

The Eye and Systemic Disease
Gregory L. Pinto, M.D.

- I. Overview
 - A. Many systemic diseases affect the eye.
 - B. A primary care provider needs to know what to look for on an eye exam
 - C. A primary care provider also needs to know when to refer a patient to an ophthalmologist.

- II. Diabetes Mellitus
 - A. Significance of Diabetes Mellitus (DM):
 1. Worldwide: 135 million with DM worldwide (90% Type 2); 300 million projected by 2025
 2. United States: 16 million Americans affected; 800,000 new cases of Type 2 diabetes per year (African Americans, Latinos and Native Americans at double risk)
 3. Diabetic retinopathy is the leading cause of blindness in working-age Americans
 - B. Diabetic Retinopathy: Clinical Stages
 1. Non-proliferative (“Background”) Diabetic Retinopathy
 - i. Characterized by microaneurysms, hard exudates, intraretinal hemorrhages
 - ii. Patients are often asymptomatic
 - iii. Diabetic Macular Edema (DME) may develop at this stage
 - iv. 5% prevalence with diabetes less than 5 years
 - v. 15% prevalence with diabetes greater than 15 years
 2. Advanced (“Pre-proliferative”) Background Diabetic Retinopathy
 - i. Characterized by venous “beading” and intraretinal microvascular abnormalities
 - ii. Risk of progression to Proliferative Diabetic Retinopathy is high
 - iii. Laser treatment at this stage may be considered
 3. Proliferative Diabetic Retinopathy (PDR)
 - i. Characterized by retinal neovascularization that can lead to
 - ii. vitreous hemorrhage and/or
 - iii. neovascular glaucoma
 - iv. Macular edema may also develop at this stage
 4. Prevalence of PDR in insulin users under 30:
 - i. 5 years’ duration = nearly 0
 - ii. 15 years = 25%
 - iii. 20 years = 55%
 5. Prevalence of PDR in insulin users over age 30: 20% in those with IDDM > 20 years

C. Laser Treatment for Diabetic Retinopathy

1. Laser treatment of clinically-significant macular edema decreased the rate of vision loss from 16% to 7% (versus controls) at 2 years and from 24% to 12% at 3 years
2. Laser treatment (Pan-Retinal Photocoagulation) of PDR showed an overall reduction of severe vision loss (worse than 5/200) from 15.9% in untreated eyes to 6.4% in treated eyes
3. Pan-Retinal Photocoagulation may lead to reduced night vision, reduced peripheral vision and reduced visual acuity
4. Vitrectomy may be needed for vitreous hemorrhage

D. Medical Treatment/Prevention

1. Control of Blood Glucose (Diabetes Control and Complication Trial)
 - i. In patients without retinopathy, intensive glucose control (insulin pump or 3 or more insulin injections per day) effected a 76% reduction in the risk of developing retinopathy compared to controls (fewer than 3 injections per day)
 - ii. In patients with mild or moderate retinopathy, intensive control effected a 54% reduction in the progression of retinopathy and a 59% reduction in the need for laser treatment
2. Blood Pressure Control (United Kingdom Prospective Diabetes Study)
 - i. Reduce HgbA1C from >7.9% to <6.9% → 21% decrease in microvascular complications for each 1% decrease in HgbA1C
 - ii. Reduce SBP from >149 mmHg to <130 mmHg → 11% decrease in retinopathy progression for each 10 mmHg decrease in SBP
 - iii. Protective effects seen with ACE inhibitors and beta blockers
3. Control of Serum Lipids
 - i. Elevated serum lipid levels in some studies were associated with increased risk of retinal hard exudates in diabetics
 - ii. Control of serum lipids makes sense to reduce cardiac risk and, perhaps, retinopathy
4. Aspirin
 - i. No evidence yet of accelerated or slowed progression of retinopathy
 - ii. No increased risk of vitreous hemorrhage
 - iii. No contraindication, therefore, to aspirin use in patients with diabetic retinopathy of any stage

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E. Screening for Diabetic Retinopathy

1. Type 1 Diabetes: annual ophthalmologic exams starting 5 years after diagnosis
2. Type 2 Diabetes: annual ophthalmologic exams starting at time of diagnosis
3. Pregnancy: ophthalmologic exams before conception and during first trimester. Follow-up exams depending on the extent of retinopathy
4. Value of Screening:
 - i. Timely screening reduces the risk of blindness from 50% to 5%
 - ii. 100% screening is estimated to save \$167 million annually

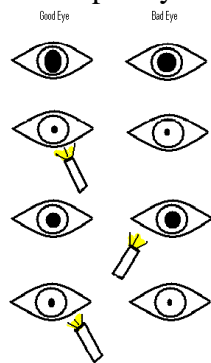
III. Hypertension (HTN)

- A. The extent of retinopathy is related to the duration and severity of HTN
- B. Damage may occur in the retina, choroid or optic nerve
- C. Clinical findings include copper- or silver-wiring changes in the arterioles; flame-shaped hemorrhages and hard exudates
- D. Edema of the optic nerve head is associated with malignant hypertension, which requires urgent, yet careful, lowering of blood pressure

IV. Retinal Vein Occlusion

- A. Central retinal vein occlusion (CRVO) involves all of the visual field
Branch retinal vein occlusion (BRVO) involves part of the visual field
- B. Significant Marcus-Gunn pupil (*vide infra*)
- C. Primary care provider needs to evaluate underlying cause, such as DM, HTN, vasculitis
- D. Ophthalmologist needs to monitor for and treat ischemia

V. Afferent Pupillary Defect (Marcus-Gunn Pupil)



- A. Testing involves the swinging flashlight test: A light is shown in the unaffected eye; both pupils constrict; the light is swung over to the affected eye; both pupils dilate.

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- VI. Hyperviscosity Syndromes
 - A. Venous tortuosity is a hallmark finding
 - B. Associated conditions include polycythemia, multiple myeloma and leukemia
 - C. Ophthalmic evaluation is indicated for patients with these conditions

- VII. Retinal Arteriolar Occlusion
 - A. central retinal arteriolar occlusion (CRAO) obliterates all of visual field (the macula may be spared)
 - B. branch retinal arteriolar occlusion (BRAO) impairs part of visual field
 - C. acute CRAO shows a “cherry red” spot on funduscopy
 - D. significant Marcus-Gunn pupil
 - E. Acute treatment: lower intraocular pressure by rebreathing CO₂, topical beta-blocker, topical or oral Diamox, digital massage
 - F. Non-acute treatment: treat underlying vasculopathy; evaluate source of emboli; rule out temporal arteritis

- VIII. Ischemic Optic Neuropathy
 - A. essentially a stroke to the optic nerve
 - B. variable degree of vision loss
 - C. prominent Marcus-Gunn pupil
 - D. need to distinguish arteritic (temporal arteritis) versus non-arteritic etiology

- IX. Temporal Arteritis
 - A. Clinical signs:
 - 1. unilateral loss of vision in elderly patient
 - 2. prominent Marcus-Gunn pupil
 - 3. optic nerve swelling and/or cherry red spot
 - 4. scalp/forehead tenderness
 - 5. 10% of patients present with cranial nerve palsy
 - B. Management:
 - 1. Obtain erythrocyte sedimentation rate
 - 2. Start systemic steroids
 - 3. Schedule temporal artery biopsy within 2 weeks

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X. Optic Neuritis

A. Features:

1. rapid vision loss that progresses over several hours to several days; usually unilateral
2. 92% have pain with eye movement
3. reduced visual acuity, visual field, color vision and light intensity
4. prominent Marcus-Gunn pupil
5. swollen disc in 33%
6. no retinal hemorrhages or exudates

B. Treatment

1. Optic Neuritis Treatment Trial (ONTT) randomized 457 patients with new optic neuritis into 3 treatment arms: placebo; oral prednisone x 14 days; and i.v. methylprednisolone x 3 days followed by oral prednisone x 11 days. The results showed that patients given i.v. steroids recovered vision faster, with no difference among the groups noted at one year. At 3 years there was no difference between the i.v. steroid and the placebo groups in the development of multiple sclerosis. Patients given only oral prednisone had more recurrences. 30% of patients develop MS at 5 years. 3 or more brain lesions on MRI were associated with a 51% risk of MS.
2. Controlled High-Risk Subjects Avonex MS Prevention Study (CHAMPS) randomized 326 patients with first demyelinating event and abnormal brain MRI to placebo or Avonex (interferon beta-1a). All patients received i.v. medrol and p.o. prednisone as per ONTT. Avonex effected a 44% reduction in the probability of developing MS at 3 years.

XI. Migraine

A. Symptoms

1. Scintillations
2. Transient homonymous hemifield loss
3. Amaurosis fugax
4. Transient cortical blindness

B. Subtypes

1. Without headache: “acephalgic” “ocular” “migraine equivalent”
2. With headache
 - i. Classic (aura precedes headache)
 - ii. Common (no aura before headache)
 - iii. Complicated (residual neurologic deficit)

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XII. Thyroid-Related Ophthalmopathy

- A. Not always correlated with serum levels of thyroid hormone
Ophthalmopathy can progress after thyroid function is normal
- B. Classification system:
 - 1. 0 No signs/symptoms
 - 2. 1 Only signs
 - 3. 2 Soft tissue involvement
 - 4. 3 Proptosis
 - 5. 4 Extraocular muscles involved
 - 6. 5 Corneal damage
 - 7. 6 Sight loss (optic nerve impaired)
- C. Treatment: Congestive Phase
 - 1. Artificial tears
 - 2. Corticosteroids for EOM or optic nerve involvement
 - 3. Orbital irradiation if steroids fail
 - 4. Surgical decompression
- D. Treatment: Cicatricial Phase
 - 1. Lid surgery
 - 2. Muscle surgery
 - 3. Orbital surgery

XIII. Autoimmune Disorders

- A. Examples
 - 1. Ankylosing Spondylitis
 - 2. Rheumatoid Arthritis
 - 3. Juvenile Rheumatoid Arthritis
 - 4. Systemic Lupus Erythematosus
 - 5. Thyroid-related ophthalmopathy
 - 6. Myasthenia Gravis
- B. DRY EYE
 - 1. the most common ocular manifestation
 - 2. Symptoms include blurred vision, FBS, photophobia, “itching” and “burning”
 - 3. Treatment: artificial tears, lubricating ointment, punctal occlusion, topical cyclosporine
 - 4. Ophthalmic evaluation is often needed
- C. Ankylosing Spondylitis
 - 1. 25% of patients develop iritis
 - 2. Symptomatic patients should be referred to an ophthalmologist

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- D. Iritis
 - = intraocular inflammation
 - 1. Deep pain, blurred vision and photophobia
 - 2. Floating cells seen on slit lamp exam; limbal conjunctival injection
 - 3. May be associated with systemic inflammatory disorder
 - Treat with topical steroids if diagnosis is certain
 - E. Rheumatoid Arthritis
 - 1. Ocular Manifestations Include:
 - i. Dry Eyes
 - ii. Iritis/Uveitis
 - iii. Episcleritis
 - iv. Scleritis
 - v. Corneal Ulcers
 - 2. Patients should be referred if any ocular symptoms develop
 - F. Juvenile Rheumatoid Arthritis
 - 1. Pauciarticular
 - 2. RF- ANA+
 - 3. Iritis OFTEN ASYMPTOMATIC
 - 4. Late findings: iritis, cataract, band keratopathy
 - 5. FREQUENT SLIT LAMP EXAMS are needed
 - G. Systemic Lupus Erythematosus
 - 1. Ocular Manifestations
 - i. Dry Eyes
 - ii. Scleritis
 - iii. Corneal Ulcers
 - iv. Retinopathy and Optic Neuropathy (incl. HTN retinopathy)
 - 2. Ophthalmic evaluation is needed with any CNS involvement or visual disturbance
 - H. Myasthenia Gravis
 - 1. Disease of acetylcholine receptors at neuromuscular junction
 - 2. 75% of patients present with ocular involvement
 - i. Ptosis
 - ii. Limited EOM
 - iii. Diplopia
- XIV. Sarcoidosis
- A. Multisystem disorder characterized by granulomatous inflammation of many organs
 - B. More common in African-Americans and Hispanics
 - C. Ocular involvement in approx. 25%
 - D. Iritis is characterized by large corneal endothelial precipitates
 - E. Retinal vasculitis is often segmental, giving an appearance of “candlewax drippings”

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XV. AIDS

A. Ocular Manifestations include

1. Dry eye
2. Cotton-wool spots
3. CMV retinitis
4. Kaposi's sarcoma of eyelid or conjunctiva

B. CMV Retinitis

1. Opportunistic Infection
2. Usu. Seen with CD4 lymphocyte counts <100 cells/ml
3. Treatable with
 - i. i.v. or intravitreal ganciclovir
 - ii. i.v. foscarnet
 - iii. p.o. valganciclovir
 - iv. i.v. cidofovir
 - v. intravitreal fomivirsen

XVI. Shaken Baby Syndrome

- A. Hemorrhages may be seen beneath the retina, within the retina or in the vitreous

XVII. Intracranial Hypertension

- A. Papilledema=optic disc swelling from intracranial HTN
- B. Transient visual disturbances (usu. asymptomatic)
- C. Causes include brain tumor, meningitis, hydrocephalus, pseudotumor cerebri
- D. Note: Optic disc edema may also be seen without intracranial HTN: sarcoidosis, syphilis, optic nerve ischemia

XVIII. Sickle Cell

- A. HbSC disease (most common form with retinopathy)
- B. HbSS disease
- C. Sickle Thalassemia
- D. Not seen with sickle trait
- E. Peripheral neovascularization
- F. Often asymptomatic until vitreous hemorrhage develops
- G. Regular dilated funduscopy needed

XIX. Herpes Zoster

- A. Usually affects adults
- B. Unilateral
- C. Skin lesions in a dermatomal distribution of the ophthalmic branch of the trigeminal nerve
- D. Keratitis/uveitis
- E. Older patients at risk for post-herpetic neuralgia
- F. Usually use Valtrex/Famvir

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