STRUCTURE AND EMBRYOLOGY OF VITREOUS

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VITREOUS HUMOR

- Transparent connective tissue
- Largest structure in the human eye
- Occupies more than ¾ of the total ocular volume
- Attached to basal lamina of lens, optic nerve, and retina
- Separated from the retina by the internal limiting membrane (ILM)
  - ILM is composed of Type IV collagen but is NOT a true basement membrane

Fincham, Gregory S., et al. "Posterior vitreous detachment and the posterior hyaloid membrane." *Ophthalmology* 125.2 (2018): 227-236.

DISCLOSURES

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VITREOUS FUNCTIONS

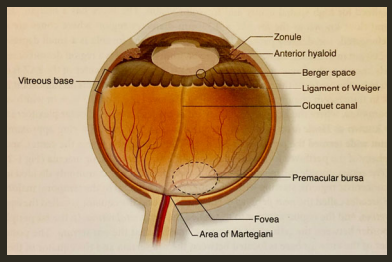
- Physically support the retina and fill the posterior segment
- Provide a diffusion barrier between the anterior and posterior segment
- Metabolic buffer against free radicals
- Be optically clear

(Spoiler: the eye continues to function well even when the vitreous is removed)

Levin, Leonard A., et al. *Adler's Physiology of the Eye E-Book*. Elsevier Health Sciences, 2011.

BASIC ANATOMY - VITREOUS

Illustration by Mark M. Miller. Retina and Vitreous: 2017-2018. Vol. 12, American Academy of Ophthalmology, 2017, p7.



NORMAL VITREOUS LOOKS... CLEAR

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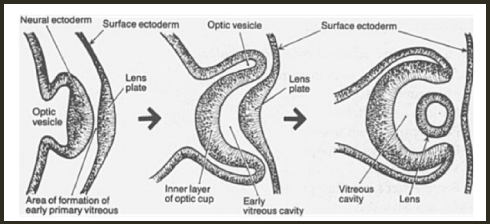
EMBRYOLOGY – PRIMARY VITREOUS

Primary vitreous forms between the lens vesicle and the fetal retina through migration of ectoderm, neuroectoderm, and mesoderm cells into the vitreous cavity.



Schepens, Charles L., and Adolphe Neetens, eds. *The vitreous and vitreoretinal interface*. Springer Science & Business Media, 2012.

HISTOLOGY OF PRIMARY VITREOUS

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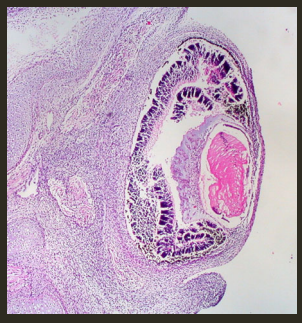
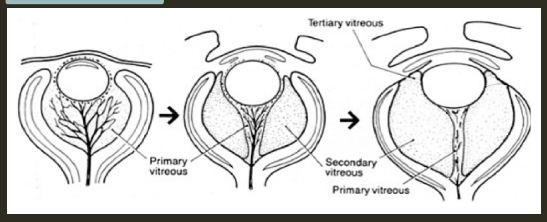


PRIMARY | SECONDARY | TERTIARY



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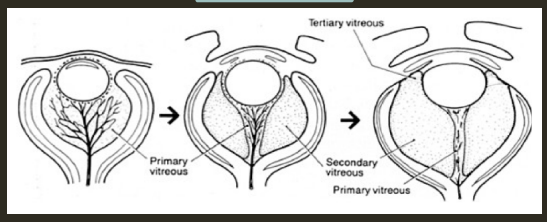
PRIMARY | SECONDARY | TERTIARY



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PRIMARY VITREOUS

- Vitreous formation begins at 3rd-4th week of gestation
- Ectoderm from the lens vesicle along with neuroectoderm cells from the optic vesicle migrate into vitreous cavity
- Glycosaminoglycans are major component of primary vitreous
- Mesoderm from the edge of the optic vesicle migrates to form beginnings of tunica vasculosa lentis anteriorly
- Hyaline lens capsule forms at 8-13mm stage
- Hyaloid vascular system from the primitive ophthalmic artery enters the vitreous cavity from the optic papilla and grows to connect with the tunica vasculosa lentis
- Vitreous is fully vascularized by the 30mm stage

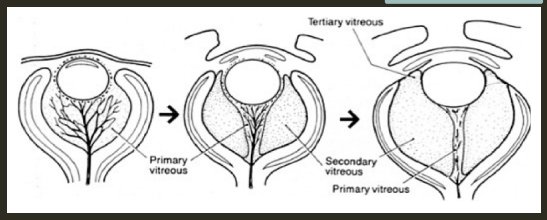
Schepens, Charles L., and Adolphe Neetens, eds. *The vitreous and vitreoretinal interface*. Springer Science & Business Media, 2012.

SECONDARY VITREOUS

- Will go on to become the largest component of adult vitreous
- Forms during the 13mm – 70mm embryonic stage (around the 6-9th week of gestation)
- First, an acellular secondary vitreous derived from neuroectoderm fills the space between the border of the inner retina and the posterior surface of the primary vitreous
  - This has a fibrillar structure that runs parallel to the surface of the retina
- Second, neuroectodermal cells differentiate into hyalocytes (90%) and fibroblasts or glial cells (10%) migrate into the acellular secondary vitreous
  - These cells synthesize hyalouronic acid (a sulfated glycosaminoglycan and the major component of secondary vitreous), collagen (types II and IX), glycosaminoglycans, soluble proteins, and glycoproteins
- Third, as an increasing amount of secondary vitreous forms, the (completely vascularized) primary vitreous begins to regress

1. Schepens, Charles L., and Adolphe Neetens, eds. *The vitreous and vitreoretinal interface*. Springer Science & Business Media, 2012.
2. Levin, Leonard A., et al. *Adler's Physiology of the Eye E-Book*. Elsevier Health Sciences, 2011.

PRIMARY SECONDARY **TERTIARY**



Schepens, Charles L., and Adolphe Neetens, eds. *The vitreous and vitreoretinal interface*. Springer Science & Business Media, 2012.

CONGENITAL AND DEVELOPMENTAL VITREOUS ABNORMALITIES

Either primary vitreous doesn't regress, or secondary vitreous doesn't grow

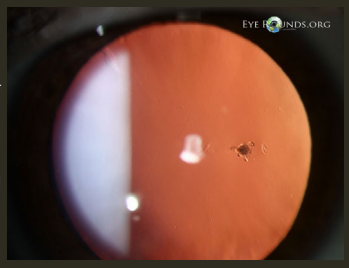
TERTIARY VITREOUS

- Zonules develop around lens / extending to attach to the ciliary body, pars plicata, and into the pars plana
  - Zonules = the tertiary vitreous
- Primary vitreous continues to regress, and continues regressing even up until the end of fetal development
  - Premature infants often have hyaloid vasculature intact
  - Cloquet's canal forms where the primary vitreous used to be
- Hyalocytes previously part of the primary vitreous migrate into the tertiary vitreous
- The volume of the vitreous continues to increase

1. Schepens, Charles L., and Adolphe Neetens, eds. *The vitreous and vitreoretinal interface*. Springer Science & Business Media, 2012.
2. Levin, Leonard A., et al. *Adler's Physiology of the Eye E-Book*. Elsevier Health Sciences, 2011.

MITTENDORF DOT

- Small remnant fibrovascular plaque at posterior lens capsule
- Inferonasal
- Can have hyaloid remnant attached
- Site of previous attachment of hyaloid artery

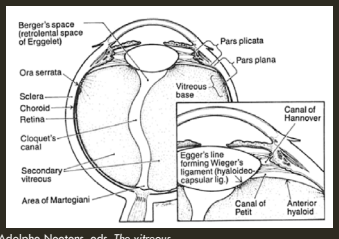


Schepens, Charles L., and Adolphe Neetens, eds. *The vitreous and vitreoretinal interface*. Springer Science & Business Media, 2012.

Weed, M; Crister, D. "Mittendorf dot." *EyeRounds*, University of Iowa, 1 May 2013, https://webeye.ophth.uiowa.edu/eyeforum/atlas/pages/mittendorf-dots.htm.

VITREOUS ANATOMY IN ADULT EYE

- Vitreous continues to grow into adulthood
  - Length of vitreous in a newborn eye = 10.5mm, growing to 16.5mm during adulthood
- Hyaluronic acid levels increase
- Vitreous begins as entirely gel; in adulthood up to 20% of the vitreous is liquefied
- Cloquet's canal begins as a straight line but then becomes more undulating with time (gravity pulls central part downward)



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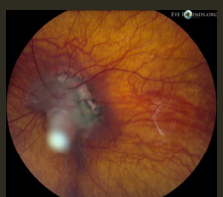
PERSISTENT HYALOID ARTERY

A residual vessel attached to the posterior lens capsule, usually inferonasal

Occurs in 95% of premature infants, almost always regresses spontaneously

Can be associated with spontaneous prepapillary hemorrhage

Rare to have active blood flow within the artery itself



Schepens, Charles L., and Adolphe Neetens, eds. *The vitreous and vitreoretinal interface*. Springer Science & Business Media, 2012.

Vislisel J, Crister, D. "Persistent fetal vasculature (PFV)." *EyeRounds*, University of Iowa, 26 May 2014, https://webeye.ophth.uiowa.edu/eyeforum/atlas/pages/PFV/index.htm.

PERSISTENT VASCULAR LOOP

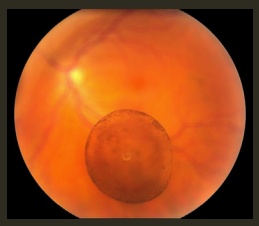
- Likely derived at least in part from remnants of hyaloid artery
- Can be associated with spontaneous vitreous hemorrhage

Schepens, Charles L., and Adolphe Neetens, eds. *The vitreous and vitreoretinal interface.* Springer Science & Business Media, 2012.

"Prepapillary Vascular Loops." *Columbia University Department of Ophthalmology*, https://www.columbiaeye.org/education/digital-reference-of-ophthalmology/vitreous-retina/hereditary-congenital/prepapillary-vascular-loops. Accessed January 9, 2020.

VITREOUS CYST

- Rare
- Develop from remnants of hyaloid system, Bergmeister's papilla, or from ciliary epithelium
- Cysts derived from hyaloid are usually single and mobile
- Cysts derived from Bergmeister's papilla are small, usually multiple, and immobile
- Cysts derived from ciliary epithelium are mobile
- Often translucent but can be pigmented



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This image was originally published in the Retina Image Bank. Calhoun J. Vitreous Cyst. Retina Image Bank. 2013; 7737. © the American Society of Retina Specialists. https://imagebank.asrs.org/file/7737/vitreous-cyst

BERGMEISTER'S PAPILLA

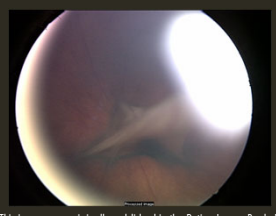
- Remnant of glial sheath that surrounds posterior 1/3 of hyaloid artery
- May represent failure of glial tissue to atrophy, and/or overgrowth of this glial tissue

Schepens, Charles L., and Adolphe Neetens, eds. *The vitreous and vitreoretinal interface.* Springer Science & Business Media, 2012.

"This image was originally published in the Retina Image Bank. Kaplan J, Piri N. Bergmeister's Papillae. Retina Image Bank. 2013; 5360. © the American Society of Retina Specialists."https://imagebank.asrs.org/file/5360/bergmeister-papillae

PERSISTENT FETAL VASCULATURE (PFV) AKA PERSISTENT HYPERPLASTIC PRIMARY VITREOUS (PHPV)

- Usually unilateral
- Can be densely amblyogenic
- Persistence of retrolental mass of primary vitreous that did not regress
- Stretched ciliary processes
- Peripheral retinal can be dragged toward retrolental mass causing tractional retinal detachment



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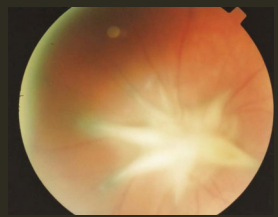
"This image was originally published in the Retina Image Bank. Berrocal A. Persistent Fetal Vasculature. Retina Image Bank. 2012; 1205. © the American Society of Retina Specialists. https://imagebank.asrs.org/file/1205/persistent-fetal-vasculature-pfv

PREPAPILLARY VEIL

- Bergmeister's papillae with mesodermal tissue hyperplasia, creating a partial or complete veil or mass of tissue covering the optic disc
- Vitreous fibrils attach to this glial epipapillary membrane



Schepens, Charles L., and Adolphe Neetens, eds. *The vitreous and vitreoretinal interface.* Springer Science & Business Media, 2012.

Morales, Maira Saad de Avila, et al. "Ophthalmic Doppler in persistent hyperplastic primary vitreous atypical presentation: case report." *Arquivos brasileiros de oftalmologia* 78.5 (2015): 320-322.

PFV

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COLOBOMA

Due to incomplete closure of the embryonic fissure (inferonasally), resulting in a sectoral area where secondary vitreous fails to evolve

Can involve choroid, optic nerve, retina, ciliary body, zonules, and iris

Formed vitreous gel is absent over the coloboma

Schepens, Charles L., and Adolphe Neetens, eds. *The vitreous and vitreoretinal interface*. Springer Science & Business Media, 2012.

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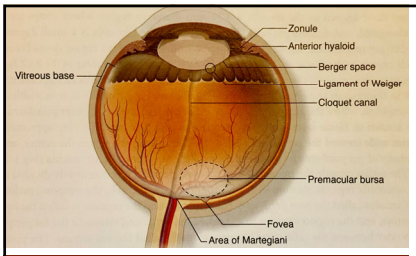
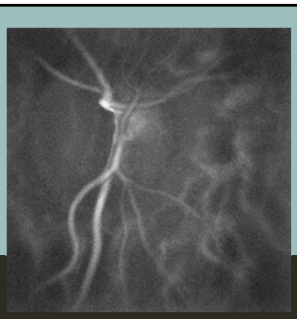


Illustration by Mark M. Miller. Retina and Vitreous: 2017-2018. Vol. 12, American Academy of Ophthalmology, 2017, p7.

QUESTIONS?

THANK YOU



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COLLAGEN STRUCTURE OF VITREOUS AND ASSOCIATED PATHOLOGIES

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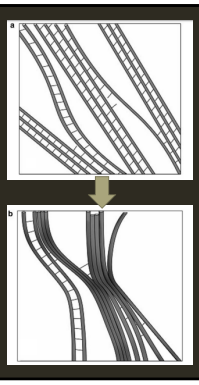
FIBRIL STRUCTURE OF VITREOUS COLLAGEN AND SYNERESIS

- Large type II collagen fibrils are organized into bundles
- These bundles are both interconnected and spaced apart by type IX collagen fibrils
- With aging, loss of type IX collagen from the fibril surfaces leads to collagen fibril aggregation and vitreous ~syneresis~



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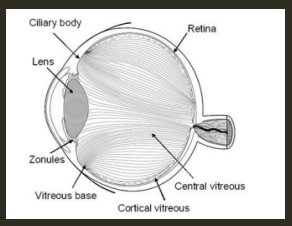
VITREOUS POLYMER ULTRASTRUCTURE

Regions of vitreous:

- Central vitreous
- Cortical vitreous
- Vitreous base

Collagen fibrillar concentration and orientation varies between these regions

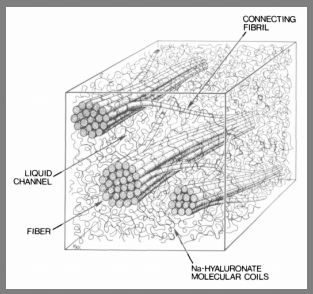


Le Goff, M. M., and P. N. Bishop. "Adult vitreous structure and postnatal changes." *Eye* 22.10 (2008): 1214-1222.

PROTEIN STRUCTURE OF COLLAGEN

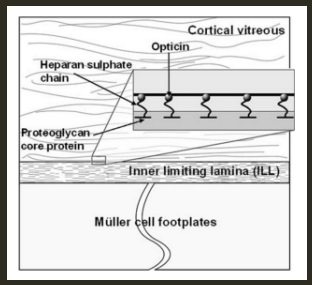
- Collagen fibrils aggregate into bundles forming visible fibers
- Hyaluronic acid, other proteoglycans, and water molecules fill the interfibrillar spaces

Sebag, J., and E. A. Balazs. "Morphology and ultrastructure of human vitreous fibers." *Investigative ophthalmology & visual science* 30.8 (1989): 1867-1871.



VITREORETINAL INTERFACE — INTERNAL LIMITING MEMBRANE

- Collagen fibers attach to internal limiting membrane (ILM) with proteoglycans including laminin and fibronectin
- Weakening of this adhesion contributes to posterior vitreous detachment
- ILM is also reduplicated during posterior vitreous detachment



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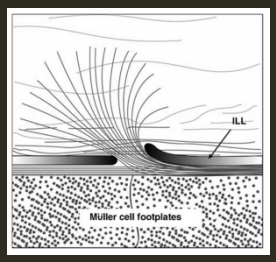
VITREOUS BASE

Vitreous collagen fibrils insert directly into posterior ciliary body and peripheral retina, forming strong adhesions

Adult peripheral retina continues to synthesize collagen, which can break through ILM and intertwine with cortical vitreous, creating further adhesions

The vitreous base remains firmly attached to the retina, except in cases of trauma which can cause an avulsion of the vitreous base

Even in vitrectomy, the vitreous base is 'shaved'



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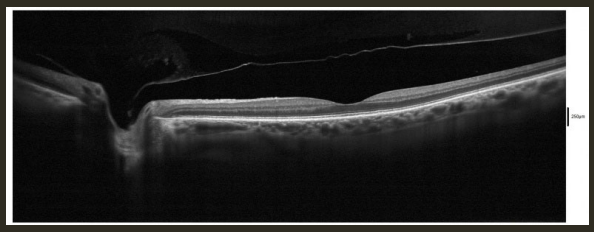
2. *Retina and Vitreous: 2017-2018*. Vol. 12, American Academy of Ophthalmology, 2017, p289.

PARTIAL PVD



Tabernero, S. Posterior vitreous detachment. EyeWiki. April 5, 2016. Accessed January 9, 2020. https://eyewiki.aao.org/w/index.php?title=File%3ADpv.jpg&oldid=22244

SYNCHYSIS AND SYNERESIS

Vitreous undergoes progressive remodeling

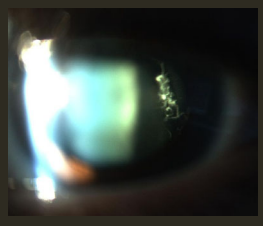
Synchysis = development of fluid filled lacunae

Syneresis = collagen fiber condensation

Synchysis and syneresis develop and progress during aging and after exposure to reactive oxygen species within the vitreous

Synchysis and syneresis are separate entities and develop independently

Detachment of anterior cortical gel from lens and ligament of Wieger (anterior vitreous detachment) historically was caused by intracapsular cataract extraction



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1. Fincham, Gregory S., et al. "Posterior vitreous detachment and the posterior hyaloid membrane." *Ophthalmology* 125.2 (2018): 227-236.
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POSTERIOR VITREOUS DETACHMENT

Clinical diagnosis

History of new-onset flashes and floaters – acute

May be asymptomatic

Exam

May or may not demonstrate epipapillary glial tissue torn form the optic nerve head (Weiss ring)

Separation of the posterior vitreous cortex from the vitreoretinal interface; can be associated with reduplication of the ILM

An alternative interpretation defines posterior vitreous detachment as the separation of the vitreous and its enveloping posterior hyaloid membrane from the surface of the retina

Image: By Jonathan Trobe, M.D. - University of Michigan Kellogg Eye Center - The Eyes Have It, CC BY 3.0, https://commons.wikimedia.org/w/index.php?curid=16116032

Text: Fincham, Gregory S., et al. "Posterior vitreous detachment and the posterior hyaloid membrane." *Ophthalmology* 125.2 (2018): 227-236.

POSTERIOR VITREOUS DETACHMENT FORMATION

With age, there is both liquefaction (synchysis) and collapse (syneresis) of the vitreous gel

Lacunae of liquefied material form within cortical vitreous, filled with hyaluronan

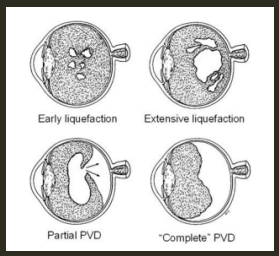
Collagen fibers surround lacunae

Contraction of gel around these lacunae (possibly due to electrostatic attraction and crosslinking of adjacent collagen fibers in the absence of hyaluronan) leads to posterior vitreous detachment (PVD)

The vitreous detaches posteriorly, remaining firmly attached at the vitreous base, and altogether moves anteriorly in the process of PVD formation

PVD = detachment of posterior cortical vitreous from its adhesions to the optic disc (area of Martegiani), the macula, and the blood vessels

Retina and Vitreous: 2017-2018. Vol. 12, American Academy of Ophthalmology, 2017, p289.



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PVD DIAGNOSIS

Often made via indirect ophthalmoscopy or slit lamp biomicroscopy

Visualize the posterior vitreous face a few millimeters in front of the retinal surface

A translucent ring of fibroglial tissue (Weiss ring) is often torn loose from the optic nerve head

Shallow and incomplete detachments may not be visible at slit lamp or via indirect ophthalmoscopy, but may be seen on Bscan

PVDs frequently begin as a localized vitreous detachment over the perifovea (posterior perifoveal vitreous detachment), which can be seen on OCT

Localized regions of posterior cortical vitreous can separate slowly and asymptomatically over years, in contrast to the sudden onset symptomatic PVD

Retina and Vitreous: 2017-2018. Vol. 12, American Academy of Ophthalmology, 2017, p289.

PVD CONTRIBUTING FACTORS

Older age

Longer axial length

History of blunt trauma

Diabetes

History of cataract extraction, particularly if there has been violation of the posterior capsule and loss of vitreous anteriorly

Inflammation - PVD increased with history of vitritis, due to loss or alteration of hyaluronan

Radiation exposure

Reactive oxygen species (any of the above may contribute)

Retina and Vitreous: 2017-2018. Vol. 12, American Academy of Ophthalmology, 2017, p289.

DIFFERENTIAL DIAGNOSIS OF POSTERIOR VITREOUS OPACITIES

Retinal detachment

Asteroid hyalosis

Synchysis scintillans

Vitreous syneresis

Vitreous inflammation (infectious or non-infectious)

Vitreous hemorrhage

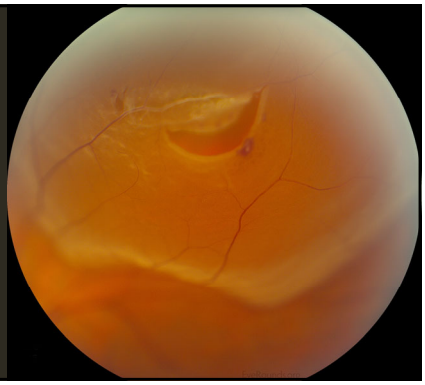
Vitreous amyloidosis

Intraocular lymphoma

Direct seeding of intraocular tumor (primary vs metastasis)

WHY DO WE CARE ABOUT PVD?

Gauger, E, et al. "Vitreous Syneresis: An Impending Posterior Vitreous Detachment (PVD)." *EyeRounds*, University of Iowa, 17 Nov. 2014, https://webeye.ophth.uiowa.edu/eyeforum/cases/196-PVD.htm.



ASTEROID HYALOSIS

Minute white opacities of calcium-containing phospholipids within otherwise normal vitreous

Variously found to be associated with older age, hypertension, diabetes, history of alcoholism, and history of cardiovascular disease

Can obscure view to retina; FA is useful in evaluating suspected retinal pathology when asteroid hyalosis blocks the view

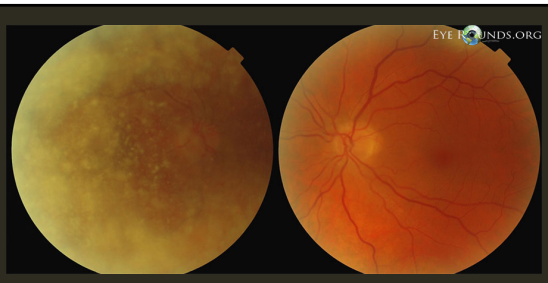
Many eyes with asteroid hyalosis have abnormal vitreoretinal interface abnormalities with vitreoretinal adhesions --- these adhesions increase risk of RD during PPV (hard to induce PVD during PPV in cases of asteroid hyalosis)

1. Mochizuki, Yasutaka, et al. "Anatomical findings of vitreoretinal interface in eyes with asteroid hyalosis." *Graefe's Archive for Clinical and Experimental Ophthalmology* 247.9 (2009): 1173-1177.
2. *Retina and Vitreous: 2017-2018*. Vol. 12, American Academy of Ophthalmology, 2017, p300.

RHEGMATOGENOUS PATHOLOGY DUE TO PVD

- PVD / vitreous contraction and traction caused by ocular saccades can lead to retinal breaks at sites of strong adhesion between retina and vitreous, particularly at the posterior edge of the vitreous base
- Retinal tears occur in 10-15% cases of acute and symptomatic PVD – overall 21.7% in meta-analysis
- 1.8% will develop or have tears not seen on initial exam
- Retinal detachment occurs when liquefied vitreous tracks through the tear and behind the retina causing retinal detachment
- Vitreous hemorrhage associated with a PVD occurs in approximately 7.5% of cases
- Vitreous hemorrhage associated with a PVD increases the chance of retinal tear to almost 70%
- Clumps of pigment in vitreous (Shafer's sign) highly sensitive and specific for retinal tear or detachment

1. Gauger, E, et al. "Vitreous Syneresis: An Impending Posterior Vitreous Detachment (PVD)." *EyeRounds*, University of Iowa, 17 Nov. 2014, https://webeye.ophth.uiowa.edu/eyeforum/cases/196-PVD.htm.
2. Coffee, Robert E., et al. "Symptomatic posterior vitreous detachment and the incidence of delayed retinal breaks: case series and meta-analysis." *American journal of ophthalmology* 144.3 (2007): 409-413.
3. Tanner, Vaughan, et al. "Acute posterior vitreous detachment: the predictive value of vitreous pigment and symptomatology." *British journal of ophthalmology* 84.11 (2000): 1264-1268.



ASTEROID HYALOSIS

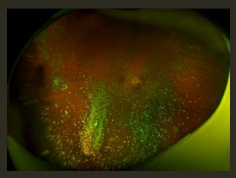
"Asteroid Hyalosis." *EyeRounds*, University of Iowa, 2 Aug. 2012, https://webeye.ophth.uiowa.edu/eyeforum/atlas/pages/asteroid-hyalosis.html

CHOLESTEROLOSIS AKA SYNCHYSIS SCINTILLANS

Yellow-white, gold, or multicolored crystals in vitreous and anterior chamber during cholesterolosis, or synchysis scintillans

Occurs almost exclusively in sick eyes with a history of multiple large VHs

PVD is frequently present, allowing crystals to settle inferiorly



"This image was originally published in the Retina Image Bank. Iglicki M, Zur D. Retinal Detachment Due to Trauma with Synchysis Scintillans. Retina Image Bank. 2018; 28102. © the American Society of Retina Specialists. https://imagebank.asrs.org/file/28102/retinal-detachment-due-to-trauma-with-synchysis-scintillans

Retina and Vitreous: 2017-2018. Vol. 12, American Academy of Ophthalmology, 2017, p302-303.

VITREOUS OPACITY – CELLS!

Clumps of brown RPE pigment
- Shafer's sign – look for tear or detachment

Red blood cells
- Vitreous hemorrhage from retinal tear, vs proliferative vascular process (PDR vs PVR vs tumors etc.)

White blood cells
- Due to uveitis (can be autoimmune vs infectious)
- Due to infection (endophthalmitis, can be exogenous or endogenous, vs related to other infection (ARN, etc.))

Vitritis Masquerade
- Intraocular lymphoma

Other White Cells - Tumor
- Lymphoma, Rb seeding the vitreous, metastatic disease, etc.

AMYLOIDOSIS

First PPV performed for this reason

Bilateral vitreous opacification can occur as an early manifestation of dominant amyloidosis

Rare to have amyloid in vitreous in nonfamilial cases

Diagnosed by PPV with vitreous biopsy

Initially, amyloidosis in the vitreous appears adjacent to retinal vessels posteriorly; develops anteriorly later. At first, opacities appear granular with wispy fringes, but as they enlarge and aggregate, the vitreous takes on a 'glass-wool' appearance. With PVD, the opacities may be displaced into the visual axis, causing blurry vision and photophobia.

DDX: chronic VH, lymphoma, Sarcoidosis, Whipple's disease (a/w chronic vitritis), in addition to retinal vasculitis and posterior uveitis

Amyloid can recur after PPV

Retina and Vitreous: 2017-2018. Vol. 12, American Academy of Ophthalmology, 2017, p303-304.

RED BLOOD CELLS

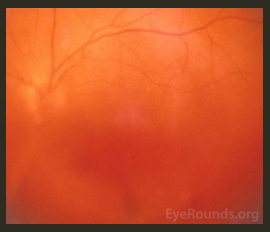
Differential diagnosis:

Retinal tear or detachment

Proliferative vascular process:
- Diabetic retinopathy (PDR)
- Other proliferative retinopathy (PVR, ROP, etc.)

Vascular tumor

Valsalva retinopathy, macroaneurysm, etc. with egress of blood from preretinal space into vitreous



"Vitreous Hemorrhage: From One Medical Student to Another." *EyeRounds*, University of Iowa, 8 Aug. 2018, http://webeye.ophth.uiowa.edu/eyeforum/tutorials/vitreous-hemorrhage-med-student/index.htm

AMYLOIDOSIS – RETINAL AND SYSTEMIC FINDINGS

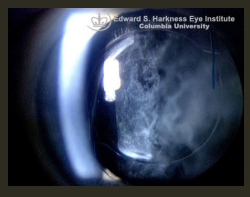
Amyloid can also deposit in retinal vasculature, choroid, and TM – however this should not be the first thing on your differential; with cloudy vitreous, retinal vascular abnormalities, first think infectious/inflammatory

Retinal findings in amyloidosis can include hemorrhages, exudates, CWS, and peripheral neovascularization

Amyloid may also deposit in orbit, EOMs, eyelids, conj, cornea, and iris

Non-ocular manifestations include polyneuropathy and CNS abnormalities

Amyloid can also deposit in the heart, skin, and GI tract / liver

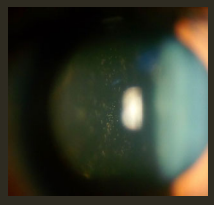


"Vitreous Amyloidosis." Columbia University Department of Ophthalmology, https://www.columbiaeye.org/education/digital-reference-of-ophthalmology/vitreous-retina/tumor-others/vitreous-amyloidosis. Accessed January 9, 2020.

WHITE BLOOD CELLS

Vitritis
- Due to uveitis (can be autoimmune vs infectious)
- Due to infection (endophthalmitis, can be exogenous or endogenous, vs related to other infection (ARN, etc.))

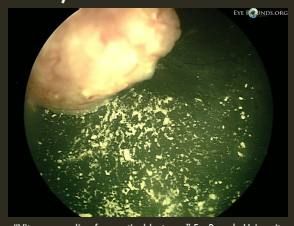
Vitritis Masquerade
- Intraocular lymphoma – painless, persistent and chronic vitreous cell in older or immunocompromised person
- Intraocular lymphoma can be a presenting sign of CNS lymphoma



By Imrankabirhossain - Own work, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=59584484

TUMOR CELLS (USUALLY WHITE)

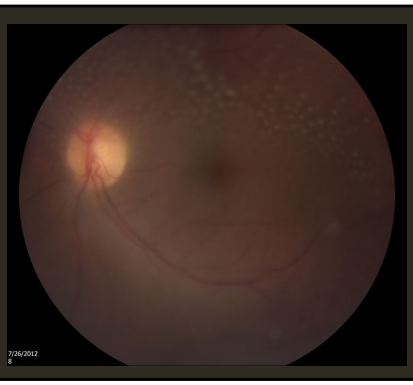
- Direct seeding of vitreous from retinal tumor
- Retinoblastoma
- Less commonly, metastatic disease



"Vitreous seeding from retinoblastoma." *EyeRounds*, University of Iowa, 2 Sept. 2014, https://webeye.ophth.uiowa.edu/eyeforum/atlas/pages/Rb-seeding/index.htm.

QUESTIONS?

This image was originally published in the Retina Image Bank. Merrill P. Syphilitis Panuveitis, Left Eye. Retina Image Bank. 2012; 1150. © the American Society of Retina Specialists. https://imagebank.asrs.org/file/1150/syphilitic-panuveitis-left-eye



7/26/2012
8

THANK YOU

VITREORETINAL INTERFACE DISEASE AND VITREOUS ANTIOXIDANT PROPERTIES

Rebecca Sieburth, MD
Northeast Eye Center
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VITREORETINAL INTERFACE DISEASE

Persistent attachment of the vitreous to the fovea can lead to vitreomacular traction syndrome

Remnants of the vitreous often remain on the internal limiting membrane after a PVD; some describe a PVD as actually being a form of posterior vitreoschisis that is either internal or external to the layer of hyalocytes on the posterior vitreous face

These vitreous remnants / hyalocytes may contribute to ERM or macular hole formation, and possibly contribute to tractional retinal detachments in patients with myopia or diabetes mellitus

Retina and Vitreous: 2017-2018. Vol. 12, American Academy of Ophthalmology, 2017, p290.

DISCLOSURES

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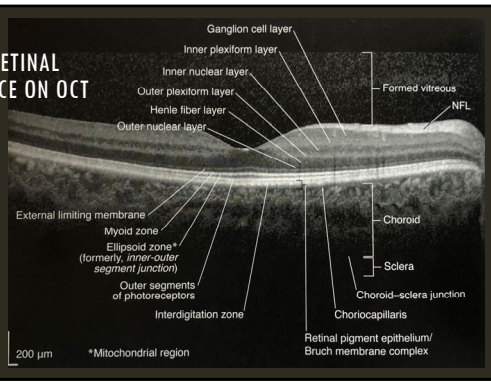
VITREORETINAL INTERFACE ON OCT



Courtesy of Colin A. McCannel, MD. Retina and Vitreous: 2017-2018. Vol. 12, American Academy of Ophthalmology, 2017, p24.

VITREORETINAL INTERFACE DISEASE

Often associated with a PVD

EPIRETINAL MEMBRANE (ERM)

A transparent, avascular, fibrocellular membrane on the inner retinal surface that adheres to and covers the ILM of the retina

Schisis of posterior vitreous may leave variable portions of posterior cortical vitreous attached to macula

This allows glial cells from the retina and/or RPE cells to proliferate along the ILM and hyalocytes to proliferate on posteriorly attached cortical vitreous remnants

Cellular origin of ERMs is still under debate – histologically, ERMs are comprised of RPE cells and retina glial cells (astrocytes and Muller cells)

- Myofibroblasts, fibroblasts, hyalocytes, and macrophages have also been identified

Retina and Vitreous: 2017-2018. Vol. 12, American Academy of Ophthalmology, 2017, p291.

EPIRETINAL MEMBRANE - EPIDEMIOLOGY

Idiopathic ERM = most common

Most common after age 50 (idiopathic)

Present in 2% of patient older than 50 years old and 20% of pts older than 75 years at time of autopsy

Both sexes equally affected

Usually asymmetric, bilateral in 10-20%

PVD is present in almost all eyes with idiopathic ERM

Secondary ERMs occur regardless of age or sex in association with abnormal vitreoretinal adhesions, areas of inflammation, and following retinal detachment or retinal bleeding

Retina and Vitreous: 2017-2018. Vol. 12, American Academy of Ophthalmology, 2017, p291.

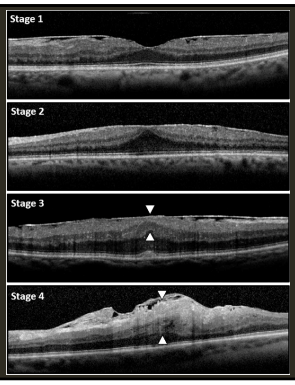
ERM STAGES - OCT

Stage 1. Mild ERM. Preserved foveal contour and retinal layers

Stage 2. Moderate ERM. Loss of foveal contour with preservation of retinal layers

Stage 3. Moderate ERM with continuous ectopic inner foveal layers covering the entire fovea (white arrows). Flat foveal contour, and all retinal layers are well defined.

Stage 4. Advanced ERM with complete foveal disorganization. Thick ectopic foveal layers covering fovea, and disorganization of foveal contour and retinal layers



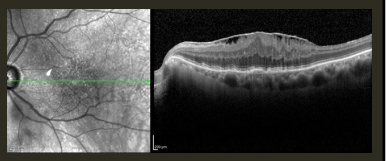
Govetto, Andrea, et al. "Functional and anatomical significance of the ectopic inner foveal layers in eyes with idiopathic epiretinal membranes: surgical results at 12 months." *Retina* 39.2 (2019): 347-357.

EPIRETINAL MEMBRANE - EXAM

Appear as mild sheen or glint on retinal surface

ERMs become more thickened and opaque over time, and can obscure underlying retinal details

If preretinal membrane (but not retina) has central open area in central macula, can give "pseudohole" appearance (differentiate via OCT)



This image was originally published in the Retina Image Bank. Garcia-Aguirre, G. Epiretinal Membrane (Macular Pucker). Retina Image Bank. 2018; 28297. © the American Society of Retina Specialists. https://imagebank.asrs.org/file/28297/epiretinal-membrane-macular-pucker

Retina and Vitreous: 2017-2018. Vol. 12, American Academy of Ophthalmology, 2017, p292.

ERM TREATMENT

If asymptomatic, do not intervene

If bothered by VA loss or metamorphopsia, refer to retina specialist for a careful discussion with patient regarding individual R/B/A/I, as an evaluation for PPV with ERM peel

Should monitor asymptomatic ERMs as they can worsen

Retina and Vitreous: 2017-2018. Vol. 12, American Academy of Ophthalmology, 2017, p292-293.

EPIRETINAL MEMBRANE STAGES - EXAM

ERM contracture produces distortion and wrinkling of the inner surface of the retina

When mild = cellophane maculopathy or preretinal macular fibrosis

Moderate = surface-wrinkling retinopathy or retinal striae

Severe = macular pucker

Increased traction can cause shallow macular detachment, diffuse thickening, or cystic changes (pseudo-IRF) on OCT

Traction on retinal vessels *can* result in increased vascular tortuosity

Retina and Vitreous: 2017-2018. Vol. 12, American Academy of Ophthalmology, 2017, p292.

VITREOMACULAR TRACTION

Vitreomacular traction includes abnormalities that arise from focal or broad posterior vitreous adhesions in the presence of detaching or otherwise detached posterior vitreous

VMA = vitreomacular adhesion – does not necessarily cause visual symptoms and can be observed

VMT = vitreomacular traction – posterior hyaloid abnormally adherent to macula

Posterior hyaloid remains tethered to macula as posterior vitreous detaches

Can cause tractional distortion of fovea, intraretinal cystic edema, and in severe cases tractional foveal detachment

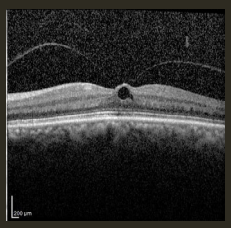
Retina and Vitreous: 2017-2018. Vol. 12, American Academy of Ophthalmology, 2017, p293-294.

VITREOMACULAR TRACTION - SYMPTOMS

Decline in BCVA

Metamorphopsia

Complaint about poor VA out of proportion to measured acuity



Retina and Vitreous: 2017-2018. Vol. 12, American Academy of Ophthalmology, 2017, p293-294.

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OCRIPLASMIN

One of a variety of treatments that can be discussed between the patient and their retina specialist

Recombinant protease with activity against fibronectin and laminin

A multicenter RCT found resolution of VMT in 26.5% of ocriplasmin-injected eyes compared to 10.1% of placebo-injected eyes over the same period. In a subset of patients with vitreomacular adhesions less than 1500microns, rate of resolution increased to 33.6%.

Ocriplasmin is one of multiple treatment options for vitreomacular traction and for early macular hole

Broad VMT and adhesions associated with an ERM are poorer candidates for ocriplasmin

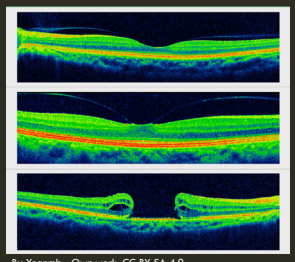
Retina and Vitreous: 2017-2018. Vol. 12, American Academy of Ophthalmology, 2017, p293-294.

VITREOMACULAR TRACTION - STAGES

Top: vitreomacular adhesion

Middle: vitreomacular traction

Bottom: full thickness macular hole



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ANTIOXIDANTS IN THE VITREOUS

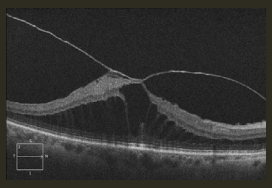
VITREOMACULAR TRACTION - MANAGEMENT

Spontaneous separation of VMT is rare but can occur

Chronic traction is generally thought to be harmful over the long term, particularly when there is cystic intraretinal edema or when vision is affected

Intervention options include PPV vs intravitreal ocriplasmin (vs intravitreal air bubble) – based on morphology of VMT and other individual factors

Macular hole = a manifestation of horizontal tractional forces on the macula resulting in separation of some or all retinal layers. Associated with VMA and VMT. Will skip detailed discussion of macular hole.



Retina and Vitreous: 2017-2018. Vol. 12, American Academy of Ophthalmology, 2017, p293-294.

"This image was originally published in the Retina Image Bank. Hunyor, A. Severe vitreomacular traction. Retina Image Bank. 2012; 2891. © the American Society of Retina Specialists. https://imagebank.asrs.org/file/2891/severe-vitreomacular-traction

COMPOSITION OF VITREOUS

Vitreous gel contains more than 99% water (associated with proteins and glycosaminoglycans that make up protein structure)

Major part of the collagen fibrils is hyaluronic acid

Vitreous pH conditions (pH 7–7.4)

Determinants of vitreous composition:

- Blood ocular barrier (with both active and passive transport across this barrier)
- Retina and ciliary body metabolism contributions
- Diffusion process through the vitreous body
- Vitreous collapse, PVD, and vitrectomy reduce diffusion barrier between anterior and posterior segment

Levin, Leonard A., et al. *Adler's Physiology of the Eye E-Book*. Elsevier Health Sciences, 2011.

ANTIOXIDANT PROPERTIES OF VITREOUS

ROS are generated in the vitreous by ultraviolet and visible light

Vitreous maintains biochemical homeostasis through multiple substances that consume ROS and molecular oxygen

Antioxidants in vitreous include ascorbic acid and glutathione

Ascorbic acid is present in 10-40x higher concentrations in vitreous than in plasma

Ascorbic acid is actively concentrated in the vitreous through the sodium-dependent vitamin C transporter in the pigmented ciliary epithelium

Ascorbic acid consumes ROS; glutathione also works to consume ROS and regenerates ascorbic acid

Formed vitreous gel (compared to a vitreous that has undergone PVD or a posterior segment where the vitreous has been removed surgically) has a higher ascorbic acid concentration and consumes oxygen at a faster rate

1. Siegfried, Carla J., and Ying-Bo Shui. "Intraocular oxygen and antioxidant status: new insights on the effect of vitrectomy and glaucoma pathogenesis." *American journal of ophthalmology* 203 (2019): 12-25.
2. Levin, Leonard A., et al. *Adler's Physiology of the Eye E-Book*. Elsevier Health Sciences, 2011.

VITREOUS AND CATARACT FORMATION

Vitreous gel helps to maintain a hypoxic environment around the lens

Consumption of oxygen/ROS may protect the lens and the trabecular meshwork from oxidative damage

Hyperbaric oxygen therapy has been shown to increase the rate of cataract formation (50% incidence of nuclear cataract within 1 - 3 years)

Nuclear sclerotic cataract often develops within the 12 - 18 months after a PPV, with 37% - 95% of patients needing cataract surgery within the next 1-2 years

Increased vitreous liquefaction increases the risk of nuclear cataract development

It is thought that oxygen and ROS exposure causes oxidative damage to the lens and contributes to cataract formation

Siegfried, Carla J., and Ying-Bo Shui. "Intraocular oxygen and antioxidant status: new insights on the effect of vitrectomy and glaucoma pathogenesis." *American journal of ophthalmology* 203 (2019): 12-25.

A NON-LINEAR RELATIONSHIP

At physiologic concentrations, ascorbic acid functions as an antioxidant

In higher concentrations achieved by pharmacological doses, ascorbic acid may no longer function as effectively as an antioxidant as they may increase levels of H_2O_2 in the vitreous

Future studies are needed to evaluate the significance of vitreous H_2O_2 produced by supraphysiologic levels of ascorbic acid

1. Schwab, Christoph, et al. "Gender differences in albumin and ascorbic acid in the vitreous antioxidant system." *Free Radical Biology and Medicine* 146 (2020): 257-263.
2. Siegfried, Carla J., and Ying-Bo Shui. "Intraocular oxygen and antioxidant status: new insights on the effect of vitrectomy and glaucoma pathogenesis." *American journal of ophthalmology* 203 (2019): 12-25.

QUESTIONS

ALBUMIN

Albumin, a 66.5 kDa protein, is an important component of plasma protein and is an antioxidant

Albumin may be involved in regenerating glutathione (GSH)

Albumin also assists in ROS consumption and pH balance

There is an inverse relation between vitreous ascorbic acid concentrations and redox state of albumin

1. Schwab, Christoph, et al. "Gender differences in albumin and ascorbic acid in the vitreous antioxidant system." *Free Radical Biology and Medicine* 146 (2020): 257-263.
2. Siegfried, Carla J., and Ying-Bo Shui. "Intraocular oxygen and antioxidant status: new insights on the effect of vitrectomy and glaucoma pathogenesis." *American journal of ophthalmology* 203 (2019): 12-25.

THANK YOU

VITREOUS ASSOCIATIONS WITH LIGHT AND RADIATION, AND FACTORS ASSOCIATED WITH ASTEROID HYALOSIS

Rebecca Sieburth, MD
Northeast Eye Center
Latham, NY

VITREOUS CHANGES IN RESPONSE TO EXPOSURE TO LIGHT AND RADIATION

The eye has the second highest exposure to visible light and radiation exposure in the body, second only to the skin

Catalase is another substance the vitreous that acts to bind free radicals

26 calf eyes were irradiated with UV-A light for 3 hours

Catalase activity in irradiated eyes increased 33%

This suggests that short-wave UV-A light increased free radical formation leading to increased catalase activity in the vitreous

Heller, S., and U. M. Mayer. "Effect of UV-A light on the catalase activity in the vitreous body of calf eyes." *German journal of ophthalmology* 3.6 (1994): 445-446.

DISCLOSURES

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I have no financial relationship with a commercial interest and have no financial disclosures.

VITREOUS CHANGES WITH PHOTOSENSITIZER - HEMATOPORPHYRIN

Calf vitreous gel decreased in collagen polymer length by 0.6% after irradiation with 24 hours of white light

With hematoporphyrin added as a photosensitizer, polymer length decreased by 1.9% after irradiation with 24 hours of white light

Kakehashi, Akihiro, Norio Ueno, and Bireswar Chakrabarti. "Molecular mechanisms of photochemically induced posterior vitreous detachment." *Ophthalmic research* 26.1 (1994): 51-59.

VITREOUS ASSOCIATIONS WITH LIGHT AND RADIATION

Animal studies

VITREOUS CHANGES WITH PHOTOSENSITIZER - RIBOFLAVIN

Bovine vitreous collagen or HA was irradiated by visible light in the presence of riboflavin (RF) as a photosensitizer

After irradiation with visible light in the setting of added riboflavin, the molecular weight of hyaluronic acid polymers decreased and the vitreous collagen became more insoluble

Cross-linking of vitreous collagen and degrading HA may contribute to vitreous syneresis, synchysis, and PVD

Akiba, Jun, Norio Ueno, and Bireswar Chakrabarti. "Mechanisms of photo-induced vitreous liquefaction." *Current eye research* 13.7 (1994): 505-512.

VITREOUS CHANGES WITH PHOTOSENSITIZER - BILIRUBIN

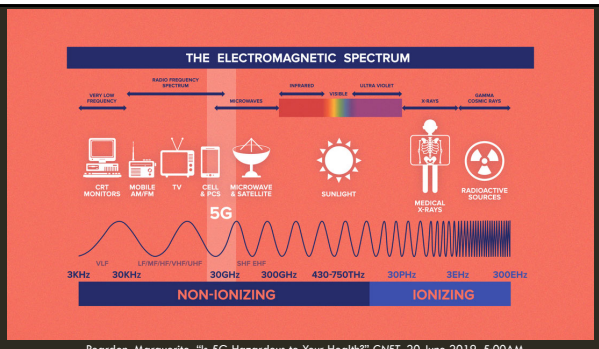
Bilirubin is a hemoglobin degradation product

Bovine collagen was irradiated by visible light in the presence of bilirubin

Free radicals released from light interacting with bilirubin-sensitized vitreous produced an increase in high-molecular-weight components and insolubilization of vitreous, greater than in controls that did not undergo addition of bilirubin

Cross-linking and breakdown of hyaluronic acid polymers may contribute to vitreous liquefaction in the setting of vitreous hemorrhage

Hikichi, Taiichi, et al. "Cross-linking of vitreous collagen and degradation of hyaluronic acid induced by bilirubin-sensitized photochemical reaction." *Japanese journal of ophthalmology* 41.3 (1997): 154-159.



Reardon, Marguerite. "Is 5G Hazardous to Your Health?" *CNET*, 20 June 2019, 5:00AM, www.cnet.com/news/5g-phones-and-your-health-what-you-need-to-know/.

VITREOUS CHANGES WITH PHOTOSENSITIZER - FLUORESCEIN

Levels of ascorbic acid in rabbit eyes exposed to visible light were measured

In the test group, fluorescein was used as a photosensitizer

Ascorbic acid levels dropped in eyes treated with fluorescein and irradiated with visible light

This suggests that ascorbic acid is consumed when vitreous is exposed to prolonged visible light, suggesting that physiologic levels of ascorbic acid may have a protective effect against ROS

Zhang, Xiao Mei, Kentaro Ohishi, and Tadahisa Hiramitsu. "Microdialysis measurement of ascorbic acid in rabbit vitreous after photodynamic reaction." *Experimental eye research* 73.3 (2001): 303-309.

FACTORS ASSOCIATED WITH ASTEROID HYALOSIS

REACTIVE OXYGEN SPECIES PRODUCED BY LIGHT MAY CONTRIBUTE TO VITREOUS LIQUEFACTION

Hyaluronic acid, a major component of vitreous, is degraded and depolymerized by ROS

Calf vitreous was irradiated with visible light from two 15-W fluorescent lamps and became liquefied thereafter

Irradiation with hematoporphyrin led to increased liquefaction of calf vitreous

Irradiation with ascorbic acid also led to increased liquefaction of calf vitreous

Inflammation of calf vitreous was simulated via addition of endotoxin; this also produced vitreous liquefaction

ROS may be a significant contributor to vitreous structural changes

Ueno, N. "Changes in vitreous structure caused by oxygen free radicals." *Nippon Ganka Gakkai Zasshi* 99.12 (1995): 1342-1360.

NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES)

Randomized sample of individuals in multiple diverse regions of the United States, sampled and weighted to be representative of the United States as a whole

Conducted by the CDC in the same areas for 2 years at a time

From 2005-2008, the NHANES included exams for vision, frequency doubling technology (FDT), and fundus photographs as well as a variety of other questionnaires, exams, and lab tests

A population-based, cross-sectional study of adults age 40 and older was performed from the 2005-2008 National Health and Nutrition Examination Survey (NHANES) to evaluate prevalence of and associated factors with asteroid hyalosis

ASTEROID HYALOSIS IN THE NHANES DATABASE

Asteroid hyalosis is an uncommon clinical entity with possible associations with systemic disease. The purpose of this study is to examine the prevalence of asteroid hyalosis and identify associated conditions in a population representative of United States adults.

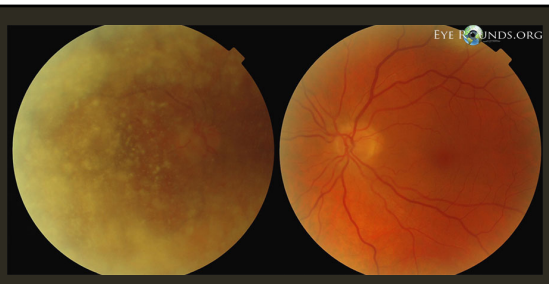
RESULTS – PREVALENCE

Of 5,578 subjects identified, 48 had asteroid hyalosis.

Overall prevalence of asteroid hyalosis was 0.86%, with gender specific prevalence of 0.97% in men and 0.76% in women.

In 16.7% of cases, asteroid hyalosis was present bilaterally.

Ophthalmic Characteristics	n (%)
Total Eyes	56 (100.0)
Right Eye	28 (50.0)
Left Eye	20 (35.7)
Bilateral	8 (16.7)



ASTEROID HYALOSIS

"Asteroid Hyalosis." *EyeRounds*, University of Iowa, 2 Aug. 2012, https://webeye.ophth.uiowa.edu/eyeforum/atlas/pages/asteroid-hyalosis.html

RESULTS – DEMOGRAPHIC ASSOCIATIONS

Demographic, Examination, and Questionnaire Associations with Asteroid Hyalosis			
Demographics	Odds Ratio	Confidence Interval	P-value
Age	1.09	0.06 - 0.12	**<0.0001**
Female Gender	0.79	-0.82- 0.34	0.43
Ethnicity			
Hispanic	0.33	-2.91 - 0.94	0.23
Non-Hispanic White	1.39	-0.75 - 1.77	0.60
Non-Hispanic Black	1.99	-0.53 - 2.20	0.30
Other	3.00	-0.94 - 2.91	0.23
Education			
9-11th Grade Education	1.52	-0.65 - 1.50	0.44
Highschool or GED	1.86	-0.28 - 1.62	0.20
Some College or Associate Degree	0.87	-1.32 - 1.01	0.80
College Graduate or Above	1.87	-0.36 - 1.69	0.22

BASELINE CHARACTERISTICS OF POPULATION

Population Characteristics	Without Asteroid Hyalosis	With Asteroid Hyalosis	Total in Sample Population
Subjects*	5530 (99.14)	48 (0.86)	5578 (100.0)
Mean Age (Years)	59.43	71.13	59.53
Sex**			
Women	2771 (99.25)	21 (0.75)	2792 (50.24)
Men	2759 (99.03)	27 (0.97)	2786 (50.13)
Ethnicity**			
Hispanic	1238 (99.12)	11 (0.88)	1249 (22.48)
Non-Hispanic White	2988 (99.14)	26 (0.86)	3014 (54.24)
Non-Hispanic Black	1125 (99.21)	9 (0.79)	1134 (20.41)
Other	179 (98.90)	2 (1.10)	181 (3.26)
*n (%) of total population; ** n (%) of subgroup			

RESULTS – SUMMARY OF ASSOCIATED FACTORS

Asteroid hyalosis was associated with older age ($p<0.0001$, 95% confidence interval [CI], 0.06-0.12; odds ratio [OR], 1.09).

There were no significant associations with ethnicity or sex.

After adjusting for age, ethnicity, and sex, asteroid hyalosis was associated with history of myocardial infarction ($p=0.022$; 95% CI, 0.07-1.55; OR, 2.36) and weight in kilograms ($p=0.049$; 95% CI, 0.001-0.04; OR, 1.02).

RESULTS - ASSOCIATED OCULAR FACTORS

Demographic, Examination, and Questionnaire Associations with Asteroid Hyalosis			
Fundus Photography*	Odds Ratio	Confidence interval	P value
Mild Nonproliferative Diabetic Retinopathy (NPDR)	1.25	-0.98 - 1.15	0.67
Moderate/Severe NPDR	3.37	-0.61 - 2.42	0.97
Proliferative Diabetic Retinopathy	0.000005	-224.64 - 25.06	0.99
Central Diabetic Macular Edema	3.97	-1.51 - 2.96	0.18
Early Age Related Macular Degeneration	1.54	-0.68 - 1.33	0.39
Late Age Related Macular Degeneration	0.000002	-171.14 - 12.26	0.98
Arteriovenous Nicking	0.87	-1.36 - 0.79	0.79
Vertical Cup to Disc Ratio	6.34	-0.46 - 4.08	0.11

RESULTS – ASSOCIATIONS WITH SERUM MARKERS

Demographic, Examination, and Questionnaire Associations with Asteroid Hyalosis			
Serum Markers	Odds Ratio	Confidence interval	P value
High Density Lipoprotein (HDL) (mg/dL)	0.98	-0.04 - 0.005	0.15
Low HDL (<60 mg/dL)	1.08	-0.56 - 0.77	0.81
Triglycerides (mg/dL)	1.00	-0.007 - 0.003	0.93
High Triglycerides (>150 mg/dL)	1.50	-0.51 - 1.30	0.37
Low Density Lipoprotein (LDL) mg/dL	1.01	-0.002 - 0.02	0.10
High LDL (>130 mg/dL)	1.11	-0.90 - 1.01	0.83
Total Cholesterol mg/dL	1.00	-0.005 - 0.009	0.53
High Cholesterol (> 200 mg/dL)	0.93	-0.68 - 0.53	0.82
C-Reactive Protein (CRP) mg/dL	1.08	-0.23 - 0.24	0.51
High CRP (>3 mg/dL)	1.37	-2.58 - 1.88	0.76
Hemoglobin A1c	1.11	-0.18 - 0.33	0.42
High Hemoglobin A1c (> 6.5)	1.84	-0.31 - 1.38	0.14
Calcium (mg/dL)	0.59	-1.29 - 0.24	0.18
High Calcium (> 10.2 mg/dL)	0.0000003	-266.30 - 14.91	0.98
Phosphorus mg/dL	1.27	-0.31 - 0.76	0.38
High Phosphorus (> 4.6 mg/dL)	1.24	-1.00 - 1.15	0.68
Uric Acid (mg/dL)	1.19	-0.02-0.36	**0.07**
High Uric Acid (> 4.0 mg/dL)	2.38	-0.34 - 2.69	0.24

RESULTS – ASSOCIATIONS WITH BODY MEASURES

Demographic, Examination, and Questionnaire Associations with Asteroid Hyalosis			
Body Measures	Odds Ratio	Confidence interval	P value
Systolic blood pressure	0.99	-0.03 - 0.004	0.18
Hypertension (Blood pressure > 140 / 90 mmHg)	0.9	-1.02 - 1.01	0.83
Weight (kg)	1.02	0.001 - 0.04	**<0.05**
BMI (kg/m^2)	1.05	-0.02 - 0.11	0.15
Obesity (BMI >30 kg/m^2)	1.33	-0.43 - 0.98	0.43
Waist Circumference (cm)	1.02	-0.002-0.04	0.07
Bone Density			
Total Femur Bone Mineral Density (BMD) (g/cm^2)	0.64	-2.75 - 1.79	0.70
Femoral Neck BMD g/cm^2	4.71	-3.41 - 1.75	0.57
Total Spine BMD in g/cm^2	0.46	-3.07 - 1.38	0.49

CONCLUSIONS

More research is needed to explore possible shared pathophysiologic mechanisms between development of asteroid hyalosis and cardiovascular disease.

RESULTS - QUESTIONNAIRE ASSOCIATIONS

Demographic, Examination, and Questionnaire Associations with Asteroid Hyalosis			
Questionnaire	Odds Ratio	Confidence interval	P value
Ever had 5 or more drinks every day	0.79	-1.02 - 0.65	0.57
Smoked at least 100 cigarettes over entire life	0.85	-0.78 - 0.44	0.61
High blood pressure	0.91	-0.70 - 0.50	0.76
High Cholesterol	1.79	-0.07-1.28	**0.09**
Diabetes	0.76	-0.95 - 0.46	0.43
Arthritis	1.14	-0.47 - 0.75	0.67
Congestive Heart Failure	0.67	-1.27 - 0.67	0.40
Coronary Artery Disease	2.04	-0.15-1.46	**0.08**
Heart Attack	2.36	0.07-1.55	**0.02**
Stroke	0.56	-1.39 - 0.41	0.20
Thyroid Problem	1.05	-0.74 - 0.97	0.91
Cancer	1.25	-0.51 - 1.08	0.58
Osteoporosis	1.12	-0.79 - 1.21	0.83

RESULTS OF OTHER STUDIES – UCLA

Asteroid hyalosis epidemiology in an autopsy population at UCLA

Total 10,801 subjects

Prevalence: 1.96%

Associated with age (<0.001), male sex (p=0.006), ARMD (p=0.02), HTN (p=0.03), atherosclerosis (p<0.001), and posterior vitreous attachment (p<0.001) (WITHOUT adjusting for age…)

WITH adjustment for age, only posterior vitreous attachment (p=0.002) and male sex (p=0.046) were statistically significant

Alcoholism and diabetes were not associated

Fawzi, Amani A., et al. "Asteroid hyalosis in an autopsy population: The University of California at Los Angeles (UCLA) experience." *Archives of Ophthalmology* 123.4 (2005): 486-490.

RESULTS OF OTHER STUDIES - WILLS

Asteroid hyalosis epidemiology in population of patients seen at Wills in Philadelphia

Total 12,305 subjects

Prevalence: 0.83%

Associated with diabetes (p=0.0007), HTN (p=0.0001), atherosclerosis (p=0.006), and hyperopia (p=0.009)

Bergren, Robert L., Gary C. Brown, and Jay S. Duker. "Prevalence and association of asteroid hyalosis with systemic diseases." *American journal of ophthalmology* 111.3 (1991): 289-293.

SUPPLEMENTS? NO EVIDENCE FOR A ROLE IN VITREOUS DISEASE

No evidence for supplements for vitreous related reasons

Vitamin C in high enough doses no longer functions well as an antioxidant

The vitreous can be removed entirely and the eye continues to function well

There is evidence that supplementation with antioxidants is of benefit in eye disease (AREDS2 for ARMD), and that unsaturated fatty acids can assist with dry eye (fish oil supplements)

Research suggests that ROS may contribute to the pathophysiology of glaucoma, diabetic retinopathy, and several corneal diseases

More research is needed

RESULTS OF OTHER STUDIES – BEAVER DAM EYE STUDY

Asteroid hyalosis epidemiology in population of patients living in Beaver Dam, Wisconsin

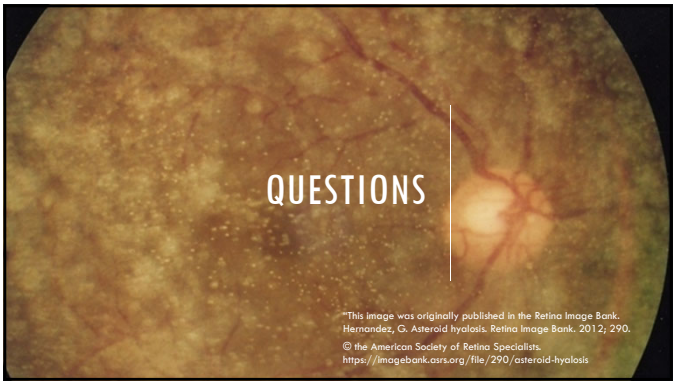
Total 4747 subjects

Prevalence: 1.2%

Associated with age (p<0.001), body mass (p=0.02), alcohol consumption (p=0.03)

Nonsignificant trends were identified for systolic blood pressure (p=0.07), serum cholesterol (p=0.09), and serum albumin (p=0.09)

Moss, Scot E., Ronald Klein, and Barbara EK Klein. "Asteroid hyalosis in a population: the Beaver Dam eye study." *American journal of ophthalmology* 132.1 (2001): 70-75.



"This image was originally published in the Retina Image Bank. Hernandez, G. Asteroid hyalosis. Retina Image Bank. 2012; 290.

https://imagebank.asrs.org/file/290/asteroid-hyalosis

ASTEROID HYALOSIS

Associated with multiple factors that are also associated with atherosclerosis

There is no direct association with calcium levels that have been found in previous studies or in this recent study

Age is associated with other calcific degenerations in the body – calcific scleral plaques (Cogan's patch), as well as systemic atherosclerosis

While asteroid hyalosis is rarely visually significant, it can obscure the view to the fundus and make vitrectomy more difficult to perform in cases when vitrectomy is necessary

THANK YOU