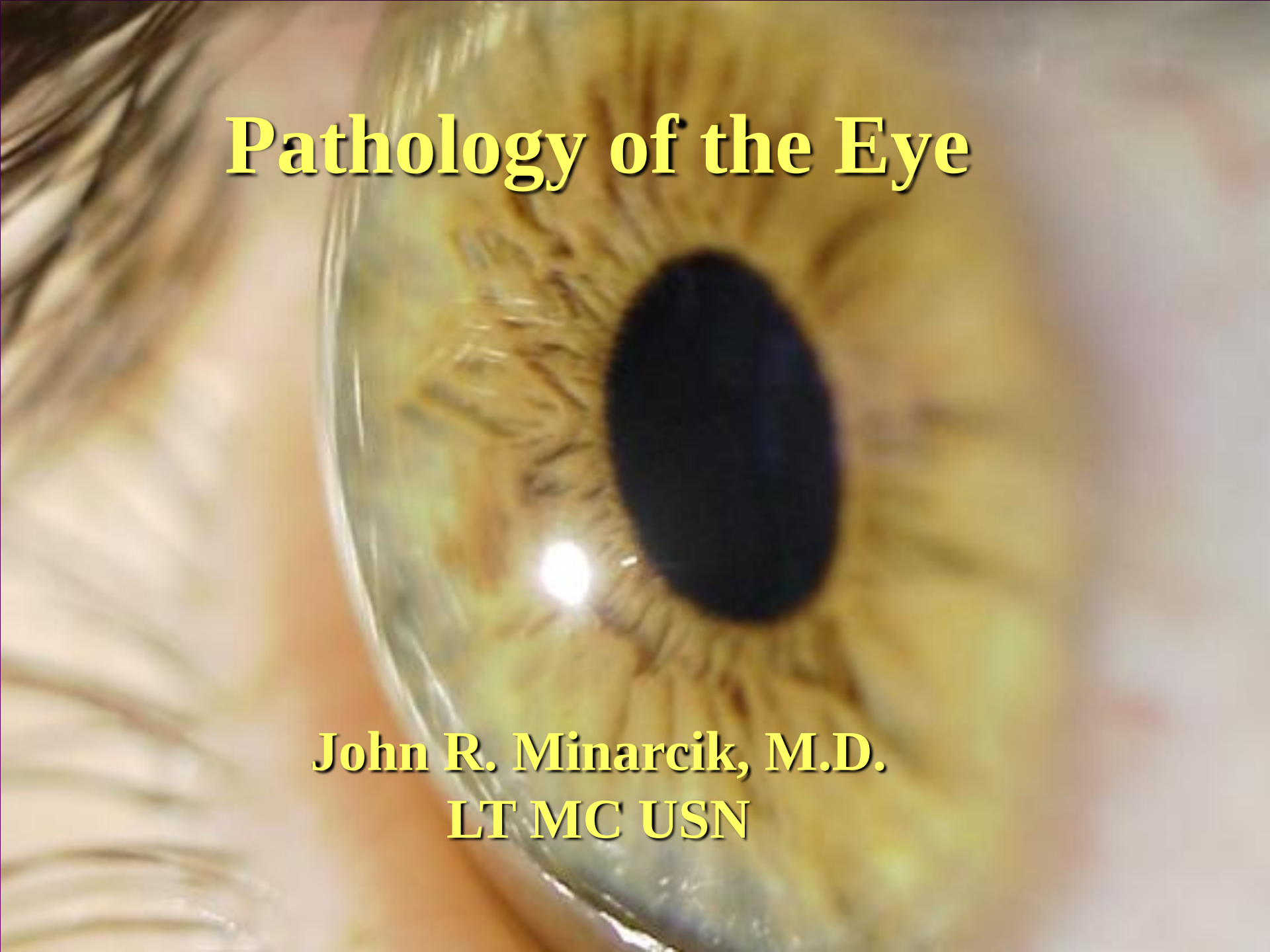
Pathology of the Eye



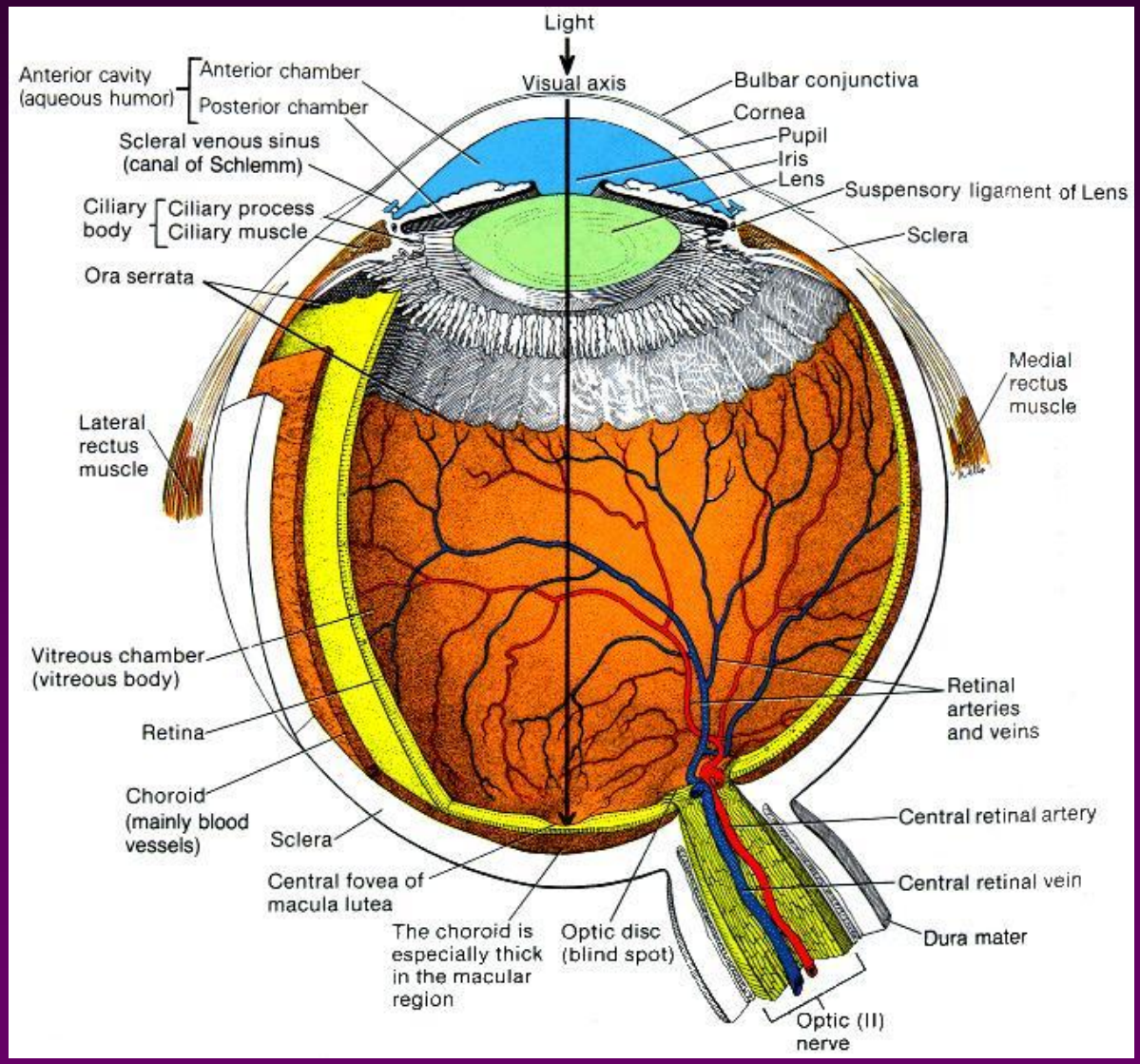
John R. Minarcik, M.D.
LT MC USN

Outline and Introduction

SECTIONS

1. Orbit
2. Eyelid
3. Conjunctiva
4. Cornea
5. Uvea
6. Lens
7. Retina/Vitreous
8. Optic Nerve/Glaucoma

Intro - Basic Anatomy



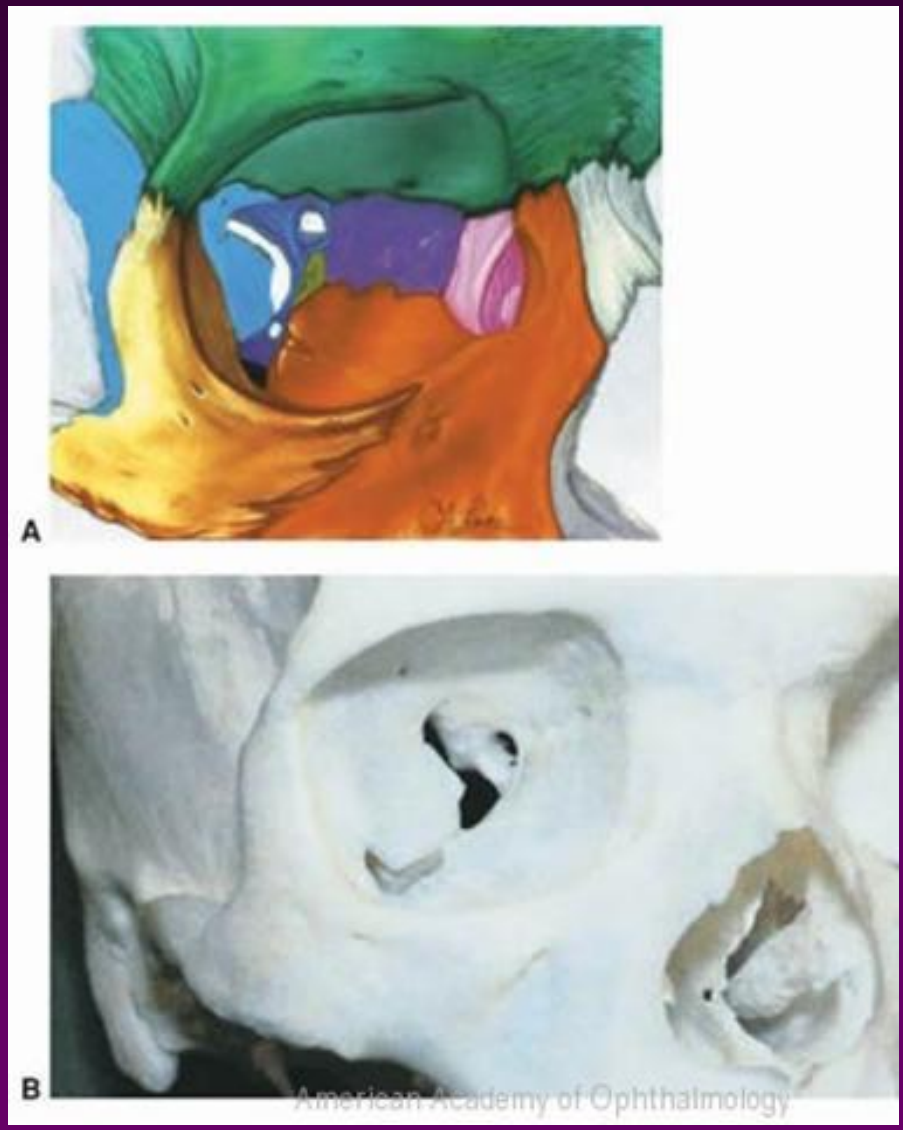
THE ORBIT

Orbit

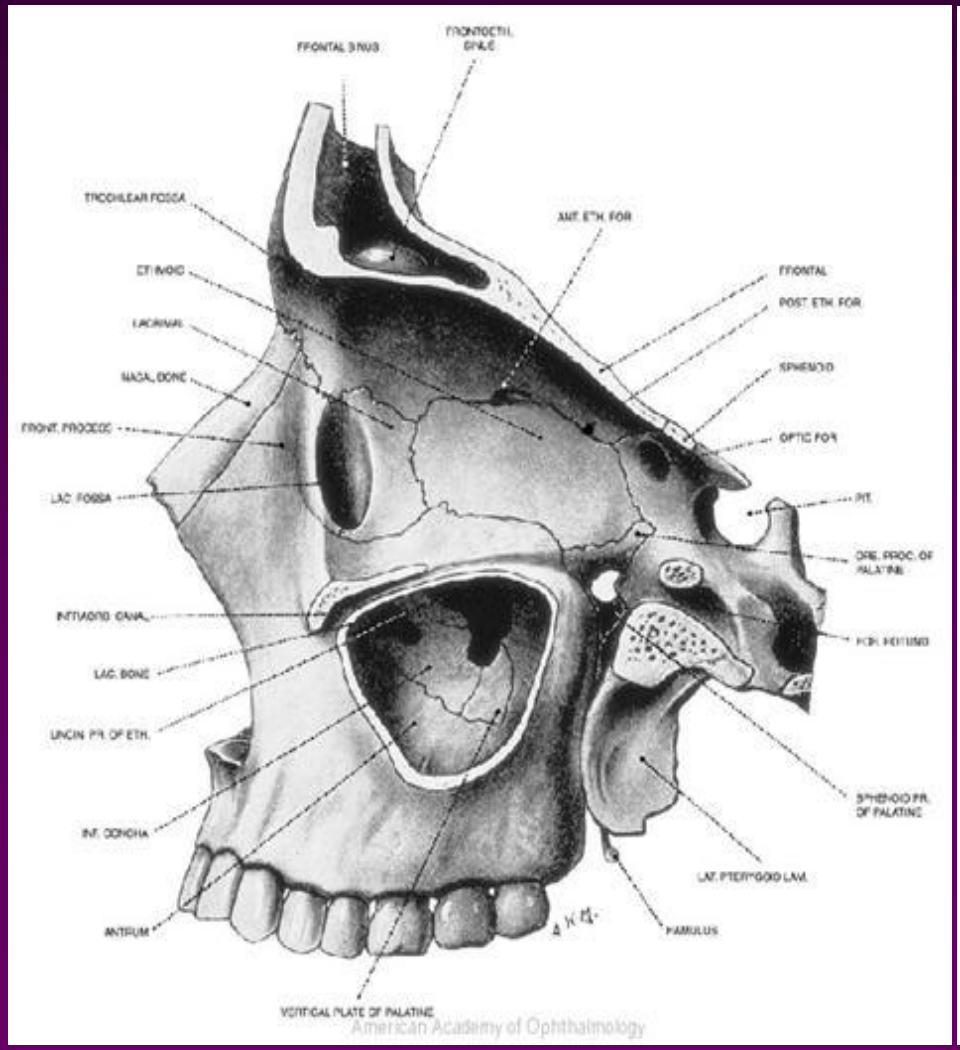
- Anatomy
- Thyroid Orbitopathy
- Tumors
- Inflammation/Infection
- Trauma

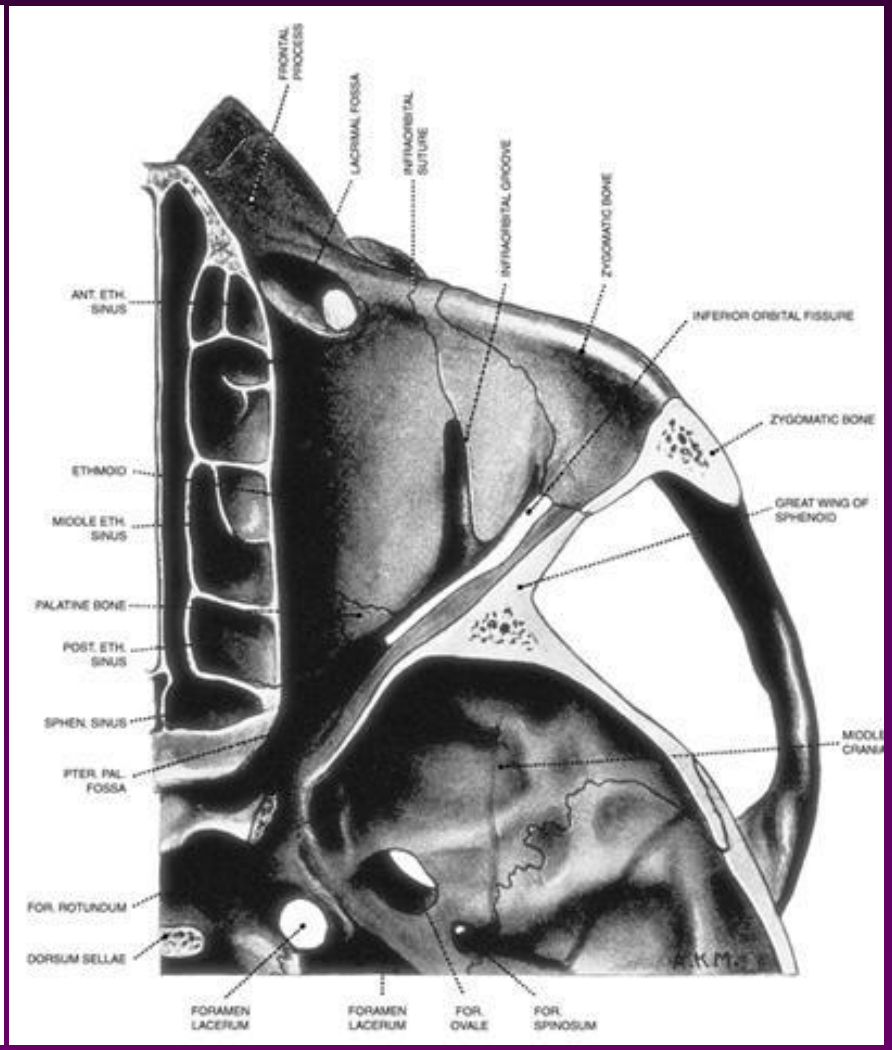
Orbit - Anatomy

- Bones of the orbit
  - Sphenoid
  - Maxillary
  - Ethmoid
  - Lacrimal
  - Zygoma
  - Palatine
  - Frontal



Orbit - Osteology

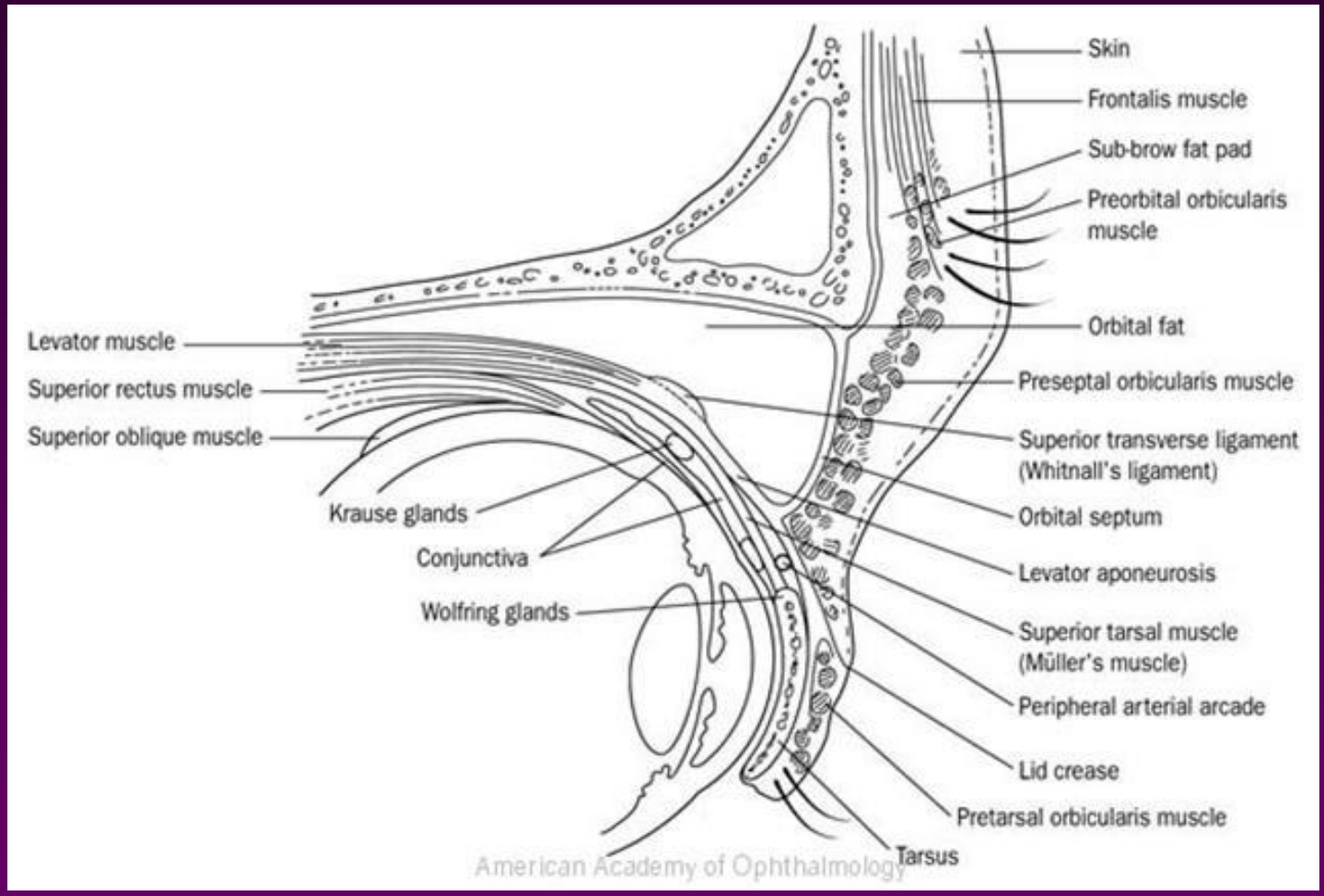




Orbit – Posterior Contents

- The ANNULUS OF ZINN is the tendon-ring that encircles the ON and acts as an origin for the muscles.

Orbit – Anterior Boundary

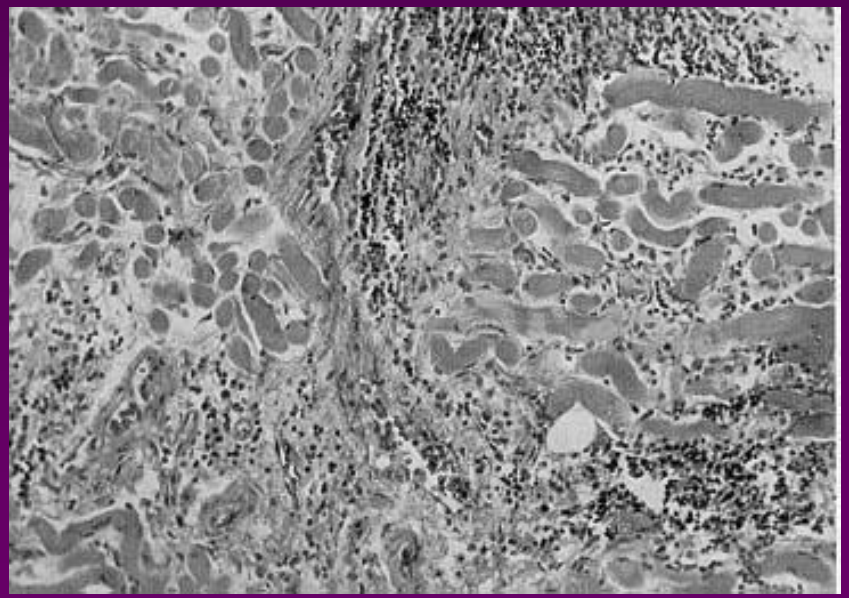


- The ORBITAL SEPTUM is the anterior fascial boundary to the orbit

Orbit – Thyroid-Related (Graves') Orbitopathy

- Autoimmune condition, triggered by ?Thyroid antigens, with lymphocytic infiltration, FIBROSIS, and ENLARGEMENT of extraocular muscles.
- Proptosis, strabismus/muscle-restriction, exposure problems (dry-eye), and compressive optic neuropathy.
- Treated with steroids, radiation therapy, or surgical decompression (opening the orbital walls into the sinuses)

Orbit – Thyroid-Related Orbitopathy



Orbit - Tumors

- Wide variety of lacrimal, lymphoid, neural, vascular, meningeal origin tumors, and metastatic tumors
- Children
  - –rhabdomyosarcoma is the most common primary malignancy of orbit.
  - – neuroblastoma is most common metastatic tumor

Orbit - Inflammation

- **<u>Orbital Cellulits</u>** frequently extends from adjacent sinus infections, or periocular trauma.
- A life and sight threatening emergency! Can extend into the cavernous sinus, and brain.
- “Pre-Septal” vs. “Post-Septal” can be distinguished by involvement of intraorbital structures

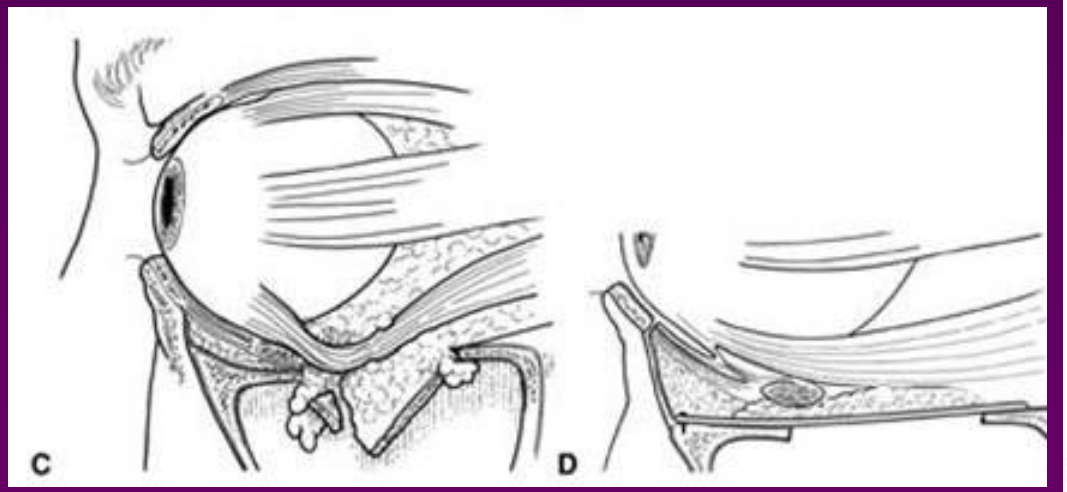
Orbit - Inflammation

Orbit - Trauma

- “Blow–out” fractures occur when blunt trauma to the eye causes the orbit to rupture
- Hemorrhages into the orbit can act like a “compartment syndrome”

Orbit - Trauma

Orbital Floor fractures can cause restricted upgaze if there is muscle entrapment



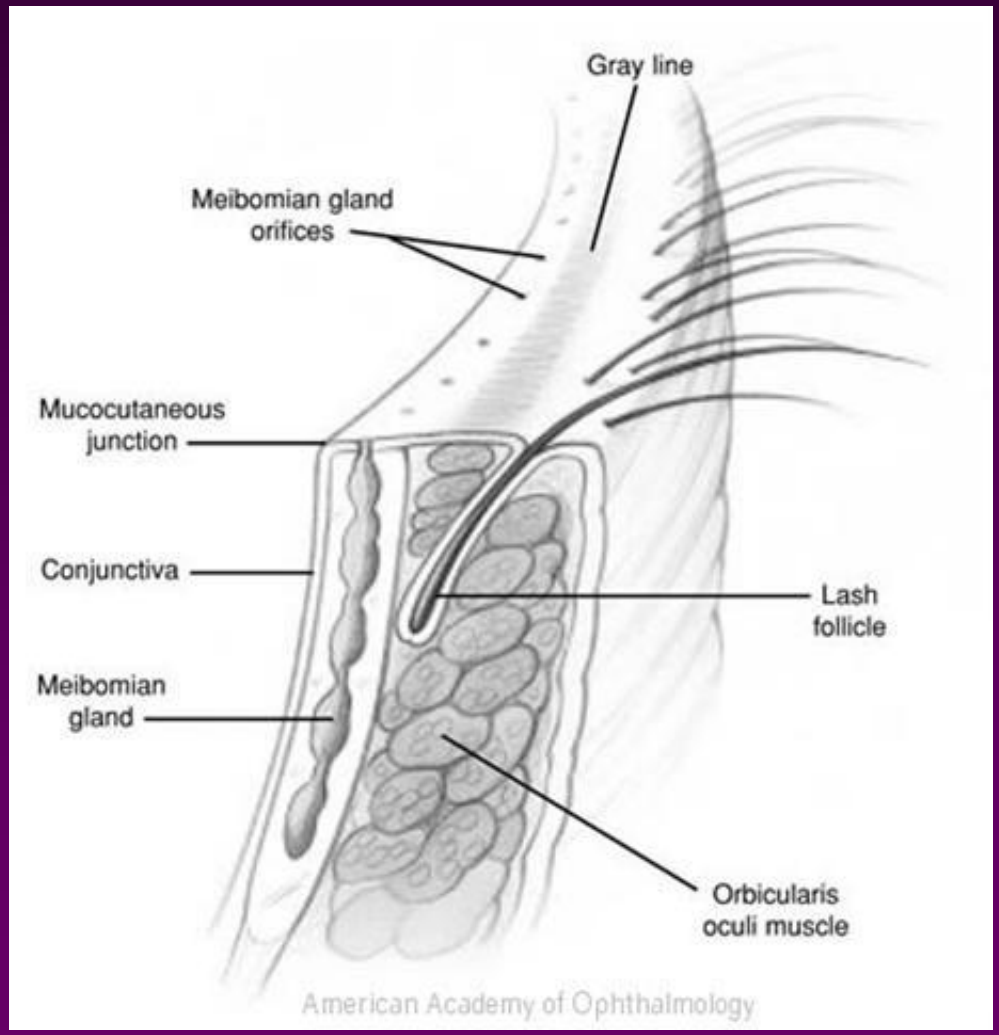
LIDS

- Anatomy
- Tumors

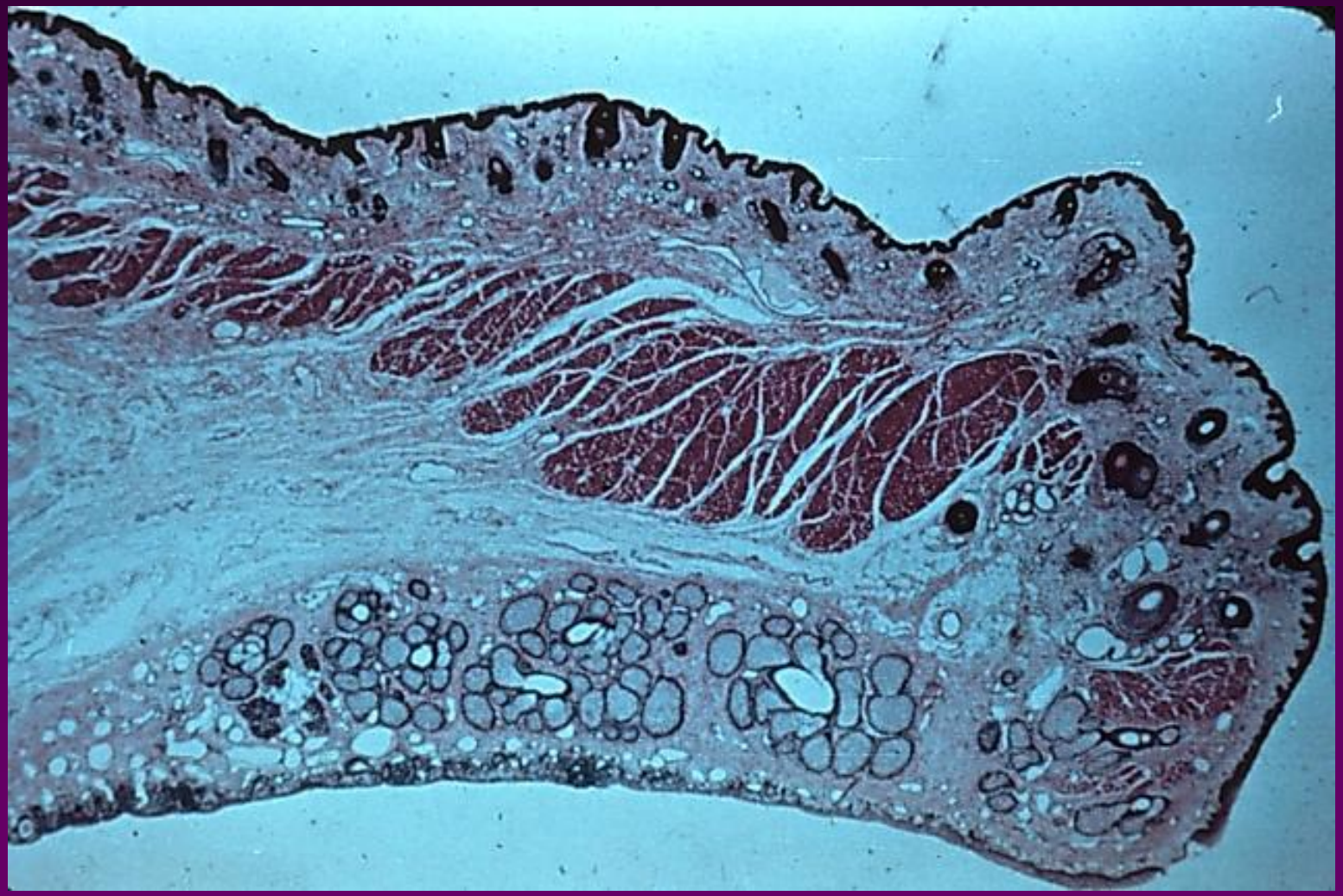
LIDS - Anatomy

LAYERS:

- Skin
- Orbicularis
- Tarsal plate
- Meibomian glands
- Palpebral conjunctiva

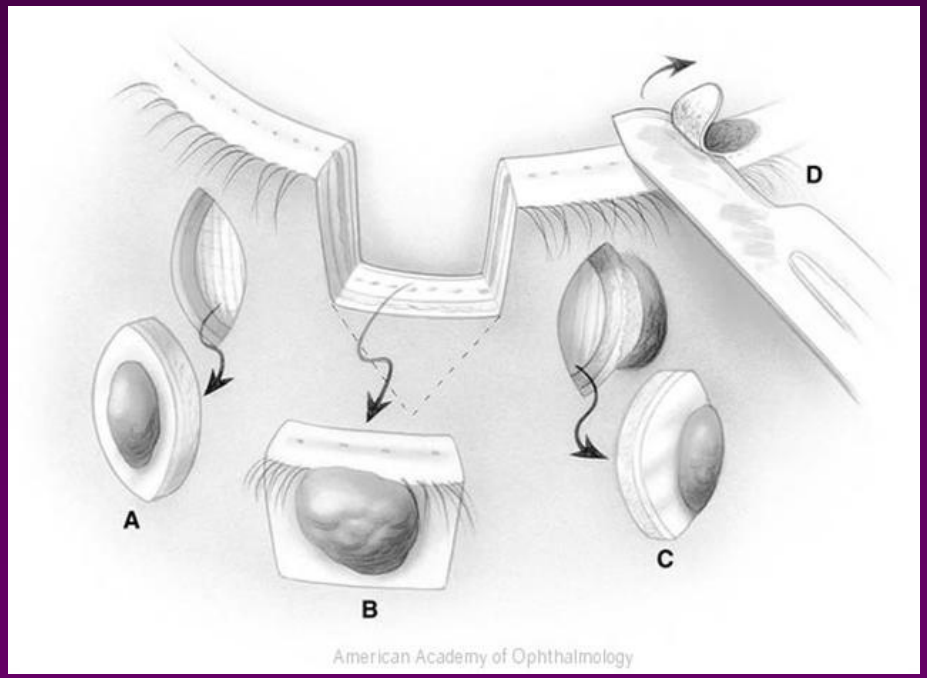


LIDS - Histology

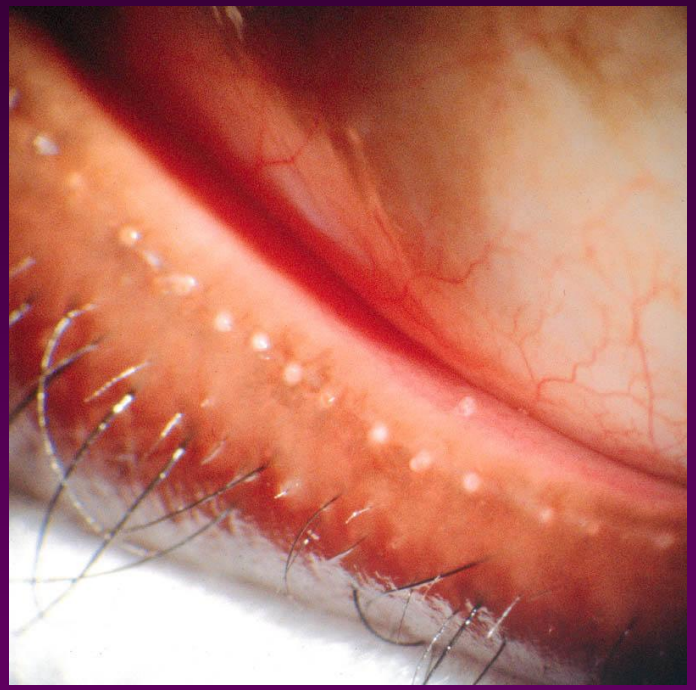


LIDS - Tumors

- Malignant
  - **Basal cell carcinoma** - most common
  - Squamous
  - Melanoma
  - Sebaceous cell carcinoma
- Benign
  - **Chalazion** vs. Hordeolum
  - Papillomas/Verrucae
  - Epidermal inclusion cysts
  - Many others…



LIDS - Tumors

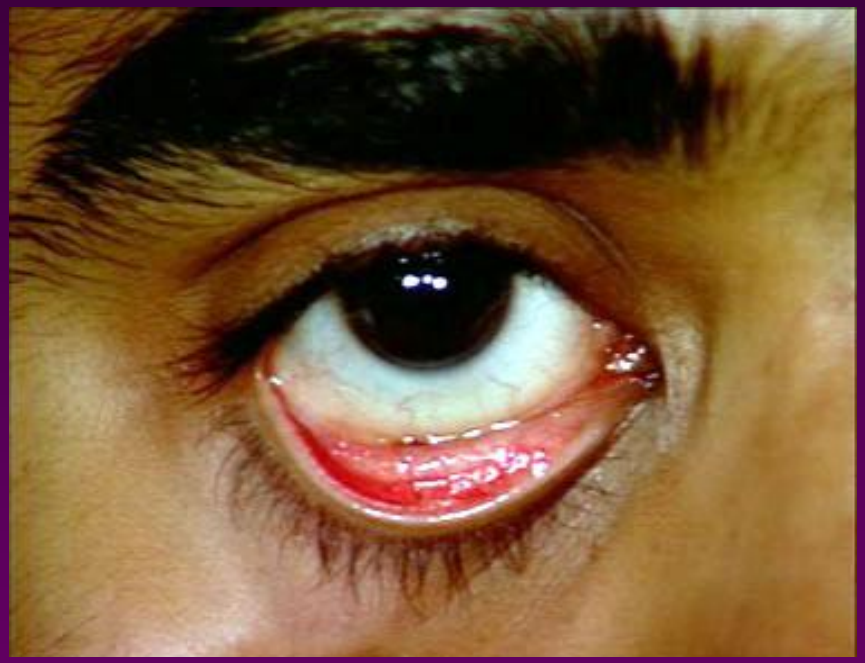


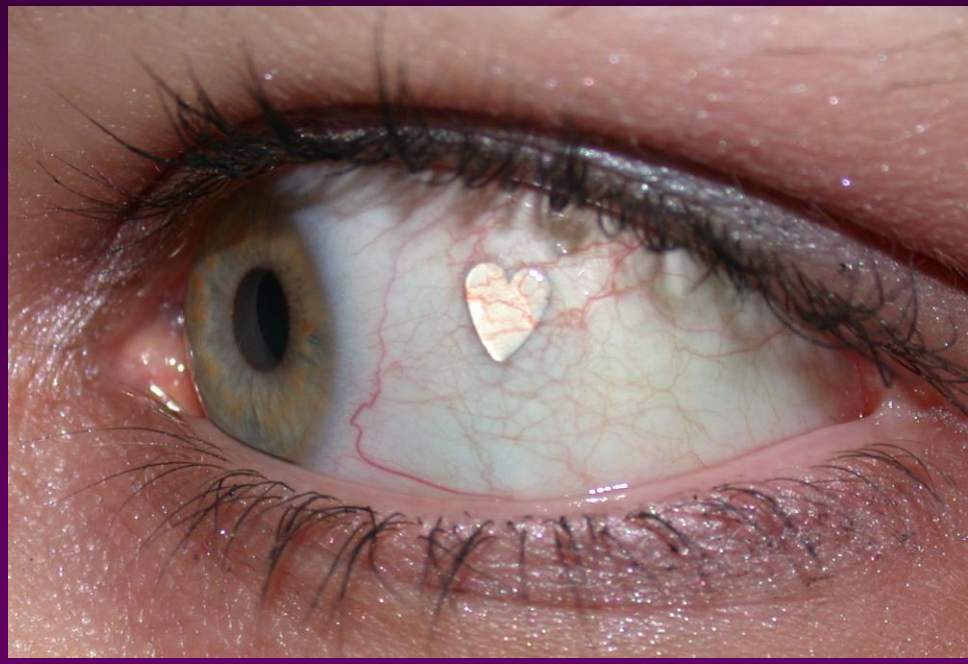
- Chalazion – a cyst of the meibomian gland
- Hordeolum – an *inflammed* cyst of the MG (foreign body granuloma)

Conjunctiva

- Thin, non-keratinized skin covering the sclera (bulbar) or the inner surface of the lid (palpebral)
- Rich in goblet cells, which secret the mucinous components of the tear film

Conjunctiva



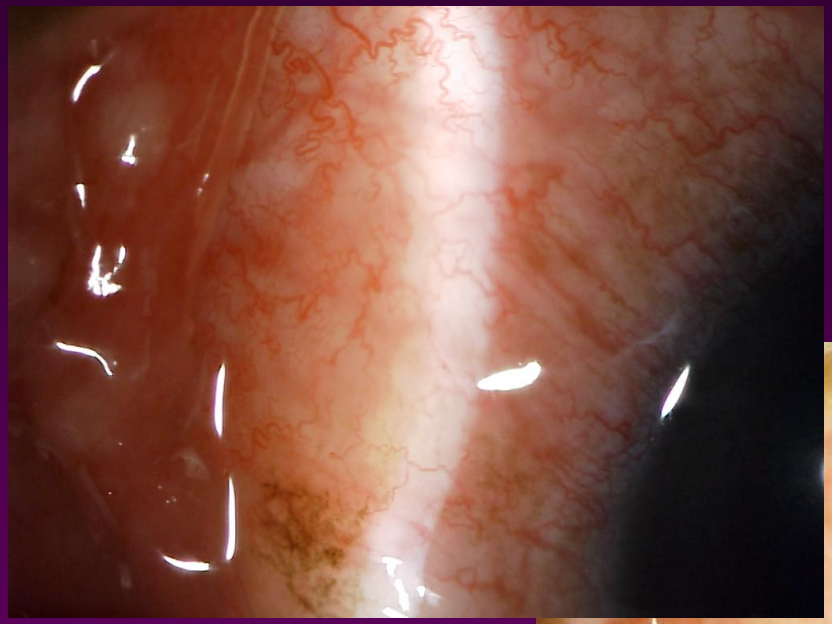


- The bulbar layer is continous with the palpebral layer

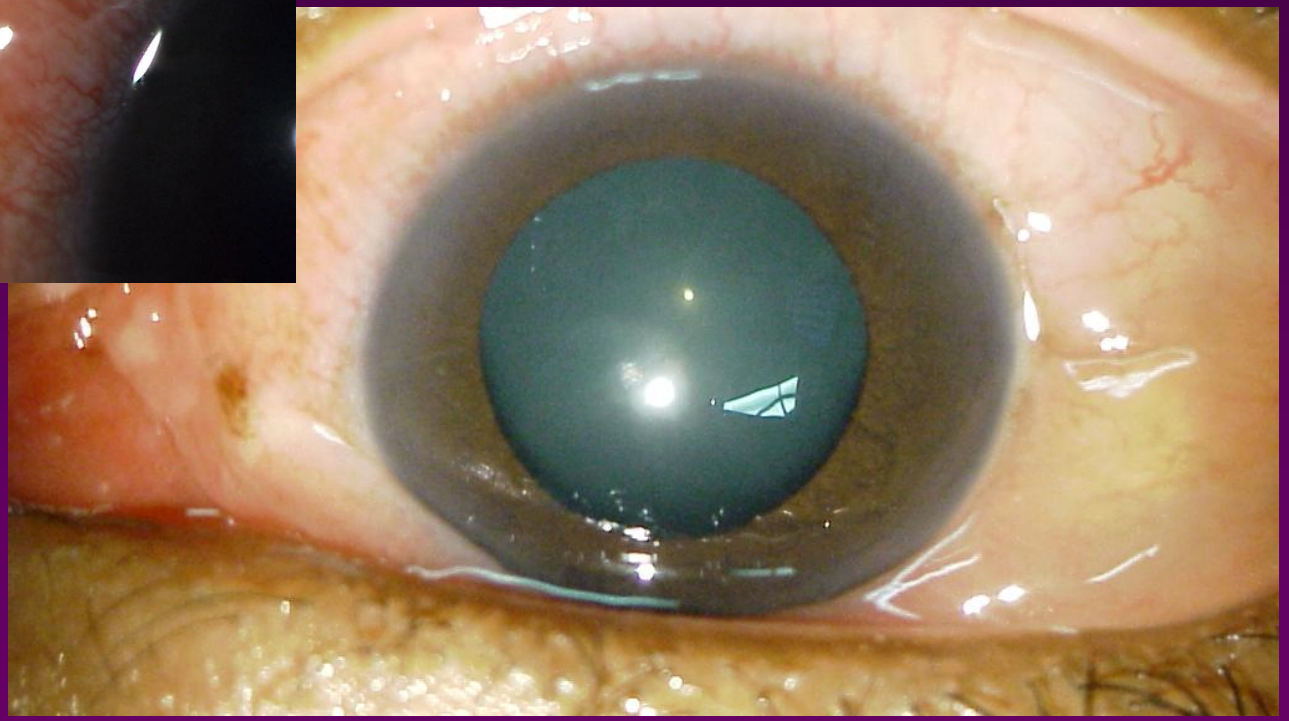
Conjunctiva – Pathologic conditions

- Conjunctivitis (“pink-eye”) – is an inflammation of the conjunctiva due to a viral (Adenovirus), bacterial, or allergic cause.
- Scarring – Can occur with serious inflammatory conditions like Stevens-Johnson syndrome and Ocular Cicatricial Pemphigoid

Conjunctivitis



- A rare granulomatous variety…
- Bartonella henselae



- Cat-scratch Fever!

Conjunctiva – Degenerative conditions

- Pinguecula – on the conj only
- Pterygium – encroaching onto cornea

- Histologically identical
- Both involve “elastotic degeneration” of the conjunctiva, usually due to chronic ultraviolet exposure.

Conjunctiva – Degenerative conditions

- Small pinguecula

- Pterygium

Conjunctiva - tumors

- Conjunctival intraepithelial neoplasia (CIN)
- Squamous Cell
- Melanoma
- Lymphoid - arising from mucosa-associated lymphoid tissue (MALT)

Conjunctiva

- CIN (squamous cell), HPV 16/18

Cornea

The cornea is a unique transparent and avascular tissue that is the most important refractive structure of the eye.

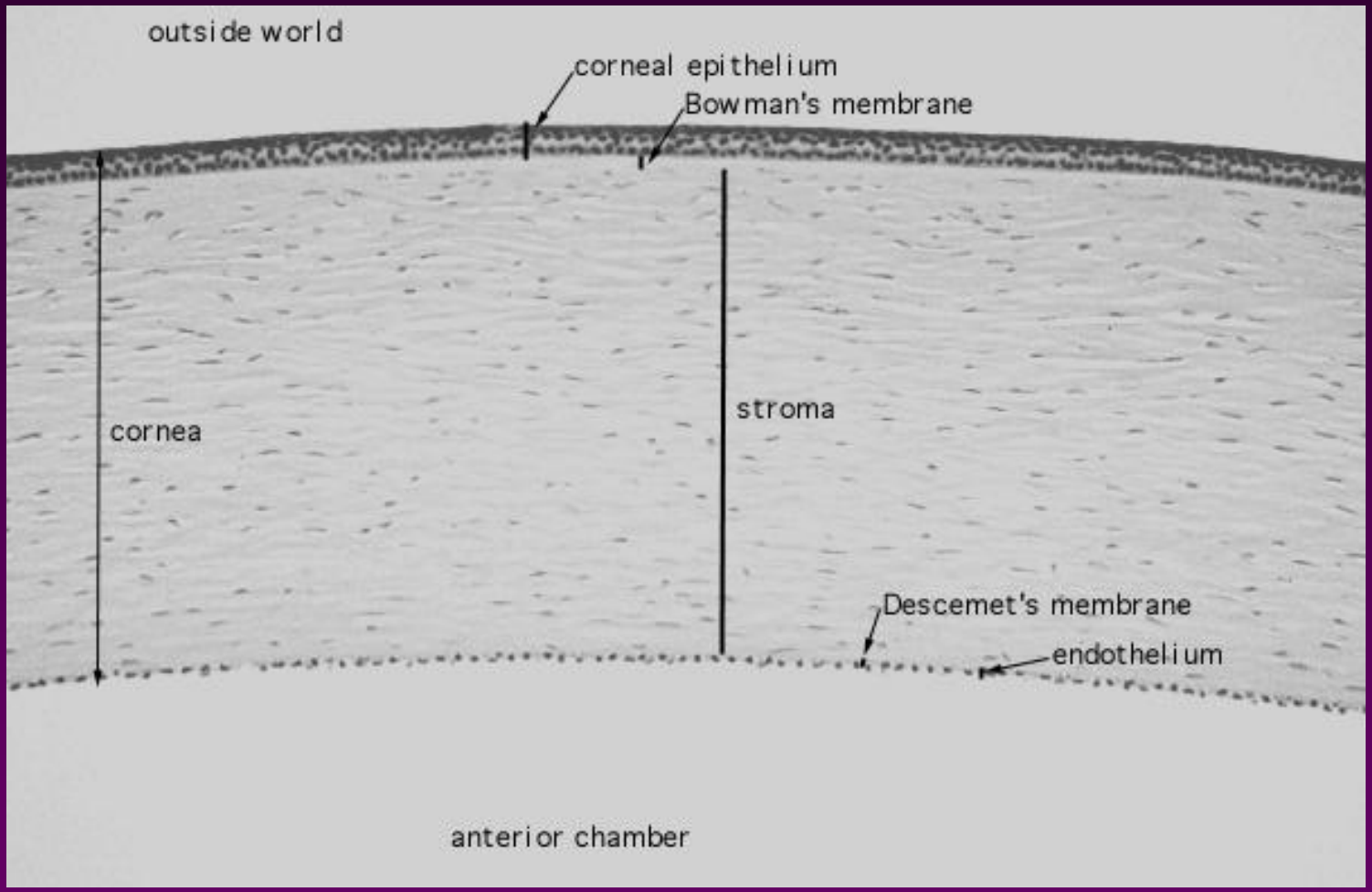
- Anatomy
- Inflammation/Infection
- Dystrophy/Ectasia

Cornea - Anatomy

5 Layers:

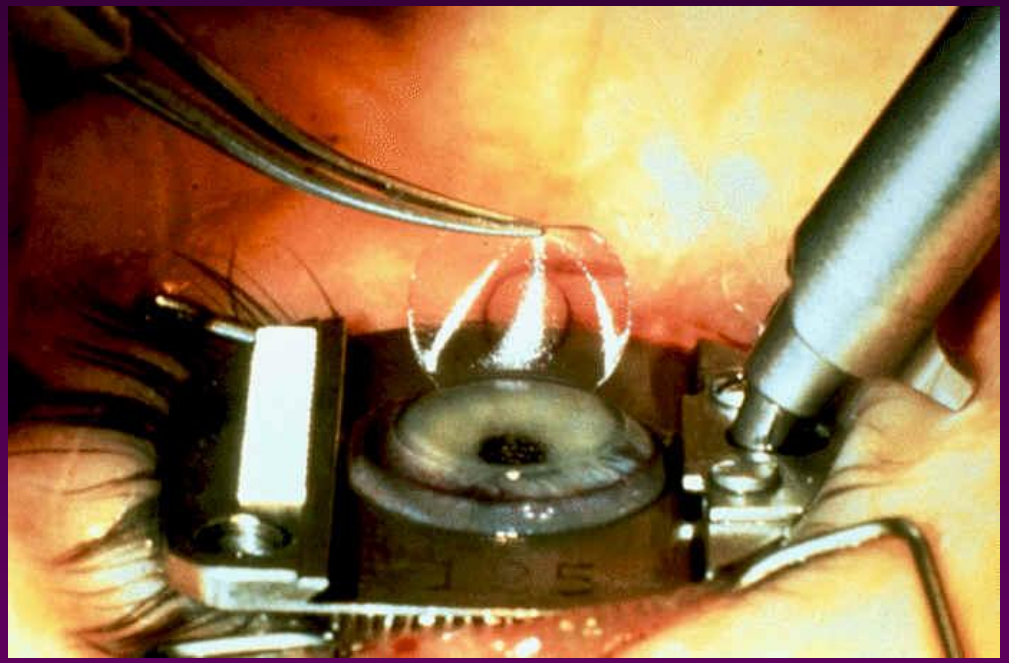
- **Epithelium** – Continuous with conj, richly innervated by CN-V_1
- **Bowman's Membrane**
- **Stroma** – The thickest central portion (90%). This is where LASIK/Refractive surgery happens! Primarily made up of Type 1 Collagen in uniformly-spaced lamellar bundles.
- **Descemet's membrane**
- **Endothelium** – pumps the water out of the cornea and keeps it clear

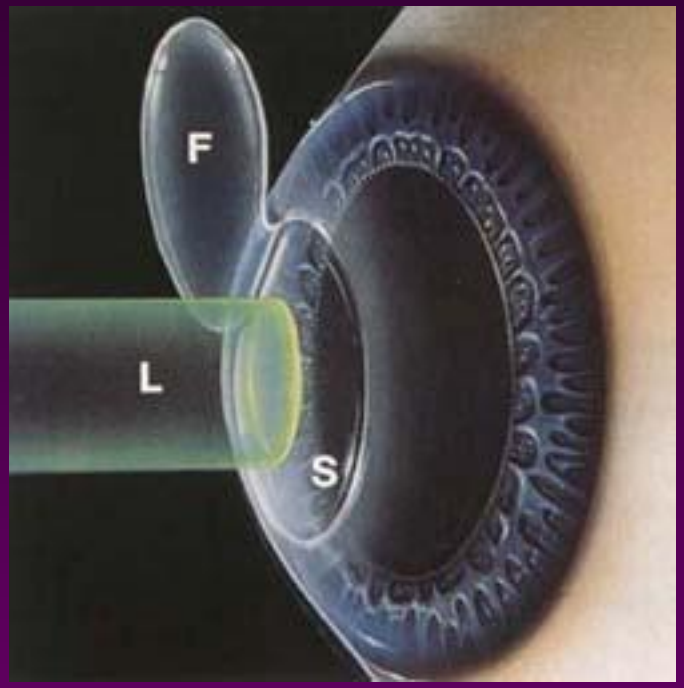
Cornea



The uniform spacing of the stromal collagen bundles at a distance of approx ¼ wavelength light allows transparency.

Cornea - Refractive Surgery





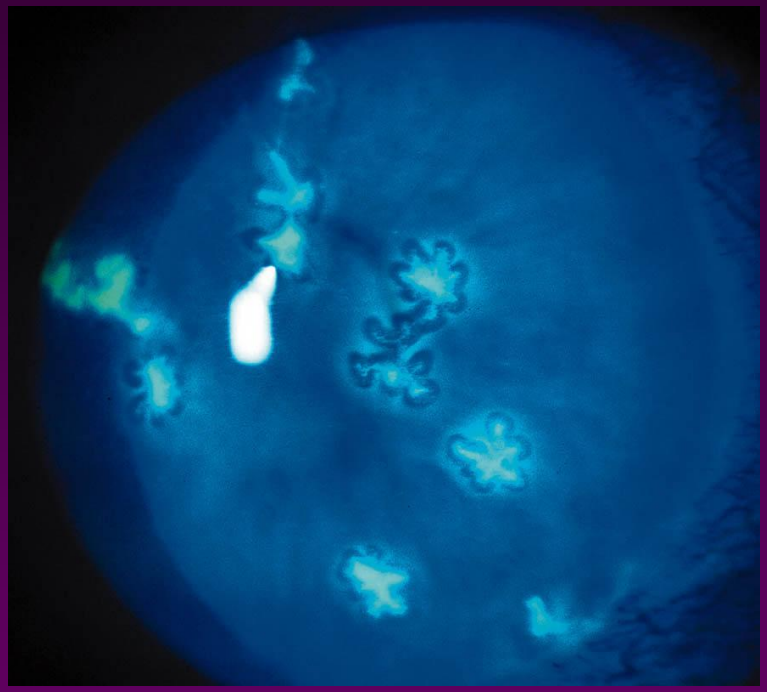
- Excimer Laser is applied to the stromal bed, underneath a reflected corneal flap (LASIK).
- The tissue is ablated precisely to counteract the refractive error of the eye.

Cornea – Inflammation/Infection

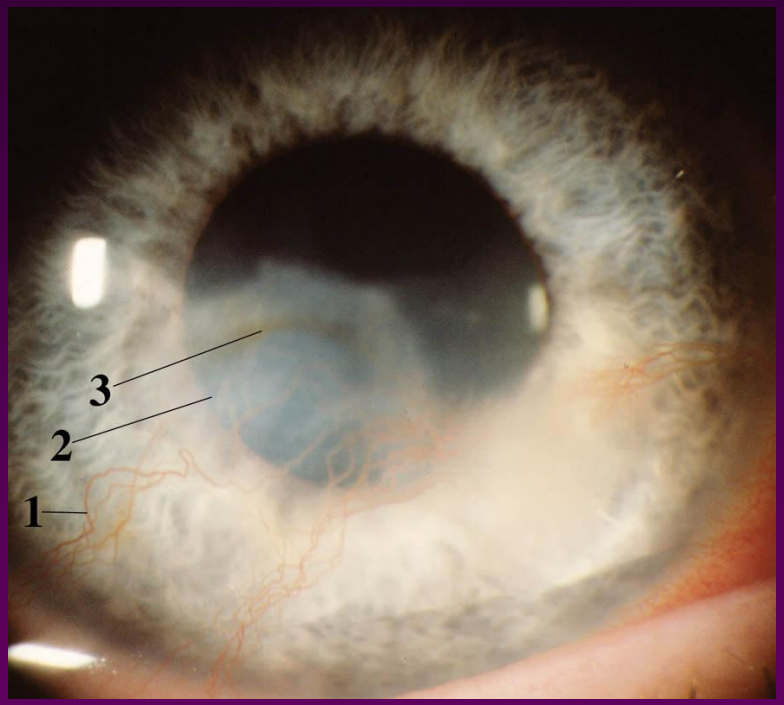
Keratitis – inflammation of cornea

- Bacterial ulcer – Frequent in contact lens users, Pseudomonas most common
- Viral – Herpes (HSV) is a frequent etiology
- Autoimmune, Syphilis, Fungal, ameobic, and many other types

Cornea - HSV Keratitis

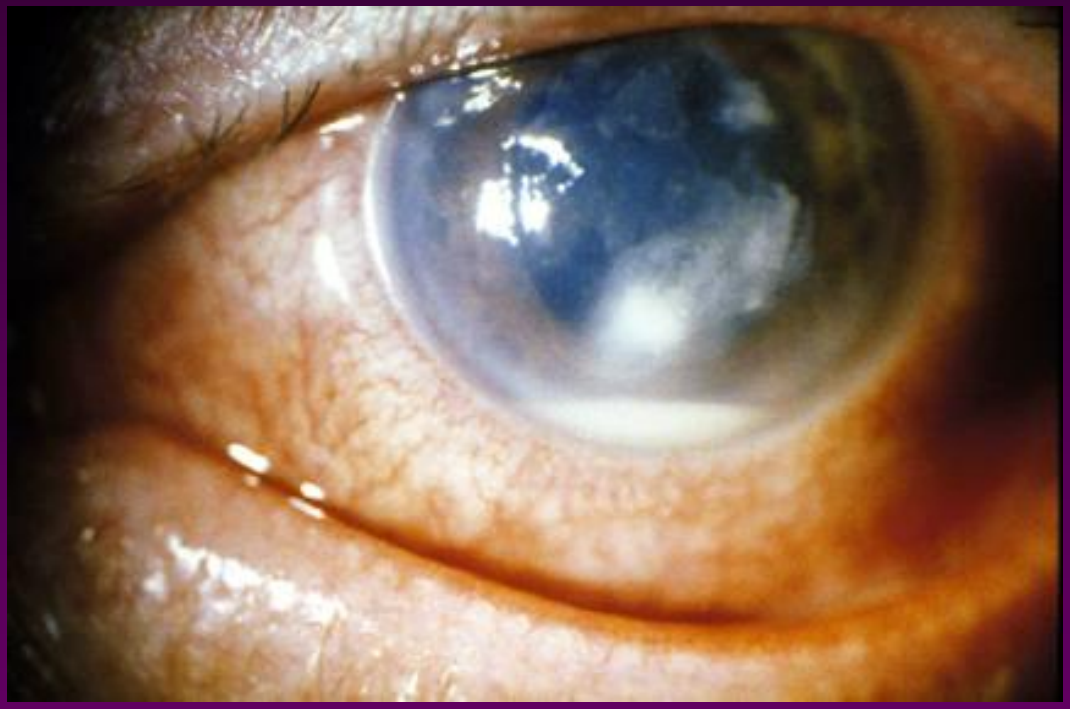


- Epithelial “dendritic” Keratitis



- Stromal Keratits (note the vessels and clouding)

Cornea - Bacterial Ulcer

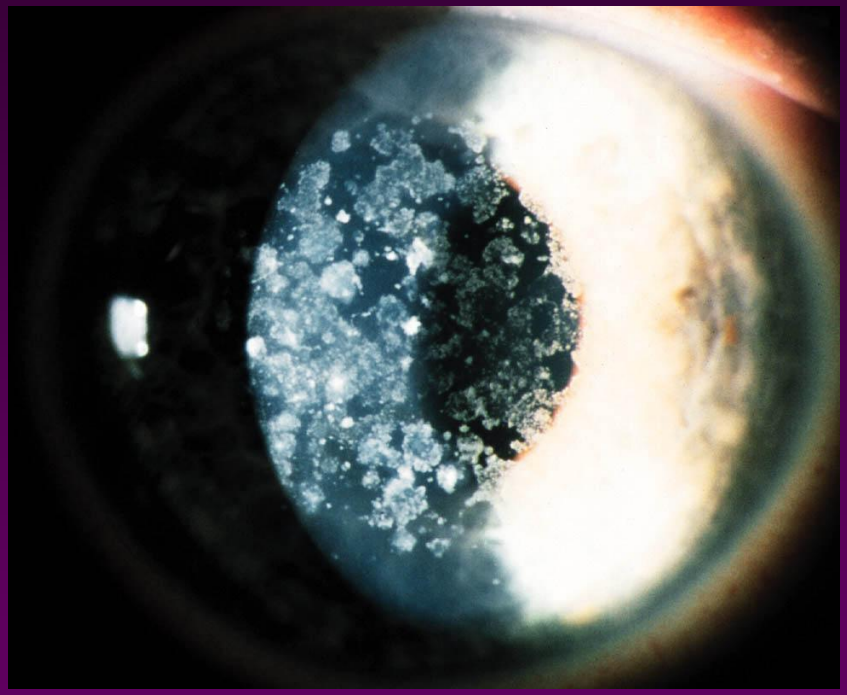


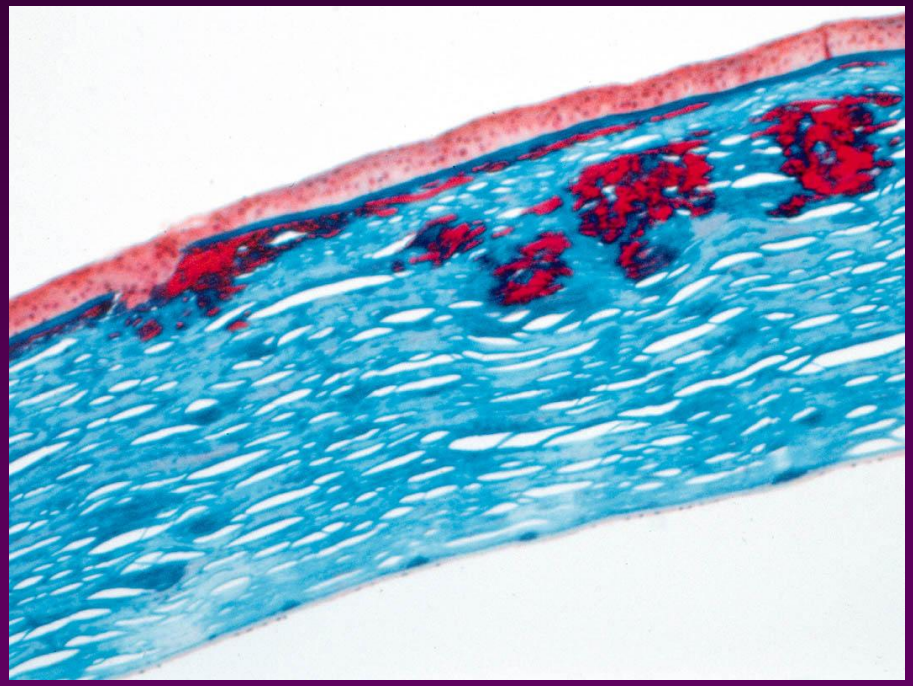
Epithelial defect, infiltrate of white cells into the cornea, and a layered leukocyte collection in the AC (Hypopyon)

Cornea – Stromal Dystrophy

- Dystrophy – a heritable disorder resulting in abnormal tissue morphology, function, or abnormal depositions of material into the cornea.
- MANY types, affecting each specific layer.

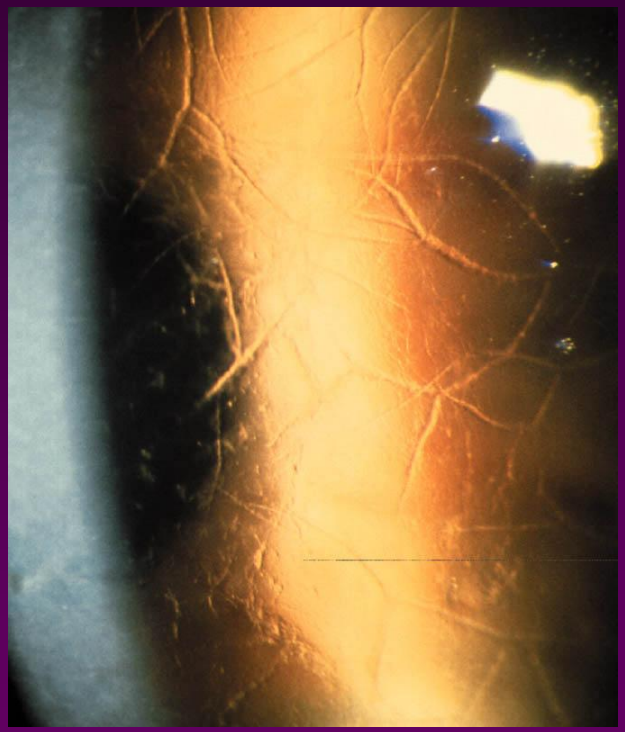
Cornea – Stromal Dystrophy



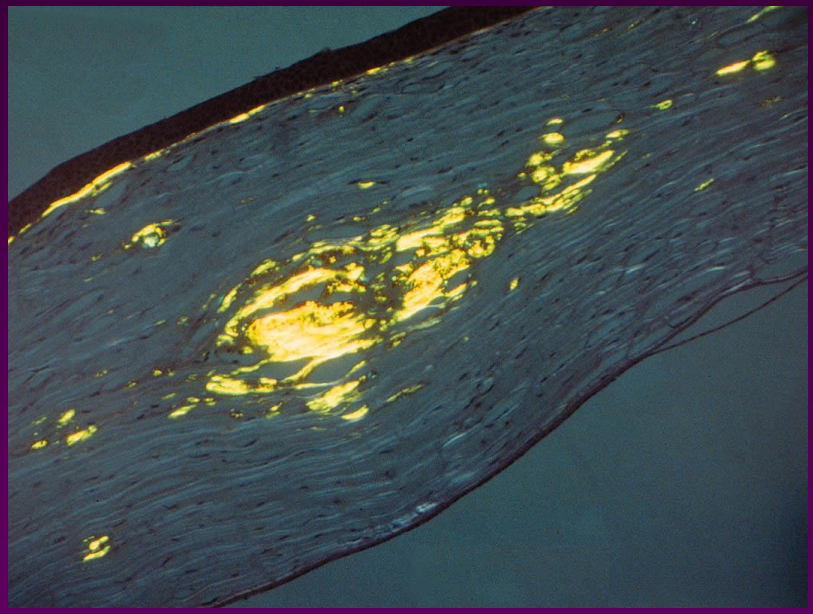


- Granular Dystrophy
- Hyaline material deposited in stroma

Cornea – Stromal Dystrophy

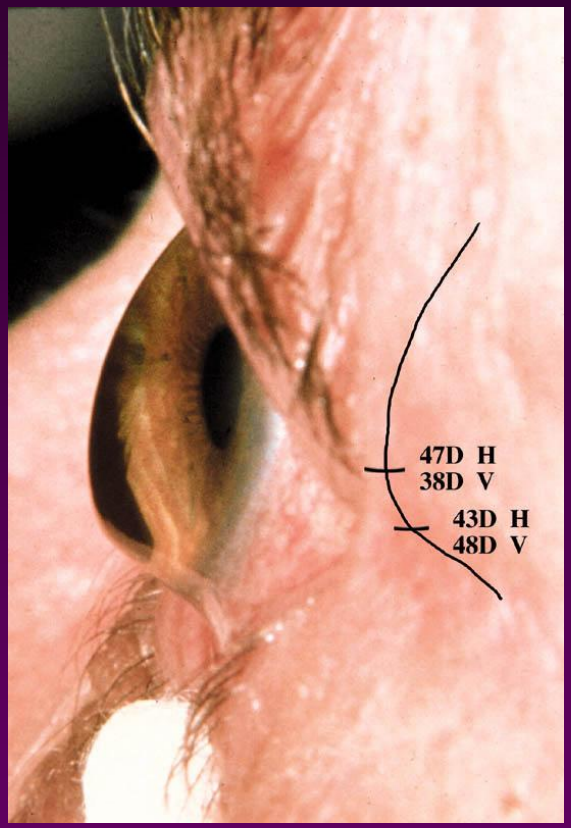


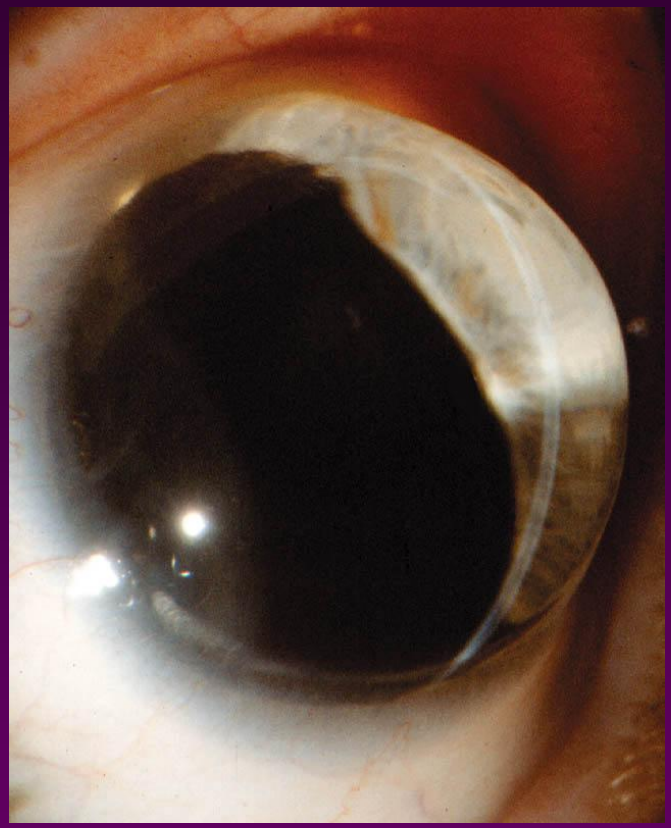
- Lattice Dystrophy



- Amyloid deposition with “apple-green” birefringence, with Congo Red staining

Cornea - Ectasia

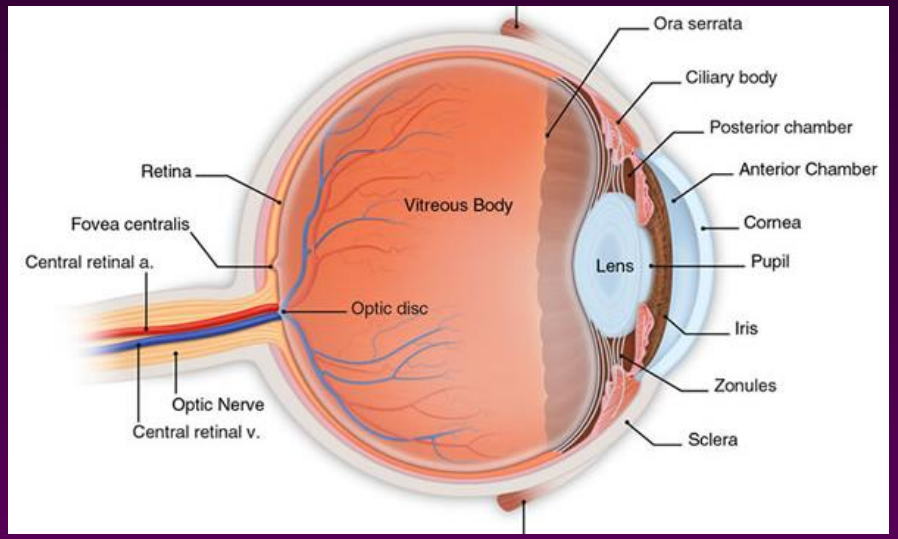




- Progressive deformation of cornea is an ectasia. Keratoconus is the most common ectatic dystrophy. Ectasia can also be a complication of refractive surgery…

THE UVEA

The Uvea



"The uvea" is:

1. The Iris
2. The Ciliary body
3. The Choroid

Each has a function

1. Iris is a diaphragm for light
2. Ciliary body suspends and "flexes" the lens, and makes the aqueous humor
3. The choroid helps nourish the outer retina

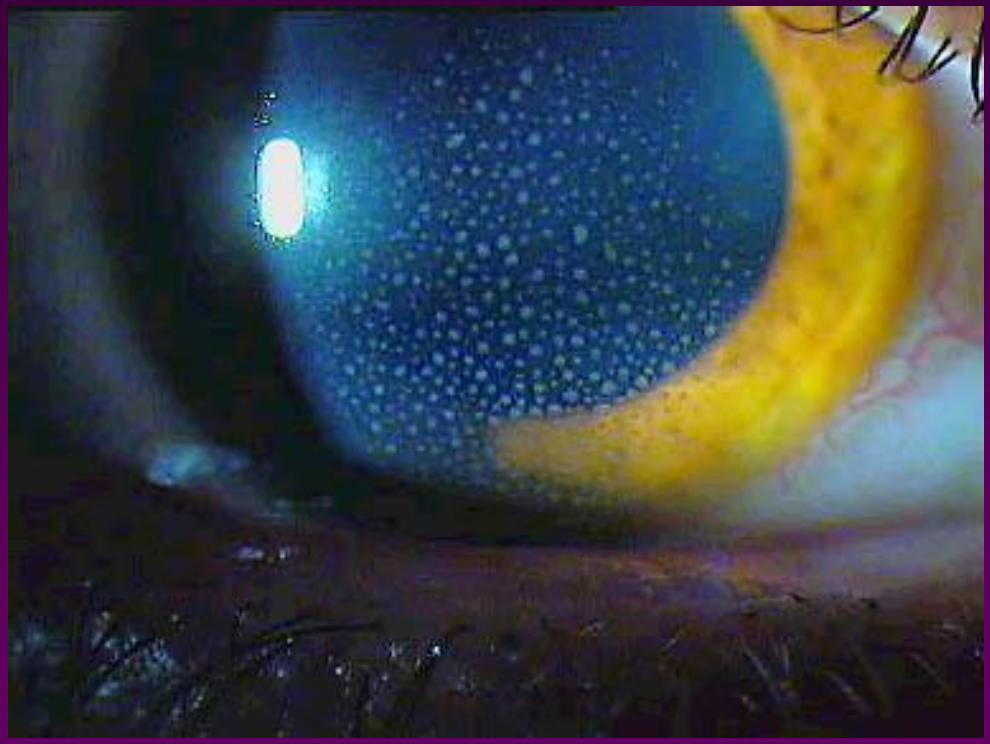
The Uvea - Angle

- The "angle" is a special region of the uvea where the iris meets the cornea
  - Regulates the outflow of Aqueous humor through the *Canal of Schlem*
  - Determines the Intraocular pressure (*Important in Glaucoma*)

The Uvea - Inflammation

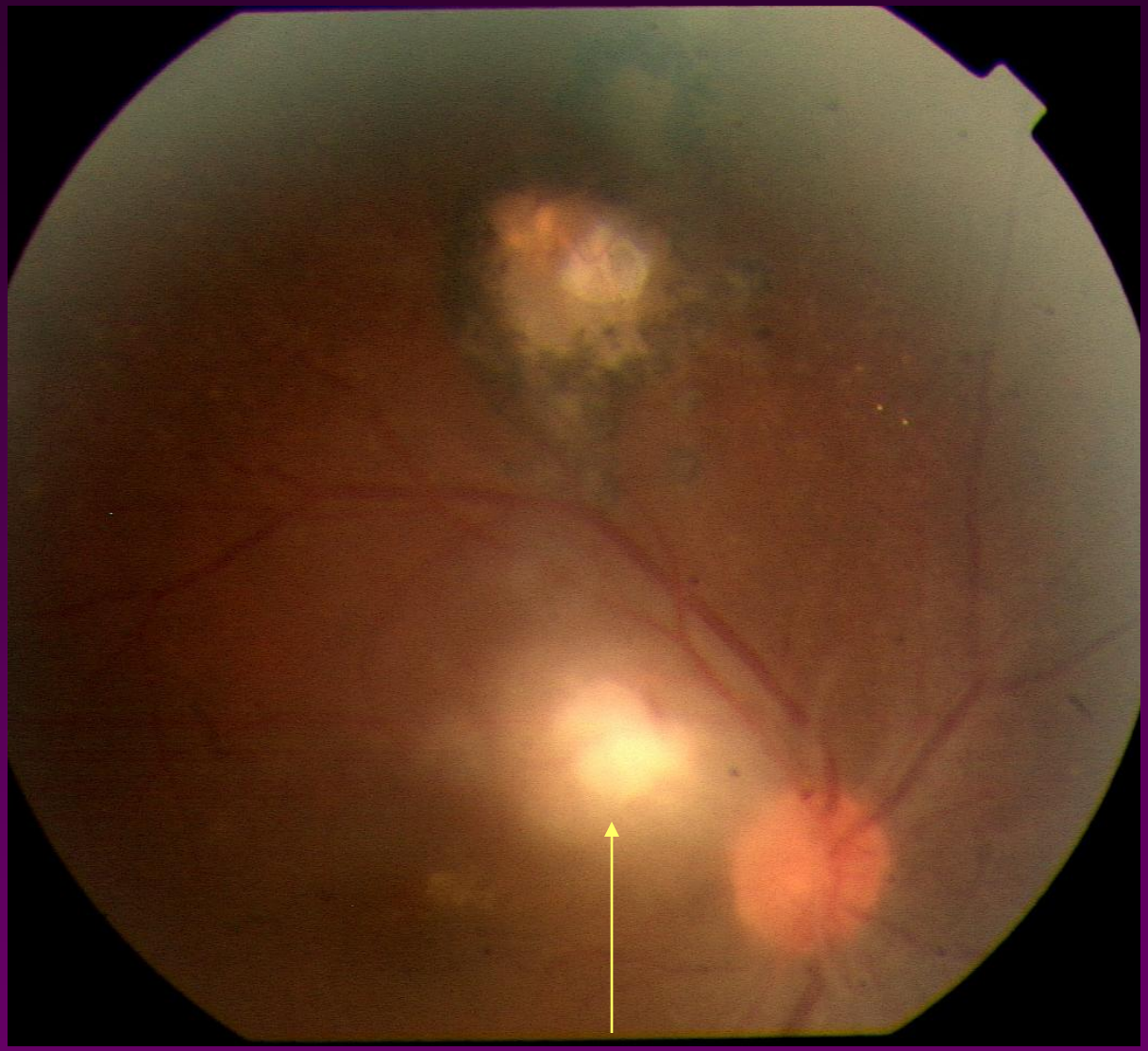
- "Uveitis" is inflamation of any combination of the iris, ciliary body, or choroid.
- Many etiologies (autoimmune, syphilis, sacrcoid, TB, HLA-B27, infectious, *idiopathic*, etc…)
- Many names (iritis, anterior uveitis, iridocylitis, choroiditis, etc…) depending on the location
- Sometimes associated with SERIOUS systemic inflamatory diseases (eg. arthritic diseases), inflamatory bowel disease, and vasculitis.

The Uvea – Anterior Uveitis



- Anterior uveitis/iritis
- WBCs floating in the aqueous

Uvea – Posterior Uveitis



- Active Toxoplasmosis Choroiditis, and old scar (above)

The Uvea - Tumors

- The Choroid is a highly perfused vascular “net” feeding the outer retina
- It is a *potential target site for metastasis* for carcinoma, such as breast and lung.

The Uvea - Tumors

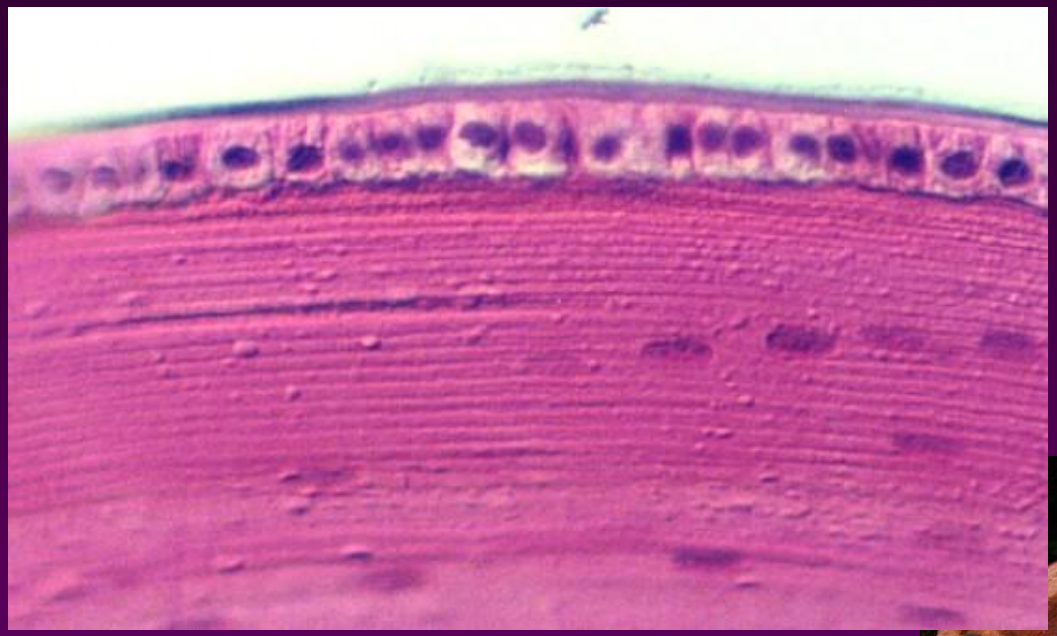
- The uvea (especially choroid) is also richly pigmented, and primary melanocytic tumors are common.
- Nevi and malignant melanomas are both relatively common, and can be difficult to distinguish, clinically.
- Tumors with “spindle-B” or epithelioid histologic patterns are malignant

THE LENS

The Lens

- A transparent, avascular structure consisting of concentric cellular fibers
- Highest protein content of the body (Crystallins), which account for a high refractive index
- Interaction of the ciliary body muscle, through the zonular fibers, cause dynamic shape changes.
- In concert with the cornea, helps to focus light on the retina.

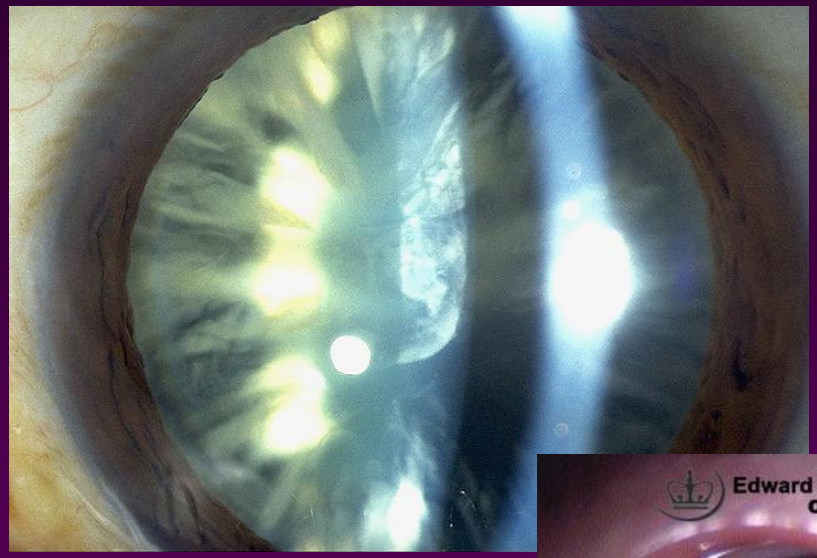
The Lens

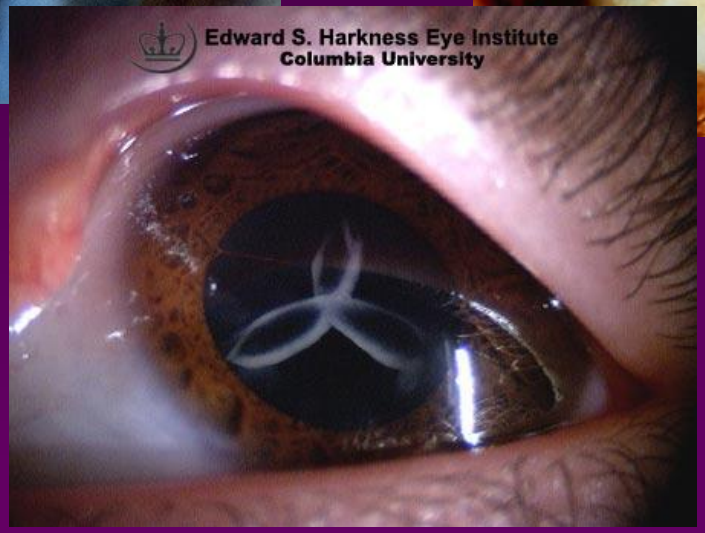


- Entire structure encapsulated
- Lens cells migrate and elongate into fibers

- The deepest fibers are the oldest ones
- The lens continues to fatten throughout life
- Central fibers become sclerotic and opaque with time

The Lens - Cataract

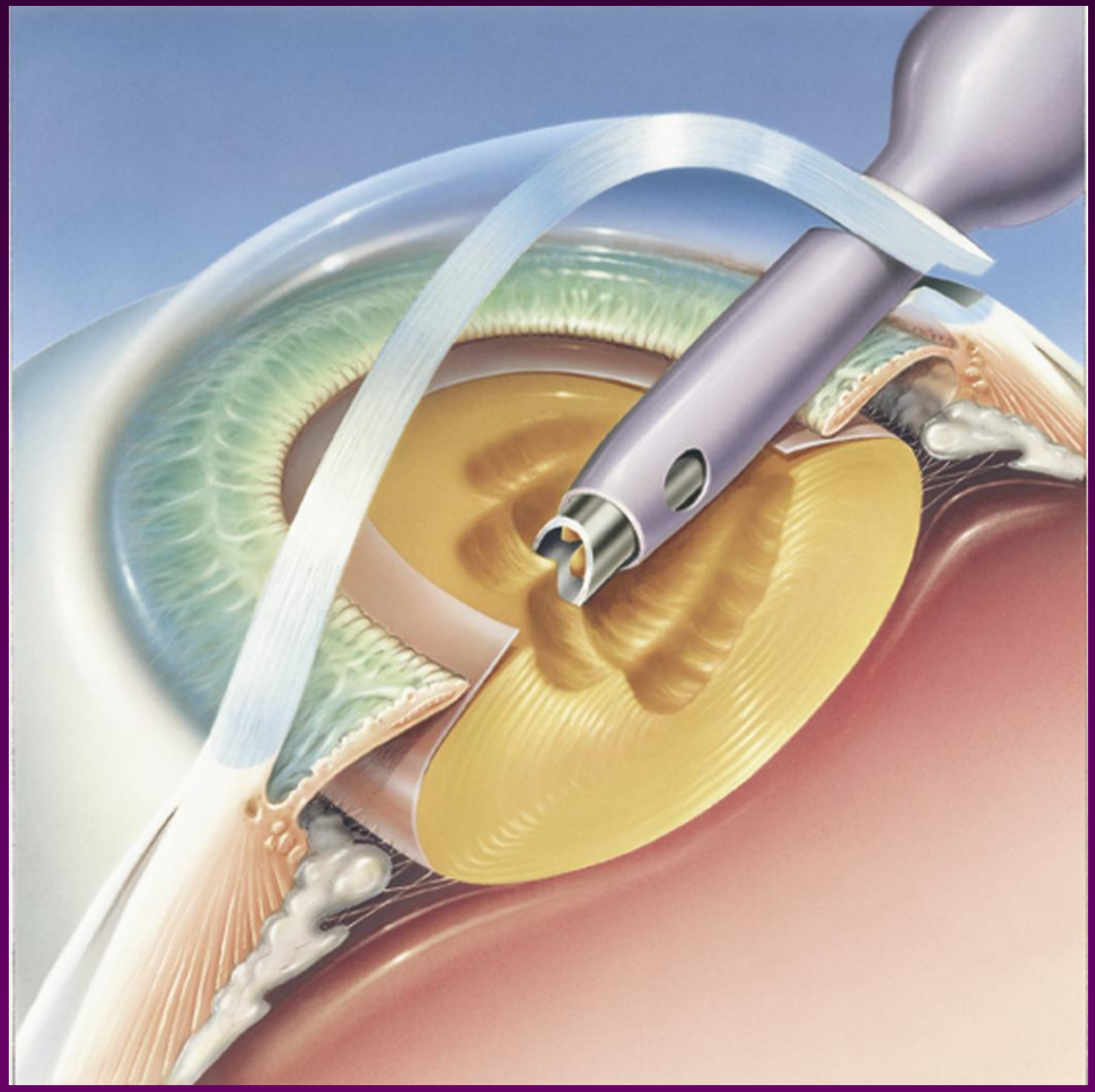




Opacities of the lens develop with time, or insult

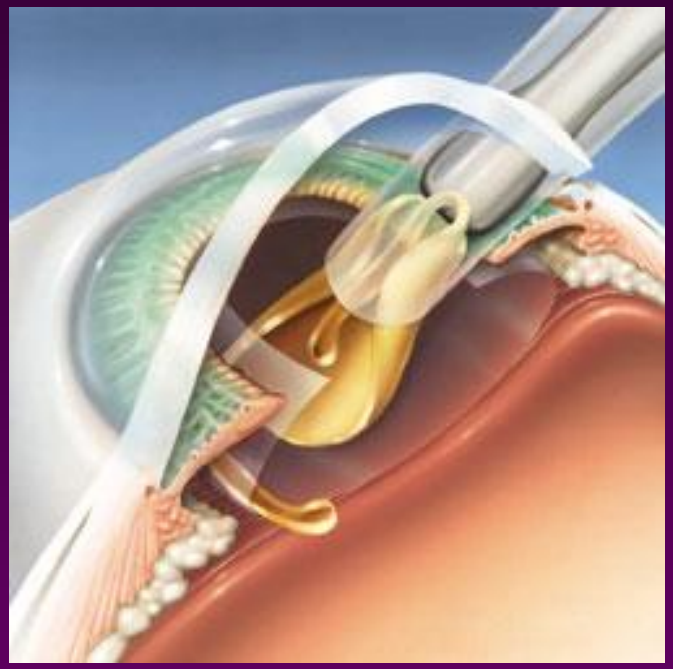
- UV light, steroids, and inflammation are pathogenic factors

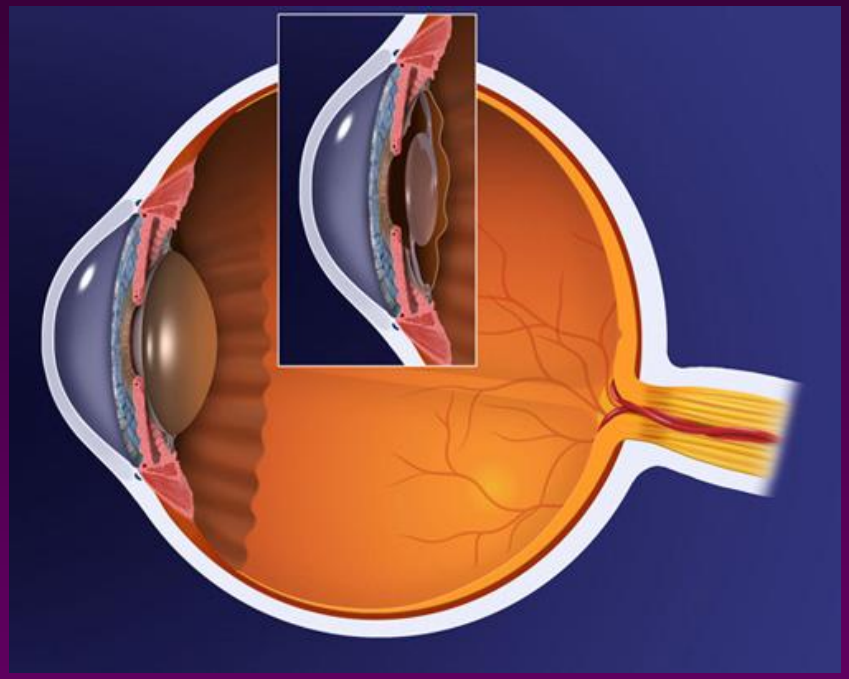
The Lens – Cataract surgery



- A opening into the lens capsule is made
- The cataract is emulsified with ultrasound energy, and aspirated out of the eye

The Lens – Cataract surgery





- The dense, cloudy crystalline lens is removed, and replaced with an optical implant.


The Retina

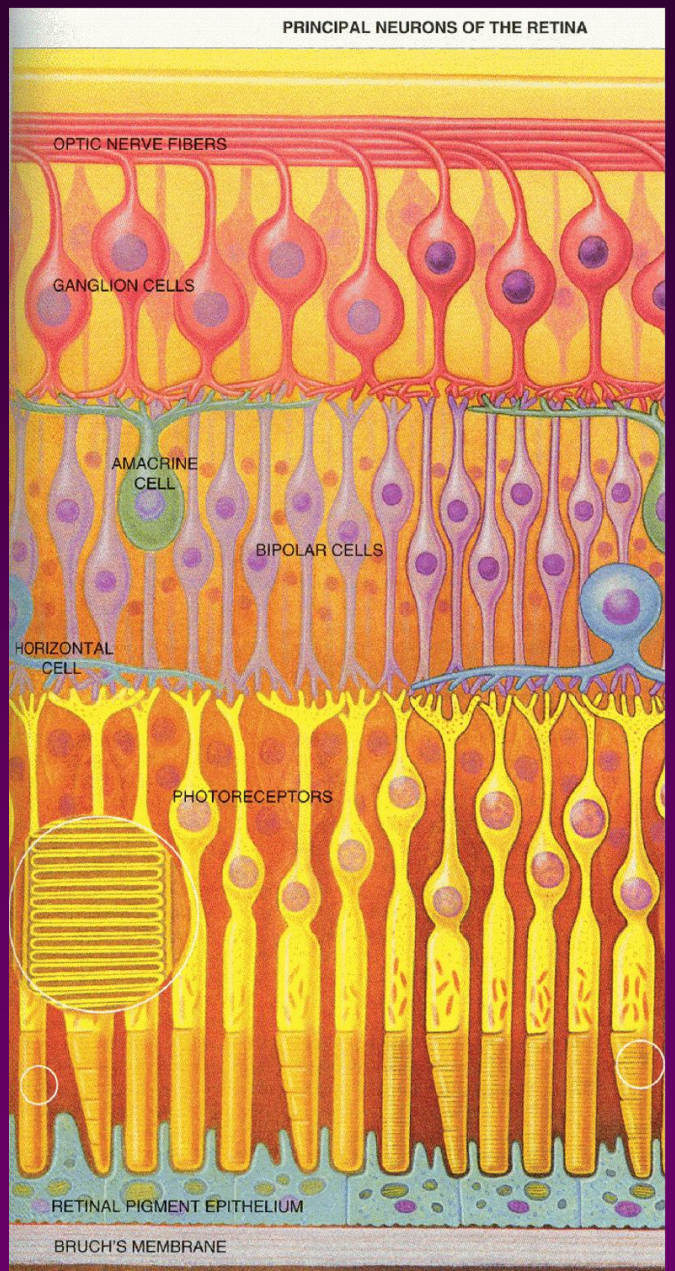
The Retina

- Anatomy
- Detachment
- Vascular disease/Ischemic retinopathy
  - Microvascular (*Diabetes*)
  - Vascular occlusion (*Vein occlusion/Arterial Occlusion*)
- Macular degeneration
- Tumors

The Retina - Anatomy

Cell types (overview)

- Photoreceptors (detect light signal)
- Bipolars transmit/modulate signal to ganglion cells
- Ganglion cells send signal by long axons through optic nerve and into visual pathways of the brain
- Other cell types…



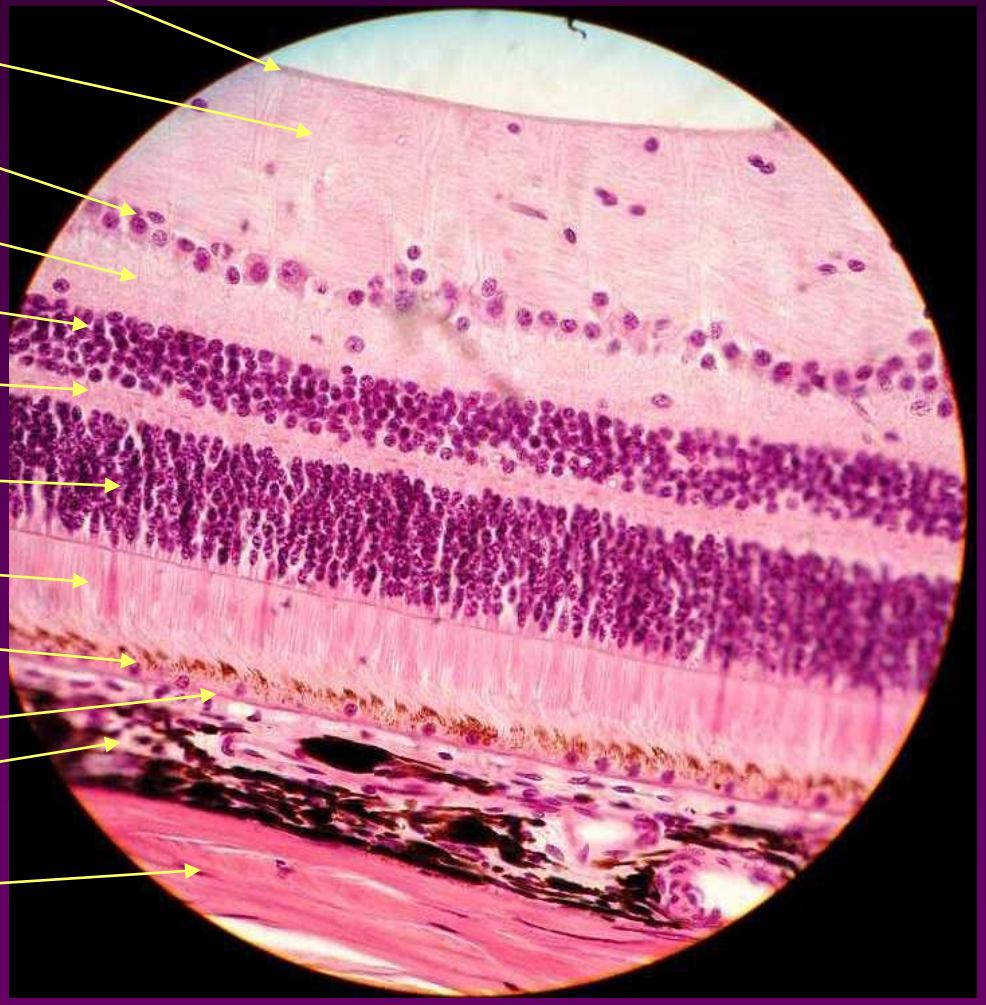
The Retina - Anatomy

Layers (inside to out):

1. Inner limiting membrane
2. Nerve Fiber Layer
3. Ganglion Cell Layer
4. Inner plexiform layer
5. Inner nuclear layer
6. Outer plexiform layer
7. Outer nuclear layer
8. Photoreceptor segments
9. Retinal Pigment Epithelium
10. Bruch's Membrane

(Choroid)

(Sclera)

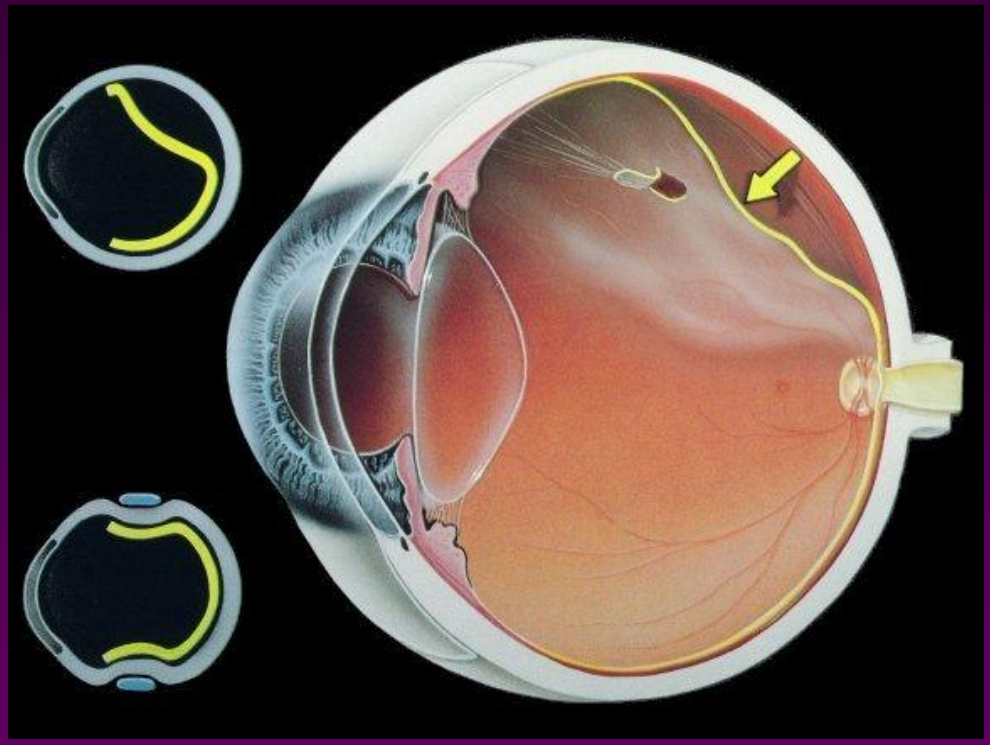


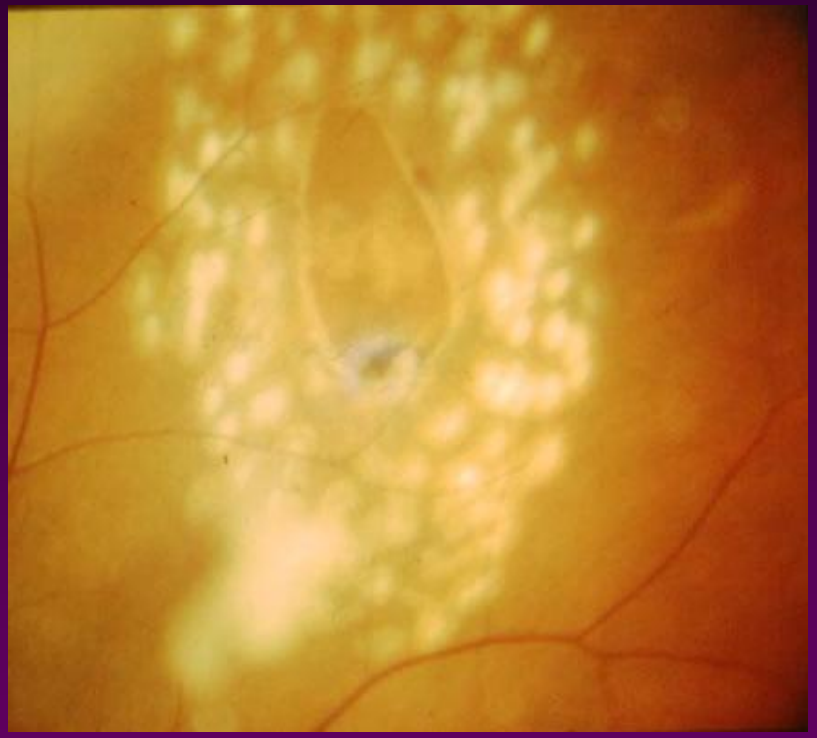
Retina – Anatomy

Pathologic conditions of layers

1) Retinal detachment: Separation between RPE and photoreceptor segments
2) Macular degeneration: Bruch's membrane damaged by deposition of *drusen*, allowing leaky choroidal vessels to grow into retina (exudative type).

The Retina - Detachment

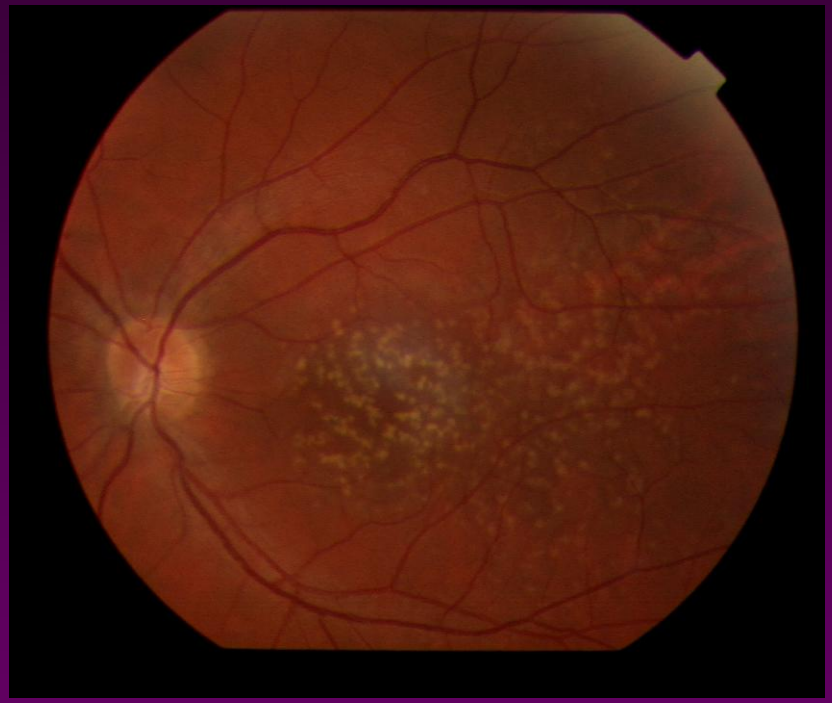




Retinal tears are the most frequent causes of detachment (rhegmatogenous RD)

Tears can be “spot welded” with laser to prevent detachment

The Retina – Macular degeneration



- Clinical appearance of *drusen* in Macular degeneration

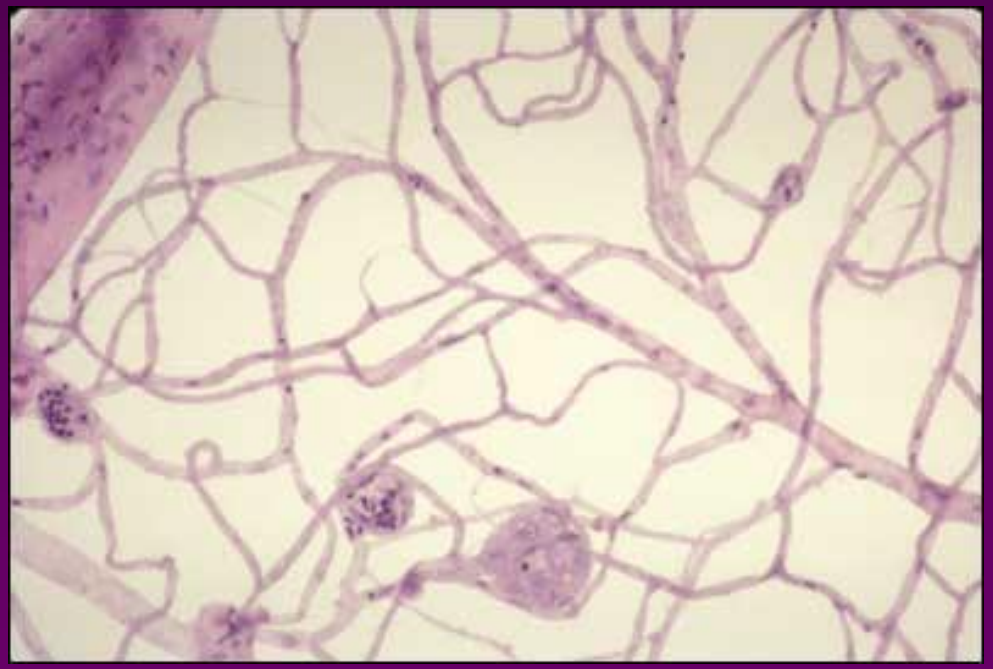
The Retina – Vasculopathy

- Microvascular (small vessel disease)
  - Diabetes
  - Sickle Cell
  - Radiation
- Macrovascular (large vessel occlusions)
  - Central retinal vein occlusion (CRVO)
  - Branch retinal vein occlusion (BRVO)
  - Central retinal artery occlusion (CRAO)
  - Branch retinal artery occlusion (BRAO)

The Retina – Diabetic Retinopathy

Microvascular dysfunction leads to tissue ischemia

- Thickened and Leaky Capillary basement membranes
- Loss of pericytes
- Microaneurysms
- Nonperfusion

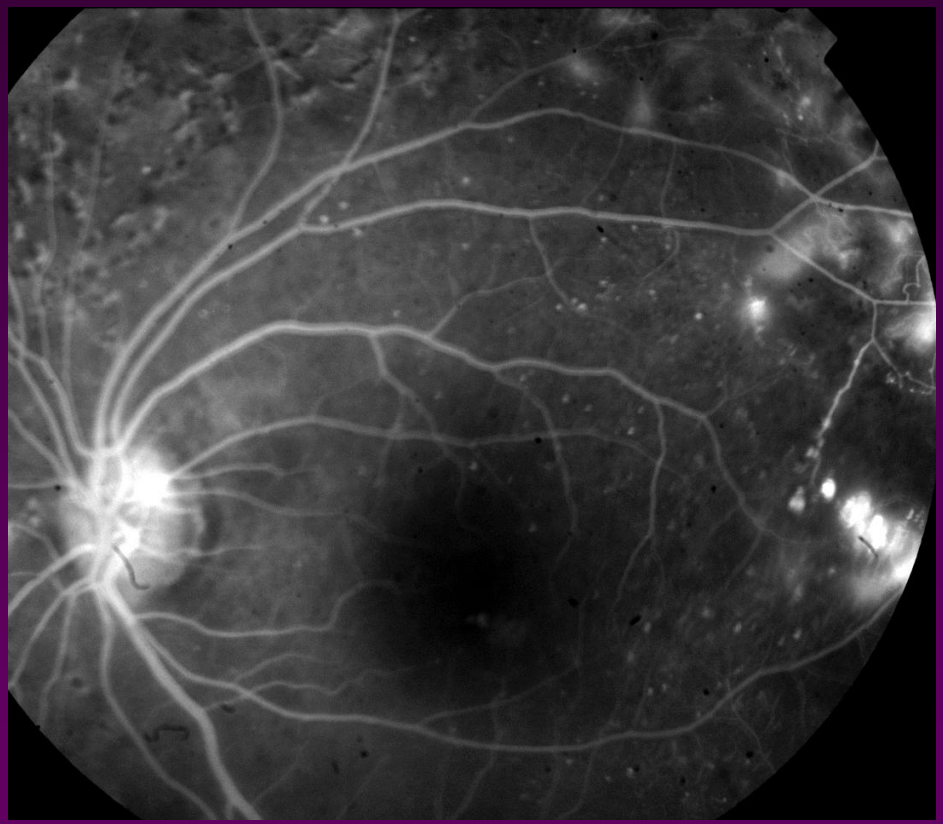


The Retina – Diabetic Retinopathy

Ischemia leads to vascular endothelial growth factor (VEGF) production from injured tissues

- Promotes Neovascularization (abnormal blood vessel growth) of the retina, optic nerve, or iris.
- Abnormal vessels can cause edema or tractional retinal detachments
- VEGF implicated in other ischemic eye diseases, like Retinopathy of Prematurity

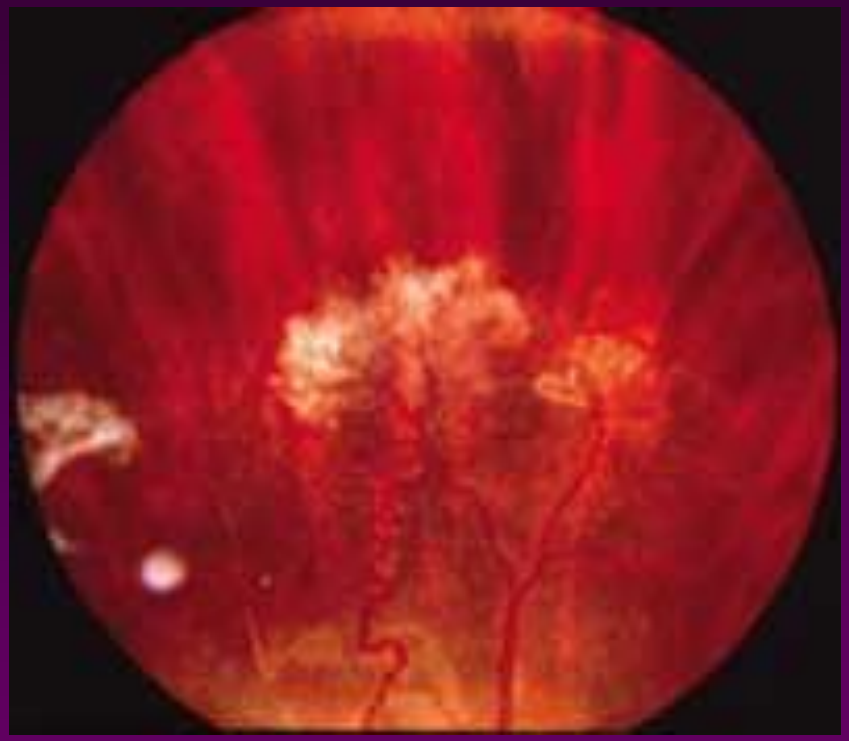
The Retina – Diabetic Retinopathy



- Microaneurysms!

- Capillary dropout and Nonperfusion!
- Neovascularization!

The Retina – Diabetic Retinopathy

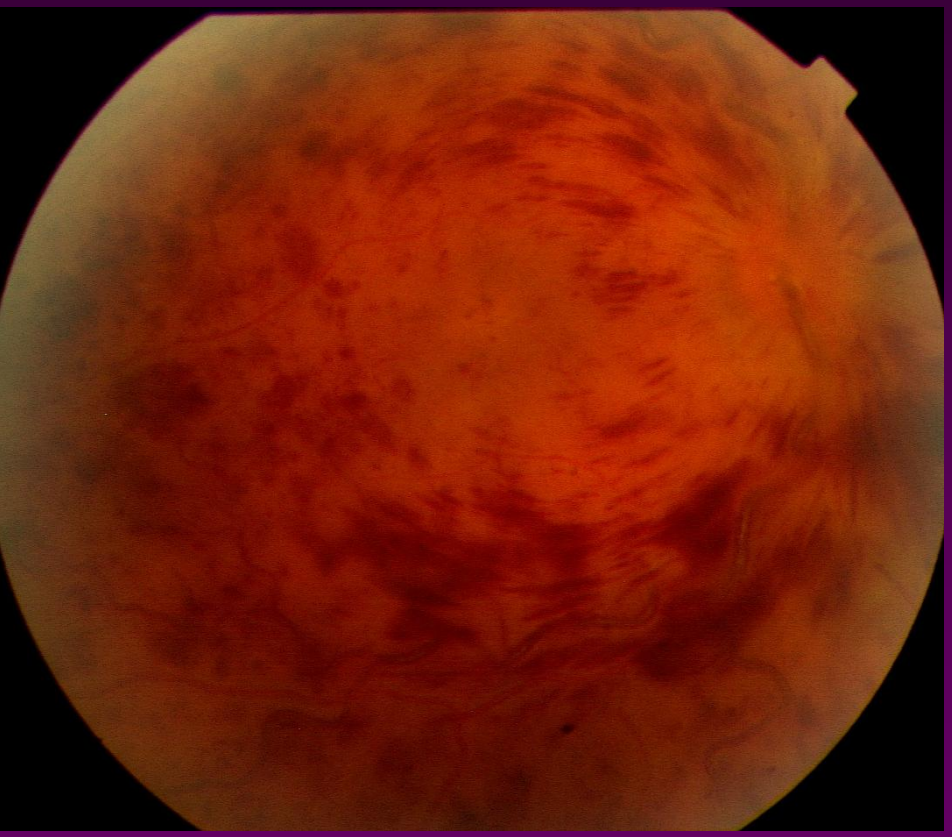


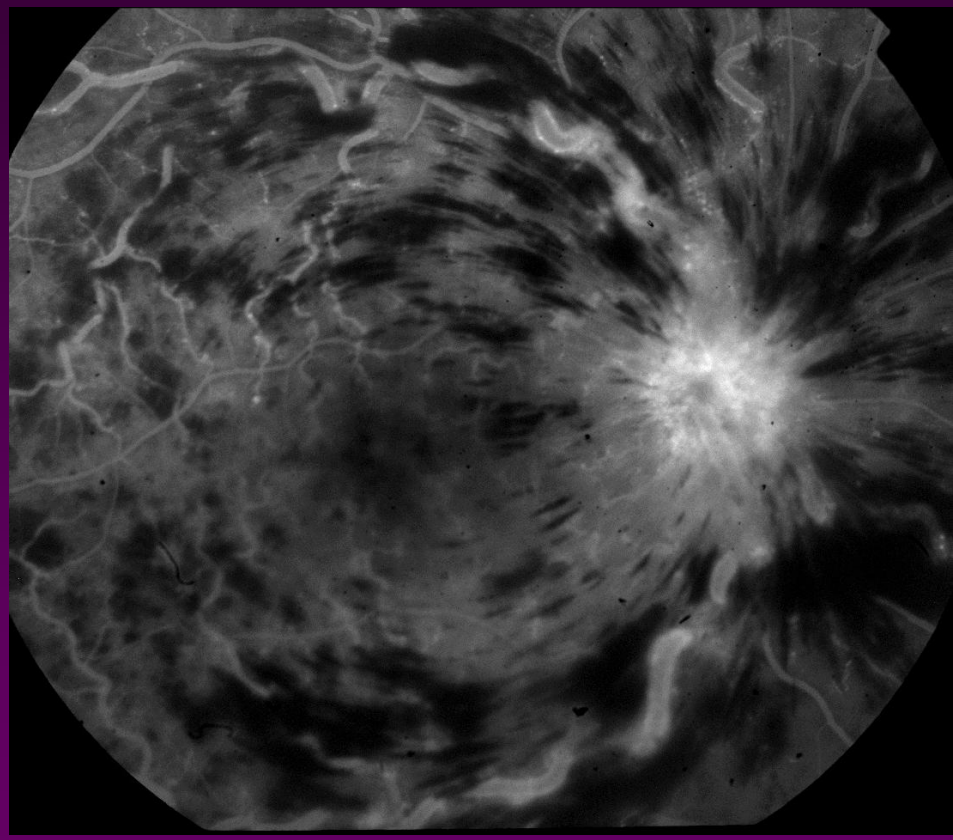
- Retinal neovascularization

The Retina – MACROvascular Disease

- CRVO/BRVO – variety of anatomical prothrombotic predispositions
- CRAO/BRAO – watch out for carotid/cardiac embolic disease, or vasculitis.

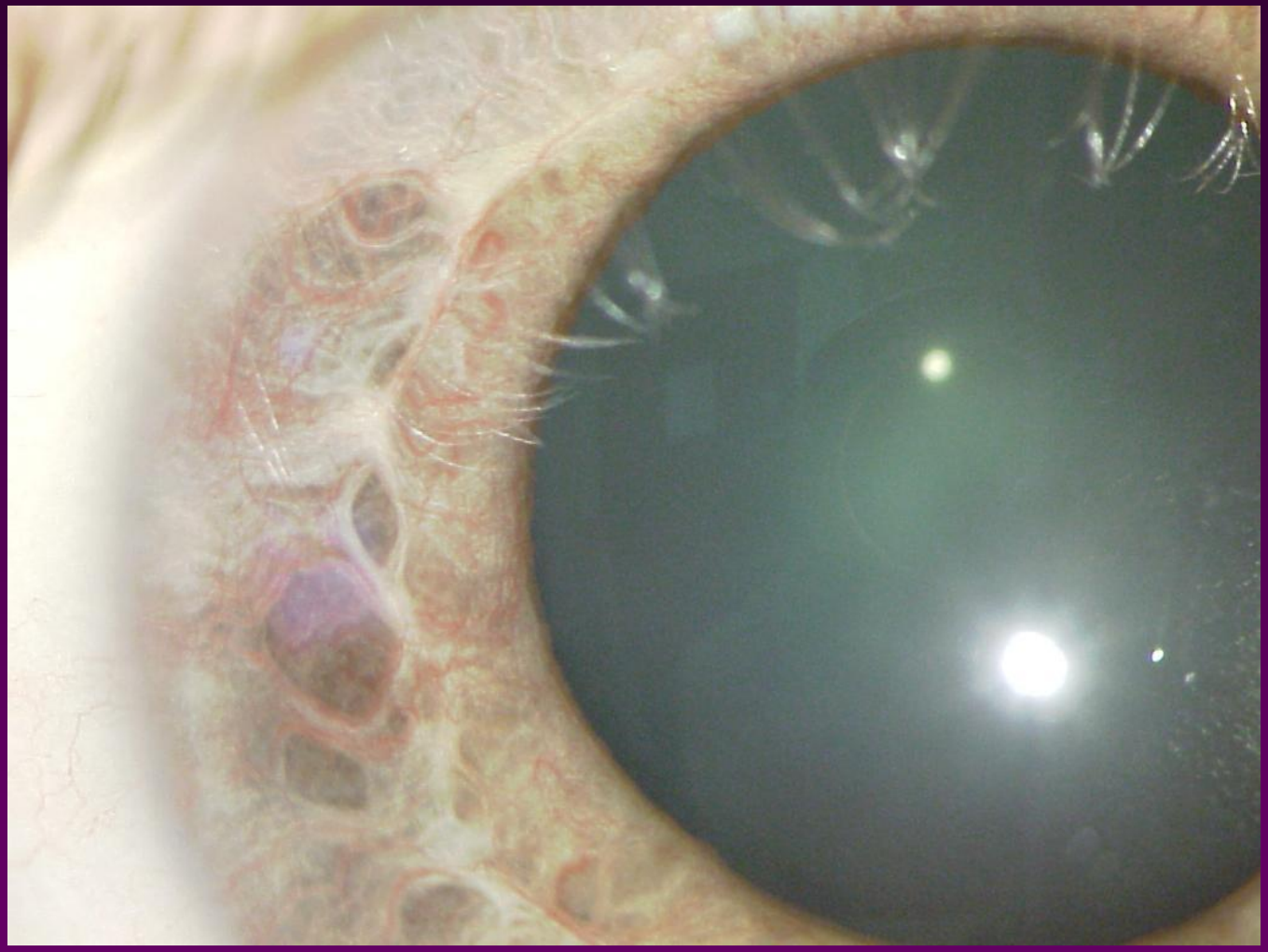
The Retina – Macrovascular disease





CRVO – Hemorrhage, congestion, ischemia

The Retina – Macrovascular disease

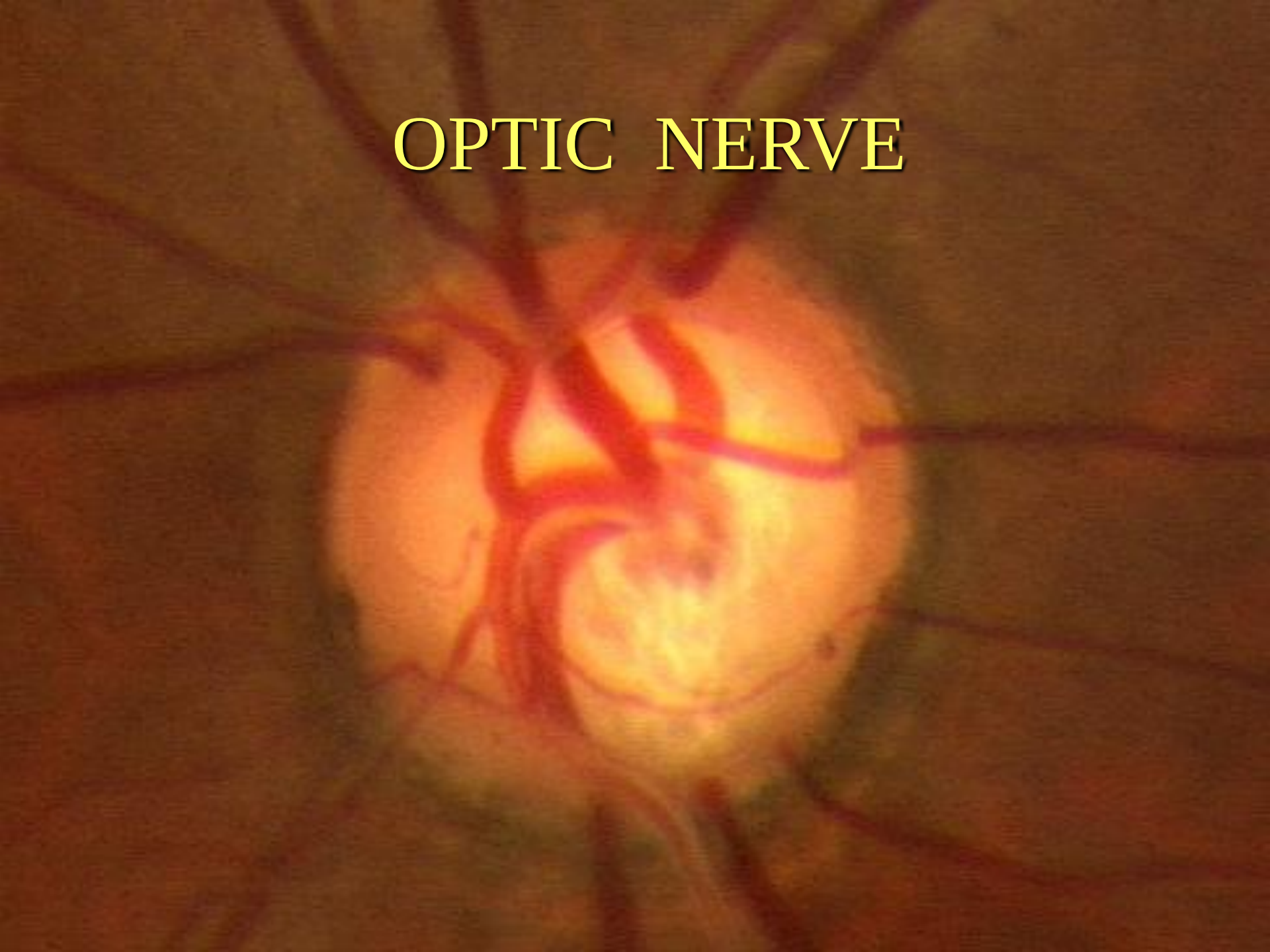


Ischemic CRVO led to VEGF production, which caused neovascularization of iris.

The Retina - Tumors

Retinoblastoma

- Classic pediatric tumor of retina
- Hereditary or Sporadic
- Requires two gene mutations (Knudsen's "two-hit" hypothesis)
- Classic histologic features of Flexner-Wintersteiner Rosettes, and fleurettes


OPTIC NERVE

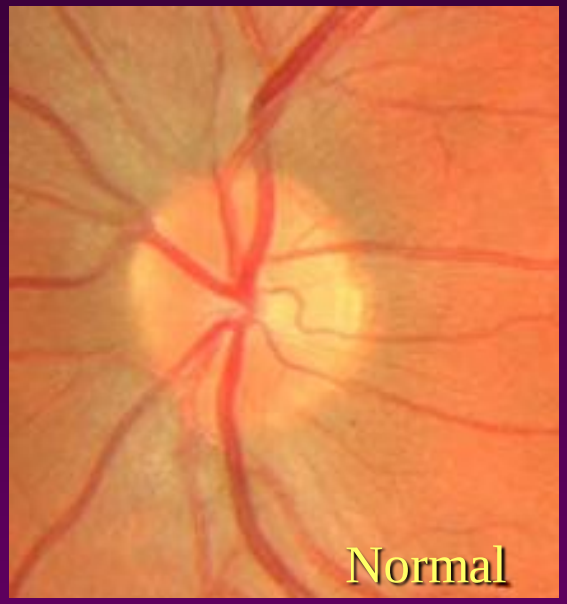
Optic nerve – Pathologic Conditions of…

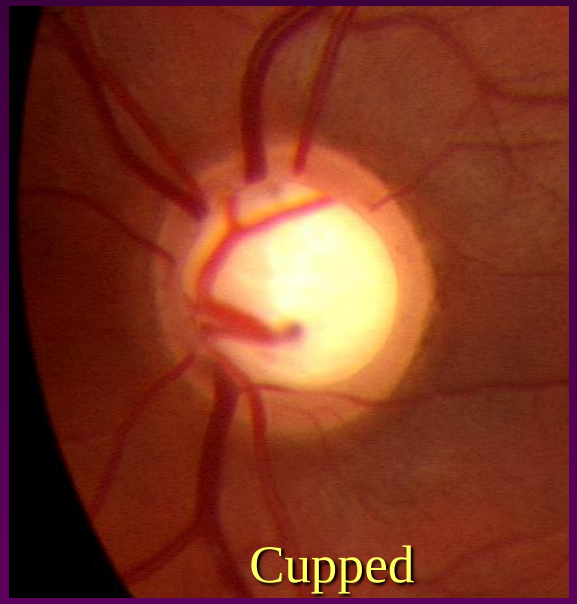
- Ischemic Neuropathy – due to arteritic (Giant Cell Arteritis) or non-arteritic causes.
- Optic Neuritis –Many causes, but demyelinating *(Multiple Sclerosis)* causes are most important
- Papilledema – swelling due to increased intracranial pressure

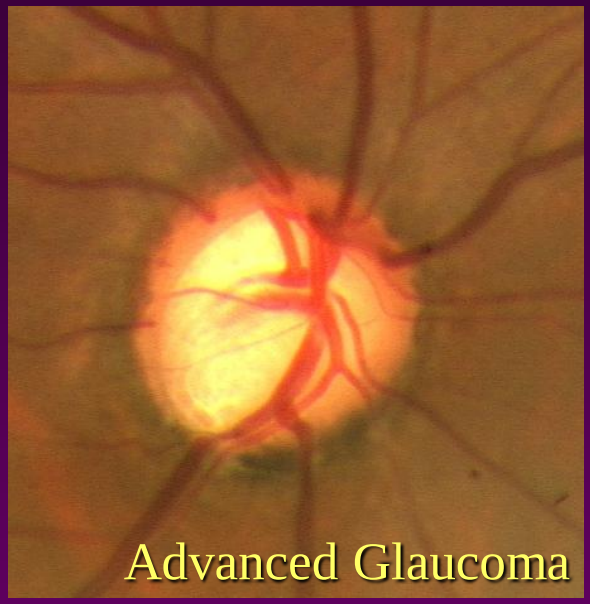
Optic Nerve – Pathologic conditions of…

- Glaucoma – progressive injury of optic nerve, frequently associated with elevated intraocular pressure
  - Characteristic “cupping” of nerve
  - Loss of retinal nerve fiber layer
  - Advancing peripheral visual field loss

Optic Nerve - Glaucoma







- Loss of rim correlates to loss of axons from ganglion cells in retina (Nerve fiber layer).
- Regions of lost ganglion cells/axons cause visual field loss.


Final discussion points?

Summary of *key* topics:

Thyroid orbitopathy

“Ditzels” on the front of the eye

Corneal layers

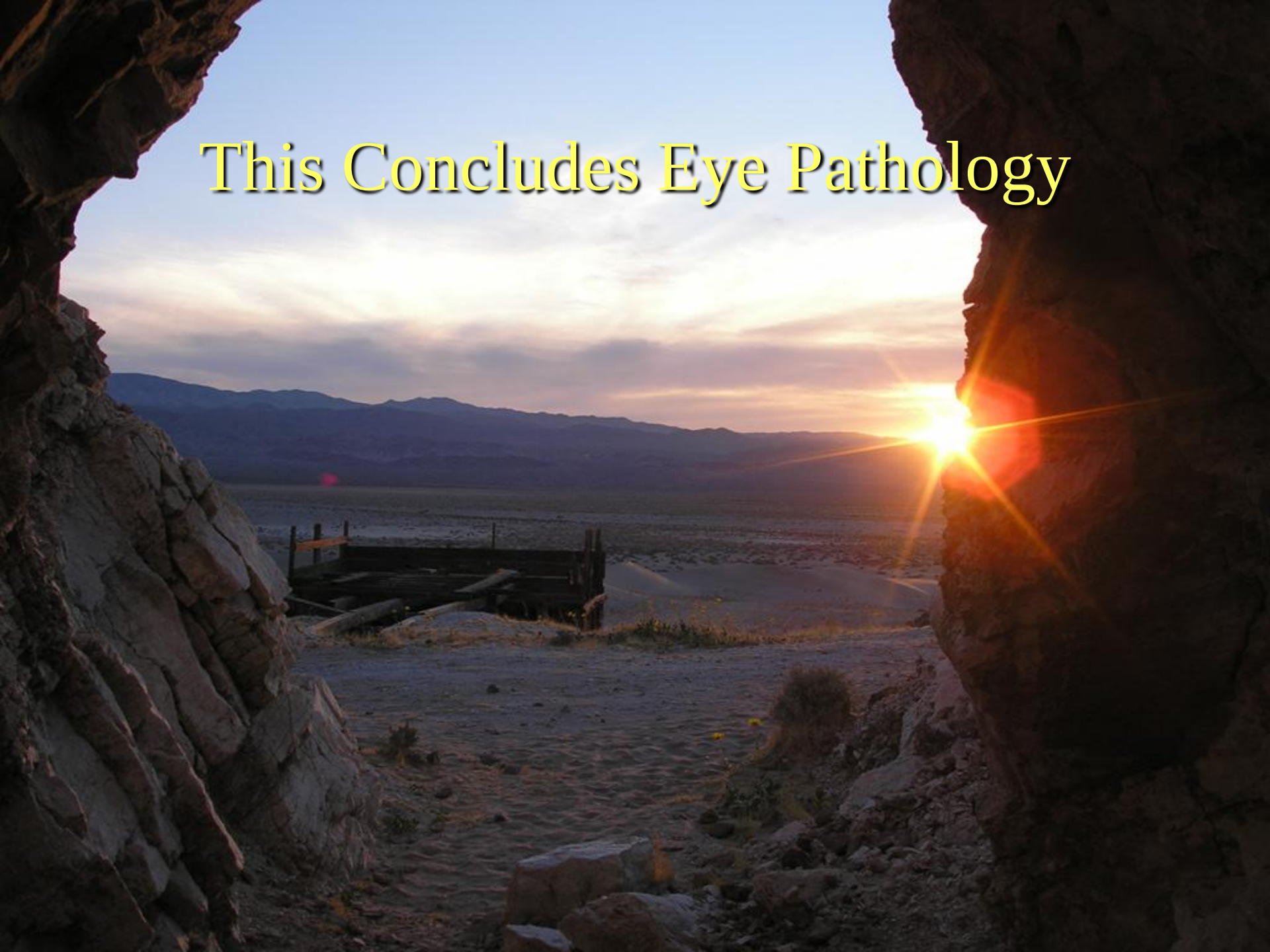
Uveitis as a manifestation of systemic disease

Lens and cataract

Diabetic Retinopathy

Retinal Detachment

Glaucoma


This Concludes Eye Pathology