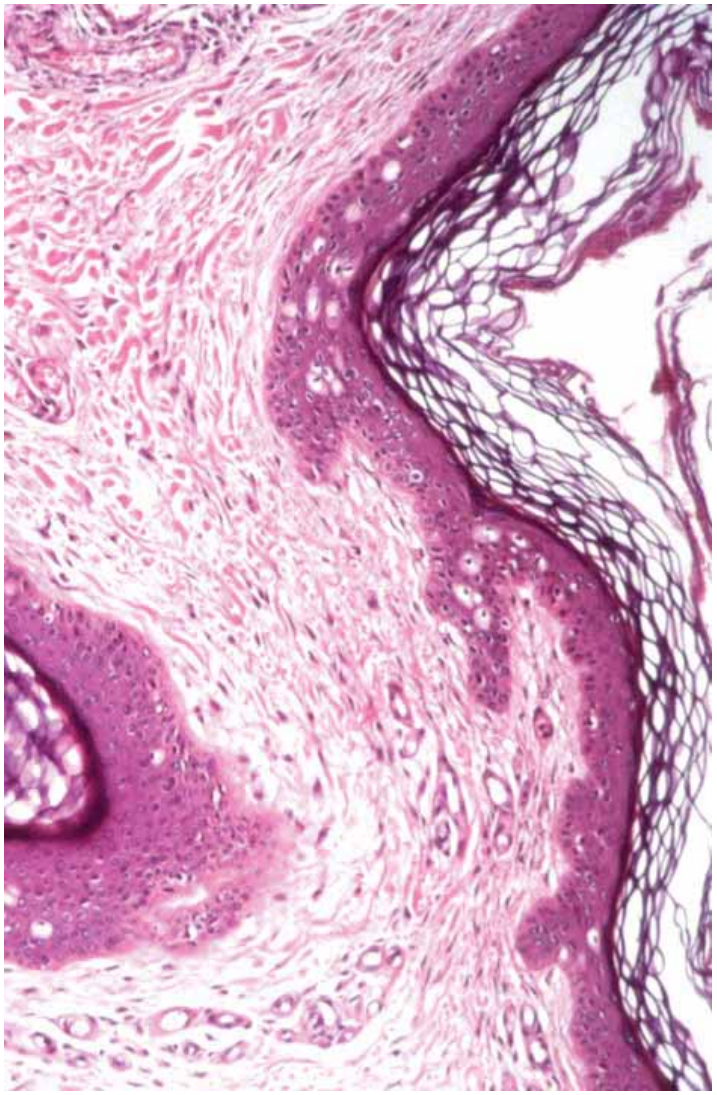


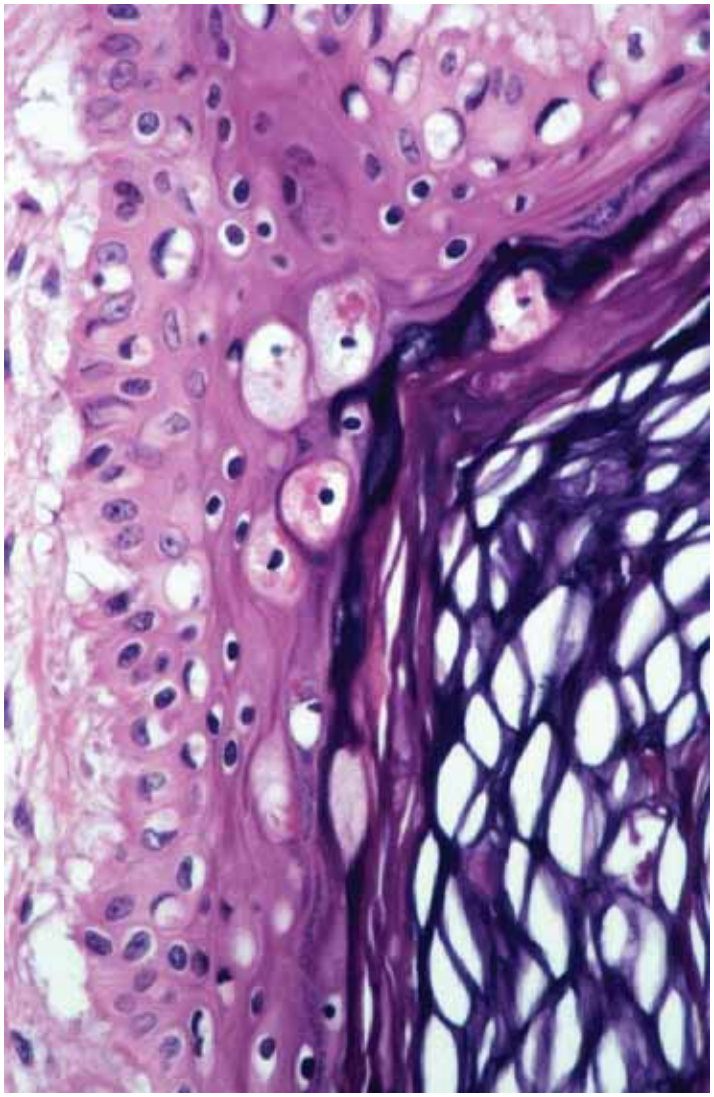
Pyknotic nucleus, clear halo, rim of stippled cytoplasm, eosinophilic granules

Mehregan, 1980, Tschen, 1988

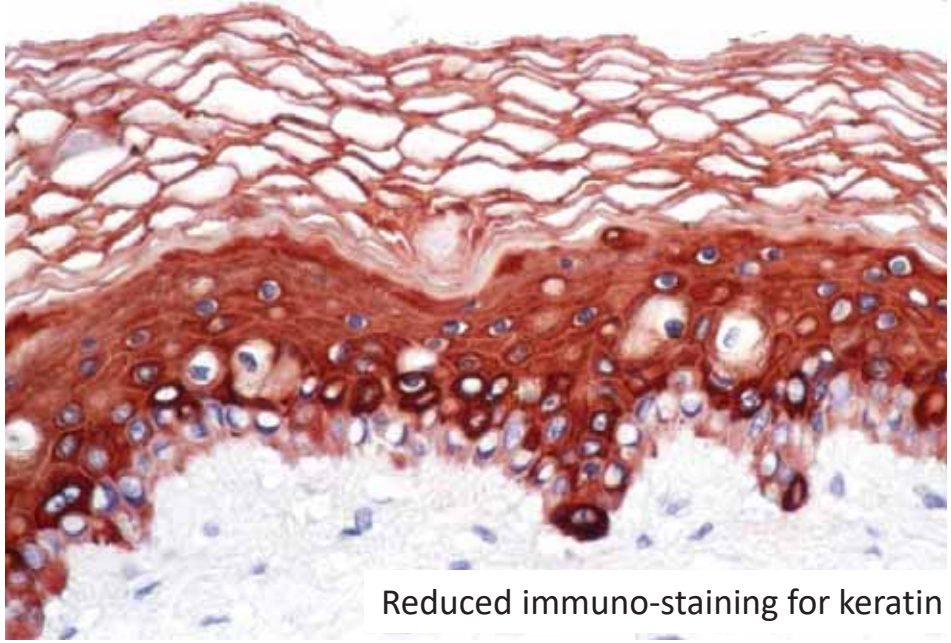


Fibroma

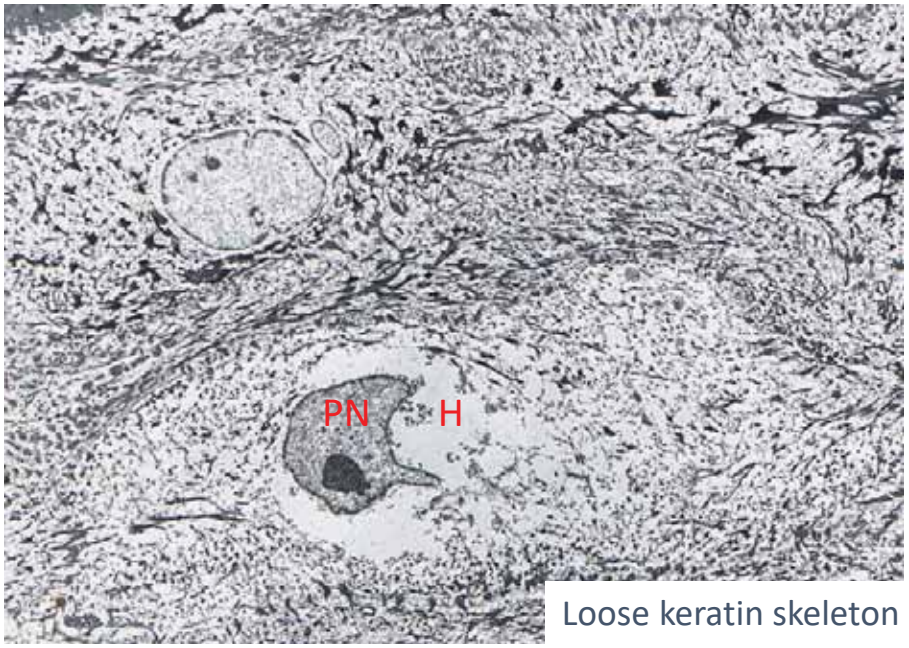




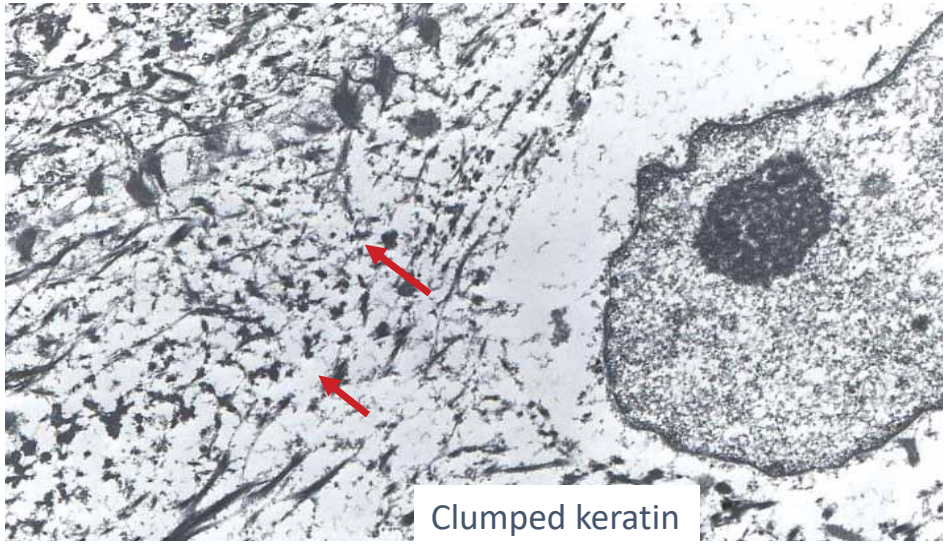
Large, pale cells



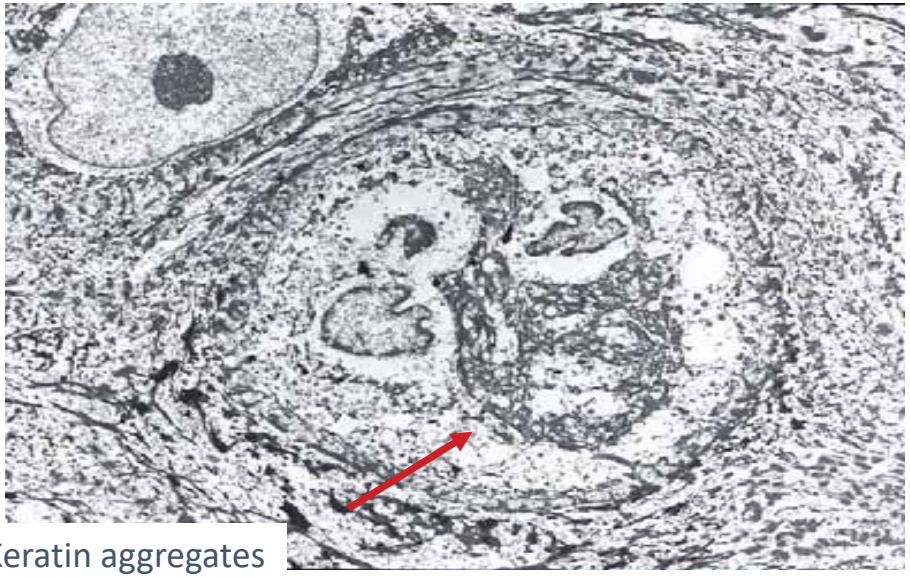
Reduced immuno-staining for keratin



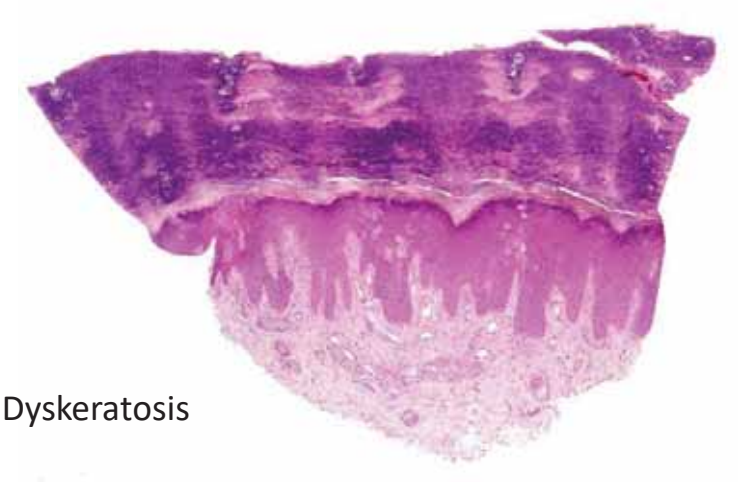
Loose keratin skeleton



Clumped keratin

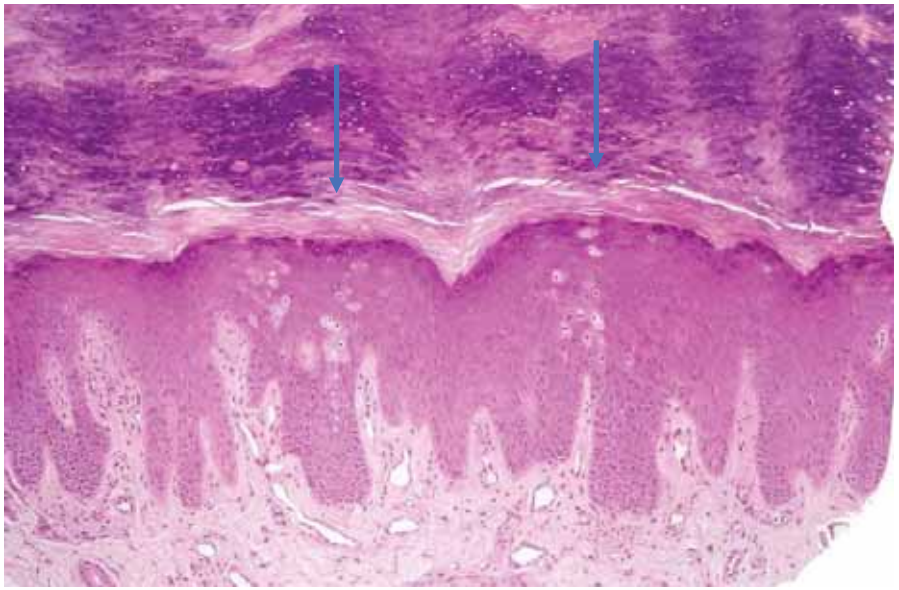


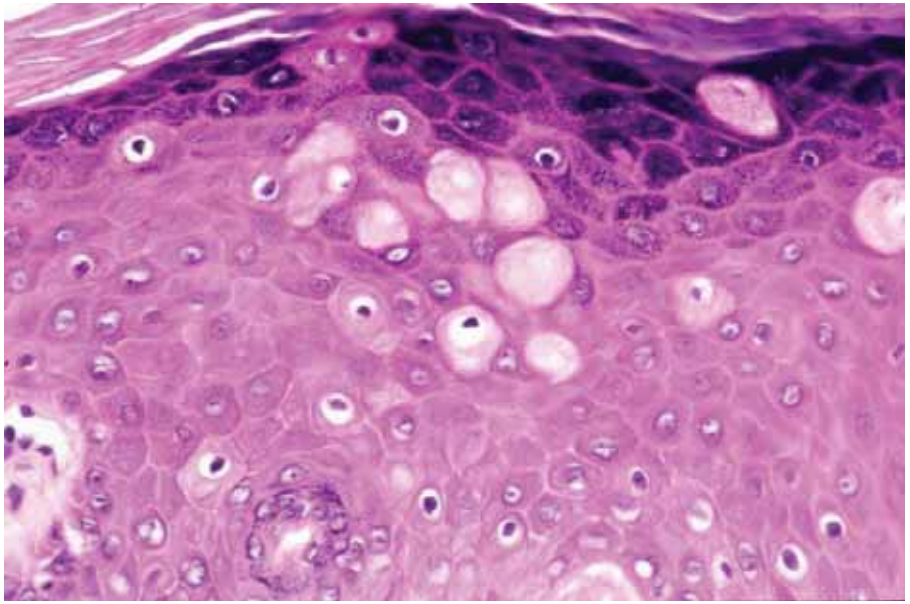
Keratin aggregates



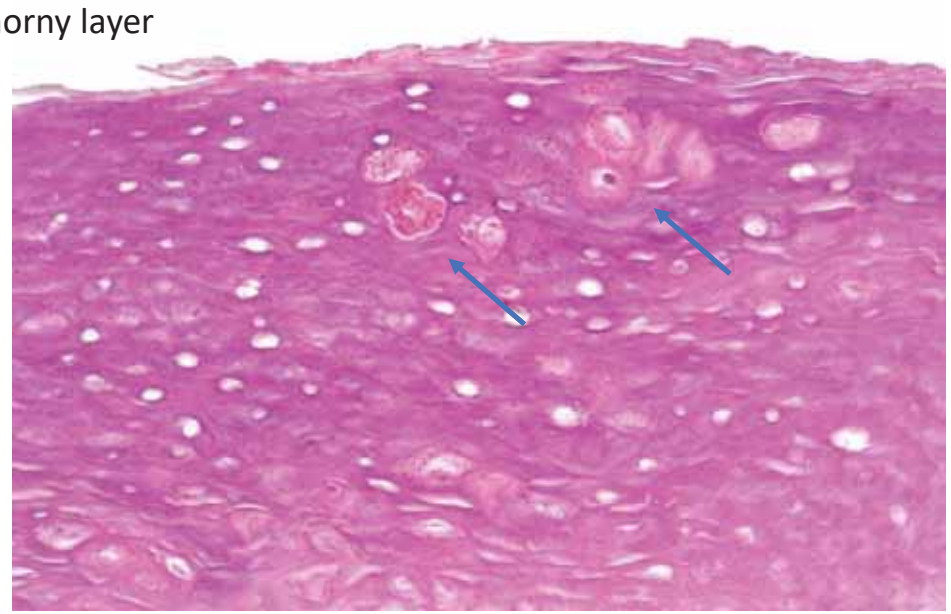
Pagetoid Dyskeratosis

Columnar distribution along ridges

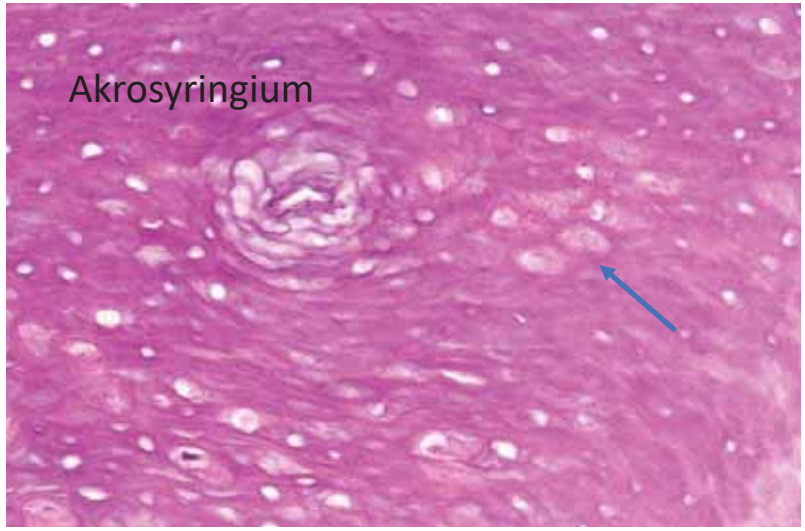


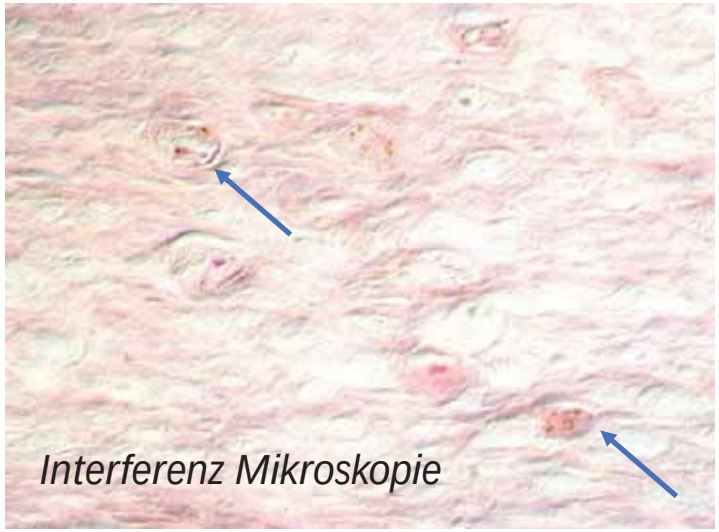


and horny layer



Immunhistochemistry: CK7, EMA, melanocytic markers negativ





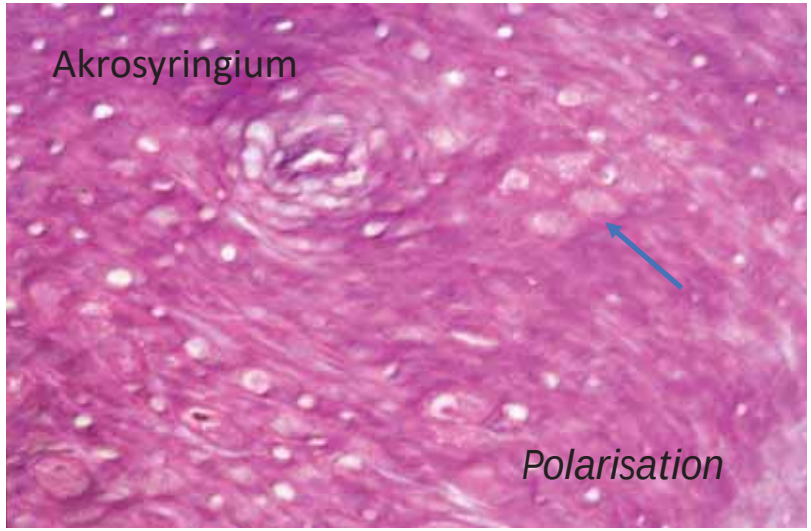
Pagetoid Dyskeratosis with

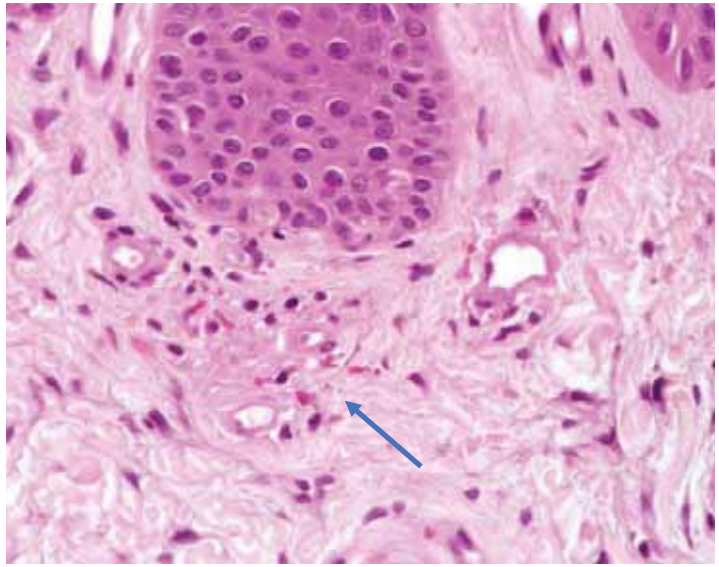
yellowish-brownish granules

Melanin stain negativ

Refraktile

Perls Prussian blue stain negativ
-> no Hemosiderin

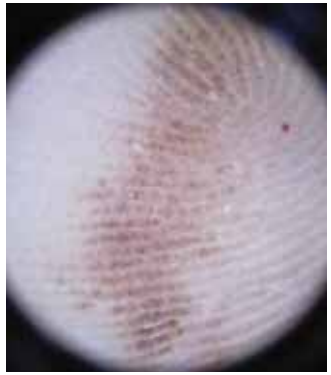




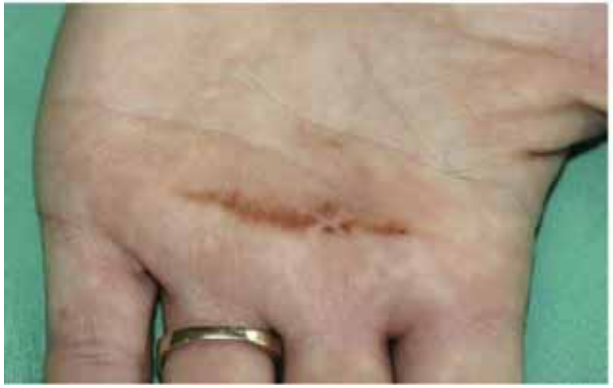
Benzidine blue stain positiv
-> Hämatoidin

Extravasated erythrozytes

Pagetoide Dyskeratosis of the Hands



- Predominantly women, middle-aged
- Circumscribed orange-brown hyperpigmentation on the palms or fingertips
- Dermatoscopy: ridged pattern, DDx Melanoma



- Mechanical irritation (Working with brooms, ….)
- Resolution after pausing

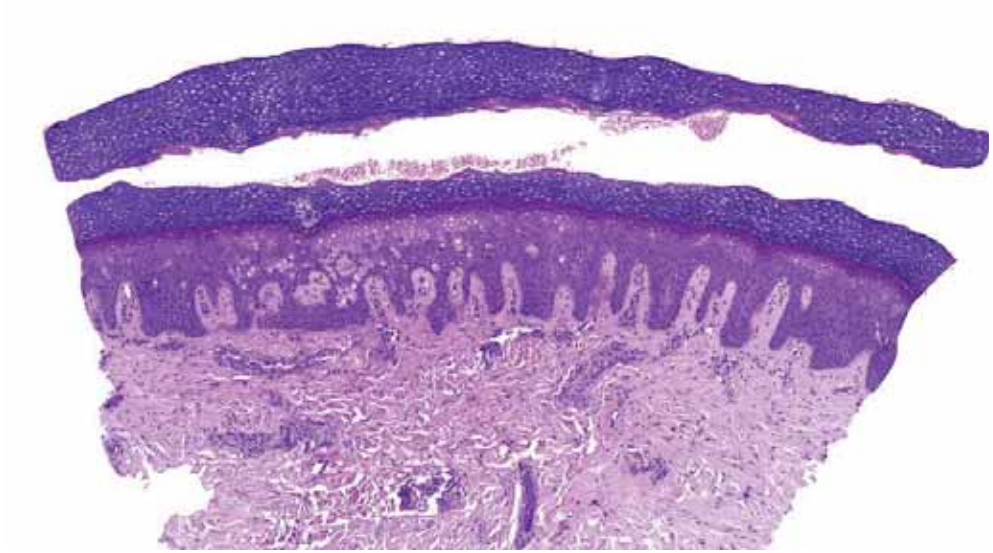
Loidi et al, Actas Dermosifiliogr., 2014

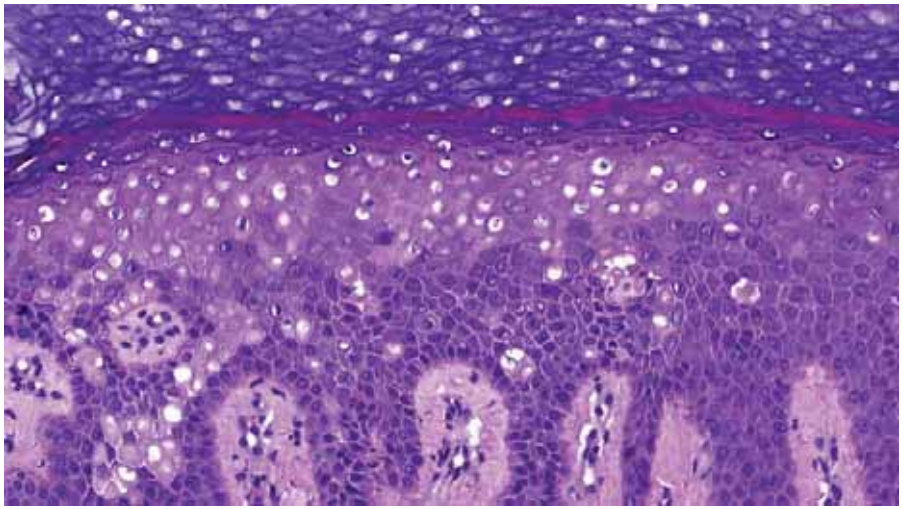
- Histological DDx Toxic Dermatitis, Acrodermatitis enteropathica

Aethiopathogenesis of pigment not metioned

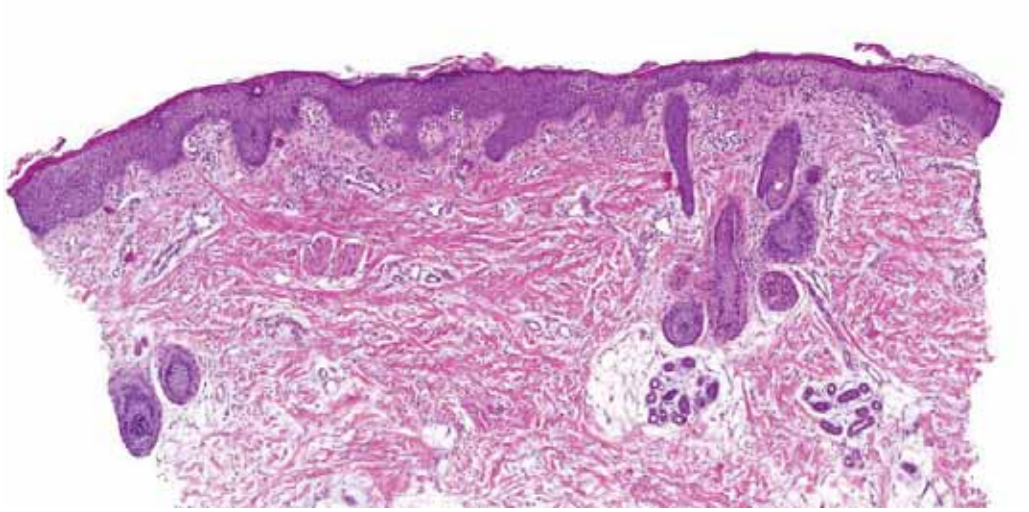
Wang et al, JAAD, 2004
Tojonaga et al, JAMAm 2013

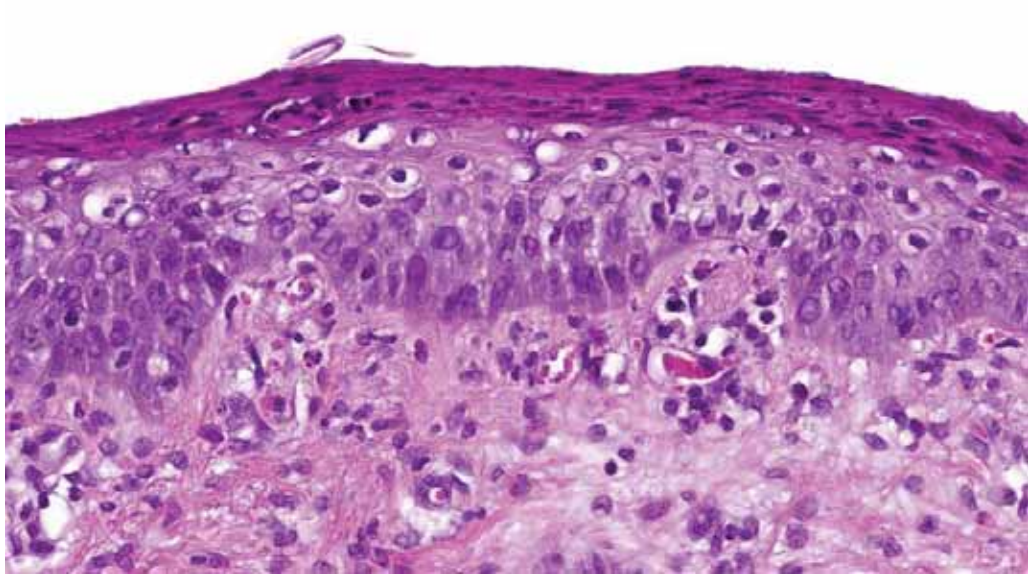
Toxische Dermatitis

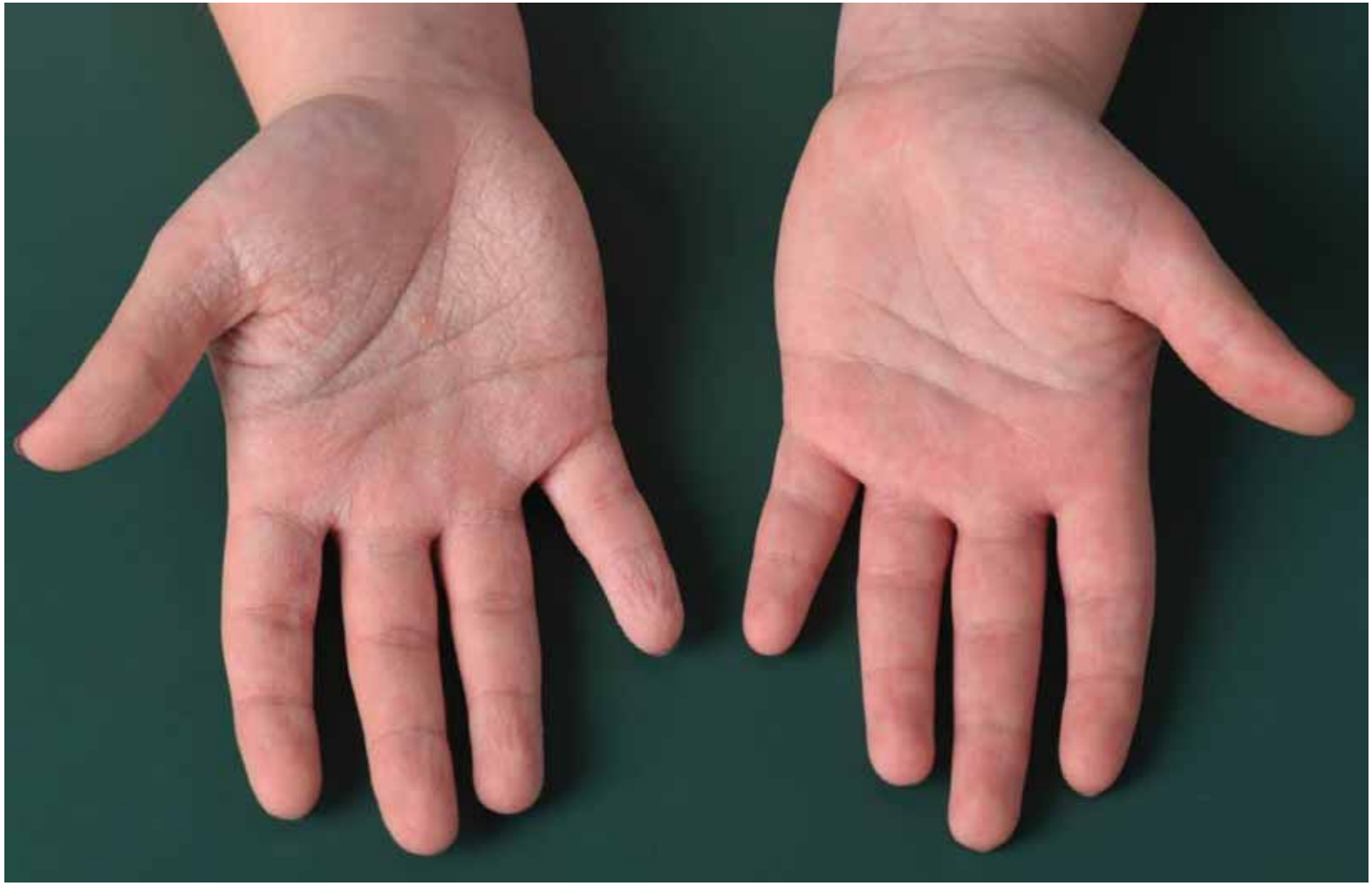




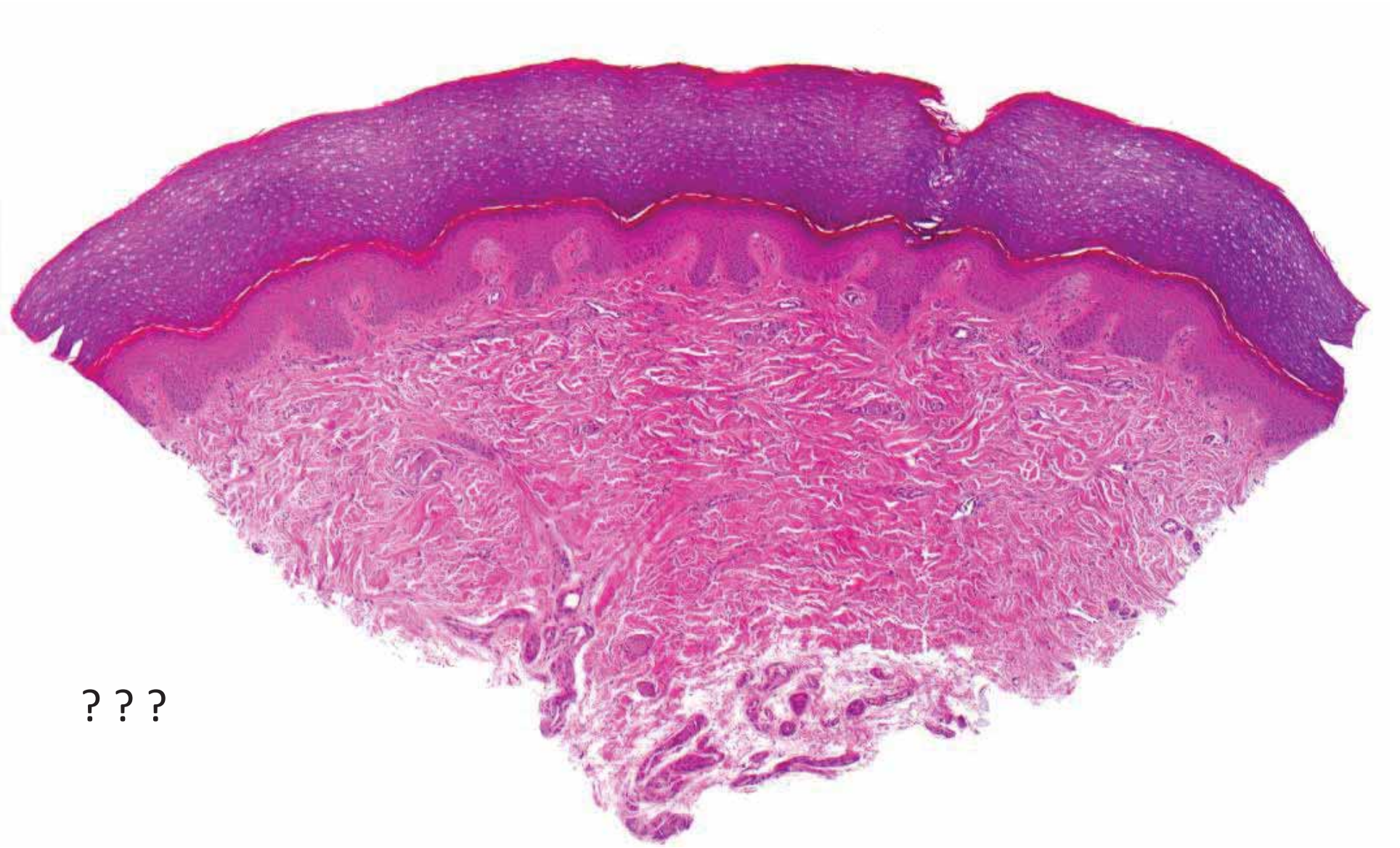
Akrodermatitis enteropathika







Young woman, shortly after immersion in water or sweating, whitish thickening with a "pebbly" surface



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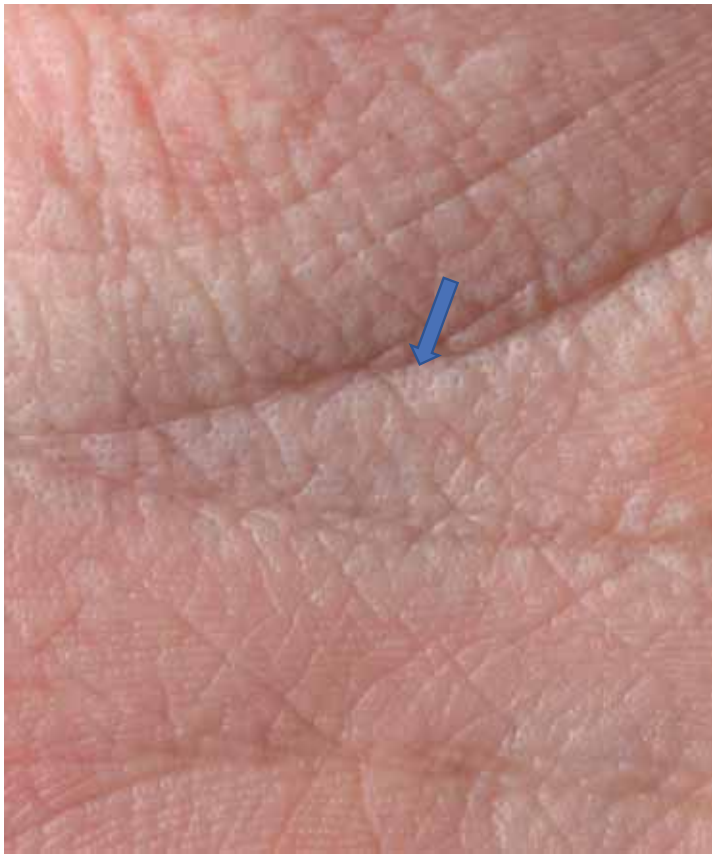
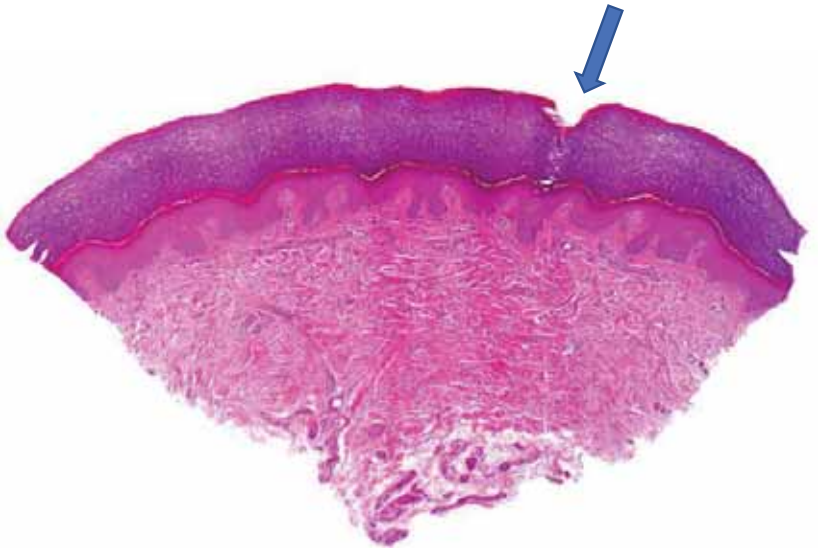
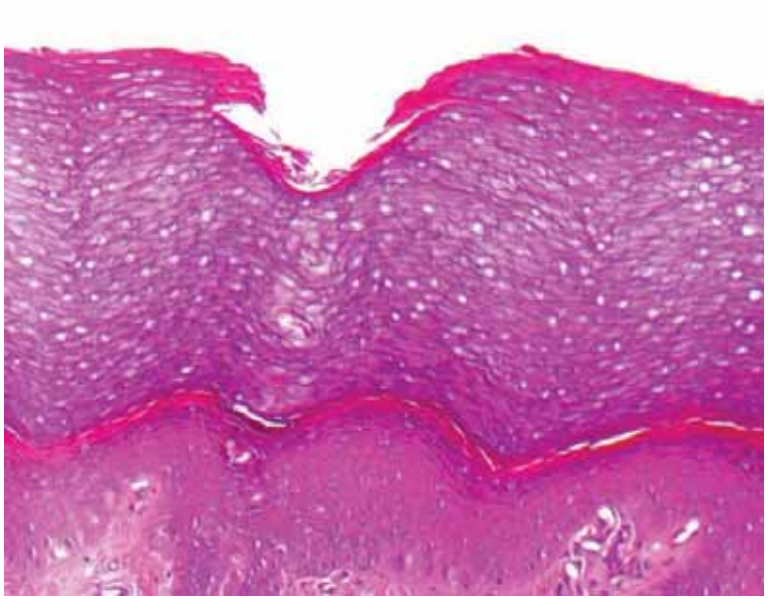
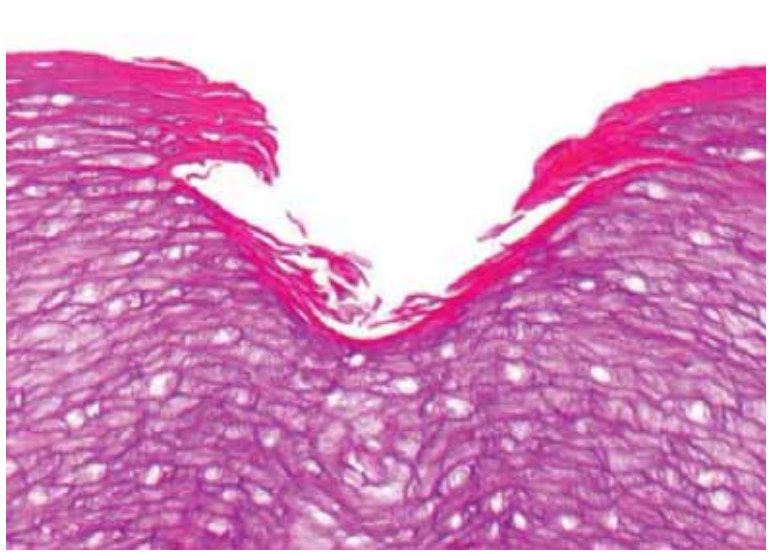


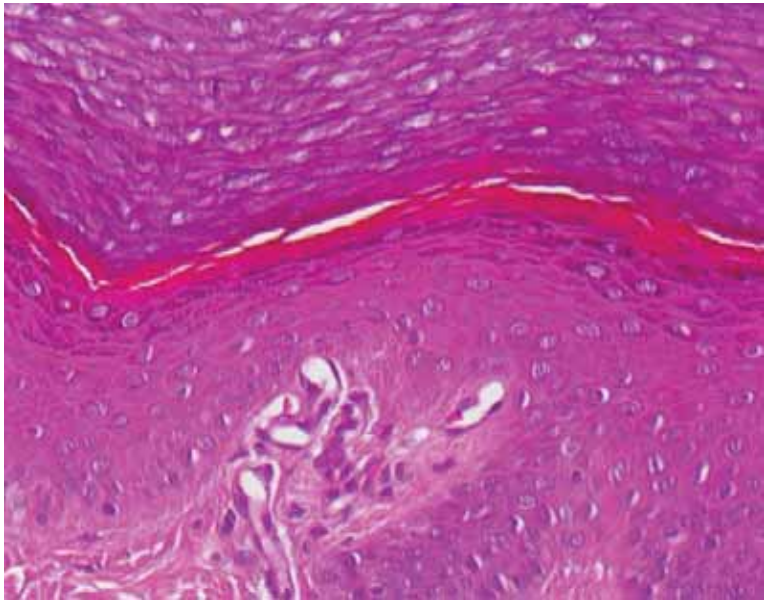
Dilated pores of acrosyringium after contact with water

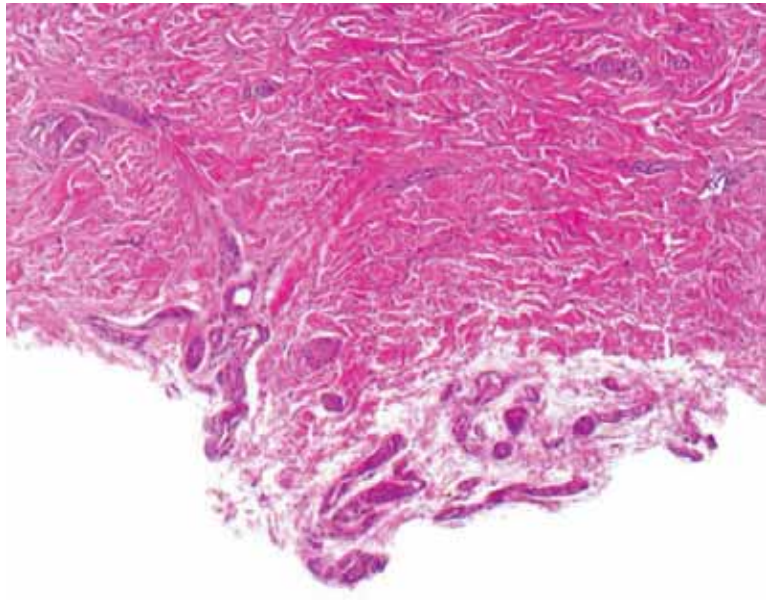


Mild orthohyperkeratosis (?),
hyperplasia of eccrine sweat glands (?)







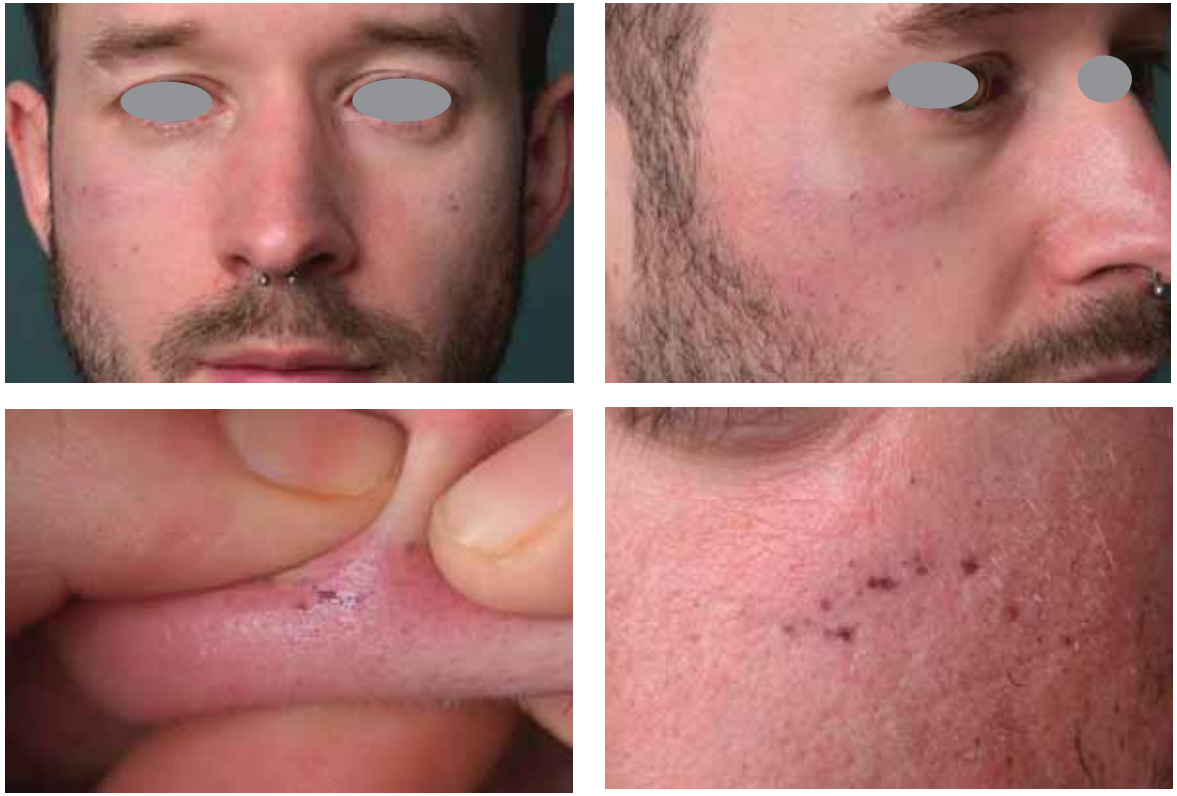


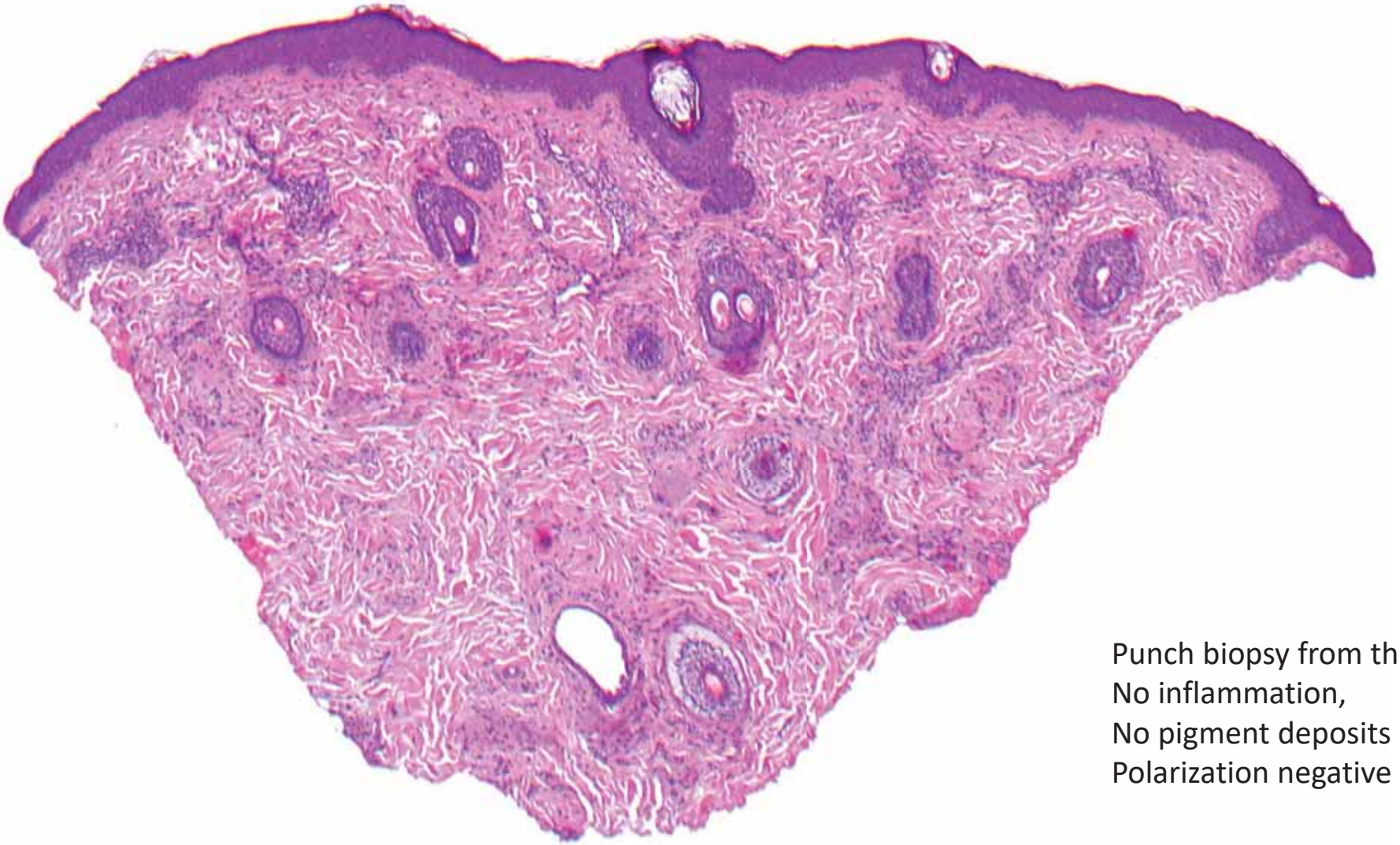
Transient aquagenic Keratodermie

- Acquired (Cox-2 inhibitor), inherited (AR, AD)
- Manifestation in the second decade of life, mainly women
- Mild keratoderma in the center of the palms
- Shortly after immersion in water or sweating, whitish thickening with a "pebbly" surface, enlarged acrosyringeal ostia (dermoscopy)
- Painful, burning or itching sensations
- Reversible after drying
- Therapy: as for hyperhidrosis
- DDx Aquagenic wrinkling of the palms in cystic fibrosis (including carriers), NEPPK type Bothnia (aquaporin), hereditary papulotranslucent acrokeratoderma (PPK punctata), acral peeling syndrome (TG5), exfoliative ichthyosis (cystatin), ...

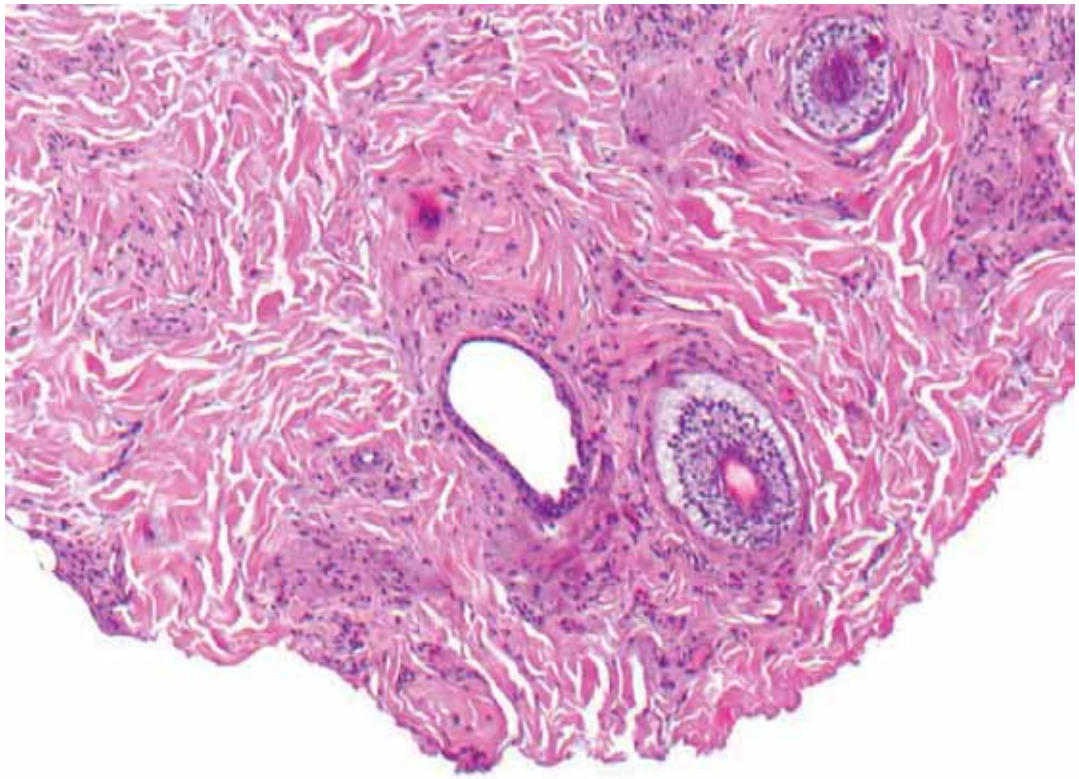
CASE

- 31-year-old man
- Since 11 years, discharge of bluish-brownish secretions from both cheeks several times a day, especially after sporting activity
- Colored secretion can be expressed on pressure. The secretion dries up on the skin surface and leaves behind punctiform, brownish-black macules.
- A nasal septum piercing in 2011
- No restrictions of the general condition
- Other integument unremarkable

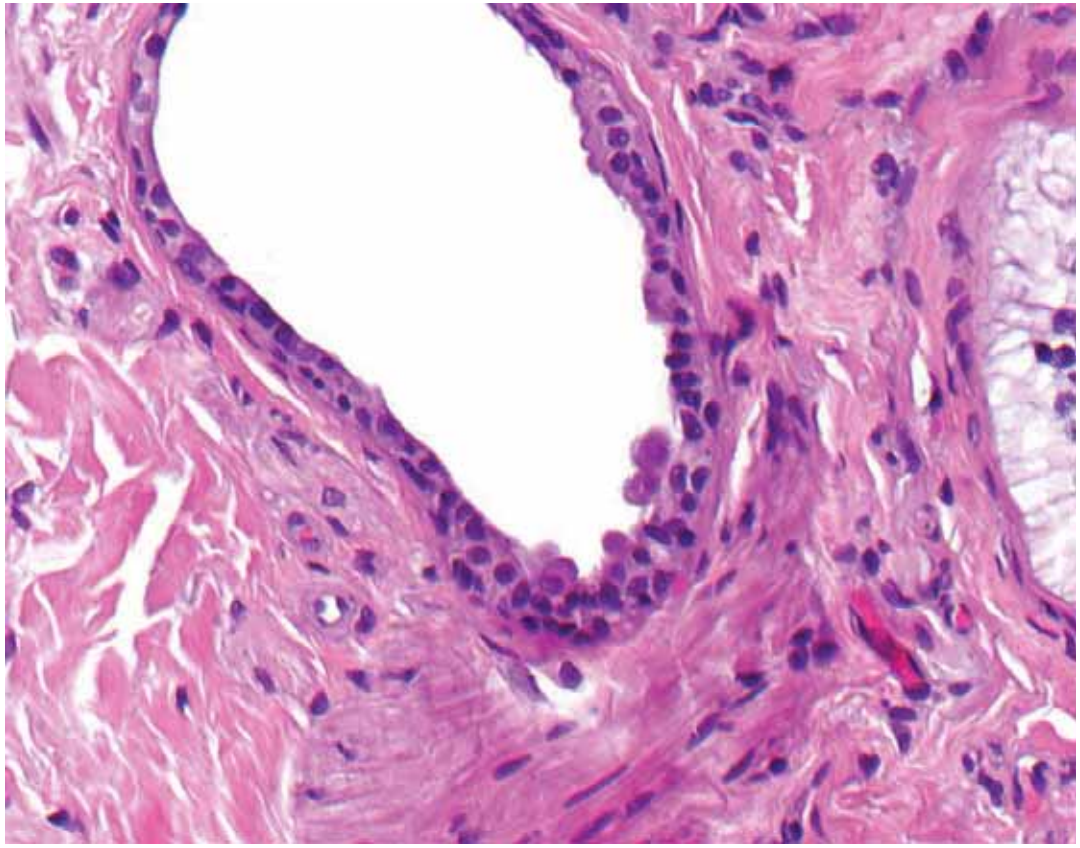




Punch biopsy from the cheek
No inflammation,
No pigment deposits
Polarization negative



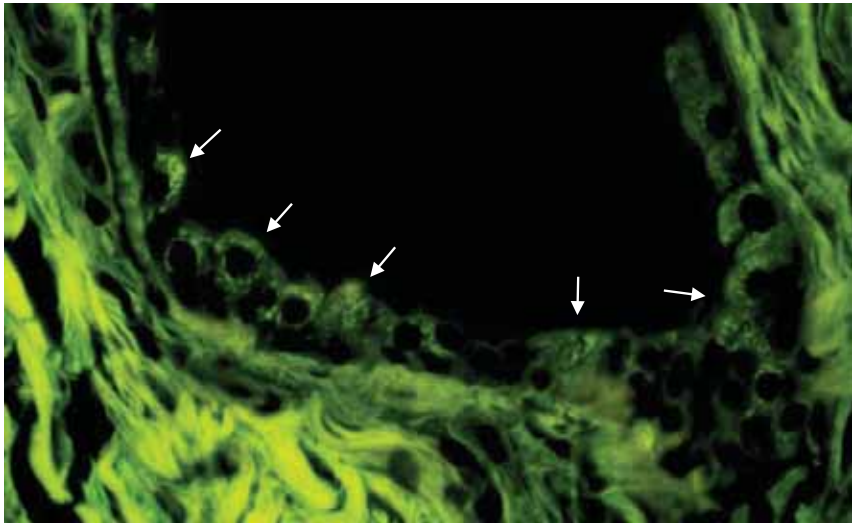
Apocrine glands

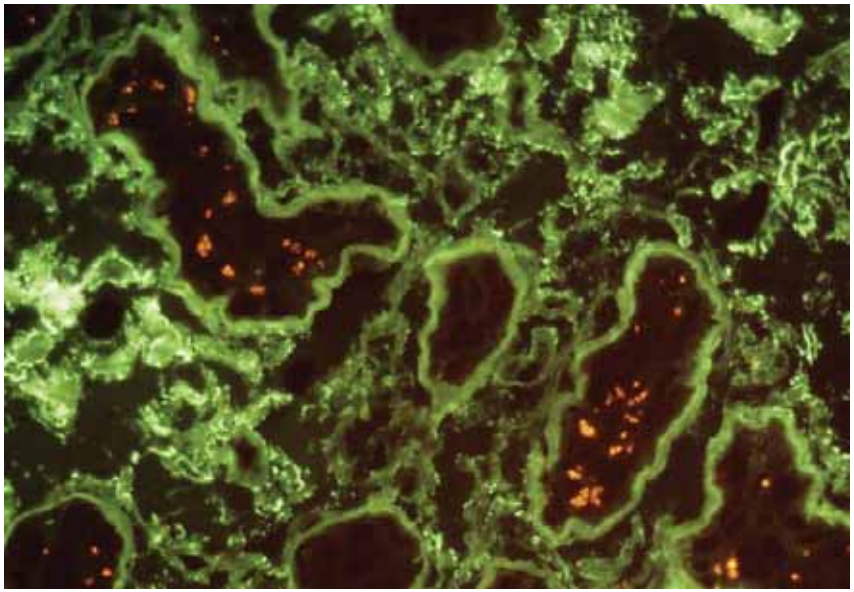


Chromhidrosis - 3 Subtypes

- *Apocrine chromohidrosis:*
  After puberty
  Genitoanal region, axilla, areolae > face
  Secretion of pigmented sweat: yellow, blue, green, blue-black
- *Eccrine chromhidrosis (systemic cause):*
  Exogenous: Medication intake, food, metals
  Endogenous: Hyperbilirubinemia in liver diseases, bilirubin oxidized -> biliverdin
- *Pseudo-eccrine chromohidrosis:*
  Colorless sweat is colored by reaction with exogenous substances such as bacteria, dyes or chemicals

Red Eccrine Chromhidrosis with Review of the Literature.
Jaiswal, AK et al. Indian J Dermatol. 2017 Nov-Dec; 62(6): 675.





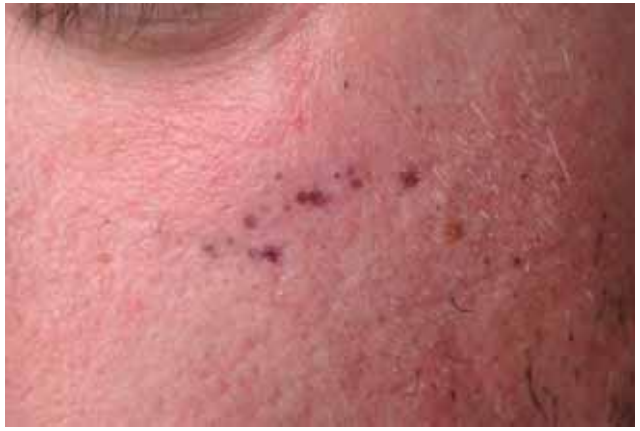
Apokrine Chromhidrosis - Pathophysiology

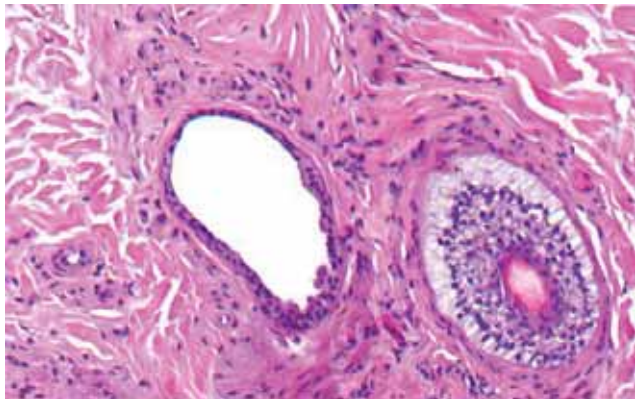
- Apocrine glands
- Lipofuscin granules in the secretory cells (PAS-positive, fluorescent at 360-395 nm): Different accumulation and oxidation levels cause the different colors of sweat - yellow, green, blue, …
- Additionally, tyrosine-, melanin-, hemoglobin-degradation possible

Apokrine Chromhidrosis. Schwarz, T et al. Hautarzt. 1989
Chromhidrosis: a rare diagnosis requiring clinicopathologic correlation. Wang, A. et al. Am J Dermatopathol. 2014.
Facial an axillary apocrine chromhidrosis. Tato, BP et al. Dermatol Online J. 2012

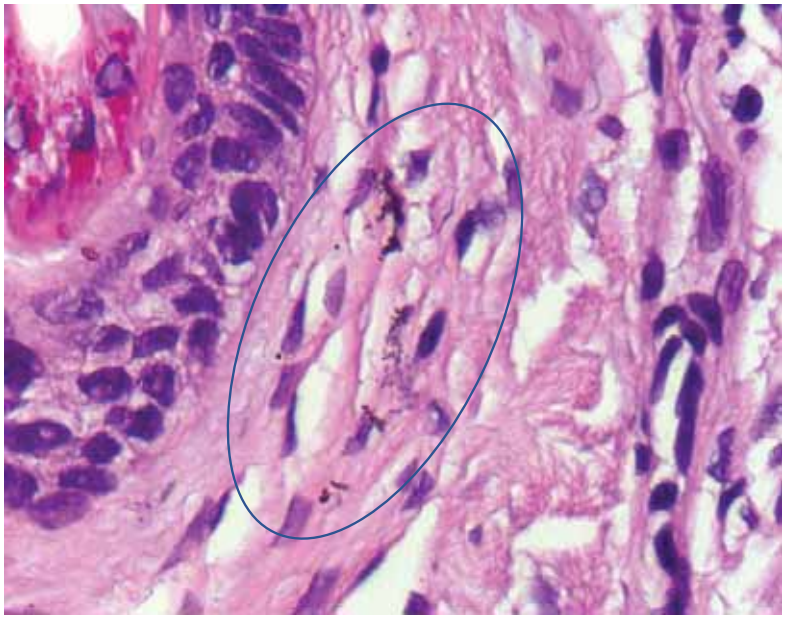
Chromhidrosis faciei

- Rare, chronic, idiopathic disease
- Onset after puberty
- Punctiform secretion of pigmented / colored sweat on the cheeks
- Ectopic apocrine glands
- Accumulation and oxidation of lipofuscin granules
- Therapy: Aluminum chloride, Capsaicin, Botulinum toxin

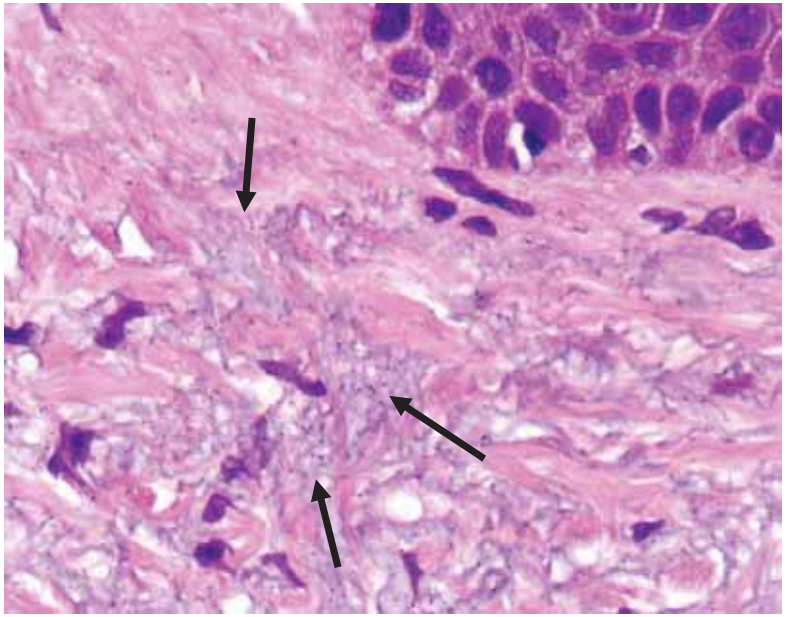




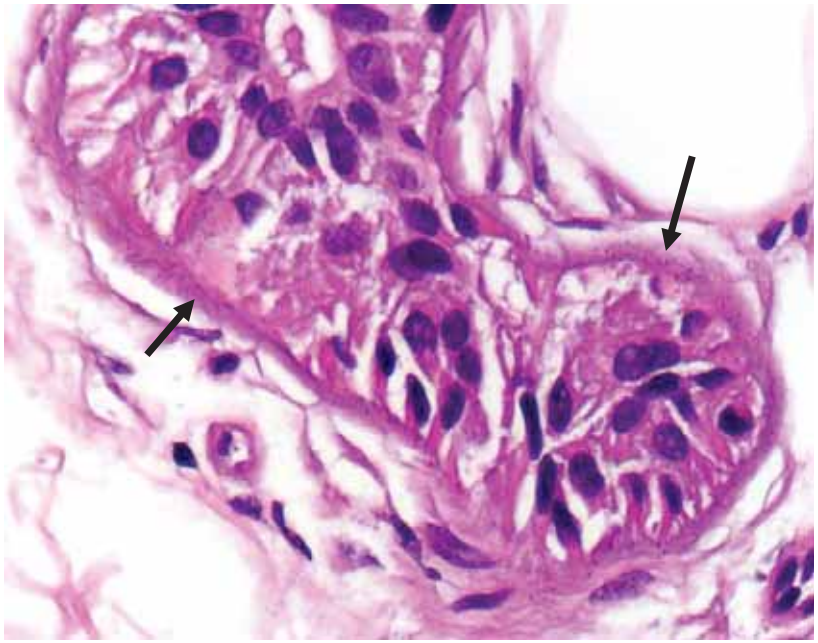
DDx Argyrosis

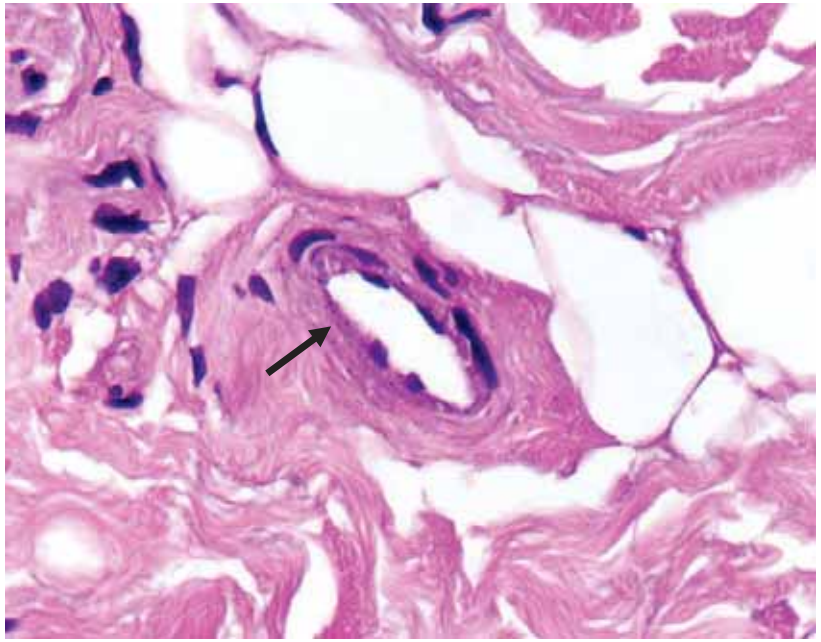


Silber particles along the adnexae

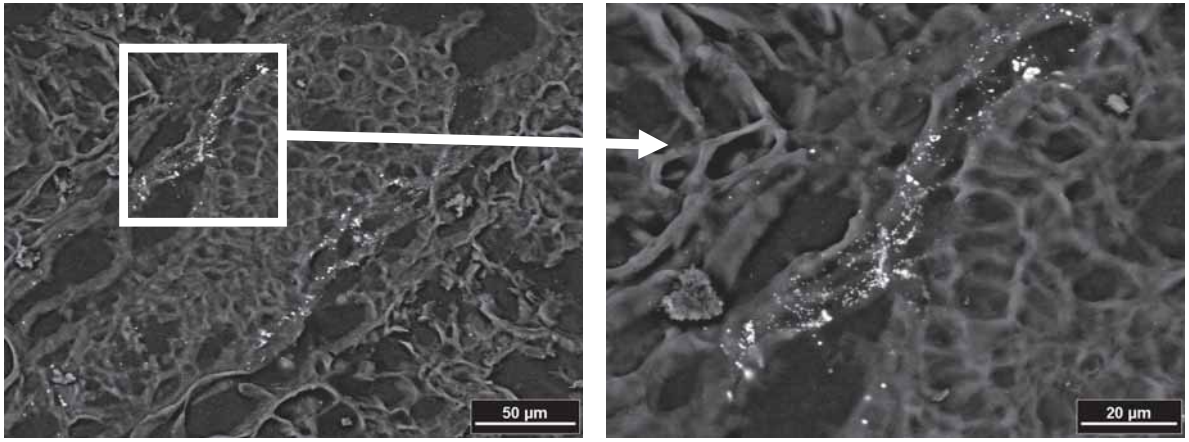


Silber particles associated with solar elastosis

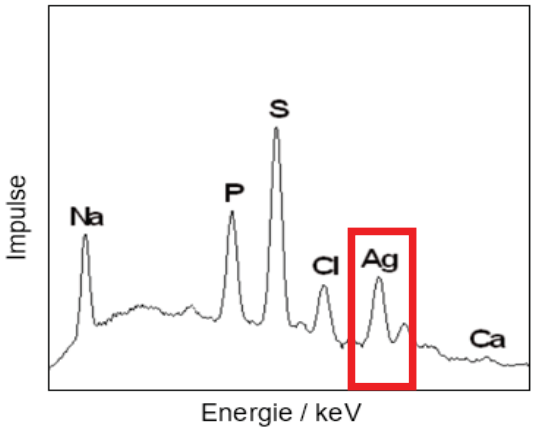




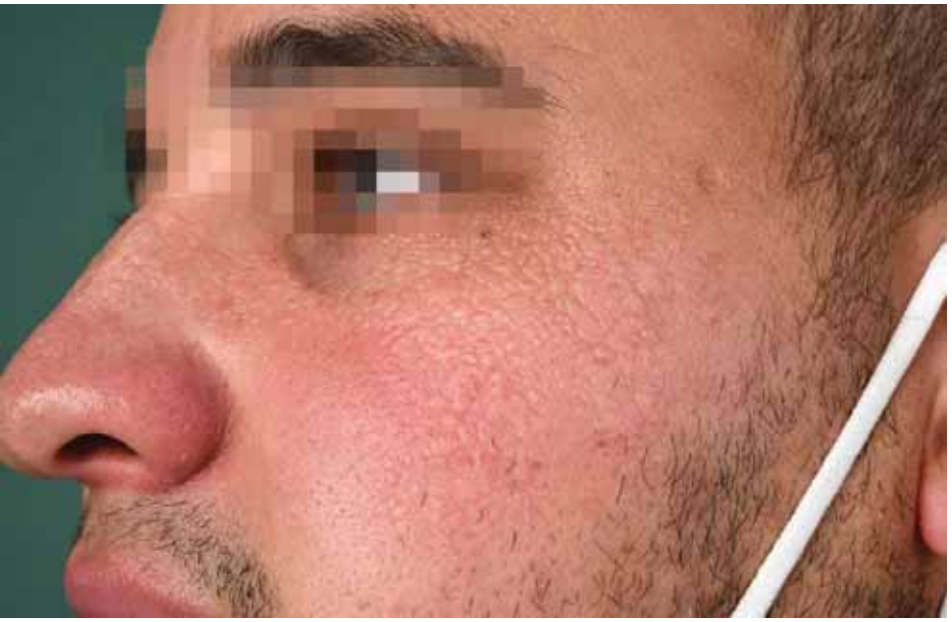
Electron dense particles
along the BM of
sweat glands
and vessels

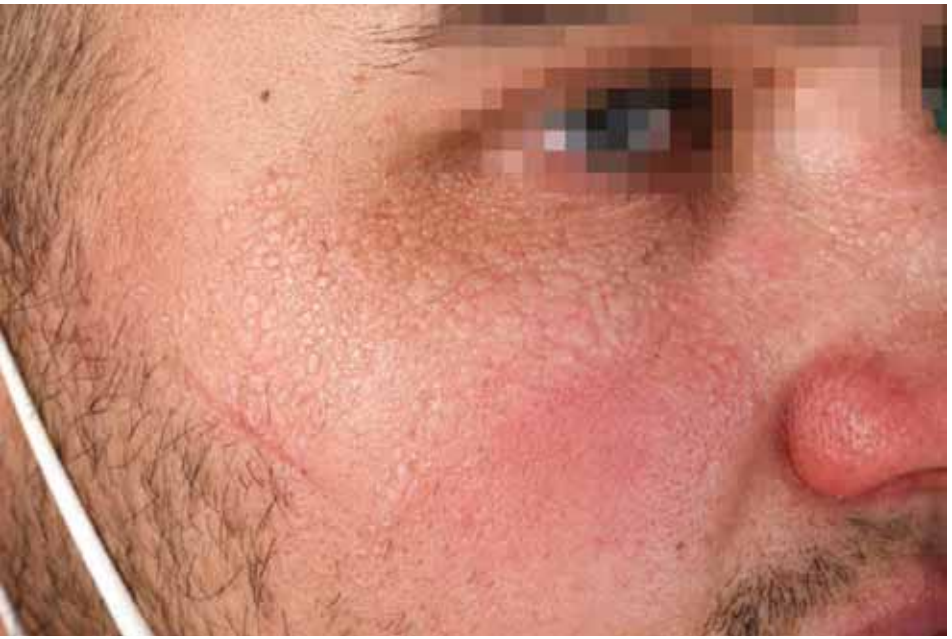


Fritz Schmidt, Akademie für Elektronenmikroskopie und Analytik, Münster



EDX Analysis of the particles





CASE

25-y-old man

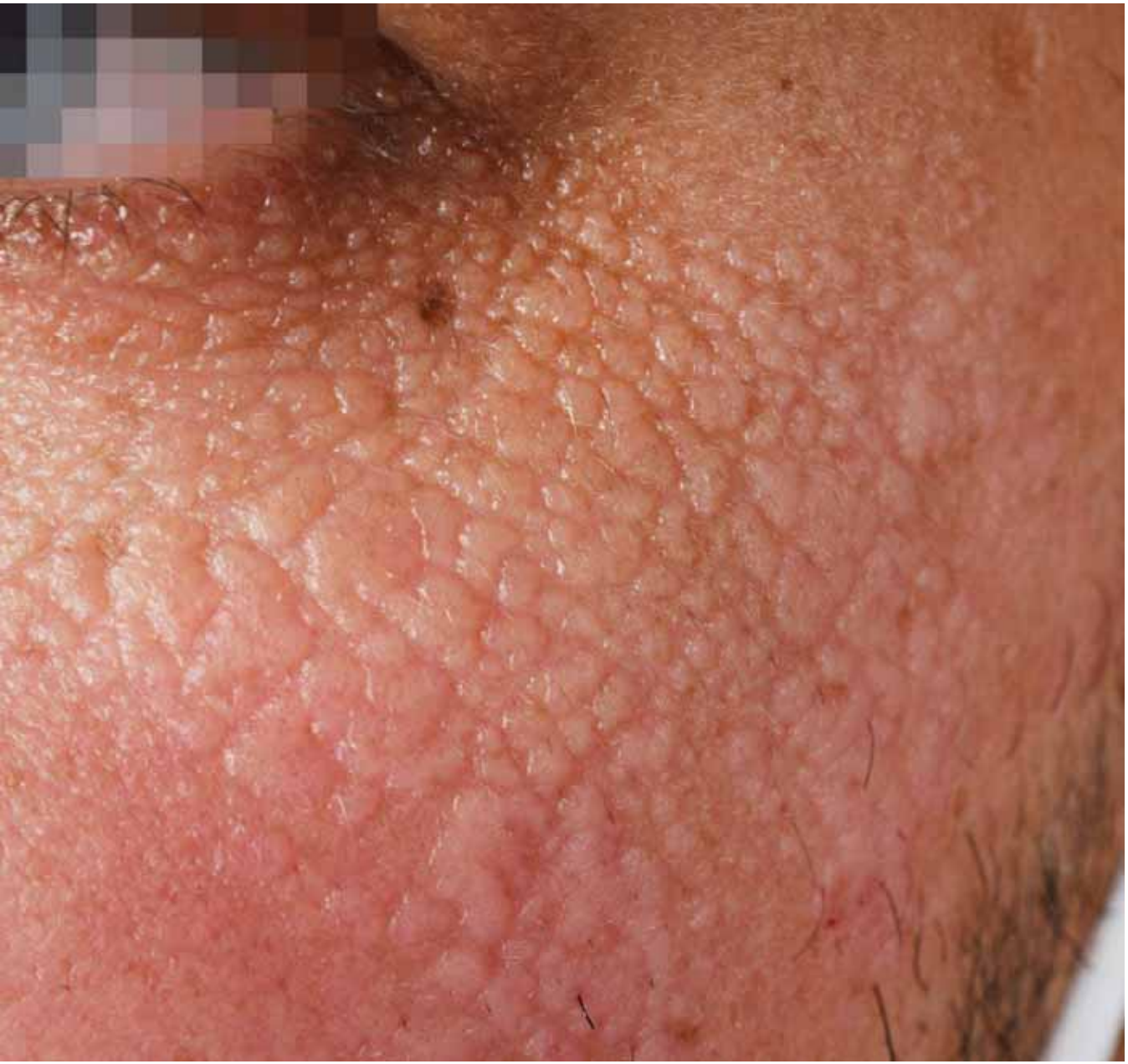
Papules on the cheeks and bridge of the nose

Since age of 12

No itching or pain

Allergic asthma and rhinoconjunctivitis

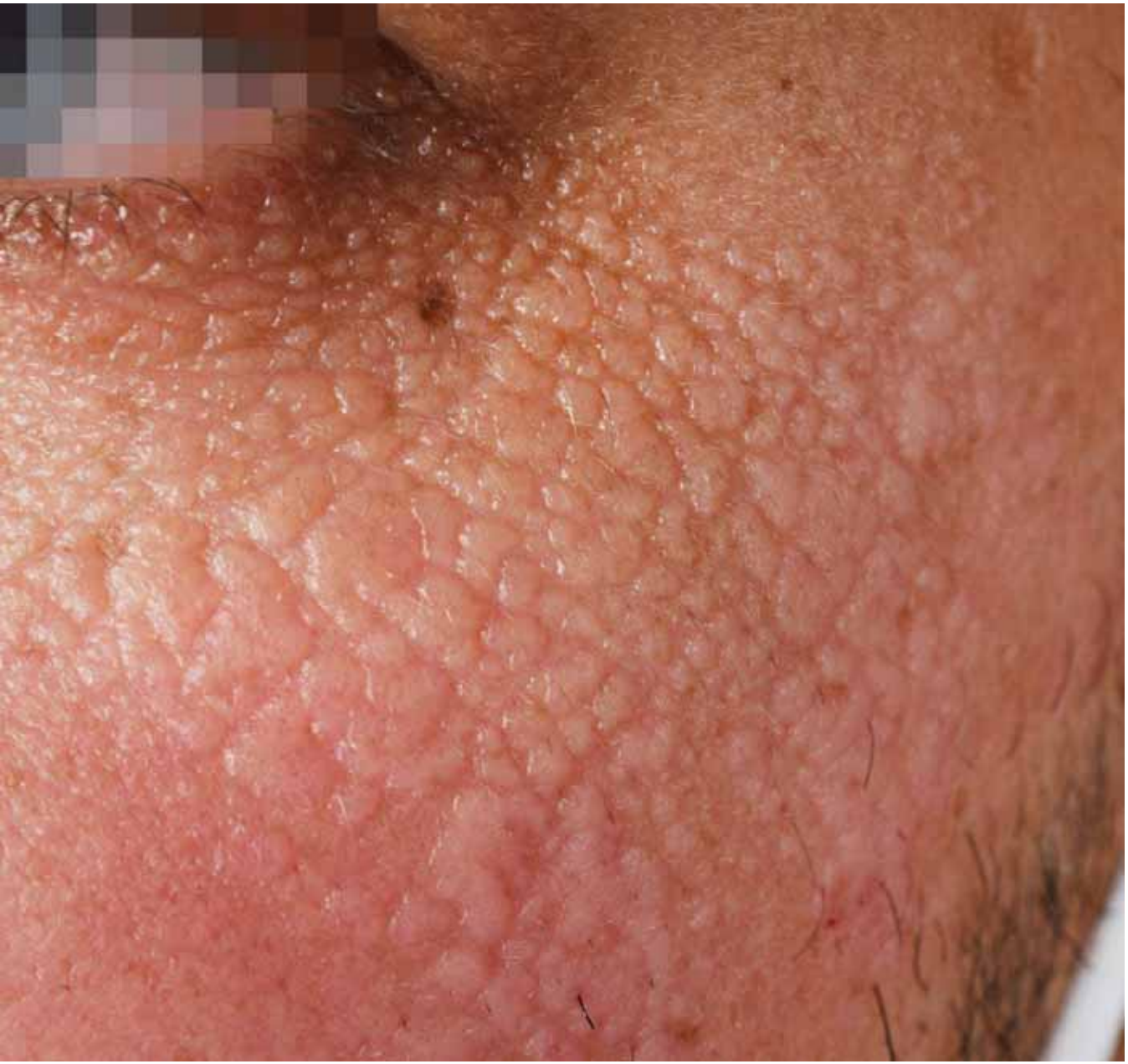
No medication



Cobblestone-like skin relief

Aggregated, skin-colored, flat, polygonal papules

No signs of solar elastosis



DDx

Syringoma

Trichoepithelioma

Zysts, Milia

Angiofibroma

Sarkoidosis

Lymphoma

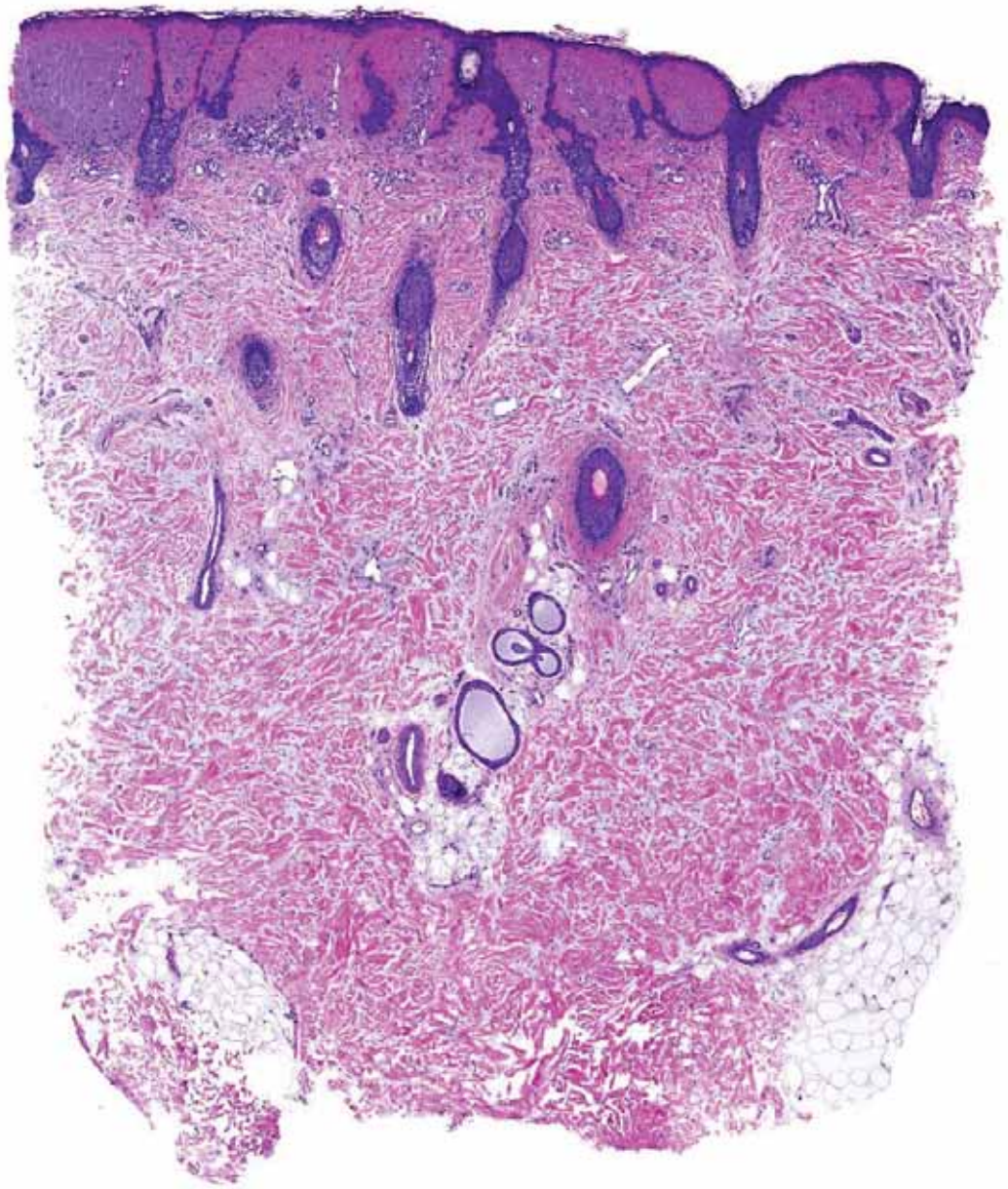
M. Favre-Racouchot

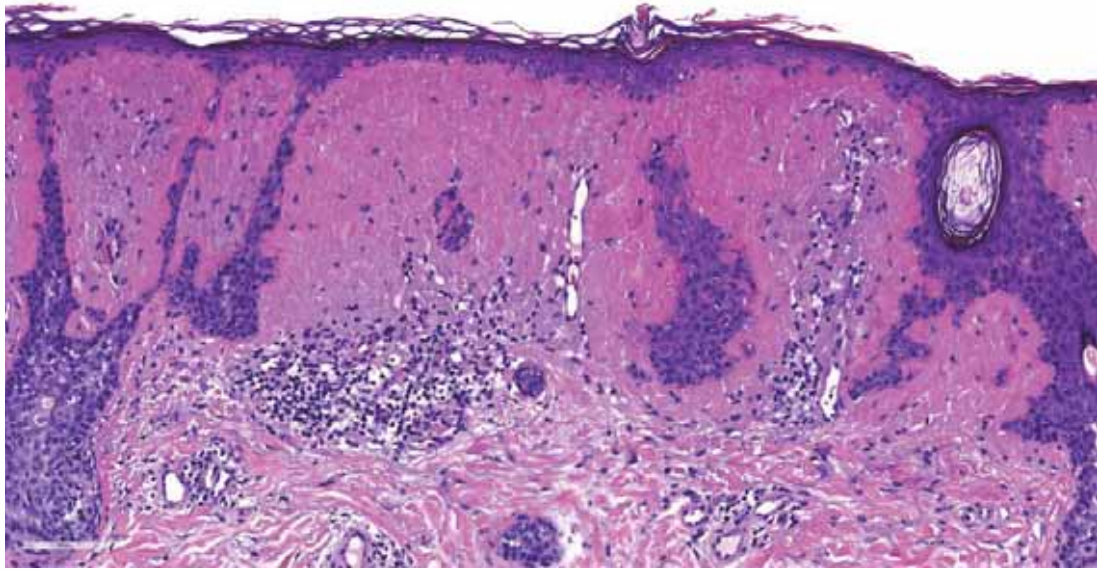
Amyloidosis

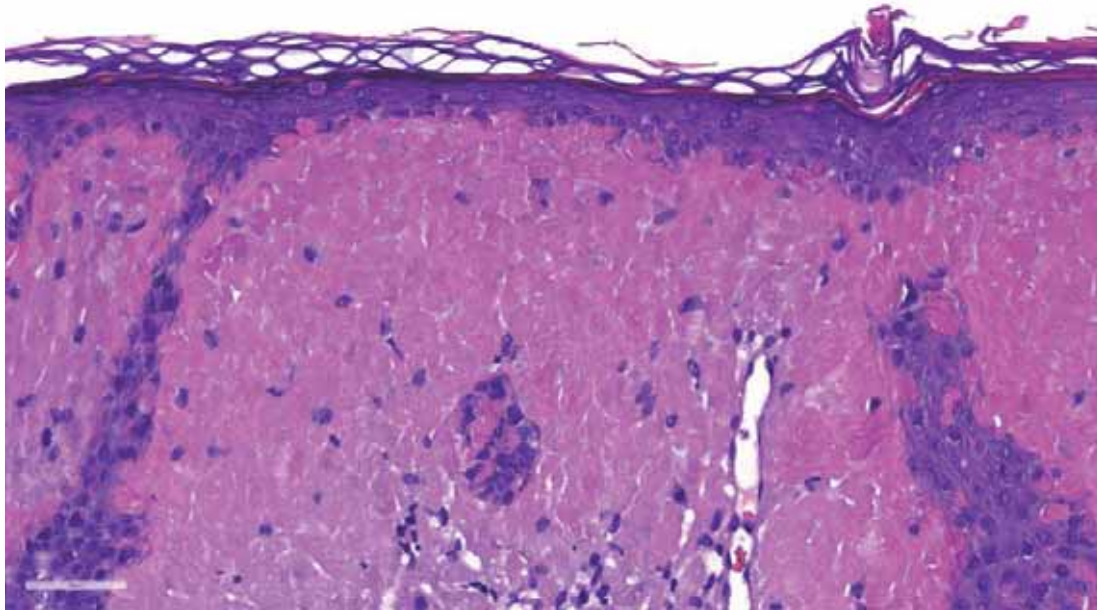
Hyalinosis cutis et mucosae

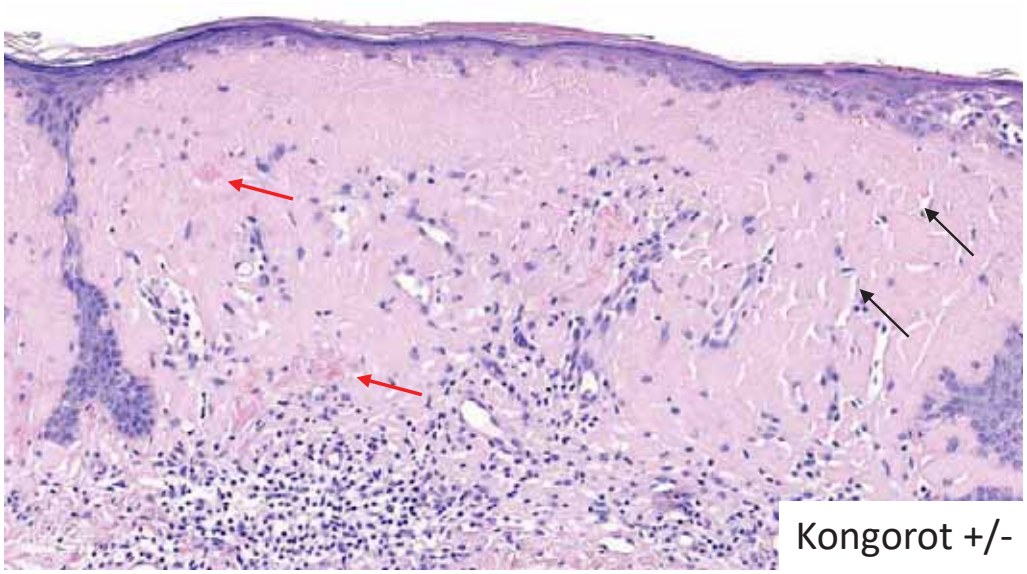
Ochronosis

….

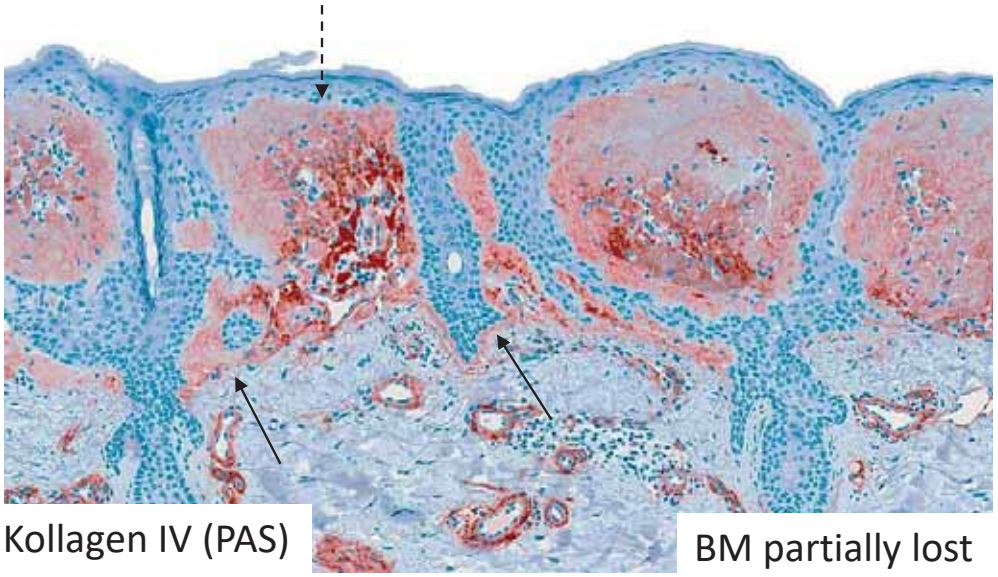






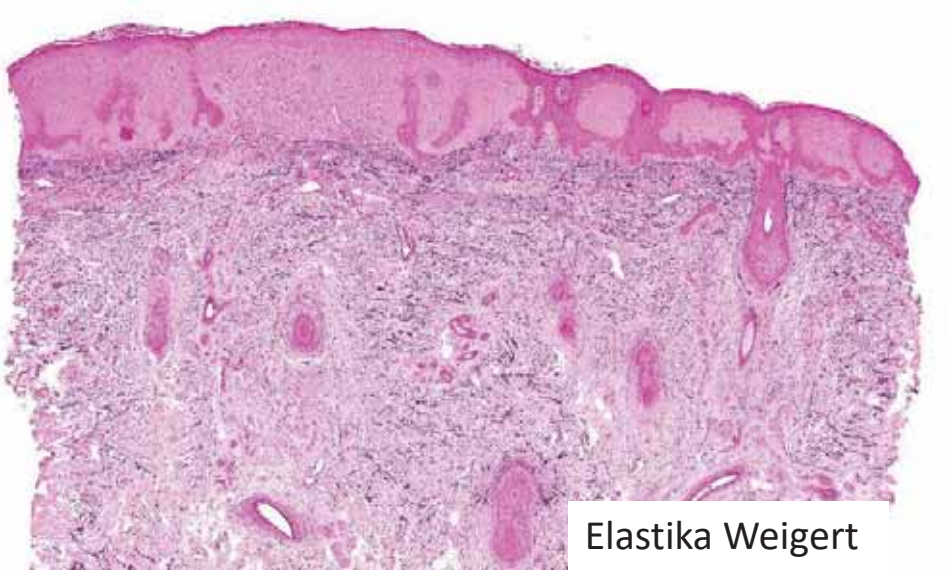


Kongorot +/-

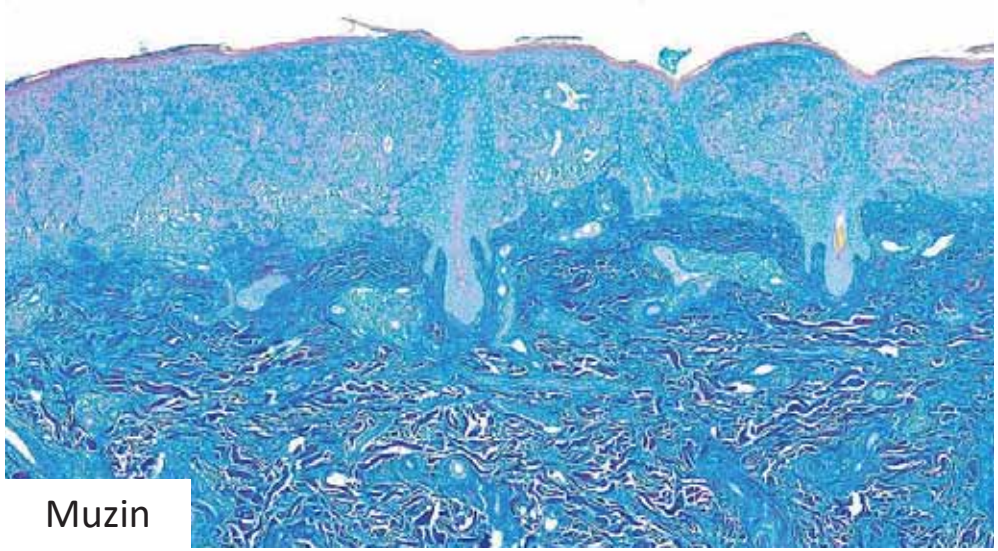


Kollagen IV (PAS)

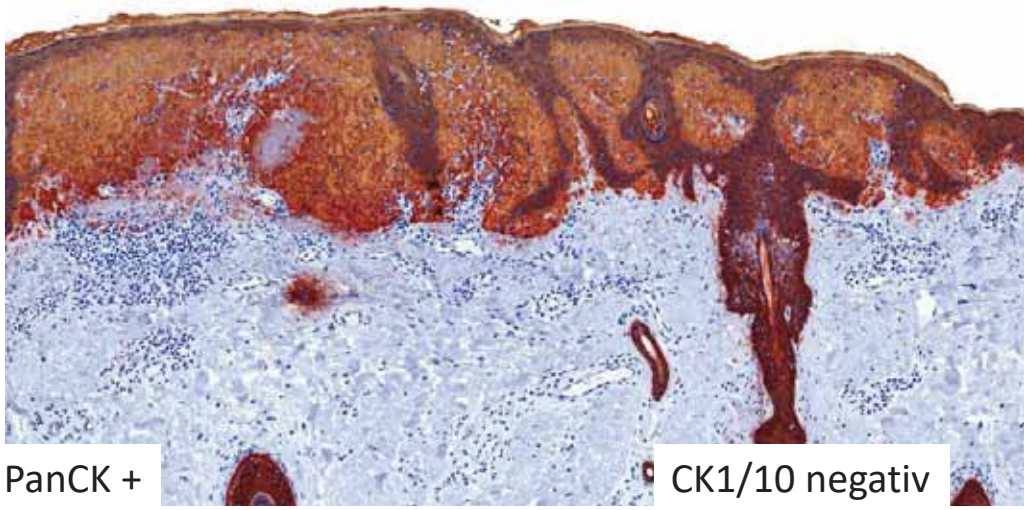
BM partially lost



Elastika Weigert

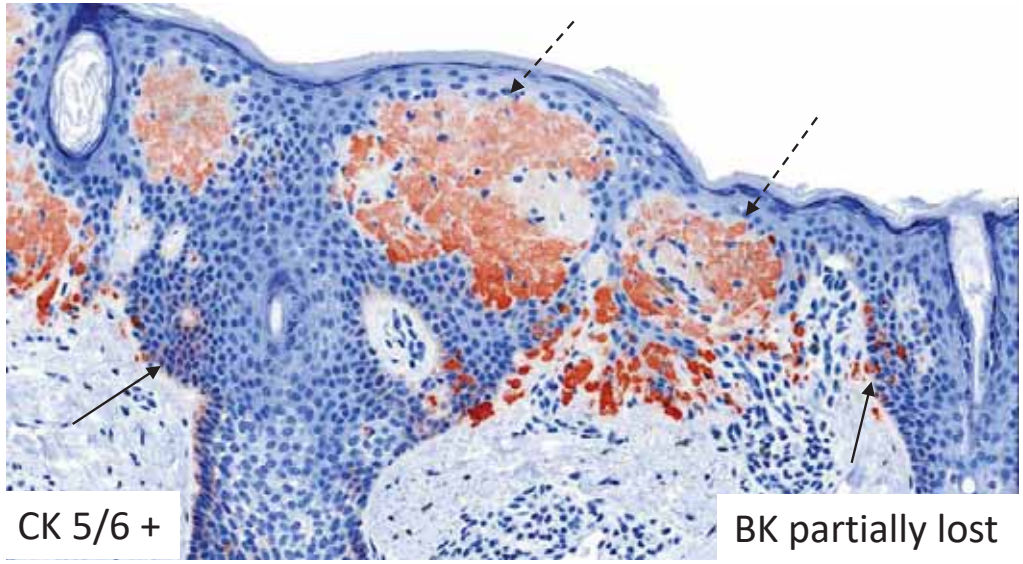


Muzin



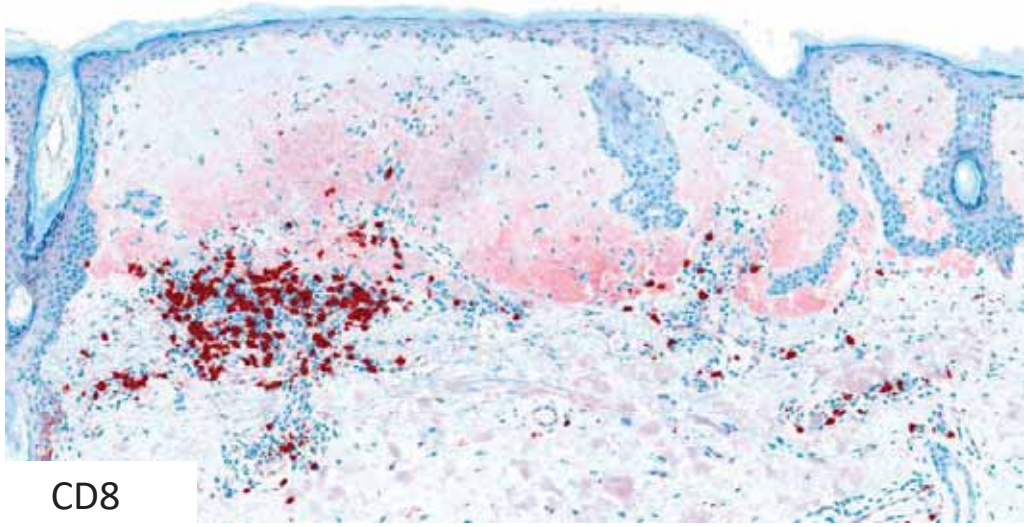
PanCK +

CK1/10 negativ

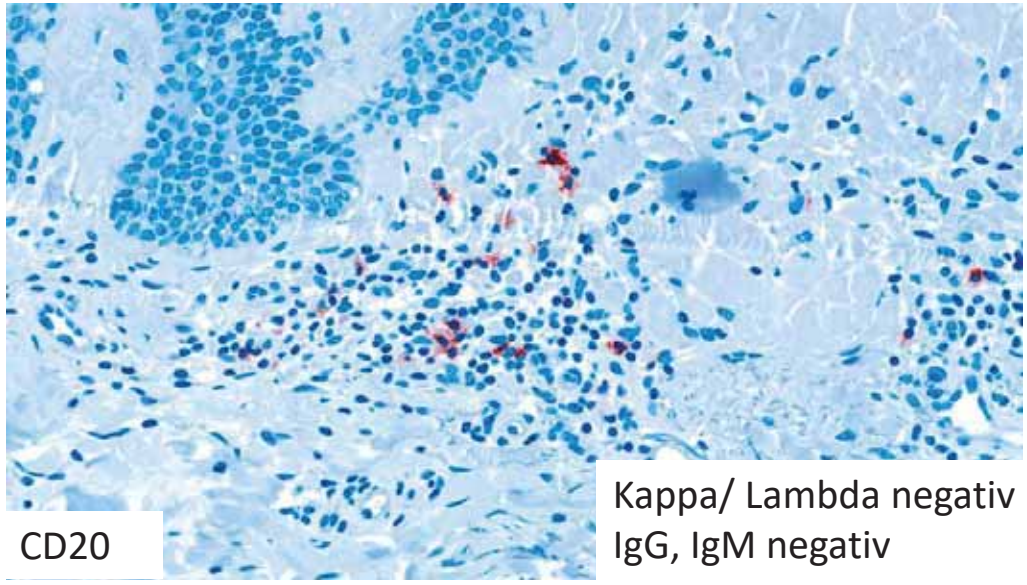


CK 5/6 +

BK partially lost



CD8



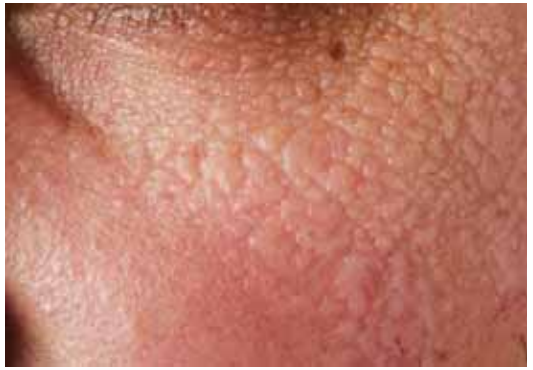
CD20

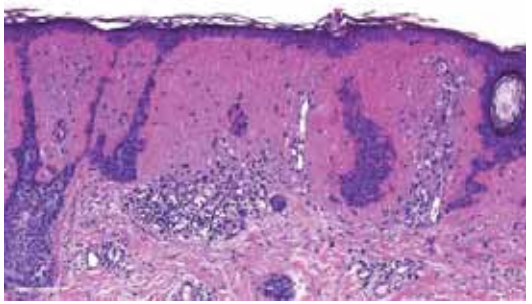
Kappa/ Lambda negativ

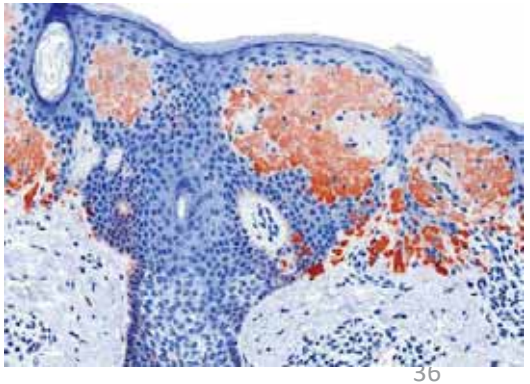
IgG, IgM negativ

Juvenile Colloid Milia

- Family history, manifestation before puberty
- Skin-colored to yellowish-brown, solitary or aggregated papules on the nose, cheeks, ears, perioral area, neck or back of the hand (conjunctiva, eyelids or oral mucosa)
- Sometimes gelatinous masses discharge from the papules when pressure is applied
- Other types of Colloid milia (CM):
  - adult CM (Elastosis „colloidalis“): Solar elastosis, Grenz zone, Keratin and CoI IV negativ
  - nodular CM: Amyloidosis
  - pigmented CM: Exogenous ochronosis

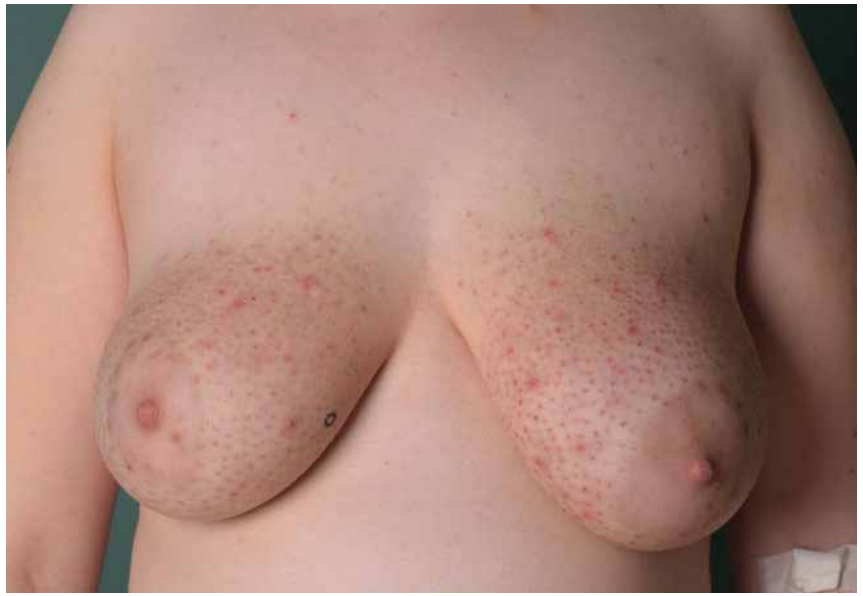




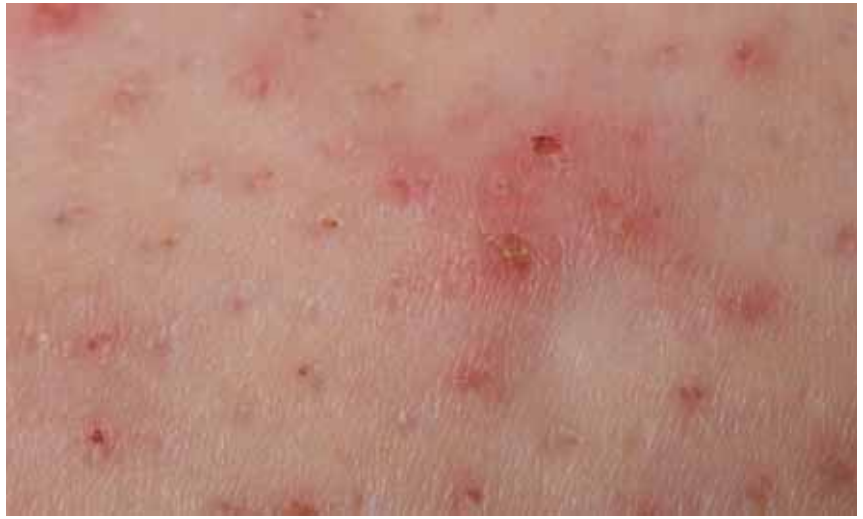


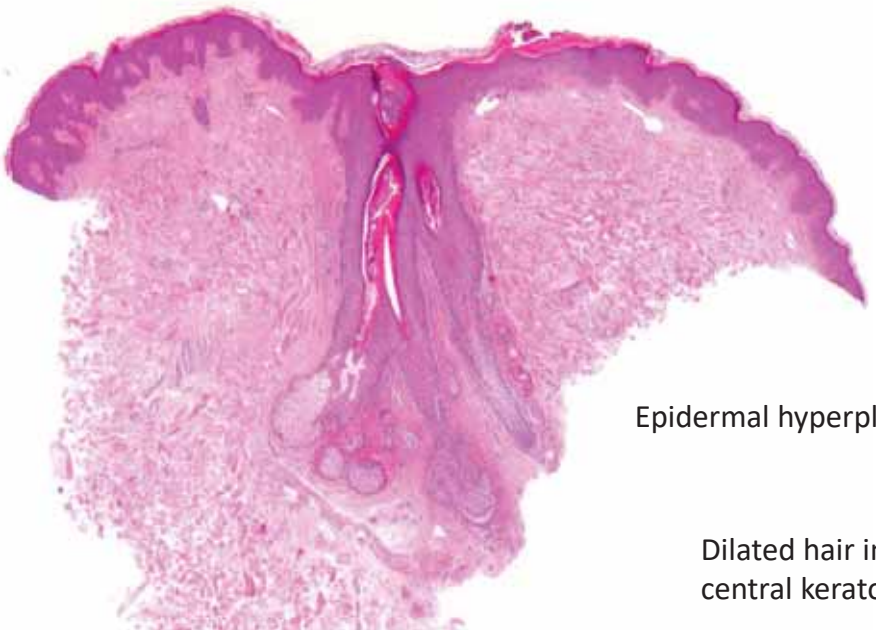
CASE

- 20-year-old white female with pruritic hyperkeratotic papules on the trunk



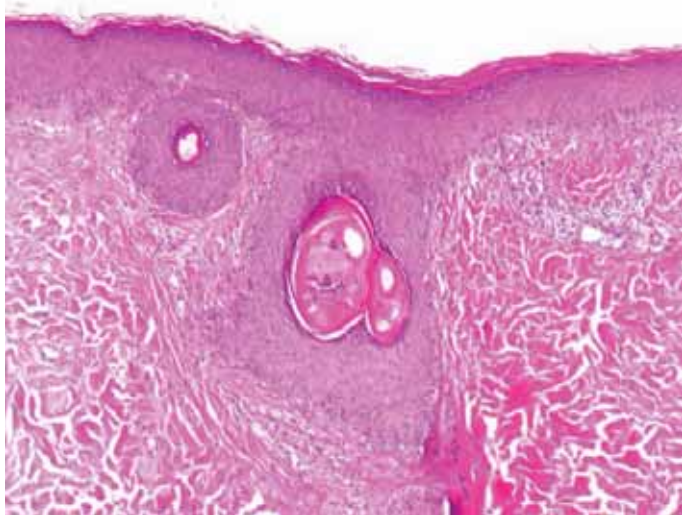
At time of biopsy
no other history

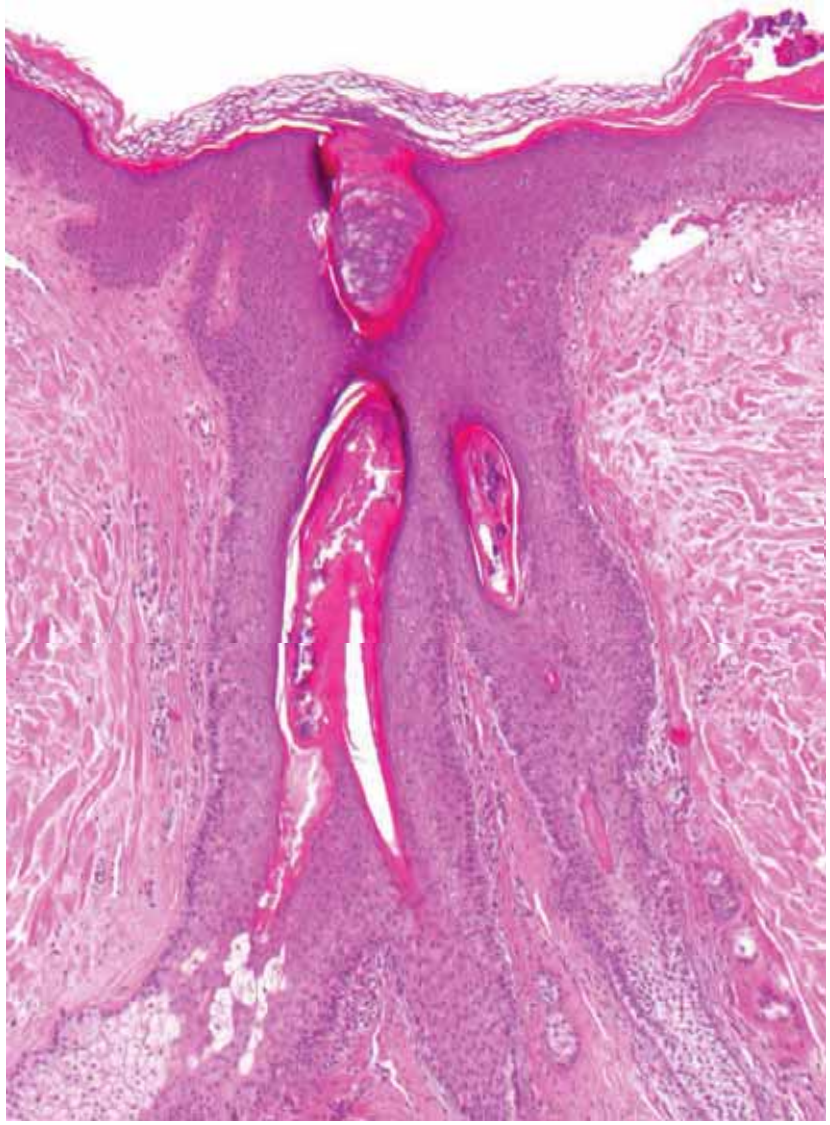




Epidermal hyperplasia with hyperkeratosis

Dilated hair infundibula with
central keratotic plugs






- 20 year-old white female with pruritic hyperkeratotic papules on the trunk

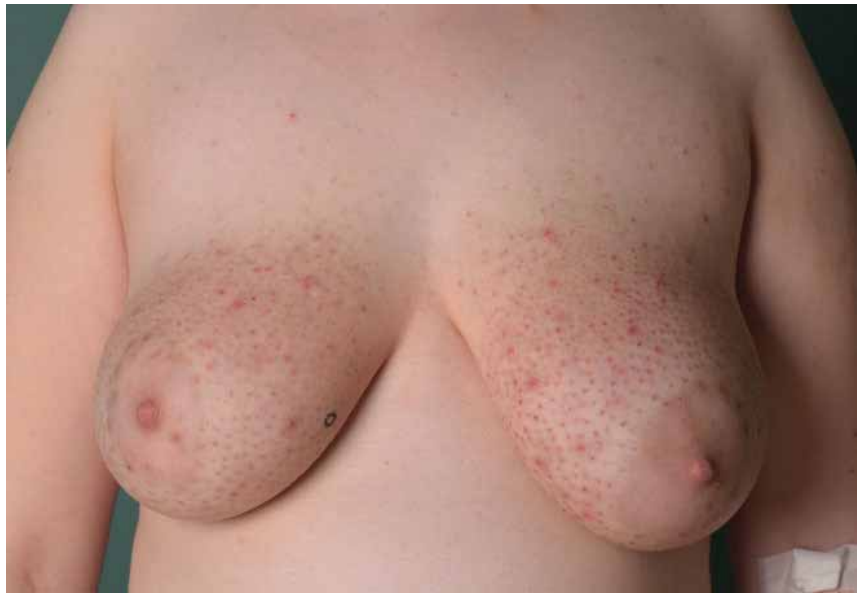
- Atopic diathesis, Coeliac disease (gluten-free diet)

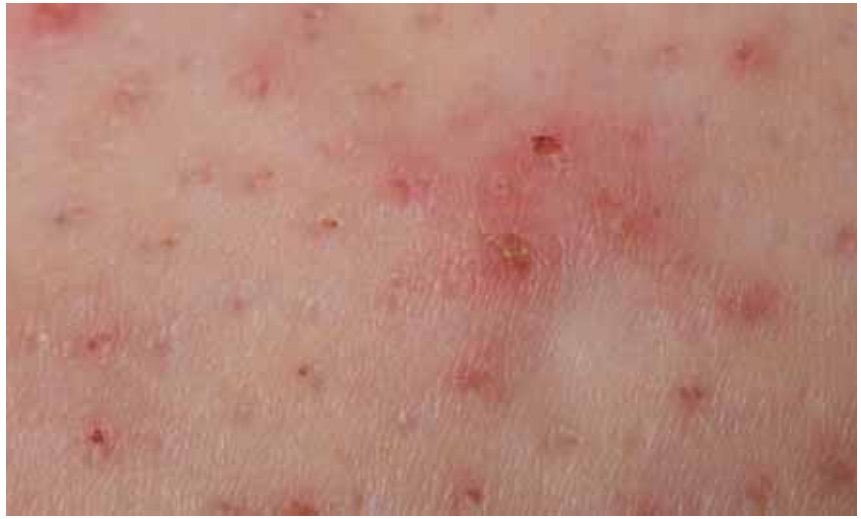
❖Vitamin B2, B12, D and zinc deficiency

✓Vitamin A normal

✓HIV negativ

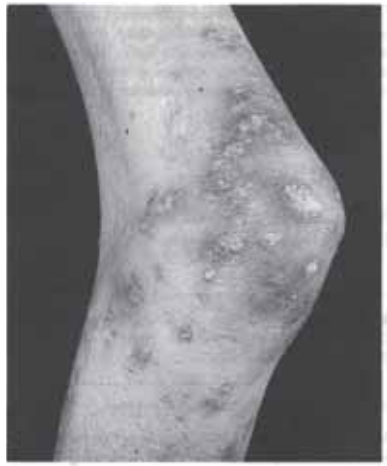
✓Anti-Gliadin and Anti-Transglutaminase negativ (under diet)





Phrynoderma
(“phryno”, toad-like skin)

Rare deficiency condition



Manifestation: 5-30 years

Follicular hyperkeratotic papules
Dry skin, pruritus

Extensor surfaces of extremities, trunk, buttock

Deficiencies of Vitamin A, B, D
and zinc or other minerals

Malnutrition, inflammatory bowel diseases,
bariatric surgery,
Co-factor friction and trauma

Substitution therapy

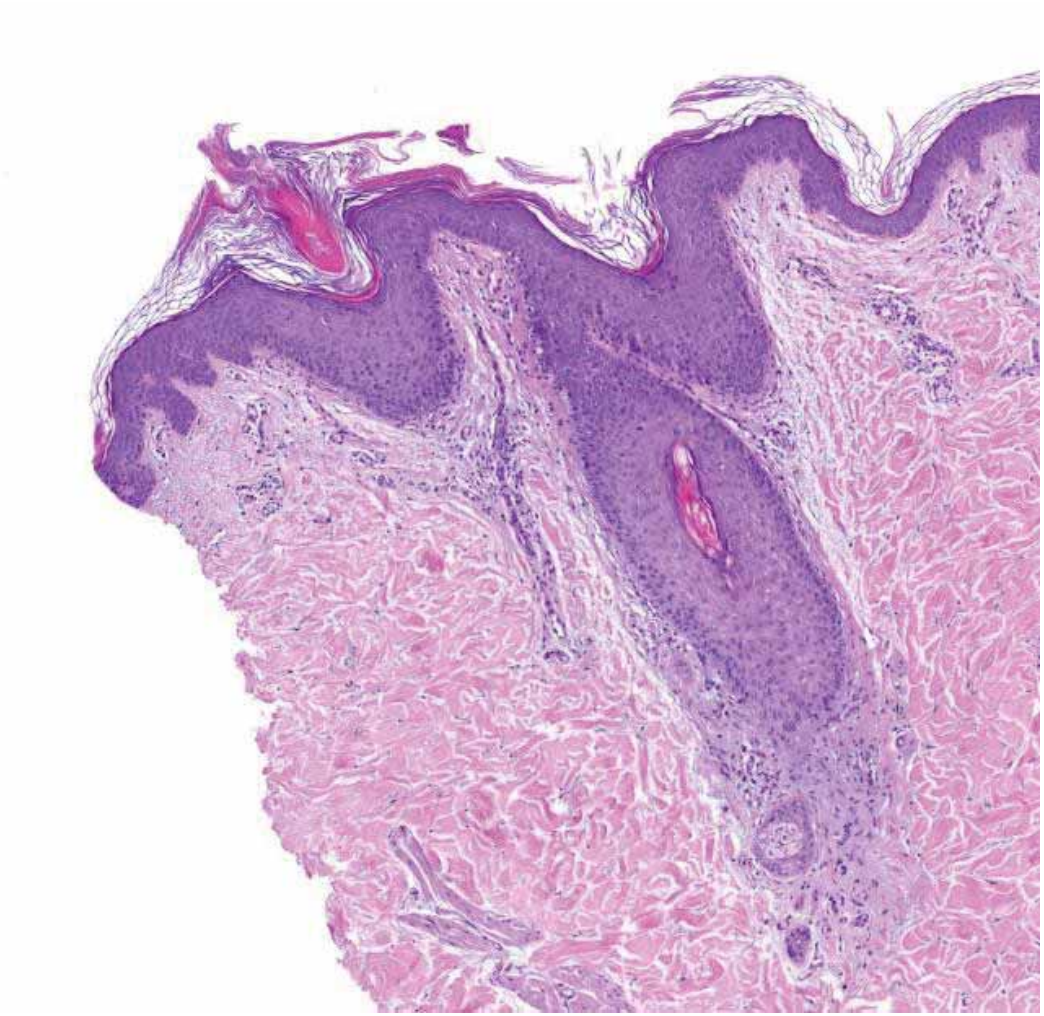
Phrynoderma,
Xerosis cutis,
Xerophthalmie
(night blindness),

Treatment: cod oil

Lucius Nicholls, South-India, 1929
Loewenthal, East-Africa, 1933

Follicular hyperkeratosis, isolated or leading finding

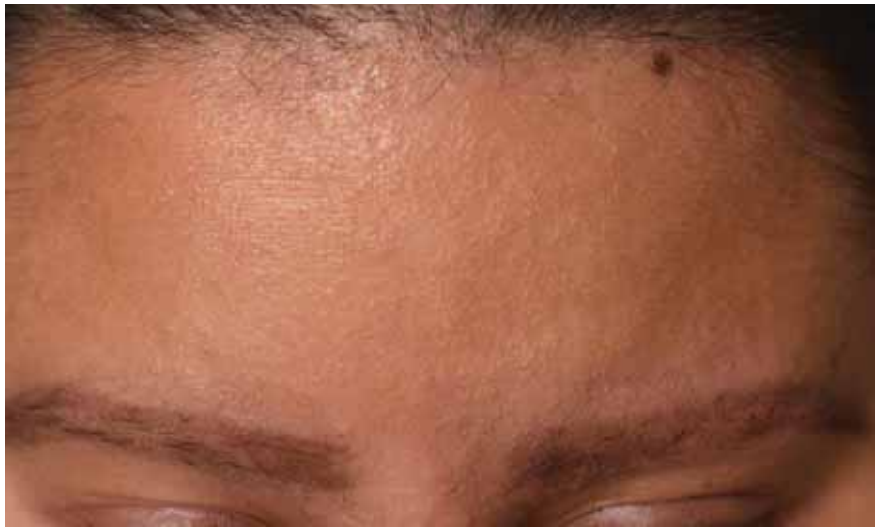
- Keratosis pilaris
- Lichen spinulosus
- Comedones, Milia
- Infundibular cysts, dilated pore of Winer
- Trichostasis spinulosa
- Phrynoderma
- Drug-induced

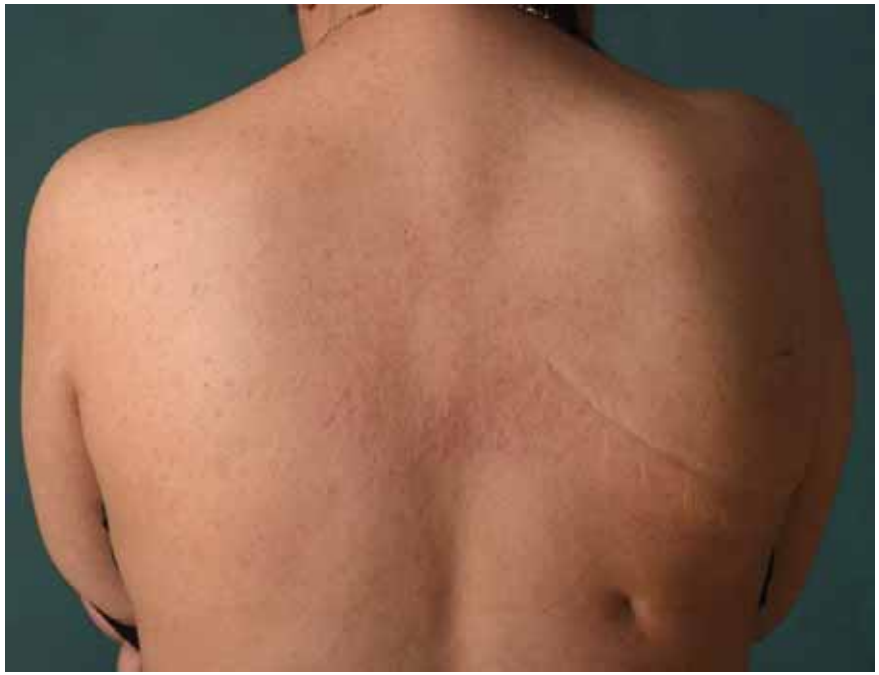


CASE

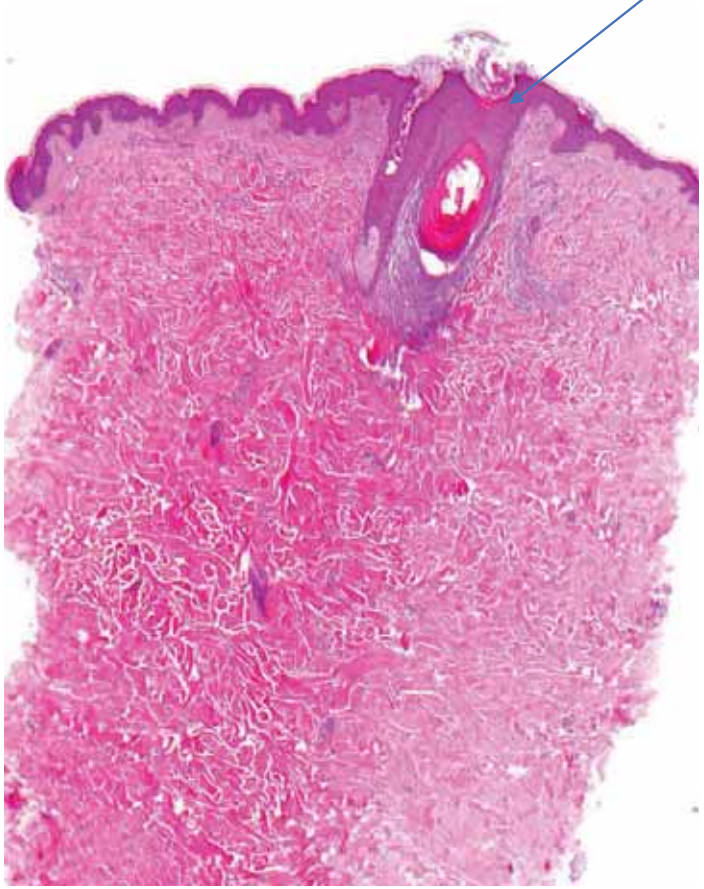
- 20-year-old female
- Eruptive occurrence of follicular papules and spiky keratosis
- Alopecia of her eyebrows

At time of biopsy
no other history





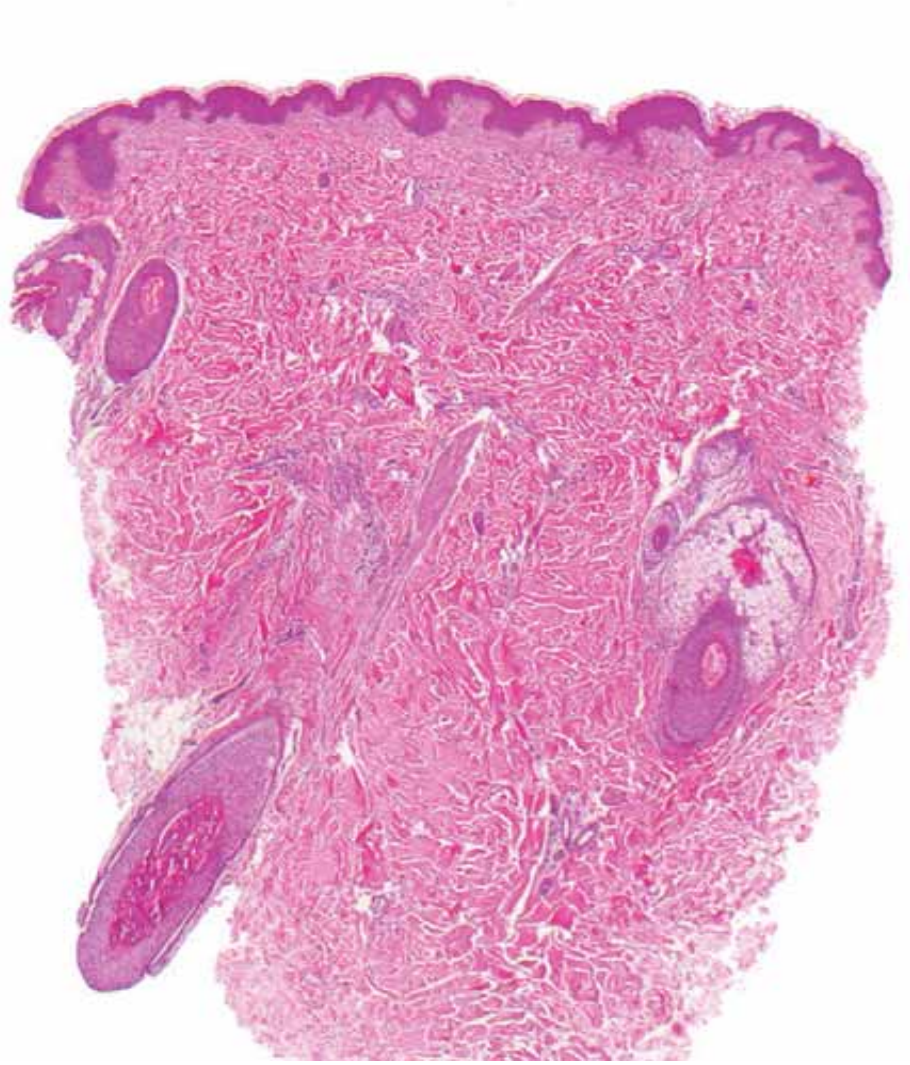
1st Biopsy



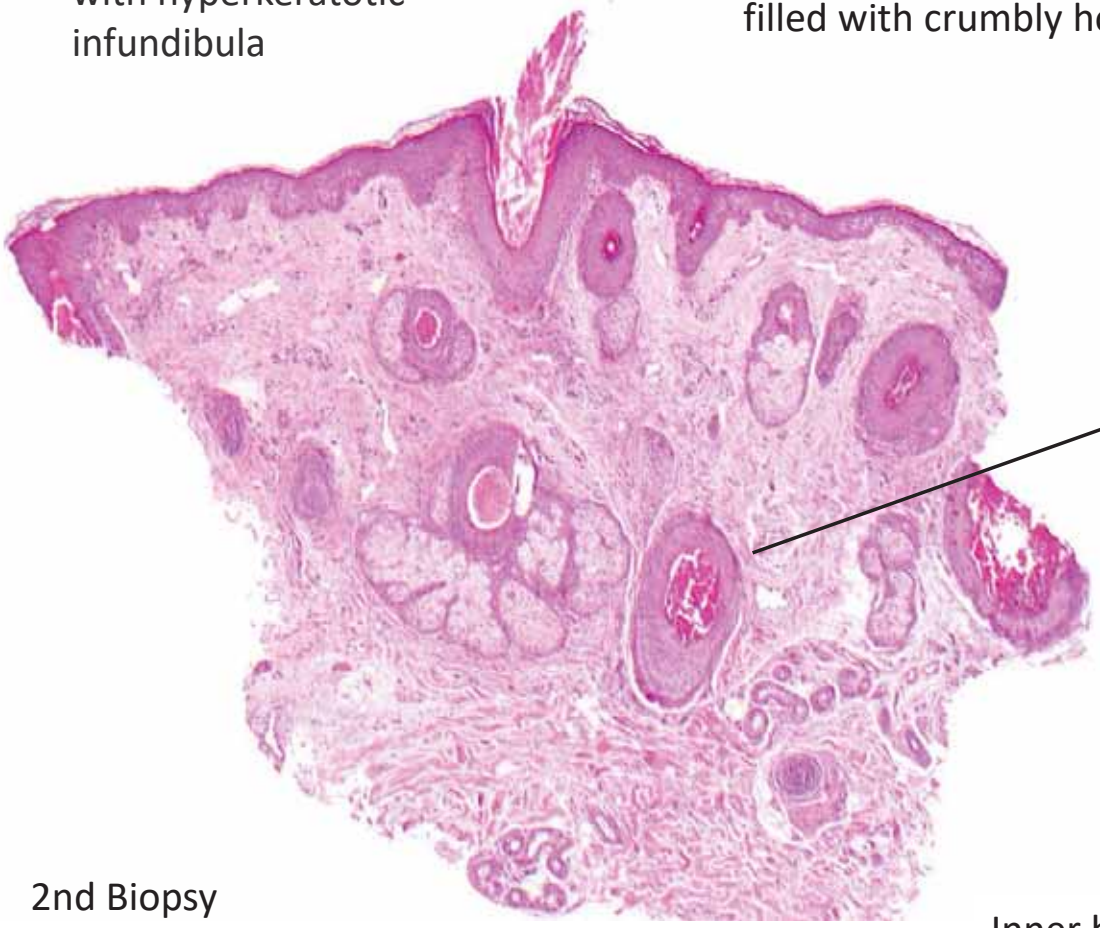
Follicular hyperkeratosis

step sections

Deeper parts:
crumbly horn masses

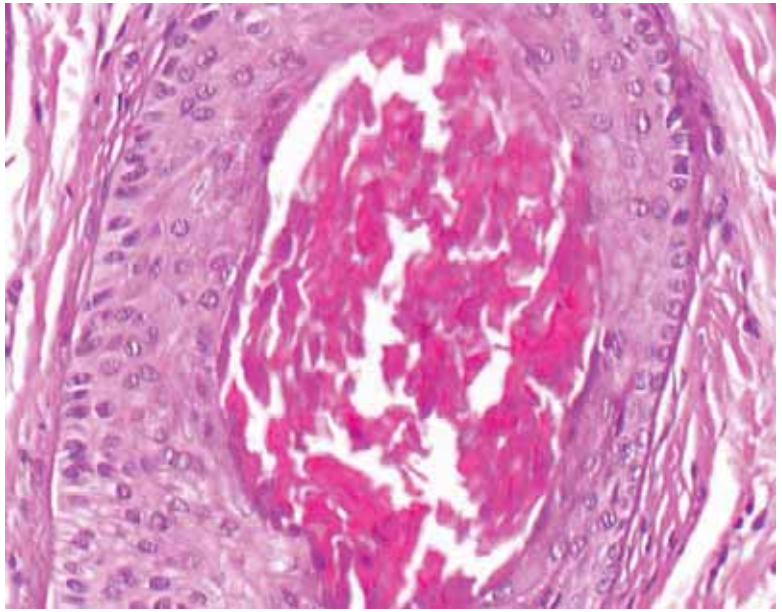


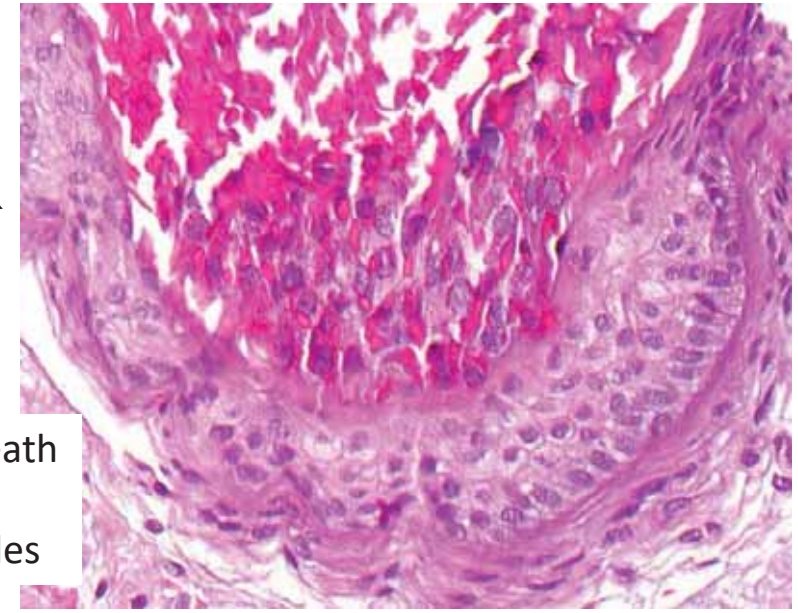
Spiky keratosis
with hyperkeratotic
infundibula



2nd Biopsy

Deeper parts of hair follicles
filled with crumbly horn masses





Inner hair root sheath
with prominent
trichohyalin granules

Biopsy sent to Heinz Kutzner

Prompt diagnosis within 24 hours by mail

Biopsy sent to Heinz Kutzner

Prompt diagnosis within 24 hours by mail:

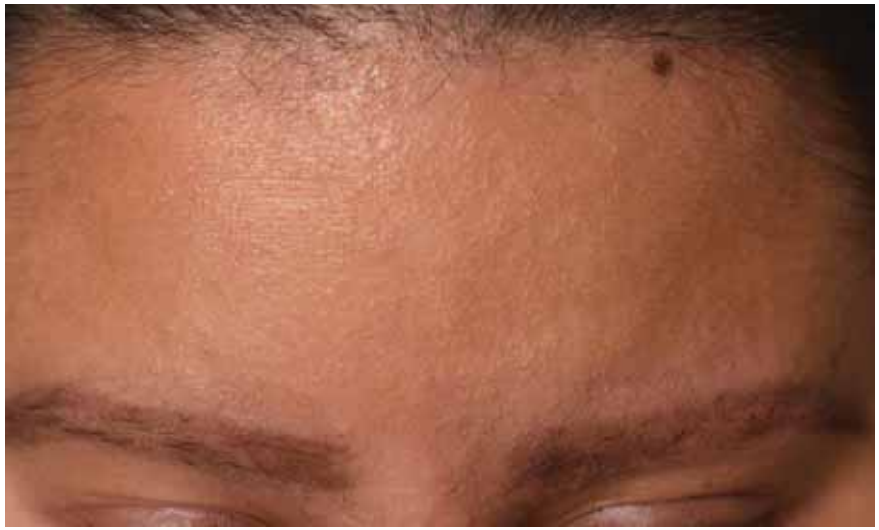
„Trichodysplasia spinulosa,
PCR for Polyoma virus will be performed“

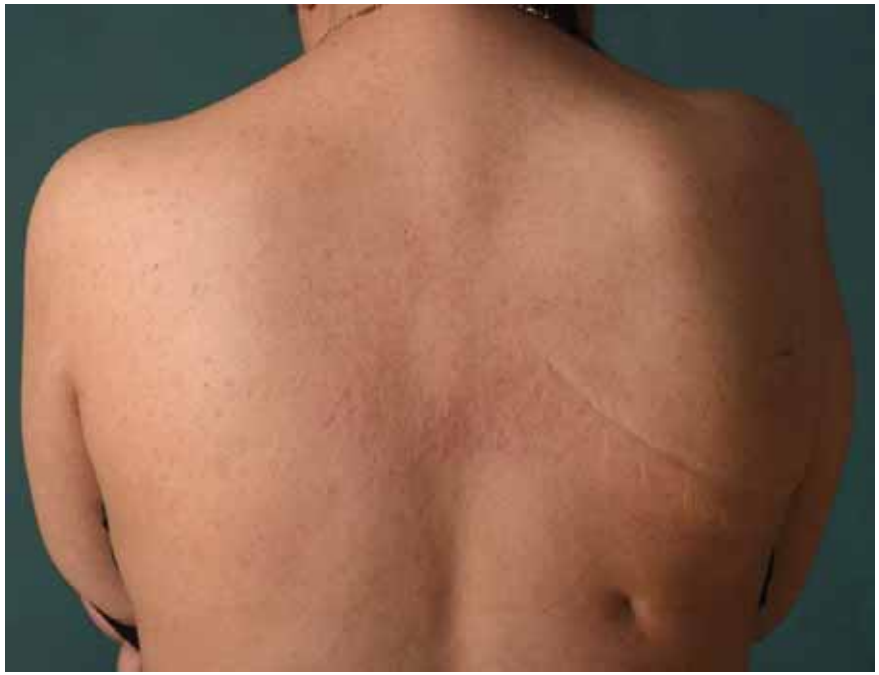
CASE

- 20-year-old woman
- Eruptive occurrence of follicular papules and spiky keratosis
- Alopecia of her eyebrows

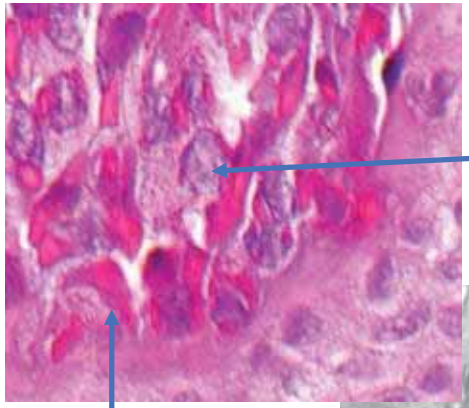
History:

- Kidney transplant 9 years ago
- Immunosuppressive therapy with mycophenolate mofetil, prednisolone, tracolimus





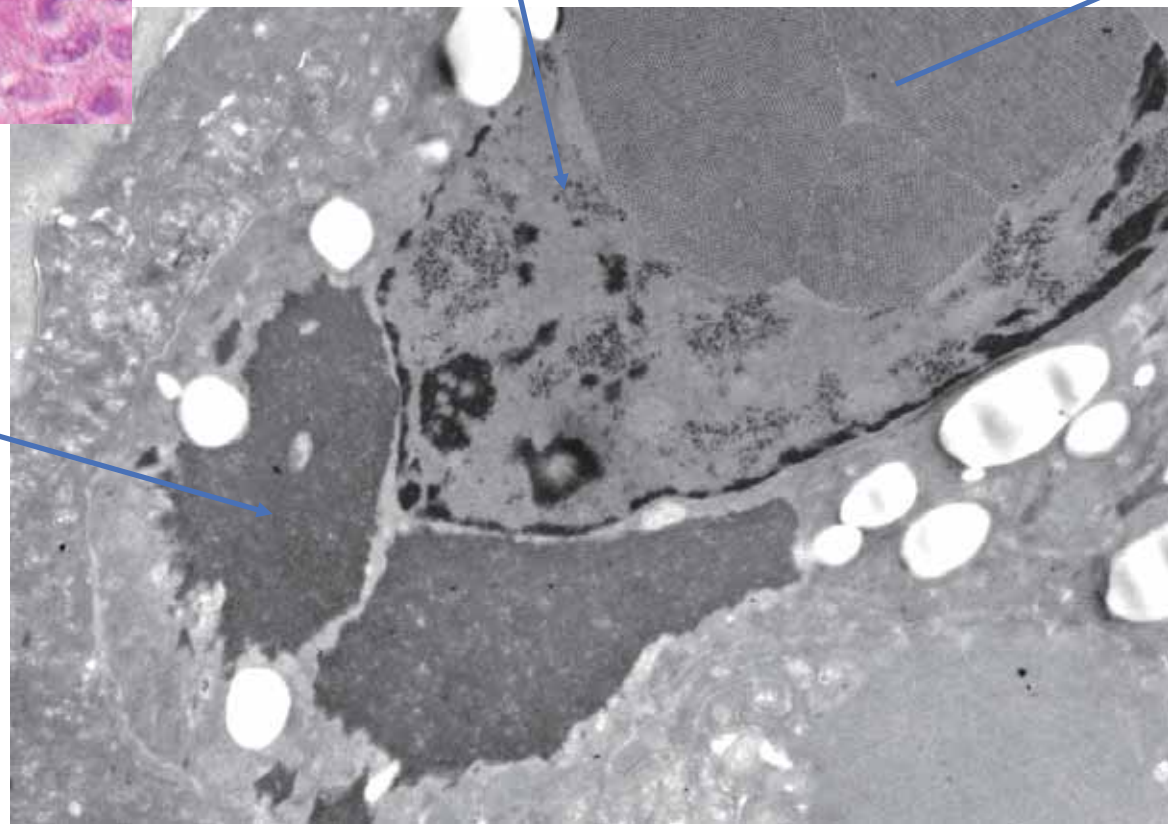
Inner root sheath of the hair follicle

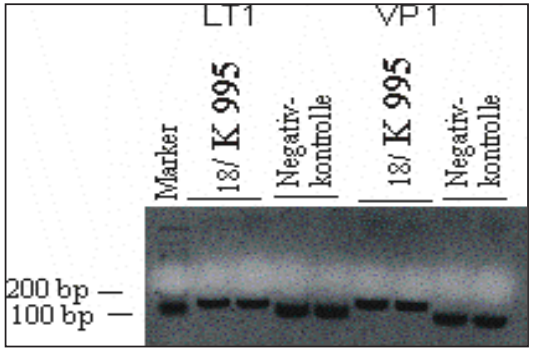


Large pale nuclei

Viral particles in a cristalloid arrangement

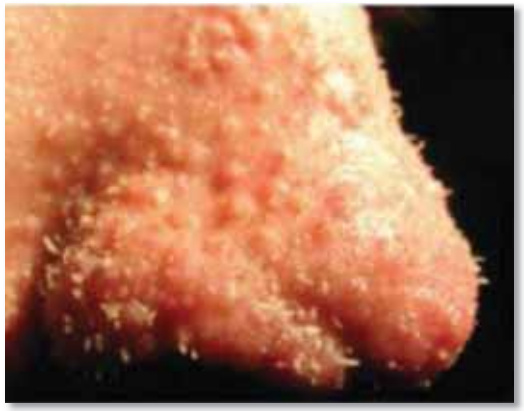
Trichohyaline granules





PCR, H. Kutzner, Friedrichshafen

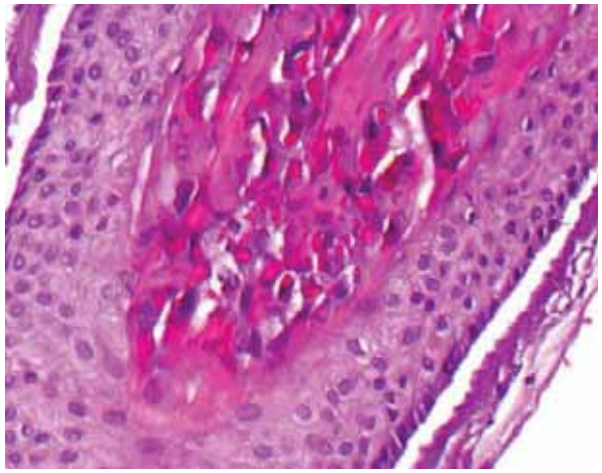
Trichodysplasia spinulosa (TS)



- Virus infection with TS-associated Polyomavirus
- Over 90% of adults showing serological evidence of previous exposure to the virus
- Immunocompromised patients (organ transplant patients)
- TS through primary infection

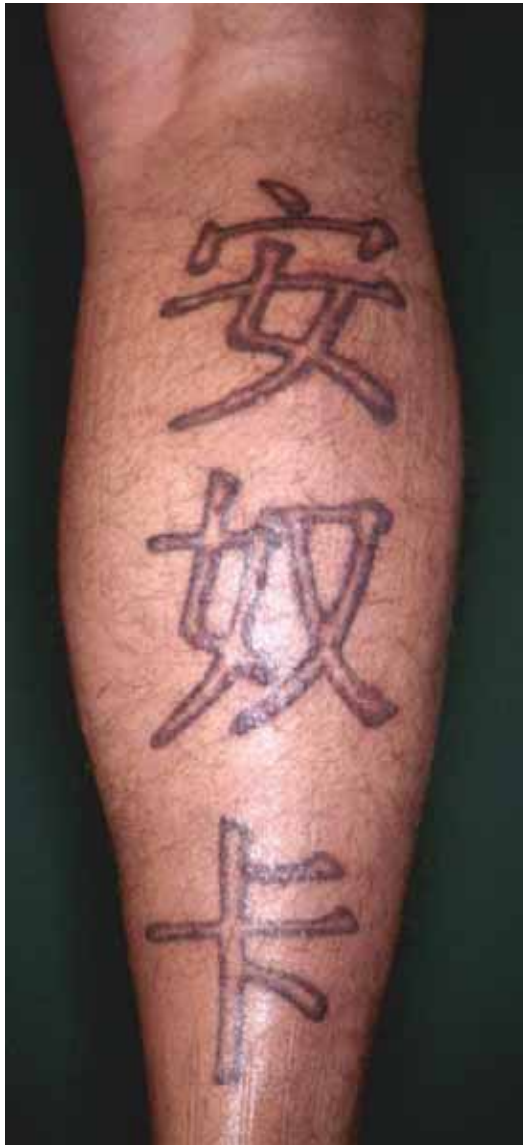
- Follicular associated papules, spiky keratoses
- Centrofacial zone
- Alopecia (eyebrows)
- No other symptoms

Additional diagnostics
Electron microscopy
Immunohistochemistry
PCR
(Serology not helpful)

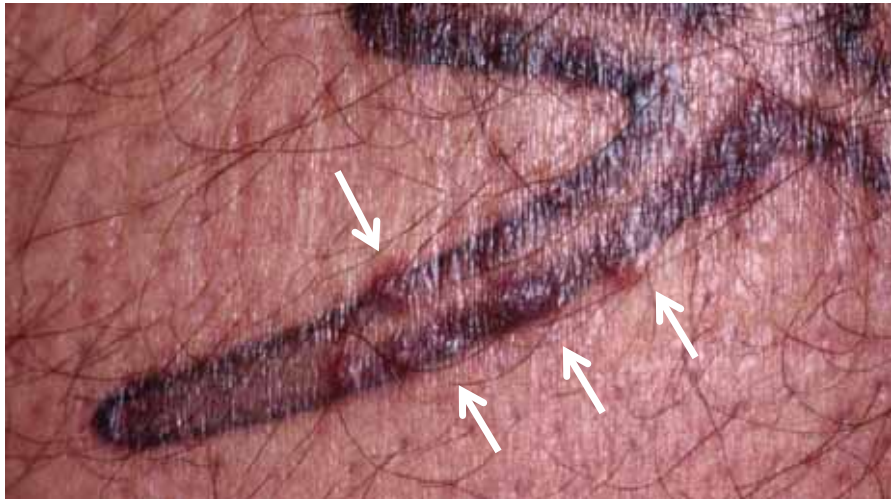


Disturbed cornification of the inner root sheath of hair follicles

Haycox et al., J Investig Dermatol Symp Proc 1999;
Van der Meijden et al., PLoS Pathog 2010
Wanat et al., Arch Dermatol 2012;
Fischer et al., Arch Dermatol 2012



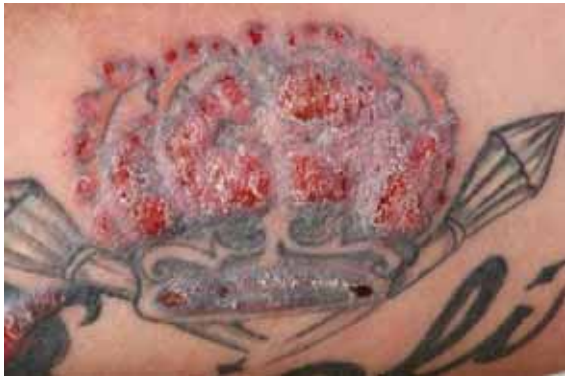
23-y-old man,
professional tattoo on lower leg,
otherwise healthy



Papules and pustules after 4 months,
no itch, no erythema
no fever, no lymphadenopathy

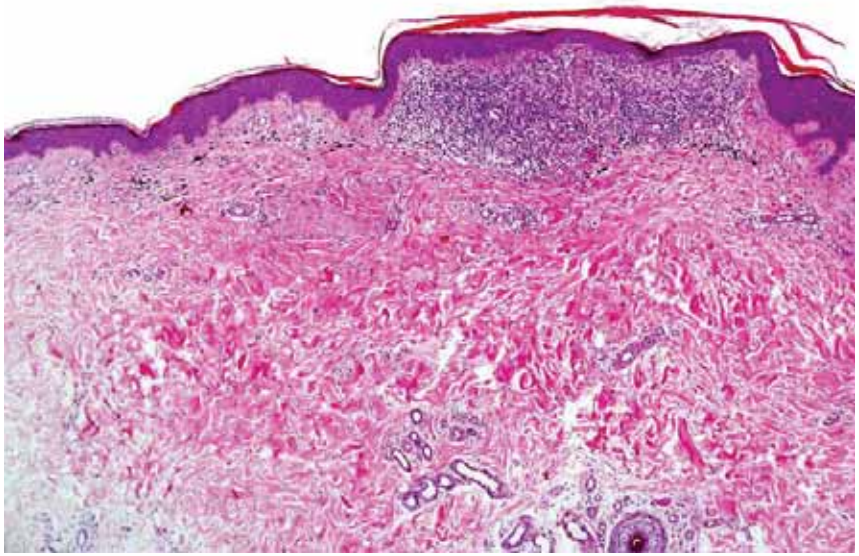
Tattoo Reactions

- Hypersensitivity reactions
- Photoallergic reaction
- Foreign body reaction
- Sarkoidosis
- Lymphomatoid reactions
- Lymphoma
- Keloid
- Pseudoepitheliomatous hyperplasia
- Köbner-phenomenon
  (Psoriasis, Lichen planus, LE, Darier, ….)
- Infection



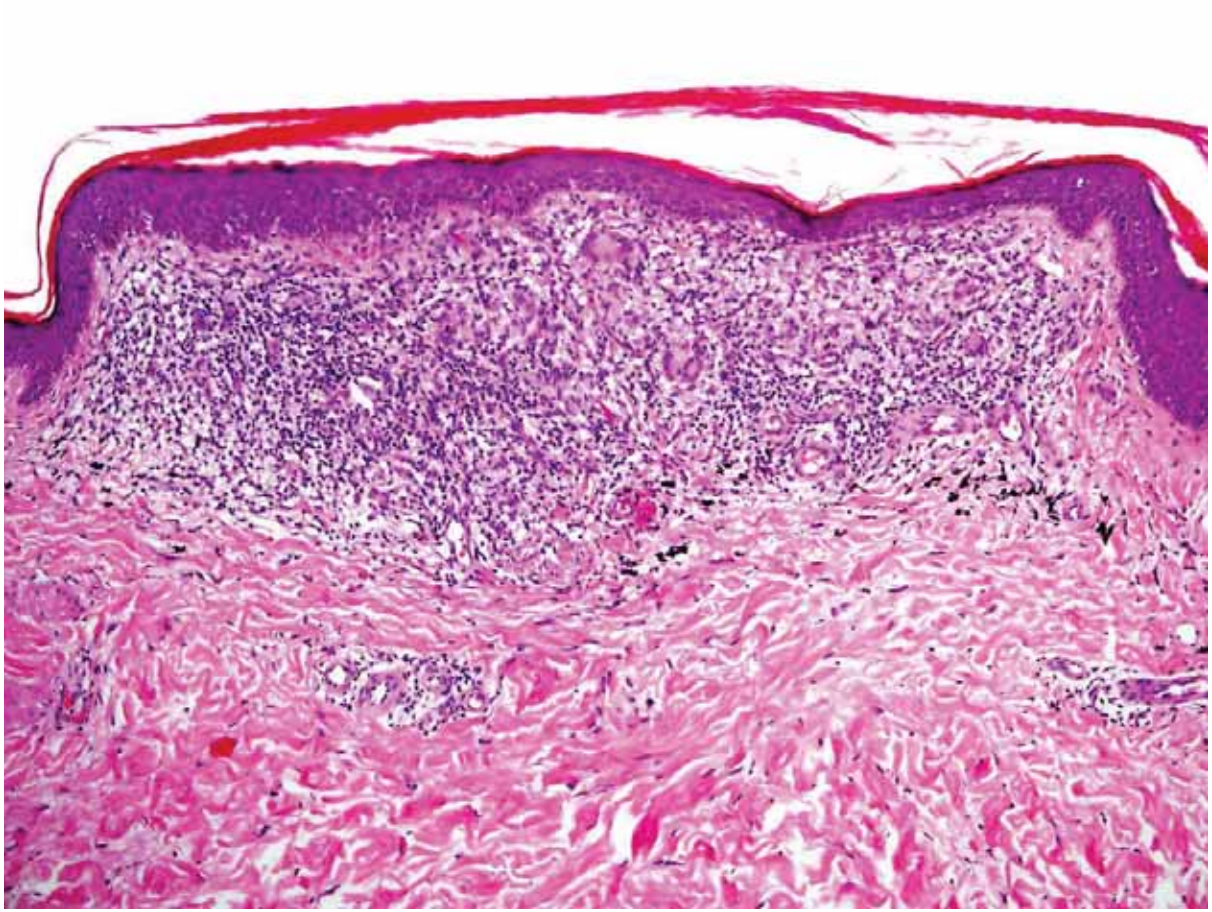
Contact Dermatitis

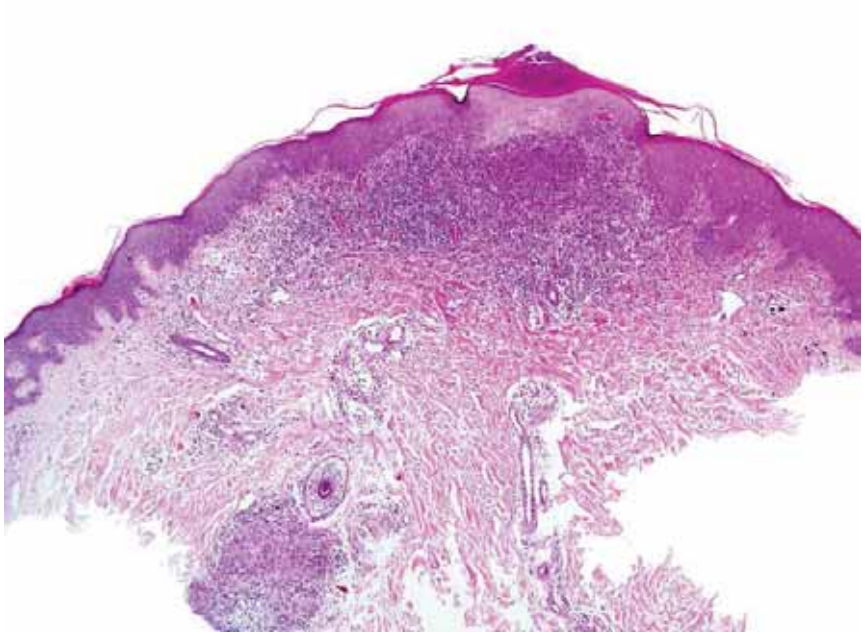
Psoriasis



Lichenoid, granulomatous Dermatitis

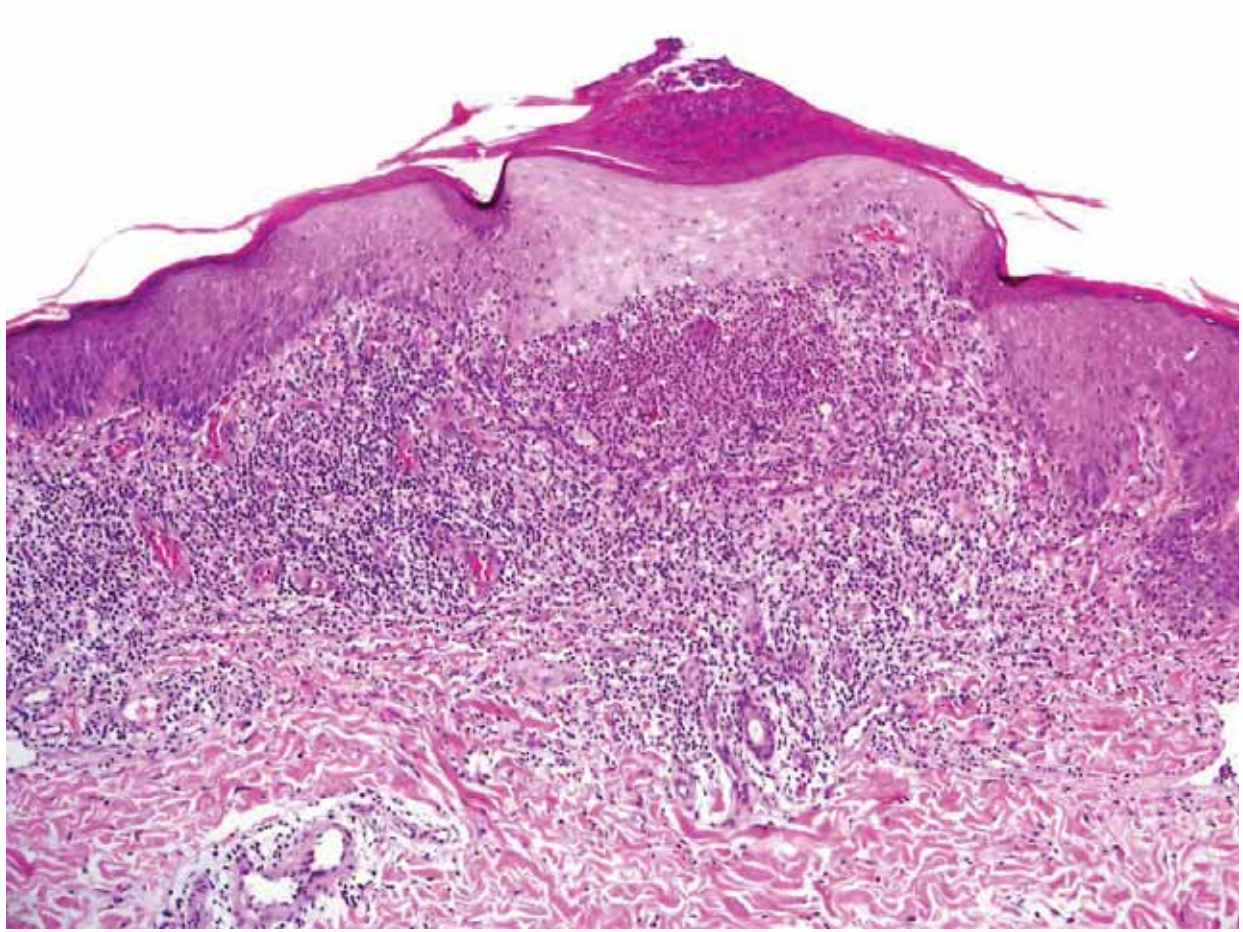
Biopsy 1, papule

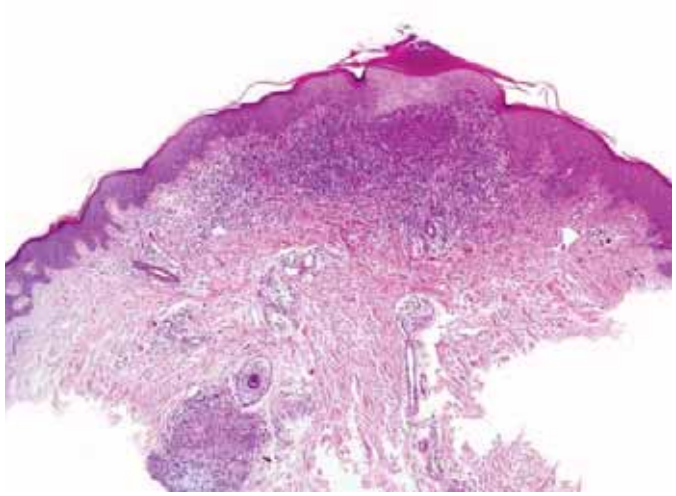




Suppurative and pustular Dermatitis

Biopsy 2, pustular lesion





Negative
Patch tests (tattoo pigments including original dyes, metals, and others)

X-ray and CT-lung
Blood test including ACE, lysozyme

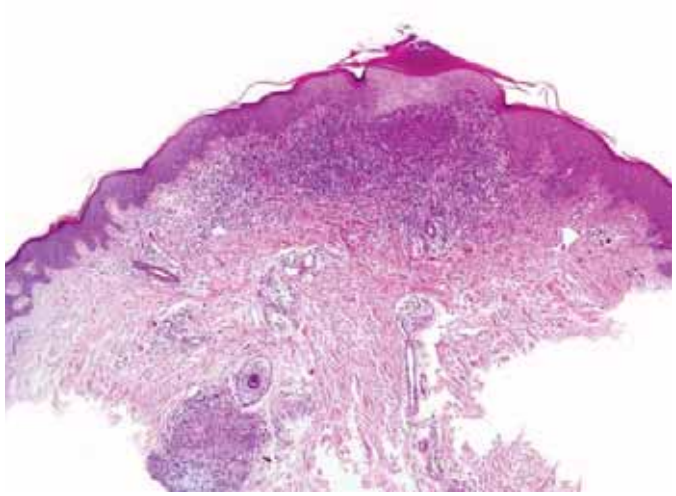
Tine-Test

Histology: Lichenoid, granulomatous, suppurative Dermatitis

Histologic stains for acid-fast-bacilli and fungi: negative

Culture from a swab: Staph. aureus positive

? ? ?



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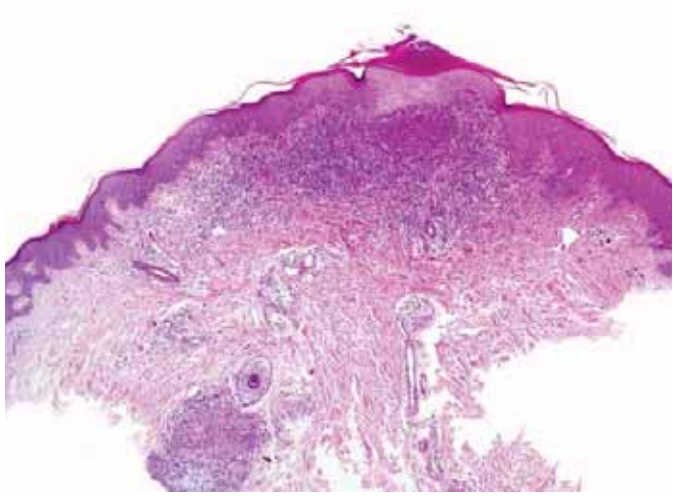
? ? ?



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Tine-Test

Histology: Lichenoid, granulomatous, suppurative Dermatitis

Histologic stains for acid-fast-bacilli and fungi: negative

Culture from a swab: Staph. aureus positive

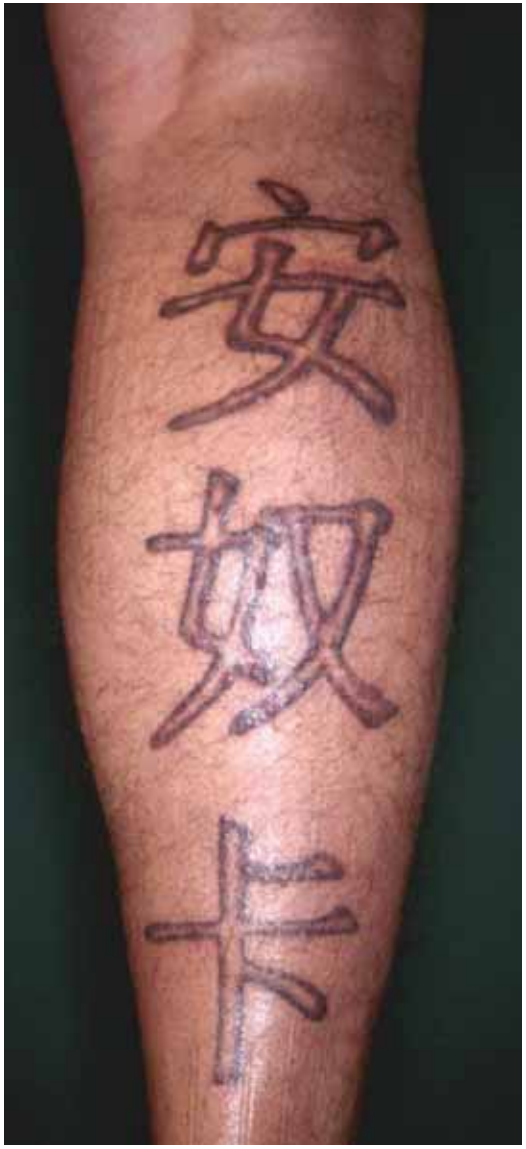
PCR for 16S RNA-gene from unfixed tissue (common to all *bacteria*): negativ

Culture from unfixed tissue (after 3 months): *Mycobacterium chelonae*

Mycobacterium chelonae infection

- Saprophyte found in water, soil, dust and animals
- Infections follow trauma, surgery, contact with contaminated medical instruments (e.g. marker pen, liposuction, mesotherapy), placement of implants (e.g. prosthetic breast implants), acupuncture, botulinum toxin, and tattooing (Local immunosuppresion by metals and azo-dyes)
- Diagnosis: Bacterial culture higher sensitivity than PCR
- Low mortality
- Spontaneous healing

- Immunocompromised patients more susceptible to severe, systemic spread to lung and heart, high mortality



Follow up

Therapeutic recommendation:

Claritrhomycin and ciprofloxacin,

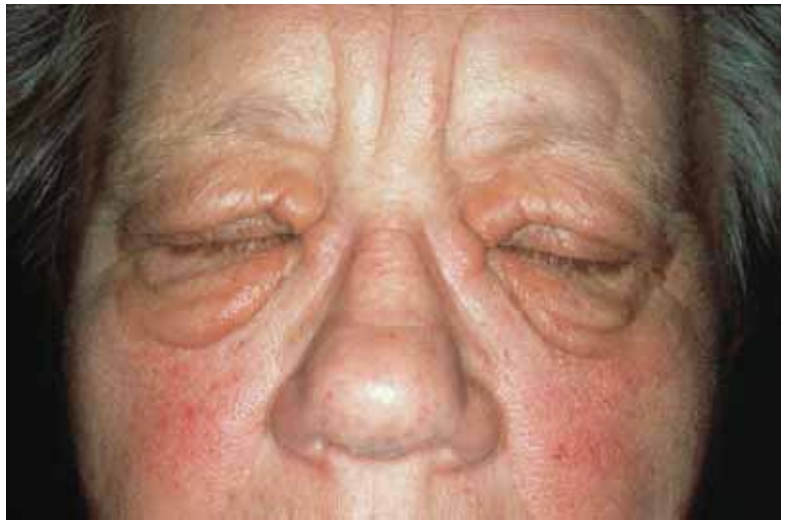
but spontaneous resolution after 5 months

CASE

- 68-year-old woman
- Sudden hearing loss, Hydroxyethyl starch (HES)

- After 15 infusions, 500 ml/d (450 g HES):
  Episodes of generalized, severe, burning pruritus
  on normal appearing skin
  Periocular swelling
- Laboratory parameters widely normal
  including lipidstatus
- After 6 months pruritus decreased
- Swelling persisted for > 4 years

- Patient‘s and family history unremarkable

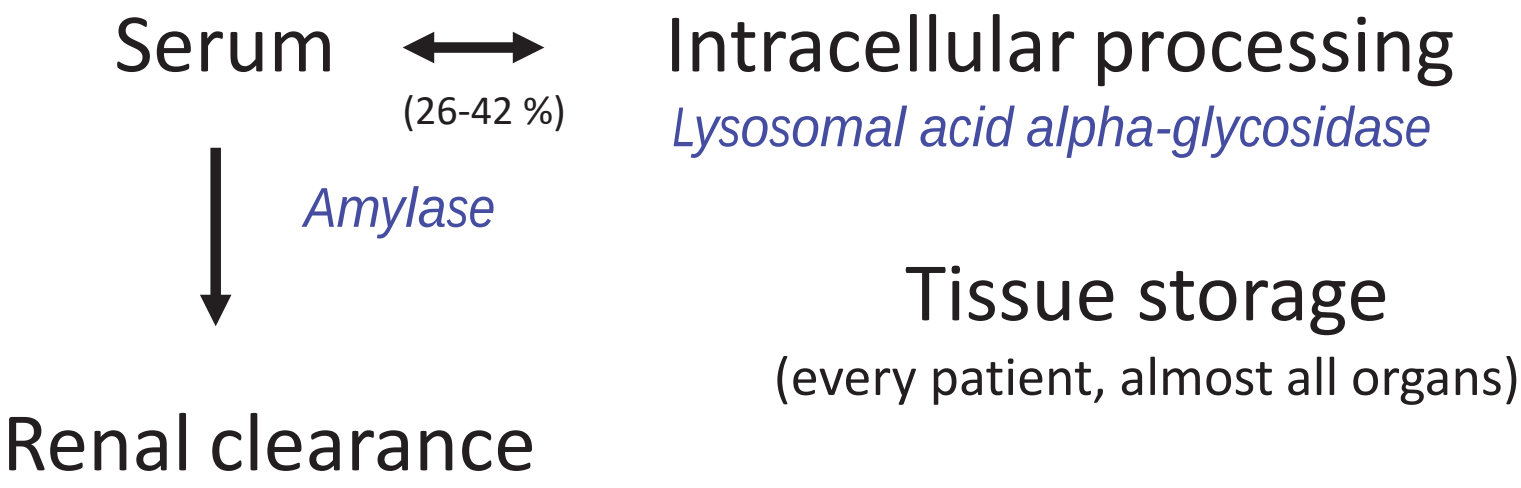


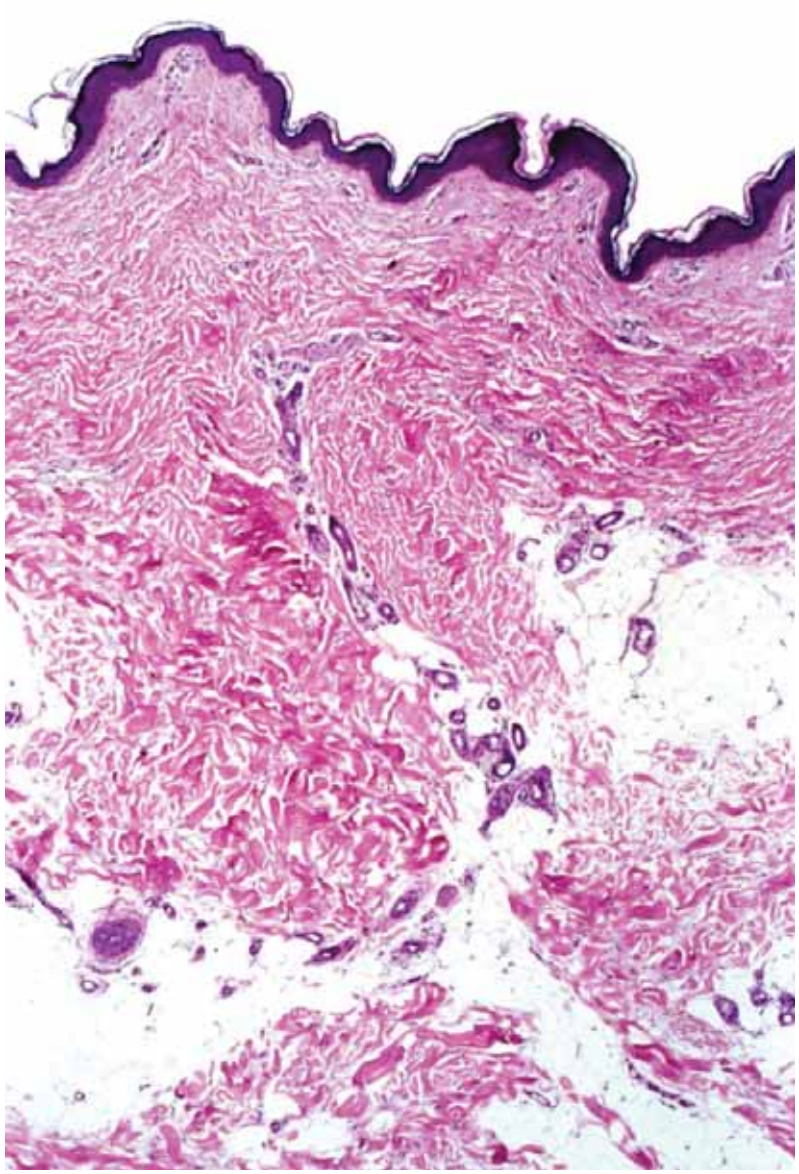
Peter Kiehl †, Hannover

Hydroxyethyl starch (HES)

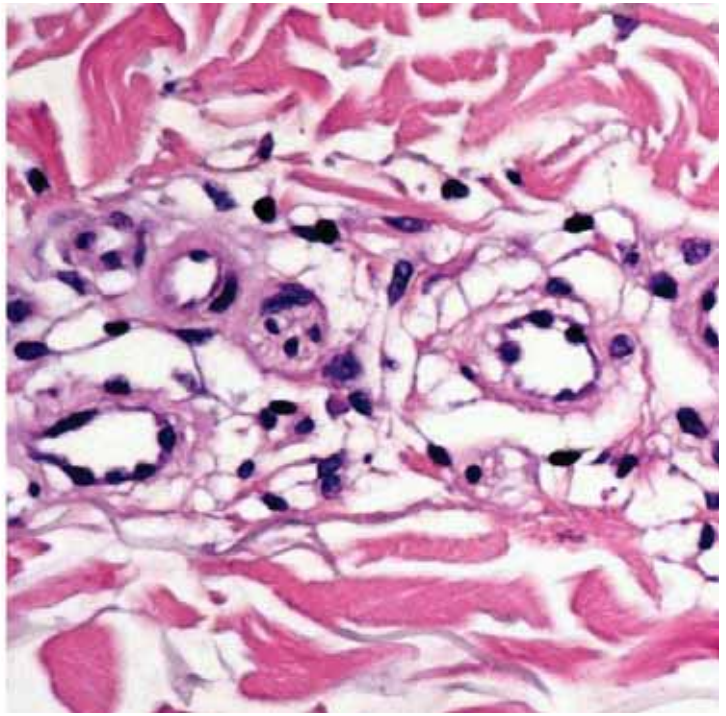
Plasmaexpander used for plasma volume substitution
and improvement of microcirculation

HES - Metabolism



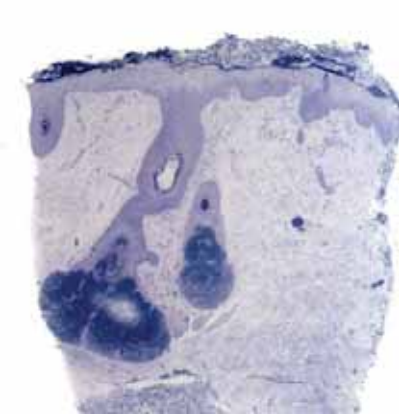


1st Biopsy, pruritic, non-inflamed arm

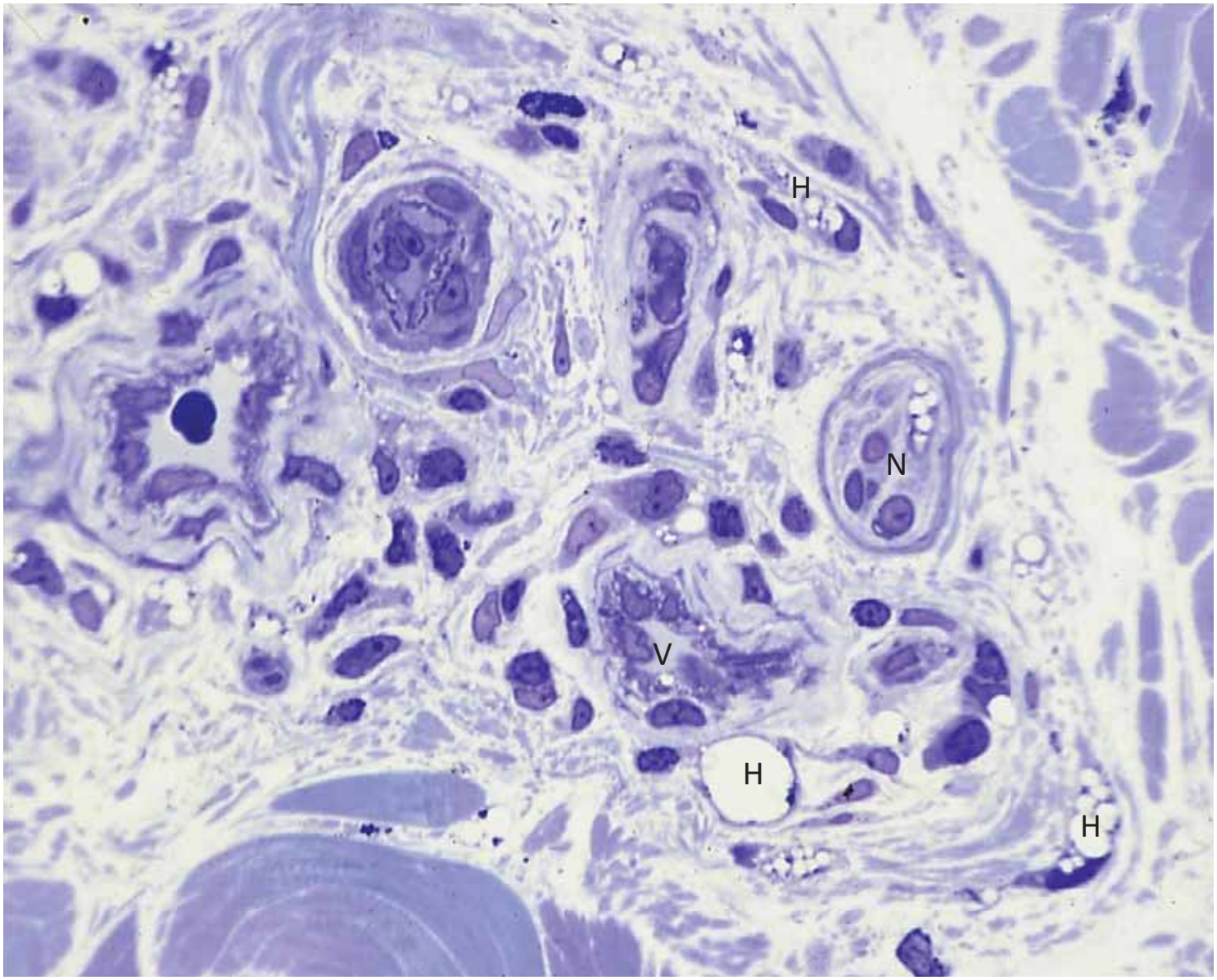


Paraffine section
Histologically - normal skin

Epon-embedding

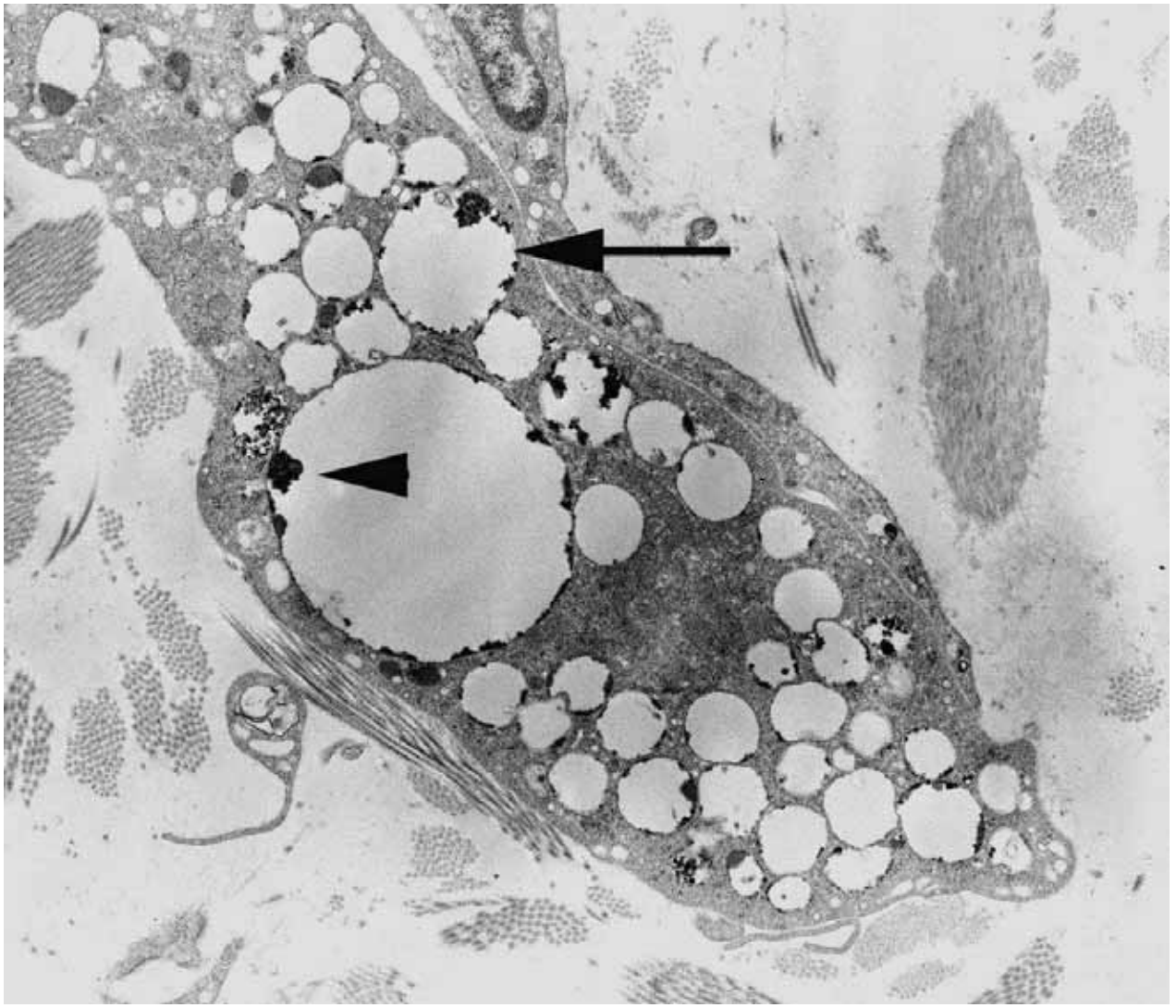


Semithin section (< 500nm),
Toluidine blue

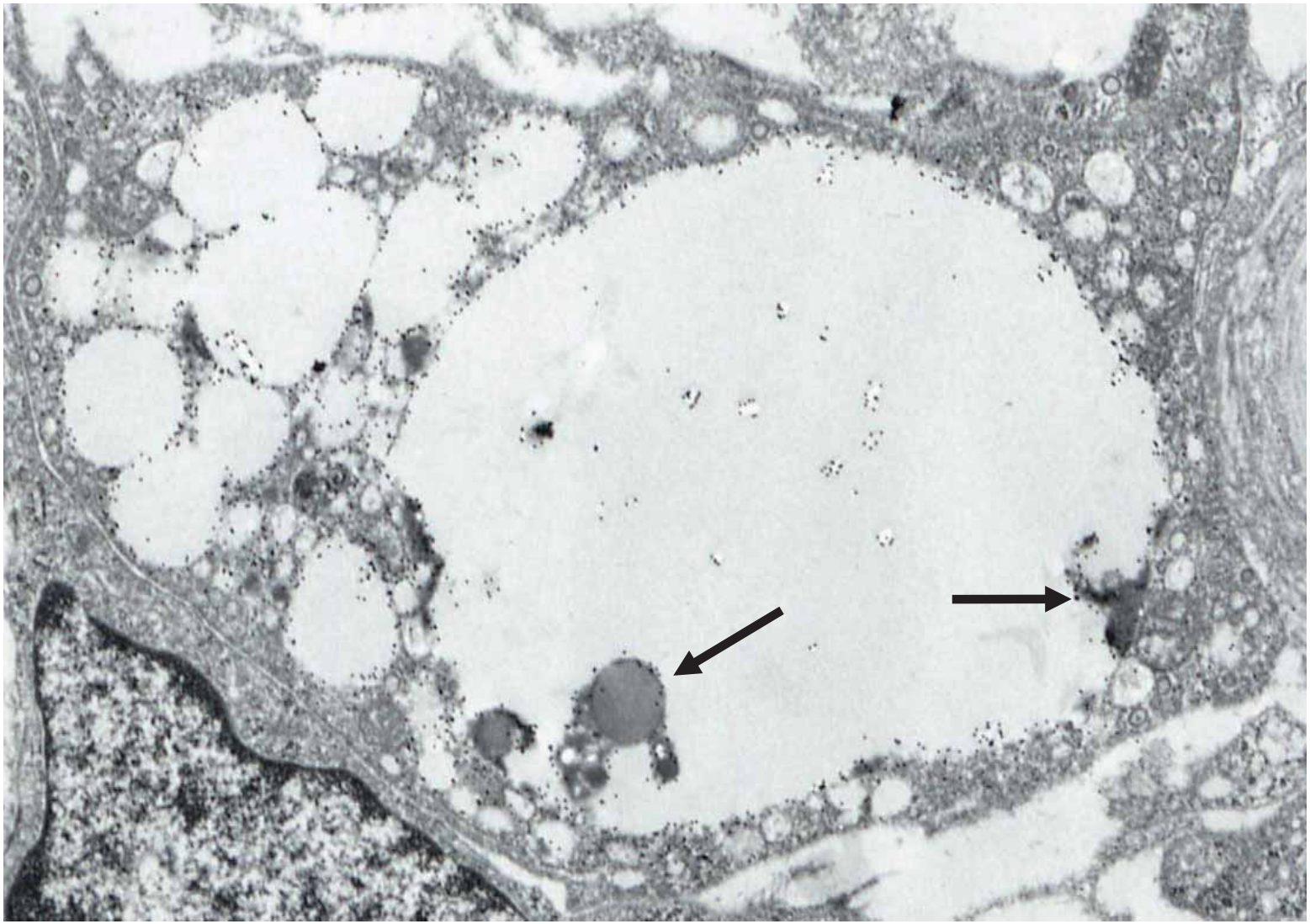


Routine electron microscopy

Ultrathin section
50-100nm

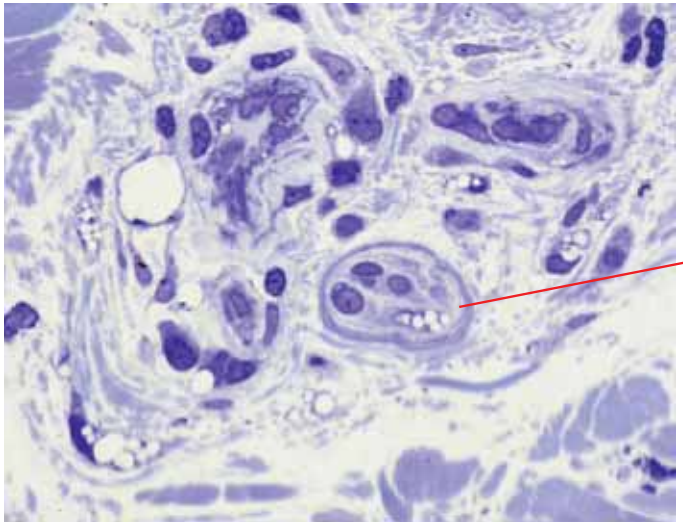


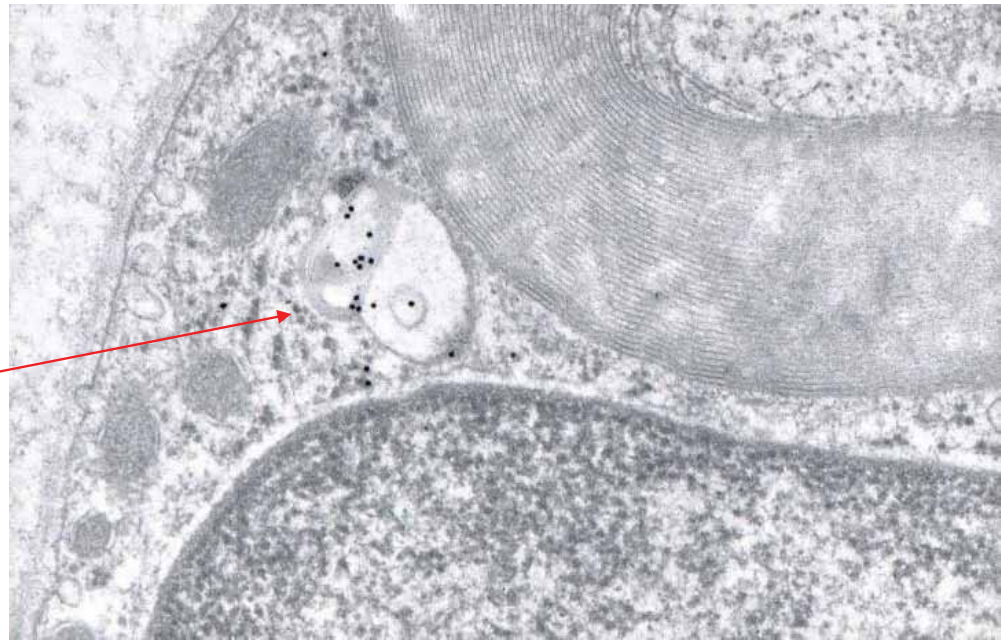
Macrophages, vacuolated with amorphous deposits

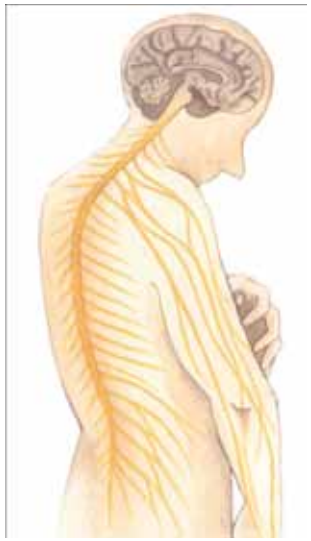


Postembedding Immuno-EM, Gold-labelled HES-Antibodies

Only patients with pruritus







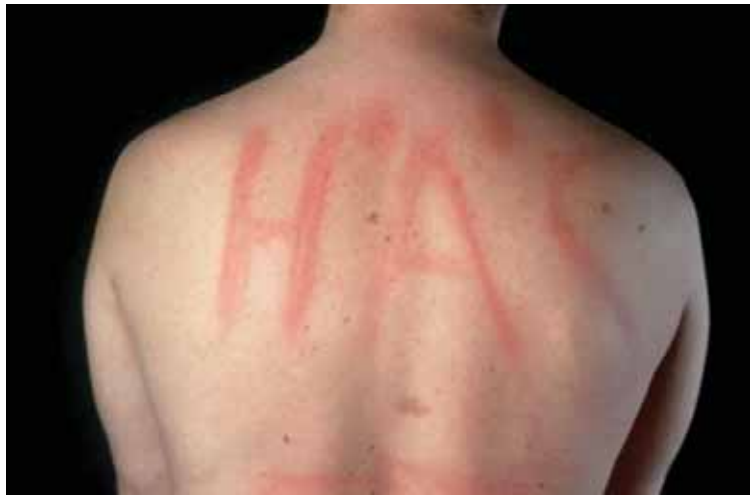
Metze D, Reimann S, et al.Efficacy and safety of naltrexone, an oral opiate receptor antagonist, in the treatment of pruritus in internal and dermatological diseases.
J Am Acad Dermatol, 41:533-539, 1999

Sonja Ständer
(Reimann)

PRURITUS
KompetenzZentrum

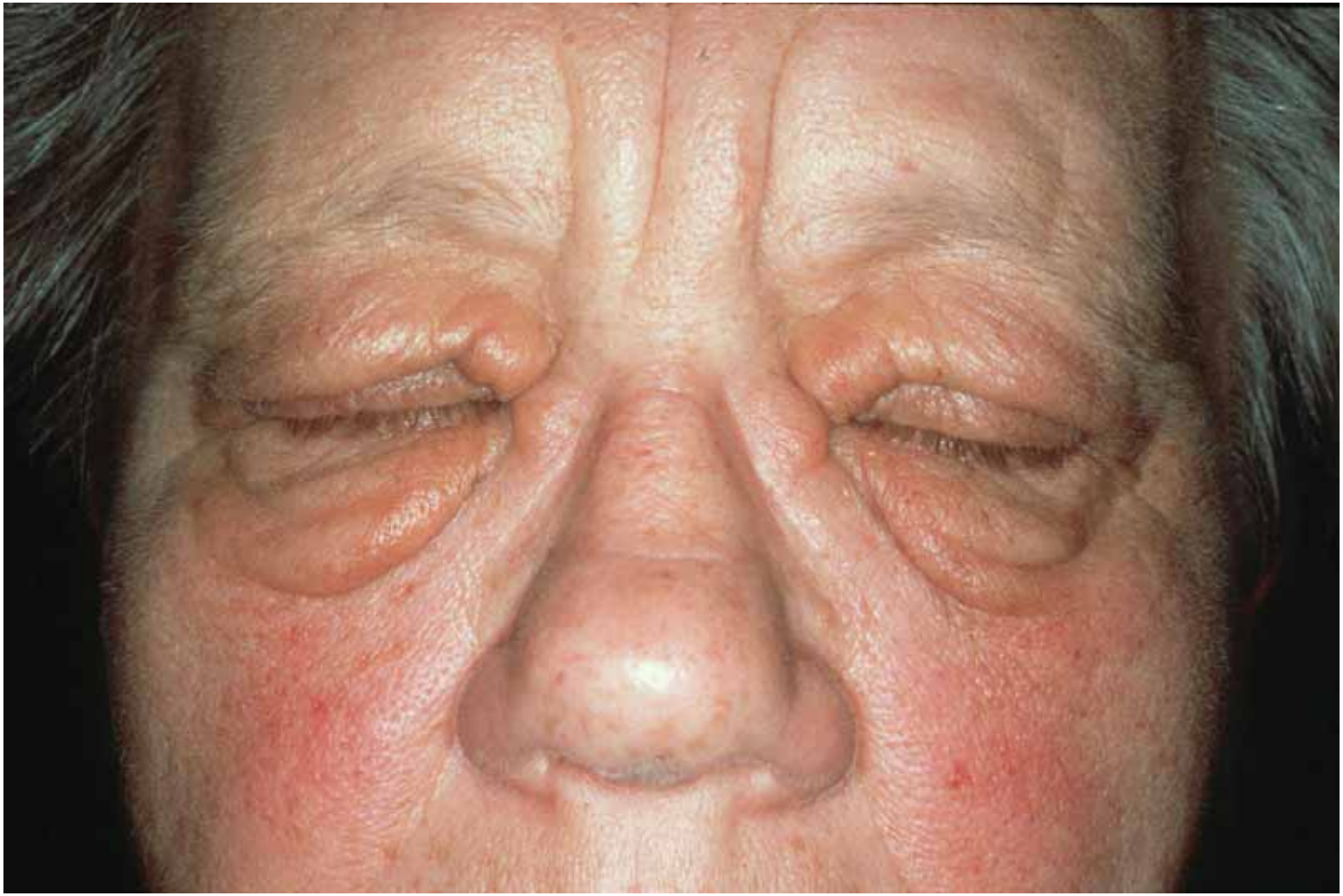
HES-induced pruritus

- Risk depends on cumulative dosage (32%, >400 g)
- Symptoms start days or weeks after last infusions
- Burning itch
- Pruritic episodes triggered by warm water, friction, physical stress (*Alloknesis*)
- Very disturbing, quality of life reduced
- Symptoms persist for months (years)

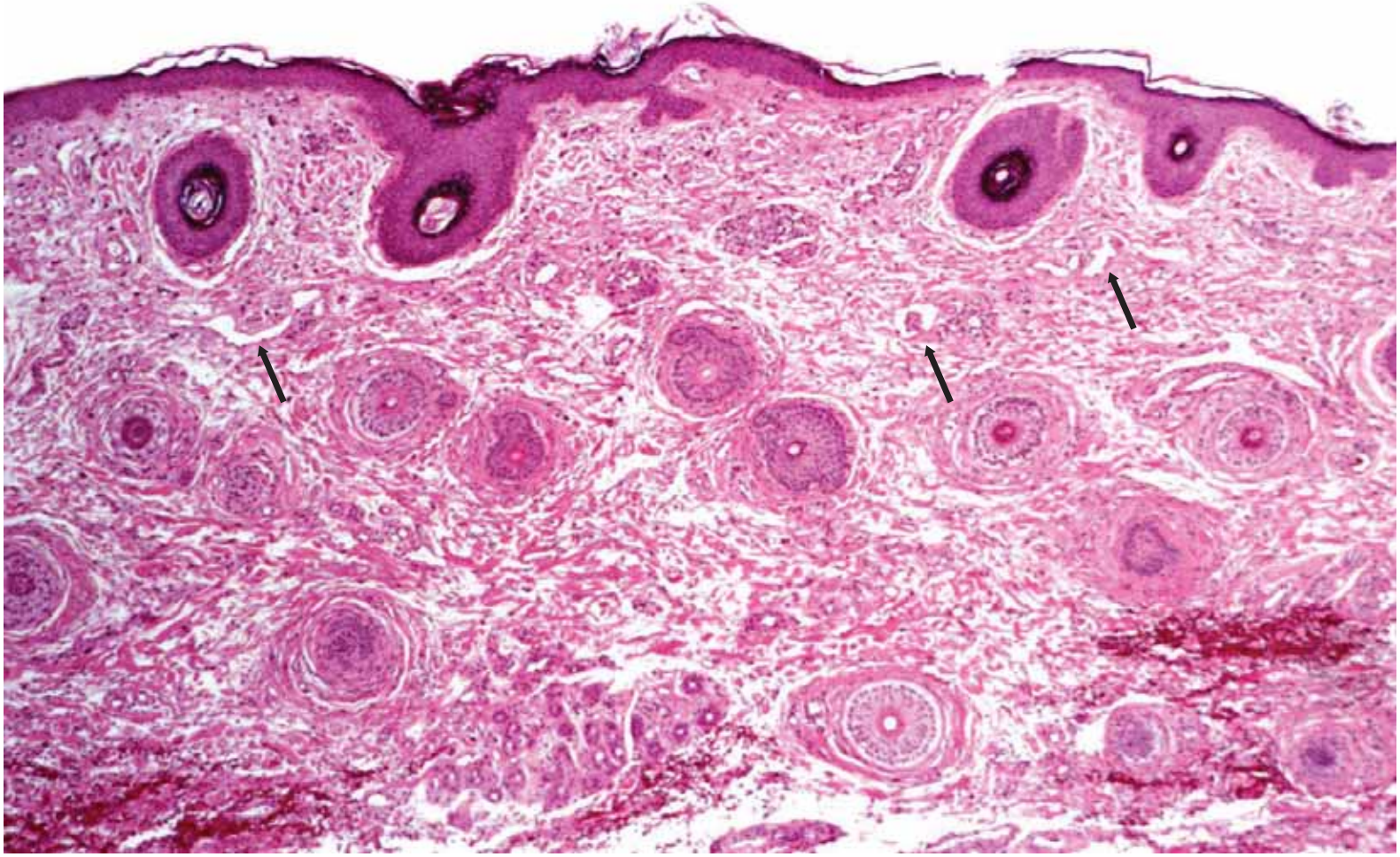


Clinical examination: no visible skin changes,
red dermographismus possible
Treatment: Capsaicin, polidocanol, naltrexone,
gabapentin …
(no effect of antihistamines, steroids, UV irradiation, ….)

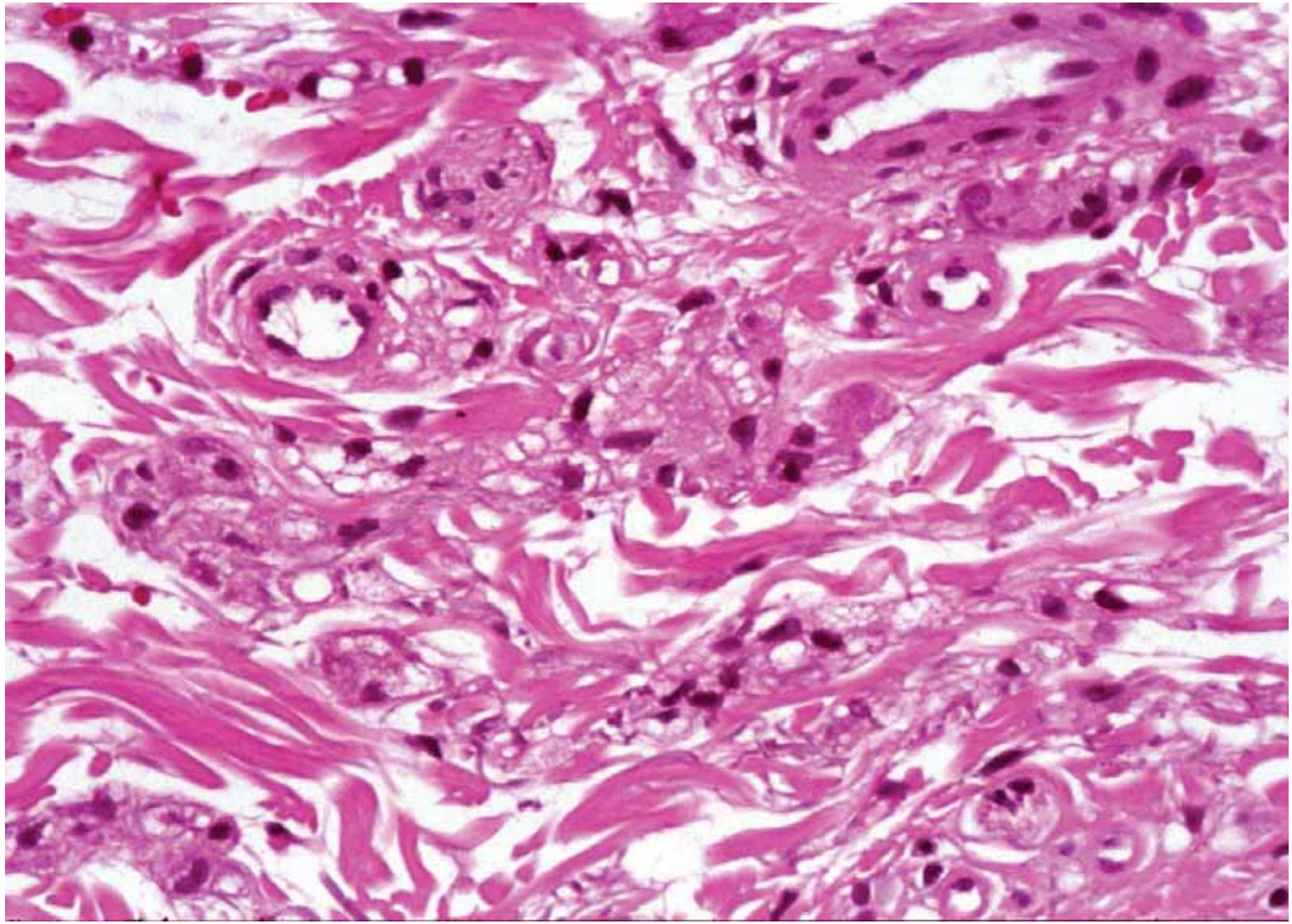
D. Metze, D. Reimann, et al, Br J Dermatol, 1997
S. Ständer, et al. Br J Dermatol, 2005
S. Ständer, et al, Acta Derm Venereol, 2013



2nd Biopsy from periorbital skin – swelling ?

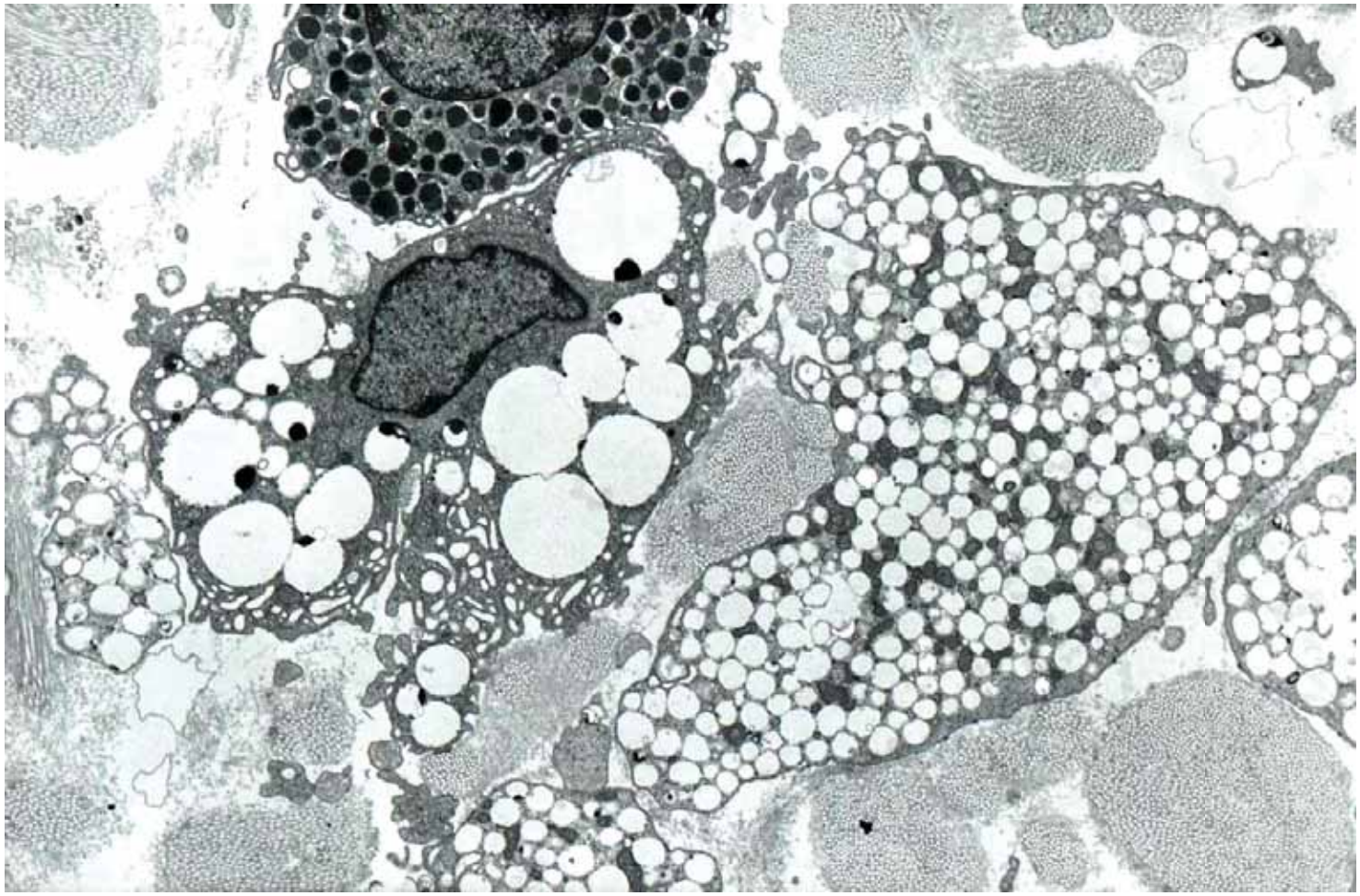


Diffuse infiltrate of macrophages, dilated lymphvessels



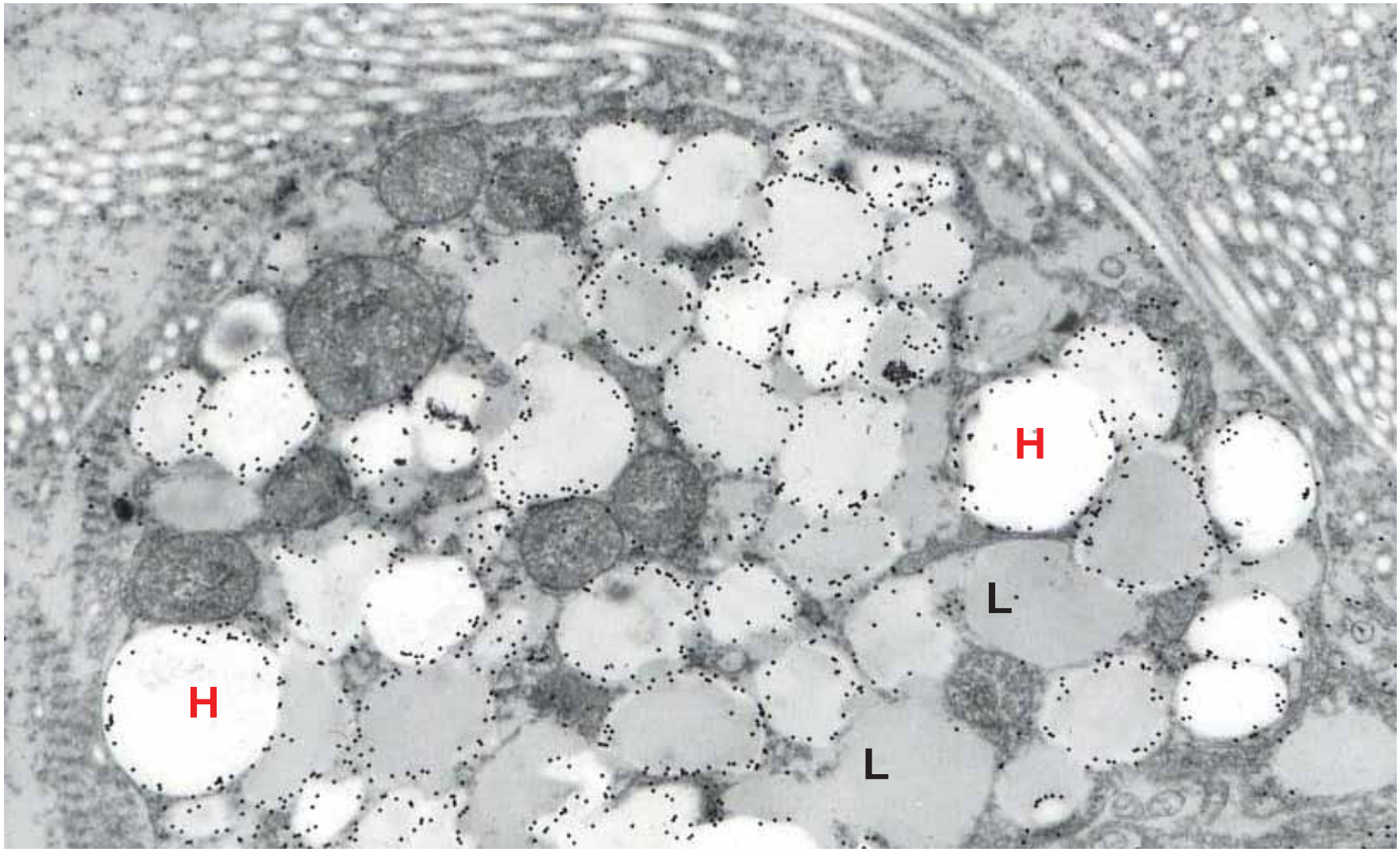
Xanthomatization of macrophages

Mast cell



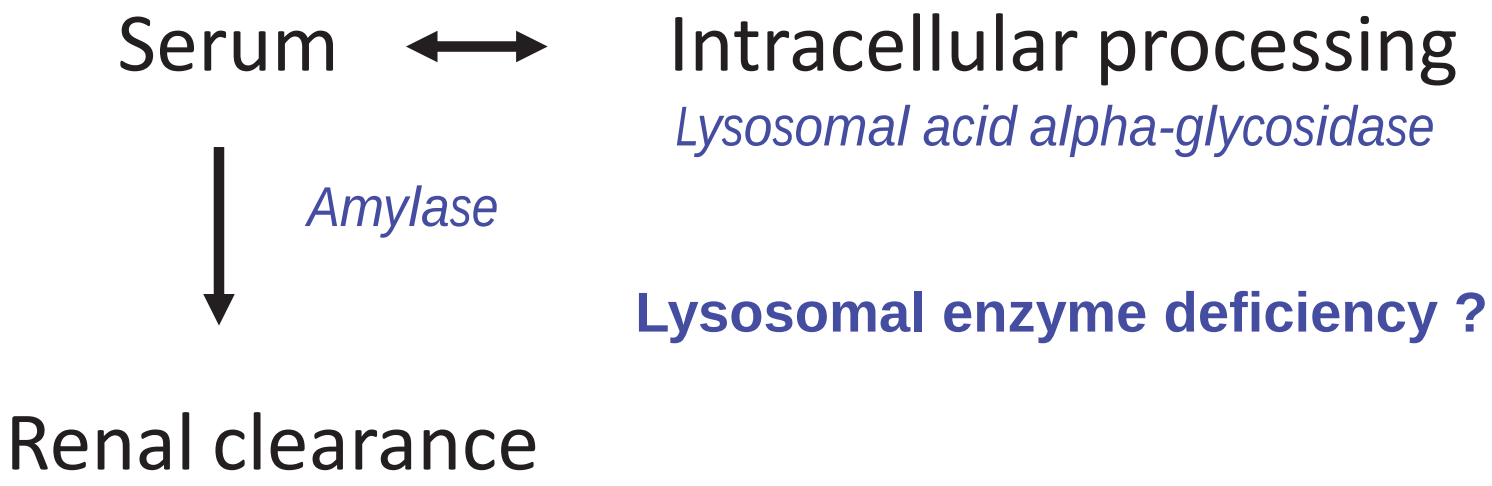
Macrophages with HES storage

Macrophages with Xanthomatization



HES-reactive Vacuoles Lipidvacuoles *Anti-HES-Immunogold*

HES - Metabolism



Cultured fibroblasts

Enzymatic activity of acid alpha-glycosidase reduced (50%)

Pompe‘s Disease (Glycogen storage disease), heterozygous carrier status

Residual enzyme activity prevents glycogen accumulation and clinical symptoms (heart, skeletal muscles)

Impaired lysosomal degradation of HES →

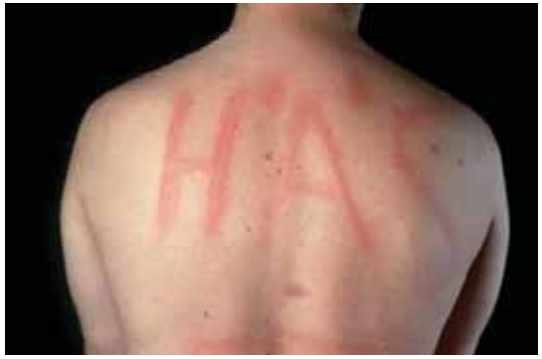
Endothelial cells – lymphedema

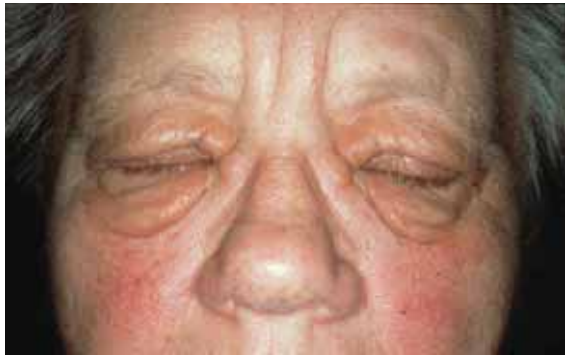
Macrophages – degenerative changes

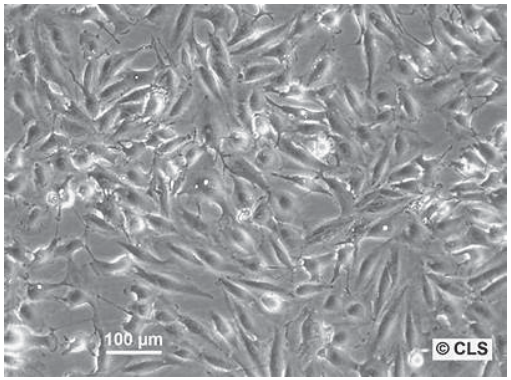
→ Xanthomatization

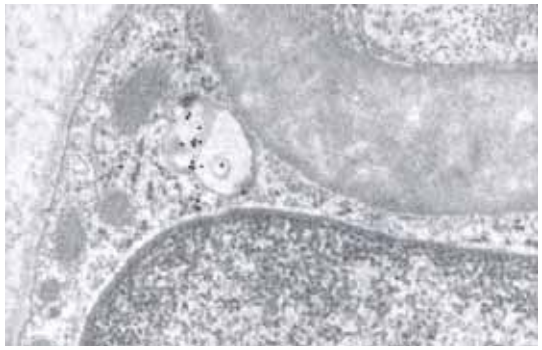
P. Kiehl †, D. Metze, et al,
Br J Dermatol 138:672-677, 1998

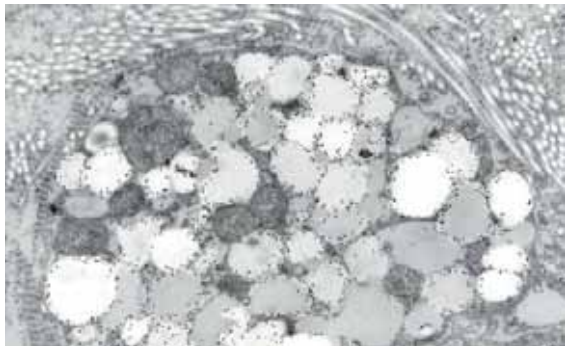
HES-associated pruritus with periorbital swelling in Pompe‘s disease











Enzymatic activity of acid alpha-glycosidase

NIRK

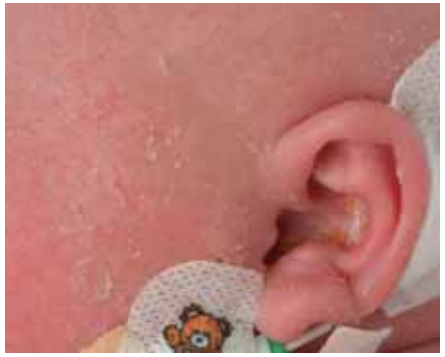
V. Oji,
K. Süßmuth,
H.Traupe

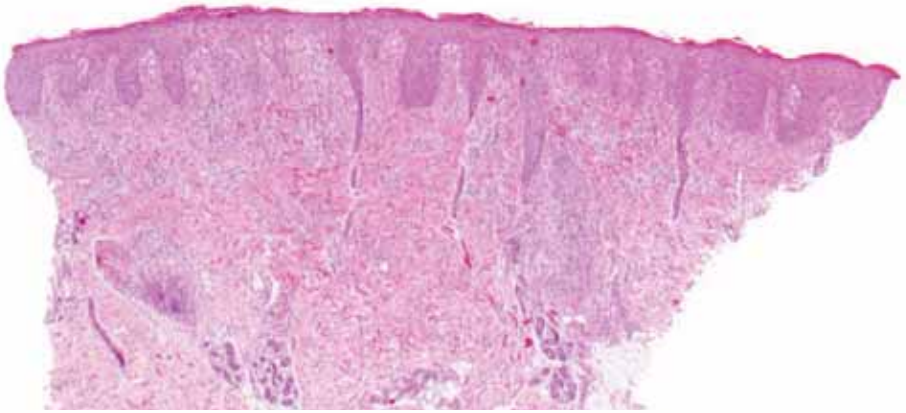
10-month-old infant, female, family history unremarkable, parents non-consanguineous

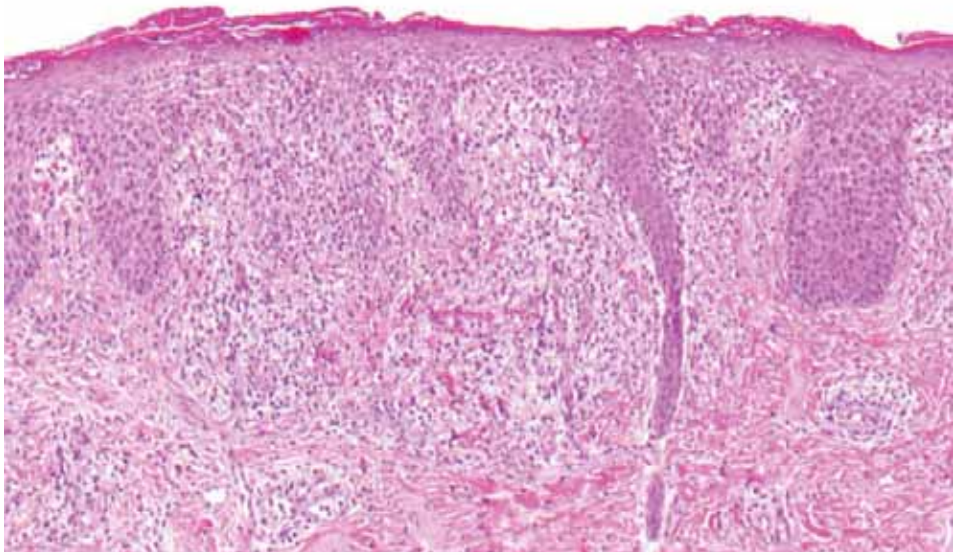
Erythroderma with translucent and fine scaling, double-sided syndactyly, failure to thrive

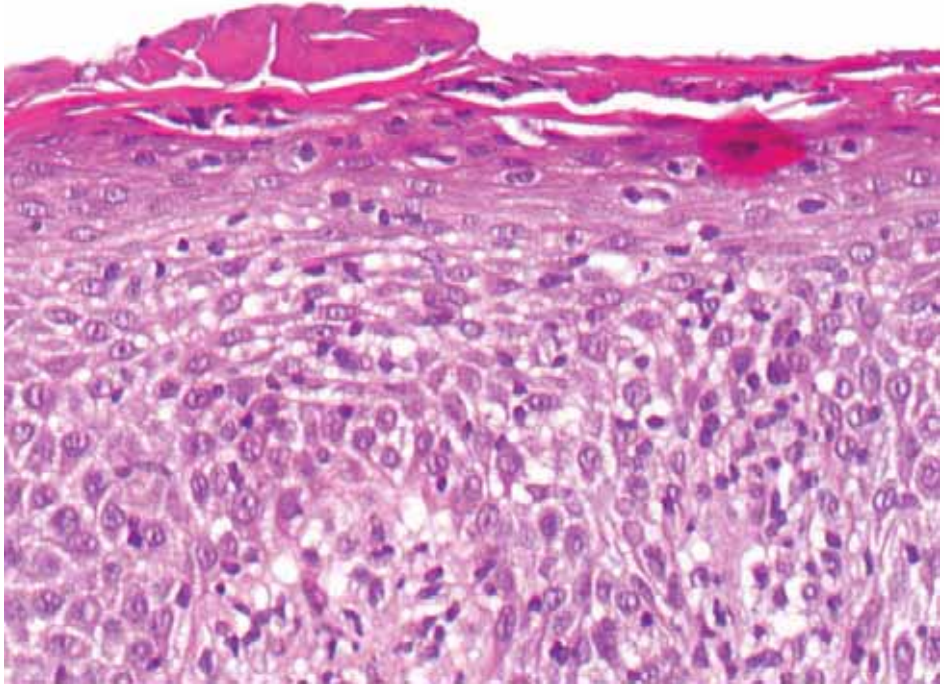
Immunodeficiency with recurrent systemic infections (influenza, pyelonephritis, pneumonia, S. aureus and E.coli sepsis), signs of immune dysregulation, increased serum IgE, macrophage-activation, hepatosplenomegaly

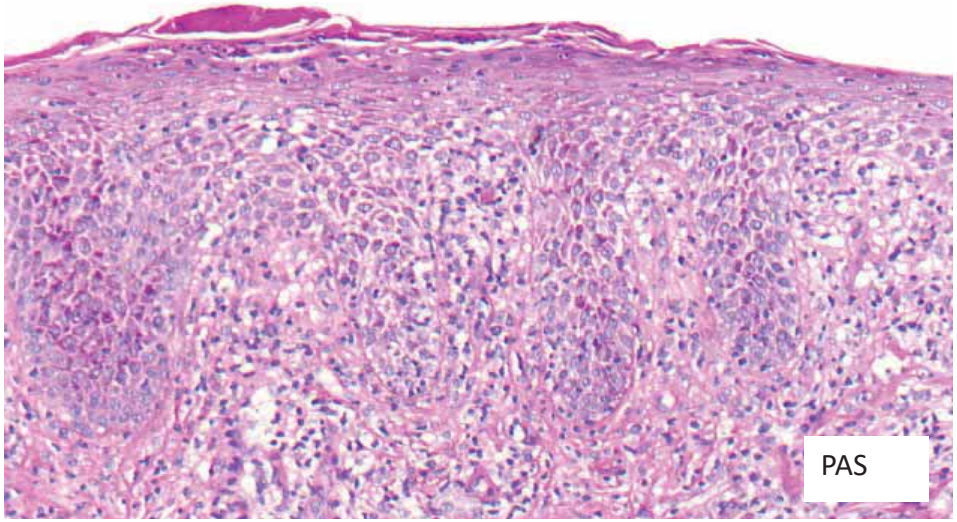
3 months later patient died of P. aeruginosa sepsis.







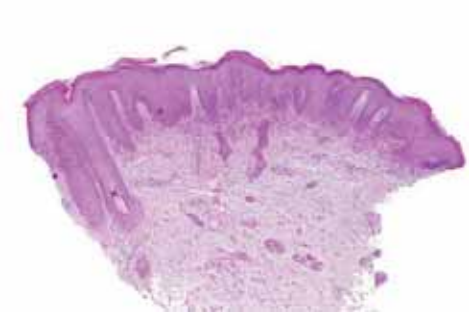


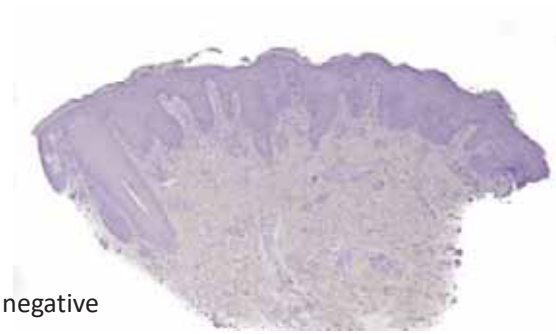

PAS

Psoriasiform Pattern in a Newborn/Child

- Comèl-Netherton Syndrome

IHC for Lympho-Epithelial Kazal Type Inhibitor (LEKTI)

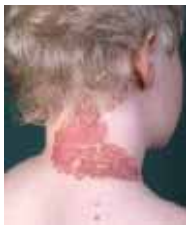


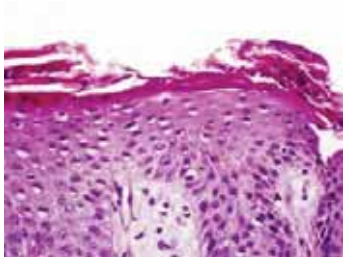


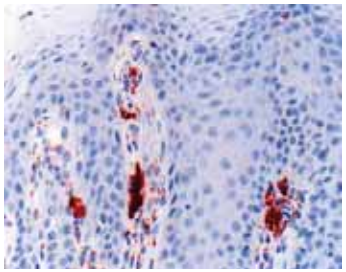
LEKTI negative

- CHILD Syndrome

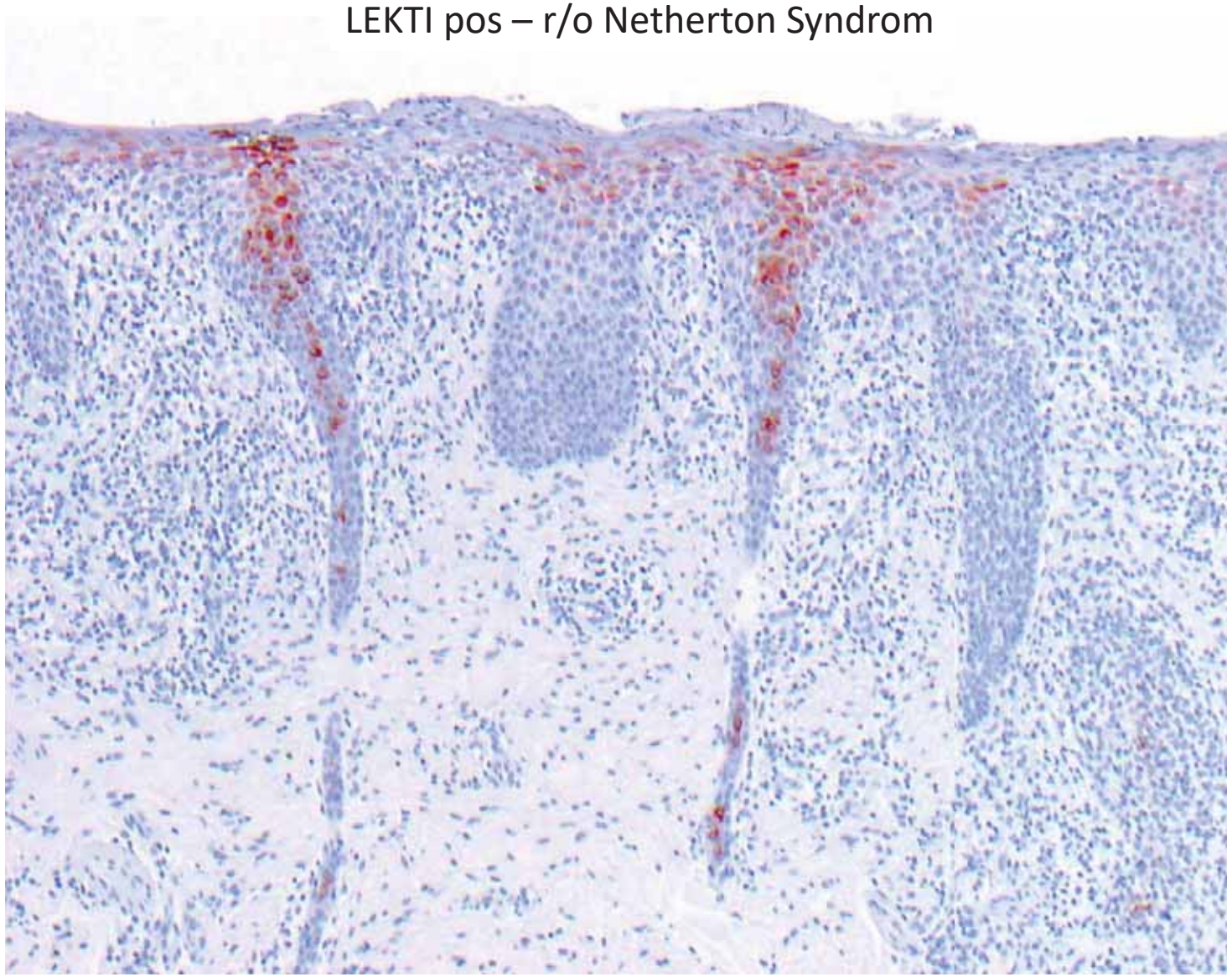
IHC for Adipophylin







LEKTI pos – r/o Netherton Syndrom

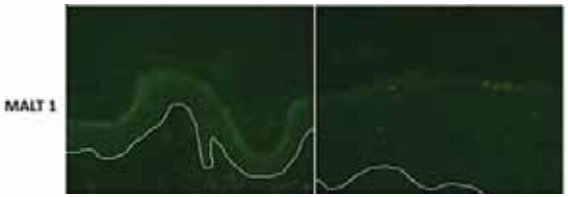


MALT1 deficiency mimicking Netherton- and Omenn syndrome

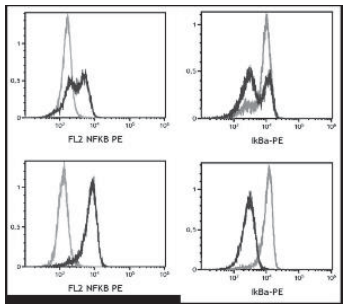
H. Wiegmann; J. Reunert, D. Metze; T. Marquardt,
V. Kunde, S. Ehl, D. Foell, I. van den Heuven,
V. Oji; H. Wittkowski. BJD, 2020

Department of Dermatology, Department of Pediatrics, Department of Pediatric Rheumatology and Immunology; University Hospital Muenster
Center for Chronic Immunodeficiency, University of Freiburg, Germany

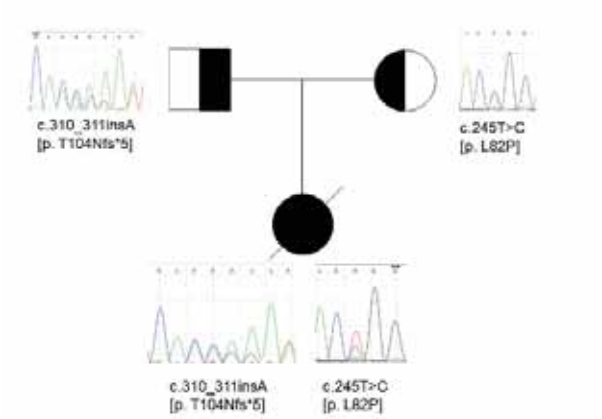
LABORATORY
Mild B-lymphopenia, hypogammaglobulinemia, absent IgA and IgM, and absent titers for tetanus, pertussis and diphtheria after two immunizations.
Leukocytosis (54.000/µl), eosinophilia (8.000/µl), highly increased IgE (30.000 IU/ml), thrombocytopenia.
Intermittent macrophage-activation markers: sCD25 (13.240 U/ml), ferritin (1.200 µg/l), S100A8/A9 (62.000 ng/ml).
Hypofibrinogenemia, hypertriglyceridemia



Control skin Patient skin



Flow cytometry analysis of NFκB activation inpatient T-cells. 5 × 105 PBMC were stimulated with PMA and ionomycin for 15 minutes at 37°C. Analysis of CD4+ cells in comparison to a healthy control revealed deficient phosphorylation of NF-κB p65 (left panels) and impaired degradation of IkB (right panels)in patient cells.

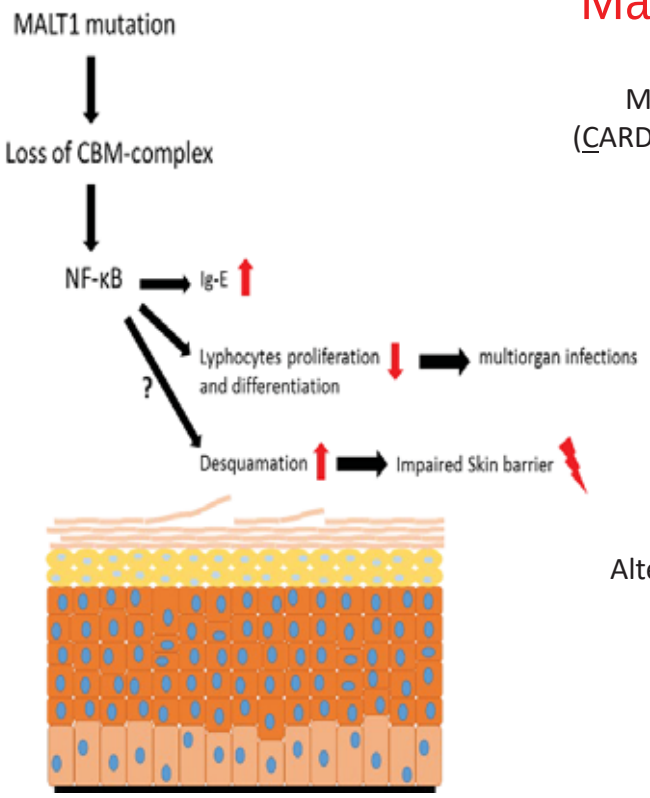


Family tree and results of the Sanger sequencing. Two compound heterozygous loss of function mutations in MALT1 (Exon 2 c.245T>C, Exon 2 c.310_311insA). Both parents heterozygous for one of the variants.

No mutation of SPINK5 and RAG1/RAG2 Mutation

Malt1 Deficiency (OMIM#615468)

MALT1 proteinase is part of the CBM (CARD11-BCL10-MALT) signalosome complex that activates NF κB



Combined immunodeficiency: adaptive and innate immune responses defect

Altered epidermal differentiation

Malt1 Deficiency (OMIM#615468)

- Loss-of-function mutations in MALT1 gene encoding proteinase MALT1

  → reduced NF-κB activation
  → defect adaptive and innate immune responses (combined immunodeficiency)
  → dysfunction of the epidermal differentiation and skin barrier

- Postpartal periodic erythroderma with scaling (rare, 3 cases)
- Failure to thrive, hypernatremic dehydration

- Immunodeficiency with recurrent systemic infections
  Signs of immune dysregulation and macrophage-activation,
  increased serum IgE

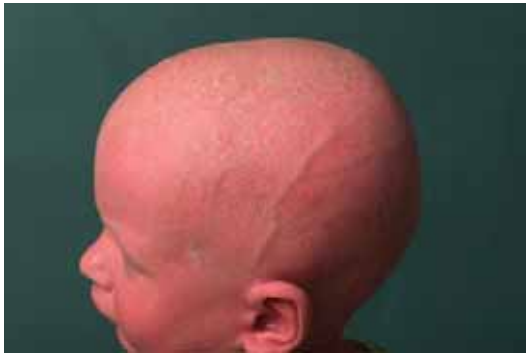
- Histology: Psoriasiform Dermatitis
  IHC: Loss of MALT1 in the epidermis

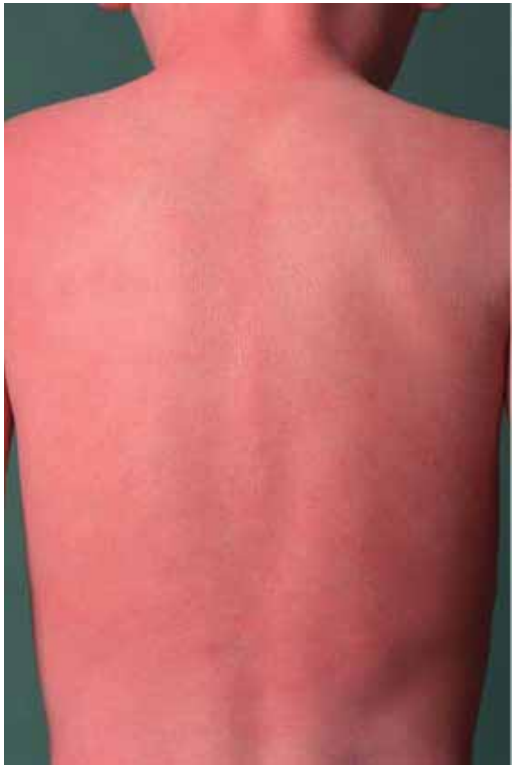
- DDx Netherton (SPINK5 Mutation)
  Omenn syndrome (RAG1/RAG2 Mutation)

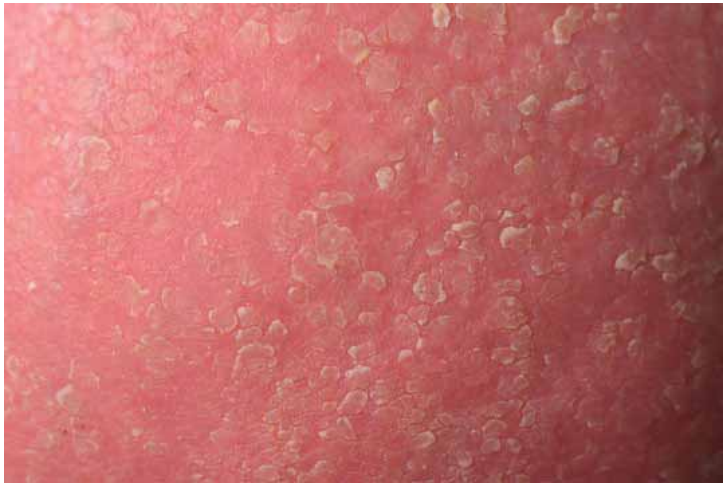
NIRK

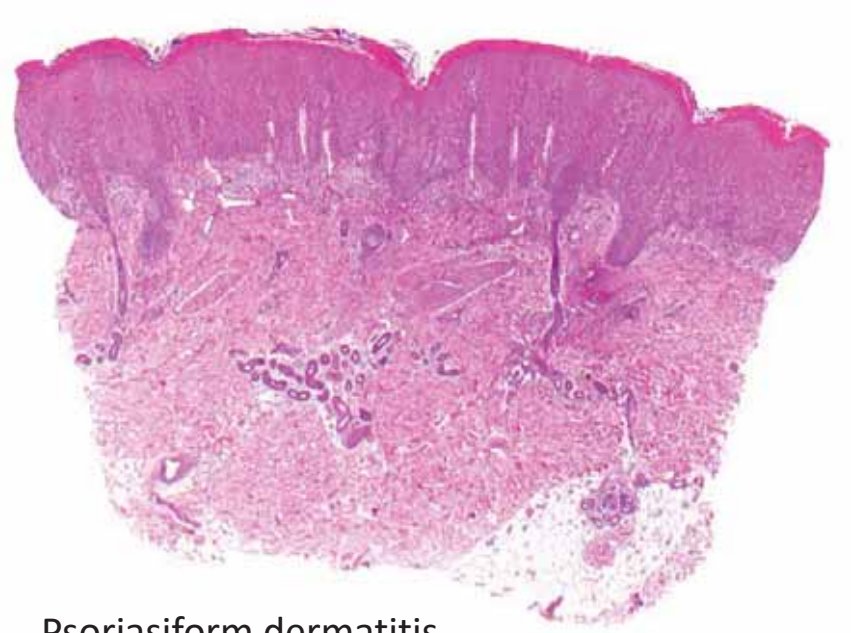
V. Oji,
K. Süßmuth,
H.Traupe

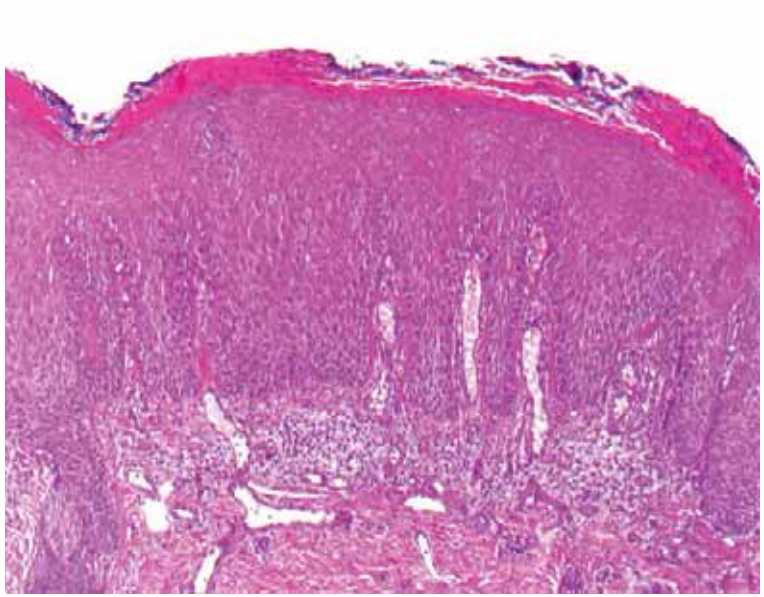
5-year-old boy
Psoriasiform Erythroderma (highly pruritic)
Palmoplantar Keratoderma (mild)
Atrichia, Nail dystrophy
Growth retardation
Recurrent infections and sepsis
Therapy: Ustekinumab



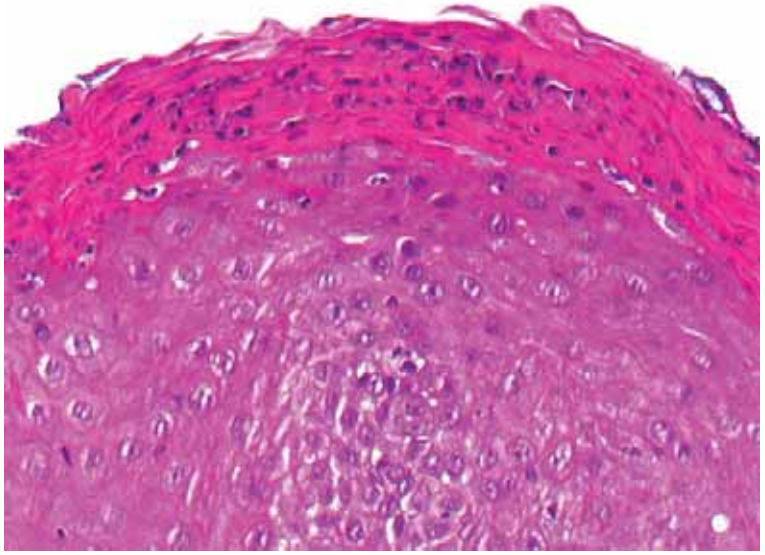


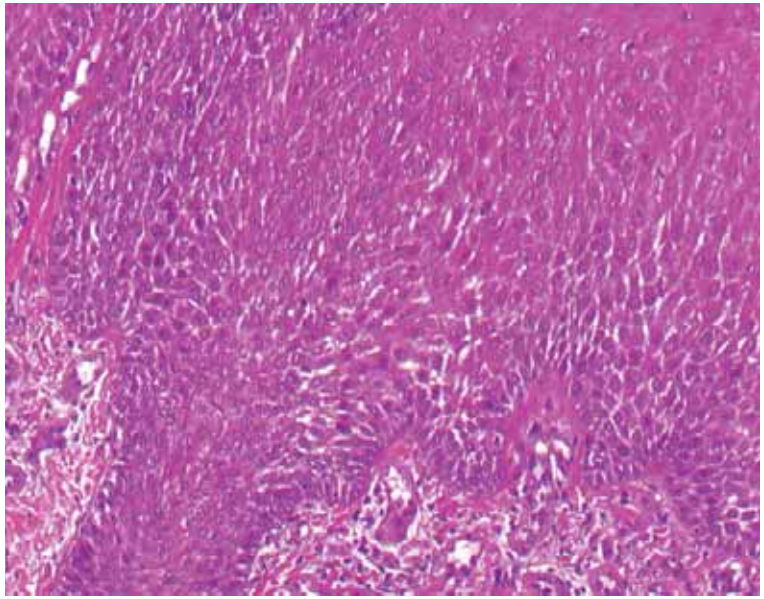




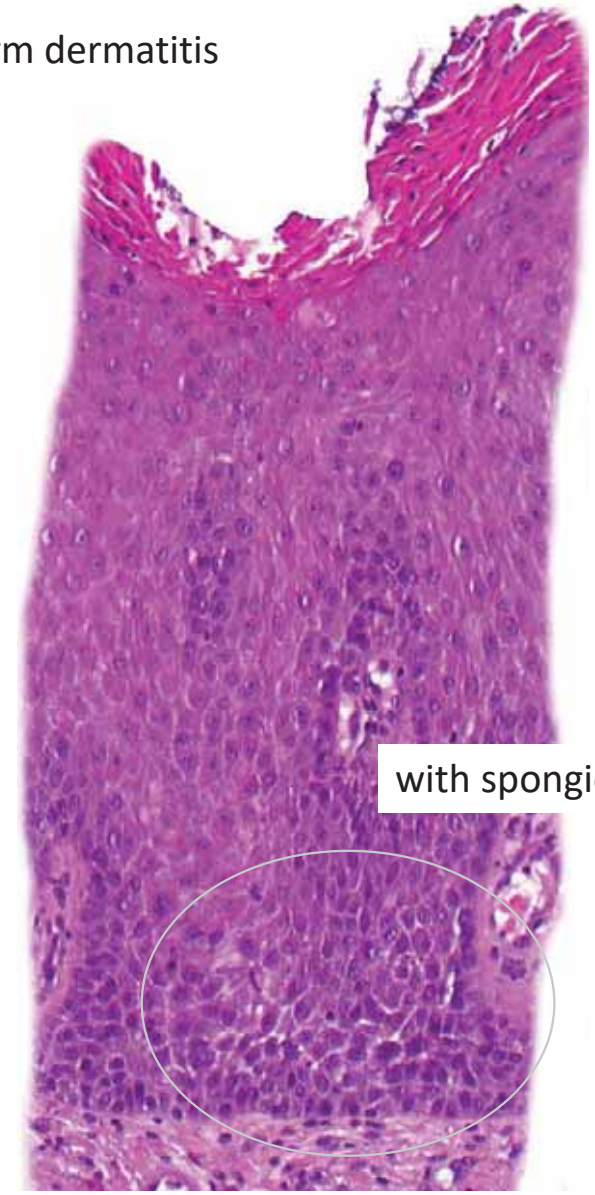


Psoriasiform dermatitis

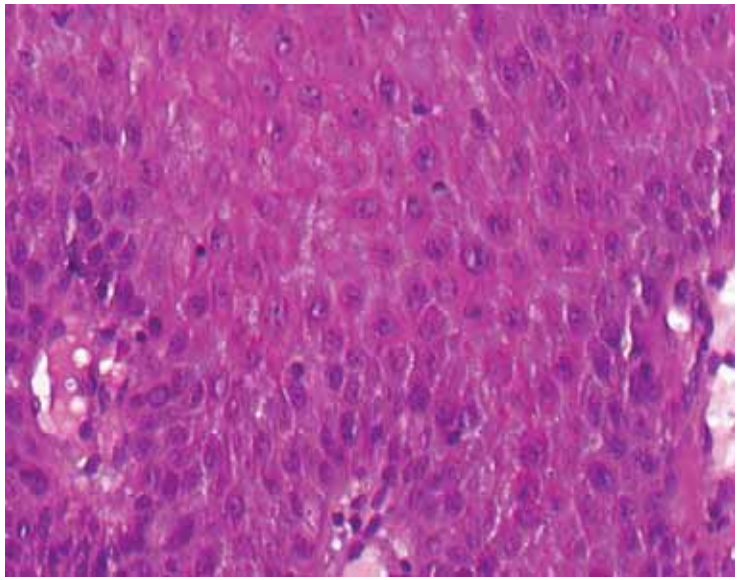


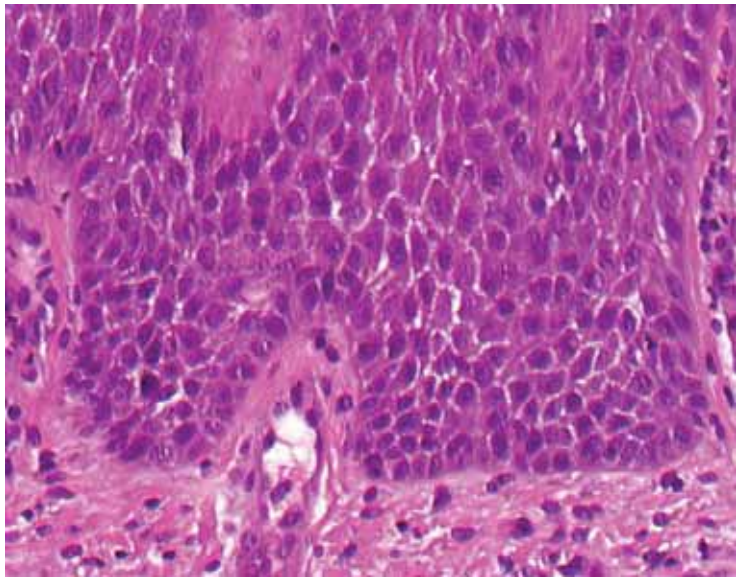


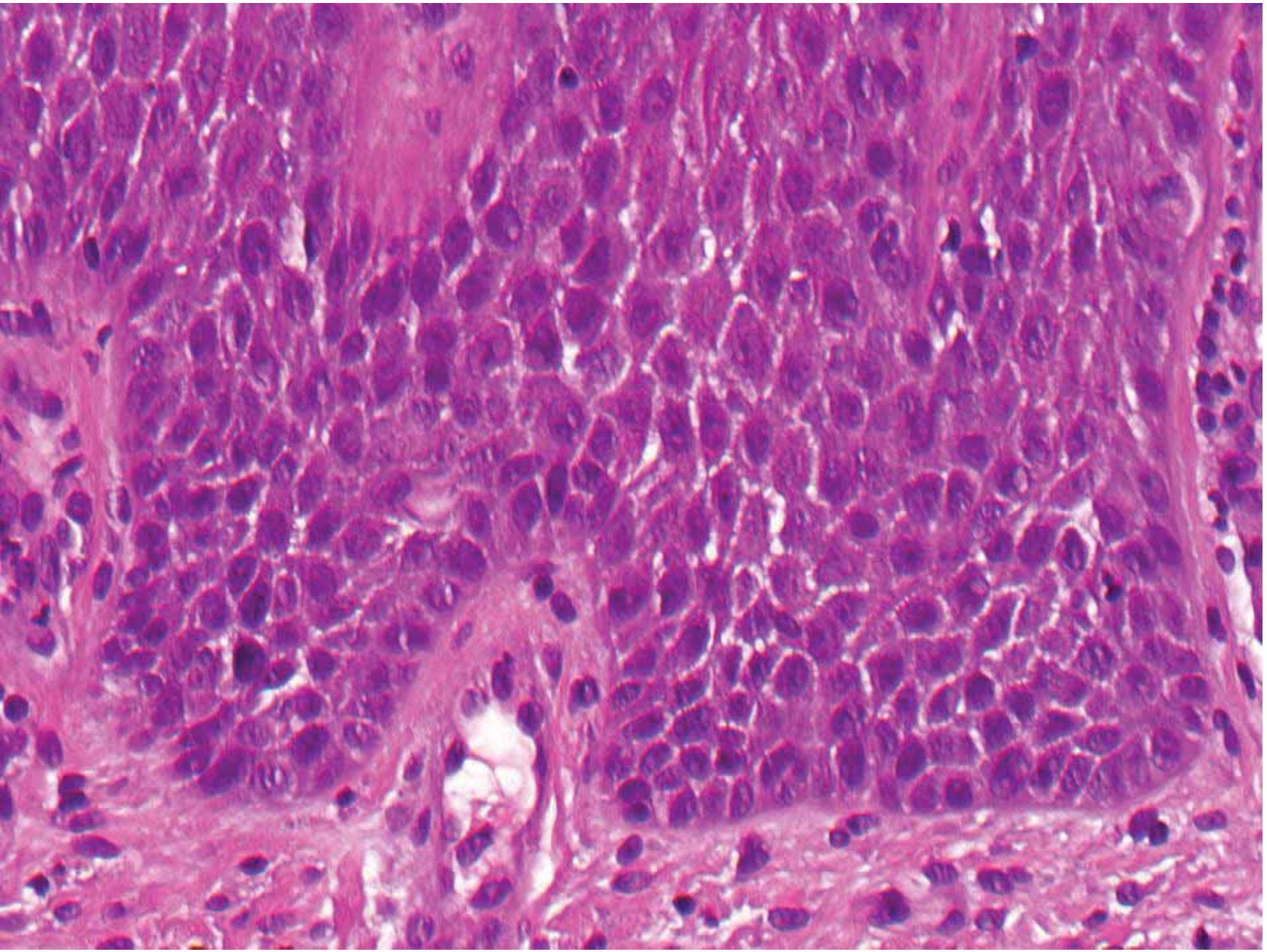
Psoriasiform dermatitis



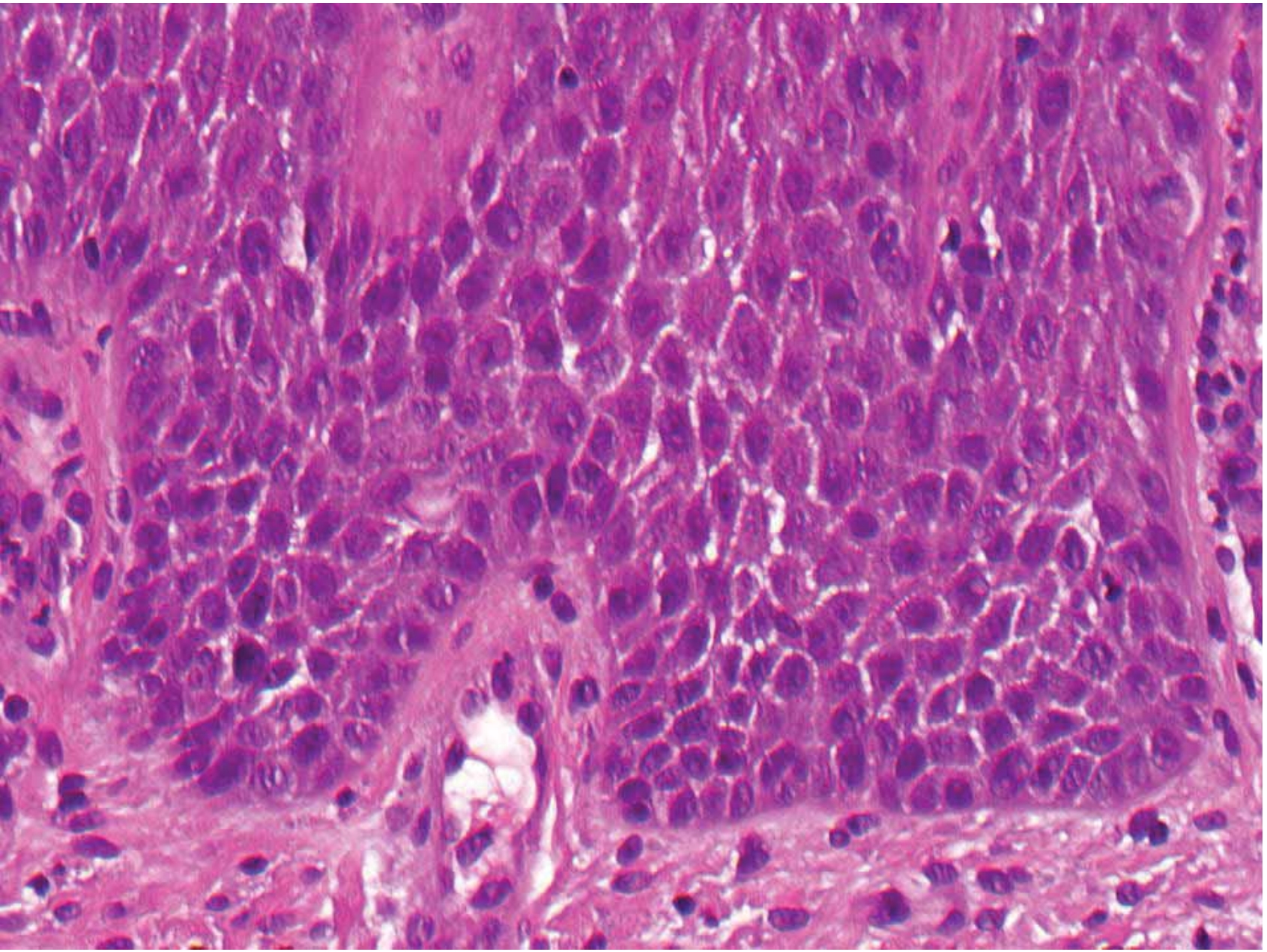
with spongiosis ?







No spongiosis
but
special type of acantholysis



Desmosomal Akantholysis

Widening of intercellular spaces
Hypereosinophilia of keratocytes

DDx Spongiosis: pale keratocytes, vesicles, crusting

Psoriasiform Pattern in a Newborn/Child

• Comèl-Netherton Syndrome	LEKTI
• CHILD Syndrome	Adipophylin
• MALT 1 Deficiency Syndrome	MALT 1

+ Akantholysis of Desmosomal Type

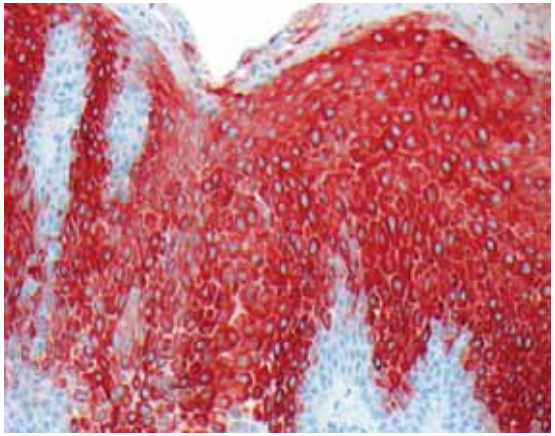
Psoriasiform Pattern in a Newborn/Child

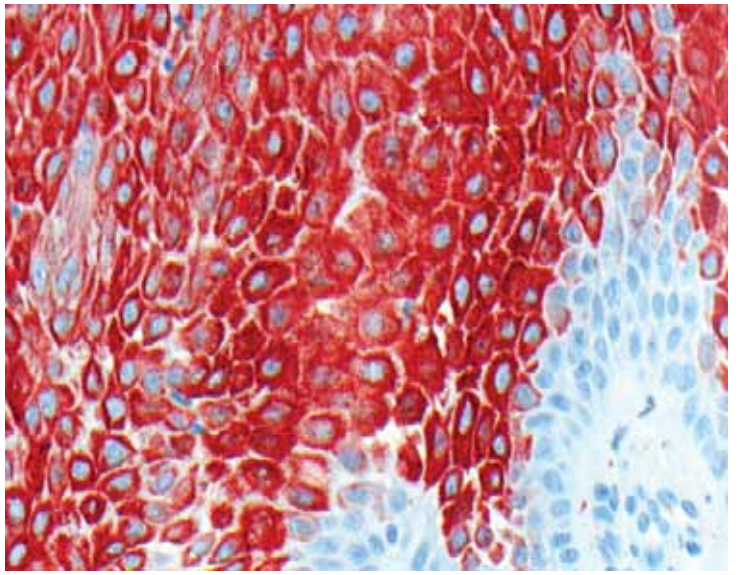
• Comèl-Netherton Syndrome	LEKTI
• MALT 1 Deficiency Syndrome	MALT 1
• CHILD Syndrome	Adipophylin

+ Akantholysis of Desmosomal Type

• SAM Syndrome	Desmoglein, Desmoplakin
• Peeling skin disease	Corneodesmosin
• Ectodermal dysplasia-skin fragility syndrome (McGrath Syndrome)	Plakophilin

Hyperproliferative Keratin 16
positiv

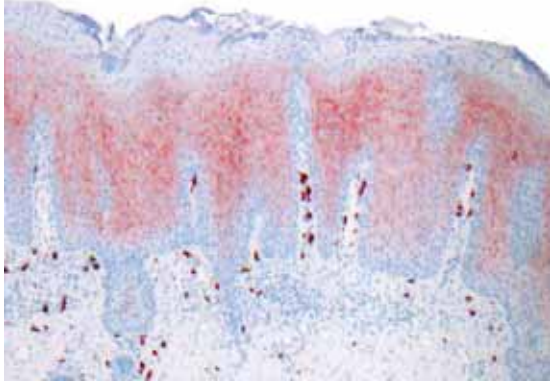


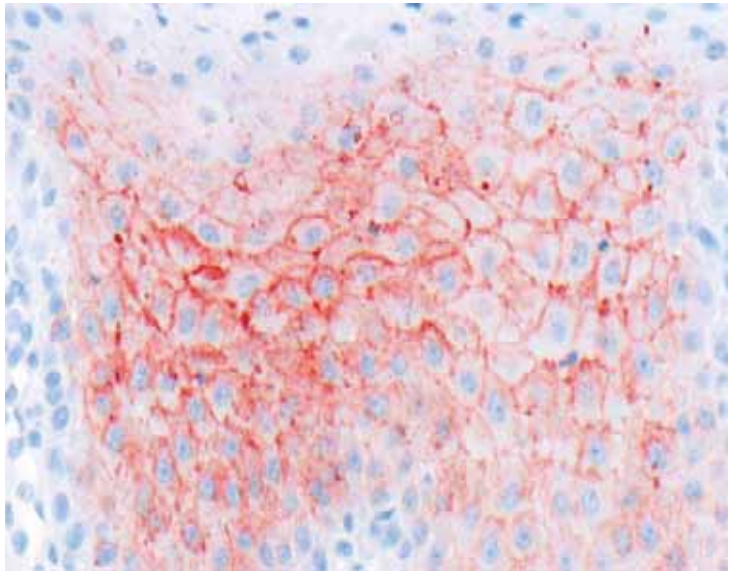


Desmoglein weak
but regular

Desmoplakin:
dominant missense mutation
c.1748C>Tp.L583P

J. Fischer, Freiburg





SAM-Syndrome
(Severe Dermatitis, Allergies, Metabolic vasting syndrom)

- Mutations of *Desmoglein 1 or Desmoplakin (OMIM 615508)*
- Congenital erythroderma reminiscent of Netherton syndrome
- Hypotrichosis, Pruritus
- Food allergies, hyper IgE, eosinophilia, recurrent skin and respiratory infections, failure to thrive, growth retardation

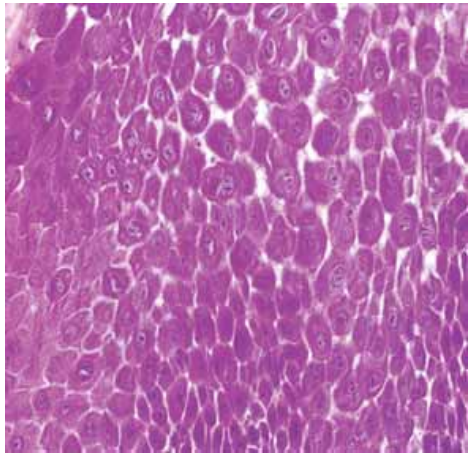
- More variably: Pustulation, palmoplantar keratoderma, onychodystrophy, dental abnormalities, eosinophilic esophagitis, nystagmus, cardiac defects

- Therapy: Ustekinumab, TNF antagonists, Dupilimumab, Calcineurin inhibitors

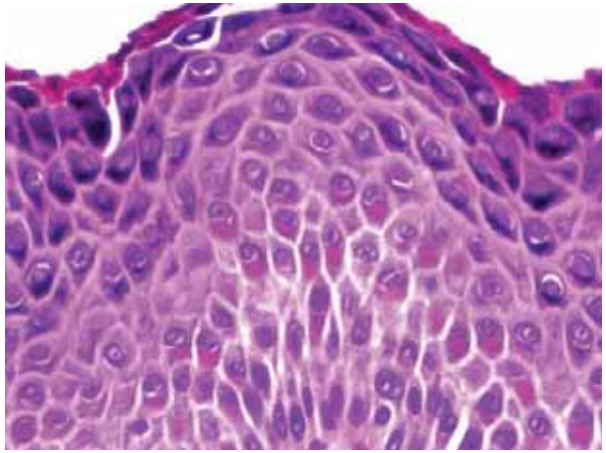
Acantholysis of the Desmosomal Type

(Acantholysis related to mutations of desmosomal proteins)

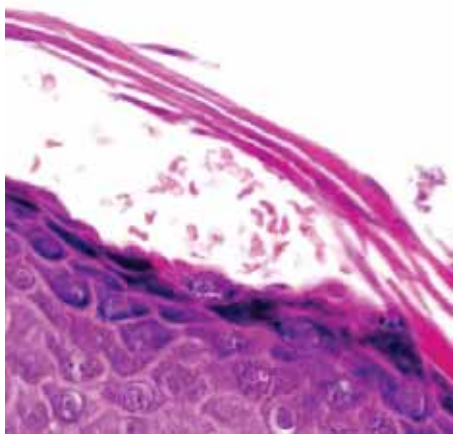
- Widening of intercellular spaces and partial dehiscence of keratinocytes with regular nuclei
- No pale keratocytes, vesiculation, crusting
- Often Hyperkeratosis and hypergranulosis (SPPK), psoriasiforme hyperplasia (SAM Syndrome)
- Hypereosinophilia and/or eosinophilic clumping of the cytoplasm (McGrath syndrome)
- Subcorneal variant (Peeling skin disease)



Striate PPK

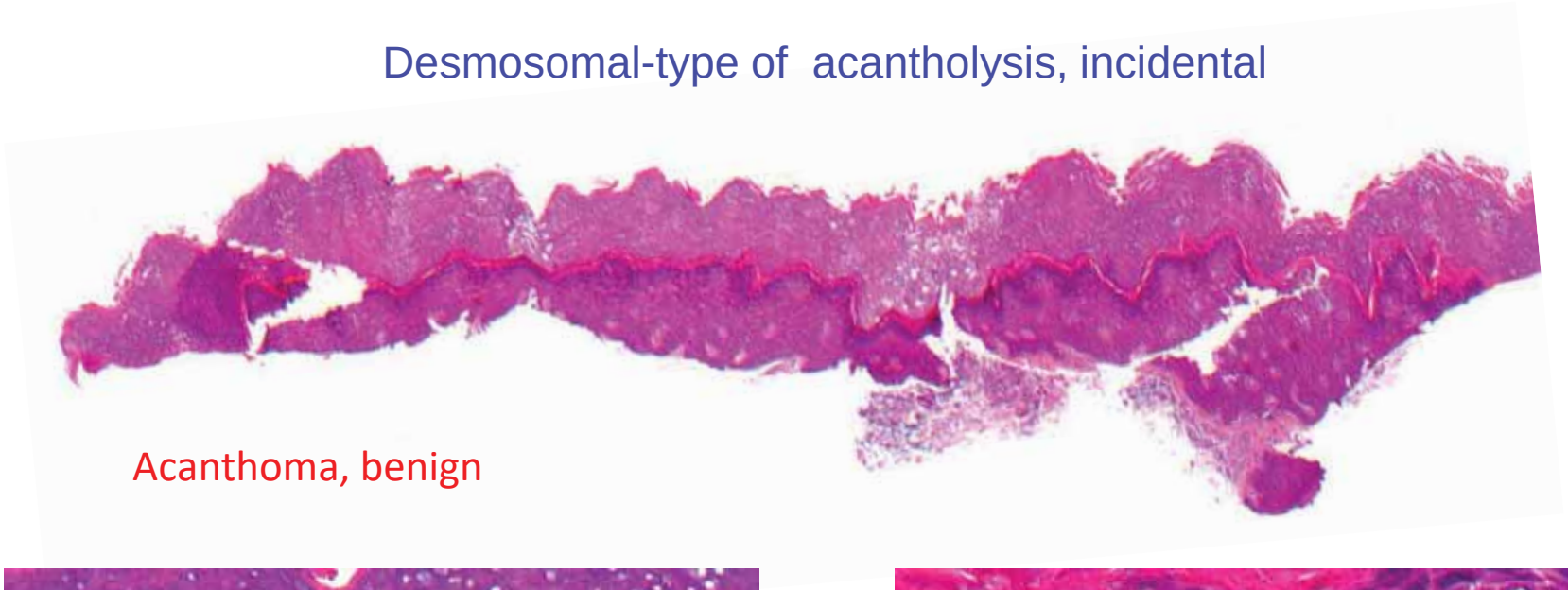


McGrath syndrome

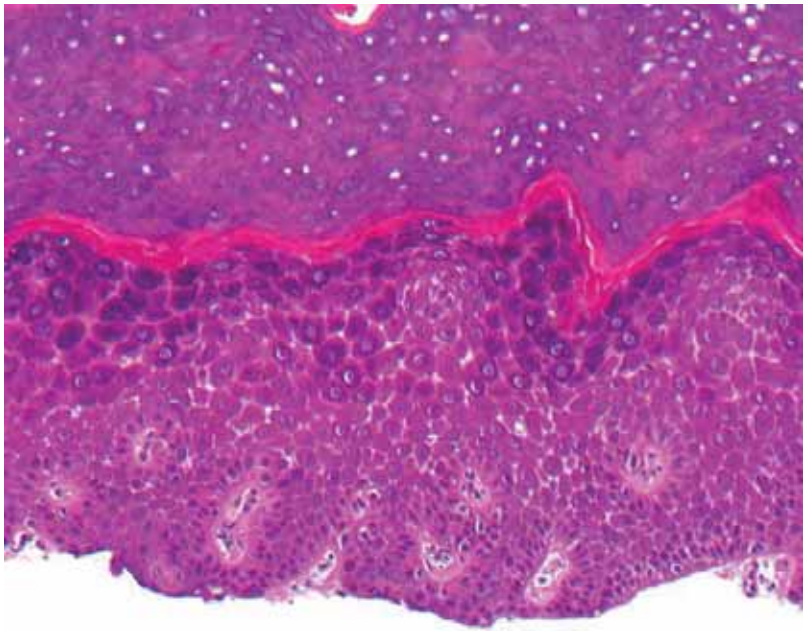


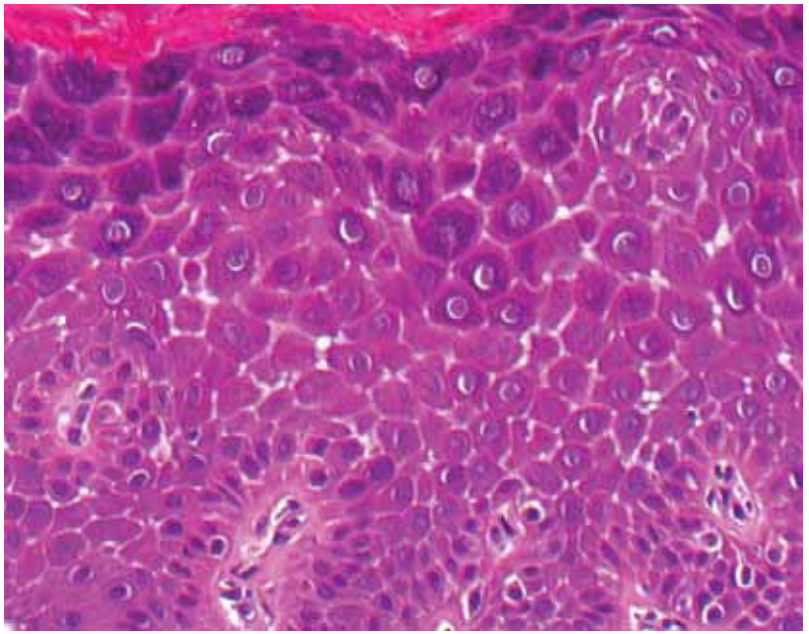
Peeling skin disease

Desmosomal-type of acantholysis, incidental

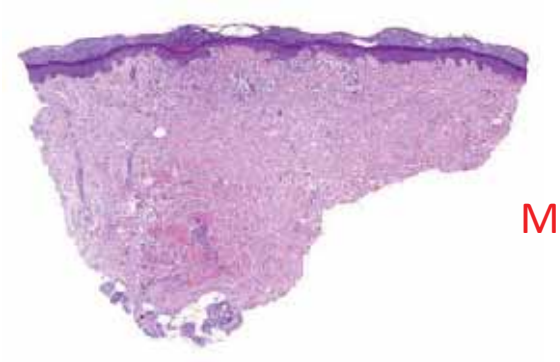


Acanthoma, benign

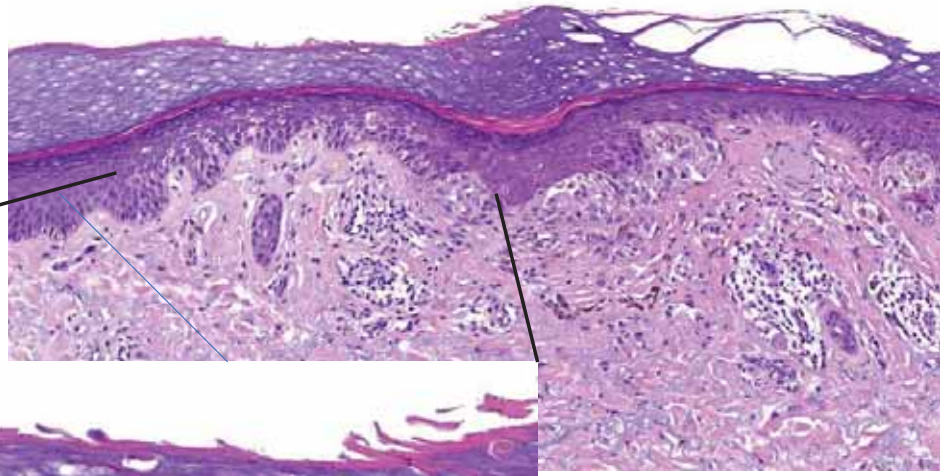


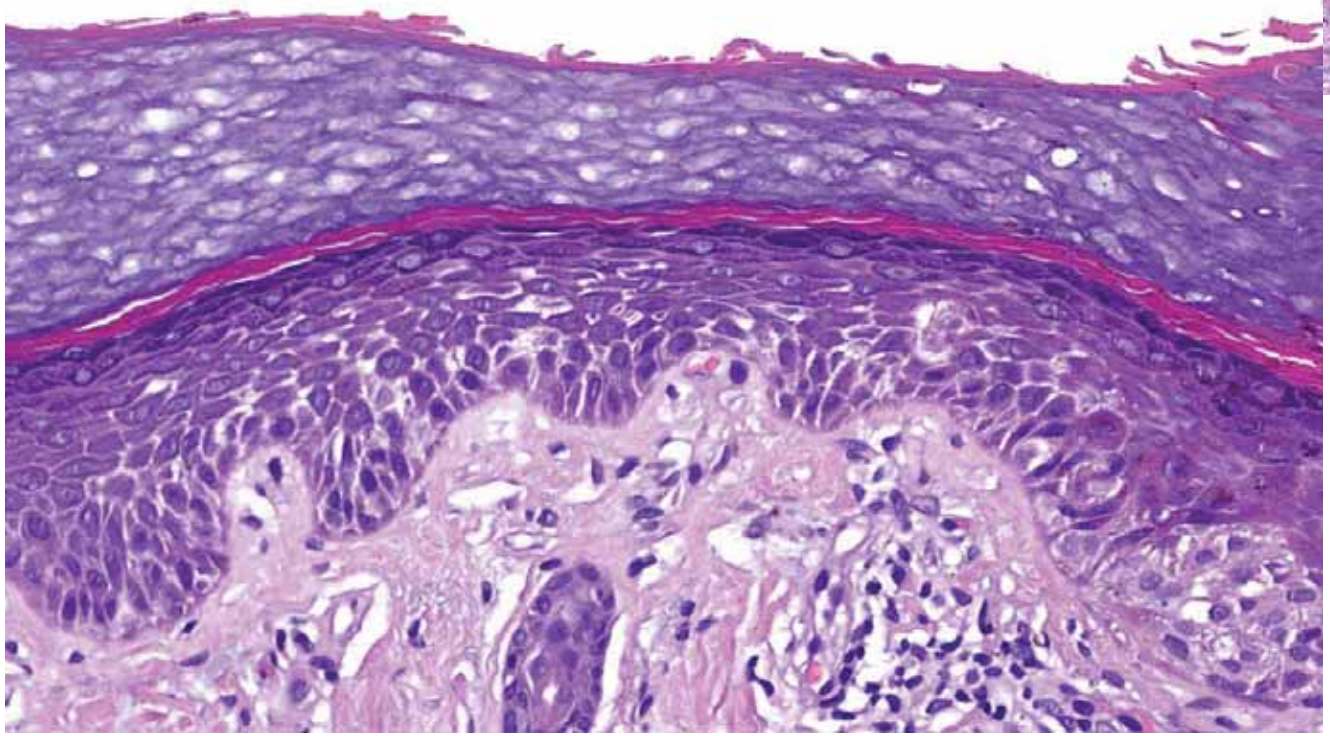


Desmosomal-type of acantholysis, incidental



Melanocytic nevus

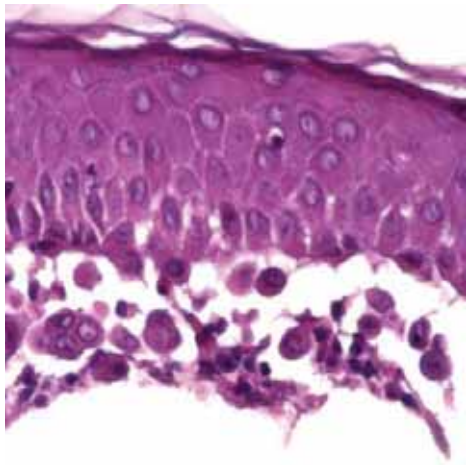




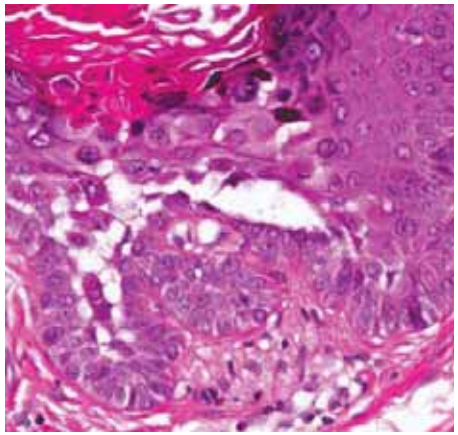
Acantholysis of the Desmosomal Type

(DDx other types of acantholysis)

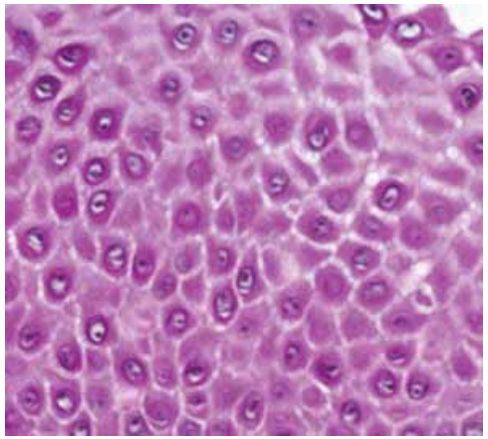
- Pemphigus: blistering with intact roof, roundish keratinocytes (fully acantholytic cells)
- Darier: pyknotic nuclei and hypereosinophilic cytoplasm (Dyskeratosis)
- Hailey-Hailey: perinuclear hypereosinophilia and pale periphery
- Herpes and other viral infections: ballooning (intracellular edema)
- (Eczema: spongiosis, vesicles, parakeratosis, crusting)



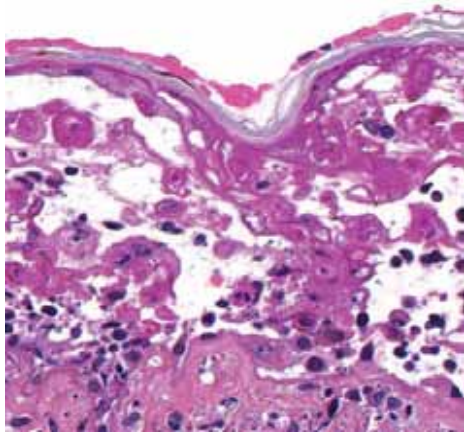
Pemphigus



M. Darier



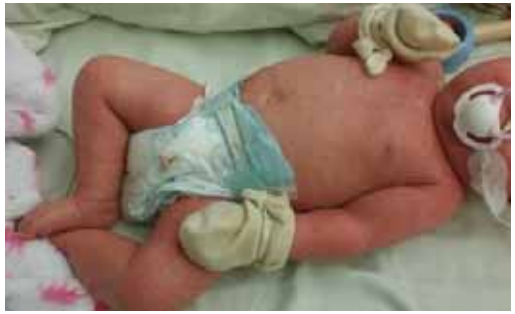
M. Haily-Hailey

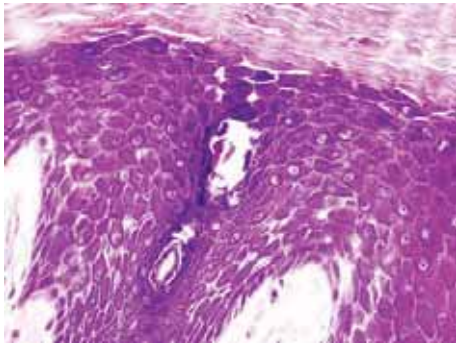


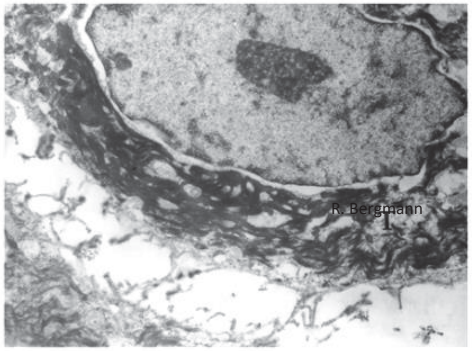
Herpes

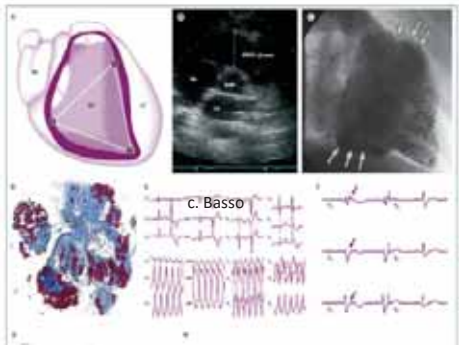
Acantholysis of the Desmosomal Type
inflammatory, non inflammatory
syndromic, non-syndromic, incidental

Keratosis palmoplantaris areata et striata (SPPK, type I,II)
Carvajal-Huerta-, Naxos-Syndrome,
SAM-, McGrath-, Peeling skin-syndrome, …







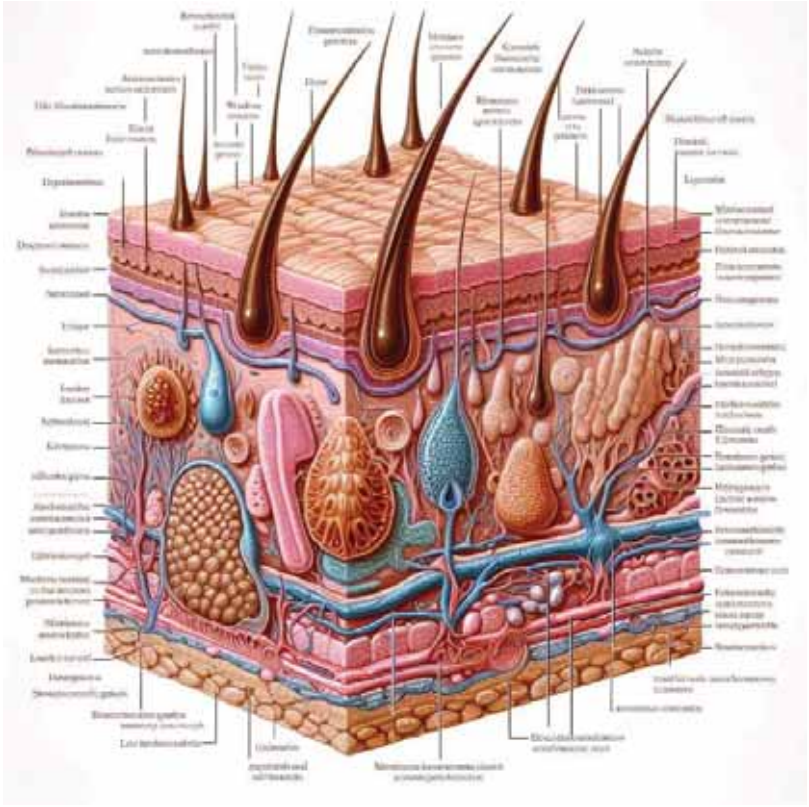


Thank you for your attention

Clinical-pathologic correlation

Klinik für Hautkrankheiten, Universitätsklinikum Münster (UKM)
Internationales Ausbildungszentrum für Dermatopathologie der ICDP und UEMS

The Future



„Anatomy of the skin“

AI, Image Generator, 2023

„Santa Clause uses the microscope“

AI, Image Generator, 2023

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