Retina Roundup

Walter O. Whitley, OD, MBA, FAAO
Director of Professional Relations and Education
Virginia Eye Consultants
Regional Medical Director
Eyecare Partners, LLC

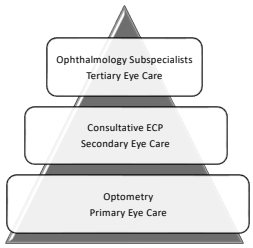
1

Disclosures - Walter O. Whitley, OD, MBA, FAAO has received consulting fees, honorarium or research funding from:

- Aerie: Advisory Board, Speaker
- Alcon: Advisory Board, Consultant, Speaker
- Allergan: Advisory Board, Consultant, Speaker
- Bausch and Lomb: Advisory Board, Speaker
- Bruder: Advisory Board
- CollaborativeEye – Co-Chief Medical Editor
- Dry Eye Coach – Co-Medical Editor
- Eyenovia: Consultant
- Heru: Consultant, Research
- I-MED Pharma: Advisory Board
- Iveric: Consultant
- Kala: Advisory Board, Speaker
- Mediprint Pharma: Consultant
- New Sight Capital: Co-Founder
- Oyster Point: Advisory Board, Speaker
- Regener-Eyes: Consultant
- Review of Optometry – Contributing Editor
- RVL Pharmaceuticals: Advisory Board, Consultant, Speak
- Santen: Advisory Board, Consultant
- Science Based Health: Advisory Board
- Sun Pharmaceuticals: Advisory Board
- Tarsus Pharmaceuticals: Advisory Board
- Thea Pharmaceuticals: Consultant
- Visus Pharmaceuticals: Advisory Board

2

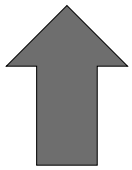
Spectrum of Eye Care

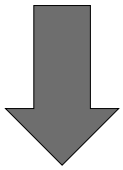


3

Current Challenges

- Increasing patient demand
- Less ECPs to available to care for patients





4

4 C's of Comanagement

- Care
- Comfort
- Collaboration
- Communication

5

Barriers of Undertreatment with Anti-VEGF Agents

- Too old for therapy
- Private/professional obligations
- Comorbidity
- Lack of support
- ***Burden for family members***
- ***Challenge accompanying persons***
- ***Travel/opportunity costs***
- ***Time commitment***
- Side effects
- Cost of treatment
- Depression
- Dissatisfaction
- Believe in need of therapy
- Uncomfortable feeling
- Shared decision-making
- Trust in physician
- Knowledge

Sobolewska B, Sabsabi M, Ziemssen F. Importance of Treatment Duration: Unmasking Barriers and Discovering the Reasons for Undertreatment of Anti-VEGF Agents in Neovascular Age-Related Macular Degeneration. Clin Ophthalmol. 2021 Oct 27;15:4317-4326.

6

What Are the Predictors of Non-Adherence?

- Distance between home and hospital
- Dissatisfaction with the results of intravitreal therapy
- Burden of regular follow-up visits
- Other considerations
  - Dependence on relative
  - Higher age
  - Poor visual acuity at baseline

Boulanger-Scemama E, Querques G, About F, et al. Ranibizumab for exudative age-related macular degeneration: a five year study of adherence to follow-up in a real-life setting. *J Fr Ophtalmol.* 2015;**38**(7):620–627.
Westborg I, Rosso A. Risk factors for discontinuation of treatment for neovascular age-related macular degeneration. *Ophthalmic Epidemiol.* 2018;**25**(2):176–182.

7

It's About Time

- A European study reviewed the burden on 131 patients with diabetic macular edema and central vein occlusion who who were undergoing anti-VEGF therapy in 2015 and 2016.[2]
  - Avg. Total Time per injection of 4.5 hours
  - For each six-month period of treatment,
    - RVO - >13 hours
    - DME - >20 hours
  - 53% need to take at least one day off
  - 71% required assistance with travel and personal needs

Sivaprasad S, Oyetunde S. Impact of injection therapy on retinal patients with diabetic macular edema or retinal vein occlusion. Clin Ophthalmol 2016;10:939-46.

8

How Can We Address?

- Patient adherence is defined as following the treatment plan on doctor's advice after shared decision-making
- Providers
  - Optimal outcomes of therapy for nAMD require not only efficacious treatment but also adherence to intravitreal therapy and visits, including optical coherence tomography (OCT) examinations.

World Health Organization (WHO). *Adherence to Long-Term Therapy: Evidence for Action*. Geneva: WHO; 2003.

9

What is Your Discussion in Regard to Treatments for nAMD and DME?

10

Preferred Practice Patterns

TABLE 5 Initial Management Recommendations for Patients with Diabetes

Severity of Retinopathy	Presence of Macular Edema	Follow-up (Months)	Panretinal Photocoagulation (Scatter) Laser	Focal and/or Grid Laser[a]	Intravitreal Anti-VEGF Therapy
Normal or minimal NPDR	No	12	No	No	No
Mild NPDR	No	12	No	No	No
	NCI-DME	3–6	No	Sometimes	No
	CI-DME	1*	No	Rarely	Usually
Moderate NPDR	No	6–12*	No	No	No
	NCI-DME	3–6	No	Sometimes	Rarely
	CI-DME	1*	No	Rarely	Usually
Severe NPDR	No	3–4	Sometimes	No	Sometimes
	NCI-DME	2–4	Sometimes	Sometimes	Sometimes
	CI-DME	1*	Sometimes	Rarely	Usually
Non-high-risk PDR	No	3–4	Sometimes	No	Sometimes
	NCI-DME	2–4	Sometimes	Sometimes	Sometimes
	CI-DME	1*	Sometimes	Sometimes	Usually
High-risk PDR	No	2–4	Recommended	No	Sometimes[b,c,d,e]
	NCI-DME	2–4	Recommended	Sometimes	Sometimes
	CI-DME	1*	Recommended	Sometimes	Usually

Anti-VEGF = anti-vascular endothelial growth factor; CI-DME = center-involved diabetic macular edema; NCI-DME = noncenter-involved diabetic macular edema; NPDR = nonproliferative diabetic retinopathy; PDR = proliferative diabetic retinopathy.

[a] Focal and/or grid laser may be considered include intravitreal corticosteroids or anti-VEGF agents (off-label use, except aflibercept and ranibizumab). Data from the Diabetic Retinopathy Clinical Research Network in 2011 demonstrated that, at 2 years of follow-up, intravitreal ranibizumab with prompt or deferred laser resulted in greater visual acuity gain and intravitreal triamcinolone acetonide plus laser also resulted in greater visual gain in pseudophakic eyes compared with laser alone.[16] Individuals receiving the intravitreal injections of anti-VEGF agents may be re-examined as early as 1 month following injections.

[*] For patients with good visual acuity (20/25 or better) and CI-DME, there is no difference between observation plus aflibercept if visual acuity decreases, focal laser plus aflibercept if visual acuity decreases.

https://www.aao.org/preferred-practice-pattern/diabetic-retinopathy-ppp
https://www.aao.org/preferred-practice-pattern/age-related-macular-degeneration-ppp

11

Treatment Options

Non-nAMD
- Observation
- Antioxidants / AREDS 2

nAMD
- Antioxidants / AREDS 2
- Anti-VEGF Agents
  - Ranibizumab 0.5 mg
  - Bevacizumab 1.25 mg
  - Aflibercept 2.0 mg

DME
- Focal laser
- Anti-VEGF Agents
  - Ranibizumab 0.5 mg
  - Bevacizumab 1.25 mg
  - Aflibercept 2.0 mg
- Intravitreal steroids
- Vitrectomy

12

Anti-VEGF treatment should be respectful of and responsive to individual patient preferences, needs, and values and ensuring that patient values guide all clinical decisions.

Vennedey V, Hower KI, Hillen H, Ansmann L, Kuntz L, Stock S; For the Cologne Research and Development Network (CoRe-Net). Patients' perspectives of facilitators and barriers to patient-centred care: insights from qualitative patient interviews. *BMJ Open*. 2020;**10**(5):e033449.

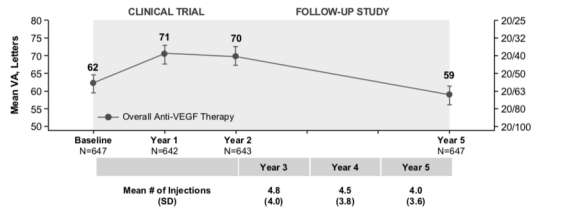
13

What are the Effect of Lapse of Treatment?

14

Poor Real-world Vision Outcomes

5-Year CATT Follow-up Study (n=647)[a]



CATT = Comparison of Age-related Macular Degeneration Treatments Trials; SD = standard deviation; VA = visual acuity.
CATT Research Group. *Ophthalmology*. 2016;123(8):1751-1761.

15

Vision Outcomes Correlated to Number of IVT Anti-VEGF Injections Received Per Year

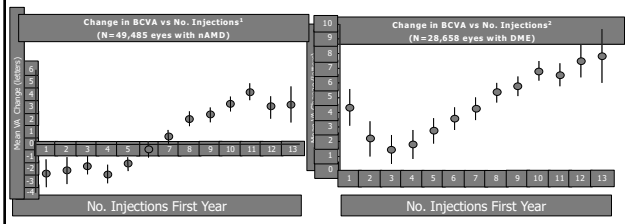
Results From 1 Year: IVT Anti-VEGF Monotherapy[a,1-11]

		Clinical Trial Data	Real-World Data
nAMD	Mean change in BCVA from baseline (ETDRS letters)	6.6-11.3	0.4-1.1
	Injections/year (mean number)	7.5-12.5	6.0-7.6
DME	Mean change in BCVA from baseline (ETDRS letters)	10.7-12.5	4.2
	Injections/year (mean number)	3.4-12.2	6.4

[a]Data from patients previously enrolled in clinical and real-world trials who received fixed and PRN dosing intervals of anti-VEGF monotherapy; trials conducted at different time periods. BCVA = best-corrected visual acuity; ETDRS = Early Treatment Diabetic Retinopathy Study; IVT = intravitreal; PRN = as needed.
1. Brown DM, et al. *N Engl J Med*. 2006;355:1432-1444; 2. Busbee BG, et al. *Ophthalmology*. 2013;120:1046-1056; 3. Heier JS, et al. *Ophthalmology*. 2012;119:2537-2548; 4. Rosenfeld PJ, et al. *N Engl J Med*. 2006;355:1419-1431; 5. Dugel PU, et al. *Ophthalmology*. 2020;127(1):72-84; 6. Martin DF, et al. *N Engl J Med*. 2011;364(20):1897-1908; 7. Khanani AM, et al. *Ophthalmol Retina*. 2020;4(2):122-133; 8. Kiss S, et al. *Ophthalmology*. 2020;127(9):1179-1188; 9. Ciulla TA, et al. *Ophthalmol Retina*. 2020;4(1):19-30; 10. Korobelnick JF, et al. *Ophthalmology*. 2014;121(11):2247-2254; 11. Ciulla TA, et al. *Br J Ophthalmol*. 2021;105(2):216-221.

16

A Higher Number of Anti-VEGF Injections Correlates With Better Vision Outcomes in nAMD and DME



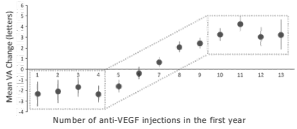
DME = diabetic macular edema.
1. Ciulla TA, et al. *Ophthalmol Retina*. 2020;4(1):19-30. Open Access. https://creativecommons.org/licenses/by-nc-nd/4.0.
2. Ciulla TA, et al. *Br J Ophthalmol*. 2021;105:216-221. Open Access. https://creativecommons.org/licenses/by-nc-nd/4.0.

17

Real-world nAMD Outcomes Data

Vision Correlates With Number of Anti-VEGF Injections

Retrospective Study of US Electronic Medical Records (2012-2016) Patients With Treatment-naive nAMD (N=49,485 eyes)[1,a]



There is a relationship between the number of injections received per year and mean change in visual acuity[1]

Results From 1 Year of Anti-VEGF IVT Monotherapy[1-5,b]

	FDA-labeling data[2,b,c]	Real-world data[1,4,5,d]
Mean number of injections/year	8-12	6.0-7.6
Mean change in BCVA from baseline, ETDRS letters	6.3-11.0	0.6-1.1

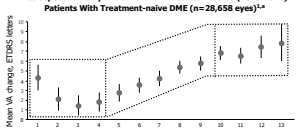
Patients with nAMD receive fewer injections in the real world compared with clinical trials[1-5]

[a]This retrospective study assessed anti-VEGF therapy intensity and its relationship with VA change in real-world patients with nAMD (N=49,485 eyes). The analyses were performed on a large database of aggregated, longitudinal medical records of treatment-naïve patients with nAMD who underwent anti-VEGF monotherapy injections between January 2012 and October 2016. [b]Table includes data from patients with nAMD previously enrolled in clinical and real-world trials who received fixed and PRN dosing intervals of anti-VEGF monotherapy. These trials were conducted at different time periods. [c]Data reflect dosing and outcomes reported in FDA-labeling for ranibizumab and aflibercept. As brolucizumab data are not yet reflected in real-world studies, FDA-labeling data for brolucizumab have been excluded. [d]Data reflect real-world dosing and outcomes for patients treated with ranibizumab, bevacizumab, or aflibercept. BCVA = best-corrected visual acuity; ETDRS = Early Treatment Diabetic Retinopathy Study; IVT = intravitreal; PRN = pro re nata; VEGF = vascular endothelial growth factor.
1. Ciulla TA, et al. *Ophthalmol Retina*. 2020;4(1):19-30. Open Access under a CC BY-NC-ND 4.0 license; Data from 2. Aflibercept. Package insert. Regeneron Pharmaceuticals, Inc; 2019; 3. Aflibercept. Package insert. Regeneron Pharmaceuticals, Inc; 2021; 4. Khanani AM, et al. *Ophthalmol Retina*. 2020;4(2):122-133. Open Access under a CC BY-NC-ND 4.0 license; 5. Kiss S, et al. *Ophthalmology*. 2020;127(9):1179-1188. Open Access under a CC BY-NC-ND 4.0 license.

18

Real-world DME Outcomes Data
Vision Correlates With Number of Anti-VEGF Injections

Retrospective Study of US Electronic Medical Records (2013-2018)
Patients With Treatment-naive DME (n=28,658 eyes)[1,a]



Results From 1 Year of Anti-VEGF IVT Monotherapy[1,2,b]

	FDA-labeling data[2,c]	Real-world data[1,d]
Mean number of injections/year	8-12	6.4
Mean change in BCVA from baseline, ETDRS letters	10.5-12.5	4.2

Patients with DME receive fewer injections in the real world compared with clinical trials[1]

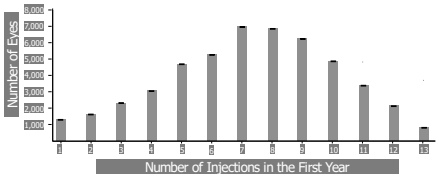
[a]This retrospective study assessed anti-VEGF monotherapy injection intensity and its relationship with changes in VA in real-world patients with DME (n=28,658 eyes). The analyses were performed on a database of aggregated de-identified electronic medical records of treatment-naive patients with DME who underwent anti-VEGF injections between January 2013 and July 2018. [b]Table includes data from patients with DME previously enrolled in clinical and real-world trials who received fixed and PRN dosing intervals of anti-VEGF monotherapy. These trials were conducted at different time periods. [c]Data reflect dosing and outcomes reported in FDA-labeling for ranibizumab and aflibercept. As brolucizumab data are not yet reflected in real-world studies, FDA-labeling data for brolucizumab have been excluded. [d]Data reflect real-world dosing and outcomes for patients treated with ranibizumab, bevacizumab, or aflibercept. DME = diabetic macular edema.

1. Ciulla TA, et al. *Br J Ophthalmol.* 2021;105(2):216-221. Open access under a CC BY-NC 4.0 license; 2. Aflibercept. Package insert. Regeneron Pharmaceuticals, Inc; 2021.

19

Real-world nAMD Patients in the US Are Receiving Fewer Injections Than Those in Clinical Trials

Retrospective Study of US Electronic Medical Records (2012-2016)
Patients with treatment-naive nAMD who underwent anti-VEGF injections[a]



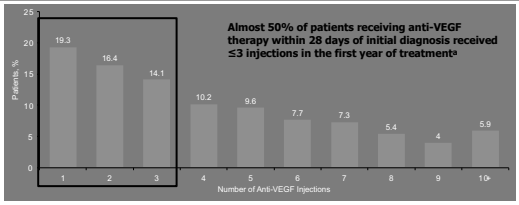
[a]This retrospective study assessed anti-VEGF therapy intensity and its relationship with VA change in real-world patients with nAMD (N=49,485 eyes). The analyses were performed on a large database of aggregated, longitudinal medical records of treatment-naive patients with nAMD who underwent anti-VEGF injections between January 2012 and October 2016.

Ciulla TA, et al. *Ophthalmol Retina.* 2020;4:19-30. Open Access. https://creativecommons.org/licenses/by-nc-nd/4.0.

20

Real-world DME Patients Receive Fewer Injections Than Those in Clinical Trials

AAO IRIS Registry Analysis (n=13,410)[1]

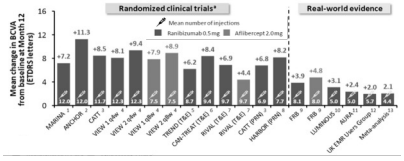


AAO = American Academy of Ophthalmology; IRIS = Intelligent Research in Sight.
[a]This large-scale, retrospective study investigated the mean number of anti-VEGF injections administered in real-world patients (n=13,410) with new-onset DME in the AAO IRIS Registry who were diagnosed between July 2013 and March 2016 and who initiated anti-VEGF treatment within the first 28 days following diagnosis.

1. Willis TA, et al. Presented to AAO Board Meeting; May 5, 2020; Virtual.

21

Intravitreal Injections of Anti–VEGF Have Limitations in the Real World



*Ranibizumab monthly and aflibercept bimonthly dosing unless stated otherwise.

BCVA = best-corrected visual acuity; ETDRS = early treatment diabetic retinopathy study; PRN = pro re nata; q#w = every # weeks; T&E = treat and extend; VEGF = vascular endothelial growth factor.

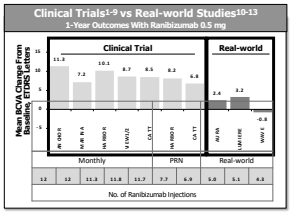
1. Rosenfeld PJ, et al. N Engl J Med. 2006;355(14):1419-1431; 2. Brown DM, et al. N Engl J Med. 2006;355(14):1432-1444; 3. CATT Research Group. N Engl J Med. 2011;364(20):1897-1908; 4. Heier JS, et al. Ophthalmology. 2012;119(12):2537-2548; 5. Silva R, et al. Ophthalmology. 2018;125(1):57-65; 6. Kertes PJ, et al. Ophthalmology. 2019;126(6):841-848; 7. Gillies MC, et al. JAMA Ophthalmol. 2019;137(4):372-379; 8. Busbee BG, et al. Ophthalmology. 2013;120(5):1046-56; 9. Gillies MC, et al. Ophthalmology. 2016;123(12):2545-53; 10. Holz FG, et al. Presented at: EURETINA 2017; Sept 7-10, 2017; Barcelona, Spain; 11. Holz FG, et al. Br J Ophthalmol. 2015;99(2):220-226; 12. Writing Committee for the UK Age-Related Macular Degeneration EMR Users Group. Ophthalmology. 2014;121(5):1092-1101; 13. Kim LN, et al. Retina. 2014;34(8):1618-1631.

22

Clinical Trial vs Real-world Anti-VEGF Results: Undertreatment May Result in Suboptimal Vision Outcomes

- Real-world visual acuity outcomes fall short of clinical trial results
- Frequent monitoring and injections are a significant burden on patients, caregivers, and physicians
- A solution is needed to reduce treatment burden and improve real-world patient outcomes

Clinical Trials[1-9] vs Real-world Studies[10-13]
1-Year Outcomes With Ranibizumab 0.5 mg



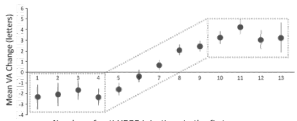
BCVA = best-corrected visual acuity; ETDRS = Early Treatment Diabetic Retinopathy Study; PRN = as-needed.

1. Brown DM, et al. *N Engl J Med.* 2006;355(14):1432-1444; 2. Brown DM, et al. *Ophthalmology.* 2009;116(1):57-65.e5; 3. Busbee DM, et al. *Ophthalmology.* 2013;120(5):1046-1056; 4. Heier JS, et al. *Ophthalmology.* 2012;119(12):2537-2548; 5. Ho AC, et al. *Ophthalmology.* 2014;121(11):2181-2192; 6. Martin DF, et al. *Ophthalmology.* 2012;119(7):1388-1398; 7. Martin DF, et al. *N Engl J Med.* 2011;364(20):1897-1908; 8. Rosenfeld PJ, et al. *N Engl J Med.* 2006;355(14):1419-1431; 9. Schmidt-Erfurth U, et al. *Ophthalmology.* 2014;121(1):193-201; 10. Cohen SY, et al. *Retina.* 2013;33(3):474-481; 11. Finger RP, et al. *Acta Ophthalmol.* 2013;91(6):549-56; 12. Holz FG, et al. *Br J Ophthalmol.* 2015;99(2):220-226; 13. Holz FG, et al. *Br J Ophthalmol.* 2013;97(9):1161-1167.

23

Real-world nAMD Outcomes Data
Vision Correlates With Number of Anti-VEGF Injections

Retrospective Study of US Electronic Medical Records (2012-2016)
Patients With Treatment-naive nAMD (N=49,485 eyes)[1,a]



Results From 1 Year of Anti-VEGF IVT Monotherapy[1-5,b]

	FDA-labeling data[2,3,c]	Real-world data[1,4-5,d]
Mean number of injections/year	8-12	6.0-7.6
Mean change in BCVA from baseline, ETDRS letters	6.3-11.0	0.6-1.1

There is a relationship between the number of injections received per year and mean change in visual acuity[1]

Patients with nAMD receive fewer injections in the real world compared with clinical trials[1-5]

[a]This retrospective study assessed anti-VEGF therapy intensity and its relationship with VA change in real-world patients with nAMD (N=49,485 eyes). The analyses were performed on a large database of aggregated, longitudinal medical records of treatment-naive patients with nAMD who underwent anti-VEGF monotherapy injections between January 2012 and October 2016. [b]Table includes data from patients with nAMD previously enrolled in clinical and real-world trials who received fixed and PRN dosing intervals of anti-VEGF monotherapy. These trials were conducted at different time periods. [c]Data reflect dosing and outcomes reported in FDA-labeling for ranibizumab and aflibercept. As brolucizumab data are not yet reflected in real-world studies, FDA-labeling data for brolucizumab have been excluded. [d]Data reflect real-world dosing and outcomes for patients treated with ranibizumab, bevacizumab, or aflibercept. BCVA = best-corrected visual acuity; ETDRS = Early Treatment Diabetic Retinopathy Study; IVT = intravitreal; PRN = pro re nata; VEGF = vascular endothelial growth factor.

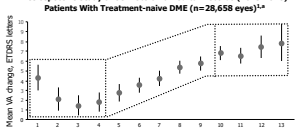
1. Ciulla TA, et al. *Ophthalmol Retina.* 2020;4(1):19-30. Open Access under a CC BY-NC-ND 4.0 license; Data from 2. Aflibercept. Package insert. Regeneron Pharmaceuticals, Inc; 2019; 3. Aflibercept. Package insert. Regeneron Pharmaceuticals, Inc; 2021; 4. Khanani AM, et al. *Ophthalmol Retina.* 2020;4(2):122-133. Open Access under a CC BY-NC-ND 4.0 license; 5. Kiss S, et al. *Ophthalmology.* 2020;127(9):1179-1188. Open Access under a CC BY-NC-ND 4.0 license.

24

Real-world DME Outcomes Data

Vision Correlates With Number of Anti-VEGF Injections

Retrospective Study of US Electronic Medical Records (2013-2018) Patients With Treatment-naive DME (n=28,658 eyes)[1,a]



Results From 1 Year of Anti-VEGF IVT Monotherapy[1,2,b]

	FDA-labeling data[2,c]	Real-world data[1,d]
Mean number of injections/year	8-12	6.4
Mean change in BCVA from baseline, ETDRS letters	10.5-12.5	4.2

Patients with DME receive fewer injections in the real world compared with clinical trials[1]

[a]This retrospective study assessed anti-VEGF monotherapy injection intensity and its relationship with changes in VA in real-world patients with DME (n=28,658 eyes). The analyses were performed on a database of aggregated de-identified electronic medical records of treatment-naive patients with DME who underwent anti-VEGF injections between January 2013 and July 2018. [b]Table includes data from patients with DME previously enrolled in clinical and real-world trials who received fixed and PRN dosing intervals of anti-VEGF monotherapy. These trials were conducted at different time periods. [c]Data reflect dosing and outcomes reported in FDA-labeling for ranibizumab and aflibercept. As brolucizumab data are not yet reflected in real-world studies, FDA-labeling data for brolucizumab have been excluded. [d]Data reflect real-world dosing and outcomes for patients treated with ranibizumab, bevacizumab, or aflibercept. DME = diabetic macular edema.

1. Ciulla TA, et al. *Br J Ophthalmol.* 2021;105(2):216-221. Open access under a CC BY-NC 4.0 license; 2. Aflibercept. Package insert. Regeneron Pharmaceuticals, Inc; 2021.

25

What is the Referral Process?

26

"Communication is KEY to successful retina co-management"

27

Process of Retina Co-management

Referring Provider
- Performs exam & identifies need for retina referral
- Discusses & educates patient regarding condition (DME, nAMD, RD, etc.)
- Discusses retina surgeon and co-management considerations
- Schedules retina referral
- Sends recent exam, special ophthalmologic testing (OCT, Fundus Photos, etc.) & consultation request

Retina Surgeon
- Evaluates and treats patients
- Discuss co-management opportunities with patient
- Sends recent exam, recommendations for treatment, next step to referring provider
- Discuss importance of follow up care with referring provider

Referring Provider
- Evaluates patients annually or PRN
- Sends recent exam, recommendations for treatment, next step to retina specialists
- Discuss importance of follow up care with retina specialist

28

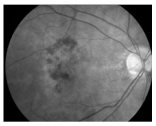
Best Practices to Improve Patient Outcomes

Risk Factor: Gives ideas of risk moving forward
- MPOD (macular pigment density)
- Genetics
- Smoking
- Family history

Diagnostic testing: Identifies presence of disease
- OCT/Fundus imaging (structural)
- Clinical exam
- Dark adaptation (functional)
- Electrodiagnostics – Flicker ERG
- Preferential hyperacuity

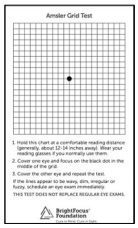
29

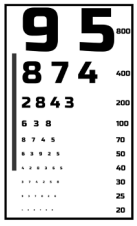
In-Office Diagnostics



30

Current and Future of At-Home Testing / Monitoring





Bellsmith KN, Gale MJ, Yang S, et al. Validation of Home Visual Acuity Tests for Telehealth in the COVID-19 Era. *JAMA Ophthalmol*. Published online March 31, 2022.
Photo access from https://www.brightfocus.org/sites/default/files/legacy/images/amsler_grid_wcag.pdf on September 26, 2022

31

Multisite Study Confirmed Automated Dark Adaptometer is Highly Sensitive, Specific & Accurate

JOHNS HOPKINS UNIVERSITY

HARVARD

PENNSTATE HERSHEY College of Medicine

High Sensitivity:
- Correctly identified **90.6%** of confirmed AMD cases

High Specificity:
- Correctly identified **90.5%** of confirmed normal cases

High Accuracy:
- **90.6%** overall accuracy

Jackson GR, et al. Invest Ophthalmol Vis Sci. 2014;55(3):1427-1431.

32

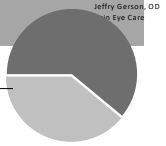
32

Undetected AMD is a Significant Problem

Sample of 100 consecutive older adults (over age 60) with **normal retinal health based on clinical exam** were tested using Dark Automated Adaptometer

GRIN EYE CARE

Jeffry Gerson, OD



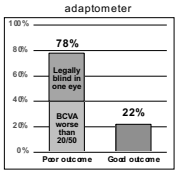
39% **(39 of 100) had previously undetected AMD**

33

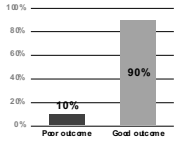
33

Primary Eye Care Has a Major Opportunity to Maintain Visual Acuity of Patients with AMD

CURRENT OUTCOMES
Without dark automated adaptometer



IDEAL OUTCOMES
with dark automated adaptometer

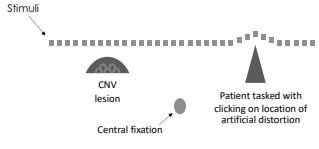


Cervantes-Castañeda RA, et al. Eye (Lond). 2008;22(6):777-781.
Olsen TW, et al. Ophthalmology. 2004;111(2):250-255.

34

34

Preferential Hyperacuity Perimetry delivers accurate, highly sensitive, specific disease detection

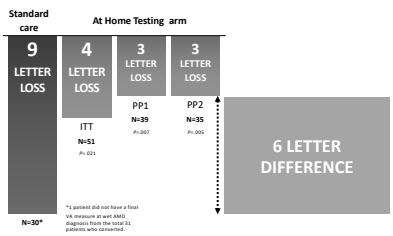


When the distortion caused by CNV is larger than the artificial distortion, the patient will preferentially pick this spot of pathological distortion

35

35

Patients who used At-Home Testing for Wet AMD lost fewer letters

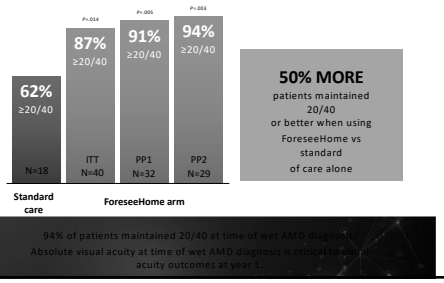


*1 patient did not have a final VA measure at wet AMD diagnosis from the total 31 patients who consented.

Reference: AREDS2-HOME Study Research Group. *Ophthalmology*. 2014;121(2):535-544.

36

More patients who used At Home Testing for Wet AMD maintained ≥20/40



50% MORE
patients maintained 20/40 or better when using ForeseeHome vs standard of care alone

94% of patients maintained 20/40 at time of wet AMD diagnosis
Absolute visual acuity at time of wet AMD diagnosis is critical for visual acuity outcomes at year 1.

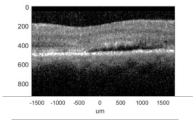
37

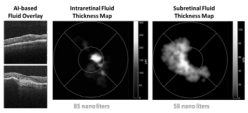
Home OCT for monitoring chronic therapy of neovascular AMD between office visits

- Monitoring of intra- and subretinal fluid based on daily patient self-imaging
- Easy-to-use, patient-operated device
- Takes less than one minute per eye
- AI algorithm analyzes images on cloud
- Remote diagnostic clinic, provider of monitoring program, reports changes meeting physician-selected fluid volume thresholds to referring physician
- 24/7 physician access to all data

Home Device

Home OCT Image



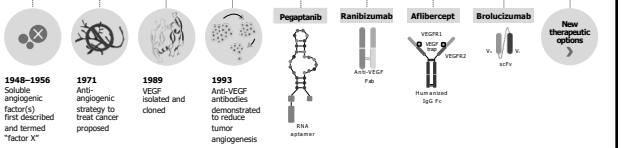


***NOT FDA APPROVED

38

Anti-VEGF Therapies Have Redefined the Care of Patients With Retinal Diseases

Historical timeline of VEGF discovery[1] | The evolution of anti-VEGF therapies for retinal disease management[2–6]



1948–1956 Soluble angiogenic factor(s) first described and termed "factor X"

1971 Anti-angiogenic strategy to treat cancer proposed

1989 VEGF isolated and cloned

1993 Anti-VEGF antibodies demonstrated to reduce tumor angiogenesis

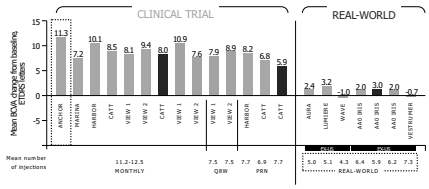
Fab = fragment antigen binding; Fc = fragment crystallizable; IgG = immunoglobulin G; scFv = single-chain fragment variable; VEGF = vascular endothelial growth factor; VEGFR = VEGF receptor; VH = heavy chain variable domain; VL = light chain variable domain.
1. Apte RS, et al. *Cell.* 2019;176(6):1248-1264; 2. Sharma A, et al. *Eye (Lond).* 2020;34(4):611-613; 3. Adamis AP, et al. *Eye (Lond).* 2020;34(11):1966-1972; 4. Ranibizumab. Package insert. Genentech; 2006; 5. Aflibercept. Package insert. Regeneron; 2011; 6. Brolucizumab. Package insert. Novartis; 2019.

39

Yet, Visual Acuity Is Not Translated From Clinical Trials to the Real World

Patients with nAMD experience worse visual outcomes in the real world because they receive fewer anti-VEGF injections compared with patients receiving fixed, frequent therapy in randomized clinical trials[1]

1 year outcomes with anti-VEGF IVT treatment[1–10]



HCPs and people living with nAMD desire a treatment that translates visual outcomes from clinical trials into the real world

AFL = aflibercept; BCVA = best-corrected visual acuity; BVZ = bevacizumab; ETDRS = Early Treatment Diabetic Retinopathy Study; HCP = health care professional; IVT = intravitreal; nAMD = neovascular age-related macular degeneration; PRN = as needed; Q8W = every 8 weeks; RBZ = ranibizumab; VEGF = vascular endothelial growth factor.
1. Ciulla TA, et al. *Ophthalmol Retina.* 2020;4(1):19-30; 2. Brown DM, et al. *N Engl J Med.* 2006;355(14):1432-1444; 3. Busbee DM, et al. *Ophthalmology.* 2013;120(5):1046-1056; 4. Heier JS, et al. *Ophthalmology.* 2012;119(12):2537-2548; 5. Martin DF, et al. *N Engl J Med.* 2011;364(20):1897-1908; 6. Rosenfeld PJ, et al. *N Engl J Med.* 2006;355(14):1419-1431; 7. Holz FG, et al. *Br J Ophthalmol.* 2015;99(2):220-226; 8. Cohen SY, et al. *Retina.* 2013;33(3):474-481; 9. Finger RP, et al. *Acta Ophthalmol.* 2013;91(6):540-546; 10. Rao P, et al. *Ophthalmologica.* 2018;[illegible]

40

Current Standard of Care for nAMD Involves Frequent Injections

Drug	Hallmark Trial	Dose	Key Finding(s)	Safety
Bevacizumab	CATT	1.25 mg Q4W	• Mean BCVA Δ +7.8 letters over 24 months • BCVA and CRT comparable to ranibizumab Q4W	• Higher systemic adverse events with bevacizumab
Ranibizumab	ANCHOR/MARINA	0.5 mg monthly	• Mean BCVA Δ +6.6 to +10 letters over 24 months	• 1.3% - 2.1% endophthalmitis • 6.2% - 10% ocular inflammation ≥1+
Aflibercept	VIEW1/VIEW2	2 mg Q4W or 2 mg Q8W	• Aflibercept noninferior to ranibizumab q4w • Mean BCVA Δ +8.4 to +9.3 letters over 52 weeks • Comparable fluid resolution between groups	• Endophthalmitis in 1% in each group in VIEW1, 0% in VIEW2
Brolucizumab	HAWK/HARRIER	6 mg Q8W or 6 mg Q12W	• Noninferior to aflibercept • Mean BCVA Δ +6.1 to +6.6 letters over 48 weeks • Superior fluid resolution compared to aflibercept	• Endophthalmitis 1% • Inflammation 4% • Rare post-marketing reports of vasculitis

CRT = central retinal thickness; Q4W = every 4 weeks; Q12W = every 12 weeks.
Rosenfeld PJ, et al. *N Engl J Med.* 2006;355(14):1419-1431; Brown DM, et al. *N Engl J Med.* 2006;355(14):1432-1444; Heier JS, et al. *Ophthalmology.* 2012;119(12):2537-2548; Dugel PU, et al. *Ophthalmology.* 2020;127(1):72-84; Boyer[illegible]

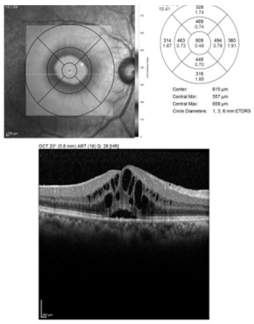
41

Novel & Pipeline Therapeutic Agents & Treatment Delivery Systems for AMD/DME in Early- or Late-stage Development to Offer Extended Duration of Action via Various Mechanisms or Delivery

- Faricimab
- Aflibercept 8 mg
- KSI-301
- OPT-302
- OCS-01
- THR-149
- UBX1325
- Port delivery system (PDS)
- Gene therapy

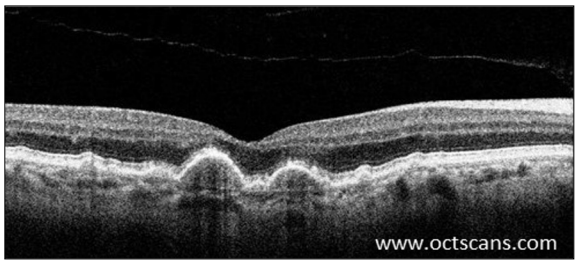
AMD = age-related macular degeneration; DME = diabetic macular edema.

42



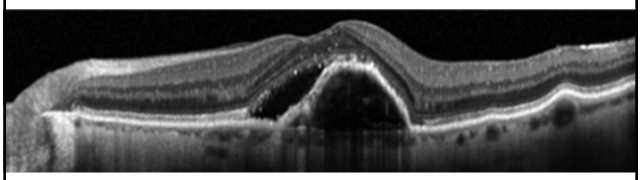
43

79 y.o. sees wavy lines

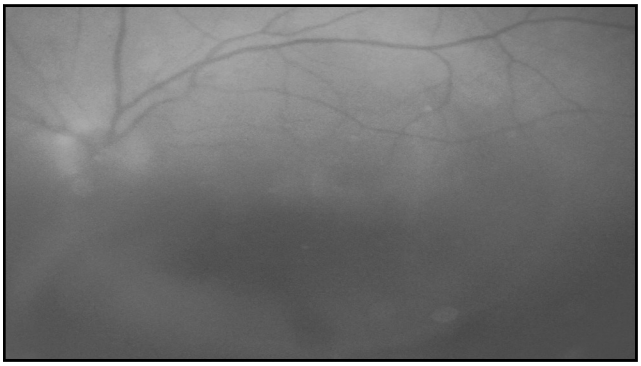


44

79 y.o. sees wavy lines



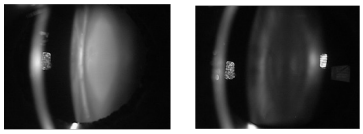
45



46

Case #1

- CC: Referred for cataract evaluation, blurred VA OD>OS
- BCVA:
  - OD -5.50+1.25X015 20/50
  - OS -1.25+1.50X180 20/20-1



47

Post-Operative One Month Follow-up

- OD phone consult – Reports decreased VA OD
- Reported VA at 1 week was uncorrected 20/20
- No observable inflammation/swelling
- Recommended f/u to clinic for OCT and start NSAIDs/Steroids

48

2nd Opinion Post Surgery

- VA OD was blurry, compliant w/ drops
- BCVA OD 20/40-1 PH/NI
- SLE: 2+SPK OD / PCIOL – 1+ PCO / (+) Macula edema
- Recommended OCT OD

49

Cystoid Macular Edema

- OCT Findings
- Fluorescein Angiography
  - If OCT findings unclear
- Assessment
  - CME OD
  - PCO OD
  - DES OD
- Plan
  - PF QID / NSAID QID
  - Refer for subtenon/intravitreal triamcinolone injection

50

Polling Question

When does cystoid macular edema most typically occur following cataract surgery?

A. 1-3 days
B. 2-3 weeks
C. 4-6 weeks
D. Anytime after surgery

51

Cystoid Macular Edema

- CME is the most frequent cause of visual decline following *uncomplicated* cataract surgery
- Late on-set (*4 to 6 weeks* post-operatively) [1]
- Estimated to occur in 1-3% of low-risk cataract cases
- CME development is due in part to prostaglandin-mediated breach of blood-retinal barrier[3]

1. Samiy N, Foster CS. The role of nonsteroidal antiinflammatory drugs in ocular inflammation. *Int Ophthalmol Clin*. 1996;36(1):195-206.
2. 2. Mishima H, Masuda K, et al. The putative role of prostaglandins in cystoid macular edema. *Prog Clin Res* 1989;31:251-264.

52

Risk Factors for CME

- Pre-existing ocular inflammation
- Diabetic retinopathy
- Any ocular vascular disease
- Cardiovascular disease
- Epiretinal / vitreoretinal membrane

53

Cystoid Macular Edema

- Self-limiting for the first several weeks
- Diagnosis: SLE, OCT, IVFA
- Treatment: *treat aggressively*
  - Steroids / NSAIDS qid X 1-3 months
    - 50% recover in 6 mos
  - Consider oral steroid, periocular steroid injection, pars plana vitrectomy
  - Acetazolamide po

54

Clinical Pearls

- All visual fluctuations are related to ocular surface disease
- Consider time course of events
- Benefit of prophylactic NSAIDs
- Communication between surgeon / referring OD

55

Case #2: JM 29 yowm

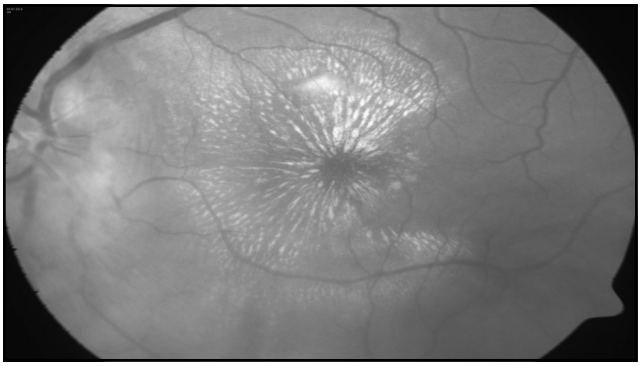
- RFV: Blurry VA OS for 2 days, yellow spot hourglass shape, constant, (-) headache, (-) N&V

56

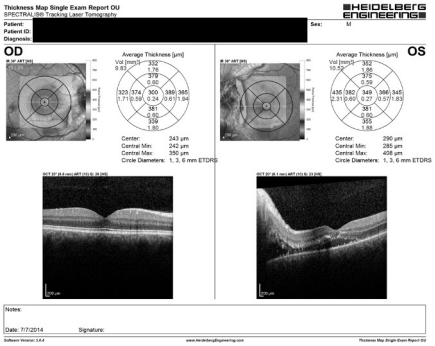
JM 29 yowm

- RFV: Blurry VA OS for 2 days, yellow spot hourglass shape, constant, (-) headache, (-) N&V
- Medical Hx: Unremarkable
- BCVA
  - OD 20/20
  - OS 20/80 NI on Pinhole
- Subjective APD OS
- Entrance tests normal except for pain on EOMs in extreme gaze OS
- SLE: Trace Cells in AC OS

57



58



59

Differentials

- Atypical Mycobacterial Diseases
- Benign reactive conditions
- Cat scratch fever
- Coccidioidomycosis (Infectious Diseases)
- Leishmaniasis
- Lyme Disease
- Lymphogranuloma Venereum (LGV)
- Malignant neoplasms
- Nocardiosis
- Sarcoidosis
- Sporotrichosis
- Syphilis
- Toxoplasmosis

60

- Assessment
  - Papillitis OS
  - Neuroretinitis OS
- Plan
  - Difluprednate QID OS
  - MRI of Head/Orbits with and without contrast
  - Order blood work to rule out infectious vs. neuro cause
  - F/u 2 weeks

61

Diagnostic Work Up

- MRI of Head and Orbits with and without contrast
- Lab Work
  - CBC with Differential
  - ESR
  - CRP
  - SMA-12
  - ANCA
  - RPR
  - Bartonella antibodies
  - Urinalysis
- Biopsy with PCR Testing
- Computed Tomography

62

1 Week Follow Up Visit

- BCVA OS 20/CF1'
- No change to SLE
- Lab Results
  - Positive for *B. Henselae* IgM and IgG
  - MRI – slight protrusion and enhancement of optic nerve
- Discuss likely cause of condition and reassured VA should improve and restore to normal levels over 1-3 months.
- Antipyretics / analgesics prn
- Doxycycline 100mg BID PO x 2 weeks

63

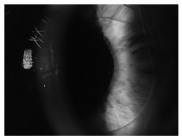
Case #3 - KS

- 74 YOWM presents for evaluation of a fog like vision and increased floaters OS since an intravitreal injection of Avastin two days prior
- Ocular History: Dry AMD OD, wet AMD OS, pseudophakic OU, macular edema OD
- Systemic Disease: Arthritis, HTN, hypercholesteremia, atrial fibrillation, hypothyroidism,
- Medications: Toprol XL, Omeprazole, Lyrica, Crestor, Synthroid, Co Q-10 and Klonopin.

64

Case Example - KS

- BCVA: OD 20/20-2 OS 20/60+2 NI with pinhole.
- Pupils: Irregular pupil OS, (-) APD
- SLE:
  - Tr injection OS
  - Fine KP and trace edema OS
  - Iris: PI @ 4:00 OS.
  - AC: 3+ cell OS
  - Lens: ACIOL in good position OS
  - 2+ Cells in PC



65

Polling Question

What is the most common symptom for patients with posterior uveitis?

A. Pain
B. Photophobia
C. Blurred vision
D. Headache

66

Diagnosis

- Acute postoperative endophthalmitis
  - Staphylococcus epidermidis accounts for nearly 60% of cases
  - Staphylococcus aureus accounts for another 20%
  - Incidence after intravitreal injection between 1/1300 to 1/10,000

67

Work Up

- Complete ocular history and examination
- Consider a B-Scan which may confirm marked vitritis and establishes a baseline against which success of therapy can be measured
- Perform culture and sensitivity studies on aqueous and vitreous samples
- TAP vs. PPV???

68

Treatment

- Intravitreal antibiotics
- Consider intensive topical steroids and intensive topical fortified antibiotics
- Atropine 1%
- Immediately pars plana vitrectomy if LP or worse
- IV antibiotics are not routinely used
- Some oral antibiotics may be considered an alternative

69

Role of Antibiotics

- Yin et al. Abx resistance of ocular surface flora with repeated use of topical abx after intravitreal injection JAMA opht. Apr 2013.
- Bascom Palmer ARVO 2011 - Topical Abs pre/post provided no benefit for reduced endophthalmitis

70

Follow-Up

- Monitor q12h
- Relief of pain is a useful early sign of response to therapy. After 48 hours patients should show signs of improvement
- Consider oral steroids
- If patient is responding well, topical fortified antibiotics may be slowly tapered after 48 hours and then switched to regular strength antibiotics
- Fortunately, endophthalmitis after intravitreal injection is rare, but clinicians should maintain a low threshold for treatment.

71

Case #4

- CC: Decreased VA OD, > 2 yrs, progressive, affects near and far, Glare OD>OS
- BCVA OD 20/70-2 PH 20/60
  OS 20/25-2 BAT 20/50-
- SLE: Cataracts OD>OS
- 12/02/08 – Unremarkable Cataract Sx OD

72

Postoperative Day 1

- Pain last night, today better
- UCVA OD: 20/40 PH 20/30
- IOP - 18 at 1:55pm
- SLE:
  - Wound secure
  - 2+ SPK
  - AC well formed with about 1+ cell
  - IOL well centered in pupil

73

Postoperative Medication

- Review medications
- No restrictions on physical activity
- Remind patient that it is normal for vision to be blurry and eyes out of balance
- F/U 1 week
- Fax results to surgeon if co-managed

74

Weekend Emergency

- CC: VA decreased and foggy, no pain
- BCVA: OD 20/200 PH/NI
- IOP: 10 mmHg
- SLE: 3-4+ cells / deep / PVD / 3+ Vitritis / Dot hemes / whitening throughout periphery
- A: Increased post op inflammation OD
- P: Prednisolone acetate q1h OD, nepafanac TID, moxifloxacin TID / F/u tomorrow

75

Thoughts???

- Sudden decrease in vision
- Increase in inflammation
- No PVD noted previously
- No pain / discomfort
- Dot hemorrhages in the periphery

76

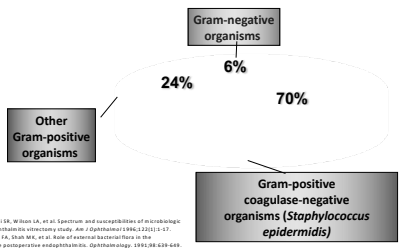
What is the Most Common Organism Found in Bacterial Endophthalmitis?

A. S. aureus
B. S. epidermidis
C. S. pneumonia
D. H. influenza

77

Endophthalmitis Vitrectomy Study

- **69% of patients with bacterial endophthalmitis were culture-positive**



1. Han DP, Wisniewski SR, Wilson LA, et al. Spectrum and susceptibilities of microbiologic isolates in the endophthalmitis vitrectomy study. *Am J Ophthalmol* 1996;122(1):1-17.
2. Speaker MG, Milch FA, Shah MK, et al. Role of external bacterial flora in the pathogenesis of acute postoperative endophthalmitis. *Ophthalmology*. 1991;98:639-649.

78

Endophthalmitis Vitrectomy Study

		VA Outcomes			
Presenting VA		20/40 or better	20/100 or better	Les than 5/100	Recommend Treatment
HM or better	TAP	62%	84%	3%	TAP
	PPV	66%	86%	5%	
Light Perception	TAP	11%	30%	47%	PPV
	PPV	33%	56%	20%	

PPV = pars plana vitrectomy and intravitreal injection of antibiotics
TAP = vitreous tap and intravitreal injection of antibiotics

http://www.nei.nih.gov/neitrials/viewstudyweb.aspx?id=29#Results

79

AMERICAN ACADEMY OF OPHTHALMOLOGY
CrossMark

Comparative Effectiveness of Antibiotic Prophylaxis in Cataract Surgery

Lisa J. Herrinton, PhD,[1] Neal H. Shorstein, MD,[2] John F. Paschal, MD,[3] Liyan Liu, MS,[1] Richard Contreras, MS,[4] Kevin L. Winthrop, MD, MPH,[5] William J. Chang, MD,[6] Ronald B. Melles, MD,[6] Donald S. Fong, MD[7]

Purpose: Intracameral injection is an effective method for preventing infection, but no controlled study has been published in the United States.
Design: We conducted an observational, longitudinal cohort study to examine the effect of topical and injected antibiotics on risk of endophthalmitis.
Participants: We identified 315 246 eligible cataract procedures in 204 515 members of Kaiser Permanente, California, 2005–2012.
Methods: The study used information from the membership, medical, pharmacy, and surgical records from the electronic health record.
Main Outcome Measures: The adjusted odds ratio (OR) and 95% confidence interval (CI) for the association of antibiotic prophylaxis (route and agent) with risk of endophthalmitis was estimated using logistic regression analysis.
Results: We confirmed 215 cases of endophthalmitis (0.07% or 0.7/1000). Posterior capsular rupture was associated with a 3.68-fold increased risk of endophthalmitis (CI, 1.89–7.20). Intracameral antibiotic was more effective than topical agent alone (OR, 0.58; CI, 0.38–0.91). Combining topical gatifloxacin or ofloxacin with intracameral agent was not more effective than using an intracameral agent alone (compared with intracameral only: intracameral plus topical, OR, 1.63; CI, 0.48–5.47). Compared with topical gatifloxacin, prophylaxis using topical aminoglycoside was ineffective (OR, 1.97; CI, 1.17–3.31).
Conclusions: Surgical complication remains a key risk factor for endophthalmitis. Intracameral antibiotic was more effective for preventing post-cataract extraction endophthalmitis than topical antibiotic alone. Topical antibiotic was not shown to add to the effectiveness of an intracameral regimen. *Ophthalmology 2016;123:287-294 © 2016 by the American Academy of Ophthalmology.*

See Editorial on page 226.

80

Next Day Visit

- Increase in pain today
- OD VA: 20/400 NI w/ Pinhole
- SLE: Central K stain w/ Dendritic appearance / 2+ Cells in AC / 3 + Cells in Vitreous / Dot hemorrhages / Retinal whitening

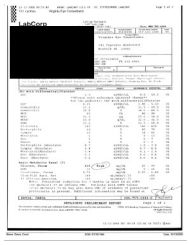
81

What's She Have????

- Possible Acute Retinal Necrosis
  - Foscarnet 2.4 mg/ 0.1cc injected intravitreally
  - Vicodin 5/325 1 tab every 4-6 hrs PRN
  - Valtrex 1000mg every 8 hrs for 10 days
  - Ordered blood cultures, fungal, PCR for VZV, HSV I, HSV 2, gram stain, CBC, Chem 7, ESR, and C-reactive protein
- Cannot r/o bacterial endophthalmitis
  - Recommend intravitreal injections of Vancomycin 1mg/0.1cc and Ceftazidime 2.25 mg/ 0.1 cc.
  - Vitreous specimen sent to lab
  - Monitor very closely

82

Lab Reports




83

Acute Retinal Necrosis

- Definition
  - Necrotizing herpetic retinitis. May present unilaterally or bilaterally (20%)
- Epidemiology
  - Usually occurs in young, healthy adults.
  - Less common are elderly and immunocompromised
  - Caused by infection with HZV or HSV
- History
  - Iritis or episcleritis
  - Rapid decline in VA with intense vitritis

84

Acute Retinal Necrosis

- Important Clinical Signs
  - Vitritis with peripheral retinal whitening that coalesces
- Associated signs
  - Iridocyclitis, photophobia, vitritis, optic neuritis, and retinal arteriolitis

85

Acute Retinal Necrosis

- Diagnosis
  - Diagnosis based on clinical exam
  - Polymerase chain reaction
  - Retinal biopsy
- Management
  - Systemic antiviral treatment
  - IV acyclovir 10mg/km tid for 7 to 10 days
  - Followed by 3 month course of acyclovir po
    - 800mg five times per day
  - Risk of RD is 8 to 12 weeks
  - Laser photocoagulation
  - Pars Plana Vitrectomy

86

Clinical Pearls

- If patient calls with symptom of sudden decrease VA or pain during the first week: the doctor *must* see the patient
- Treat as infectious until proven otherwise
- Importance of communicating with surgeon

87

Case #5

- 29 yo Caucasian female presents for evaluation of "black spot" in central vision of her left eye starting 4 days ago.
  - States sometimes spot gets very bright like "she has stared at the sun for too long"
  - Reports stable visual acuity, OU. Denies any flashes or floaters.
  - Reports constant pressure-like pain in eyes and front of face for past few months

88

Medical Hx

- Longstanding myopia, OU
- Cesarian section NOV 2019; gall bladder removed 5x ablations of endometriosis
- Latex allergy, NKDA; no current medications
- Family Hx: of HTN, Fibromyalgia, and possibly ALS
- Social history: Never smoker

89

Exam:

- BCVA: 20/20 (OD); 20/20 (OS)
- Lensometry: -5.25 OD; -5.00 OS
- IOP:17 / 19
- Confrontation Visual Fields: Full to finger count, OU
- Pupils: PERRLA (-) APD OD, OS

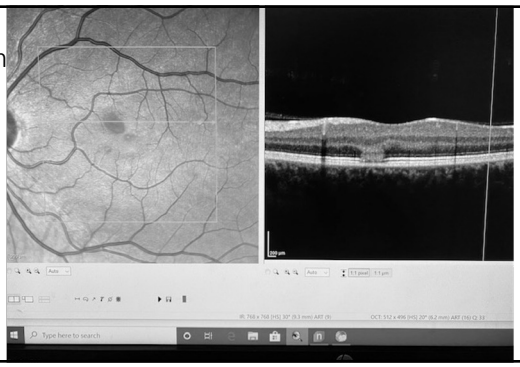
90

Exam

- Anterior Segment:
  - Cornea: Clear (-)SPK, (-) guttata, OU, (-) KPs
  - Lids/lashes/adnexa: normal, OU
  - AC: Deep & Quiet, 4/4 (-) cells/flare, OU
- Posterior Segment
  - Clear vitreous
  - ONH: Round/pink/distinct margins, 0.4 C/D ratio;
  - No pathology noted throughout OD
  - OS: RPE changes @ nasal fovea (+)FLR

91

Im



92

Differentials for Unilateral Acute Onset Scotoma in Young Female

- Idiopathic choroidal neovascularization
- Central serous chorioretinopathy
- Unilateral acute idiopathic maculopathy
- Acute posterior multifocal placoid pigment epitheliopathy (APMPPE)
- Acute macular neuroretinopathy

93

Acute Macular Neuroretinopathy

- AMN is a rare disease w/ sudden onset of unilateral, paracentral scotomas in white females in their 30s[1]
- Unclear etiology, but currently thought to originate from an ischemic attach in the deep capillary plexus of the retina
- Associated most commonly w/ fever and flu
  - Also oral contraceptives, hypotension, IV contrast, IV ephedrine, preeclampsia, and caffeine use[2]

94

Presentation

- Lesions occur 3 days—2 months after onset
  - Lesions are visible as dark gray petaloid perifoveal lesions w/ their tips pointed toward the fovea[3]
  - In OCT imaging; Hyperreflective plaques initially at the ONL and OPL which gradually resolve and are replaced by thinning
  - OCT- A show reduced blood flow
  - Can present with 20/30 vision, scotoma, floaters, metamorphopsia and photopsia[4]
- Tx and Management - None

95

Case #6

- 92 year old male presents to clinic for cataract evaluation as a referral by outside provider
- VA:
  - OD: 20/400 OS: CF @ 1ft
- Mrx:
  - OD: -3.00 Sph BCVA: 20/400
  - OS: Plano + 0.50 x 180 BCVA: 20/400
- IOP: 11OD/12OS

96

Slit Lamp Findings

- Posterior pole largely unremarkable on Dilated Fundus Exam with difficult view

97

1 Day Post Op

- VA: 20/400 OS PH: NI
- IOP: 15
- Cornea: 3+ central MCE, 1+ folds
- A/C: 1+ cell
- PCIOL in good position
- Plan
  - Continue Abx and NSAID
  - Increase steroid q2h

98

1 Week Post Op

- VA: 20/200 OS PH: NI
- Mrx: +0.50 Sphere BCVA: 20/150
- IOP: 7
- K: 1+ K edema
- A/C: trace cell
- PCIOL in good position
- Thoughts on decreased vision??
  - K edema?
  - Rotated toric axis?
  - CME?

**OD Sx scheduled for next week

99

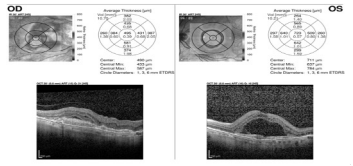
This Doesn't Make Sense??

- Dilation and OCT performed today
- IOL on axis at 175
- Posterior Segment:
  - Macula: RPE changes, loss of foveal reflex, sub-macular hemorrhages inferior to fovea

100

Diagnosis

- Exudative age related macular degeneration with active choroidal neovascularization



101

Wet AMD Treatment Options

- Photodynamic Therapy (PDT)
  - IV injection of photosensitizing dye which is concentrated in abnormal vessels
- Laser
  - Coagulates CNV
- Anti-VEGF Agents
  - Lucentis (ranibizumab)
  - Avastin (bevacizumab)
  - VEGF Trap Eye (aflibercept, Eylea)
    - Similar to Lucentis
    - Higher binding affinity

102

CASE #7 55 YO Male, New Patient

- **CC: blurry vision OD x 2 weeks**
  - Associated with mild discharge; no redness, itching, pain
  - Treated with Erythromycin ointment, oral Amoxicillin, and Refresh Tears by outside provider → no improvement

Case Courtesy of Hannah Calvelli, OD

103

EXAM FINDINGS:

OD:

- **VA:** 20/80+1
- **BEST CORRECTED:** 20/70
- **ANTERIOR SEGMENT:**
  - No active inflammation or infection
  - Posterior synechiae 12-6
- **IOP:** 12/12
- VITREOUS: Clear
- ONH: Flat, sharp, good color; c/d 0.7
- Macula: Slightly elevated

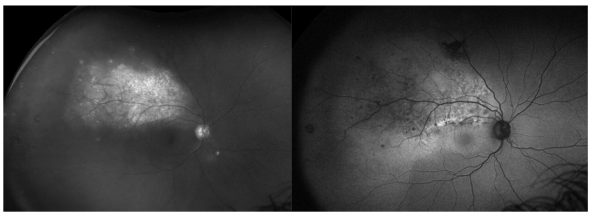
PERIPHERY:

- Elevated mass with associated hemorrhage superior arcades

- OS - Unremarkable

104

OPTOS OD: sub-retinal yellow white lesion noted sup arcade measuring ~8DD with overlying pigment mottling, mild SRF

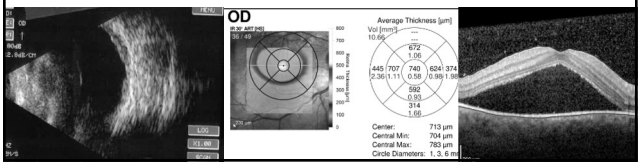


105

FA OD: area of hyper-fluorescence in the macula in the early phases which increases in intensity and size in the late phases, consistent with leakage

B-Scan OD: multiple vitreous opacities, no obvious mass, retina attached

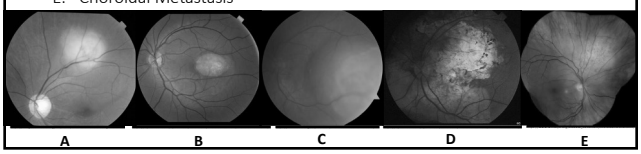
OCT OD: SRF through macula



106

DIFFERENTIAL DIAGNOSIS:

A. Choroidal Granuloma
   - Sarcoidosis, Syphillis, TB, Toxoplasmosis
B. Choroidal Hemangioma
C. Amelanotic Melanoma
D. Choroidal Osteoma
E. Choroidal Metastasis



107

ASSESSMENT/PLAN:

- **PANUVEITIS, OD**
  - Choroidal granuloma
  - History of sarcoidosis (biopsy proven)

- **MANAGEMENT:**
  - Prednisone 80mg daily taken with Prilosec.
  - Durezol QID OD and Atropine BID
  - Consult with PCP about potential steroid sparing agents in the future

108

SARCOIDOSIS:

- Systemic inflammatory disease of unknown etiology leading to formation of non-caseating granulomas
  - Exogenous agent triggers response in genetically predisposed individuals
- Can impact any organ
  - Most common = skin, lungs, lymph nodes, and eyes
- 2 peaks of incidence → 20-30 yo and 50-60 yo
  - Females 2x more likely than males
  - African American 2x more likely than Caucasians

109

OCULAR SARCOIDOSIS:

- 13-79% of systemic sarcoidosis cases
  - Presenting symptom in 20-30%
- No single defining feature
- Most common = bilateral anterior uveitis
- Posterior uveitis:
  - Usually bilateral, can be asymmetric
  - Granulomas unifocal or multifocal; various sizes
  - Perivascular sheathing/ mid-peripheral periphlebitis common ("candle-wax drippings")
  - #1 cause of vision loss = CME
- Long term complications = chronic maculopathy, cataract, glaucoma

TABLE 3 Involvement of Ocular and Adnexa in Sarcoidosis

Orbit	Orbital, lacrimal gland or extraocular muscles granulomas
Lid	Granuloma
Conjunctiva	Granuloma Conjunctivitis
Sclera	Scleritis episcleritis
Cornea	Interstitial keratitis
Anterior chamber	Granulomatous or nongranulomatous anterior uveitis
Pars Plana	Intermediate uveitis
Vitreous	Vitreitis
Retina	Periphlebitis Retinitis
Choroid	Multifocal choroiditis Granuloma Coalescent choroidal infiltration
Optic nerve	Papillitis Papilledema Granuloma Retrobulbar optic neuropathy

Bonfioli AA, Orefice F. Sarcoidosis. *Seminars in Ophthalmology*. 2005; 20: 177-182. Doi: 10.1080/08820530500231938.

110

IWOS CLASSIFICATION:

- IWOS = International Workshop on Ocular Sarcoidosis
- Gold standard for diagnosis = tissue biopsy
- Ocular granulomas rarely biopsied due to potential risk
- **Initial IWOS criteria 2009** → revised 2017
  - ***Definite*** = biopsy proven with compatible uveitis
  - ***Presumed*** = diagnosis not supported by biopsy, but bilateral lymph adenopathy (BHL) present with 2 ocular signs
  - ***Probable*** = diagnosis not supported by biopsy and BHL absent, but 3 ocular signs and 2 suggestive systemic labs

I. Other causes of granulomatous uveitis must be ruled out.
II. Intraocular clinical signs suggestive of OS.
1. Mutton-fat keratic precipitates (large and small) and/ or iris nodules at pupillary margin (Koeppe) or in stroma (Busacca).
2. Trabecular meshwork nodules and/or tent-shaped peripheral anterior synechia.
3. Snowballs/string of pearls vitreous opacities.
4. Multiple chorioretinal peripheral lesions (active and atrophic).
5. Nodular and/or segmental periphlebitis (±candle wax drippings) and/or macroaneurysm in an inflamed eye.
6. Optic disc nodule(s)/granuloma(s) and/or solitary choroidal nodule.
7. Bilaterality (assessed by ophthalmological examination including ocular imaging showing subclinical inflammation).
III. Systemic investigation results in suspected OS.
1. Bilateral hilar lymphadenopathy (BHL) by chest X-ray and/or chest computed CT scan.
2. Negative tuberculin test or interferon-gamma releasing assays.
3. Elevated serum ACE.
4. Elevated serum lysozyme.
5. Elevated CD4/CD8 ratio (>3.5) in bronchoalveolar lavage fluid.
6. Abnormal accumulation of gallium-67 scintigraphy or 18F-fluorodeoxyglucose positron emission tomography imaging.
7. Lymphopenia.
8. Parenchymal lung changes consistent with sarcoidosis, as determined by pulmonologists or radiologists.

Mochizuki M, Smith JR, Takase H, Kaburaki T, Acharya NR, Rao NA. Revised criteria of International Workshop on Ocular Sarcoidosis (IWOS) for the diagnosis of ocular sarcoidosis. *Br J Ophthalmol*.

111

MANAGEMENT OPTIONS:

- Steroids = 1st line therapy
  - Topical, intraocular, oral
- Immunosuppressants
  - Methotrexate, mycophenolate mofetil, azathioprine, cyclosporine
- Biologics
  - TNF-a inhibitors (Infliximab)

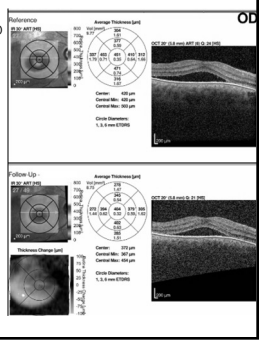
** Prognosis depends on severity & timing of treatment initiation

112

FOLLOW UP #1 (2 weeks post-dx):
- OCT: improved SRF, improved choroidal thickening OD
- Begin to taper Prednisone by 10mg every week
- Taper Durezol to BID. Continue Atropine BID

FOLLOW UP #2 (3 weeks post-dx):
- 1mL Sub-Tenon Kenalog 40mg injection performed without complication
- Continue Prednisone taper
- Continue with Durezol BID OD and Atropine BID OD

FOLLOW UP #3 (4 weeks post-dx):
- s/p Sub-T Kenalog injection
- OCT: improving SRF, no IRF OD
- Labs ordered: ACE, CBC, FTA-ABS, RPR, TOXO IGG
- Continue Prednisone 40mg/day. Continue Atropine BID OD. D/C Durezol.



113

CONCLUSION:

- Sarcoidosis should be on the differential for any ocular inflammatory findings!
- Posterior manifestations hold a higher risk of long-term complications
- Timely treatment and coordination with rheumatology/PCP are critical for long term management

114

Case #8

34-year-old female
Referred by OD for central retinal artery occlusion

- **Chief Complaint**
  - Blurry vision OU for 14 days. Noticed stomach discomfort around the same time. Vision gradually became worse. Hospitalized for 5 days – acute pancreatitis
- **Review of Symptoms:** negative
- **Medical History:** Anxiety
- **Medications:**
  - Wellbutrin, Xanax, Zoloft
- **Ocular History:** Unremarkable
- **Family History:** Unremarkable

Case Courtesy of James Dowgin, 4th Year Extern, PUCO

115

VA's
- OD: CF3 PH: NI
- OS: CF3 PH: NI

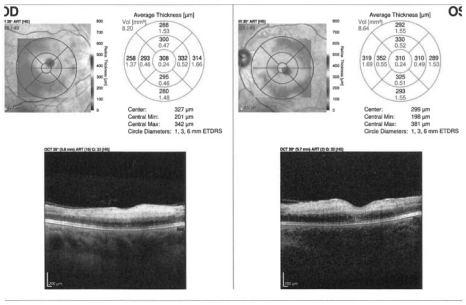
Pupils
- OD sluggish pupil
- OS: APD +1

CVF abnormal – poor central vision

Pressures
- 12 mmHg OU

- **Anterior segment** Unremarkable
- **Posterior segment**
  - Vitreous: clear
  - ON: Cotton wool spots around optic nerve OU
  - Macula: cherry red spot OU
  - Vessels: attenuated OU
  - Periphery: dot heme superior OS

116



117

Impression:
- Central retinal artery occlusion, bilateral
  - Purtscher's retinopathy – h/o pancreatitis
  - OCTM
    - OD: VMA with extensive inner hyper reflectivity
    - OS: ellipsoid zone disruption with VMA with extensive inner retinal hyper reflectivity
  - OCTA: macular ischemia OU

Plan:
- Observe. Educated that vision expected to improve over time, although it will never return to normal. Explained there is no proven treatment. Steroid injections around the eye are a potential treatment option in the future, will hold off for now. Recheck in 1 month with FA.

118

1 month later

Blood work came back with increased Toxoplasmosis IgM titers

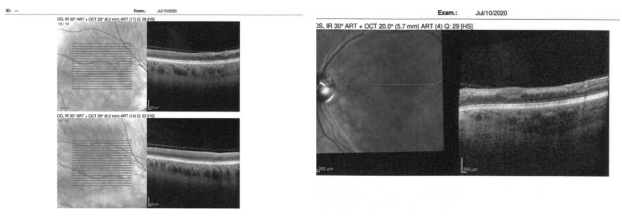
VA's
- OD 20/400 PH: NI
- OS 20/400 PH: NI

Pupils No APD OU

CFV Full to finger count

Posterior Segment
- Vitreous: Clear
- ON: mild pallor
- Macula: improving soft exudates
- Vessels: Normal
- Periphery: Normal

119



120

Impression:
- Central retinal artery occlusion, bilateral
  - Purtscher's retinopathy – h/o pancreatitis
  - FA: early patchy hyperflourescence with very mild increase in intensity seen in late phases, no increase in size oh hyperflourescence, no leakage OU
  - Fundus photos: OD improving soft exudates around posterior pole, mild pallor of nerve and macula, mild arterial attenuation, no signs of peripheral NVE OU

Plan:
- Condition is improving. Observe, recheck in 1 month. Discussed seeing infectious disease physician

121

Purtscher Retinopathy

- Usually due to a compression injury to the head, chest, or lower extremities – without direct trauma to the globe
- With features like Purtscher retinopathy without trauma, it is called Purtscher-like retinopathy.
  - Can be caused by acute pancreatitis, chronic renal failure, autoimmune diseases, fat embolism, amniotic fluid embolism, retrobulbar anesthesia, and orbital steroid injection among other things.[2]
- Symptoms:
  - Decreased vision – usually sudden (within 2 days of trauma)[3]
- Signs:
  - Multiple cotton wool spots around optic nerve, sometimes accompanied with superficial hemorrhages.
  - Can have larger areas of superficial retinal whitening, serous macular detachment, tortuous vessels, hard exudates, optic disc edema, RAPD, and optic atrophy of chronic.[1]
  - Usually bilateral, but may be asymmetric

122

Purtscher Retinopathy

Incidence of symptomatic Purtscher's estimated to be 0.24 cases per million per year – however, many cases or asymptomatic.

Differential diagnosis:
- Hypertensive retinopathy
- Lupus retinopathy
- Partial CRAO
- Endogenous endophthalmitis
- Retinitis
- Giant cell arteritis
- HIV retinopathy
- Ischemic central retinal venous occlusion
- Post-febrile retinitis
- Commotio retinae

Tripathy K, Patel BC. Purtscher Retinopathy. [Updated 2020 Jul 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK542167/

123

Purtscher Retinopathy

Etiology
- Possible due to occlusion of small arterioles in peripapillary retina via compliment activation, fibrin clots, platelet-leukocyte aggregates, or fat emboli.

Evaluation
- FA - blockage of choroidal fluorescence by the whitened opaque retina, macular ischemia/infarction, capillary nonperfusion, focal areas of arteriolar occlusion, paravascular staining and leakage from the optic nerve head
- OCT
  - acute: inner retinal hyperreflectivity.
  - Late: retinal thinning, photoreceptor loss.
- Visual Field – may show central, paracentral, or arcuate scotoma
- Others
  - Amylase/lipase levels, MRI, ANA, compliment component C5.

Tripathy K, Patel BC. Purtscher Retinopathy. [Updated 2020 Jul 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK542167/

124

Purtscher Retinopathy

Prognosis can be variable. Poor prognostic factors include:
- Macular infarction
- A long duration of acute retinal changes
- Optic disc swelling
- Choroidal hypoperfusion
- Severe retinal capillary nonperfusion
- Prior episode of Purtscher retinopathy in the same eye
- Involvement of the outer retina

Long term complications:
- Optic atrophy/ optic disc pallor
- Retinal pigment epithelial atrophy
- Thinning of the retinal nerve fiber layer
- Foveal thinning
- Attenuation or sheathing of retinal vessels

Treatment:
- None, treat underlying condition if present.

Tripathy K, Patel BC. Purtscher Retinopathy. [Updated 2020 Jul 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK542167/

125

Conclusions

- Numerous advances in retina procedures and treatments
- Embrace technology to improve patient care
- Continuous communication is key to effective comanagement

THANK YOU!!!

wwhitley@cvphealth.com

126