DIABETIC RETINOPATHY

Didactic lecture in Hotel Krishna main hall by Dr. H. S. Ray M.S., Ophthalmology, FRF (Ahemdabad) - Drishti Eye Hospital, Madan Mahal Main Road, Jabalpur 2.

Session Sponsor:_____

TYPES OF DIABETES MELLITUS

o **TYPE -I or IDDM**
o 10% 0f Diabetics
o Insulinopenia due to Beta Cell failure
o Abrupt in Onset & Prone to Ketosis
o Diagnosed before 40 Years, Majority in Childhood

o **TYPE -II or NIDDM**
o Slow Onset & Progression
o Serum level of Insulin varies- Normal, Above & Low
o Displays Tissue Resistance to Insulin (Abnormal Insulin)
o Usually occurs above 40 years (M:F Ratio 2:3)

DIAGNOSIS

Symptoms
o Polyuria,
o Polyphagia,
o Rapid Weight Loss.

Lab findings
o Elevated Plasma Glucose Level:
* Fasting Plasma Glucose >/= 140mg/dl
* Post Prandial Plasma Glucose (GTT) >/= 200mg/dl

PATHOGENISIS OF DIABETIC RETINOPATHY

o Hypoxia - Low 2,3 DPG, & High HbA -Lower tissue Oxygen
o Polyol Pathway of glucose metabolism
o Intracellular Sorbitol & Fructose
o Release of Growth hormone, Fibrinogen & Alpha 2 Globulin
o Hyperaggragation of RBCs & Platelets- Sludging of blood flow
o Prostaglandins cause Vascular Insult
o Prostacyclin (PGI 2)
o Thromboxane (TXA 2)
o Leukotrienes inhibits PGI 2 & promotes TXA 2
o Disparity between PGI 2 & TXA 2 plays a role in Diabetic Microangiopathy.

PATHOGENISIS OF POLIFERATIVE DIABETIC RETINOPATHY

o Angiogenic Factors (Peptides)
o bFGF (basic Fibroblast Growth Factor)
o IGF (Insulin Growth Factor)
o VEGF (Vascular Endothelial Growth Factor)
o Role of PVD
o Mechanical effect for developing Proliferative Tissue
o Complete PVD occurs due to Aging
o Partial PVD is more common in Diabetics with PDR
o Scafolding for Fibro-Vascular Proliferation
o Vitreo-Retinal Traction - TRD
o Precocious PVD before PDR prevents TRD

Anatomic Lesions & Pathogenesis of DR

Microscopic Level Changes

o Capillary Basement membrane thickning, Increases in thickness to 5 Times from 0.5
o Loss of Intramural Pericyte (Pericytes:Endo.Cells= 1:1)
o Capillary Acellularity
o Microaneurysms
o Impairment of Autoregulation

EPIDEMIOLOGY

o Type-1, Males are at higher risk of developing PDR than Maculopathy
o Maculopathy is more common in Type-2
o Retinopathy is a consequence of long term sustained Hyperglycemia, but often modified by Genetics & acquired Systemic factors.
o Tight long term Control of Diabetes, Hypertension, Proteinuria, & Smoking can prevent or retard Diabetic Retinopathy.

EPIDEMIOLOGY of PDR

o Wisconsin Epidemiologic Study of DR (WESDR)
o Younger-Onset group (YOG): (Before 30 Yrs.)
o Prevalence of DR : 2% in of <2 Yrs. 98% in >15 Yrs.
o PDR: 0% in <5Yrs. 25% in 15Yrs. 56%in >20Yrs.
o Macular Edema:Rare before 10Yrs. 21% in>20Yrs
o Older-Onset group (OOG): (After 30 Yrs)
o DR: 30% in (IT) & 23% in (NIT) in DM of 2 Yrs.
o PDR: 20% in (IT) & 4% in (NIT) after 15 Yrs.
o 4-Year Incidence & Progression
o YOG : 59% Retinopathy, 41% Progression, & 10.5% to PDR
o OOG(IT) : 47% Retinopathy, 34% Progression, & 7% to PDR
o OOG (NIT) : All incidences are Low, 34% show Retinopathy
o WESDR found an Increase in PDR Risk:
o Elevated HbA- in all group
o Proteinuria- in YOG with DM of 10 Yrs.
o Elevated Diastolic BP & Male Sex in Younger-Onset.
o Elevated Systolic BP in Older-Onset group.
o Legal Blindness: 3% in Older-OG, 1.5% in Y-OG
o Mortality risk : Increases in patients of PDR with
o Diabetic Nephropathy
o Genetic Factors (Histocompatibility Antigen)
o HLA-DR Phenotypes 4/0, 3/0, X/X (neither 3 nor 4) have 3 - 4 times higher risk than HLA-DR 3/4 , 3/X, 4/X, ones found in DM

LABORATORY- INVESTIGATIONS

o FBS & PPBS (1½ hrs).
o Urine - Sugar, Albumin, M/E
o Glycosylated Hb (Normal 5-8)
o Lipid Profile - Cholestrol, Triglyceride, HDL / LDL / VLDL
o RFT- Serum Creatinine & Blood Urea
o Cardiovascular Workup - CPK, LDH
o RA Factor - If h/o Joint pain.

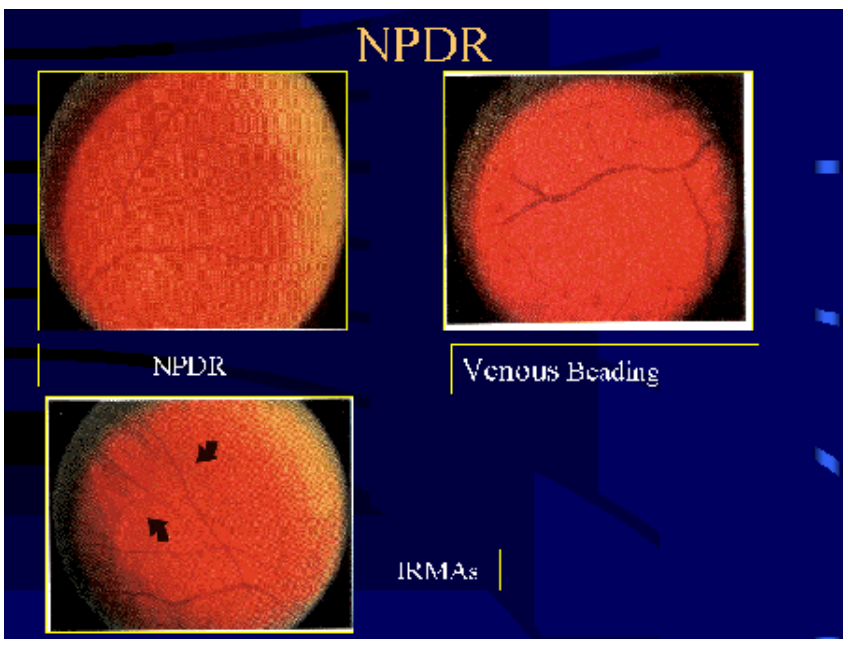
Clinical Classification DRS / ETDRS

o Background diabetic retinopathy (NPDR).
o Pre-proliferative diabetic retinopathy. (Severe NPDR).
o Proliferative diabetic retinopathy (PDR).
o Advanced diabetic eye disease.
* Persistent New vessels * Traction RD.
* Neovascular glaucoma.
5. End stage diabetic eye disease.
6. Maculopathy.
* Focal * Diffuse * Ischaemic * Mixed.

Background Retinopathy (NPDR)

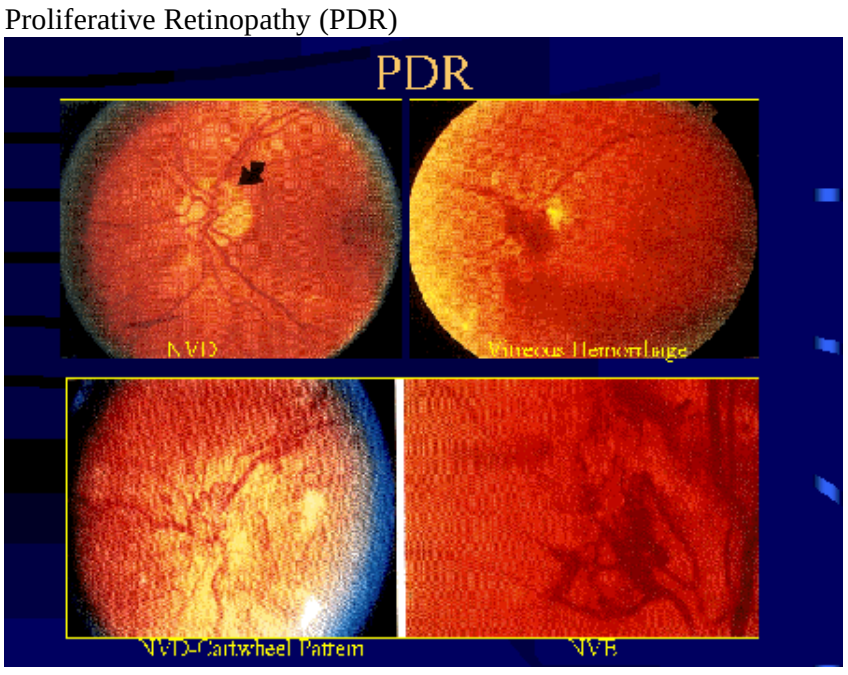
o Microaneurysms
o Retinal Hemorrhages
o Hard Exudates
o Retinal Oedema

NPDR

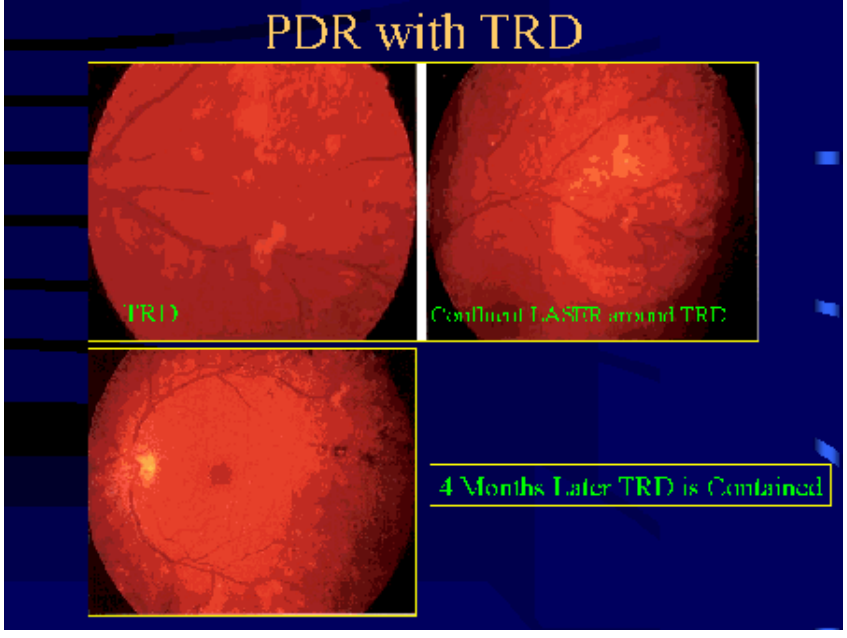


Pre-proliferative Retinopathy
Severe / Very Severe NPDR

Proliferative Retinopathy (PDR)



PDR with TRD



Steps of Neovascularization

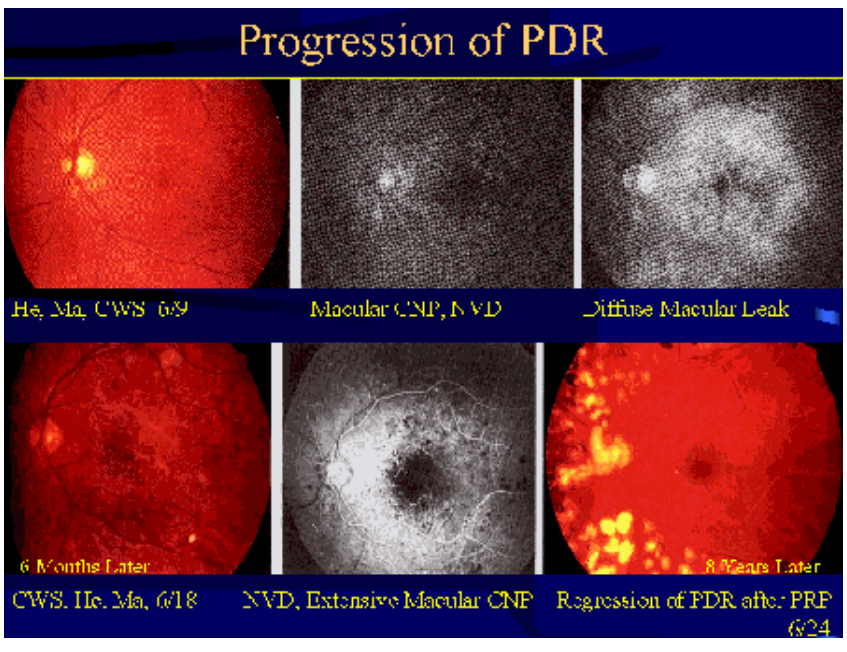
o Destruction of Basement Membrane
o Extension of Cytoplasmic Bud from Endothelial cells
o Migration & Division of Endothelial cells
o Tubes unite to form Capillaries as Flat Fronds
o NV grows through ILM into Vitreous, accompanied by Proliferative Fibrous Tissue

Types of Neovascularizition:

o Epipapillary
o Peripapillary
o Papillo-vitreal- a.Columnar b.Arcuate c.Confluent
o Retino-vitreal
o Preretinal (Surface)

High-Risk Characteristics of PDR (HRC)

o NVD that is covering ¼ to 1/3 disc area or more in size
o NVD less than ¼ disc area in size with fresh Vitreous or Pre-retinal hemorrhage.
o NVE greater than or equal to ½ DD in size with fresh Vitreous or Pre-retinal Hemorrhage



Glial Proliferation - PDR

Grade 1 : Patchy Gliosis in the Posterior pole or along the Midportion or Distal aspect of the vascular
arcades, not involving the Optic Disc. FPE

Grade 2 : Gliosis involving the Optic Disc only. FPD

Grade 3 : Gliosis of the Arcade region & Optic Disc Moderate FPE & FPD

Grade 4 : Circular Band of Gliosis involving the Optic Disc,Vascular arcade, & Temporal Interarcade retinal area. Severe FPE & FPD

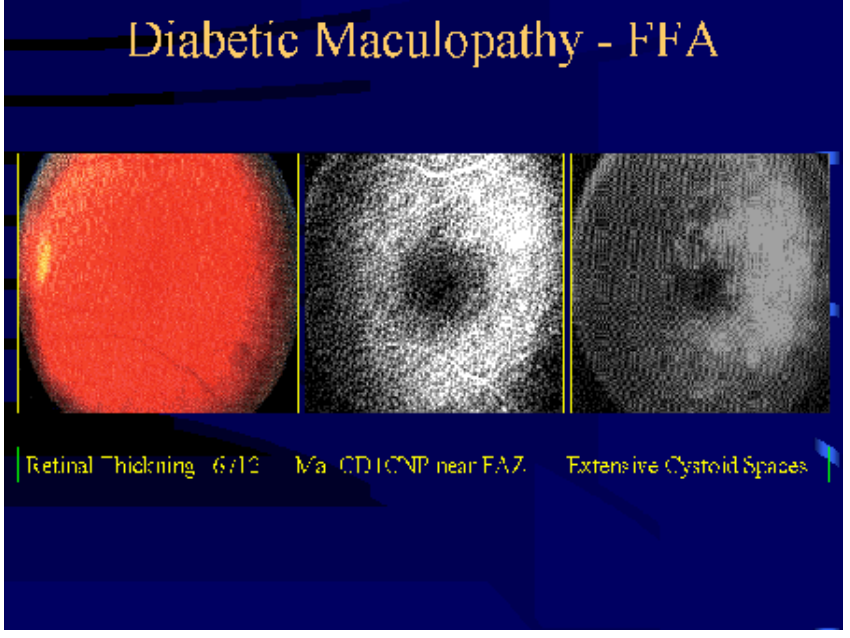
Grade 5 : Indicates a Shallow, Circular, Centrally located TRD around the Optic Nerve & Posterior pole
caused by traction from a shallow PVD

Grade 6 : Moderately elevated central TRD caused by a highly detached Cone shaped PVD extending to
the region of Ora Serrata

Grade 7 : Markedly elevated Total TRD by a highly detached posterior hyaloid adherent to the
vitreous base .

Grade 8 : Total TRD caused by excessive traction from a highly detached posterior hyaloid & cyclitic
membrane pulling the retina into the Retrolental space. Triangular Syndrome.

Diabetic Maculopathy



Mechanisms of Macular affection in Diabetes

o Collection of interstitial fluid within the Macula with or without lipid exudates or cystoid changes
o Nonperfusion of parafoveal capillaries with or without intraretinal fluid.
o Traction in the Macula by Fibrous Tissue Proliferation causing dragging, surface wrinkling, or detachment of macula
o Intraretinal or Preretinal Hemorrhages in the Macula
o Lamellar or Full-thickness Macular Hole

CSME

o Retinal Thickening at or within 500 micron of the center.
o Hard Exudates at or within 500 micron of the center + Thickening of adjacent retina.
o Area of Retinal Thickening at least 1 Disc Diameter in size, A part of which is at least within 1 DD of the center.
* Focal * Ischaemic
* Diffuse * Mixed

CSME Criterion
Levels of Retinopathy

NPDR

o Mild NPDR 5% 15% At least One Microaneurysm
o Moderate NPDR 12-27% 33% Ma, Soft Exudates (CWS), Venous Beading (VB) & IRMAs
o Severe NPDR "4-2-1 rule" 52% 60% Hge / Ma in all 4 quadrants, or V B in 2 or more quadrants, or IRMA in atleast 1 quadrant.
o Very Severe NPDR 75% 75% Two or more lesions of Severe NPDR but no NV

PDR Composed of
o NVD,or NVE
o Pre-Retinal or Vitreous Hemorrhage
o Fibrous Tissue Proliferation (FPD & FPE)
o Early PDR 75% NVD or NVE (Definition not met for High-Risk PDR)
o High-Risk PDR
o NVD => 1/3 to ½ Disc Area
o NVD less than ¼ Disc area with fresh Vitreous or Pre-retinal Hge.
o NVE => ½ DD in size with fresh Vitreous or Pre-retinal Hge.

Progression of PDR

PDR at 1-Year Visit
by Severity of Individual Lesion
Lesion Grade PDR in 1-year(%)
Hge / Ma Present in 2-5 fields 9
Very severe >5 fields 57
IRMA None 9
Moderate in 2-5 fields 57
VB Absent 15
Present in 2-5 fields 59

Management of Diabetic Retinopathy

o There is No known Cure for Diabetic Retinopathy & Diabetic Maculopathy.
o Laser minimizes the risk of MVL & SVL(<5/60)
o Meyer Schwickerath- Pioneer Photocoagulation in 1955
o Four Major Clinical Trial- DCCT, DRS, ETDRS, & DRVS have largely determined the strategies for management of DR.

Diabetic Control & Complication Trial (DCCT)

o To study Primary prevention & Secondary Intervention
o An average of 3 years Intensive Rx reduction in Risk.
o Rapid Glycemic control in previously uncontrolled Diabetics is detrimental for Diabetic Retinopathy.
o Intensive Rx of DM slowed the development of DR- 9 Yrs Trial
o Benefit of Intensive Rx is more in Early NPDR Stage of DR than in More Advanced Severe NPDR or PDR Stage.
o A 10% reduction of Hb-A level significantly reduced the Risk of Onset & Progression of DR, also reduced the need for Laser Therapy.

DRS (Diabetic Retinopathy Study) Major Conclusions

o Photocoagulation Reduces the risk of severe visual loss by 50% or more (SVL= < 5/60)

o Modest Risk of decrease in Visual Acuity (usually only 1 line) & Visual Field Following Laser Photocoagulation.
o Treatment benefit Outweighs Risk for eyes with High-Risk PDR (50% 5-year rate of SVL in such eyes without treatment was reduced to 20% by treatment).

ETDRS (Early Treatment Diabetic Retinopathy Study) DRVS (Diabetic Retinopathy Vitrectomy Study)

Major Conclusions:
Group H -Recent Vitreous Hemorrhage
o Chances of recovery of Visual acuity > 6/12, increased by 50% in Early Vitrectomy group verses 12% in Conventional Management group at 4 year follow-up in Type-I Diabetes who were younger & had Severe PDR.
Group NR- Very Severe PDR With Useful Vision
o Chance of VA > 6/12, increased by Early Vitrectomy (rather than Delayed Vitrectomy) for eyes with Very Severe New Vessels

Role of Fluorescein Angiography & Fundus Photography

o BDR- Baseline Photo / Maculopathy
o CSME- Ischaemia / Extent / Location
o PPDR- Extent of CNP / NVD / NVE / IRMAs
o PDR- Resudial or Recurrent Proliferation
o Angiographic Risk Factors (EDTRS)
o Fluorescein Leakage
o CNP on FA
o Capillary dilatation on FA
o Colour Fundus Photo Risk Factors
IRMAs, Venous Beading, Hemorrhage, Ma, Hard & Soft Exudates (CWS)

Perifoveal Capillary Network
Diabetic Maculopathy - FFA

Eye Examination Schedule

Age at Onset of Diabetes Time of 1st Ex. Minimum Follow-up
0-30 yrs 5 yrs after onset Every year
31 yrs or > At Diagnosis Every year
During Pregnancy 1st Trimester 3 monthly & for 1styr

Diabetic Status of Retina Follow-up (Months)

Normal or Mild NPDR 12
NPDR without Macular edema(ME) 6-12
NPDR + ME (non-significant) 4-6
NPDR + CSME 3-4
Severe NPDR 3-4

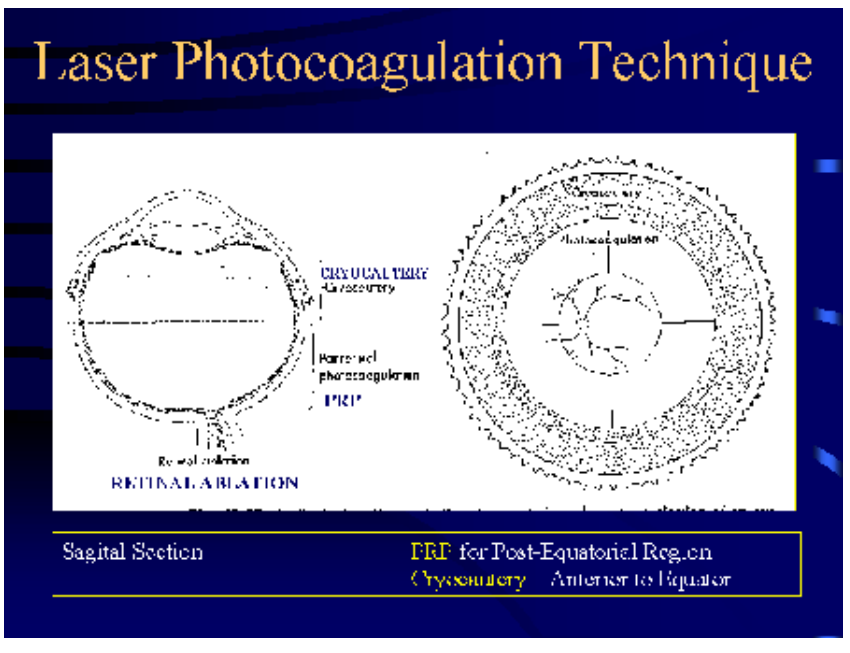
General Management Recommendations

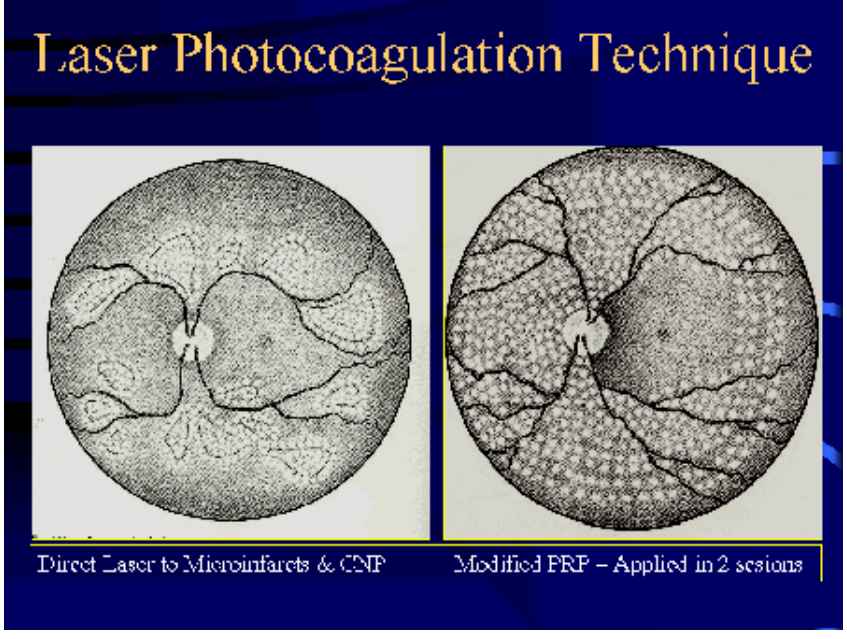
General Management Recommendations (Contd,)

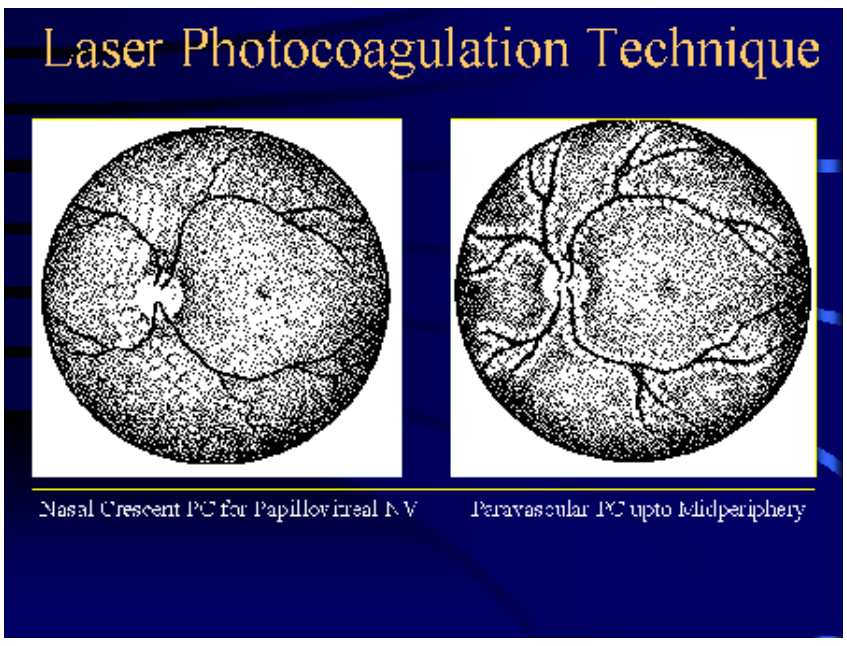
Laser Management of Diabetic Maculopathy

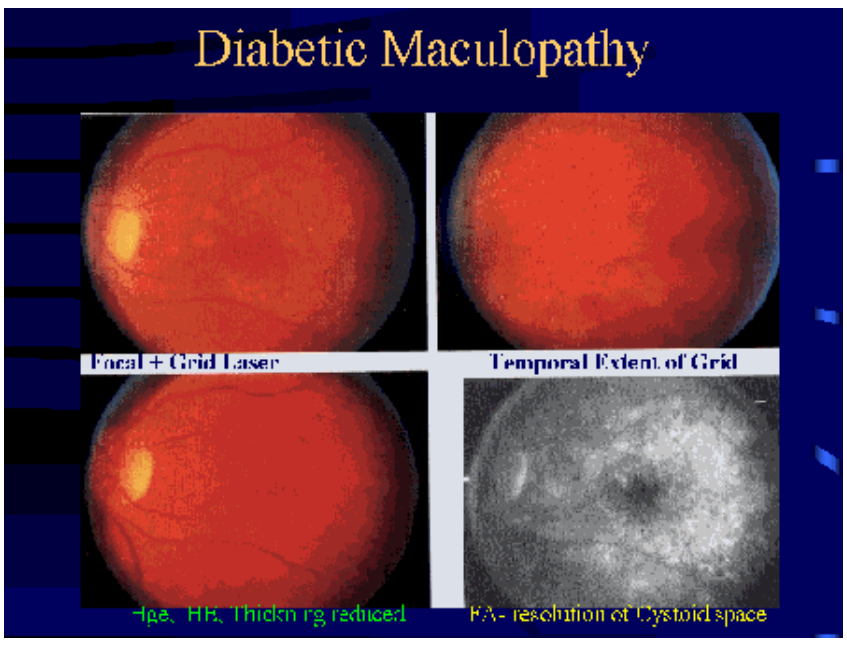
ETDRS Protocol for CSME:
o FA is done prior to deciding treatable lesion
o Discrete points of retinal hyperfluorescence or focal leakage that are >500 micron from the center.
o Focal Leaks 300-500 micron from the center of the macula, causing retinal thickening or hard exudates.
o Areas of Diffuse leak within the retina (IRMA or leaking capillary bed)
o Thickened retinal avascular zones (except normal FAZ).

Laser Photocoagulation Technique









Focal photocoagulation:

Prefebrably Pure Green Laser
Spot size: 50 – 200 micron
Power: 200 – 300 mW
Duration: 0.1- 0.2 sec
Burns: Light to Moderate Intensity
Lesions : focal leaks, MA, IRMAs, or Short capillary segments, Advanced Macular edema- Cystic changes, Patchy NVE< 1DD (1500 micron), Macroaneurysms.

Grid photocoagulation:

Pure Green Laser
Spot Size: 50 –200 micron
Power: 200 mW
Duration: 0.1- 0.2 sec
Burns: light to Moderate
Lision: Diffuse Macular edema , CSME

Pan-Retinal Photocoagulation:

Spot Size(micron) Duration (sec) Power (mW)
100 to 200 0.05 to 0.2 100 to 400
200 to 500 0.05 to 0.2 400 to 500Burns of Moderate intensity are placed 2-3 DD away from the macula. 1600 – 2000 burns at 1 burn width apart.

Standard Therapeutic Approach

Stage I PRP 2-3 months
Stage II Additional PRP 2-3 months
Stage III Anterior Retinal Cryocautery 2 months
Stage IV Focal Photocoagulation 2 months
Stage V Vitrectomy

EDTRS guidlines for follow up

Changes in the New Vessel
Appearance of the New Vessel (Calibre, Degree of Network, Extent of Fibrous tissue
Frequency & Extent of Vitreous hemorrhage
Status of Vitreous detachment
Extent of photocoagulation scar
Extent of TRD & fibrous proliferation

Additional PC is considered if:

Active NV (increase in size, fibrous tissue)
Extent of NV is Greater than earlier

Recurrent Vit. or Preretinal Hge.Without PVD
“Skip Areas”

Additional PC is less urgent if:

Decreased Calibre of NV
Developing Fibrous proliferance
Extensive or Complete PVD
Single episode of Vit. Hge. following PVD

Contraindications of Pan-Retinal Laser Photocoagulation

Presence of Grade IV or greater Glial proliferation
Grade IV or greater Vitreo-Retinal Traction
CNP areas in more than 60% of Macula & Paramacula –Poor Visual prognosis
Florid surface NVE posteriorly - Pituitary Ablation
Surface glial proliferation & Vitreous membranes
Grossly edematous posterior retina.
Severe Renal Retinopathy with edema, intraretinal yellowish serum accumulates, attenuation & tortousity of vascular elements and general deterioration of retina.
Diabetic retinopathy with Advanced Hypertensive retinopathy. Massive edema, exudates, extensive CNP areas, as seen in Renal retinopathy.

Complications of PRP

Field Constriction & Night Blindness
Foveal / Macular Burn
Macular Edema & Poor Colour Discrimination
Foveal Traction –Macular Detachment
Serous Choroidal Detachment- acute ACG
Anterior Segment:
Post. Synaechia – Iris & Pupillary Abnormality
Corneal Burn & Lens Opacities –Blurred Vision
Internal Ophthalmoplegia - Transient Myopia-Accomodation Cilioretinal / Choriovitreal NV
Pain – Younger diabetics & Peripheral Retina – More Painful
RBH – Due to Retrobulbar Anaesthesia

Peripheral Cryoablation for PDR

Indication:
Hazy media
Repeated Vitreous hemorrhage
Non regressing NVD despite complete PRP

Benefits:
Acclerated absorption of Vitreous Hemorrhage
Regression of NVE & NVD

Complications:
PVR Changes
TRD- Cryo should be avoided in areas of VR Adhesion

Technique:
Careful B-scan USG performed to detect areas of TRD
Transconjunctivally - Two rows of 3 – 4 applications in each quadrant at 12mm & 16mm from the limbus
After Limbal Peritomy - 20 spots in 4 rows in each quadrant, usually in 2 treatment sessions one week apart.
Applications are monitored under visualisation with Indirect Ophthalmoscope.
Otherwise in hazy media application can be for 10 – 15 sec at –60 degree centigrade

Vitrectomy for PDR

Indications:
Severe non clearing Vitreous Hemorrhage
>3 months in Type-I
>6 months in Type-II
TRD involving Macula
Combined TRD & Rhegmatogenous RD
Severe progressive Fibrovascular Proliferation
Anterior Segment NV with Posterior segment opacity
Dense Premacular Hemorrhage
Ghost Cell glaucoma
Macular edema with Premacular Traction
Cataract preventing Laser treatment for severe PDR

Aims of Vitrectomy:
Removal of all Vitreous opacities & the Scafolding along which Fibrovascular tissue proliferates
Division of all membranes & strands
Treat Retinal Breaks
Division of Retino-vitreo-retinal bands, ERM Peeling.
Endophotocoagulation

Complications / Risk:
Progressive Rubiosis
Cataract
Glaucoma
Recurrent Vitreous Hemorrhage
RD

Benefits:
Vitrectomy Prevents or Delays
Persistant Intra-gel Hemorrhage

RD
Opaque Membranes
Rubiosis
Burnt out stage

Poor Prognostic Factors:
Age > 40
Preoperative Rubiosis
Cataract
Visual Acuity < 5/60
RD
No previous Laser Photocoagulation.

Major modes of visual loss and presentation:

Maculopathy
FA, Control DM,
Grid / Focal Laser
Vitrectomy

Vit. Hemorrhage
PRP after Vitrectomy/
Spontaneous Clearing

PDR + TRD Threatning
Vitrectomy + PRP
or Involving Macula

Involuted Retinopathy
Leave it alone
