Diabetic Retinopathy

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Acknowledgment

- **Several of the slides used in this presentation come from slide sets prepared for diabetes education by:**
  - ✓ **Pennsylvania Diabetes Association**
  - ✓ **American Academy of Ophthalmology**

Disclaimer

- **PI for Genetech sponsored clinical trial using ranibizumab (Lucentis) for treatment of diabetic macular edema, ARMD and other retinal vascular diseases.**

Off label medications

- **Ranibizumab (Lucentis)**
- **Bevicizumab (Avastin)**
- **Pegaptanib (Macugen)**
- **Triamcinolone (Triessence, Kenalog)**
- **Dexamethasone**

Objectives

- Review the risk factors, presentations and clinical manifestations of DR
- Review current treatment options, goals and outcomes
- Review screening and management roles played by non-ophthalmologic physicians

1976
Diabetic Retinopathy Study

- Demonstrated effectiveness of panretinal photocoagulation for proliferative retinopathy

Pre-1974

- Blindness
- Pituitary ablation

Late 1970's – Early 1980's

- Refinement of laser procedures
- Development of vitreo-retinal microsurgical instrumentation and procedures

1982
Early Treatment Diabetic Retinopathy Study

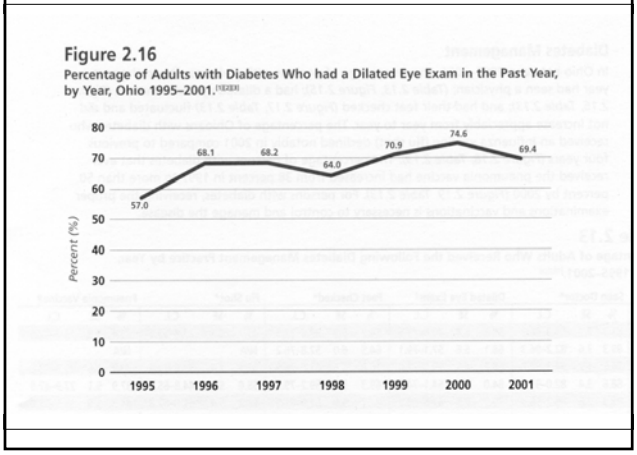
- Demonstrated effectiveness of focal photocoagulation for macular edema

2009

- Diabetic Retinopathy remains one of the most significant complications of diabetes and continues to be the leading cause of blindness

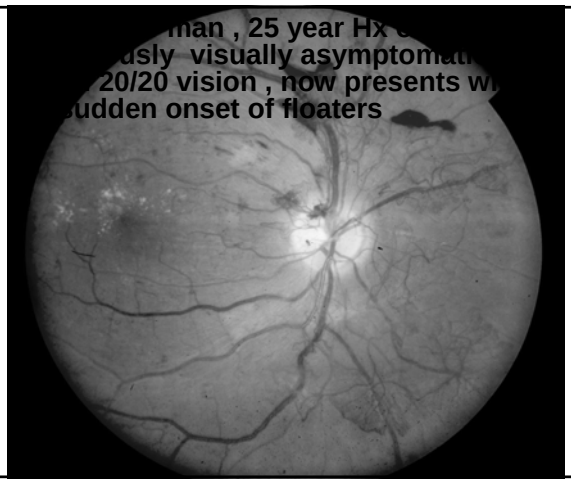
2005

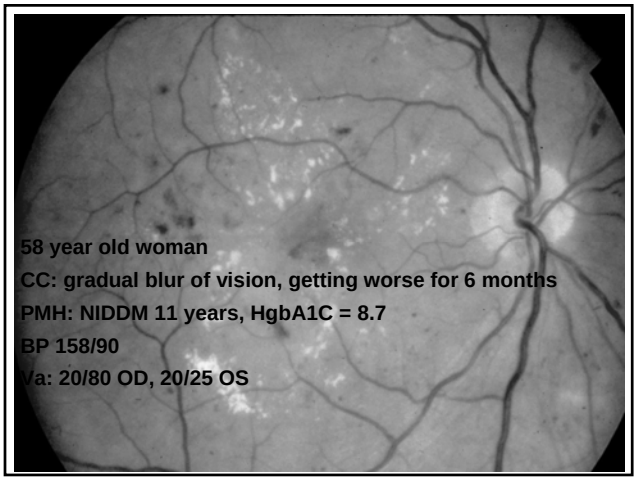
First use of VEGF inhibitors



Diabetic Retinopathy

- **Early detection and early treatment are crucial for the prevention of blindness**





Who Gets Retinopathy?

Factors include

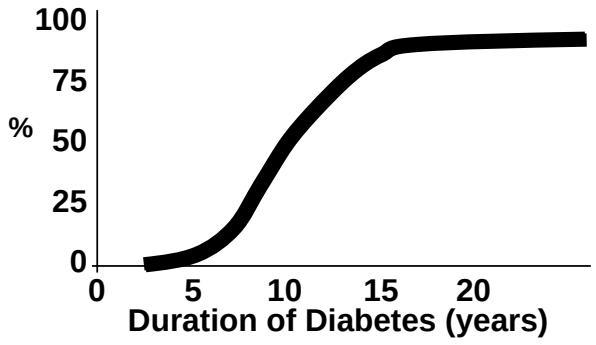
- Age of onset
- Duration of disease
- Degree of control
- Hypertension

Age of Onset and Duration

Prior to age 30

- Duration less than 5 years
  - ✓ 17% have some retinopathy
  - ✓ Macular edema unusual, PDR rare
- Duration greater than 15 years
  - ✓ 98% have some retinopathy
  - ✓ Approximately 1/3 have macular edema
  - ✓ Approximately 1/3 have PDR

Prevalence of Retinopathy



Age of Onset and Duration

After age 30

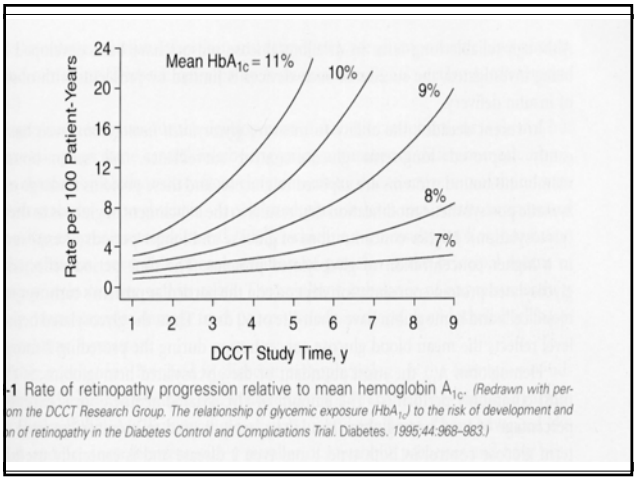
- Duration less than 5 years
  - ✓29% have some retinopathy
  - ✓Macular edema unusual, PDR 2%
- Duration greater than 5 years
  - ✓78% have some retinopathy
  - ✓Approximately 28% have macular edema
  - ✓Approximately 16% have PDR

DCCT and UKPS

- **Intense glucose control reduced rates of progression of retinopathy**
- **Blood Pressure control reduced progression of retinopathy**

Diabetes Control and Complications Trial

- **Intensive glucose control**
- **No baseline retinopathy**
  - ✓**76% reduction in the risk of developing significant retinopathy**



-1 Rate of retinopathy progression relative to mean hemoglobin A_{1c}. *(Redrawn with permission from the DCCT Research Group. The relationship of glycemic exposure (HbA_{1c}) to the risk of development and progression of retinopathy in the Diabetes Control and Complications Trial. Diabetes. 1995;44:968–983.)*

Diabetes Control and Complications Trial

- **Intensive glucose control**
- **Mild to moderate retinopathy**
  - ✓**54% reduction in progression**
  - ✓**47% reduction in development of severe NPDR or PDR**
  - ✓**56% reduction in need for laser surgery**

Hypertension and Diabetes

- There is a positive correlation between elevated systolic blood pressure and the development of exudative complications of retinopathy

Pathophysiology *Known*

- VEG-F
  - ✓ Stimulates proliferation of new vessels
  - ✓ Increases vascular permeability
  - ✓ Has pro-inflammatory activity
- PEDF
  - ✓ Decreases in DR
  - ✓ Inhibits neovascularization

Pathophysiology *Known*

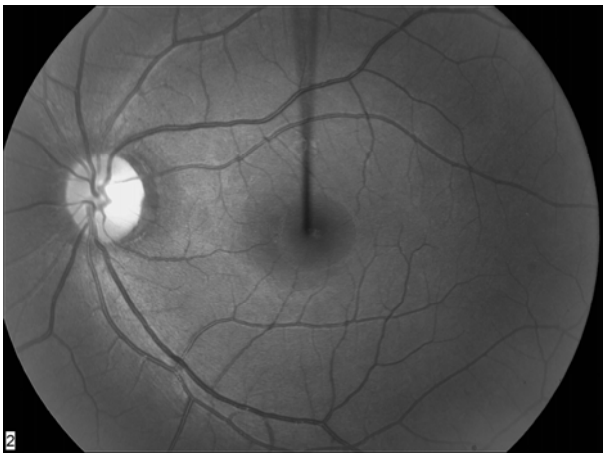
- Hyperglycemia > loss of pericytes
- Loss of pericytes > loss of capillary endothelia and capillaries
- Loss of capillaries > hypoxia and ischemia
- Hypoxia > release of VEGF
- Decrease PEDF

Other Possible Mechanisms

- Aldose reductase: glucose to sorbitol causing osmotic cell damage
- Protein Kinase C upregulates VEGF, enhanced by hyperglycemia
- Reactive oxygen species causes oxidative damage – increased VEGF
- Growth hormone plays permissive role for VEGF, reduction in GH prevents neovascularization

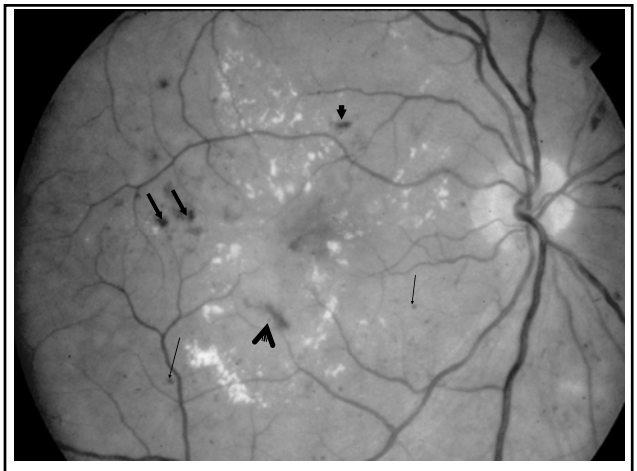
Classification and Lesions of Diabetic Retinopathy

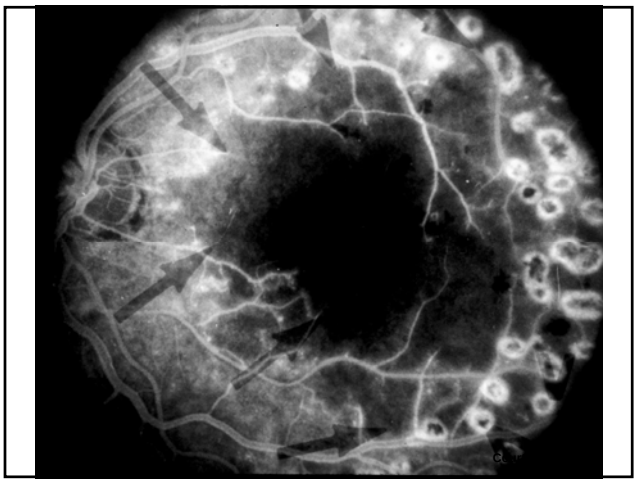
- NonProliferative Diabetic Retinopathy (NPDR)
- Proliferative Diabetic Retinopathy (PDR)

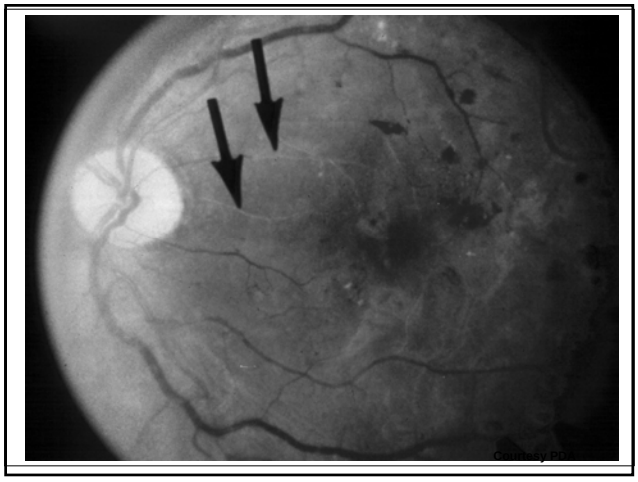


Early NonProliferative Diabetic Retinopathy

- Microaneurysms
- Hard exudates
- Intraretinal hemorrhages
- Macular edema*





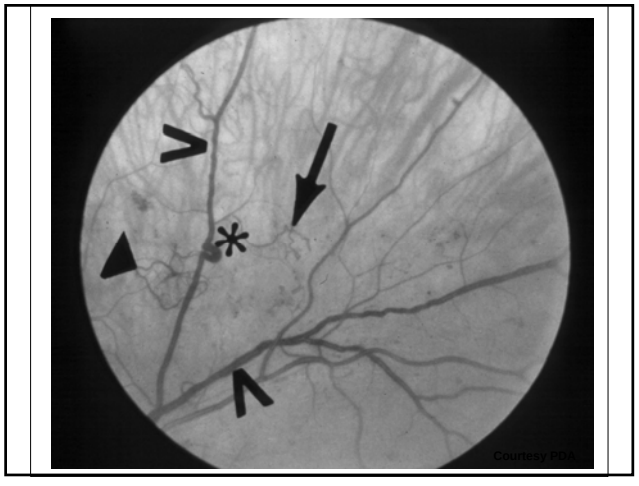


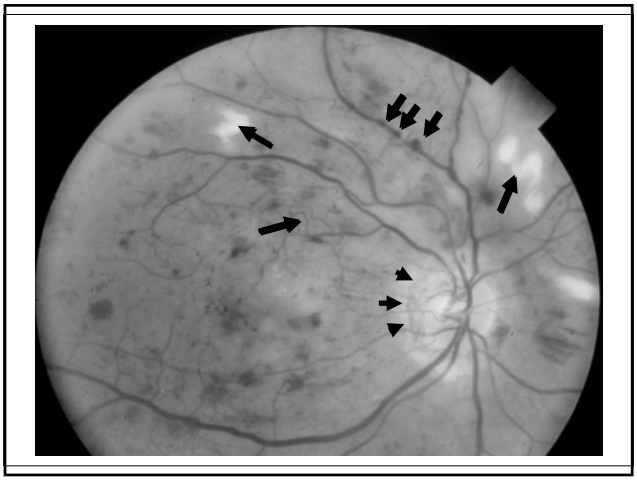
Advanced NonProliferative Diabetic Retinopathy

- Cotton wool spots
- IntraRetinal Microvascular Abnomalities (IRMA)
- Venous Bleeding

Advanced NonProliferative Diabetic Retinopathy

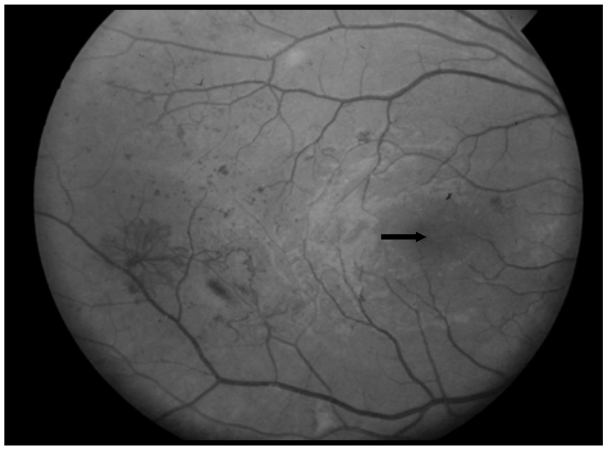
- High risk of imminent PDR
- No immediate treatment
- Patient needs re-evaluated in 2-4 months

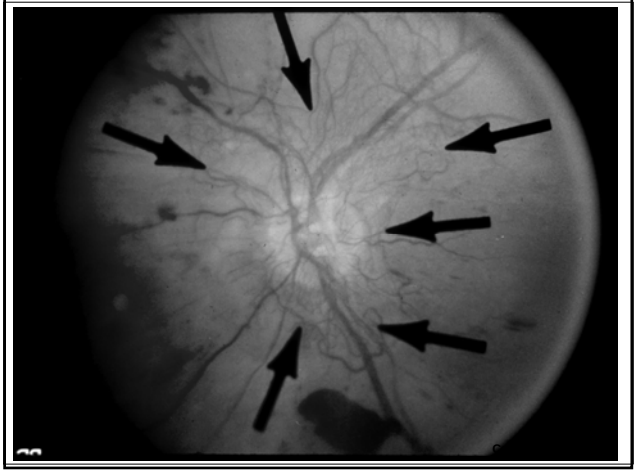


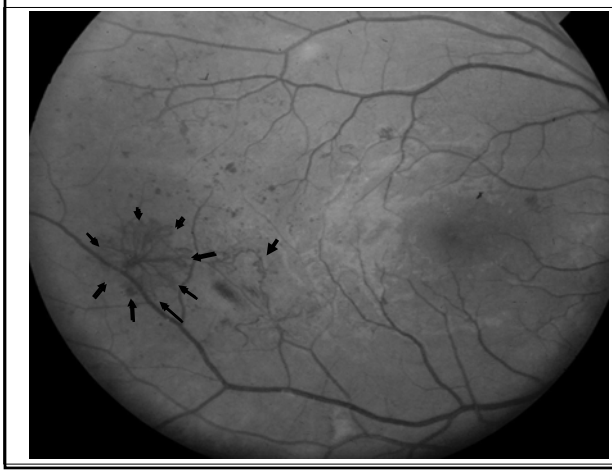


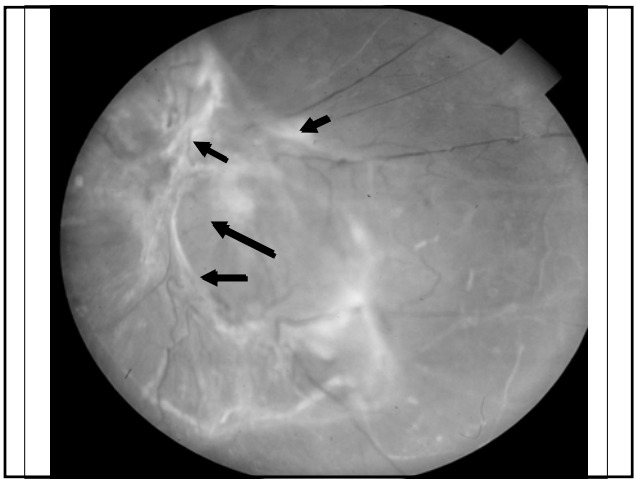
Proliferative Diabetic Retinopathy

- Signs of NPDR including macular edema
- Neovascularization of disc (NVD) or retina (NVE)
- Vitreous hemorrhage
- Fibrous proliferation with retinal detachment









What Causes Vision Loss?

- **Macular edema can occur in NPDR or PDR**
- **Vitreous hemorrhage PDR**
- **Traction Retinal Detachment PDR**

Diabetic Maculopathy Includes

- Macular edema (retinal swelling)
- Lipid exudation (hard exudates)
- Ischemia (capillary nonperfusion)

When is Maculopathy Treated?

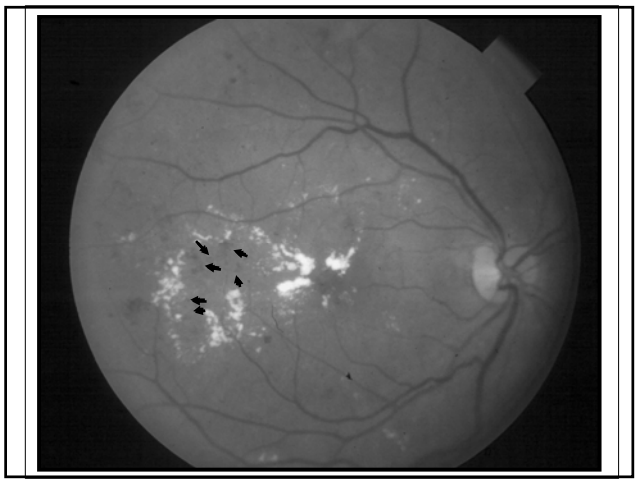
- Retinal edema within 1/3 disc diameter from the center of the fovea
- Hard exudate within 1/3 DD associated with edema
- Edema greater than 1 DD in area within 1 dd from fovea

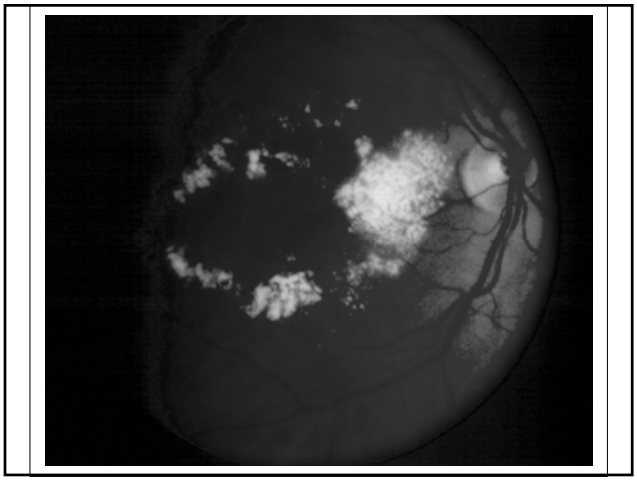
What Are Symptoms of Maculopathy?

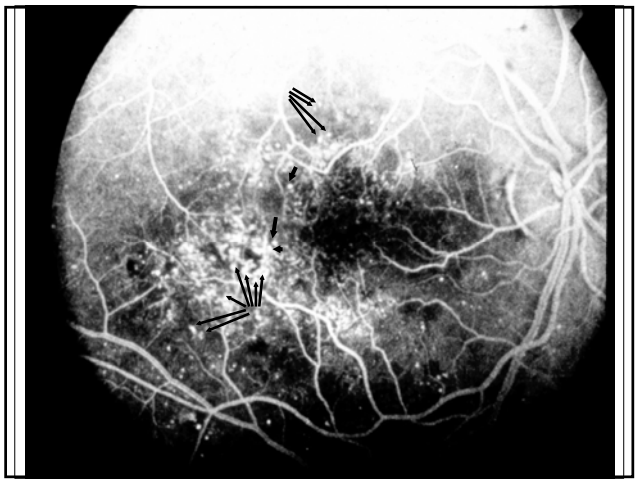
- None
- Gradual progressive loss of central vision
- Vision is “smeared”, “oily”, “filmy”, “scum”, “dirty glasses”
- Central scotoma

How do We Treat Macular Edema?

- Treatment guided by Fluorescein angiography
- Focal laser coagulation of microaneurysms
- Grid laser to areas of retinal edema and non-perfusion

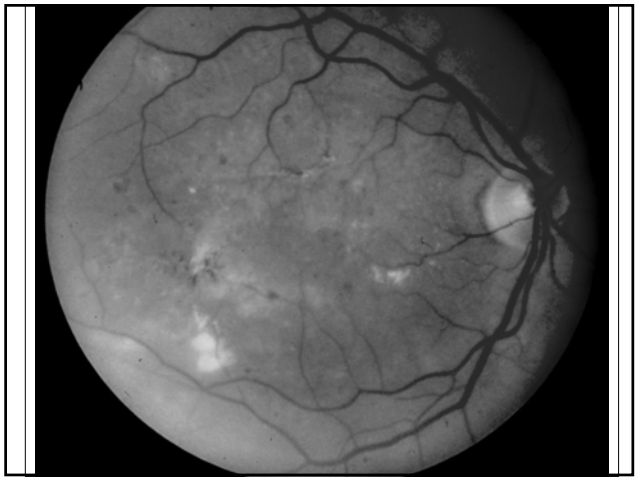






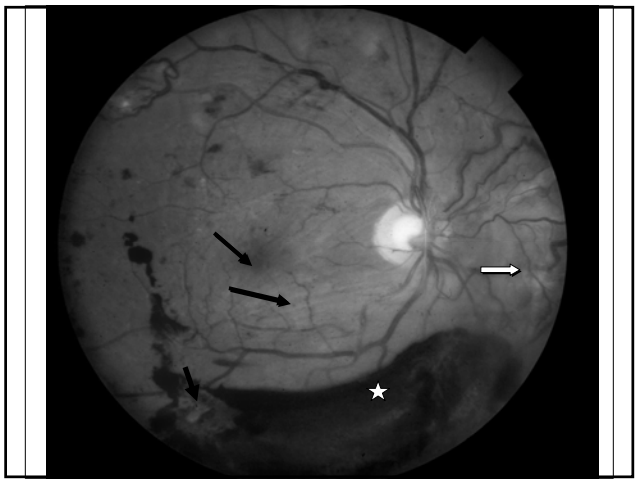
Results of Treatment for Macular Edema

- 50% reduction in rate of vision loss
- 20% improved vision
- 60% stable vision
- 20% will show progressive vision loss in spite of treatment



What are Symptoms of Proliferative Diabetic Retinopathy?

- None
- Floaters and cobwebs
- Rapid dramatic vision loss
- Visual field loss

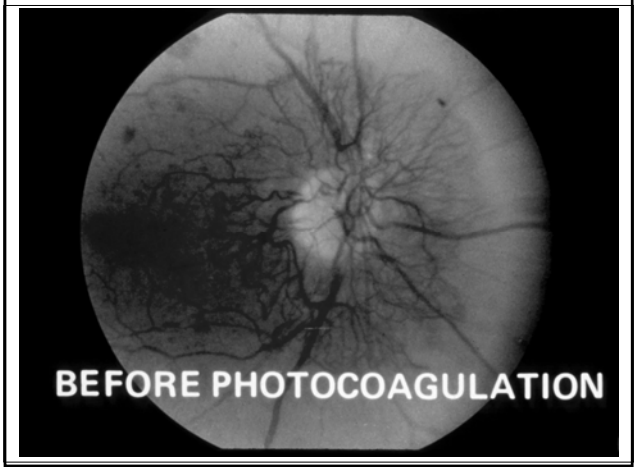


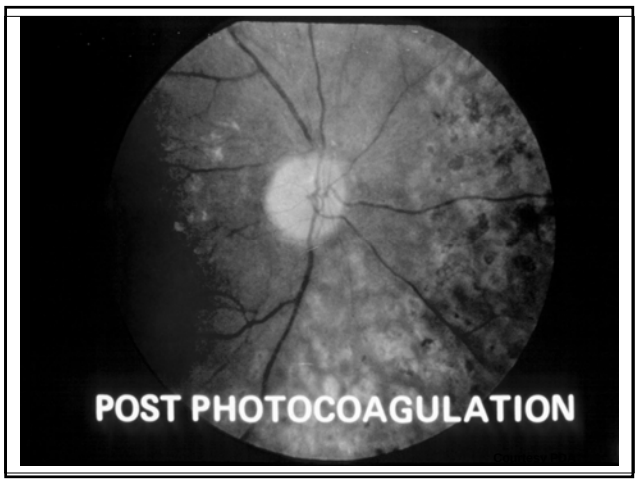
Pan Retinal Photocoagulation (PRP)

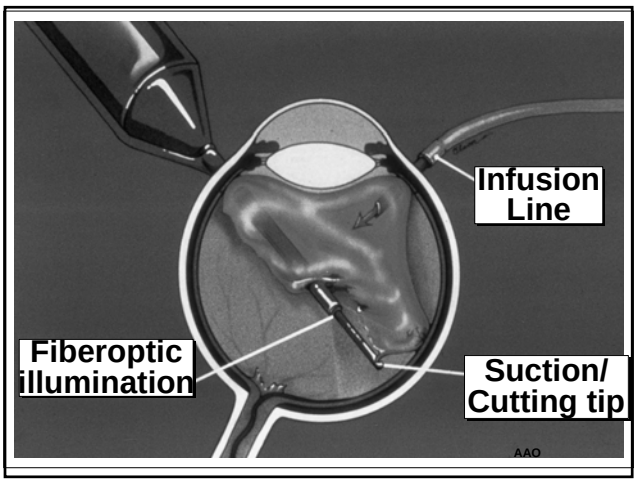
- Outpatient procedure
- 1000-2000 laser burns
- 1 to 3 sessions
- Side effects:
  - ✓ Decreased night vision
  - ✓ Decreased peripheral vision
  - ✓ Decreased central vision

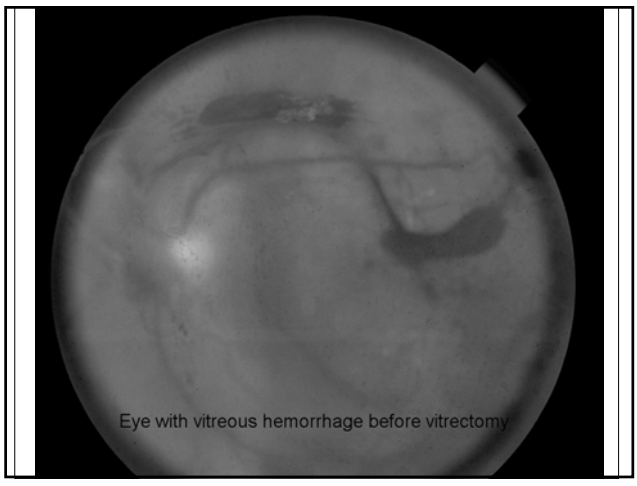
When is Proliferative Diabetic Retinopathy Treated?

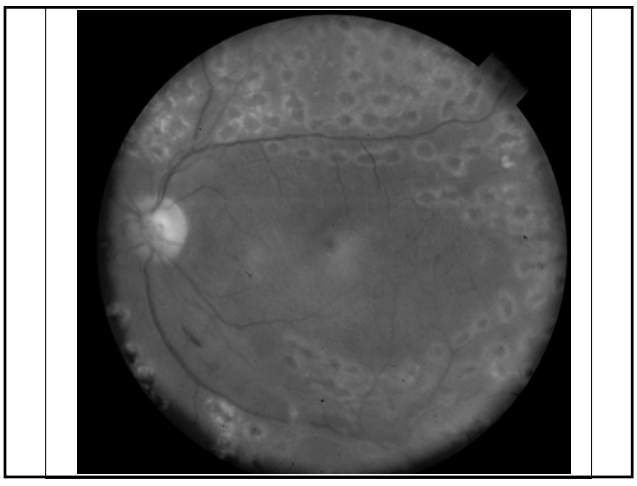
- Pan Retinal Photocoagulation for High Risk PDR:
  - ✓NVD
  - ✓NVD or NVE with preretinal bleeding
- Vitrectomy for non-clearing vitreous hemorrhage or TRD




POST PHOTOCOAGULATION


Infusion Line
Fiberoptic illumination
Suction/ Cutting tip
AAO


Eye with vitreous hemorrhage before vitrectomy



Results of Treatment for Proliferative Diabetic Retinopathy

- **Laser reduces risk of severe vision loss by 60%**
- **Vitrectomy restores pre-hemorrhage vision in 85% and allows completion of treatment with laser**
- **Vitrectomy restores vision in 65% for repair of TRD**

Medical Management *Hgb A1C < 7.0*

- **Good Glucose control**
  - ✓**Both DCCT and UK study show reduction in ocular complications**

Emerging Therapy

- **VEG-F inhibitors –off label, in clinical trial**
  - ✓ **Macugen (pegaptanib) PDR, CSDME**
  - ✓ **Lucentis (ranibizumab) CSDME, CRVO, BRVO**
  - ✓ **Avastin (bevacizumab) CSDME, PDR, NVG, CRVO**
- **Intra-vitreal steroid injection – off label, in clinical trial**
  - ✓ **Triamcinolone CRVO, BRVO, CSDME**
  - ✓ **Dexamethasone CRVO, BRVO, PDR, CSDME**

Medical Management *Hypertension*

- **A significant risk factor for development and progression of retinopathy**
- **Systolic < 130 mmHg**
- **Risk reduction similar for ACE inhibitors or other agents (Beta-blockers)**

Medical Management
Renal Disease

- **Renal disease may aggravate retinal edema**
- **Role of dialysis in regard to stabilizing retinopathy is not clear (many have already had laser)**
- **Heparin – increased risk of bleeding**

Medical Management
Anemia

- **Frequently overlooked**
- **Significant effects on retina**
- **Hgb < 12gms = 2x risk for retinopathy**
- **Increased risk of macular edema**

Medical Management
Lipid Abnormality

- **Increased retinal exudation with:**
  - ✓**Elevated serum cholesterol**
  - ✓**Elevated triglycerides**
  - ✓**Manage lipid abnormalities**

Medical Management
Anemia

- **Low hematocrit is an independent risk factor for developing PDR and severe vision loss**
- **Frequently related to renal disease and associated lack of erythropoeitin production**
- **Correction reduces retinal exudation and edema**

Medical Management
Medication FAQs

- **Aspirin – no increase in severity or frequency of hemorrhage**
- **ASA did decrease death from Cardiovascular disease by 17%**
- **Anti-oxidants - ? Benefit of Vitamins C, E, beta-carotene**

Medical Management
Screening Criteria

- **Pregnancy: discuss risk before conception**
  - ✓ **Existing retinopathy may worsen**
  - ✓ **Retinopathy may develop**
  - ✓ **Retinal evaluation before conception or in first trimester**

Medical Management
When to refer?

- **Situations requiring referral**
  - ✓ **Macular edema**
  - ✓ **NVD/NVE**
  - ✓ **Vitreous bleeding**
  - ✓ **Sudden unexplained vision loss**

Medical Management
Screening Criteria

- **Diabetes Dx < age 30:**
  - ✓ **Annual ophthalmologic exams beginning 5 years after diagnosis**
  - ✓ **Ophthalmoscopy by PCP at other intervals**

Medical Management
Screening Criteria

- **Diabetes Dx > age 30:**
  - ✓ **Annual ophthalmologic exams beginning at the time of diagnosis**
  - ✓ **Ophthalmoscopy by PCP for signs at other intervals**

Final Comment

- **Team Event: patient, ophthalmologist and physician managing diabetes.**
- **With good team play, the prognosis for maintaining functional sight is good**