

# Interface Disorders

Elizabeth A. Mauldin, Dip ACVP & ACVD  
Assistant Professor  
University of Pennsylvania  
School of Veterinary Medicine



# Interface pattern

- Superficial perivascular dermatitis with obscuring of the DEJ interface
- Due to
  - (1) vacuolar alteration
  - (2) lichenoid infiltrate
  - Or both
- Immune rxn targeting basal keratinocytes and BMZ



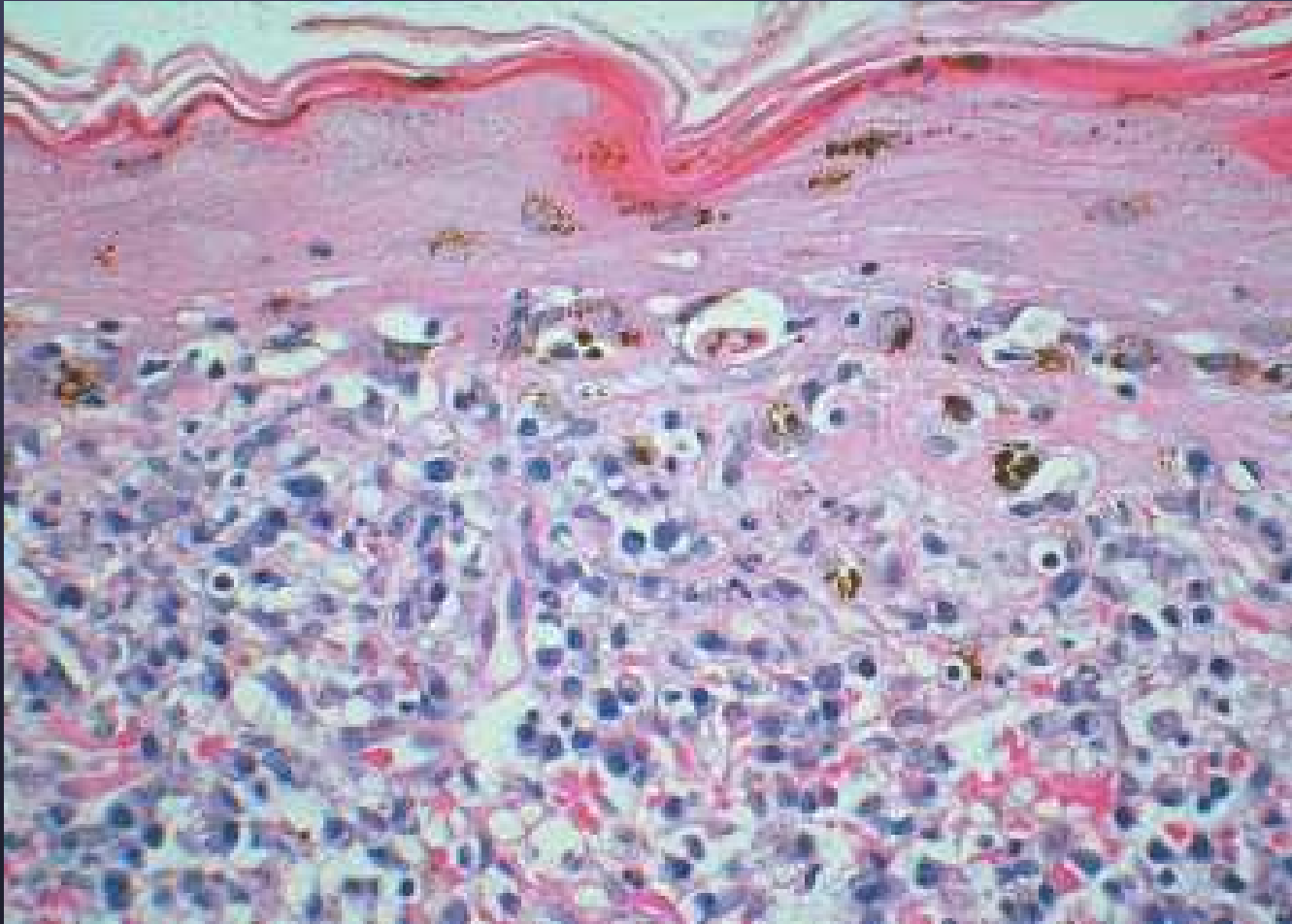
# Interface

- Vacuolar alteration (hydropic degeneration/vacuolar change)
  - Does not always have a lichenoid infiltrate
- Lichenoid Infiltrate
  - Always associated with vacuolar alteration

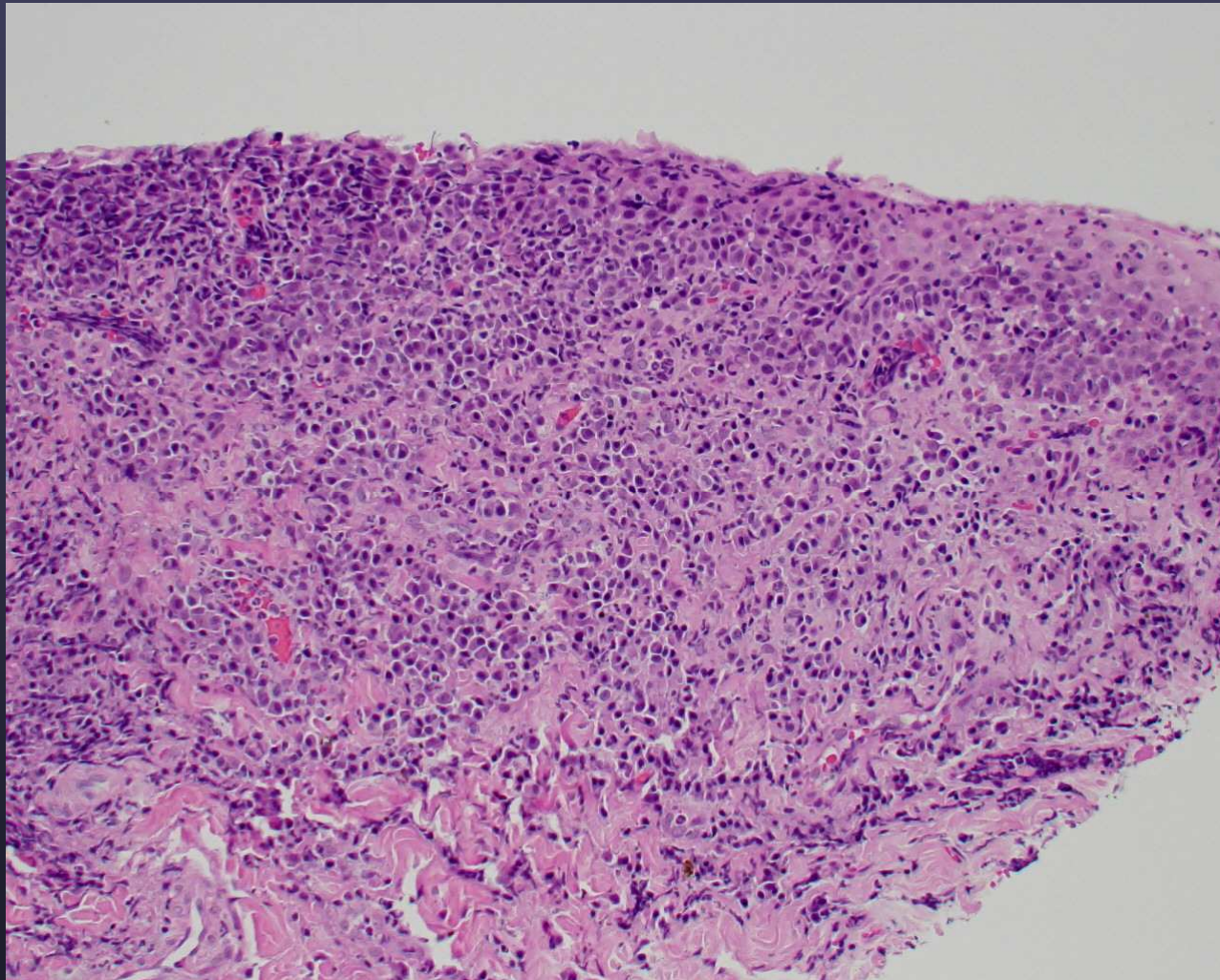
# Problems with “Lichenoid” and “Interface” in Veterinary Dermopath

- Both terms are often used incorrectly
- #1 Can see subtle “interface-type” changes in many inflammatory reactions
- #2 Lichenoid has two interpretations
  - Should imply interface change
  - Also used to describe a band of inflammatory cells without interface change
- “Lichenoid interface”- now being used when there is lichenoid inflammation with interface change

# Lichenoid



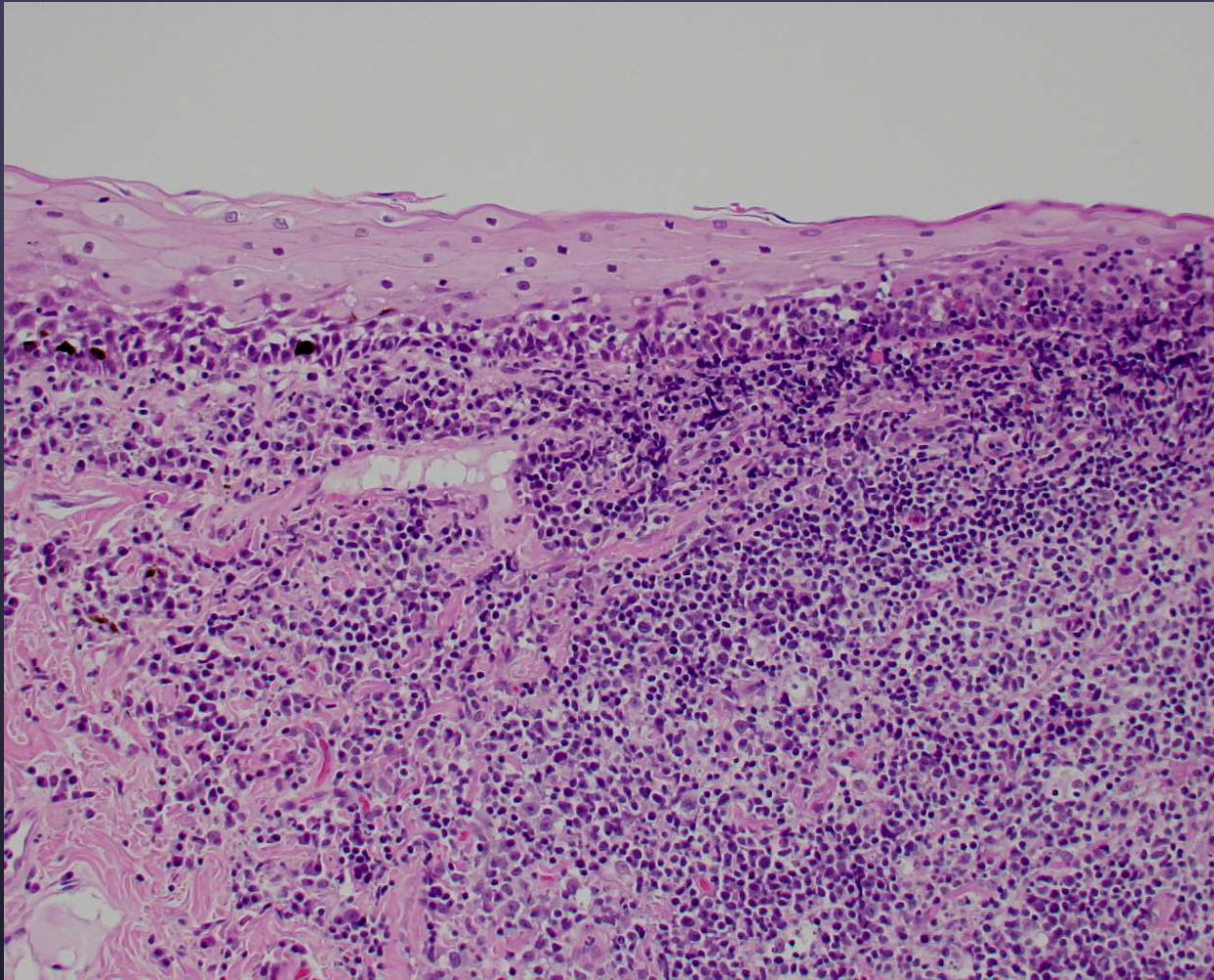
# Is this Lichenoid?



Plasmacytic gingivitis in a cat

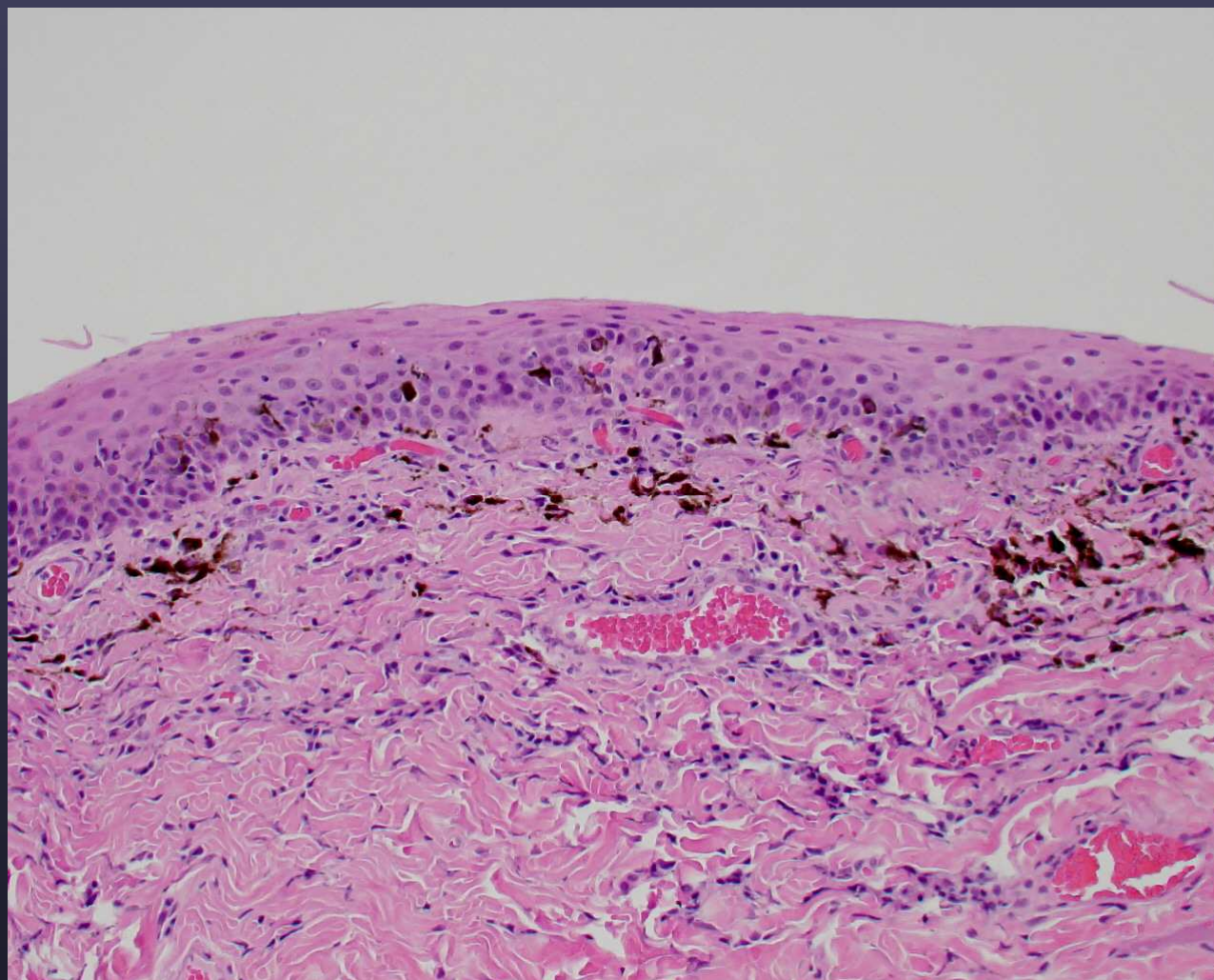


# Is this lichenoid?



Chronic gingivitis in a dog

# Interface or Not?



Same case as last slide, pigmentary incontinence

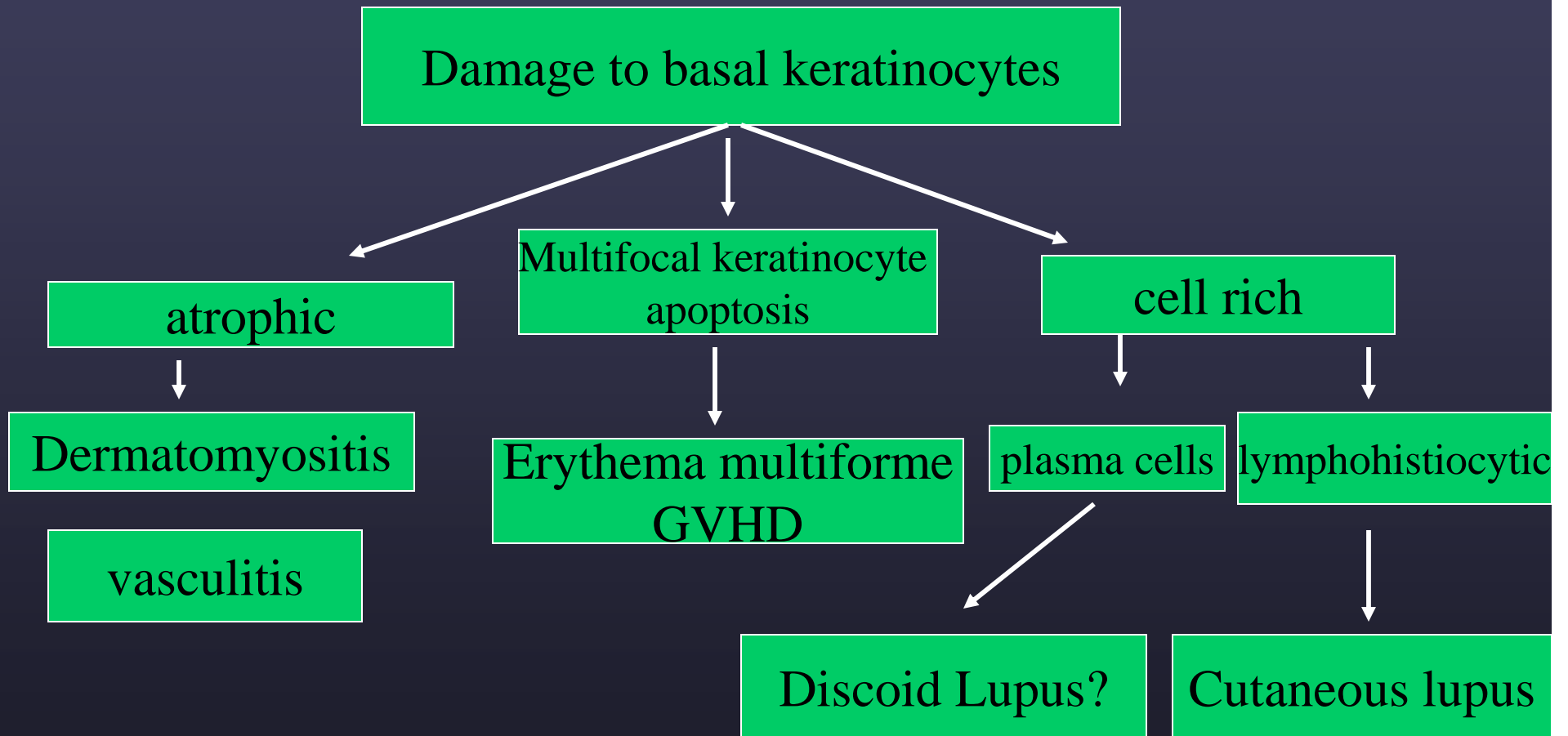
- Lichenoid?: inflammation of mucous membranes  
nonspecific band of inflammatory cells
- Vacuolar alteration: seen with any inflammatory  
infiltrate that extends to the DEJ
- Apoptotic or necrotic keratinocytes can be seen  
incidentally in many inflammatory rxns
- Pigmentary incontinence is not a specific change  
to interface rxns
- Use terms carefully!

# Interface disorders

- Erythema multiforme/drug eruption
- Thymoma associated dermatosis
- Lupoid disorders
  - Cutaneous vesicular lupus
  - Exfoliative lupus
  - Discoid lupus
- Dermatomyositis
- Rabies vaccine associated ischemic dermatopathy
- Graft vs. Host disease
- Symmetric lupoid onychodystrophy (onychitis)



# Interface dermatitis



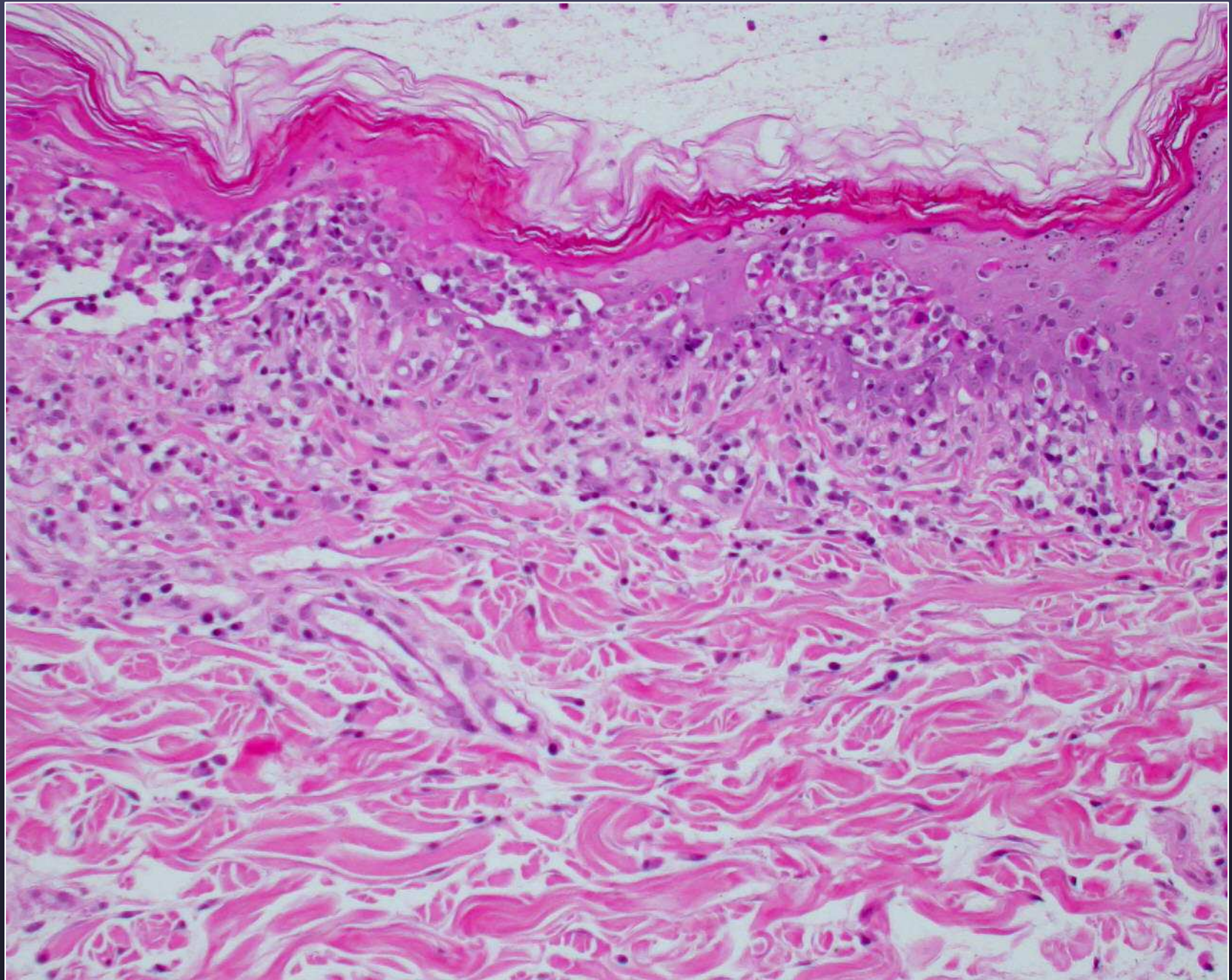


**Graft vs  
Host Disease  
(GVHD)**



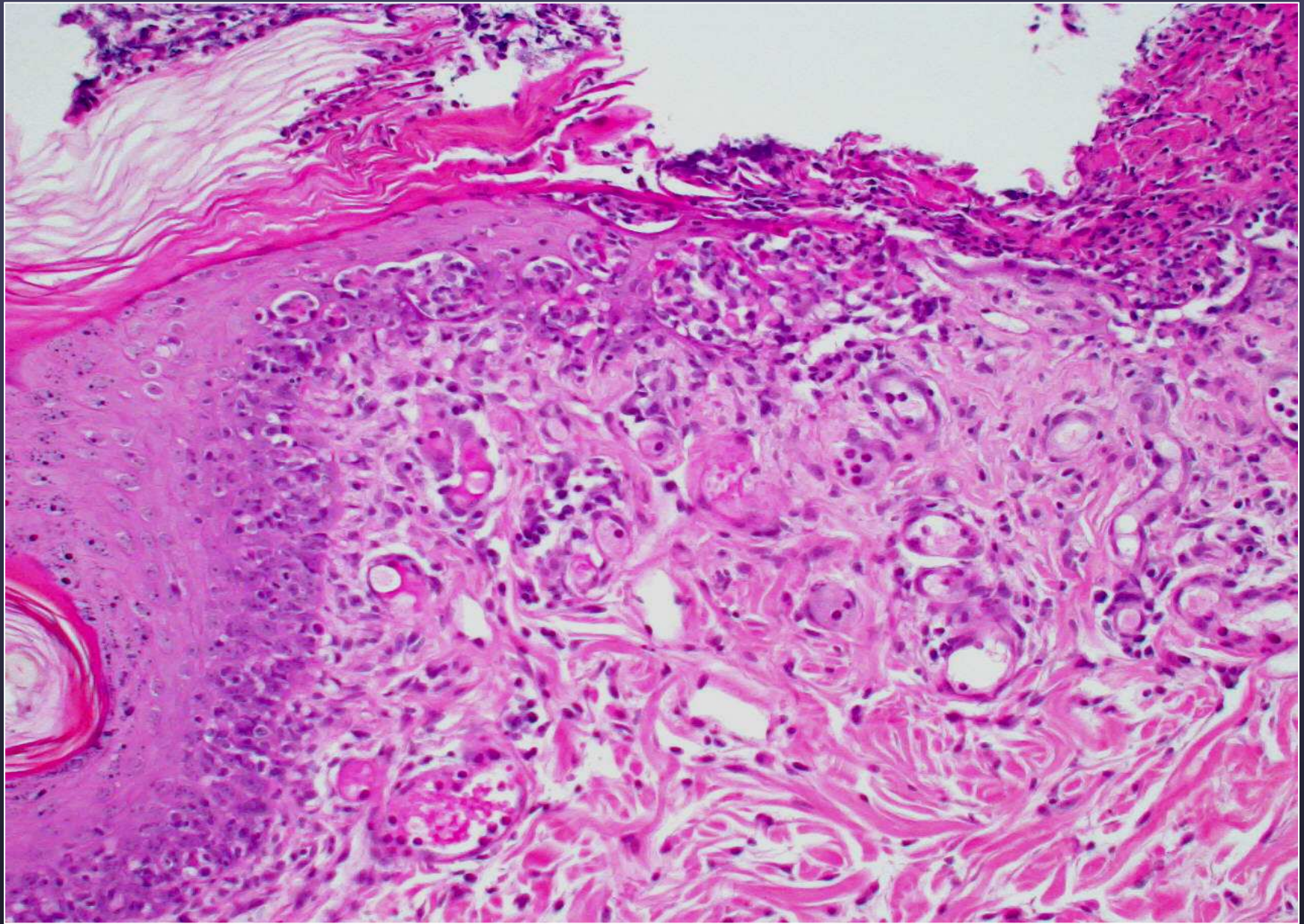


GVHD



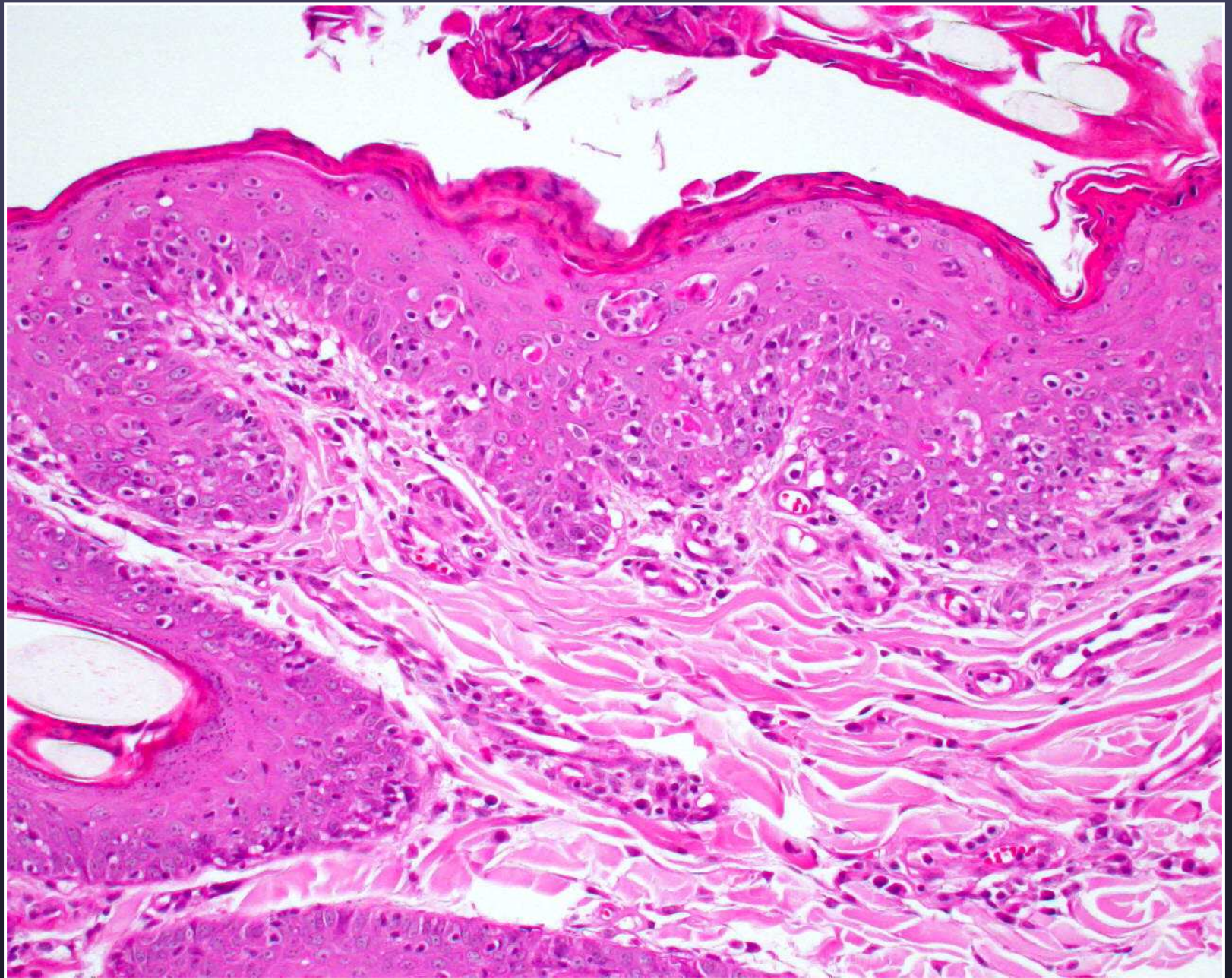
GVHD





GVHD





Erythema multiforme

# Erythema Multiforme

- Multifactorial \*cutaneous rxn pattern\*
- EM Major/SJS
  - Drugs, infectious dz, neoplasia
  - Young dogs- more likely drug-associated
  - Old dogs- more likely idiopathic
- TEN/SJS distinction- clinical features
  - Pathologists view TEN

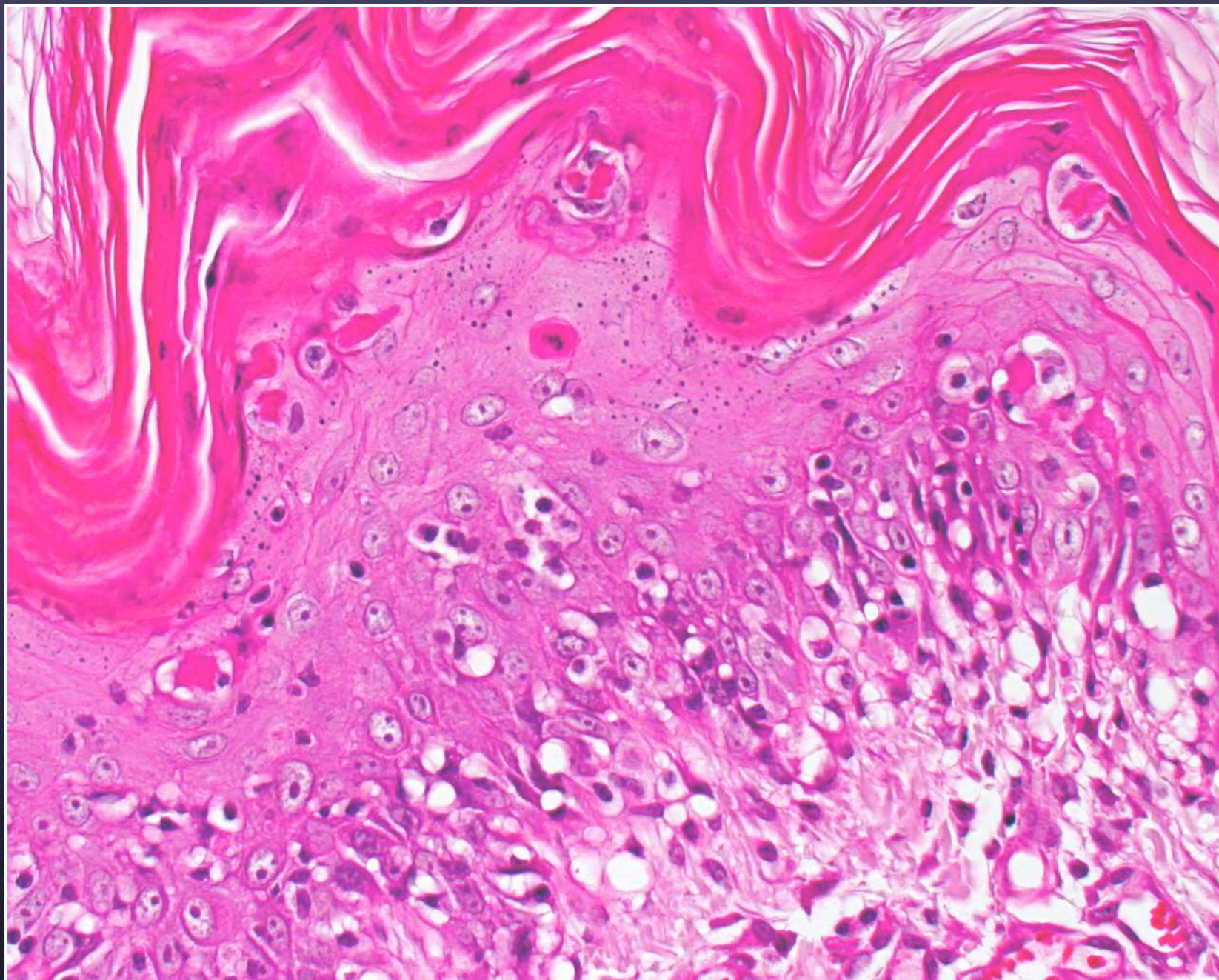
# Erythema Multiforme

- Ulcerated serpiginous to targetoid erythematous ulcers and plaques
  - Hyperkeratotic and ulcerated
- +/- mucous membrane involvement



# Interface Disorders – cell poor

- Erythema multiforme
- Multiforme = MULTIPLE FORMS!
  - Transepidermal individual keratinocyte necrosis/apoptosis
  - Satellitosis
  - Hyperkeratosis (orthokeratotic to parakeratotic) with multifocal ulcers



Erythema multiforme

# EM/SJS/TEN

- Many diseases with individually necrotic/apoptotic cells  $\neq$  equivalent with EM
- Limited in our identification and documentation of patterns of eruptions
- Histopathology provide DDX for drug eruption in veterinary medicine





Idiopathic Erythema Mulforme



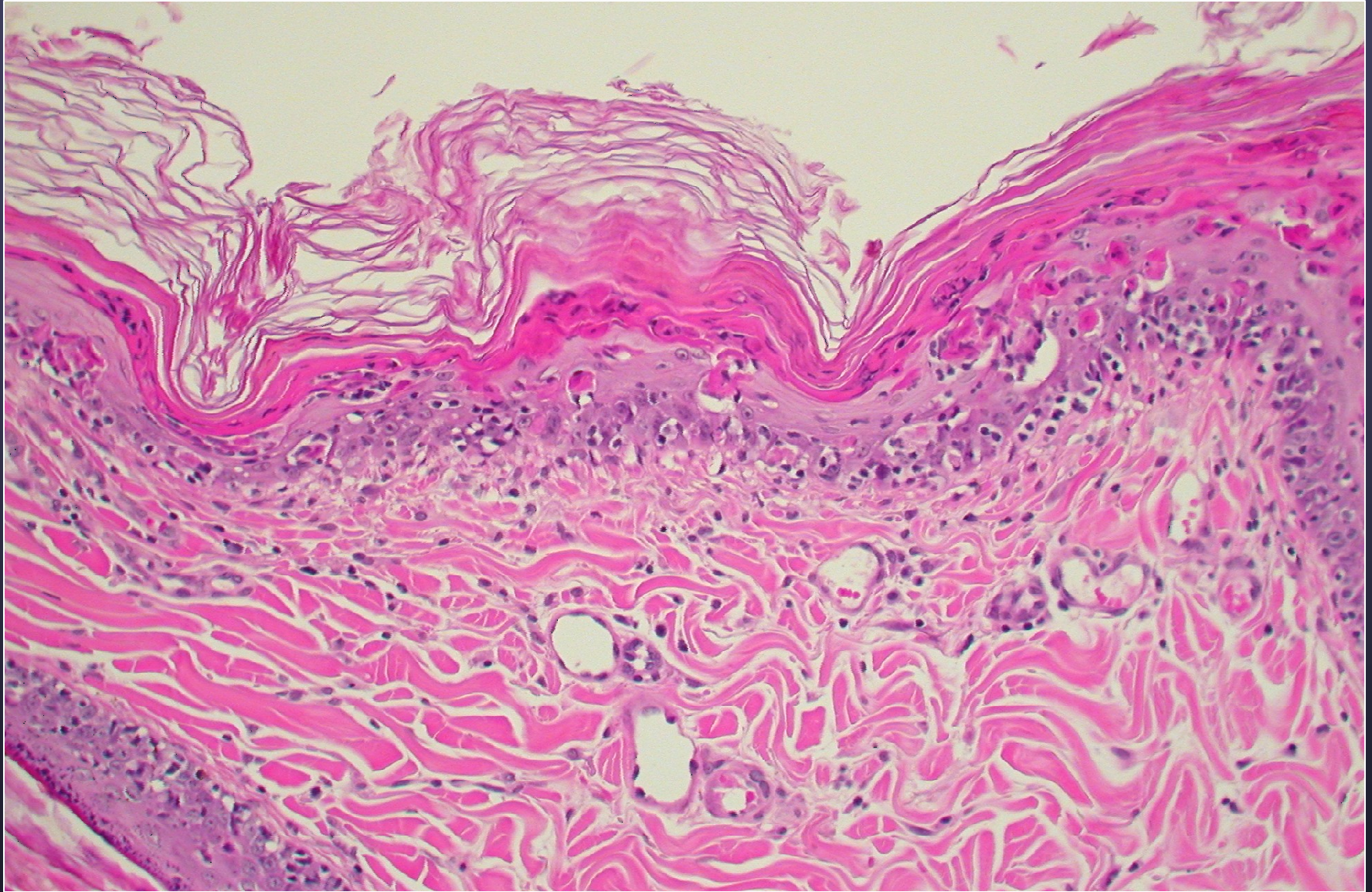
Erythema multiforme Major/  
Stevens Johnson Syndrome





EMM/SJS

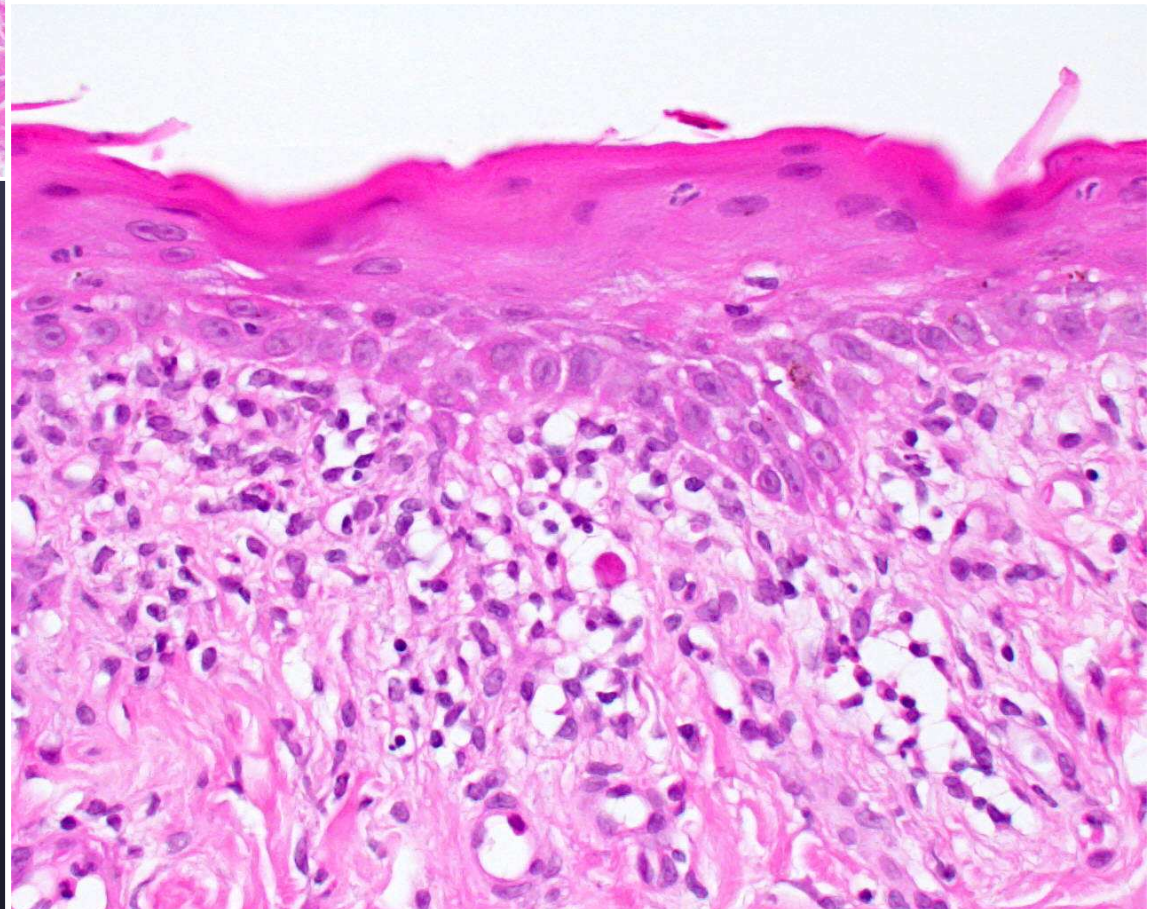
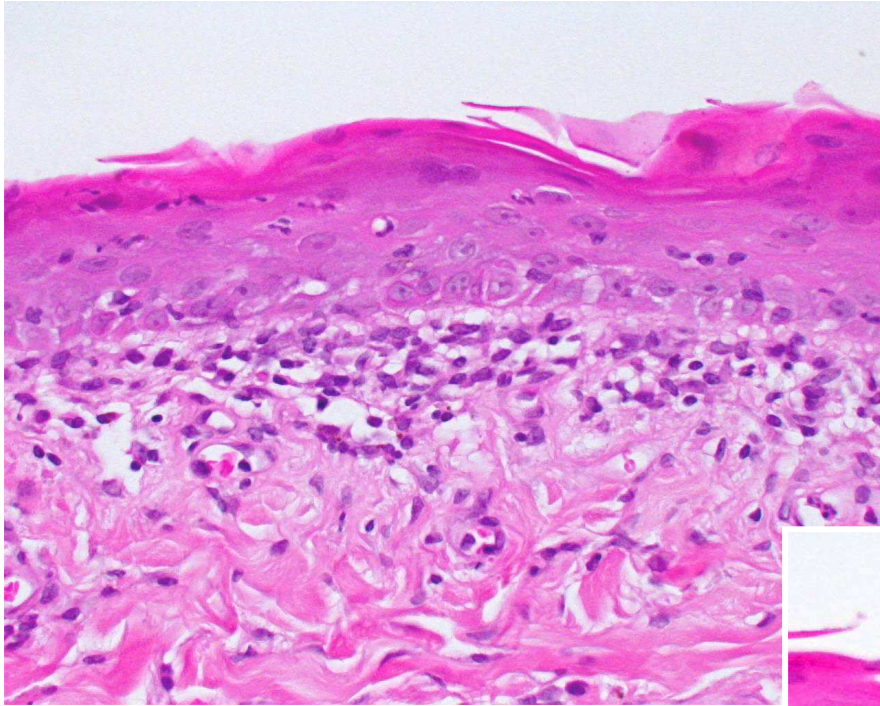




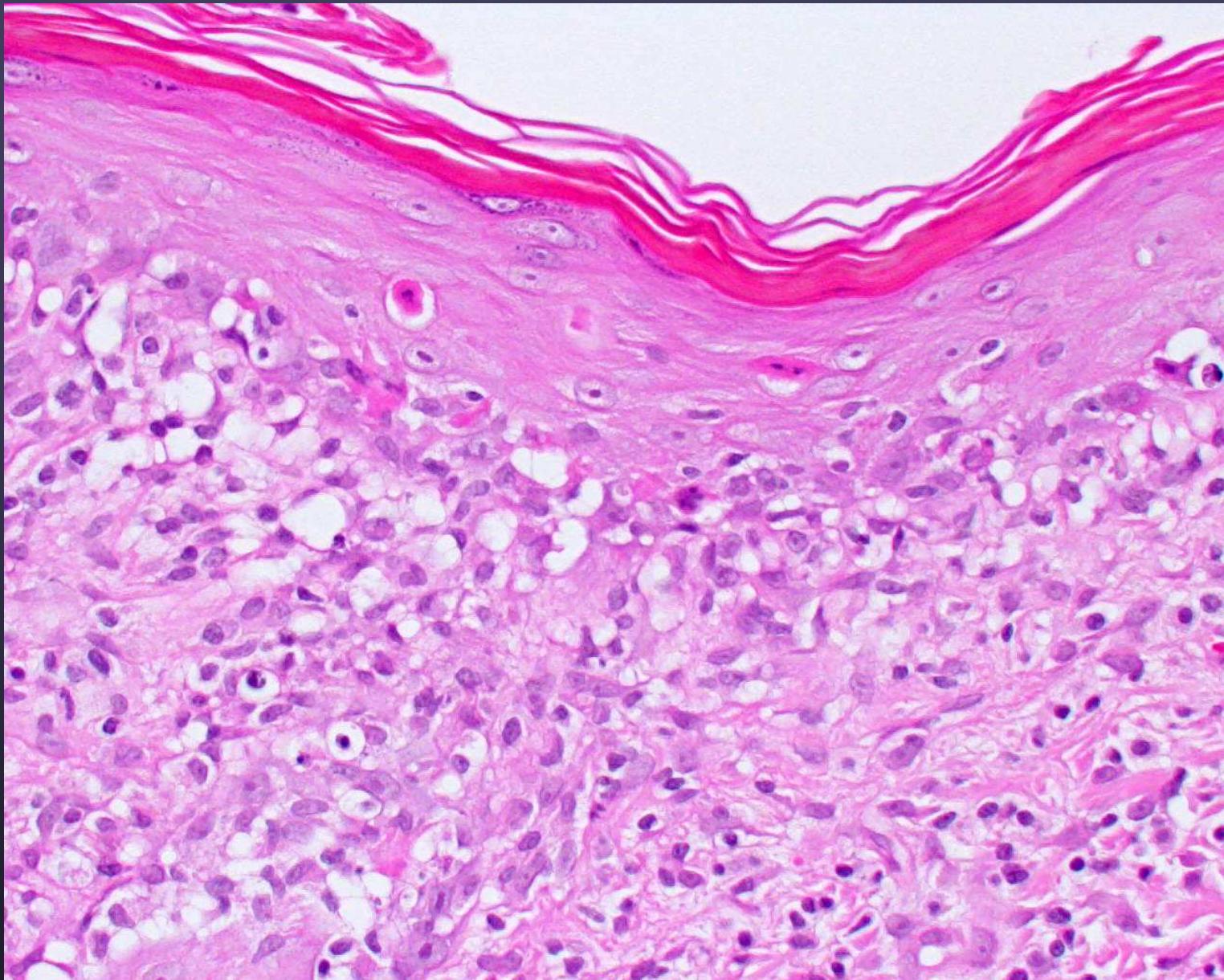
Erythema multiforme



# Early EM







Erythema multiforme



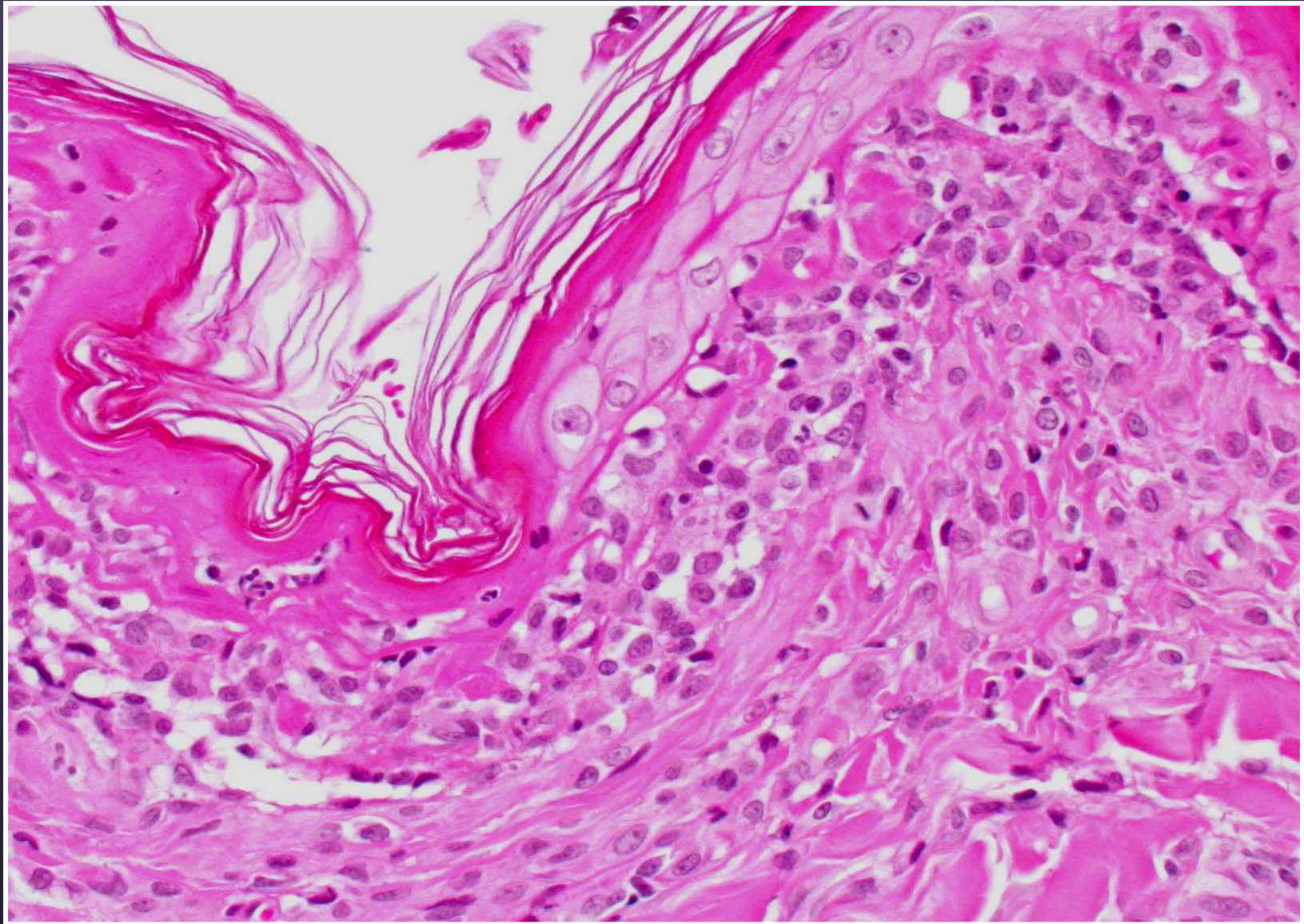


*Necrotic epidermis  
peels with gentle pressure*

**9 yr, old, MixB**

EMM/SJS

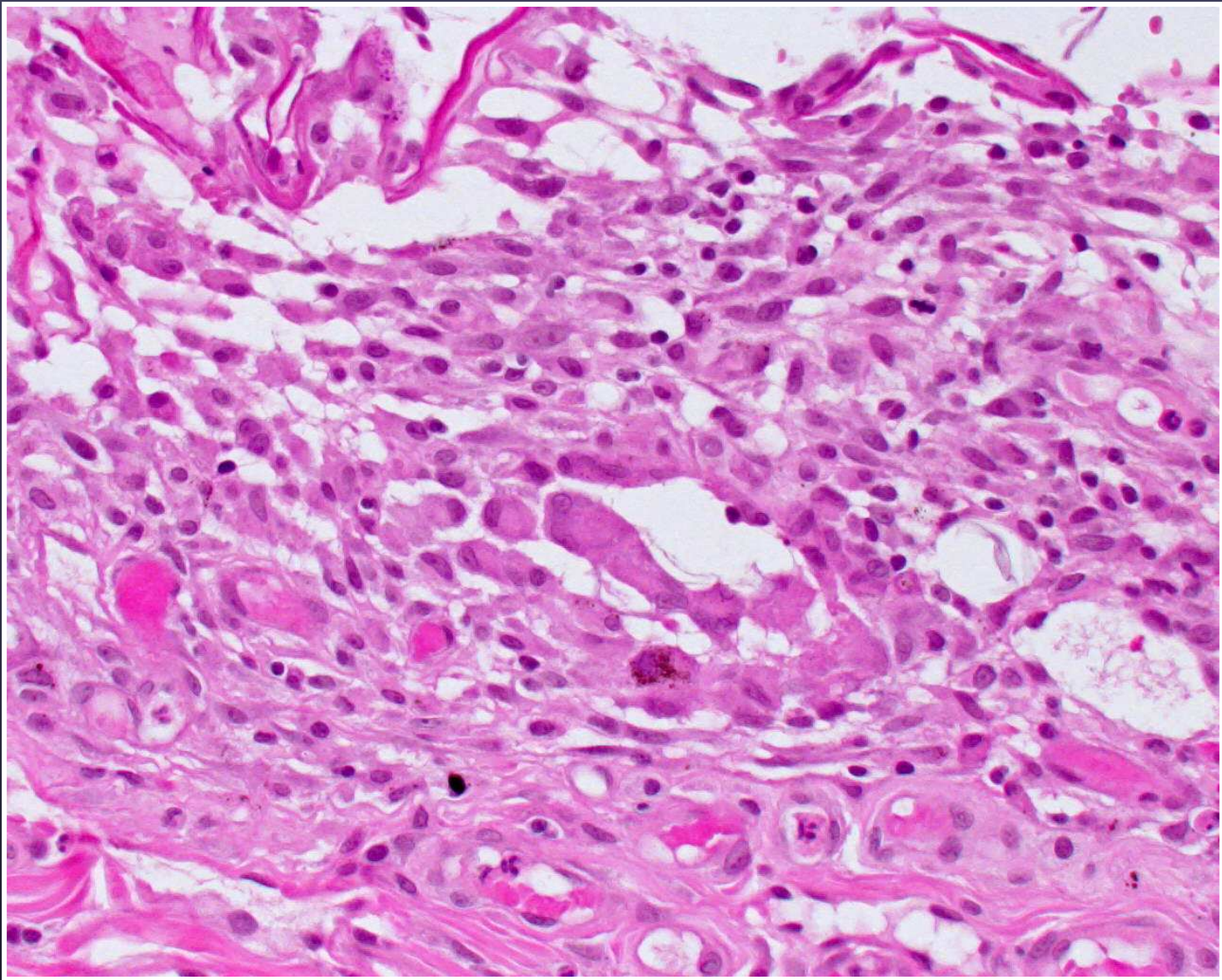




**Sept 2002**

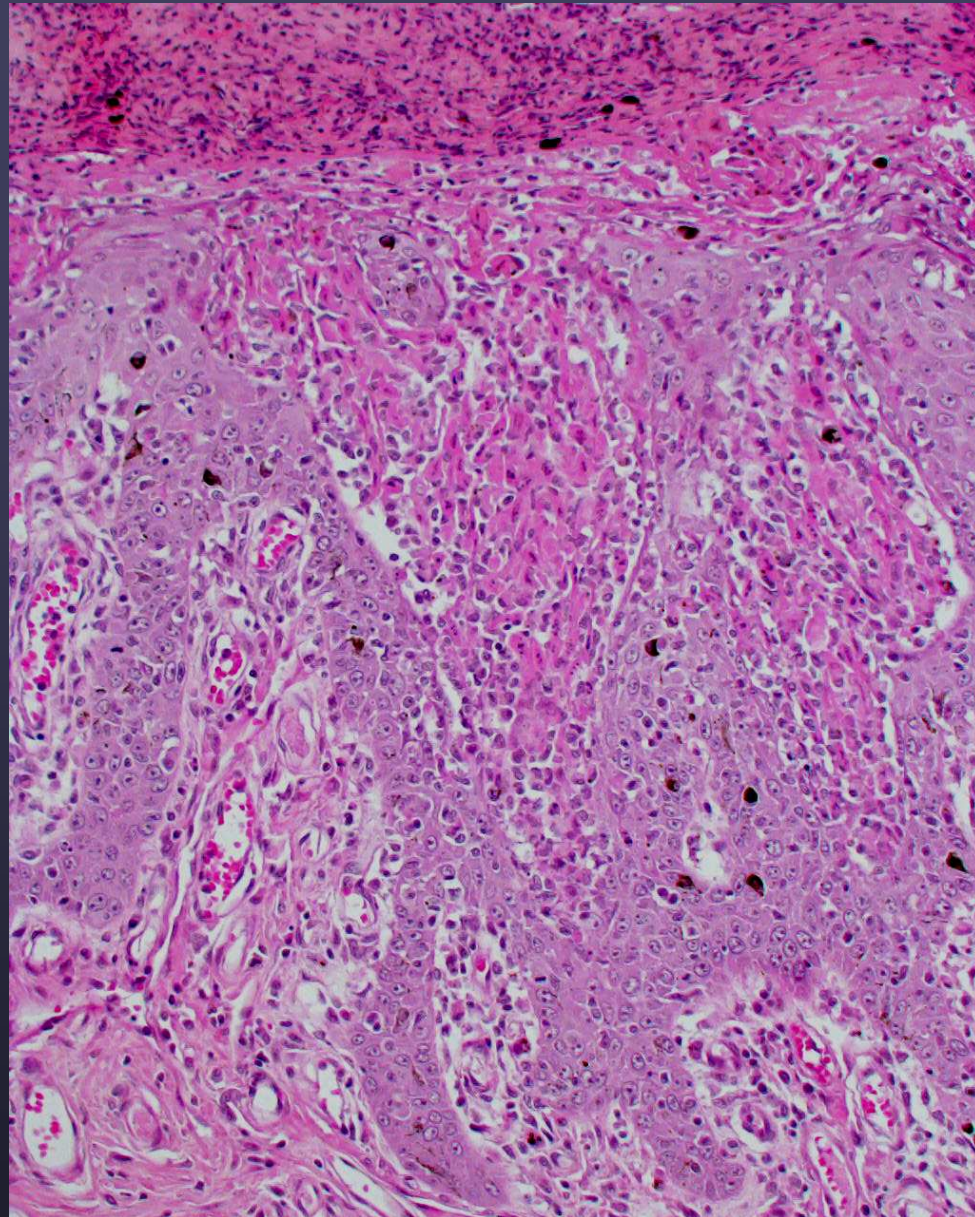
*This case is erythema multiforme with prominent lymphoid cell infiltrate  
Note: early cutaneous lymphoma can have a interface-like pattern*





*In your EM cases, look for giant cells in or just below necrotic epidermis-foreign body rxn to free keratin*

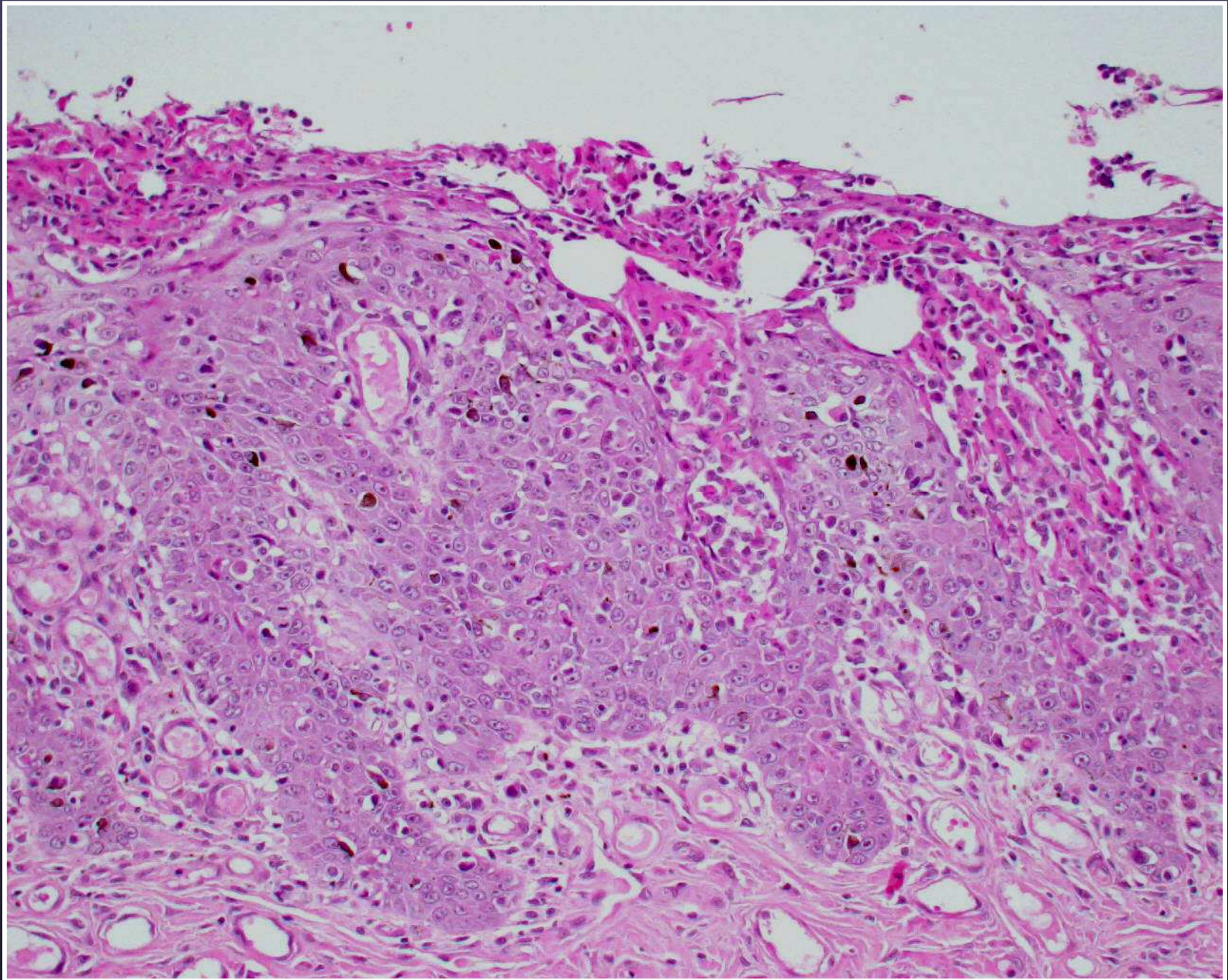




**Dec 2002**

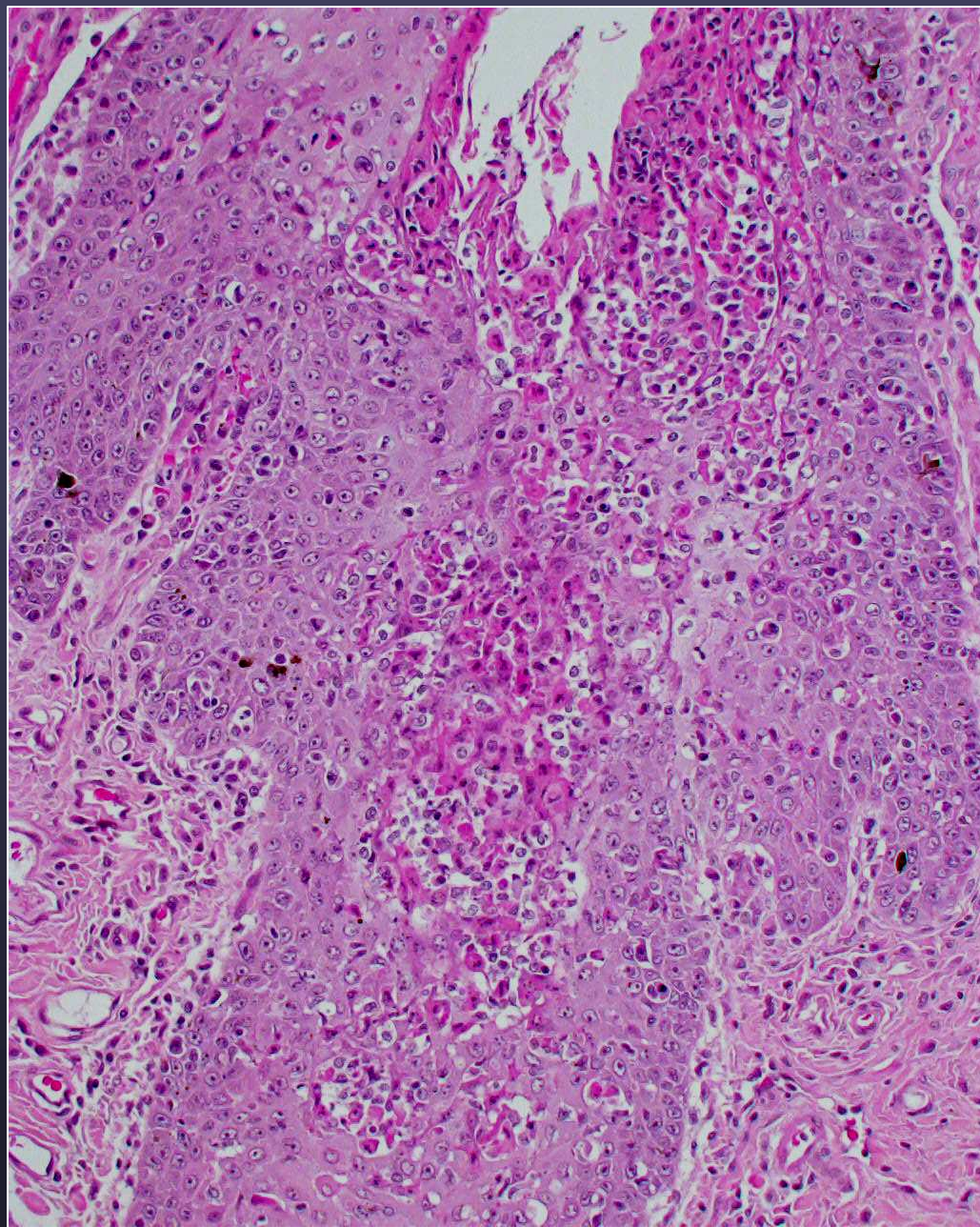
*Over time, this case developed more florid individual keratinocyte necrosis*



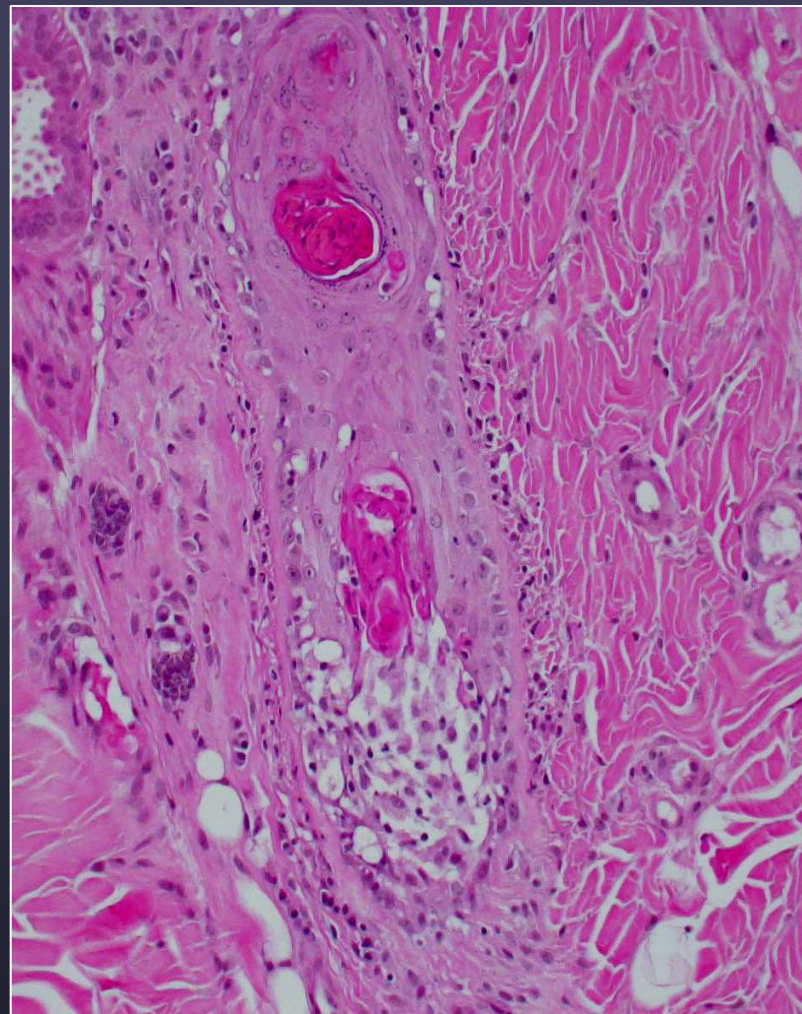


Erythema multiforme





**Dec 2002**



**Sept 2002**



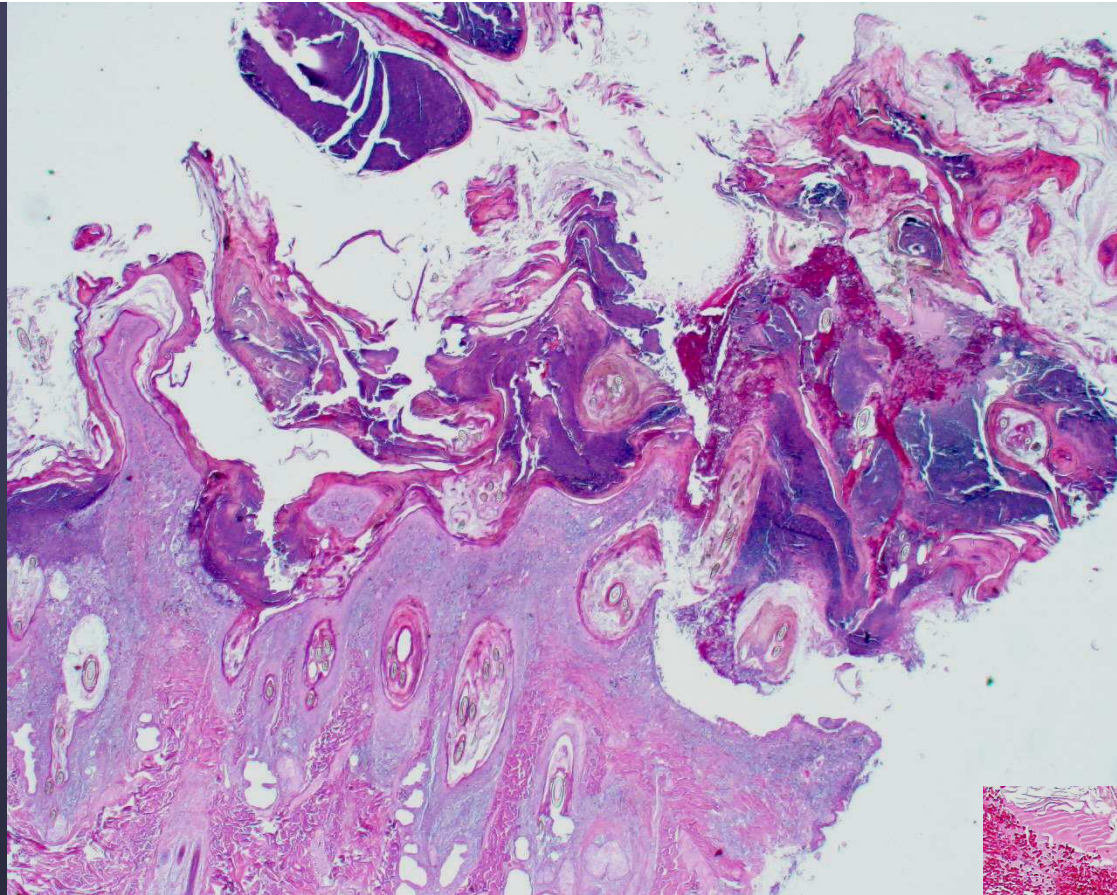


VHUP DERMATOLOGY

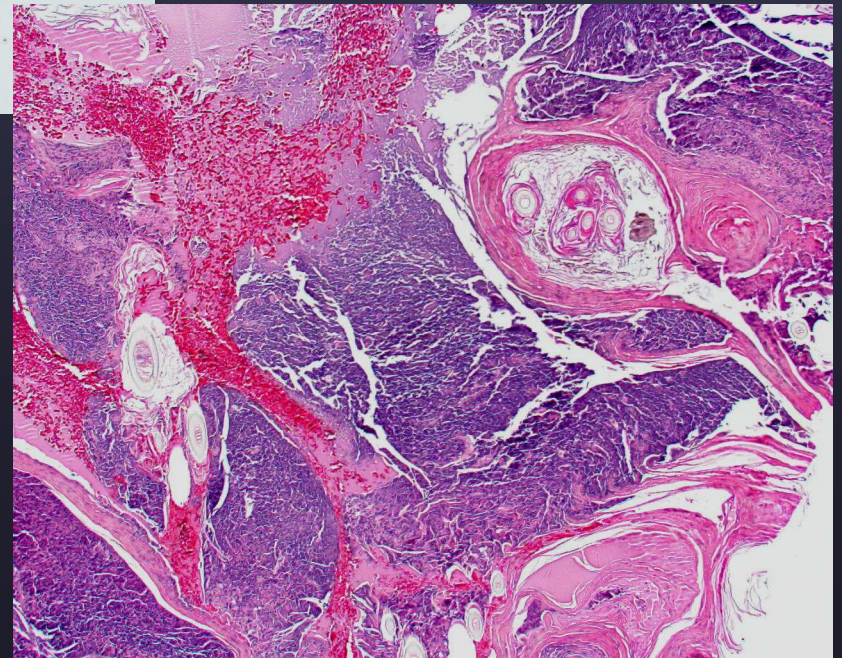
**6.5 yr old, M, Labr**

**April 2001**

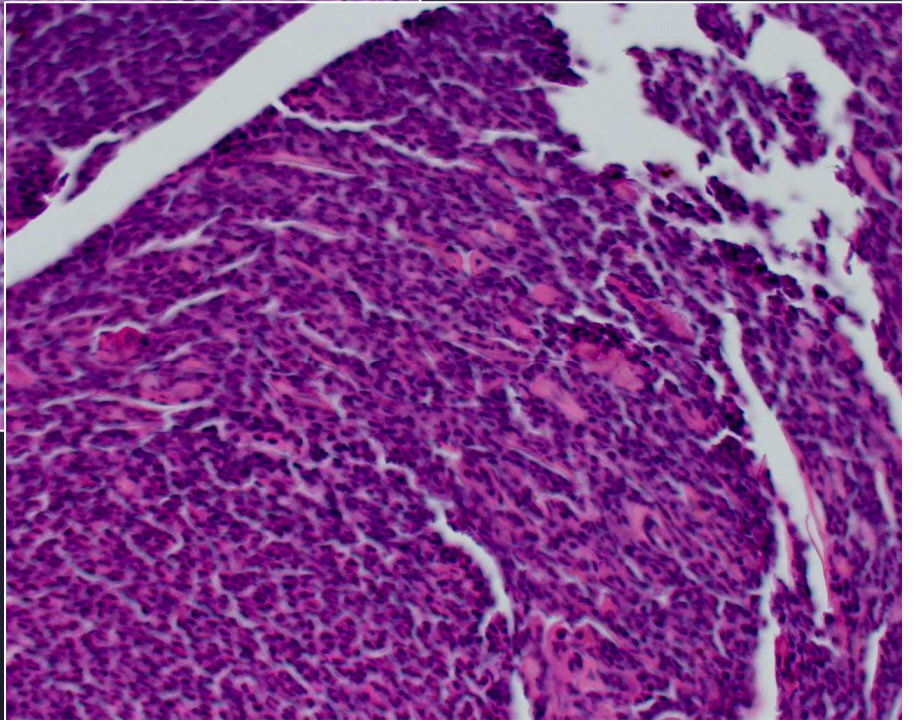
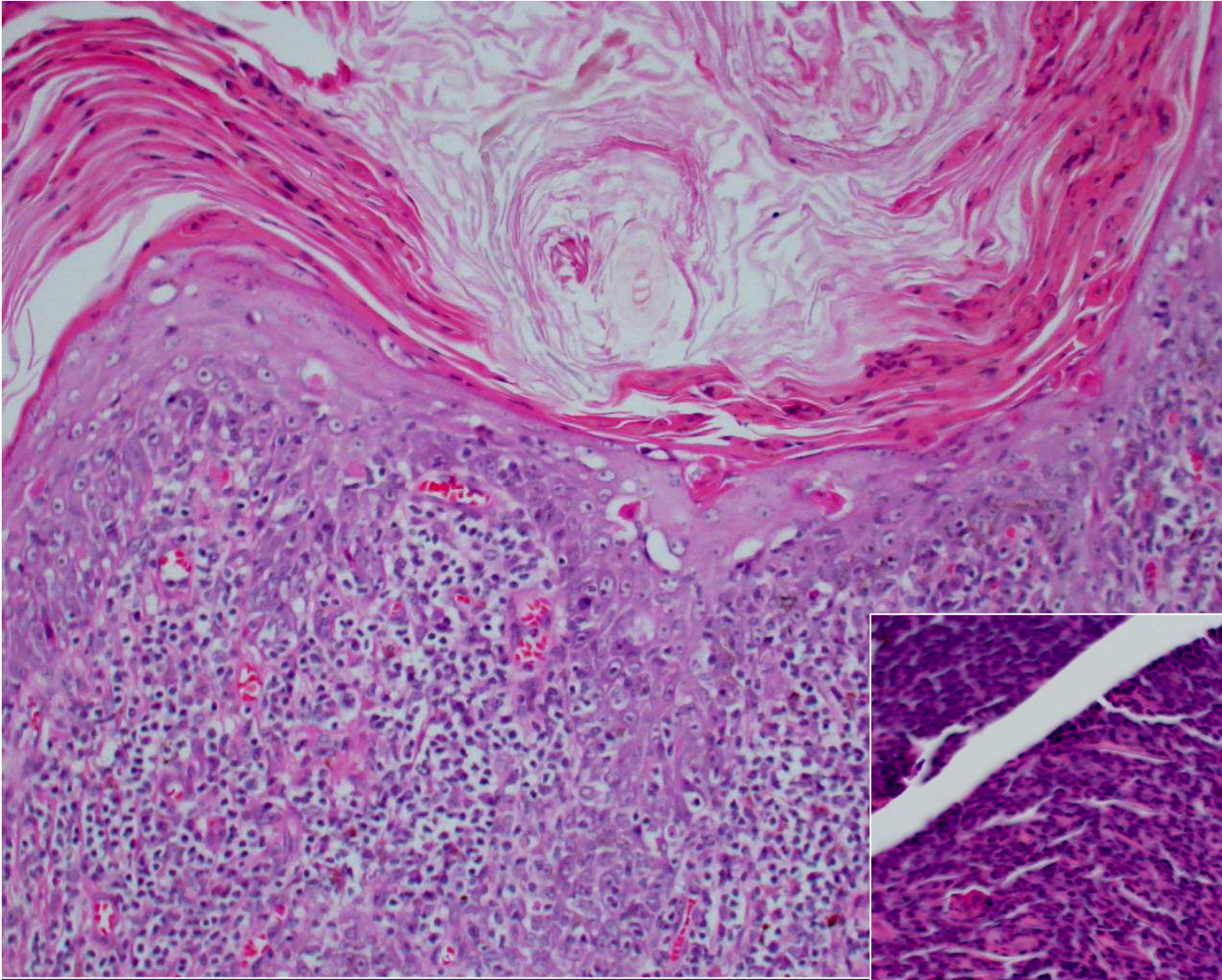




Acantholytic  
EM?











**Oct 2003**

*Severe hyperkeratosis and crusting and alopecia in dog with EMM*





**Oct 2003**

*Severe hyperkeratosis and crusting and alopecia in dog with EMM*



Concurrent pseudomonas otitis





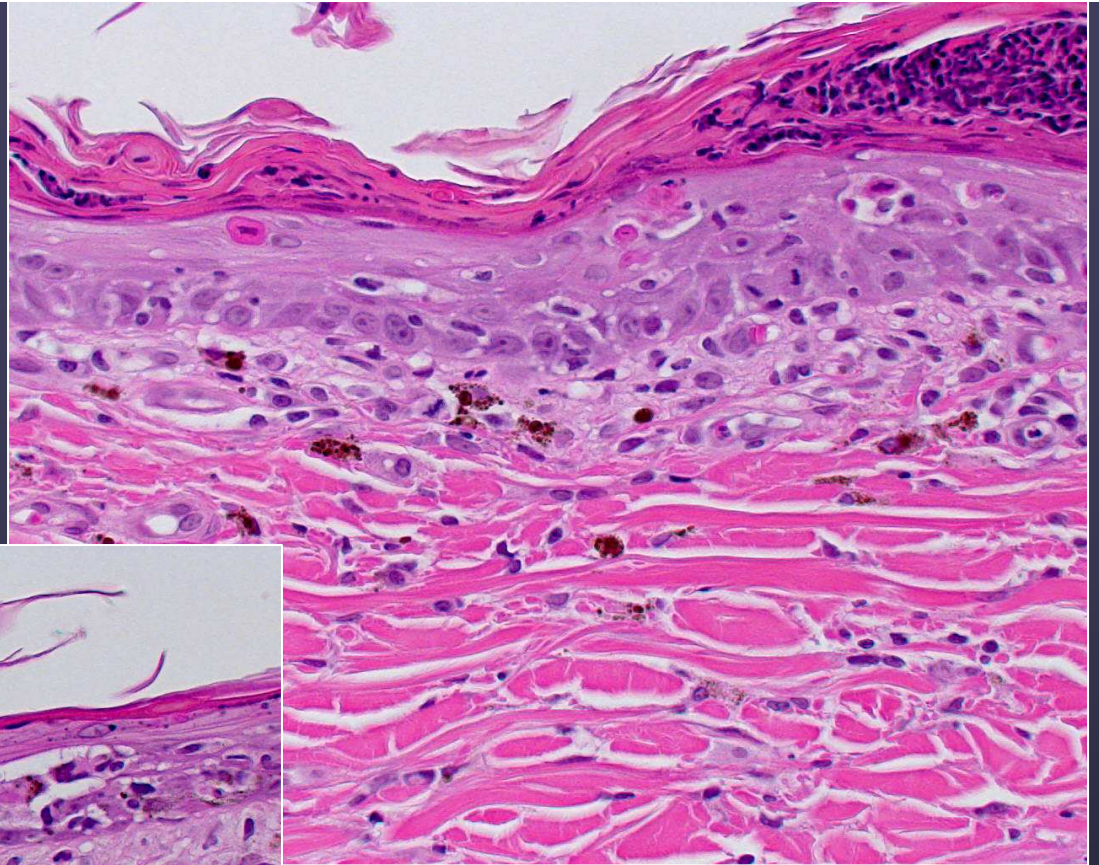
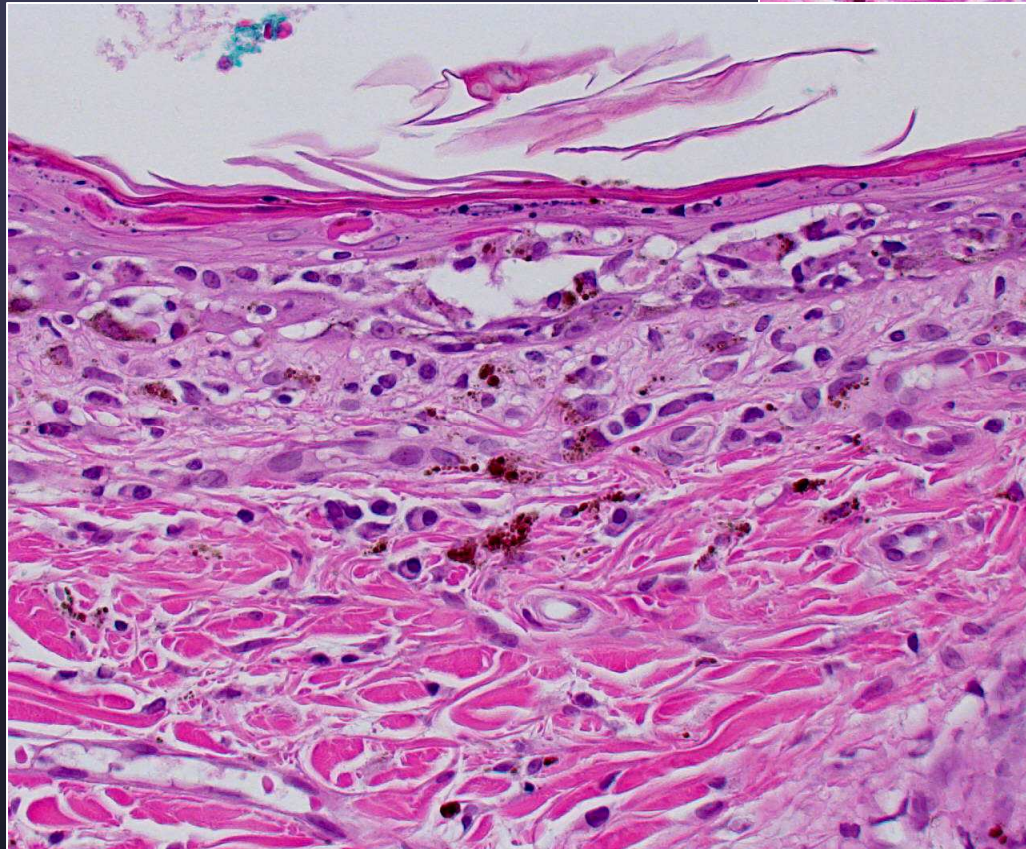
EMM/SJS associated with repositol injectable heartworm preventative





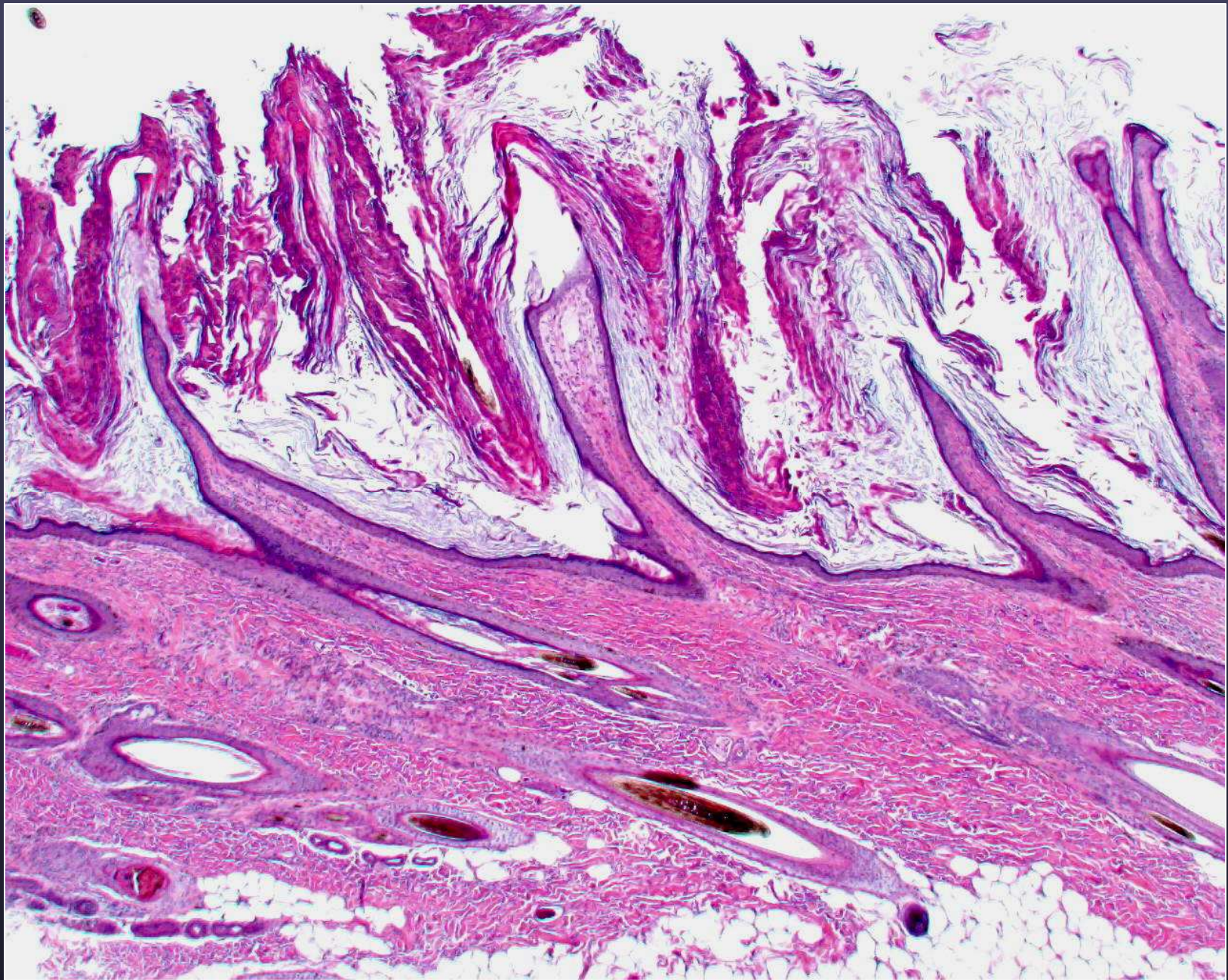
Drug-induced EMM/SJS





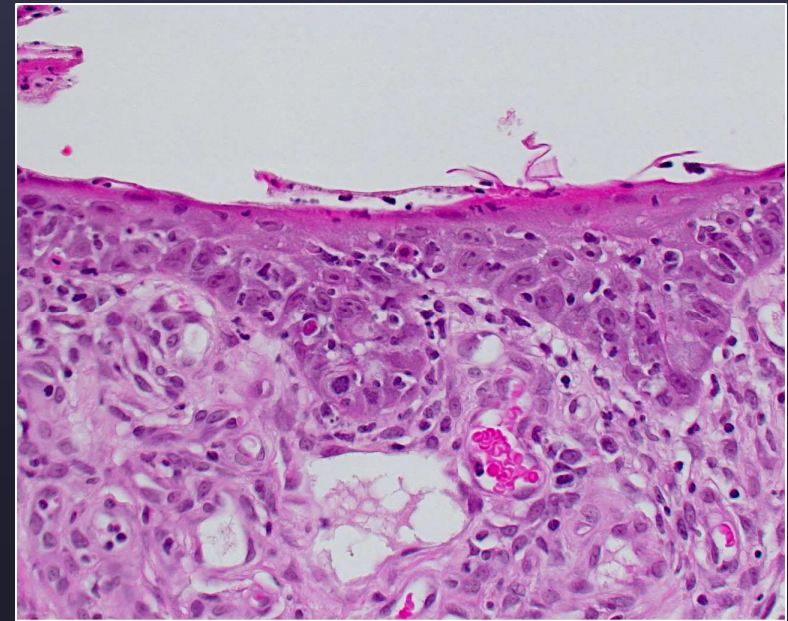
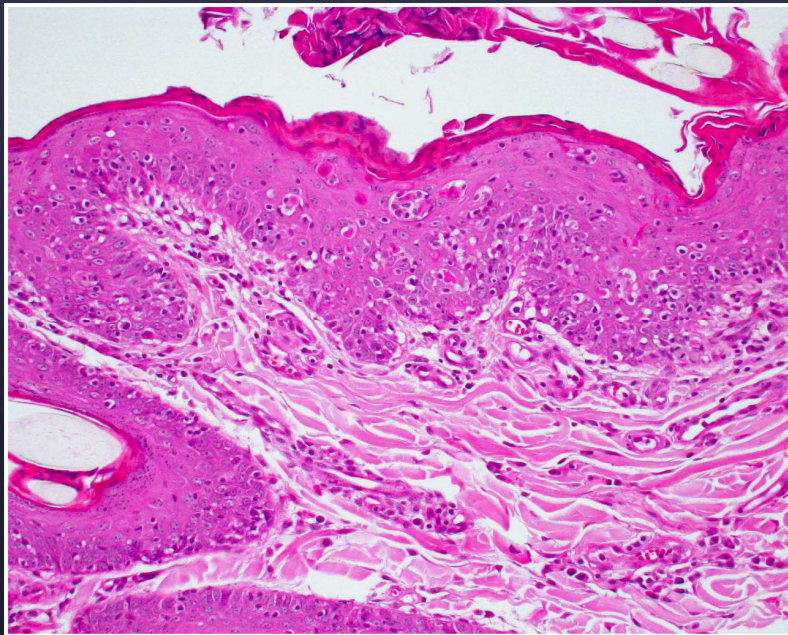
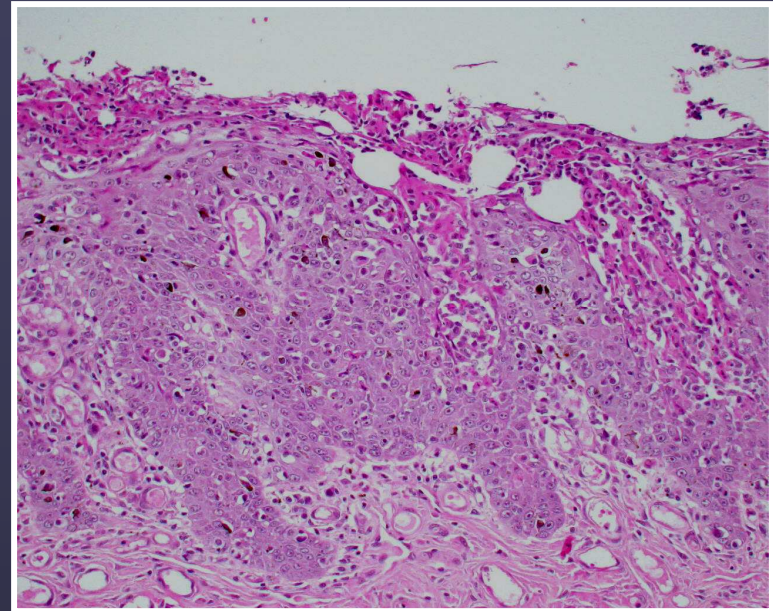
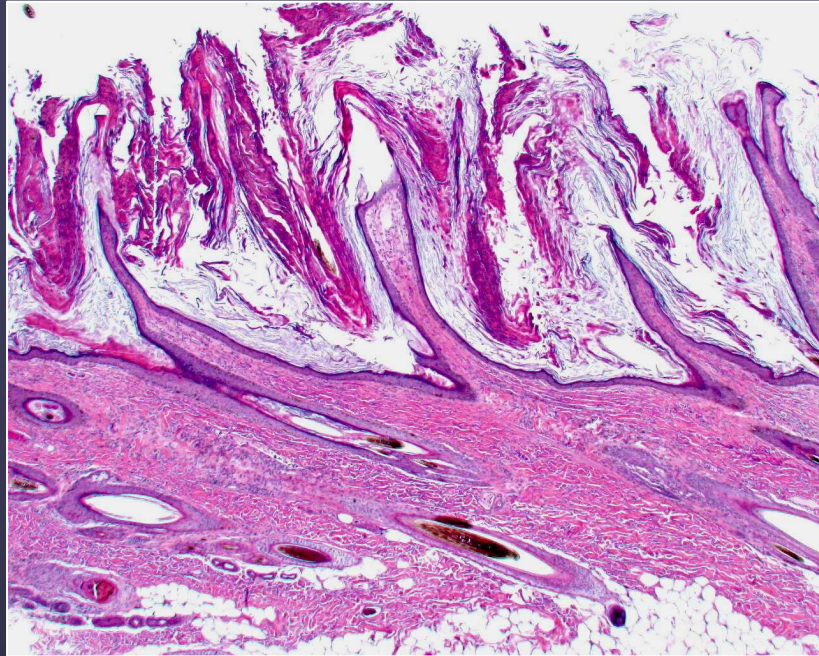
*This case is of a German shorthaired pointer  
cutaneous exfoliative lupus  
Be aware of the marked histopathologic  
variants of EMM/SJS and possible overlap  
with other disorders*





Superficial EM





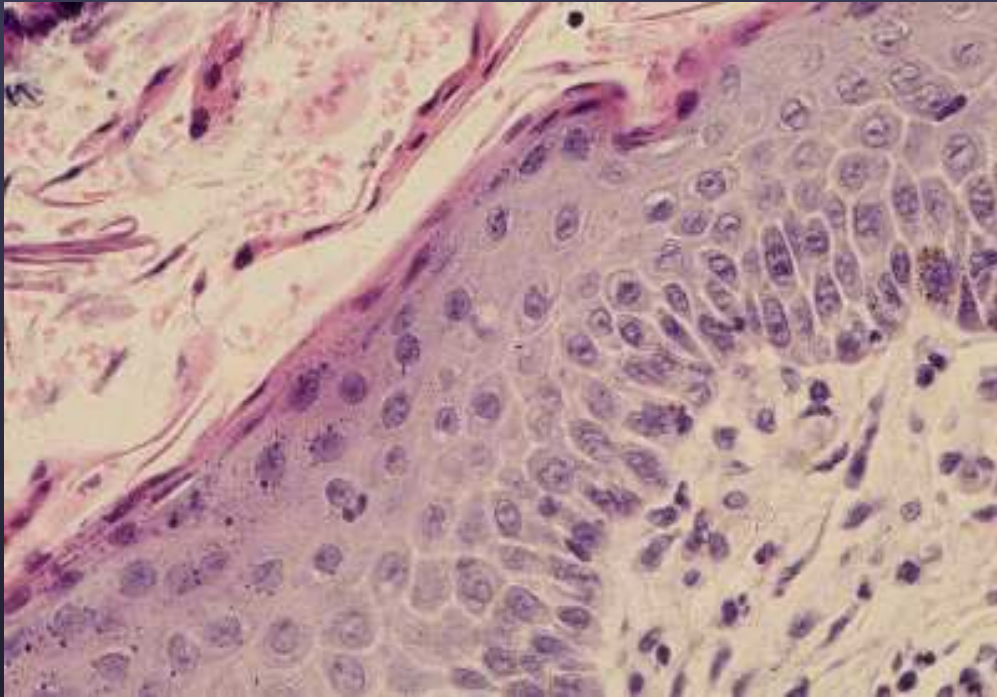
Histopath of EM variants



# Possible Variants

- Hyperkeratotic
- Acantholytic
- Papillated
- Follicular
- Ulcerative/atrophic
- Duration/Age of the lesion/Site Selection
- Multiple yet un-named disorders

# Individual Necrosis of Keratinocytes



← Superficial pattern

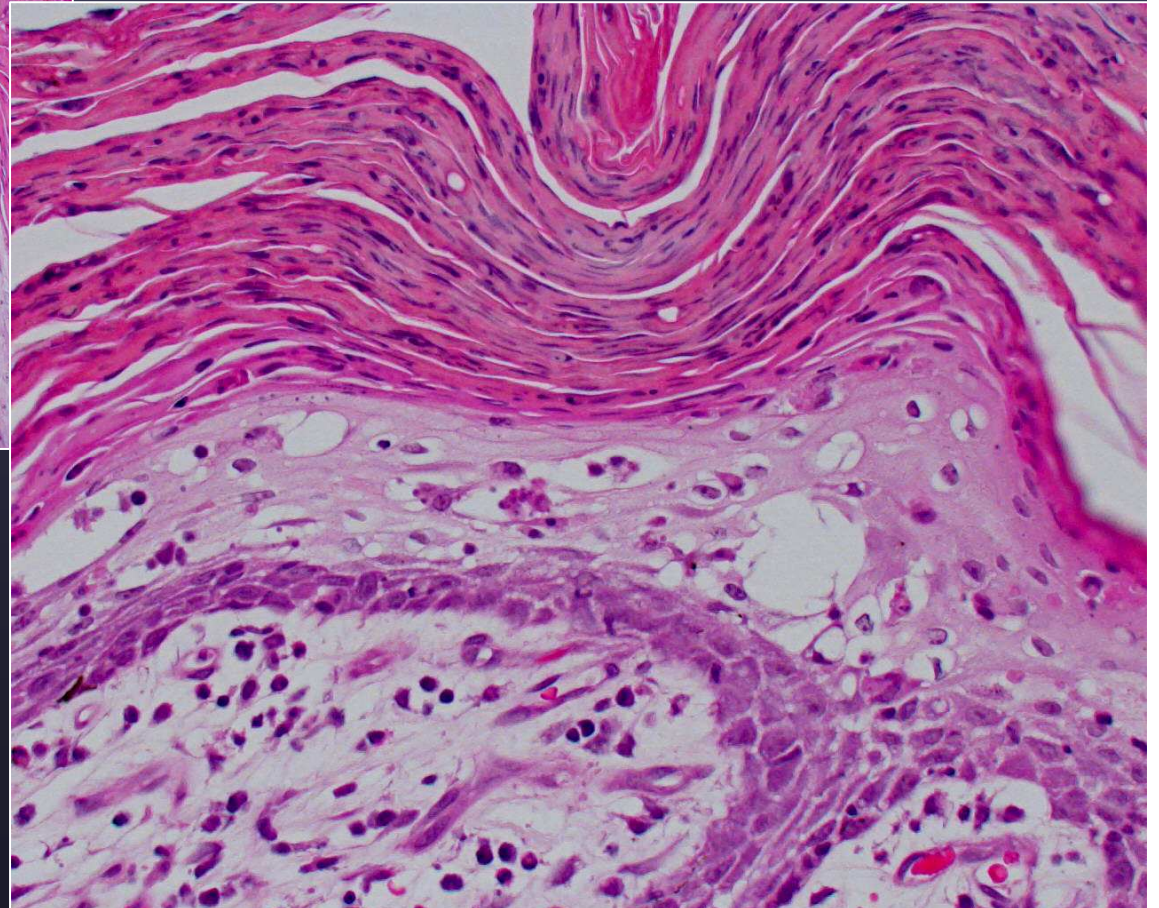
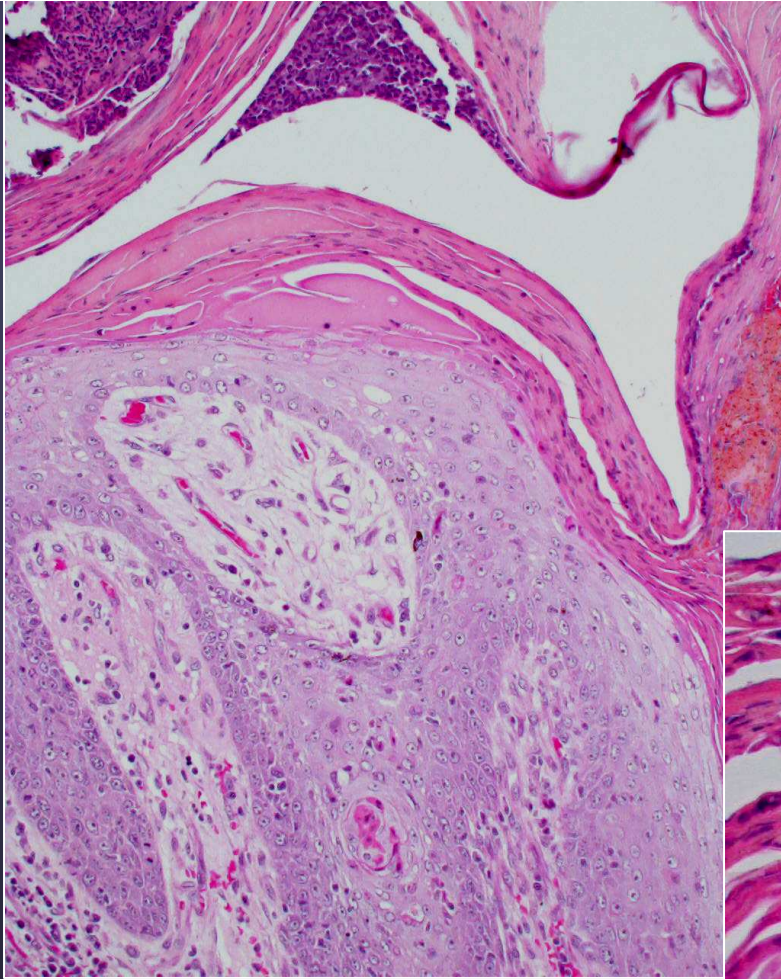
⎵ Erythema multiforme pattern

← Lupoid pattern

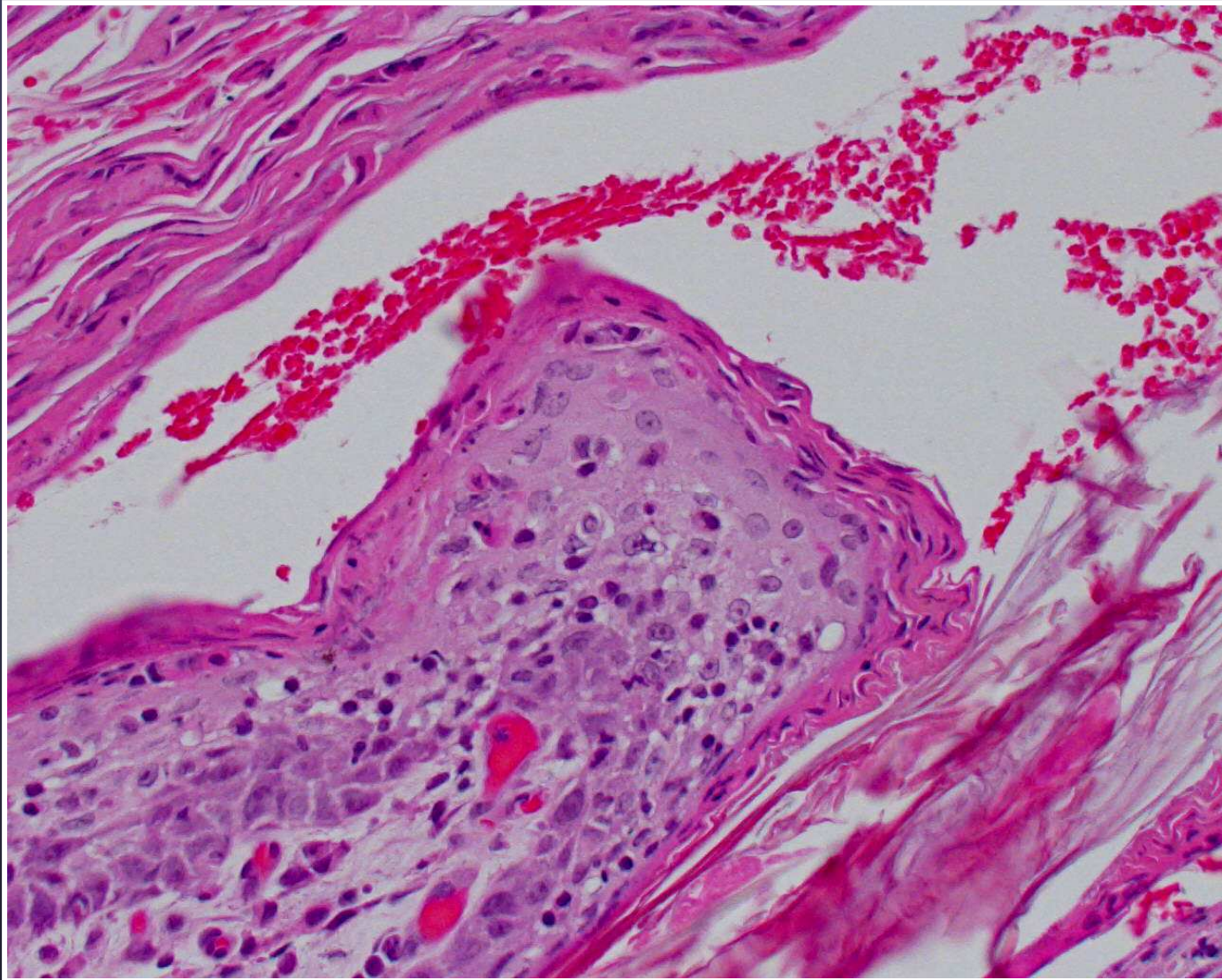
*Maybe explained by underlying immune mechanism and site targeted in epidermis*



*Individually necrotic keratinocytes  
often seen in  
Superficial necrolytic dermatitis  
(hepatocutaneous syndrome)*

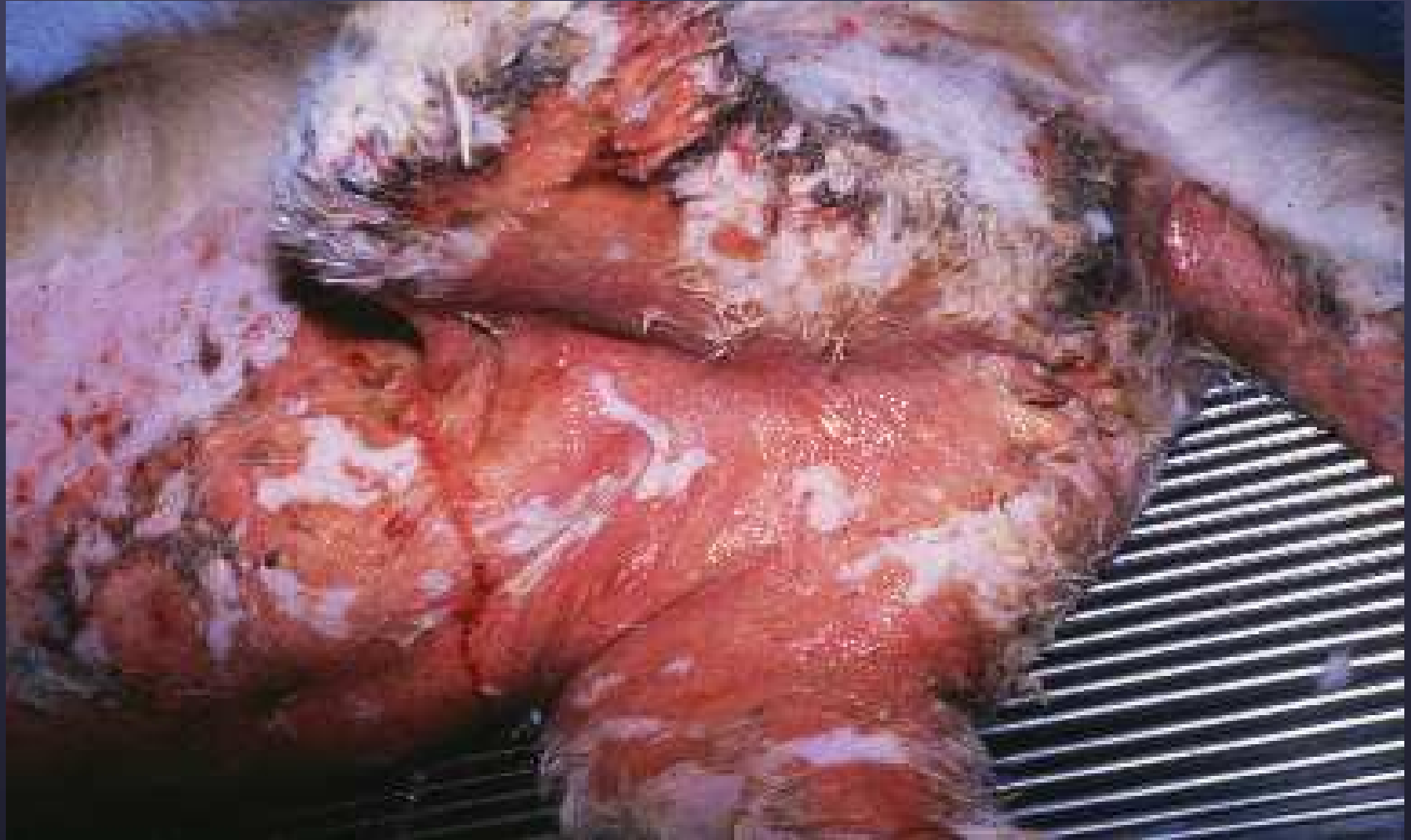






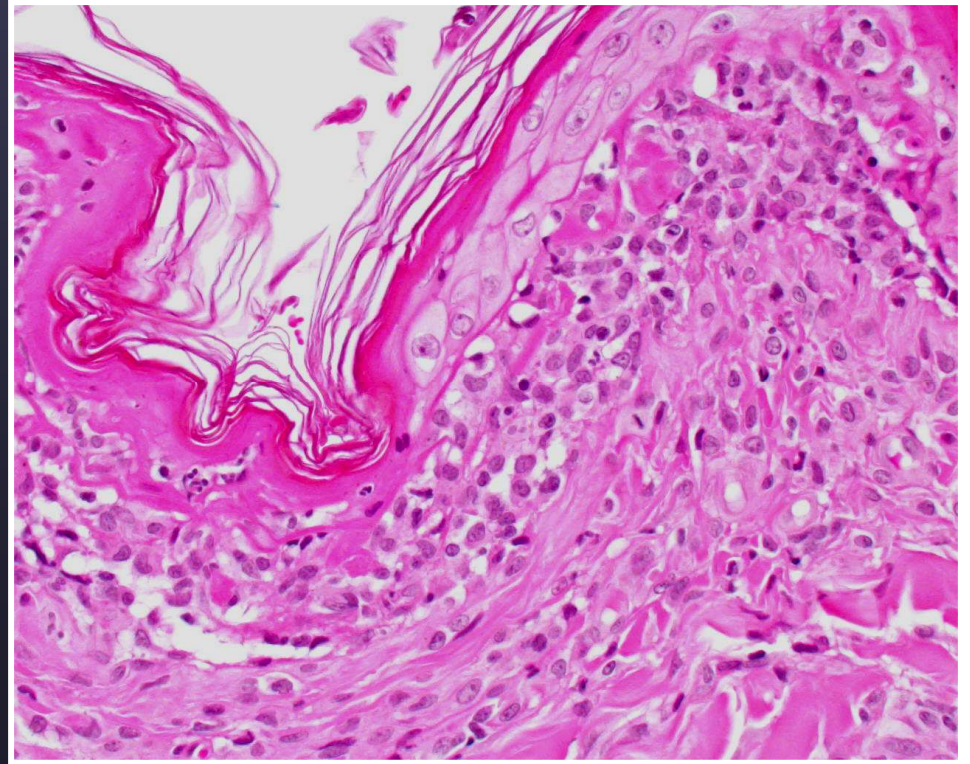
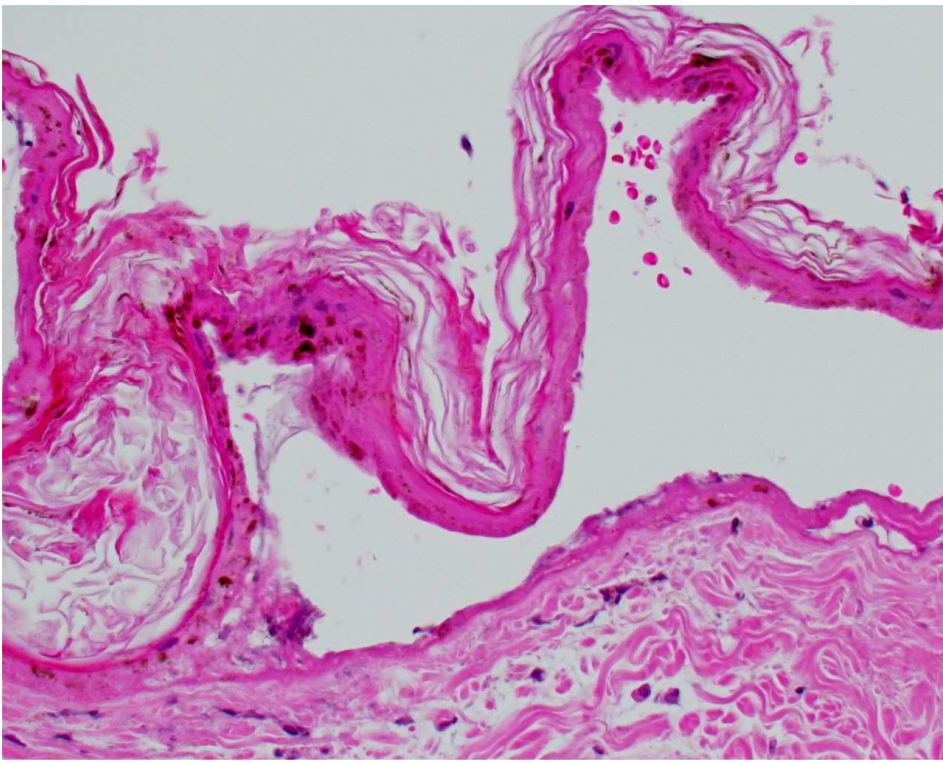
Superficial necrolytic dermatitis



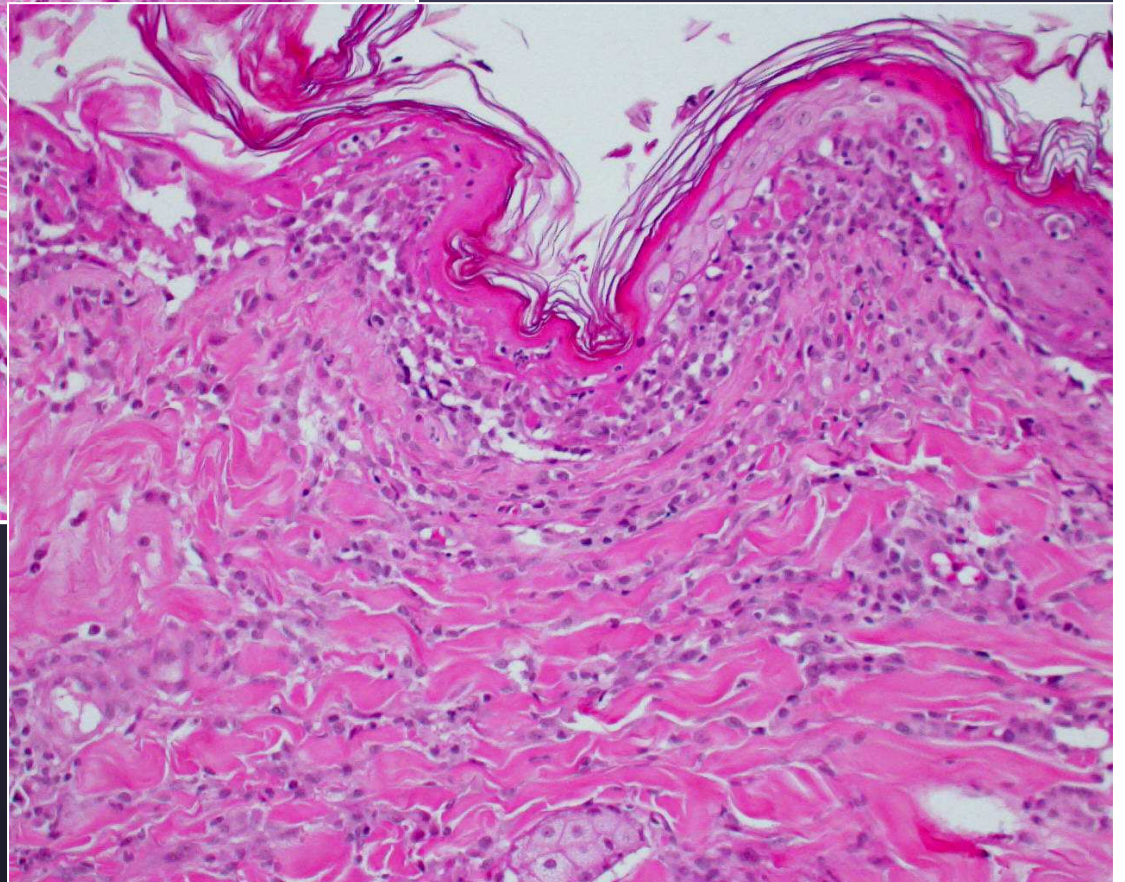
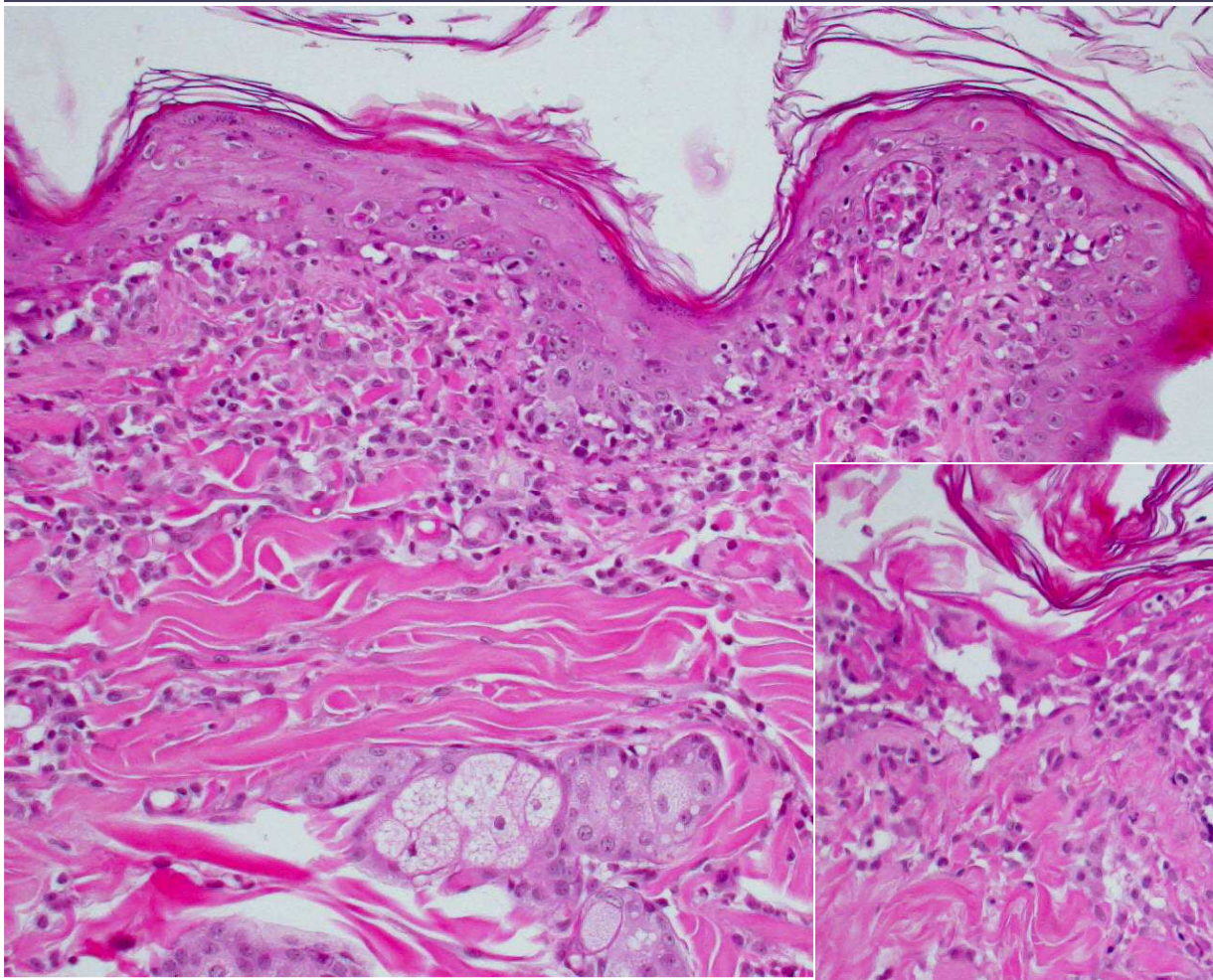


Toxic epidermal necrolysis

# EM/TEN Overlap??





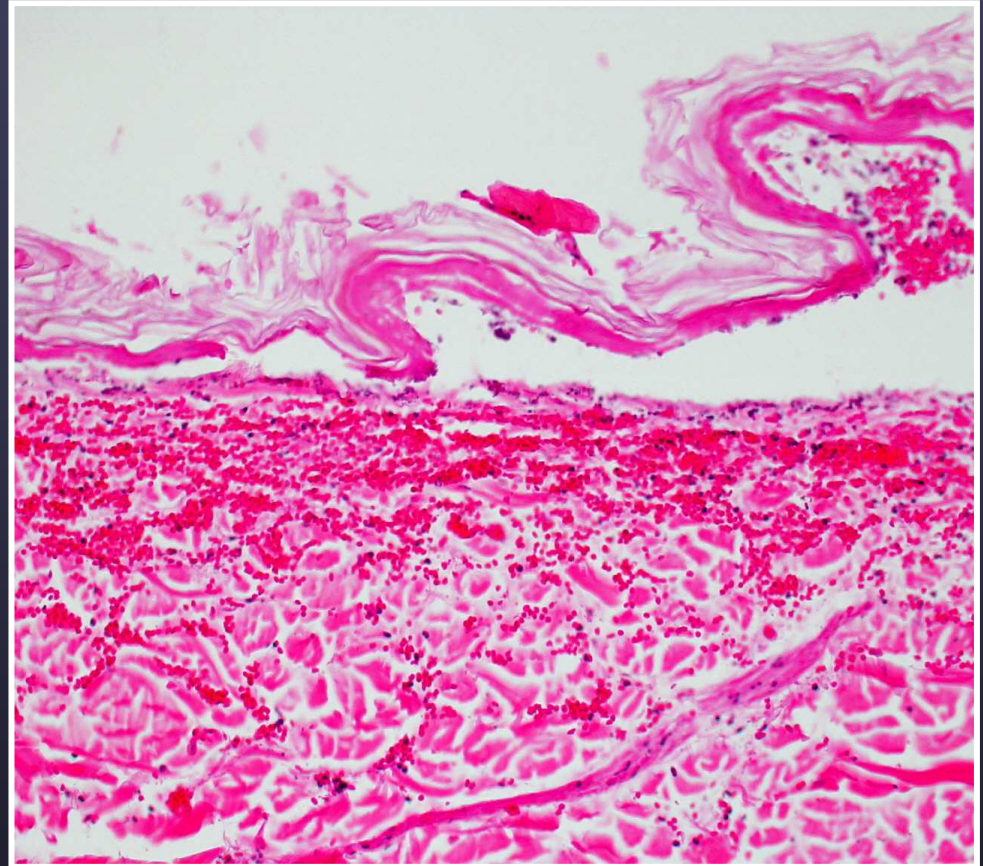


*Current theory is that clinical extent  
and distribution distinguishes EM from EMM/SJS  
and TEN and not histopath?*

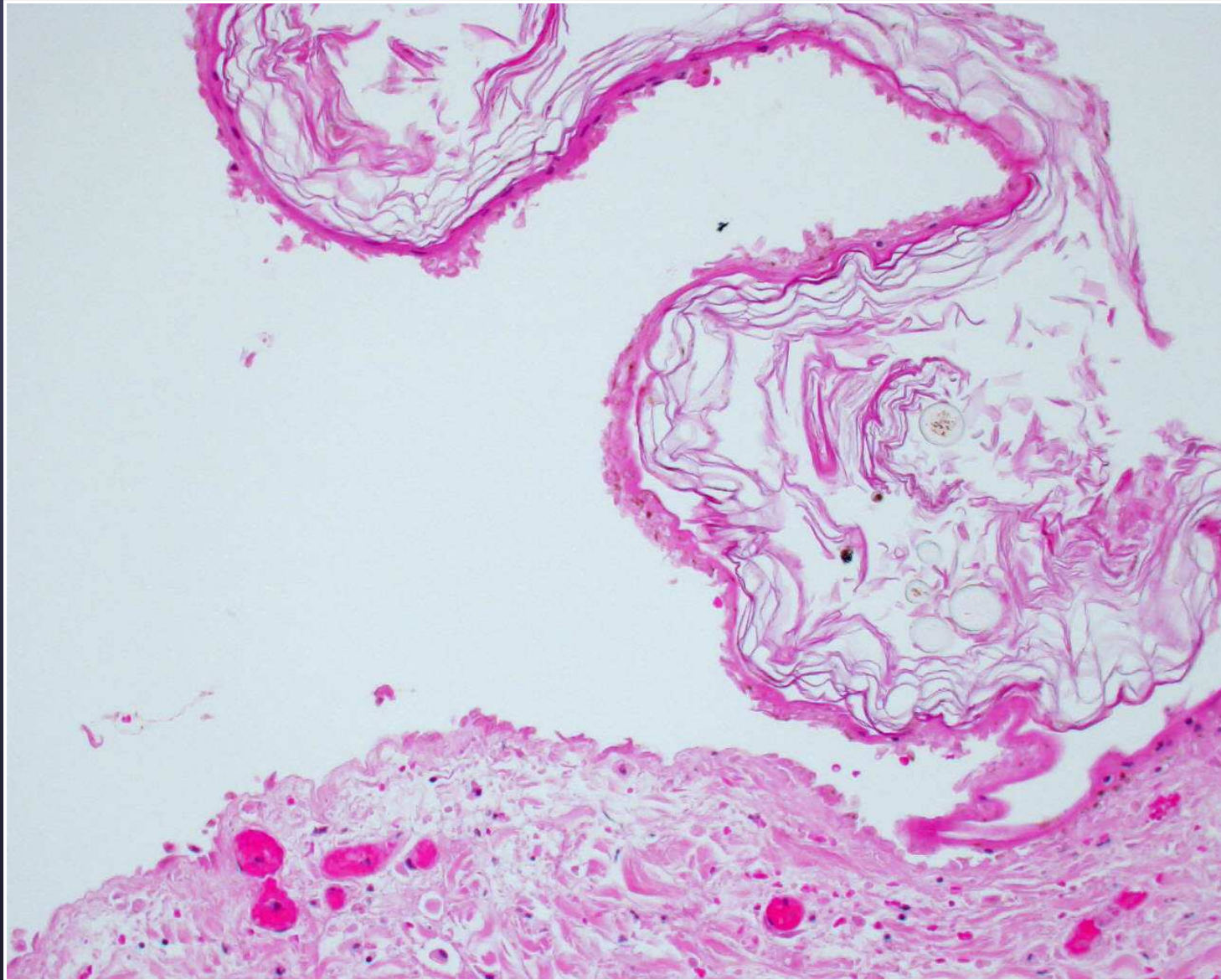


# TEN and Coagulation Necrosis

- Preservation of architecture
- Loss of cellular detail
- Typical of hypoxic cell death

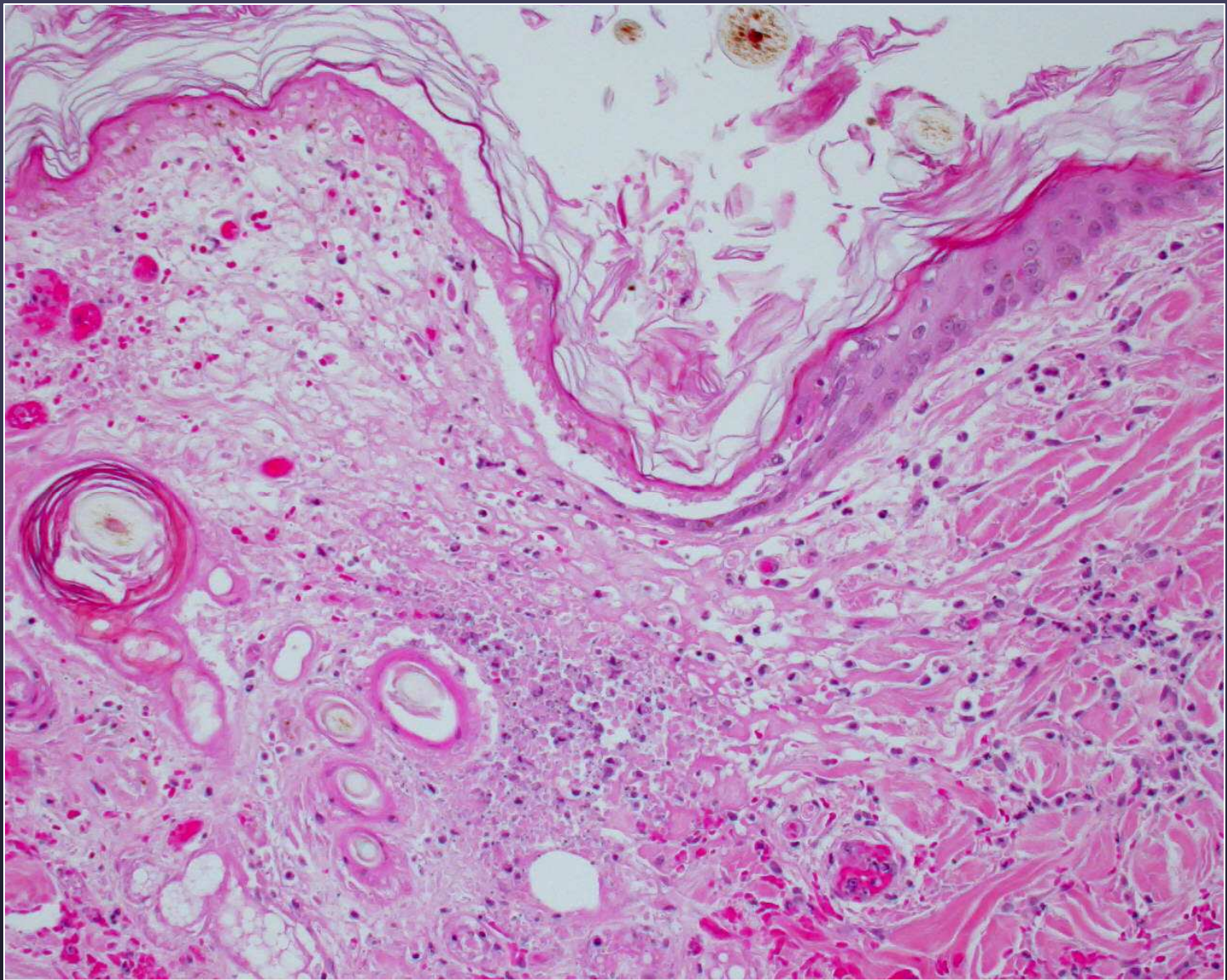






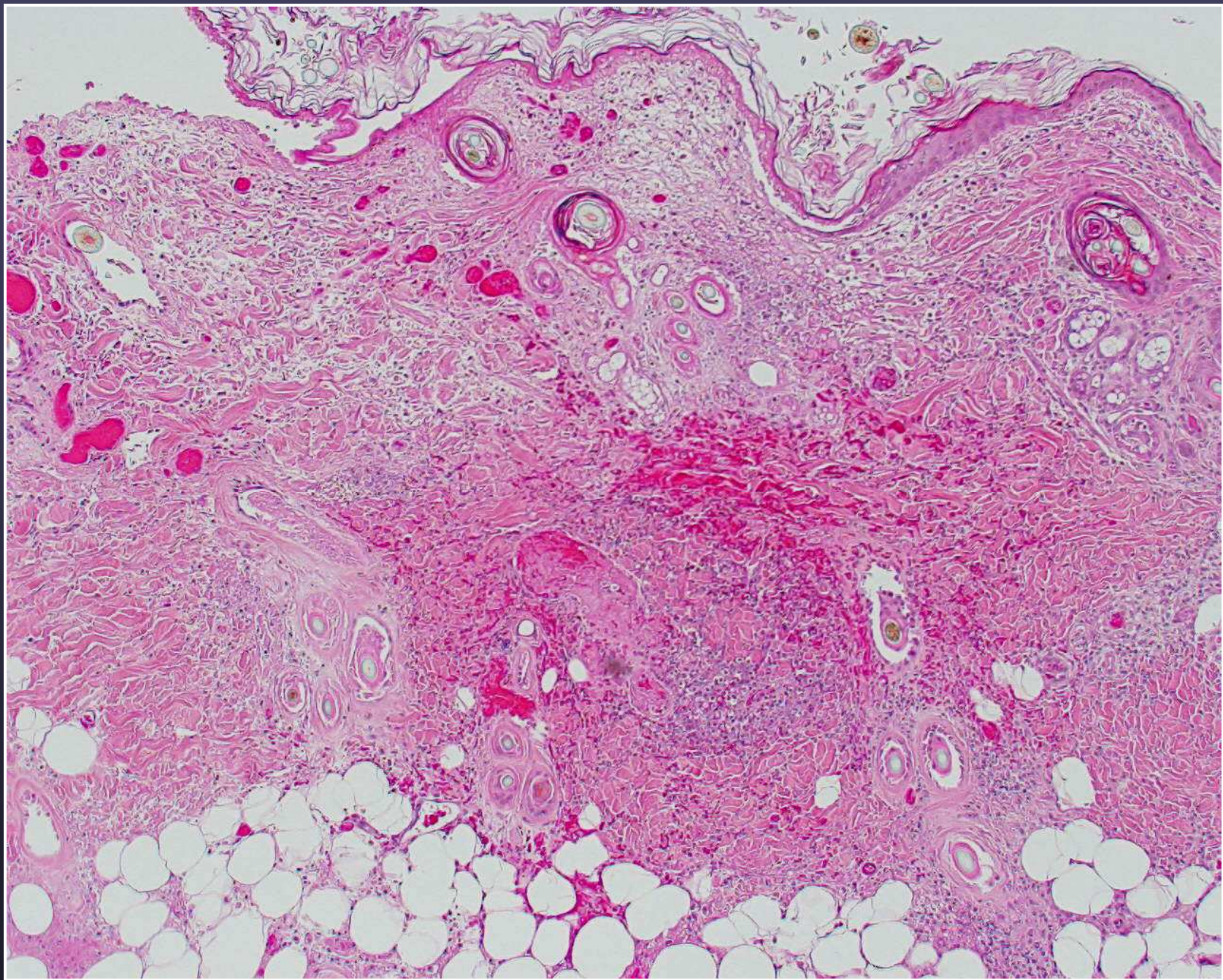
Acute epidermal necrosis



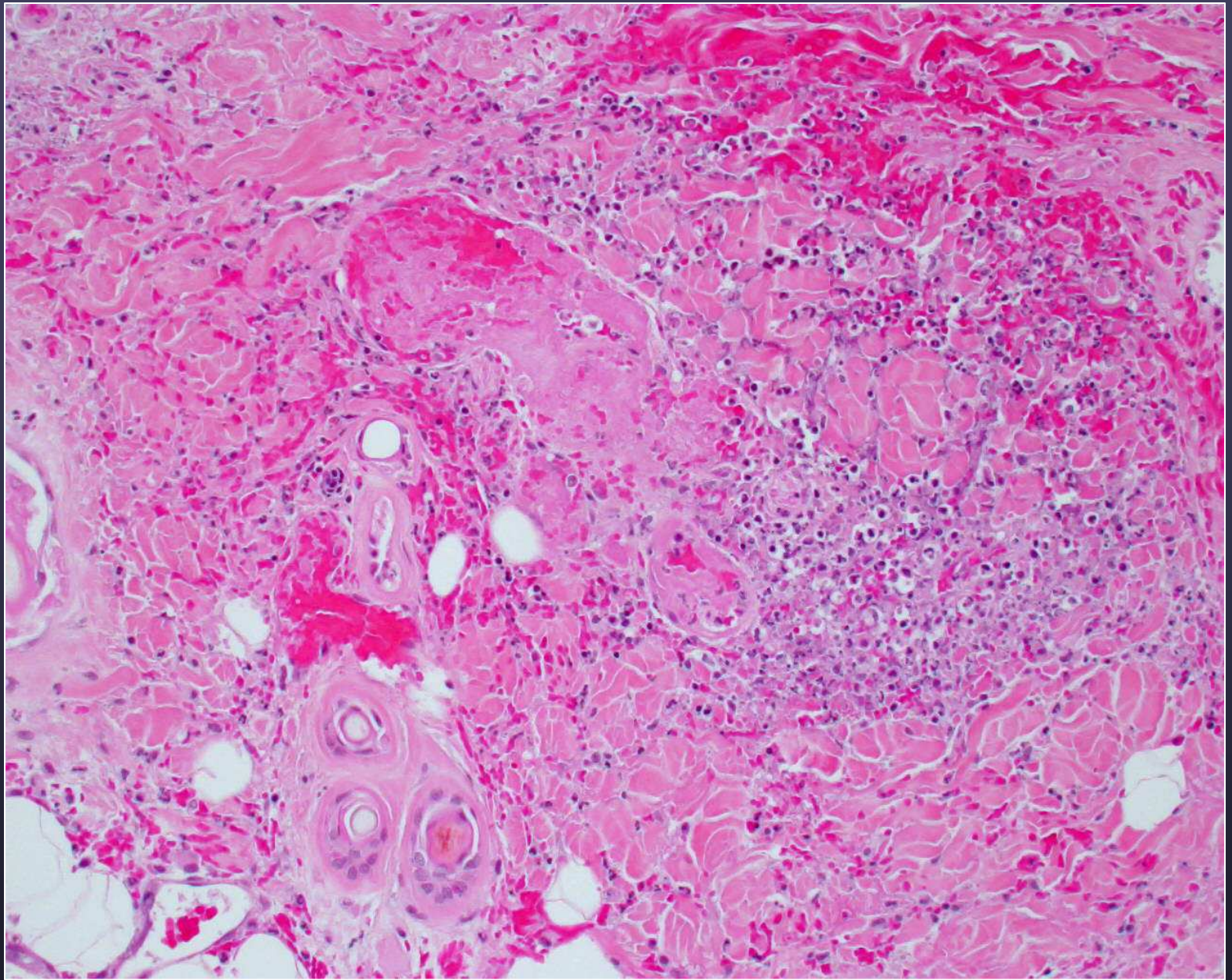


**Cutaneous Infarct**



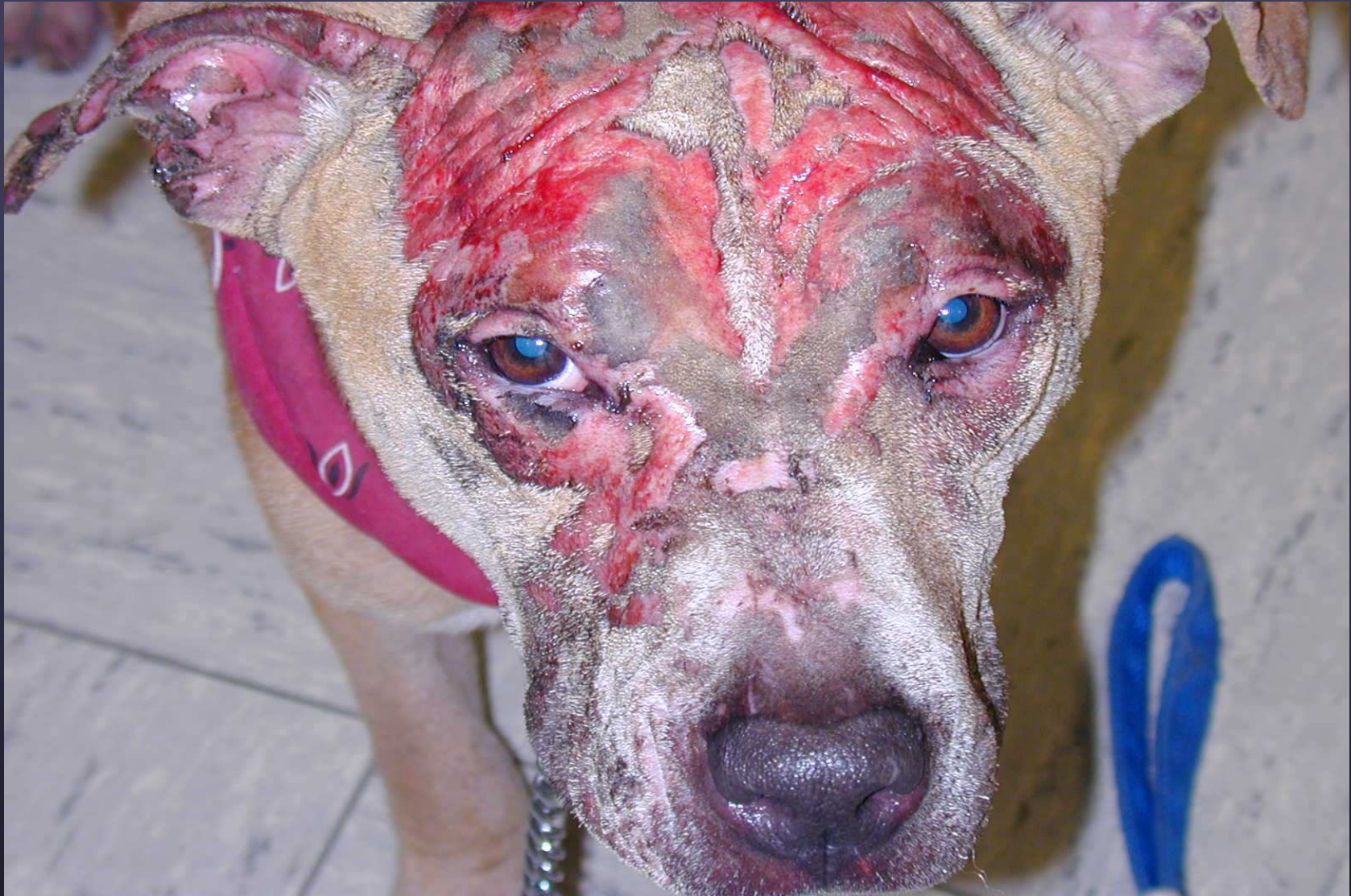






Fibrin thrombus

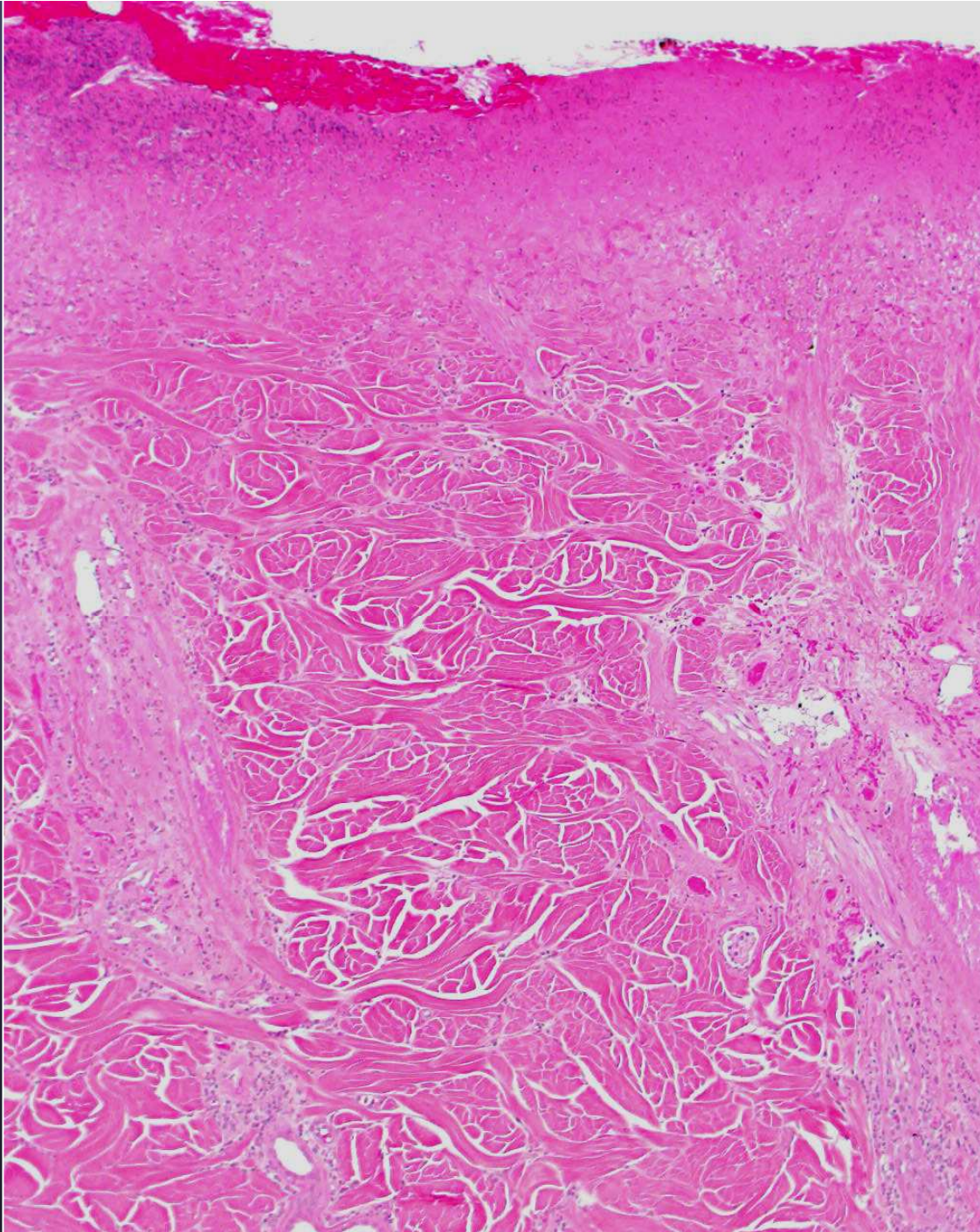




Acute thermal burn



# Thermal Burn



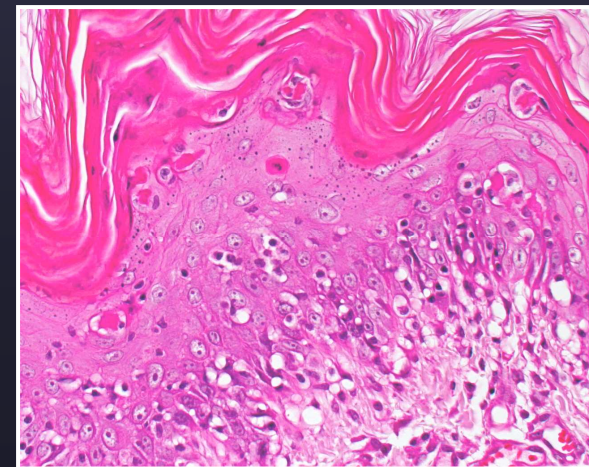
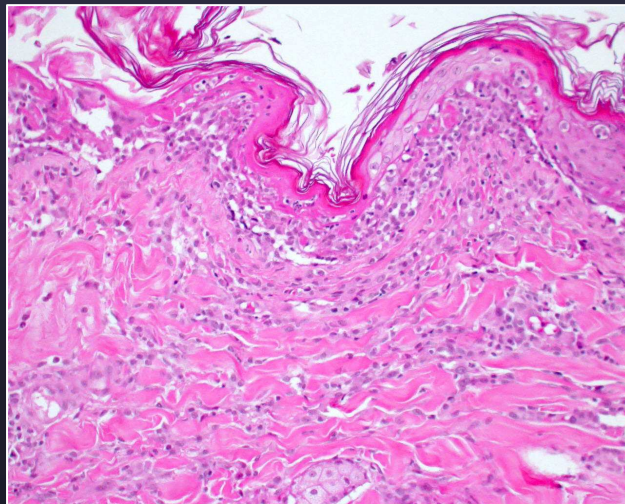
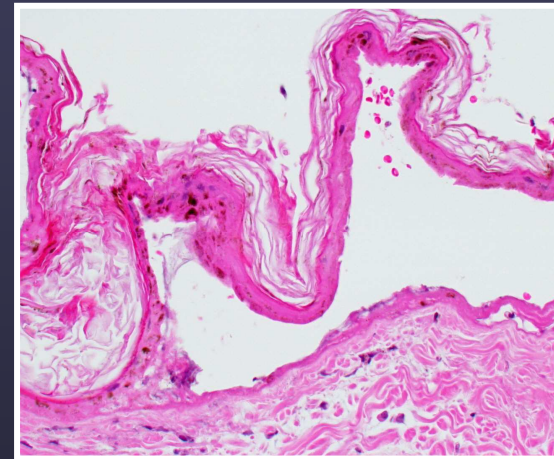
*The epidermal necrosis  
“wicks” down hair follicles*



# EM/SJS/TEN

## Conflicting Literature and Histopathology

- SJS/TEN= apoptosis?
- EMM= necrosis?
- Both are incorrect
- Both are correct



# Hypotheses

(1) Multiple pathways of cell death in drug eruptions

apoptosis

necrosis

(2) Diffuse basal cell apoptosis → ischemic necrosis

(3) Apoptotic mechanisms to tissue undergoing constant programmed cell death?

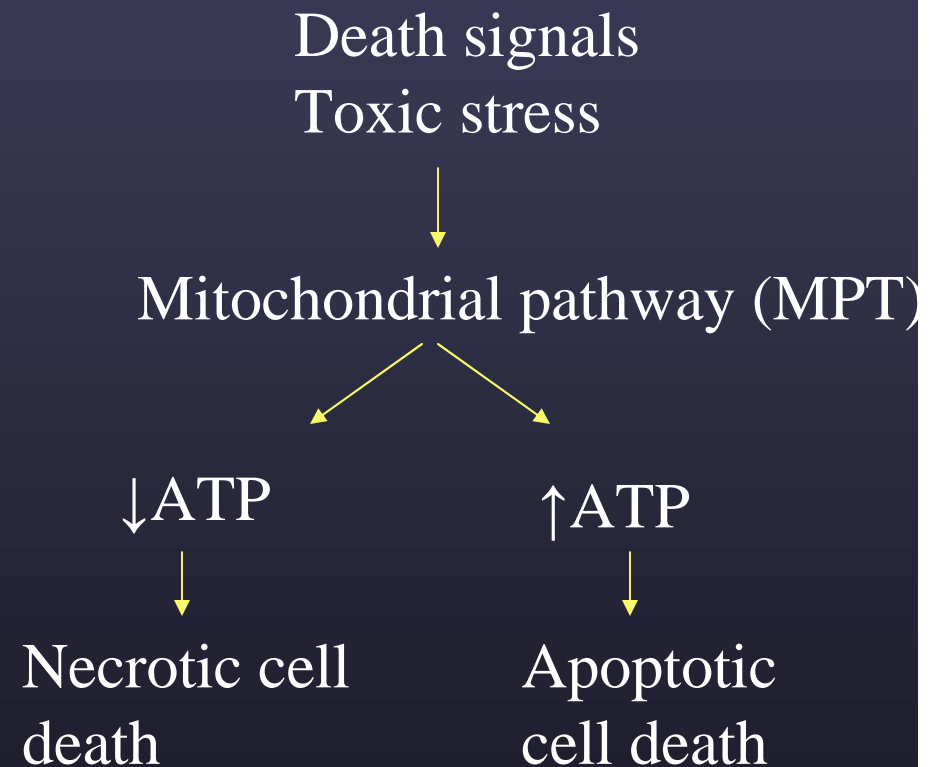
(4) Basic histopathology is a poor indicator of the type of cell death?

(3) Animal diseases not equivalent to human



# Shared pathways leading to cell death??

- Necroapoptosis
- New models of cell death



Lemasters, John J. American Physiologic Society, 1999

# Drug eruptions and the Literature



*Courtesy of R.Dunstan, modified*



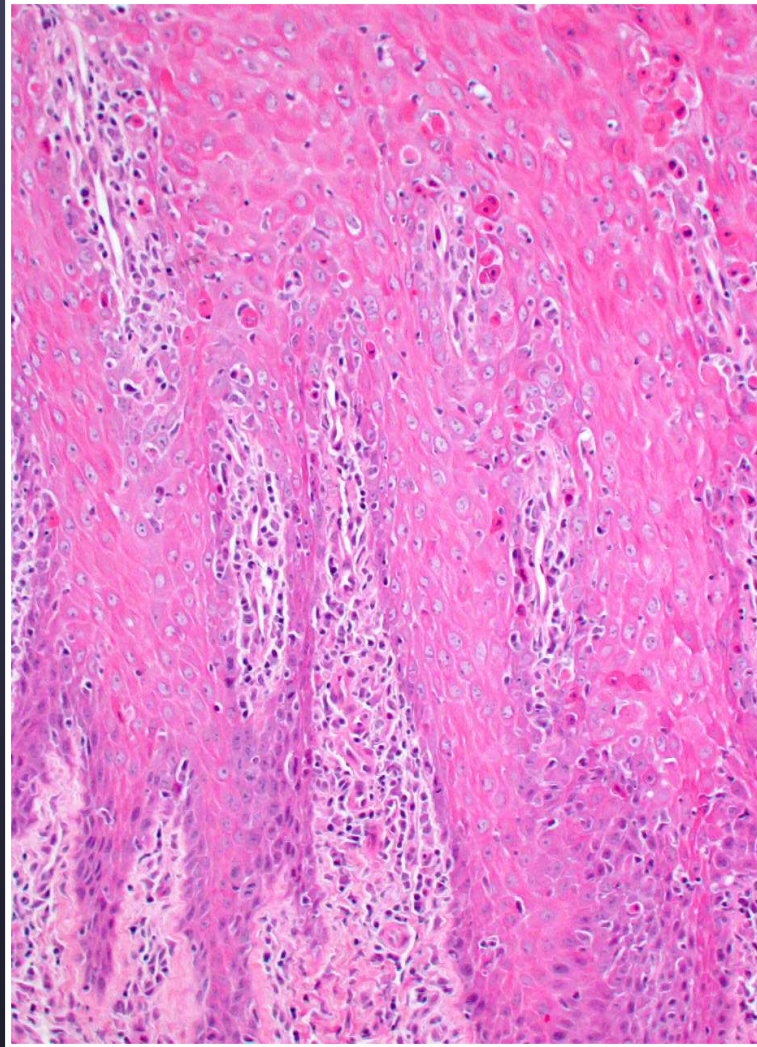
# EM in an Alpaca



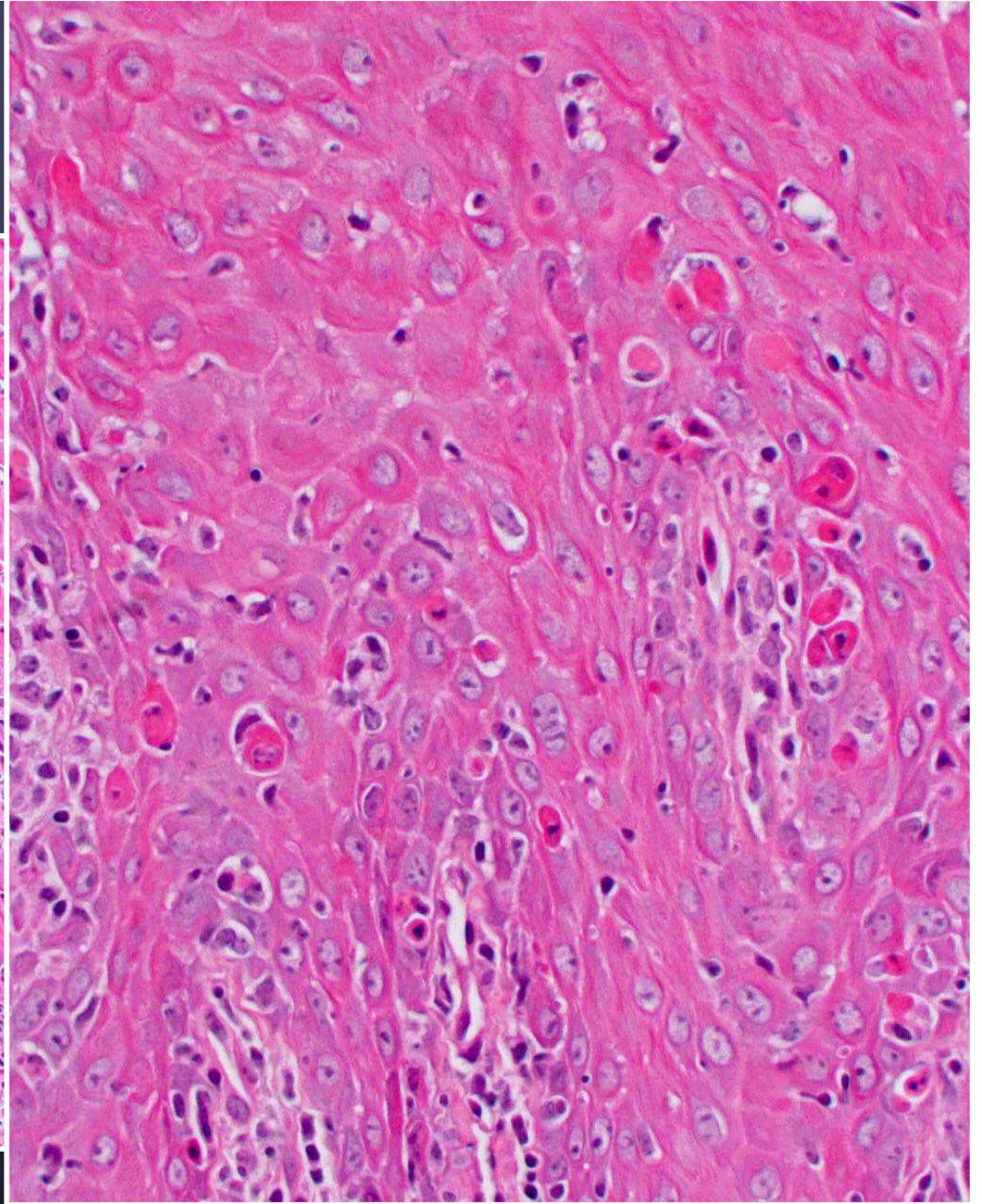


EM



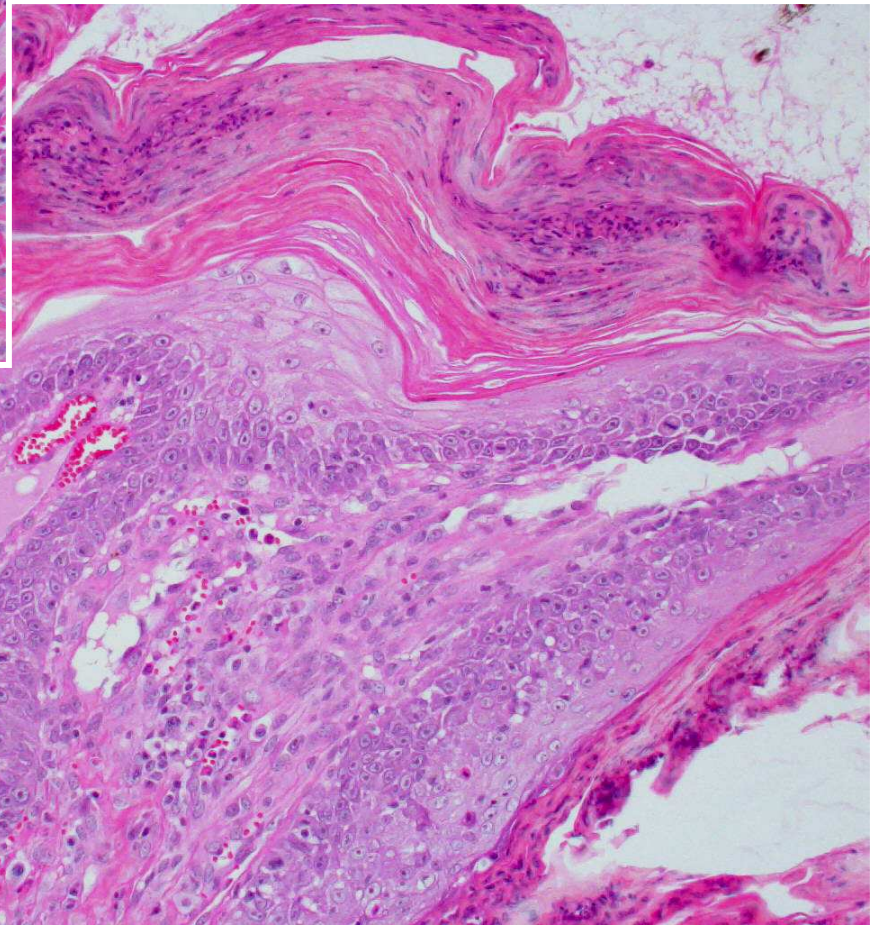
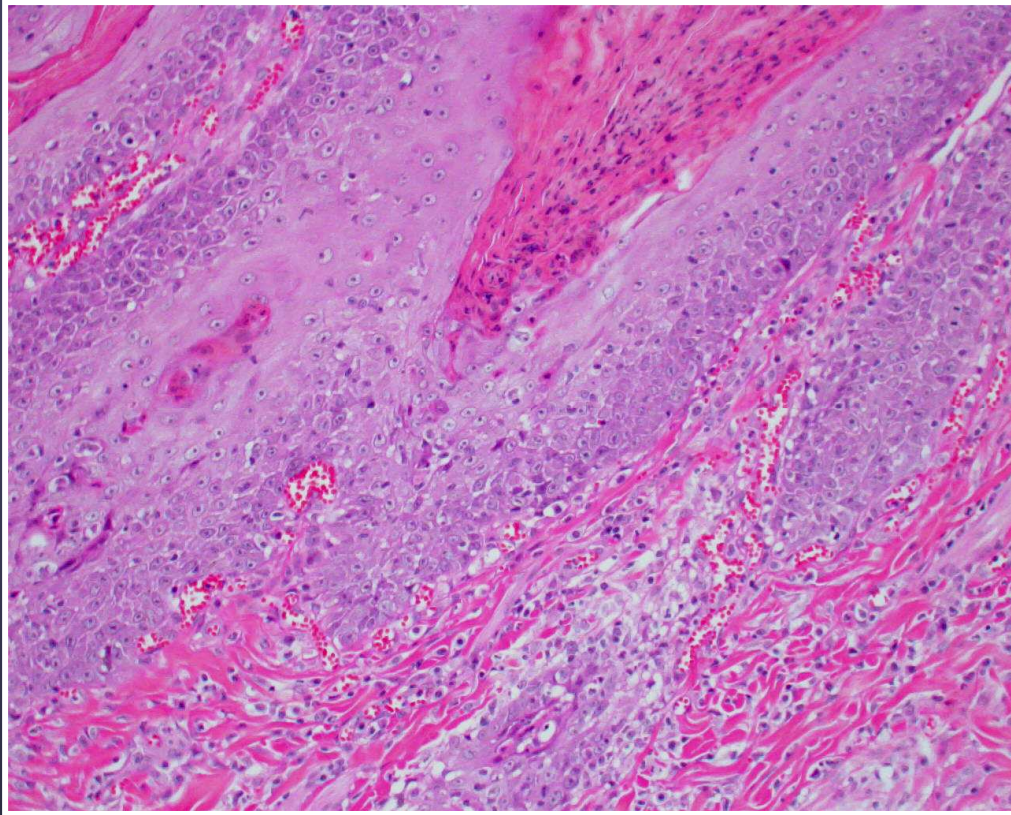


EM



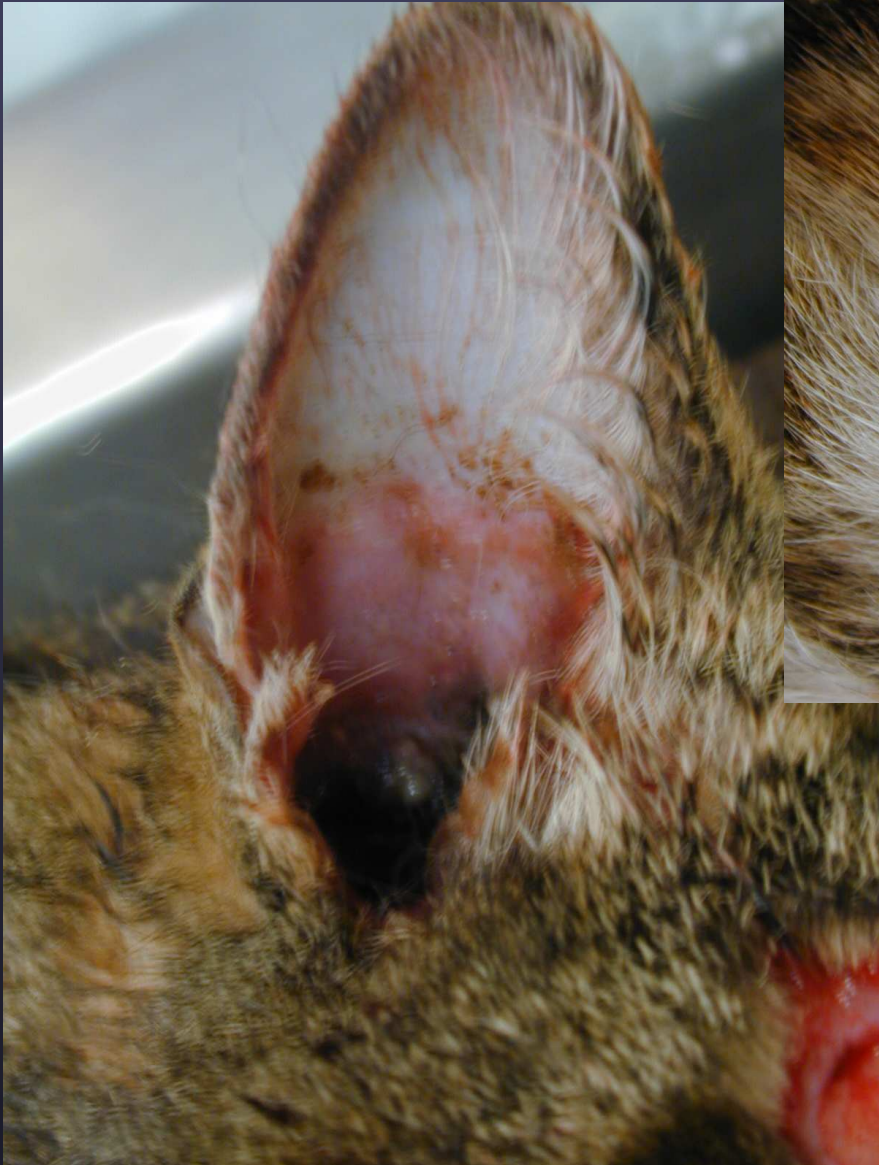


# Feline Erythema Multiforme



**6 mo., DSH, post-  
rabies vaccine**





**9 yr, DSH**

*Post-mortem  
Thymoma associated dermatosis*

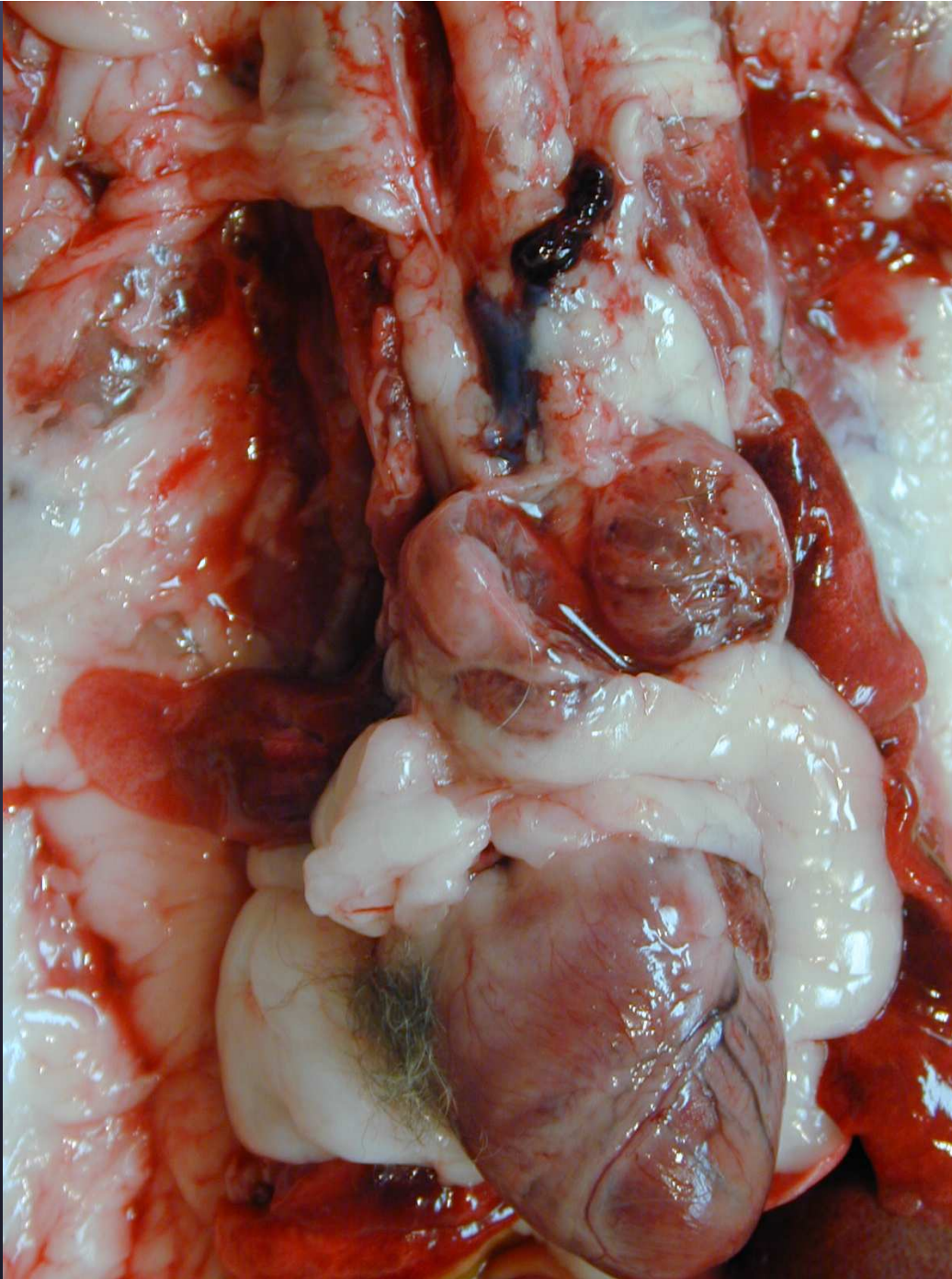


*Severe scaling is difficult to photograph  
in a deceased wet animal--sorry*



*Erosive perianal dermatitis- unusual finding*

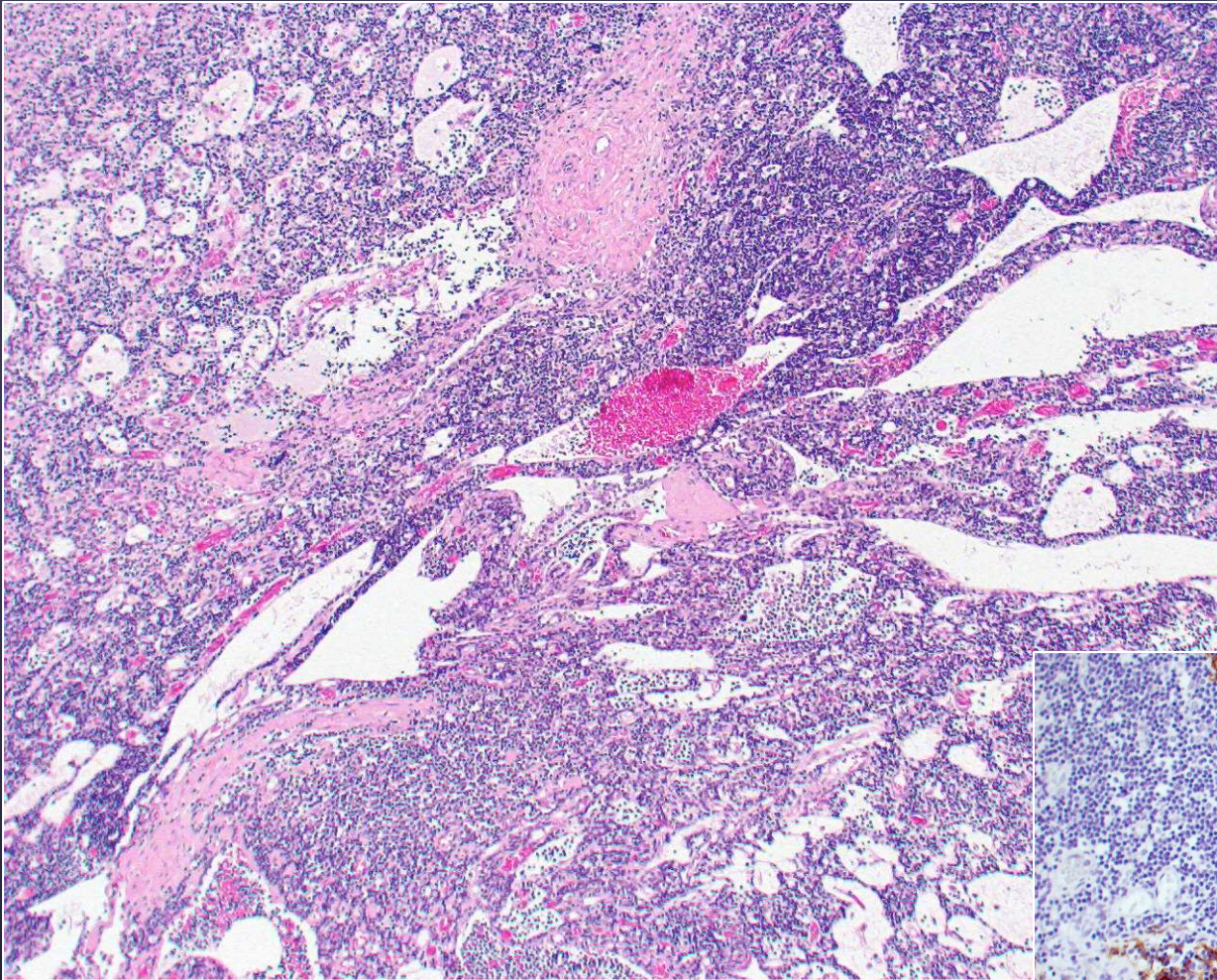




**Thymoma-  
Associated  
Dermatosis**

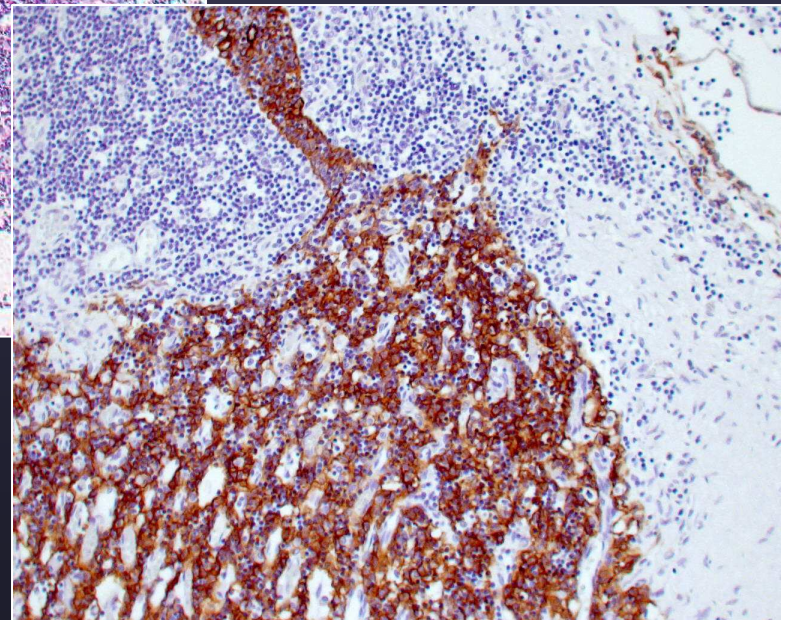


# Thymoma-associated Dermatosis



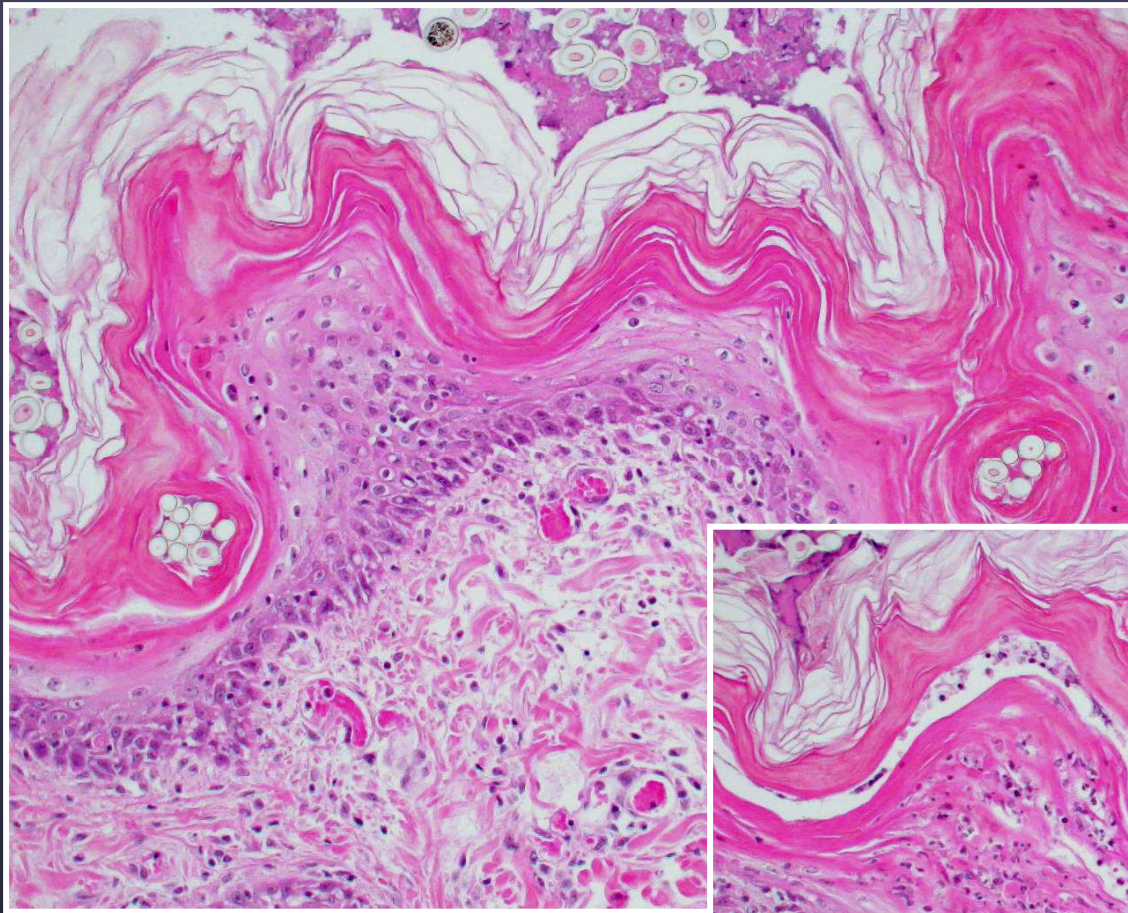
Thymic mass

**AE1/AE3**

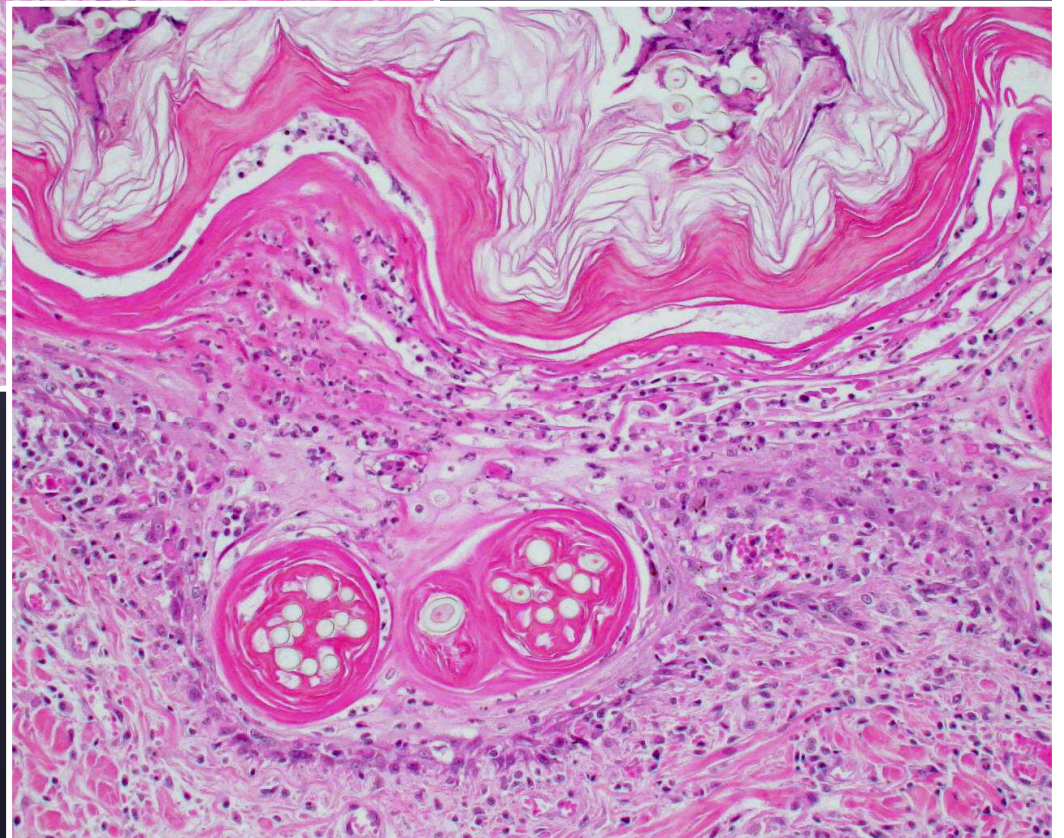




# Thymoma-associated Dermatosis



*Note that the histo resembles EM*



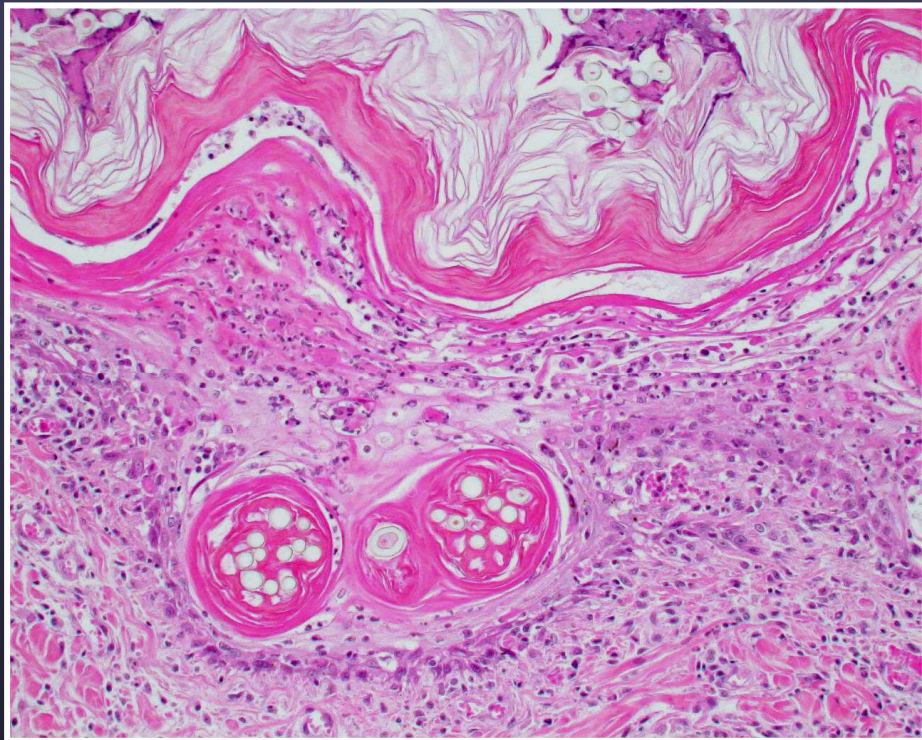
# Thymoma-associated dermatosis

- Middle-aged to older cats
- Begins with scaling→ thick adherent scale that epilates with entrapped hair→ erosions
- Lethargy and anorexia
- Dyspnea uncommon

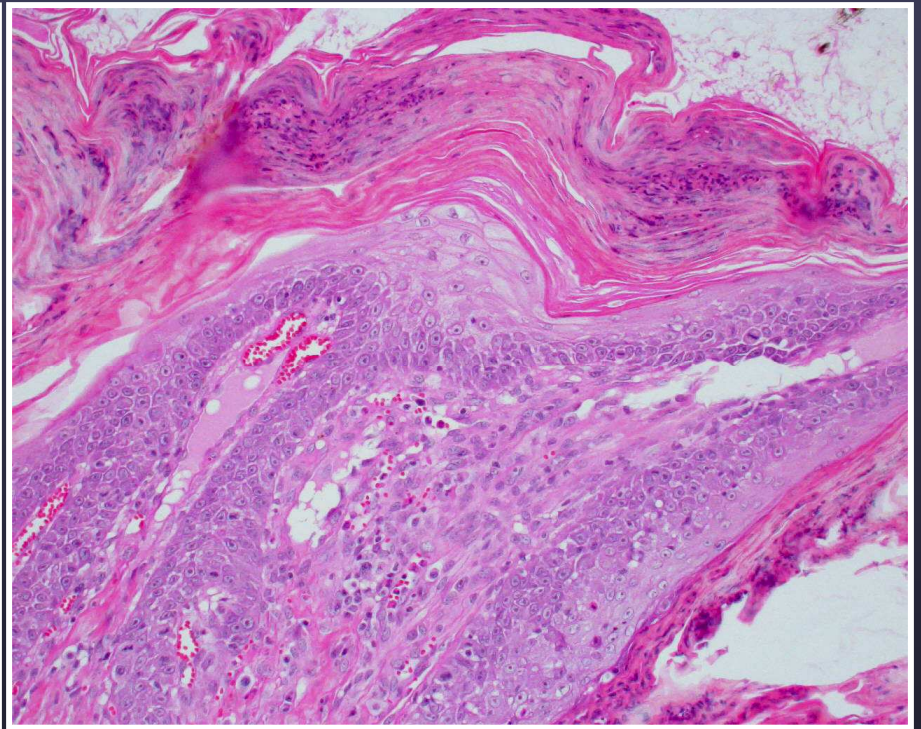


# TAD

- Scattered apoptotic KCs (basal layer and spinous)
- Diffuse and severe hyperkeratosis (parakeratotic and orthokeratotic)
- Interface change can involve ORS leading to sebaceous gland loss
- Malassezia in corneal layer



Thymoma-associated dermatosis



Erythema multiforme



# Histopathology

Erythema multiforme-like disease

Thymoma *(can be very small and missed on radiographs)*

Drugs

Herpesvirus

Systemic disease process

→ Look for Mixed patterns in cats!

*(→ Mixed patterns associated with neoplasia or systemic illness)*

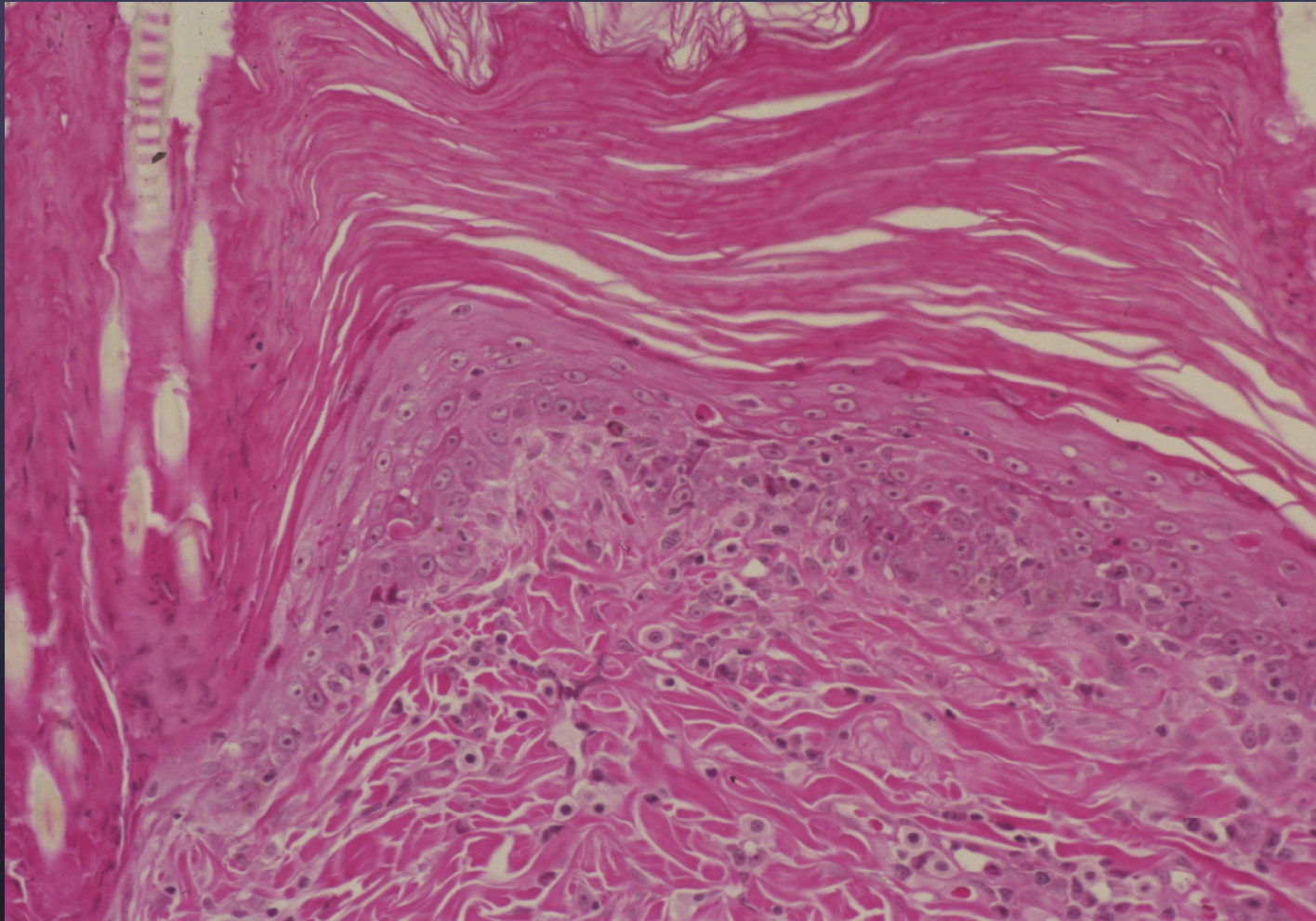


*Another case of thymoma associated dermatosis (TAD)*

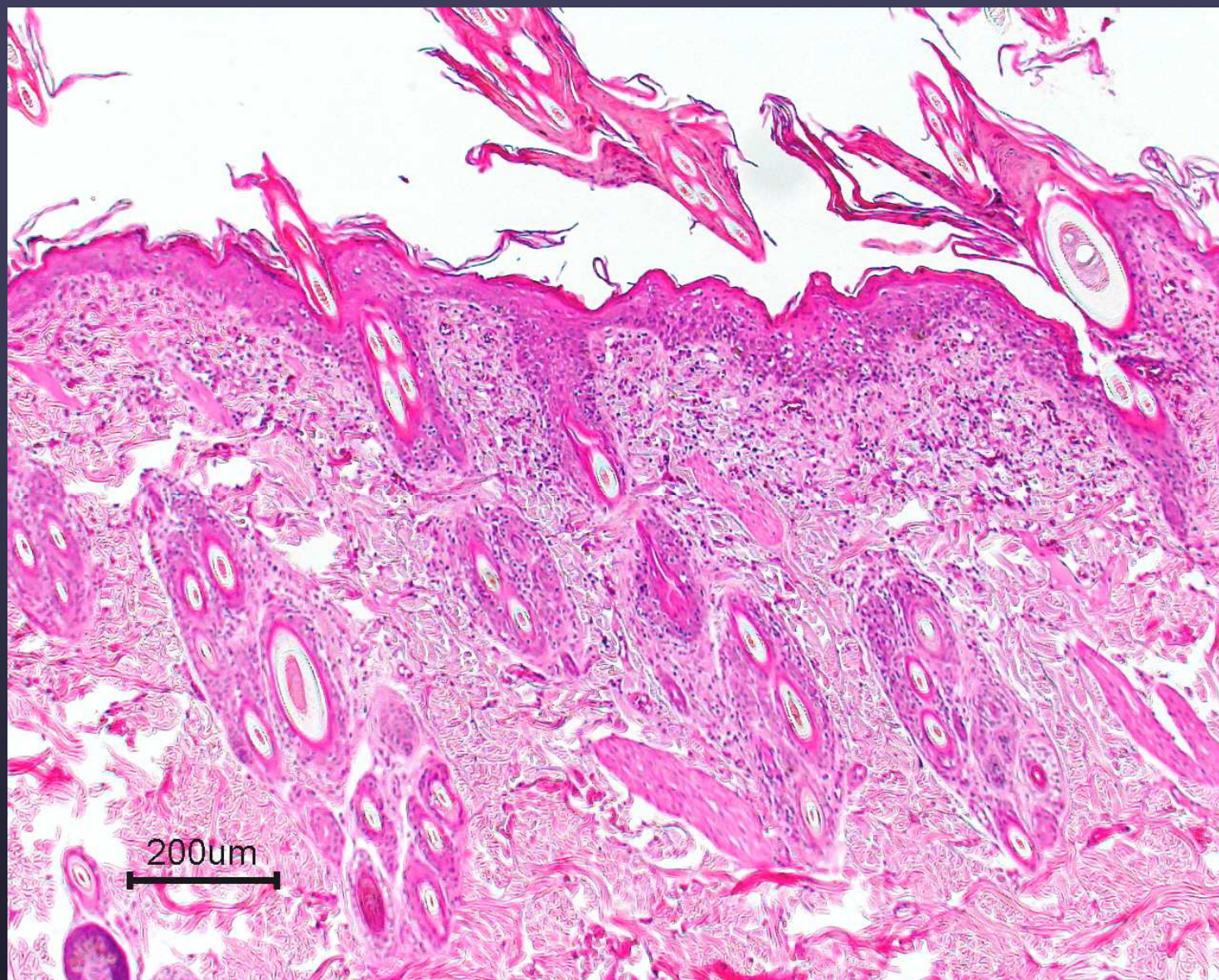
Dr. Aiden Foster



# Thymoma-Associated Dermatositis (TAD)





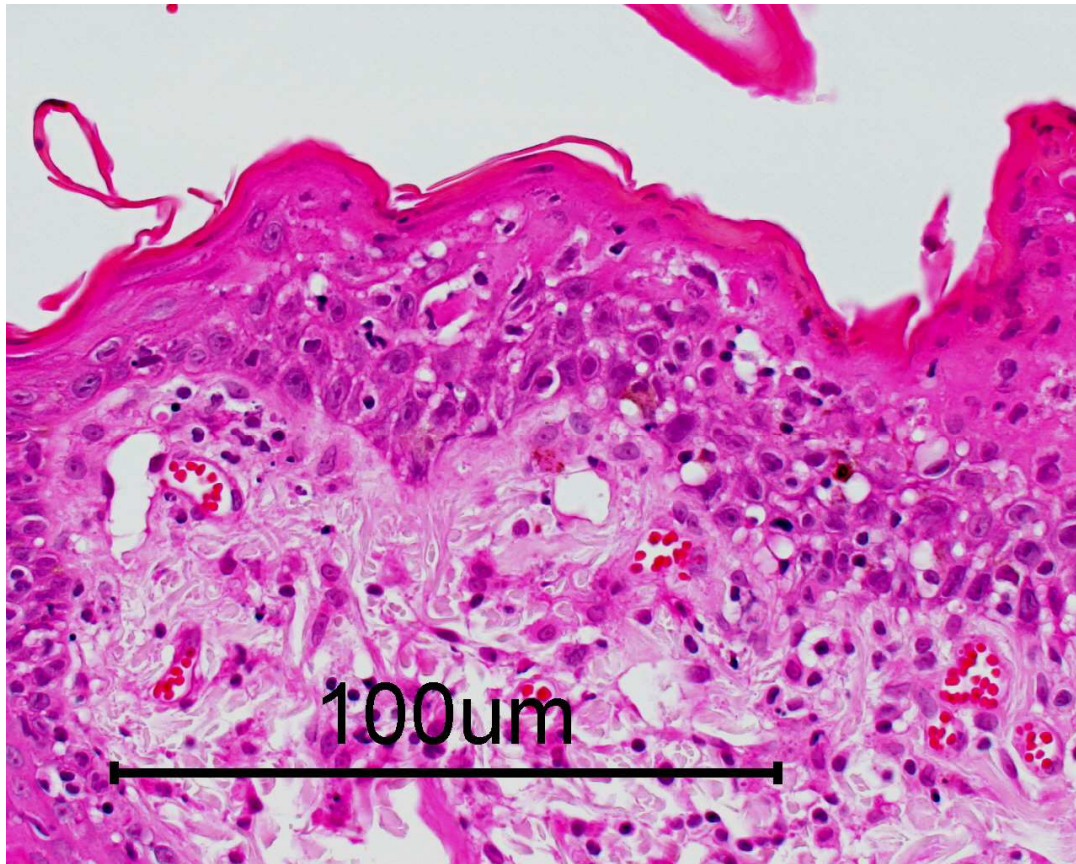


**9 yr, FS, Siamese**

**May 2002**

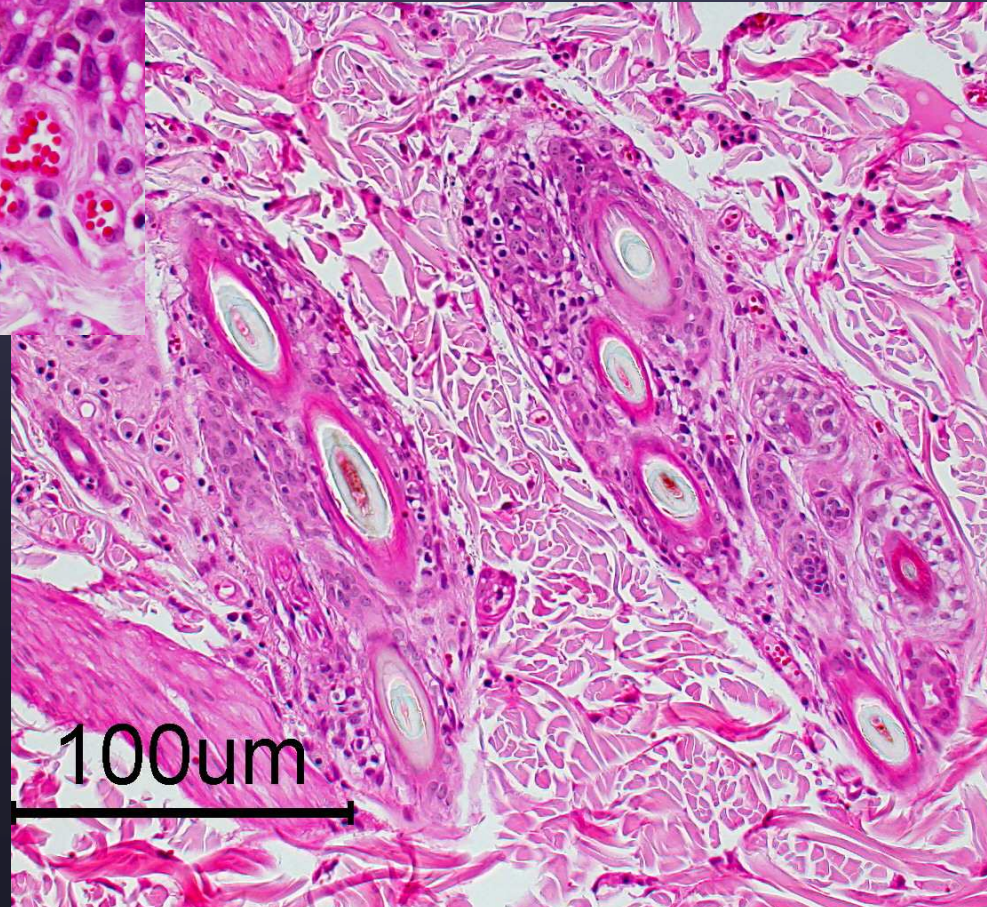
*TAD- not uncommon to see diffuse sebaceous gland loss*





TAD

May 2002





# Thymoma-associated Dermatitis



**9 yr, FS, Siamese**

**4 wks post-thymectomy**



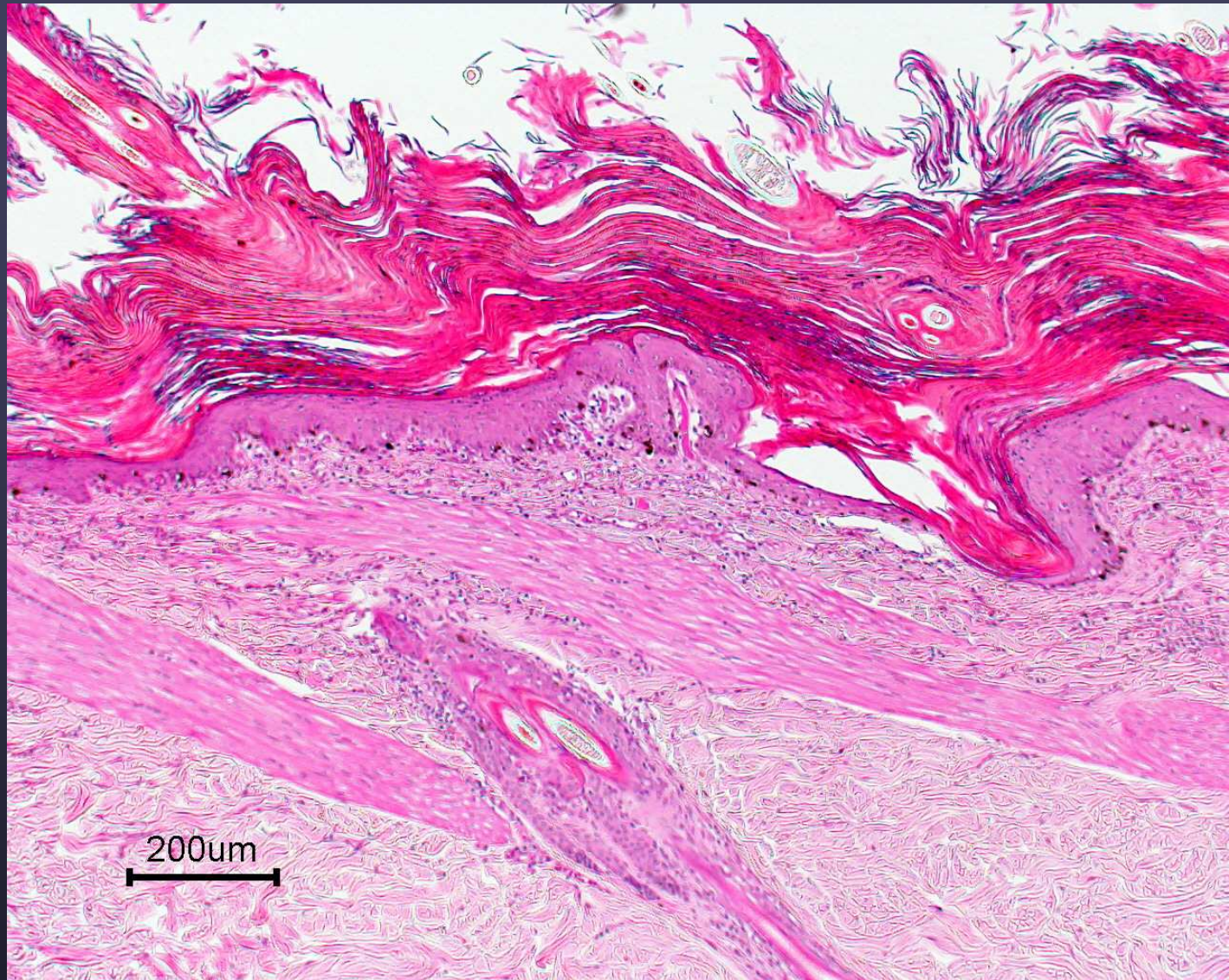


*TAD- hair mats with thick adherent keratin scale and easily exfoliates → erosions*



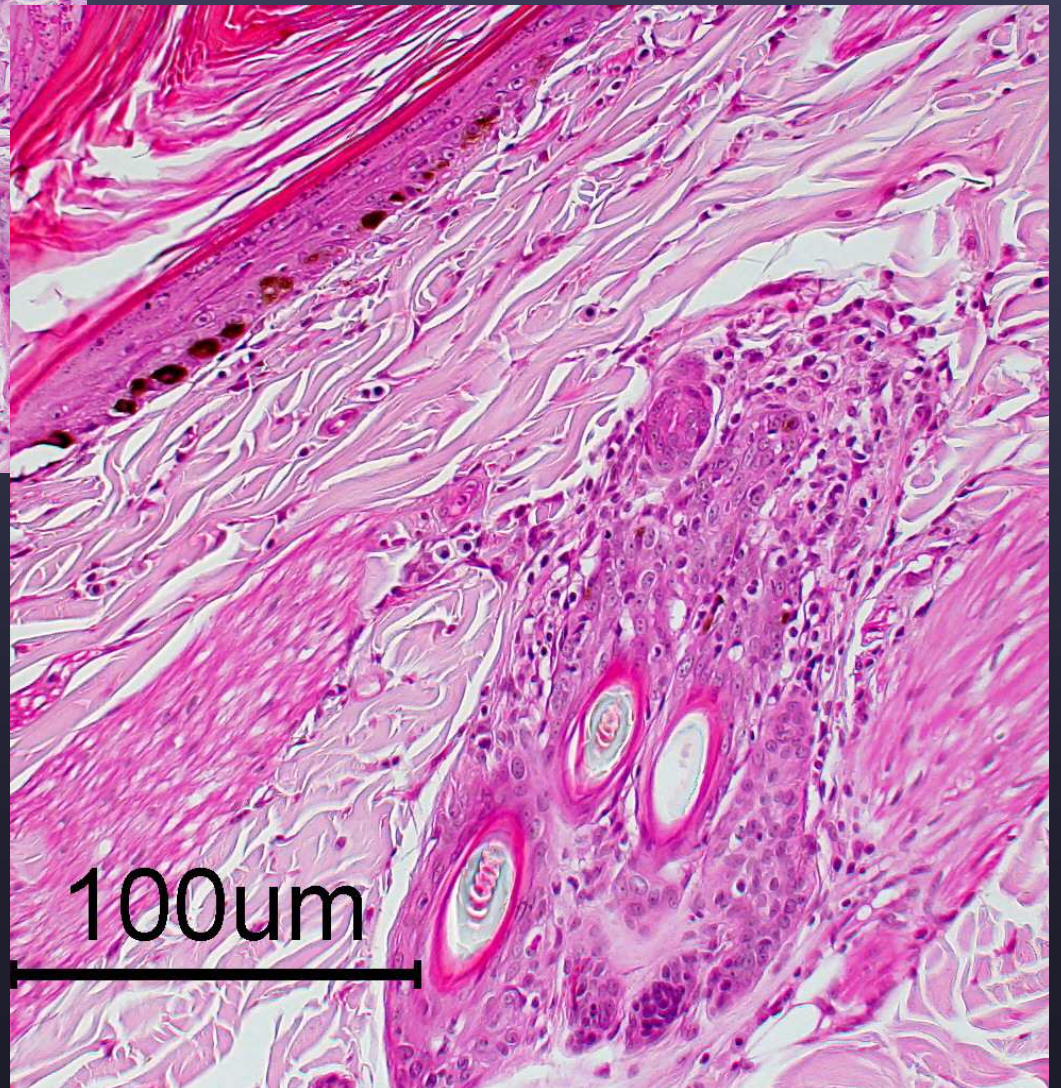
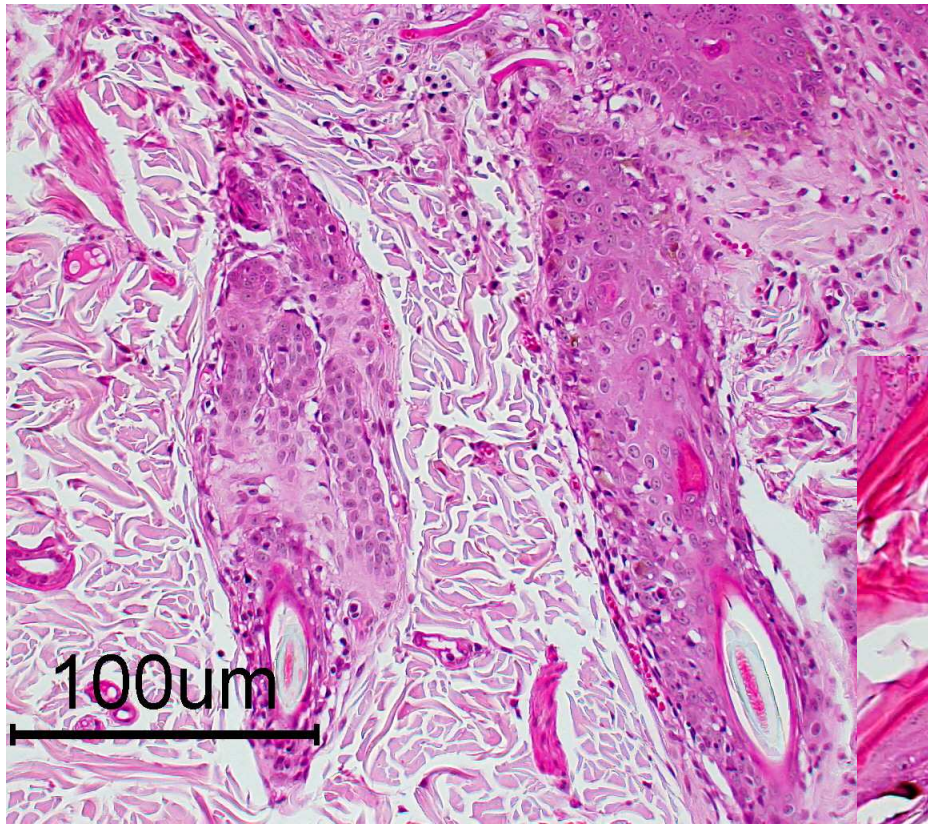
*TAD- note the severe scaling; hair mats with thick adherent keratin scale and easily exfoliates*





**TAD 4 weeks post op**





**4 weeks post op  
Sebaceous gland loss**







1 yr post-op



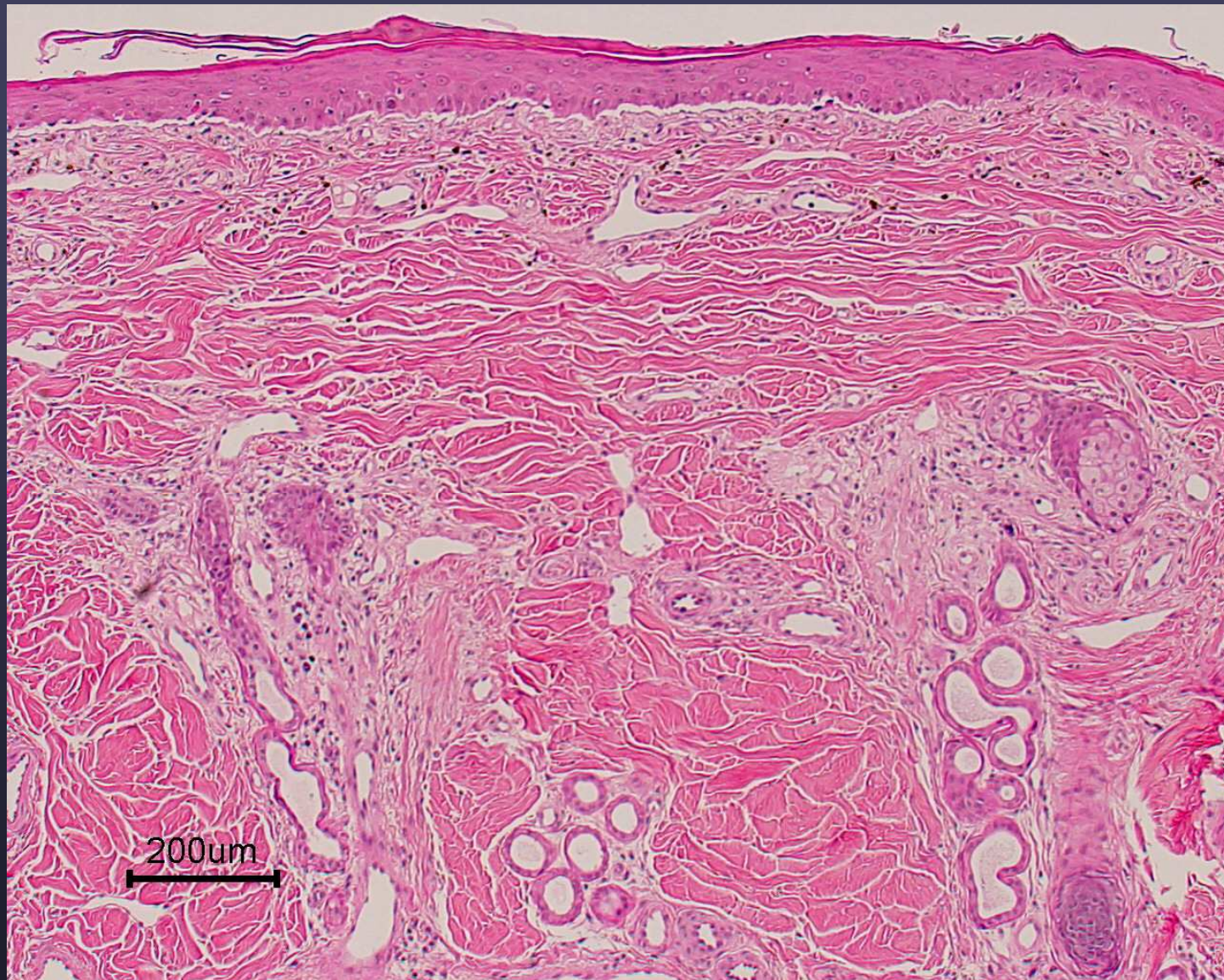


Terminal dermatomyositis in a Sheltie



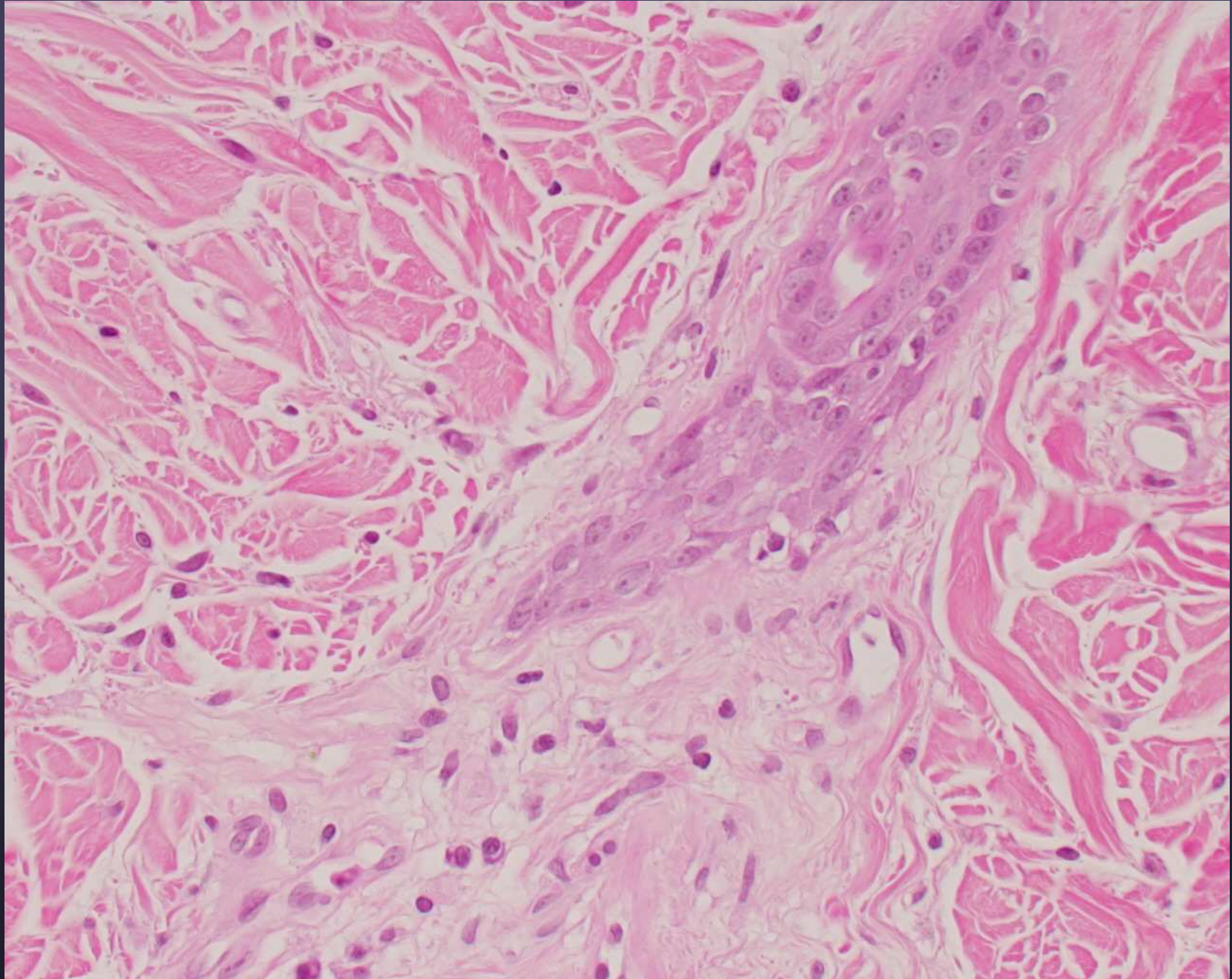
Note the skeletal muscle atrophy





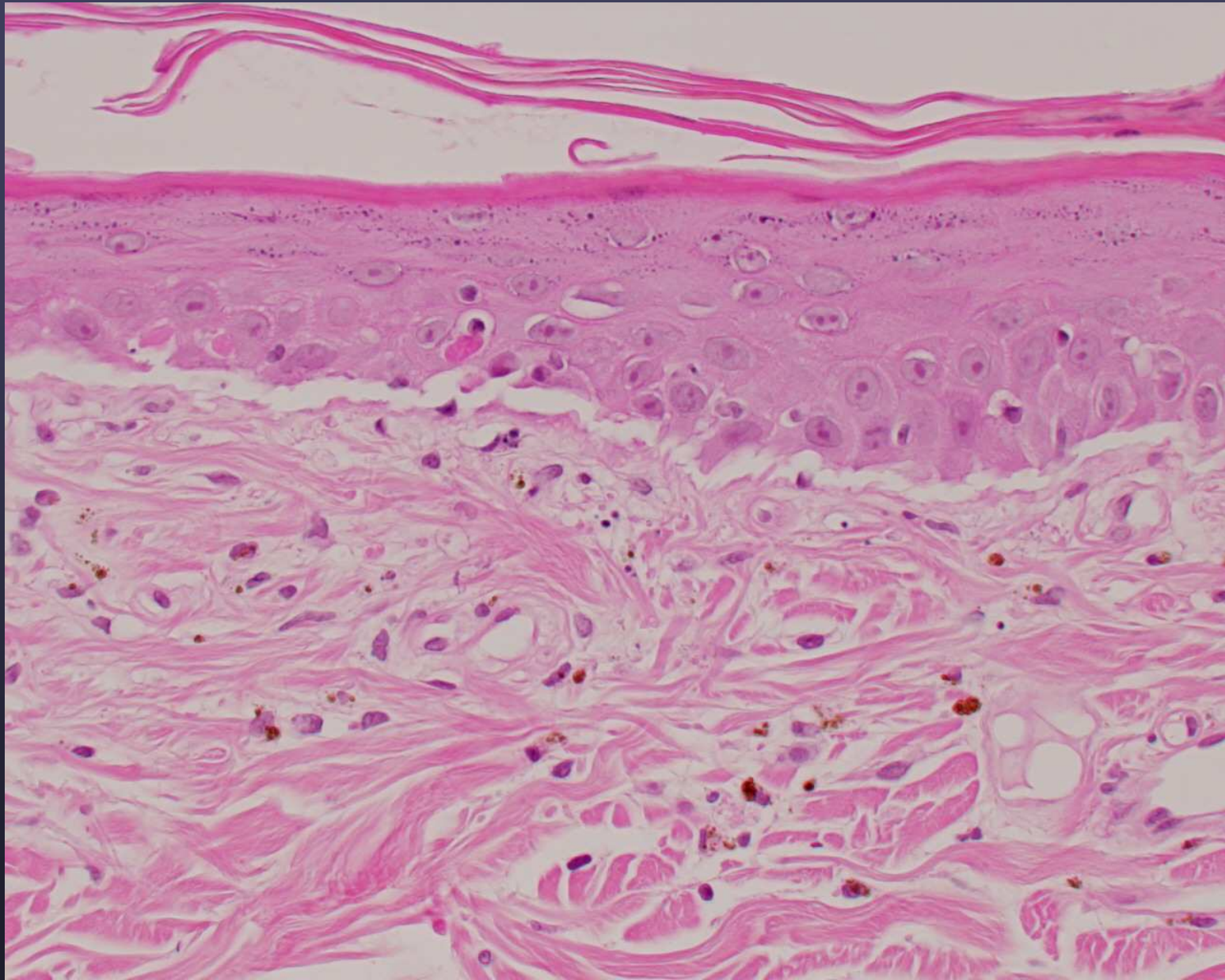
Dermatomyositis (DM)





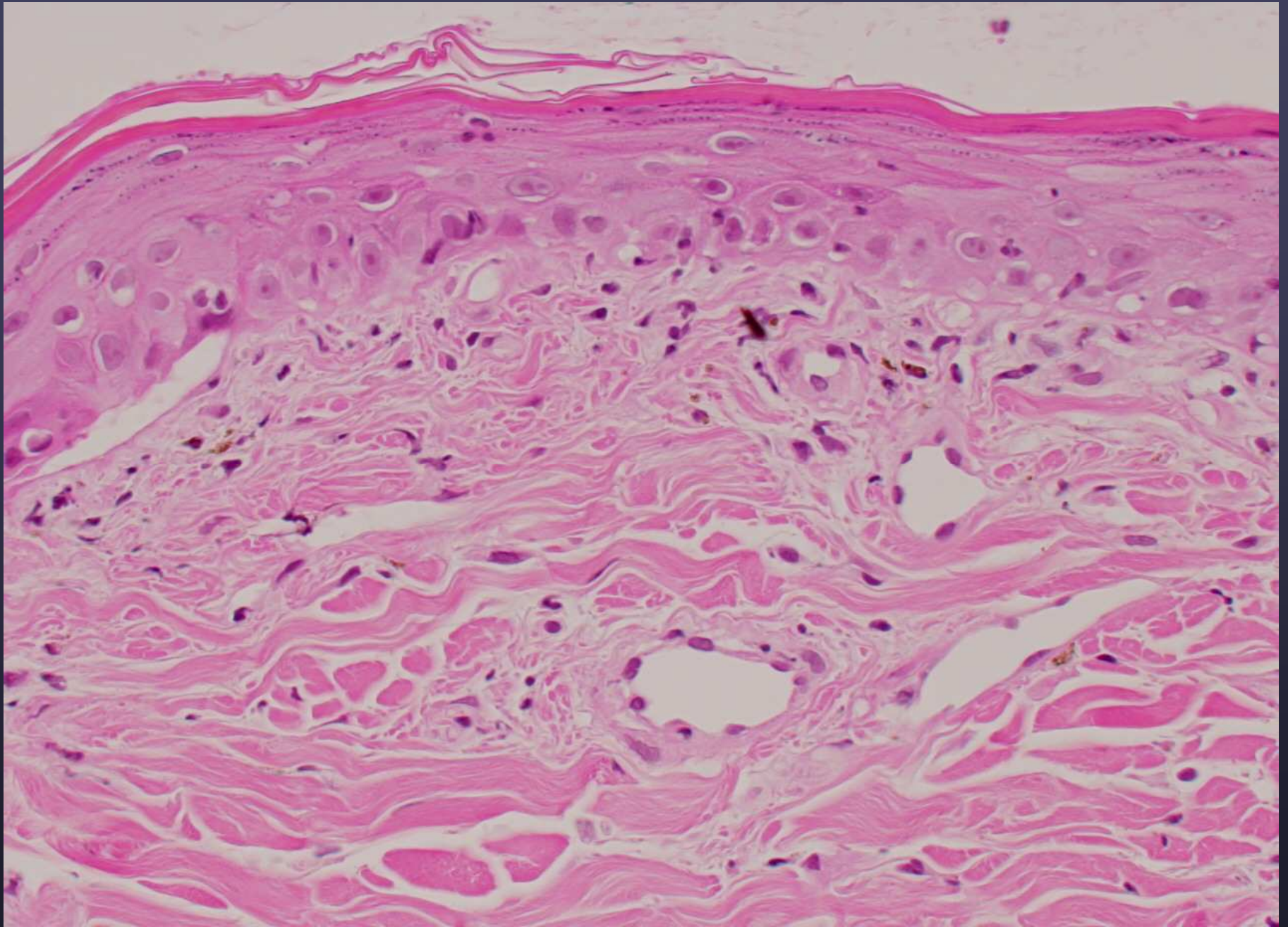
*DM- faded follicle with prominent glassy membrane*





*DM: Cell poor interface with clefting and necrotic basal cells*





DM





*More typical DM in a Sheltie*





*DM- vesicles are exceedingly rare, often periocular and muzzle alopecia/hyper or hypopigmentation and mild scale*

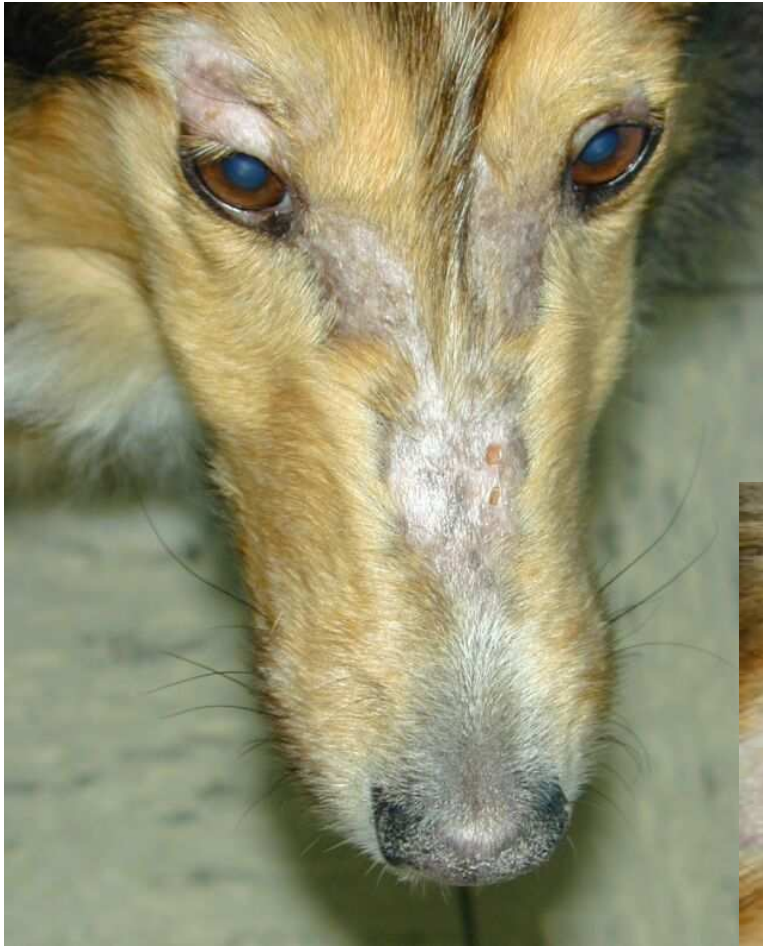


# Dermatomyositis



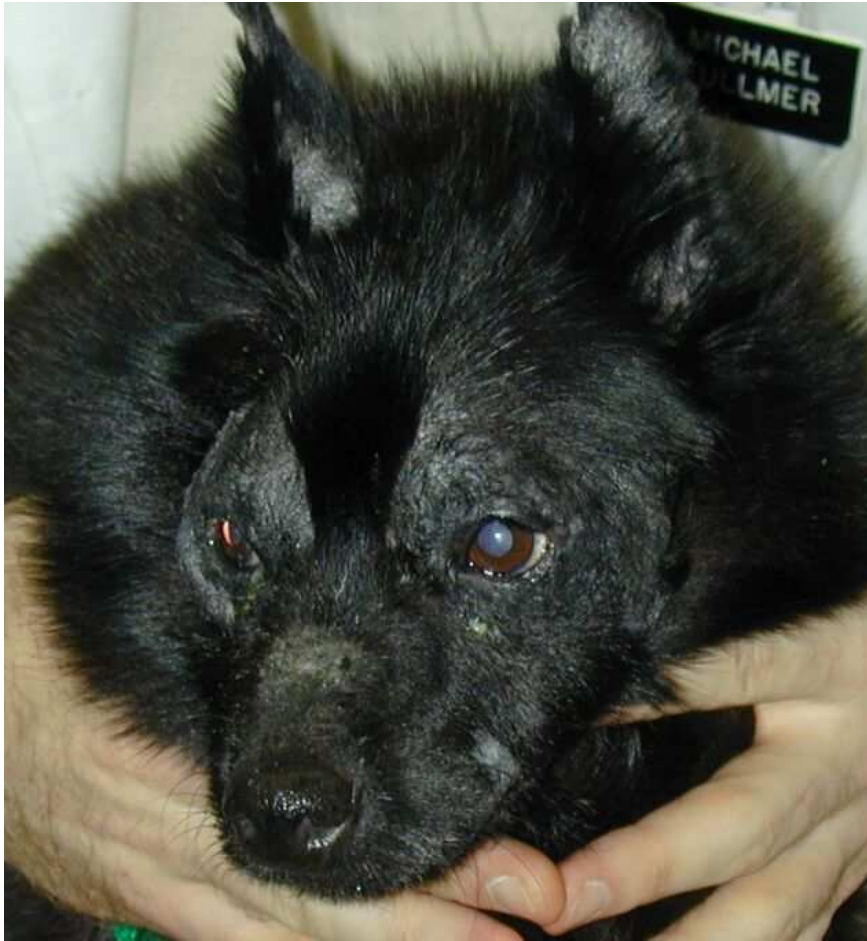
*Dog developed cruciate rupture on corticosteroids*



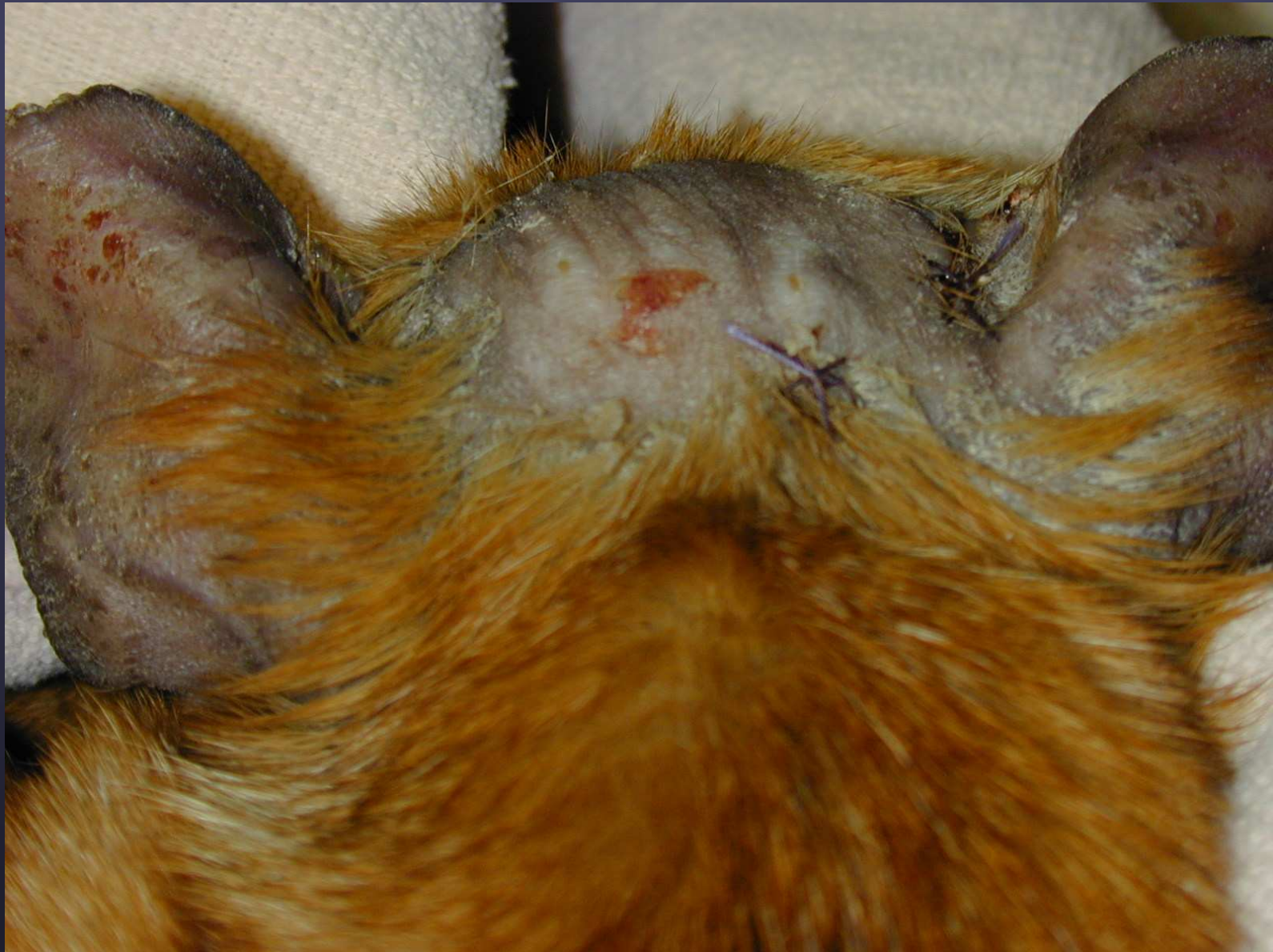


Familial dermatomyositis





Nonfamilial DM/ischemic dermatopathy



*Post-vaccinal ischemic dermatopathy*





*Post-vaccinal ischemic dermatopathy*

# Familial in collies and shelties

- Juvenile-onset; rarely adult-onset cases
- cell poor interface- scattered apoptotic basal keratinocytes with mild vacuolar change (also seen in ORS)
- hair follicles- severe atrophy with prominent glassy membrane
- Smudged dermal collagen  
Myositis occasional



# Ischemic Dermatopathy

- Localized vaccine reaction (rabies) with panniculitis
  - Dermal/epidermal changes like dermatomyositis
  - Panniculitis- lymphoplasmacytic with lymphoid follicles with foamy macrophages +/- blue-gray vaccine product



Rabies vaccine-associated localized ischemic dermatopathy

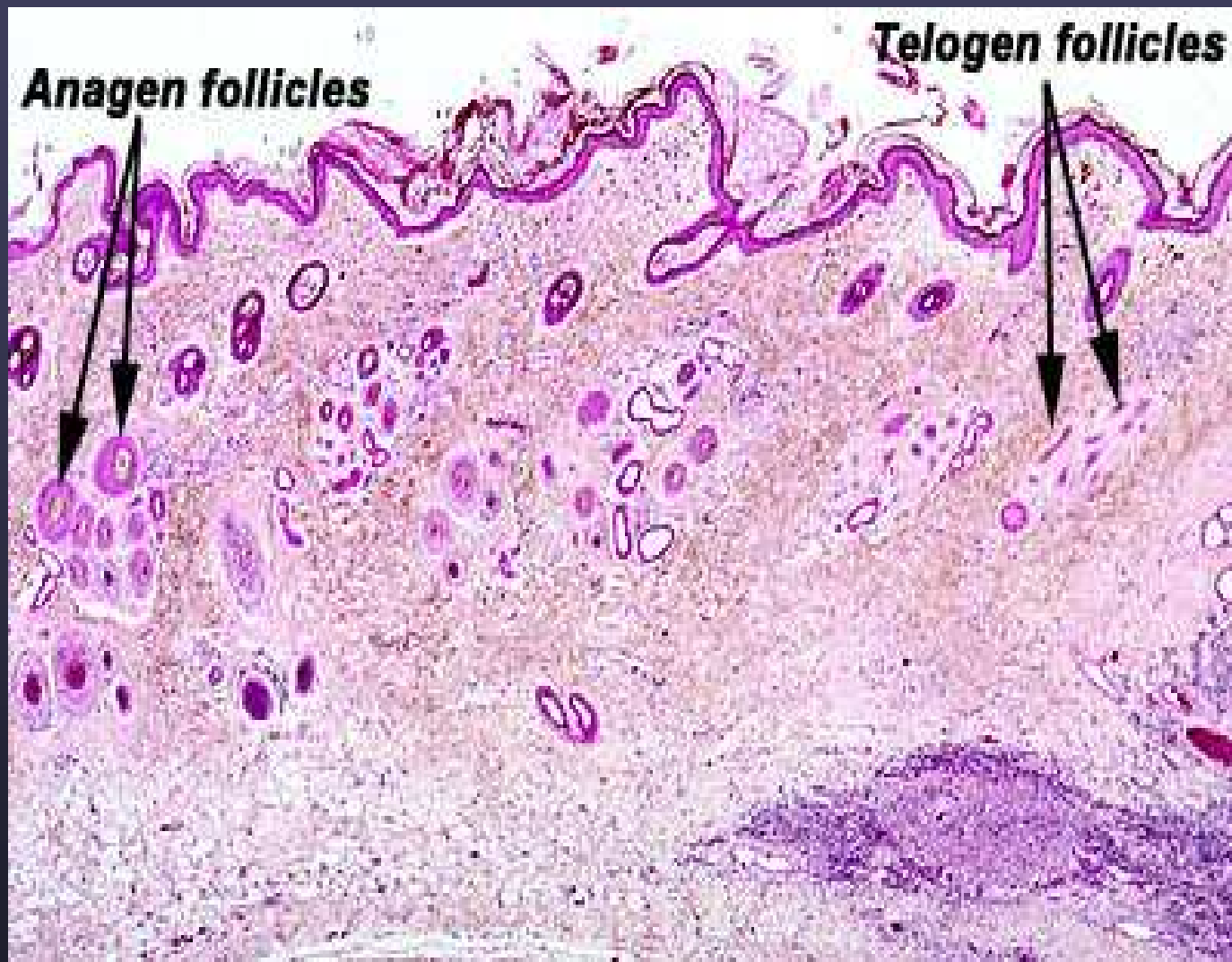


- Generalized/extremities
  - Lesions identical to DM
  - May be post-vaccinal (lacks panniculitis)



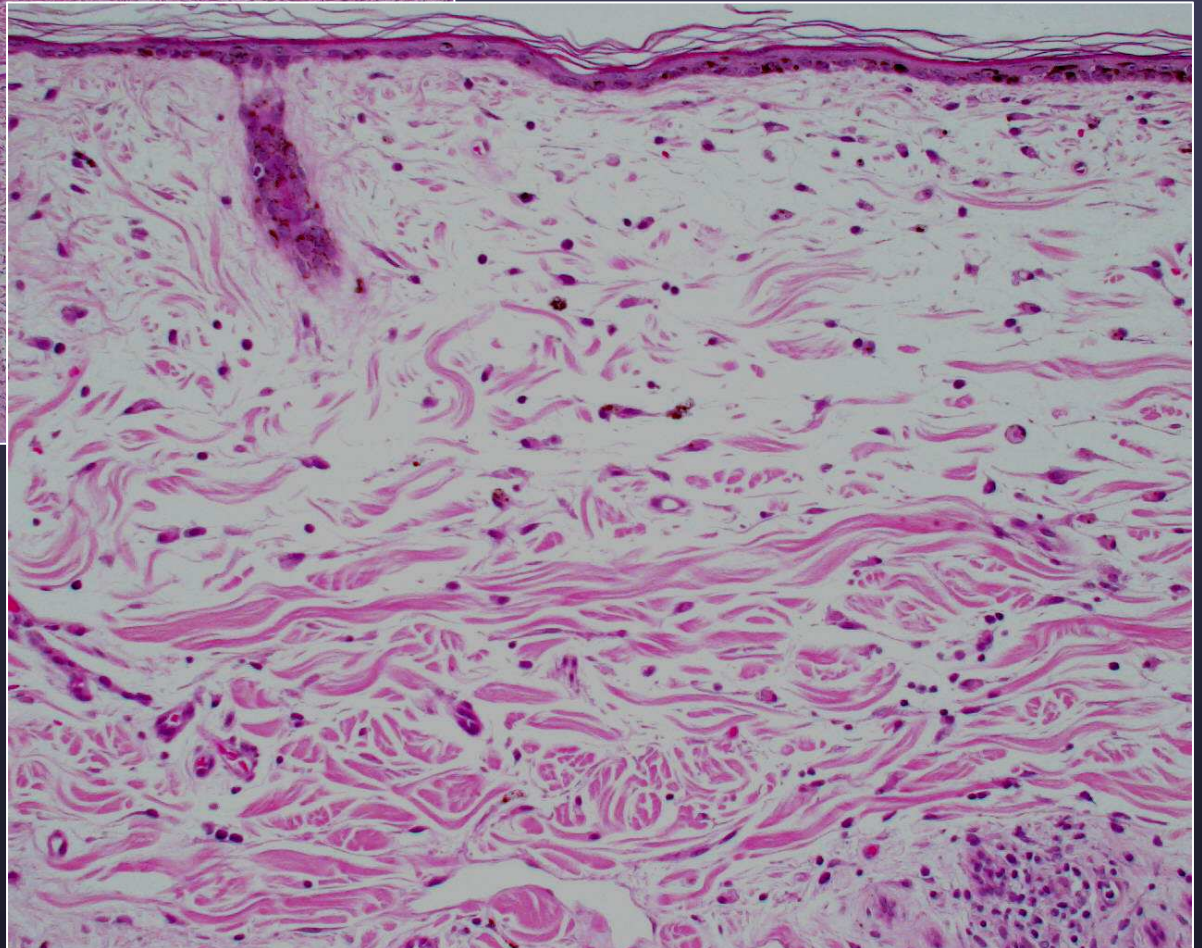
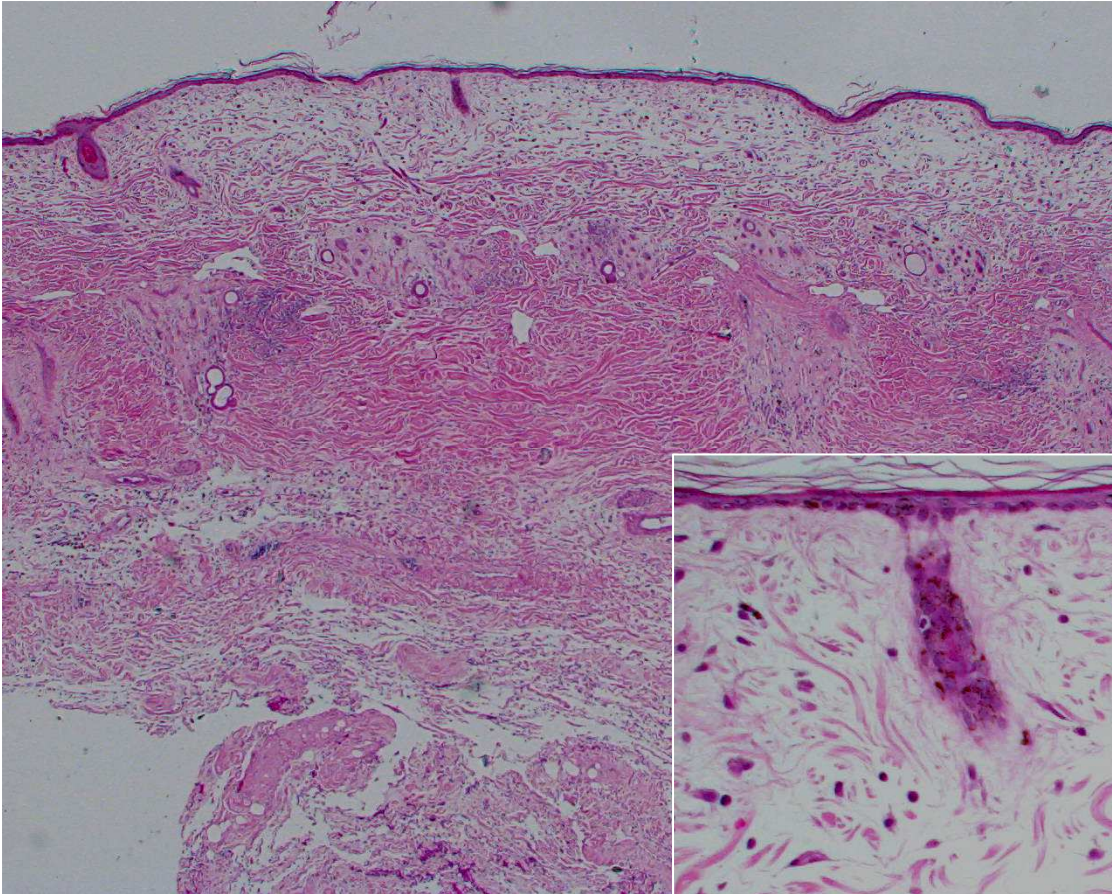
Rabies-vaccine rxn: panniculitis with severe follicular atrophy





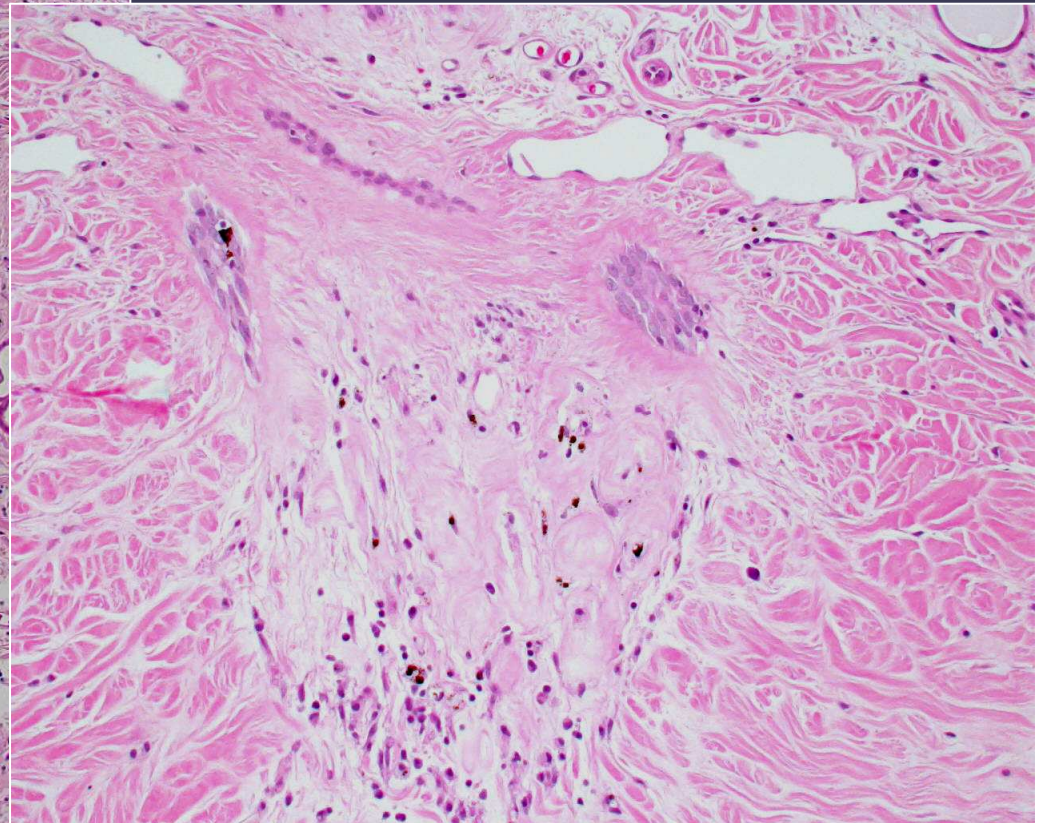
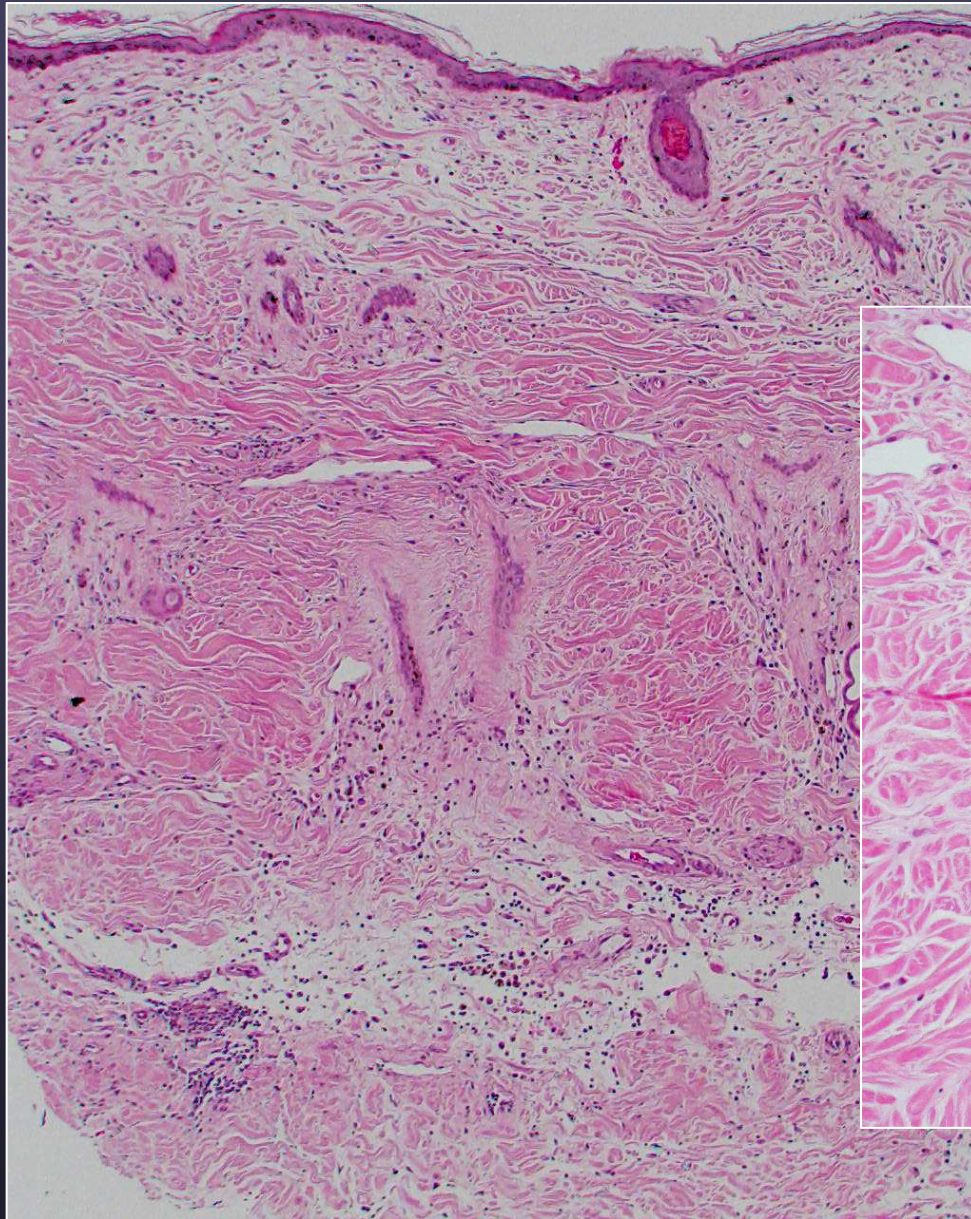
*Rabies vaccine reaction*

# Injection Site Alopecia



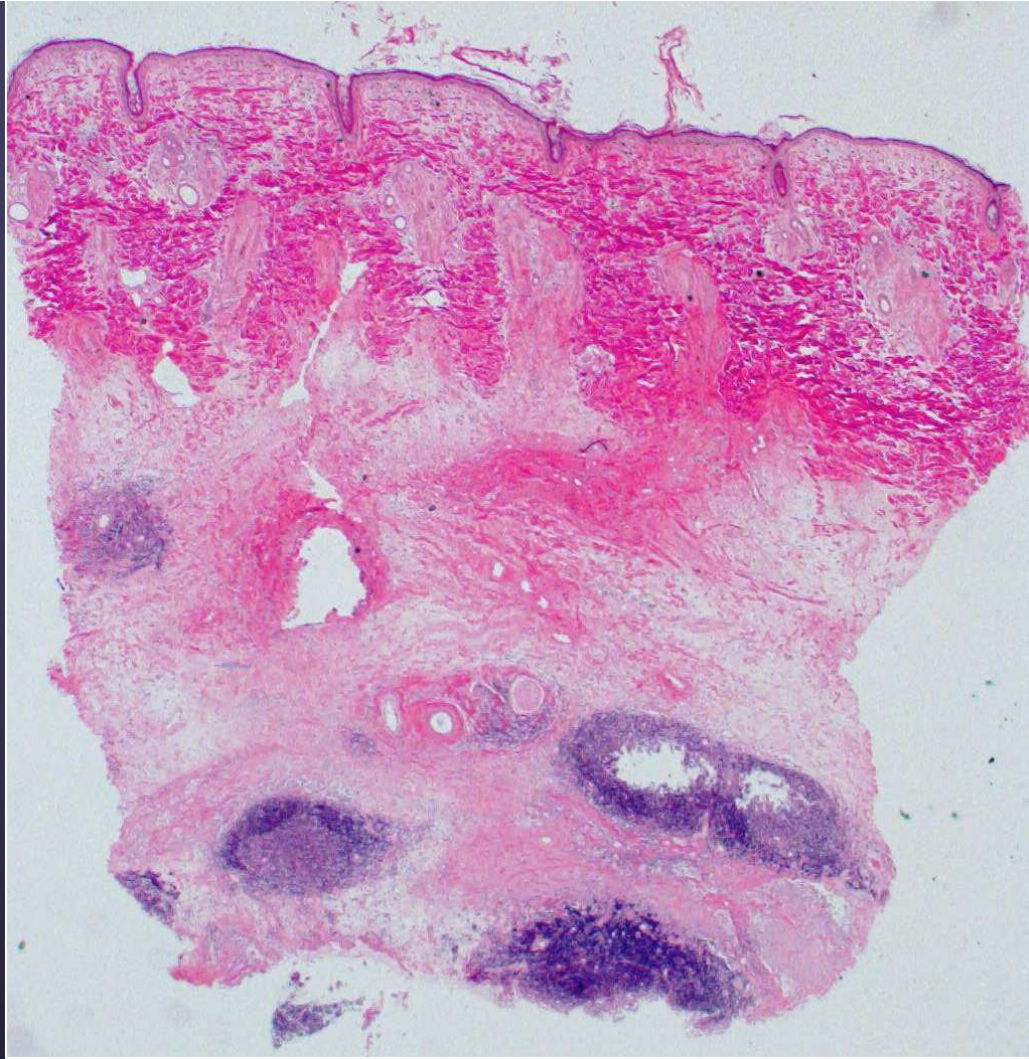
*Rabies-vaccine associated*



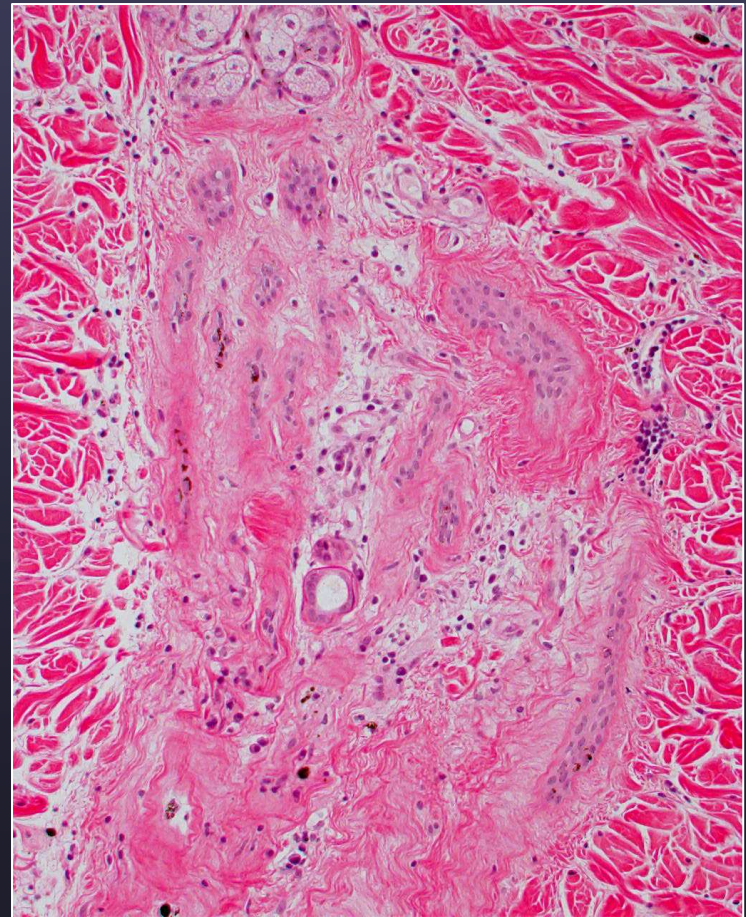


*Rabies reaction- histopath resembles DM*





# Injection Site Alopecia







*Dog with generalized ischemic dermatopathy  
associated with rabies vaccine rxn*



Ischemic dermatopathy



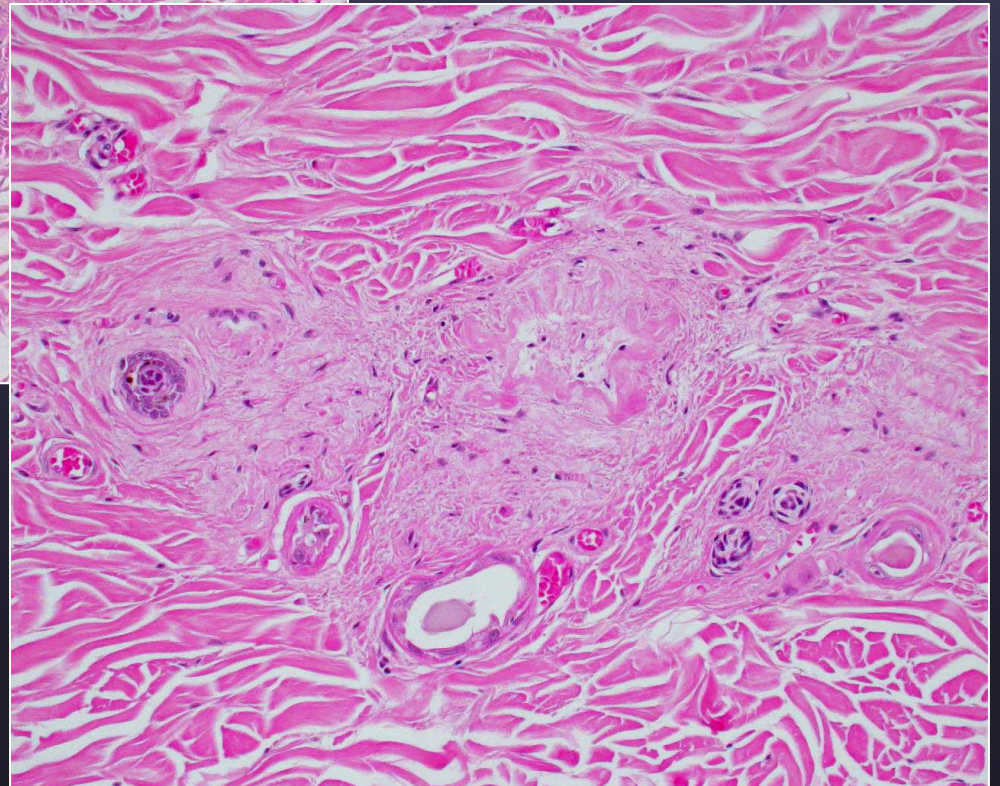
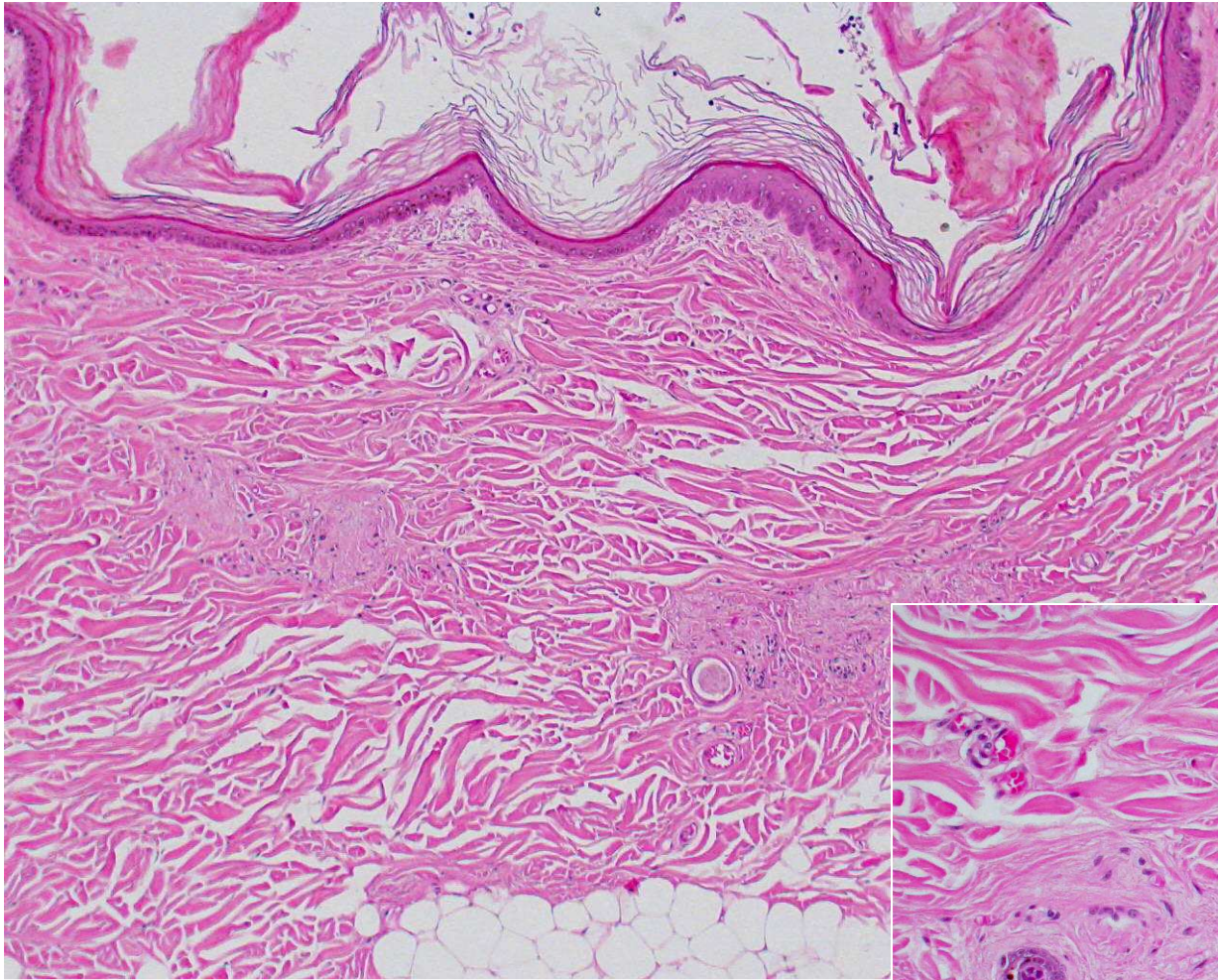


Alopecia at vaccine site

Ischemic dermatopathy







*Profound follicular atrophy*



# Idiopathic Ulcerative dermatosis of Collies and Shelties (cutaneous vesicular LE)

- Adult-onset
- Transient vesicles with large ulcers on abdomen/inguinal area/axilla
- lesions on mucous membranes/pinna less common
- Hydropic basal cell change with scattered keratinocyte apoptosis and cleft/vesicle formation; also affects outer root sheaths
- may have mild to moderate lichenoid lymphocytic infiltrate



Vesicular lupus (aka ulcerative dermatosis) of Collie and Sheltie





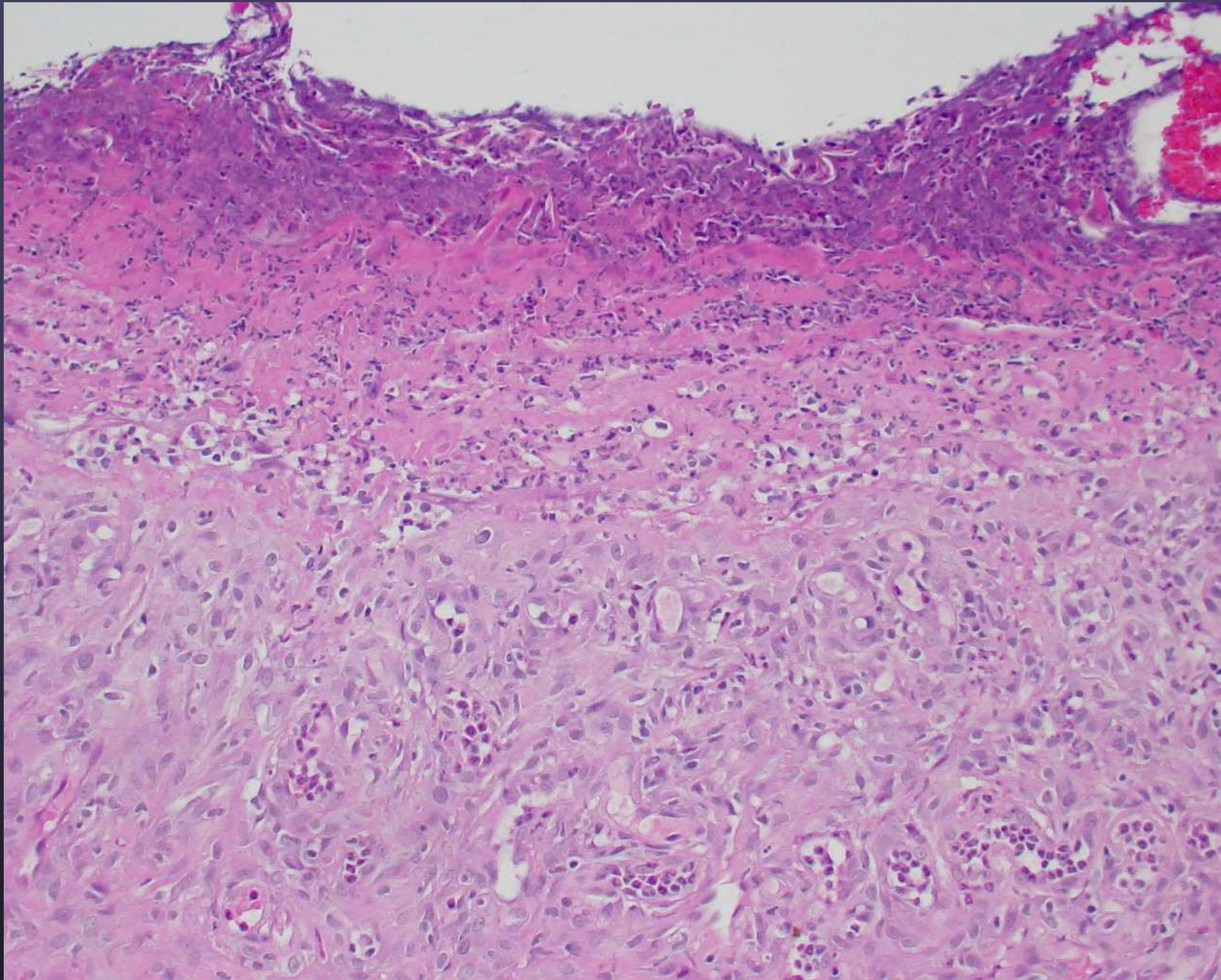
Vesicular lupus (aka ulcerative dermatosis) of Collie and Sheltie





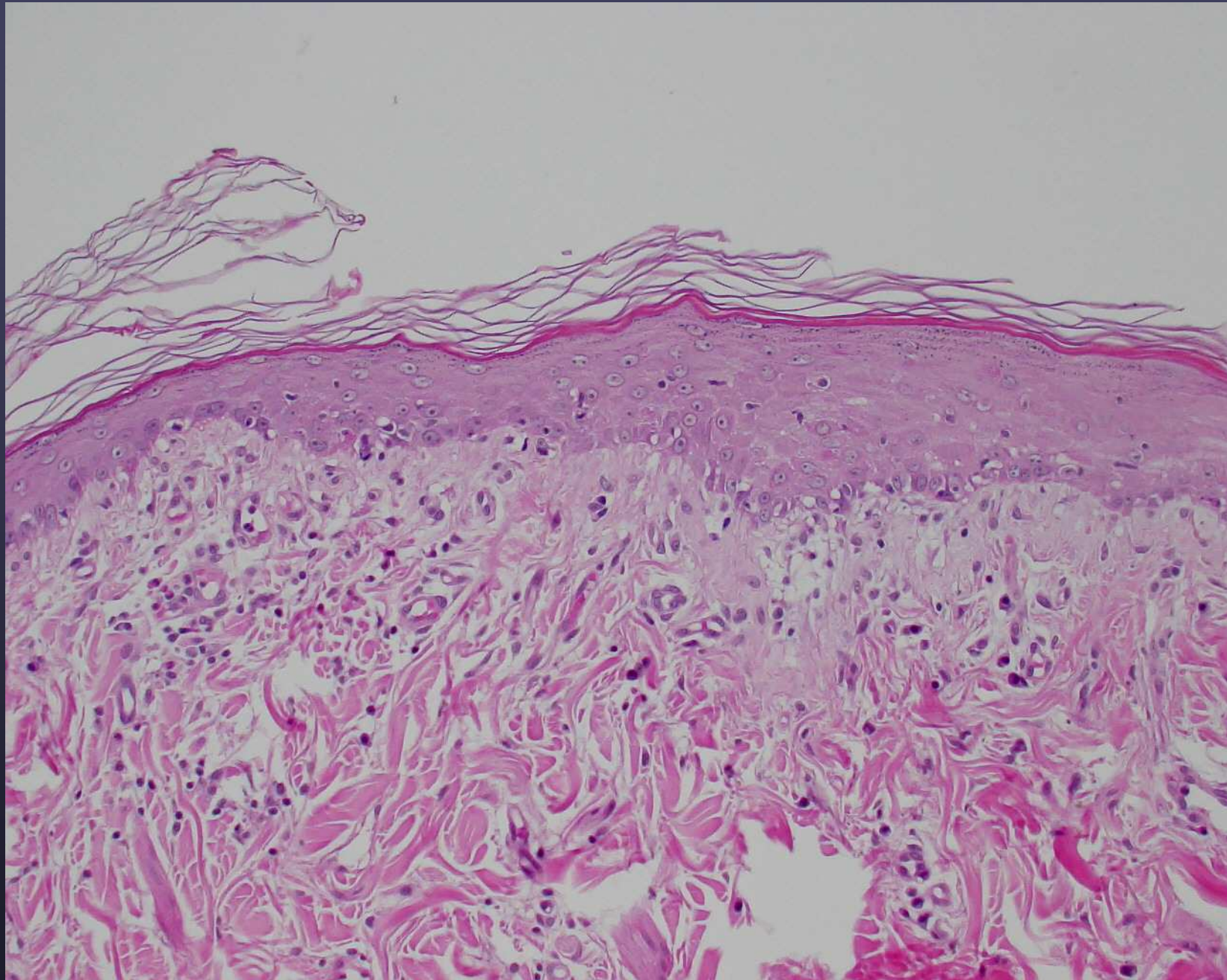
Vesicular lupus (aka ulcerative dermatosis) of Collie and Sheltie





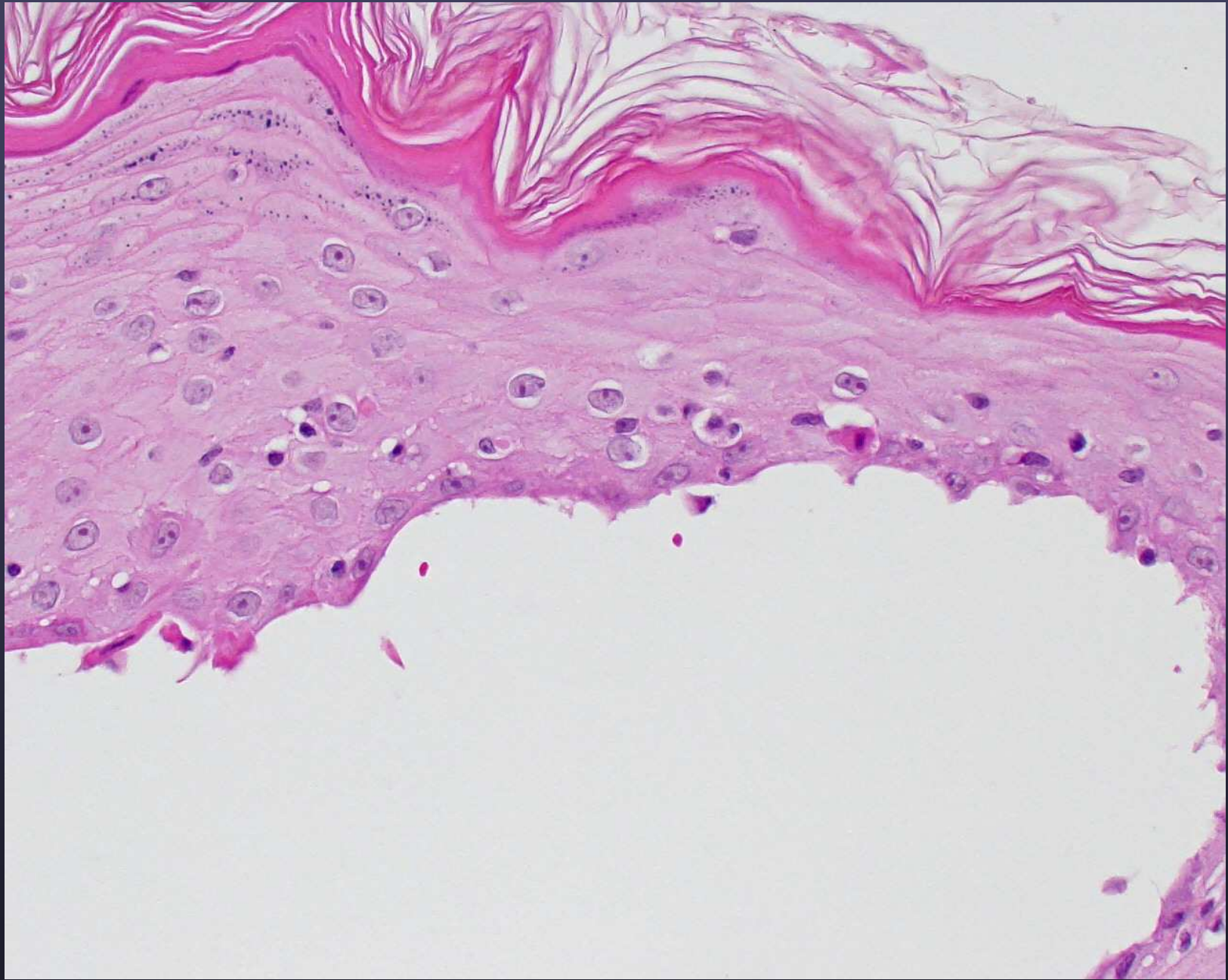
*Ulcer- may be better to use elliptical biopsies*



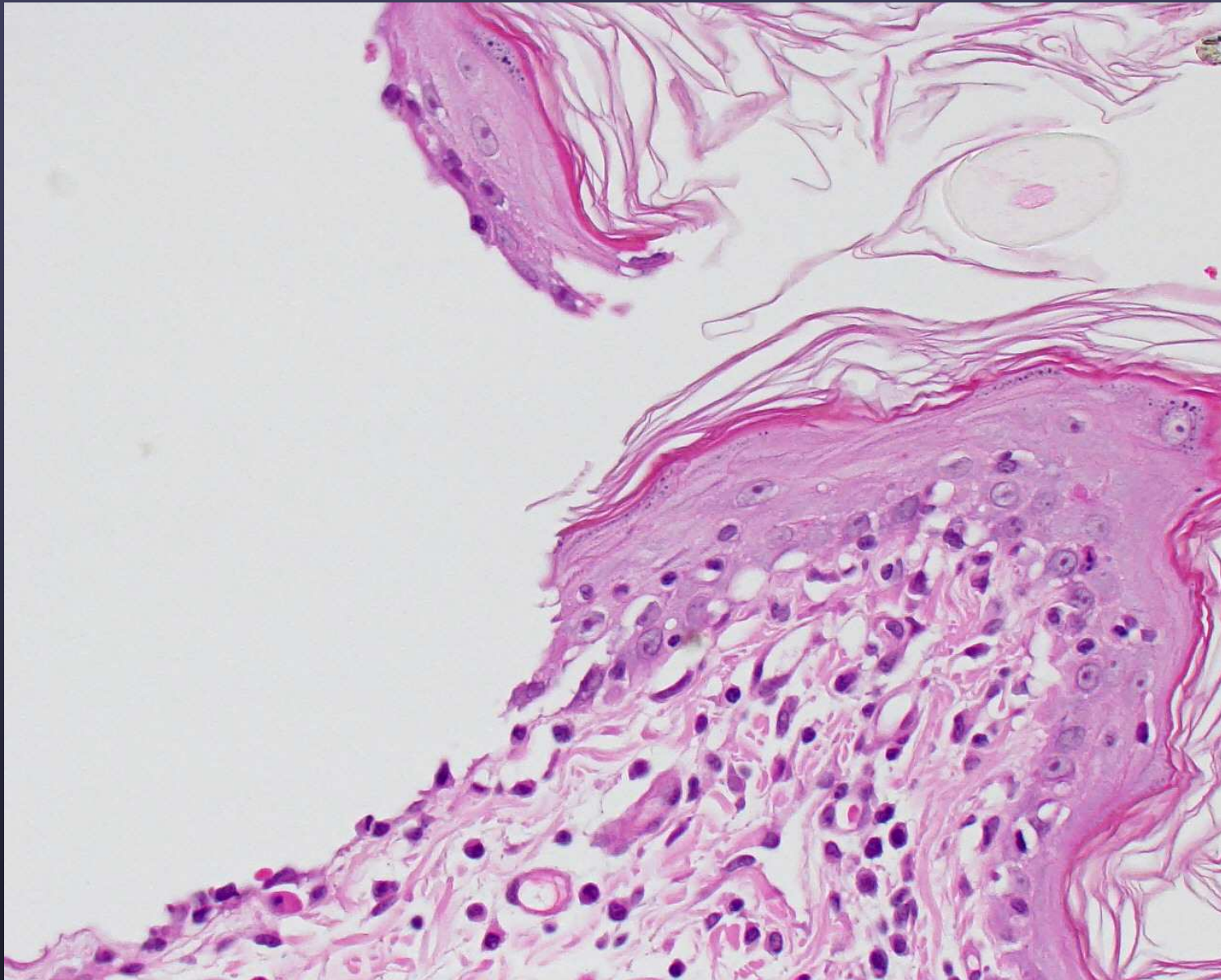


*Vesicular lupus- cell poor interface*



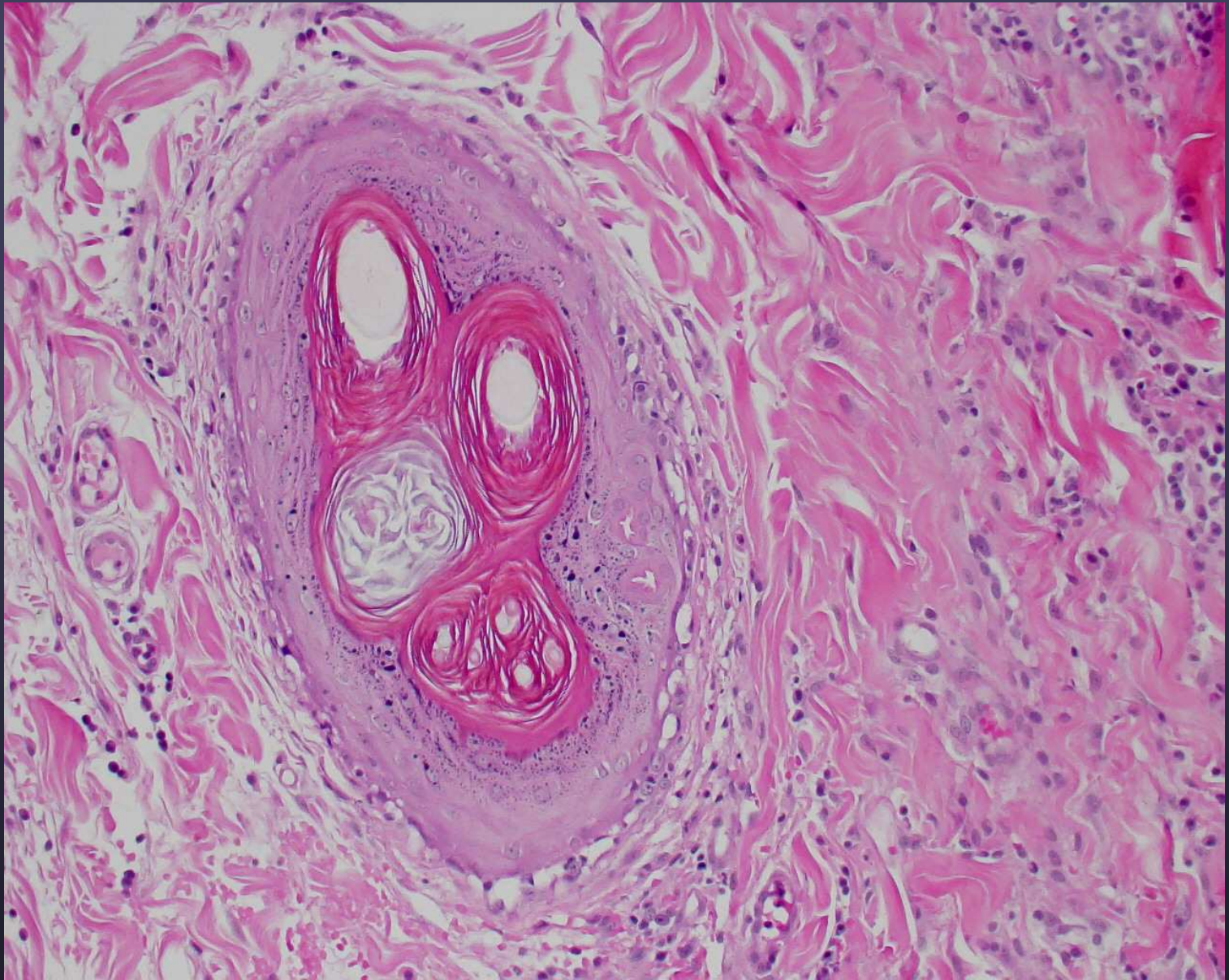


*Cell poor interface with clefting in vesicular lupus*



*Cell poor interface with clefting in vesicular lupus*





*Vesicular lupus: Hair follicle with cell poor interface*

## Lupoid dermatosis of GSP (cutaneous exfoliative lupus erythematosus)

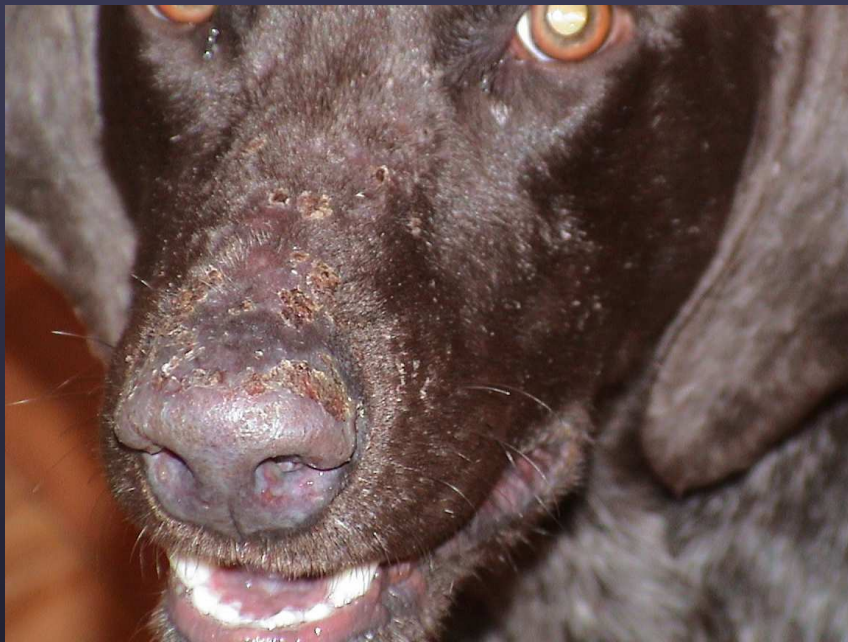
- Identified as early as 6-8 weeks of age
- Begins with scaling→ erythema, hair loss, large plate-like adherent scale with atrophy and erosions
- Joint pain (shifting leg lameness, and crouched stance)
- Progresses to generalized and severe Peripheral lymphadenopathy



# Histopathology of Lupoid Dermatositis

- Basal cell apoptosis and vacuolar change that also affects ORS
- progresses to sebaceous gland loss; dermal scarring and permanent hair loss
- apoptosis can occur in all epidermal layers and resemble erythema multiforme

# GSD Lupoid Derm



*Early onset- becomes more severe with time*



# GSP Lupoid Derm (cutaneous exfoliative lupus erythematosus)



April 2004

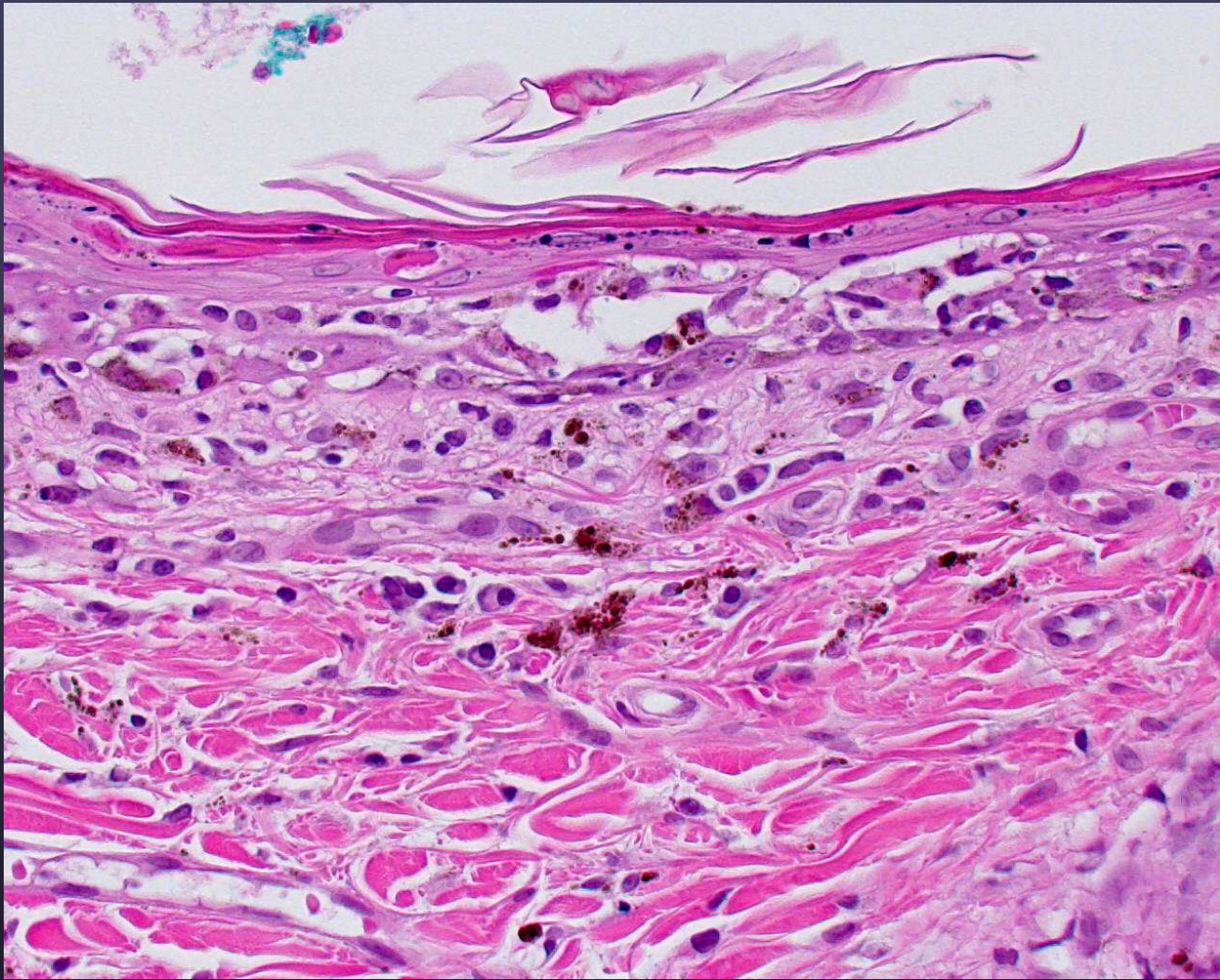
# GSP Lupoid Derm

(cutaneous exfoliative lupus erythematosus)



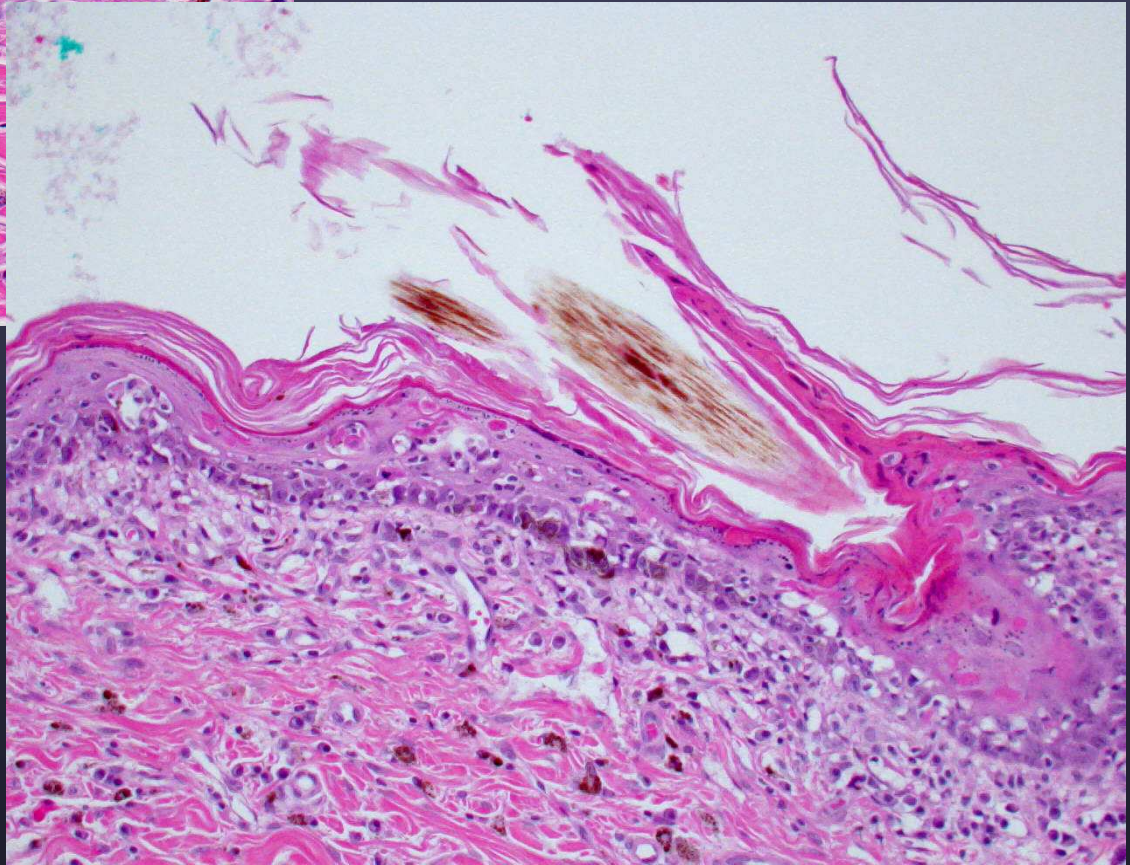
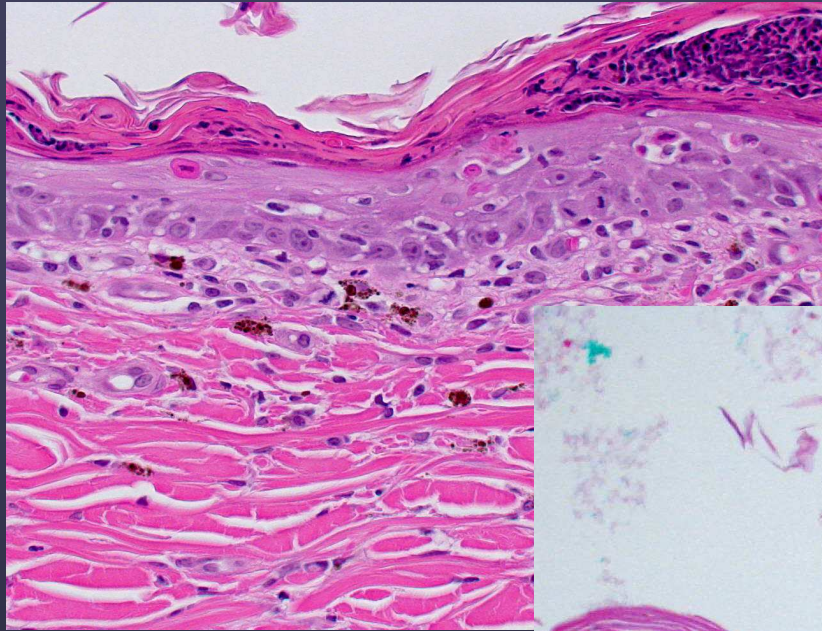
April 2004





*Exfoliative vesicular lupus of GSP*





*Exfoliative vesicular lupus of GSP*



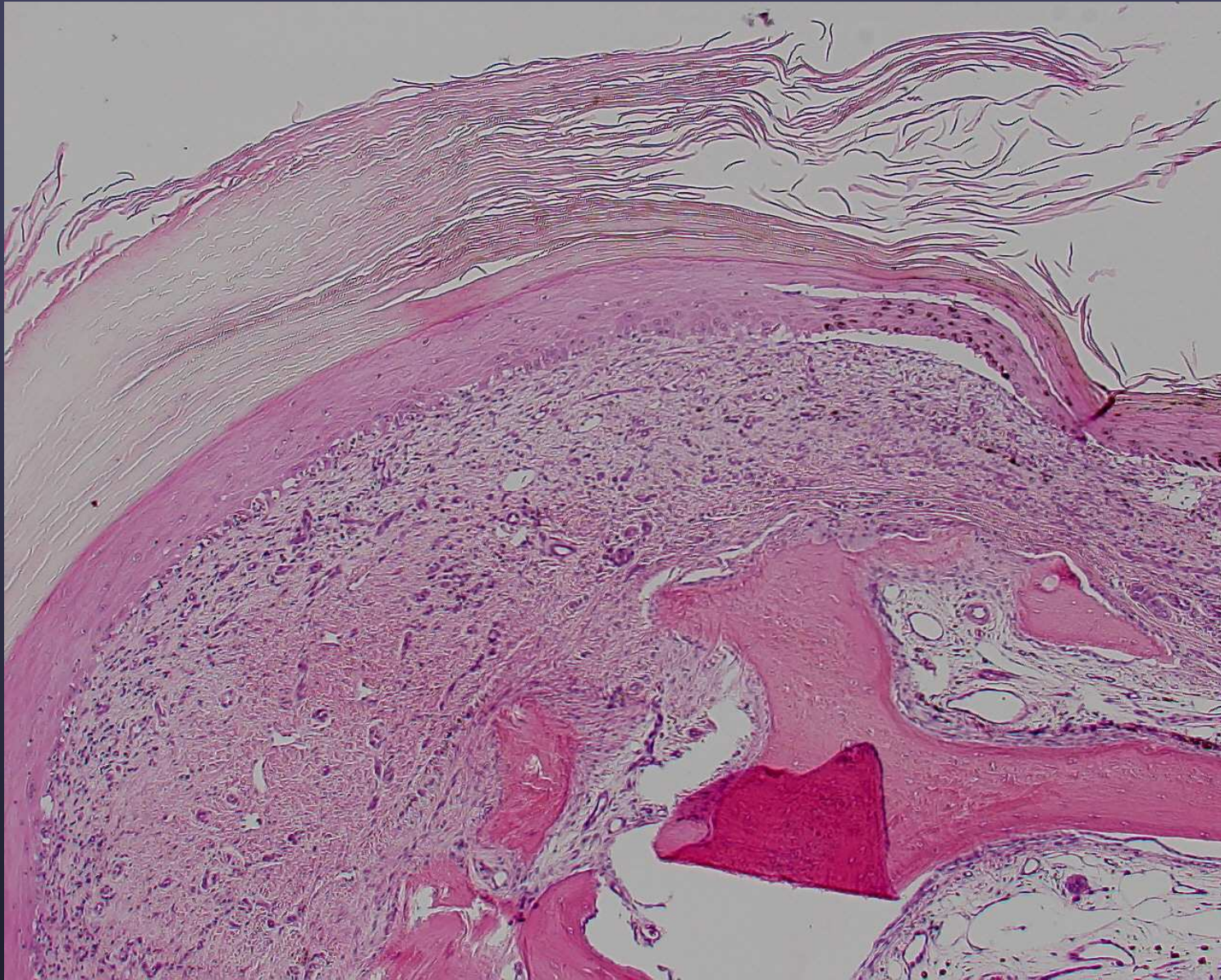


*Lupoid onychitis*



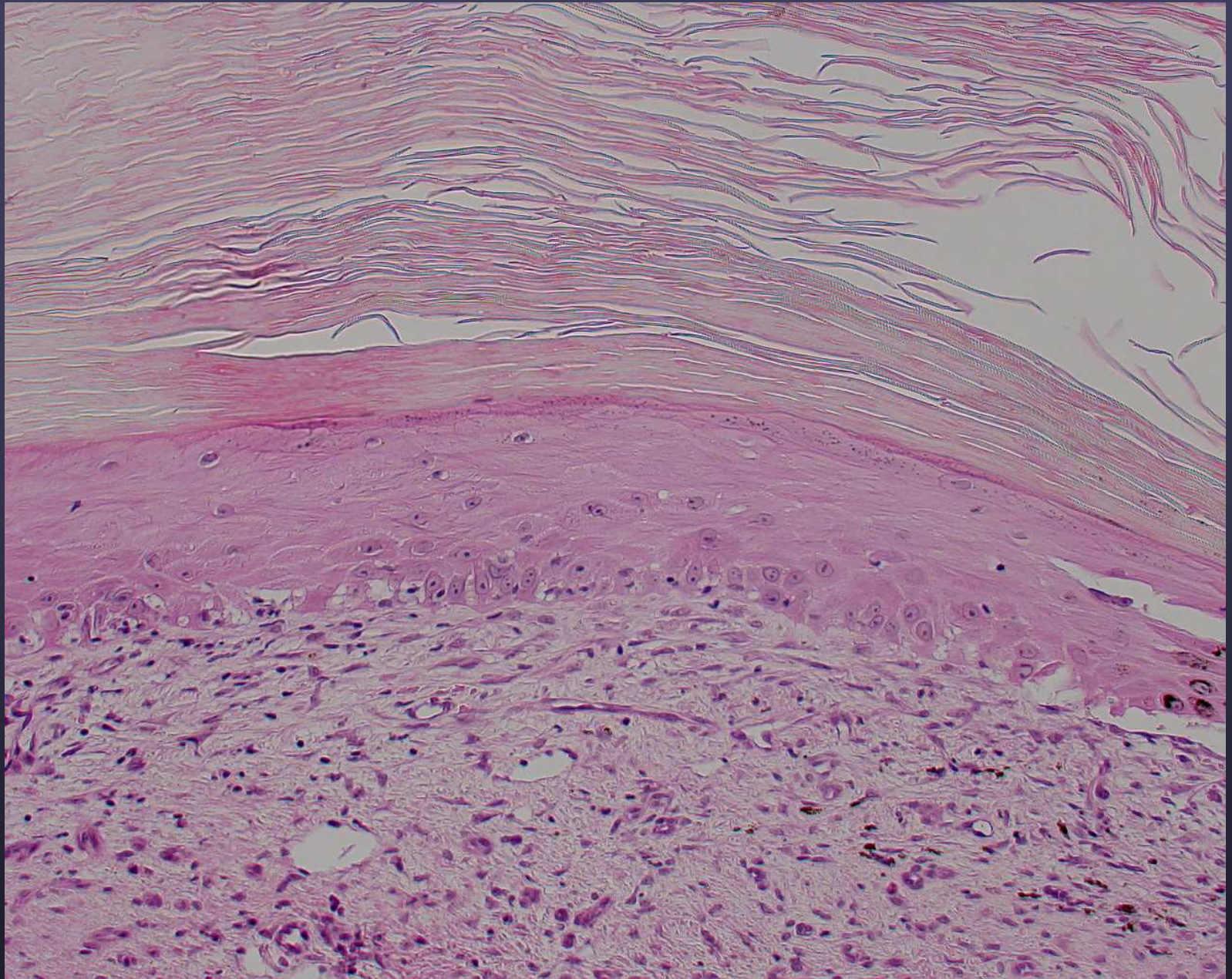
*Lupoid onychitis*





*Lupoid onychitis*





*Lupoid onychitis: Interface dermat with clefting*



# Symmetric Lupoid Onychodystrophy (Onychitis)

- Aka “SLO”
- Interface rxn of claw folds only
- Characteristic clinical presentation
  - “10 nail dz”
  - Sloughing, brittle, soft nails

# Lupoid onychodystrophy (Idiopathic Onychomadesis)

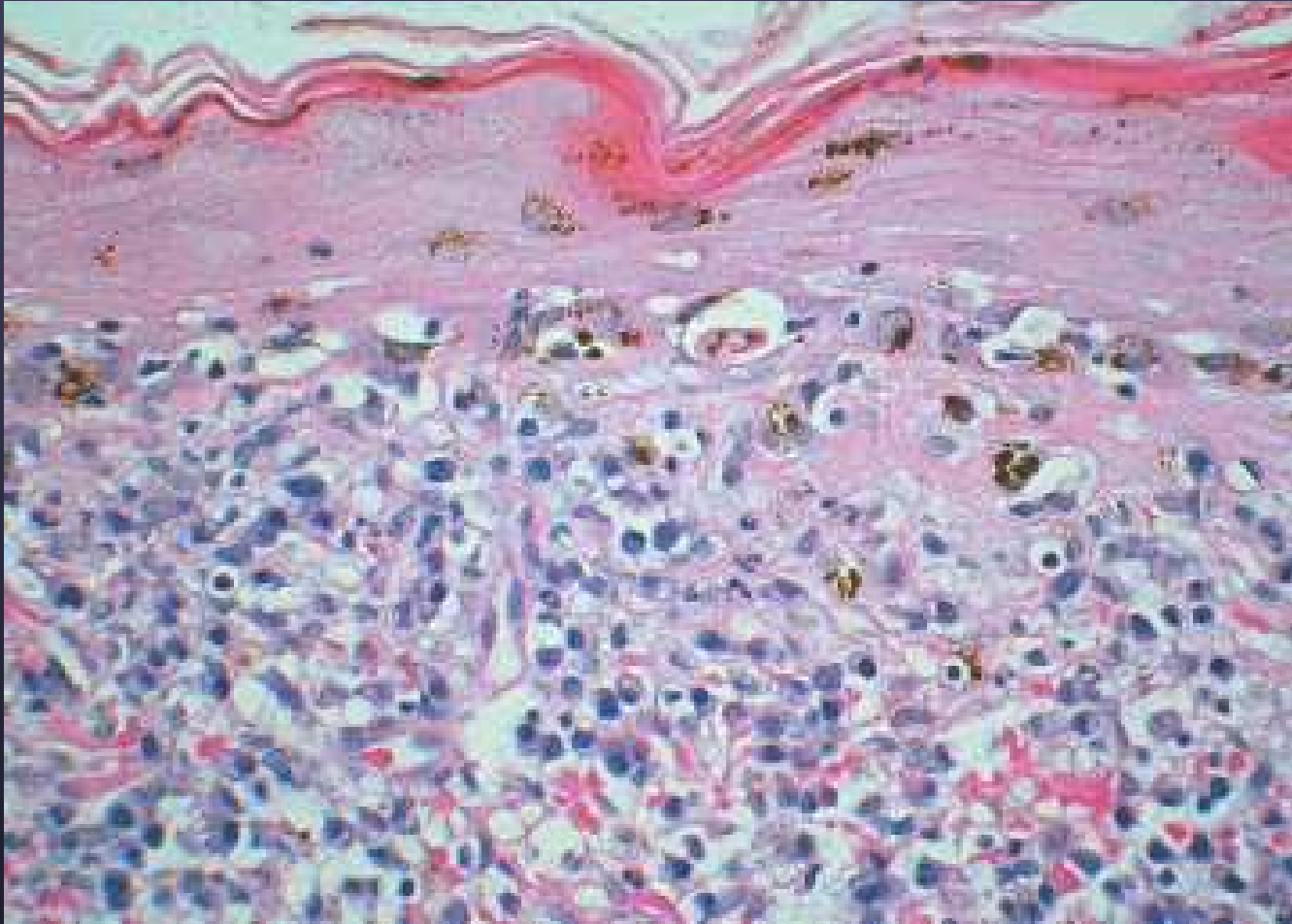
- Sudden onset onychomadesis
- Multiple nails
- Brittle, deformed, nails
- +/- pain, lameness
- GSD predisposed



**onychomadesis**



# Lichenoid





*Idiopathic lichenoid dermatosis*





*Idiopathic lichenoid dermatosis*

# Lichenoid dermatosis

- Seen in Labradors and few other breeds
- Hyperkeratotic plaques – often on face can be truncal or abdomen
- Histopath- lymphoplasmacytic lichenoid dermatitis with prominent parakeratotic hyperkeratosis