


Current Approaches to the Evaluation and Management of Diabetic Retinopathy


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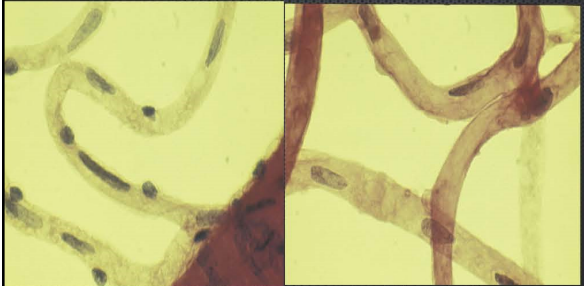
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Etiology

- Microvascular disease
- Precise cause unknown
 - Decompensation of vascular endothelium, pericyte damage
 - Growth factors (VEGF, HGF, TNF) and cytokines play a role
 - Inflammation implicated
 - Role of retinal pigment epithelium unclear



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Normal pericytes **Trypsin digest:**
Loss of pericytes


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Microaneurysms



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- NPDR affects vision by:
 - Loss of capillaries supplying the fovea
 - Macular edema



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Treatment of Diabetic Retinopathy

- General Medical Literature
- Ophthalmic Literature



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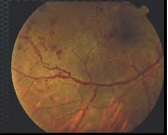
Effect of Systemic Conditions on Diabetic Retinopathy

- Glycemic control is the key
 - Diabetes Control and Complications Trial
 - Randomized, Controlled Trial of Type 1 Diabetes
 - Intensive sugar control reduced both the frequency and severity of retinopathy, nephropathy, and neuropathy
 - During start of intensive treatment, can have worsening of retinopathy, needs closer follow up

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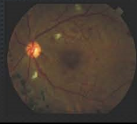
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- United Kingdom Prospective Diabetes Study
 - Randomized, controlled trial for Type 2 diabetes
 - Intensive treatment - goal was fasting glucose of 110 mg/dL
 - Conventional control was diet



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- Intensive treatment achieved HbA1c of 7.0% vs. 7.9% in conventional group (there was a loss of control with time)
 - 29% reduction in the need for laser treatment
 - For every 1% point decrease in HbA1c, there is a 35% decrease in risk of microvascular complications



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- UKPDS also compared tight blood pressure control (<150/85) vs. less tight control (<180/105)
 - Tight BP control led to a 35% in laser treatments and 47% reduced risk of losing 3 lines of visual acuity at 7.5 years

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American Diabetic Association

- Guidelines
- Goals:
 - HbA1c: less than 7% (fasting glucose of less than 120)
 - Blood pressure: systolic less than 130 mm Hg, diastolic < 85 mm Hg
 - Diet management

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Diabetic macular edema

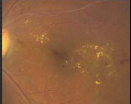
- Diabetic macular edema is the leading cause of vision loss in diabetics
 - Assess damage by visual acuity, fundus exam
 - Fluorescein angiography, and ocular coherence tomography (OCT)

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ETDRS

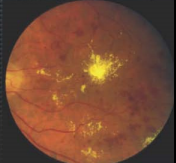
- 1) Is laser effective in the treatment of DME?
 - Yes, reduces risk of vision loss by 50%
- 2) Is aspirin effective in preventing progression of DR?
 - No
- 3) Is scatter PRP earlier better?
 - Maybe



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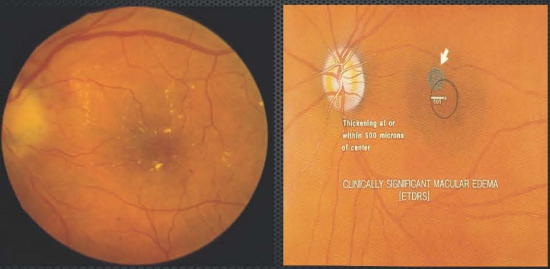
CSME

- 20 years later, the criteria remain the same




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CSME: Retinal thickening \leq 500um from foveal center



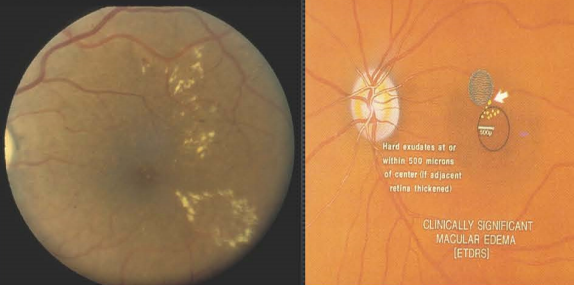
Thickening at or within 500 microns of center

CLINICALLY SIGNIFICANT MACULAR EDEMA (ETDRS)




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CSME: Hard exudates with contiguous retinal thickening \leq 500um from foveal center



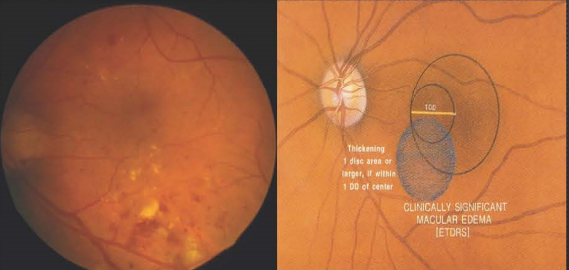
Hard exudates at or within 500 microns of center if adjacent retina thickened

CLINICALLY SIGNIFICANT MACULAR EDEMA (ETDRS)




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CSME: Retinal thickening of 1 DD within 1DD of foveal center



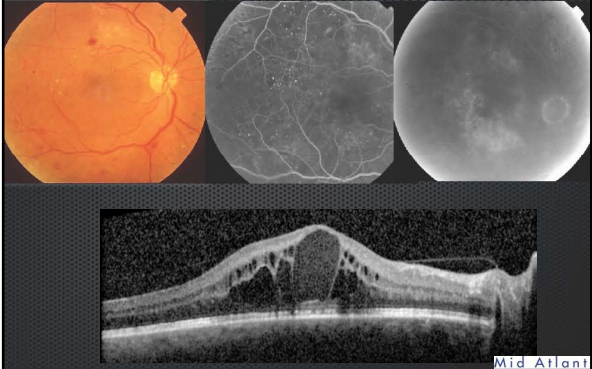

Thickening of 1 DD or more, at or within 1 DD of center

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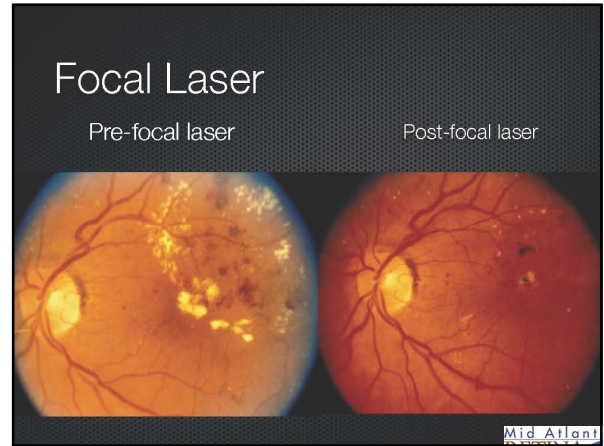
Role of Angiography and OCT

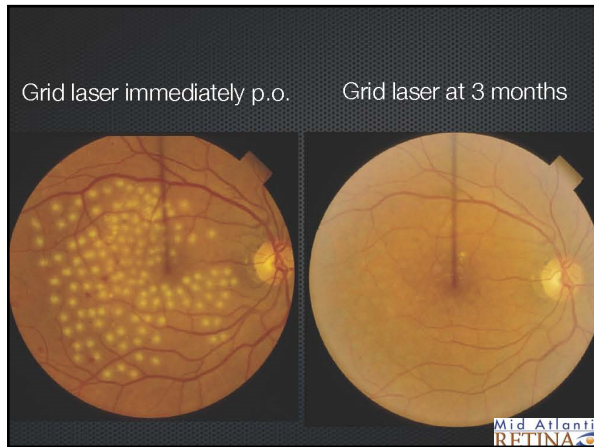
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- Complications of focal laser in CSME
 - Foveal sizzle
 - Scotoma
 - CNVM

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- ### Intravitreal Kenalog Injection
- Innovative use of steroid in reducing edema
 - Likely acts by reducing cytokines and inflammation
 - Initially, impressive results in patients refractory to laser
 - 90% have improvement of edema
 - 60% have improvement in vision
 - May have a role as first line treatment
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Diabetic Retinopathy Clinical Research network (DRCR.net)

- Eyes with DME and VA of 20/40 to 20/320 randomized to focal laser, 1 mg or 4 mg of triamcinolone.
- At three years, the laser group improved by one line, and did not change in either triamcinolone group.
- Probability of cataract surgery by 3 years was 31% for laser, 46% for 1-mg triamcinolone, and 83% in the 4-mg triamcinolone group.
- IOP increased by more than 10 mm Hg at any visit in 4% of laser, 18% of 1-mg triamcinolone, and 33% of eyes in 4-mg triamcinolone.



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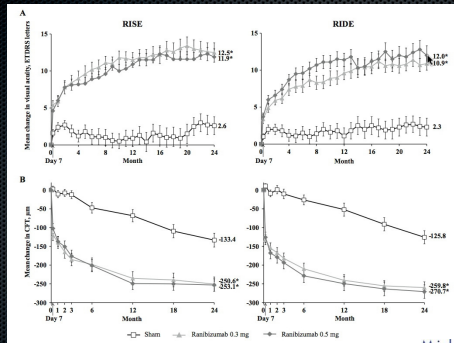
Anti-VEGF Agents

- Bevacizumab and Ranibizumab
- Case series for bevacizumab
- Randomized controlled trial ranibizumab
 - Need three year follow up
 - RISE/RIDE
 - Expanded 2-Year Follow-up of Ranibizumab Plus Prompt or Deferred Laser or Triamcinolone Plus Prompt Laser for Diabetic Macular Edema. DRCR.net Ophthalmology April 2011 (q monthx6, then PRN)



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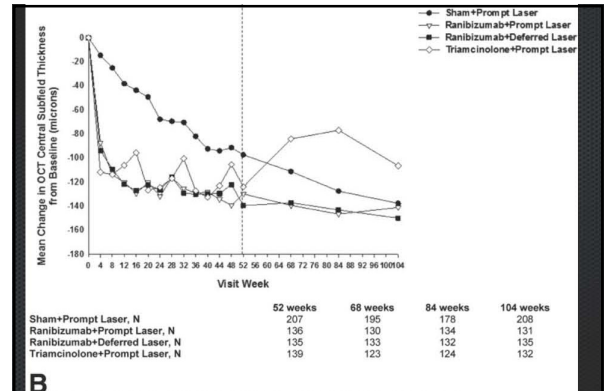
Ranibizumab DME Phase III Studies RIDE and RISE*



* Nguyen et al. Ophthalmology 2012;119:789-801.

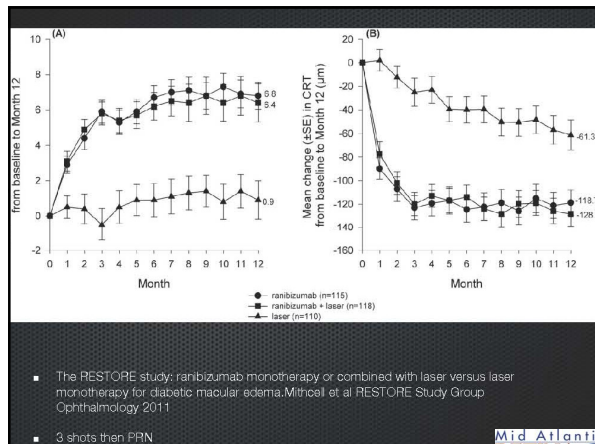


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Expanded 2-Year Follow-up of Ranibizumab Plus Prompt or Deferred Laser or Triamcinolone Plus Prompt Laser for Diabetic Macular Edema. DRCR.net Ophthalmology April 2011 (q monthx6, then PRN)

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• The RESTORE study: ranibizumab monotherapy or combined with laser versus laser monotherapy for diabetic macular edema. Mitchell et al RESTORE Study Group. Ophthalmology 2011

• 3 shots then PRN



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Current Treatments in DME

- **Anti-VEGF Injections**
 - Bevacizumab 1.25 mg (Avastin)
 - Ranibizumab 0.3 mg (Lucentis)
 - Afibercept 2 mg (Eylea)
- **Steroids**
 - Intravitreal Triescence
 - Ozurdex
 - Iluvien
- **Laser**
 - Focal/grid laser
 - Micropulse laser

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Summary

- Blood sugar, blood pressure, and cholesterol control are crucial
 - Educate patients
- The standard of care is changing
 - Focal photocoagulation
 - Anti-VEGF injections
- Future Directions
 - Avastin vs Lucentis
 - Eylea
 - Slow release steroid implants




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Bevacizumab for DME

- Mostly smaller, retrospective studies
- Pan-American Study: Retrospective (n=139)*
 - 1.25 vs. 2.50 mg bevacizumab (24 months)
 - Mean visual acuity change: 2-3 lines gained
 - 2 or more lines gained: 39-64%
 - Mean number treatments: 5.8
- BOLT Study: Prospective (n=80)**
 - Bevacizumab vs. focal laser (12 months)
 - Mean visual acuity change: + 8 vs. -0.5 letters
 - 2 or more lines gained: 31% vs. 7.9%
 - Mean number treatments: 9 vs. 3

*Arevalo et al. *Ophthalmology* 2009; 116:1488-149

**Michaelides et al. *Ophthalmology* 2010; 117:10778-1086



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THANK YOU

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