Pattern Diagnosis: Part I

Diseases characterized by perivascular dermatitis

E Mauldin
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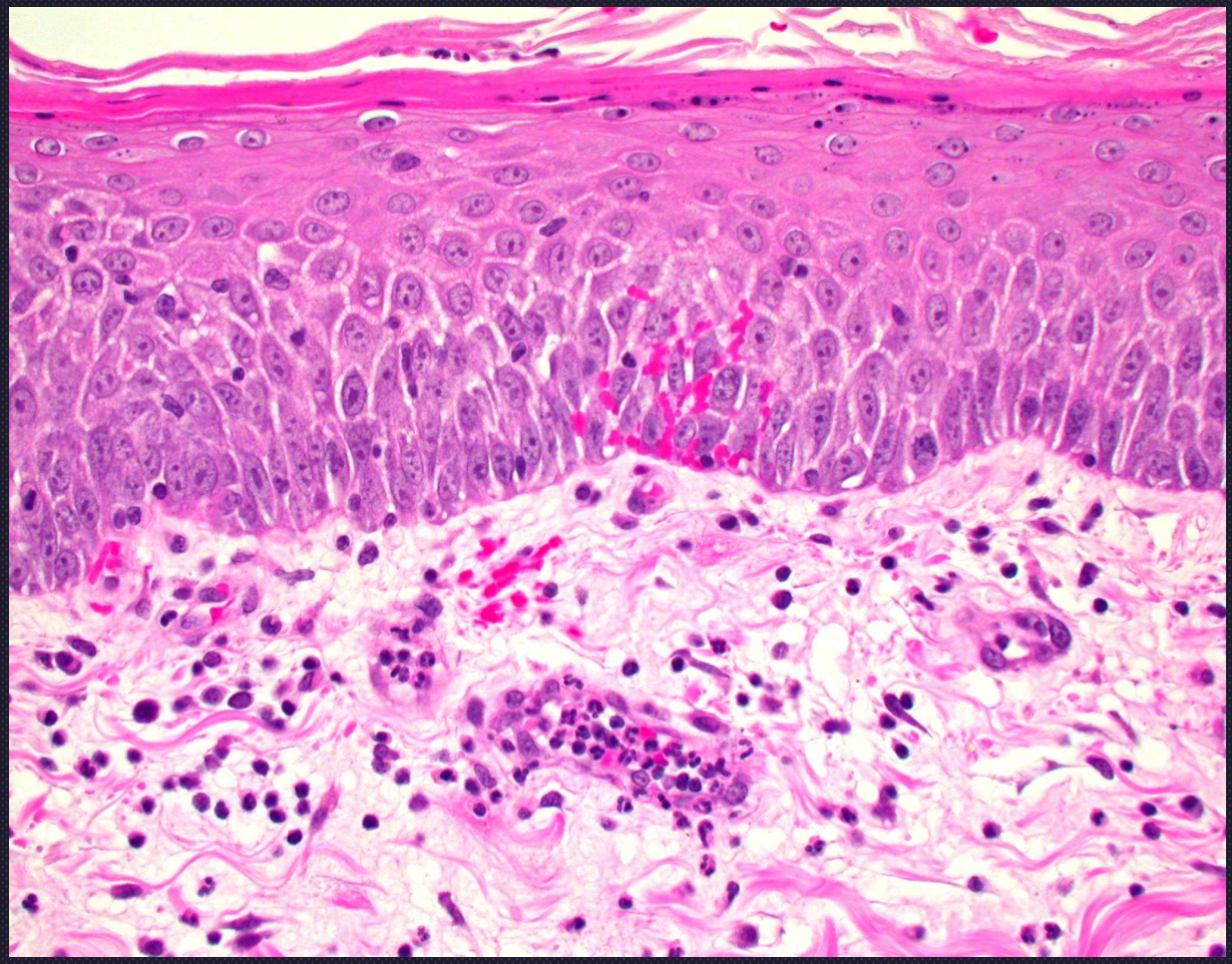
- Any (all) inflammatory processes have perivascular inflammatory cells at some point in time

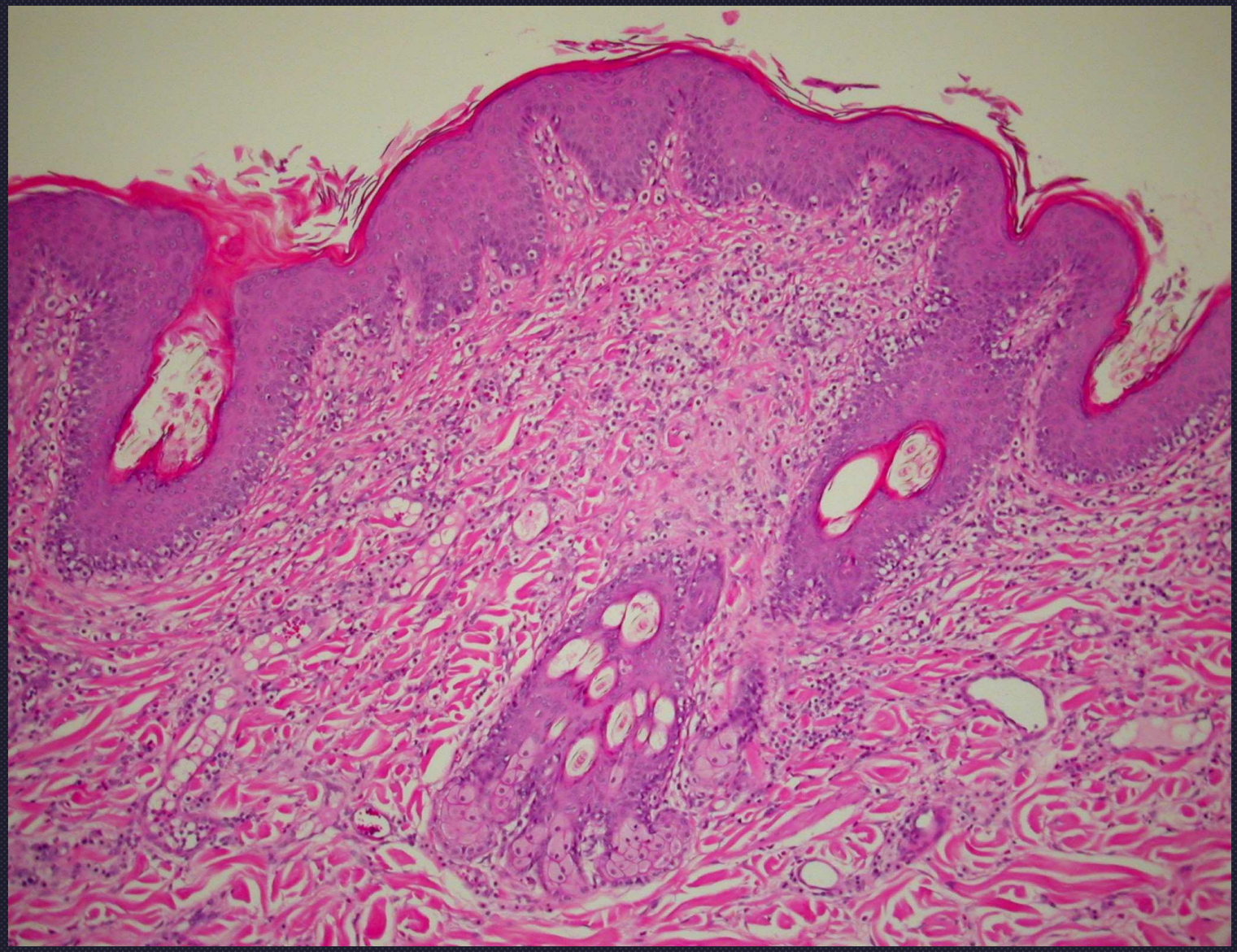
- Perivascular dermatitis is the hallmark pattern of “allergic dermatitis”
  - Type I (late phase)
  - Type IV
  - Also Type III

Perivascular Dermatitis

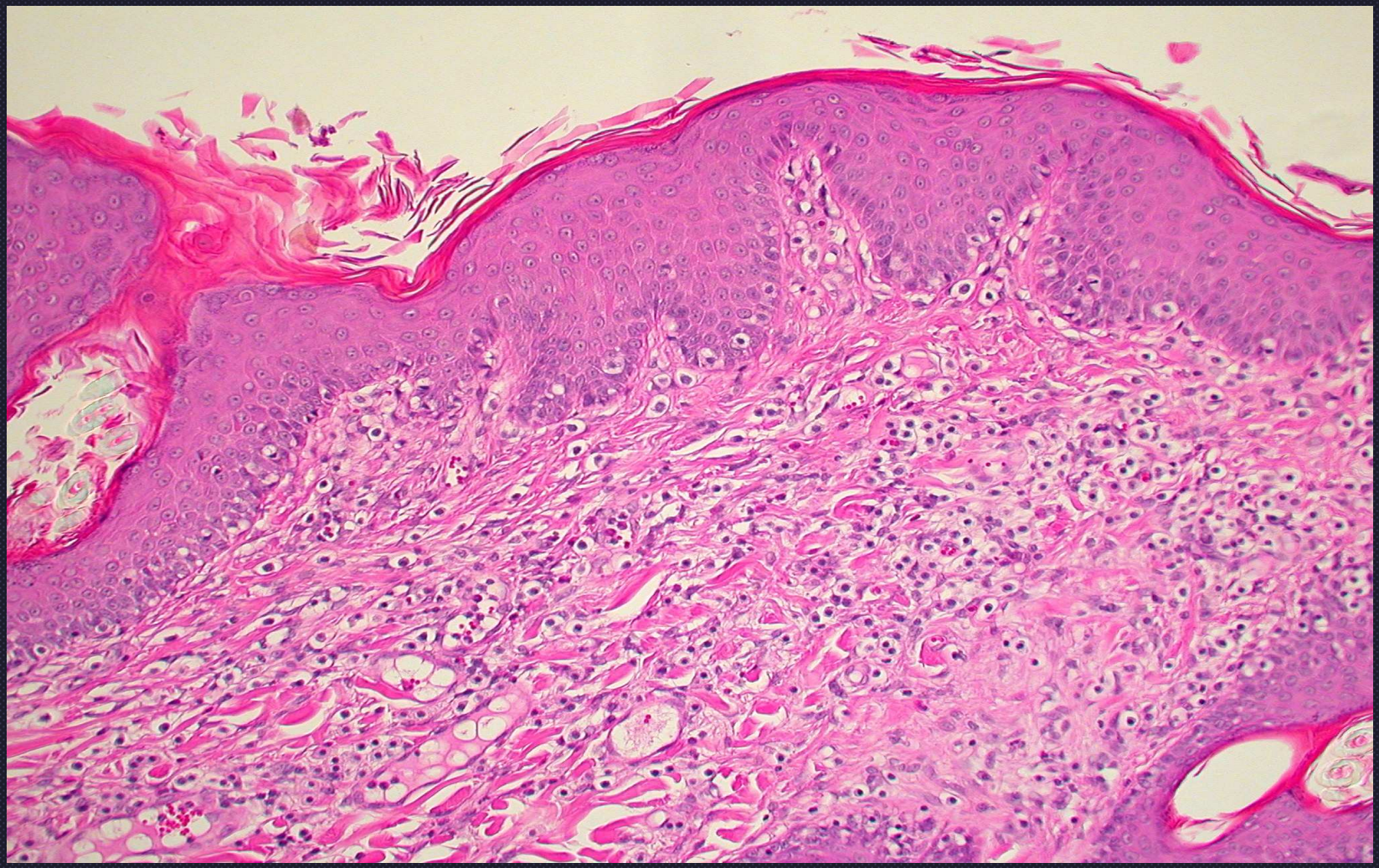


ACVD Task Force on Atopic Dermatitis

- Hyperplastic and spongiotic perivascular dermatitis
  - Mixed infiltrate (T cells, dermal dendritic cells, mast cell hyperplasia)
  - Eosinophils usually present in small numbers
- Scattered lymphocytes in epidermis
- Aggregates of Langerhans cells in epidermis
- +/- exocytosis of eosinophils, subcorneal eosinophilic microabscesses



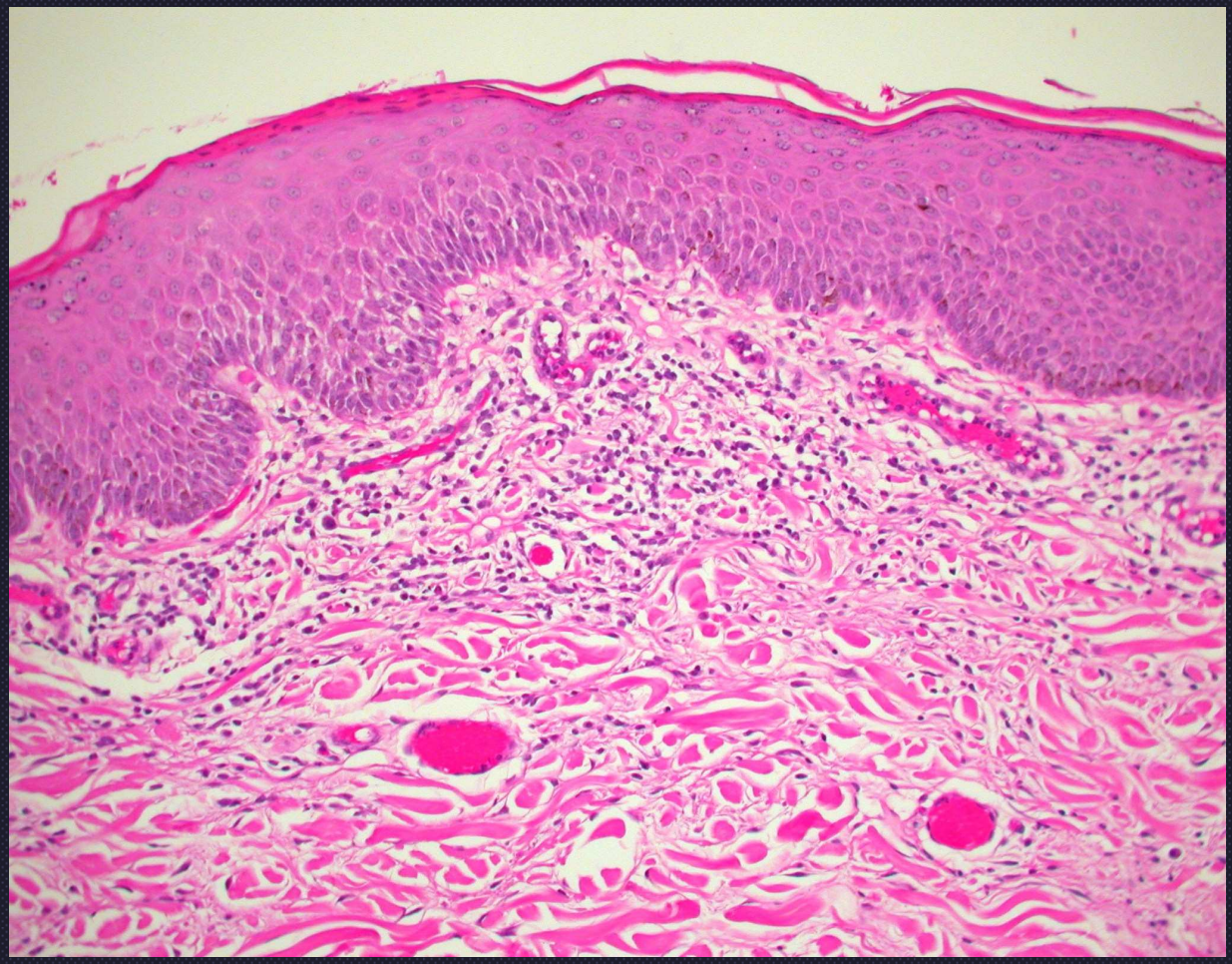
Feline allergic derm- perivascular to interstitial with intraepidermal mast cells



Feline allergic derm- perivascular to interstitial with intraepidermal mast cells

Perivascular Dermatitis

Allergic Dermatitis

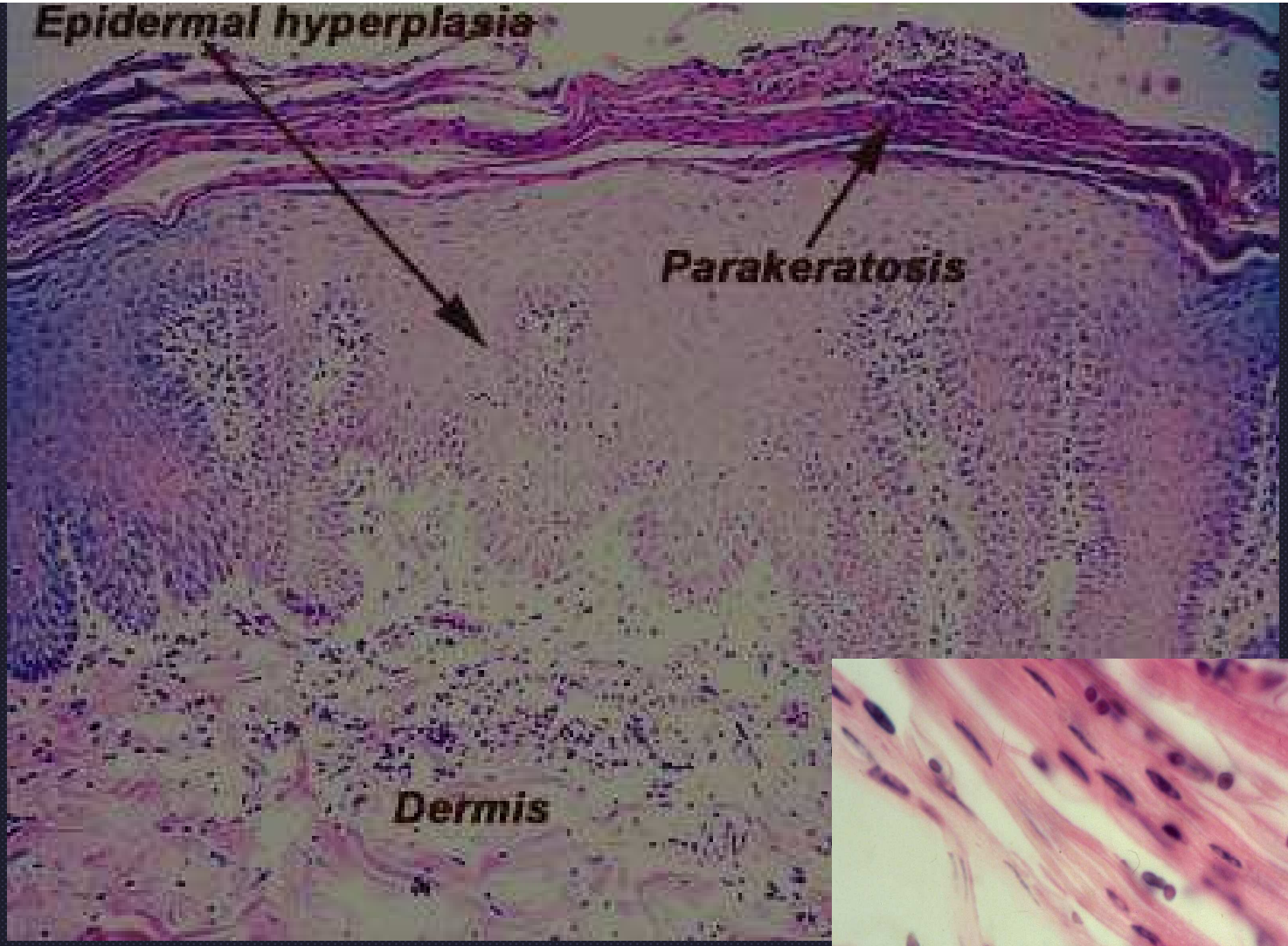


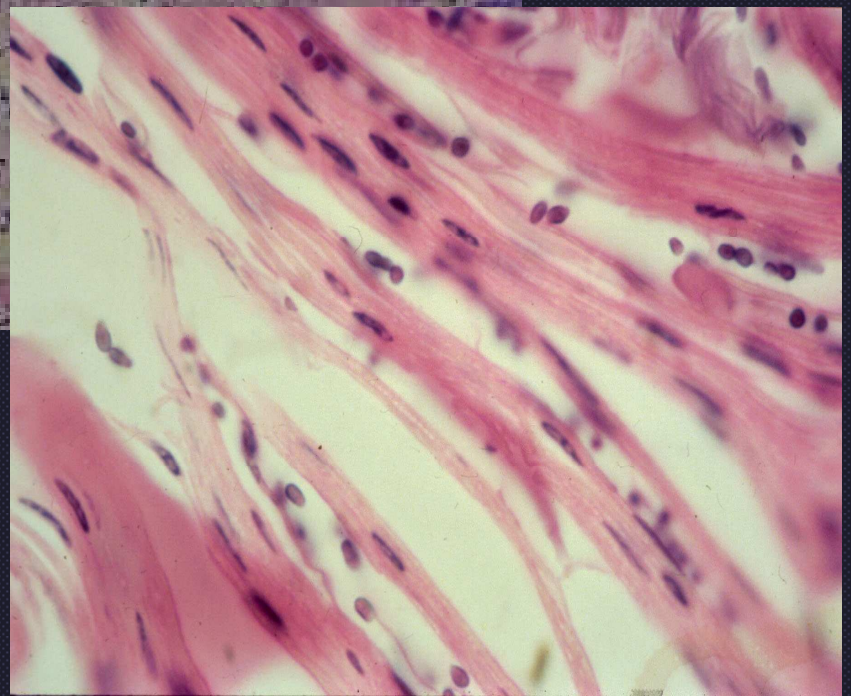
Secondary complicating factors

- Superficial trauma
- Bacterial
- Fungal

“Armadillo Westie”
chronic hypersensitivity to malassezia + environmental
+/- food allergens

Lichenification with malassezia dermatitis





Malassezia dermatitis
Parakeratosis is typically patchy
Usually secondary to allergy

- Suspect malassezia if alternating orthokeratotic and patchy parakeratotic hyperkeratosis with acanthosis
- Allergic reaction pattern
- Intertriginous areas
- Recommend tape stripping to quantitate organisms
  → Lost in histopathology processing

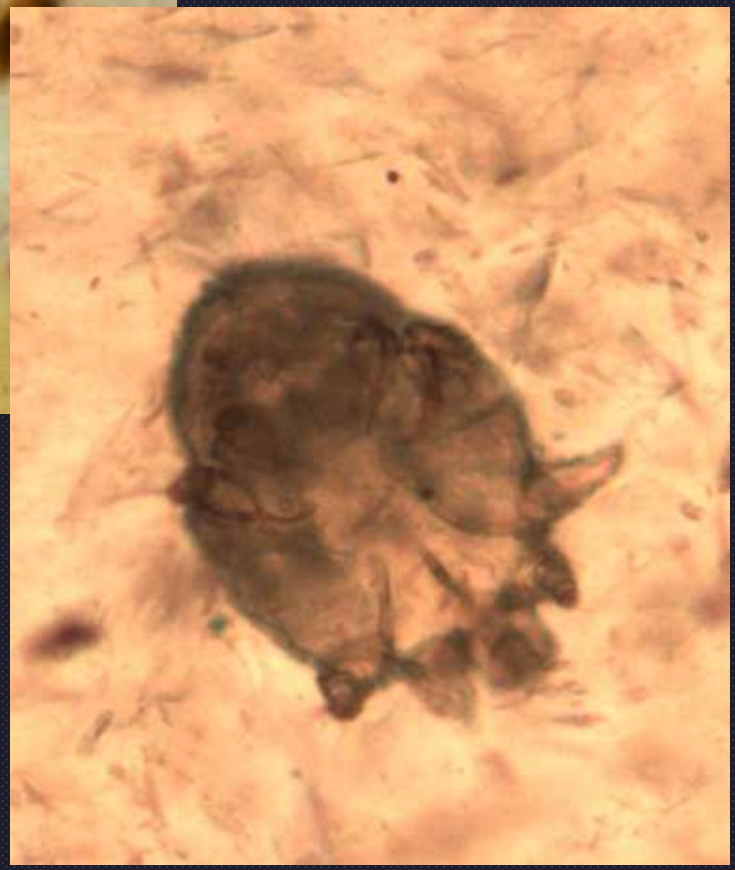
Intradermal skin test for allergen specific immunotherapy

Severe facial pruritus in a food allergic cat

Flea allergy dermatitis

Sarcoptic mange– It is a hypersensitivity rxb to the mites!

Notoedres dermatitis



Skin scraping: sarcoptic mange mites and fecal pellets

Yellow crusts on elbow in a dog with scabies

Increase yield of "chronic perivascular dx "

- Inform clinician of components in crusts
  - Malassezia, bacteria (type)
  - Always note type of inflammatory cells in pustules
- Compare with clinical presentation
  - Bx cannot *rule-out* scabies!
  - Bx of PF in a cat without crust = allergy
- Address clinical diagnosis

Perivascular dermatitis with **diffuse parakeratotic hyperkeratosis**

Parakeratosis

- Parakeratosis
  - Increased epidermal turnover
    - e.g. 8 days to complete cornification vs 21 d
    - Trauma; malassezia infection, etc.
    - Patchy
- Metabolic disease
    - More diffuse and severe
- Can be seen with EM and PF

Diffuse- limited number of differentials

DDX for Diffuse/Severe Parakeratosis

- Zinc Responsive Dermatosis
- Superficial Necrolytic Dermatitis
- Labrador retriever hereditary nasal hyperkeratosis
- Lethal Acrodermatitis of Bull Terriers
- Congenital follicular parakeratosis of Rottweiler and Labrador retriever
- Thallium Toxicity

- Know the clinical distribution of lesions
- Breeds affected
- Age of onset

- Diffuse parakeratosis in a cat??
  - Rare
  - Internal disease?
  - Erythema multiforme?

Zinc Responsive Dermatosis

Zn responsive derm

Zn responsive derm

Scrotum: Zn responsive derm

Zn responsive derm

Zn responsive derm- hyperkeratosis on elbow

Footpad hyperkeratosis- often seen in Zn responsive derm

Zinc responsive derm in a samoyed

Zn Responsive Derm

Syndrome I- nordic breed dogs

- Young dogs
- Genetic defect
- Stress exacerbation
- Decreased zinc absorption
- Late Fall and Winter?

Zinc-Responsive Dermatosis Syndrome II

- Any breed, “large breed’
- Puppies
  - Poor diet; high cereal diet, poor zinc absorption due to high phytate (binds zinc)

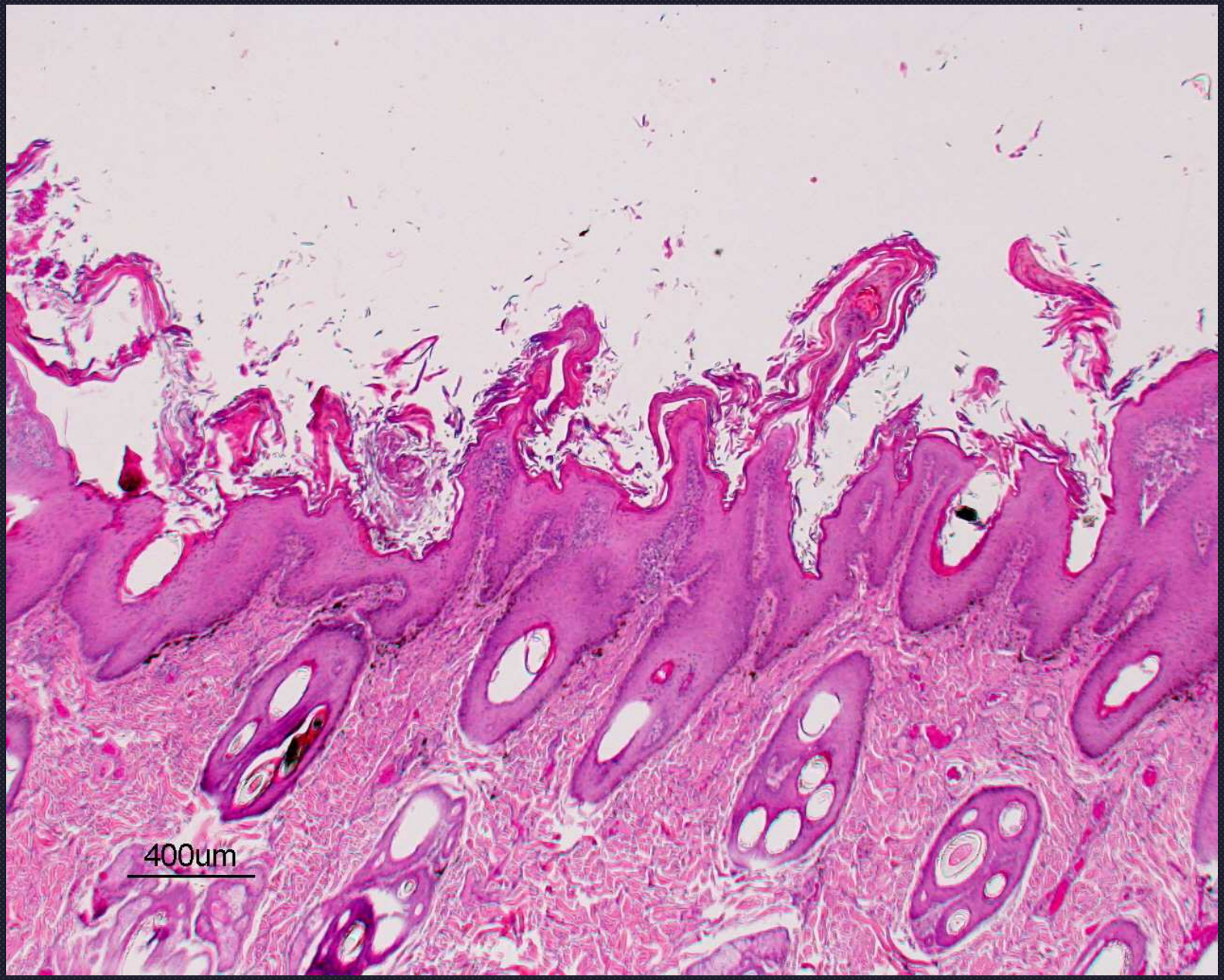
Lesions

- Hyperkeratosis, crusts, erythema
- Periocular, Perioral, muzzle >> elbows, hocks, footpad hyperkeratotis
- +/- pruritus
- Secondary pyoderma

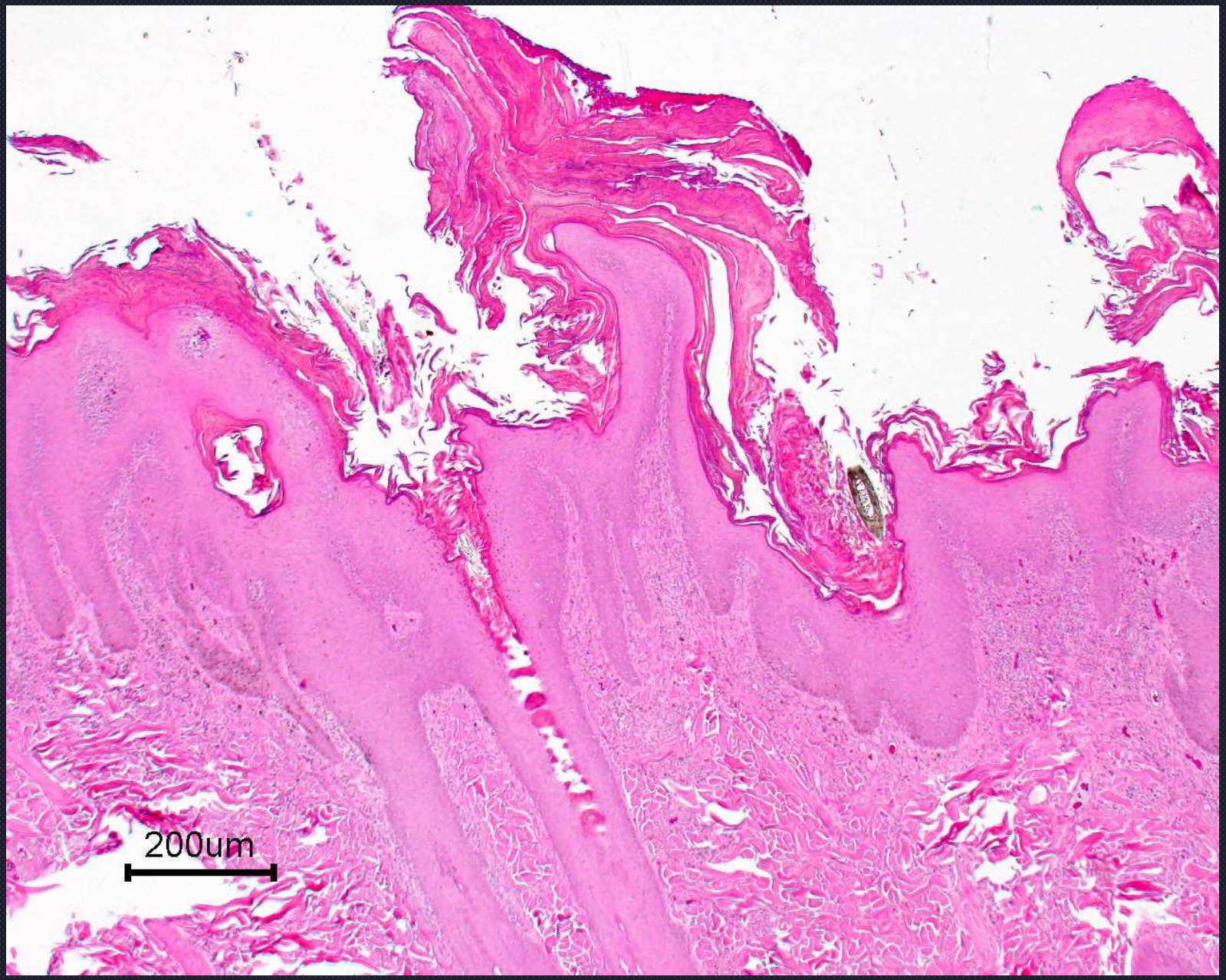
Zinc Responsive Dermatosis

- Parakeratotic hyperkeratosis
- Follicular caps or “church spires”
- May have perivascular dermatitis

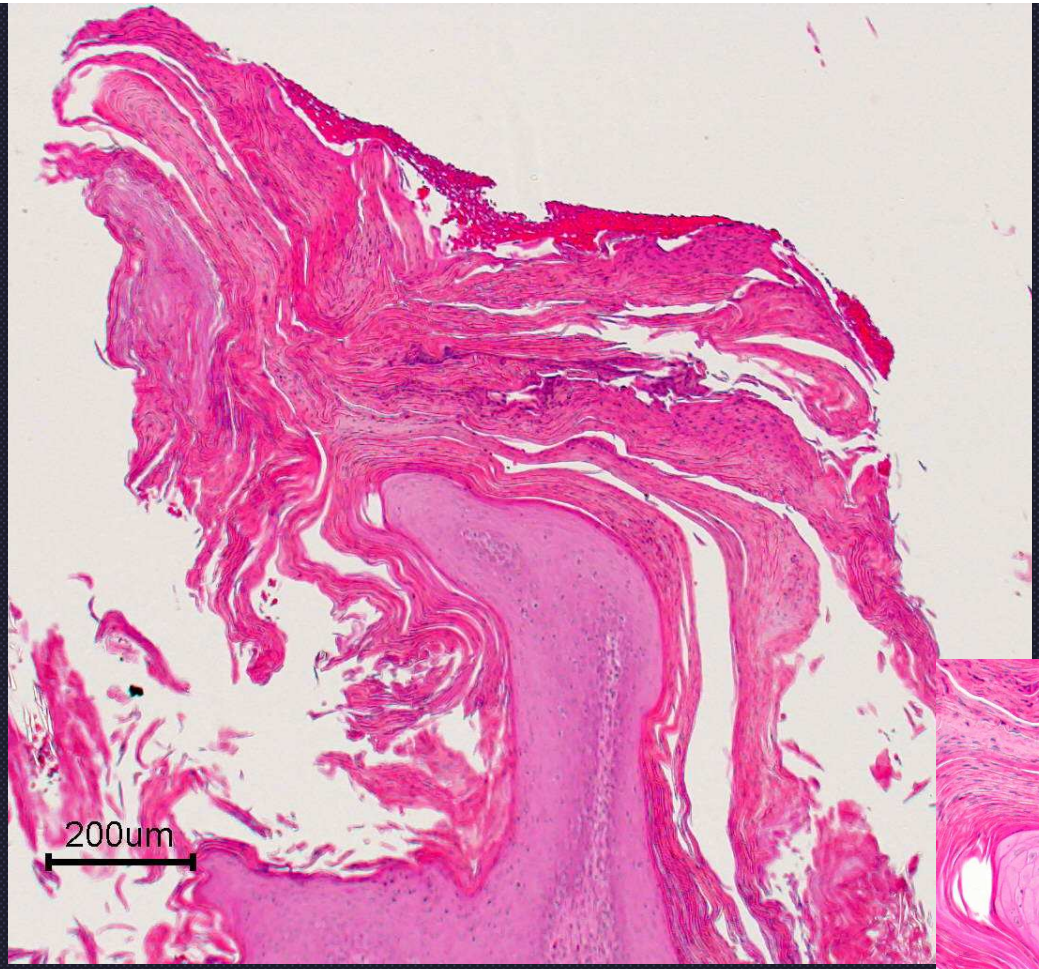
  Not unusual to have eosinophils

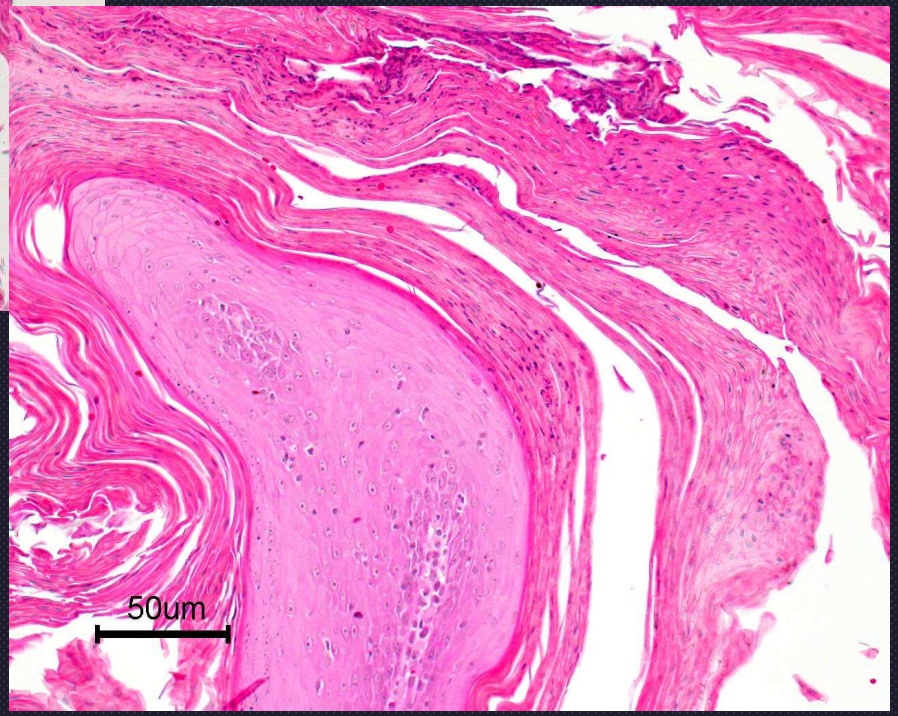


Zinc responsive derm



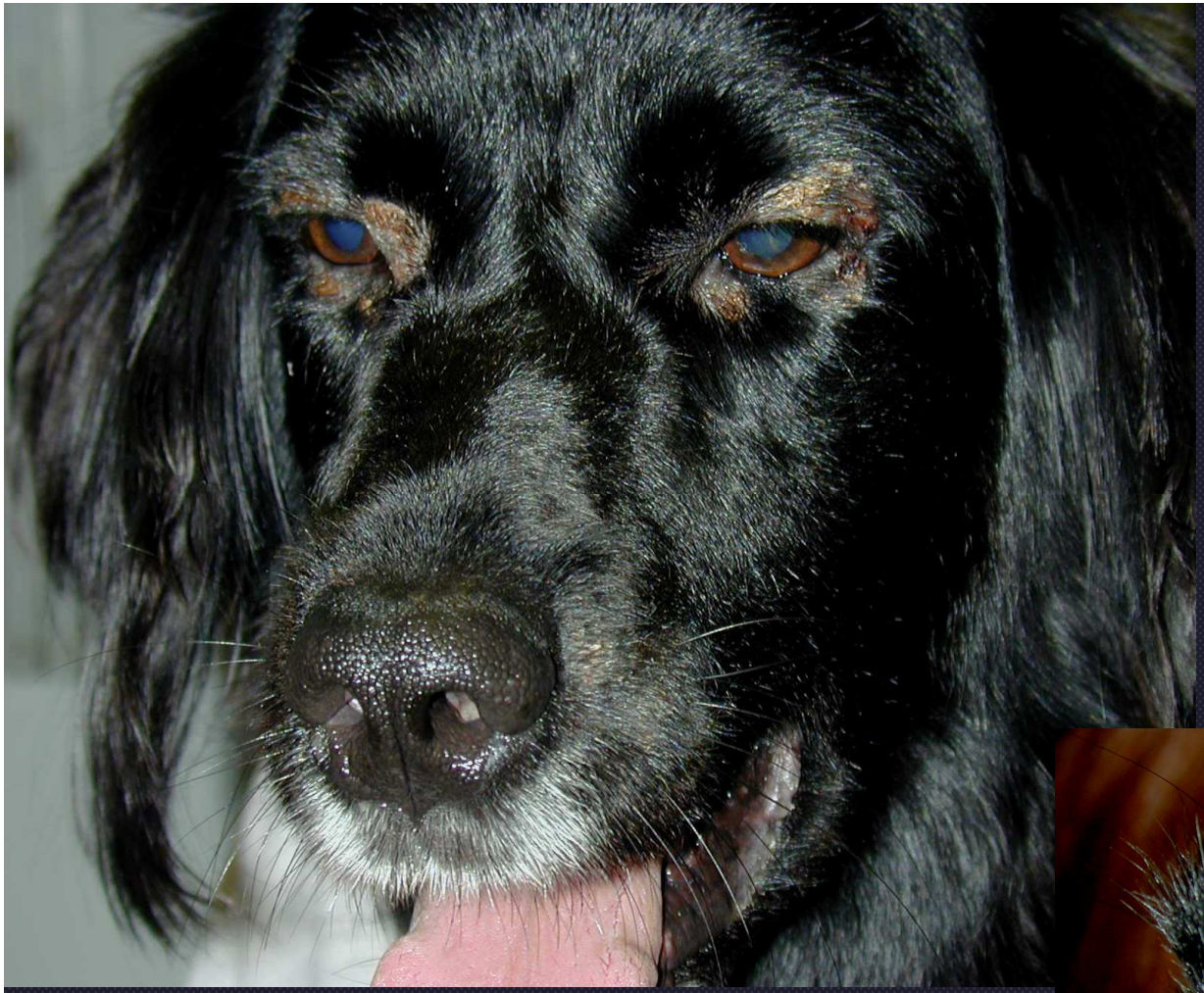
Zn responsive derm

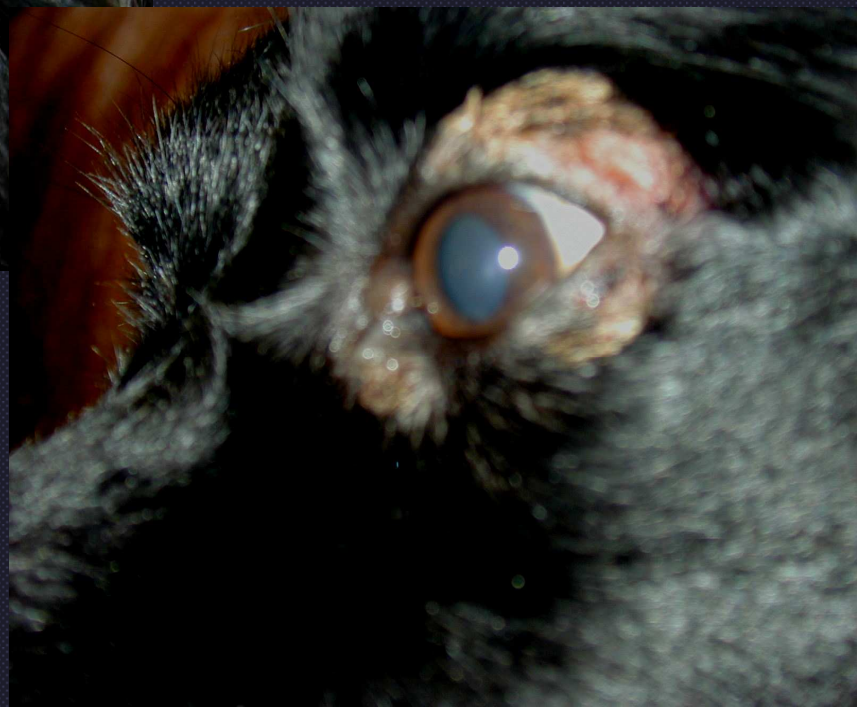




Zn responsive derm

Zinc responsive derm in a miniature pinscher





Zn responsive derm in a dog
from a rescue shelter;
responded completely to good diet

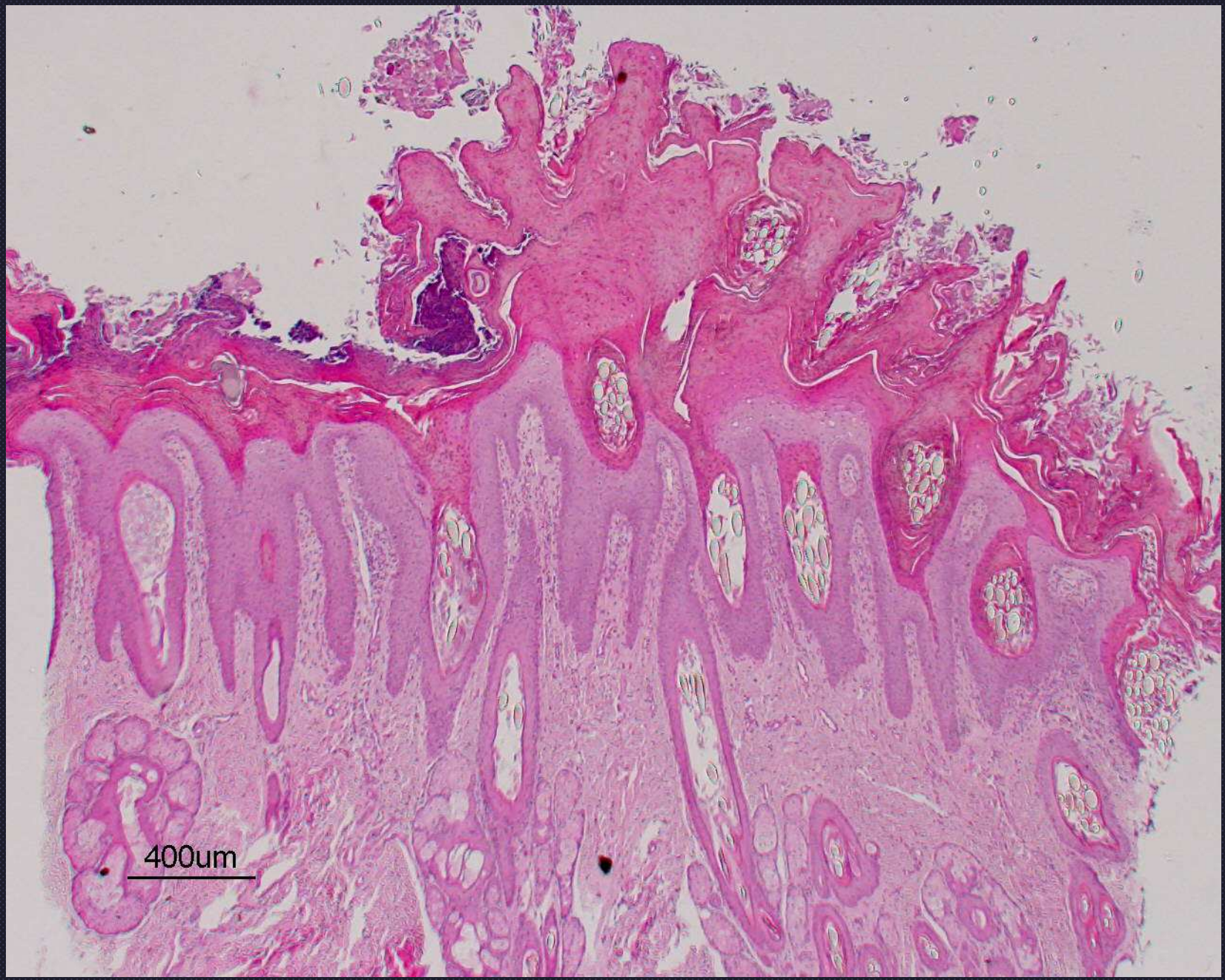
Know the Pitfalls

- Superficial trauma + malassezia/bacterial infection
  - Patchy parakeratosis
- PF in bx without acantholytic cells

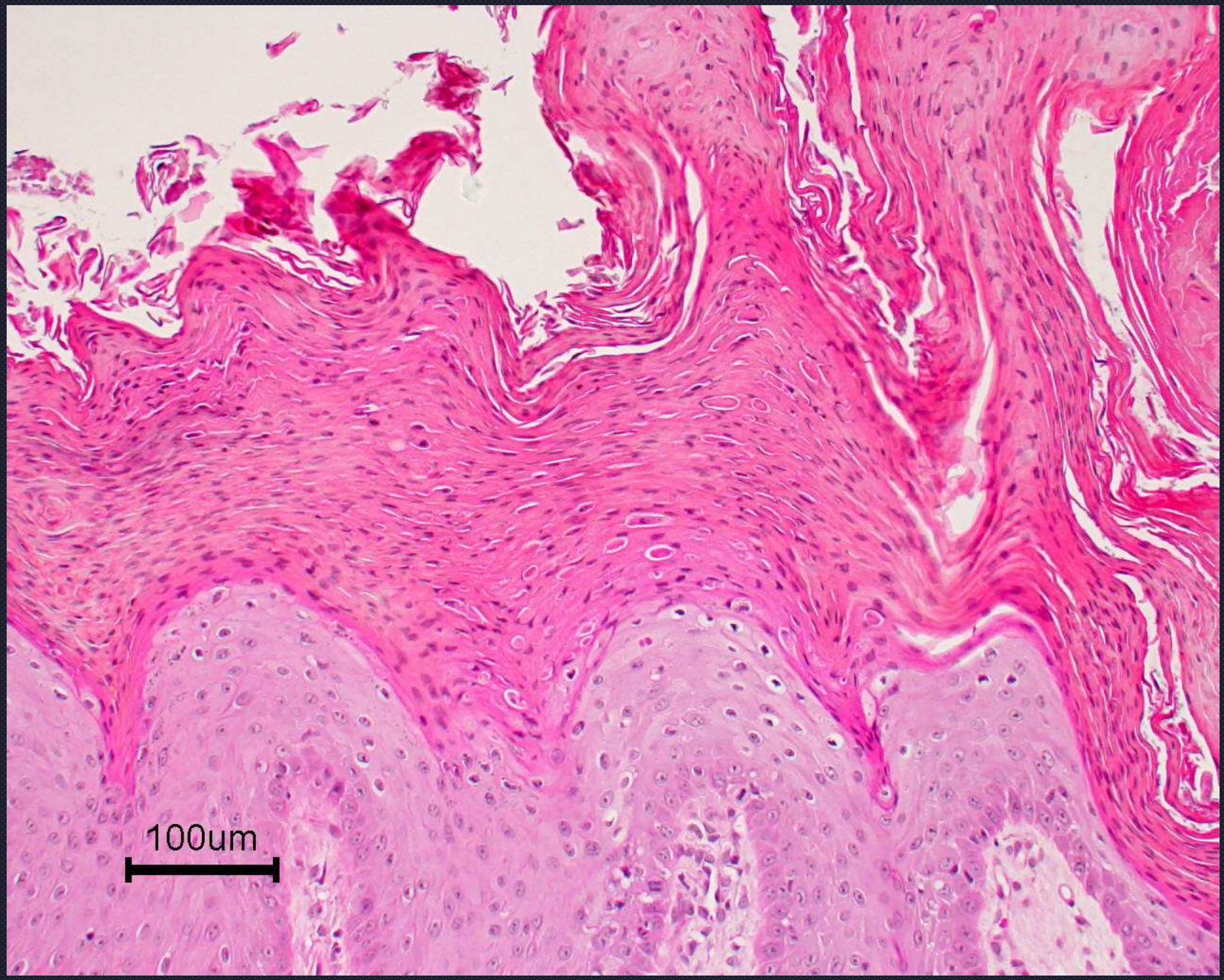
  Look for large pustules/crusts
- Superficial erythema multiforme (rare)

  - Look for individually necrotic keratinocytes

Lethal acrodermatitis



Lethal acrodermatitis

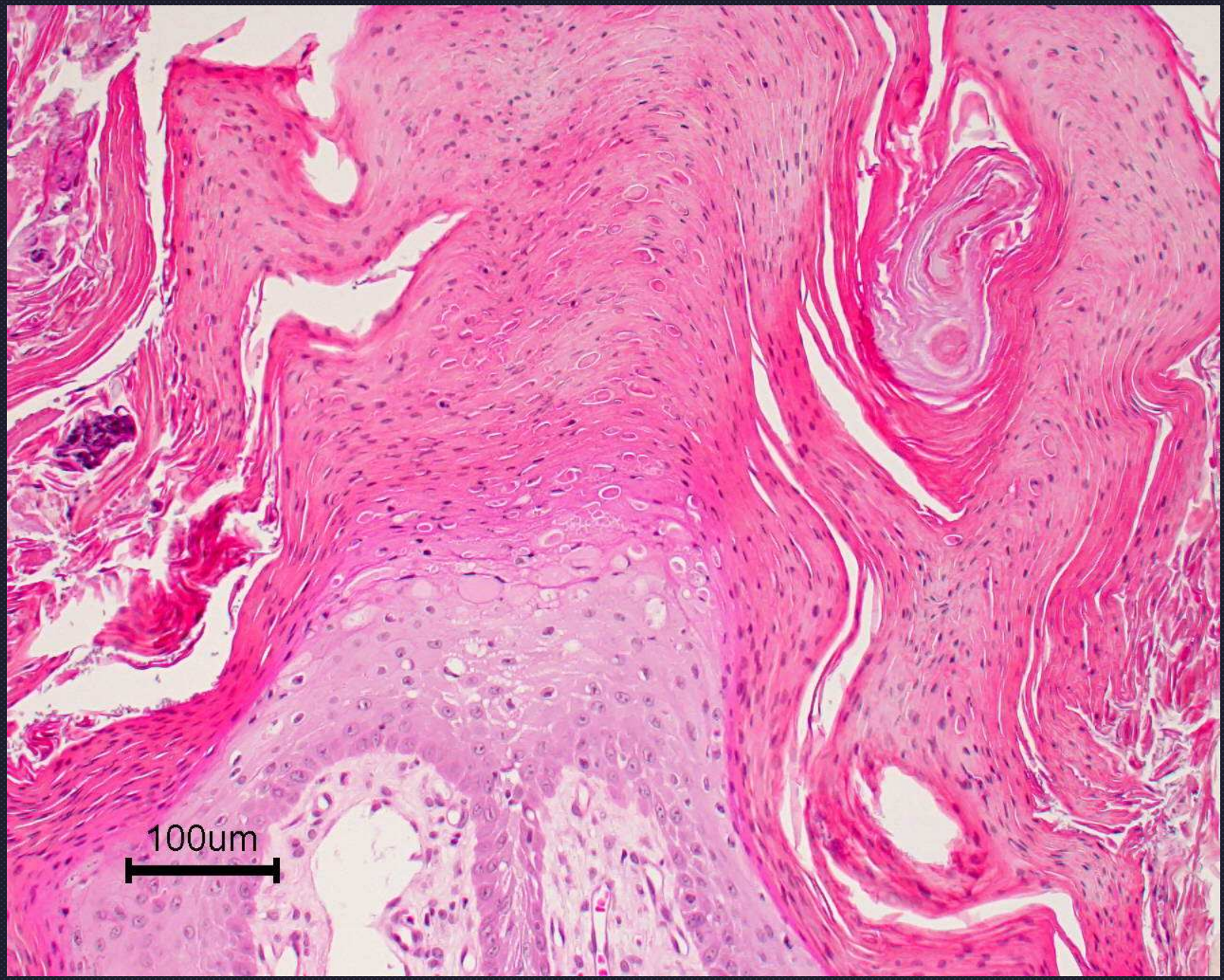


Lethal acrodermatitis

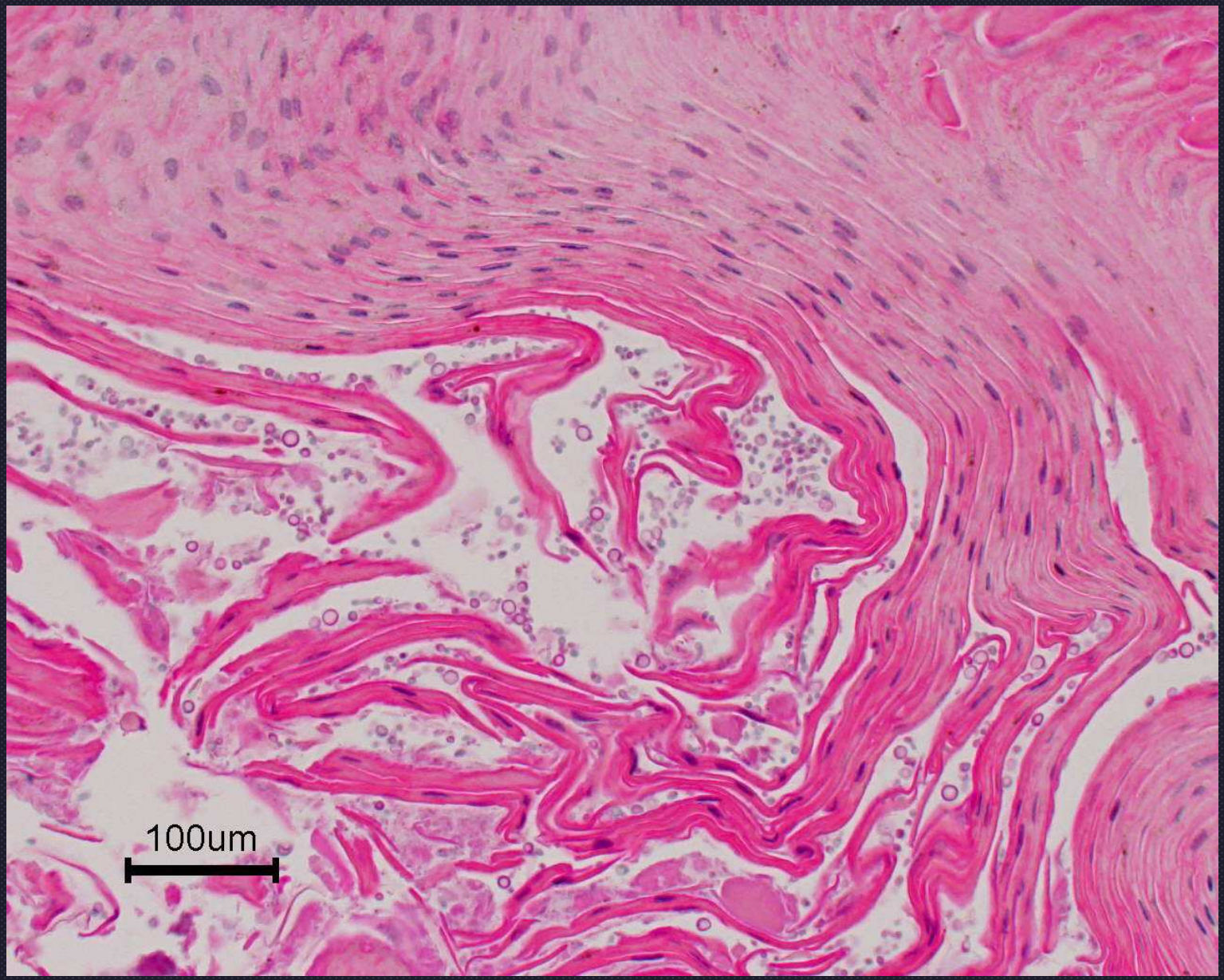
Lethal acrodermatitis of Bull terriers

Lethal acrodermatitis-
severe pododermatitis

Lethal acrodermatitis



Lethal acrodermatitis



Malassezia and candida in a dog with LAD

Oldest living LAD dog

LAD + langerhans cell histiocytosis

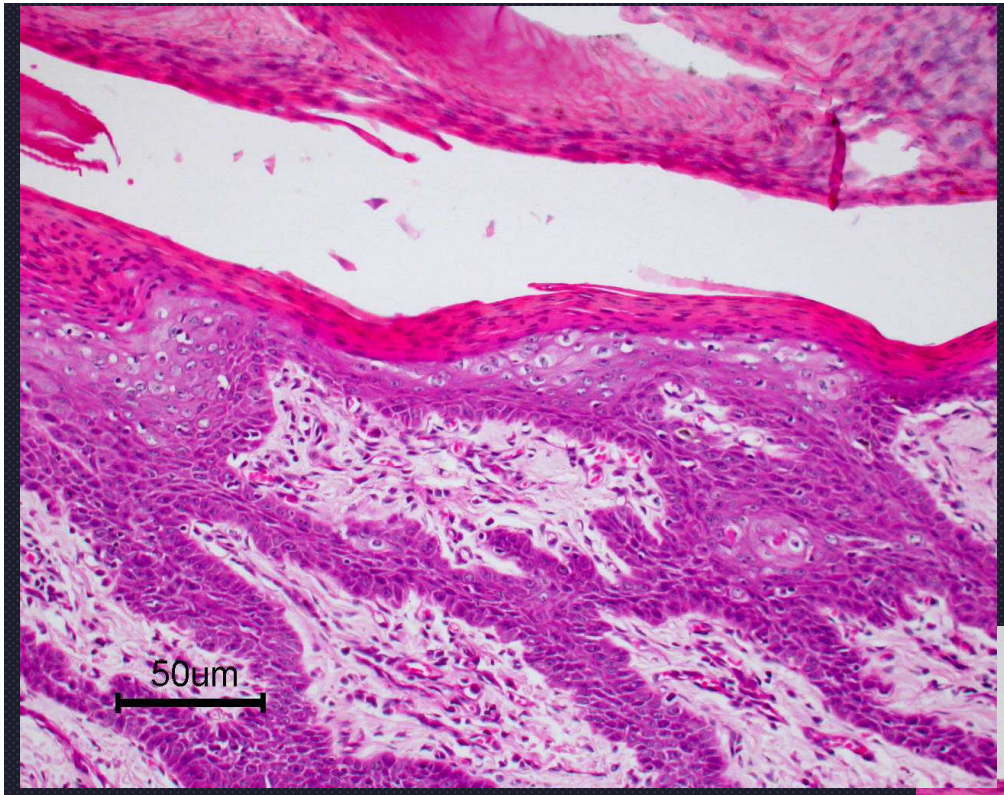
LAD + probable langerhans cell histiocytosis
Note the onychodystrophy and footpad hyperkeratosis

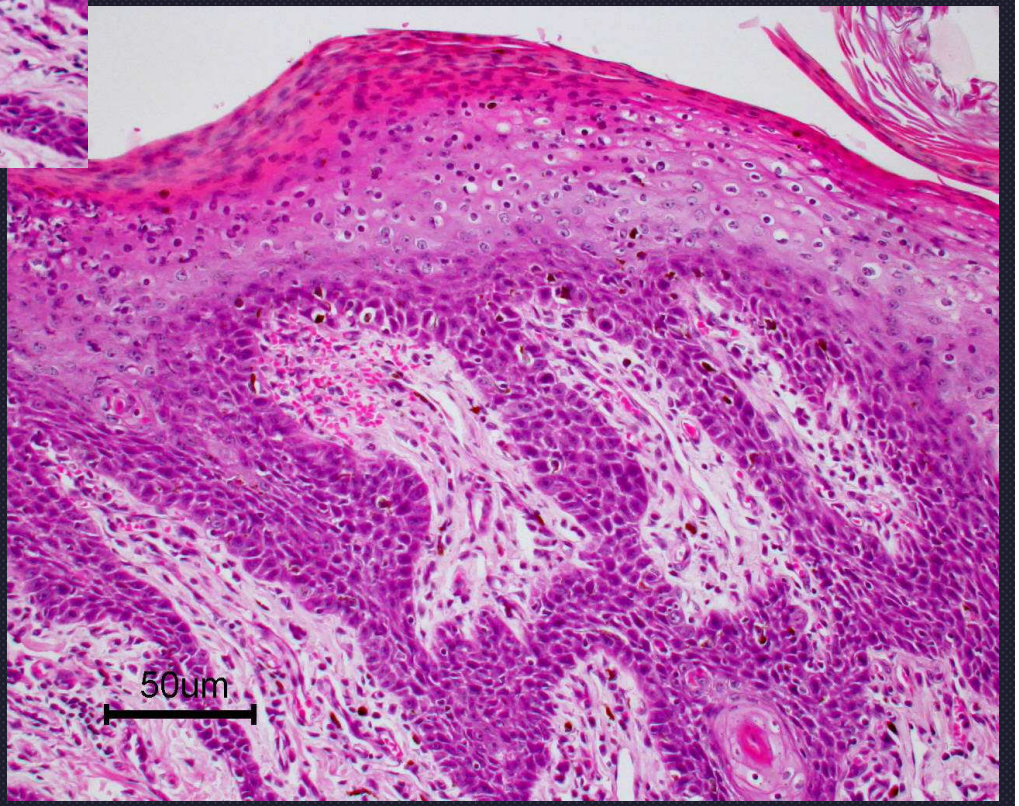
LAD + probable langerhans cell histiocytosis
Note the onychodystrophy and footpad hyperkeratosis

LAD + probable langerhans cell histiocytosis
Note the onychodystrophy and footpad hyperkeratosis

Differentials

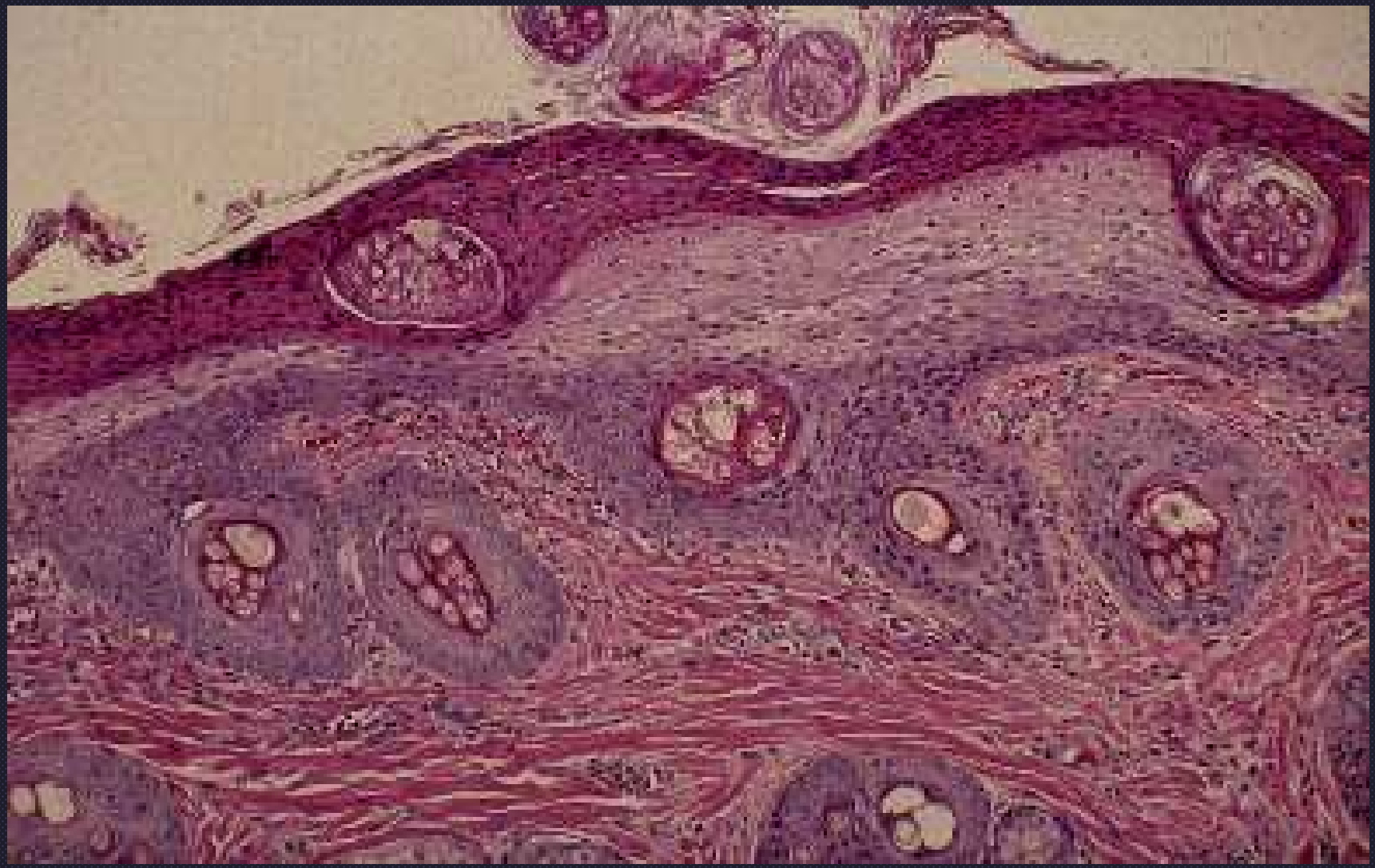
- Superficial necrolytic dermatitis
- Zinc responsive dermatosis
- Pemphigus foliaceus
- Contact dermatitis
- Senile Digital Hyperkeratosis
- Cutaneous lymphoma





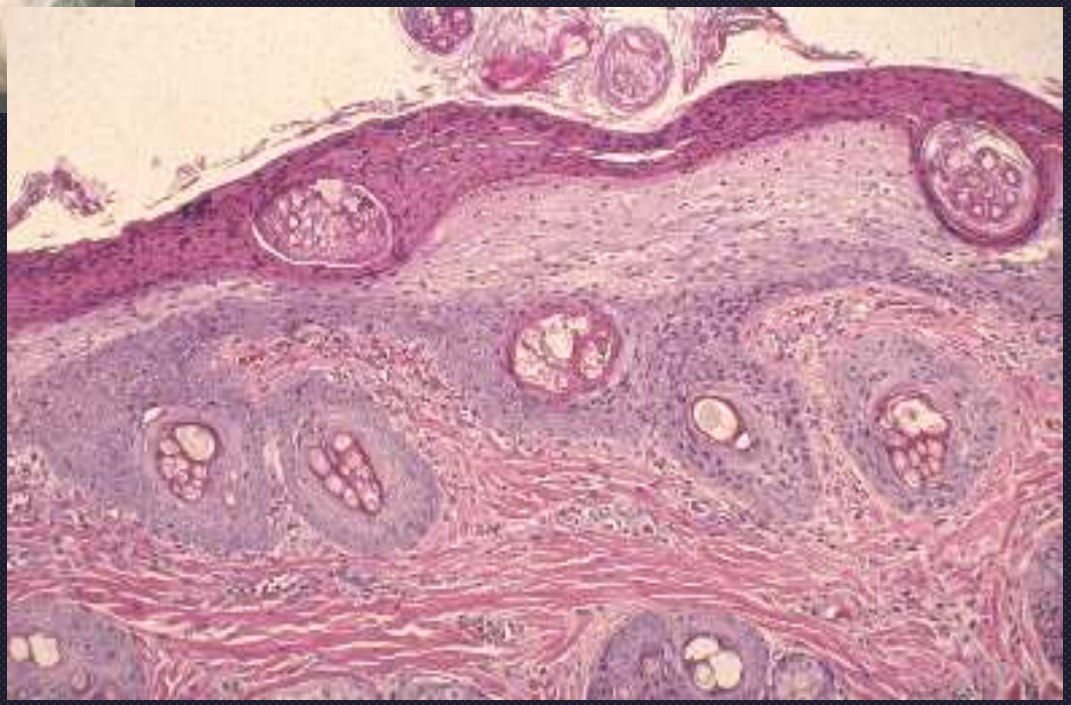
Superficial necrolytic dermatitis due to hepatocutaneous syndrome

“red, white and blue”



Superficial necrolytic dermatitis due to hepatocutaneous syndrome
“red, white and blue”

Superficial necrolytic dermatitis
hepatocutaneous syndrome
“red, white and blue”



Nomenclature

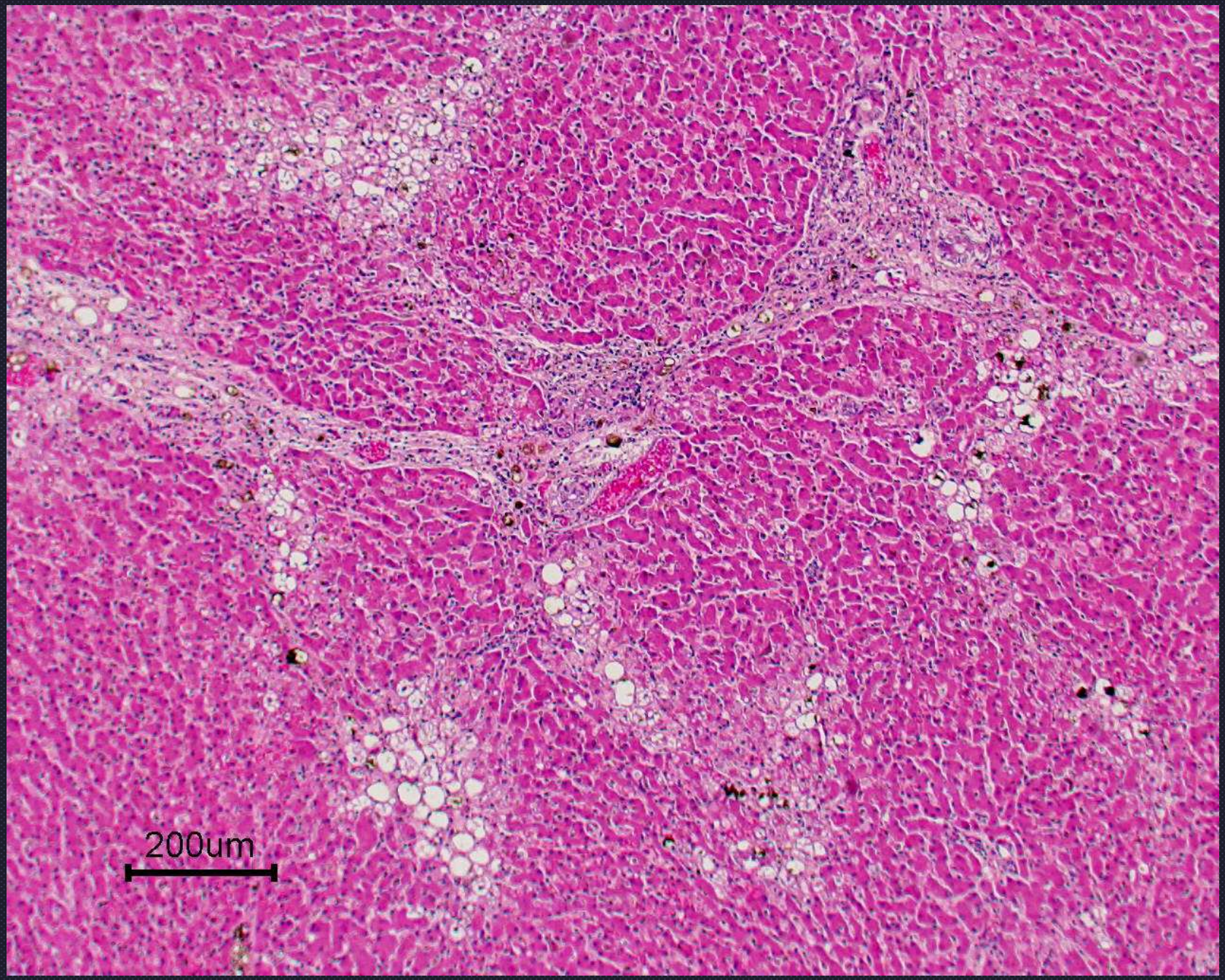
- Superficial Necrolytic Dermatitis- SND
  aka Necrolytic migratory erythema-NME
  aka Metabolic epidermal necrosis-MEN

- Is caused by either:
  - Hepatocutaneous syndrome
  - Glucagonoma syndrome

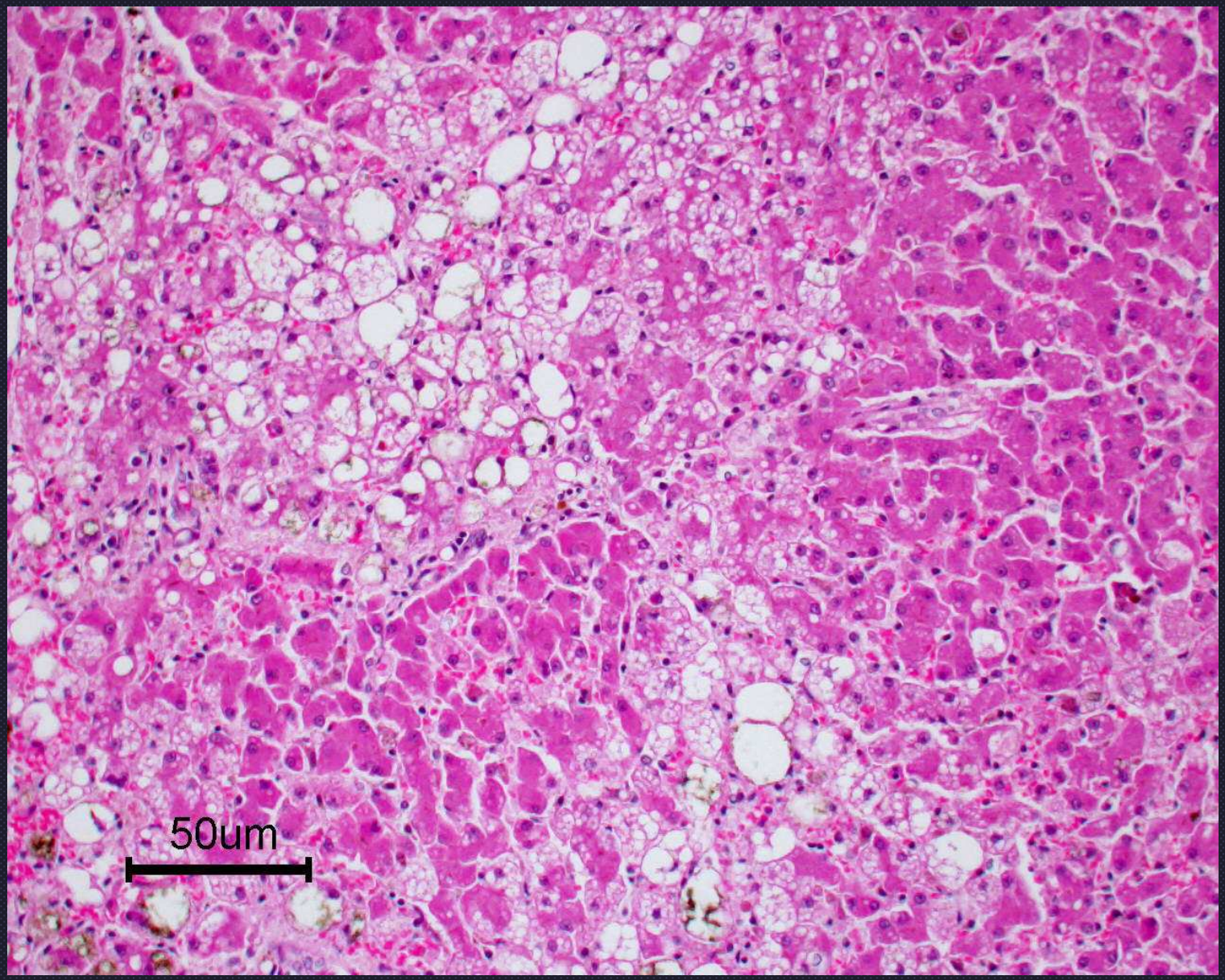
WSAVA Liver Standardization Group

- *Specific hepatopathy*
- Macronodular cirrhosis
- Regenerative hyperplastic nodules divided by bands of fibrous connective tissue (+/- duct hyperplasia)
- Minimal to mild inflammation
- Ballooned hepatocytes similar to steroid hepatopathy

Hepatocutaneous syndrome



hepatocutaneous syndrome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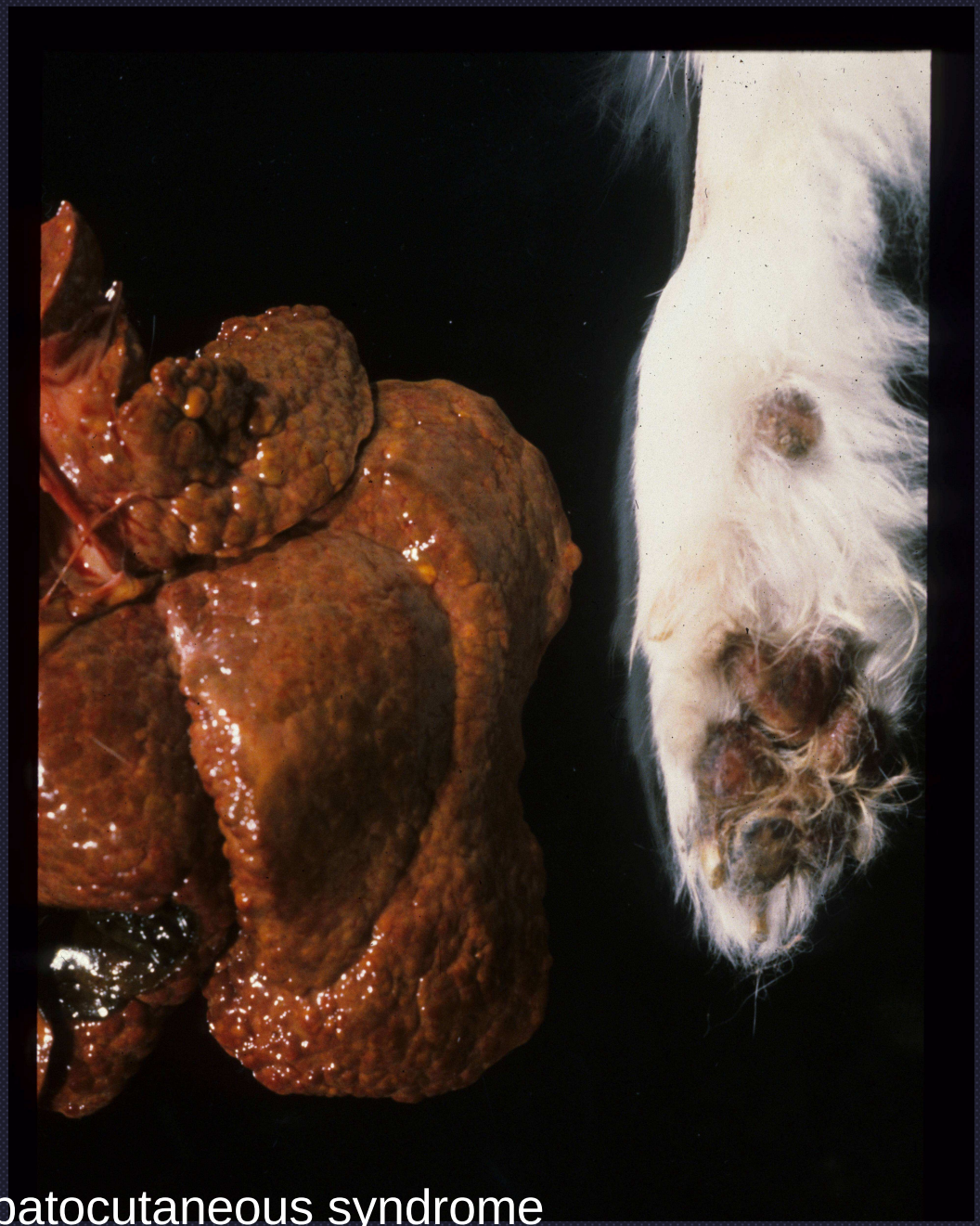


hepatocutaneous syndrome

Gross Lesions

- Surface crusts
- Hyperkeratosis
  - Secondary infection/trauma→Erosions/Ulcers
- ALL Canine cases have FOOTPAD lesions
- Periocular, Perianal, Perivular, Preputial, Scrotal

Pathogenesis?

- Abnormal protein metabolism?
  - Low circulating amino acids
  - Skin has high protein requirement
- Abnormal Zinc and fatty acid metabolism?
- Abnormal glucagon metabolism?

Hepatocutaneous Syndrome

- **Hyperkeratosis, crusting, ulcers on footpads, +/- mc junction**
- Hypoalbuminemia
- **Inc liver enzymes/ inc bile acids**
- +/- Diabetes mellitus; h/o anticonvulsant therapy
- Typical ultrasonographic findings
- Characteristic liver histopathology
- **Diagnostic skin histopathology**

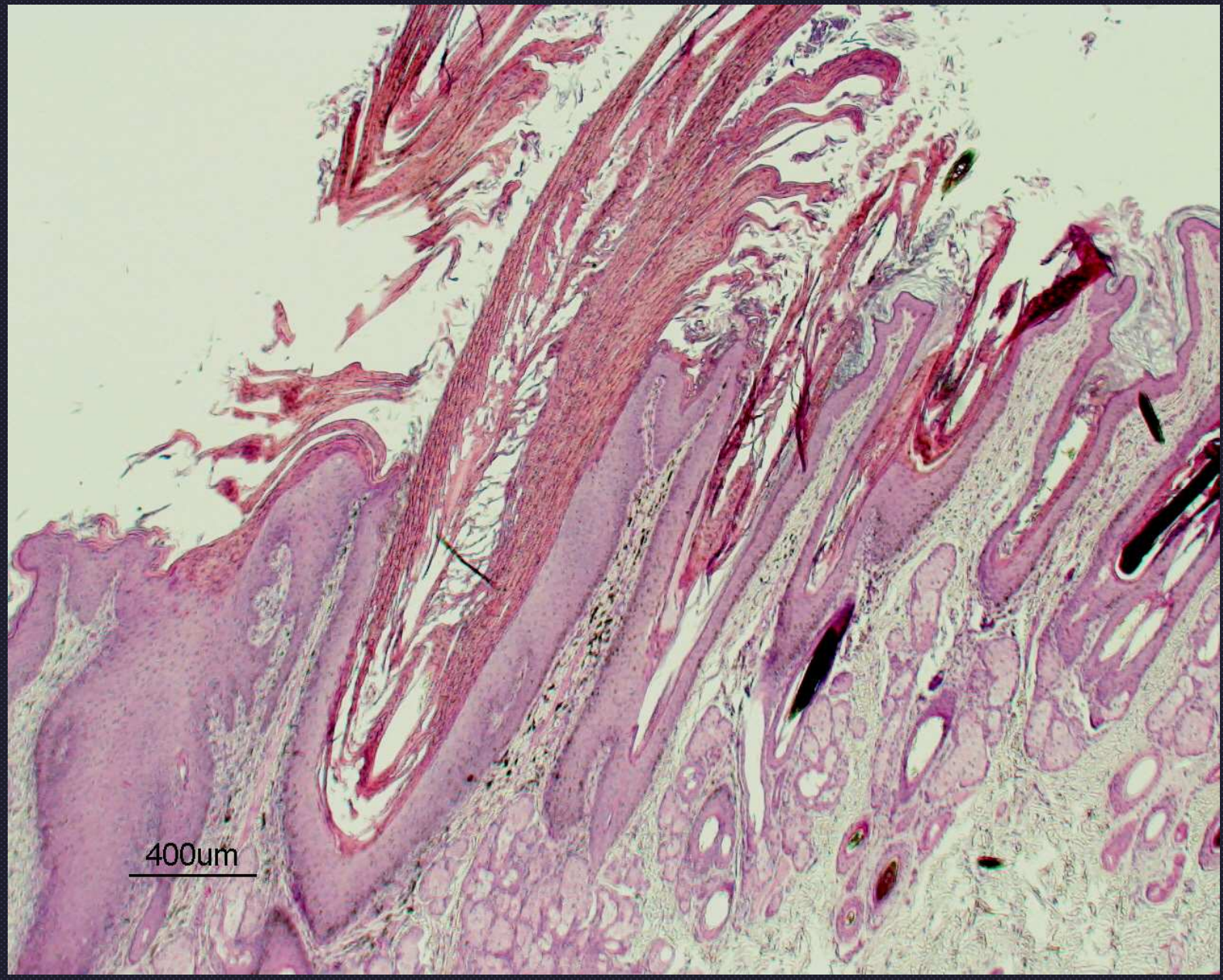
“Swiss cheese” liver

Zinc

- All Tissues contain Zinc
- Important Co-Factor in many enzymatic pathways
- In the skin, Zn is concentrated in the epidermis
- Also concentrated in hair

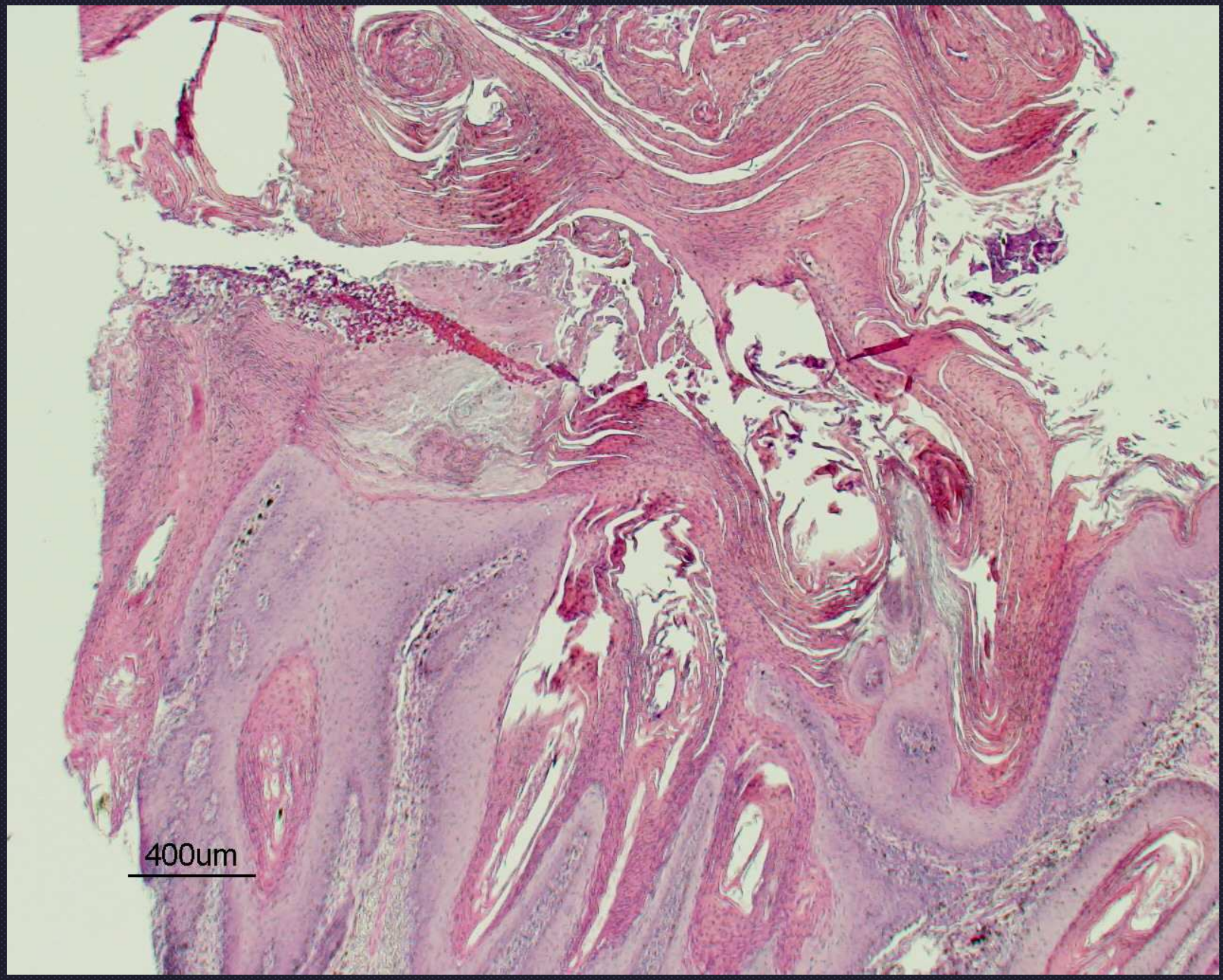
Zinc Absorption

- Required for normal cornification
- Deficiency- delayed wound healing, abnormal cornification of hair, wool, horny appendages

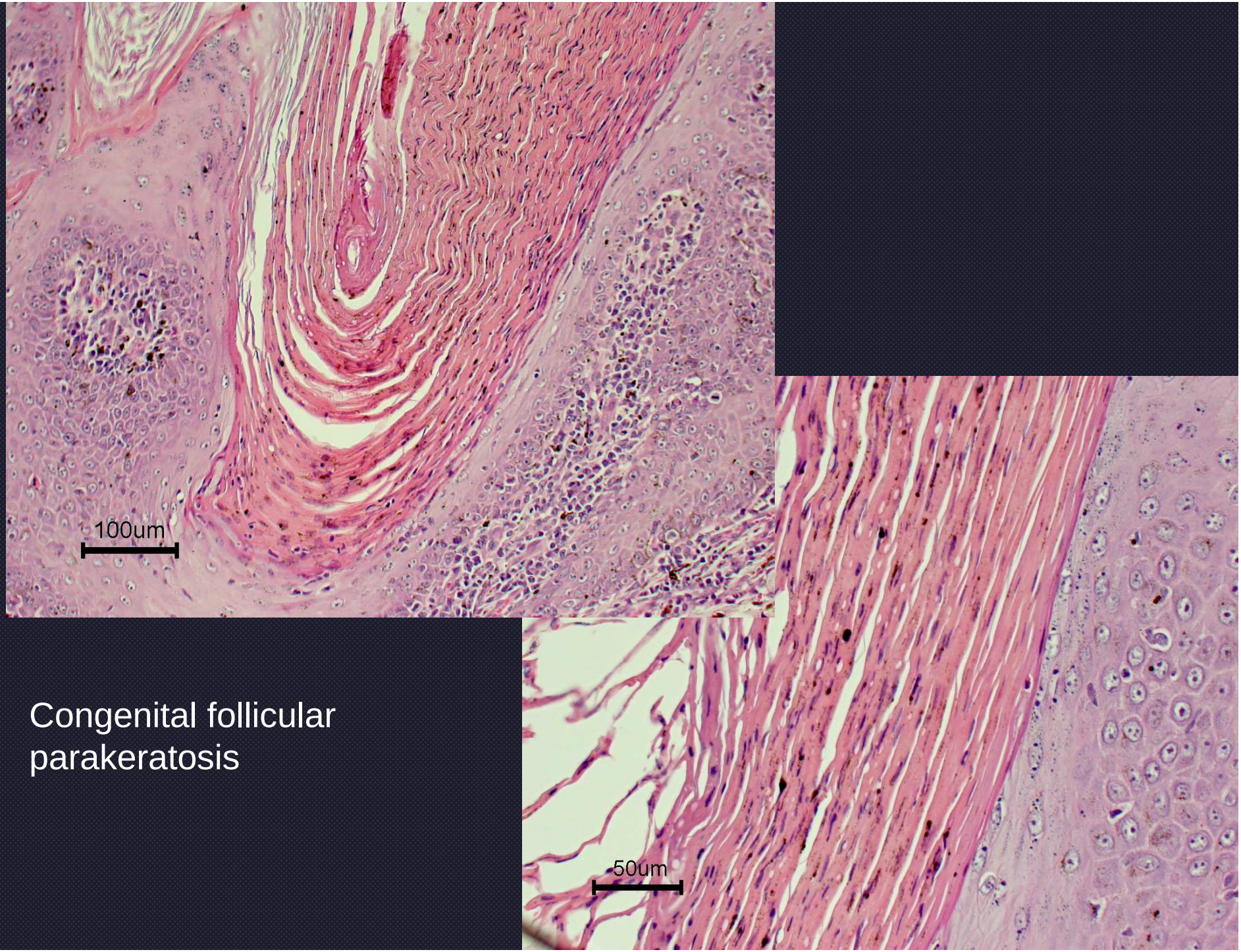


Congenital follicular parakeratosis

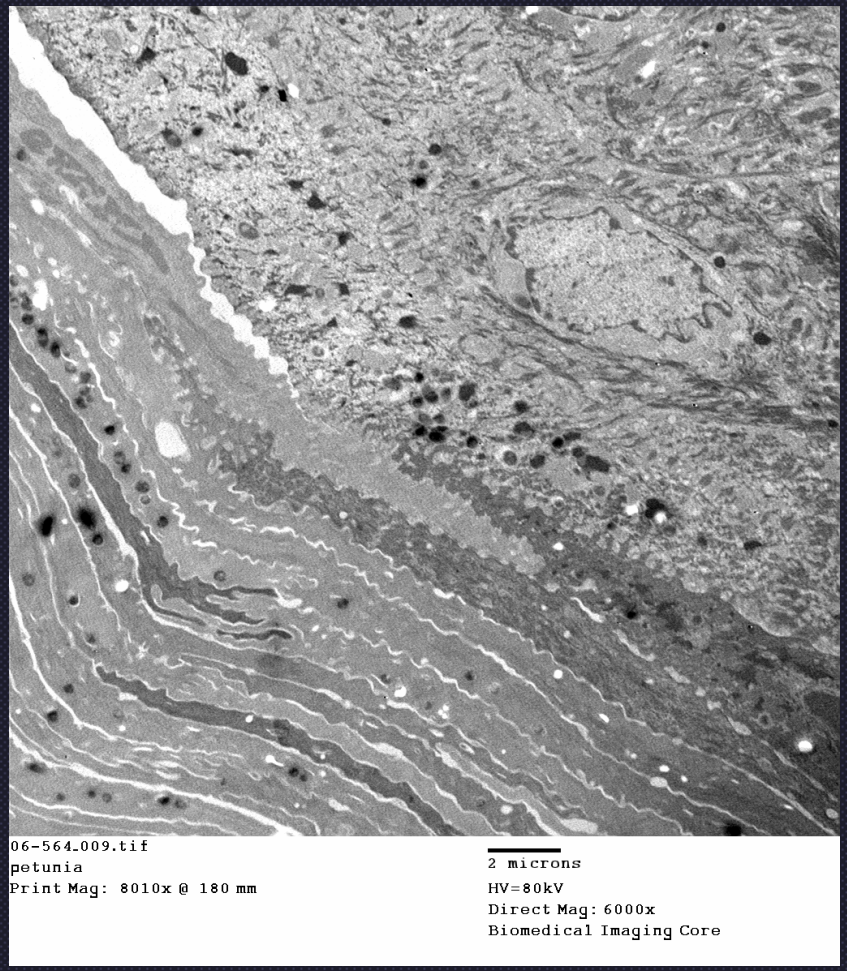
Congenital follicular parakeratosis



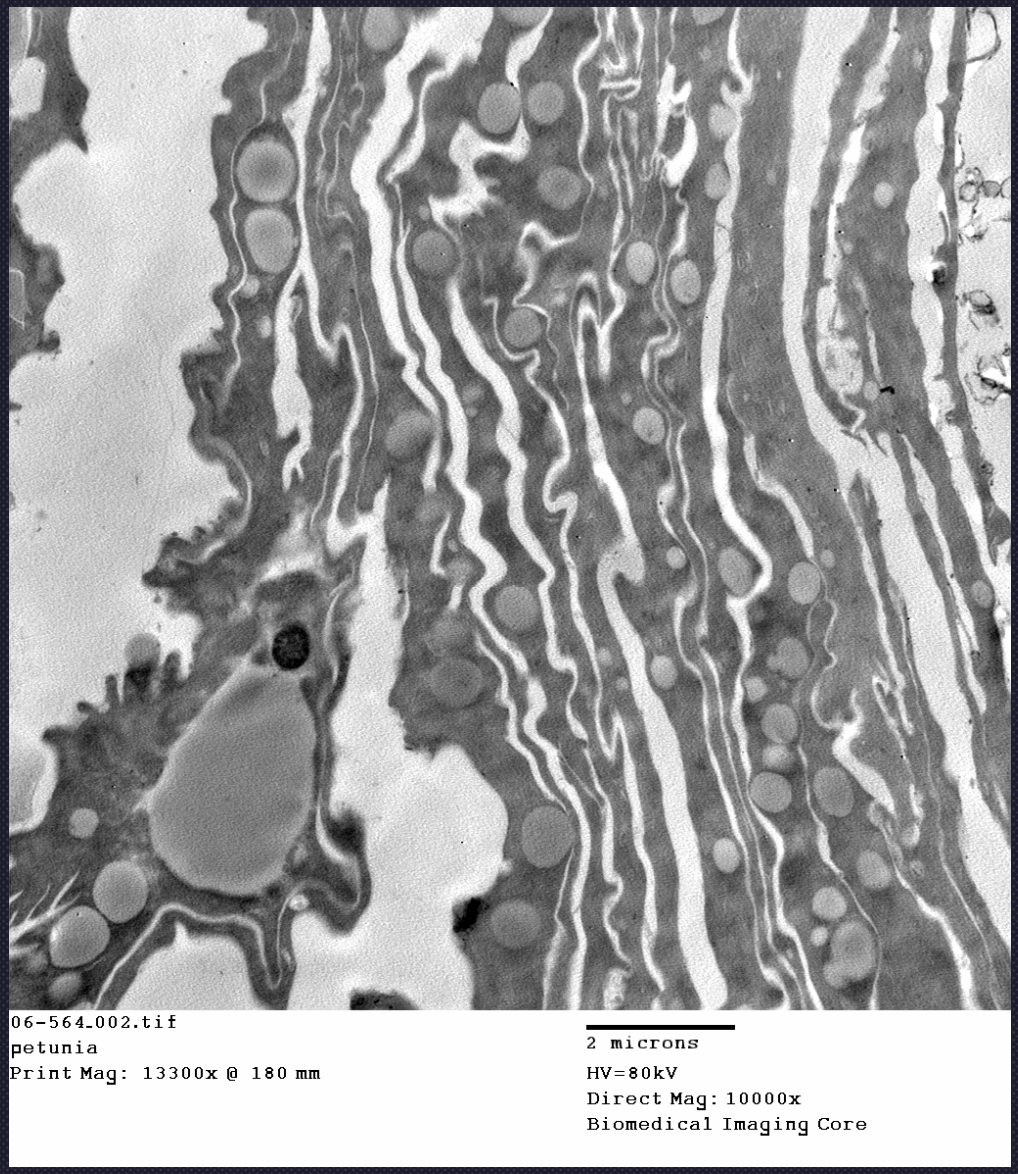
Congenital follicular parakeratosis



Congenital follicular parakeratosis



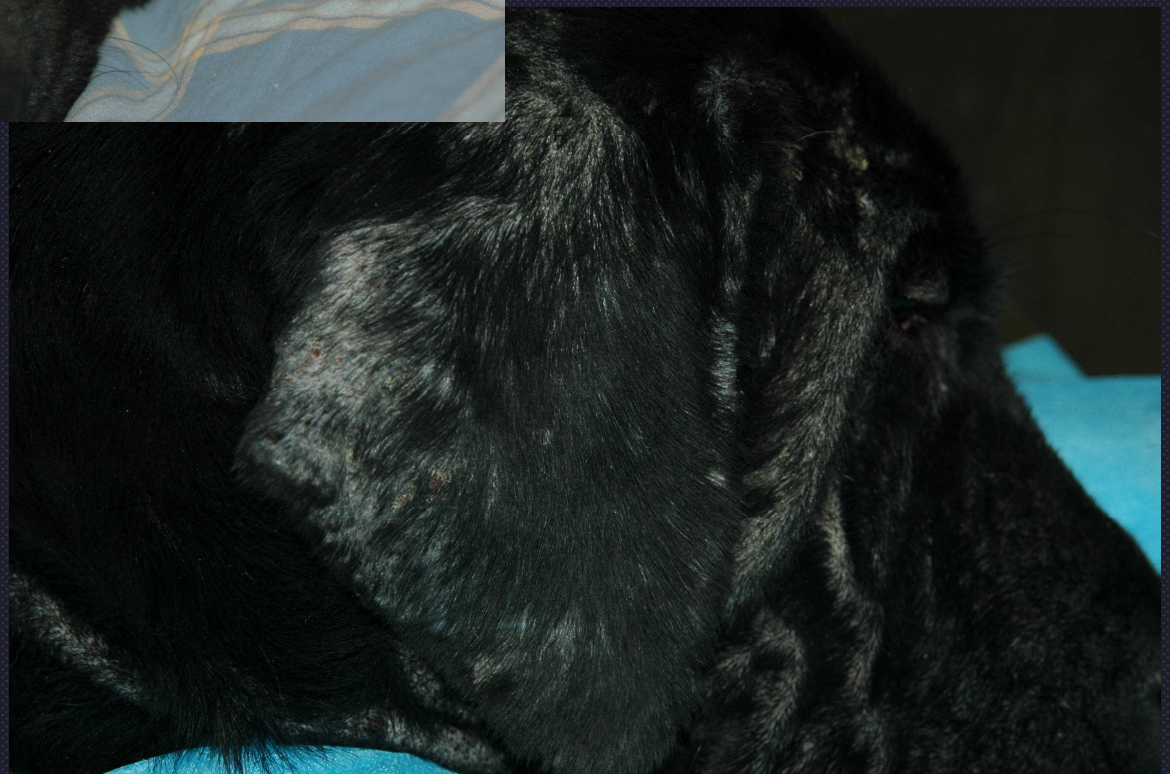
Congenital follicular parakeratosis
EM- lipid droplets in stratum corneum



Congenital follicular parakeratosis
EM- lipid droplets in stratum corneum

Congenital Follicular Parakeratosis

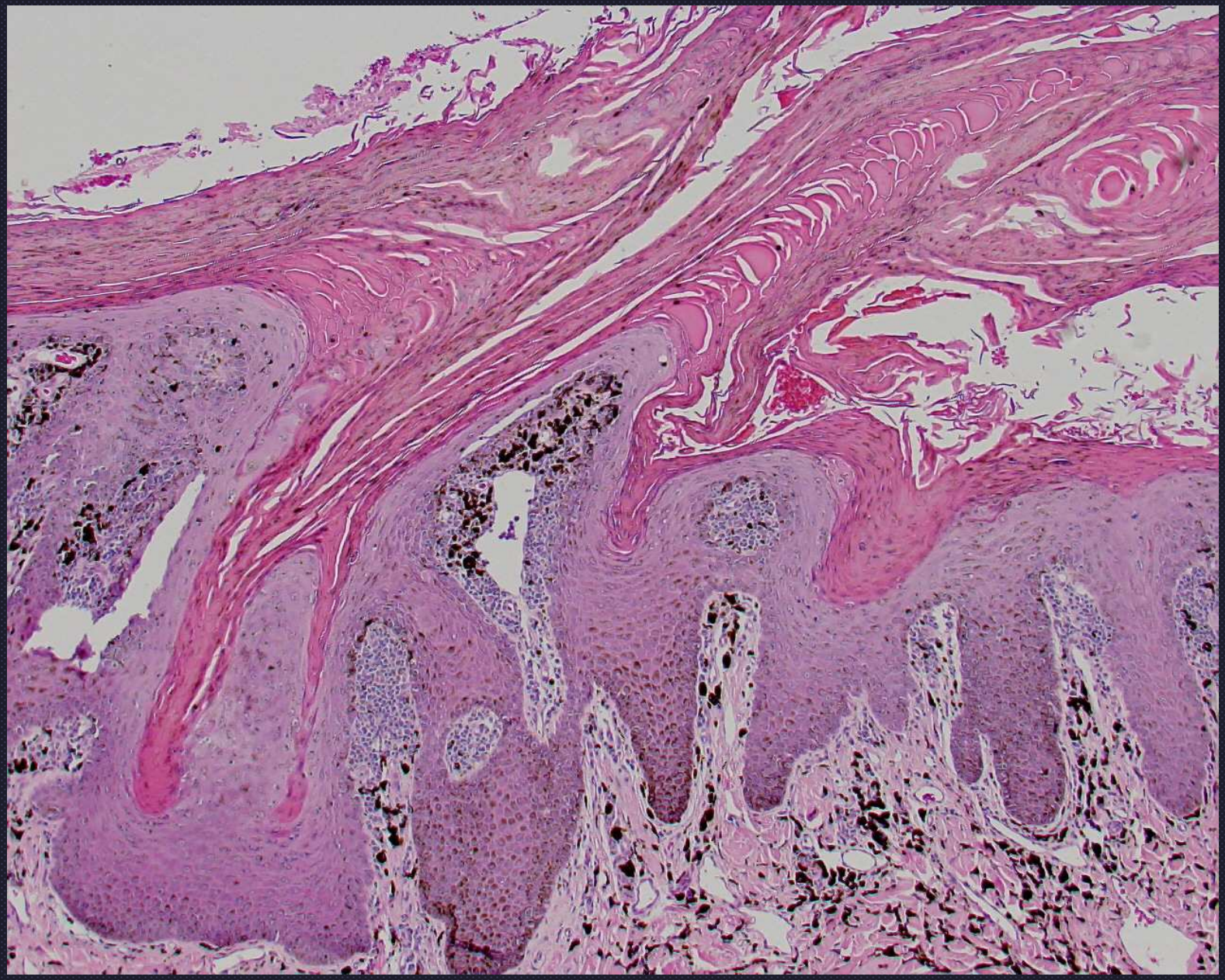
“follicular spires”
Congenital follicular parakeratosis



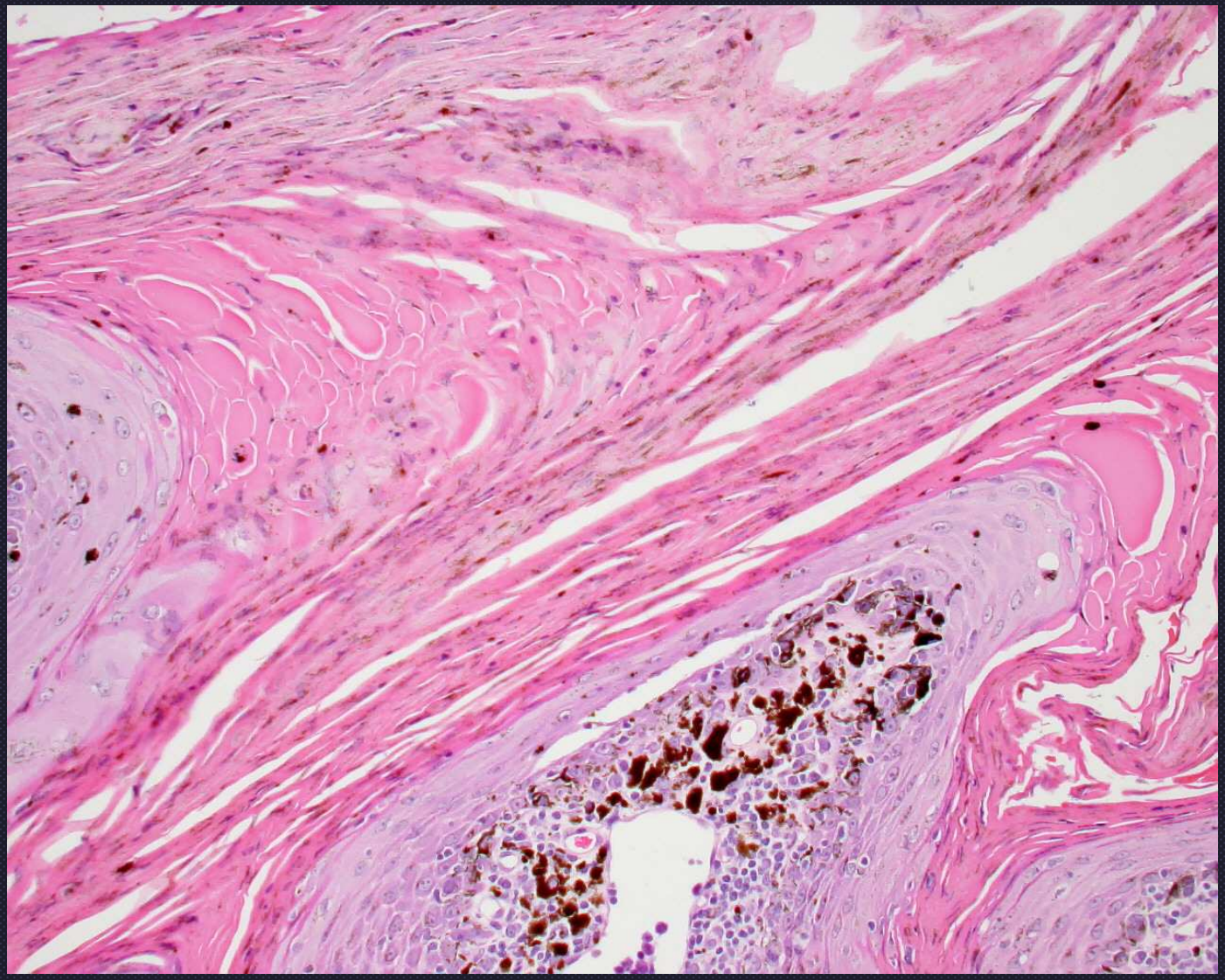
Congenital follicular
parakeratosis
2 yr old lab

Congenital follicular parakeratosis
Basset hound

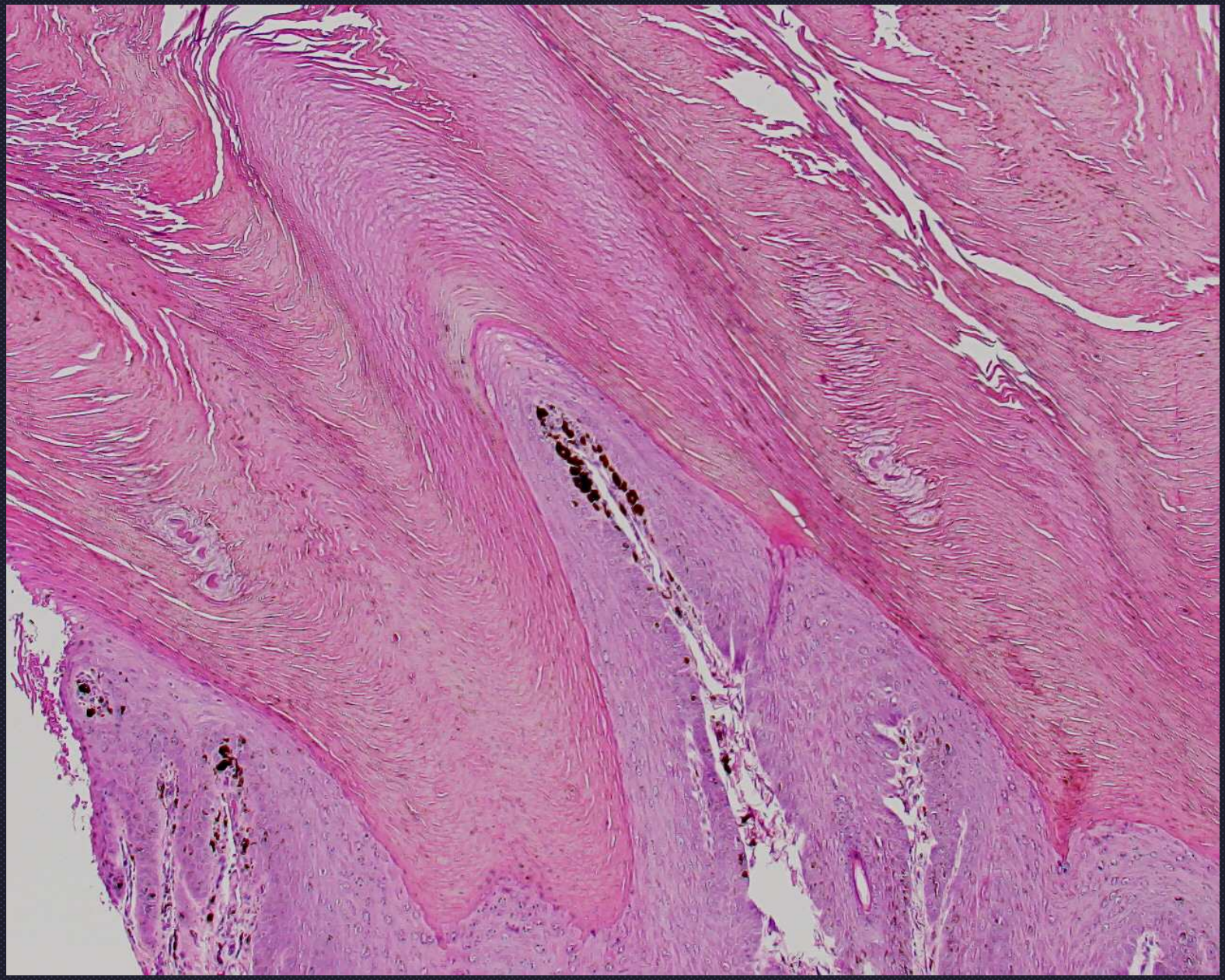
Hereditary nasal hyperkeratosis of Lab retriever



Hereditary nasal parakeratosis of the Lab retriever



Hereditary nasal parakeratosis of the Lab retriever
Note the serum lakes in stratum corneum



Few dogs may have concurrent footpad hyperkeratosis

Beautiful (not- pesty!) prickly pear cactus flower in Utah

Pattern Diagnosis: Part II

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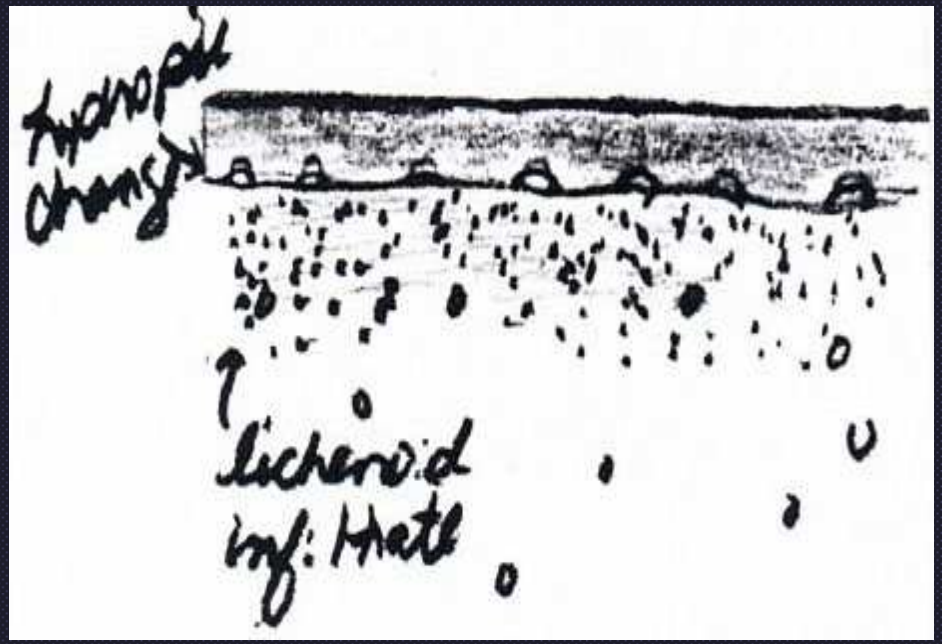
Interface Dermatitis



Interface Dermatitis

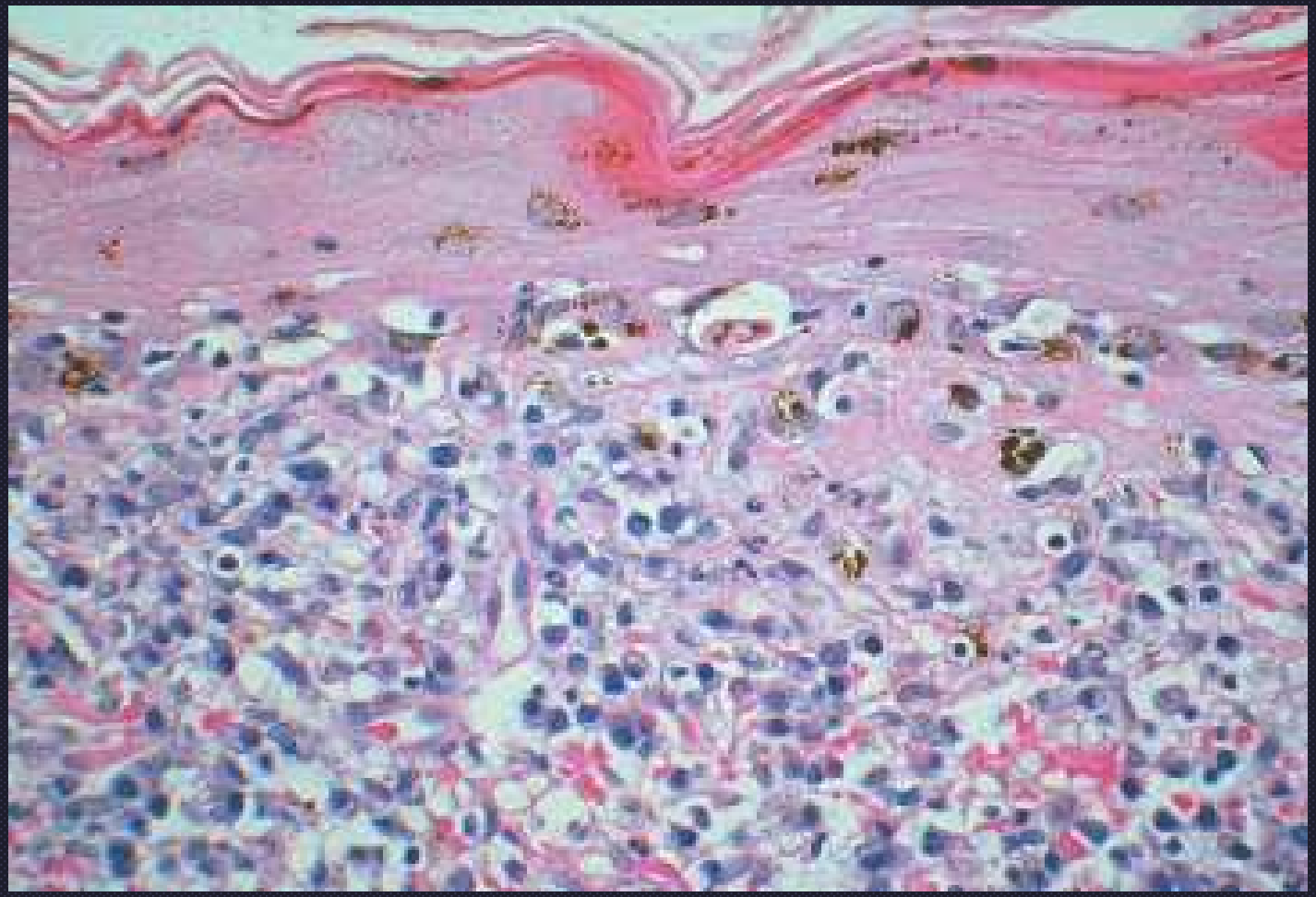
- Reaction pattern due to pathologic events which target **basal keratinocytes and dermoepidermal junction**
- Variety of Mechanisms??
  - Immune complex deposition
  - Type II hypersensitivity reaction
  - Autoreactive cytotoxic T cells

Cat vs Dog

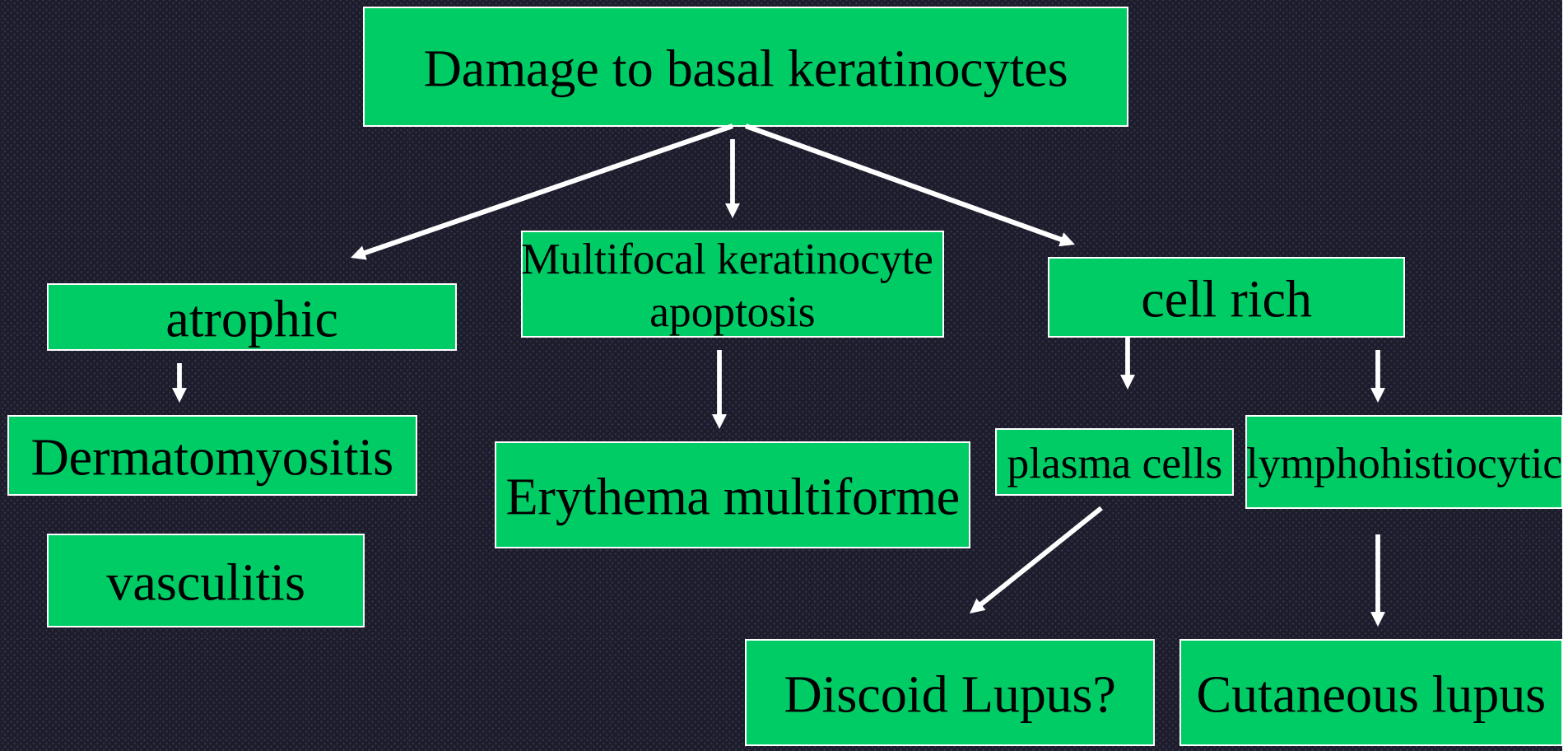
- Thymoma-associated dermatosis
- Erythema multiforme
- Mucinotic mural F/F?
- GVH
- Others

- Erythema multiforme
- Dermatomyositis
- Vaccine-associated ischemic dermatopathy
- Cutaneous vesicular lupus of Collie and Sheltie
- Exfoliative lupus of GSHP
- VKH
- Lichenoid dermatosis
- Others

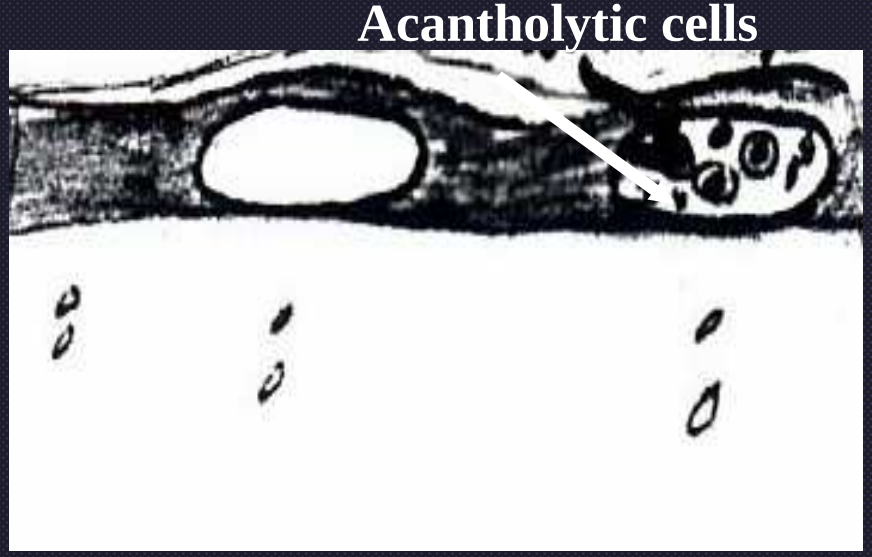
Interface Dermatitis



Interface dermatitis



Intraepidermal Pustular/Vesicular Dermatitis



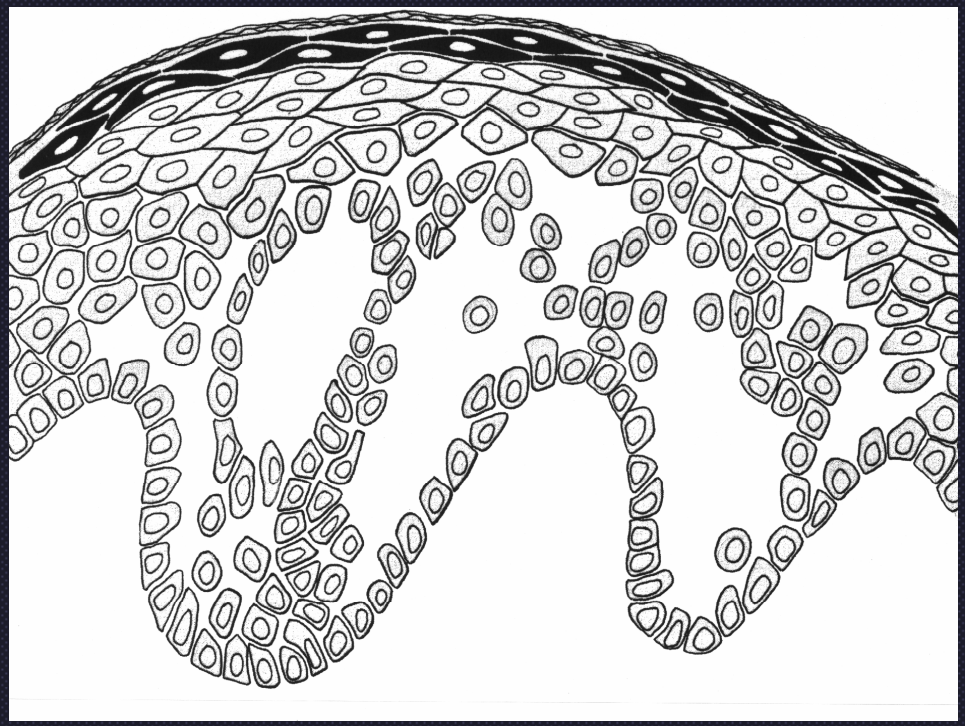
Definitions

- **Vesicle**- fluid filled cavity within or beneath the epidermis less than .5 cm diameter.
- **Bulla**- a vesicle greater than .5 cm dia.
- **Pustule**- a vesicle or bulla with purulent rather than clear liquid content.

Definitions

- **Acantholysis** ***(loosening of the spines Gk.)*** is the loss of cohesion between epidermal cells or keratinocytes. This loss of cohesion results in the formation of clefts, vesicles and bullae.
- **Acantholytic cells-** keratinocytes which separate completely from their neighbors, become round, with a round nucleus and eosinophilic cytoplasm
- Do not confuse with **ACANTHOSIS!!**
- **Use "acantholytic cell" or "acantholytic keratinocyte"**

Acantholysis



Methods of Acantholysis

- #1 Autoimmune disease due to autoantibody production to cell adhesion molecules

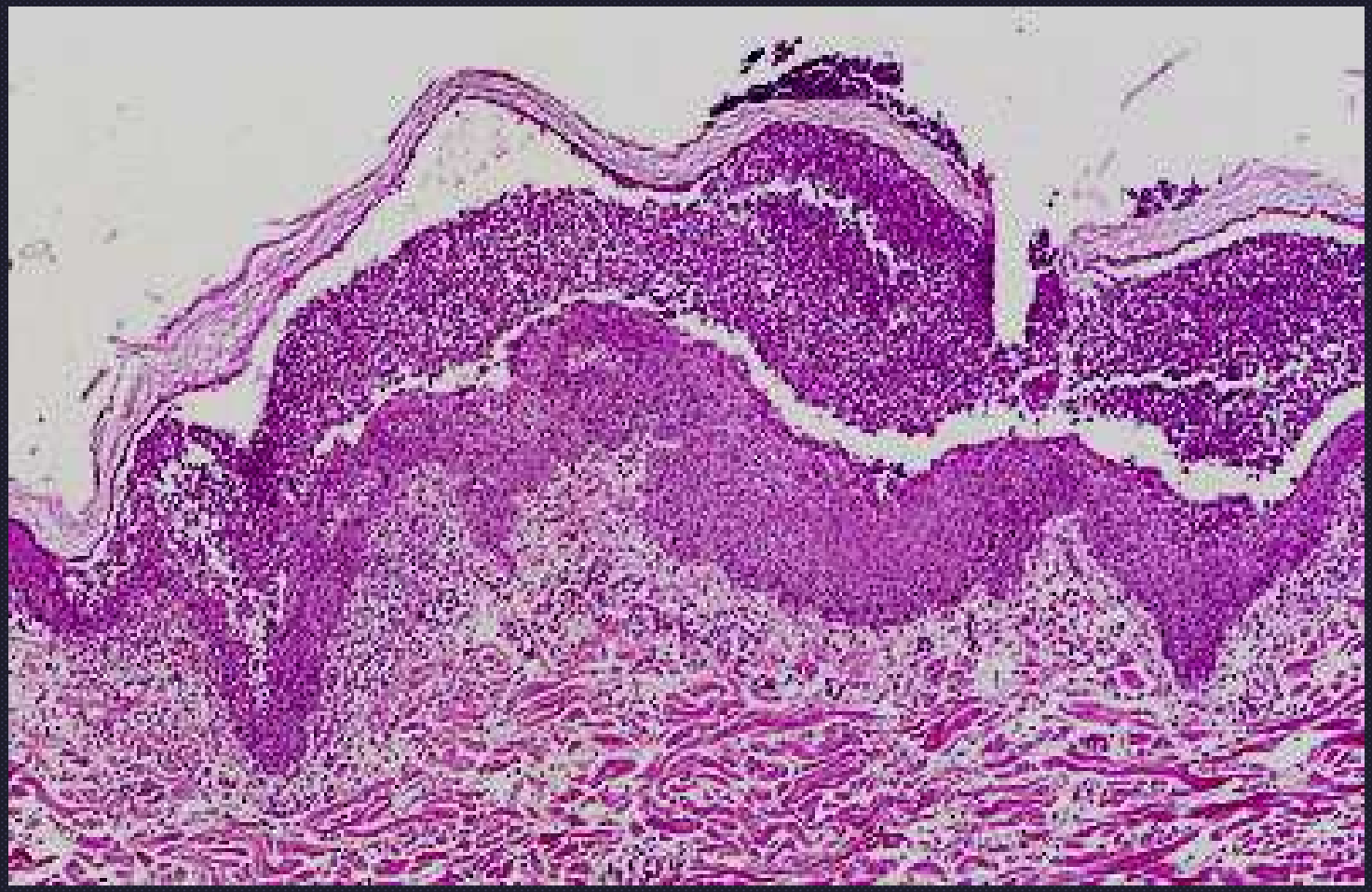
Methods of Acantholysis

- Bacterial infection with release of proteolytic enzymes and bacterial toxins
  - **mild acantholysis
  - **bacteria usually present
  - ** small pustules
- Dermatophytosis
  - Trichophton sp. (equine and canine)

Methods of Acantholysis

- *SEVERE!!* edema
  - Intercellular edema- Spongiosis
  - Intracellular edema- "Ballooning degeneration" ??? *Is this true*?

  - Equine urticarial reaction



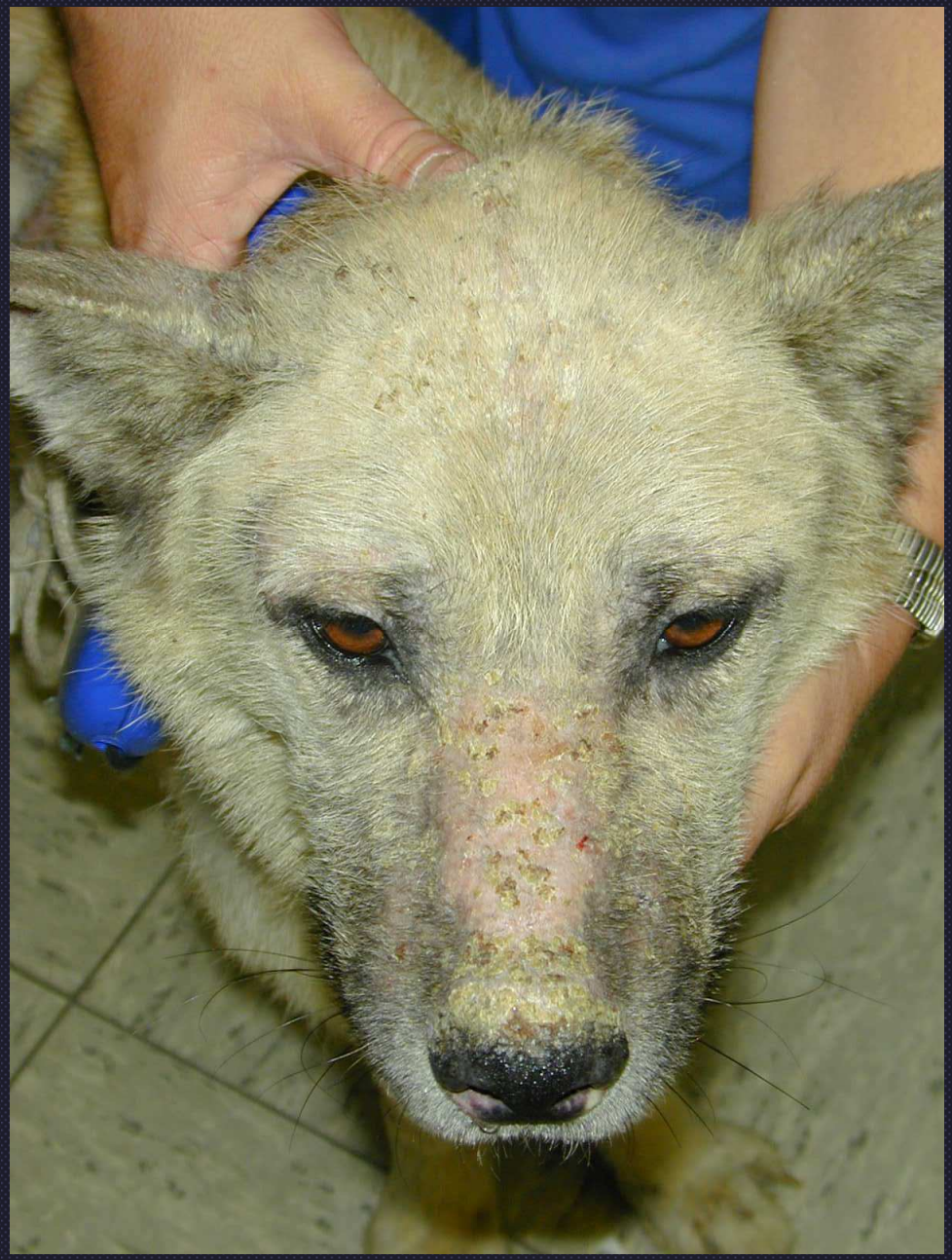
Intraepidermal pustular dermatitis
Pemphigus foliaceus (PF)

Pemphigus foliaceus

Pemphigus foliaceus

Pemphigus foliaceus

Pemphigus foliaceus



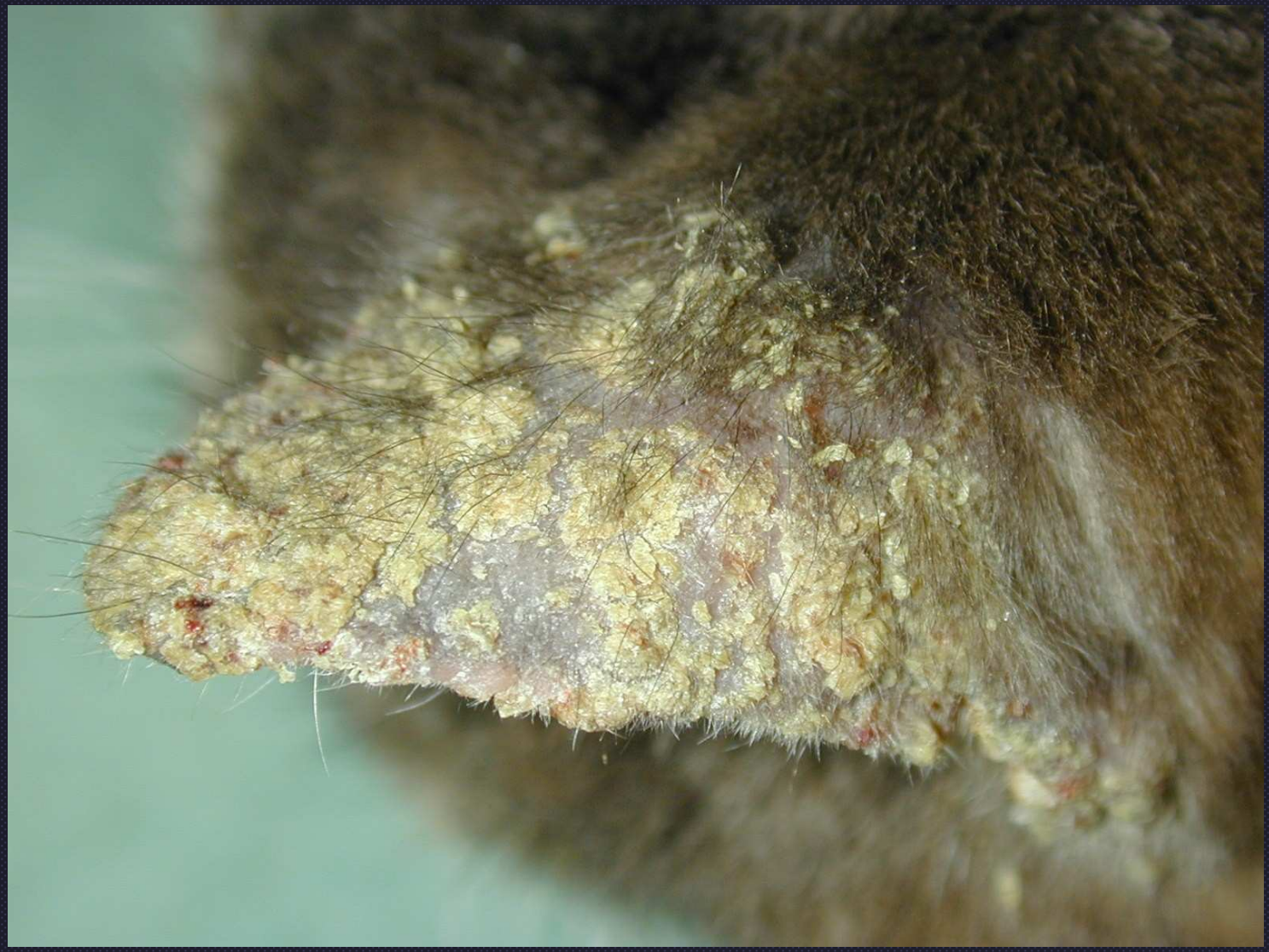
Footpad hyperkeratosis and crusting due to pemphigus foliaceus

PF vs Pyoderma

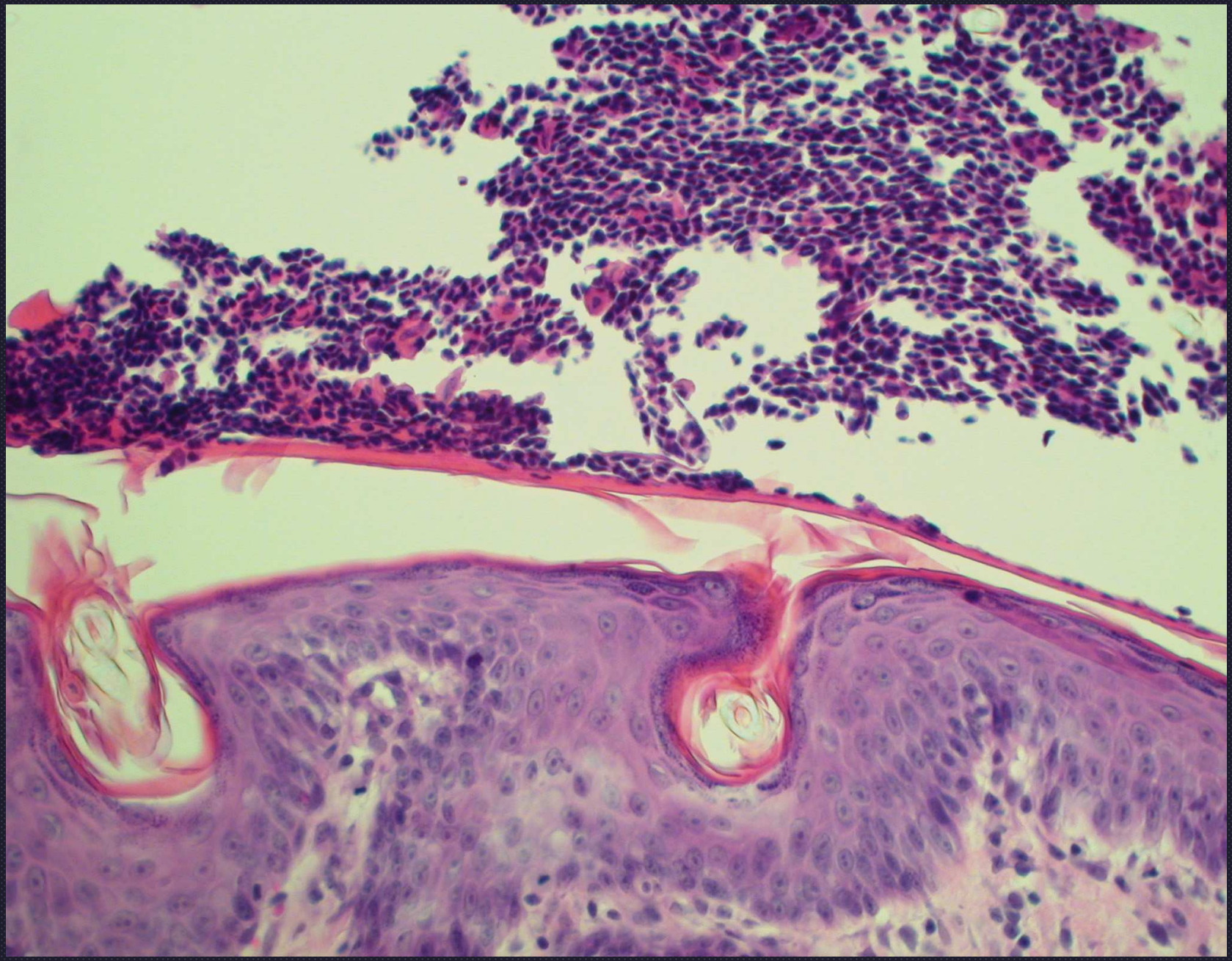
- Large subcorneal pustules (span several adnexal units) and crusts
- Corneal layer contains waves of pustules
- Nondegenerate neutrophils
- Absence of bacteria

Kuhl and Goldschmidt Vet Pathol 1996

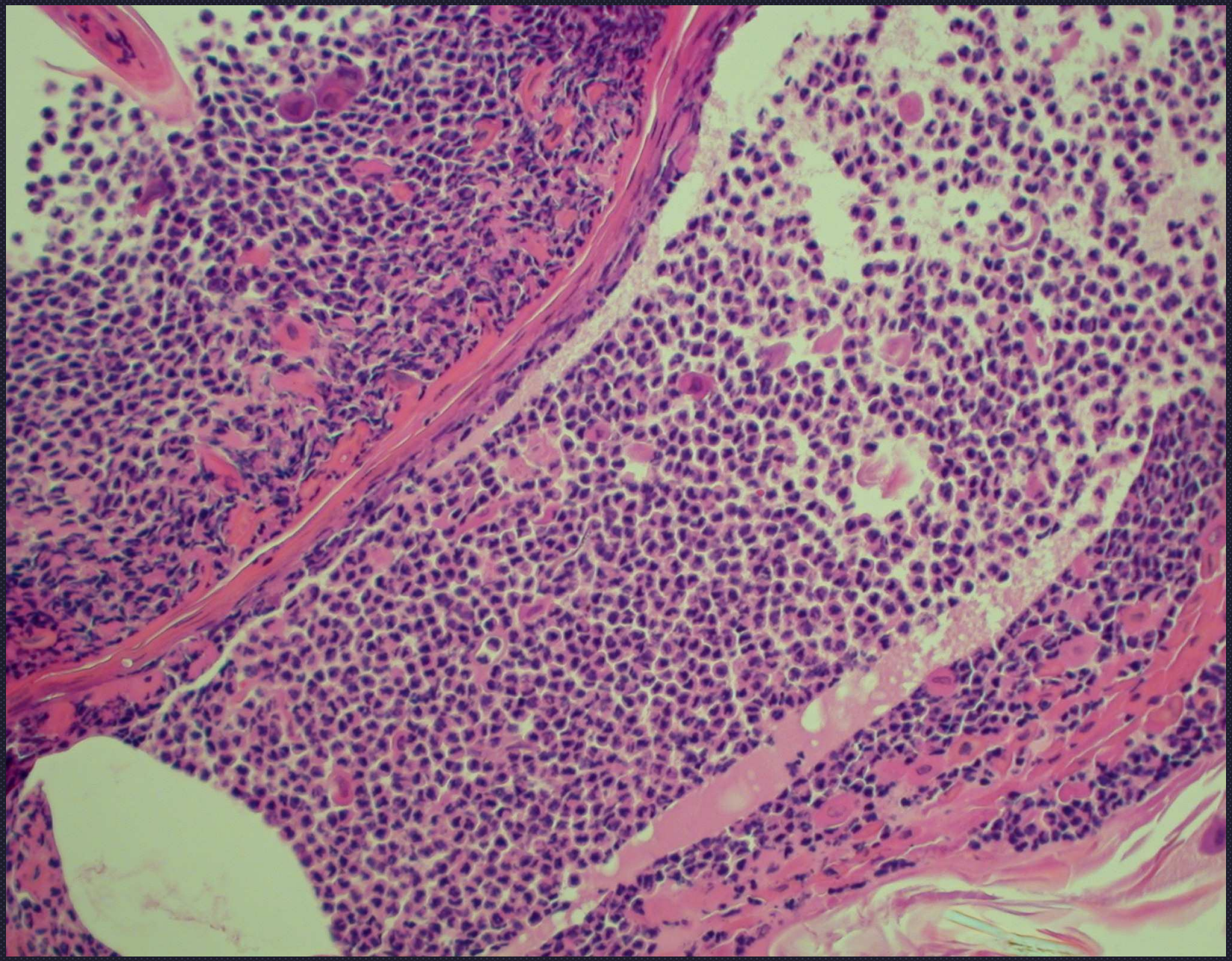
Feline Pemphigus Foliaceus



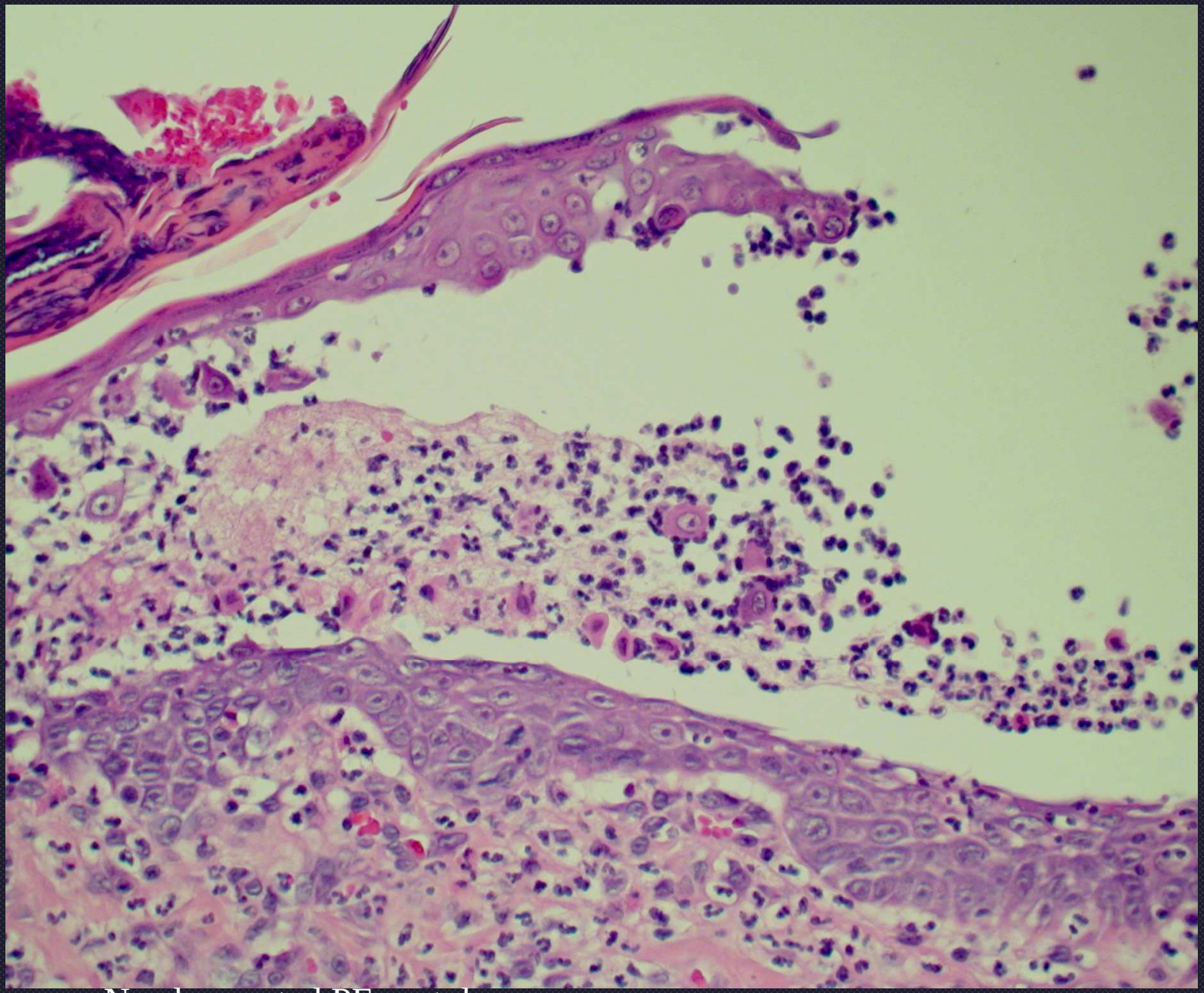
Ear margin crusting is common in cats with PF



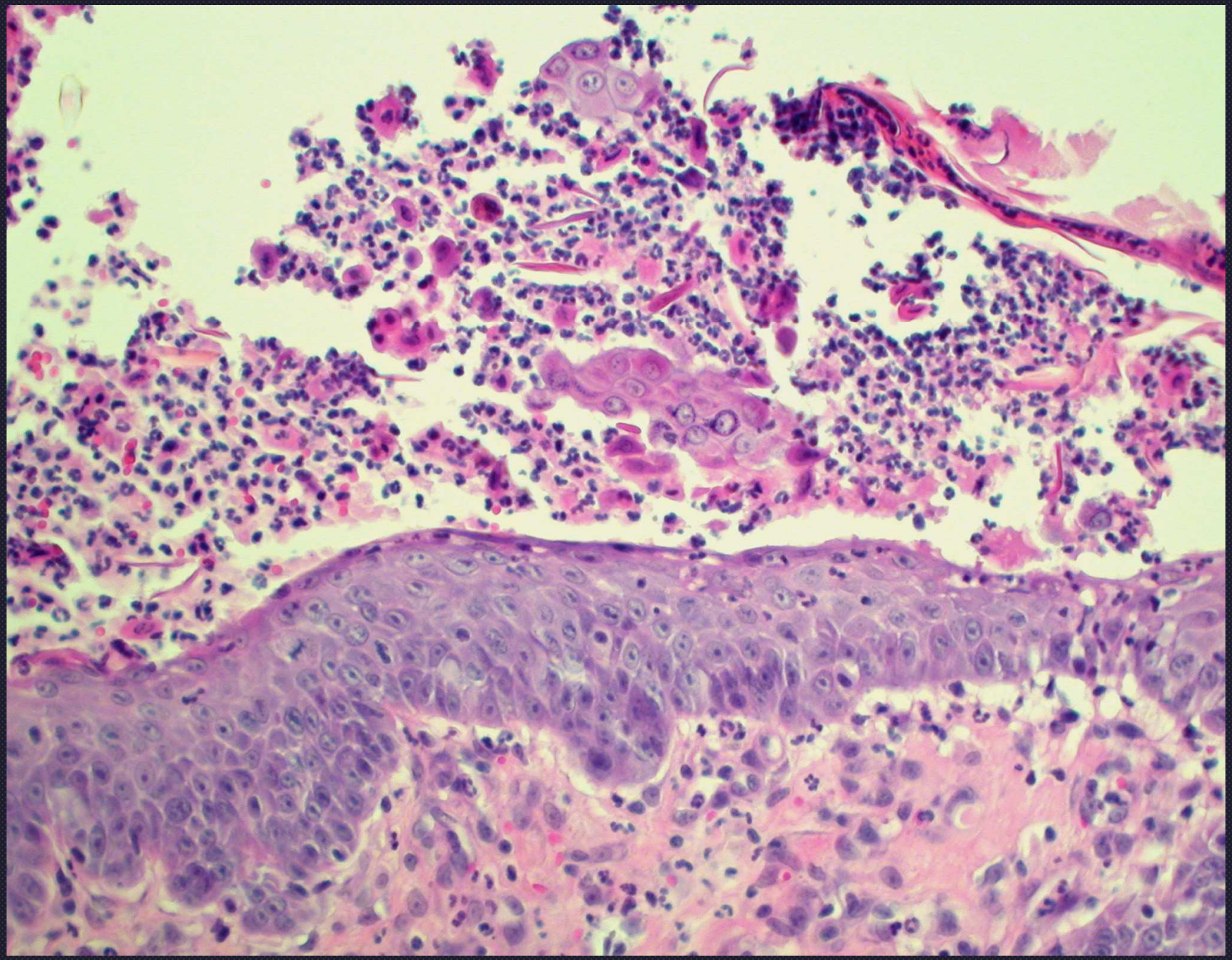
Feline PF



Waves of pustules and multiple zones of cornification in feline PF



Newly erupted PF pustule



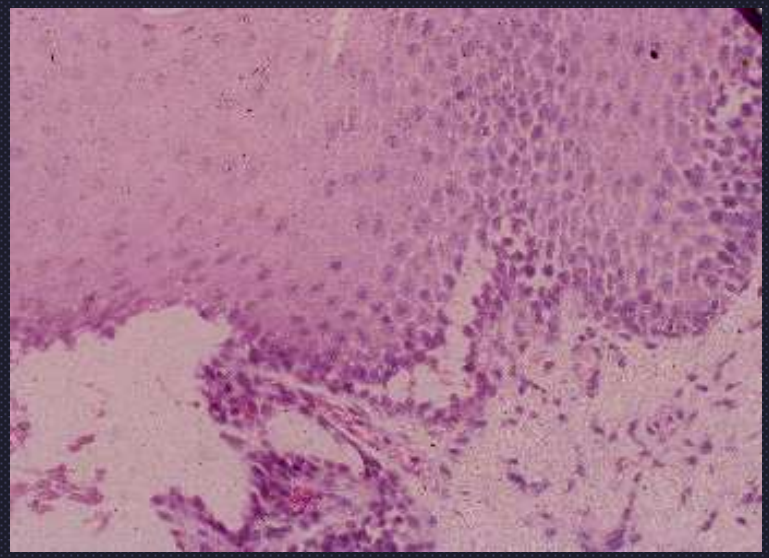
Rafts of acantholytic cells in PF

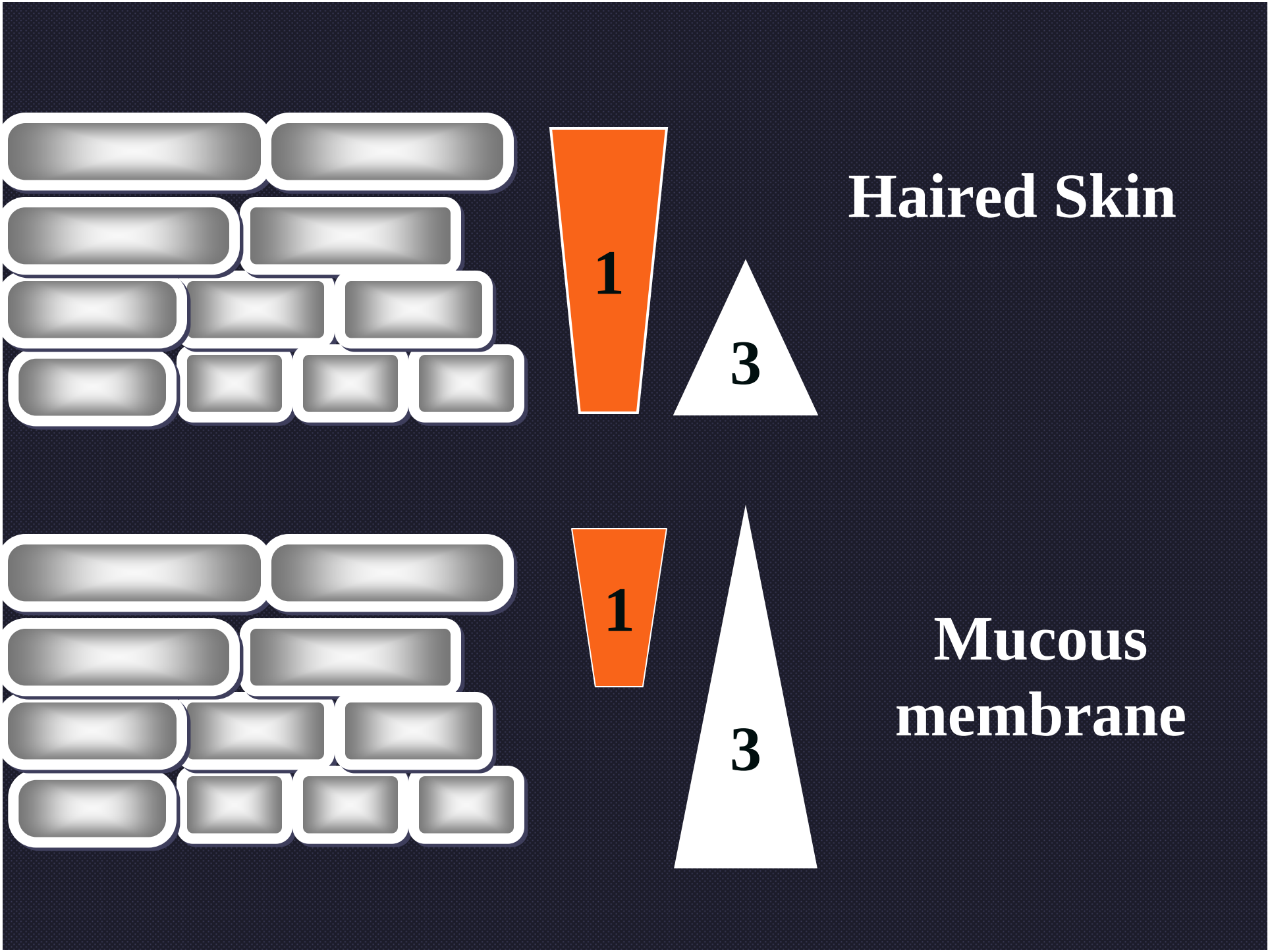
Be careful!

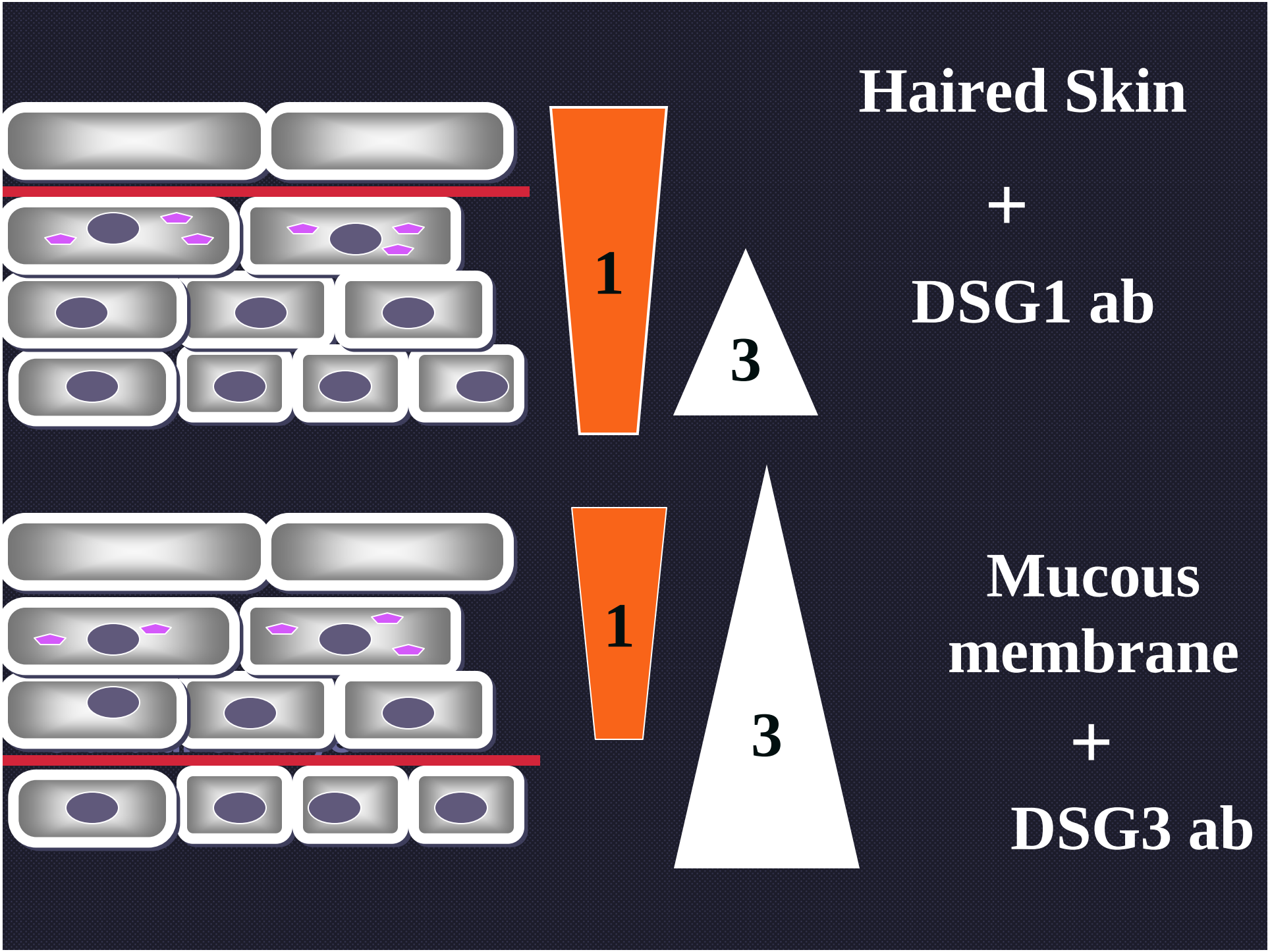
- Acantholytic dermatophytosis!
- When in doubt
- Do a PAS or GMS stain!!!

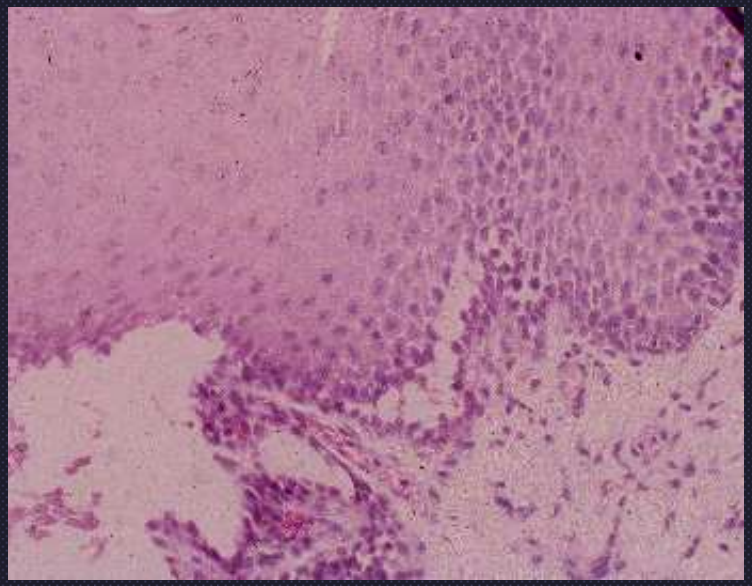
Pemphigus vulgaris

- Acantholysis with suprabasilar clefting
- Desmoglein-3 autoantibody
- Oral mucosa

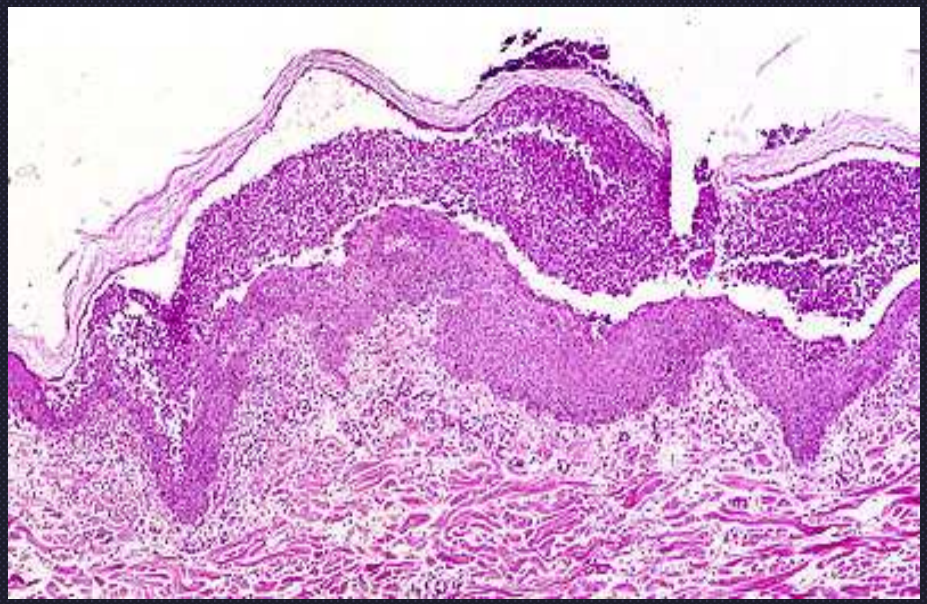



1
3
Haired Skin
1
3
Mucous membrane


Haired Skin
+
DSG1 ab
1
3
Mucous membrane
+
DSG3 ab
1
3



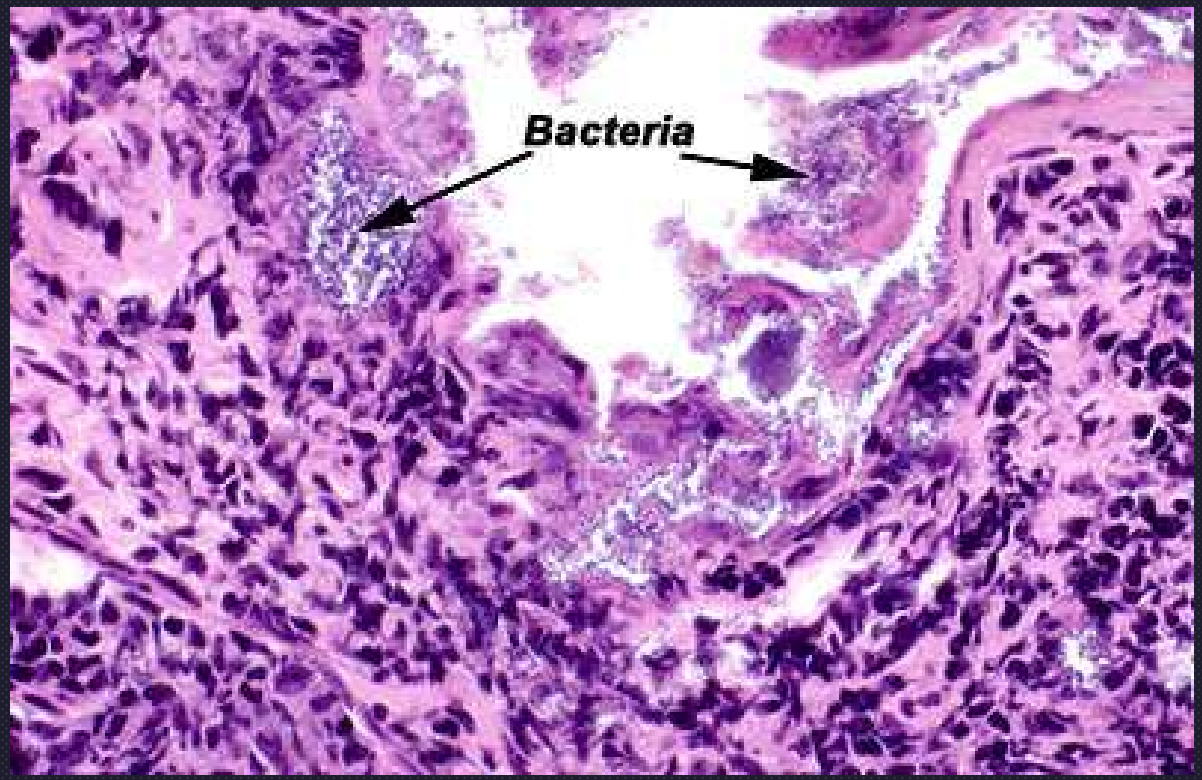
PV



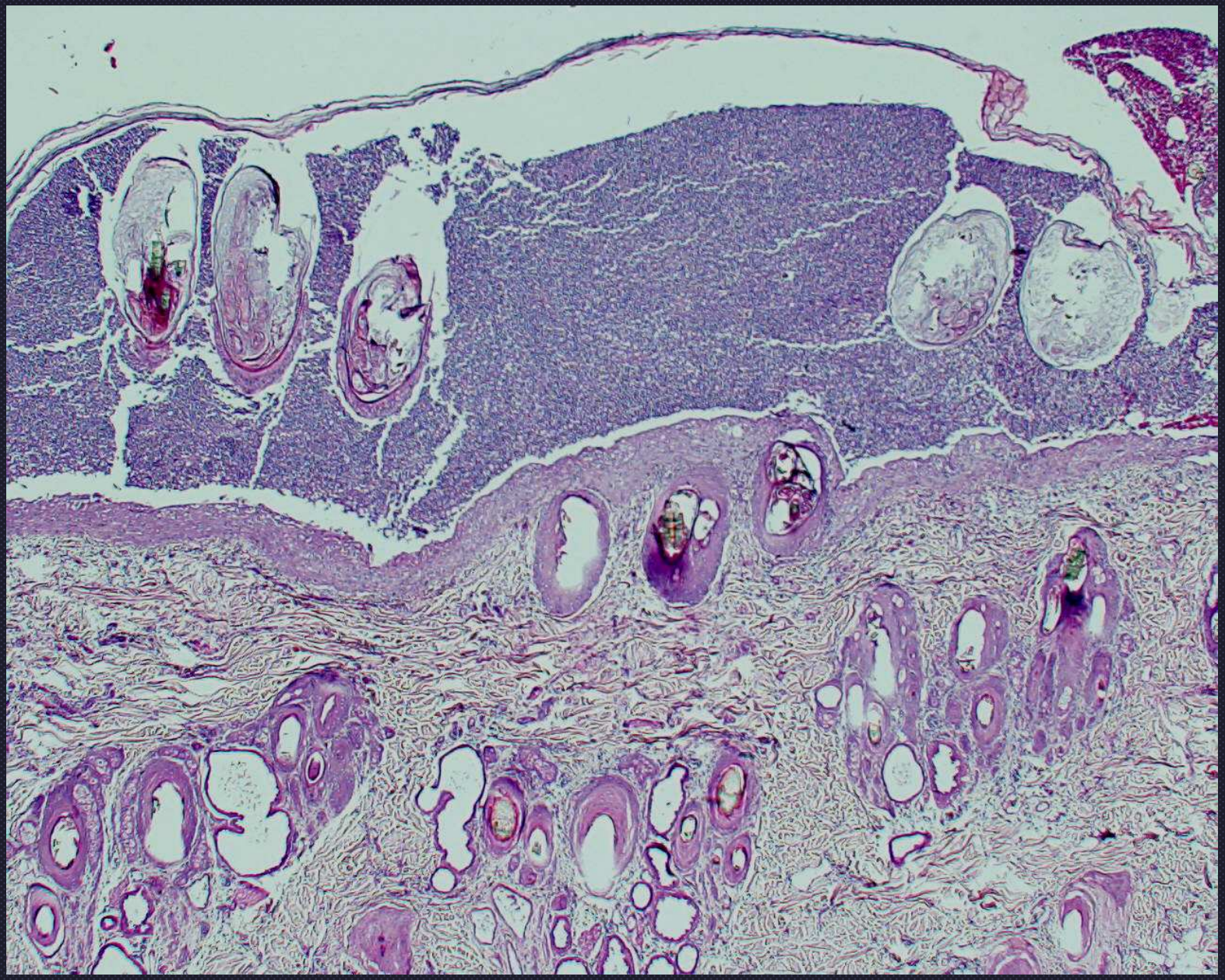
PF

Bacterial Disorders

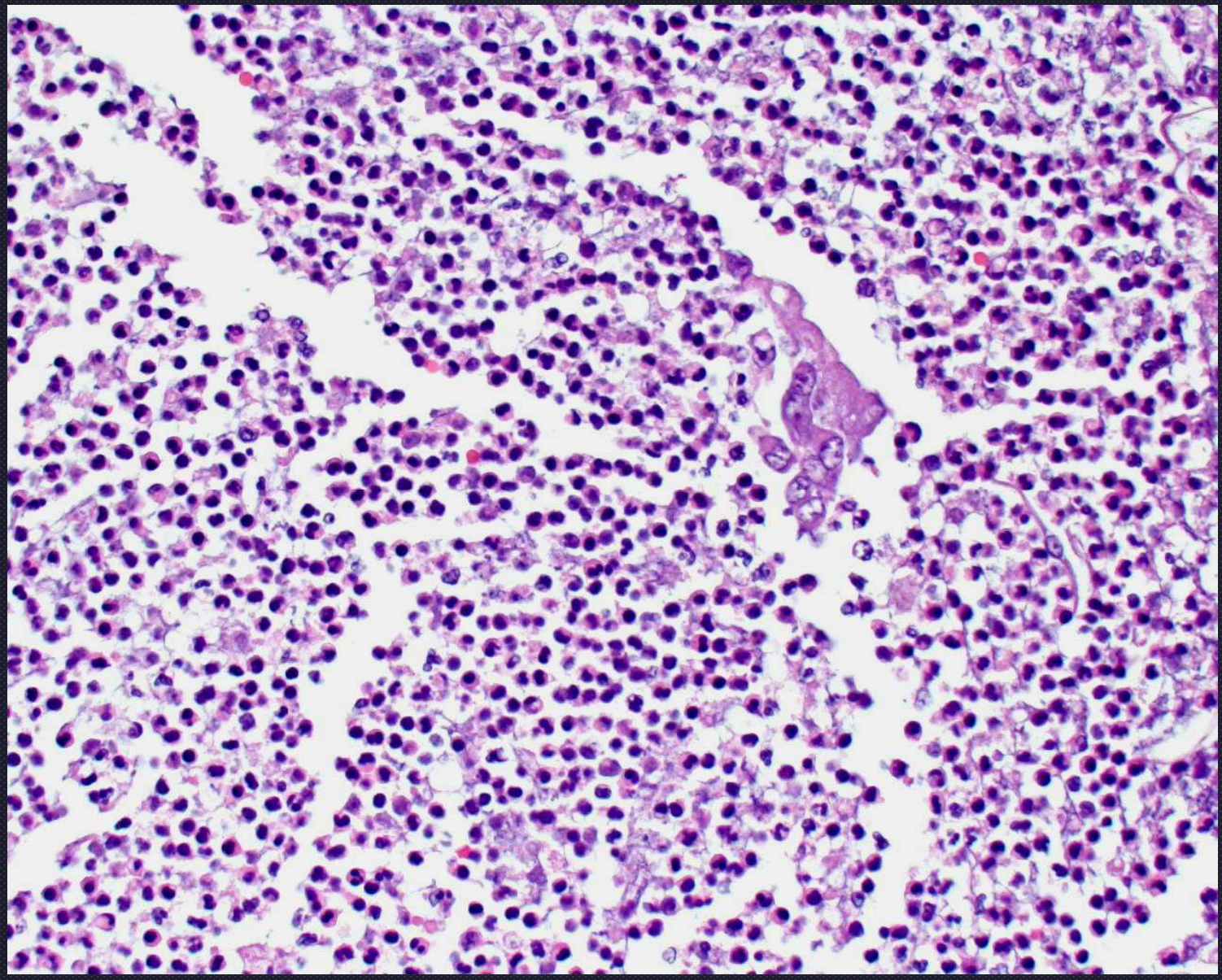
Greasy pig disease


Bacteria

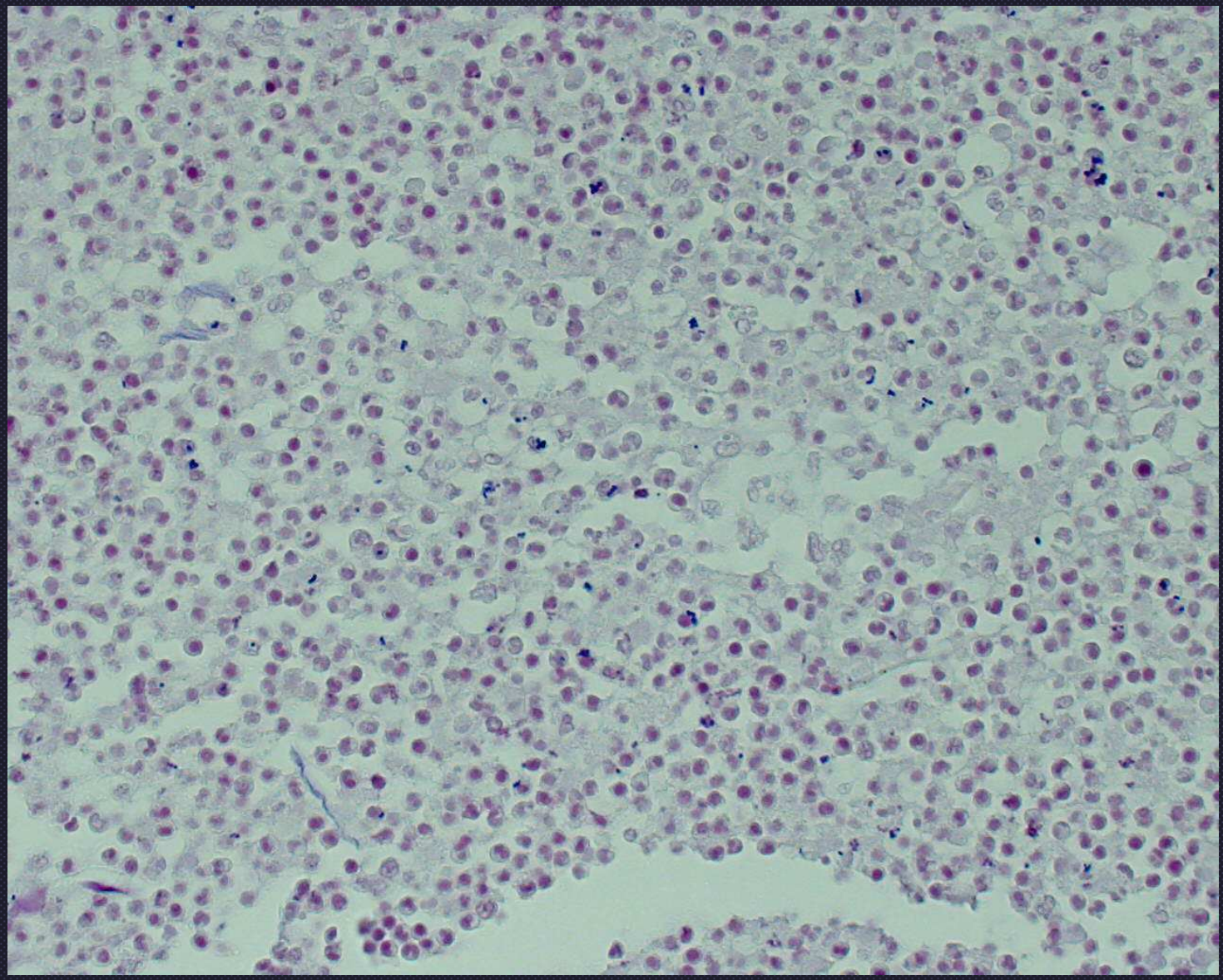
Small pustules on the abdomen of a puppy
“puppy pyoderma”



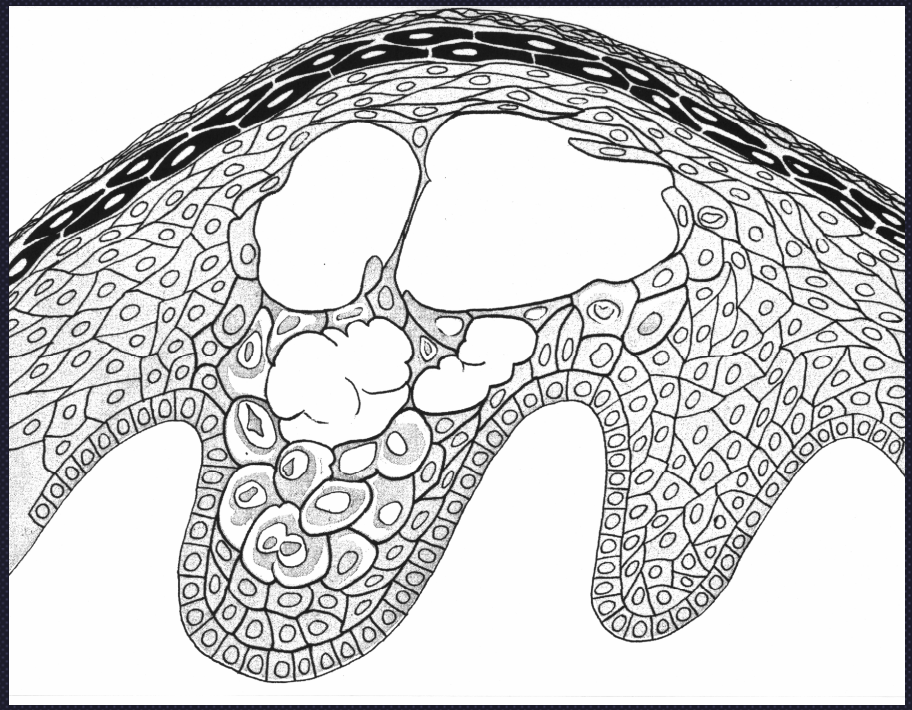
Bullous impetigo



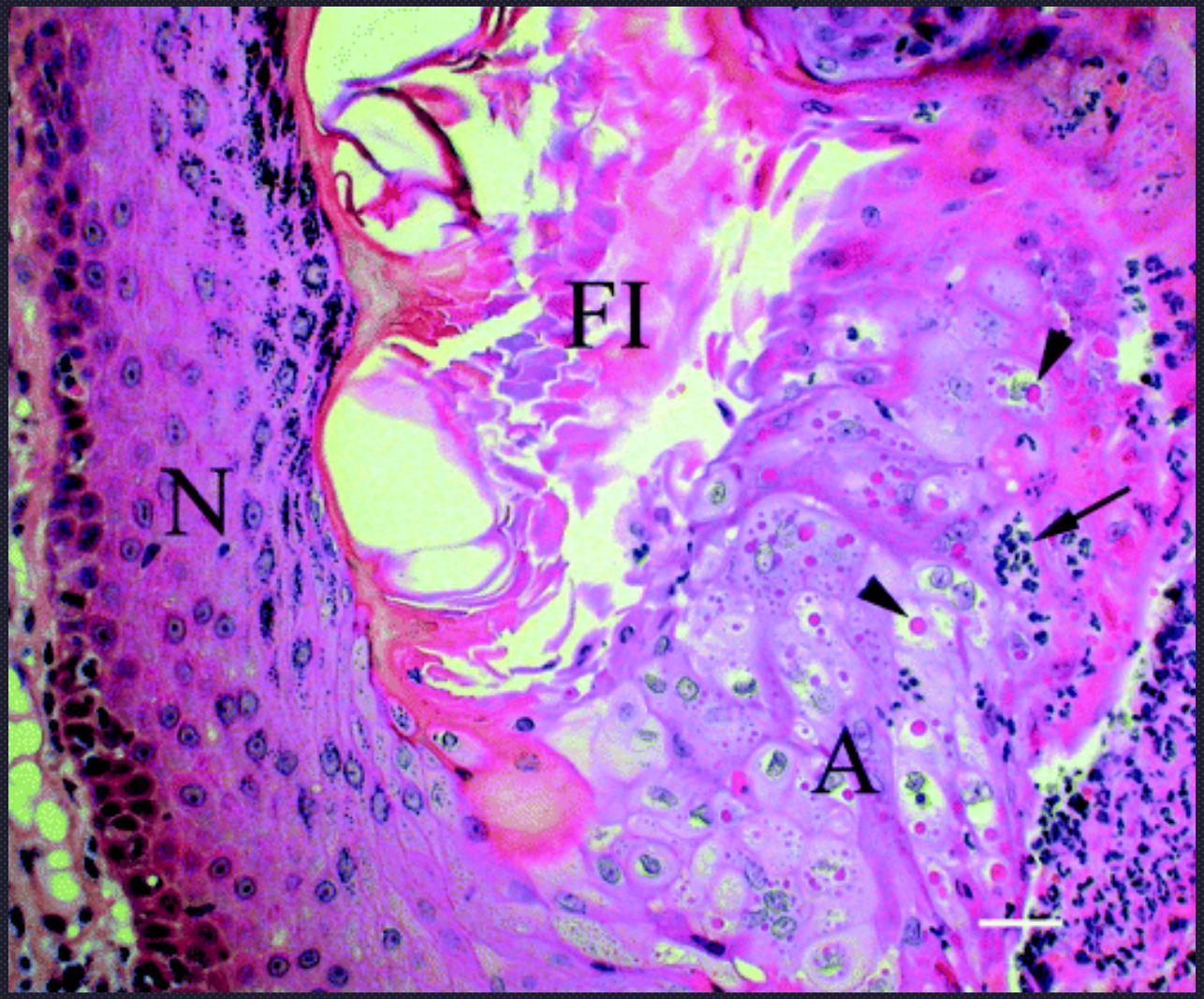
You may find a few acantholytic cells; degenerate PMNs, cocci
Bullous impetigo



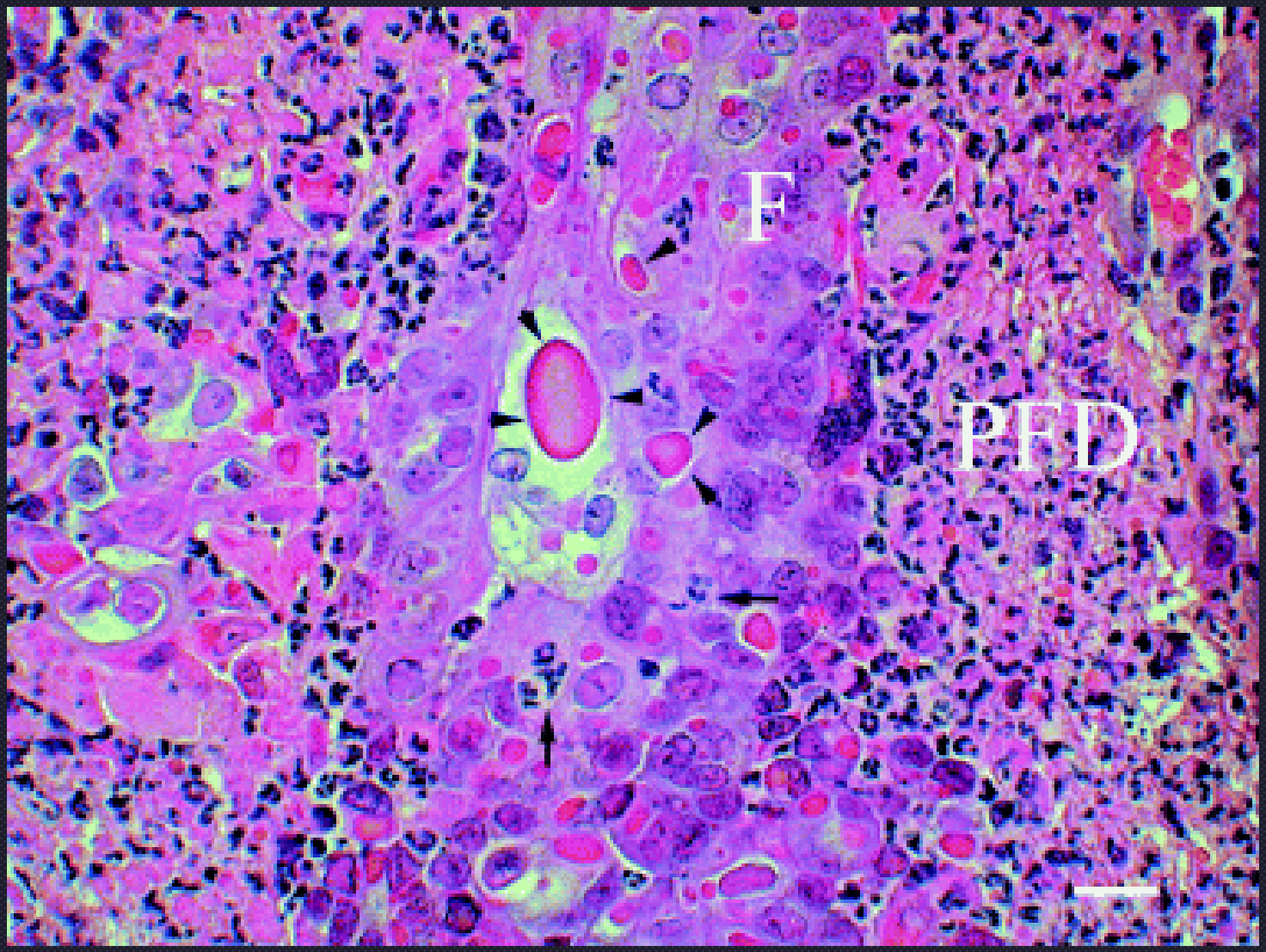
Gram positive cocci
Bullous impetigo



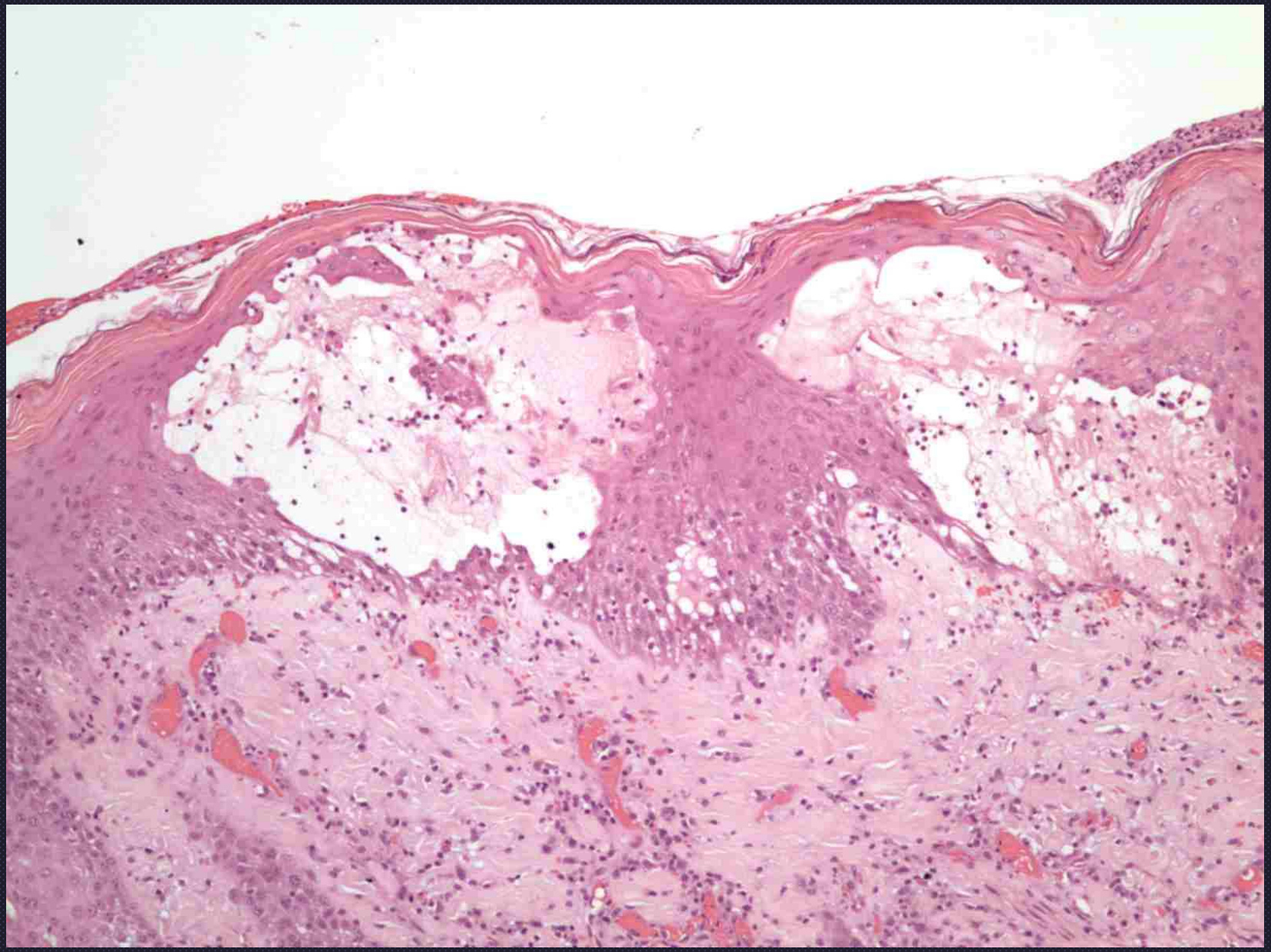
Intracellular edema **(ballooning degeneration)** results in an increase in the size of the spinous cells, associated with pallor of their cytoplasm. Severe intracellular edema results in rupture of the cell membranes and the formation of multiloculated intraepidermal vesicles (reticular degeneration).



Yager, *et. al* Raccoon pox in a cat Vet Derm 2006



Yager, *et. al* Raccoon pox in a cat Vet Derm 2006

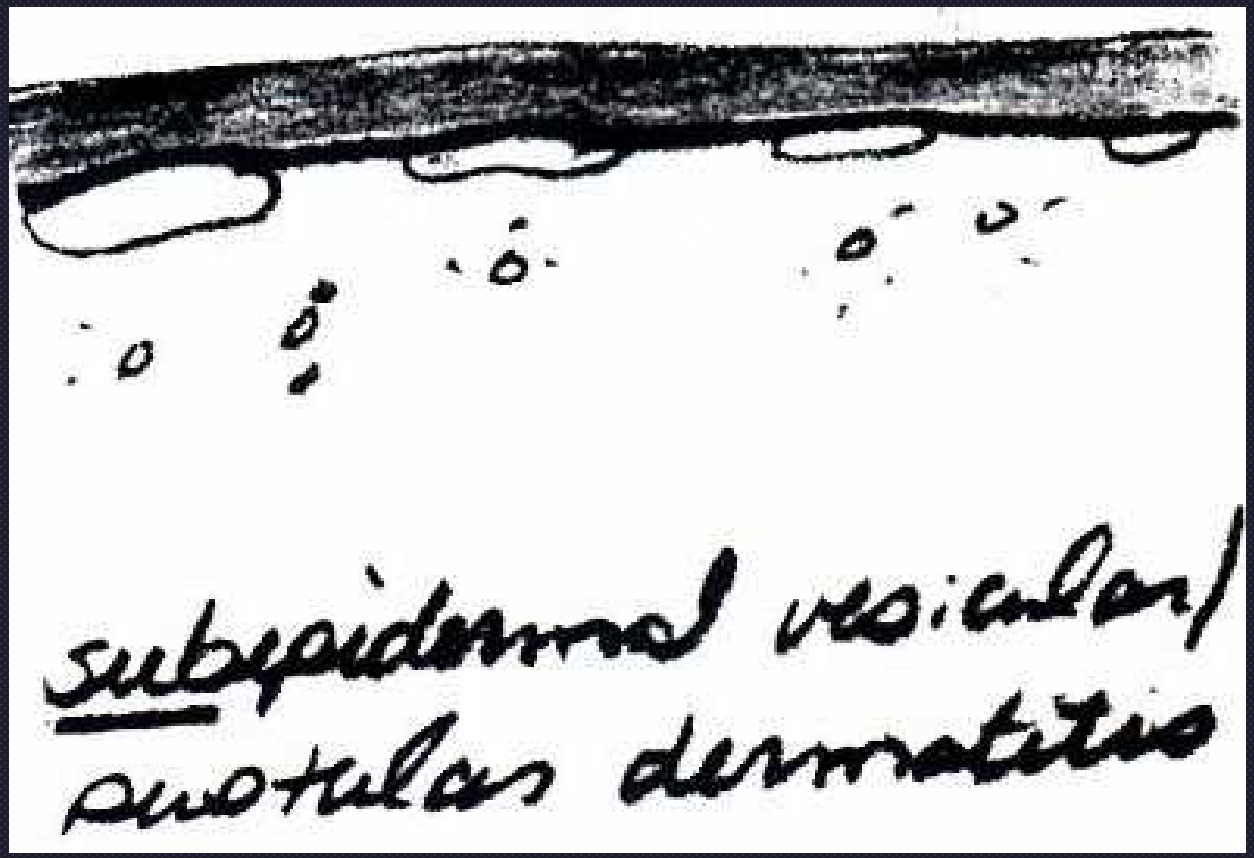


Spongiotic vesicular dermatitis in a horse
Note the mild acantholysis

Courtesy of Ann Harais

“orf’

Subepidermal vesicular dermatitis



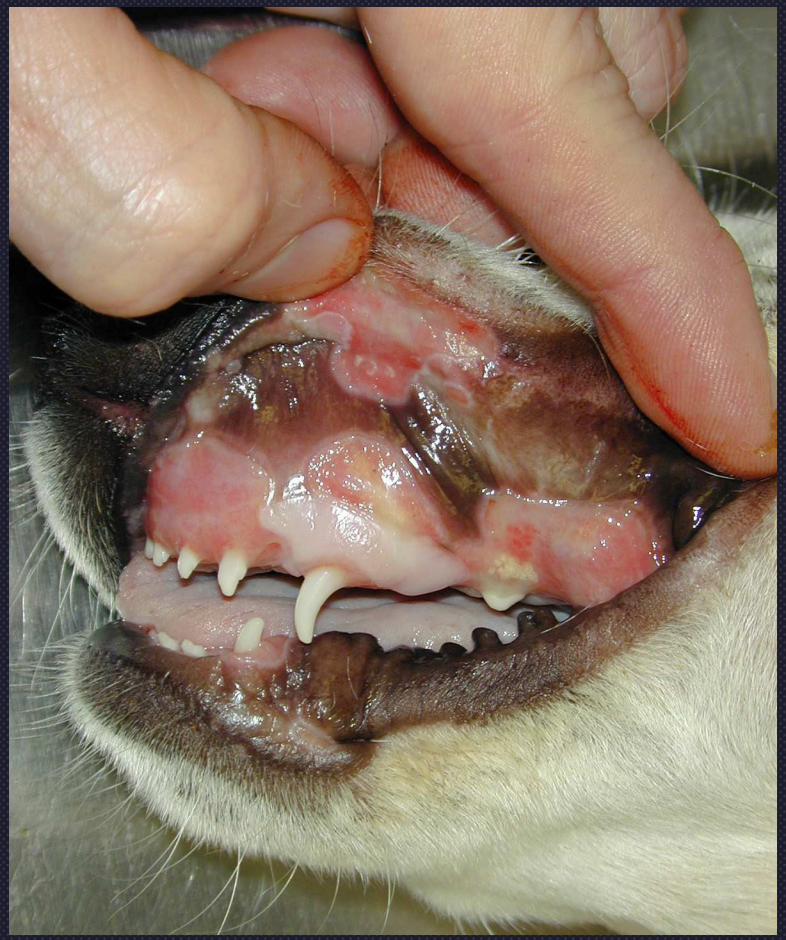
Blistering Disorders of the BMZ

- Autoab formation
  - Example: Bullous pemphigoid (OUT)
  - Mucous membrane pemphigoid (IN)
- Congenital Defect
  - Epidermolysis bullosa
    - Junctional- affects lamina lucida
    - Dystrophic- affects anchoring fibrils

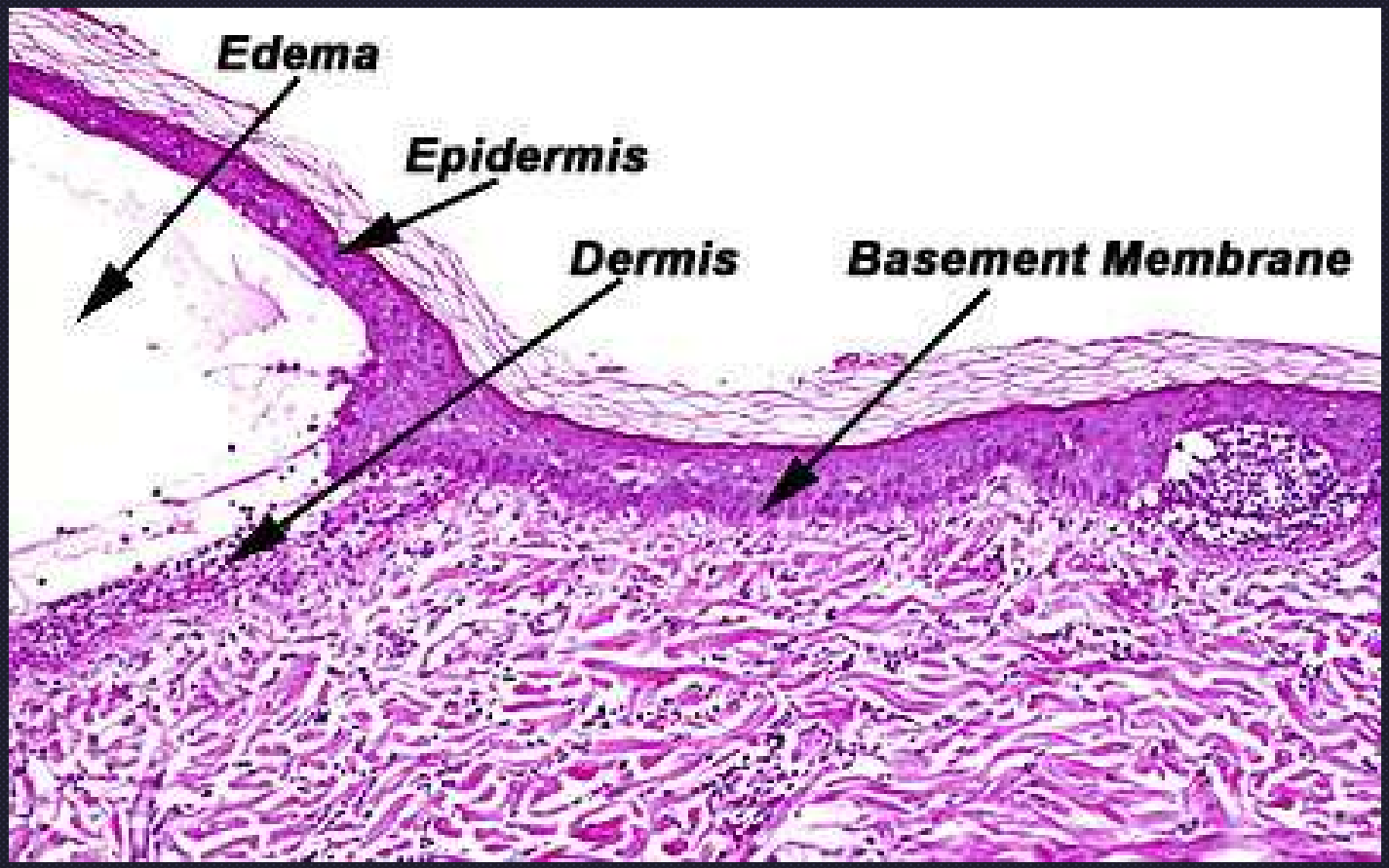
Junctional Epidermolysis Bullosa

Congenital- autosomal recessive

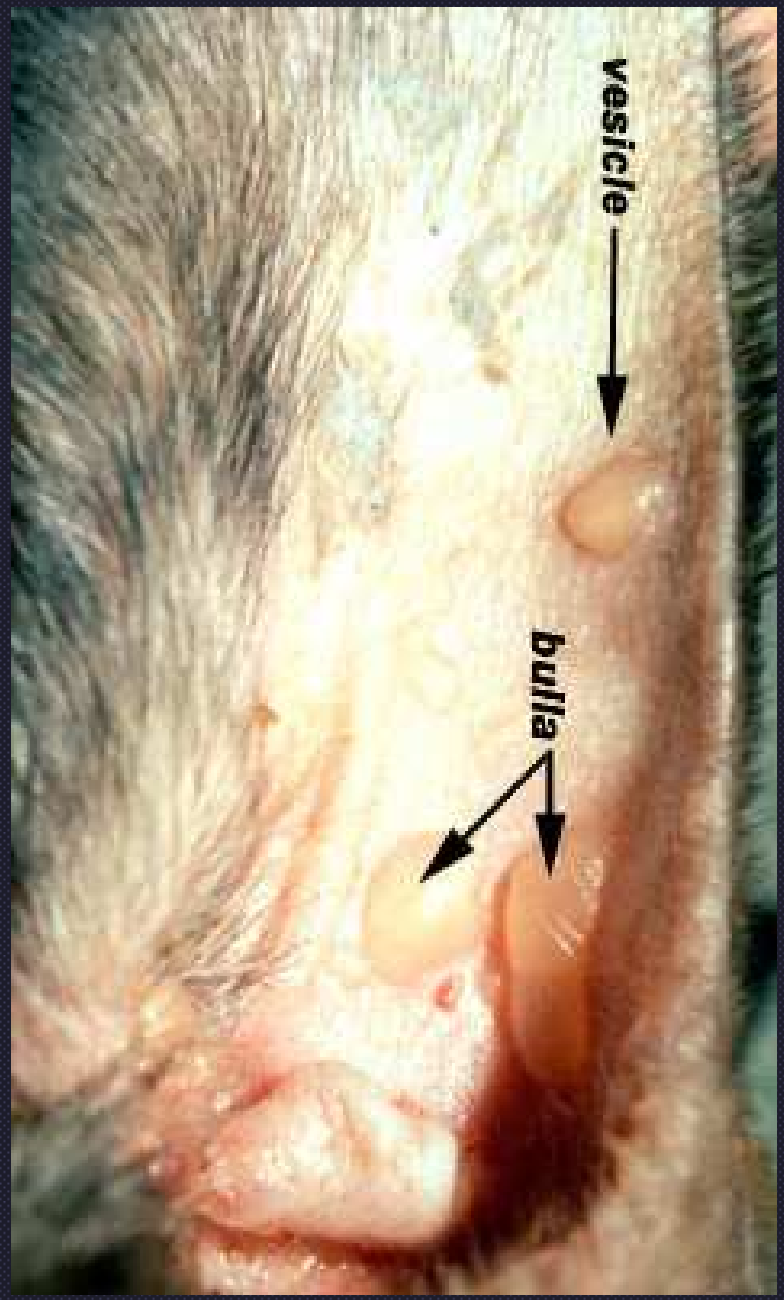
Junctional Epidermolysis Bullosa



Epidermolysis Bullosa Acquista

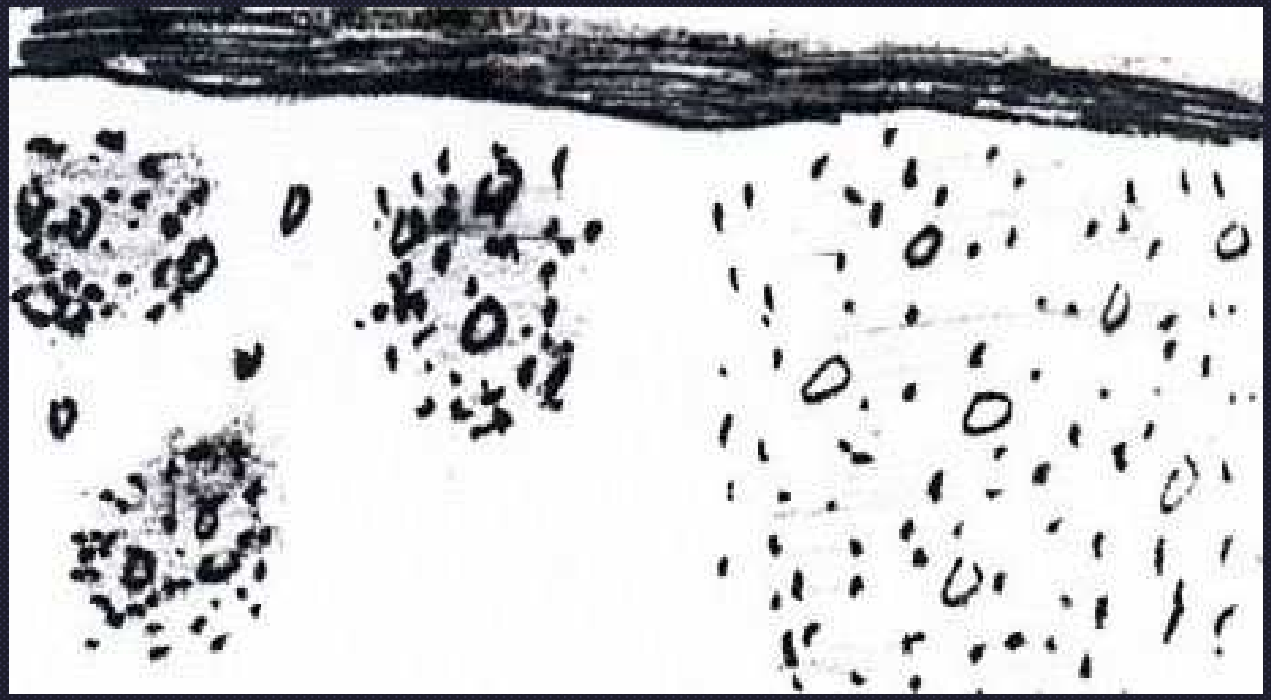


Acquired auto ab to collagen VII



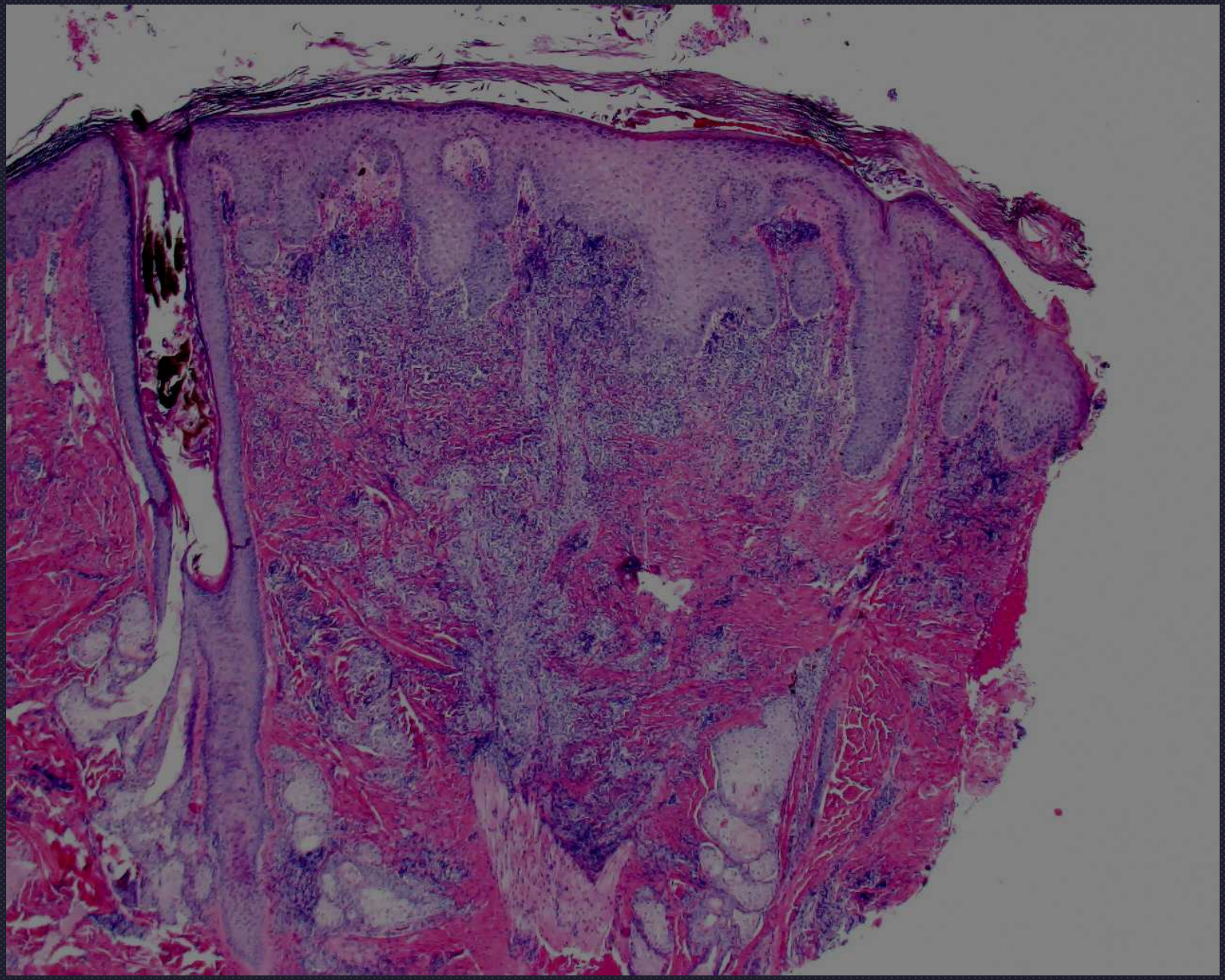
Epidermolysis bullosa aquista in a Great Dane

Nodular/Diffuse Dermatitis

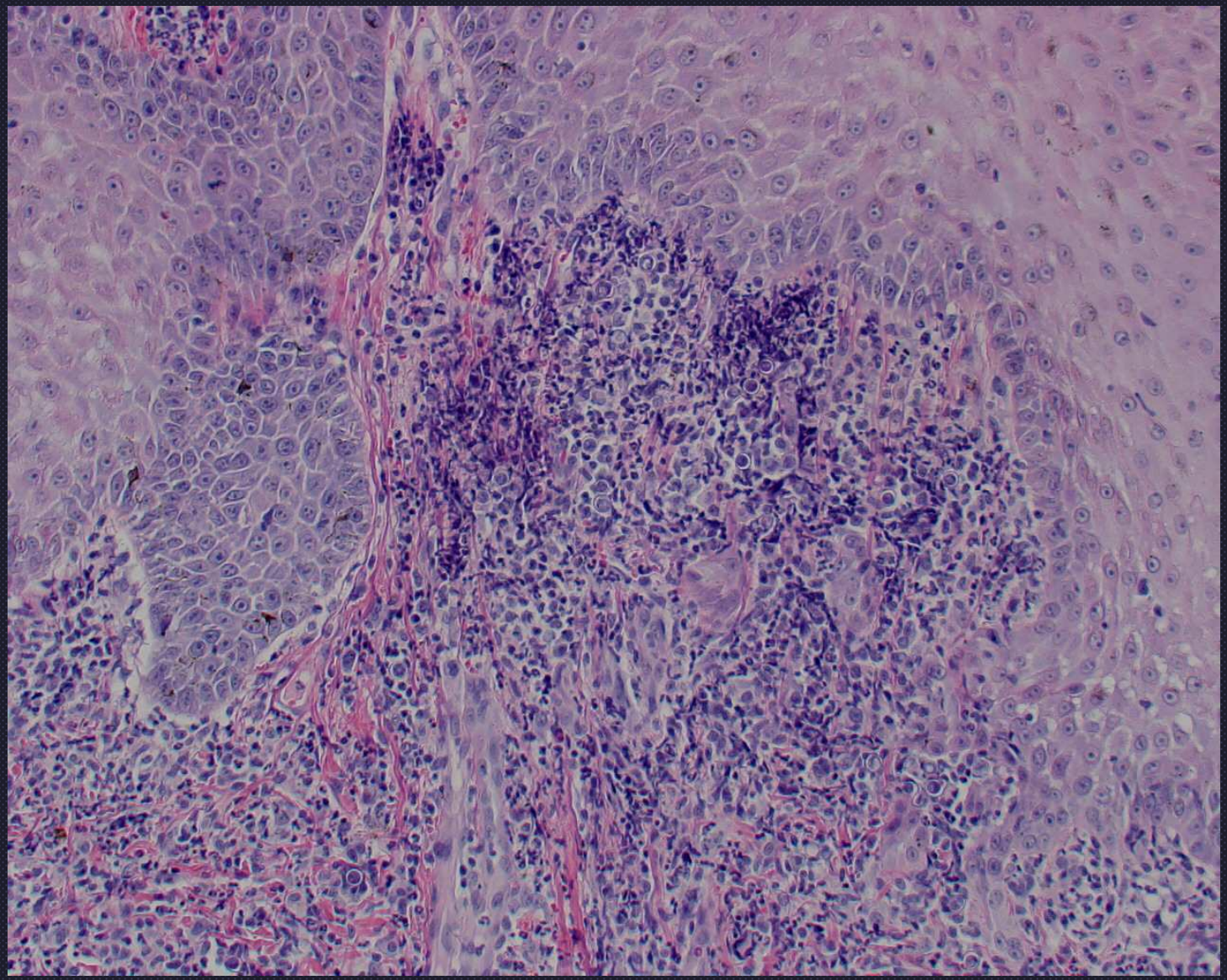


Character of Infiltrate

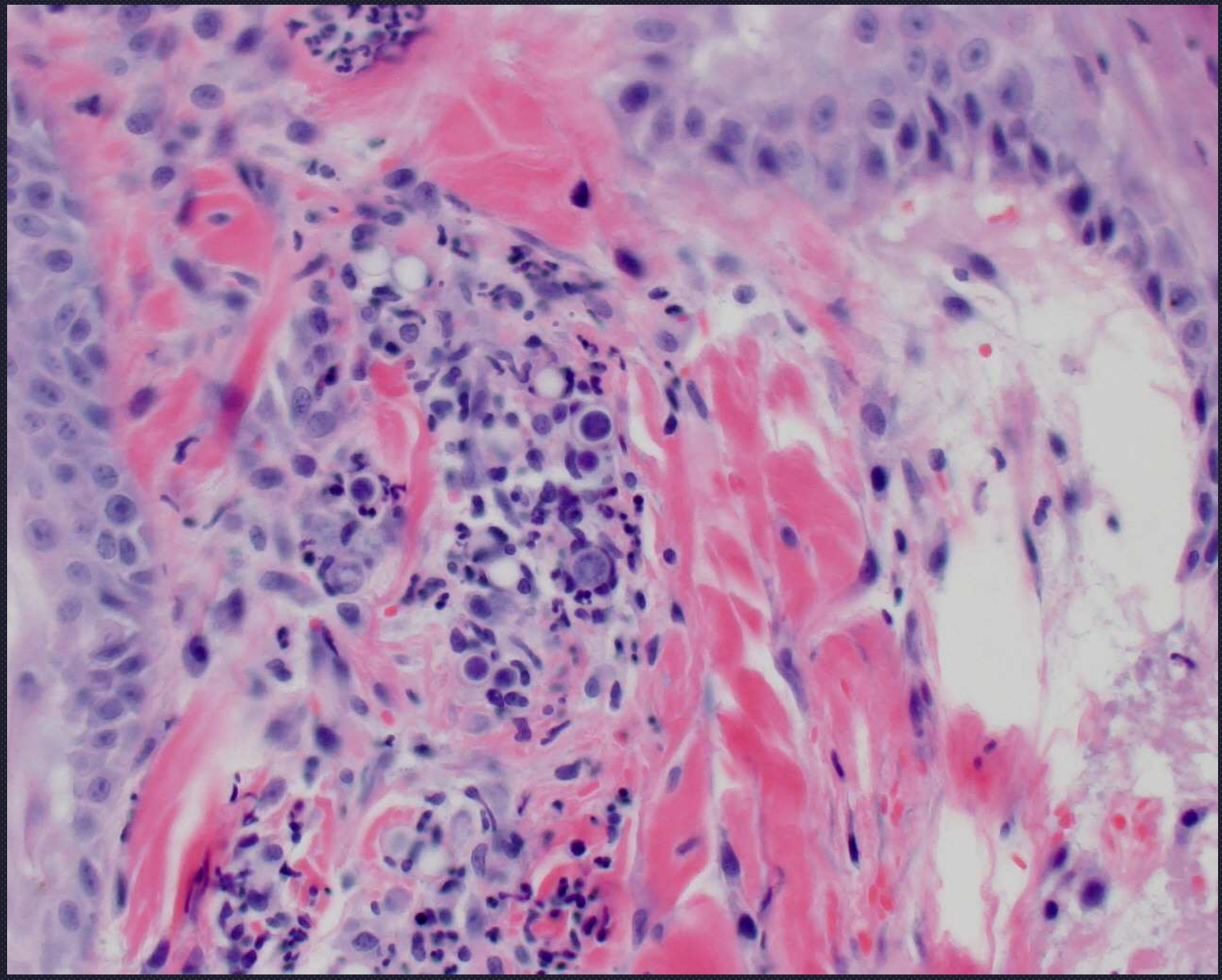
- (1) neutrophilic (e.g. bacterial)
- (2) eosinophilic (e.g. parasitic or eosinophilic granuloma)
- (3) histiocytic - chronic granulomatous or pyogranulomatous lesions (e.g. mycobacteria, fungal, foreign body)



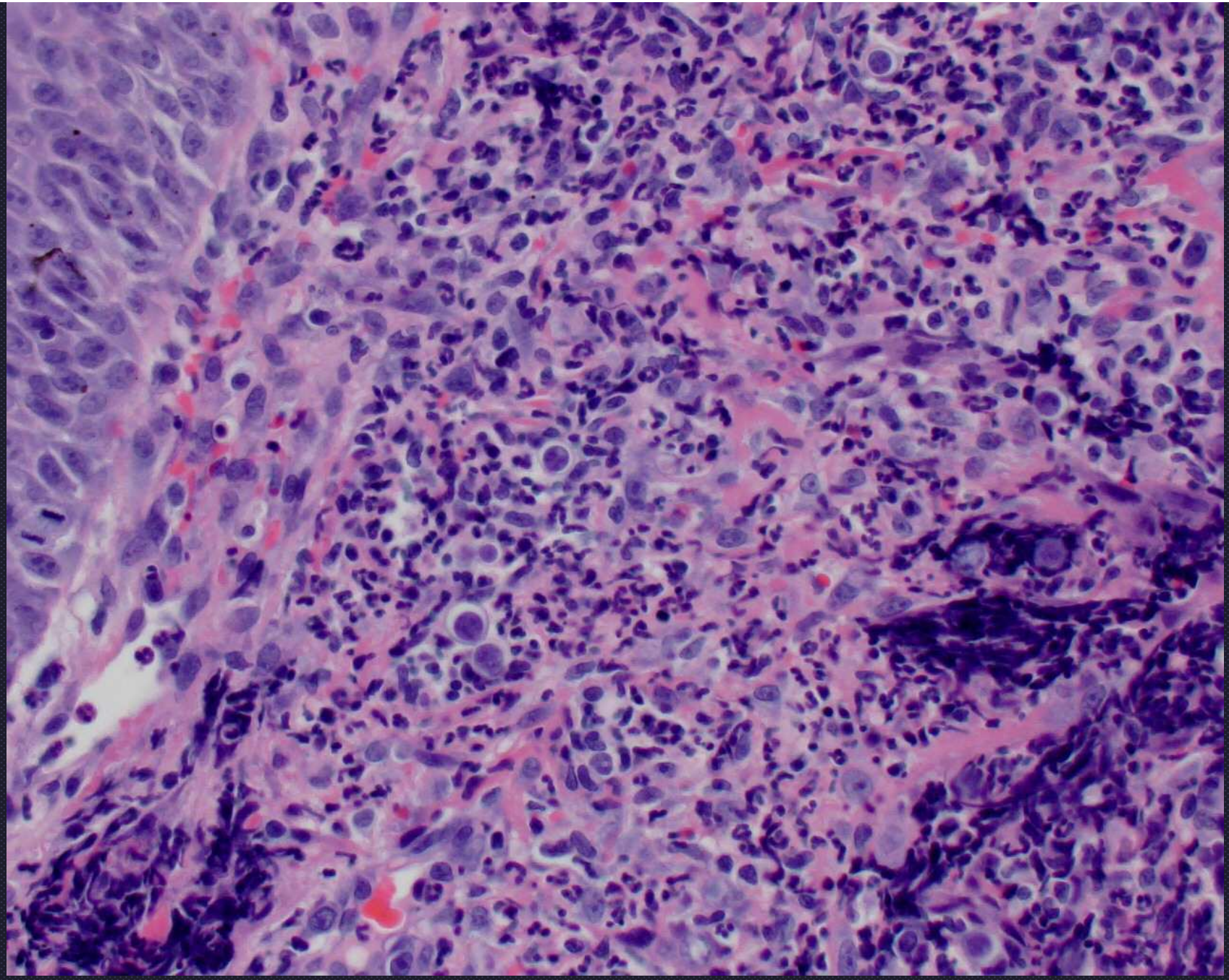
Blastomycosis



Blastomycosis

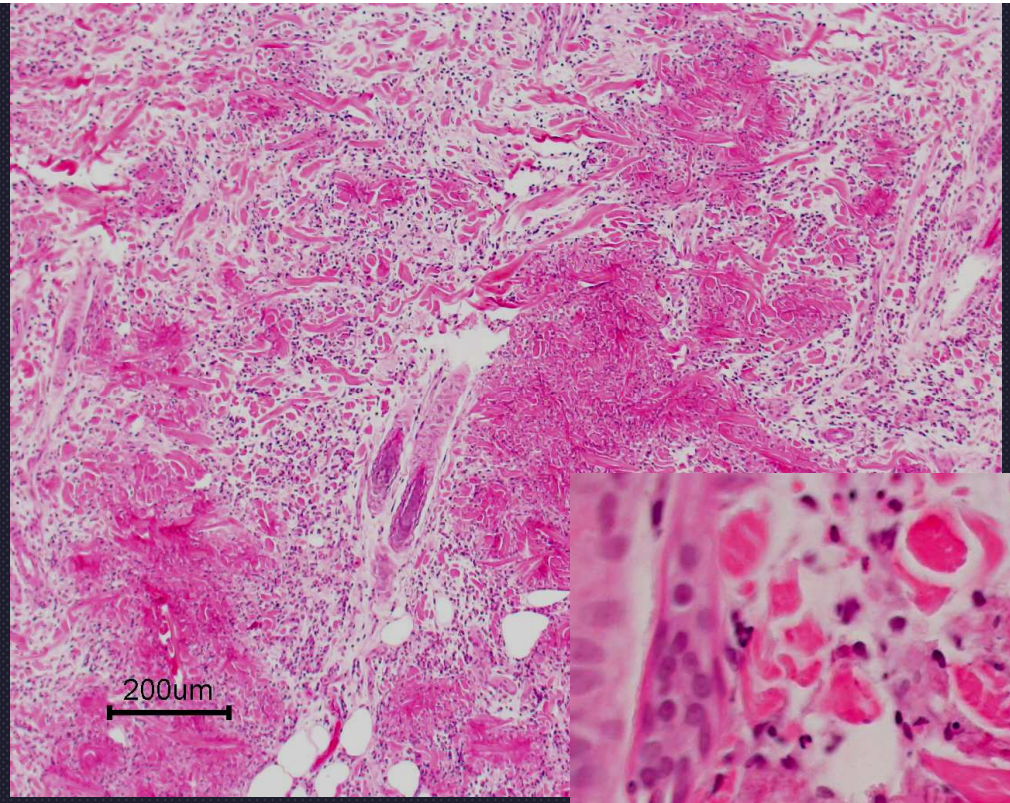


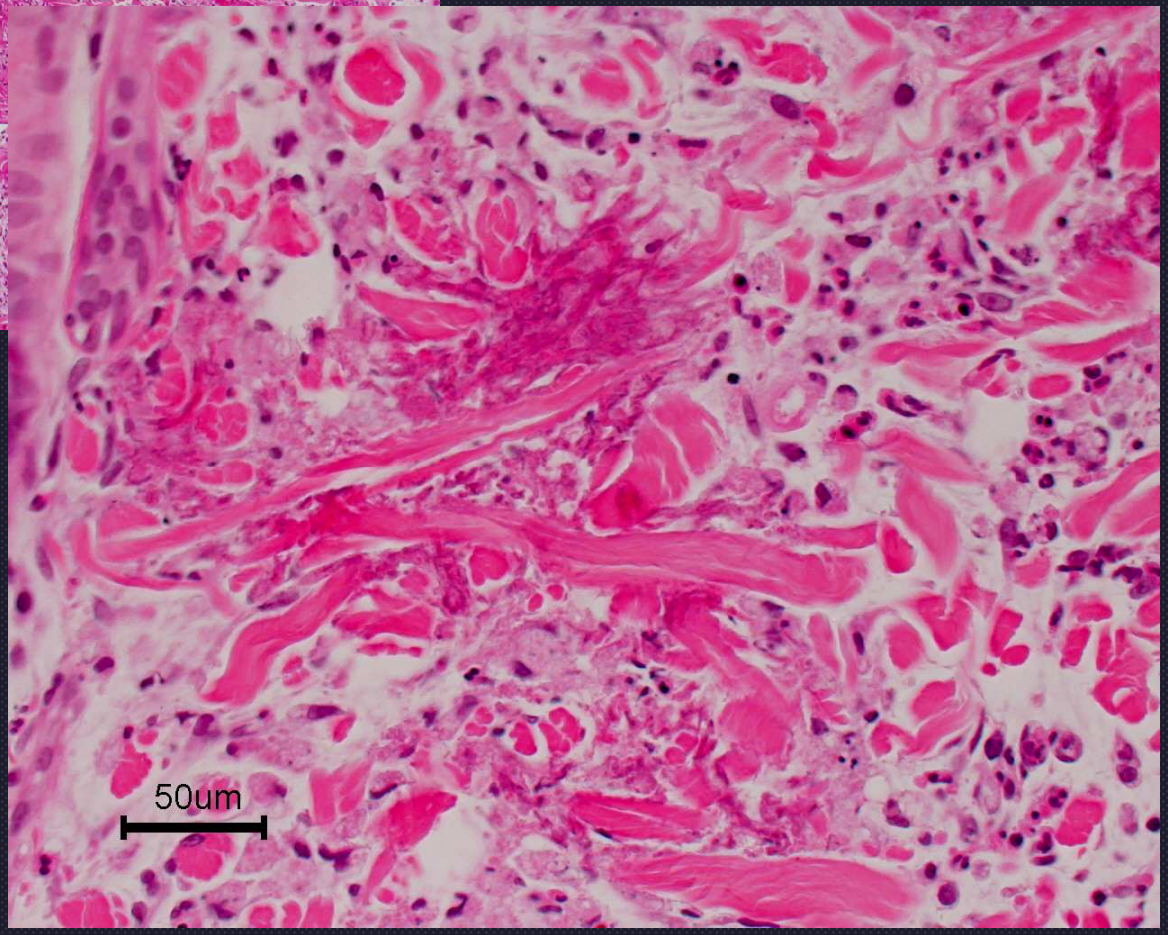
Blastomycosis



Blastomycosis

Feline eosinophilic granuloma





Eosinophilic granuloma

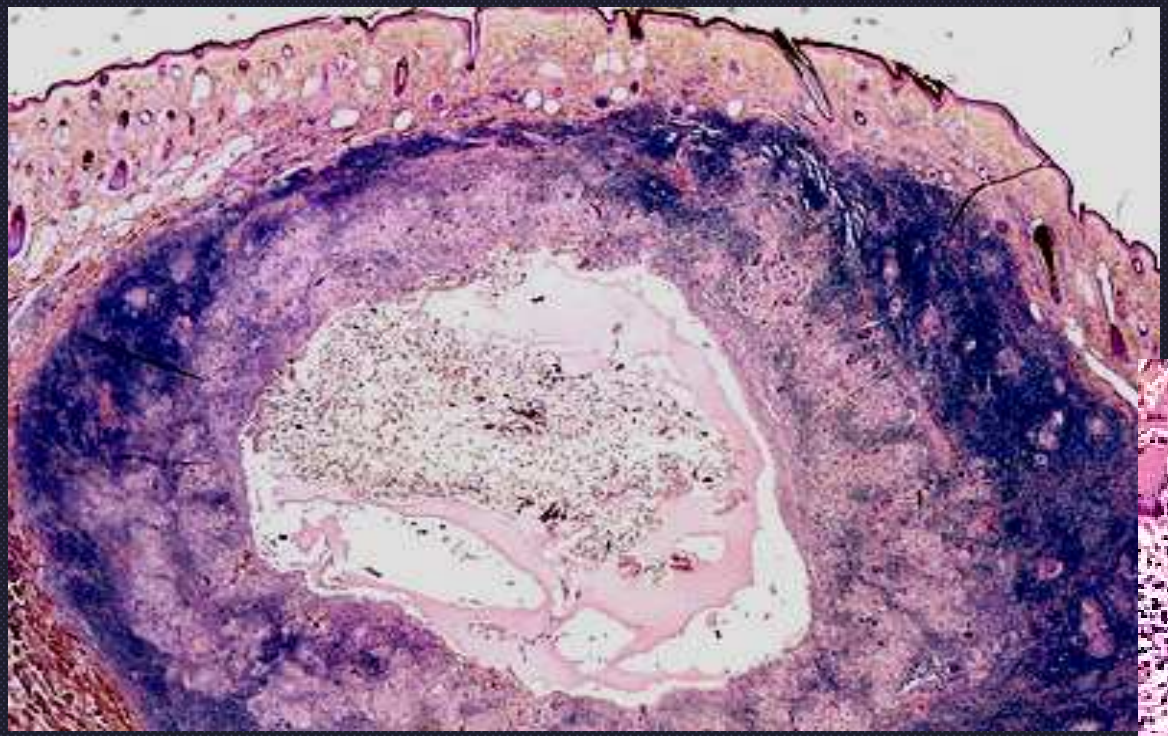
Eosinophilic granulomas

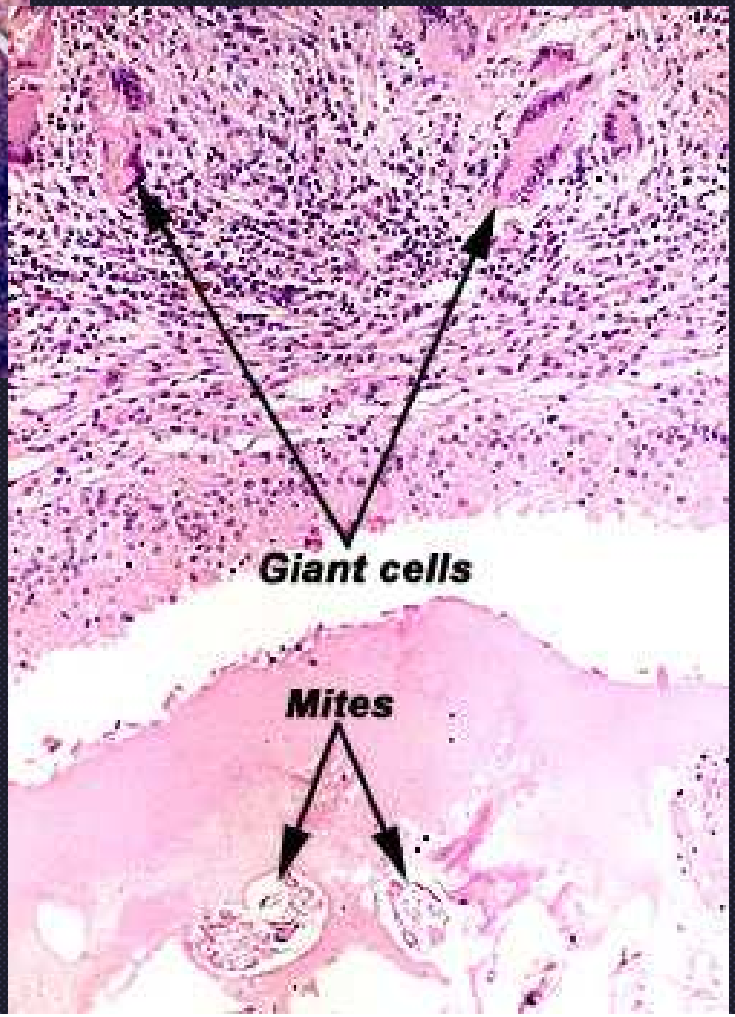
- Correct term “flame figures”
- Do not use “collagen degeneration” or “collagenolysis”

Coalescing eosinophilic granulomas

Eosinophilic granuloma

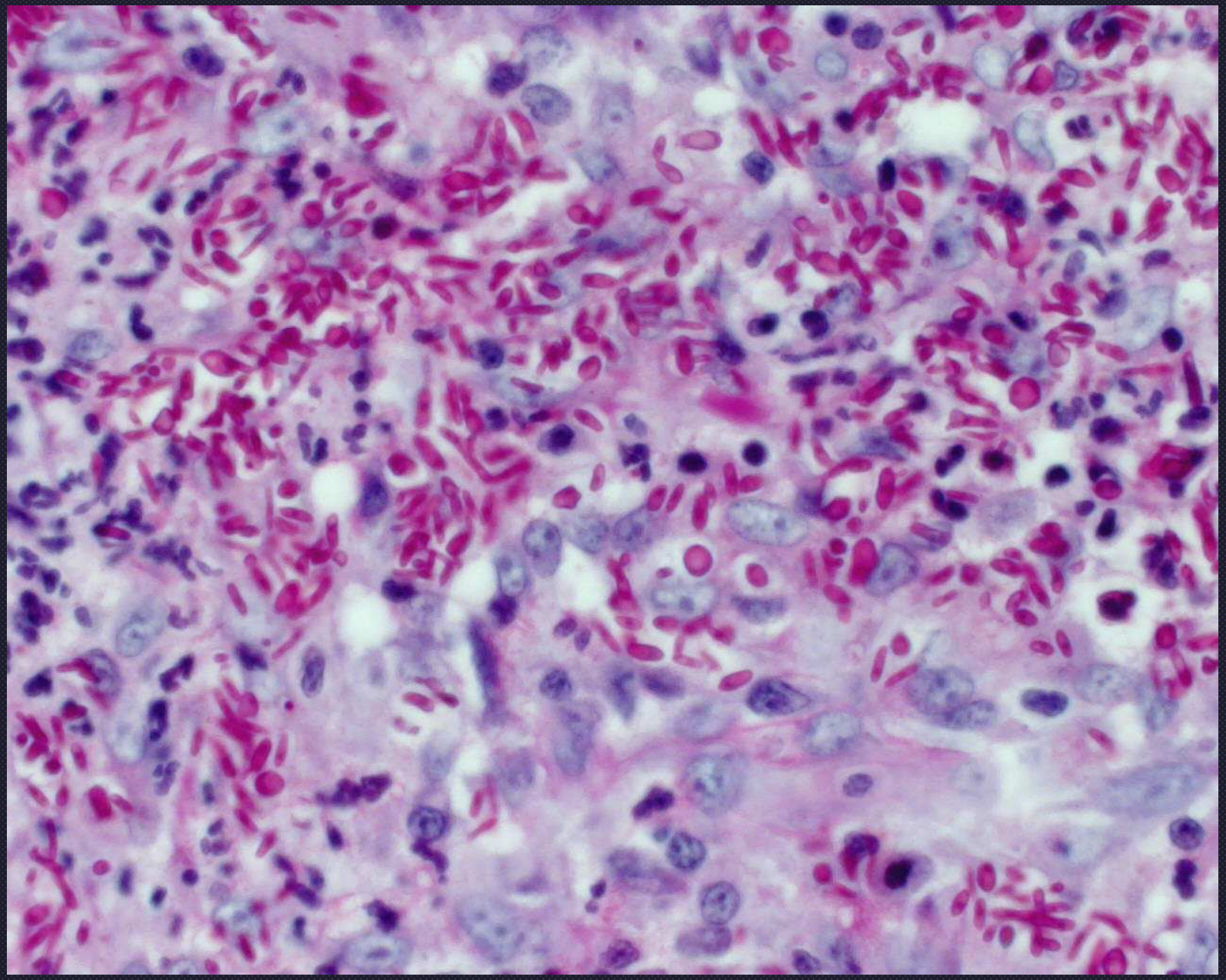
Eosinophilic granulomas do occur in the interdigital skin and footpads but less common



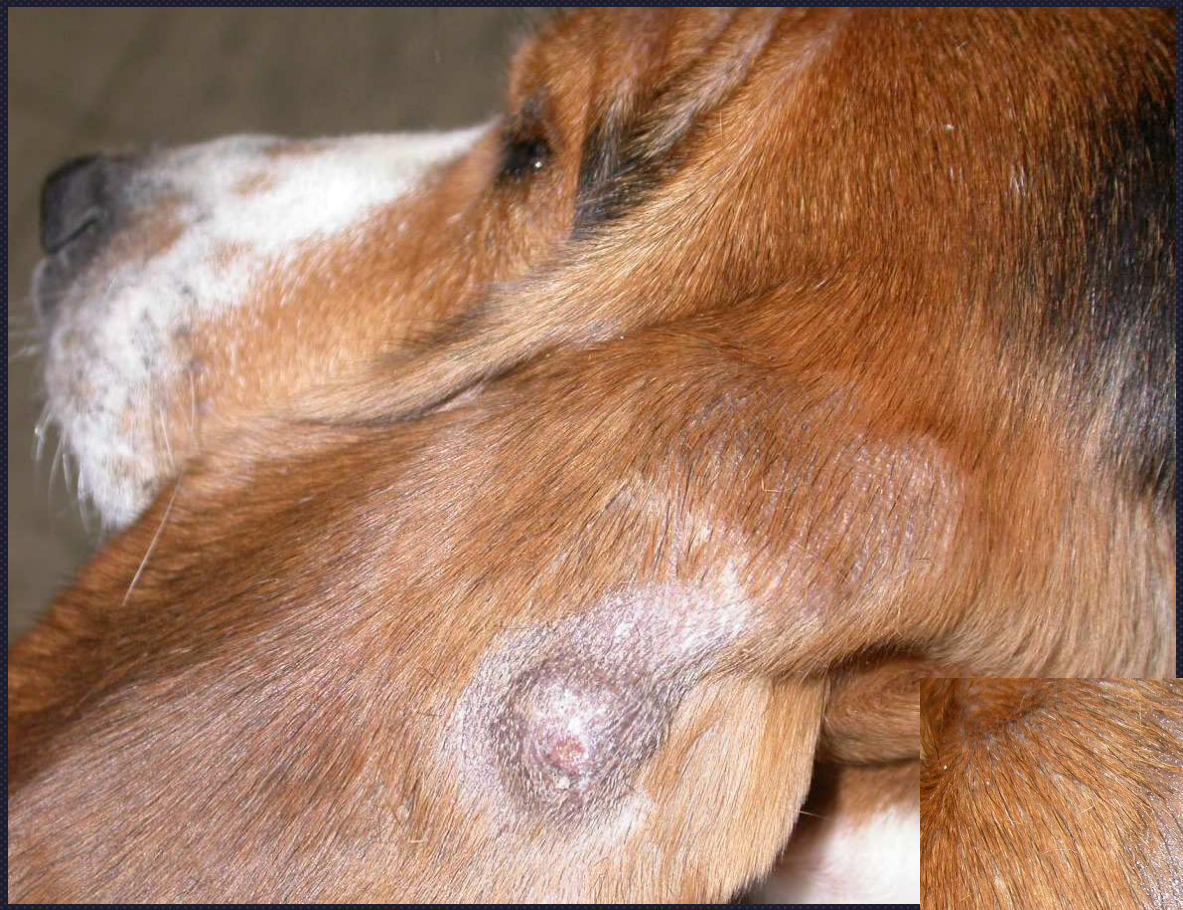


Bovine demodicosis

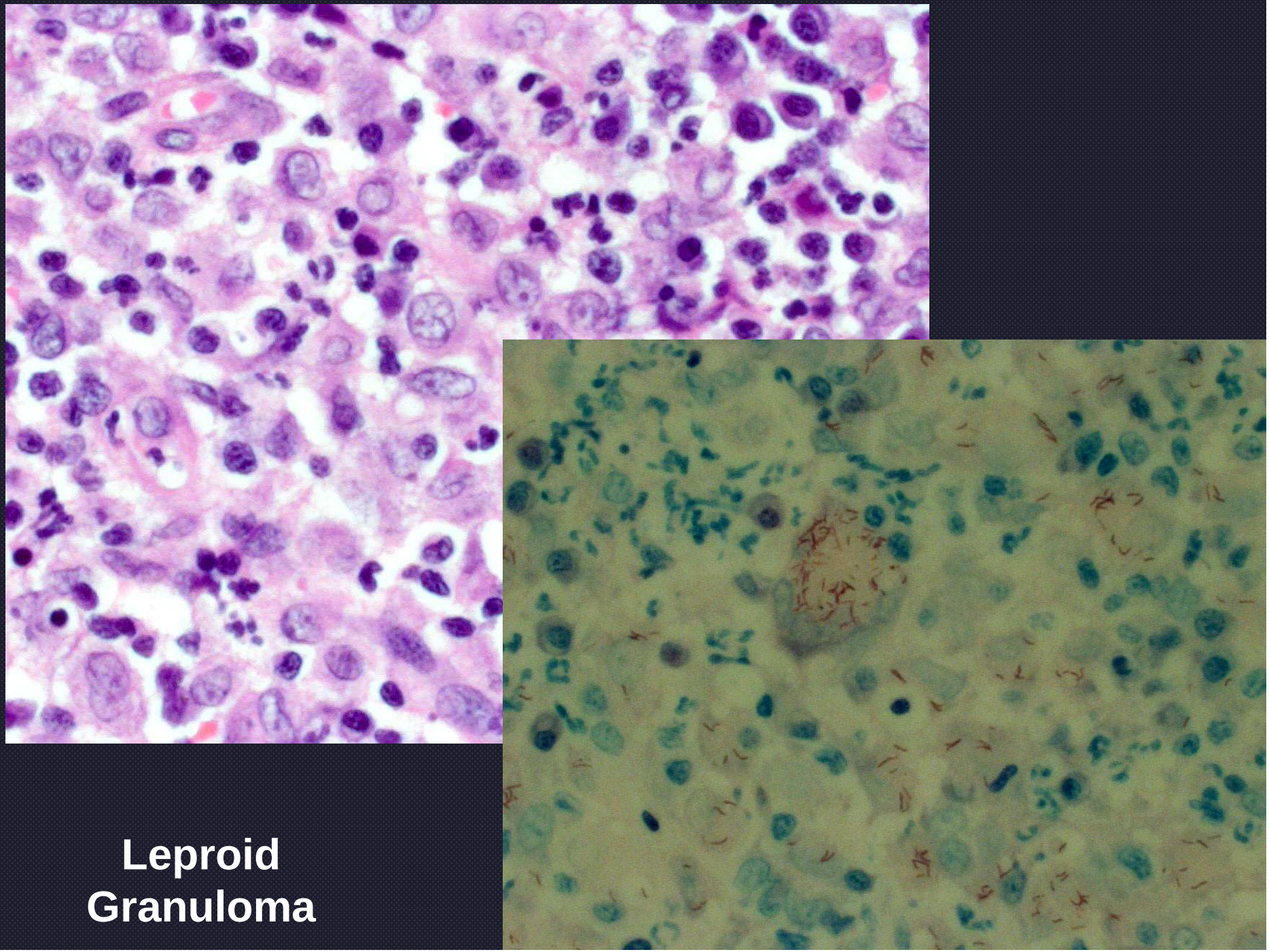
Sporotrichosis



Sporotrichosis
PAS stain



Leproid granuloma in a hunting beagle

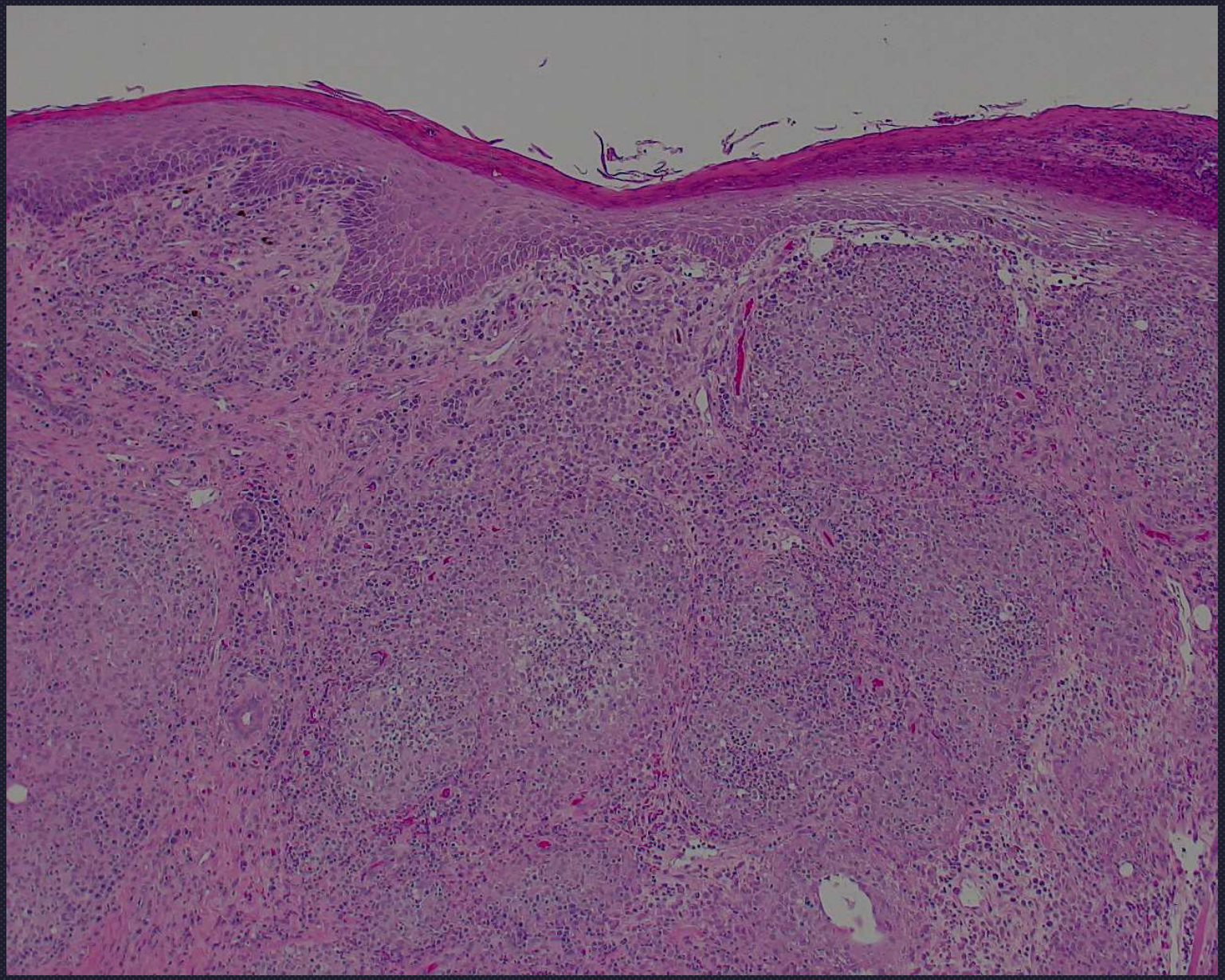


Leproid Granuloma

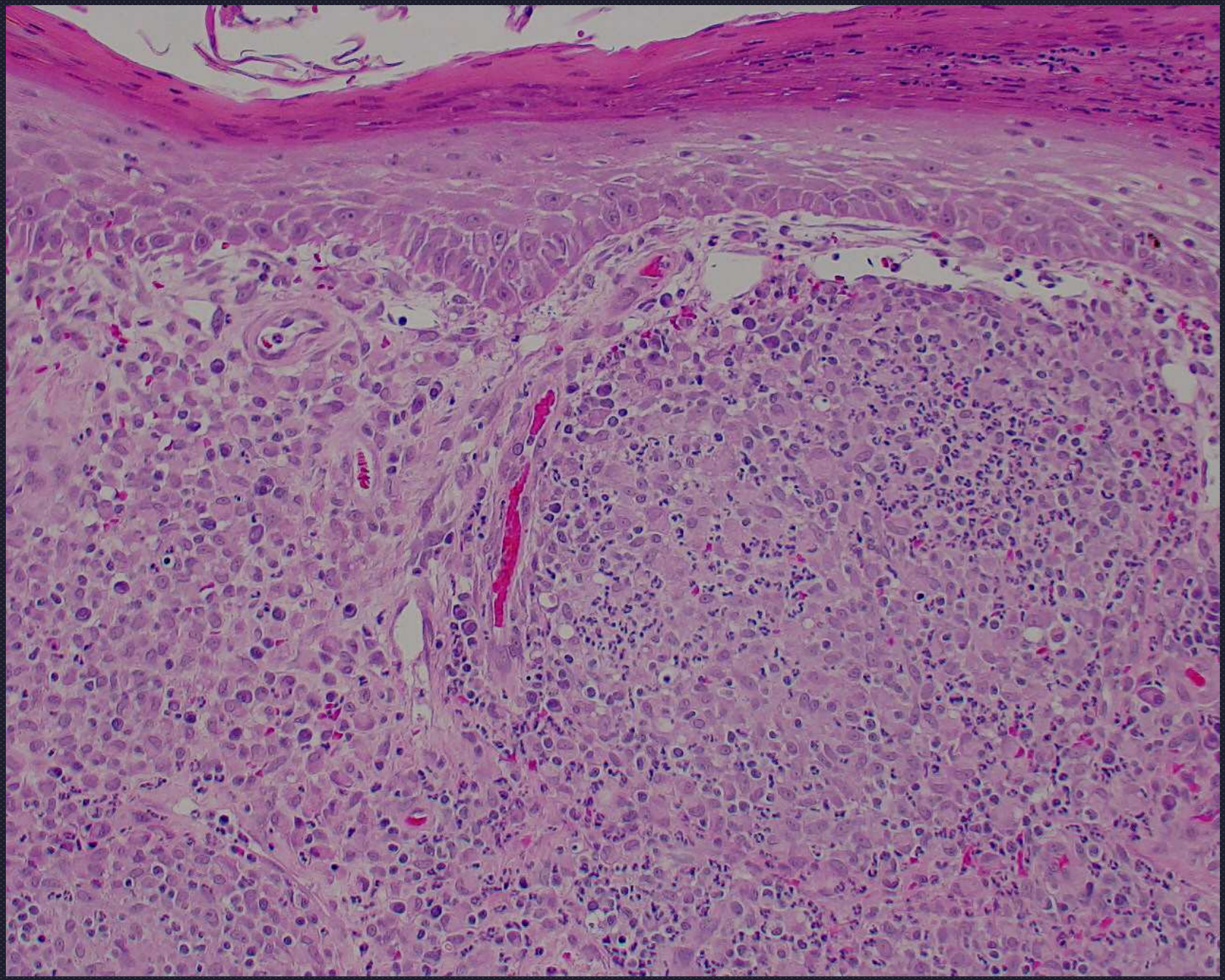
Juvenile cellulitis

Juvenile cellulitis

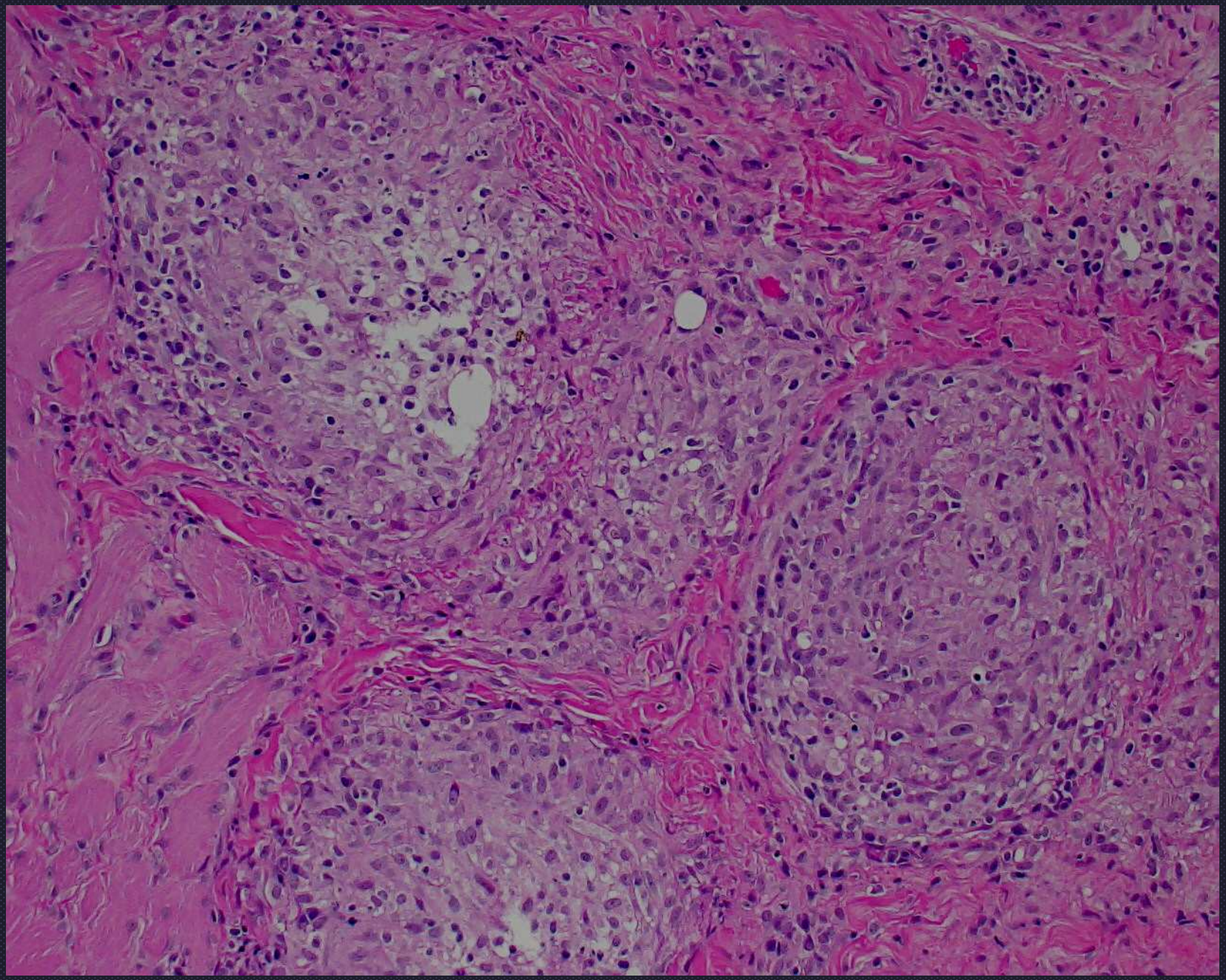
Juvenile cellulitis



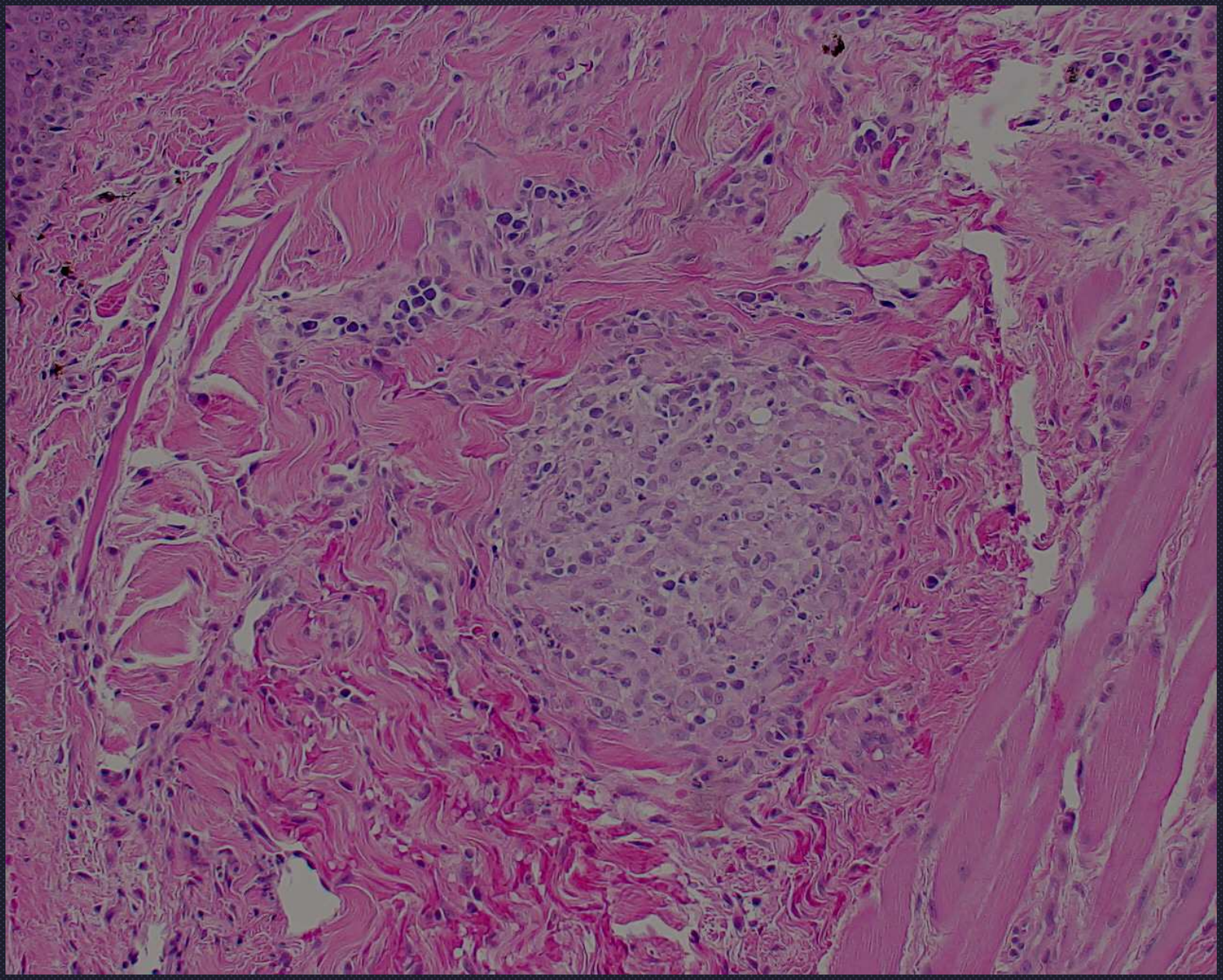
Juvenile cellulitis



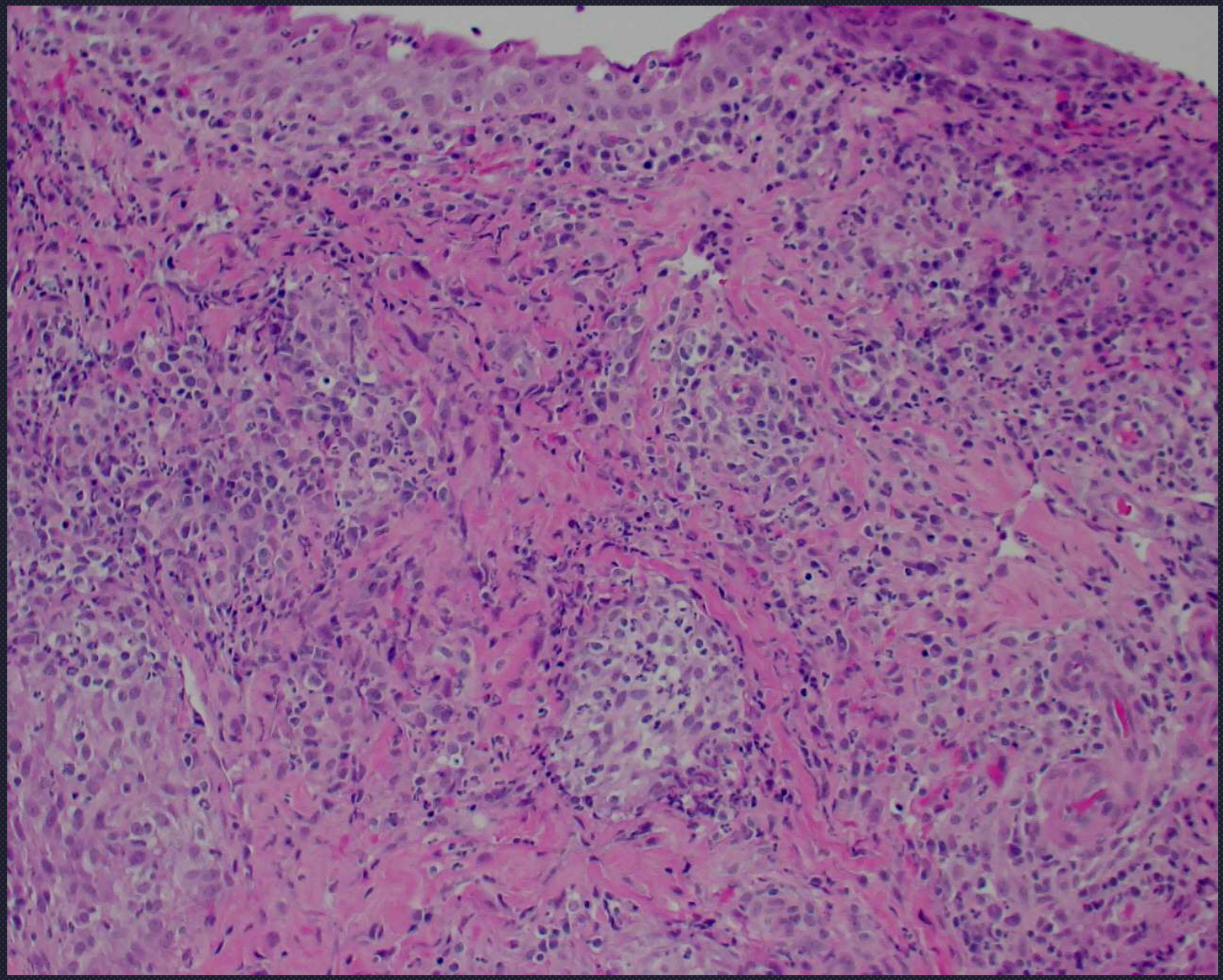
Juvenile cellulitis



Juvenile cellulitis



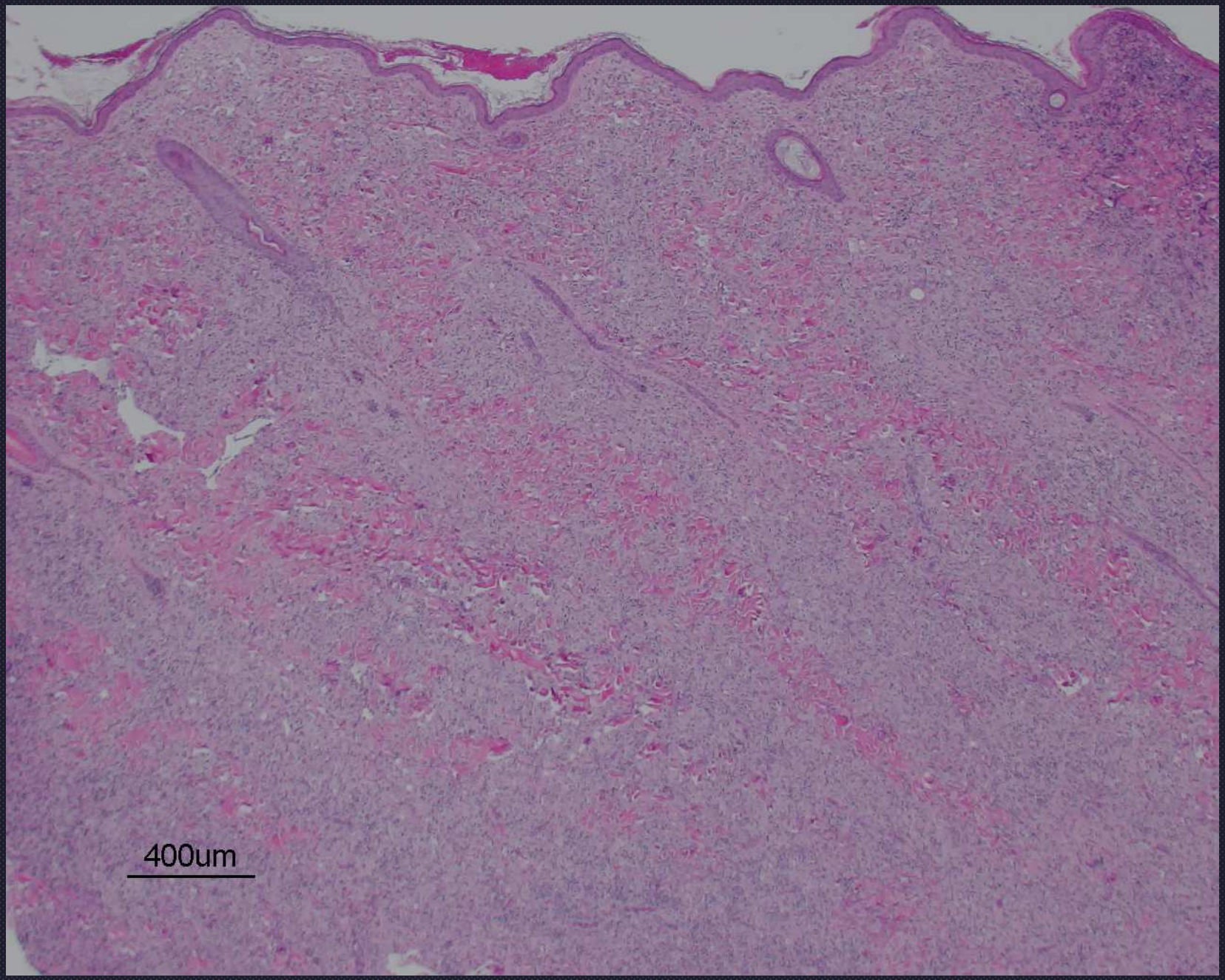
Juvenile cellulitis



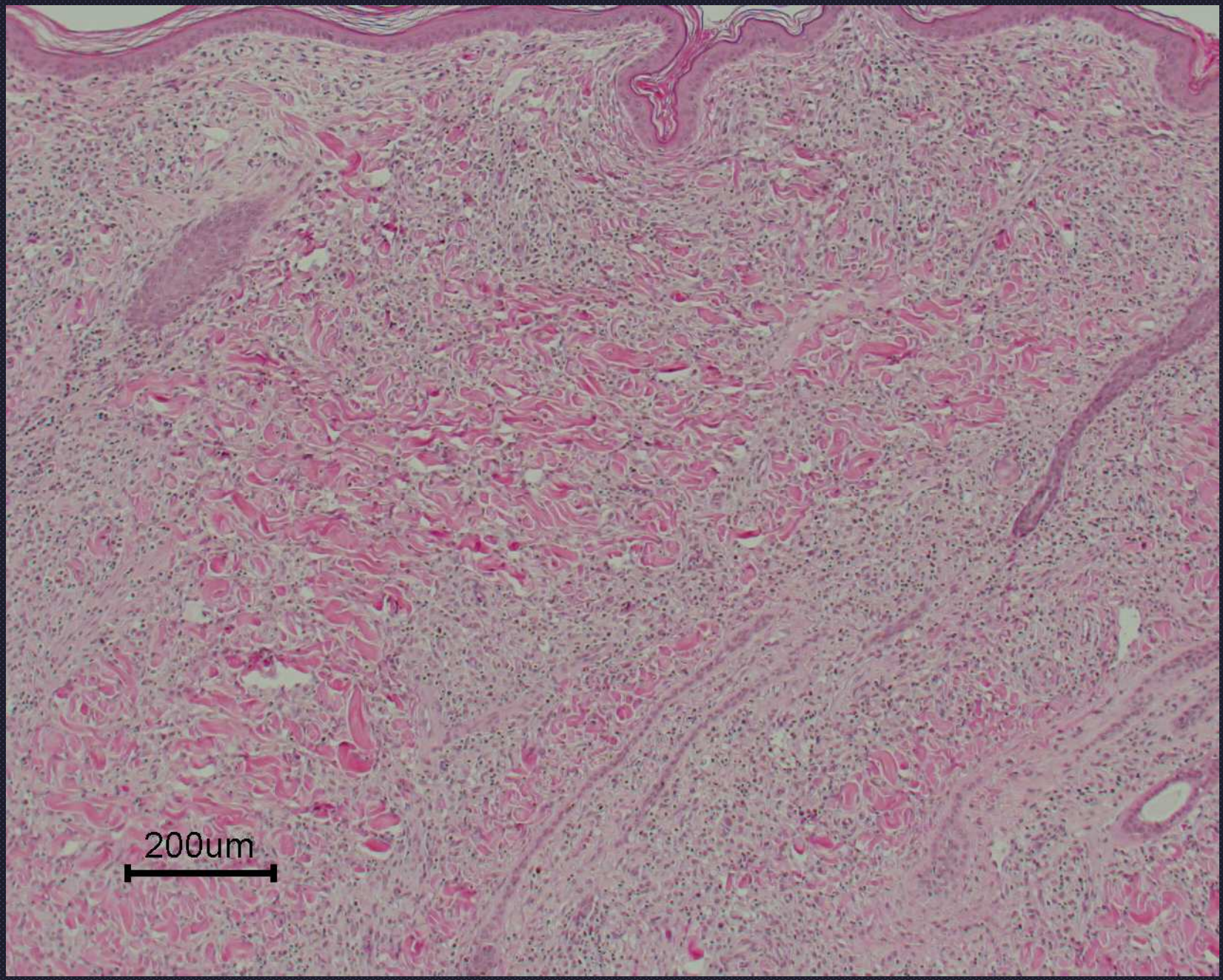
Juvenile cellulitis- look for granulomas in the upper dermis

Cutaneous reactive histiocytosis

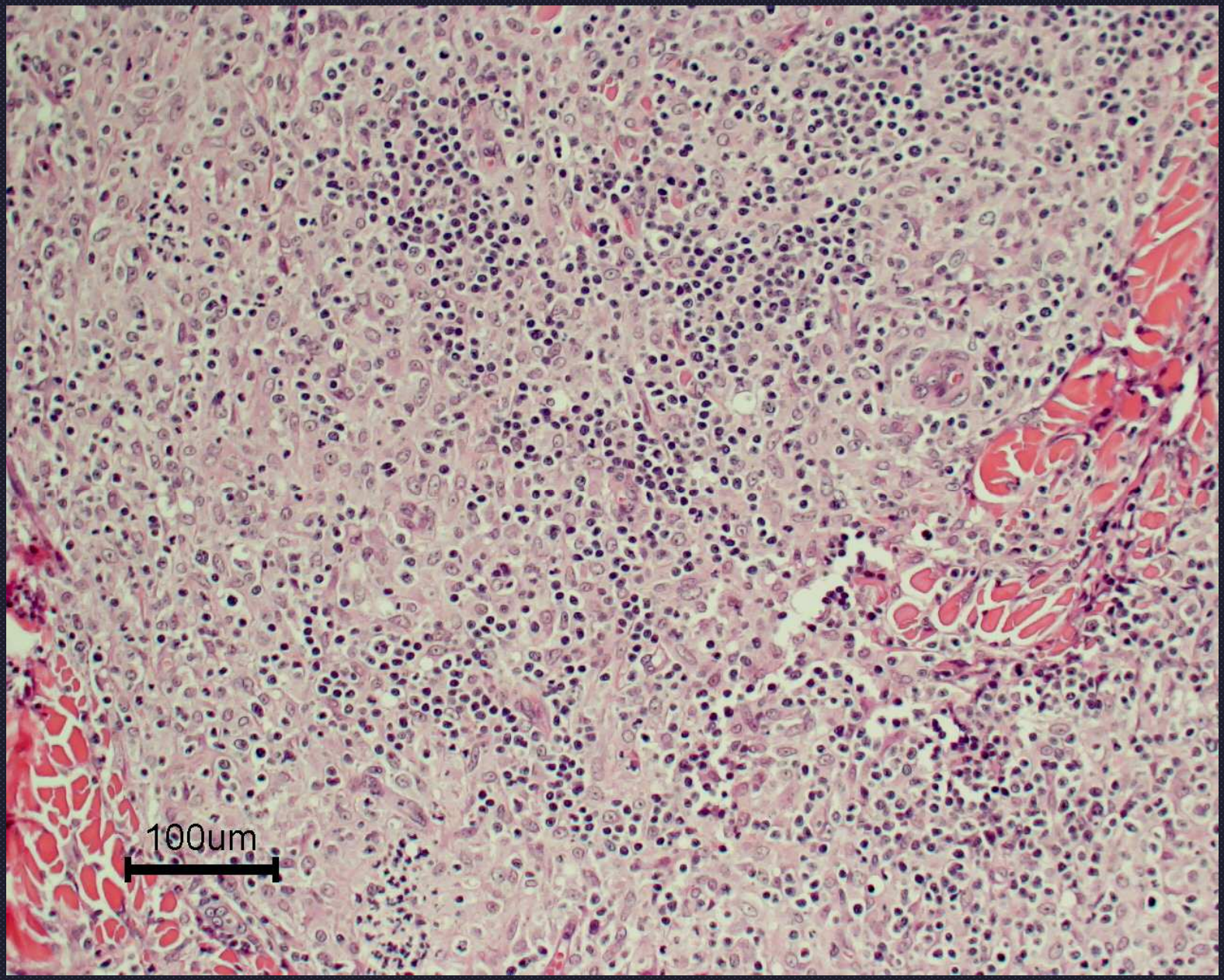
Cutaneous reactive histiocytosis
“clown nose”



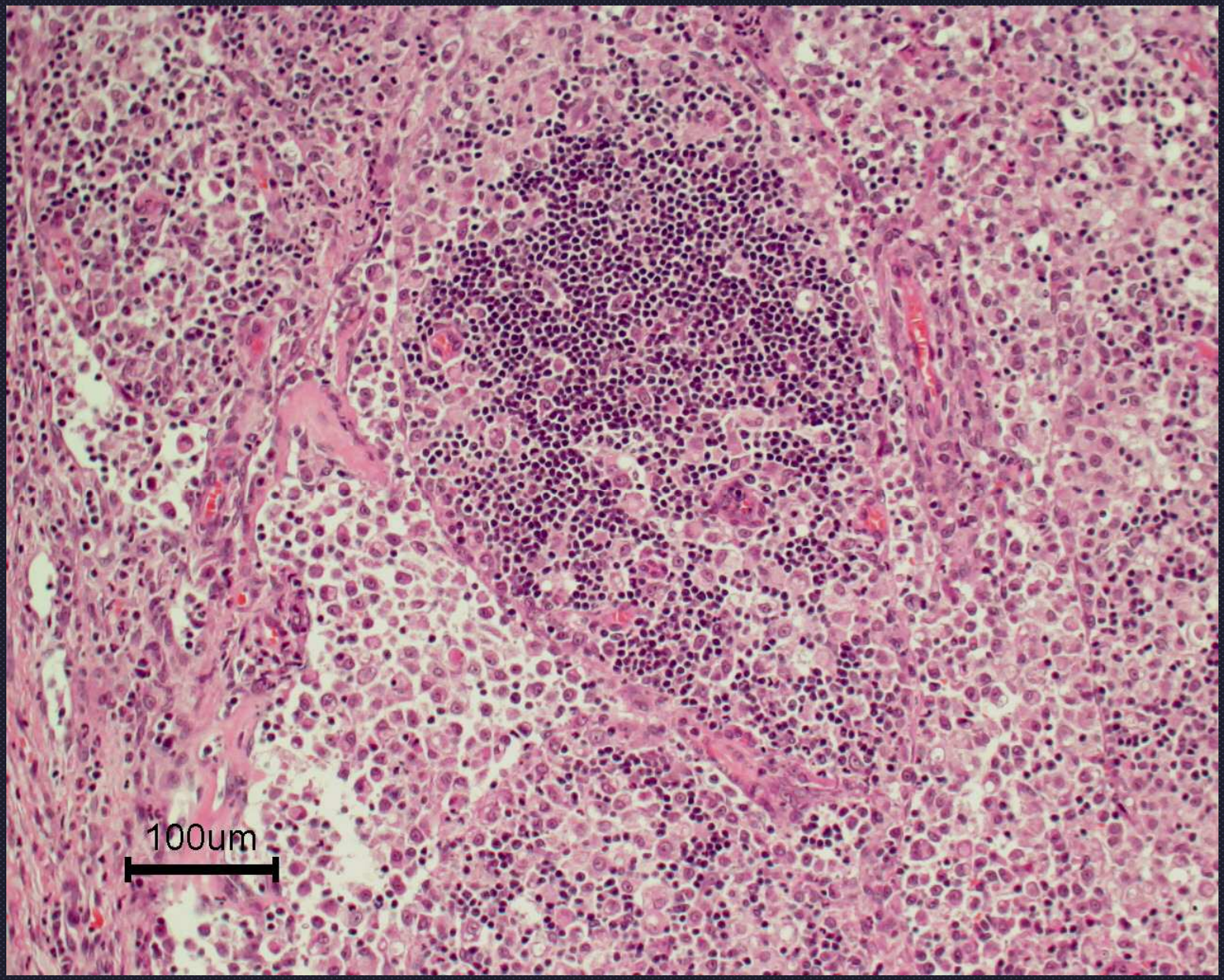
Cutaneous reactive histiocytosis



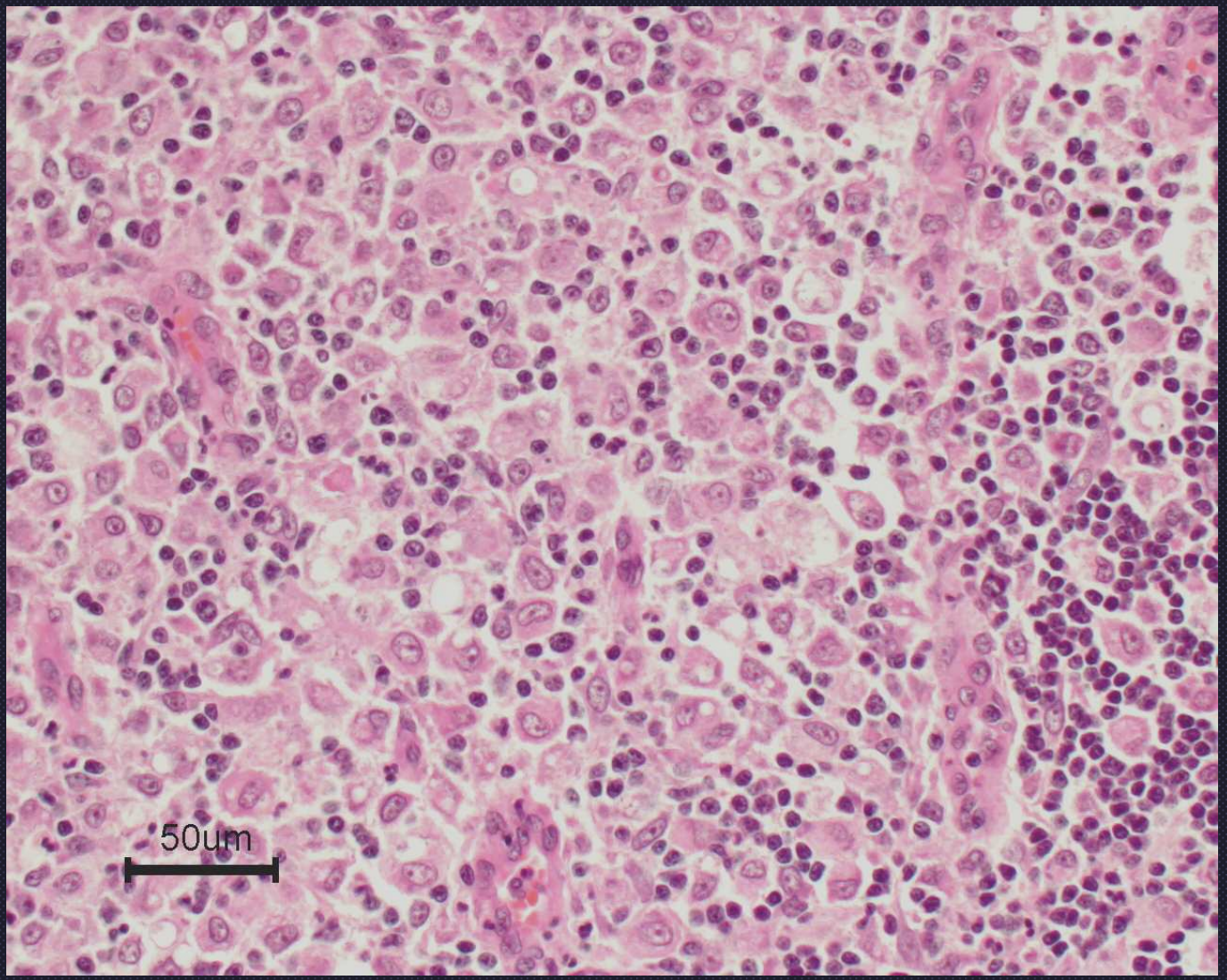
Cutaneous reactive histiocytosis



Cutaneous reactive histiocytosis

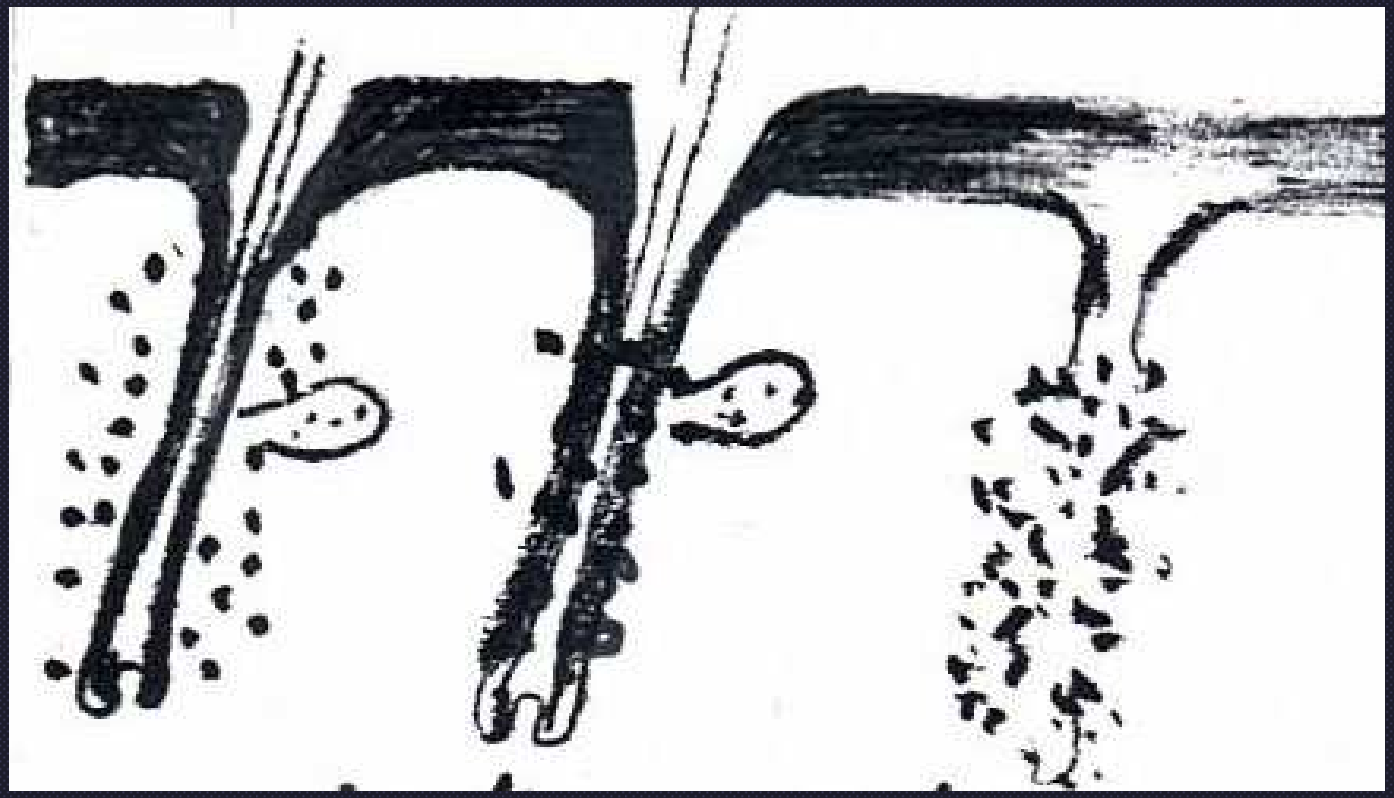


Peripheral LN
Systemic reactive histiocytosis



Peripheral LN
Systemic reactive histiocytosis

Perifollicultis/Folliculitis/Furunculosis



Disorders of Hair follicles

- Inflammation→ Folliculitis
- Hair follicle dysplasia
- Hair cycling Disorders
- Atrophy/Miniaturization
- Neoplasia

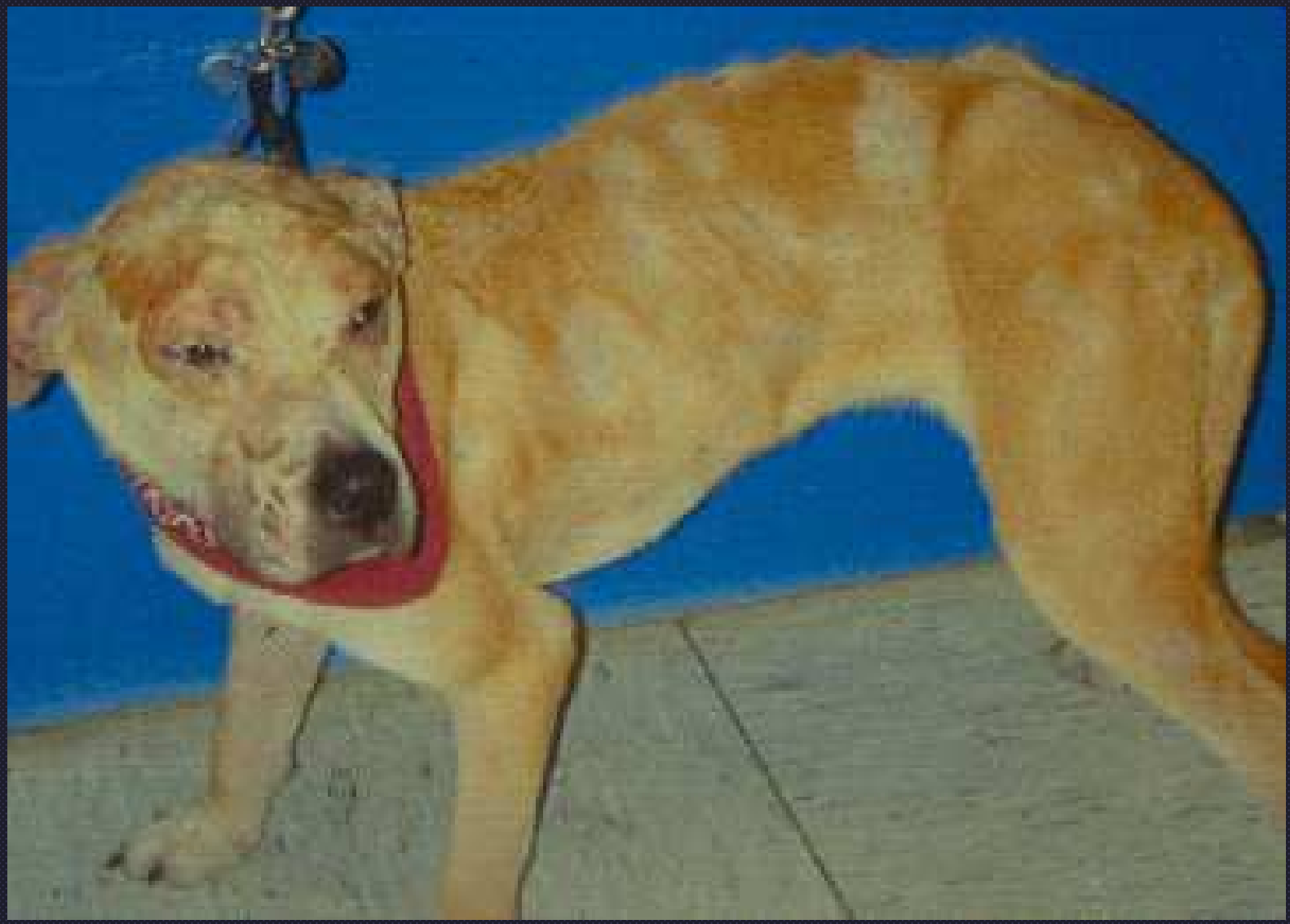
Definitions

- **Perifolliculitis**- inflammation around hair follicle
- **Luminal Folliculitis**- inflammation of the lumen of the hair follicle
- **Mural folliculitis**- inflammation within the wall of the outer root sheath

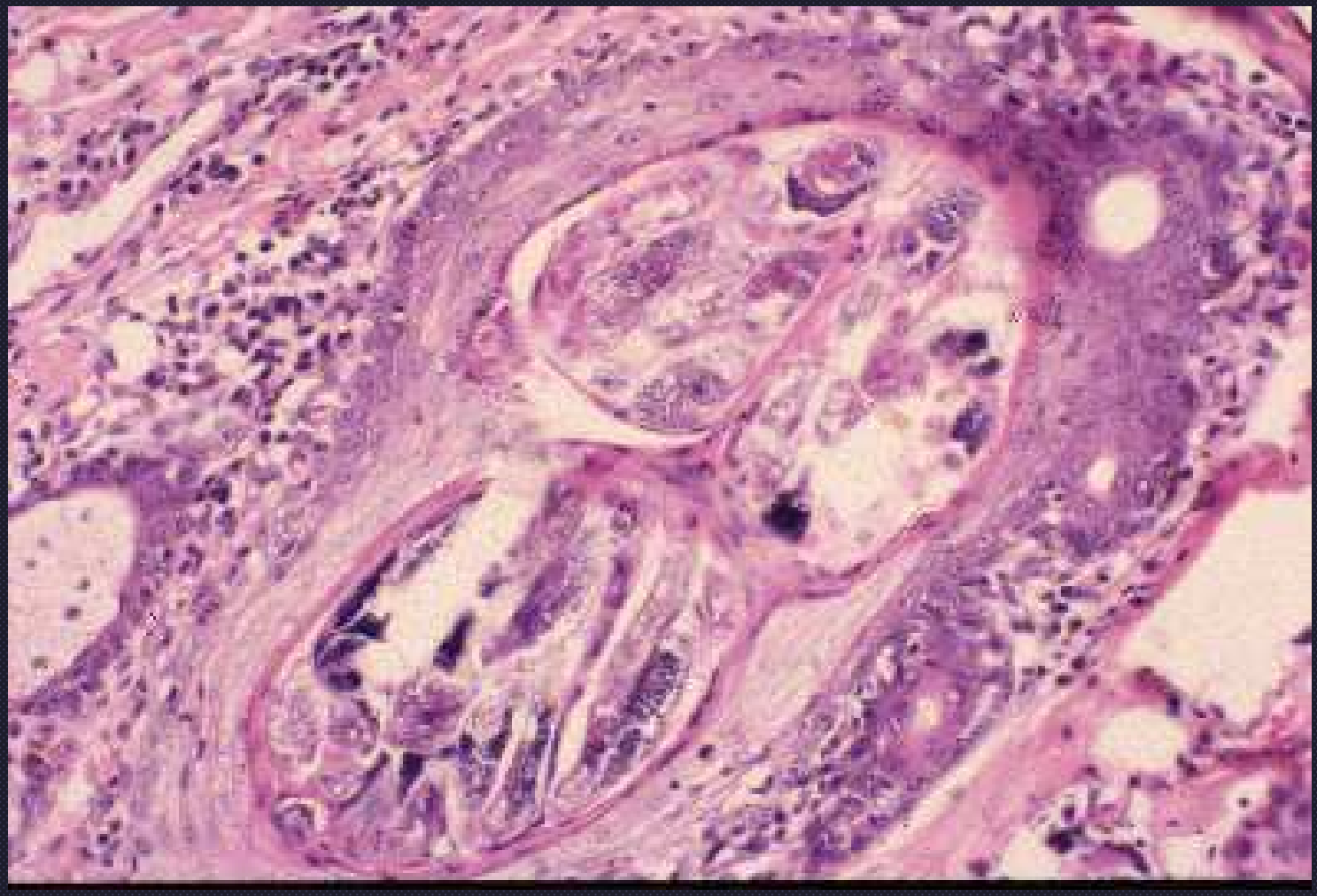
- **Furunculosis-** follicle rupture with inflammation; foreign body reaction to keratin in dermis; lesions often progress from folliculitis and furunculosis

Lip- dog with demodicosis

Demodicosis
Note the blue-black pigment due to hair follicle hyperpigmentation

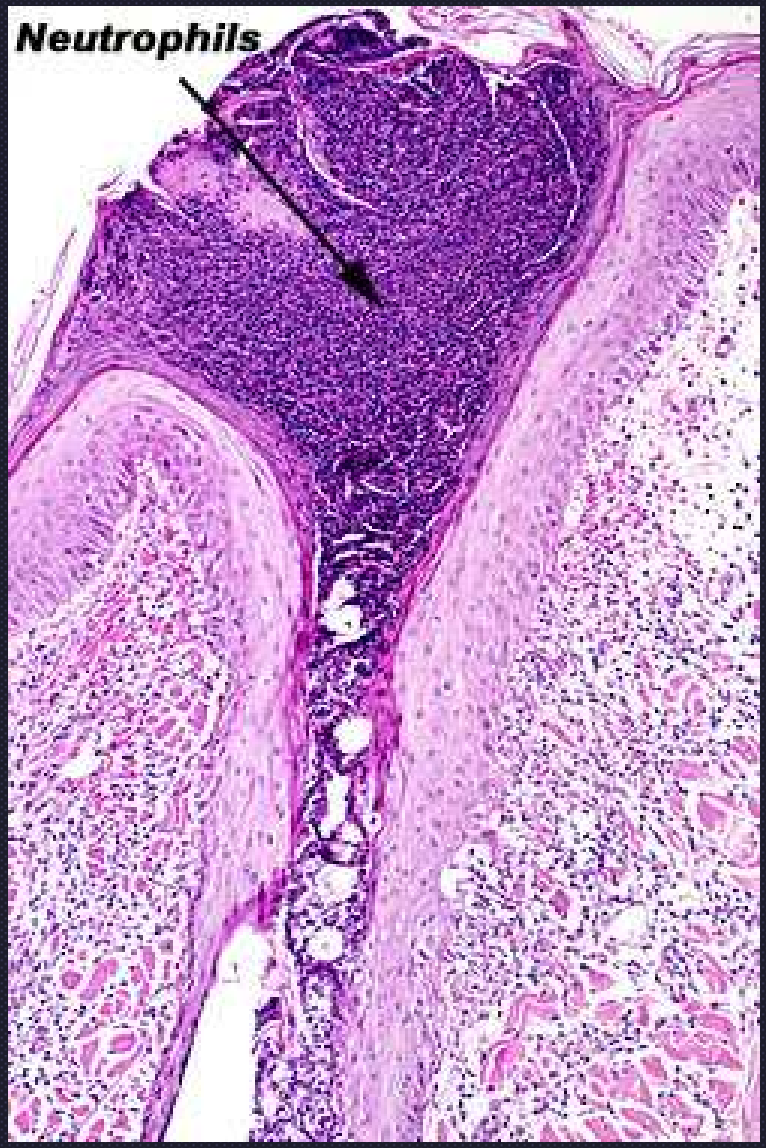


Demodicosis in a dog with thermal burn on head



Demodicosis

Demodicosis



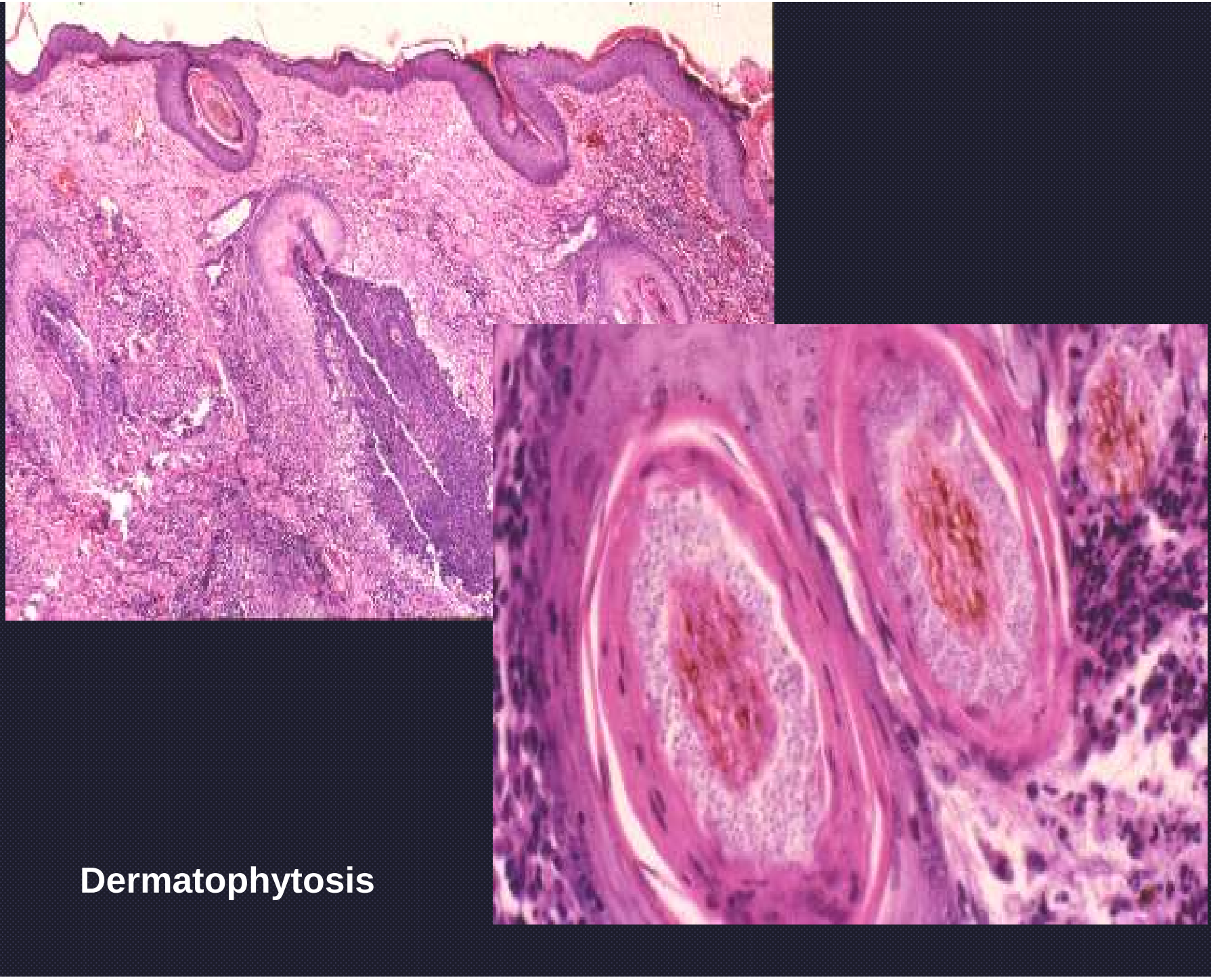
Luminal folliculitis

Short-coated breed folliculitis

"Classic" dermatophytosis in a cat

Dermatophytosis

M canis macroconidia



Dermatophytosis

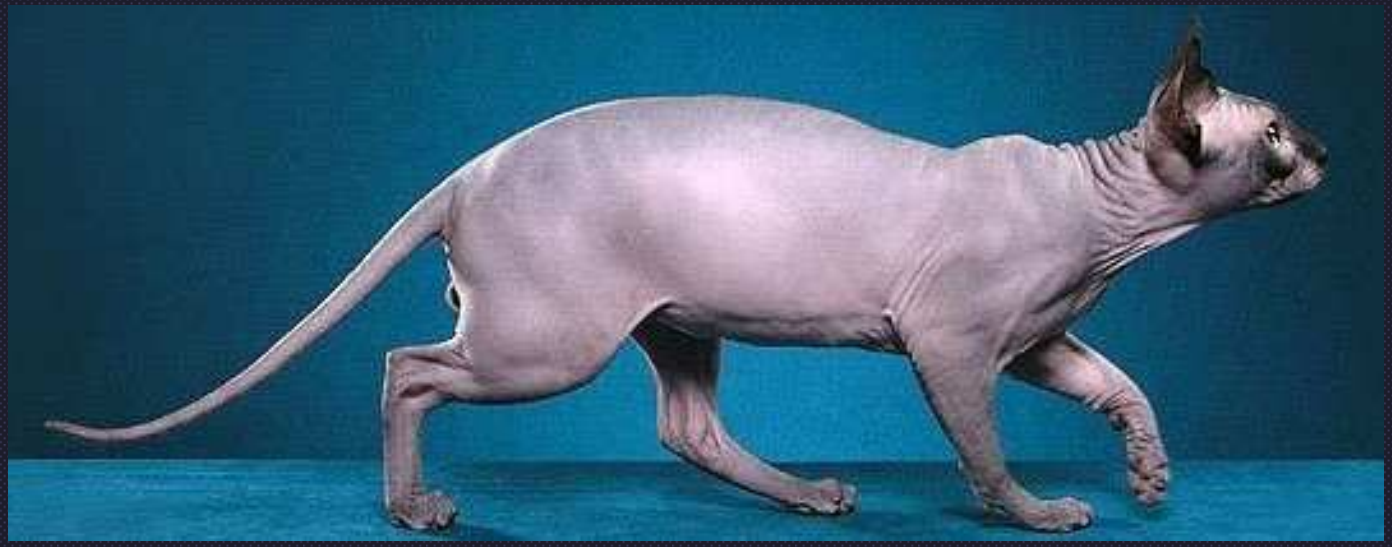
Dermatophytosis

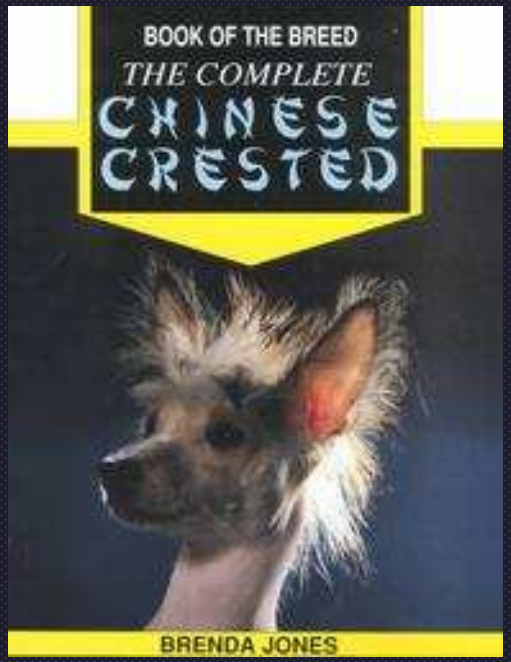
- Specific group of fungal organisms that utilize keratin in hair
- Microsporum, trichophyton, epidermophyton
- Mural folliculitis in cats and horses
- Luminal folliculitis, furunculosis, arthrospores, hyphae in shafts

Hair follicle Dysplasia
Color Dilution Alopecia

Color Dilution Alopecia

Black hair follicular dysplasia



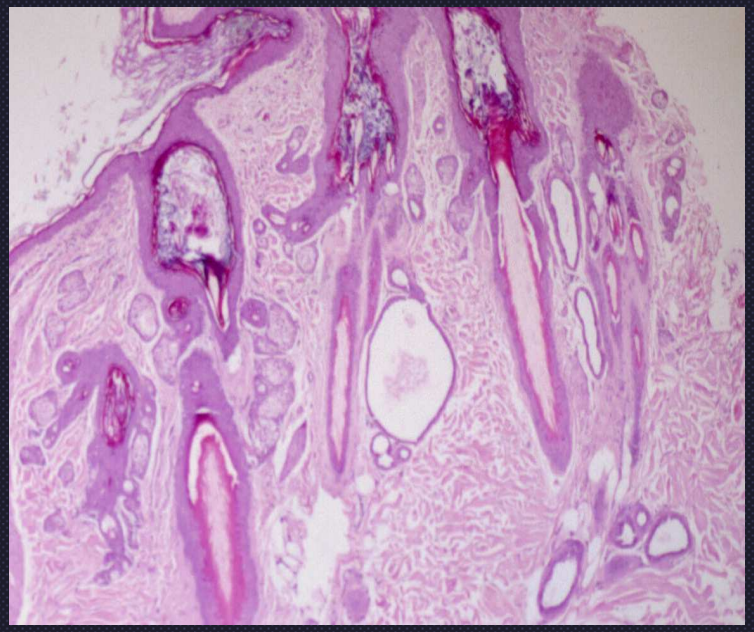


Follicular dysplasia

Follicular Changes

- Outer root sheath can undergo same changes as epidermis
- Folliculitis
- Follicular keratosis
- Follicular atrophy- different forms
  - “faded follicles”
  - excessive trichilemmal keratinization
  - miniaturization
- Follicular dysplasia- Color dilution alopecia
- Follicular neoplasia

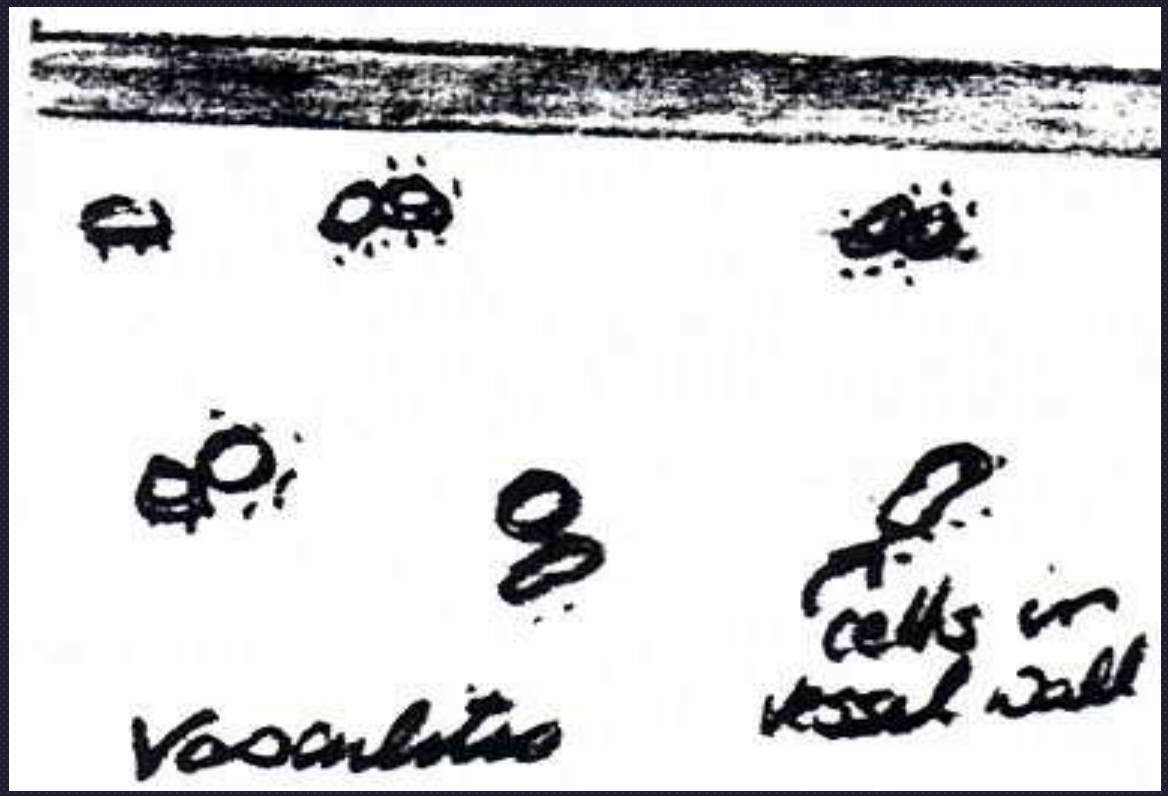
Cyclic Flank Alopecia



Follicular Atrophy

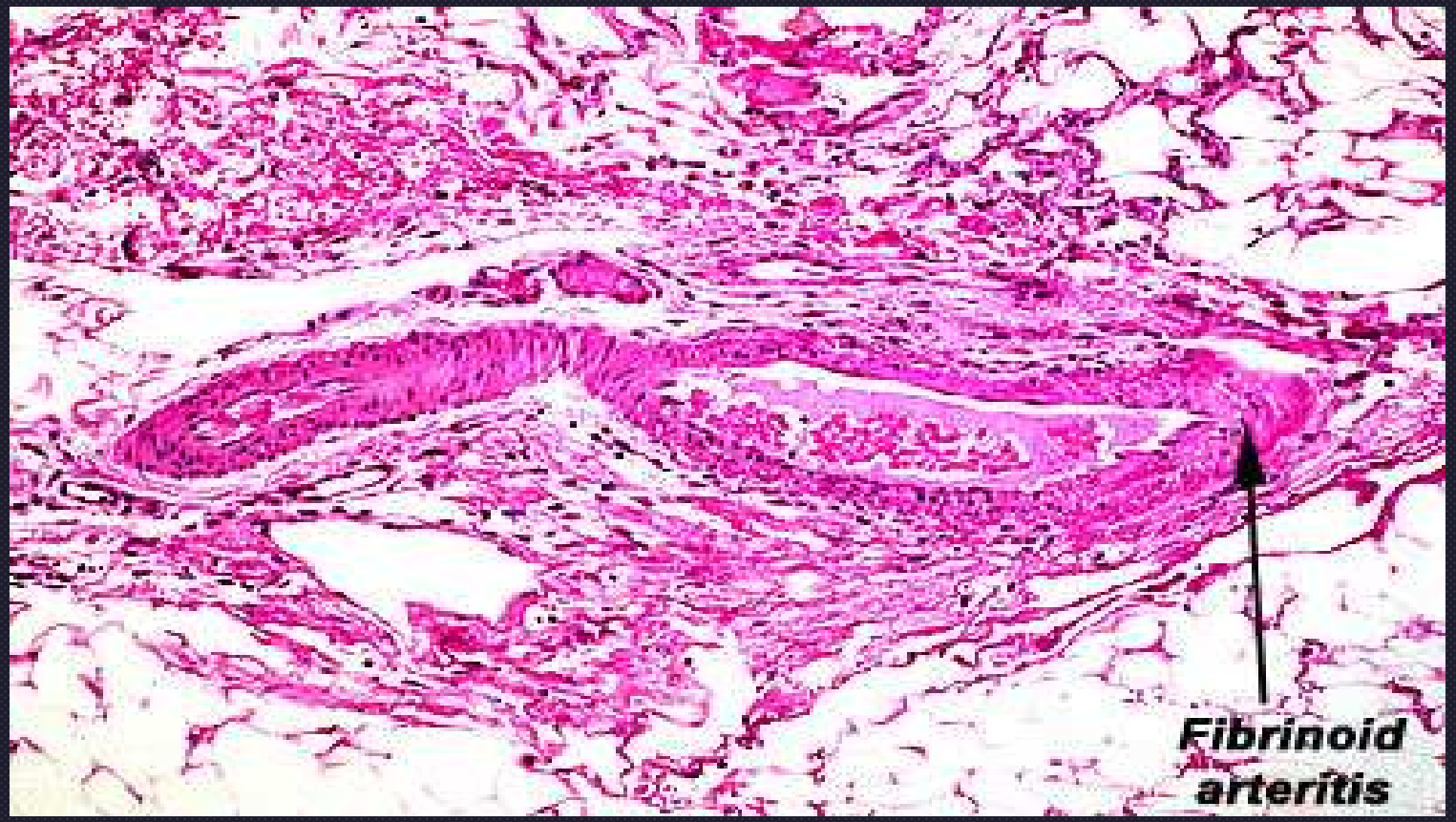
Alopecia X

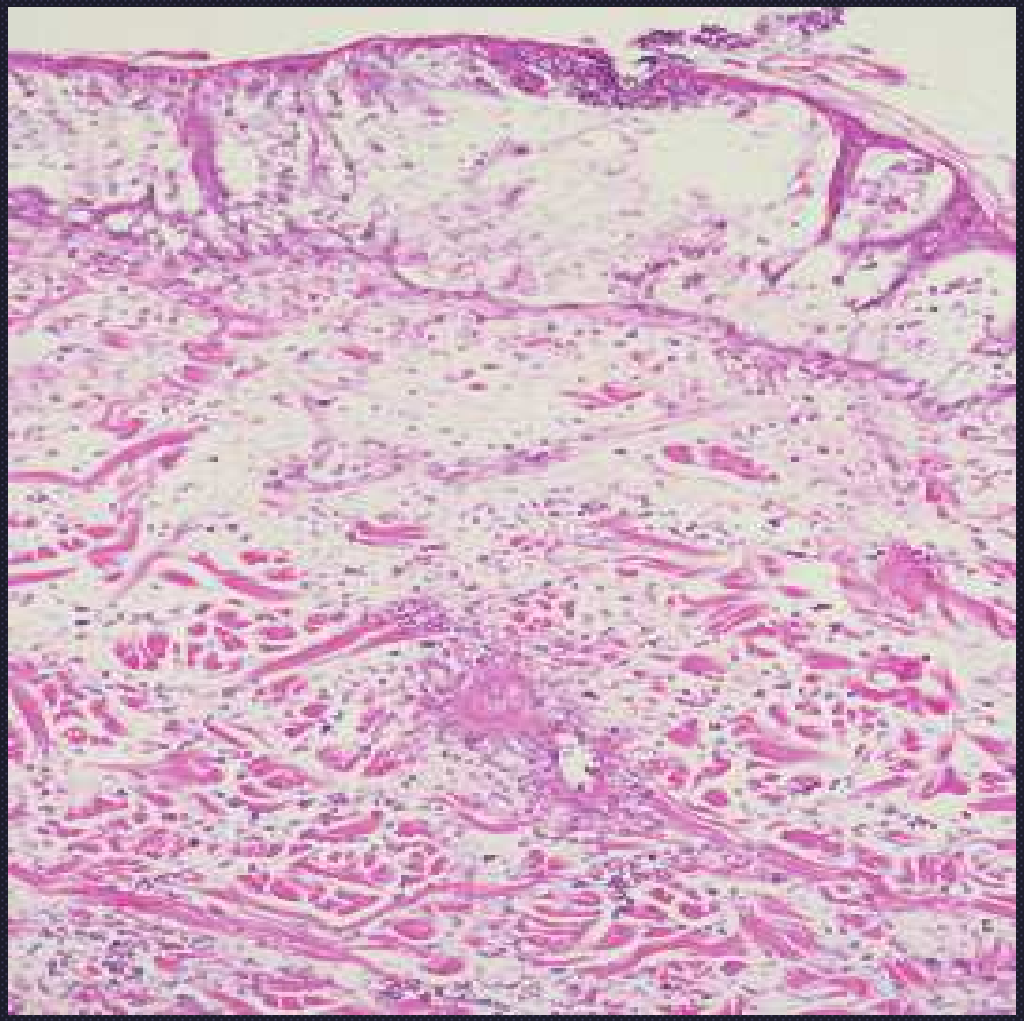
Vasculitis



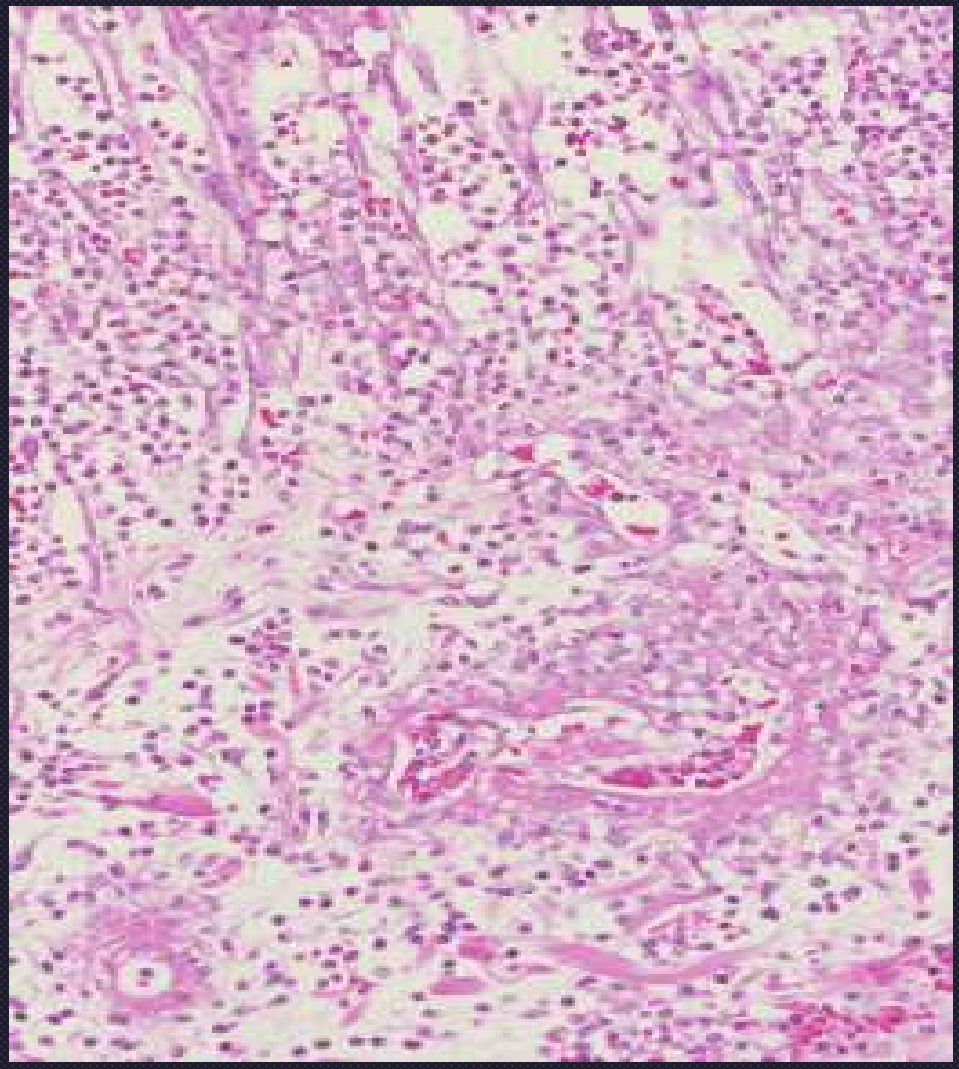
- An inflammatory cell infiltrate within or around the vessel wall (leukocytoclasia)
- Vascular injury (e.g. endothelial swelling or necrosis, fibrinoid change, intravascular fibrin thrombi)

Vasculitis


Fibrinoid
arteritis



Fibrinoid vasculitis

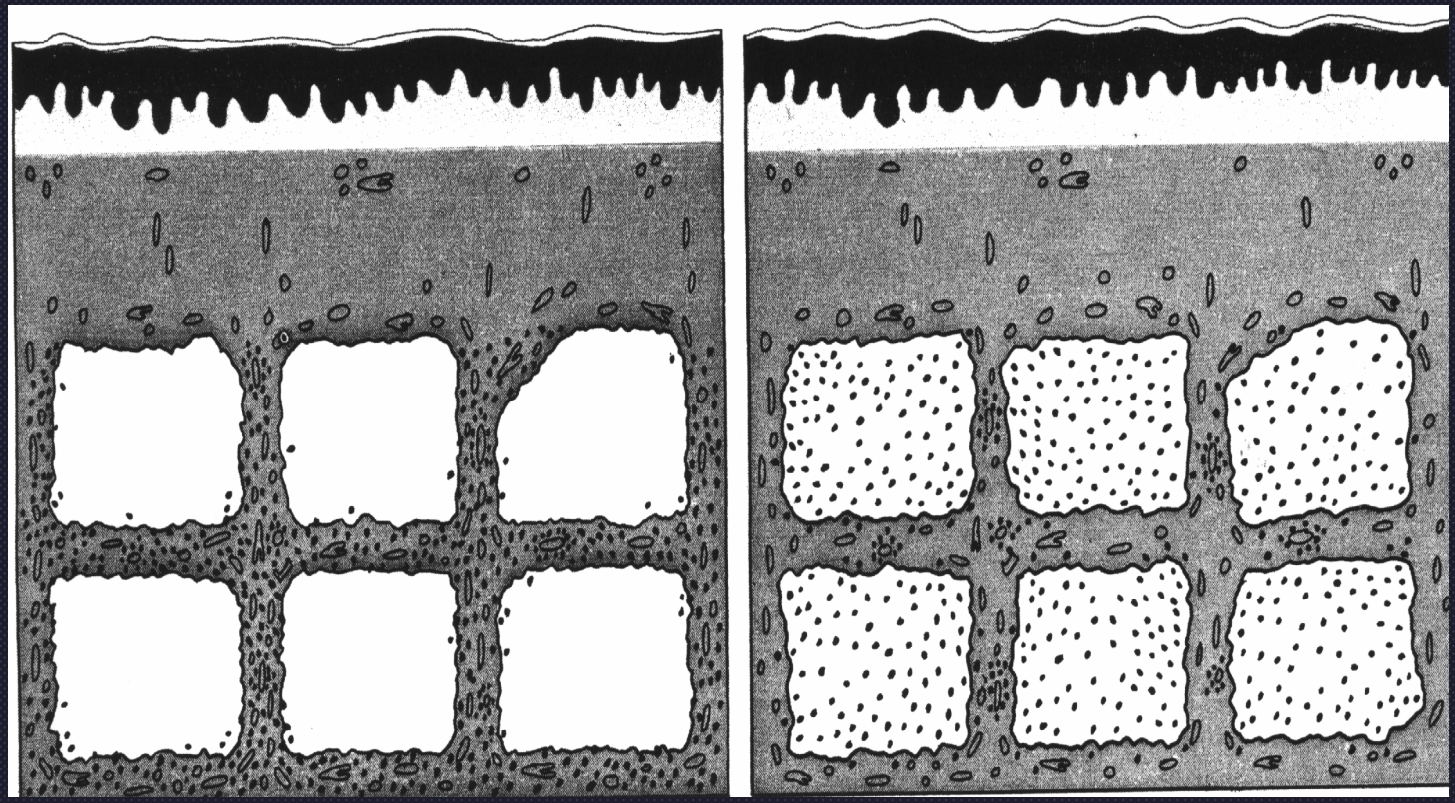


Fibrinoid vasculitis

Cutaneous vasculitis in a horse

Rabies vaccine associated alopecia

Panniculitis



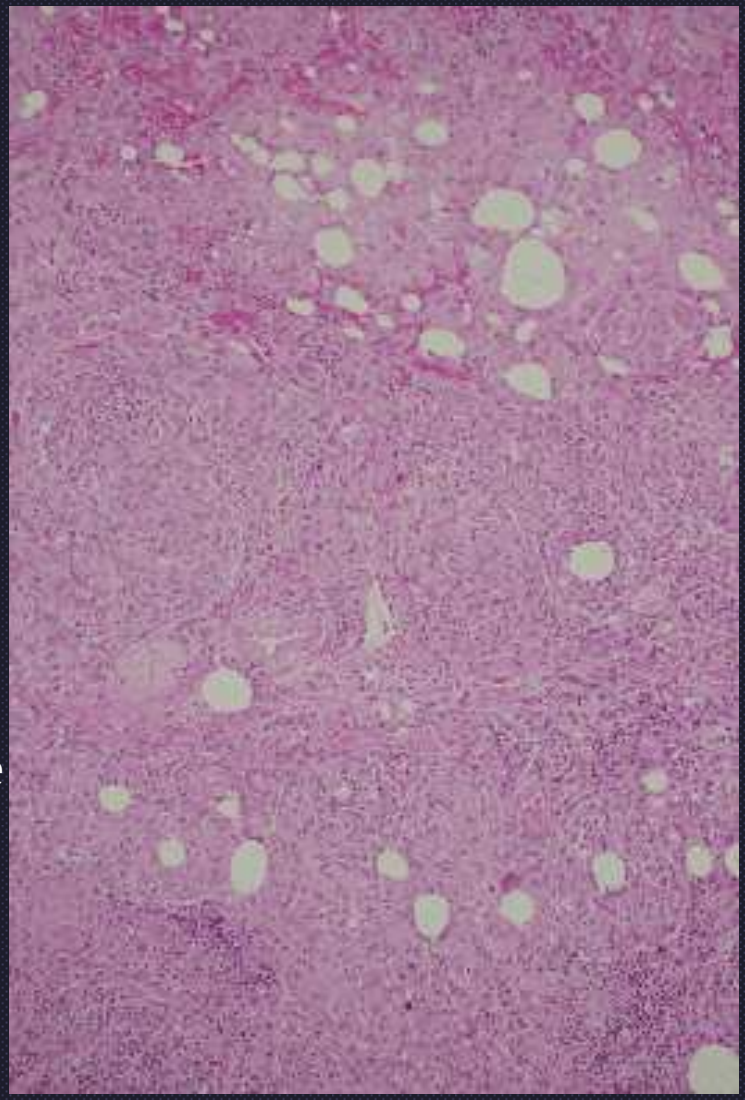
Panniculitis

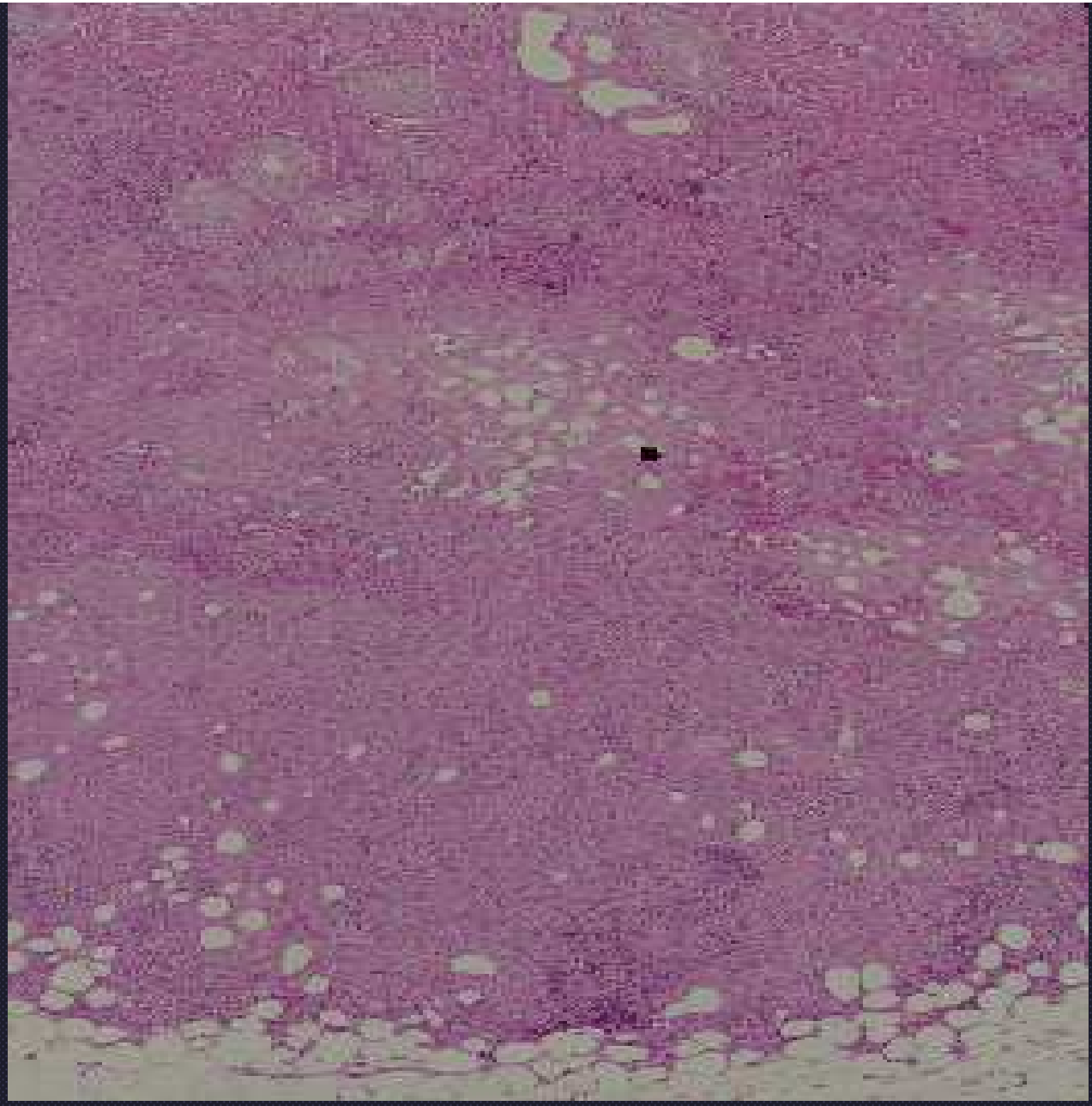
- Trauma
- Foreign body
- Infectious- must rule-out
- Rarely autoimmune
- **Often idiopathic and sterile**

“Teddy”

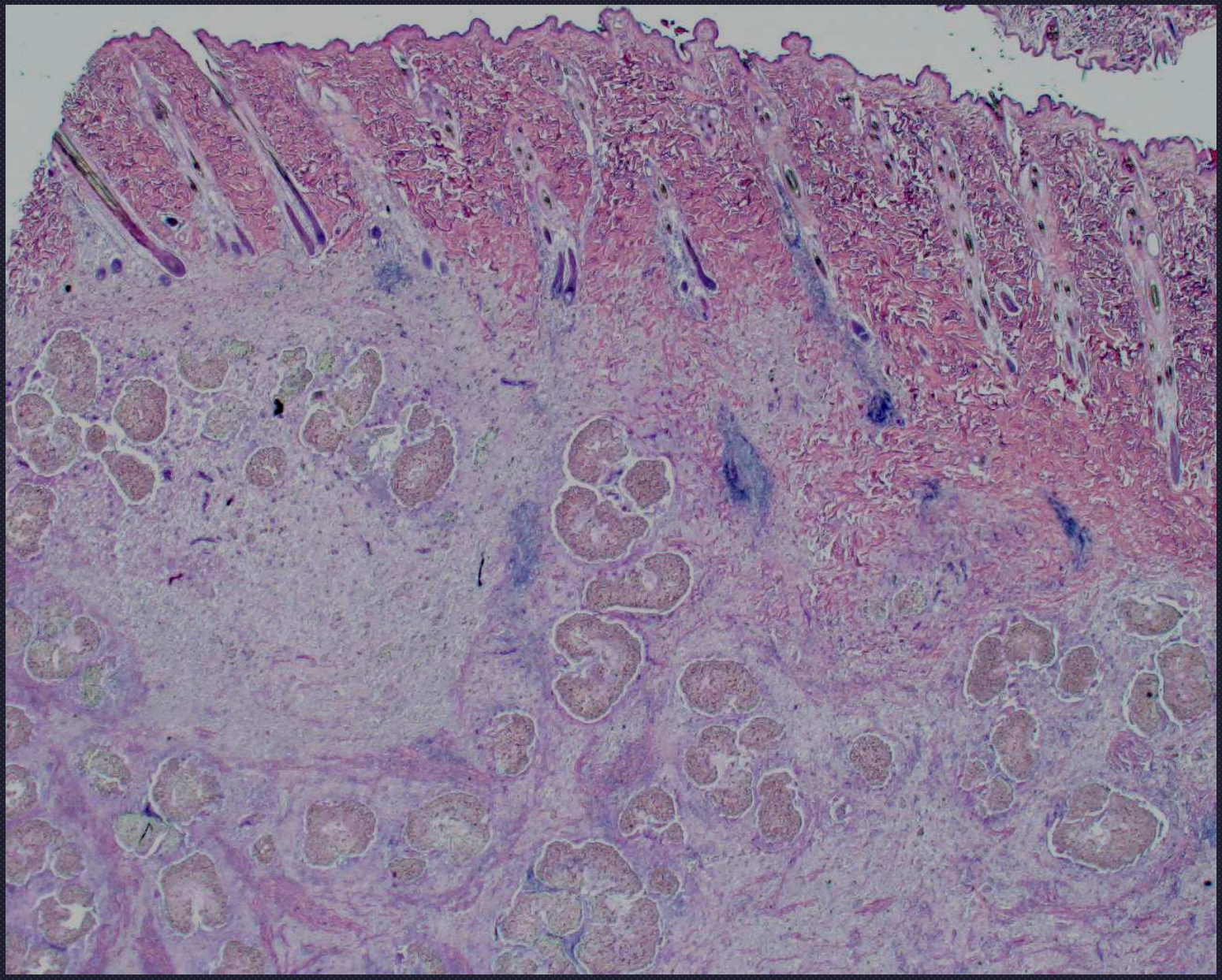
Nodule which drains “oily” exudate
Nodular panniculitis

Idiopathic nodular panniculitis
Special stains and C/S negative

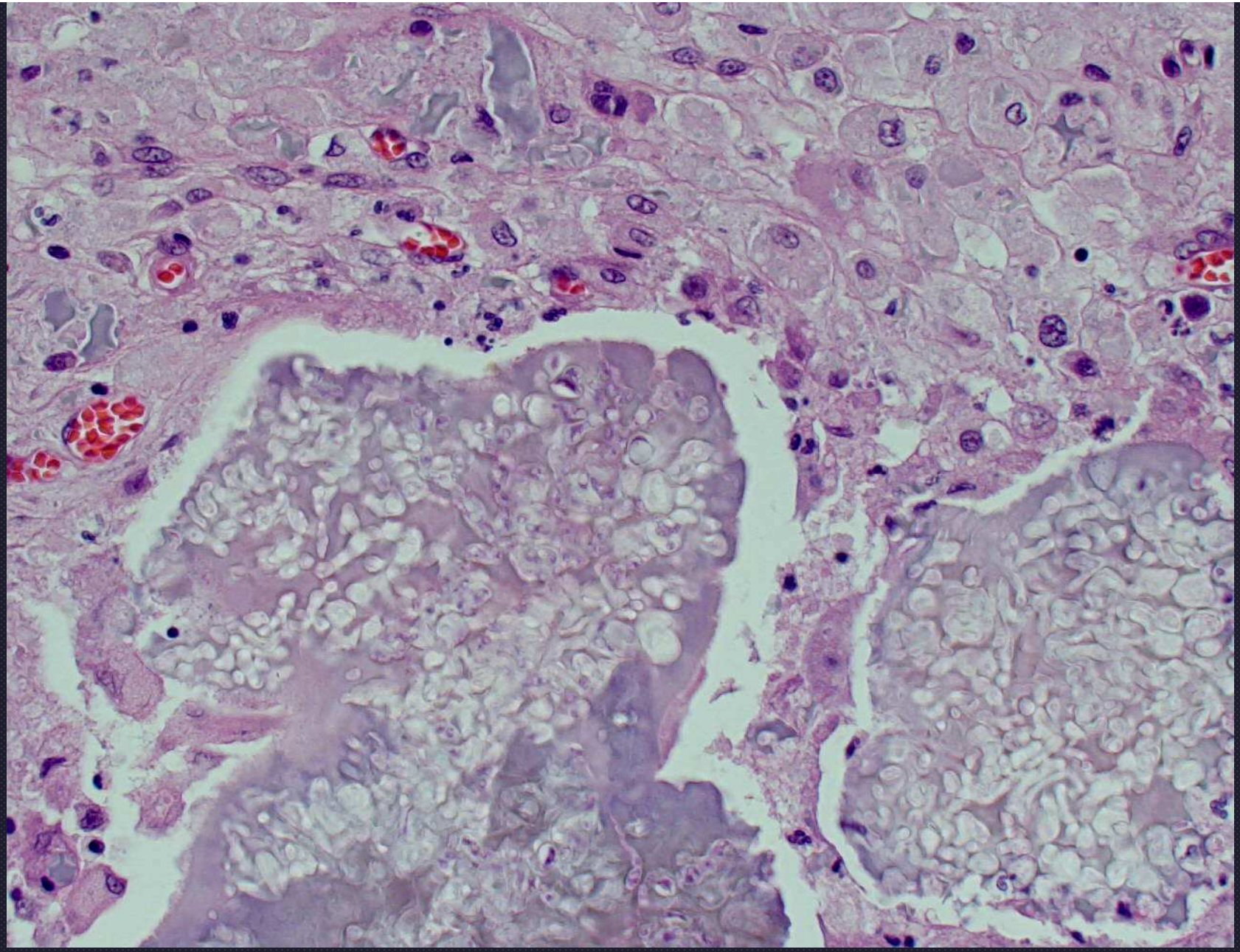




Idiopathic nodular panniculitis
Special stains and C/S negative

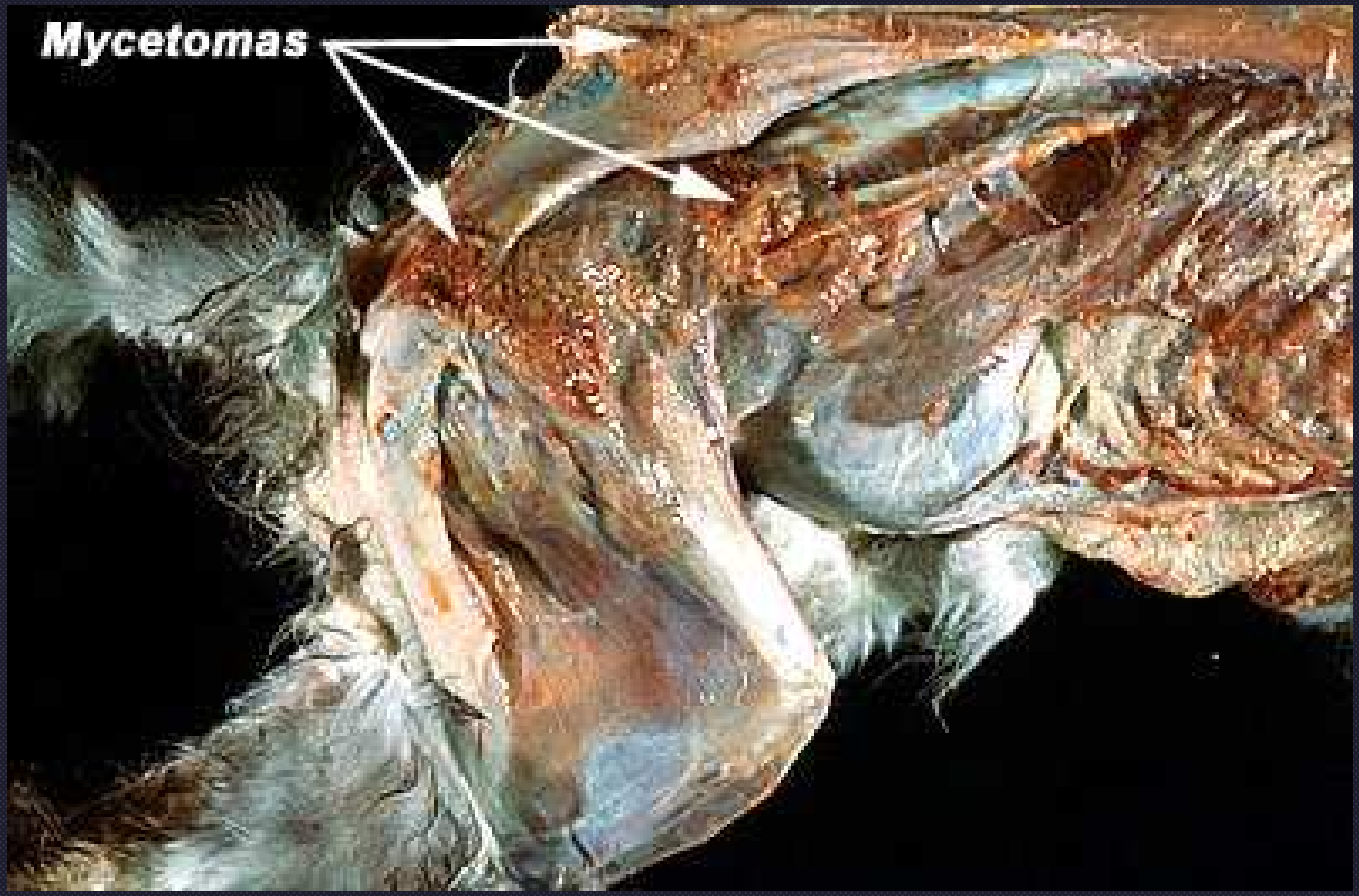


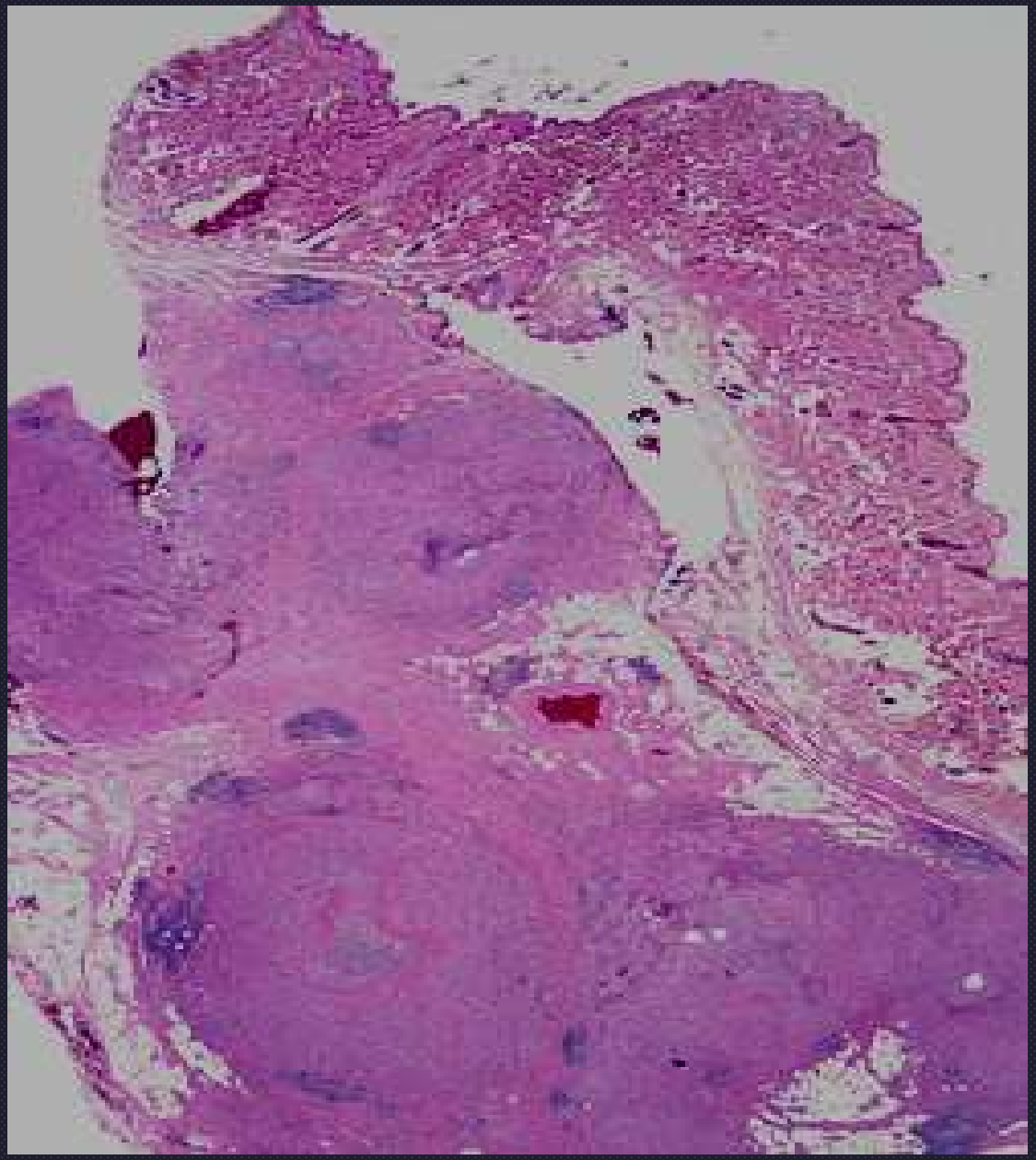
Dermatophyte pseudomycetoma



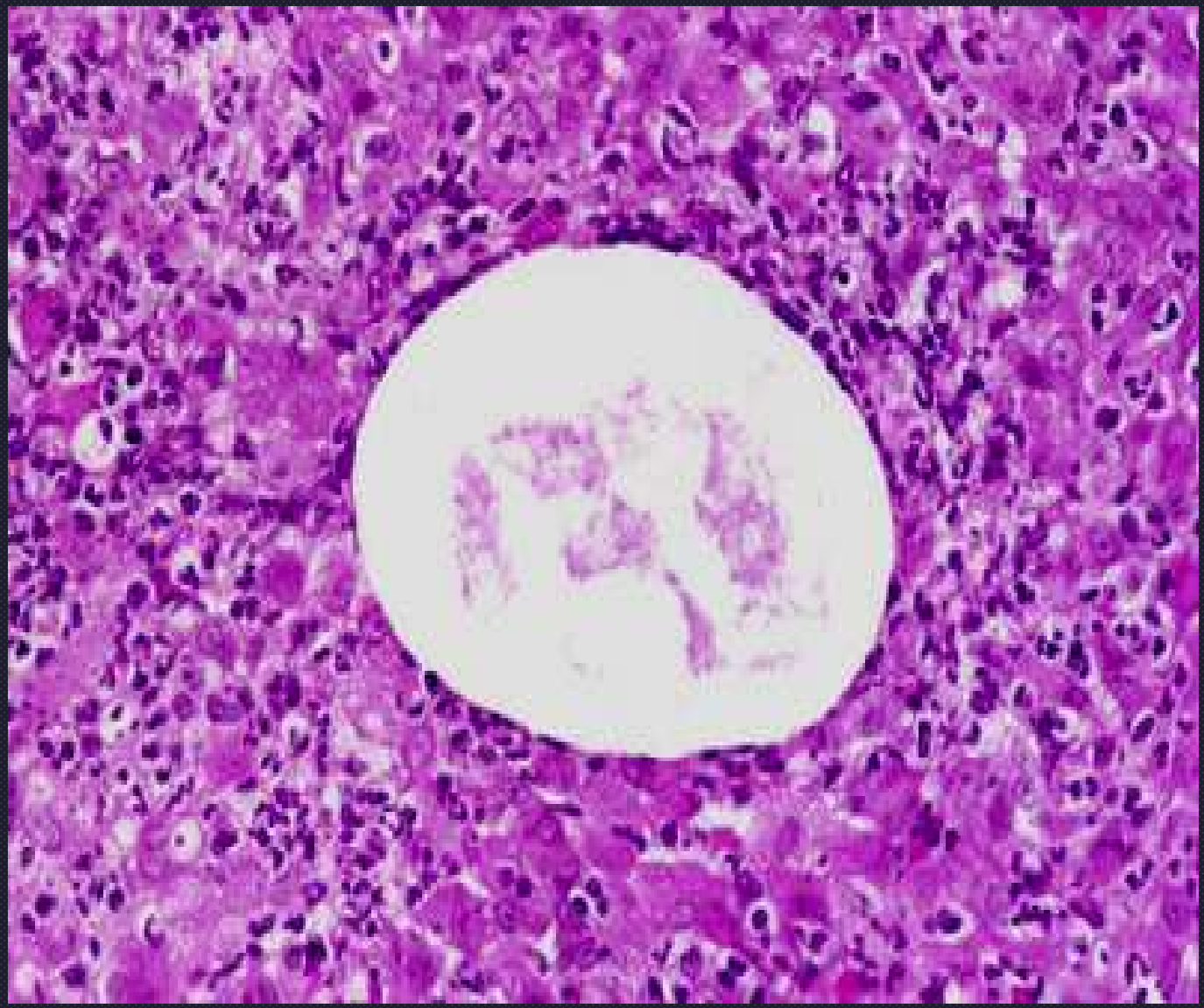
Dermatophyte
Pseudomycetoma

Dermatophyte pseudomycetoma


Mycetomas

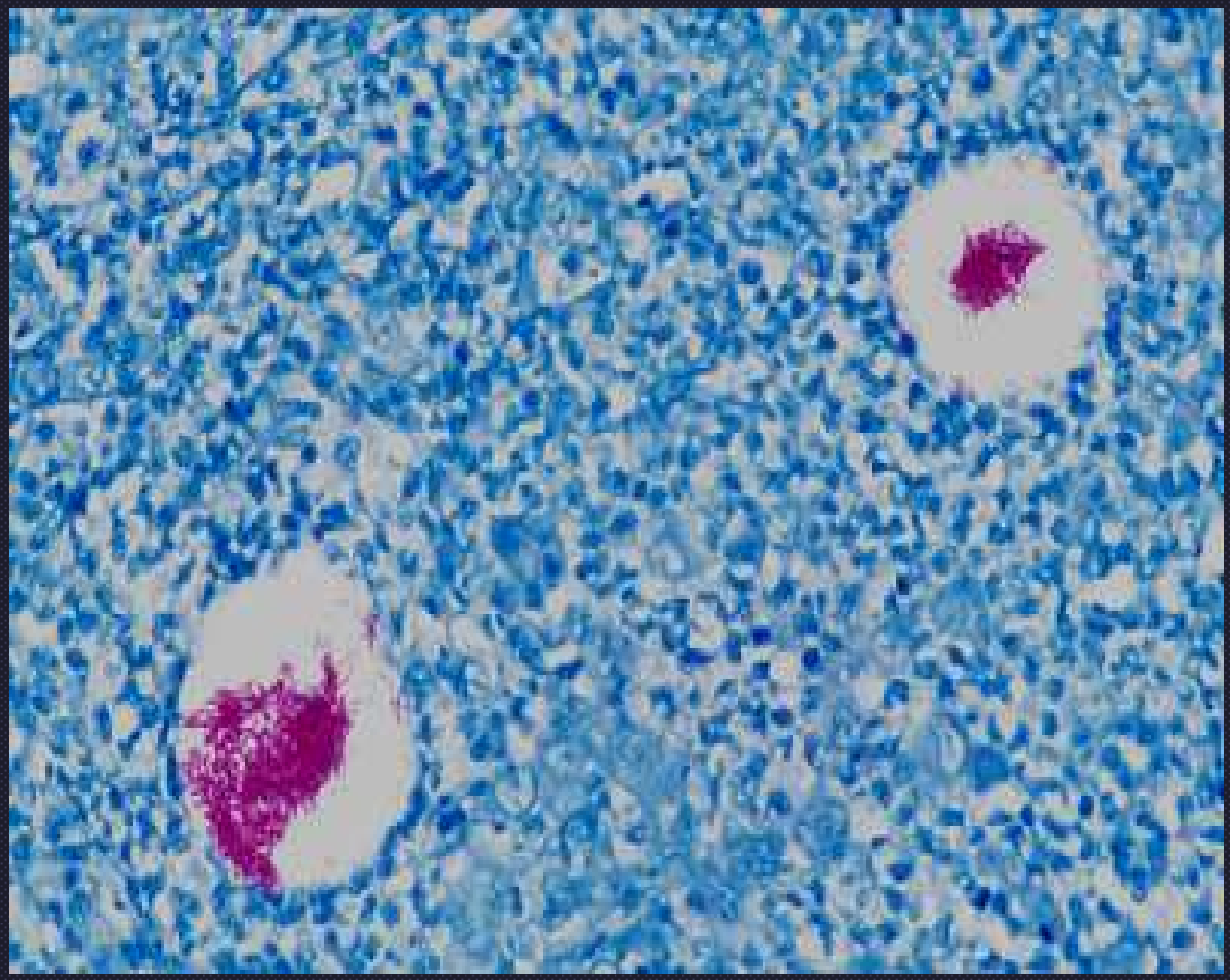


Nocardia



Nocardia

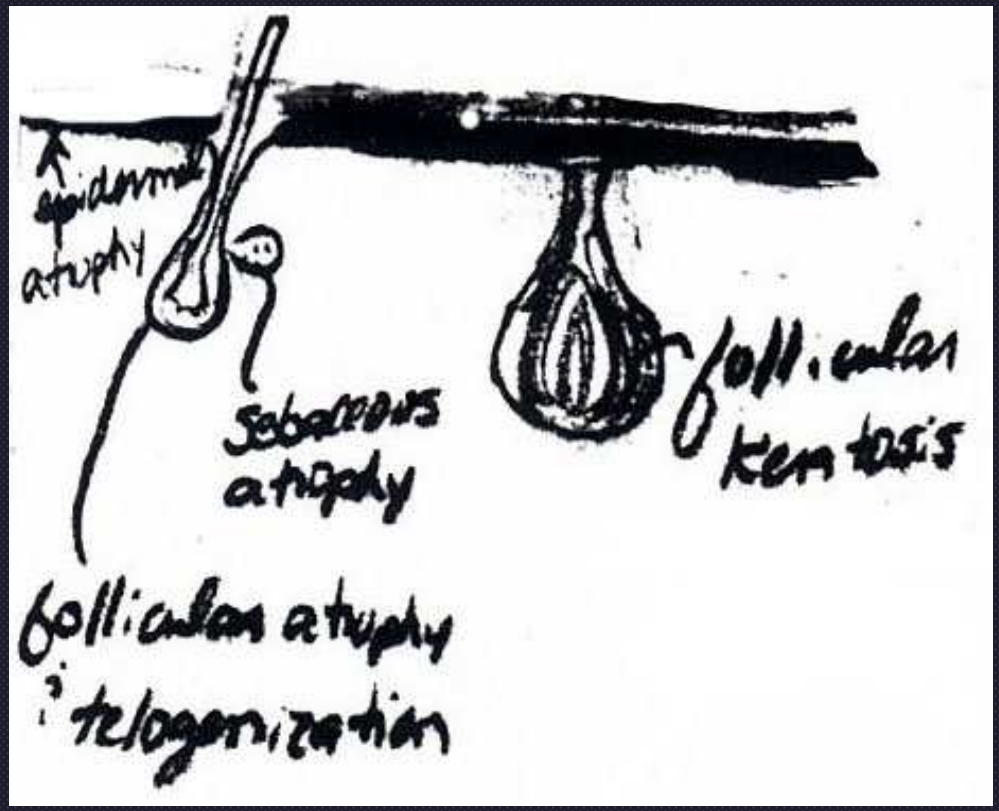
Nocardia sp.



Nocardial infection

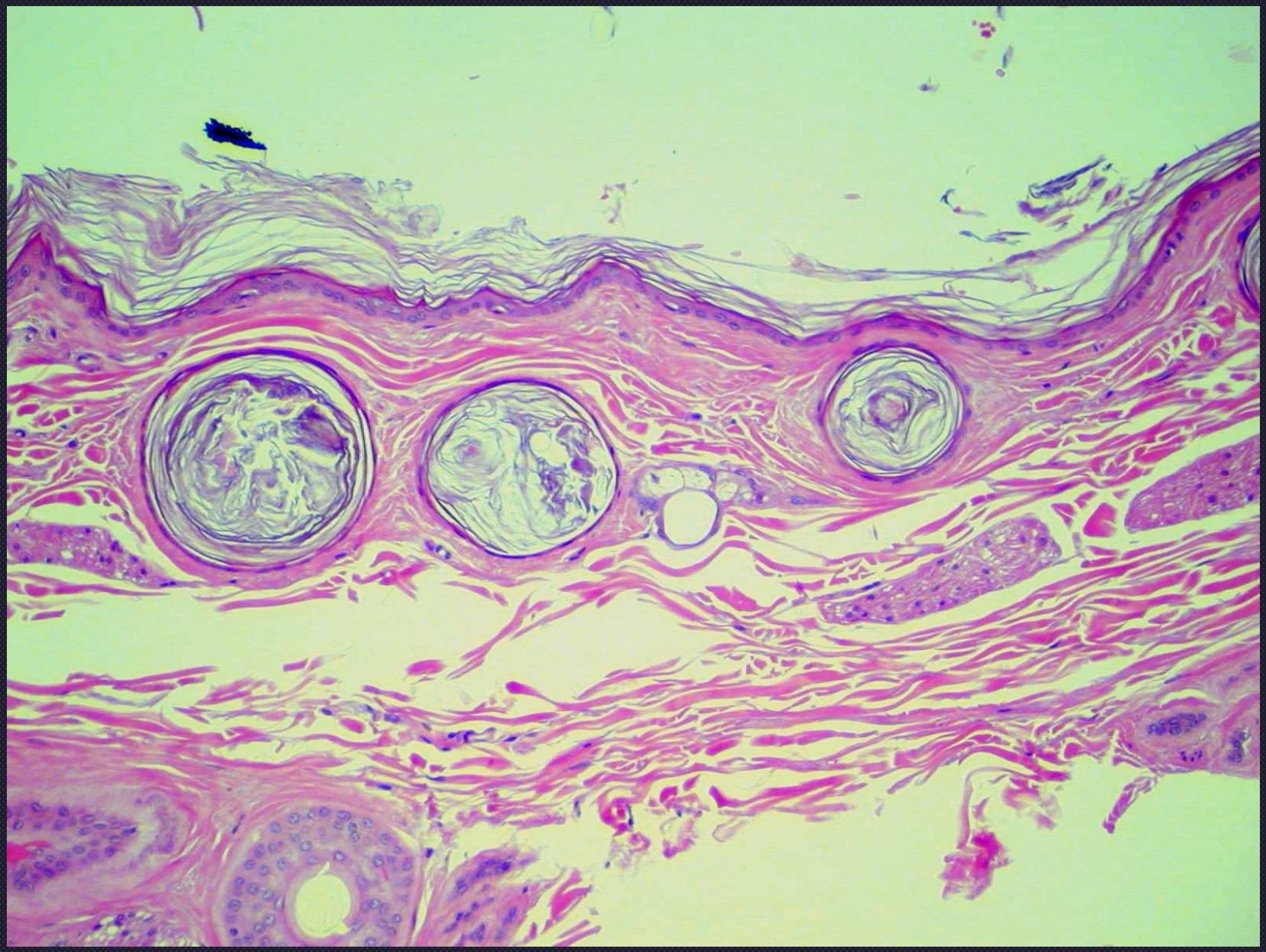
Nocardial infection

Atrophic Dermatoses



Endocrine Disease

- Hyperadrenocorticism
- Epidermal, dermal atrophy



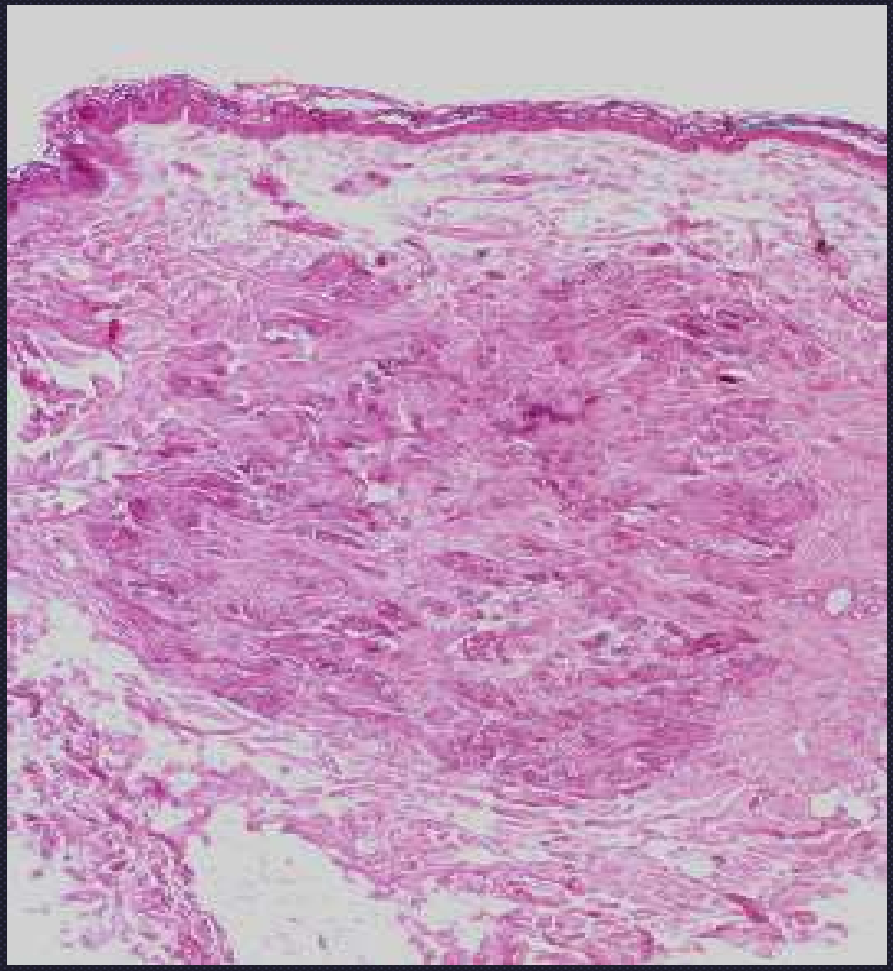
Cutaneous atrophy due to hyperadrenocorticism

Topical Corticosteroids

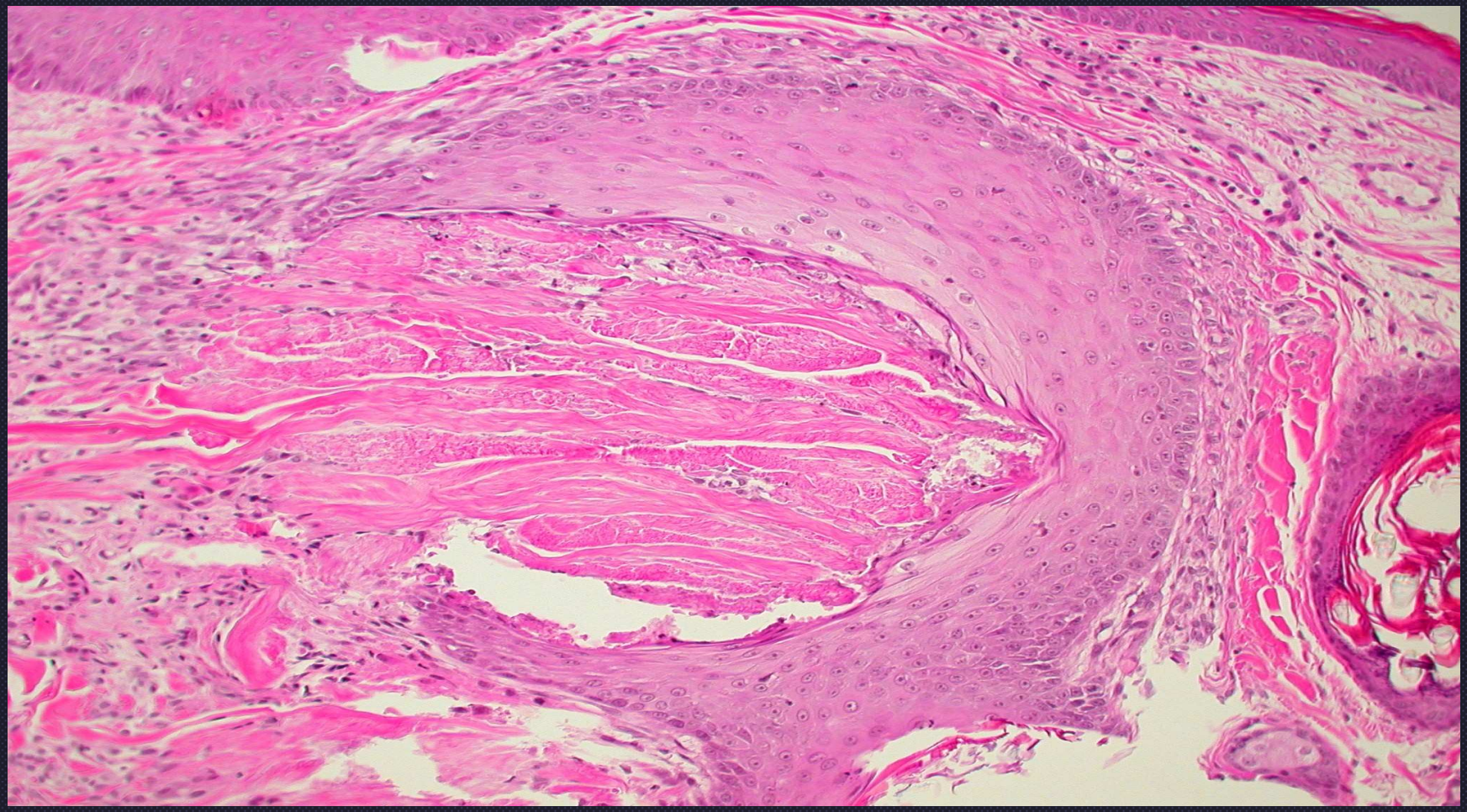
Cutaneous atrophy

Calcinosis cutis

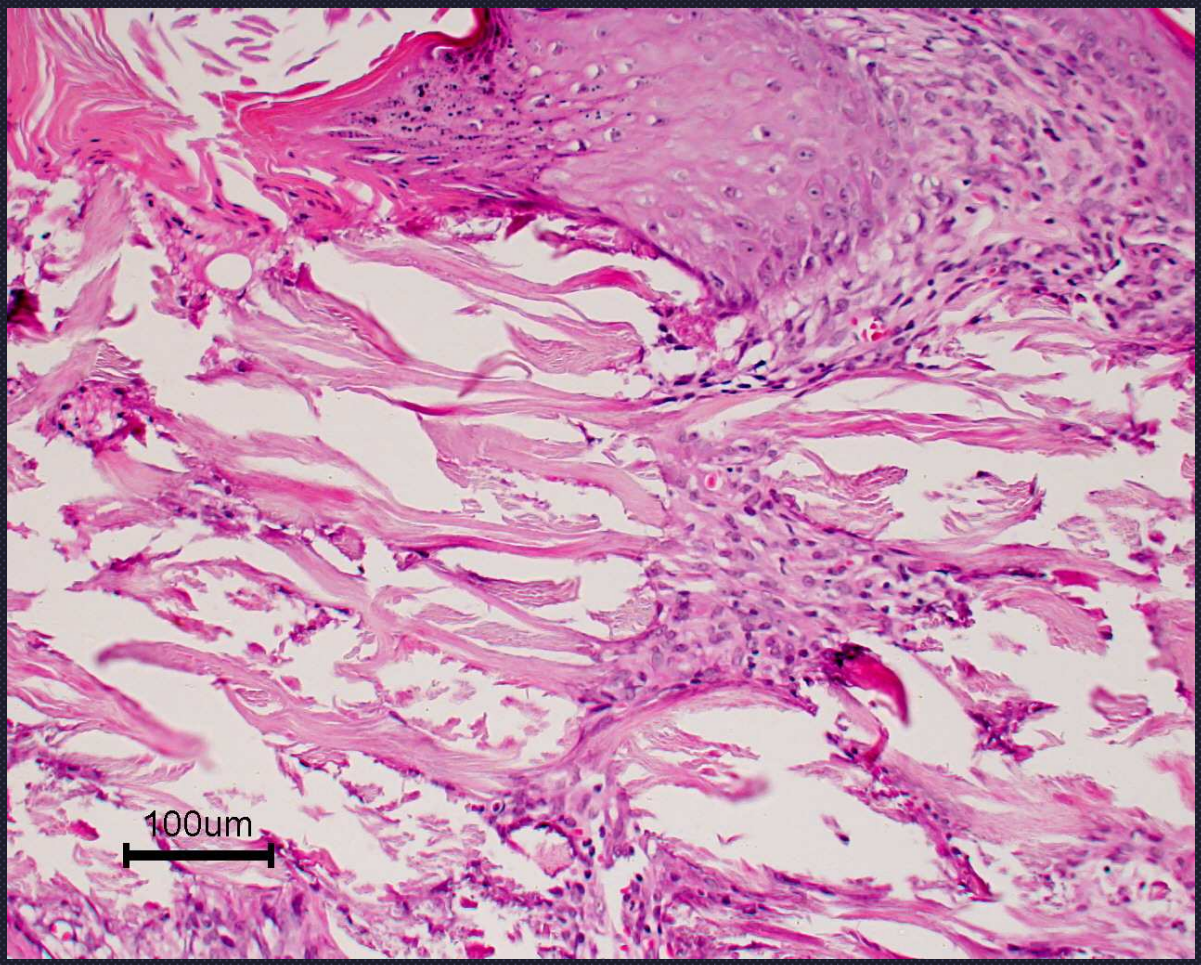
Calcinosis Cutis



Calcinosis Cutis

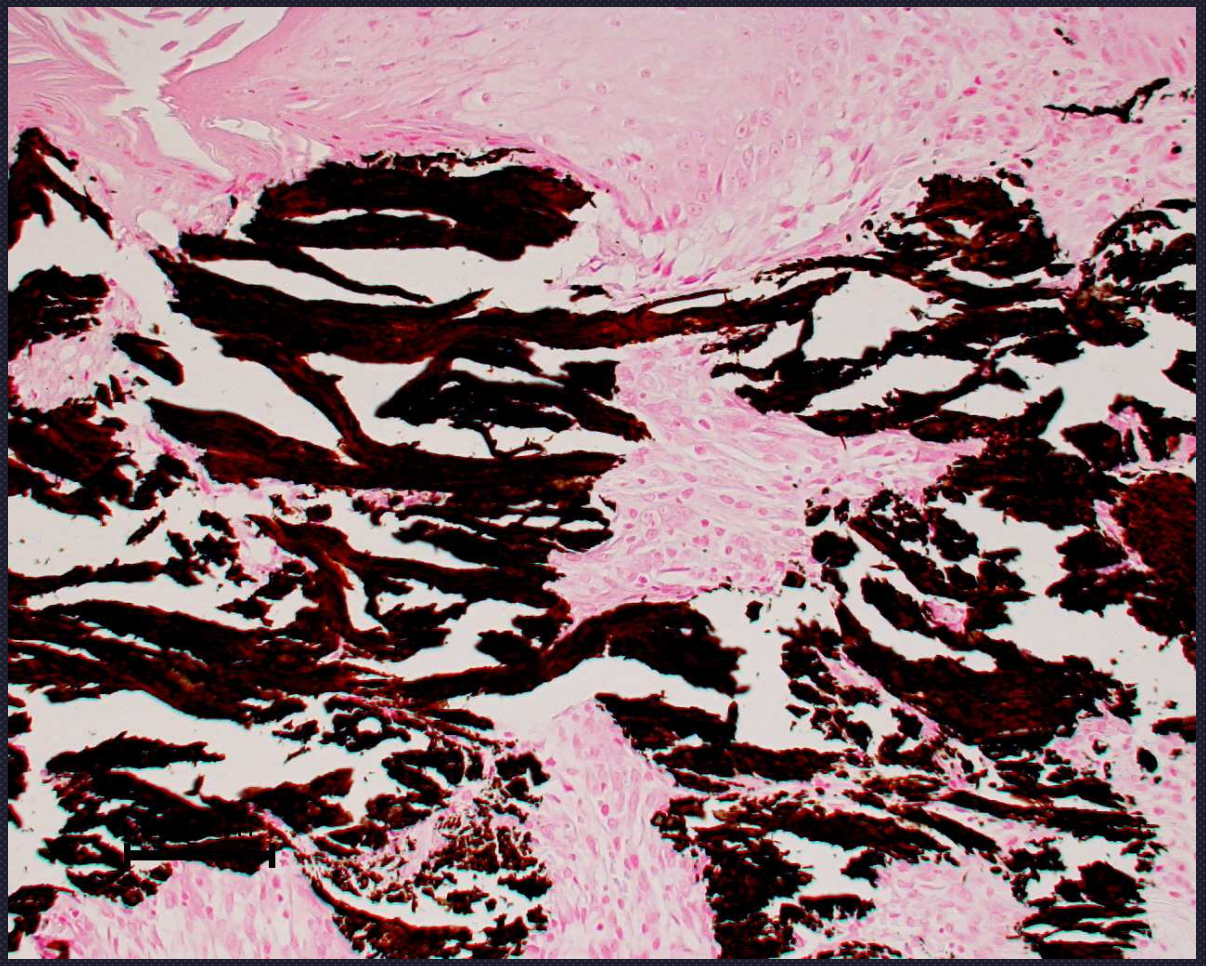


“follicular vomiting”



Calcinosis cutis

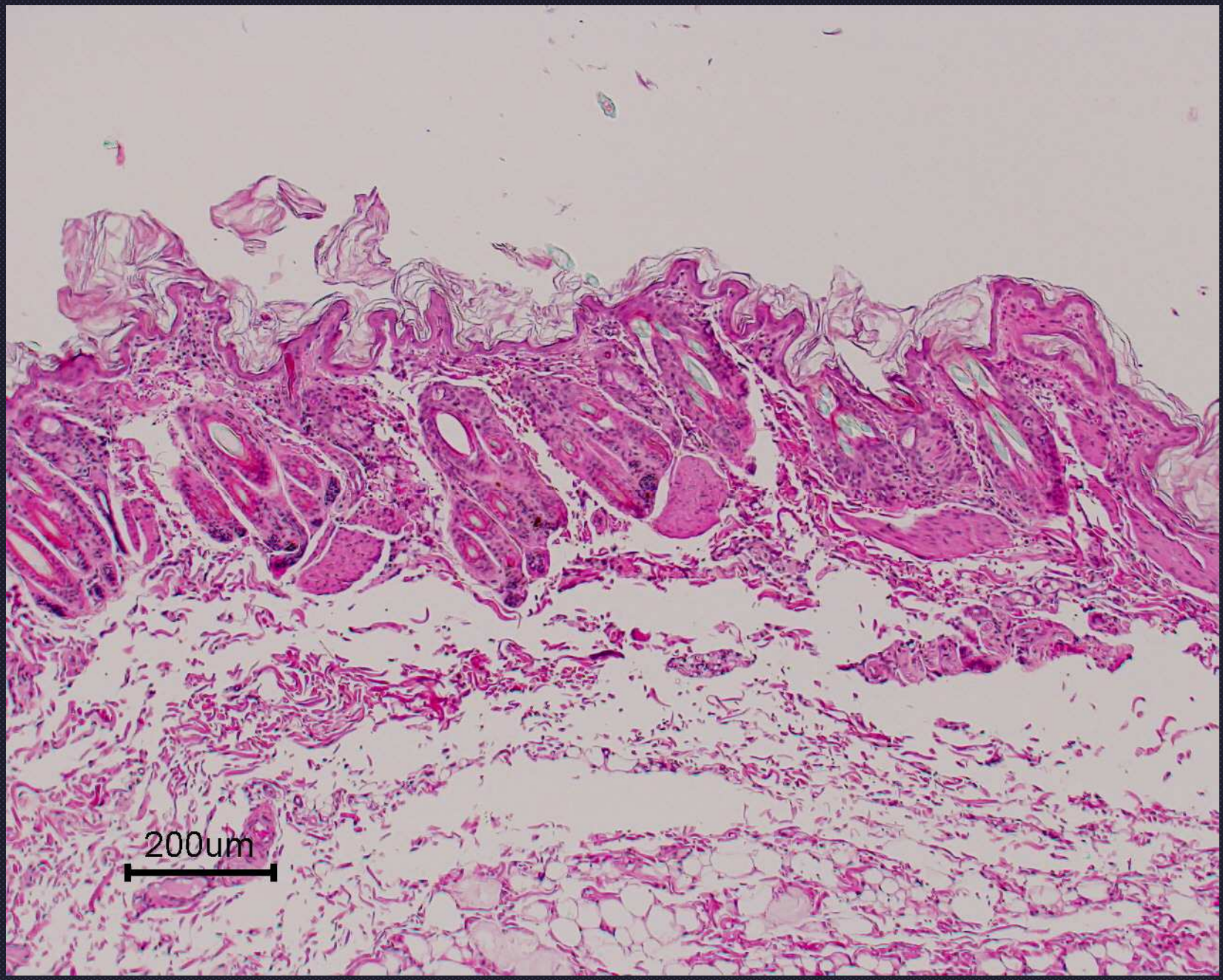
Calcinosis Cutis



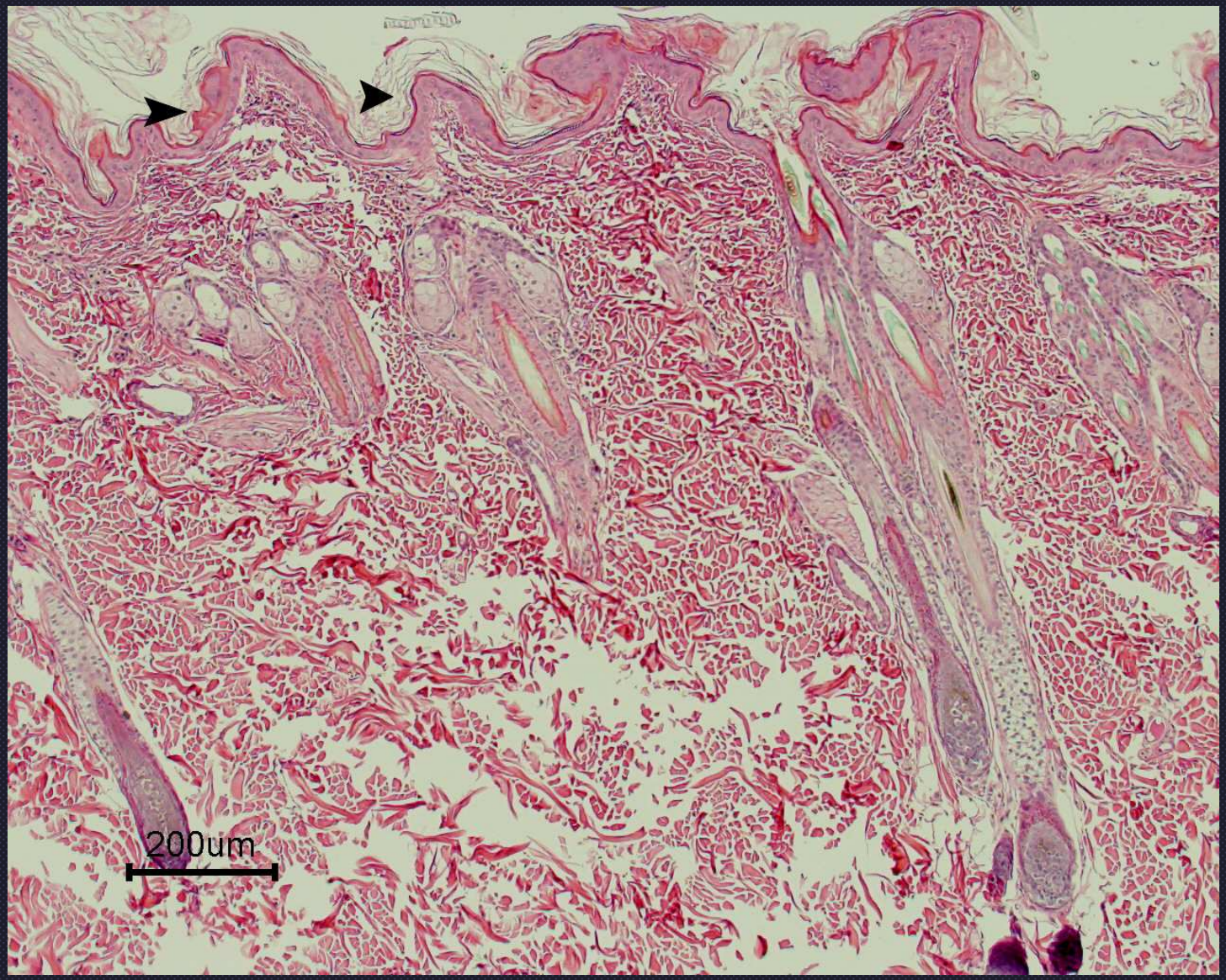
Von kossa stain

Feline acquired skin fragility syndrome

Feline acquired skin fragility syndrome



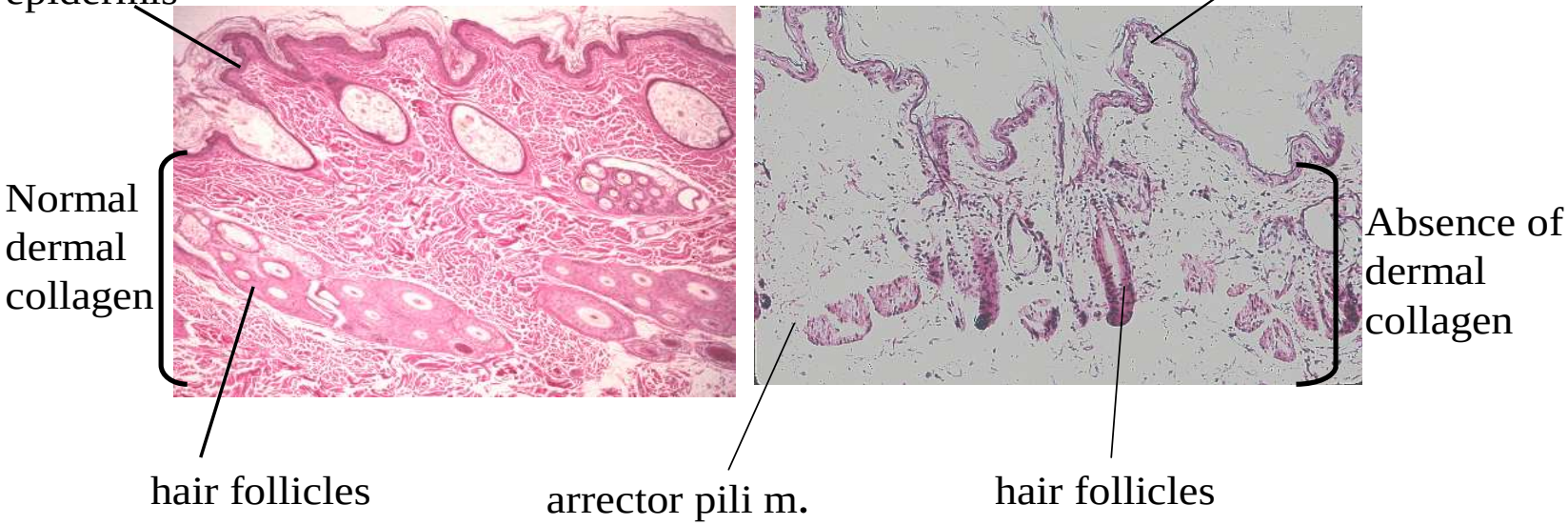
Profound dermal atrophy- feline acquired skin fragility syndrome



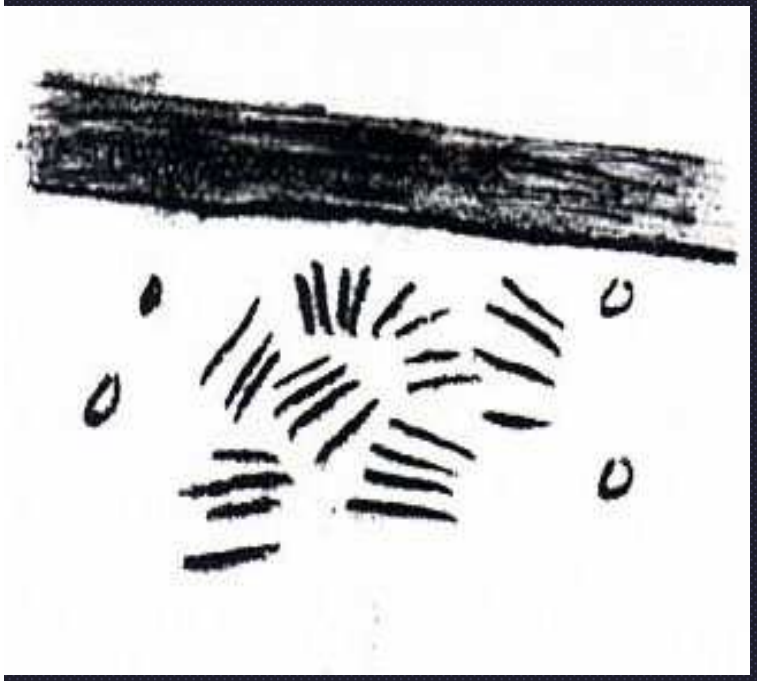
Normal feline skin

Normal animal

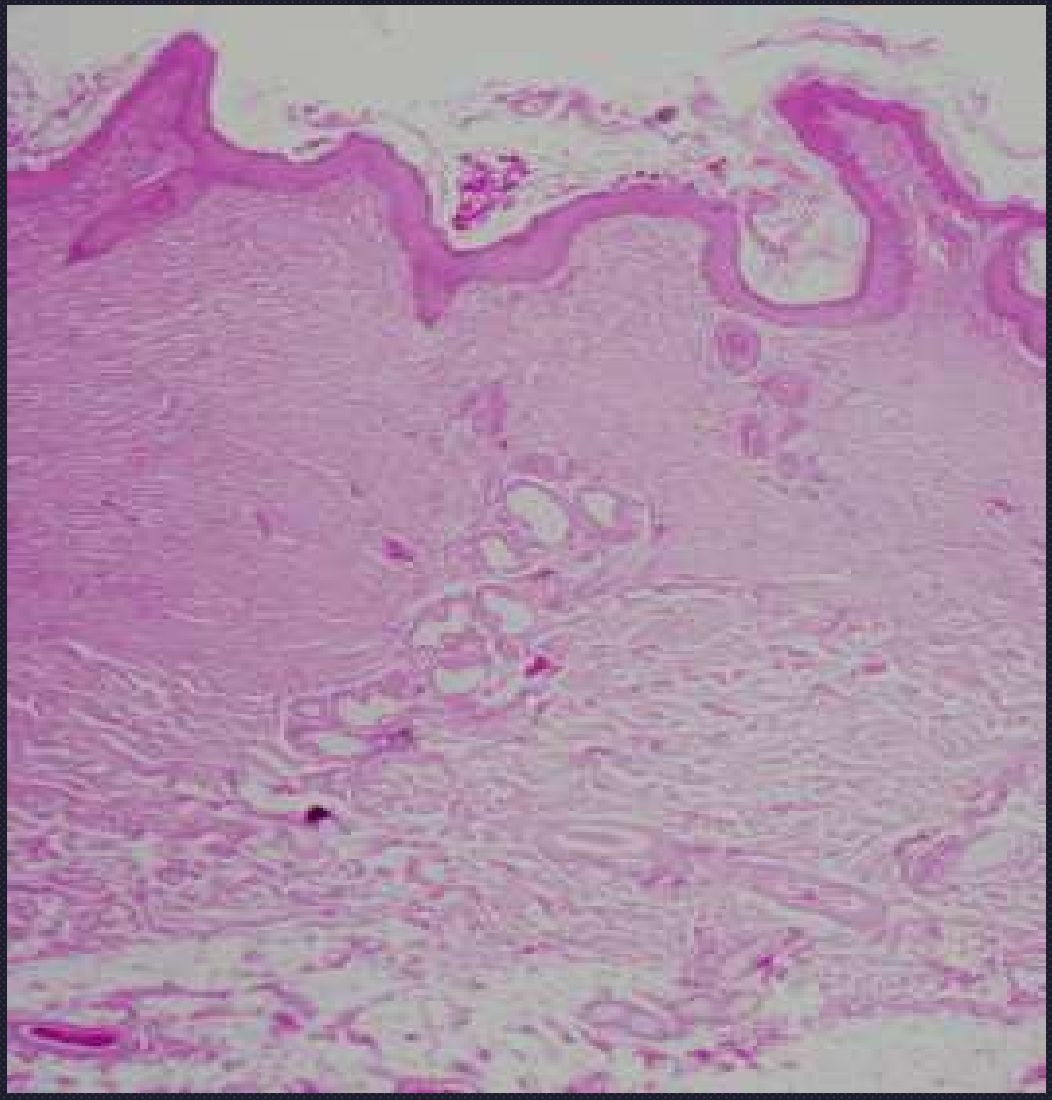
Affected cat



Feline acquired skin fragility syndrome



Fibrosing Dermatitis



Definitions

- **Fibrosis** is the end stage of fibroplasias. There is increased collagen deposition with an altered arrangement. May still find a few remaining fibroblasts.
- **Hyalinization** is the confluence and increased eosinophilia of the collagen**.**
- **Sclerosis** is an increased amount of collagen in an altered arrangement with a homogeneous, eosinophilic, hyalinized appearance