He that is stricken blind cannot forget the precious treasure of his eyesight lost.

William Shakespeare
Romeo and Juliet

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A Review of Ocular Anatomy

Most Common Vision-threatening Eye Diseases in Our Society

• Cataract
• Glaucoma
• Macular Degeneration
World Blindness
- Number of blind increasing
  - Increase in population size
  - Increased longevity
- Cataract
- Glaucoma
- Macular degeneration
- Distribution
  - Peak of blindness at birth: congenital disease
  - Exponential increase after the age of 40

Cataract

What is a Cataract?
- A waterfall
- A shiny marble
- An opacity in the natural lens of the eye
- An expensive American car

Cataract - Epidemiology
- A worldwide health problem
- 17 million people affected
- Significant economic impact on society
- A disease of poverty

Adult Cataracts
- Age is the primary risk factor
- 50% of people 65 to 74 years old have cataracts
- 70% of people 75 years or older
Other Causes of Cataract
- Genetic/congenital
- Trauma
- Systemic disease (diabetes, metabolic diseases)
- Medications
- Radiation
- Nutritional
- Inflammation

The Normal Lens

The Anatomy of a Cataract

Types of Cataract
- Cortical
- Nuclear
- Capsular

Symptoms of a Cataract
- "things seem blurry"
- "foggy"
- "haloes" (rings around lights)
- "glare"
- "I can't see street signs when I drive"
- A gradual painless decline in vision

View through a cataract
Who can name the artist?

Claude Monet (1840-1926)

The House Seen From the Rose Garden
Oil on canvas, c. 1923
Claude Monet

What is the treatment for cataracts?
- Treatment = surgical removal
- High frequency ultrasound NOT laser
- Glasses cannot reverse visual loss from a cataract
- Avoidance of UV exposure helpful in prevention
When to Consider Surgery?

- Cataract surgery is an elective procedure
- Performed when someone has functional difficulty seeing and doing activities of daily living such as driving, reading, and watching TV
- LASIK will not help cataracts (only corrects for refractive errors)

Cataract Surgery

- Done as an outpatient surgery
- Typically use topical or local anesthetic
- Very high success rate and low risk for complications
- A clear, artificial lens implant is placed in the eye
- Frequently, one does not need glasses to drive after surgery

Modern Cataract Surgery

- Phacoemulsification
- Ultrasound emulsification and aspiration of the cataractous
- Insertion of an intraocular lens

Lens Implants

- Replaces focusing power of the natural lens
- Placed within the natural lens capsule
- Most are foldable
- Power calculated by measuring the length of the eye and focusing power of the cornea

The Modern Cataract Operation

Glaucoma: The Thief in the Night
Glaucoma

What is the definition of Glaucoma?

a. High pressures inside the eye
b. An opacity in the natural lens of the eye
c. A fancy Greek dessert
d. Optic nerve damage that occurs in a specific pattern

The optic nerve is a bundle of more than 1 million nerve fibers. It connects the retina, the light-sensitive tissue at the back of the eye, to the brain. A healthy optic nerve is necessary for good vision.*

Optic Nerve

Elements of Glaucoma Management

- Optic nerve damage
- Intraocular Pressure
- Visual field loss

Normal healthy optic nerve

The Optic Nerve in Health and Disease
Eye pressure = a glaucoma risk factor

Who is at risk?
- Family history of glaucoma
- African-American population
- High eye pressures detected on eye exam
- Serious eye injury in the past
- Taking steroid medications
- Diabetes
- Nearightedness

What are the symptoms of glaucoma?
- Painless
- Does not affect vision until late stages of disease
- "The silent thief of vision"

Testing for Glaucoma:
- Measurement of Eye Pressure
- Visual Field Test
Visual loss in glaucoma

Visual Loss in Glaucoma

Glaucoma Screening

- Anyone with the aforementioned risk factors
- People 50 years of age and older should have an eye exam every 1 to 2 years

Glaucoma Treatment

- Medical
  - Primarily eye drop medication
- Surgical
  - Laser
  - Trabeculectomy

Glaucoma can be controlled not cured

- Primary goal is to lower eye pressure
- Current medication either promote outflow or decrease production of fluid in the eye
- New medication being tested that directly protects the nerve "Neuroprotection"
Age-related Macular Degeneration

- Most frequent cause of vision loss in people over 50 years old in developed countries.
- Average age of onset of vision loss is 75.
- Affects the central vision (reading, driving, recognizing faces), not the periphery.
- 200,000 new cases of wet AMD/year in North America
Projected Prevalence of Advanced* AMD in the United States

![Graph showing number of cases (millions) vs. year]

*Defined as neovascular AMD and/or geographic atrophy in at least one eye. Prevalence figures were calculated using 2000 US census data.


Advanced AMD: Risk Factors

- Emerging risk factors
  - Age
  - Race
  - Smoking
  - Family history
  - Variation in the complement factor H gene and other genes


Risk Factors for AMD

- Cardiovascular disease
  - Systolic htn, increased pulse pressures
  - Atherosclerosis
  - Increased body mass
  - Increased waist-circumference
  - Waist-hip ratio

- Diet low in antioxidants
  - High fat intake (3x)
  - Animal fat (2x)
  - Vegetable fat-ω6 fatty acid (omega-6; 4x)
    - sat., mono, poly, trans unsat., processed bakery foods

Risk Reduction for AMD

- Exercise 3x per week
- Increased antioxidant diet
- Diet low in ω6 fatty acid
  - Nuts (increase in ω3 fats)
  - Fish (salmon, cod, tuna, "oily fish")
  - Baby Aspirin

Visual Perception in AMD
Two Forms of AMD

- **Dry AMD**
  - Deposit of abnormal material in the retina
- **Wet AMD**
  - Deposit of abnormal material in the retina
  - Growth of abnormal blood vessels into the retina

**Dry AMD**
- No abnormal blood vessels
- Accumulation of abnormal material "drusen"
- 90% of cases

**Wet AMD**
- Abnormal blood vessels grow under the retina
- 10% of AMD
- 90% of severe vision loss

**EXUDATIVE AMD**

The Angiogenic Cascade is a Complex Process

Endothelial cell activation
Basement membrane degradation
Endothelial cell proliferation, migration
Tube formation

Tube elongation, remodeling
Fluorescein Angiography

- Identifies type and position of the abnormal vessels.
- Fluorescein dye injected into a vein.
- Photographs taken every few seconds for a minute then every few minutes.

Fluorescein Angiogram “Wet AMD”

Georgia O’Keeffe (1887-1986)

O’Keeffe and Macular Degeneration

- Georgia O’Keeffe developed macular degeneration in 1964 at age 77.
- Affected central visual acuity.
- Diminished ability to judge contrast.

“I can’t see straight on very well. But around the edges, one little hole where I can see quite clearly.” Georgia O’Keeffe.

Treatment Options

- Dry
  - Observation/Observation
  - Vitamin supplementation
- Wet
  - Observation
  - Laser
  - Anti-VEGF factor injections
Treatment for Dry AMD

- Stop Smoking
- Healthy Diet
  - Low Fat
  - Green Leafy Vegetables
  - Fruits
  - Fish
  - No Junk Food
- Vitamin Supplement
  - AREDS Formula

The Age-Related Eye Disease Study

- Evaluated the effects of high levels of antioxidants and zinc on the progression of Dry age-related macular degeneration

Age-related Eye Disease Study (AREDS) Formula

- Vitamin A (Beta-Carotene) 573% RDA
- Vitamin C 753%
- Vitamin E 1333%
- Zinc 464%
- Copper 80%

AREDS Study Population: Demographics

- Total participants: 4,757
- Age: 55-80; median age: 69
- Gender: 56% F
- Race: 96% Caucasian
- Duration: average F/U = 6.3 yrs.
- Current Smokers: 8%

AREDS Study Design: Oral Preparations

- Placebo
- Antioxidants
  - Vitamin C (500 mg)
  - Vitamin E (400 IU)
  - Beta-Carotene (25,000 IU or 15 mg)
- Zinc (80mg + 2 mg Cupric Oxide)
- Antioxidants + Zinc
AREDS Formulation

- Ocuvite Preservision
- I-CAPS (AREDS Formulation)
- Formulation
  - Vitamin C 500 mg
  - Vitamin E 400 IU
  - Beta-carotene 15 mg
  - Zinc oxide 80 mg
  - Cupric oxide 2 mg

AREDS

Conclusions and Recommendations:

- Category 3+4 patients should be considered for antioxidant and zinc therapy to reduce the progression of their disease.
- ≥ 55 years old
- Extensive intermediate drusen or at least one large drusen (≥ 125 µm)
- Geographic atrophy not located in center of fovea
- Advanced AMD in one eye

AREDS Results

- The supplement reduced the risk of advanced AMD by 25% over 5 years in patients with high-risk changes
- The risk of vision loss was reduced by 19% in these patients
- There was no benefit for patients with mild AMD

AREDS 2

- Is evaluating the effect of oral supplements lutein and zeaxanthin, omega-3 fatty acids and combination of above on the development of advanced AMD and moderate vision loss
- Uses prior AREDS study design

AREDS II Dietary Supplement Study

- Duration: 2006 to 2013
- Enroll 4000 patients in 60 centers
- Intermediate AMD with good Vision
  - Lutein 10 mg/day
  - Zeaxanthin 2 mg/day
  - Omega 3-Fatty Acid

AMSLER GRID: Self-Monitoring for Wet AMD
Wet AMD: Treatment

- Thermal Laser
  - “Hot Laser”
- Photodynamic Therapy
  - “Light Laser”
- Intraocular Injections
  - Macugen, 2004
  - Avastin
  - Lucentis, 2006

Photodynamic Therapy (PDT) Principles

- A light-activated dye is given intravenously and builds up in abnormal vessels
- The dye is activated in the eye using a non thermal (cold) laser
- The abnormal vessels are damaged by the activated dye

Disadvantages of PDT

- Only works for certain types of wet AMD
  - Cost
    - Medicare reimburses only for some types of wet AMD
    - Drug is very expensive ($1500/treatment)
  - Multiple treatments (average of 5 over 2 years) needed

Smart Drugs

- New nondestructive “smart drugs” are in clinical trials
  - Lucentis
  - Macugen
  - Avastin
  - Eylea

MACUGEN

- FDA Approved December, 2004
- Block VEGF-165 Only
  - Decrease Risk of Severe Vision Loss
  - Average Vision Worstens with Time
- Injection Intraocular Every 6 weeks
- Safe

Avastin for Wet AMD

- Salvage Therapy
- Intraocular Injection
  - 1/400 IV Dose
- Lower Cost: $50

* FUTURE TRIAL: Avastin vs Lucentis for AMD
LUENTIS
(rhu-Fab, ranibizumab)
- Formulated for AMD
- Small Fragment of Antibody to VEGF
- Better Retinal Penetration
- Rapidly Cleared Systemically
  - Intraocular Injection
    - every Month
- FDA Approved July, 2006

Treatments for Age-Related Macular Degeneration
- End-stage AMD ("geographic atrophy")
  - No medical treatment options
  - Low vision devices

Implantable Miniature Telescope (IMT)
(VisionCare Ophthalmic Technologies, Saratoga, California, USA)
- First ever technology for end-stage AMD
- FDA-approved in July 2010


Postoperative Results
- 20/400 vision in the left eye at week 1
- 20/150 at month 3!
Summary

**Cataract**
- Better implantable lenses
- Highly successful surgery

**Glaucoma**
- Those with risk factors and > 50 years of age should be screened

**Age Related Macular Degeneration**
- Vitamins may help prevent worsening of AMD
- New medications that may control wet AMD

To Maintain Our Sight

- Healthy diet (Eat your vegetables!)
- Take your vitamins
- Exercise
- Avoid smoking
- Avoid excessive UV exposure

The most pathetic person in the world is someone who has sight but no vision.

Helen Keller

Thank You