Corneal Dystrophies and Simulating Lesions

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OF NEUROPATHOLOGISTS

Disclosures

- I have no relevant financial relationships to disclose

Learning Objectives

- Learning Objective #1
  - Classify key corneal dystrophies
- Learning Objective #2
  - Identify pertinent clinical and pathologic features of key corneal dystrophies
- Learning Objective #3
  - Distinguish key corneal dystrophies from simulating dystrophic, degenerative, and neoplastic disease processes

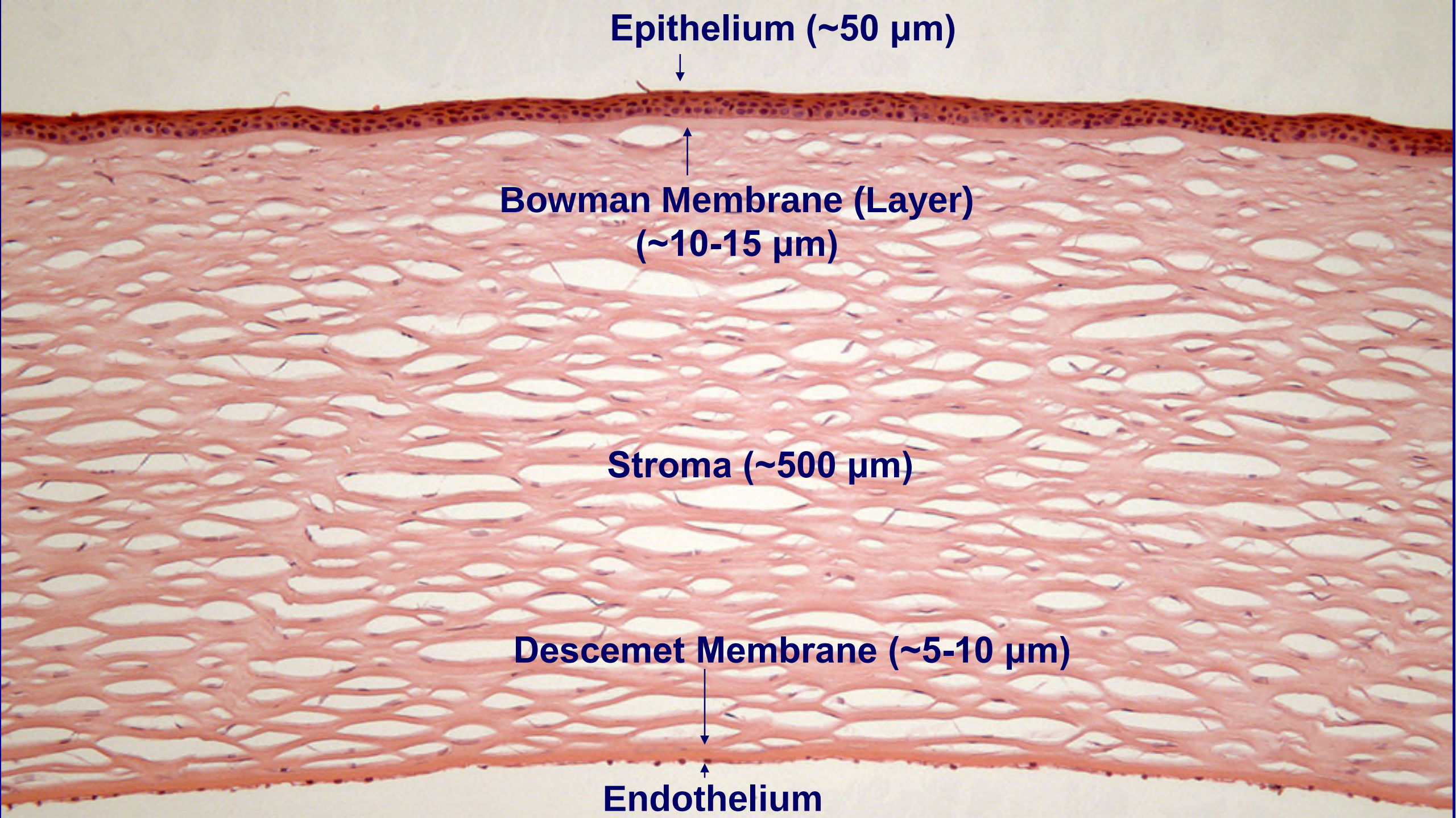
Corneal dystrophies and simulating lesions

I. Normal histology

II. Dystrophies

- Epithelial and subepithelial dystrophies
- Epithelial-stromal TGFBI dystrophies
- Stromal dystrophies
- Endothelial dystrophies

III. Virtual slides


Epithelium (~50 µm)
Bowman Membrane (Layer)
(~10-15 µm)
Stroma (~500 µm)
Descemet Membrane (~5-10 µm)
Endothelium

keratocyte

stromal lamellae

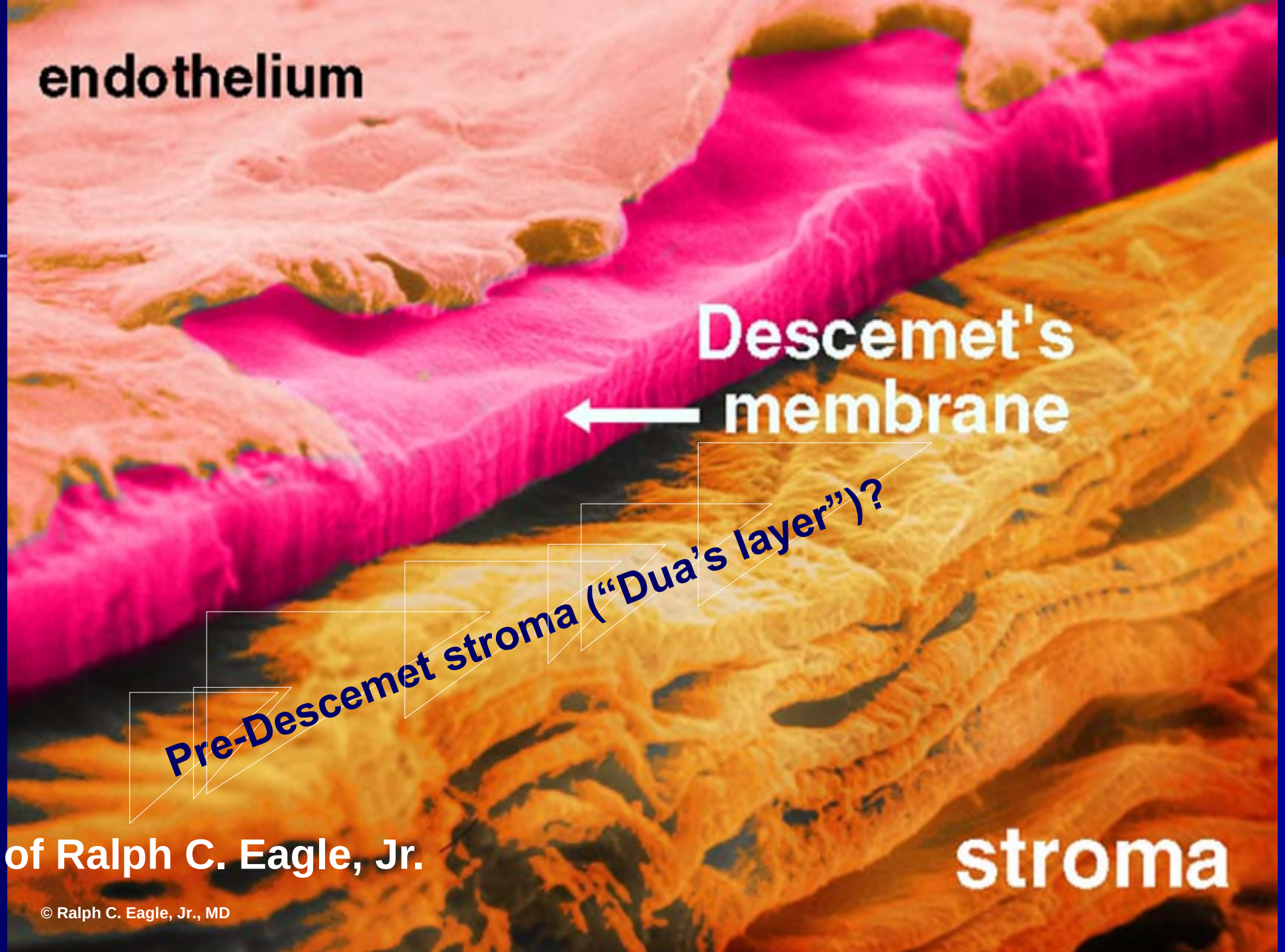
Bowman's membrane stroma – Dua's layer

Descemet membrane

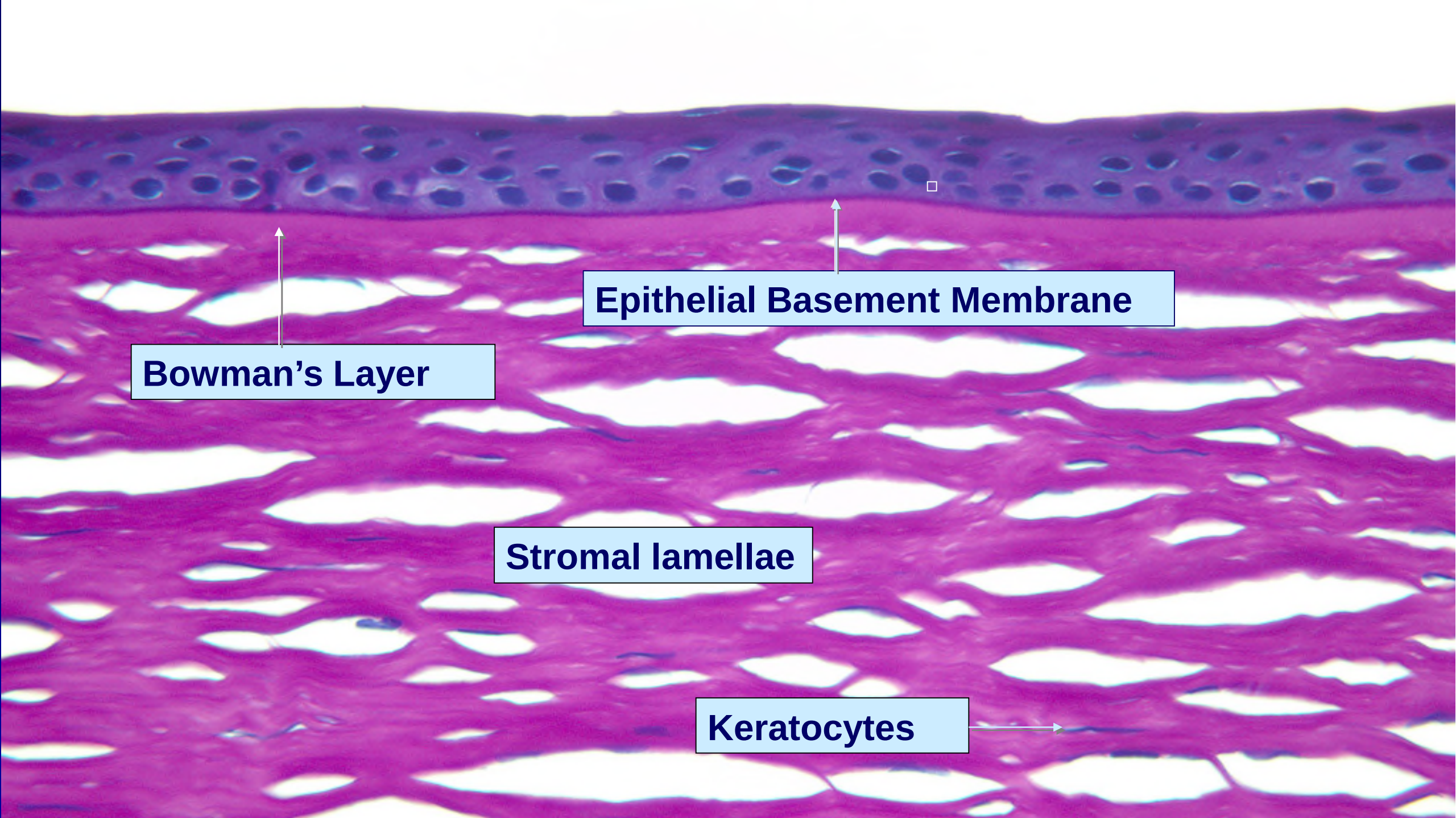
endothelium

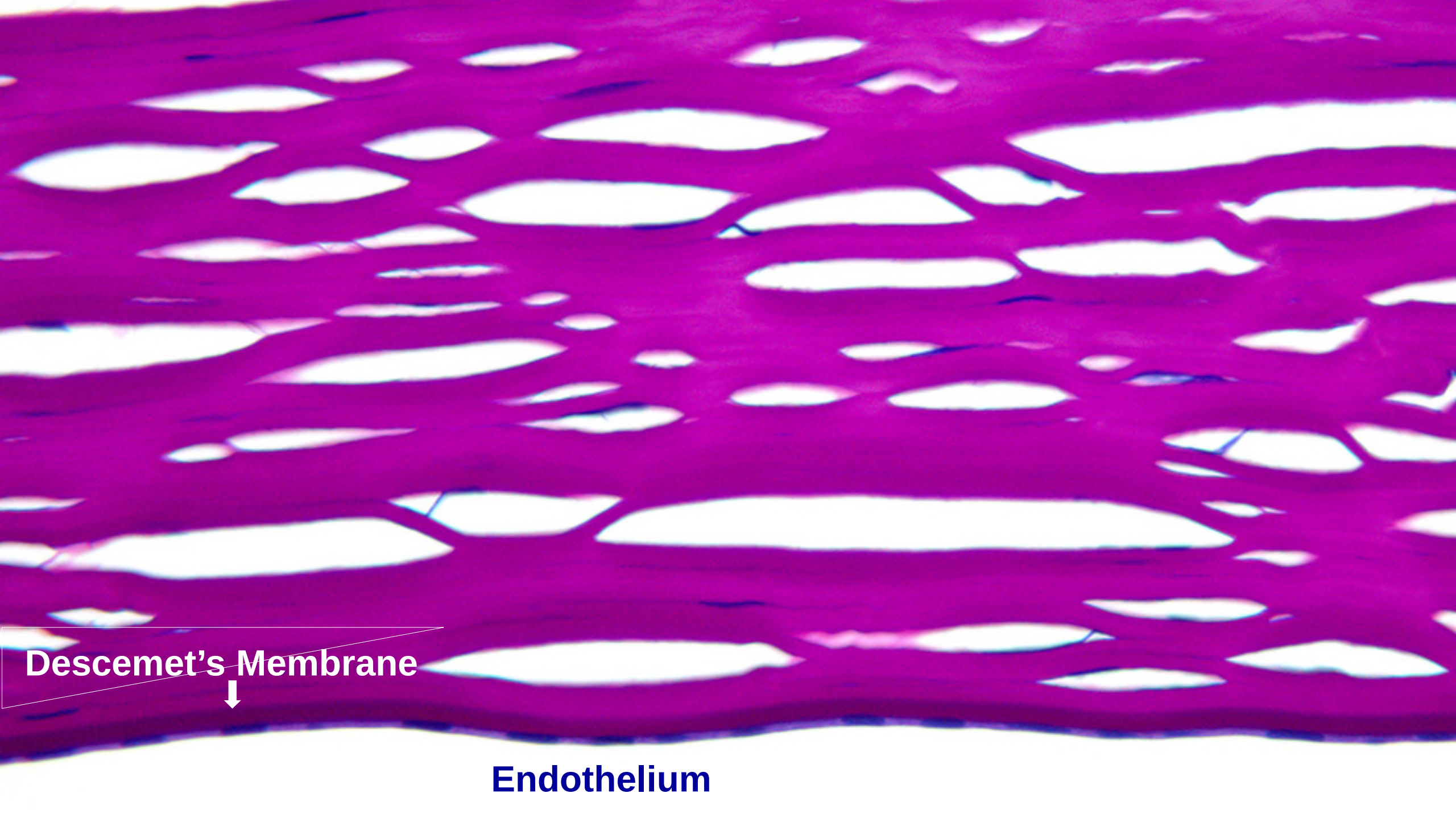
6

Courtesy of Ralph C. Eagle, Jr.

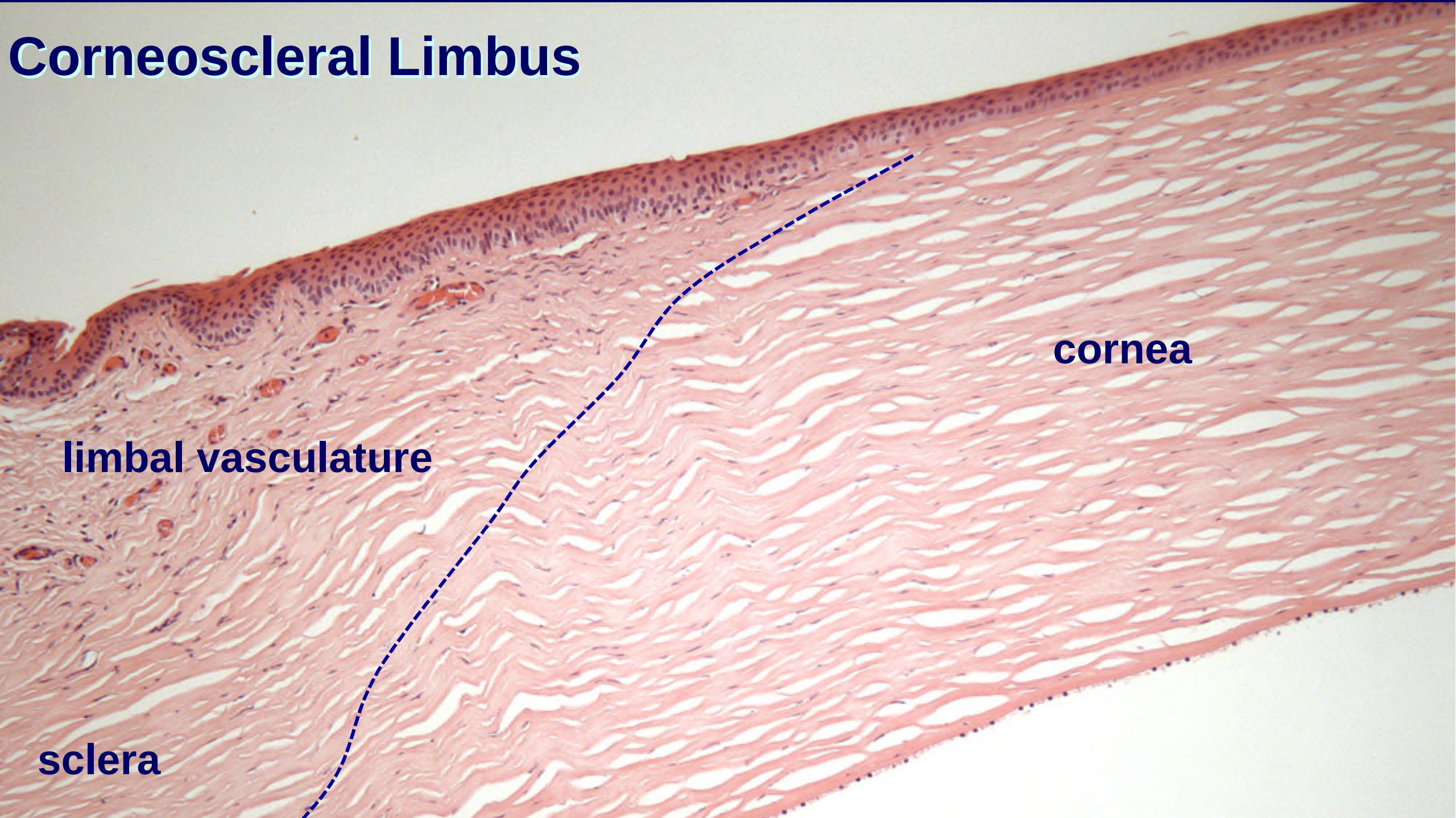


Courtesy of Ralph C. Eagle, Jr.


Epithelial Basement Membrane
Bowman’s Layer
Stromal lamellae
Keratocytes


Descemet’s Membrane
Endothelium

Corneoscleral Limbus



Corneal dystrophies and simulating lesions

I. Normal histology

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- Epithelial-stromal TGFBI dystrophies
- Stromal dystrophies
- Endothelial dystrophies

III. Virtual slides

IC3D Classification of Corneal Dystrophies—Edition 2

Jayne S. Weiss, MD, Hans Ulrik Møller, MD, PhD,† Anthony J. Aldave, MD,‡ Berthold Seitz, MD,§ Cecilie Bredrup, MD, PhD,¶ Tero Kivelä, MD, FEBO,‖ Francis L. Munier, MD,** Christopher J. Rapuano, MD,†† Kanwal K. Nischal, MD, FRCOphth,‡‡ Eung Kweon Kim, MD, PhD,§§ John Sutphin, MD,¶¶ Massimo Busin, MD,‖‖ Antoine Labbé, MD,*** Kenneth R. Kenyon, MD,††† Shigeru Kinoshita, MD, PhD,‡‡‡ and Walter Lisch, MD§§§*

Cornea 2015 Feb;34(2):117-59. doi: 10.1097/ICO.0000000000000307.

Purpose: To update the 2008 International Classification of Corneal Dystrophies (IC3D) incorporating new clinical, histopathologic, and genetic information.

Methods: The IC3D reviewed worldwide peer-reviewed articles for new information on corneal dystrophies published between 2008 and 2014. Using this information, corneal dystrophy templates and anatomic classification were updated. New clinical, histopathologic, and confocal photographs were added.

actually includes a number of potentially distinct epithelial dystrophies (Franceschetti corneal dystrophy, Dystrophia Smolandiensis, and Dystrophia Helsinglandica) but must be differentiated from dystrophies such as *TGFBI*-induced dystrophies, which are also often associated with recurrent epithelial erosions. The chromosome locus of Thiel-Behnke corneal dystrophy is only located on 5q31. The entity previously designated as a variant of Thiel-Behnke corneal dystrophy on chromosome 10q24 may represent a novel corneal dystrophy. Congenital hereditary endo-

The Cornea

I. Normal histology

II. Dystrophies

- Epithelial and subepithelial dystrophies
- Epithelial-stromal TGFBI dystrophies
- Stromal dystrophies
- Endothelial dystrophies

III. Keratoectasia

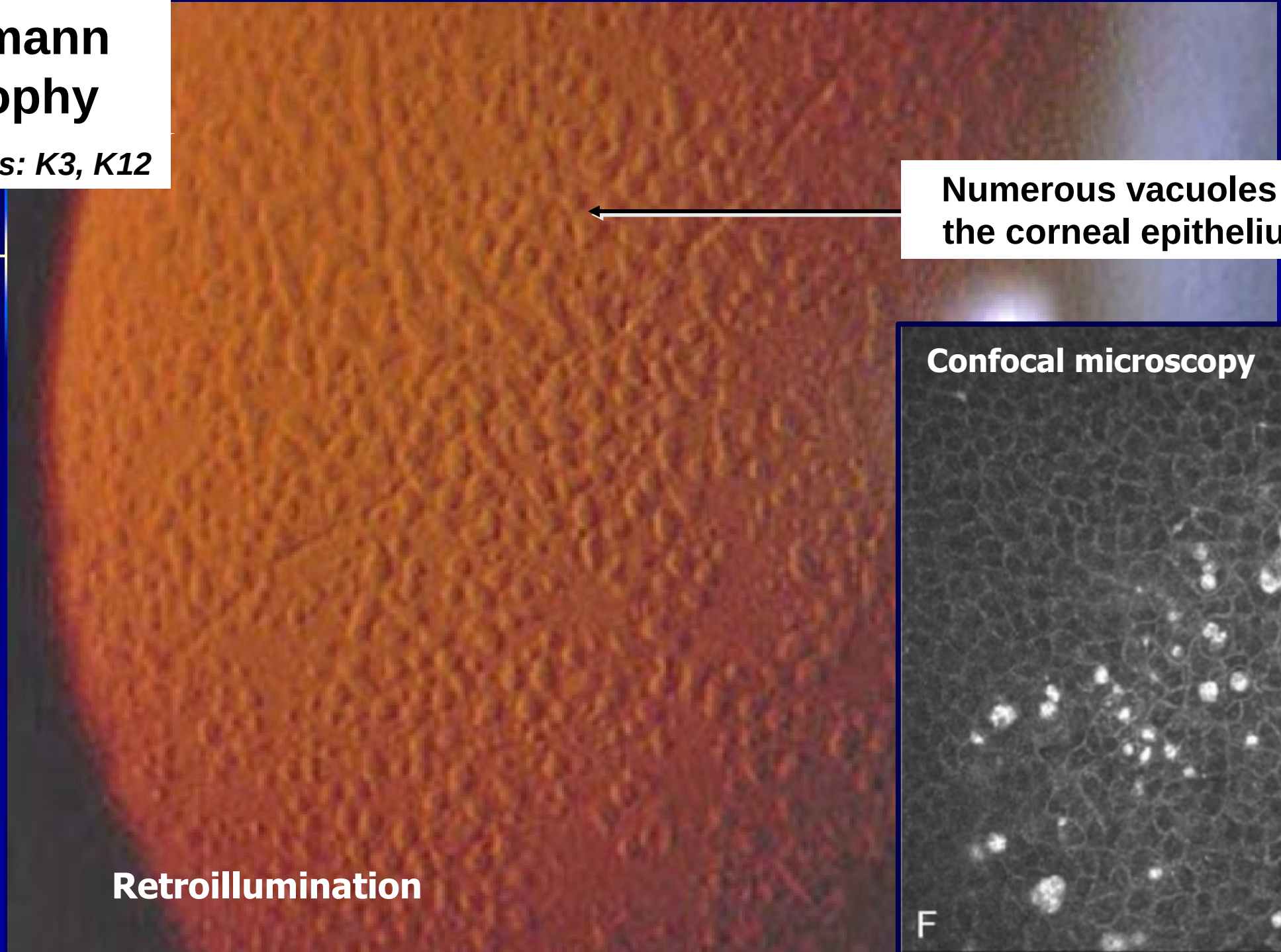
Epithelial and subepithelial dystrophies

1. Epithelial basement membrane dystrophy (EBMD)
2. Lisch epithelial corneal dystrophy (LECD)
3. Meesmann corneal dystrophy (MECD)
4. Gelatinous drop-like corneal dystrophy (GDLD)
5. Epithelial recurrent erosion dystrophies (EREDs)
6. Subepithelial mucinous corneal dystrophy

Meesmann Dystrophy

AD, Genes: K3, K12

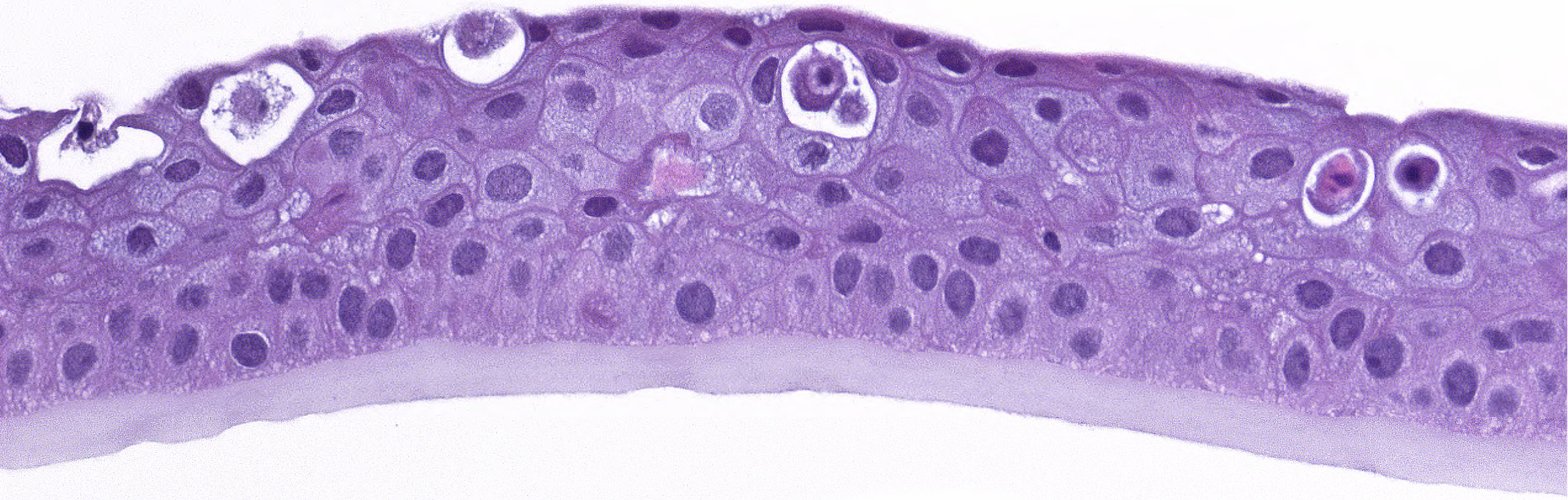
Numerous vacuoles in the corneal epithelium



Meesmann Dystrophy

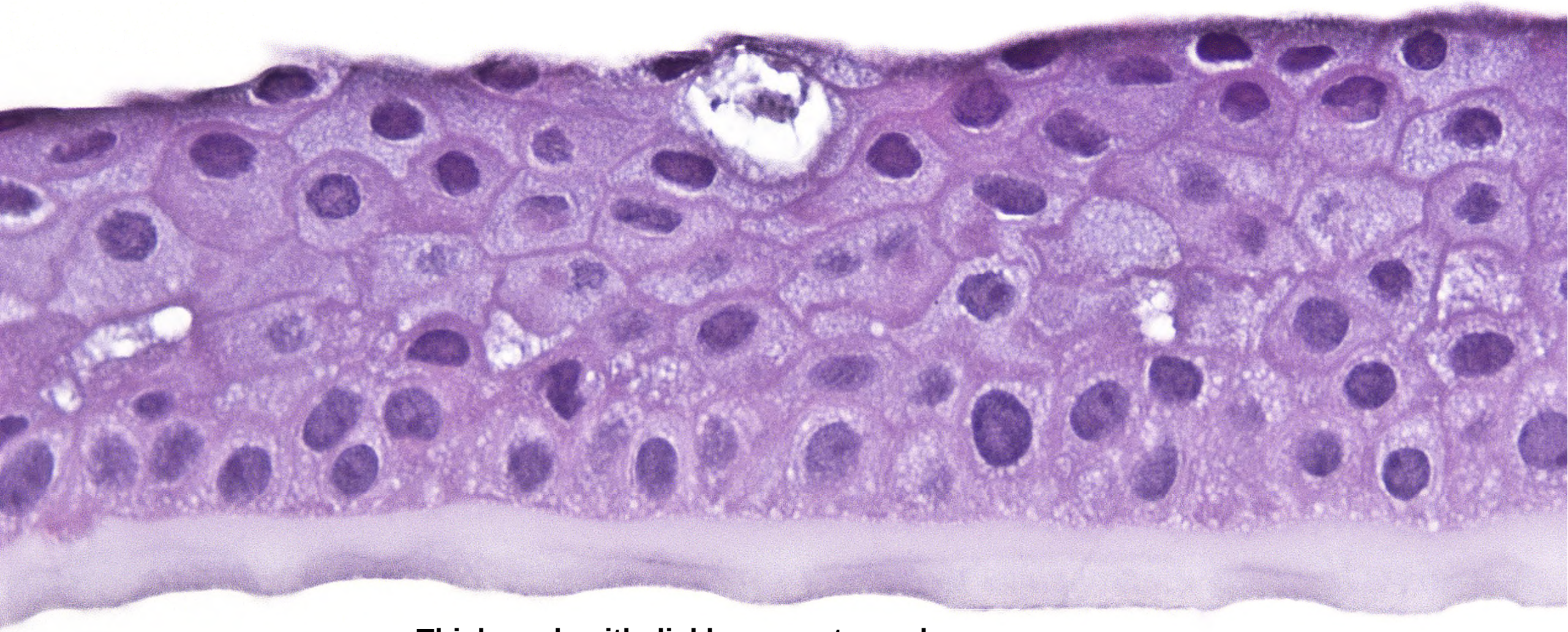
AD, Genes: K3, K12

Morphologically abnormal, vacuolated epithelial cells and intraepithelial cysts (degenerated epithelial cells)



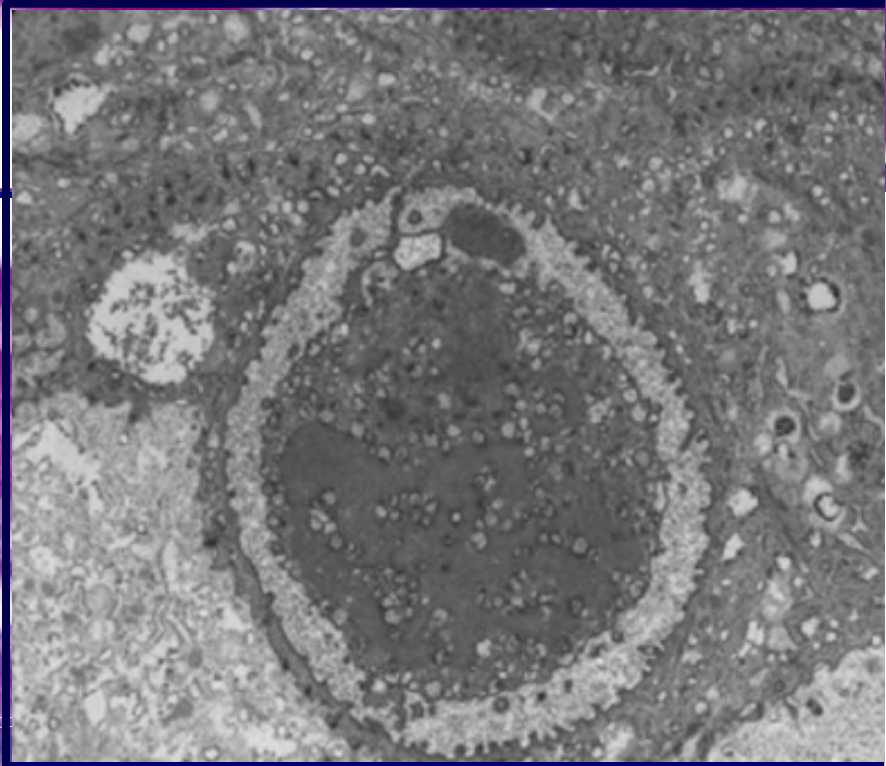
Thickened epithelial basement membrane

Morphologically abnormal, vacuolated epithelial cells and intraepithelial cysts (degenerated epithelial cells)



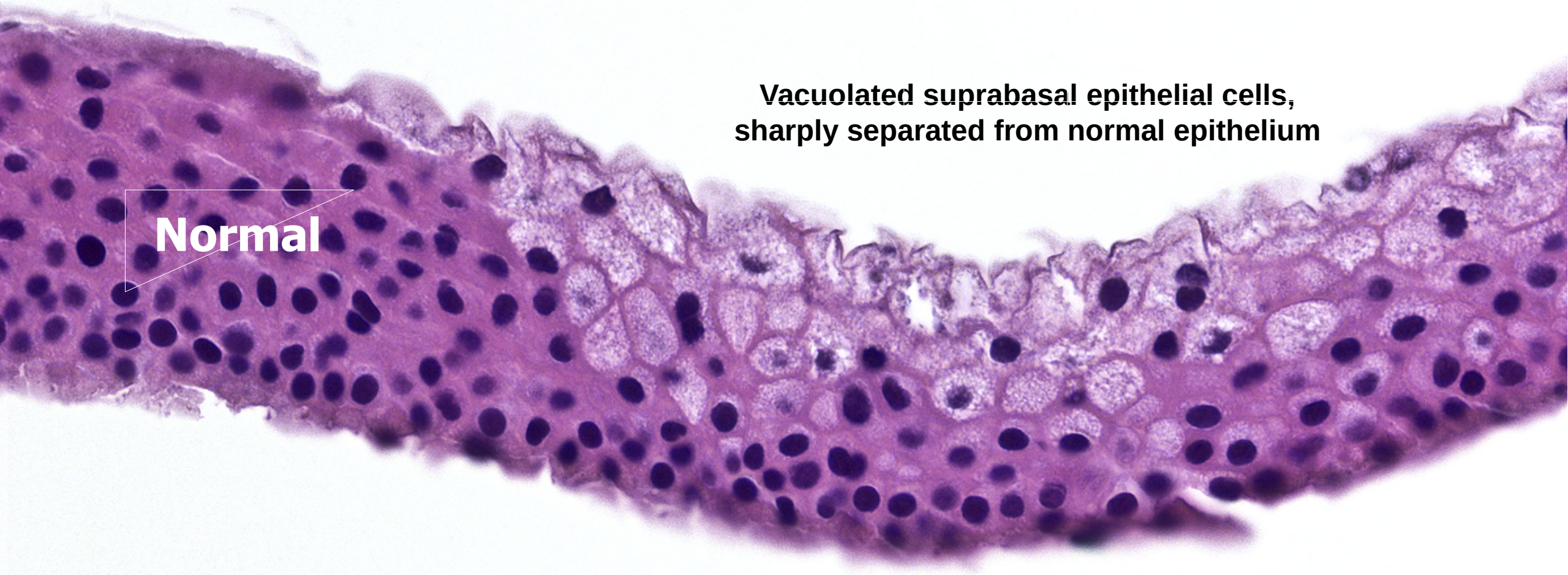
Thickened epithelial basement membrane

Thickened epithelial basement membrane



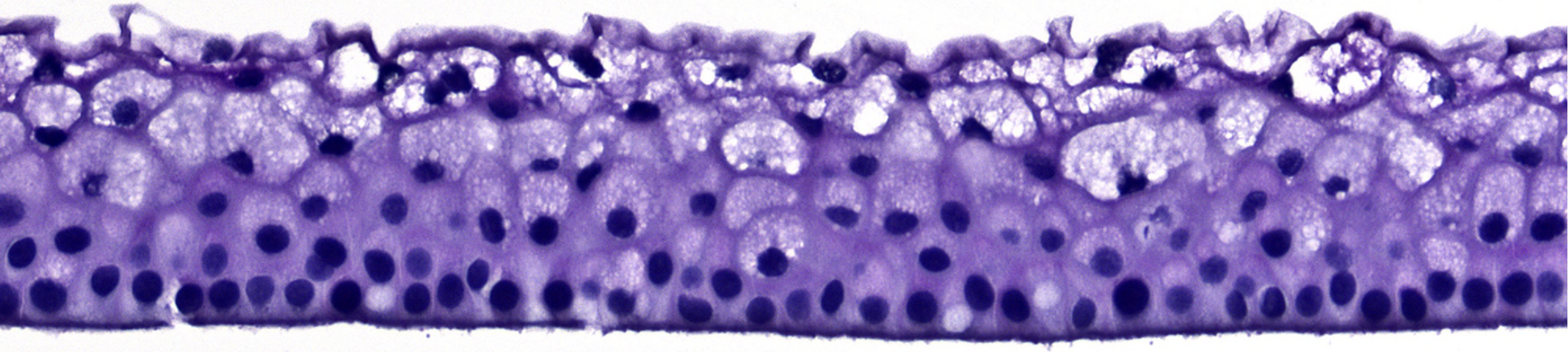
"Peculiar substance" – tangle of cytokeratins surrounded by fibrogranular material

Morphologically abnormal, vacuolated epithelial cells and intraepithelial cysts with PAS-positive, partially diastase-sensitive debris



Vacuolated suprabasal epithelial cells,
sharply separated from normal epithelium

No appreciable thickening of epithelial basement membrane



Suprabasal vacuolated epithelial cells, **mostly PAS-negative**

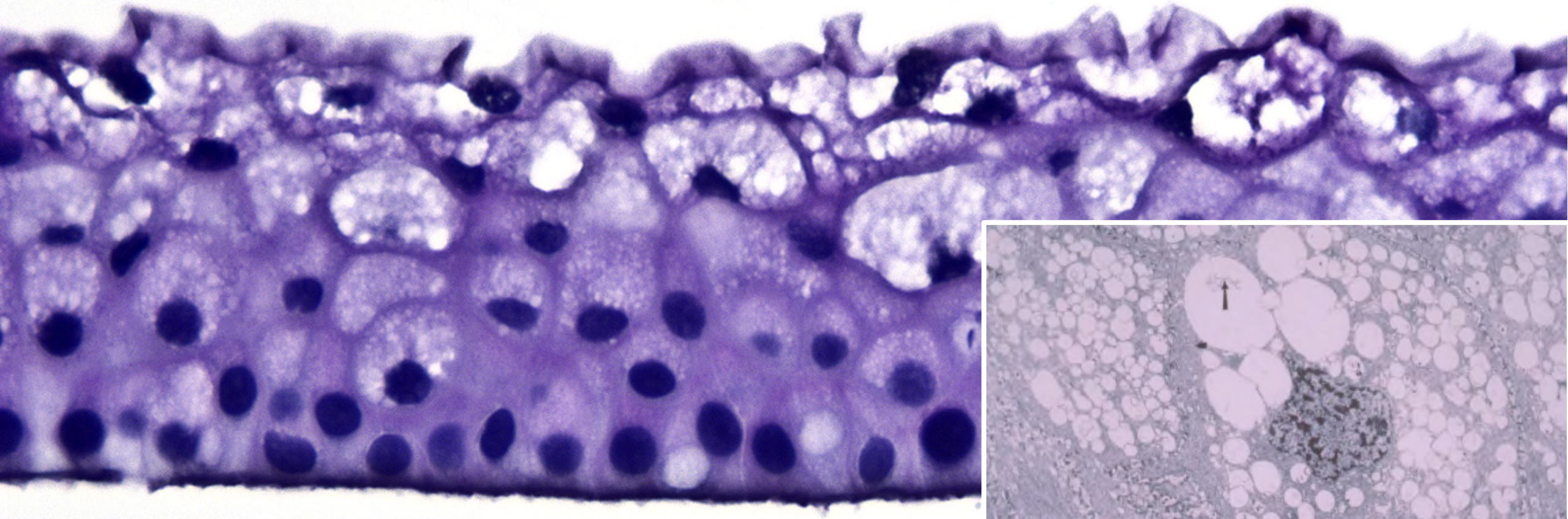
Rare foci of **PAS-positive, diastase-sensitive debris (glycogen)**

No appreciable epithelial basement membrane thickening

Suprabasal vacuolated epithelial cells, **mostly PAS-negative**

Rare foci of **PAS-positive, diastase-sensitive debris (glycogen)**

No appreciable epithelial basement membrane thickening

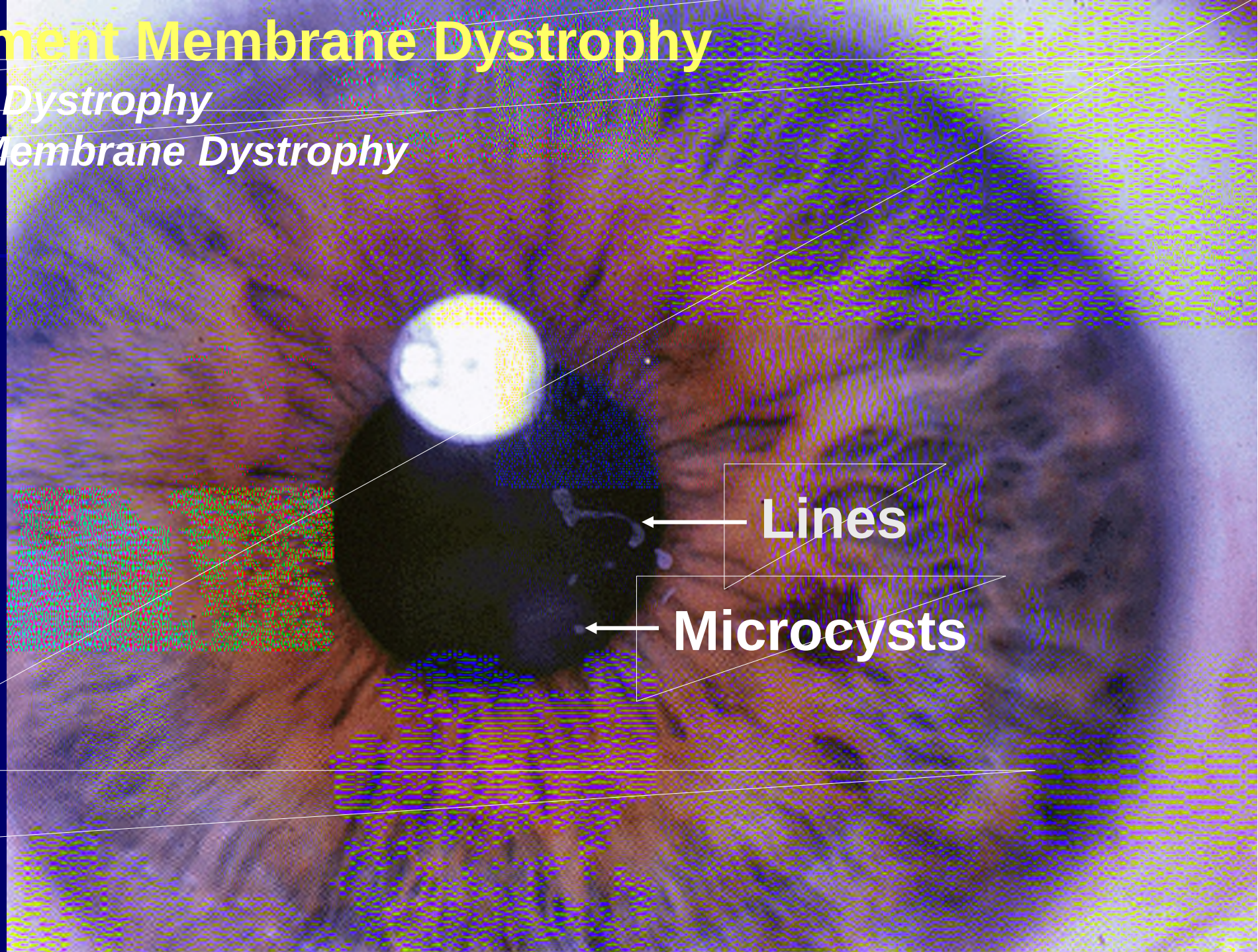


Intracytoplasmic empty vacuoles

Epithelial Basement Membrane Dystrophy

Map-Dot-Fingerprint Dystrophy

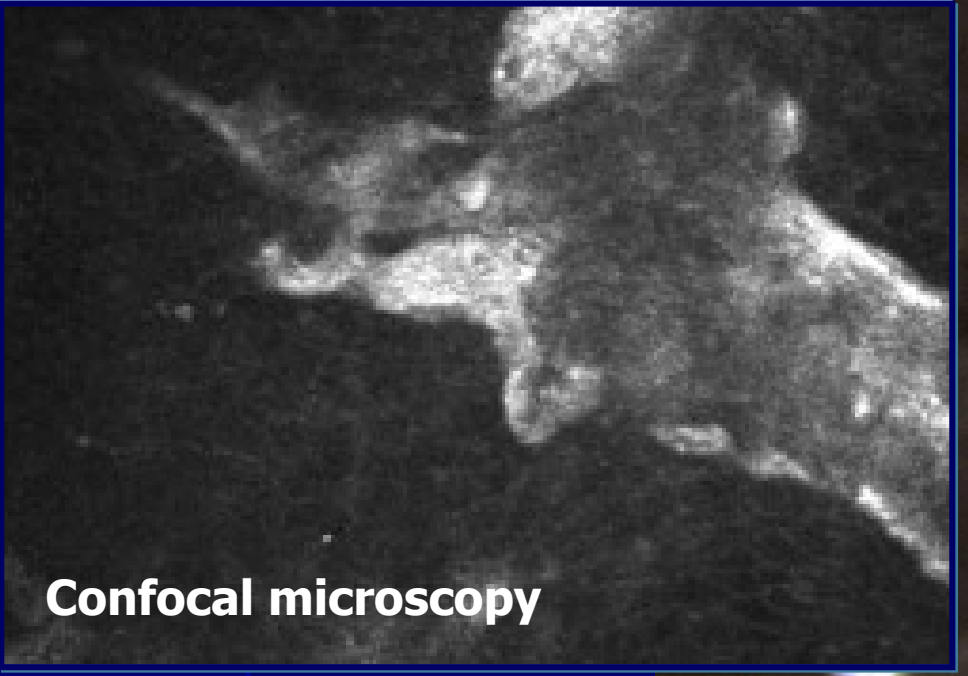
Anterior Basement Membrane Dystrophy



AD, 5q31,

***TGFβI* gene**

Most cases sporadic or degenerative



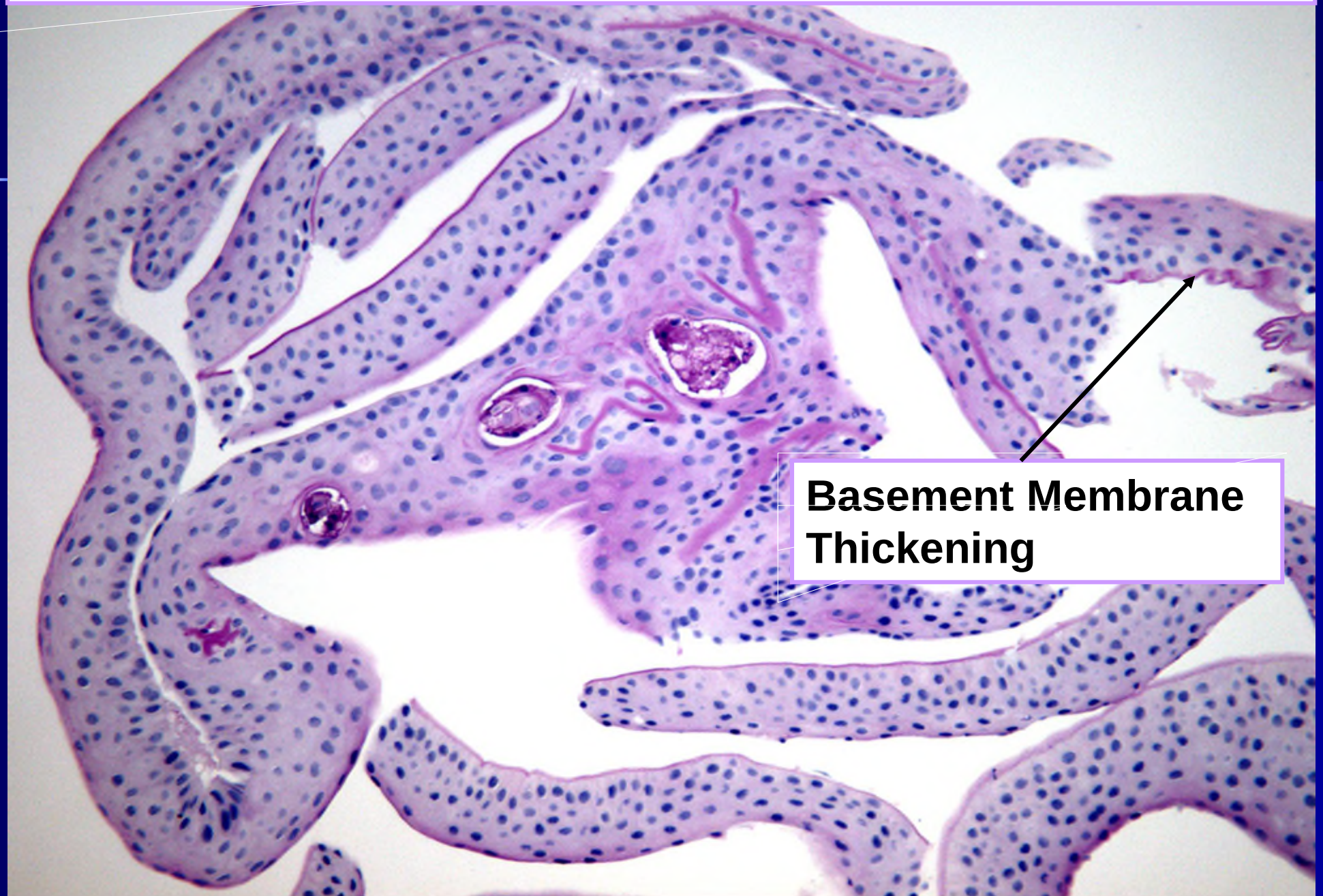
Confocal microscopy

Microcysts

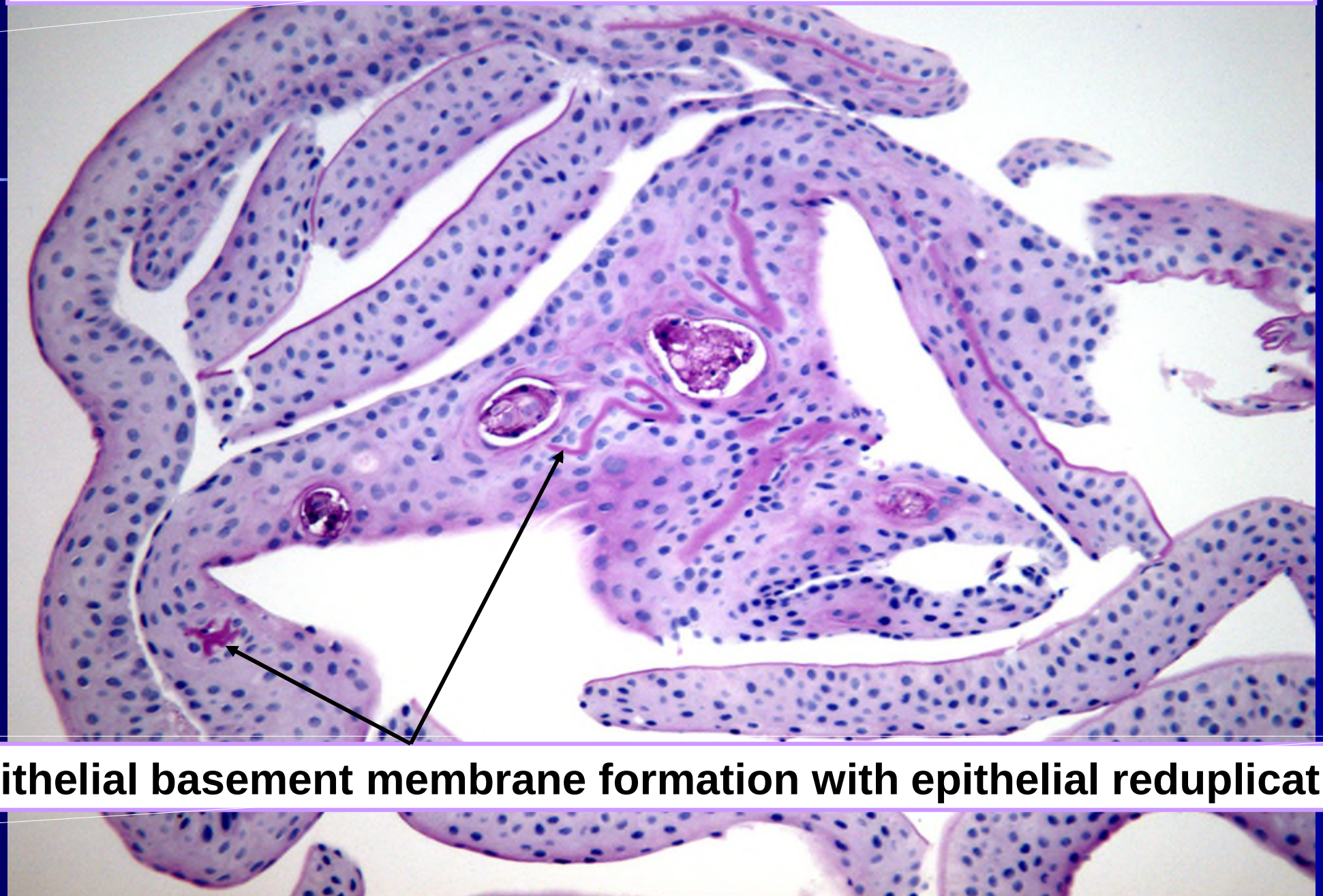
Geographic map-like opacities

Fingerprint-like lines

Epithelial Basement Membrane Dystrophy

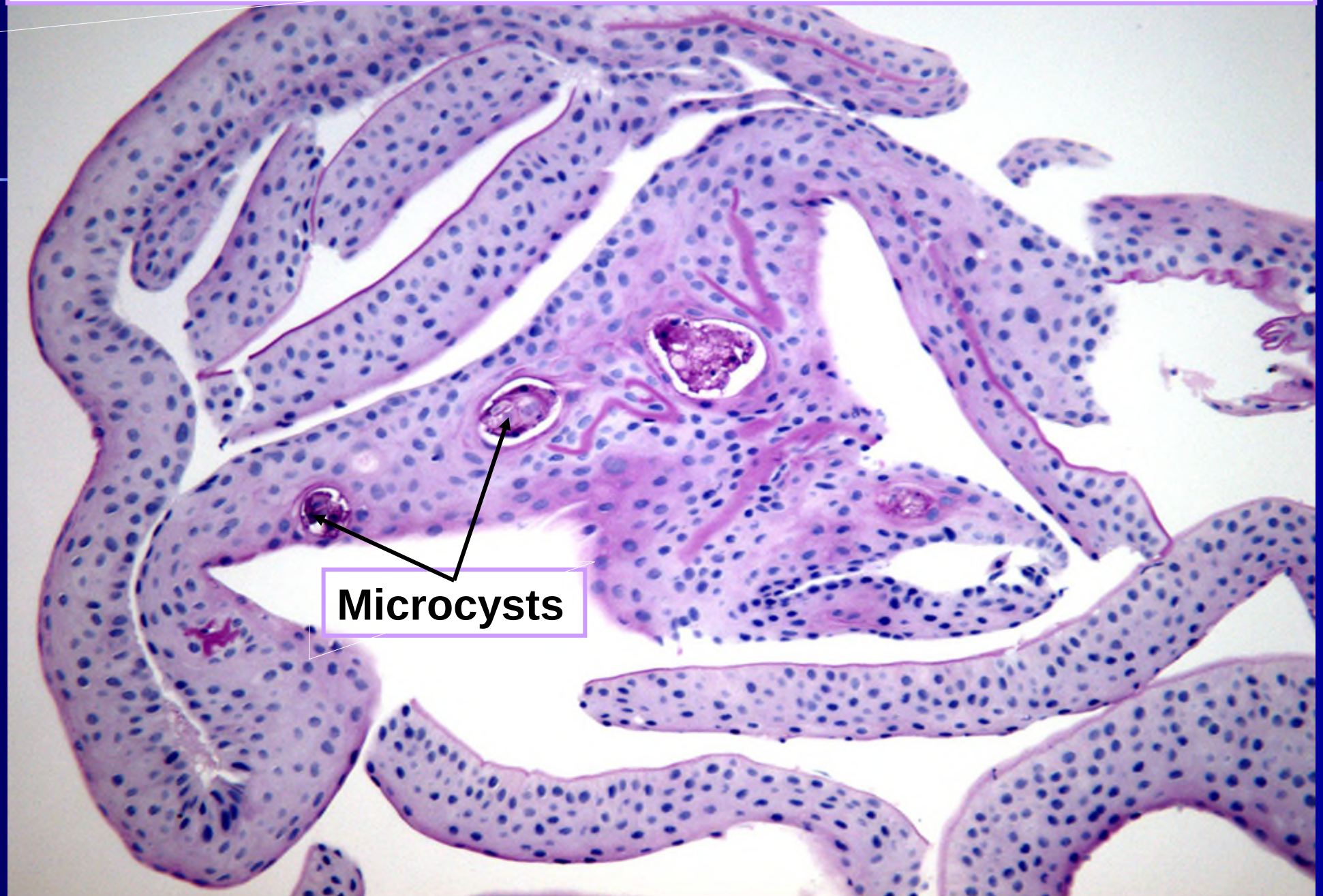


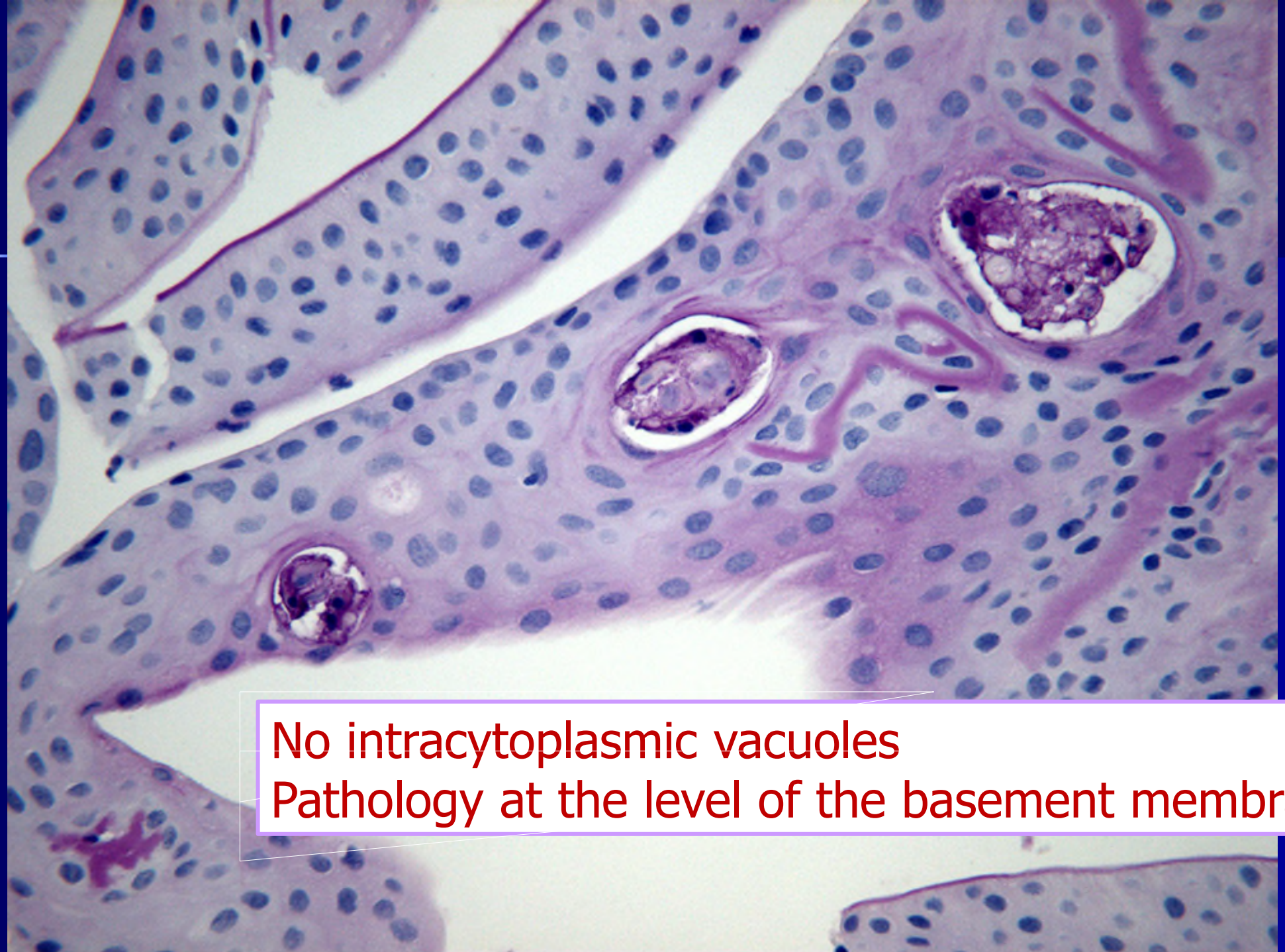
Epithelial Basement Membrane Dystrophy



Intraepithelial basement membrane formation with epithelial reduplication

Epithelial Basement Membrane Dystrophy





No intracytoplasmic vacuoles
Pathology at the level of the basement membrane

Epithelial and subepithelial dystrophies

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2. Lisch epithelial corneal dystrophy (LECD)
3. Meesmann corneal dystrophy (MECD)
4. Gelatinous drop-like corneal dystrophy (GDLD)
5. Epithelial recurrent erosion dystrophies (EREDs)
6. Subepithelial mucinous corneal dystrophy

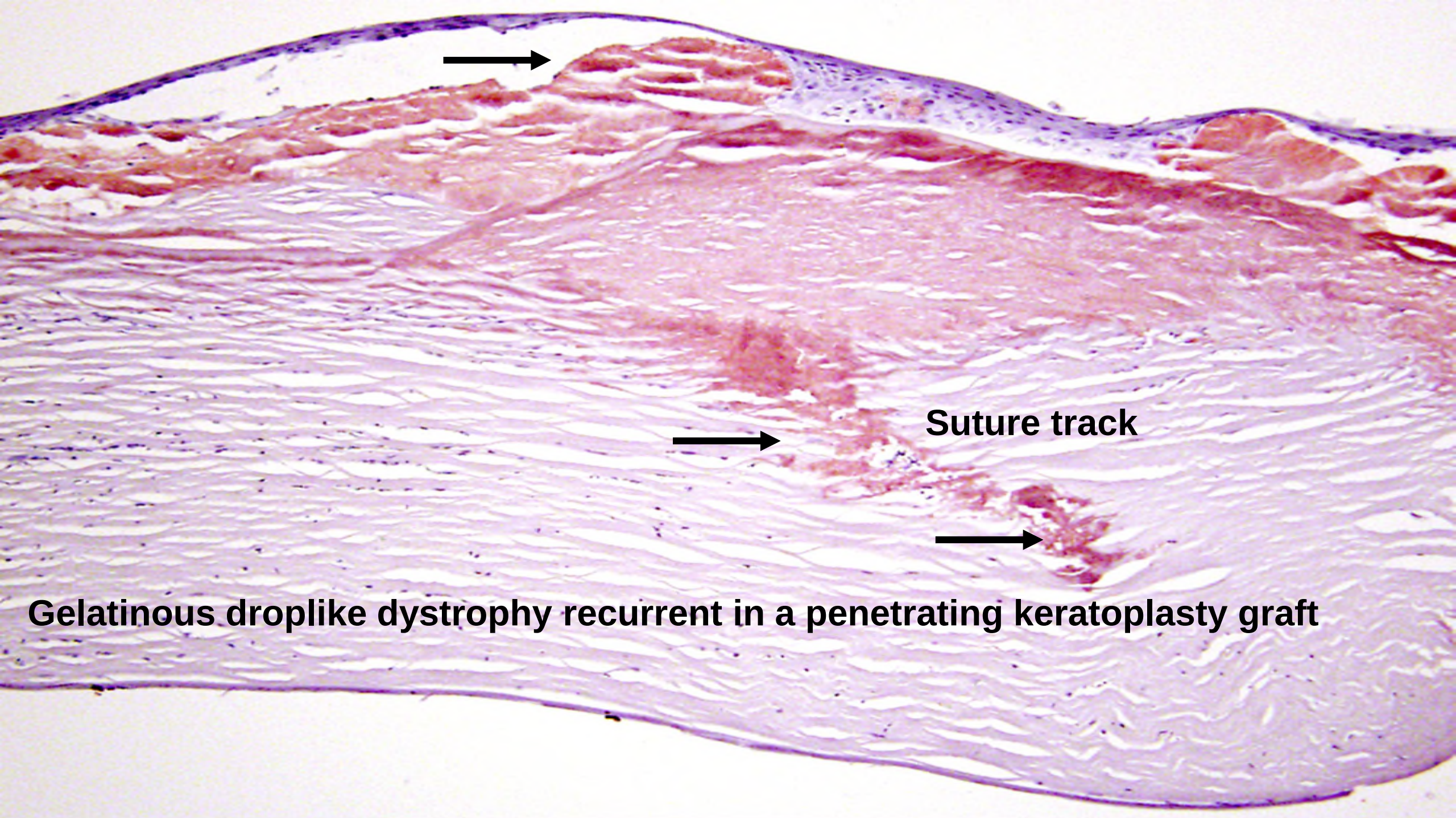
Gelatinous Droplike Dystrophy

AR, 1p32, tumor-associated calcium signal transducer 2 gene

apple green
birefringence

Amyloid deposits stain with antibodies to lactoferrin

Congo red with polarization



Gelatinous droplike dystrophy recurrent in a penetrating keratoplasty graft

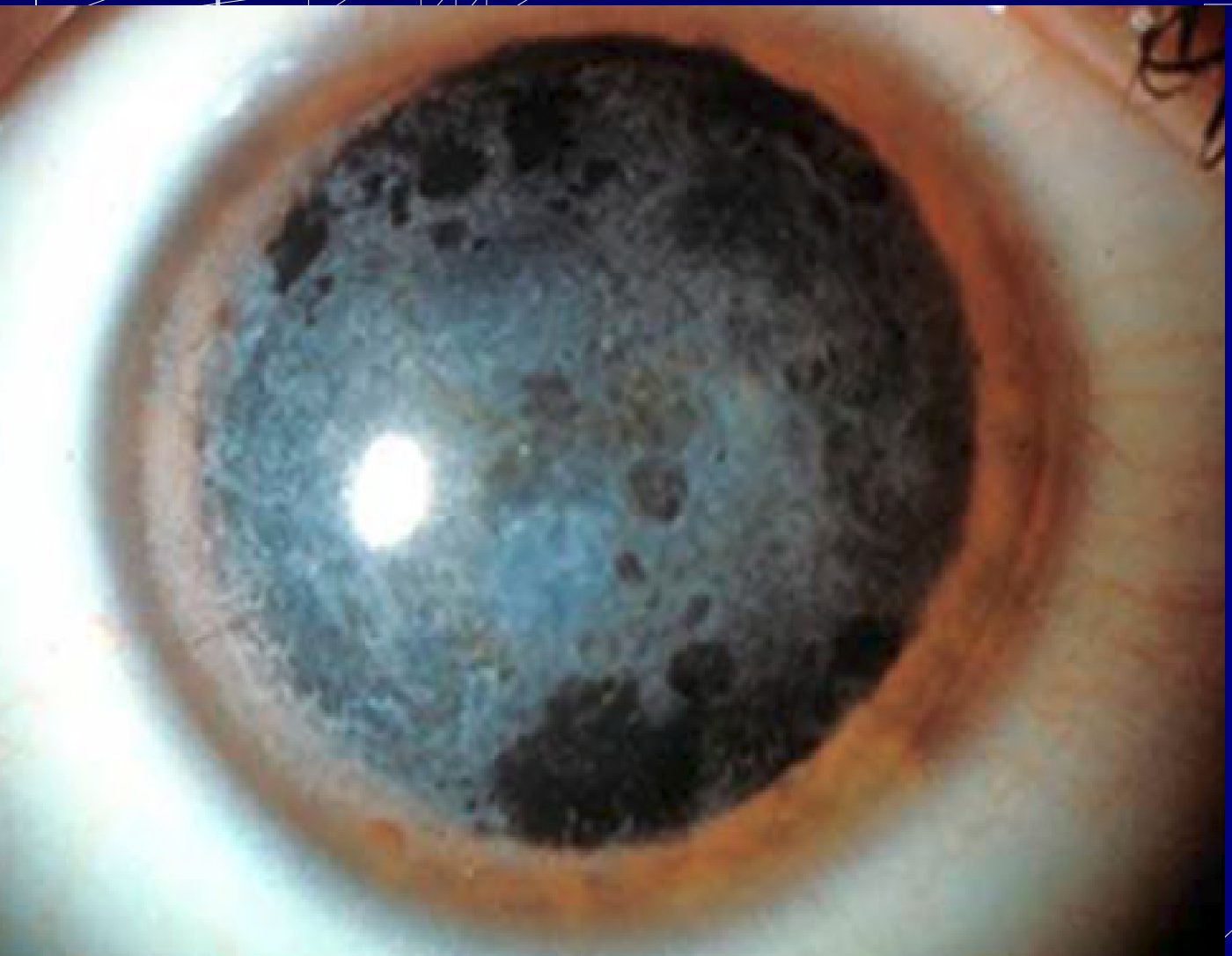
Epithelial-stromal TGFBI dystrophies

1. Reis–Bücklers corneal dystrophy (RBCD)
2. Thiel-Behnke corneal dystrophy (TBCD)
3. Lattice corneal dystrophy, type 1 (LCD1) and variants (III, IIIA, I/IIIA, IV) of LCD
4. Granular corneal dystrophy, type 1 (GCD1)
5. Granular corneal dystrophy, type 2 (GCD2)

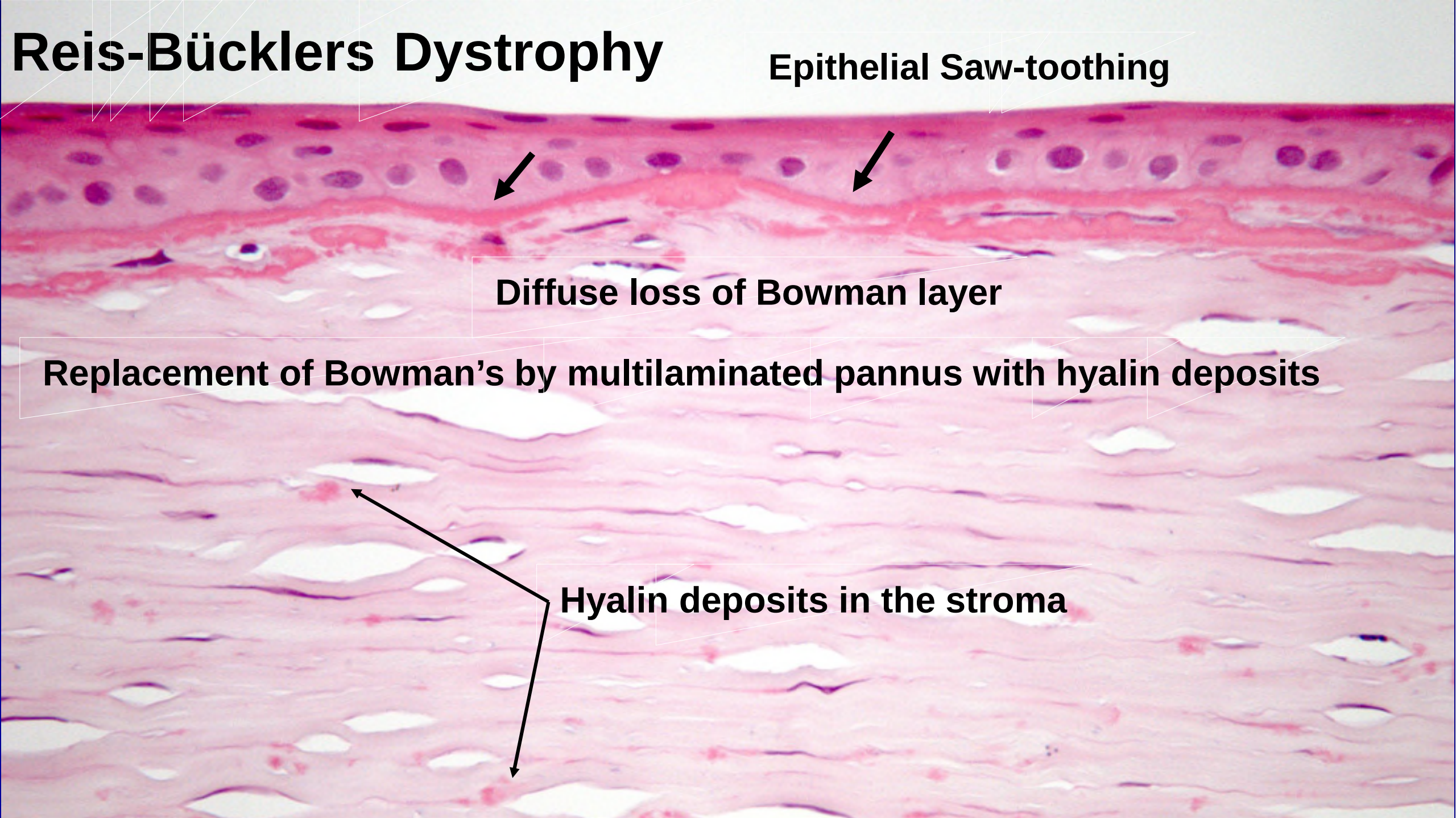
Reis-Bücklers Dystrophy

Corneal Dystrophy of Bowman Layer Type I

AD, 5q31, *TGFβI* gene

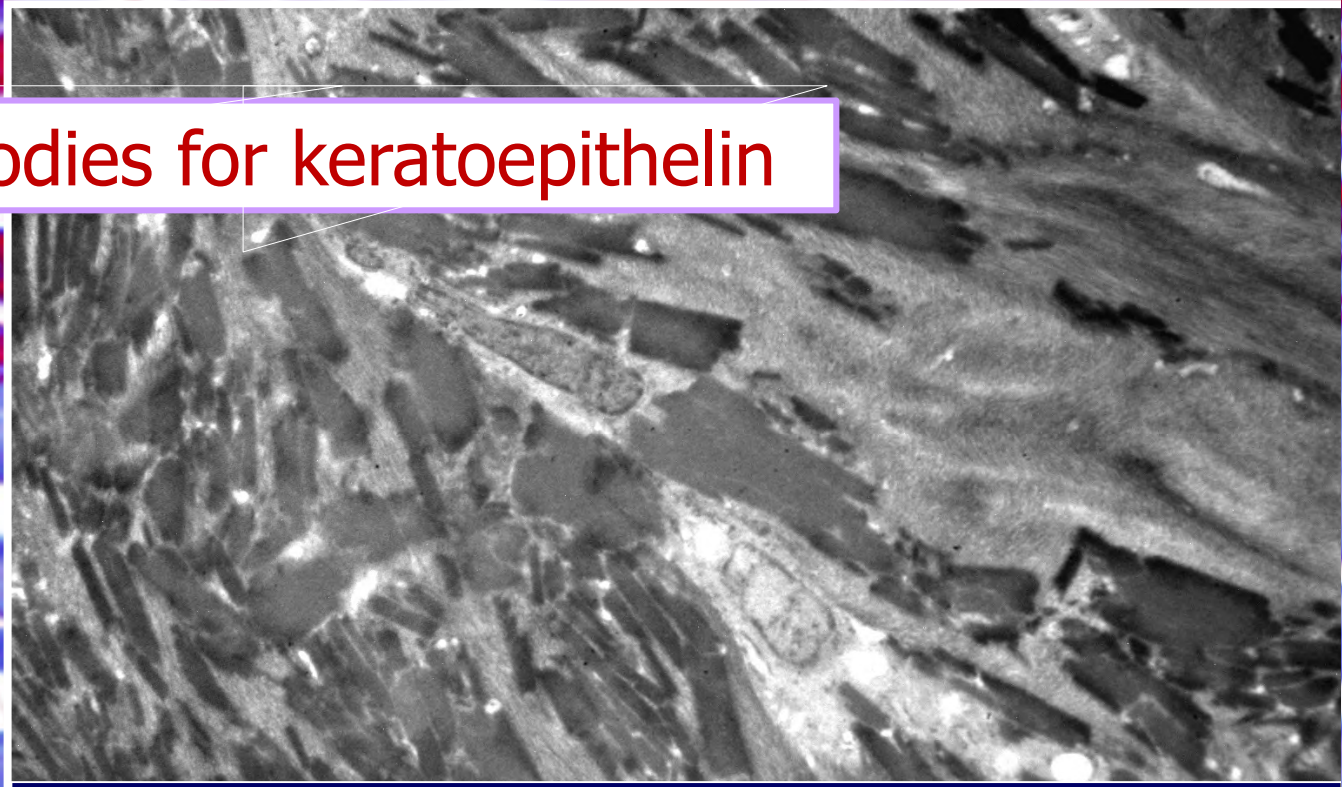


Reis-Bücklers Dystrophy



Reis-Bücklers Dystrophy (Masson-Trichrome)

Deposits stain with antibodies for keratoepithelin



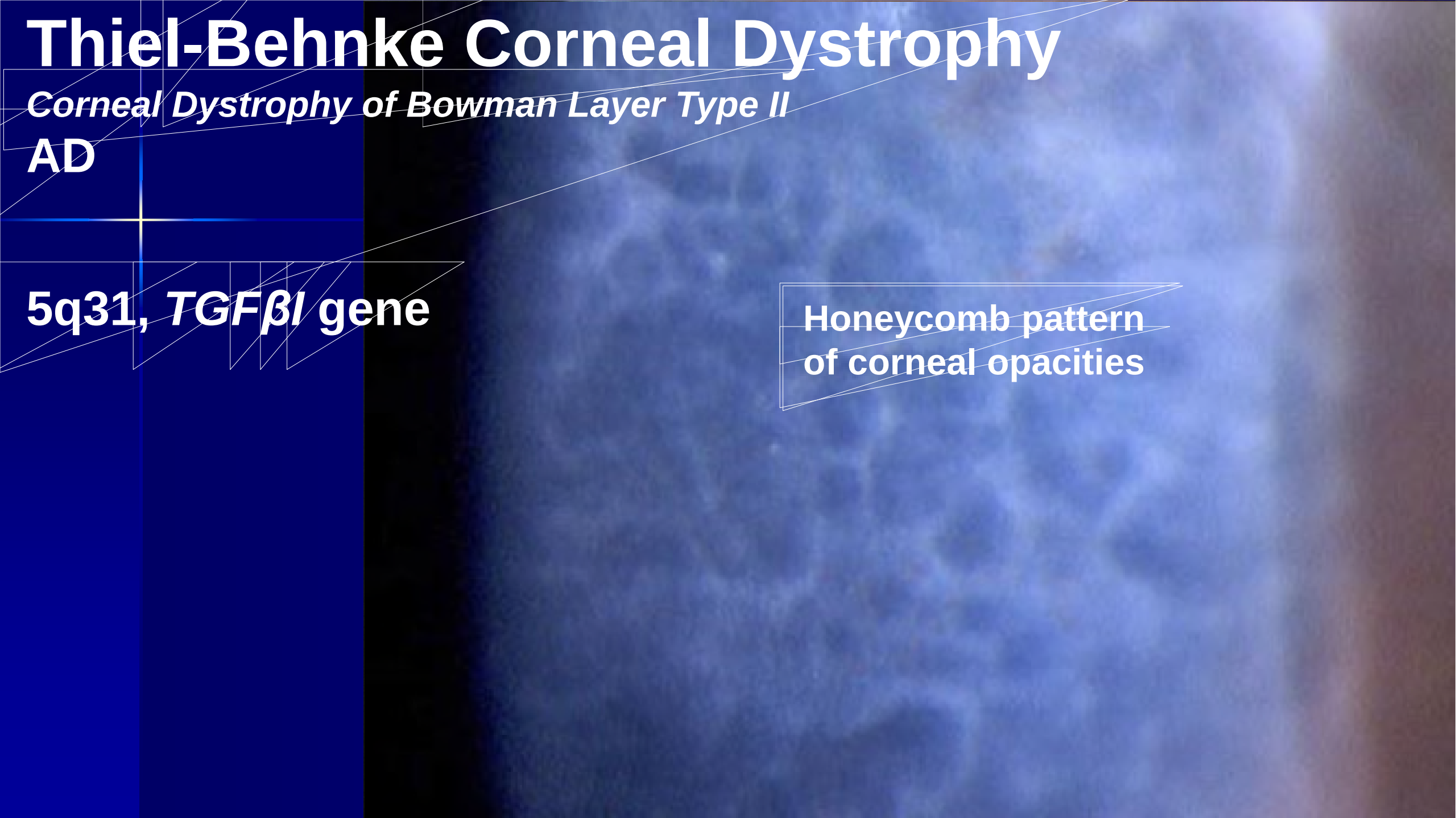
Paracrystalline rhomboid and rectangular deposits

Thiel-Behnke Corneal Dystrophy

Corneal Dystrophy of Bowman Layer Type II

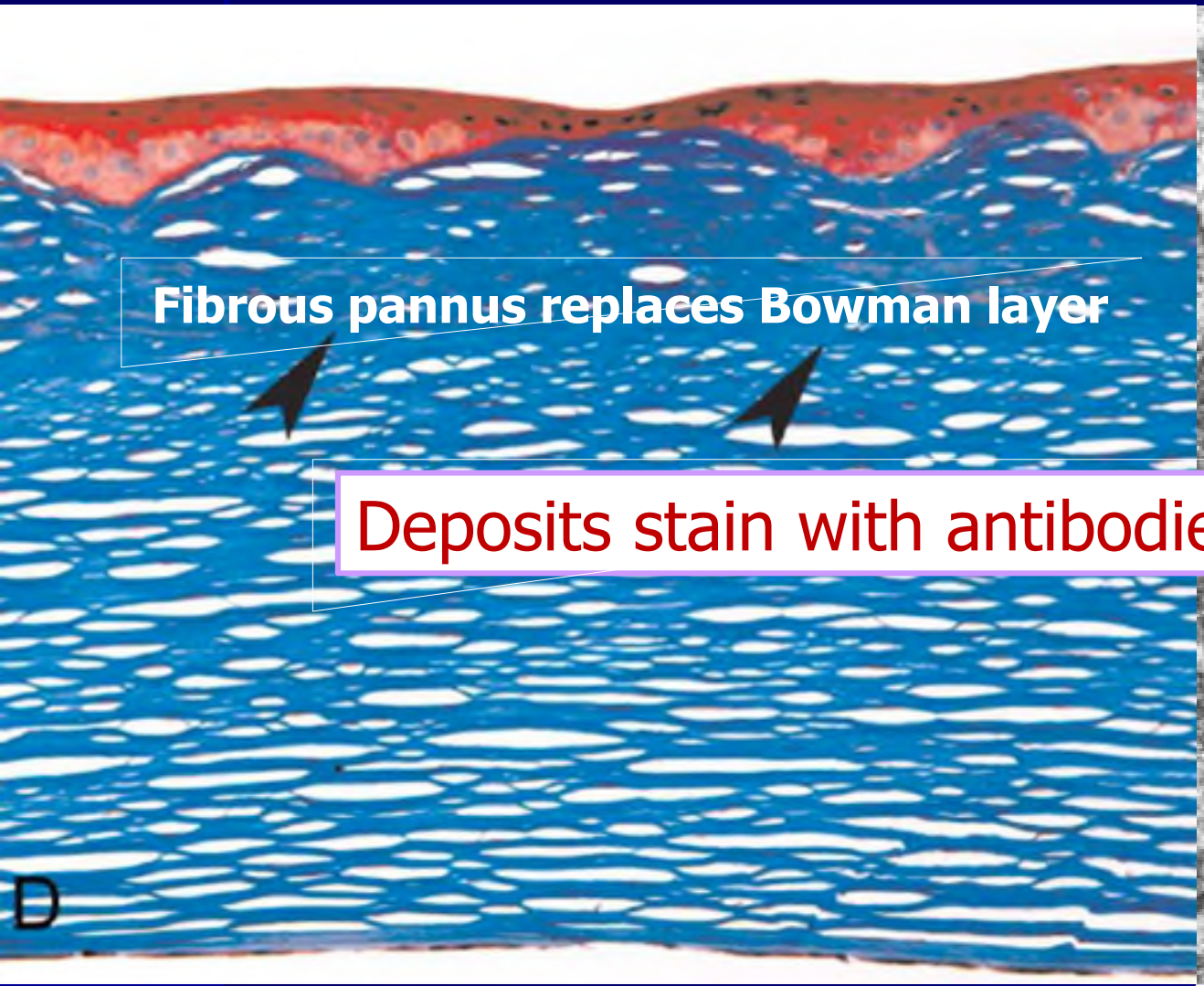
AD

5q31, *TGFβI* gene

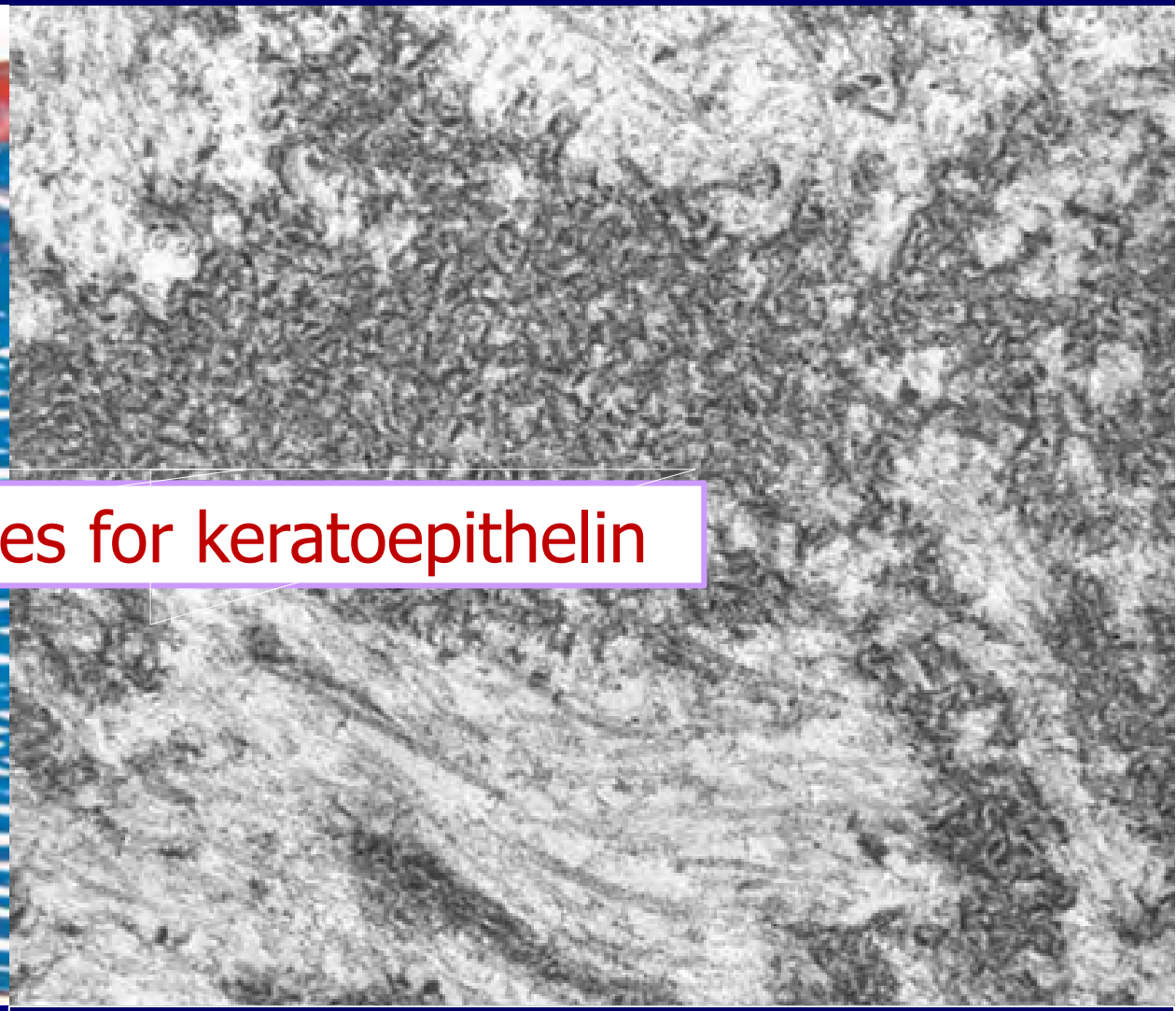


Honeycomb pattern
of corneal opacities

Thiel-Behnke Dystrophy



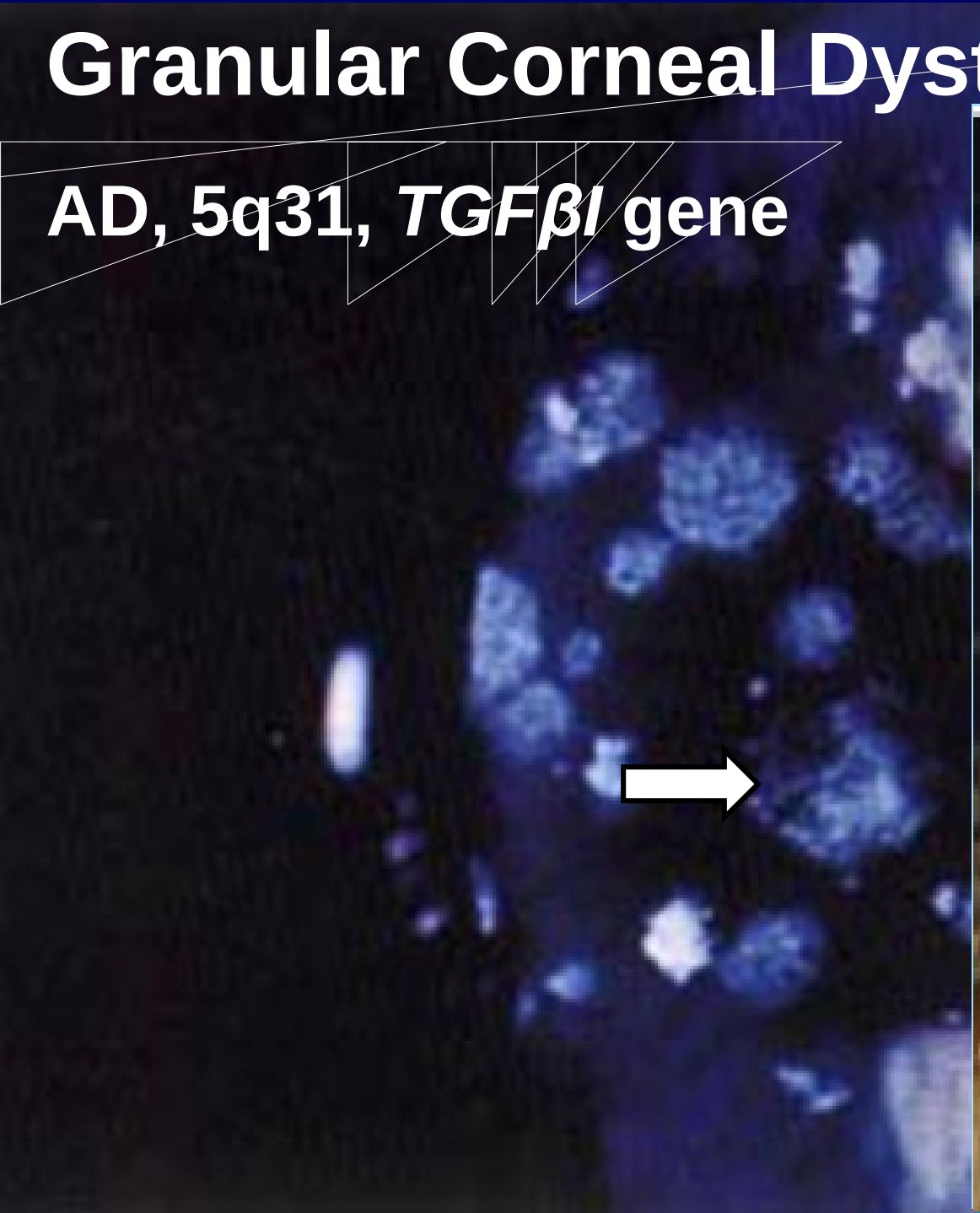
Deposits stain with antibodies for keratoepithelin



Curly filaments at the level of Bowman layer (keratoepithelin)

Granular Corneal Dystrophy, Type I

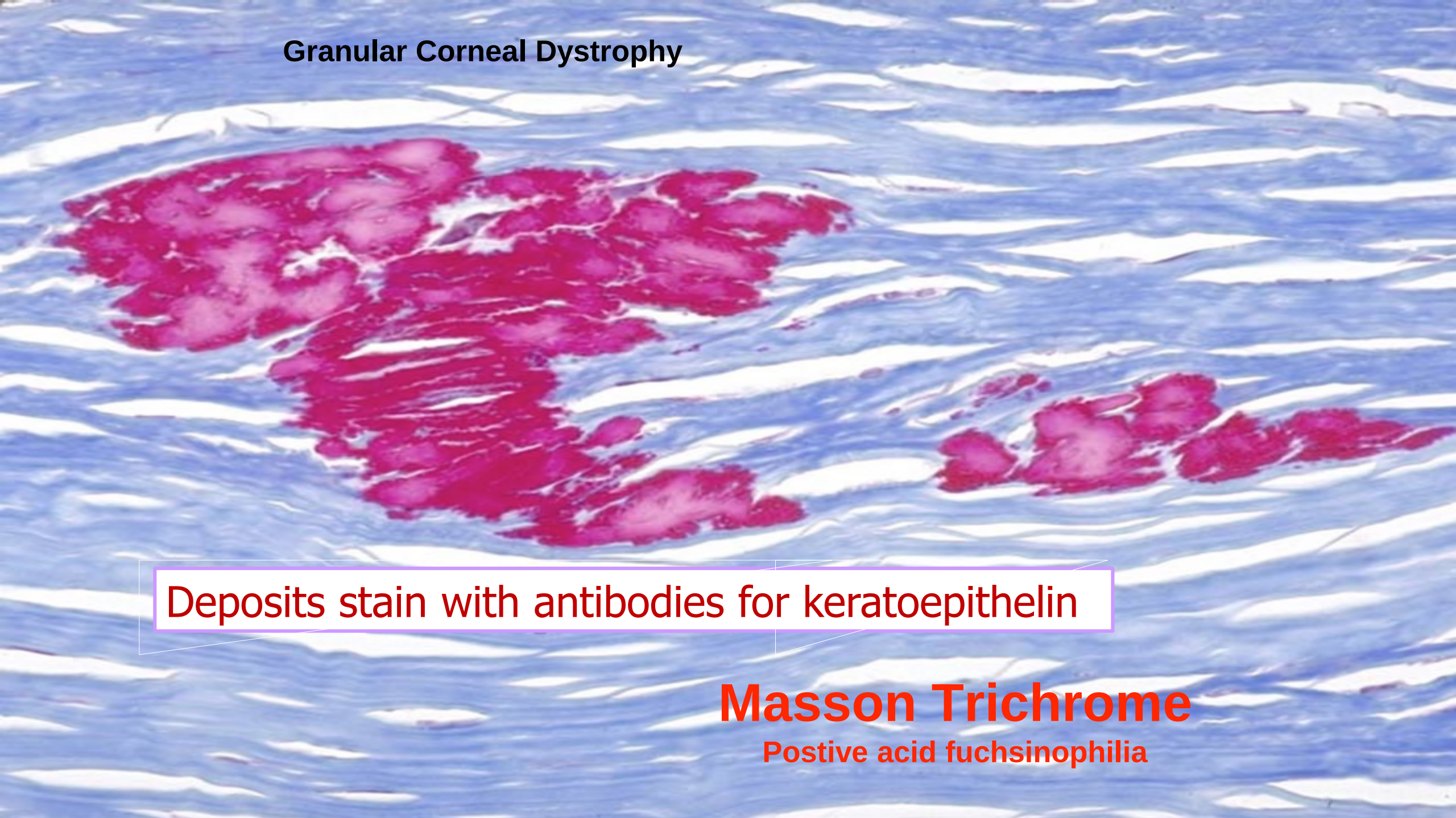
AD, 5q31, *TGFβI* gene



Granular Dystrophy

Hyalin “Rock Candy” Deposits

Granular Corneal Dystrophy



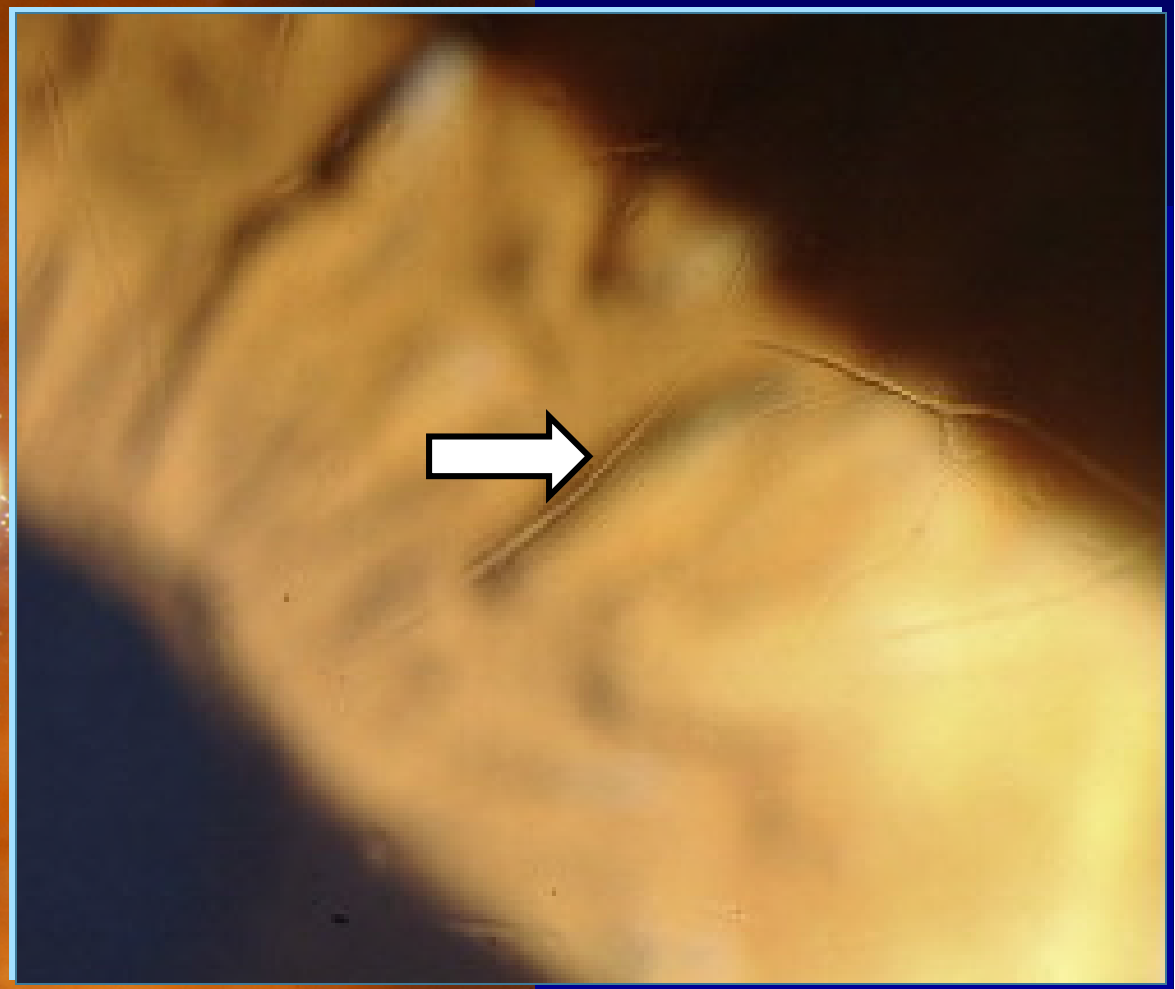
Deposits stain with antibodies for keratoepithelin

Masson Trichrome

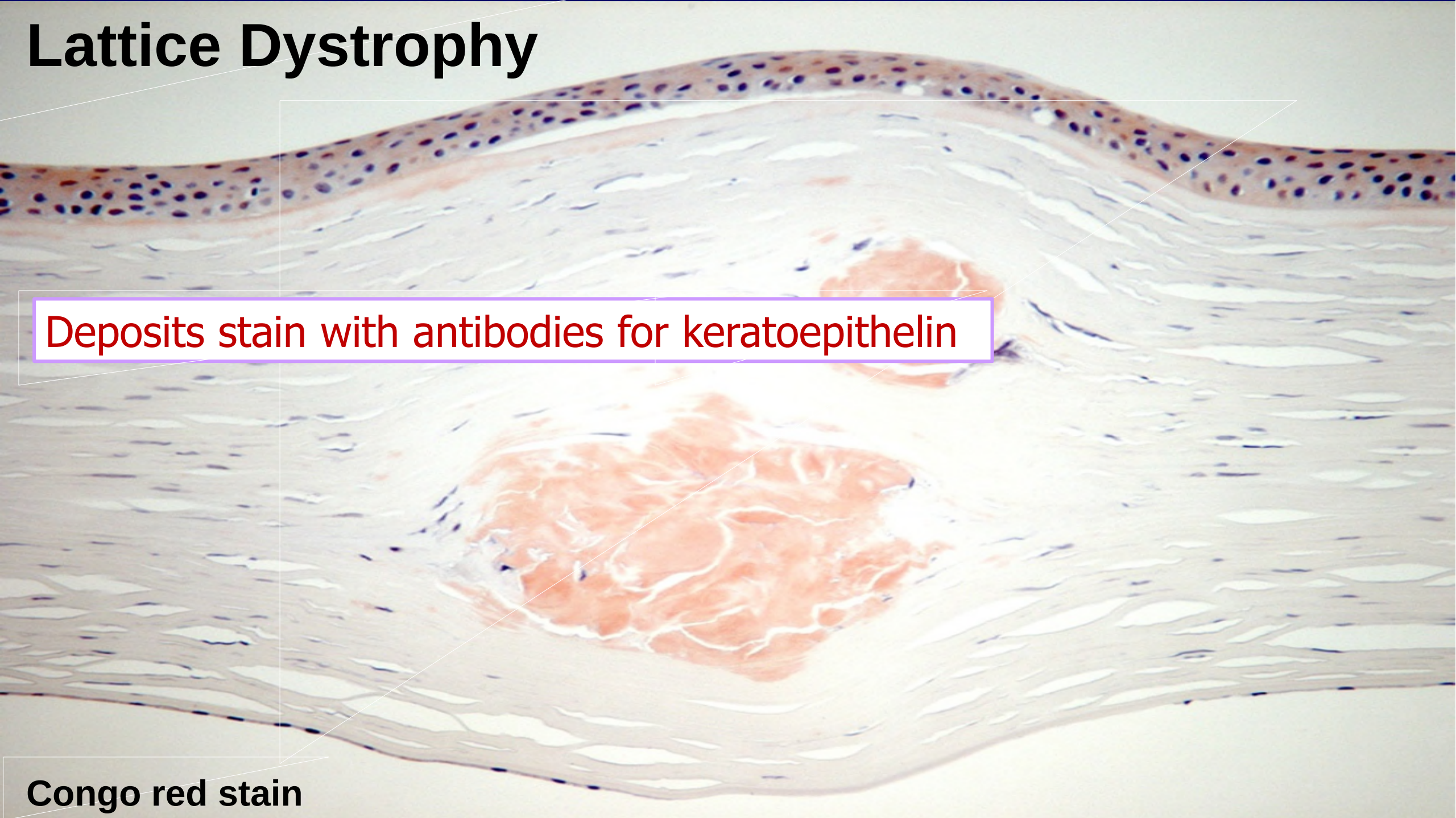
Postive acid fuchsinophilia

Lattice Corneal Dystrophy (Classic), TGFβI Type

AD, 5q31, *TGFβI* gene



Lattice Dystrophy

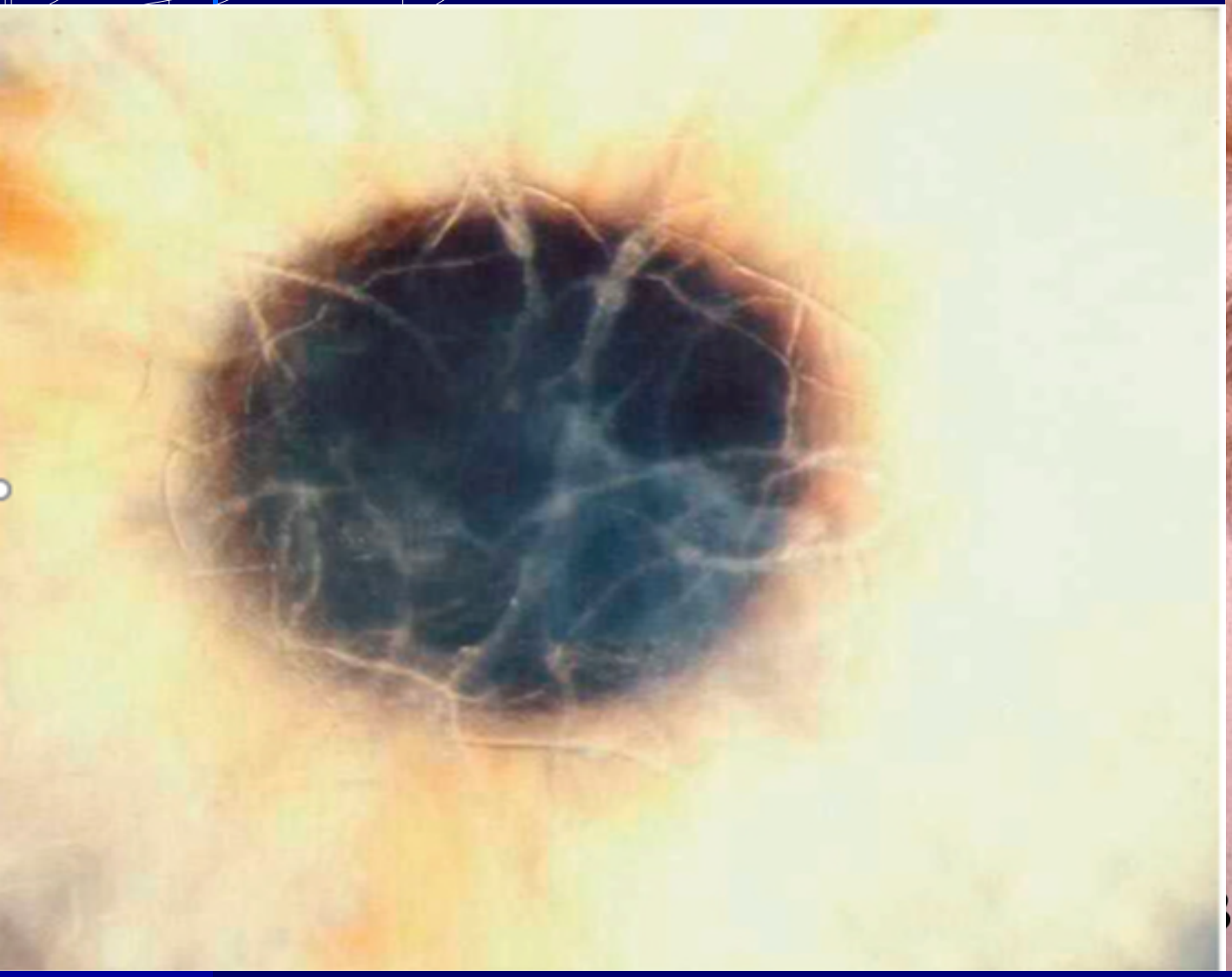


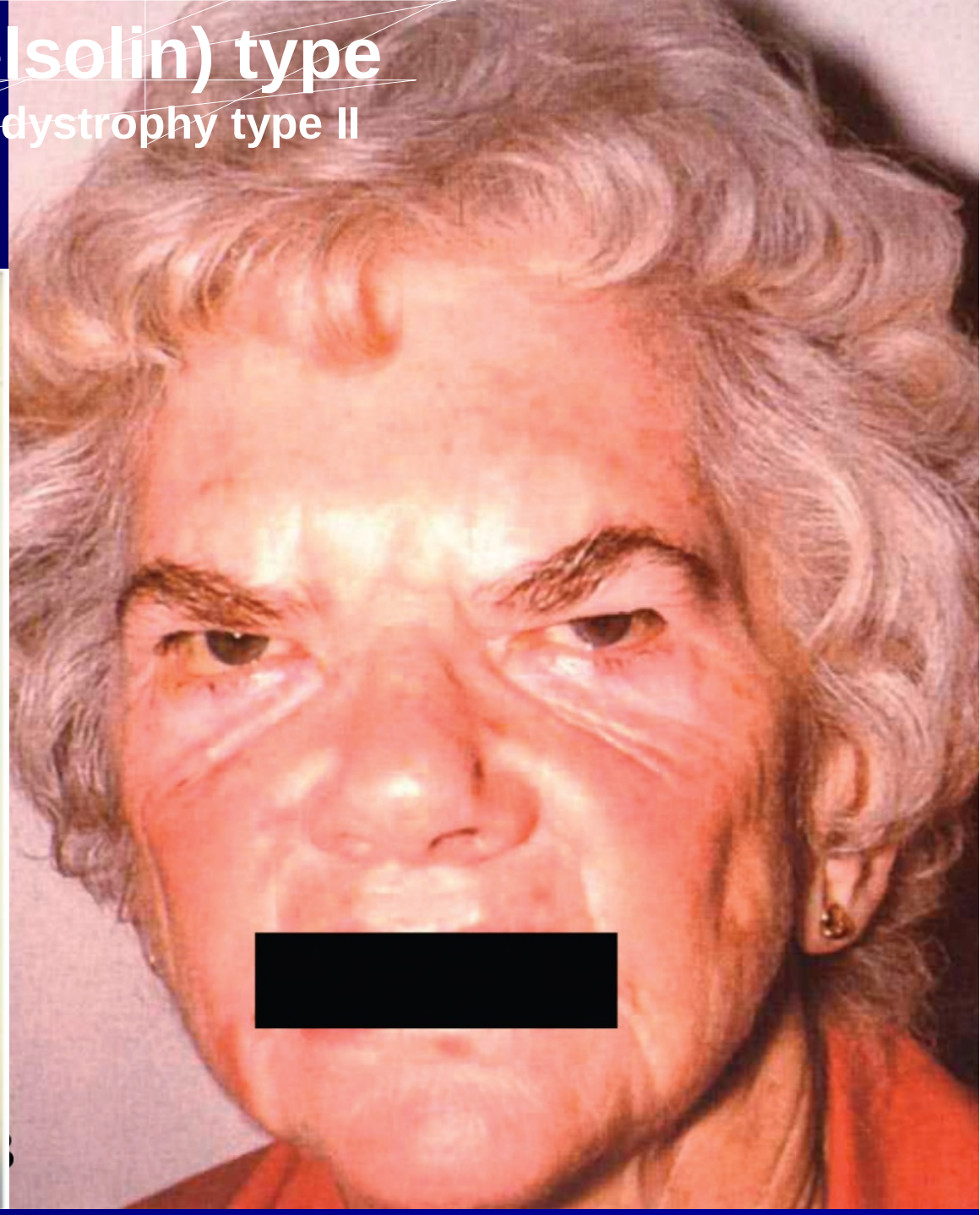
Congo red stain

Familial amyloidosis, Finnish (Gelsolin) type

Meretoja syndrome; FAF; FAP-IV; Formerly Lattice dystrophy type II

9q34, *Gelsolin* gene

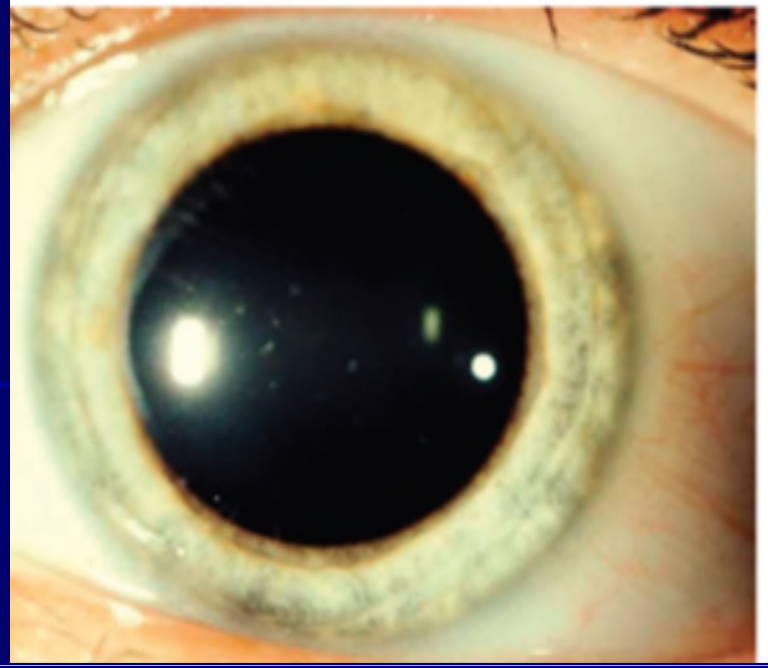


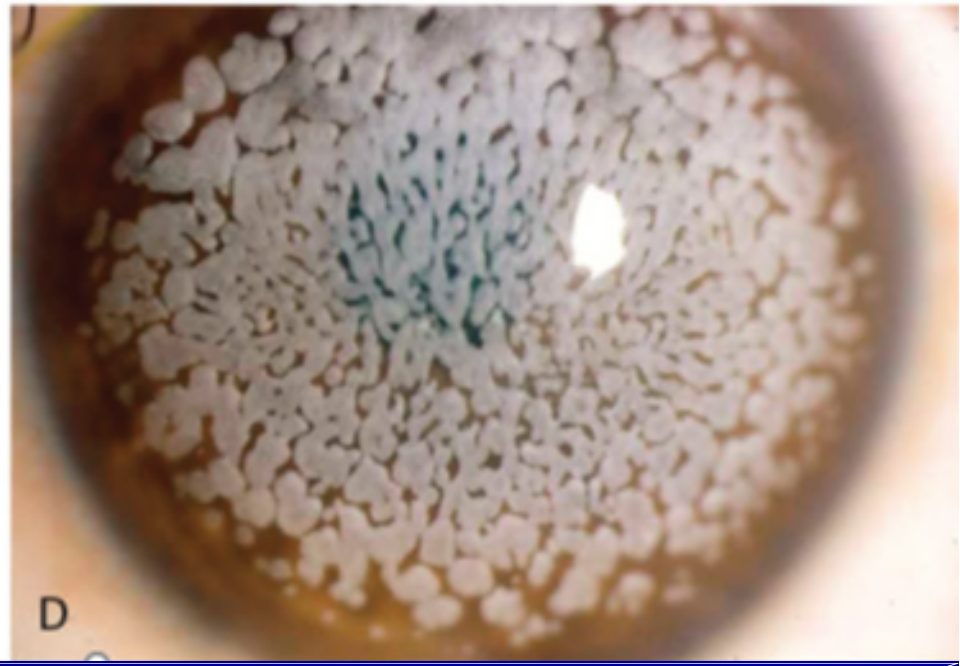


Granular Corneal Dystrophy, Type II

Avellino Dystrophy

AD, *TGFβI* gene





Stromal TGFBI dystrophies

1. Macular corneal dystrophy
2. Schnyder corneal dystrophy
3. Congenital hereditary stromal dystrophy
4. Fleck corneal dystrophy
5. Posterior amorphous corneal dystrophy

Macular Corneal Dystrophy

AR, 16q22, Carbohydrate sulfotransfarase 6 gene

Macular corneal dystrophy type I:

No AgKS reactivity in the cornea or in the serum

Macular corneal dystrophy type IA:

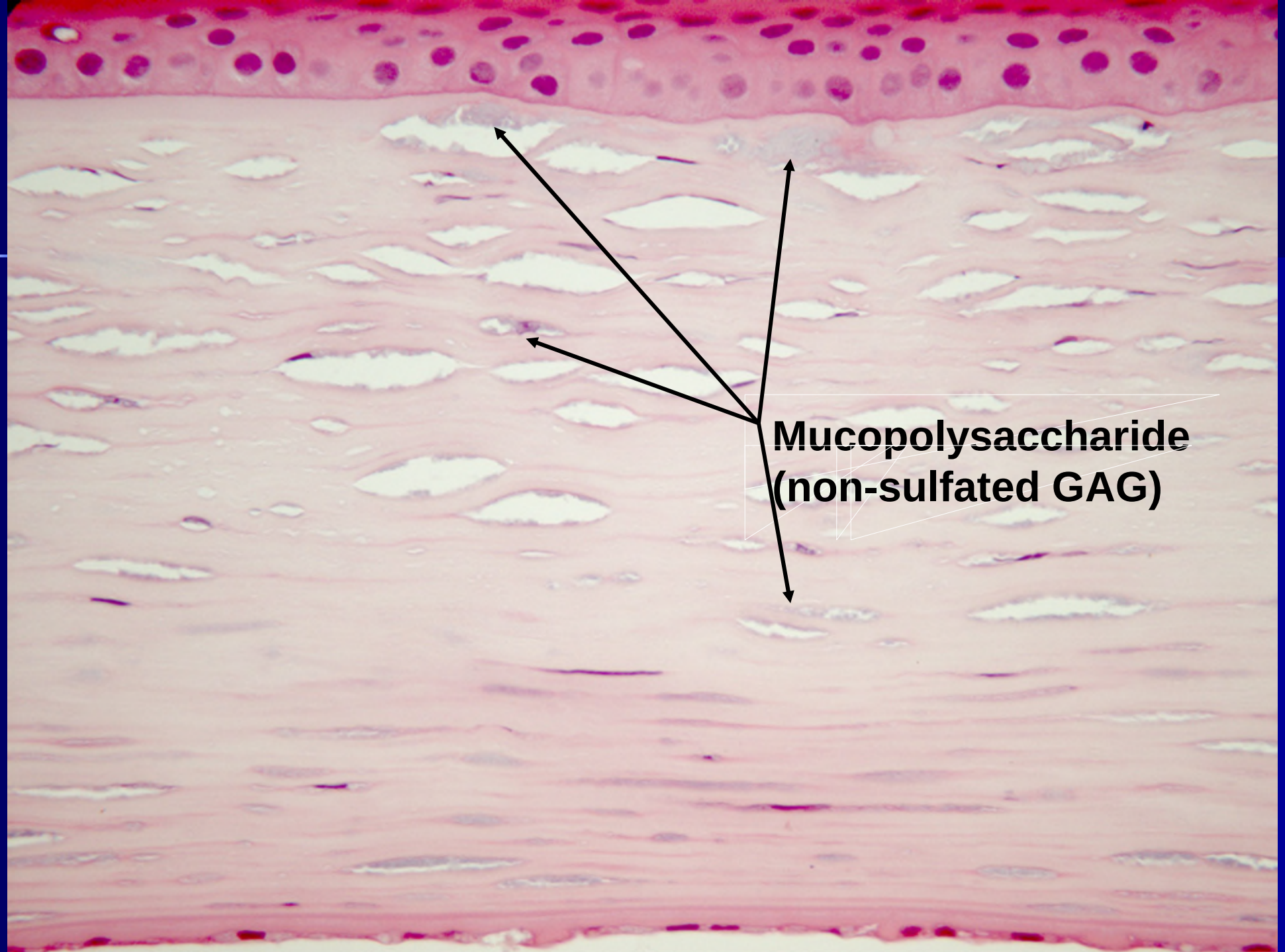
Keratocytes manifest AgKS immunoreactivity

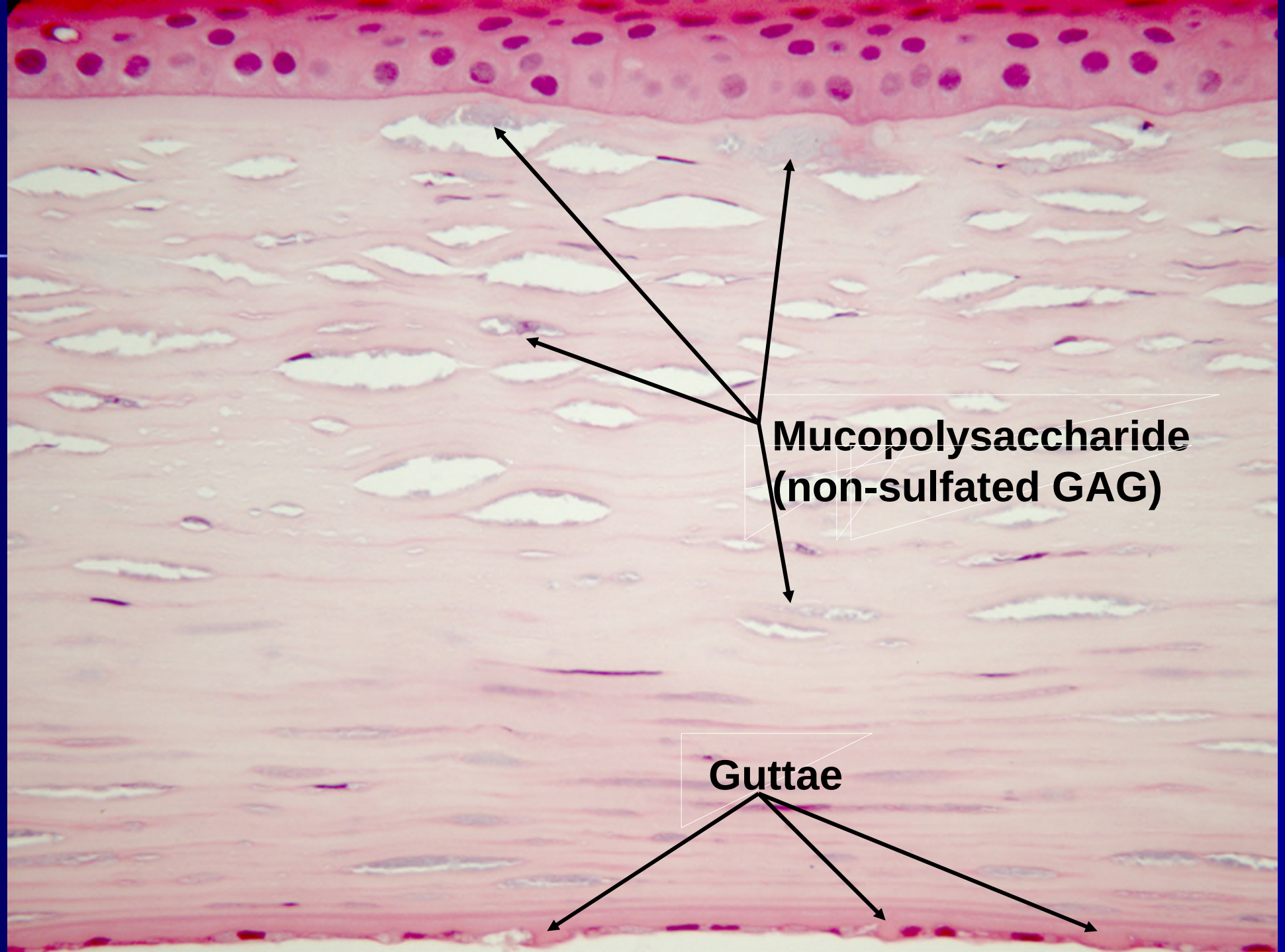
No AgKS in extracellular material or serum

Macular corneal dystrophy type II:

All corneal abnormal accumulations manifest AgKS immunoreactivity

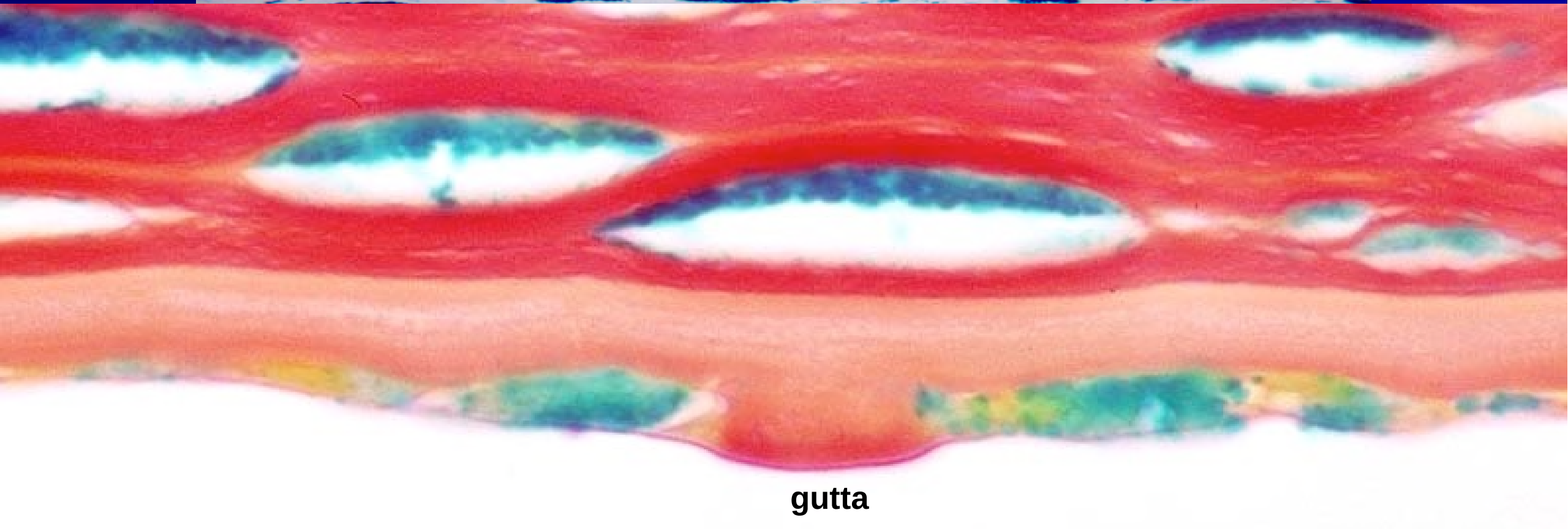
Serum has normal or lower levels of AgKS


Mucopolysaccharide
(non-sulfated GAG)

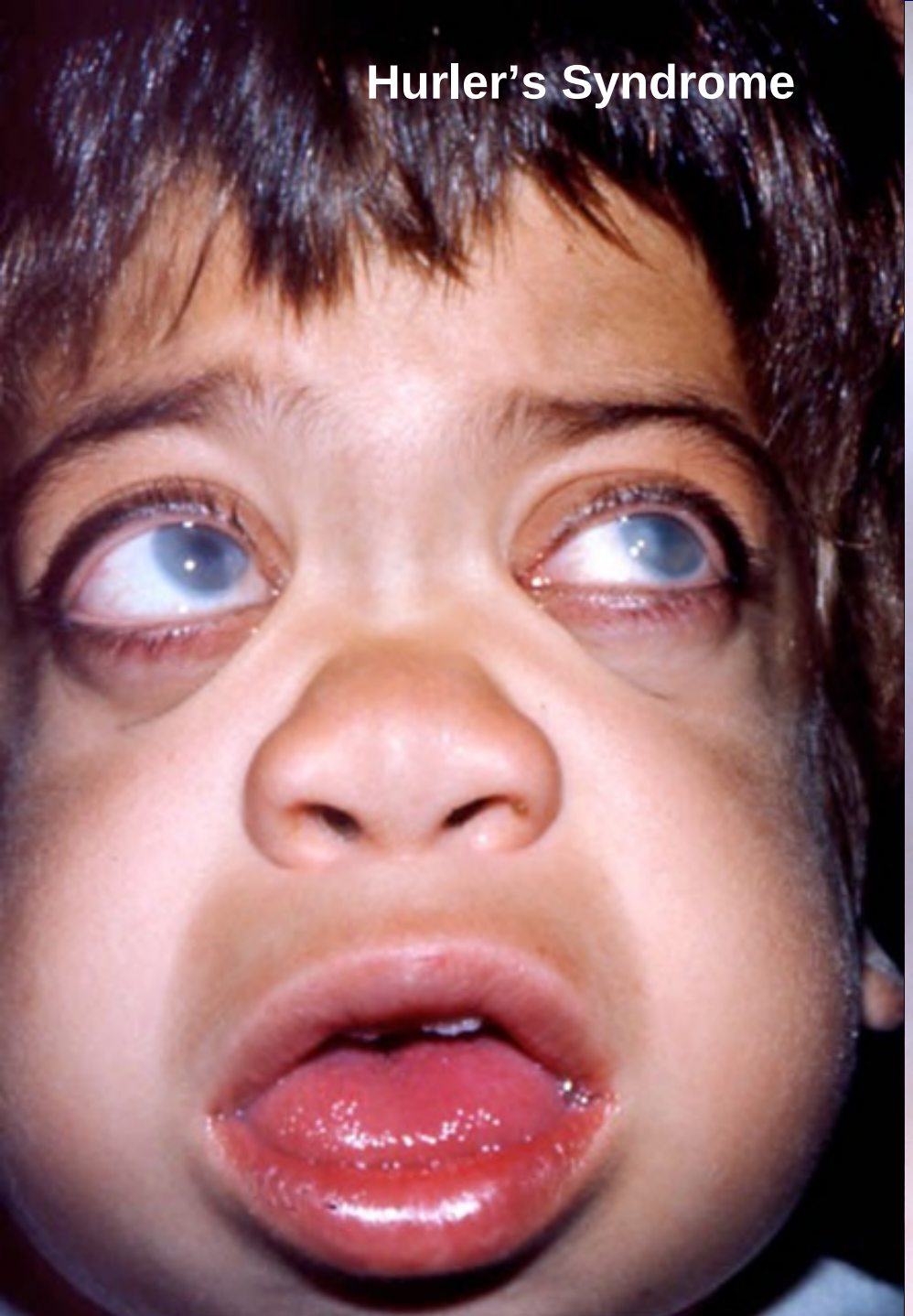

Mucopolysaccharide
(non-sulfated GAG)
Guttae

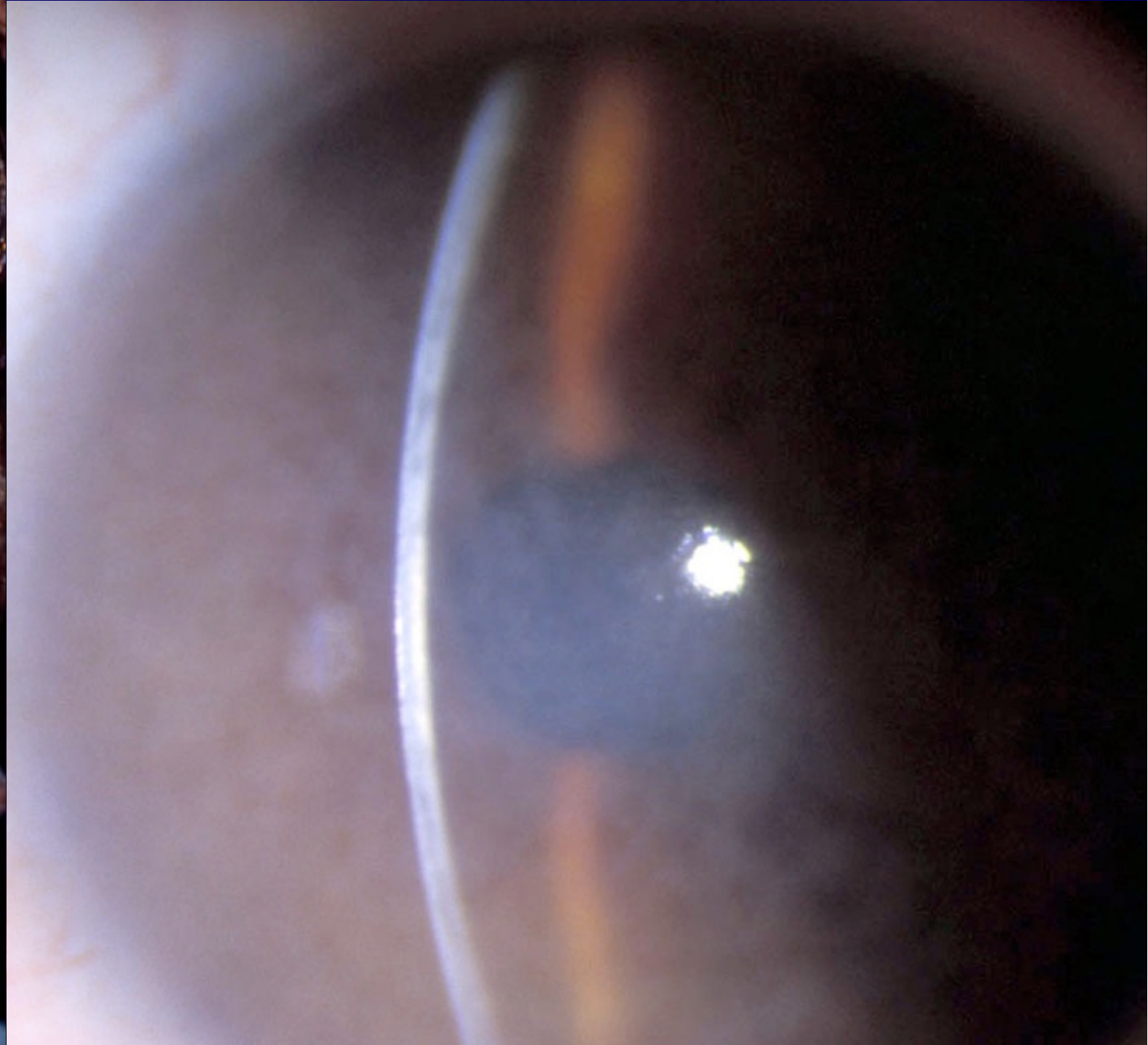
Macular Dystrophy

Epithelium not involved

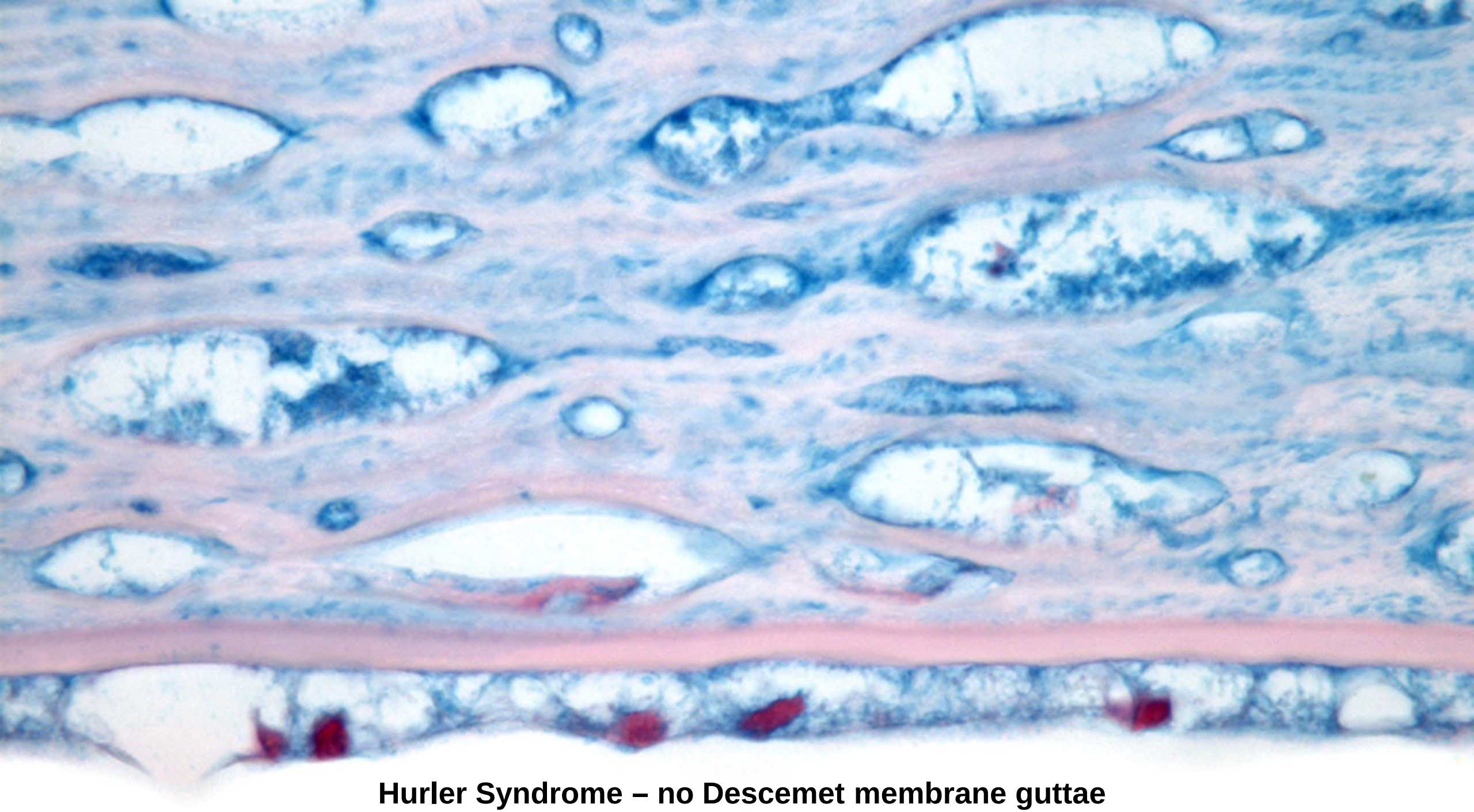


gutta


Hurler’s Syndrome



Hurler Syndrome – intraepithelial mucopolysaccharide deposits



Hurler Syndrome – no Descemet membrane guttae

Corneal Stromal Dystrophies

Marilyn Monroe Always Gets Her Men in LA, CA

Marilyn – Macular
Monroe – Mucopolysaccharide
Always – Alcian Blue (acid mucopolysaccharide)

Gets – Granular
Her – Hyalin
Men – Masson trichrome
in
L – Lattice
A – Amyloid
C – Congo Red
A – Avellino (granular + lattice)

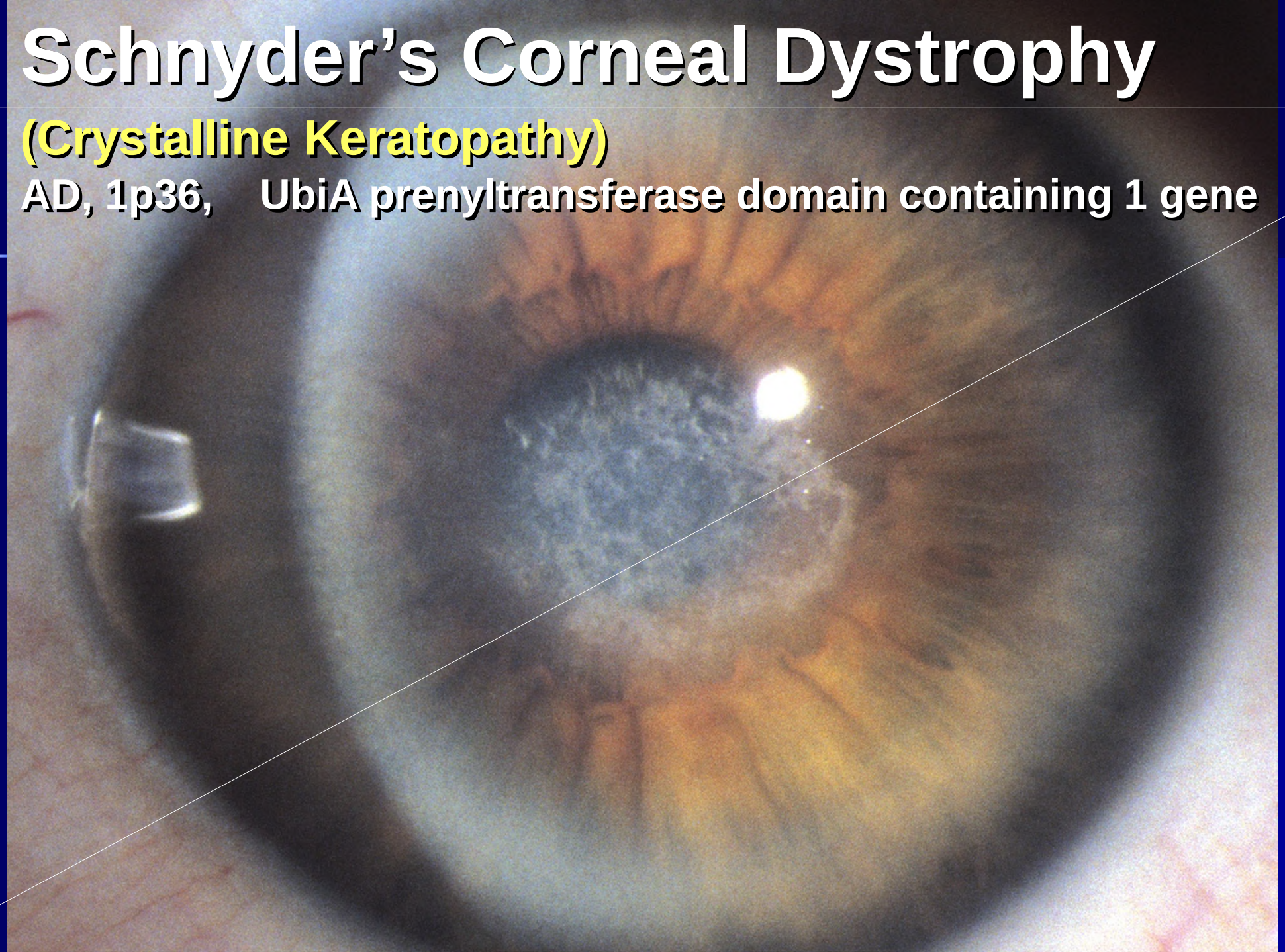
AD
5q
TGF-beta I

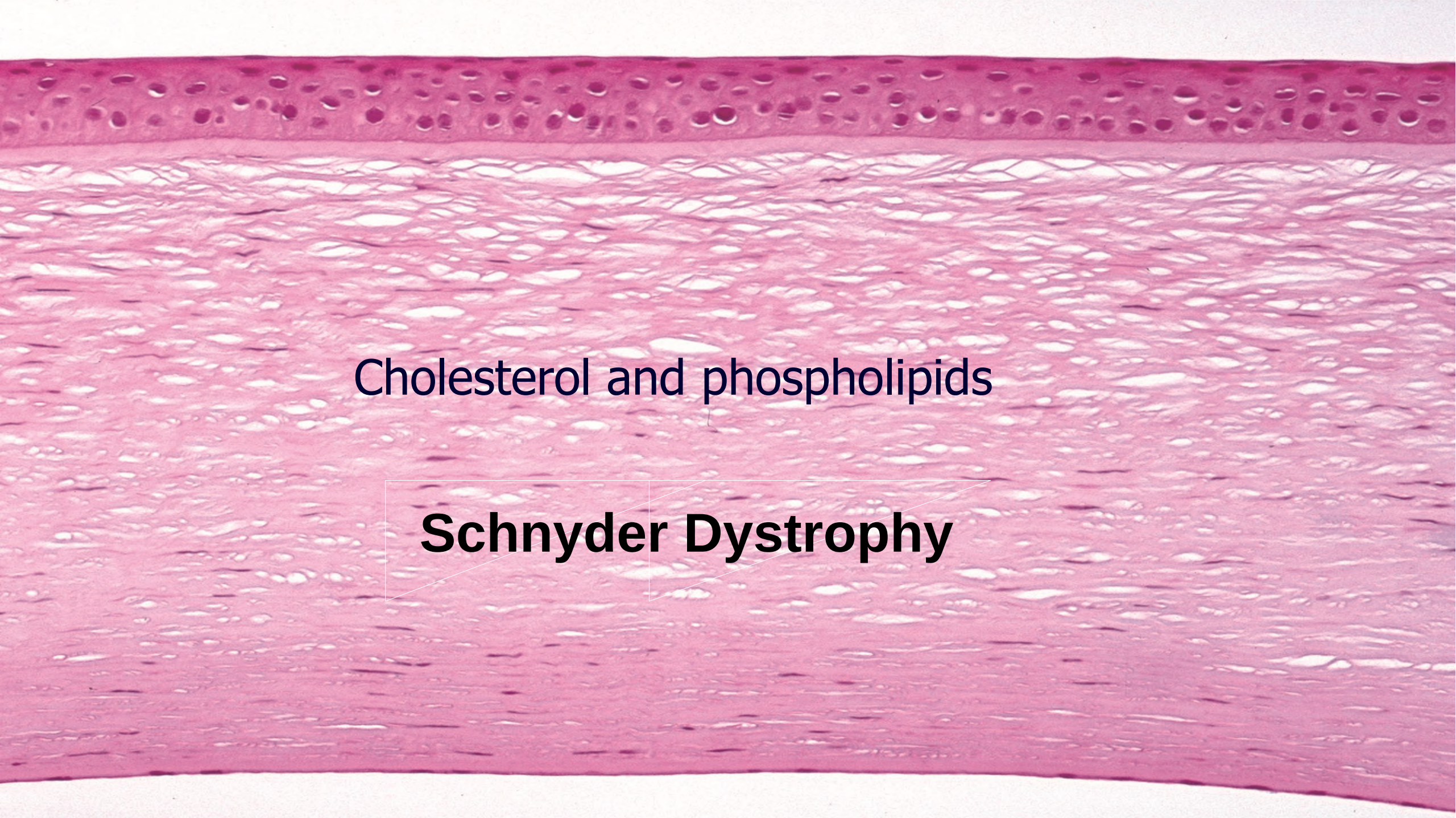
Keratoepithelin
(extracellular matrix protein; modulates cell adhesion)

Schnyder’s Corneal Dystrophy

(Crystalline Keratopathy)

AD, 1p36, UbiA prenyltransferase domain containing 1 gene




Cholesterol and phospholipids
Schnyder Dystrophy

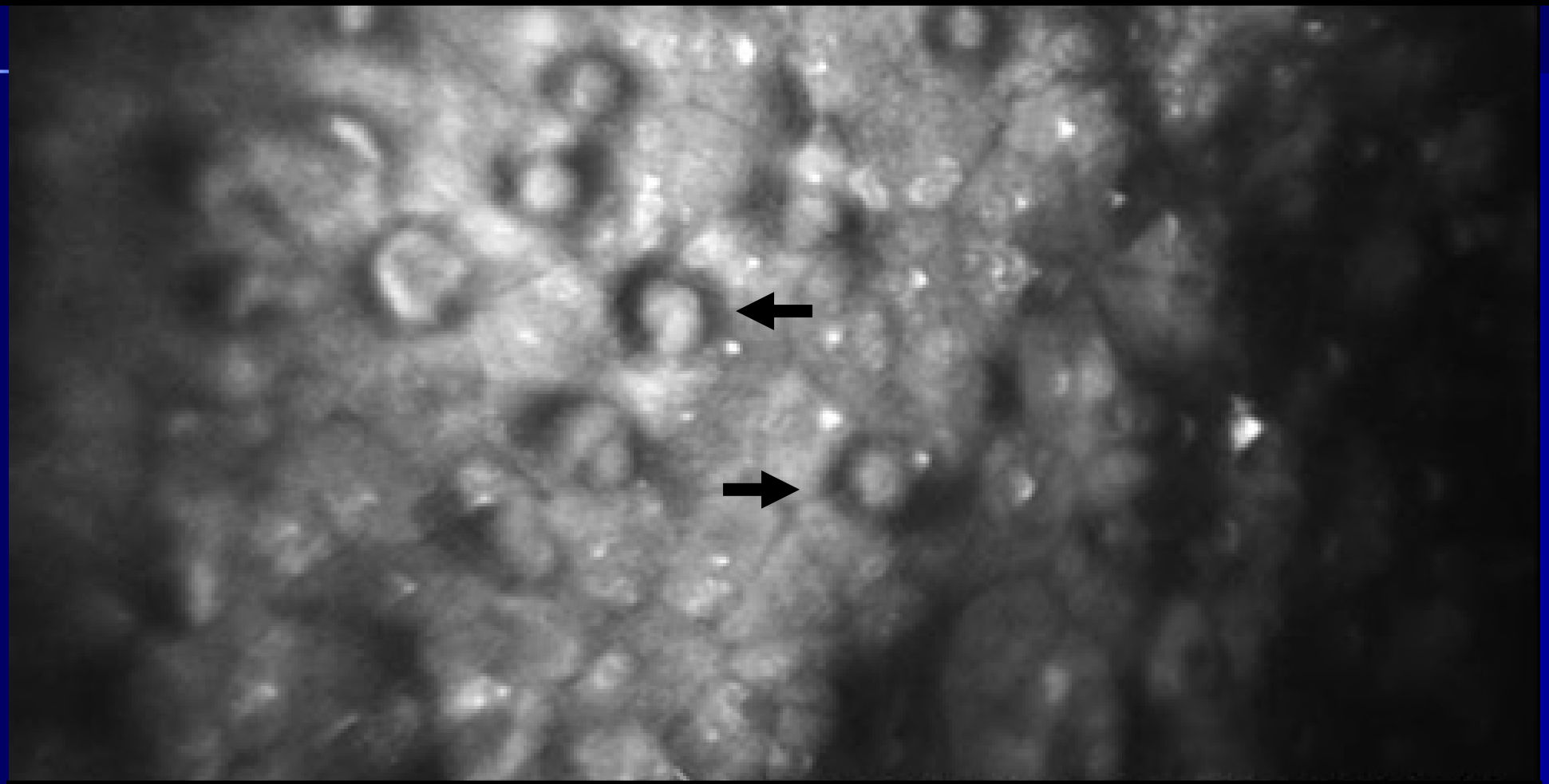
Endothelial dystrophies

1. Fuchs endothelial corneal dystrophy (FECD)
2. Posterior polymorphous corneal dystrophy (PPCD)
3. Congenital hereditary endothelial dystrophy (CHED)
4. X-linked endothelial corneal dystrophy (XECD)

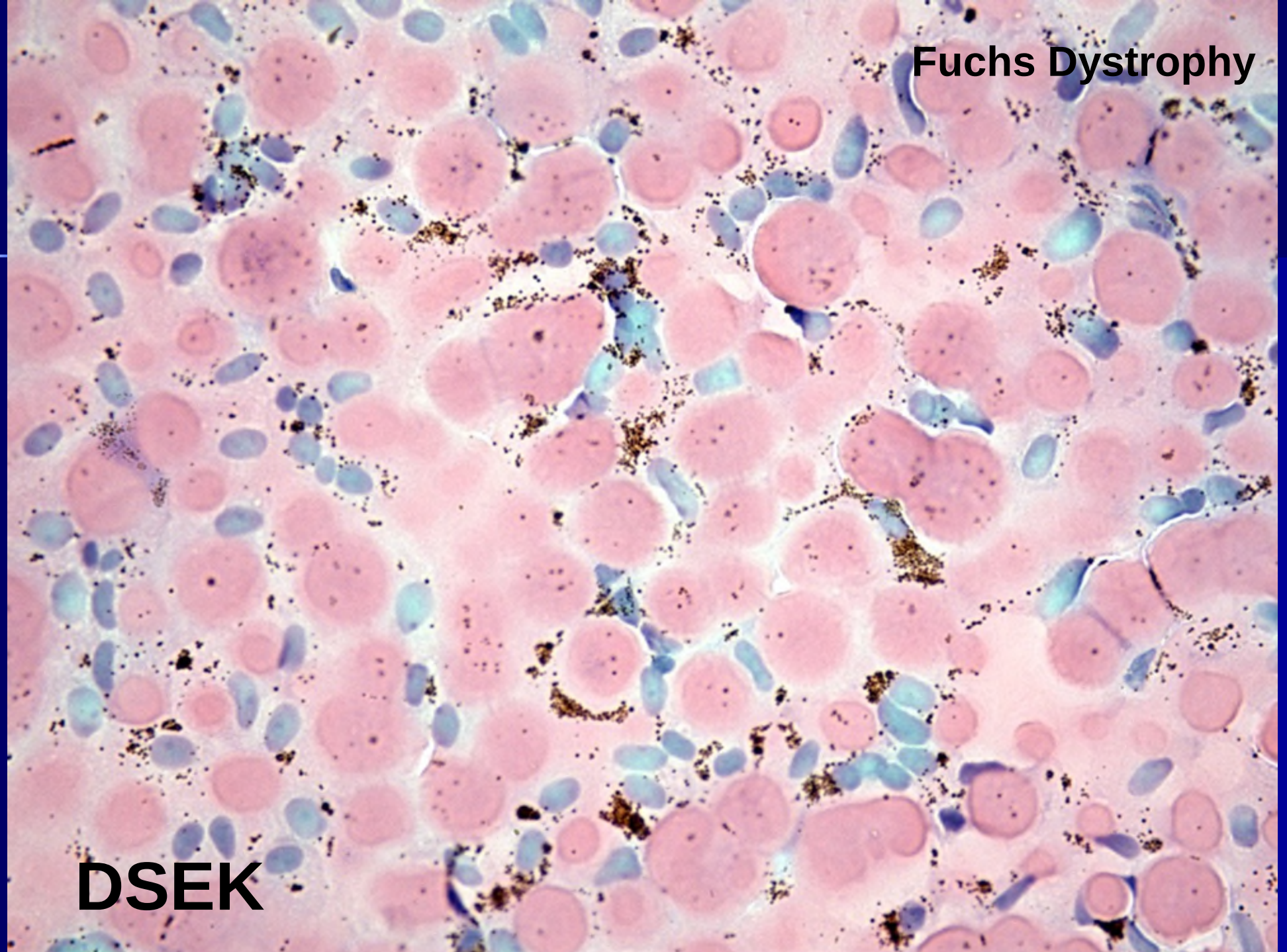
Fuchs Endothelial Dystrophy

Some AD, Chr 18 (*TCG4* gene intronic CTG18.1 repeat expansion), Multiple other genes

Early onset: 1p34, Collagen VIII gene

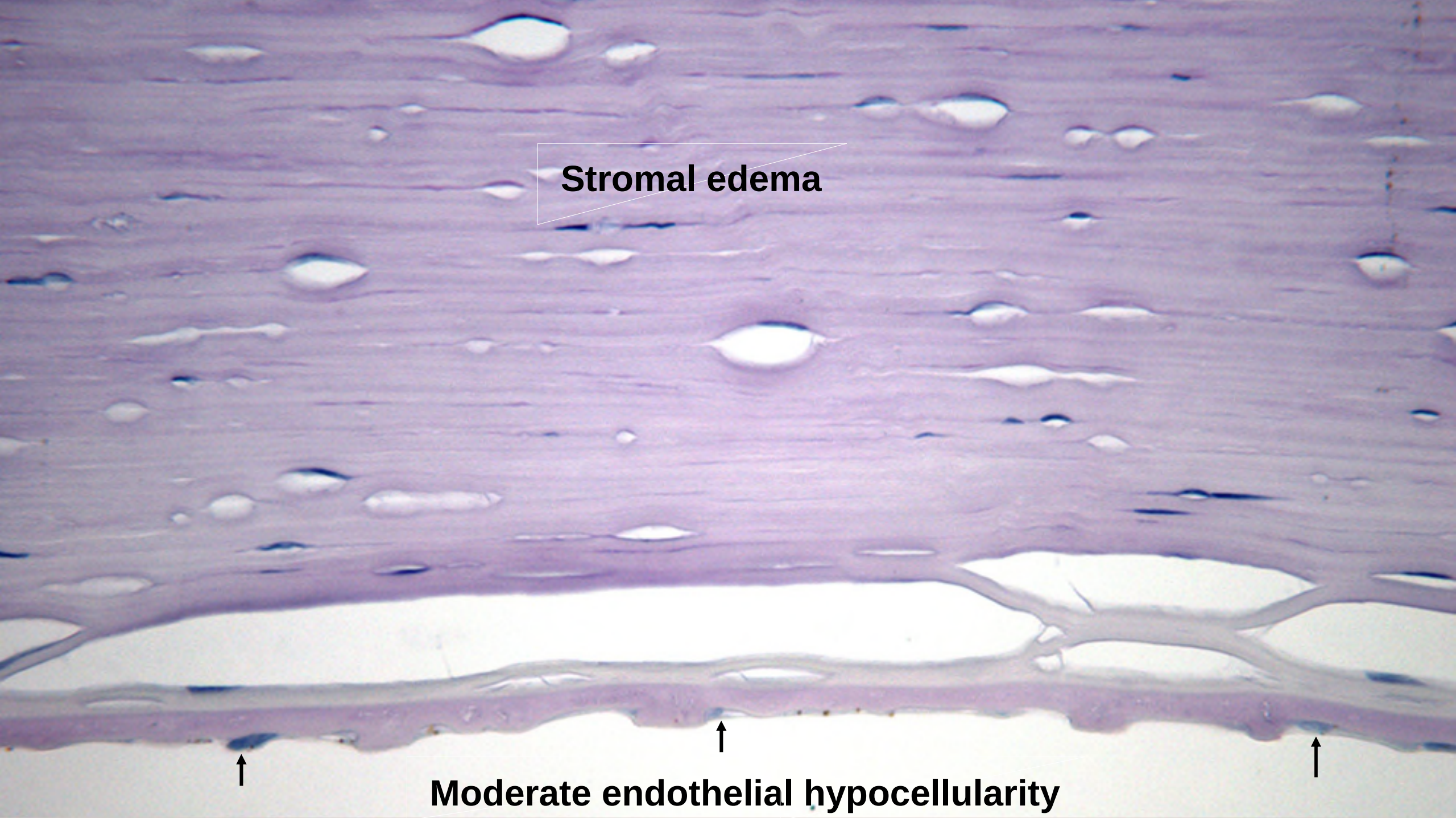


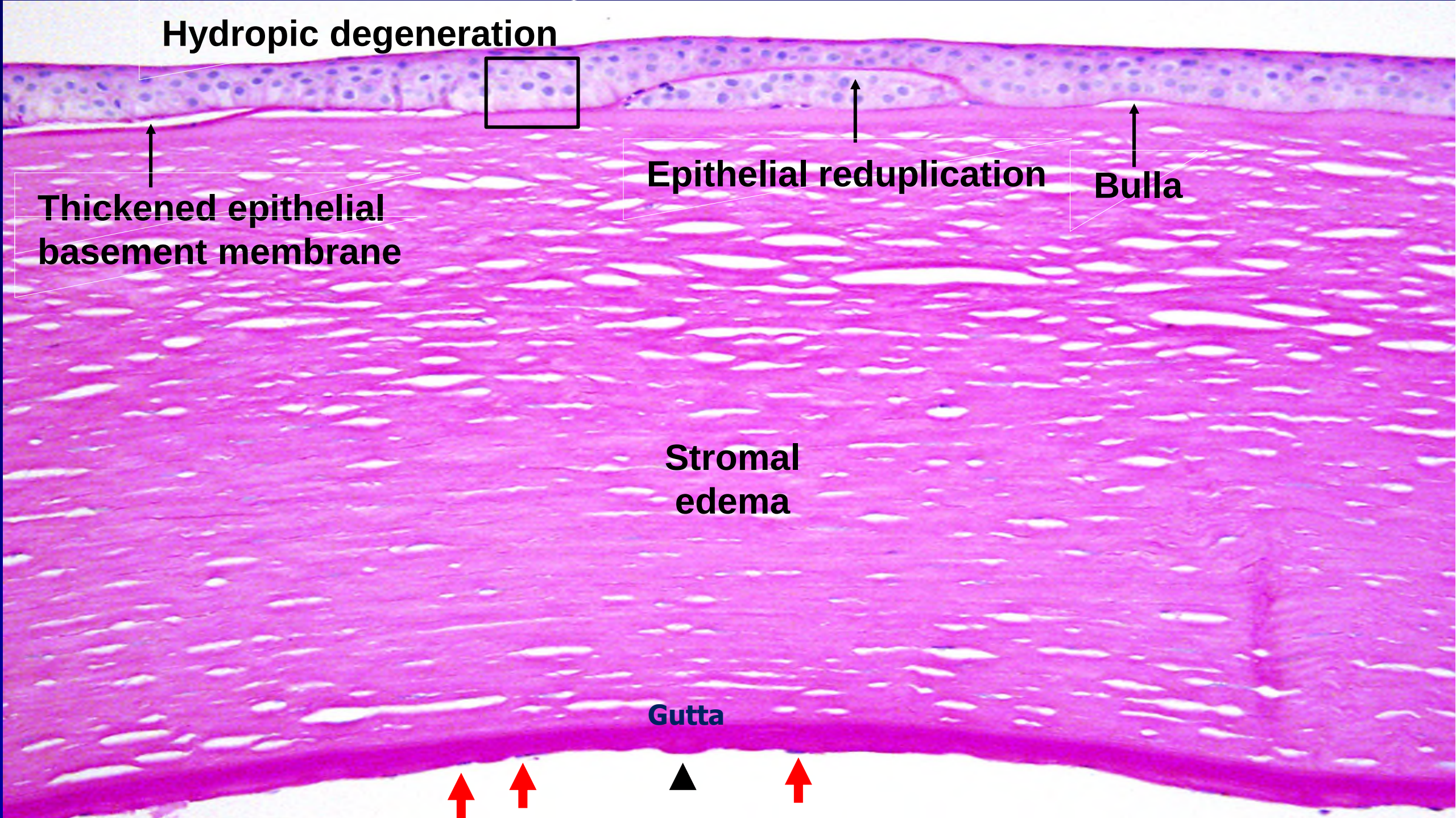

Fuchs Dystrophy
Courtesy of Ralph C. Eagle, Jr. MD


Fuchs Dystrophy
DSEK

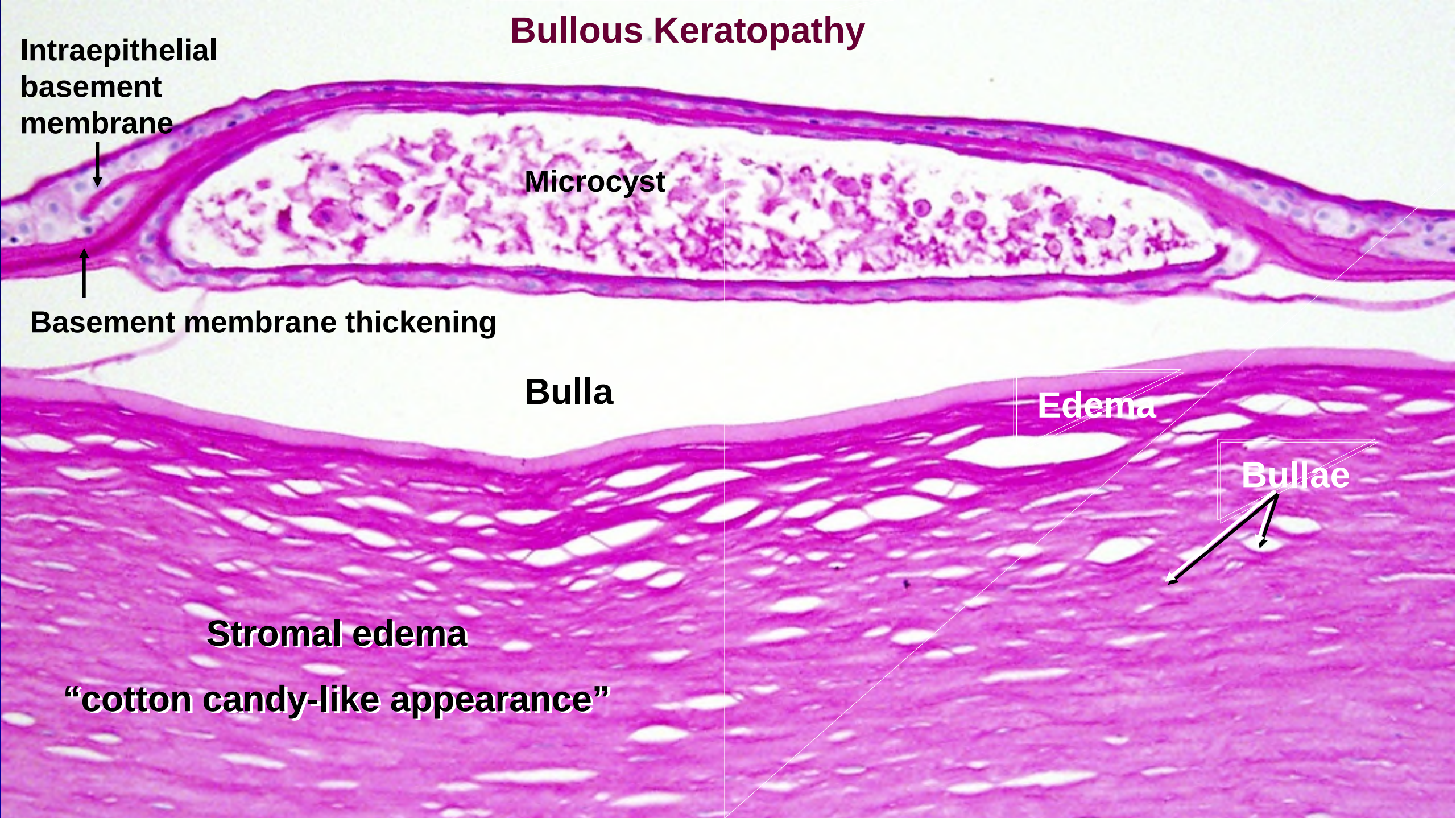
Thickened Descemet membrane

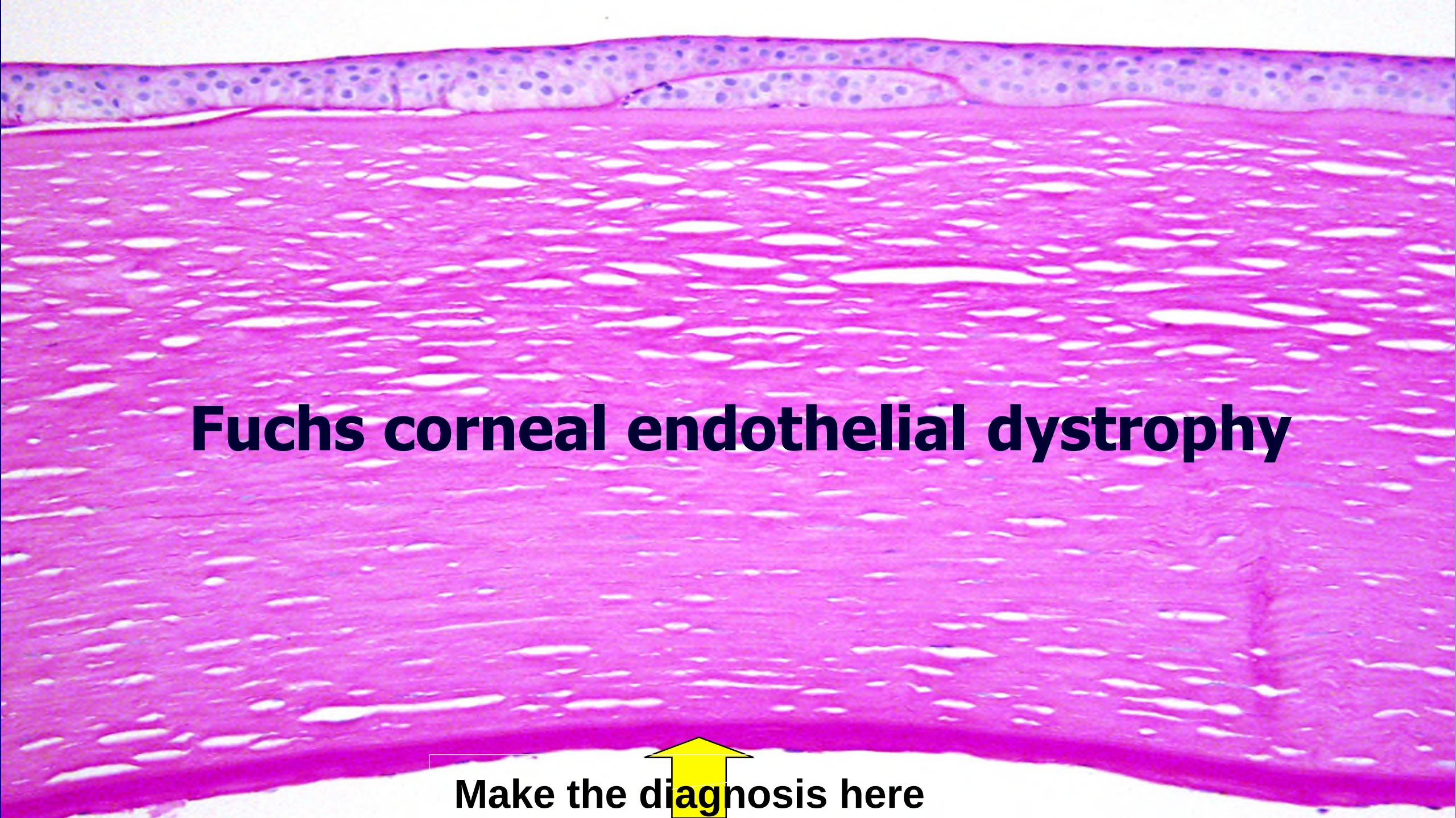
Guttate Excrescences

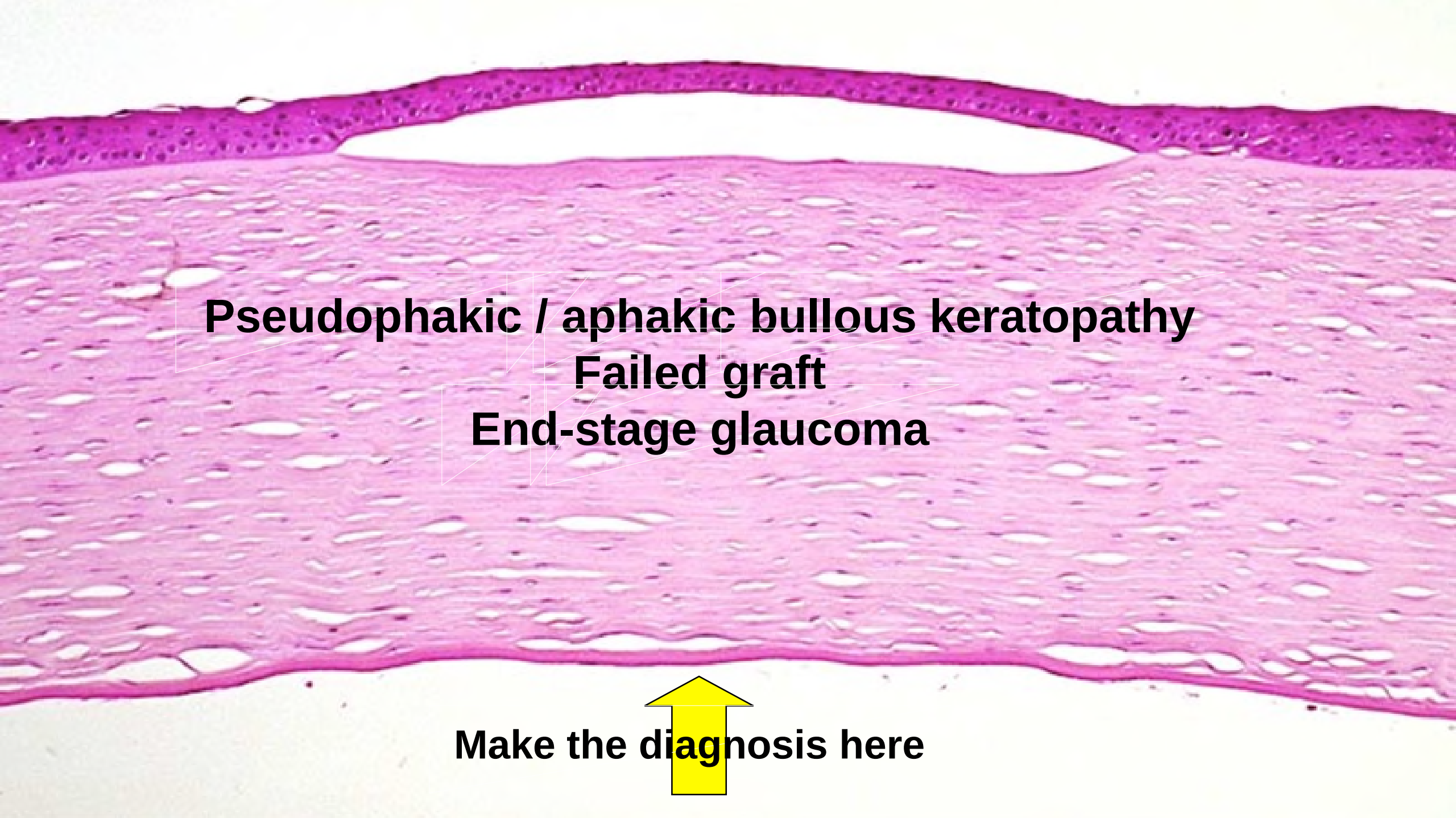

Stromal edema
Moderate endothelial hypocellularity


Hydropic degeneration
Thickened epithelial basement membrane
Epithelial reduplication
Bulla
Stromal edema
Gutta

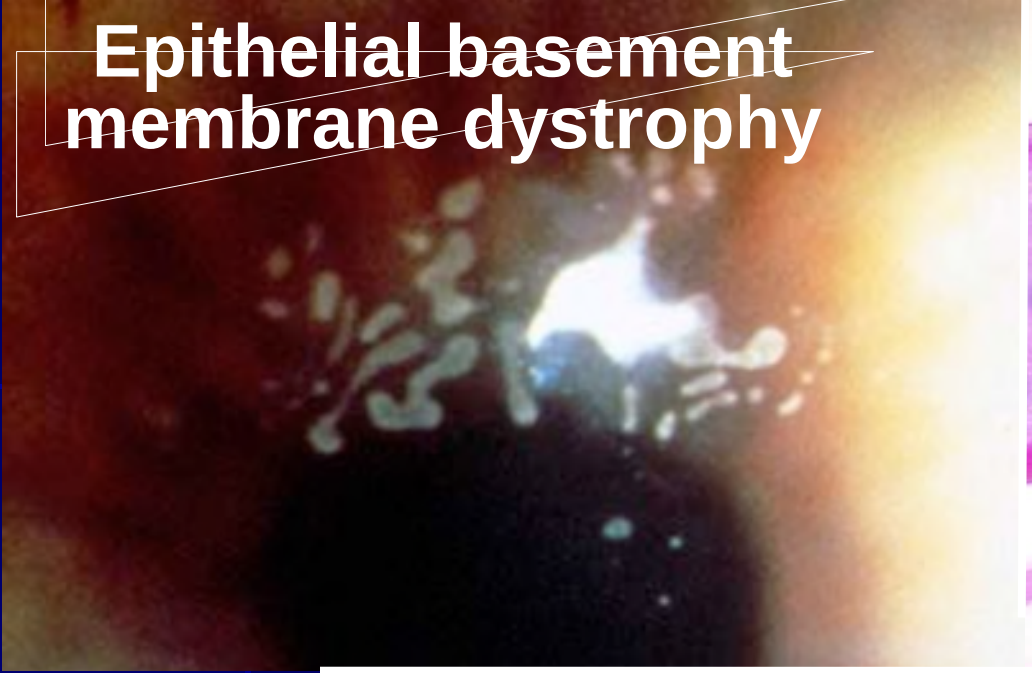
Bullous Keratopathy

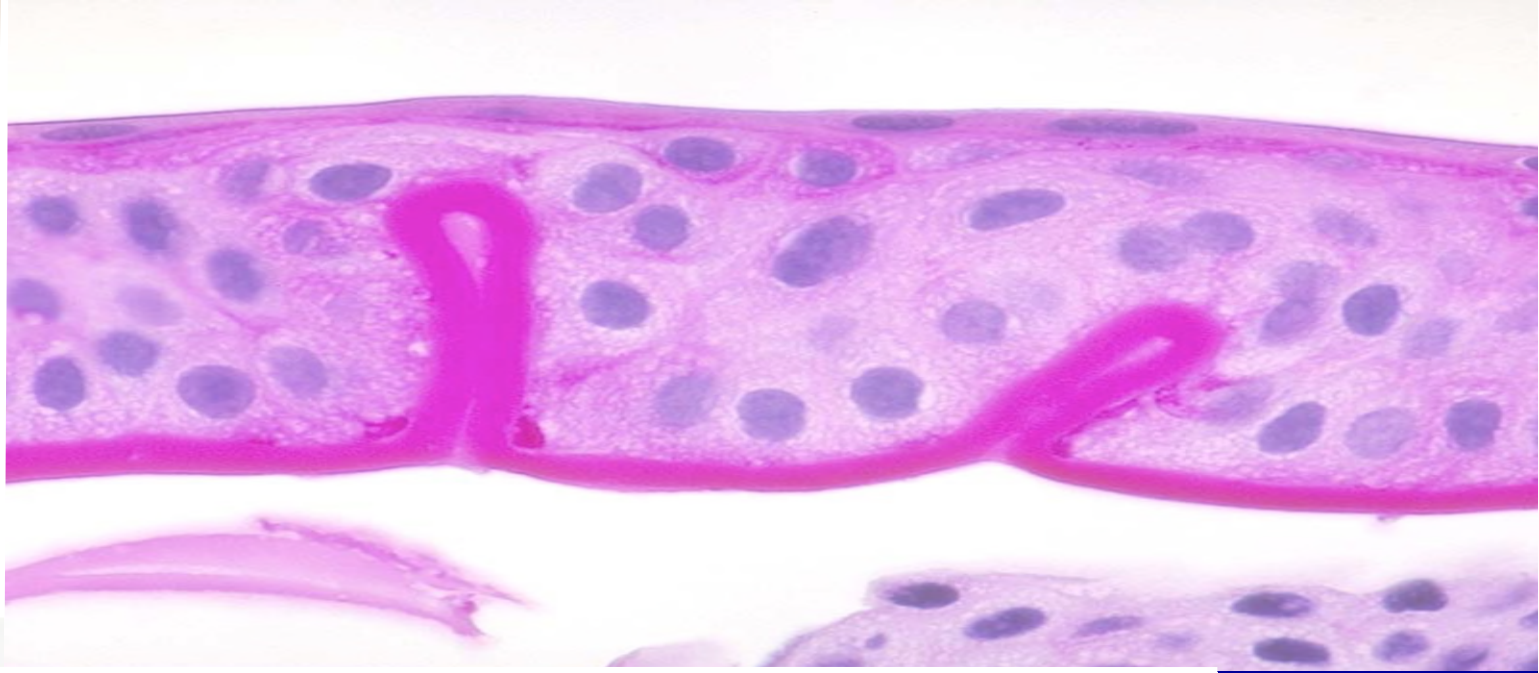


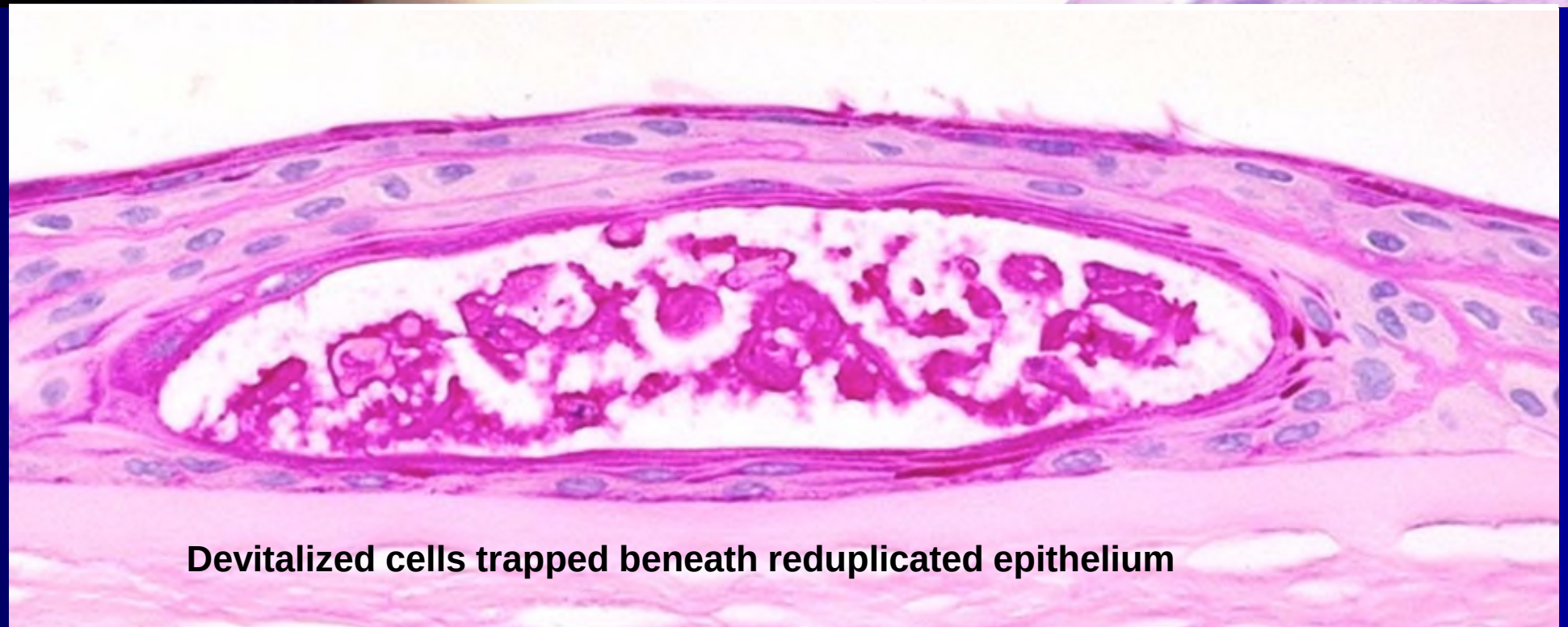

Fuchs corneal endothelial dystrophy
Make the diagnosis here


Pseudophakic / aphakic bullous keratopathy
Failed graft
End-stage glaucoma
Make the diagnosis here

Epithelial basement membrane dystrophy

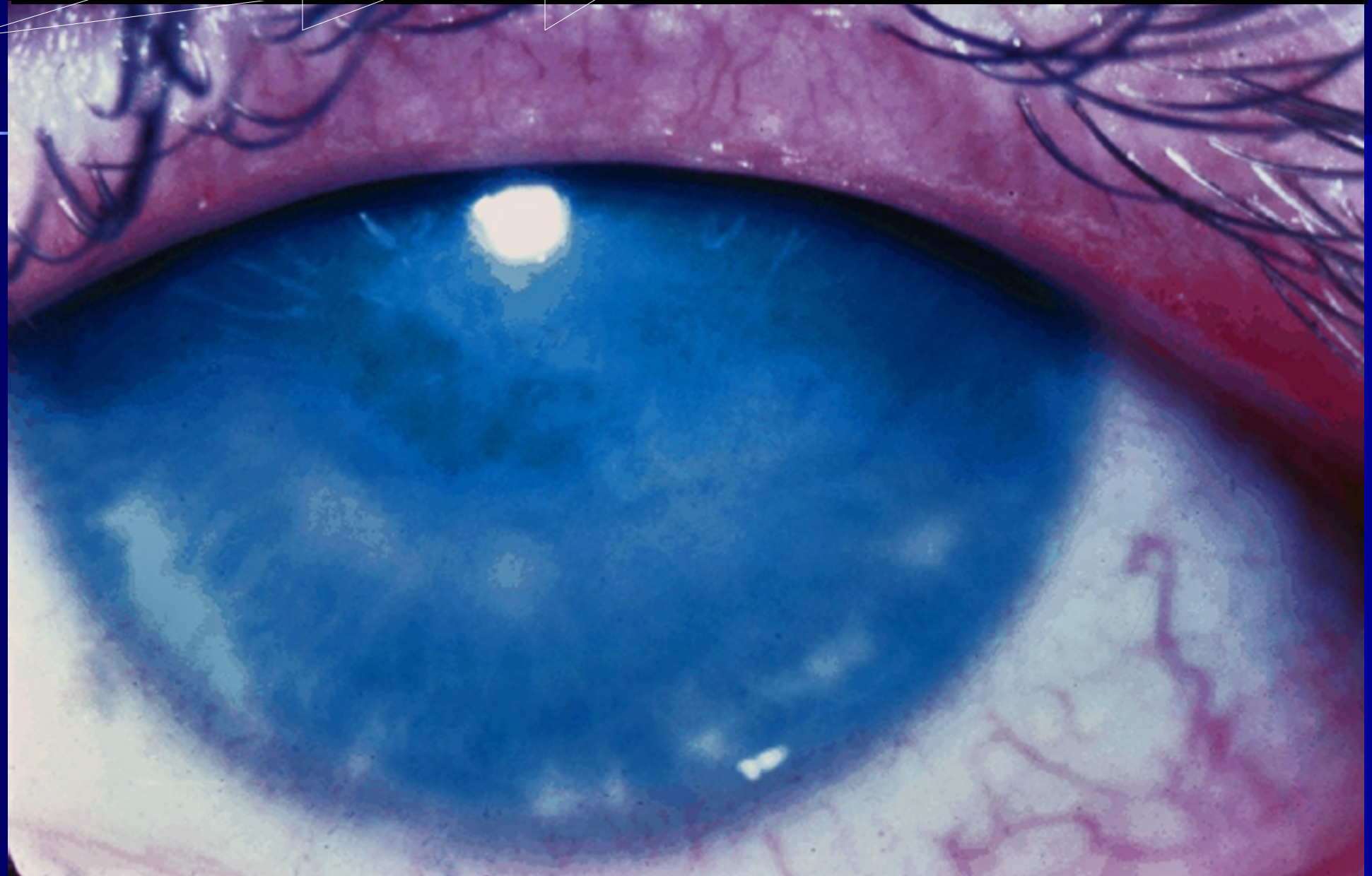




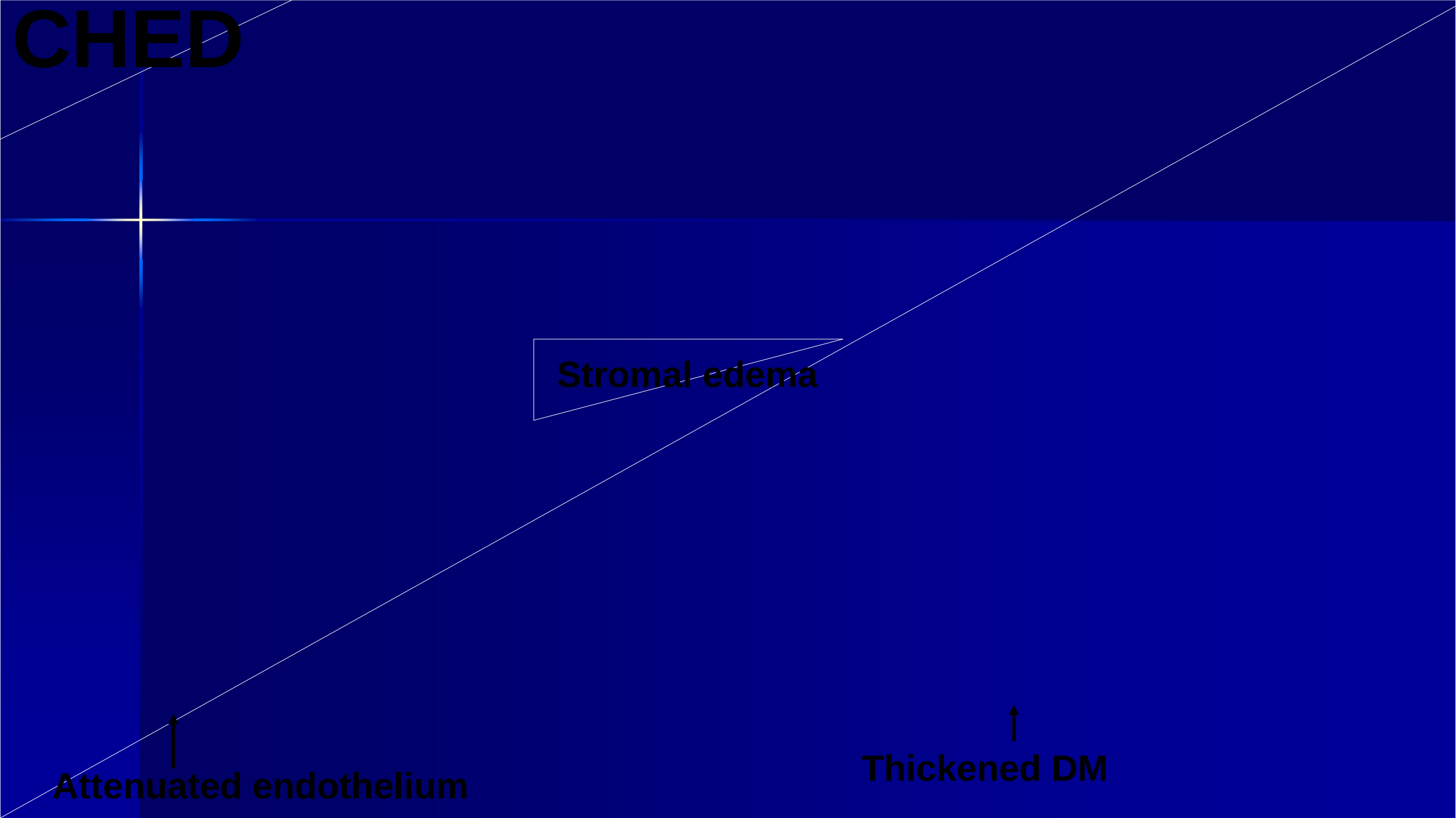


Devitalized cells trapped beneath reduplicated epithelium

Congenital Hereditary Endothelial Dystrophy (CHED)
AR, 20p13 *SLC4A11* gene



CHED



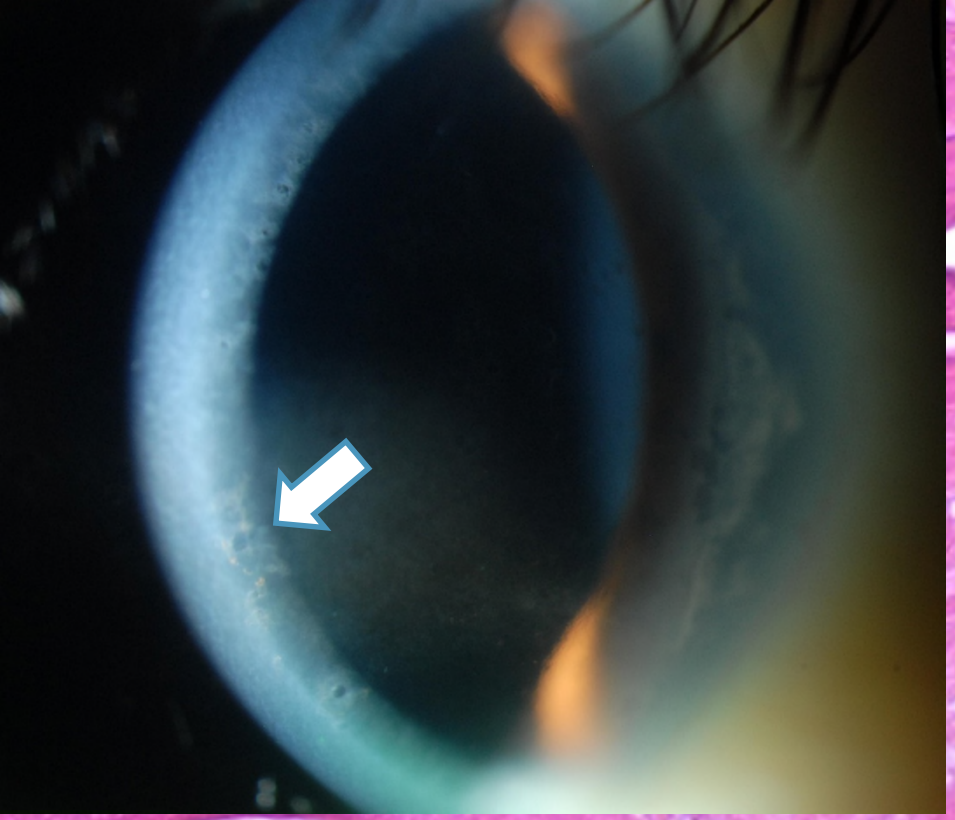
Posterior Polymorphous Dystrophy

AD

PPCD 1: 20p11.2-q11.2, Gene unknown

PPCD 2: 1p34.3-p32.3
collagen, type VIII, alpha-2 (*COL8A2*)

PPCD 3: 10p11.22
zinc finger E box–binding homeobox 1 (*ZEB1*)



CK5/6

Multilaminated Descemet membrane

IC3D Classification of Corneal Dystrophies—Edition 2

Jayne S. Weiss, MD, Hans Ulrik Møller, MD, PhD,† Anthony J. Aldave, MD,‡ Berthold Seitz, MD,§ Cecilie Bredrup, MD, PhD,¶ Tero Kivelä, MD, FEBO,‖ Francis L. Munier, MD,** Christopher J. Rapuano, MD,†† Kanwal K. Nischal, MD, FRCOphth,‡‡ Eung Kweon Kim, MD, PhD,§§ John Sutphin, MD,¶¶ Massimo Busin, MD,‖‖ Antoine Labbé, MD,*** Kenneth R. Kenyon, MD,††† Shigeru Kinoshita, MD, PhD,‡‡‡ and Walter Lisch, MD§§§*

Cornea 2015 Feb;34(2):117-59. doi: 10.1097/ICO.0000000000000307.

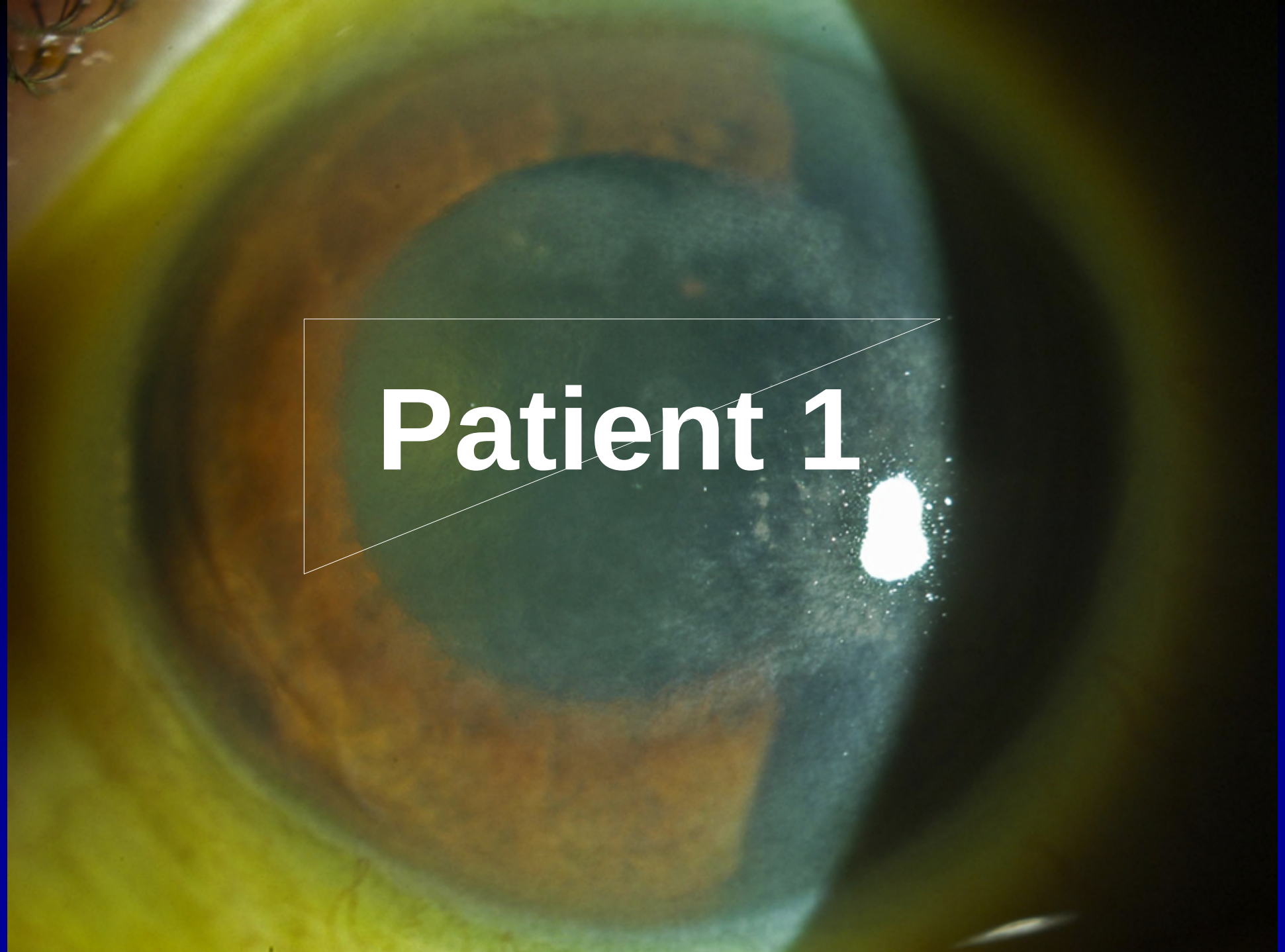
Purpos update the 2008 International Classification of Corne Dystrophie (IC3D) incorporating new molecul, histopathologic and genetic information.

Method The IC3D reviewed worldwide peer-reviewed articles for new information on corneal dystrophies published between 2008 and 2014. Using this information, corneal dystrophy templates and anatomic classification were updated. New clinical photographs, and confocal photographs were added.

Results: On the basis of revisiting the cellular origin of corneal dystrophy, a modified anatomic classification process consisting of (1) epithelial and subepithelial dystrophies, (2) epithelial–stromal *TGFBI* dystrophies, (3) stromal dystrophies, and (4) endothelial dystrophies. Most of the dystrophy templates were updated. The entity "Epithelial recurrent erosion dystrophies" actually includes a number of potentially distinct epithelial dystrophies (Francescheti corneal dystrophy, Dystrophia Smolandensis, and Dystrophia Helsinglandica but must be differentiated from dystrophies such as *TGFBI*-induced dystrophies, which are also often associated with recurrent epithelial erosions. The chromosome locus of Thiel-Behnke corneal dystrophy is only located on 5q31. The entity previously designated as a variant of Thiel-Behnke corneal dystrophy on chromosome 10q24 may represent a novel corneal dystrophy. Congenital hereditary endothelial dystrophy (CHED, formerly CHED2) is most likely only an autosomal recessive disorder. The so-called autosomal dominant [illegible] (CHED1) is insufficiently distinct to continue to be considered a unique corneal dystrophy. On review of almost all of the published cases, the description appeared most similar to [illegible] posterior polymorphous corneal dystrophy linked to the same chromosome 20 locus (PPCD1). Confocal microscopy also has emerged as a helpful tool to reveal in vivo

Genetic testing
Diagnosis
Genetic counseling
Prognostication

Illustrative Case Examples


Patient 1

74 year old Caucasian man Italian descent

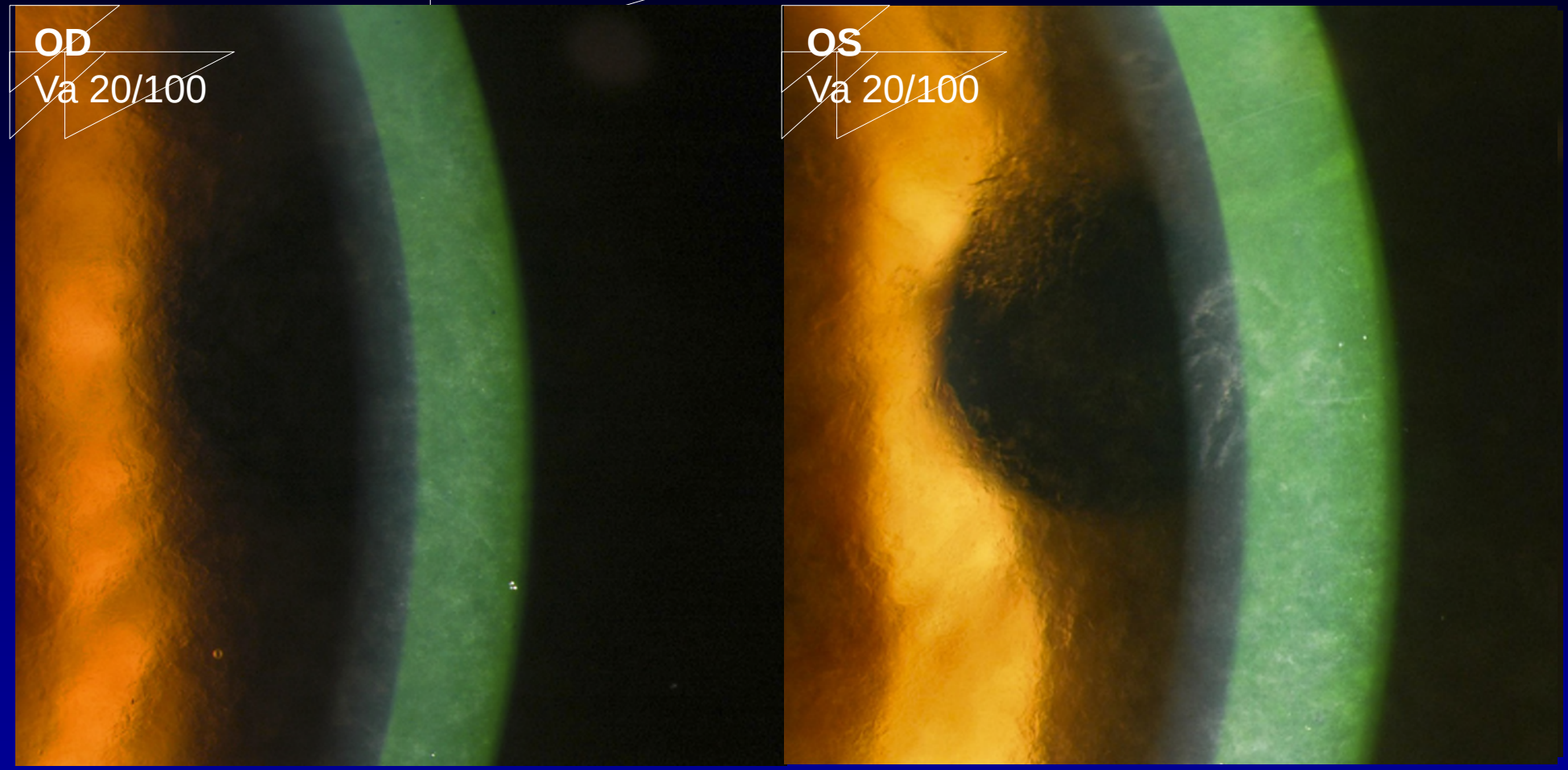
CC: **Progressive visual loss OU over 8 – 10 months**

POH: **RGPs and soft contact lenses for astigmatism**

PMH: **HTN, DM, high cholesterol**

FH: **Non-contributory**

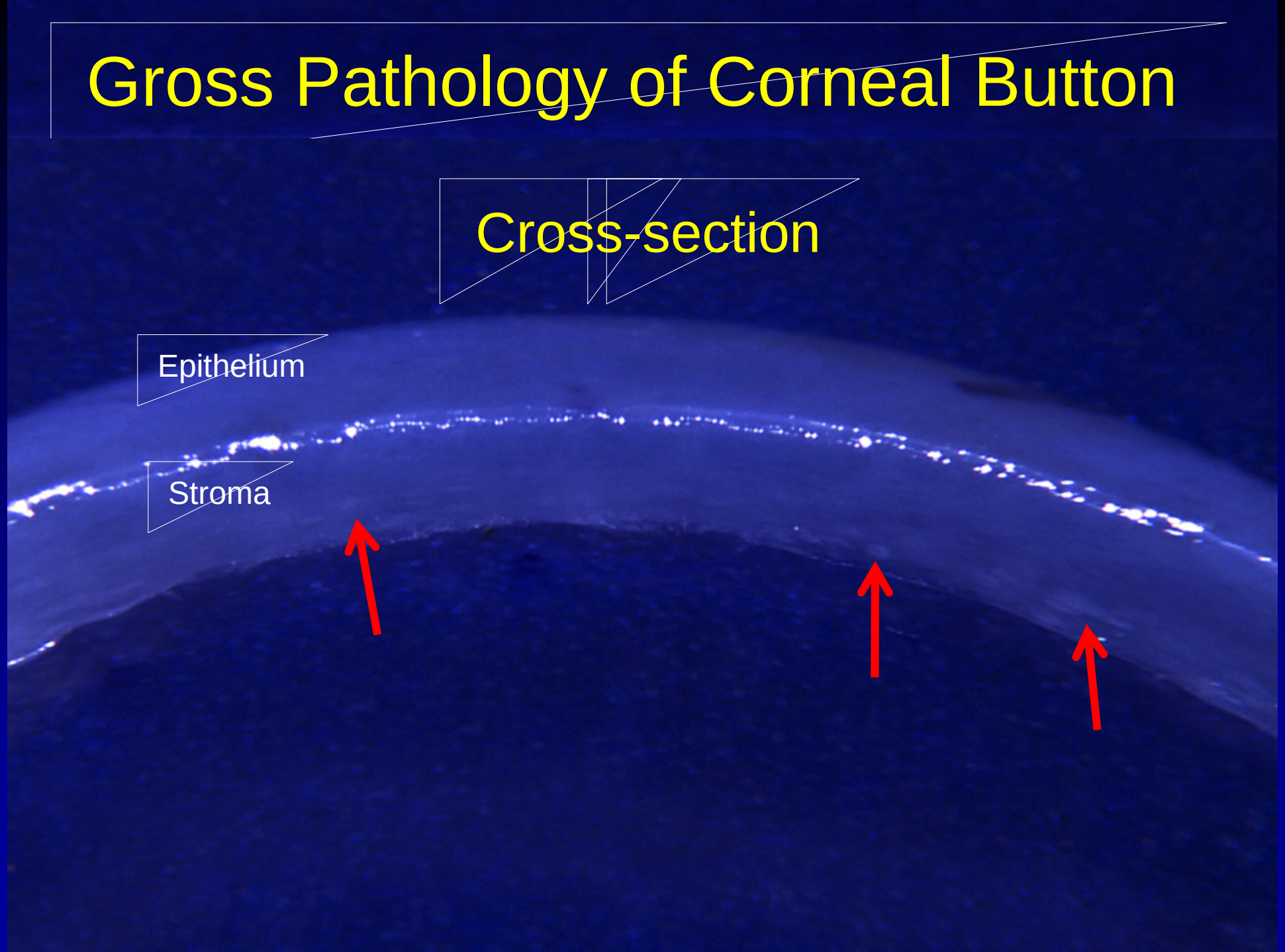
Clinical Exam

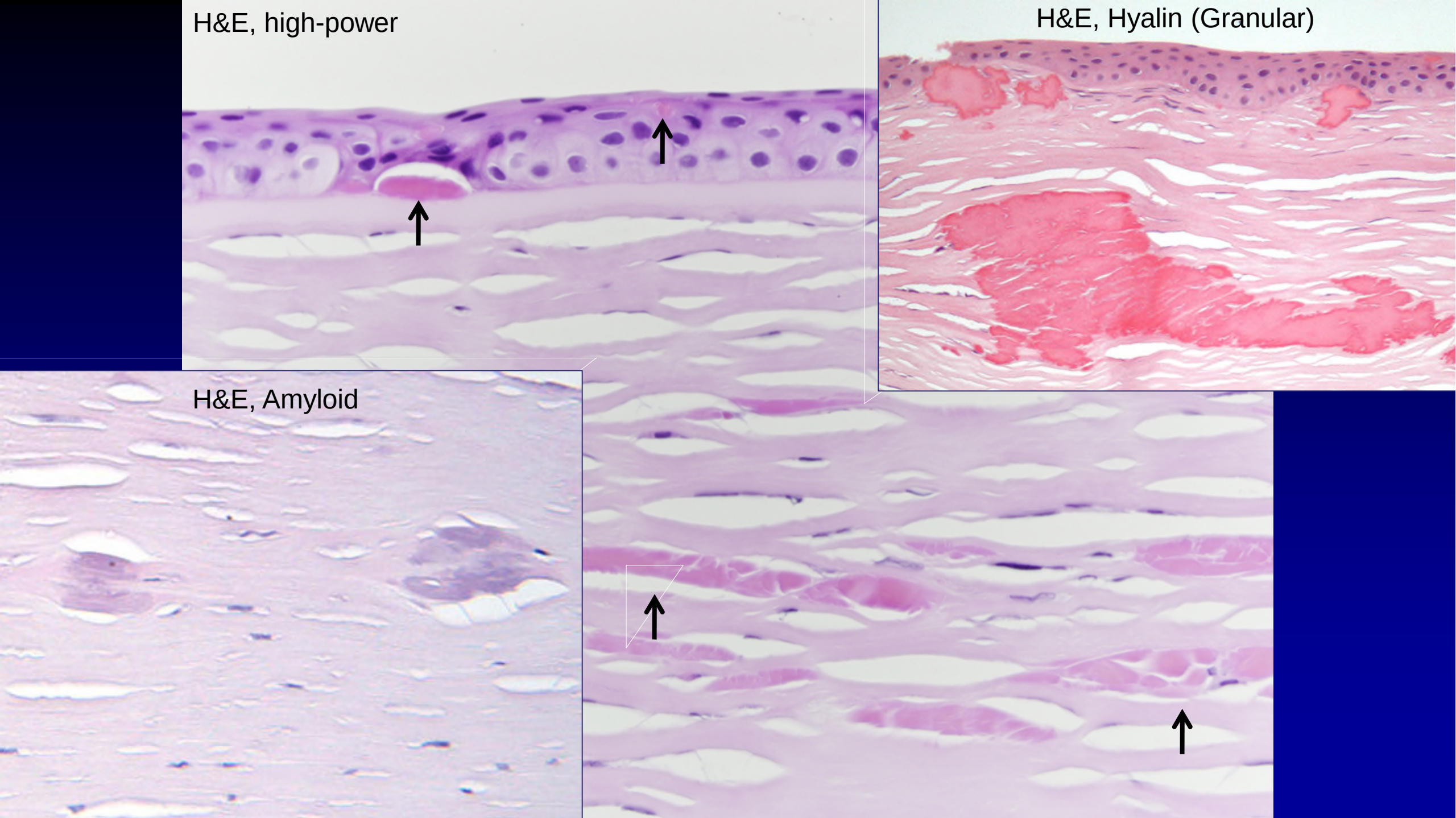


Pt seen by 3 corneal specialists

DDx: Dystrophy (Lattice, granular, Avelino, PPMD), IK (HSV, VZV, EBV), non-dystrophic amyloid deposition, Acanthamoeba, Staph hypersensitivity

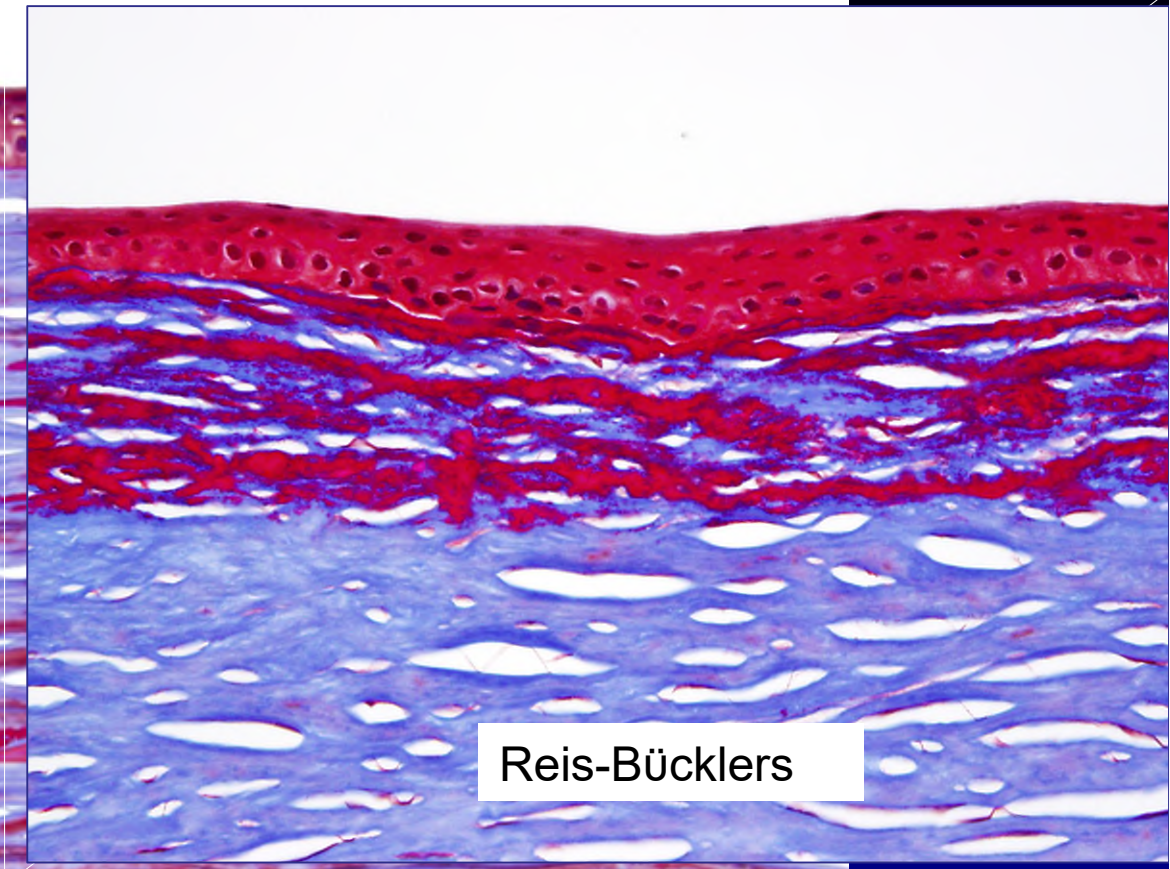
Gross Pathology of Corneal Button




H&E, high-power
H&E, Hyalin (Granular)
H&E, Amyloid

Masson-trichrome, intermediate-power

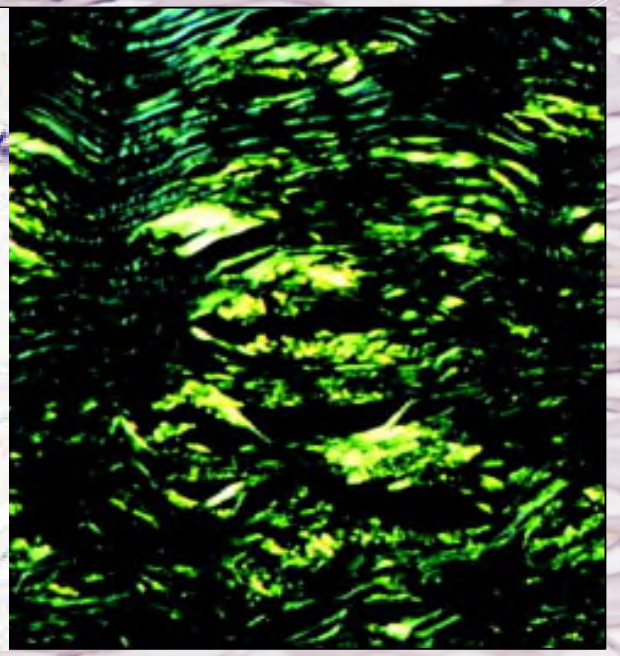
Granular, type 1



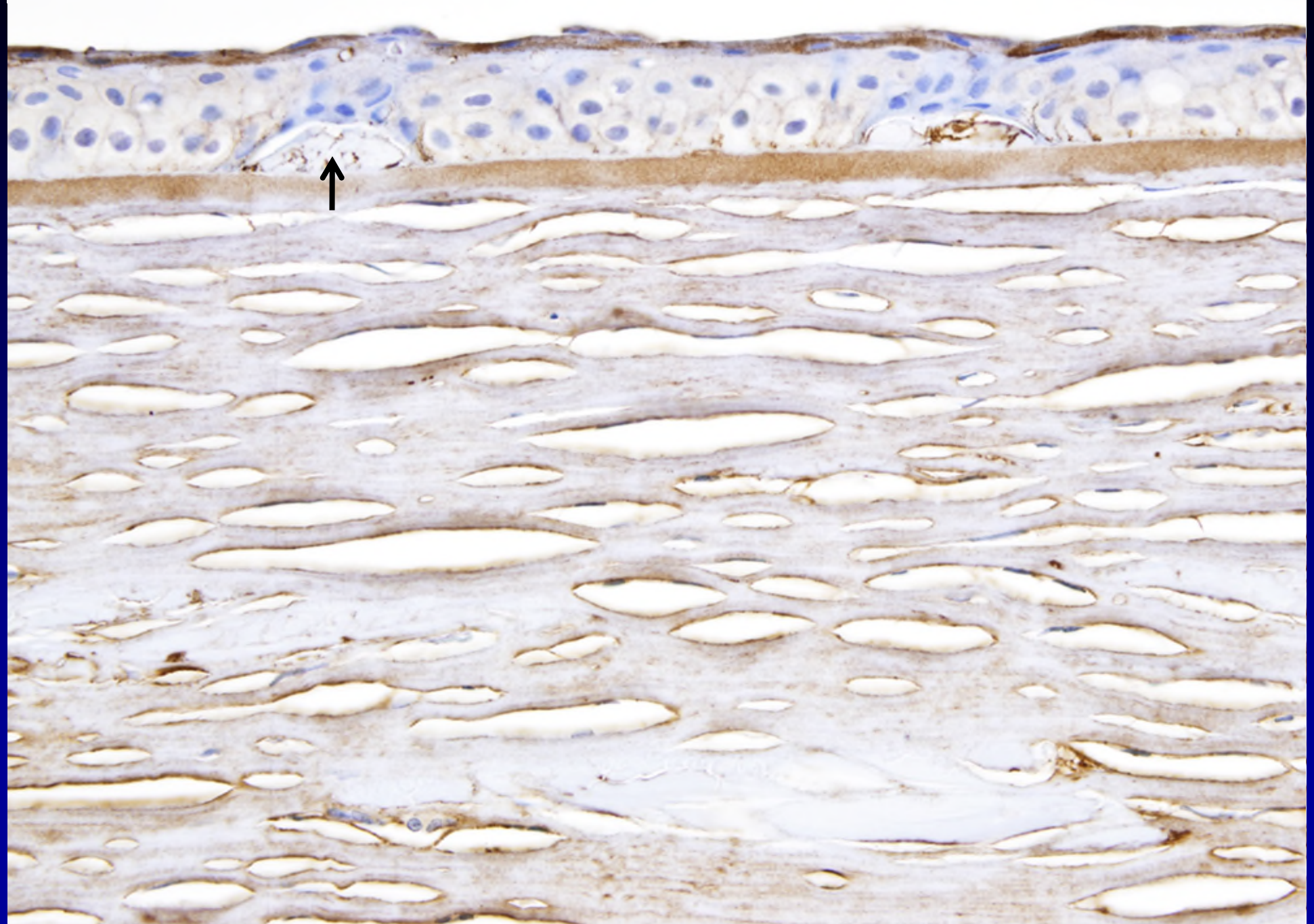
Reis-Bücklers

Congo red, intermediate-power

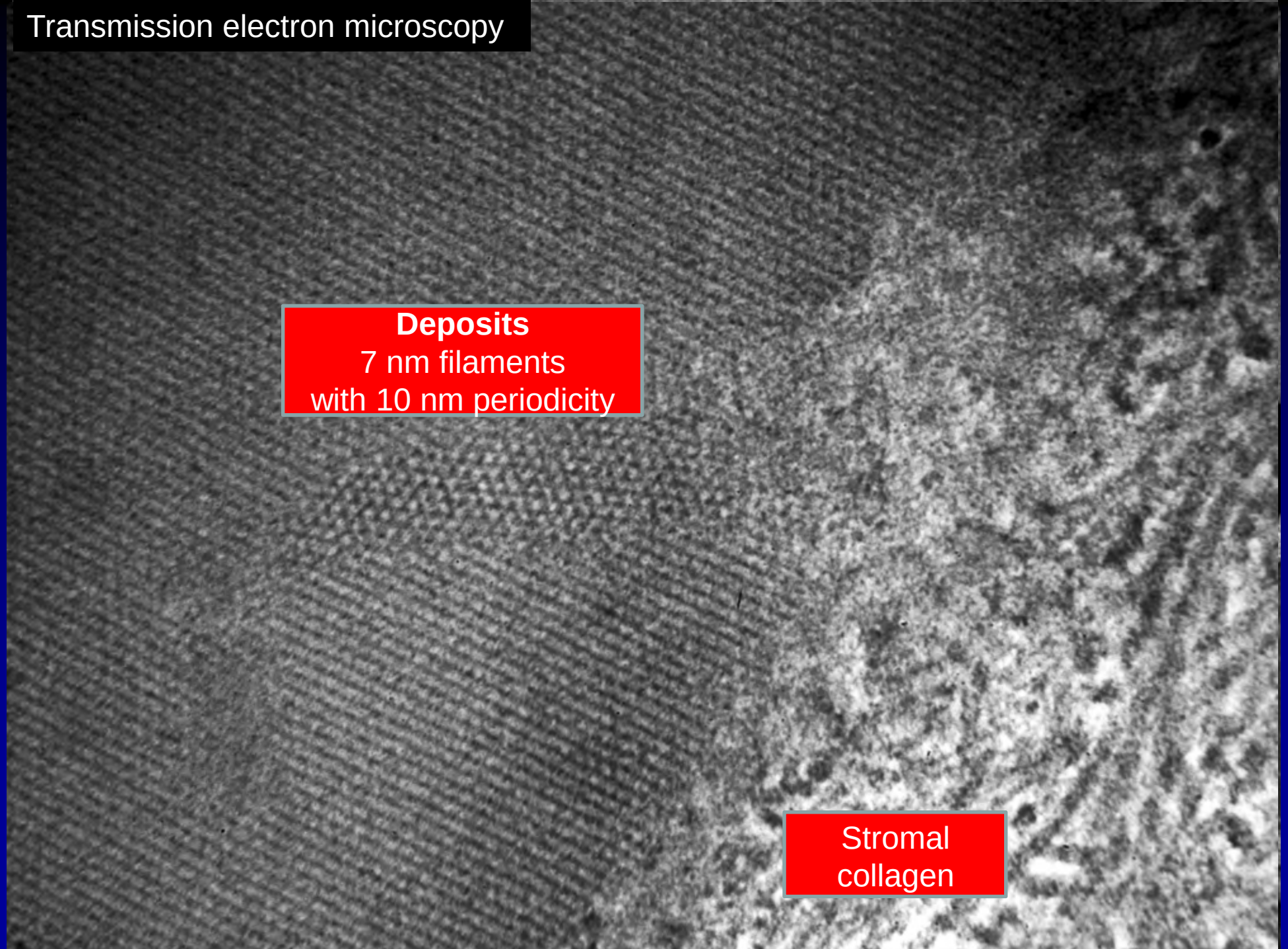
Congo red, Amyloid

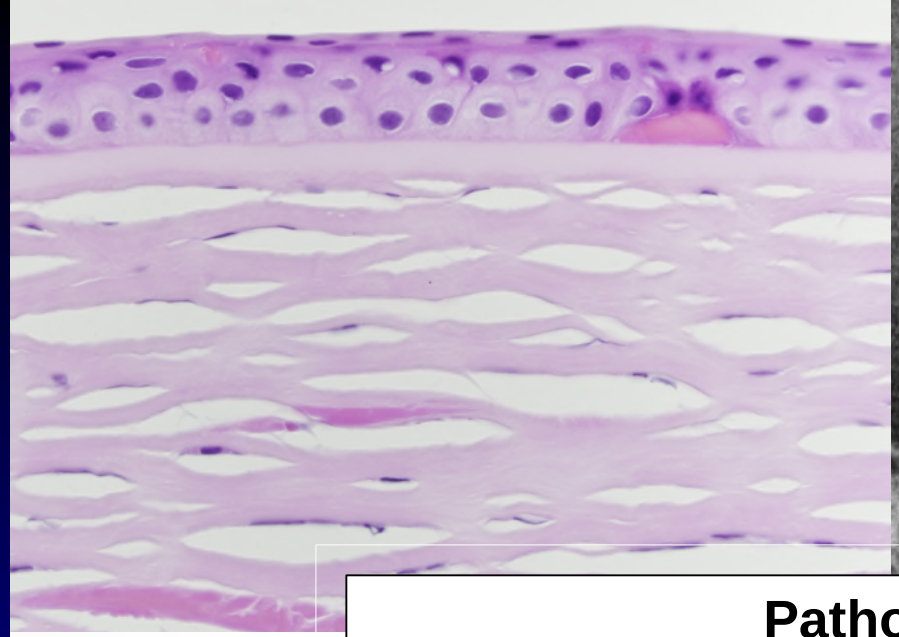


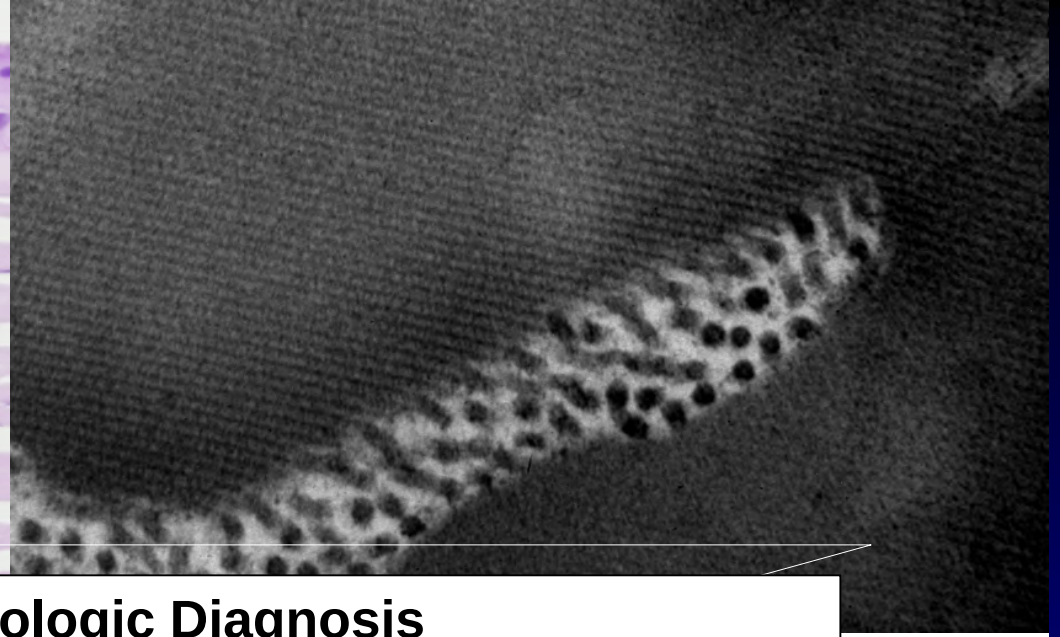
Kappa light chain antibody immunostain, high-power



Transmission electron microscopy



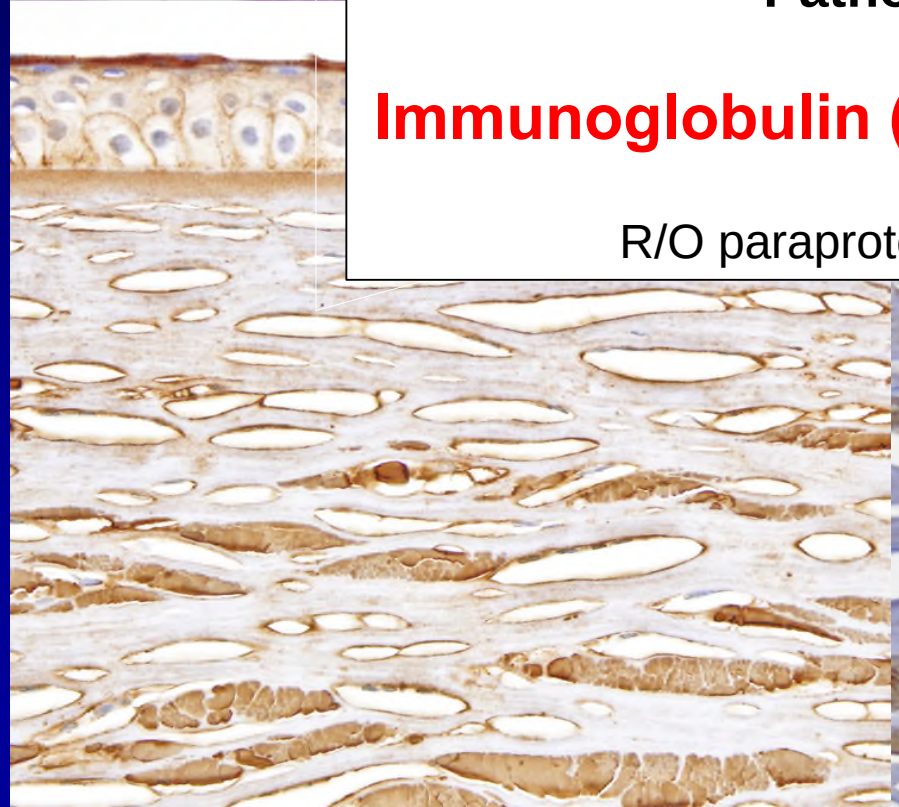


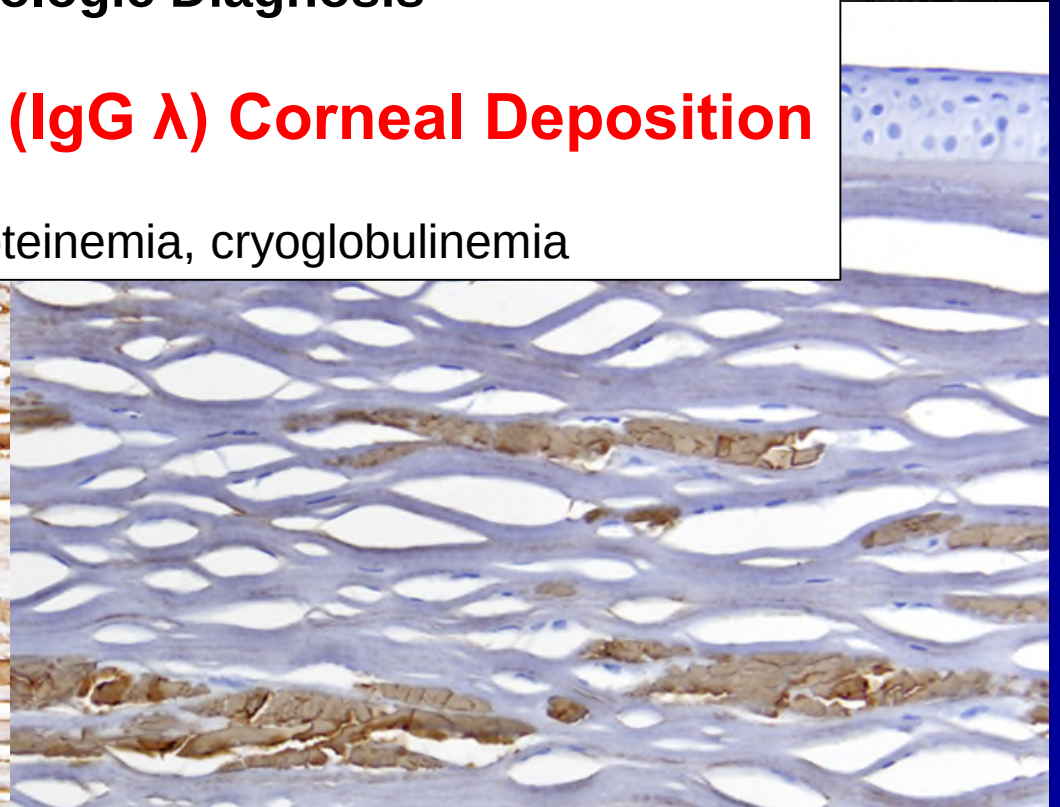


Pathologic Diagnosis

Immunoglobulin (IgG λ) Corneal Deposition

R/O paraproteinemia, cryoglobulinemia





Follow-up Oncology

- ***SPEP***
  - M-protein band (7 g/L)
  - IgG λ paraprotein by immunofixation
- ***UPEP***
  - Trace immunoglobulin
  - No free light chains
  - Normal renal function tests

Follow-up Oncology

- ***Bone marrow biopsy:***
  - Mild plasmacytosis (8% plasma cells)
  - B cells represent <10% of marrow cellular elements
  - Amyloid stain (Congo red): negative

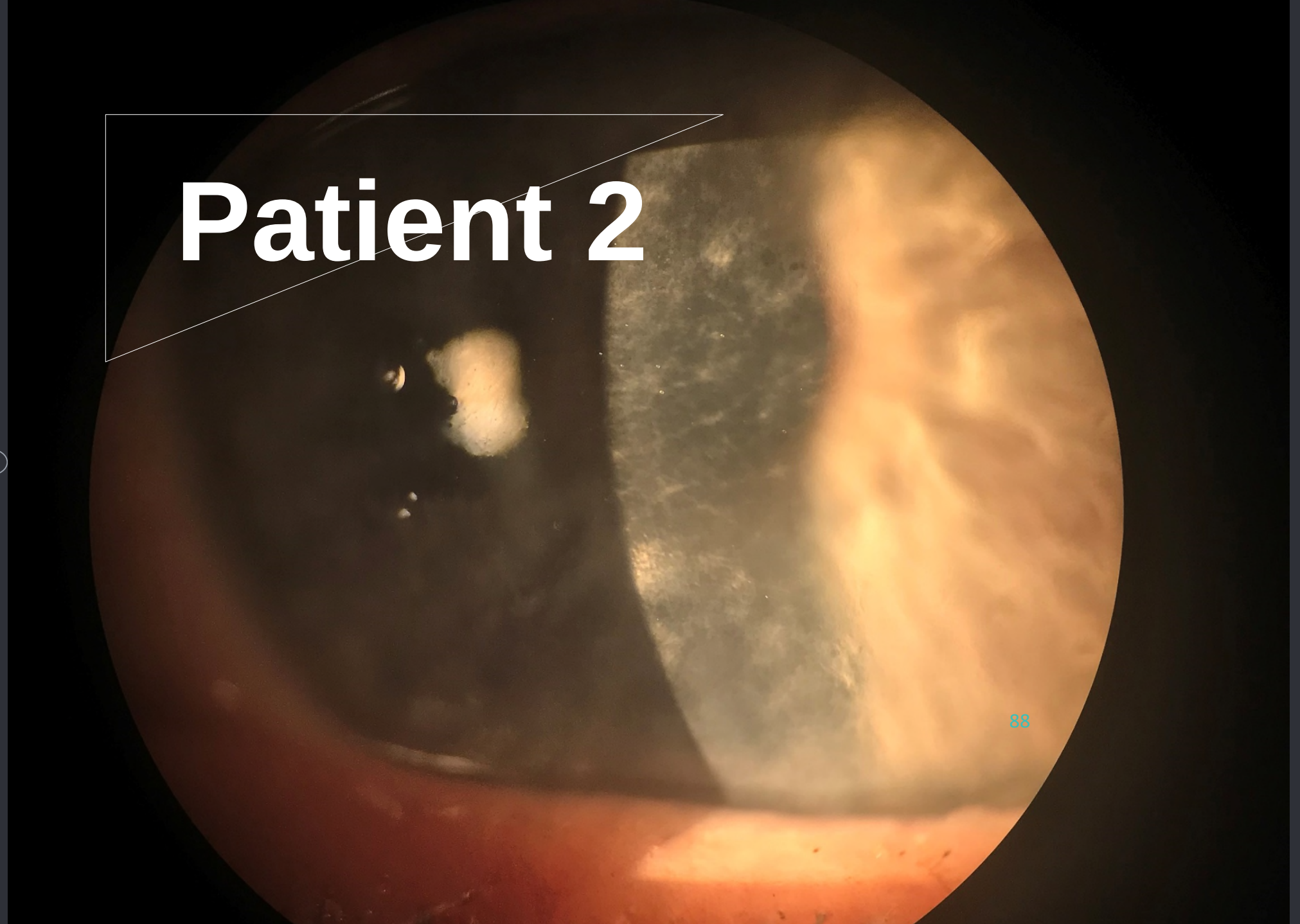
- ***Bone Scan:*** No disease
- No anemia or hypercalcemia

Diagnosis: MGUS (now smoldering myeloma)

(Monoclonal Gammopathy of Undetermined Significance)


Teaching Points:
As classic
as it gets!

Patient 2



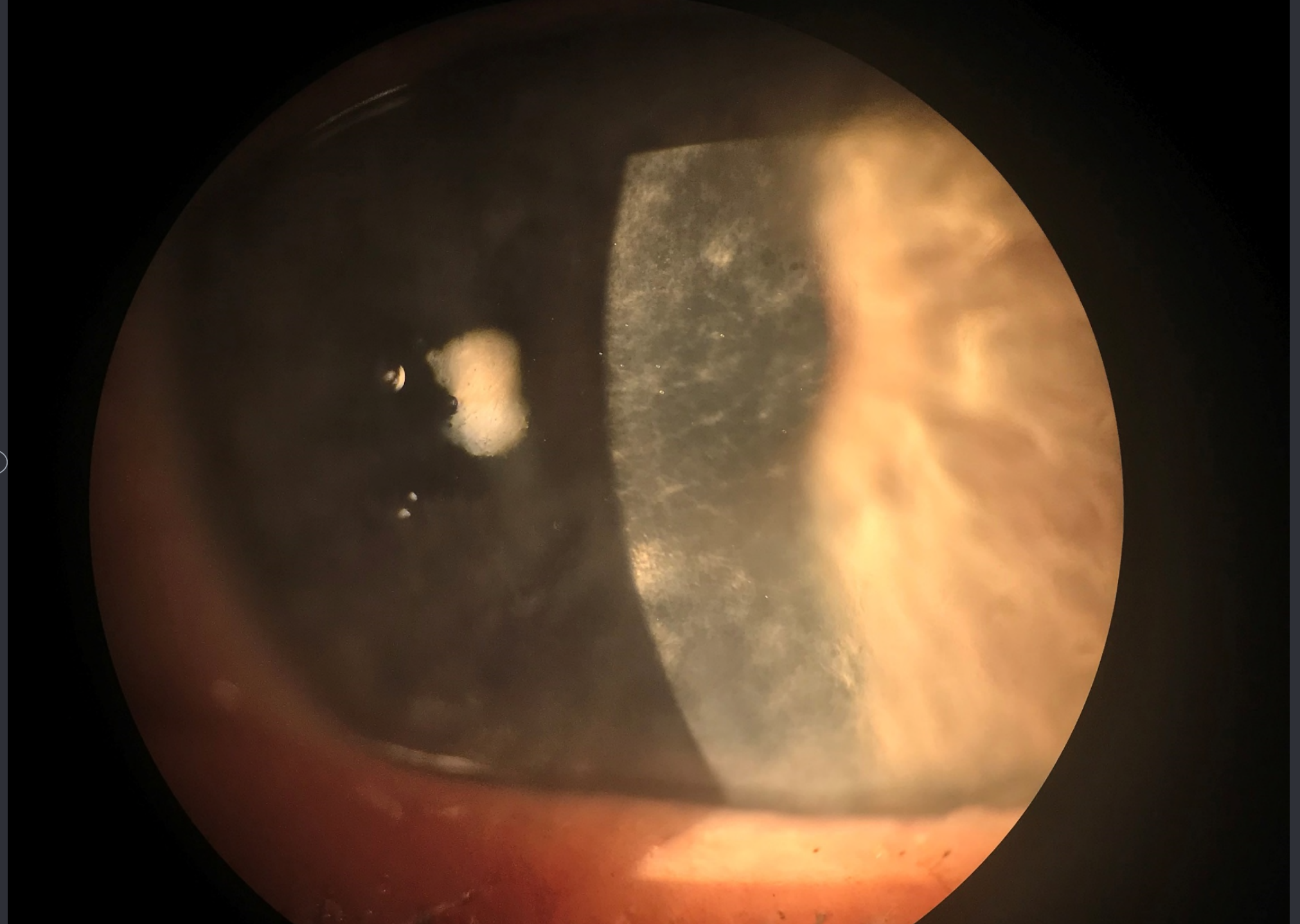
88

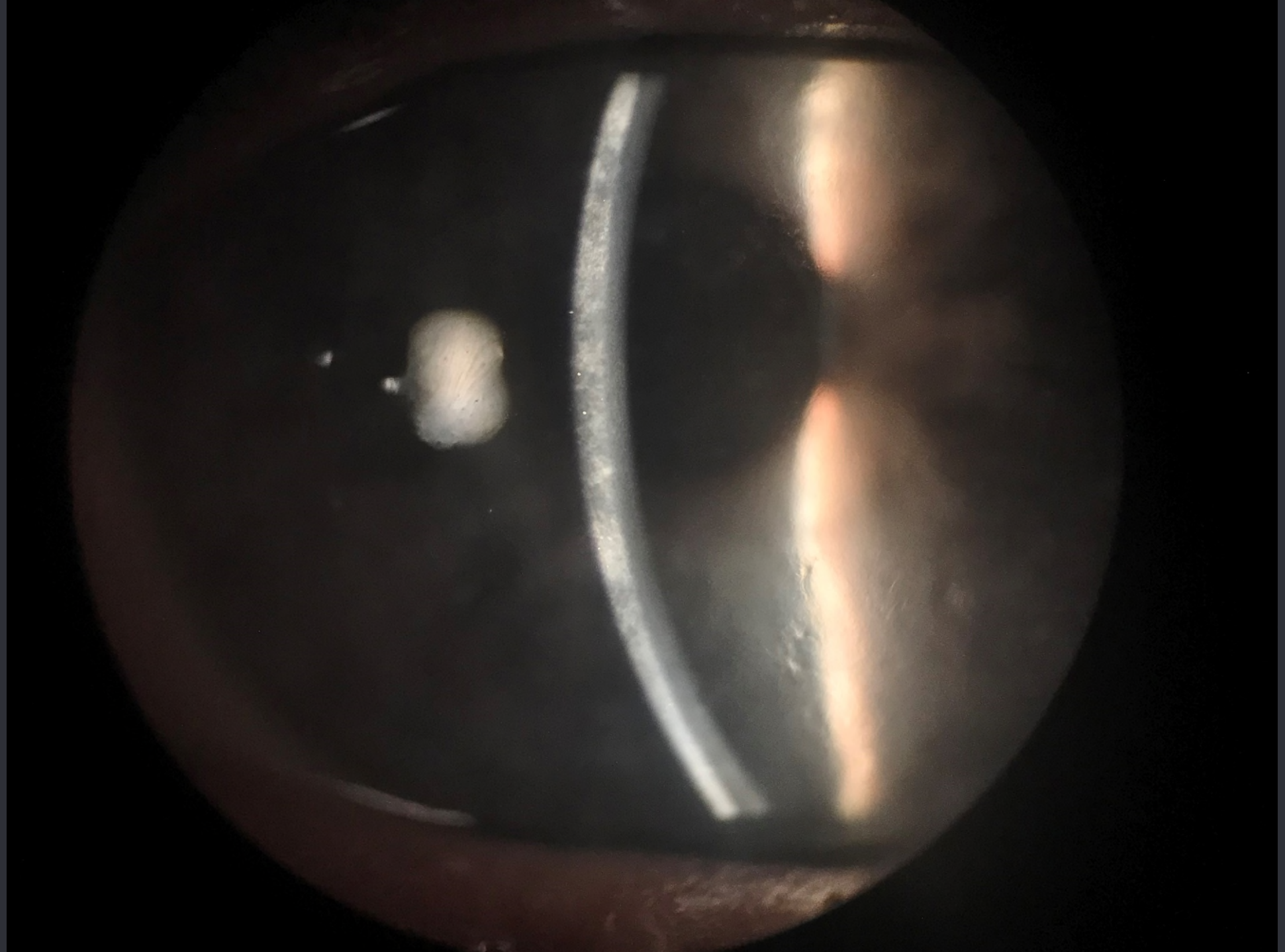
My vision is cloudy in both eyes…

69 year-old woman

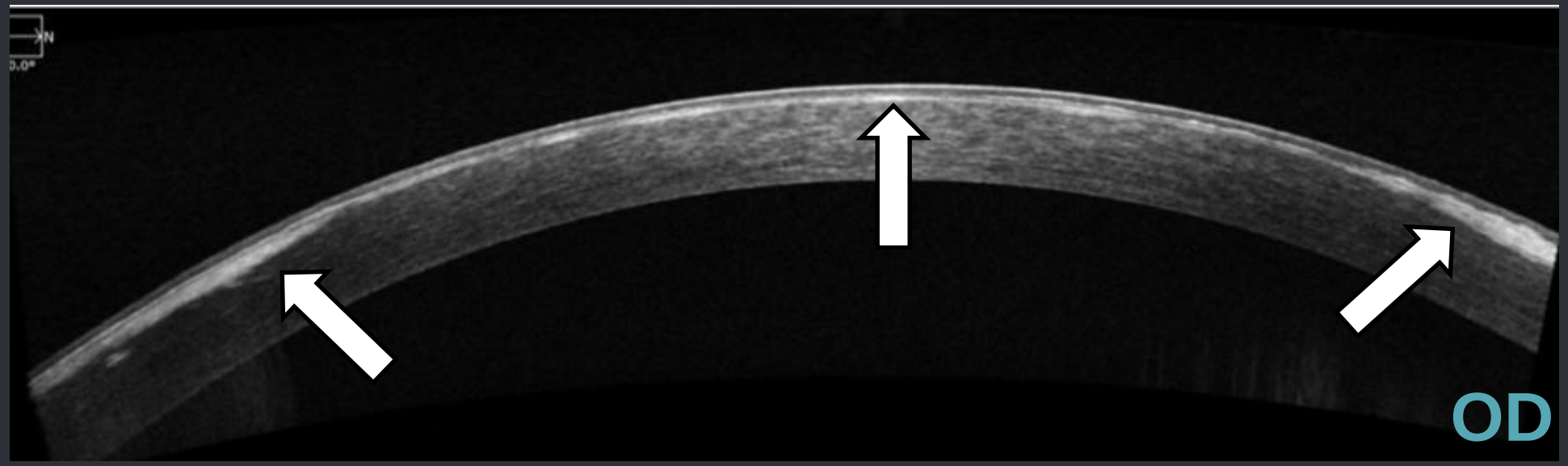
Progressive, painless blurry vision OU x 6 months

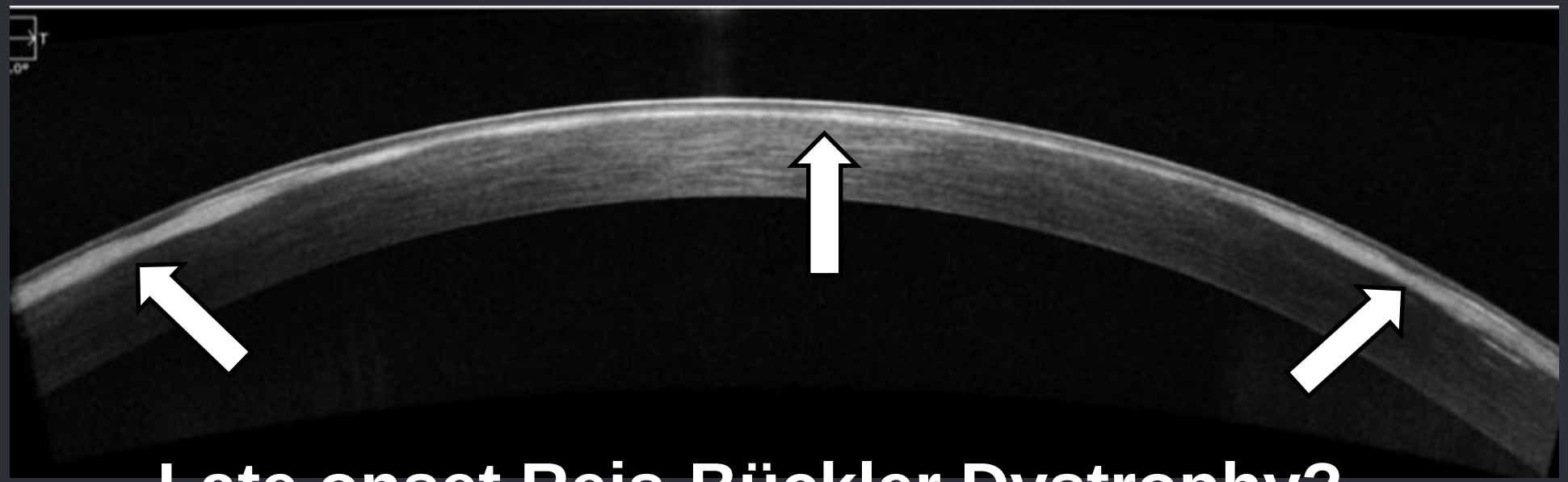
89





Anterior Segment OCT

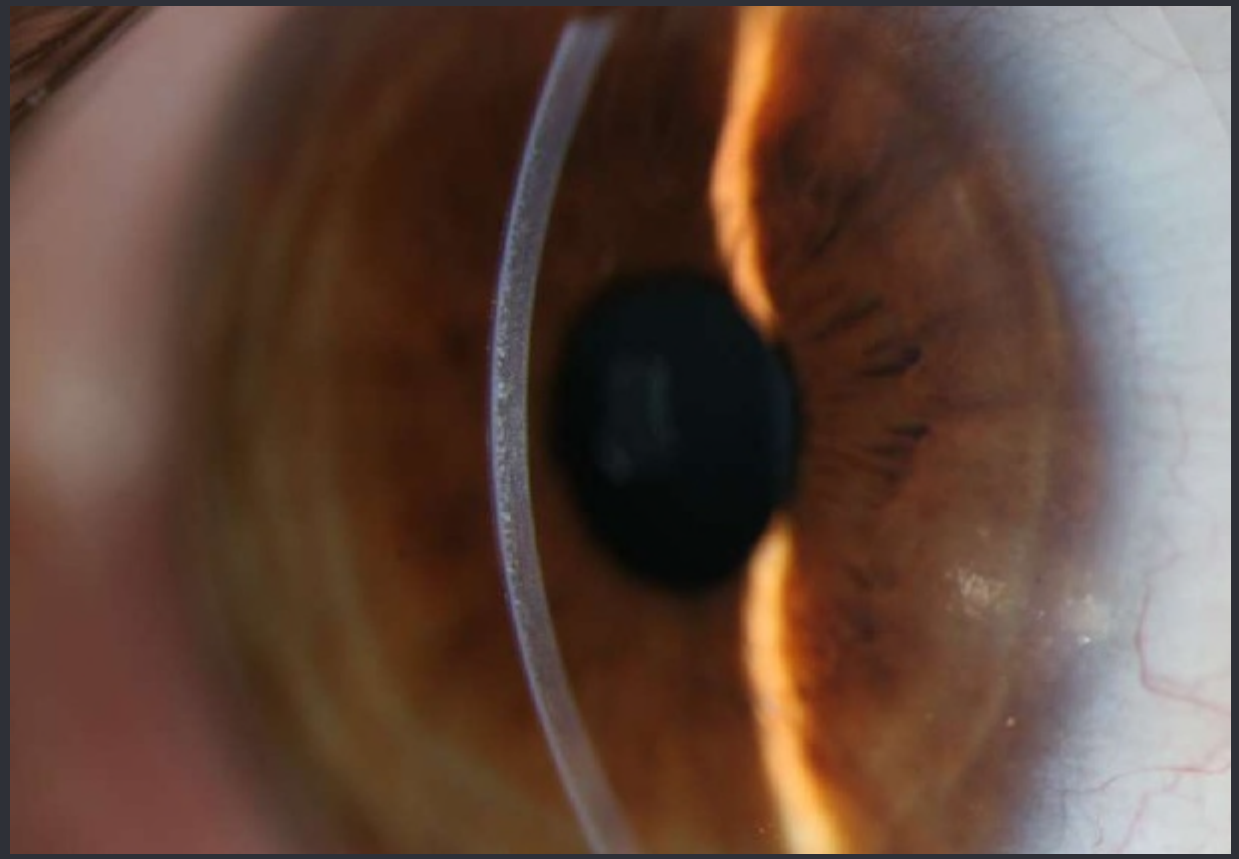


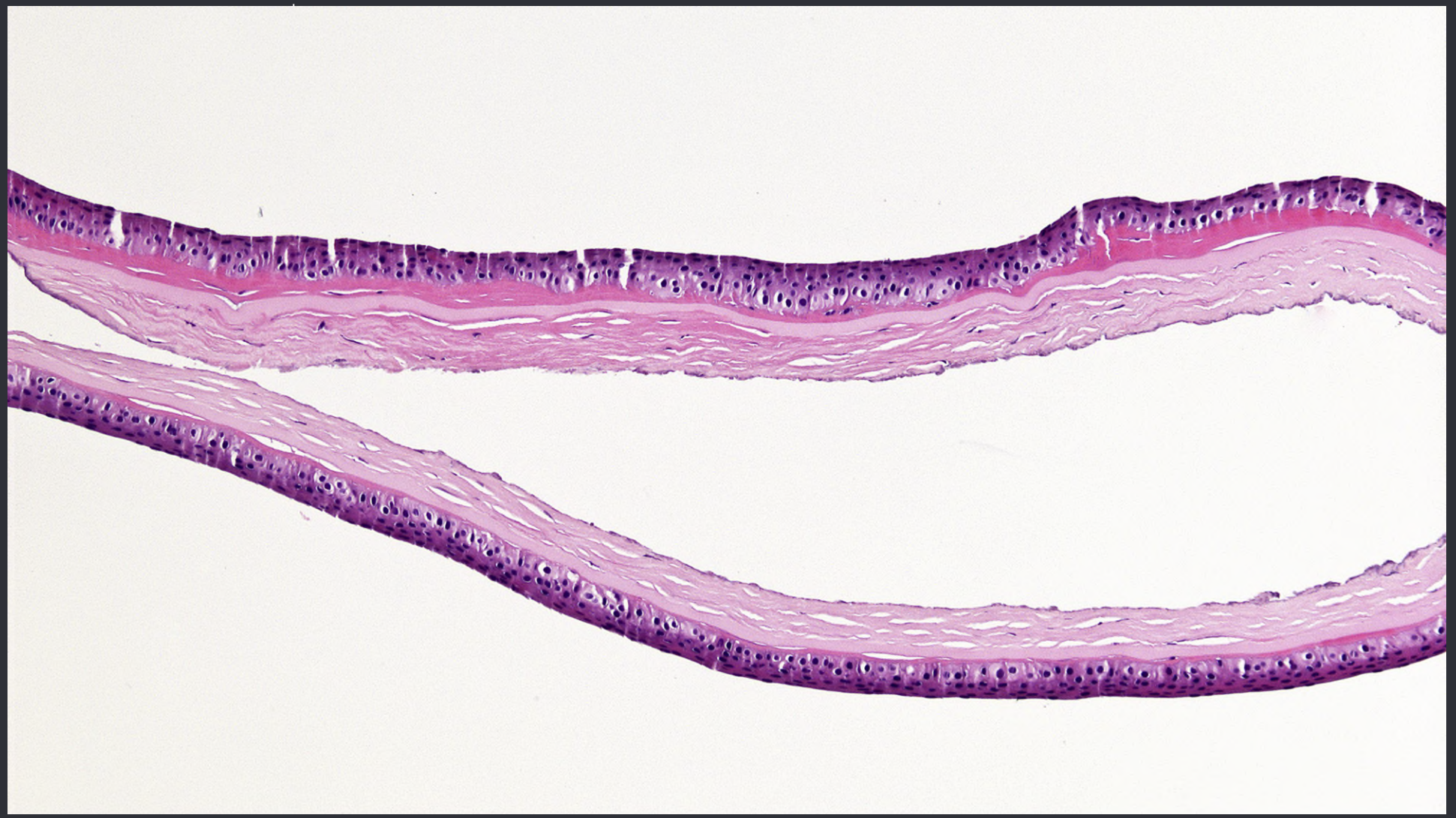


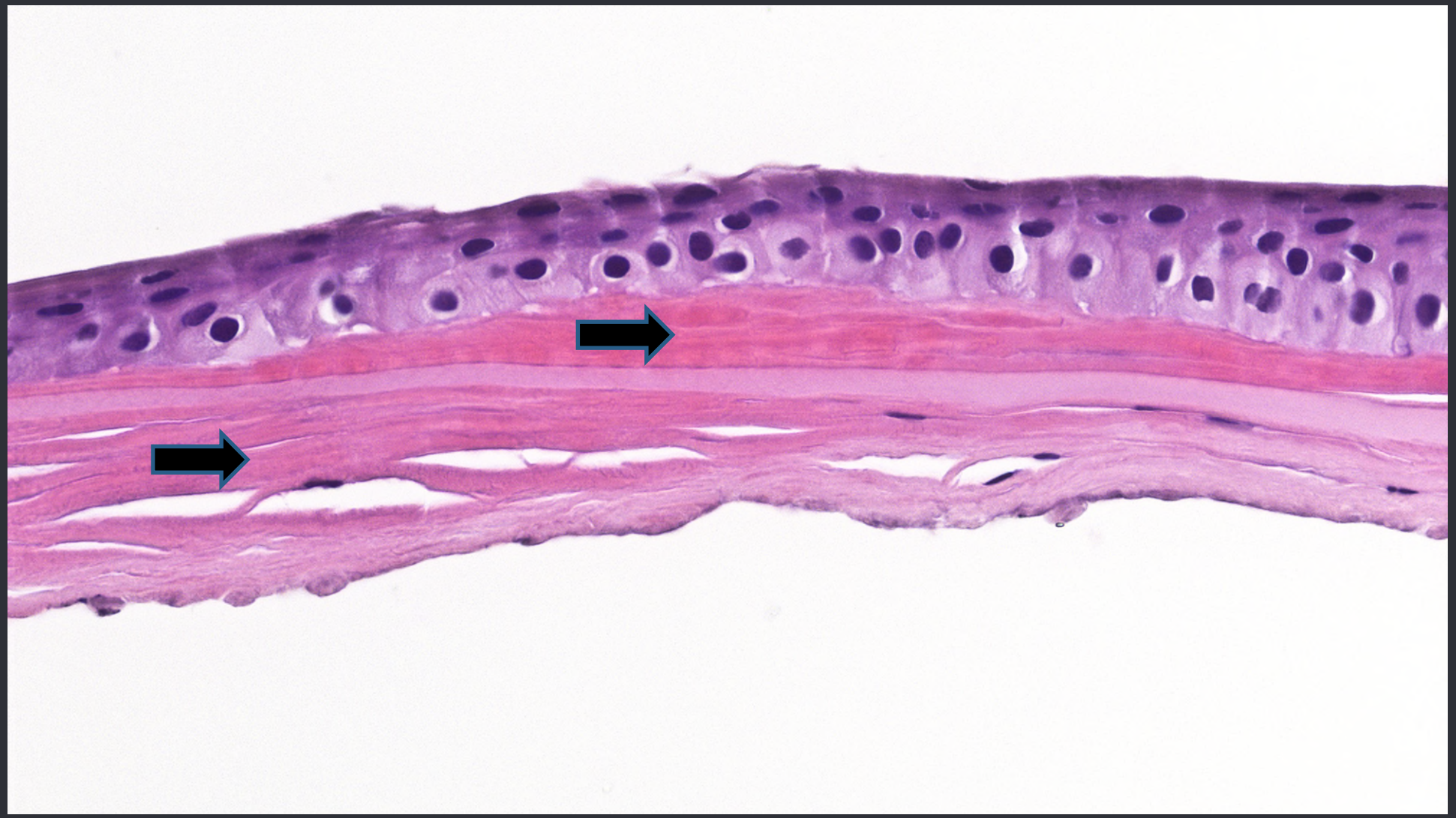
Late onset Reis-Bückler Dystrophy?

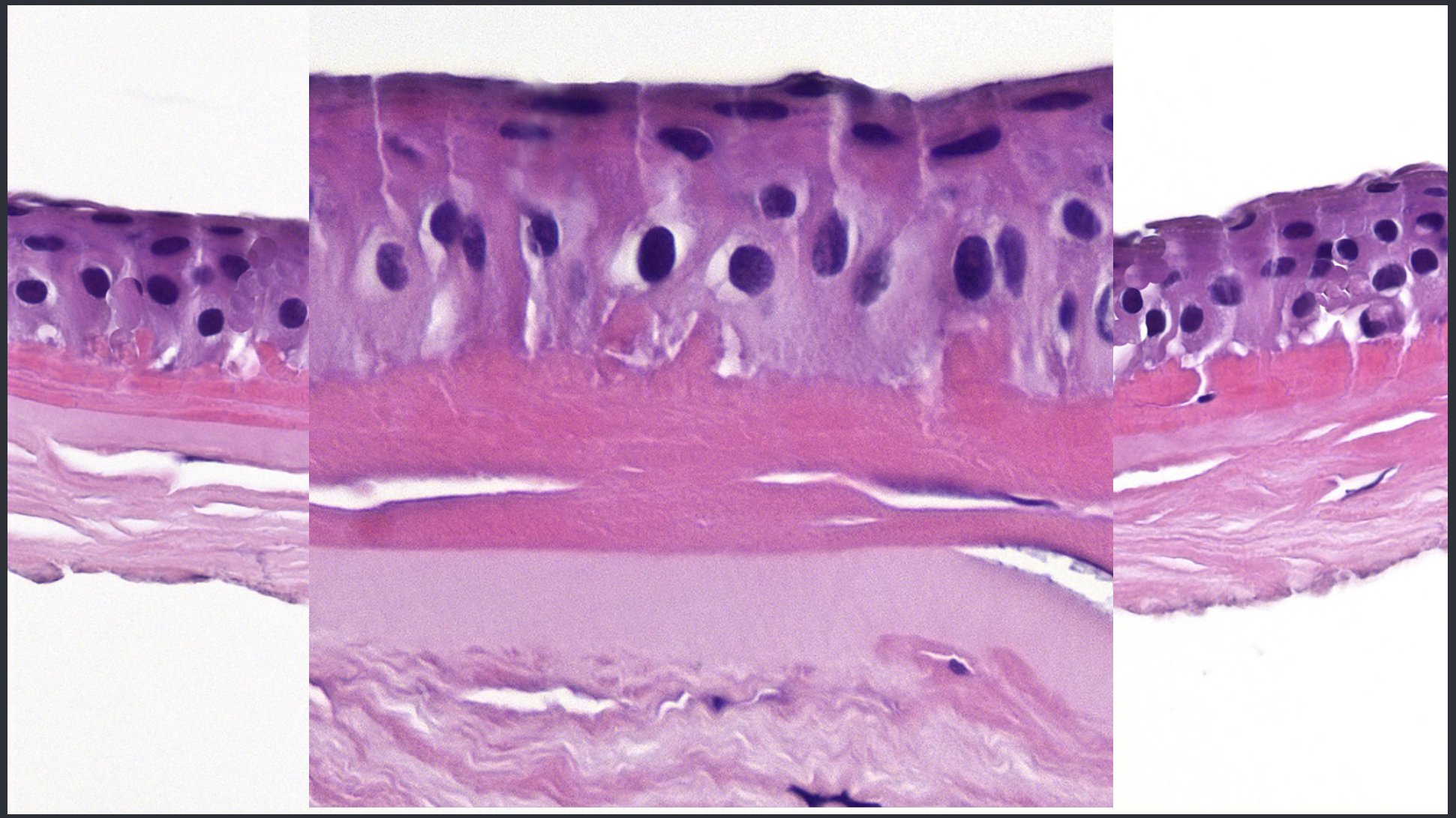
Daughter and Son Exam

Normal anterior segment both eyes

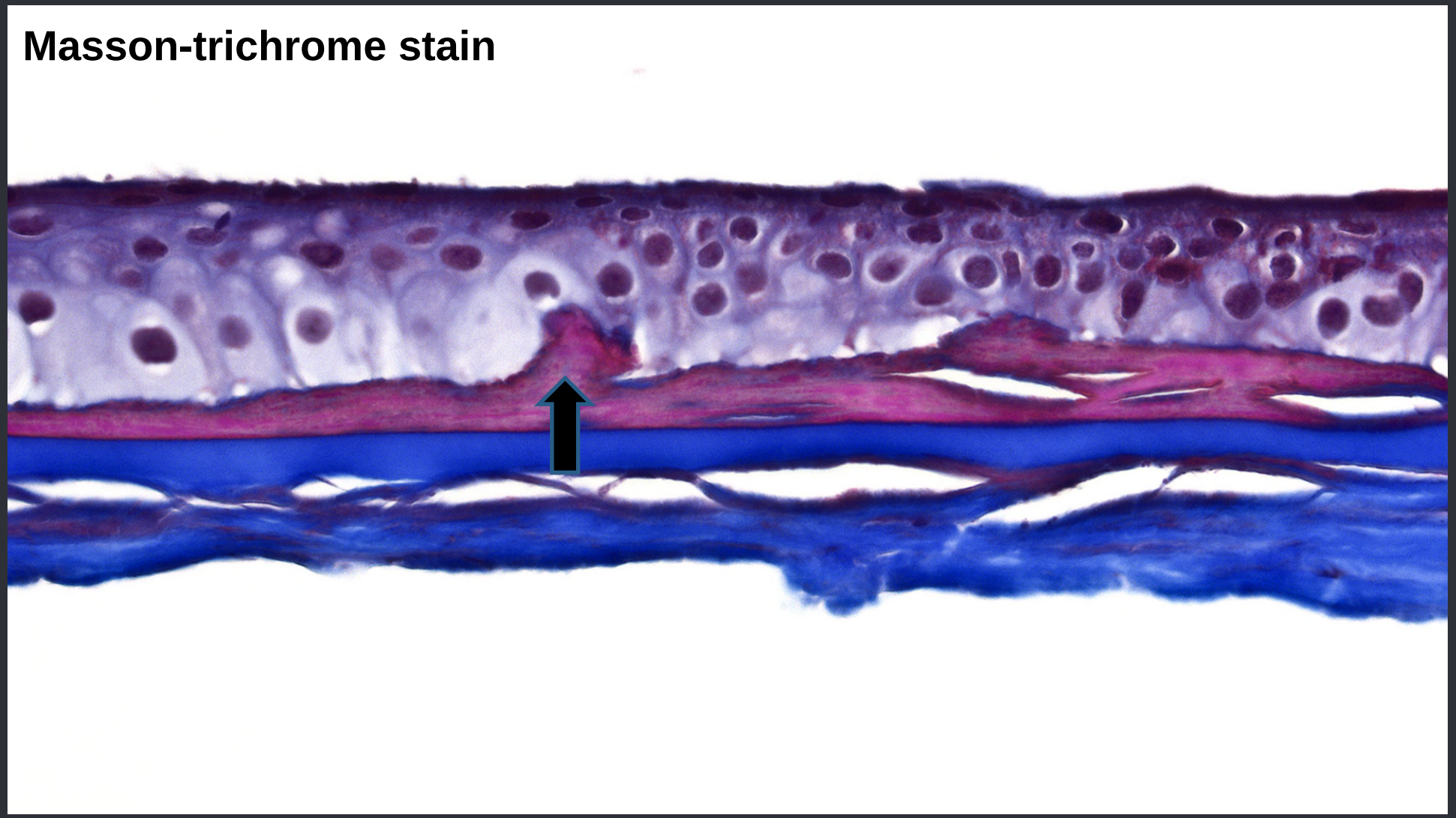




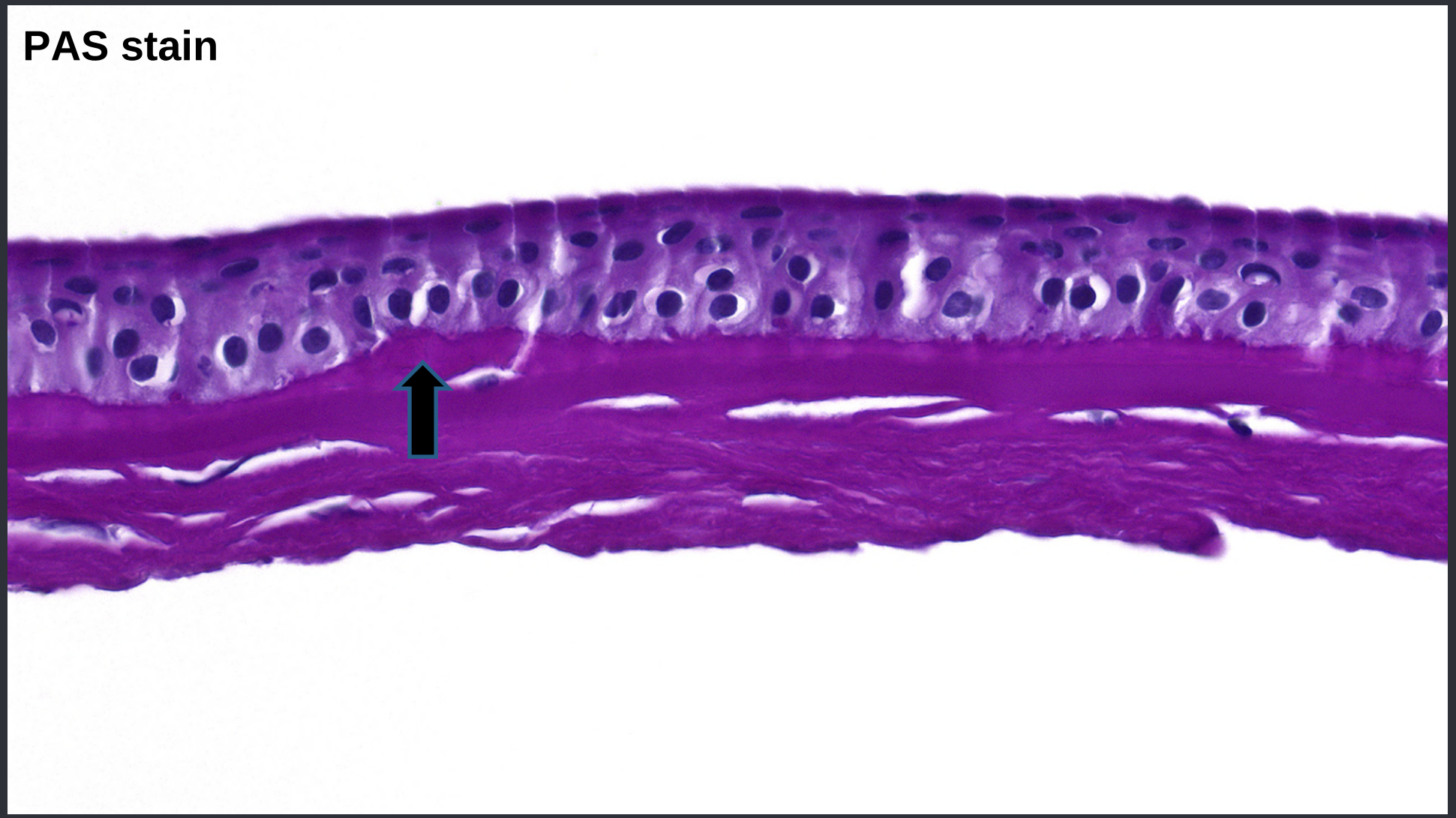




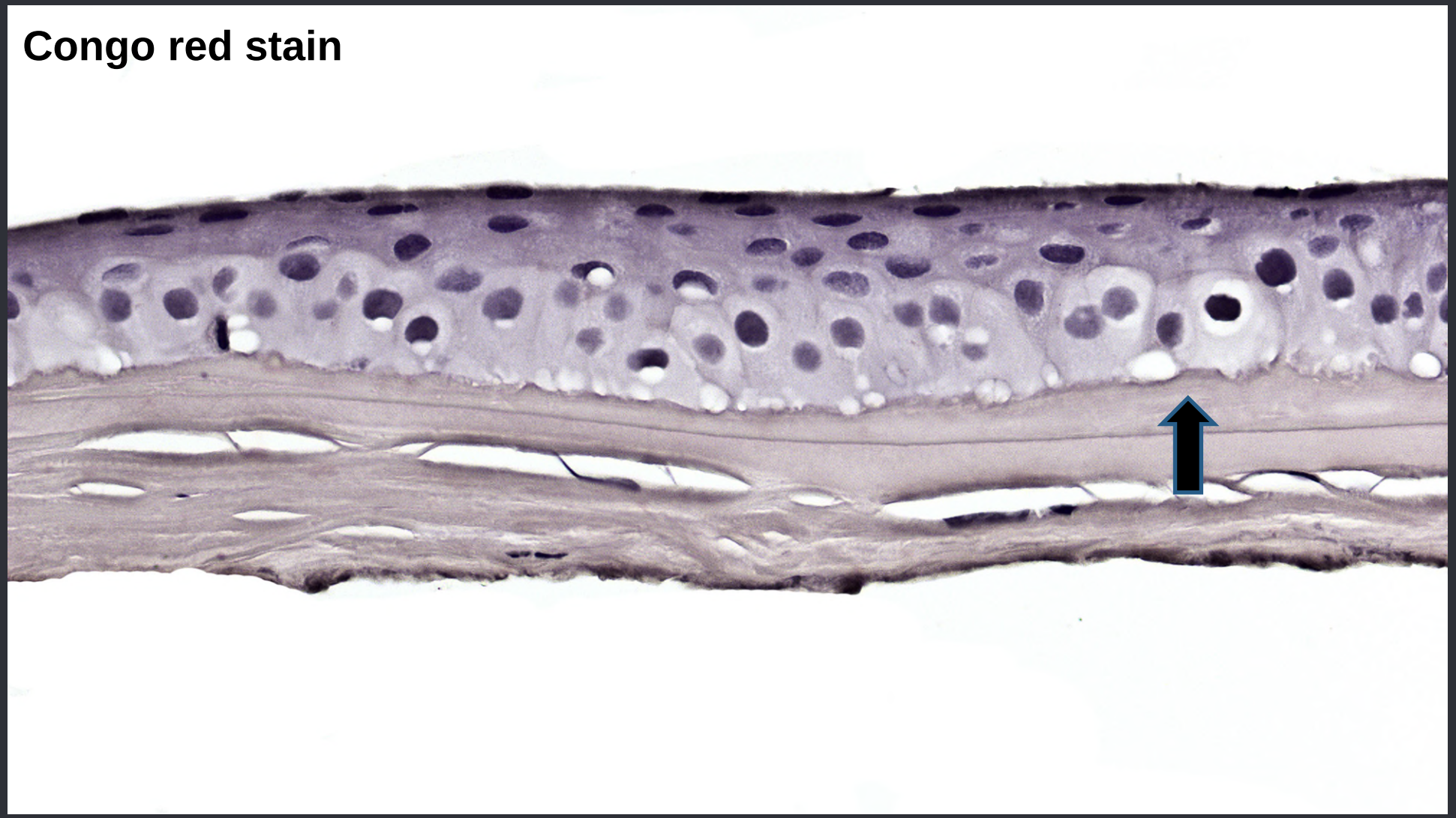
Masson-trichrome stain



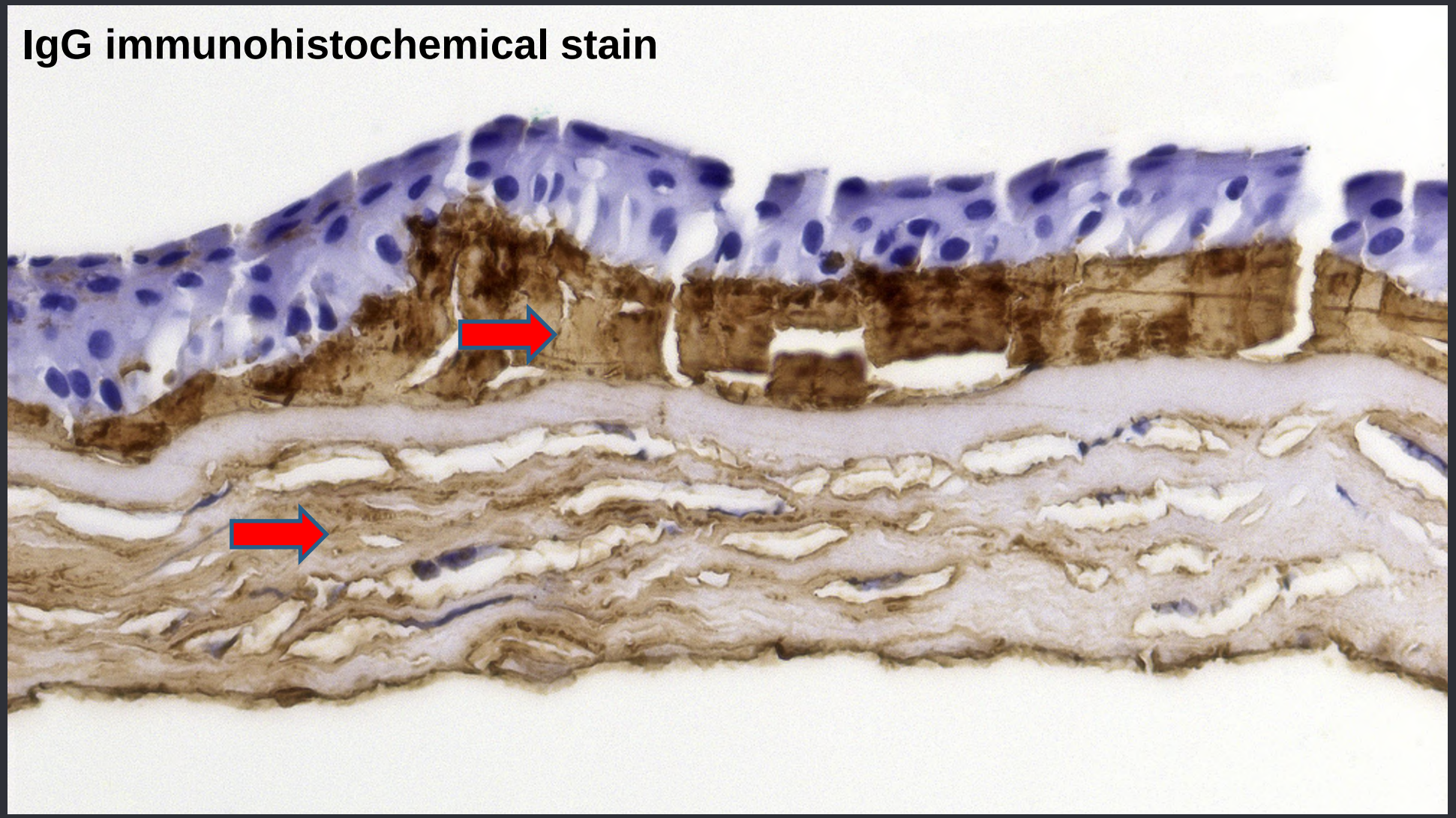
PAS stain



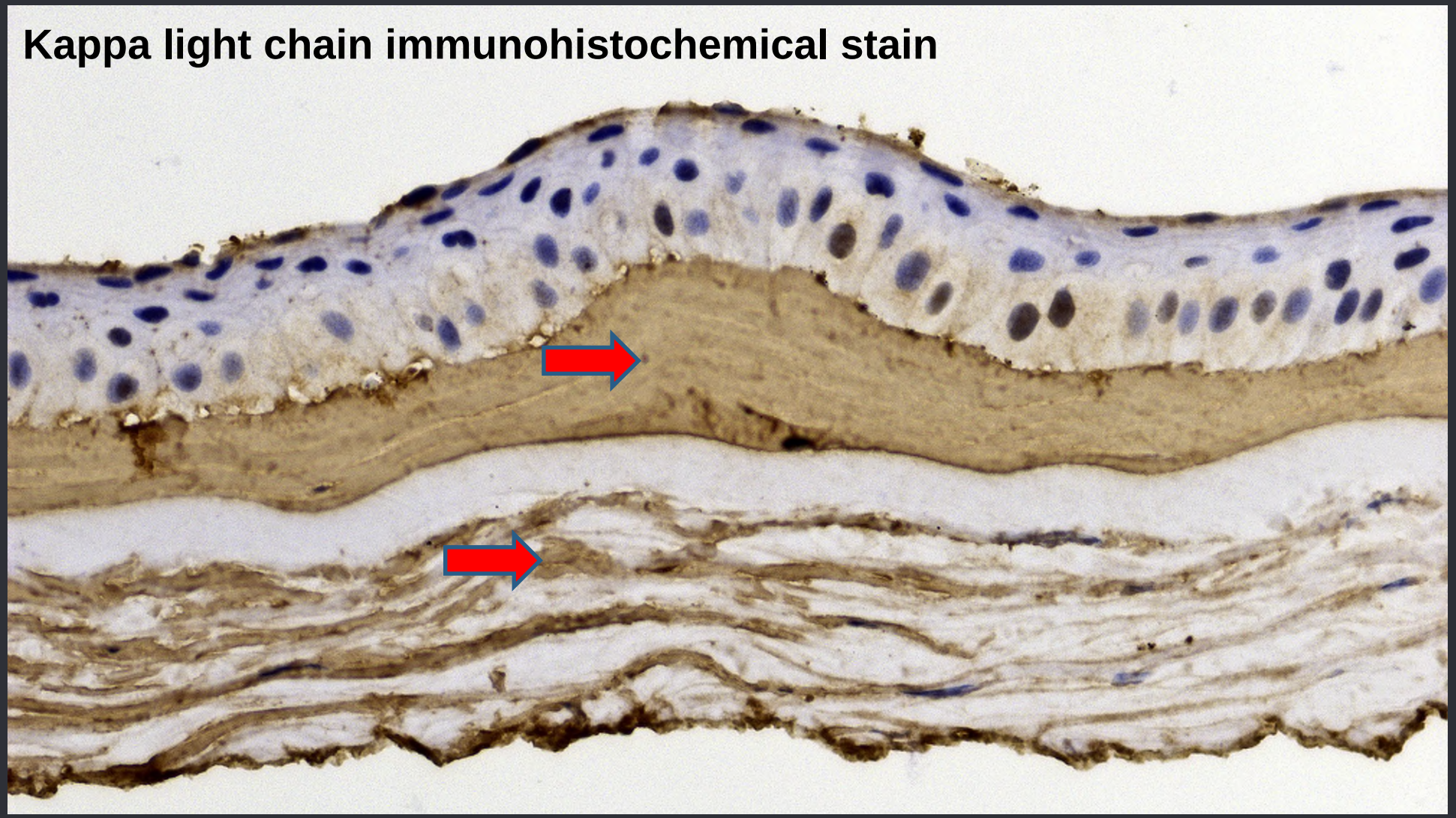
Congo red stain



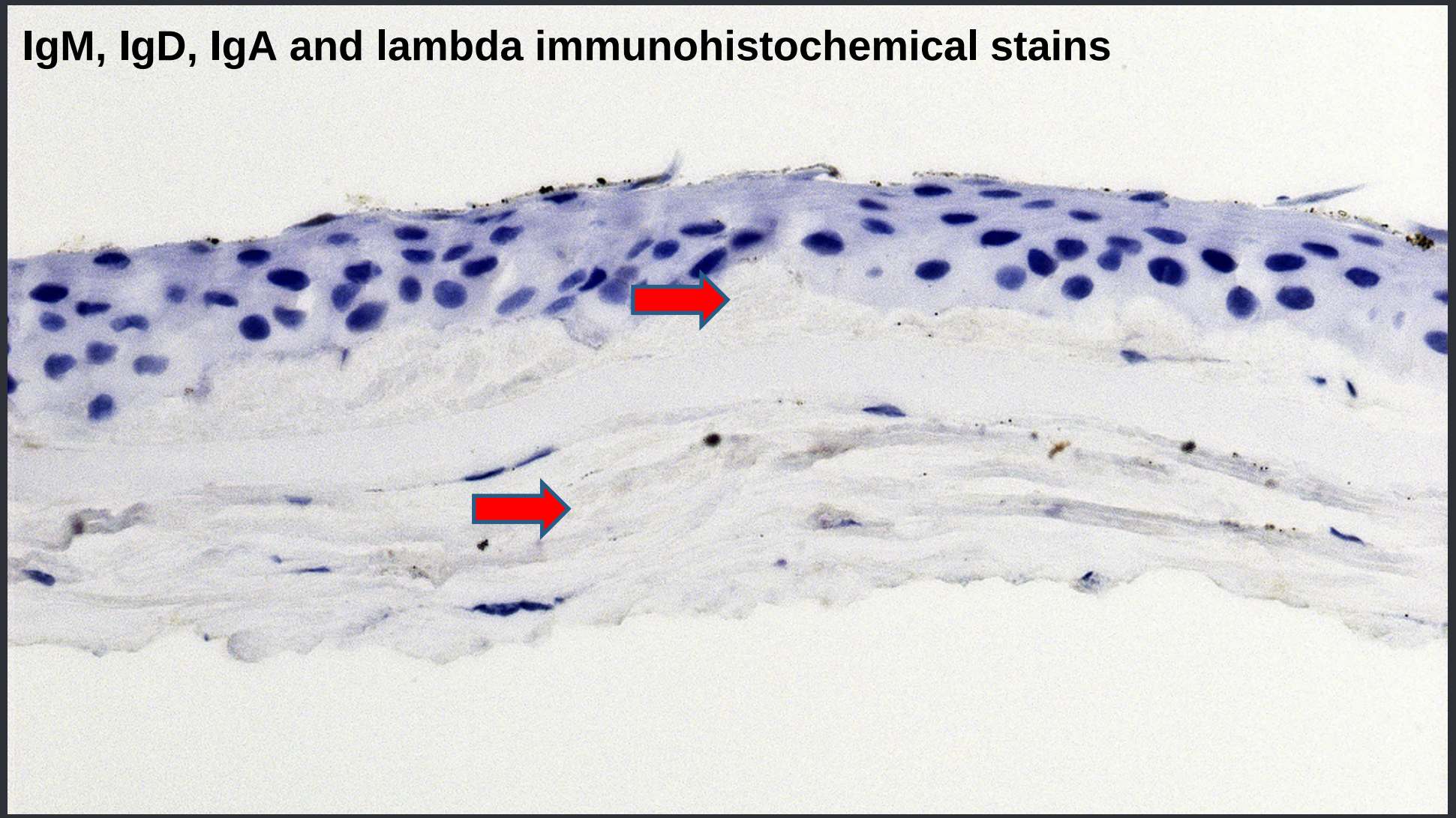
IgG immunohistochemical stain



Kappa light chain immunohistochemical stain



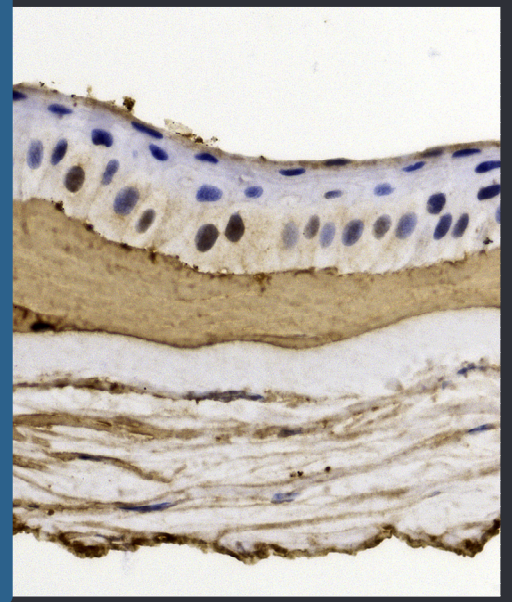
IgM, IgD, IgA and lambda immunohistochemical stains

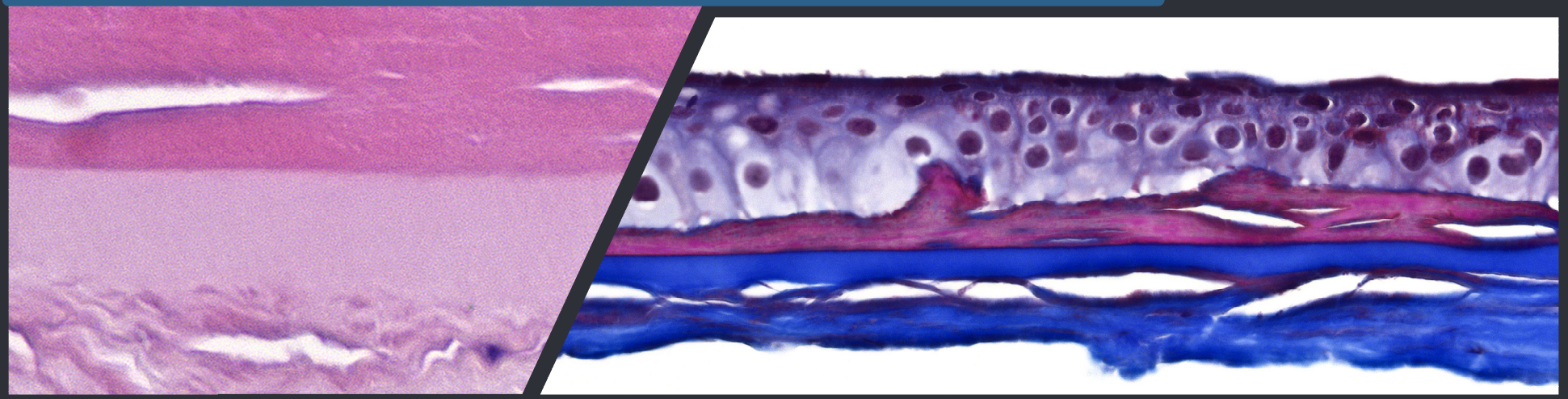


Final Pathology Diagnosis

Paraproteinemic keratopathy

Recommend evaluation
for plasma cell proliferative and
lymphoproliferative disorders

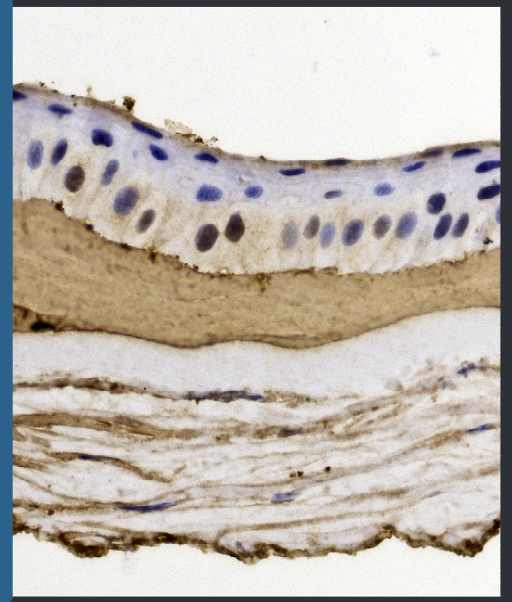


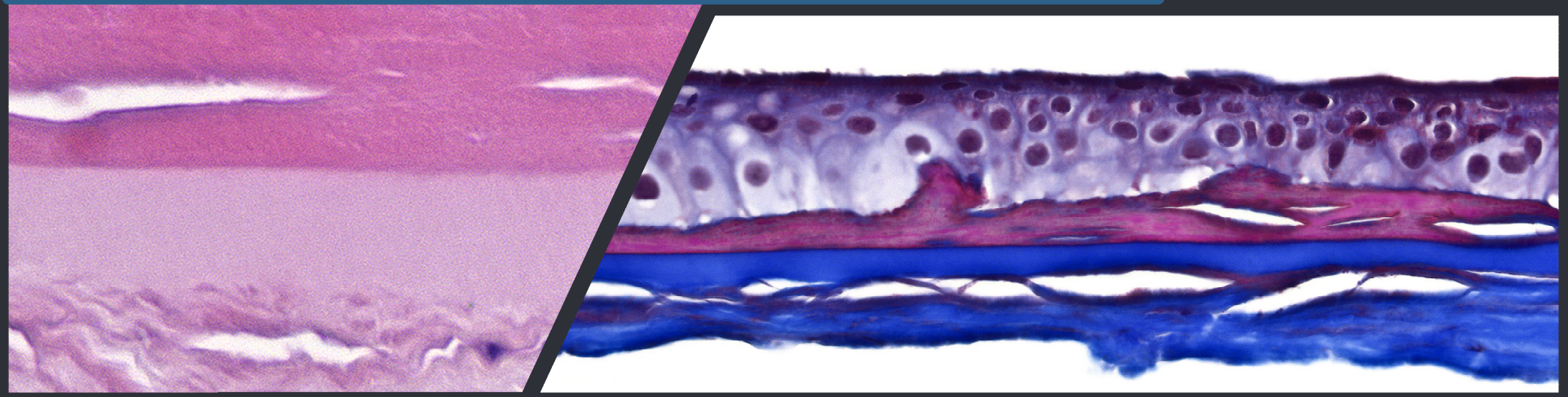


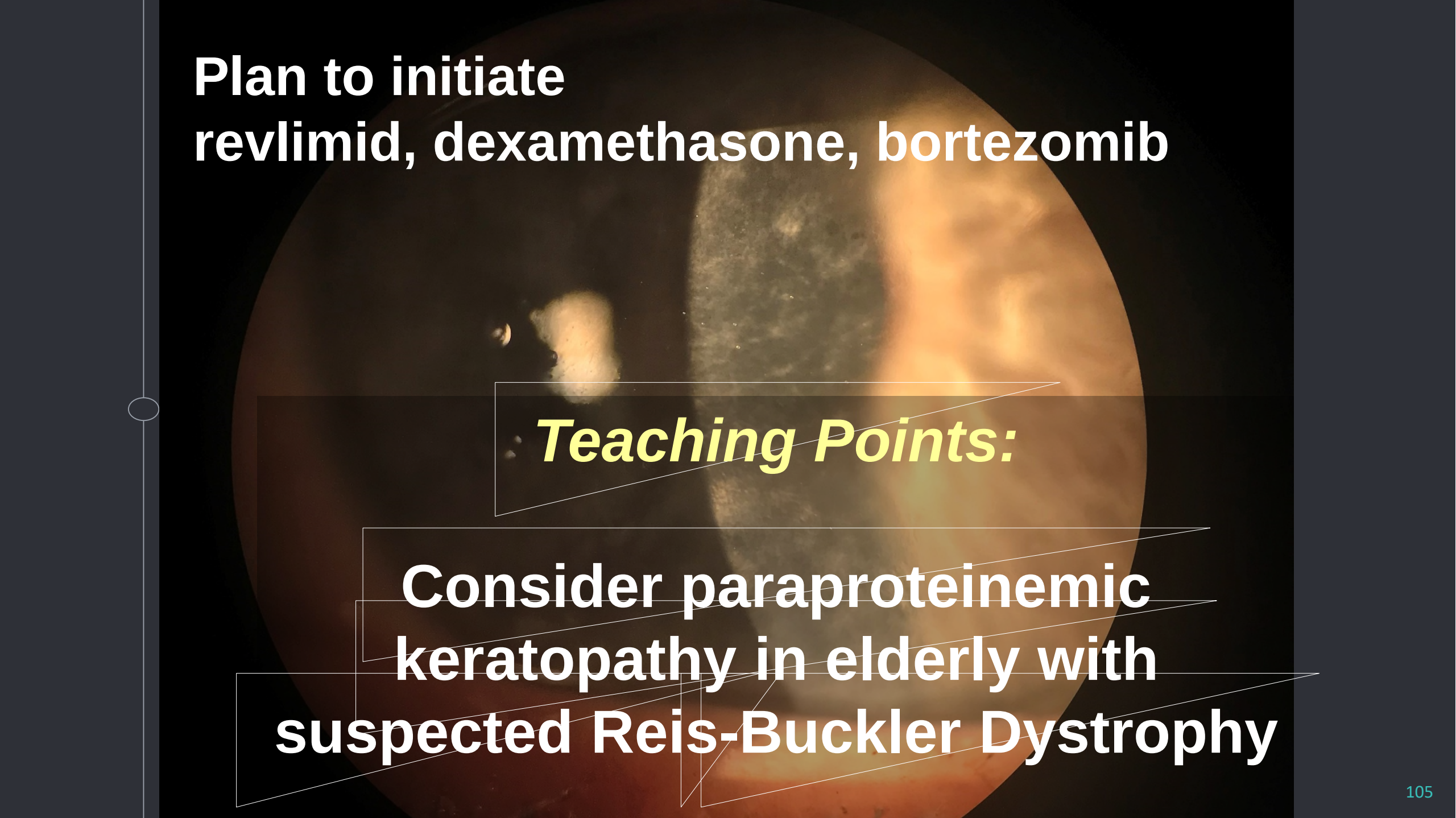
Systemic work-up

- Bone marrow bx – 15% clonal plasma cells
- UPEP, SPEP – K light chains (<10 mg/dl)
- MRI, PET/CT, skeletal survey – Negative
- No end organ damage

“SMOLDERING MYELOMA”



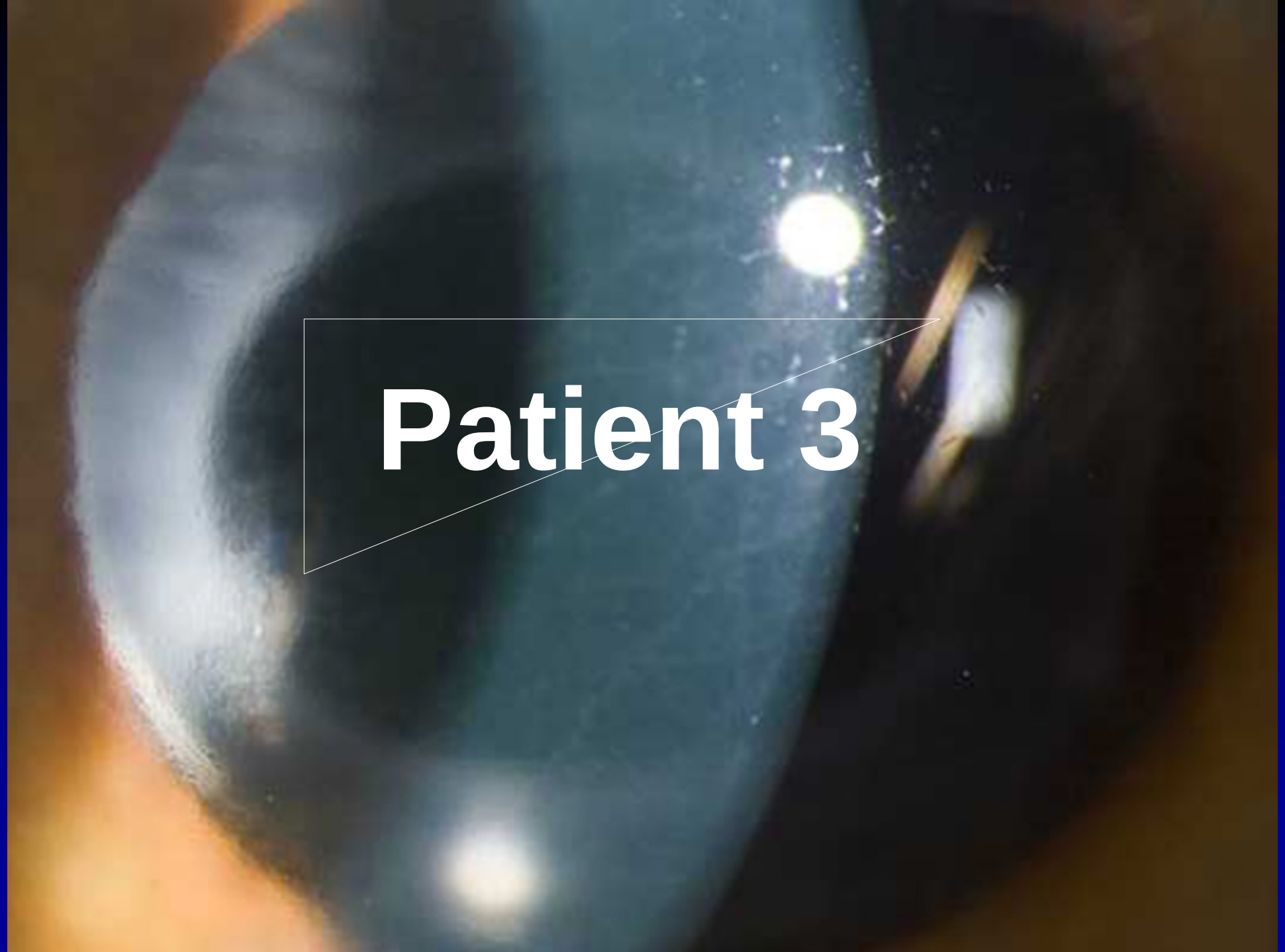




Plan to initiate
revlimid, dexamethasone, bortezomib

Teaching Points:

Consider paraproteinemic keratopathy in elderly with suspected Reis-Buckler Dystrophy


Patient 3

60 year old woman

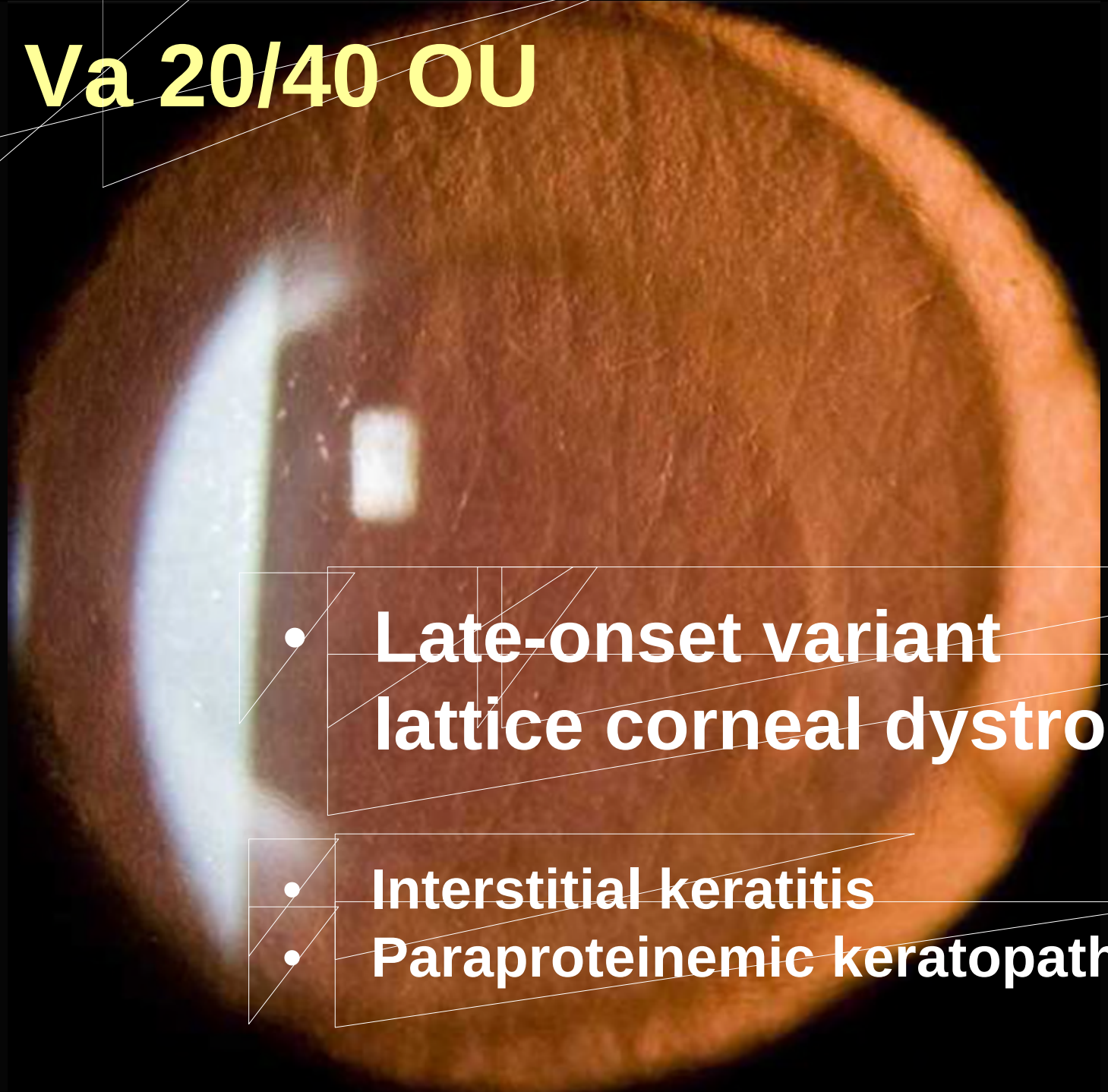
CC: **Progressive visual loss over 6 months**

POH: **RGPs for myopia**

PMH: **HTN**

FH: **Negative for corneal disorders**

Va 20/40 OU



- Late-onset variant lattice corneal dystrophy

- Interstitial keratitis
- Paraproteinemic keratopathy

WORKUP

***TGFBI* mutation studies: Negative for mutation**

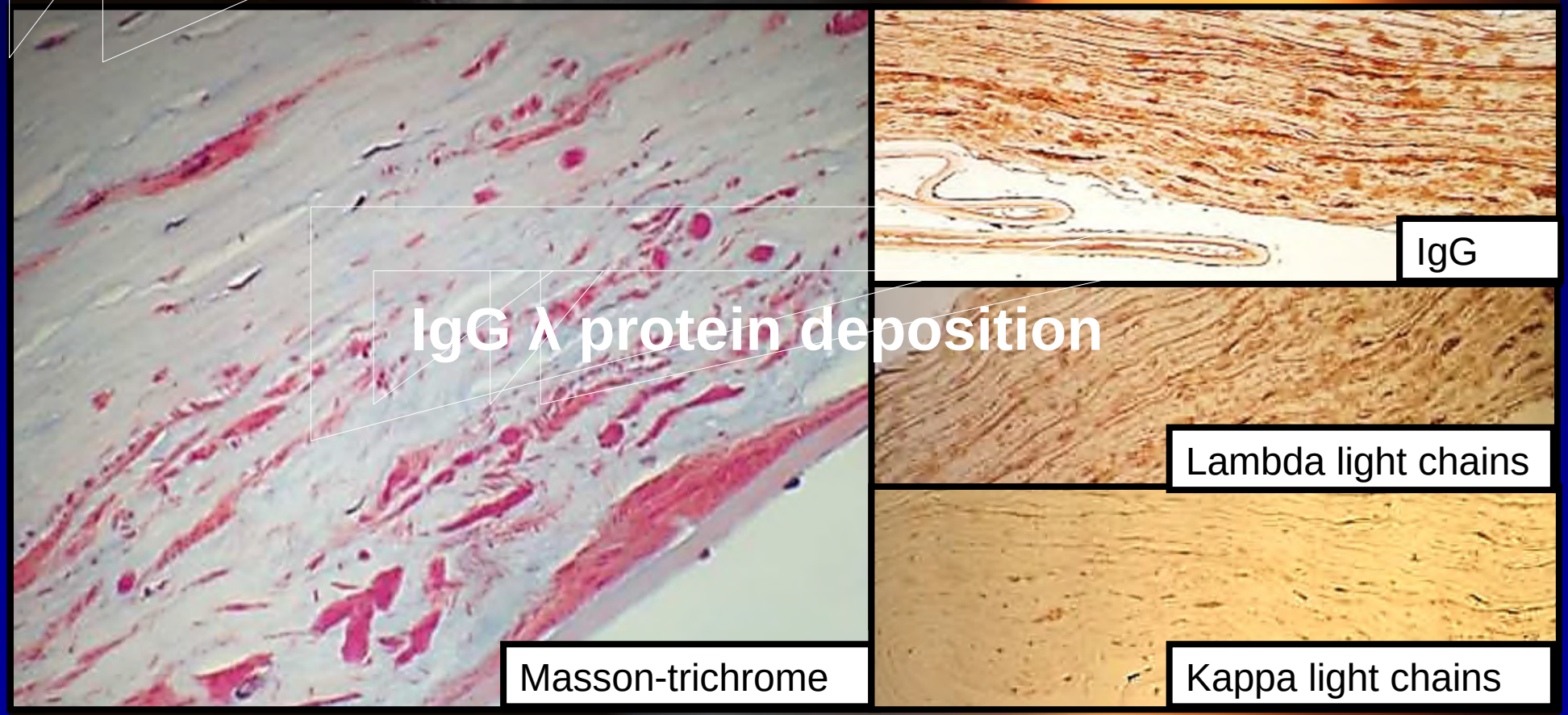
Oncologic evaluation

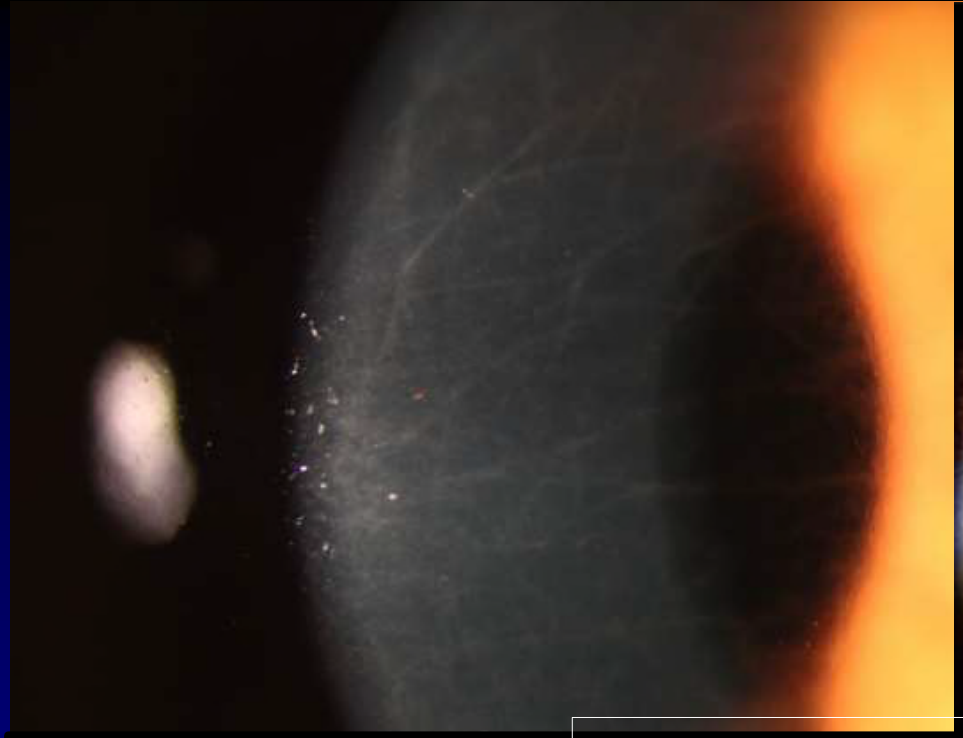
- **Elevated serum IgG (1.7 g/dL)**
- **Free urine lambda light chain (32.6 mg/dL)**
- **UPEP: Monoclonal protein (λ light chain)**
- **Bone marrow biopsy: 8% monoclonal λ light chain expressing plasma cells**

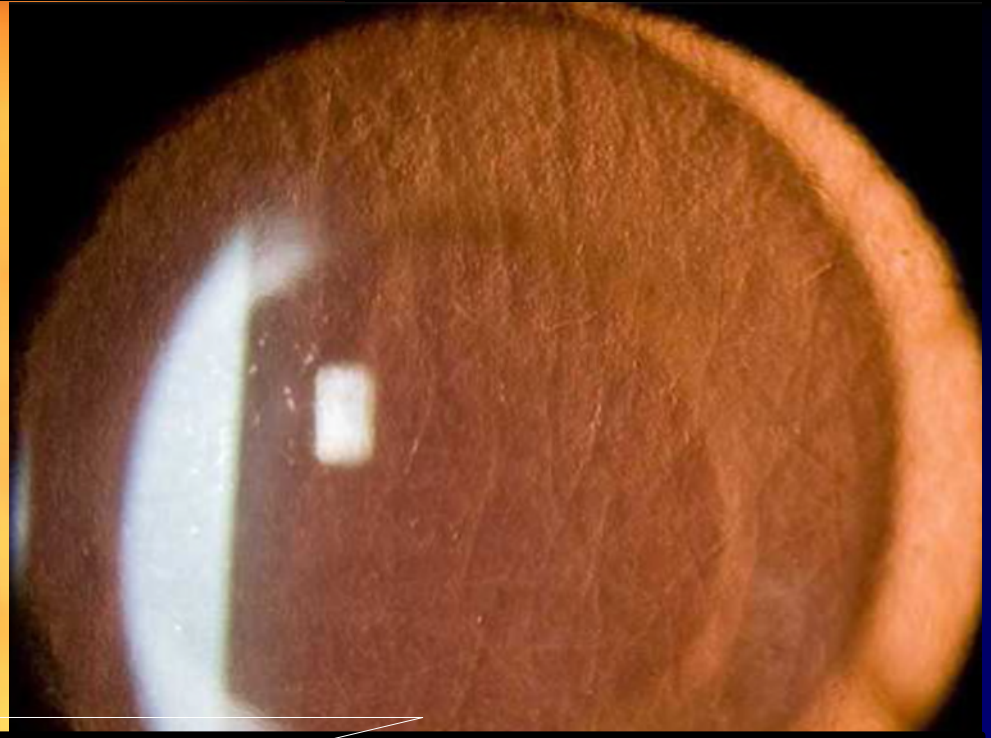
MGUS

CLINICAL COURSE (F/U 3 years)

- Va 20/60 OU
- PKP OD

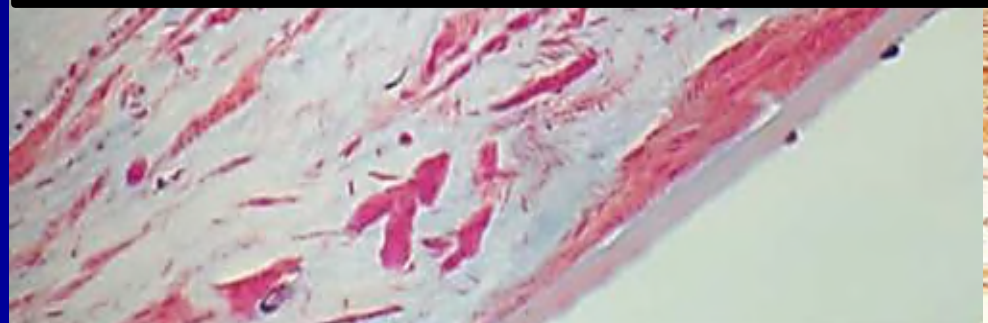


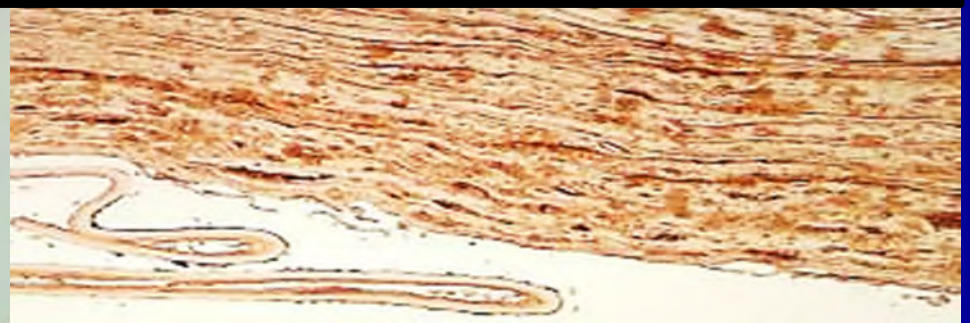




Teaching Points:

Atypical late-onset variant lattice corneal dystrophy?
…Consider paraproteinemic keratopathy





67 year old woman

CC: **Decreased vision OU for several months**

POH: **SCL-associated corneal ulcers**

PMH: **High cholesterol**

FH: **Negative for corneal disorders**

Va 20/30 OD

20/25 OS

Bilateral, axially-distributed, needle-like crystalline deposits

Schnyder corneal dystrophy?

WORKUP

UBIAD1 **mutation analysis**

- **Negative**

Oncology

- **MGUS**

CLINICAL COURSE (F/U 1 YEAR)

- Stable vision
- Observed without therapy

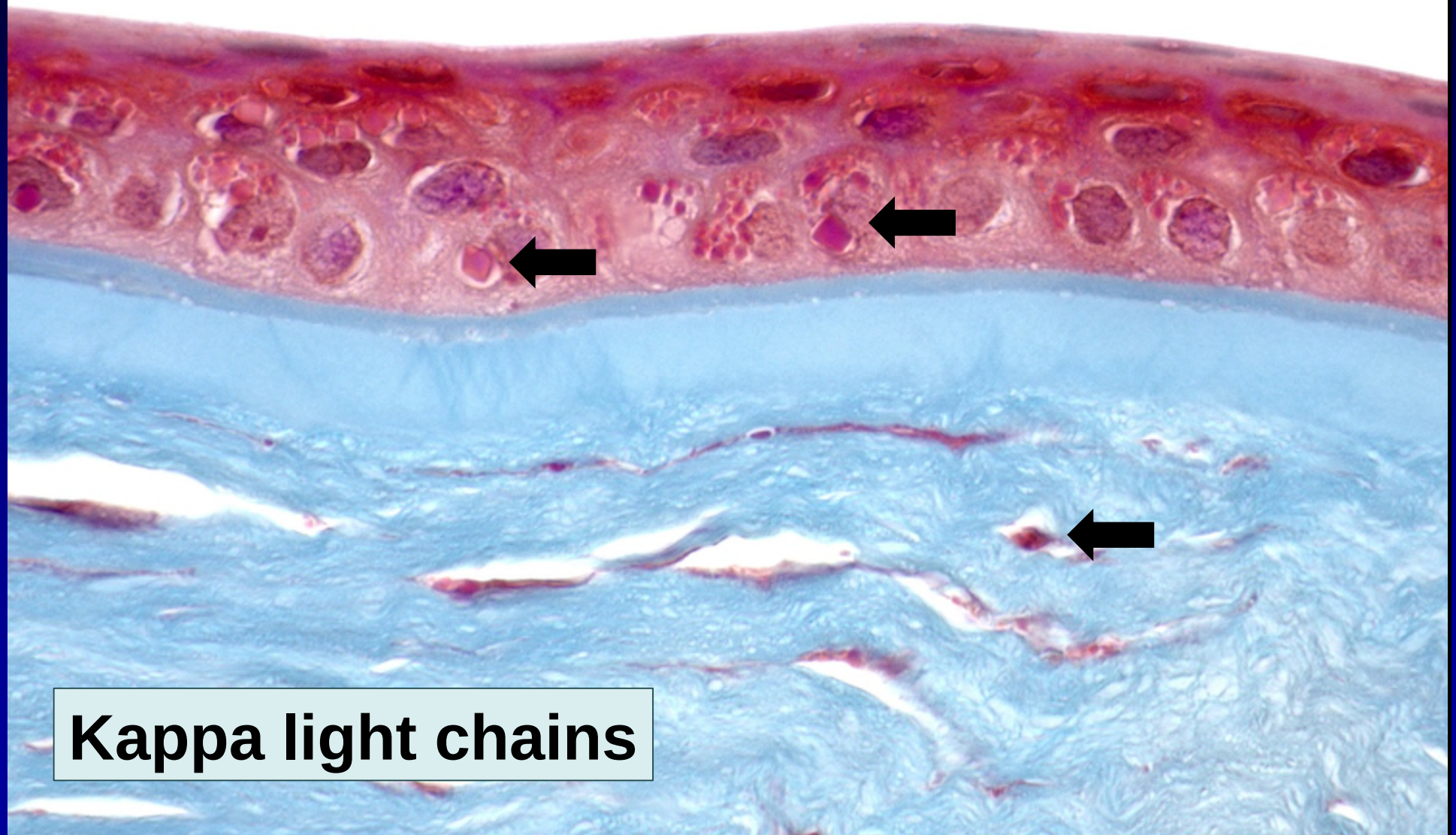
No Pathology

Different patient

WALDENSTROM MACROGLOBULINEMIA

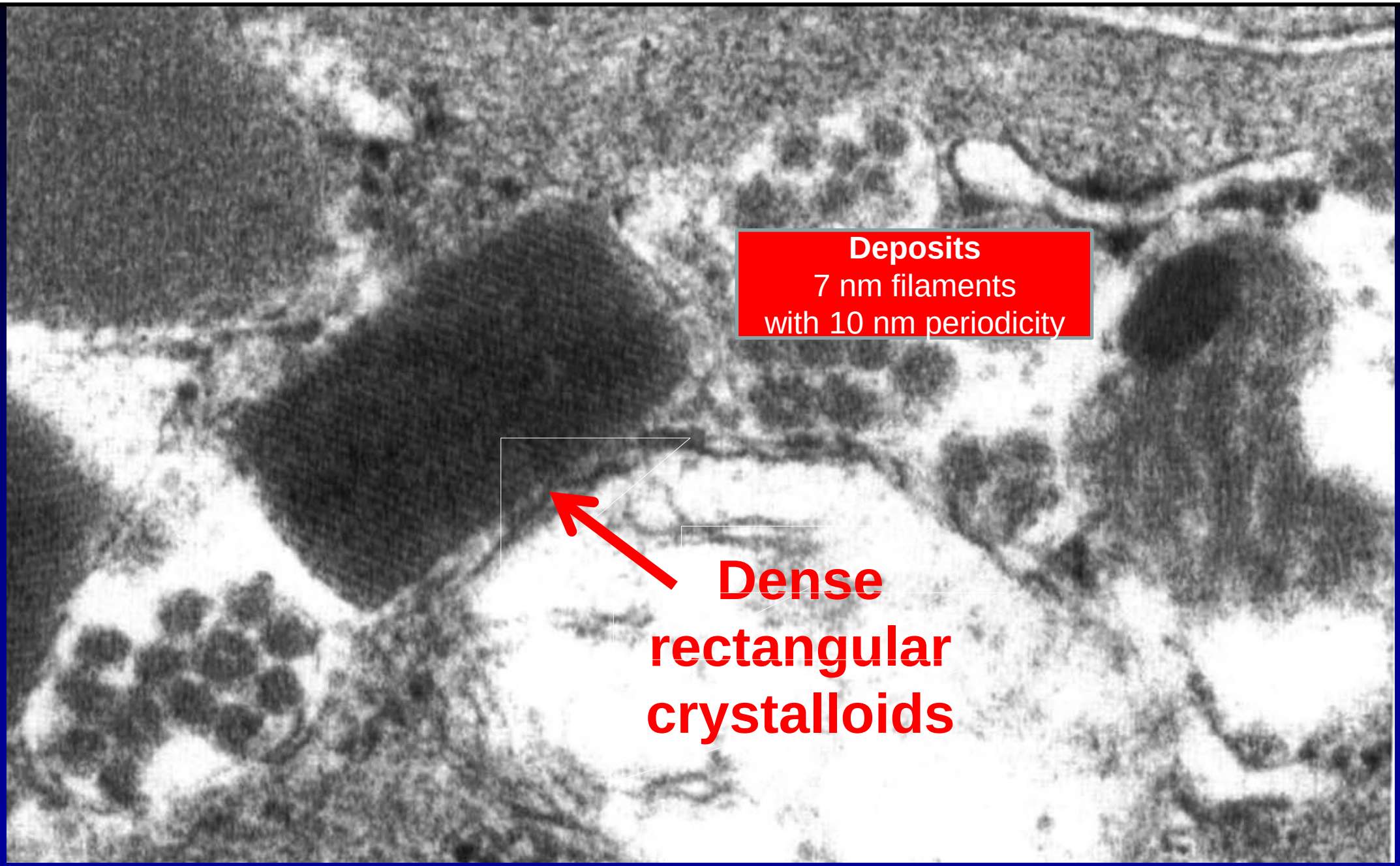
- IgM kappa paraprotein

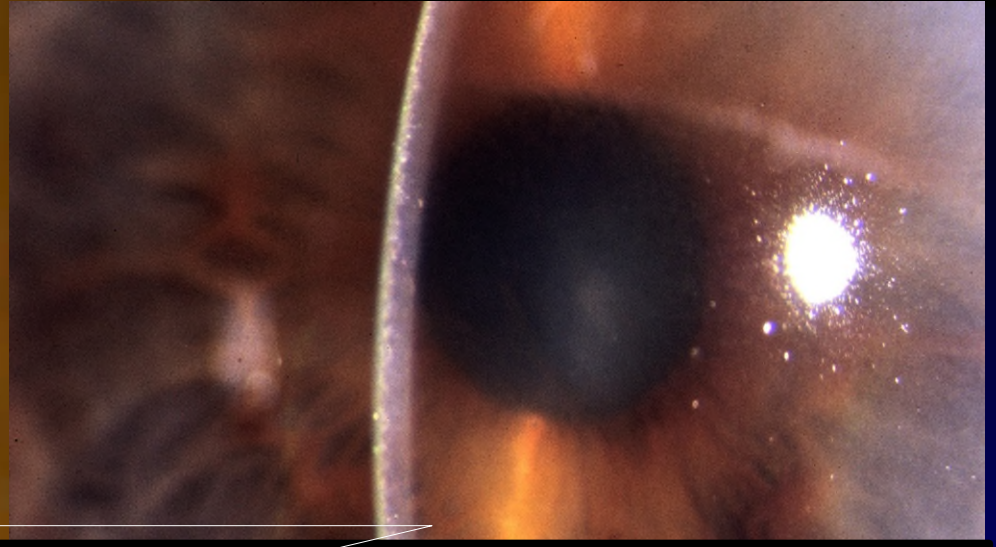
Immunoglobulin crystals



Kappa light chains

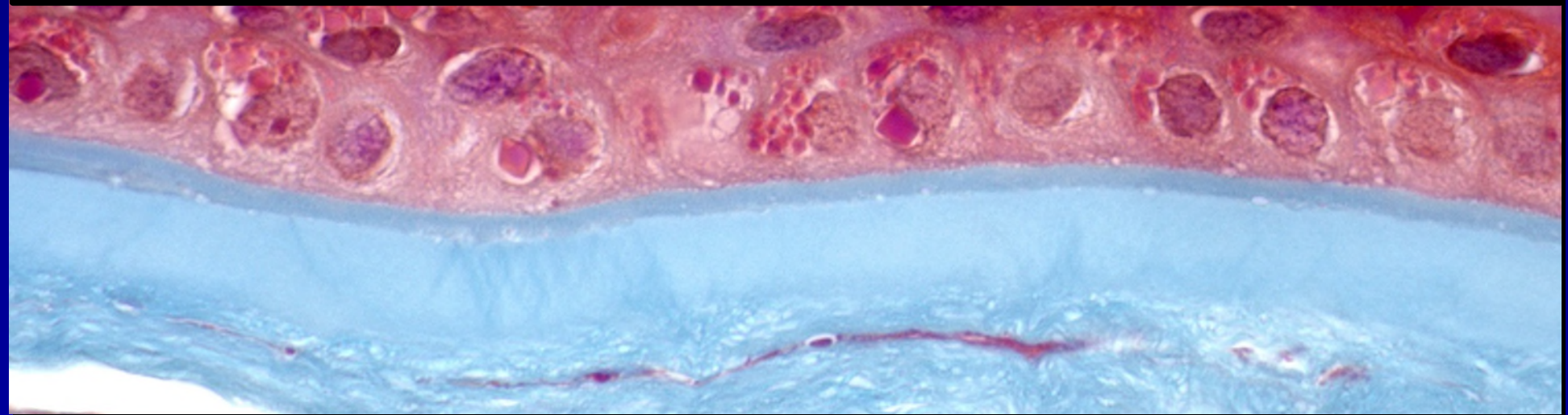
Henderson DW et al. Paraproteinemic crystalloidal keratopathy: an ultrastructural study of two cases, including immunoelectron microscopy. Ultrastruct Pathol 1993;17:643-68.





Teaching Points:

Atypical Schnyder corneal dystrophy?
…Consider paraproteinemic keratopathy



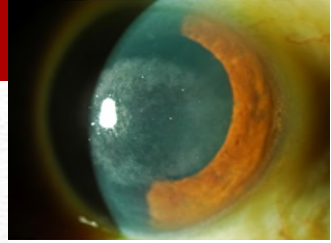
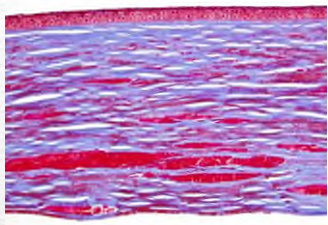
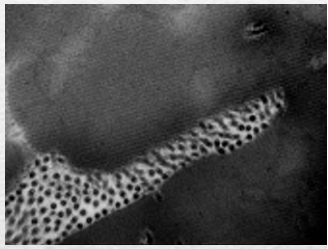
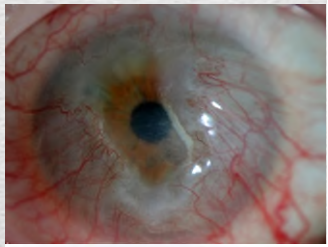
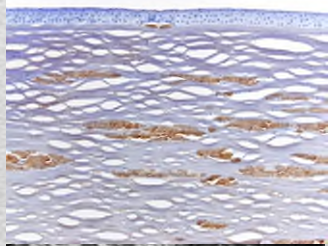
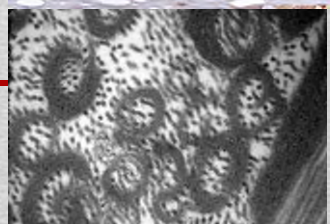
Paraproteinemic keratopathy

First described by Meesmann in 1934

Subsequently identified by Klintworth in 1978

Diagnosis implies paraproteinemia

- Plasma cell myeloma
- Monoclonal gammopathy of undetermined significance (MGUS)
- Lymphoma
- Cryoglobulinemia
- Autoimmune disorders

Summary

- Learning Objective #1
  - Classify key corneal dystrophies
- Learning Objective #2
  - Identify pertinent clinical and pathologic features of key corneal dystrophies
- Learning Objective #3
  - Distinguish key corneal dystrophies from simulating lesions

SPECIAL ARTICLE

IC3D Classification of Corneal Dystrophies—Edition 2

Jayne S. Weiss, MD, Hans Ulrik Møller, MD, PhD,† Anthony J. Aldave, MD,‡ Berthold Seitz, MD,§ Cecilie Bredrup, MD, PhD,¶ Tero Kivelä, MD, FEBO,|| Francis L. Munier, MD,** Christopher J. Rapuano, MD,†† Kanwal K. Nischal, MD, FRCOphth,‡‡ Eung Kweon Kim, MD, PhD,§§ John Sutphin, MD,¶¶ Massimo Busin, MD,||| Antoine Labbé, MD,*** Kenneth R. Kenyon, MD,††† Shigeru Kinoshita, MD, PhD,‡‡‡ and Walter Lisch, MD§§§*

Purpose: To update the 2008 International Classification of Corneal Dystrophies (IC3D) incorporating new clinical, histopathologic, and genetic information.

Methods: The IC3D reviewed worldwide peer-reviewed articles for new information on corneal dystrophies published between 2008 and 2014. Using this information, corneal dystrophy templates and anatomic classification were updated. New clinical, histopathologic, and confocal photographs were added.

Results: On the basis of revisiting the cellular origin of corneal dystrophy, a modified anatomic classification is proposed consisting of (1) epithelial and subepithelial dystrophies, (2) epithelial–stromal *TGFBI* dystrophies, (3) stromal dystrophies, and (4) endothelial dystrophies. Most of the dystrophy templates are updated. The entity "Epithelial recurrent erosion dystrophies" actually includes a number of potentially distinct epithelial dystrophies (Franceschetti corneal dystrophy, Dystrophia Smolandiensis, and Dystrophia Helsinglandica) but must be differentiated from dystrophies such as *TGFBI*-induced dystrophies, which are also often associated with recurrent epithelial erosions. The chromosome locus of Thiel-Behnke corneal dystrophy is only located on 5q31. The entity previously designated as a variant of Thiel-Behnke corneal dystrophy on chromosome 10q24 may represent a novel corneal dystrophy. Congenital hereditary endothelial dystrophy (CHED, formerly CHED2) is most likely only an autosomal recessive disorder. The so-called autosomal dominant inherited CHED (formerly CHED1) is insufficiently distinct to continue to be considered a unique corneal dystrophy. On review of almost all of the published cases, the description appeared most similar to a type of posterior polymorphous corneal dystrophy linked to the same chromosome 20 locus (PPCD1). Confocal microscopy also has emerged as a helpful tool to reveal in vivo features of several corneal dystrophies that previously required histopathologic examination to definitively diagnose.

Conclusions: This revision of the IC3D classification includes an updated anatomic classification of corneal dystrophies more accurately classifying *TGFBI* dystrophies that affect multiple layers rather than are confined to one corneal layer. Typical histopathologic and confocal images have been added to the corneal dystrophy templates.

Key Words: cornea, cornea dystrophy, cornea pathology, cornea, genetics, genetic disease, hereditary disease, confocal microscopy, histopathology, epithelium, Bowman membrane, stroma, Descemet membrane, endothelium, *TGFBI*, epithelial and subepithelial dys-

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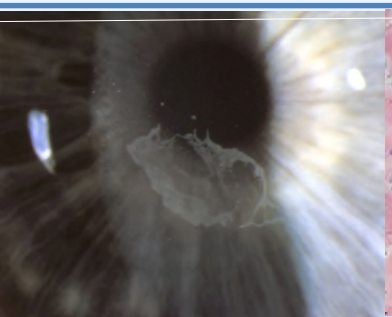
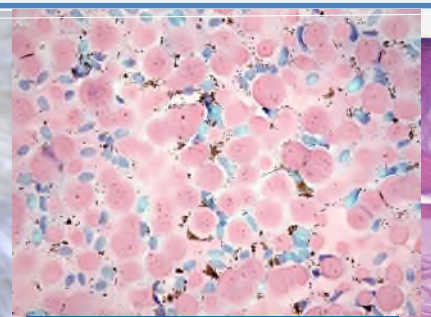
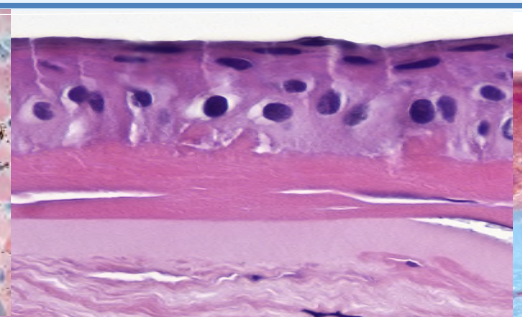
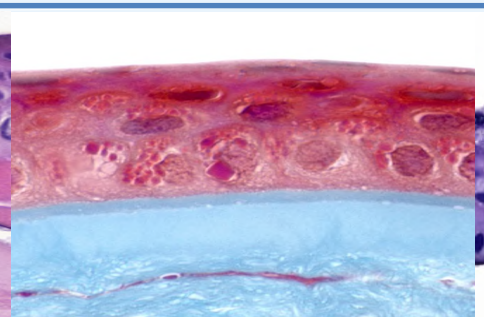
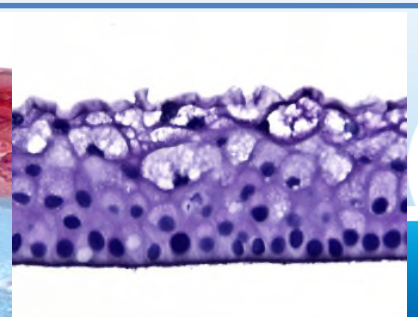

Corneal dystrophies and simulating lesions

I. Normal histology

II. Dystrophies

- Epithelial and subepithelial dystrophies
- Epithelial-stromal TGFBI dystrophies
- Stromal dystrophies
- Endothelial dystrophies

III. Virtual slides

QUESTIONS?

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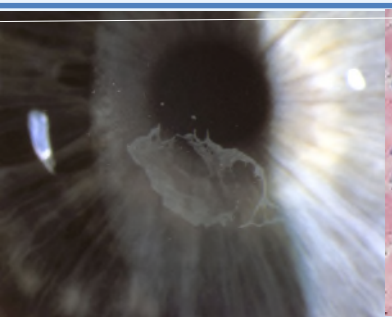
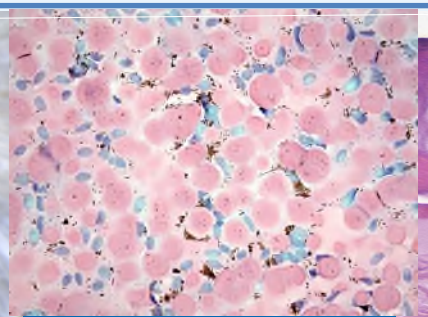
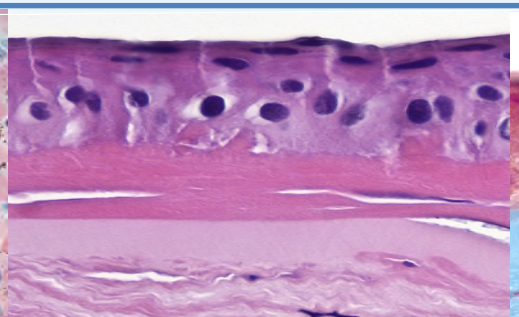
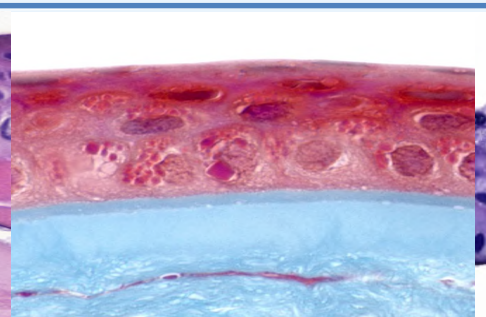
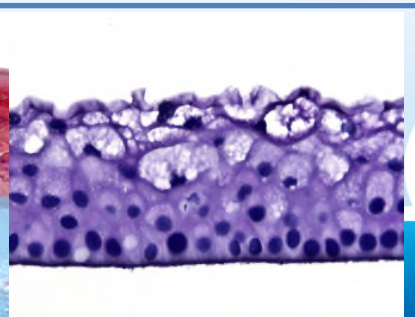

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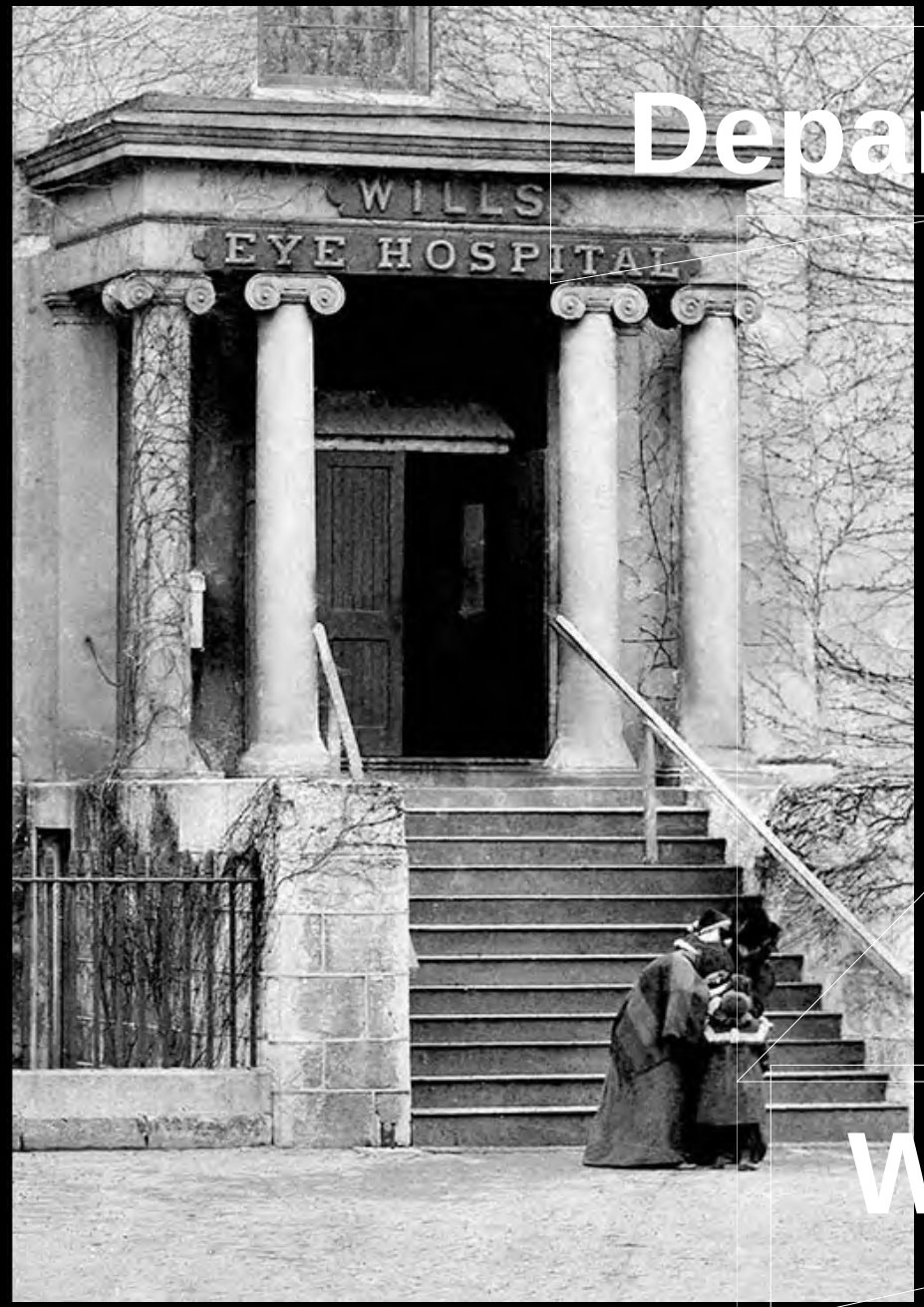

Wills Eye Hospital