Macular Degeneration and Diabetic Retinopathy: Past, Present & Future

Daniel K. Bennett, M.D.

Disclosures

- Genentech – Speaker and Advisor
AMD Statistics

- Health Care Cost
  - $98 billion in U.S., Canada and Cuba
  - $343 billion worldwide
- Cost of Vision Loss (All Causes)
  - ~$700 billion in U.S.
  - ~$3 trillion worldwide
- Substantially higher cost >64yo

Diabetes Statistics

HOW COMMON IS DIABETES?
Age-adjusted prevalence of diagnosed diabetes in US adults


<4.5%
4.5%-5.9%
6.0%-7.4%
7.5%-8.9%
≥9.0%

Please see selected important safety information provided throughout this presentation and the provided full prescribing information.

Imaging

![Fundus photo of Wet AMD](image)

Physiology

- Family of Genes:
  - VEGF-A
    - Dimeric 36-46 kDa glycosylated protein
    - 4 isoforms with varying amino acid chain lengths: 121, 165, 189, 206
    - Longer chains are matrix bound, shorter are freely diffusible
  - VEGF-B/C/D/E
  - PlGF (placental growth factor)
  - PDGF (platelet growth factor)
“You have to know the past to understand the present.”
- Carl Sagan
Learning from our mistakes...

Laser Photocoagulation

- Macular Photocoagulation Study (MPS)
  - Argon or krypton laser for extra- and juxtafoveal classic SRNVM versus observation alone
  - Slowed progression, but eventual loss of foveal vision
- Photodynamic Therapy (PDT)
  - Non-thermal, reactive O₂ molecules
"I am in the present. I cannot know what the future will bring forth. I can only know what the truth is for me today. That is what I am called upon to serve, and I serve it in all lucidity."

- Igor Stravinsky

Bevacizumab (Avastin, Genentech/Roche)

- Complete IgG molecule, weight 149 kDa
- Binds all forms of VEGF
- FDA approved to treat metastatic colorectal, breast, and lung cancer in 2004
Ranibizumab (Lucentis, Genentech/Roche)

- Approved June, 2006
- 48 kDa Fab fragment of a recombinant humanized IgG1 kappa monoclonal Ab binds to VEGF-A (including biologically active form VEGF110)}
Ranibizumab Trials

- MARINA (ranibizumab 0.3 or 0.5 mg vs sham)
- ANCHOR (ranibizumab vs PDT)
- SAILOR (long-term safety and efficacy of ranibizumab)
- FOCUS (ranibizumab + PDT vs PDT)
- PIER (ranibizumab at fixed intervals)
- PrONTO (PRN tx with ranibizumab)
- HORIZON (extension of MARINA, ANCHOR and FOCUS)
- RADIANCE (tx in mCNV)
- Protocol S (tx in DR)
RISE and RIDE

Protocol S
Aflibercept (Eylea, Regeneron)

- Fusion protein of key domains from VEGFR1 and VEGFR2 with human IgGFc
  - Produced in recombinant Chinese hamster ovary cells
  - Binds VEGF-A and PIGF

- VIEW1 and VIEW2
  - aflibercept vs ranibizumab (4 groups)
  - Year 2 was a capped PRN regimen across tx and comparator arms

- Results:
  - aflibercept 2 mg dosed every 2 months (after 3 monthly injections) showed equivalence to monthly ranibizumab
Surgical Case

- 75yo white male
- Significant decrease VA OD over the past week
- PMHx: Atrial fibrillation
- Meds: Eliquis, ASA 81mg

Count Fingers at 2'  20/32
Tissue Plasminogen Activator
Follow Up

20/40 PH: 20/25

Have we peaked?
“For time and the world do not stand still. Change is the law of life. And those who look only to the past or present are certain to miss the future.”
- John F. Kennedy
ForSight VISION4 (Genentech)

- Port Delivery System
- Refillable, non-biodegradable

Brolucizumab (Novartis)
All RTH258 patients start on q12w immediately following loading; if disease activity is seen, interval adjusted to q8w. Aflibercept is dosed every 8-weeks per label.
DARPin (Allergan)

- Abicipar Pegol
  - Currently in phase III
  - Designed ankyrin repeat proteins
  - Inhibits all relevant subtypes of VEGF-A with high potency
  - Dosing every 3-4 months
  - E. coli = CHEAP
Primary Endpoint: STABLE VISION Abicipar Q8 and Q12 Non-Inferior to Ranibizumab Q4 With Fewer Injections

SEQUOIA – Study 006
BCVA: Percent of Patients with Stable Vision (PP)

Primary Endpoint: STABLE VISION Abicipar Q8 and Q12 Non-Inferior to Ranibizumab Q4 With Fewer Injections

CEDAR – Study 005
BCVA: Percent of Patients with Stable Vision (PP)
Fovista (Ophthotech)

- Anti-PDGF drug
- Promising results in combo with Lucentis in phase I/IIa trial, but did not meet phase III endpoint
- Patients not responsive to monotherapy
- Dual mechanism of action
  - Anti-angiogenic
  - Anti-fibrotic

Treatment-Emergent Adverse Events:
- Overall Summary - SEQUOIA
- Treatment-Emergent Adverse Events:
- Overall Summary - CEDAR

* Company hypothesis with respect to MOA.
Squalamine Lactate (Ohr)

- Counteracts VEGF, PDGF and bFGF (basic fibroblast growth factor)
- IMPACT study failed in phase III
- Early results showed improvement in subretinal hyperreflective material (SHRM)
- Anti-angiogenic and anti-fibrotic effects

Bevasiranib (Opko) - Discontinued
- RNA induced protein silencing complex (siRNA) designed to silence VEGF-A mRNA
- CARE (Cand5 Anti-VEGF RNAi Evaluation) study
  - 1st time siRNA has made a phase III trial
**Tyrosine Kinase Inhibitors**

- Vatalanib (Novartis)
  - Binds intracellular kinase domain of all VEGF receptor subtypes
  - Benefit: High bioavailability provides advantage of **PO dosing**

- Pazopanib (Glaxo-Smith-Kline)
  - Inhibits VEGFR1, -2, -3, c-kit, and PDGFR
  - Benefit: **Topical administration**

- TG10081 (Targegen)

**Epiretinal Strontium-90**

- VIDION system (NeoVista)
- Monotherapy or combo with Avastin
- Phase III trials

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<table>
<thead>
<tr>
<th>Tissue</th>
<th>Effect</th>
<th>Reported thresholds for clinically observable radiation damage</th>
<th>Dose delivered during epimacular brachytherapy</th>
<th>Dose delivered during stereotactic radiosurgery</th>
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</thead>
<tbody>
<tr>
<td>Lens</td>
<td>Cataract</td>
<td>2 Gy</td>
<td>0.00056 Gy</td>
<td>0.12-0.13 Gy</td>
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<tr>
<td>Retina</td>
<td>Radiation retinopathy</td>
<td>35-55 Gy</td>
<td>24 Gy</td>
<td>16-24 Gy</td>
</tr>
<tr>
<td>Optic nerve</td>
<td>Optic neuropathy</td>
<td>&gt;55 Gy</td>
<td>2.4 Gy</td>
<td>0.2-0.37 Gy</td>
</tr>
</tbody>
</table>
The Power of Wine…

- CABERNET (CNV Secondary to AMD Treated with Beta Radiation Epiretinal Therapy)
  - Epimacular brachytherapy using a prototype device
  - Goal to reduce treatment burden

- MERLOT (Macular Epiretinal Brachytherapy Versus Lucentis Only)
  - Extension of CABERNET with identical anti-VEGF regimen in control and treatment arms

IRay (Oraya Therapeutics)

- Low-voltage, stereotactic, highly targeted X-rays
- + Lucentis
Tissue Engineering

- Maculoplasty
  - Reconstitution of normal submacular architecture
  - Repair patchy loss of RPE cells and disruption of RPE-photoreceptor interface by fibrovascular tissue
- 3 Steps:
  1. Repair damaged cells
  2. Immune suppression
  3. Replace Bruch’s

Geographic Atrophy
APL-2 (Apellis Pharmaceuticals)
- Complement C3 inhibitor
- Intravitreal injection

FILLY

Primary Endpoint: GA Lesion Growth

- APL-2 Monthly (n=84)
- APL-2 EOM (n=78)
- Sham Pooled (n=80)

LS Mean (SE) Change from Baseline in Squint Root GA Lesion (mm)

- p=0.067 vs Sham
- p=0.008 vs Sham
Thank You!

Questions?
Sudden Vision Loss

Daniel K. Bennett, M.D.

Causes

- Opacity
  - Cornea
  - Vitreous
- Retinal
  - Detachment
  - Vascular
  - Hemorrhage (Retina and Vitreous)
- Optic nerve and visual pathways
  - Ischemic optic neuropathy
  - CVA
  - Migraine
- Trauma
Macular Hemorrhage

- Causes:
  - CNVM
    - Wet AMD
    - Myopia
    - Angioid Streaks
  - Retinal arterial macroaneurysm
  - PDR
  - Valsalva
  - CRVO/BRVO
  - Terson Syndrome
  - Trauma
Retinal Vein Occlusion

- Central vs Hemiretinal vs Branch
  - Central: level of the optic nerve
  - Hemiretinal: primary superior or inferior branch
  - Branch: distal branch

Pathophysiology

- CRVO
  - Fibrin and platelet thrombus at or posterior to the lamina cribrosa
  - Virchow triad: venous stasis, endothelial injury, and hypercoagulability

- BRVO
  - Compression of the vein by atherosclerotic retinal arteries
  - Common sheath
Ischemic vs Nonischemic

- Nonischemic CRVO
  - 75-80% of cases, can progress to ischemic
  - Milder clinical presentation
  - Better overall prognosis
  - Neovascularization rare

- Ischemic CRVO
  - Marked vision decrease (often 20/400 or worse)
  - Anterior segment neovascularization

Angiography
Complications

- Macular edema
- Macular ischemia
- Retinal neovascularization and vitreous hemorrhage
- Rubeosis irides and neovascular glaucoma
Treatment

- Anti-VEGF
  - Avastin (bevacizumab)
  - Lucentis (ranibizumab)
  - Eylea (aflibercept)
- Corticosteroids (IVT or STK)
- Panretinal or focal photocoagulation

Diabetic Retinopathy

- Leading cause of new blindness ages 25-74
- Increasing incidence:
  - Sedentary lifestyle
  - High fat diets
  - Decreasing exercise habits
- Ophthalmic manifestations:
  - Cornea
  - Cataract
  - Iris NV and glaucoma
  - Retinopathy
  - Neuropathy
Diabetes Control & Complications Trial

- Intensive glycemic control
  IDDM reduced
- Goal hemoglobin A1c 6-7%
- Patient education critical!!

Signs

- Non-proliferative diabetic retinopathy
  A. Mild: 1 or more microaneurysms
  B. Moderate: hemorrhages, microaneurysms, hard exudates
  C. Severe: 4-2-1 rule
     I. 4 quadrants of microaneurysms and intraretinal hemorrhages
     II. 2 quadrants of venous beading
     III. 1 quadrant of intraretinal microvascular abnormalities
Proliferative diabetic retinopathy

A. Neovascularization (disc or elsewhere)
B. Pre-retinal hemorrhages
C. Vitreous hemorrhage
D. Fibrovascular proliferation
E. Traction retinal detachment
**Workup**

- History and detailed exam
- Fundus photography, OCT, and IVFA
- B-scan ultrasonography
- Discussion with PCP and determination of glycemic control (Hgb A1c)

**Treatment**

- Patient education
- Anti-VEGF: quickly becoming mainstay of treatment
- Laser photocoagulation
  - Panretinal photocoagulation: PDR
  - Focal/grid: macular edema
- Intravitreal steroids
- Vitrectomy
Retinal Artery Occlusion

- Painless monocular vision loss
- Occlusion of the central retinal artery or downstream branches
- >60 years old
- Men > women
Embolic, thrombotic, inflammatory, or traumatic
- Cardiac embolus, valvular disease, myxoma
- Atherosclerosis
- Carotid embolus
- Coagulopathies
- Collagen vascular diseases
- Ocular abnormalities
  - Disc drusen
  - Arterial loops

Giant Cell (Temporal) Arteritis
- Order ESR and CRP
- Temporal artery biopsy
- Typically ≥55yo
- Tx:
  - High dose intravenous corticosteroids
    - Solu-Medrol
    - 1,000 mg qd x 3 days
Types of Emboli

- Platelet-Fibrin
- Calcium
- Cholesterol

Workup

- Carotid doppler ultrasound
- Cardiac echocardiography
- Labs:
  - CBC – RBCs, platelets
  - Atherosclerotic disease – lipid panel, TGs
  - Coagulopathies – PT/PTT, SPEP, antiphospholipid Abs, fibrinogen
  - ESR/CRP
  - Sickledex
Treatment

- Lowering the IOP:
  - Topical timolol
  - Oral acetazolamide
  - Anterior chamber paracentesis
  - Ocular massage
  - Carbogen (95% O₂, 5% CO₂)
    - Choroidal O₂
    - CO₂ vasodilation
  - Hyperbaric oxygen
  - Hyperventilation
  - Anticoagulation

Ischemic Optic Neuropathy

- Painless unilateral visual loss
- Most commonly upon awakening
- Non-arteritic vs Arteritic
  - NAION ~90%
  - Can also occur operatively
  - Typically >50yo
Pathophysiology

- Infarction of the retrolaminar portion of the optic nerve head
  - Short posterior arteries

Non-Arteritic

- Optic disc anatomy
  - “Disc-at-risk”
- Vasoactive autoregulation
- Nocturnal hypotension
- Venous insufficiency
- Vasculopathic risk factors
  - Hypertension
  - Diabetes
  - Cholesterol
  - Obstructive sleep apnea
Prognosis

- 40% experience partial improvement
- 15% risk for involvement of fellow eye in 2 years
- <5% risk of recurrent ION in same eye
- Persistent visual field defect

Arteritic

- Giant Cell (Temporal) Arteritis
- Systemic lupus erythematosus
- Wegener's granulomatosis
- Behcet's disease
- Churg Strauss
- Polyarteritis nodosa
- 30% have preceding transient visual loss
- >50% visual acuity of count fingers to NLP
- >50% second eye AAION within hours to weeks

Peri-Operative

- Anemia
- Hypotension
- Fluid balance
- Type of surgery
  - Spine
  - Cardiac
- Positioning
  - Prone/face down
**Optic Neuritis**

- Acute, monocular vision loss
- Can be painful
  - Inflammation of the optic nerve and nerve sheath
  - Pain with eye movement
- Loss of color vision

**Other Findings**

- Pulfrich phenomenon
  - Pendular motion appears elliptical due to delayed conduction in the demyelinated nerve
- Uhthoff’s symptom
  - Worsening of symptoms with heat or exercise
- Phosphenes
  - Light flashes with eye movement or sound
- Auditory clicks
  - CN 7 innervates stapedius
Exam

- Decreased color vision and contrast sensitivity
- + RAPD
- VF defect
  - 50% diffuse, 20% central, rarely altitudinal
- Optic nerve often appears normal
  - 35% show edema
- Late disc pallor

Multiple Sclerosis

- Demyelinating autoimmune CNS degeneration
- White matter lesions on MRI
- Worsens over several weeks
- Generally improves over a 1-2 month period
Workup

- CSF studies
  - Cell count
  - Protein
  - Glucose
  - VDRL
  - Electrophoresis for oligoclonal bands
- VDRL and FTA-ABS
- ACE, lysozyme, chest X-ray
- ANA
- Possible Lyme titers

Prognosis

- 70% regain 20/20 vision
- Optic Neuritis Treatment Trial (ONTT)
  - 0 white matter lesions = 25% risk of MS in 15 years
  - 1 white matter lesion = 72% risk in 15 years
  - Progression typically within 5 years
Treatment

- Based on findings of ONTT
  - IV methylprednisolone 250 mg IV q6h x 3 days
  - PO prednisone 1 mg/kg/day x 11 days
- Reduces symptoms by 1-2 weeks
- No long term visual benefit
- Oral prednisone alone increased risk of recurrence

Retinal Detachment

- Progressive monocular shadow
  - Eventual loss of central vision
- Flashes and floaters
- “Heaviness” in the eye
Types

1. Rhegmatogenous
   - Breaks in the retina allow fluid to access the subretinal space

2. Serous/Exudative
   - Subretinal fluid collects due to damaged RPE and increased choroidal vascular permeability

3. Tractional
   - Fibrovascular proliferation pulls the retina away from the RPE and choroid

Rhegmatogenous

- Findings
  - Retinal break/tear
  - Tobacco dust/Shafer’s sign
    - Pigment liberated into the vitreous
  - Decreased IOP
  - Non-shifting subretinal fluid
  - +/- Vitreous hemorrhage
Long-standing
- Thin, atrophic retina
- Multiple small breaks
- Demarcation lines
- Proliferative

Treatment
- Pneumatic retinopexy
  - Single break in the superior 8 clock hours
  - Multiple breaks within 1-2 clock hours
  - Phakic > aphakic
  - Cryotherapy or laser
  - Typically SF₆ or C₃F₈ gas
**Scleral buckle**
- Elevate peripheral retina to support retinal breaks
- Alleviate vitreous traction
- Brings retina and choroid into contact
- Less likely to induce a cataract

**Indications:**
- Younger patients
- No PVD
- Lattice defects
- PVR
- Inferior pathology

**Vitrectomy**
- Remove vitreous
  - Alleviates vitreous traction on tears
- Laser around all defects
- Air, gas or oil to tamponade breaks
Thank You

- Questions?
Interesting Retina Clinic Cases

Daniel K. Bennett, MD

Case 1
Case 1: 23yo White Female

20/32  20/16

Case 1: 23yo WF
Fluorescein Angiogram
Initial Visit

20/32

4 Months

20/20
Multiple Evanescent White Dot Syndrome (MEWDS)

- Unilateral inflammatory condition
- Healthy young adults (15 – 50 years old)
- Self-limited, no treatment required

Case 2
Case 2: 51yo Black Male

Case 2: 51yo BM
Fluorescein Angiogram

OD

OS

Workup and Treatment

- ACE: normal
- ESR: 92 (high)
- CRP: 15.7 (high)
- Viral PCR: negative for CMV, HSV, VZV
- HIV 1/2: positive
- CD4: 159
- RPR: 1:64
- FTA-Abs: positive
- Quantiferon gold: negative

- Acyclovir 800mg po 5x/day
- ID workup through ER
- Lumbar puncture
- Penicillin G 3 million U q4h x 14 days
- Home with PICC
Follow Up: 3 Months

Case 3
Case 3: 18yo Black Female

20/20

CF @ 6'

[Eye images and OCT scans]
Fluorescein Angiogram

Follow Up: 3 Days

20/80

CF @ 3'
Workup and Treatment

- **History:**
  - Alopecia
  - Worsening headaches

- **Labs:**
  - ESR/CRP: normal
  - ACE: normal
  - RPR/FTA-Abs: negative/NR
  - Quantiferon gold: negative
  - Chest x-ray: normal

- **Treatment:**
  - Prednisone 60mg po qday
Vogt-Koyanagi-Harada (VKH) Disease

- Bilateral granulomatous panuveitis
- Extraocular manifestations
  - Neurologic/Auditory
    - Meningismus
    - Tinnitus/Dysacusis
    - CSF pleocytosis
  - Integumentary
    - Poliosis
    - Vitiligo
    - Alopecia

Case 4
Case 4: 67yo Asian Male

Fluorescein Angiogram
OCT

Follow Up: 1 Month
Ophthalmomyiasis Interna

- Insect-mediated ocular disorder
- Bot fly larvae (order Diptera)
  - Oestrus ovis
  - Hypoderma bovis
  - Hypoderma tarandi
  - Cuterebra spp
- Externa – invades ocular surface structures

Case 5
Case 5: 23yo Black Male

20/25    20/25
IVFA

Vitelliform Macular Dystrophy (Best Disease)

- Stages:
  - 1: Previtelliform 20/20
  - 2: Vitelliform 20/20 – 20/50
  - 3: Pseudohypopyon 20/20 – 20/50
  - 4: Vitelliruptive 20/20 – 20/100
  - 5: Atrophic <20/200
Case 6: 24yo White Female

- No visual complaints, retinal lesion discovered on routine exam
- No constitutional symptoms or systemic findings
- No significant ocular/systemic family history
Fundus Photo

Fluorescein Angiogram
Retinal Capillary Hemangioblastoma

- Enlarged retinal capillary endothelial cells
- Normal pericytes and basement membrane
- Typically superotemporal/inferotemporal mid-periphery or juxtapapillary
- High association with von-Hippel Lindau syndrome
  - Retinal lesions present between 10-40 years old (mean age of 25)
  - If no systemic association, more likely:
    - Unilateral
    - Isolated
    - Present later

Von-Hippel Lindau Syndrome

- Autosomal dominant inheritance pattern
- Mapped to chromosome 3p25.3
  - Regulation of transcription factors and hypoxia-inducible genes
  - Detection rates of 99% with genetic testing
- 1:36,000 live births
- Other findings:
  - Renal cell carcinoma
    - Leading cause of mortality (40% by age 60)
  - Central nervous system hemangiomas
  - Pheochromocytomas
  - Other tumors
  - Renal, pancreatic and hepatic cysts
# Tumors in VHL

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Most Common Age at Diagnosis</th>
<th>Frequency of Tumor</th>
<th>Tumor</th>
<th>Most Common Age at Diagnosis</th>
<th>Frequency of Tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head and Neck</td>
<td></td>
<td></td>
<td>Trunk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retinal Hemangioblastoma</td>
<td>12-25 years</td>
<td>25-60%</td>
<td>Renal Cell Carcinoma/Cyst</td>
<td>25-50 years</td>
<td>25-60%</td>
</tr>
<tr>
<td>Cerebellar Hemangioblastoma</td>
<td>18-25 years</td>
<td>44-72%</td>
<td>Pheochromocytoma</td>
<td>12-25 years</td>
<td>10-20%</td>
</tr>
<tr>
<td>Brainstem Hemangioblastoma</td>
<td>24-35 years</td>
<td>10-25%</td>
<td>Pancreatic Tumor/Cyst</td>
<td>24-35 years</td>
<td>35-70%</td>
</tr>
<tr>
<td>Spinal cord Hemangioblastoma</td>
<td>24-35 years</td>
<td>13-50%</td>
<td>Epididymal Cystadenoma</td>
<td>14-40 years</td>
<td>25-60% males</td>
</tr>
<tr>
<td>Endolymphatic Sac Tumor</td>
<td>16-28 years</td>
<td>11-16%</td>
<td>Broad Ligament Cystadenoma</td>
<td>16-46 years</td>
<td>10% females</td>
</tr>
</tbody>
</table>

# VHL Workup - Labs

- CBC for polycythemia vera
- Electrolytes and renal function tests (BUN and creatinine)
- Plasma catecholamines and urinary catecholamine metabolites
  - Pheochromocytoma
- Urinalysis (hematuria) and urine cytology (renal cell ca)
VHL Workup - Imaging

- Ophthalmic ultrasound
- Abdominal ultrasound
  - Renal and pancreatic lesions
  - Cysts of the epididymis and broad ligament
- Abdominal CT and MRI
  - Renal, pancreatic and adrenal gland lesions
- Brain CT
- CNS MRI

Cambridge Screening Protocol

<table>
<thead>
<tr>
<th>Affected Asymptomatic Patient&lt;sup&gt;a&lt;/sup&gt;</th>
<th>At-Risk Relatives: Same Protocol as Above but With Age Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical examination</td>
<td>Retinal examination&lt;sup&gt;b&lt;/sup&gt; Annually, beginning at age 5 years</td>
</tr>
<tr>
<td>Retinal examination&lt;sup&gt;b&lt;/sup&gt;</td>
<td>FA Annually, from age 10-60 years</td>
</tr>
<tr>
<td>FA</td>
<td>Brain MRI/CT Every 3 years from age 15-40 years, then every 5 years until age 60 years</td>
</tr>
<tr>
<td>Renal ultrasound</td>
<td>Abdomen MRI/CT Every 3 years from age 20-65 years</td>
</tr>
<tr>
<td>Brain MRI/CT</td>
<td>Every 3 years until age 50 years, then every 5 years</td>
</tr>
<tr>
<td>Abdomen MRI/CT</td>
<td></td>
</tr>
<tr>
<td>24 hour urine for VMA</td>
<td></td>
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</tbody>
</table>
Treatment

- **Observation**
  - Peripheral lesions <500 µm
  - No exudation/subretinal fluid
  - Not visually threatening
  - Juxtapapillary lesions
    - Significant collateral damage to nerve/macula

- **Argon laser photocoagulation**
  - Peripheral lesions <3 mm
  - No subretinal fluid
  - Green, yellow, blue laser

- **Cryotherapy**
  - Peripheral lesions >3mm
  - Subretinal fluid
- Photodynamic therapy
- Proton beam irradiation
- Surgery with cryotherapy and scleral buckle
  - Bullous RD or traction
- Possible adjunctive anti-VEGF?
  - Of particular interest to VHL patients

Anti-VEGF in Juxta papillary RCH
Prognosis

- Guarded
  - >25% of eyes with permanent vision loss
  - 20% with VA <20/100 in at least one eye
- Variables
  - Number of lesions
  - Size
  - Location
  - Degree of exudative or traction retinal detachment

Case 7
Case 7: 52yo White Male

- No visual symptoms
- Retinal lesion discovered on routine exam
- No constitutional symptoms or systemic findings
- No significant ocular/systemic family history

Fundus Photo
Fluorescein Angiogram

Fluorescein angiogram showing retinal cavernous hemangioma.

Retinal Cavernous Hemangioma

- Dilated, thin-walled vascular saccules and white fibrovascular tissue
  - “Cluster-of-grapes”
  - Plasma-erythrocyte separation
- Typically unilateral and static in size
- Rarely symptomatic unless:
  - Macular involvement
  - Vitreous hemorrhage
Fluorescein Angiogram

- Fluorescein pools in upper vascular spaces
- Erythrocytes pool in lower vascular spaces

Systemic Associations
- Skin hemangiomas
- Central nervous system hemangiomas
  - Headaches
  - Seizures
  - Focal neurologic deficits
- Gastrointestinal hemangiomas
  - Hemorrhage and anemia
- Rarely autosomal dominant
Treatment

- Observation
- Laser photocoagulation or cryotherapy
  - Recurrent vitreous hemorrhage

Bonus
Retinal Racemose Hemangioma

- Congenital arteriovenous malformation without interposed capillaries
- Multiple presentations:
  - Localized vascular communication near the nerve or periphery
  - Prominent tangle of tortuous vessels throughout the fundus

Wyburn-Mason Syndrome

- Retinal hemangioma plus AVM in the midbrain region
- Unilateral and non-hereditary
- Additional locations:
  - Brain
  - Face
  - Orbit
  - Mandible
Clinical Presentation

- Depends on location of lesions
- CNS
  - Mental status change
  - Headache
  - Seizure
  - Intracerebral hemorrhage
  - Visual field changes
  - Increased ICP
- Extracranial
  - Epistaxis
  - Oral hemorrhages

Workup

- IVFA
  - No leakage
- Cerebral imaging
  - MRI
  - Angiogram
Treatment

- Retinal lesions rarely progress or become symptomatic
- Directed toward intracranial/facial lesions
  - Catheter embolization
  - Surgery
  - Gamma-knife radiation

Thank You!

- Questions?