Revisiting Diabetes and Retinopathy: Advanced Diagnosis and Treatment Options
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• The content of this course was prepared independently by Dr. Gerstner without any input from members of the ophthalmic industry.
• Dr. Gerstner does not have financial interests in any companies, products, or services mentioned in this presentation.

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• Diplomate, American Board of Optometry

Course Description
• This course explores imaging technology utilized for improved diagnosis and progression analysis of ocular disease associated with diabetes mellitus. An in-depth discussion will familiarize the optometric physician with emerging and changing treatment protocols for the treatment of diabetic retinopathy. Case-based presentations will illustrate imaging interpretation and techniques. Systemic diabetes mellitus and levels of diabetic retinopathy will be thoroughly reviewed. Evidence-based medicine and clinical trials will be discussed.

Clinical Decision Making
• Who needs what treatment, and when do they need it?
• Subjectivity in every patient encounter
• Data collection and constructing an argument based on “facts”
• Perhaps there is more than one way to apply diagnostic or therapeutic options
• Elements of uncertainty
• Technology
• Still no substitute for your own judgment and experience
Evidence Based Medicine

- Occam’s Razor, or “common things happen commonly”
- Simple: take the path that gives the best outcome
- Follow the studies that help us make better decisions
- Use the GPS, not the map…

DCCT and EDIC

- Diabetes Control and Complications Trial and Epidemiology of Diabetes Interventions and Complications

- Type 1 diabetes mellitus: 50% will have retinopathy 10 years after diagnosis
- Type 2 diabetes mellitus: 95% will have retinopathy 10 years after diagnosis
- Intense blood glucose control reduces risk by 76%

Diabetes – Control to Prevent Complications

- Intense blood glucose control (DCCT)
  - Hemoglobin A1c (HbA1c) to monitor control
    - 6.0% or less for diabetics
    - 40% reduction of complications if HbA1c is reduced one percentage point

Diabetes – Control to Prevent Complications

- Blood pressure control
  - 33% to 50% reduction in heart disease or CVA
  - Reduction of diastolic pressure from 90 mmHg to 80 mmHg decreases a major cardiovascular event by 50%

- Lipid control
  - Strict LDL control can reduce cardiovascular complications 20% - 50%

Metabolic Syndrome

- Abdominal obesity
- Dyslipidemia
- Elevated blood pressure
- Diabetes or pre-diabetes
- Pro-thrombotic state
- Pro-inflammatory state

Clinical Studies and the Standard of Care

- Early Treatment Diabetic Retinopathy Study (ETDRS) facts on macular edema and laser photoacogulation:
  - Generally stabilizes visual acuity but often does not improve it
  - Comprises of directly treating focal areas of leakage and placing a grid in areas of diffuse capillary leakage – guided by IVFA
  - Should be avoided in presence of significant loss of perifoveal capillaries
  - May take months to show resolution of thickening and resolution may take longer for exudates
Clinical Studies and the Standard of Care – PRP Facts

- Visual acuity will not improve
- Macular edema may actually worsen
- Significant night and peripheral vision loss
- Neovascularization will not always regress
- Indicated for neovascularization of the iris

Clinical Studies and the Standard of Care

<table>
<thead>
<tr>
<th>Diabetic Retinopathy Study (DRS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYO &gt; 1/2 to 1/4 of disc area</td>
</tr>
<tr>
<td>Any NVO with associated VH</td>
</tr>
<tr>
<td>NVE with associated VH</td>
</tr>
</tbody>
</table>

Overview of Diabetes Mellitus

- Diabetes is a group of metabolic disorders defined by elevated blood glucose resulting from insulin production defects, impaired insulin action, or both
- The 1997 International Expert Committee on Diabetes Mellitus changed the classification of diabetes, criteria for the diagnosis of diabetes, and control guidelines
- Revised guidelines were published in 2003

Overview of Diabetes Mellitus

- Type 1 (no longer considered IDDM or Type I)
  - Pancreatic beta cell destruction
  - Viral/environmental insult and autoimmune injury
  - 5% of all diagnosed cases

- Type 2 (no longer considered NIDDM or Type II)
  - Pancreatic beta cell inefficiency or insulin resistance
  - Age, obesity, and family history
  - 90% - 95% of all diagnosed cases
  - Pre-diabetes (formally known as impaired glucose tolerance)

- Gestational diabetes
  - 2% to 10% of all pregnancies
  - 5% to 10% will have diabetes immediately following pregnancy
  - 35% to 60% will develop diabetes in the next 10 – 20 years

- Other types
  - MODY 1 – 6
  - 1% to 5% of all diagnosed cases
### Diagnostic Ranges of Diabetes

<table>
<thead>
<tr>
<th>Disease</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Mellitus</td>
<td>1. FPG &gt; 126 mg/dL</td>
</tr>
<tr>
<td></td>
<td>2. Two hour PG &gt; 200 mg/dL with the OGTT after 75 g glucose load challenge</td>
</tr>
</tbody>
</table>

Revised guidelines 2003

### Diagnostic Ranges of Pre-Diabetes

<table>
<thead>
<tr>
<th>Disease (impaired glucose tolerance)</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1. FPG level 100 – 125 mg/dL</td>
</tr>
<tr>
<td></td>
<td>2. Two hour PG 140 – 199 mg/dL with OGTT after 75 g glucose load challenge</td>
</tr>
</tbody>
</table>

### Hemoglobin A1C or Random Plasma Glucose?

- Which one do we do in clinic?
- Better understanding of the overall blood glucose control
- Why?
- Did you check your BG today, Mrs. Jones?
- When do we do this in the clinic?
- When we have time...
- Who?
- Not engaged in care

### Pharmacological Treatment for Diabetes

- Insulin
  - Rapid acting
  - Short acting
  - Intermediate acting
  - Long acting

### Pharmacological Treatment for Diabetes – Oral

- Insulin secretagogues
- Insulin sensitizers
- Metformin
- α-glucosidase inhibitors
- Dipeptidyl peptidase IV inhibitors
- Incretin mimetics
- Sodium glucose transport inhibitor
How Many People Are Affected?
• Total: 25.8 million children and adults or 8.3% of the population
• Diagnosed: 18.8 million people
• Undiagnosed: 7.0 million people
• Pre-diabetes: 79 million people
• New Cases: 1.9 million

How Many People Are Affected?

<table>
<thead>
<tr>
<th>Total prevalence of DM, US 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 20 years of age</td>
</tr>
<tr>
<td>Age 20 years or older</td>
</tr>
<tr>
<td>Age 65 or older</td>
</tr>
<tr>
<td>Men</td>
</tr>
<tr>
<td>Women</td>
</tr>
</tbody>
</table>

The Diabetes "Belt"

Diabetes Diagnosis

Diabetes – Lack of Activity

It is impossible to discuss retinopathy without knowing this slide.
Retina Anatomy Review: Structure and Function
- Inner retina – what we are mostly reviewing today
- Outer retina – external limiting membrane and posterior
  - Photoreceptors
  - Retinal pigment epithelium
  - Bruch’s membrane
  - Choriocapillaris
  - Choroid

Retinal Vasculature
- Arteries and arterioles v. veins and venules
- Location – located in the nerve fiber or ganglion cell layers
- Function – supplies the inner retina with blood, nutrients, and O₂

Retinal Anatomy Review: Capillary Networks
- Superficial or inner network
  - Located within the ganglion cell layer
  - Think post-arteriole and affected in artery based disease
- Deep or outer network
  - Located in the inner nuclear layer
  - Think pre-venule and affected in venous based disease

Inner Capillary Network Compromise
- Flame-shaped hemorrhages
- Cotton wool spots

Outer Capillary Network Compromise
- Intra-retinal hemorrhages
- Exudative changes

Microaneurysm
Nonproliferative Diabetic Retinopathy – Mild

- Micro-aneurysms
- Occasional hemorrhages
- Occasional exudate
- ? Maybe - clinically significant macular edema or CSME

Nonproliferative Diabetic Retinopathy – Moderate

- Increased number of hemorrhages
- Increased size of hemorrhages
- More evidence of exudate
- Evidence of capillary occlusive disease
- ? Maybe – clinically significant macular edema (CSME)

Diabetic Maculopathy

- Focal maculopathy – well developed or circumscribed retinal thickening
- Diffuse maculopathy – severe and diffuse retinal thickening
- Ischemic maculopathy – capillary non-perfusion and poor visual acuity

Clinically Significant Macular Edema

- Retinal thickening within 500 μm of the center of the fovea

Clinically Significant Macular Edema

- Exudate within 500 μm of the center of the fovea with adjacent thickening
Clinically Significant Macular Edema

• Thickening of at least one disc diameter within one disc diameter of the center of the fovea

Nonproliferative Diabetic Retinopathy – Severe

<table>
<thead>
<tr>
<th>Worsening of everything with macular edema</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-2-1 RULE</td>
</tr>
<tr>
<td>Severe retinal hemorrhages in 4 quadrants</td>
</tr>
<tr>
<td>Venous beading in 2 quadrants</td>
</tr>
<tr>
<td>IRMA in 1 quadrant</td>
</tr>
</tbody>
</table>

50% risk of developing PDR within one year

Proliferative Diabetic Retinopathy

• NVD – neovascularization of the disc
• Neovascularization development within one disc diameter of the optic nerve
• NVE – neovascularization elsewhere
• Neovascularization anywhere within the retina that is not NVD
• Junction between perfused and non-perfused retina
• NVI – neovascularization of the iris
• Threatening sign of neovascular glaucoma
• Vitreous hemorrhage
• Bleeding from NVD or NVE

4 – 2 – 1

Recent Clinical Trials for Diabetic Macular Edema

• READ
  - Ranibizumab 0.5 mg
  - Focal and grid laser photocoagulation

• RESTORE
  - Ranibizumab 0.5 mg followed by laser photocoagulation

Case Presentation

• 53-year-old male
• “My vision has been blurry in both eyes for awhile”
• HTN
• Type 2 diabetes
Recent Clinical Trials for Diabetic Macular Edema

- RESOLVE
  - Ranibizumab 0.5 mg v. sham
- RISE
  - Ranibizumab 0.5 mg v. sham
- RIDE
  - Ranibizumab 0.5 mg v. sham

Diabetic Macular Edema – Local Treatment Trends

- Lucentis or Avastin or Eylea
- Combination of focal and grid laser photocoagulation
- Possible needed for sustained effect
- Laser at one week after injection if continued marked edema
- Lower intensity and shorter duration laser photocoagulation

Diabetic Macular Edema – Local Treatment Trends

- NSAIDS and topical steroids?
- Implantable steroids?
- Injectable steroids?
- PRP

Proliferative Diabetic Retinopathy – Local Treatment Trends

- Lucentis or Avastin or Eylea followed by PRP
- Not approved as initial therapy
- Pre-vitrectomy to reduce bleeding
- Vitreous hemorrhage with neovascularization followed by PRP
- NVI or neovascular glaucoma

A Brief History of OCT

Time domain (old) versus spectral domain (new)
CIRRUS HD – OCT 5000

- Macular cube 512 x 128
- Macular cube 200 x 200
- HD 5 - line raster
- Optic disc cube 200 x 200
- Anterior segment 5 - line raster
- Anterior segment cube 512 x 128

CIRRUS HD – OCT 5000

- Macular analysis
  - Macular thickness
  - Ganglion cell analysis
  - Macular change analysis
  - Advanced RPE analysis
  - 3-D and advanced visualization

Macular analysis

5 – line raster

- High definition image

Case Presentation

- 50-year-old male
- Type 2 diabetes x 20 years
- HTN and kidney disease
- Blurred vision OD for one day

Case Presentation

- 59-year-old female
- “I have noticed blurred vision OD for a few weeks”
- Type 2 diabetes for 20 years
- Well controlled
- Compliant patient that is followed annually at TEC
- No previous retinopathy identified
- Her vision has dropped OD compared to previous

Optos Daytona

- Pros
  - Wide field
  - Magnification
  - Patient education
- Cons
  - You be the judge…
Billing and Coding
- Coding and Medicare allowable fee structure 2014 – Tennessee
  - 92134: Retina = 42.79
  - 92250: Fundus Photography = 74.43

Billing and Coding – Pitfalls
- Vision insurance, medical insurance, or both?
- ICD-9 codes and "baseline" testing
- Photography and OCT
  - Calendar year and OCT
  - The eye is considered to be a single organ
  - Clear documentation and interpretation

Case Presentation
- 54-year-old male
- Type 2 diabetes x 24 years
- HTN
- Blurred and fluctuating vision OU
- New patient – vision benefit