Diabetic retinopathy

DR. ASIWOME KWESI SENEADZA

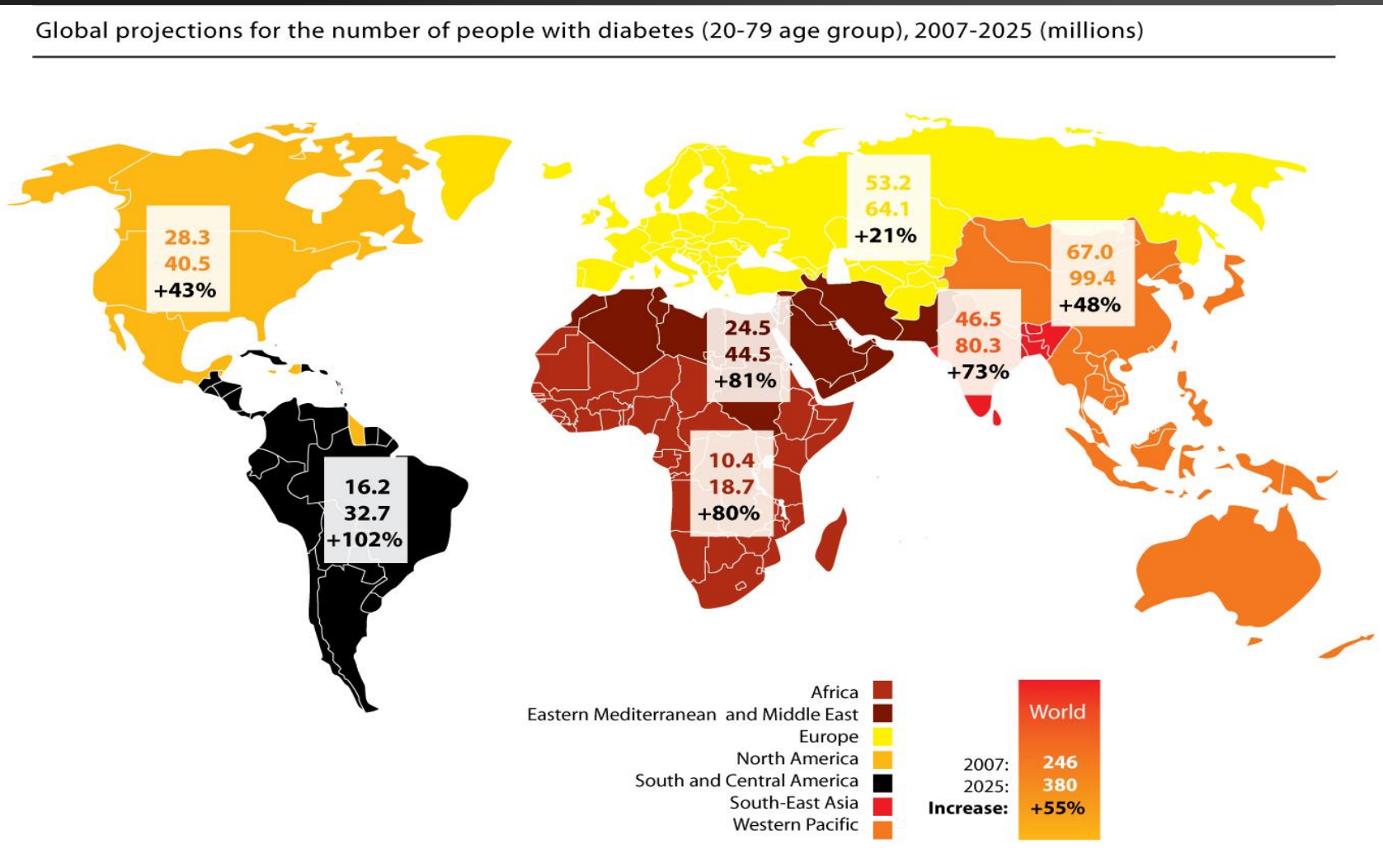
Diabetes mellitus

- Heterogeneous disorder of carbohydrate metabolism with multiple etiologic factors that ultimately lead to hyperglycemia.
  - **Type 1 (IDDM)** Autoimmune disease (loss of pancreatic islet cells)
    Begins < 30 yo (childhood)
  - **Type 2 (NIDDM)**
    - Deficiency in the regulation of insulin secretion and or in its action at the cellular level in the liver and peripheral tissues.
    - Late onset (obese patients)
  - Secondary types

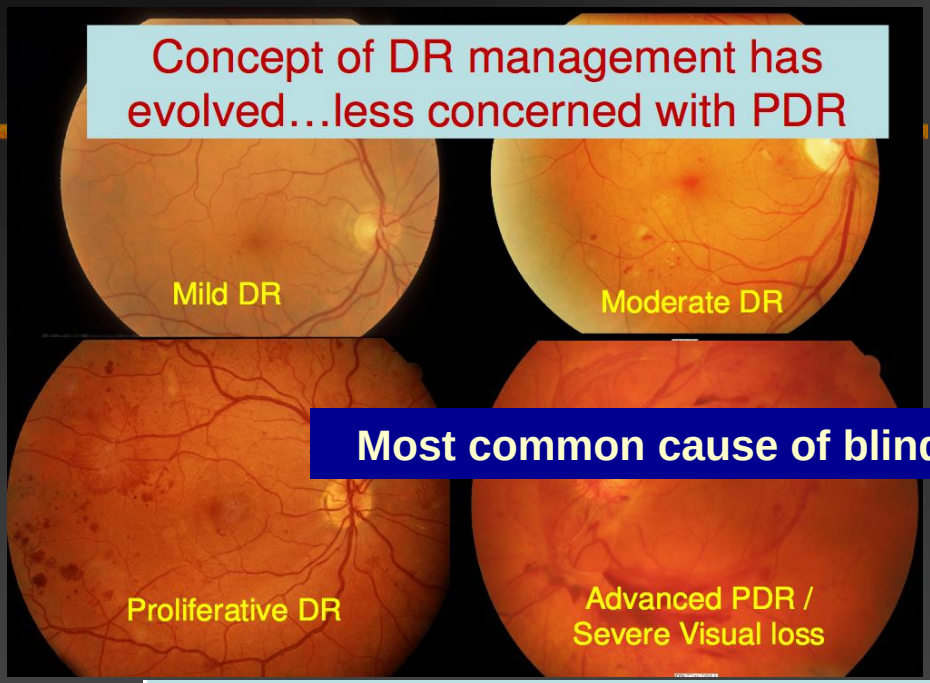
Hyperglycemia

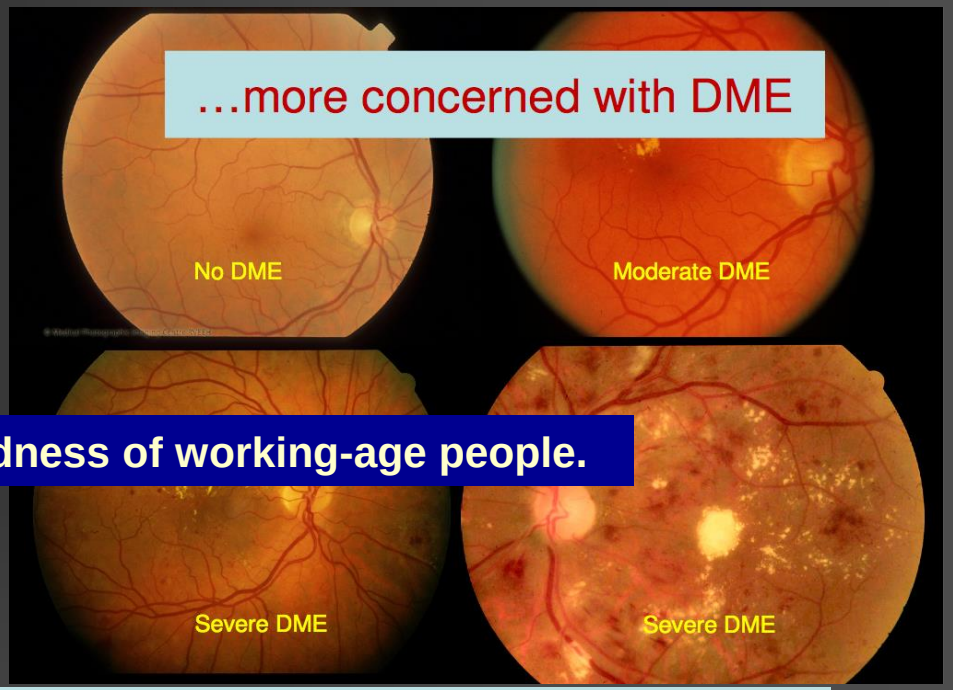
Aldose reductase-mediated cell damage, vasoproliferative factors produced by hypoxic retina, growth hormone and platelet, erythrocyte and blood viscosity abnormalities.

GLOBAL MAGNITUDE OF DIABETICS



NEED & MAGNITUDE - PARADIGM





Most common cause of blindness of working-age people.

Global prevalence and nos. with DR & DME 2010 and 2030

	% (95% CI)*	No (millions) 2010	No (millions) 2030
Any DR	35.4 (35.2-35.6)	119.6	≈200
PDR	7.2 (7.1-7.3)	20.9	≈25
DME	7.5 (7.4-7.6)	19.1	≈35
VTDR	11.7 (11.6-11.8)	30.5	≈50

MANAGEMENT OF DIABETIC RETINOPATHY

MEDICAL SYSTEMIC MANAGEMENT

DIABETIC MACULOPATHY

PROLIFERATIVE DIABETIC RETINOPATHY

PHARMACOTHERAPY

LASER THERAPHY

VITRECTOMY

LASER THERAPHY

VITRECTOMY

ANTI – VEGF
- **LUCENTIS**
- **AVASTIN**
- **AFLIBERCEPT**

CORTOCOSTERIOD
- **TRIAMCINALONE**
- **DEXAMETHASONE**
- **FLOUROCILONE**

LASER
- **FOCAL LASER**
- **GRID LASER**
- **SUPERTHRESHOL**

VITRECTOMY ± ILM PEELING

PRP

DELAM, VCO,

MANAGEMENT OF RETINOPATHY

- Evidence: visual loss could be avoided
  - Control of glycaemic levels and
  - Risk factors
  - Improving screening programs

Epidemiology of Diabetes Interventions and Complications (EDIC): design, implementation, and preliminary results of a long-term follow-up of the Diabetes Control and Complications Trial cohort. Diabetes Care. 1999;22: 99-111

SYSTEMIC MANAGEMENT
Control of diabetes And Risk Factors

RISK FACTORS

- **Non-modifiable:**

Genetic factors, gender and duration of diabetes

- **Modifiable:**

Glycaemia, blood pressure, lipid levels, anemia, tobacco and obstructive apnea.

- **Additional factors:**

Carotid arterial disease, pregnancy and renal impairment.

SYSTEMIC MANAGEMENT
Glycemic Control

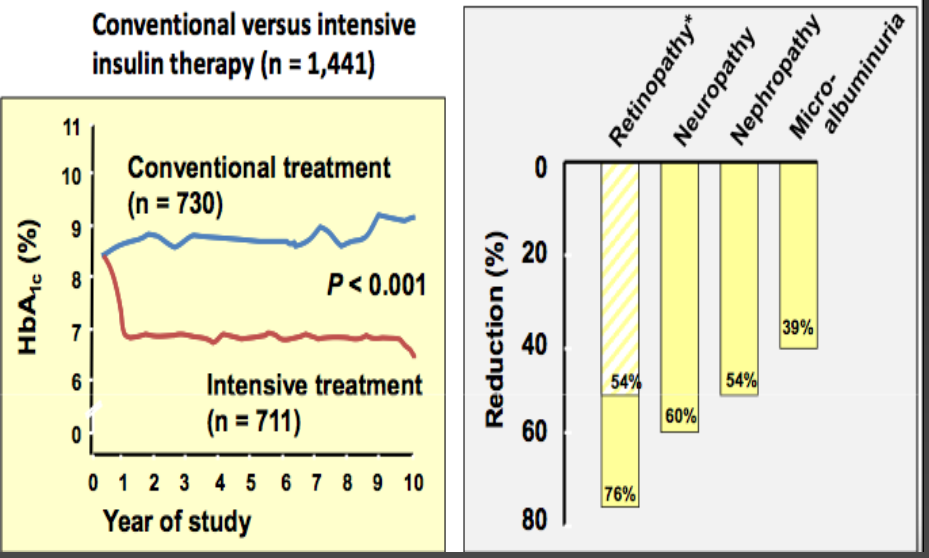
Different studies that have provided good evidence on the importance of glycaemic control on the development of retinopathy and its progression

DRS[3]: Diabetic Retinopathy Study, 1978
ETDRS[4]: Early Treatment for Diabetic Retinopathy Study, 1984
DRVS[5]: Diabetic Retinopathy Vitrectomy Study, 1981
DCCT[6]: Diabetes Control and Complications Trial, 1993
UKPDS[7]: United Kingdom Prospective Diabetes Study, 1998
WESDR[8]: Wisconsin Epidemiologic Study of Diabetic Retinopathy, 1979 Onward

Good glycaemic control early in the course of diabetes has an important impact on long-term outcome of retinopathy. (Level A)

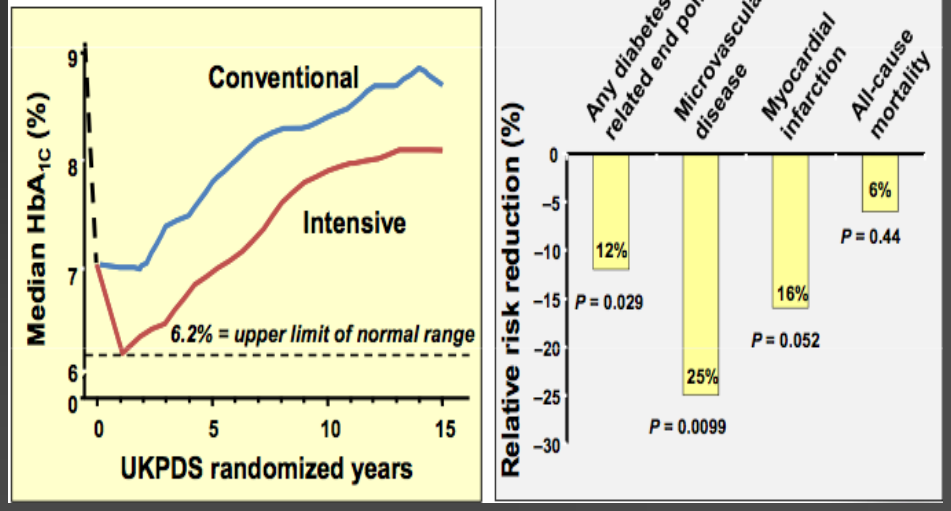
SYSTEMIC MANAGEMENT
Glycemic Control (EVIDENCE)

DCCT: Intensive Control Reduces Complications in Type 1 Diabetes



Interventional Study (6 years): Comparing conventional (standard) insulin therapy vrs intensive insulin therapy reduced the risk of development and progression of: Retinopathy 63%, Nephropathy 54%, Neuropathy 60%

UKPDS: Intensive Control Reduces Complications in Type 2 Diabetes

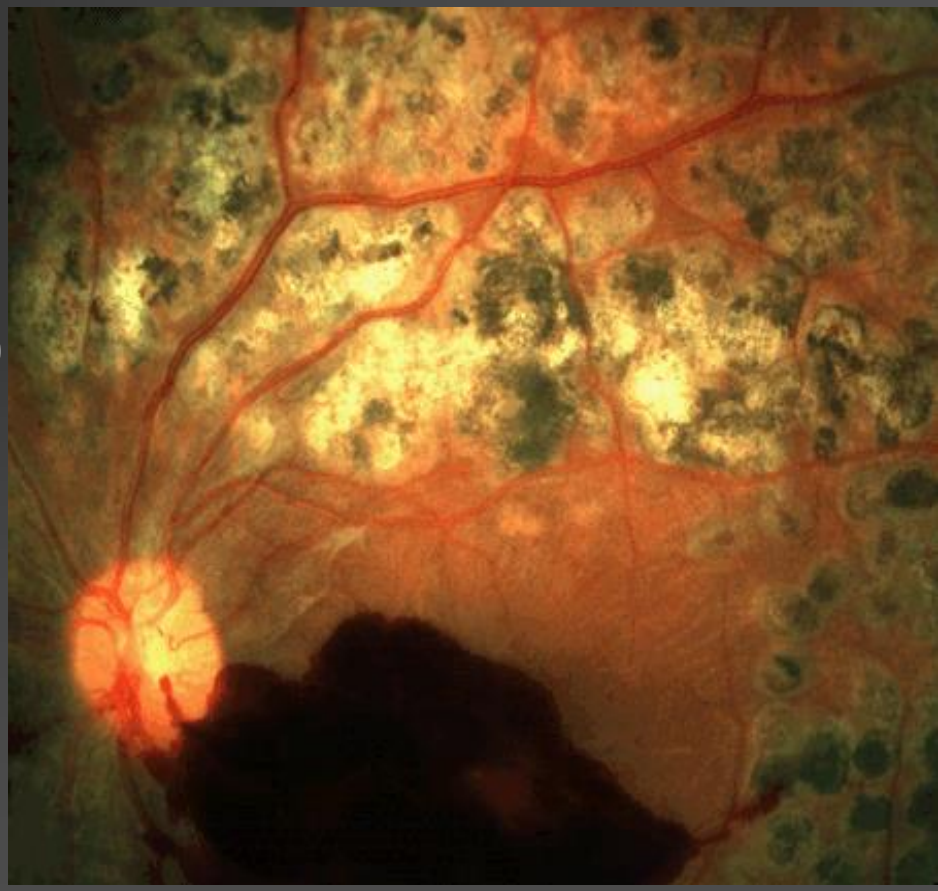


Interventional Study (20 years multi-centre prospective Randomized Interventional Trial): Comparing conventional (standard) insulin therapy vrs intensive insulin therapy reduction in: Retinopathy progression 34%, Laser 29%, Blindness 16%

SYSTEMIC MANAGEMENT
Glycemic Control (Type 1)

HBA1C < 7.0%:

- Delayed onset of DR
- Delayed progression
- Risk-reduction of 52-75% for:
  - Laser coagulation
  - csME
  - severe NPDR
  - PDR



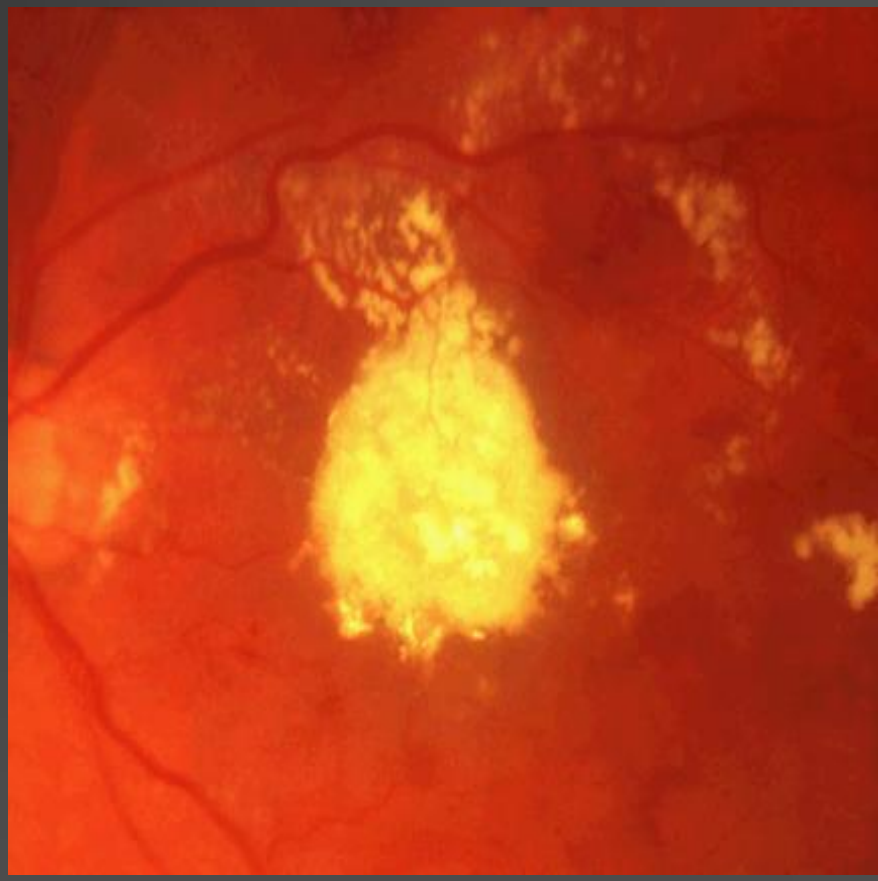
* Diabetes Control & Complications Trial Research Group: NEnglJMed 1993; 329 (877-986)
** UK Prospective Diabetes Study Group 33: Lancet 1998; 352 (837-853)

SYSTEMIC MANAGEMENT
Glycemic Control (Type 2)

Already 36% DR on Dx!*

HBA1C reduction of 1%:

- After 12 years moderate Risk-reduction of:
  - 21% for DR
  - 24% for Cataract
- No significant effect before 6 years of intensified BS control!



*UK Prospective Diabetes Study Group: Lancet 1998; 352 (837-853)

SYSTEMIC MANAGEMENT
Blood Pressure Control

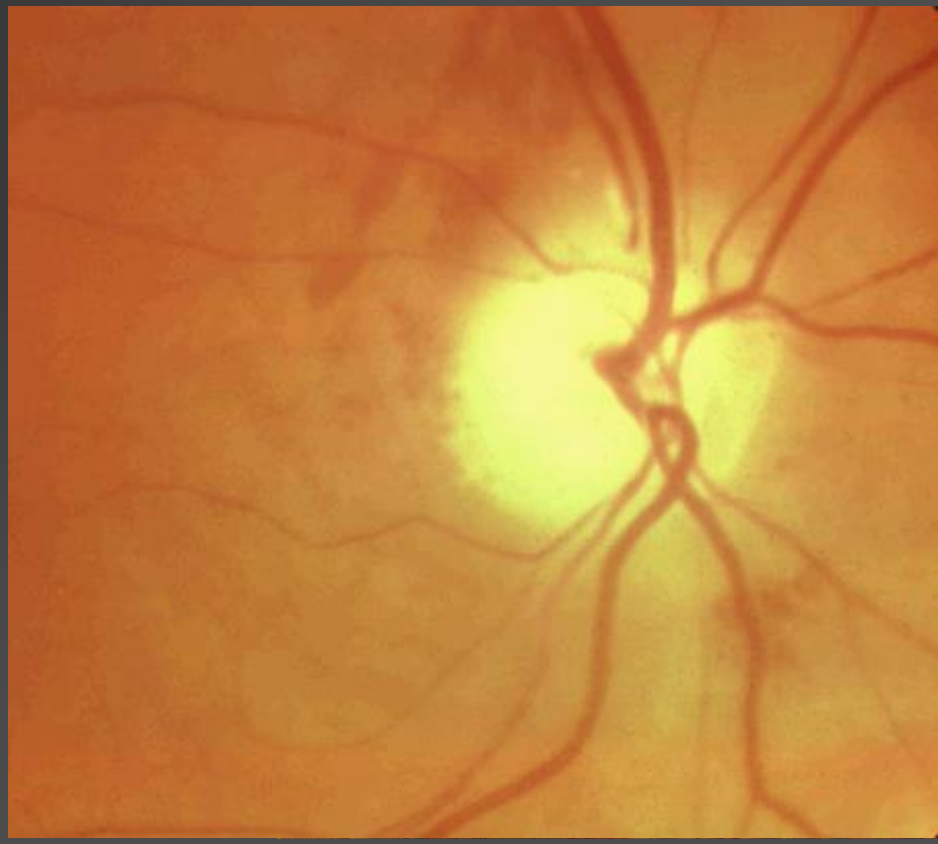
ANTIHYPERTENSIVE TREATMENT:

Type 2:

- 34% risk-reduction for progression of DR
- 47% risk-reduction for decreasing VA

Type 1:

- No sufficient data
- Indication of beneficial effect (ACE-inhibitors)***



* Gaede P et al: NEnglJMed 2003; 348 (383-393)
** UK Prospective Diabetes Study Group: Lancet 1998; 352 (837-853)
*** Chaturvedi N et al: Lancet 1998; 351 (28-31)

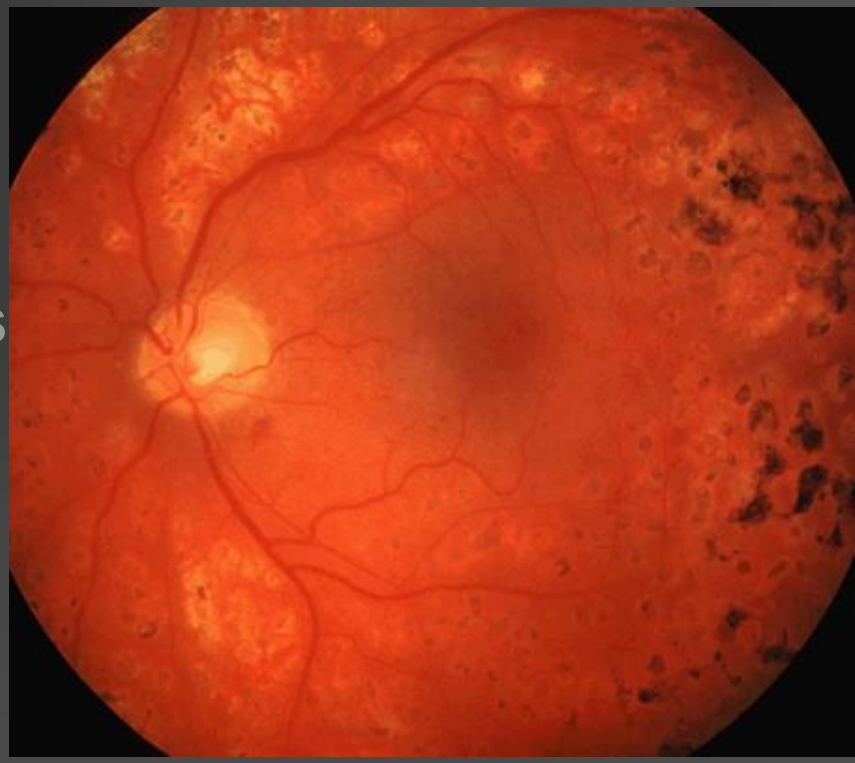
SYSTEMIC MANAGEMENT
Nephropathy

MANAGEMENT	Procedure	Pathology	Prognosis
Haemodialysis	simple	csME ↑ VA ↓	↓
Peritoneal Dialysis	more difficult	csME ↓ VA ↑	↑
Kidney Transplant	complex	csME ↓ VA ↑	↑
Kidney & Pancreas Transplant	complex	csME ↓ VA ↑	↑

SYSTEMIC MANAGEMENT
Pregnancy

DIABETIC RETINOPATHY often <u>worsens</u> considerably during pregnancy:

- discuss risks before pregnancy
- stabilize existing DR 6-8 months before / early in pregnancy (laser?)
- good metabolic control (don't adjust too aggressively!)
- examine at frequent intervals



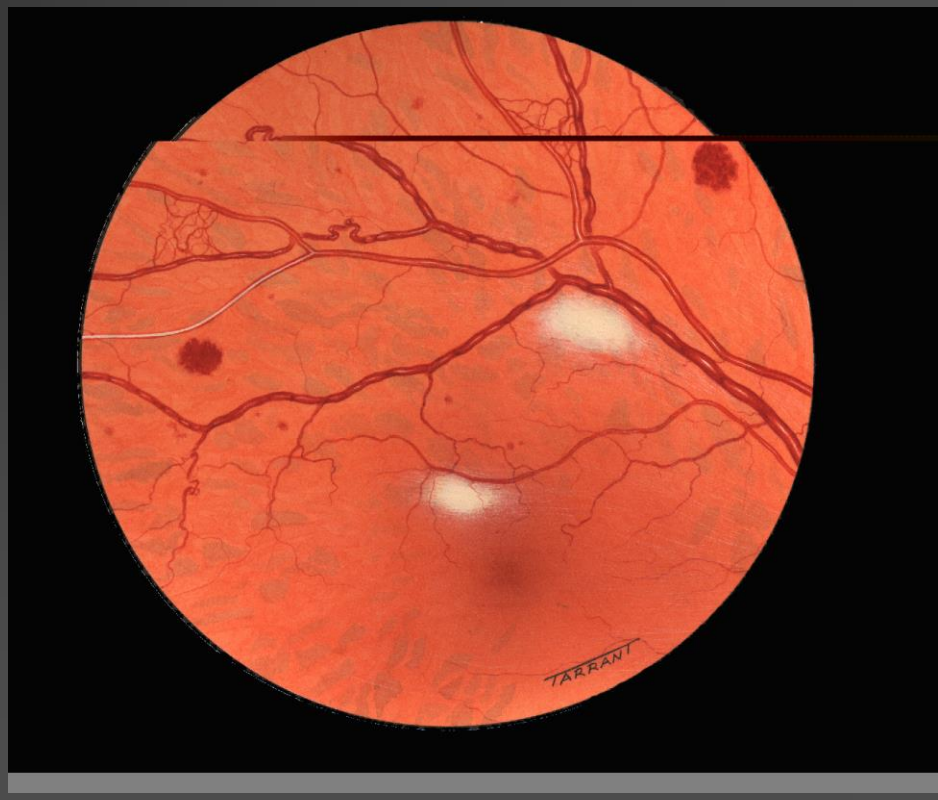
PDR after prLC

Women with GESTATIONAL-DM do <u>NOT</u> develop DR.

SYSTEMIC MANAGEMENT
Pregnancy

RISKS FOR VISUAL LOSS FROM DM (PREGNACY):

- pre-existing DR
- duration of DR
- csME
- PDR
- hypertension
- chronic hyperglycaemia
- too rapid BS-adjustment



Severe NPDR: CWS / D&P haemorrhages / venous irregularities

SYSTEMIC MANAGEMENT

Chronic **HYPERGLYCEMIA** and **ARTERIAL HYPERTENSION** are the most important risk factors for micro-vascular damage in DM

Early **DIABETIC RETINOPATHY** earmarks the vascular high-risk patient with DM

Early manifestation & rapid progression of DR indicate **high CARDIO-VASCULAR RISK**

Gaede P et al: NEnglJMed 2003; 348 (383-393)
Hammes HP: Ophthalmologe 2004; 101 (1159-1164

SYSTEMIC MANAGEMENT

Treatment Target To Improve Diabetic Outcome

Treatment	Outcomes
Aggressive glucose control	Reduces microvascular events; improves lipids
Aggressive weight loss	Improves lipids, glucose, BP, other risk factors
Aggressive lipid-lowering	Reduces CVD event rates; possible effect on retinopathy
Aggressive blood pressure control	Reduces kidney damage, eye damage, and CVD
Anti-thrombosis therapy	Reduces macrovascular event rates

Diabetes Care. 2006;28:S4-S38. Colwell JA, Nesto RW. *Diabetes Care.* 2003;26:2181-2188.

ADA Recommendations for BP & Lipids for People with Diabetes

Parameter	Goal
Blood pressure	<140/80 mm Hg
LDL	<100 mg/dL*
Triglycerides	<150 mg/dL
HDL	>40 mg/dL (men) >50 mg/dL (women)

*LDL <70 mg/dL is a therapeutic option

- Controlled BP <130/80mmHg
  - 51%
- LDL at the goal level <100mg/dl
  - 56%
- A1C at the goal level <7%
  - 53%

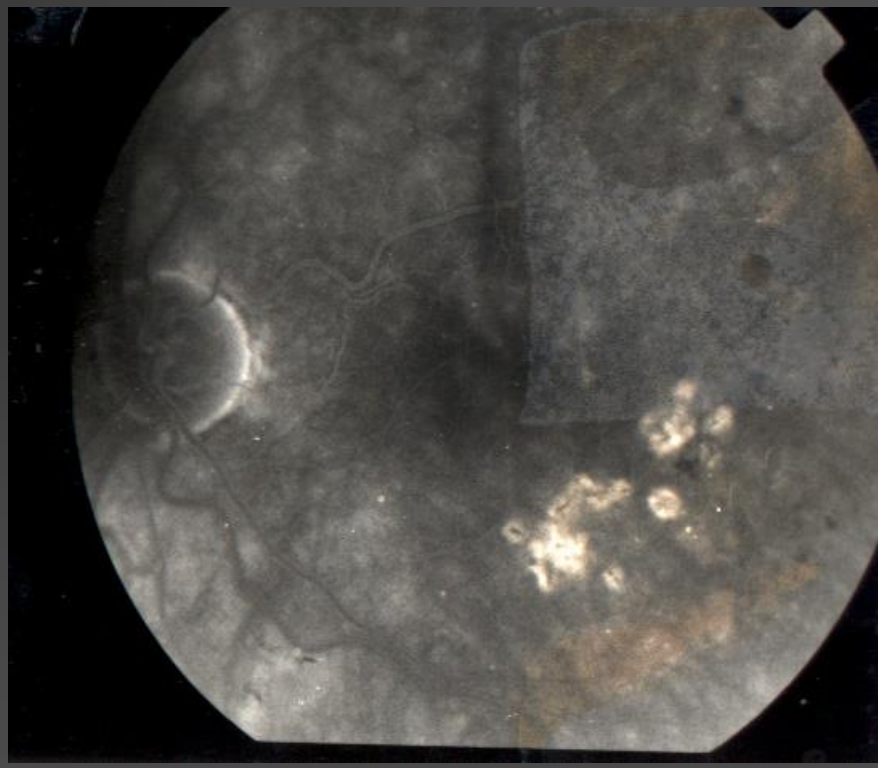
- What proportion have met all three?
  - 18.8%

OCULAR (LOCAL) MANAGEMENT

VA may be endangered before any subjective symptoms

At the time of first symptoms the optimal time for LASER TREATMENT may already have passed

PROGNOSIS clearly depends on optimal timing of local treatment



Central focal laser for focal maculopathy

INVESTIGATION - CLASSIFICATION BASED ON FFA FINDINGS

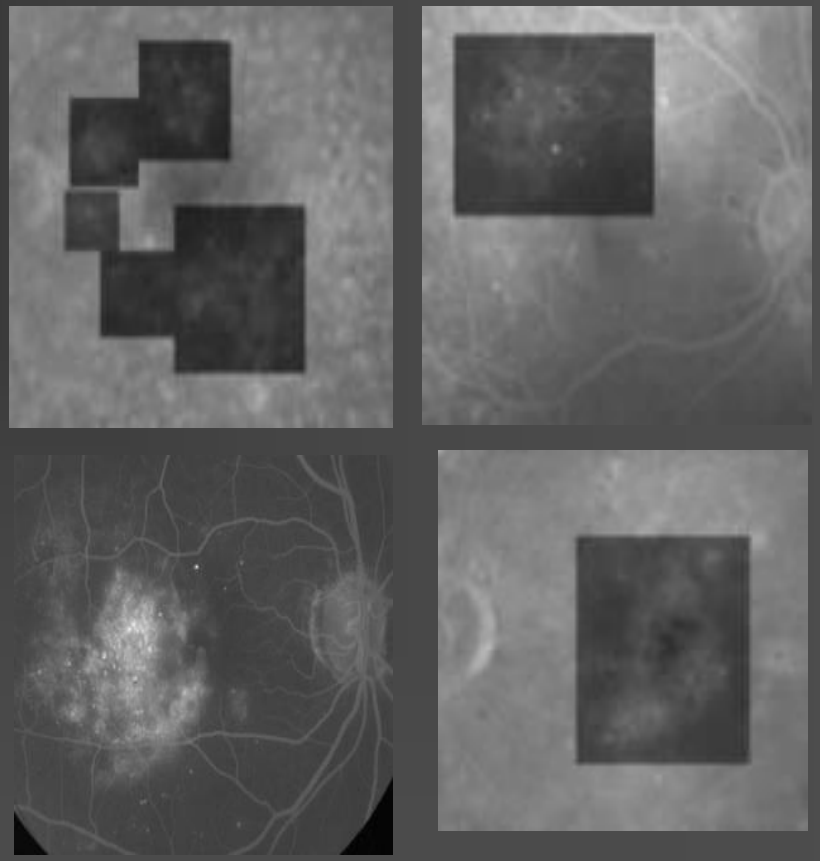
Depending on the location of leakage or loss of blood supply due to capillary loss. DMO can be classified as:

•Focal maculopathy: localized leakage (from 1 or more microAn)

• Diffuse/indeterminate maculopathy: generalised thickening of the central macula caused by widespread leakage from dilated capillaries.

•Ischaemic maculopathy: enlargement and alteration of the FAZ.

•Mixed maculopathy: combined pathology, particularly of diffuse oedema and ischaemia



Classification of diabetic retinopathy from fluorescein angiograms. ETDRS report number 11. Early Treatment Diabetic Retinopathy Study Research Group. Ophthalmology. 1991;98(5):807-22.

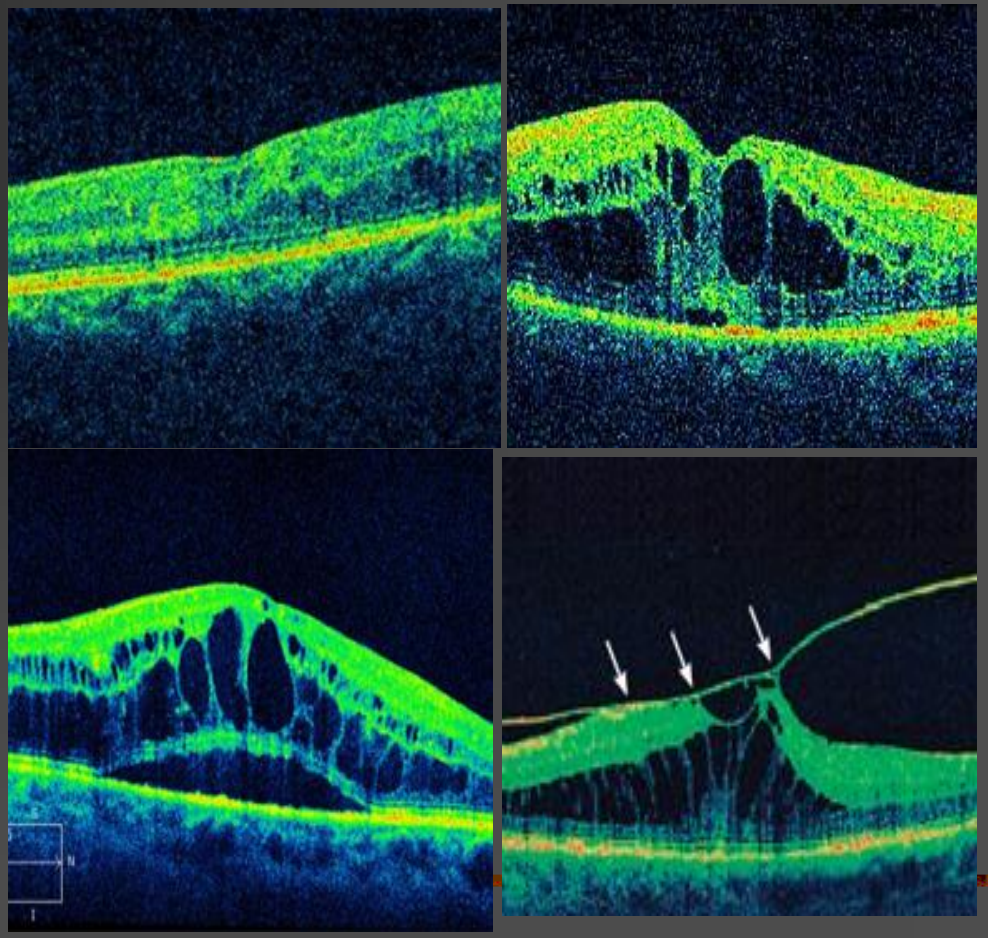
INVESTIGATION - CLASSIFICATION BASED ON OCT FINDINGS

1. DIFFUSE MACULAR EDEMA– (SPONGELIKE EDEMA)

2. CYSTOID MACULAR EDEMA

3. WITH SERIOUS RETAINAL DETACHMENT SRD

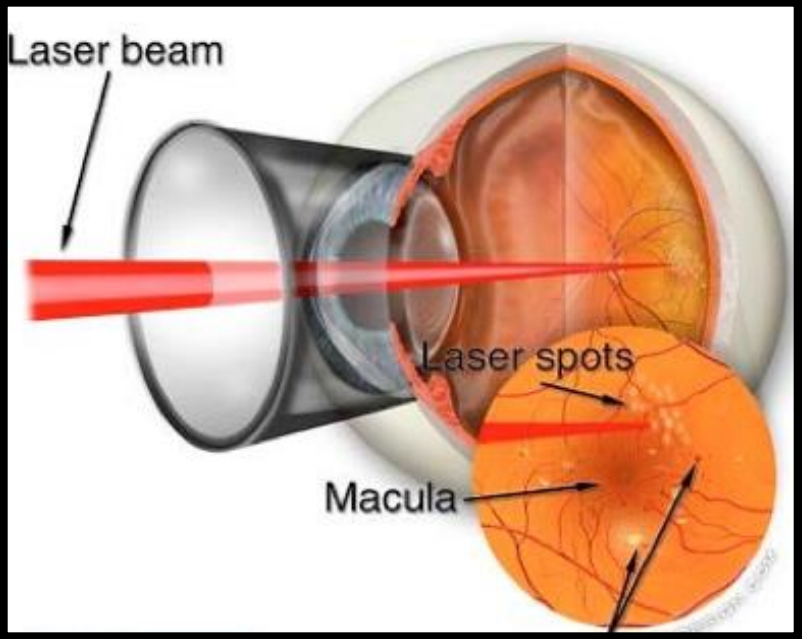
4. WITH VITREOMACULAR TRACTION



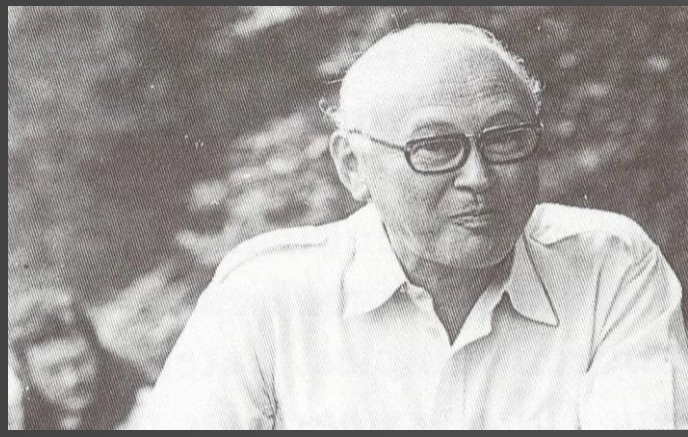
FLA (guidelines)

DIABETIC RETINOPATHY:	FLA:
NPDR without ME	NO!
ME (non-significant)	?
csME	+/- (laser?)
Severe NPDR	?
Non-HR-PDR • without csME • with csME	(NV?) +/- (laser?)
HR-PDR	?

MANAGEMENT – LASER TRETAMENT



PHOTOCOAGULATION
(HISTORY)



1640 BONETUS (Geneva)

- eclipse blindness

1949 MAYER-SCHWICKERATH (Germany)

- therapeutic use of light-damage to retina
- retinal photocoagulation

1960 MAIMAN (USA)

- first working laser
- ruby crystal (stimulated by light flash)
- use in Ophthalmology from **1963**

LASER

VISIBLE LIGHT

- 380 – 780 nm

LASER

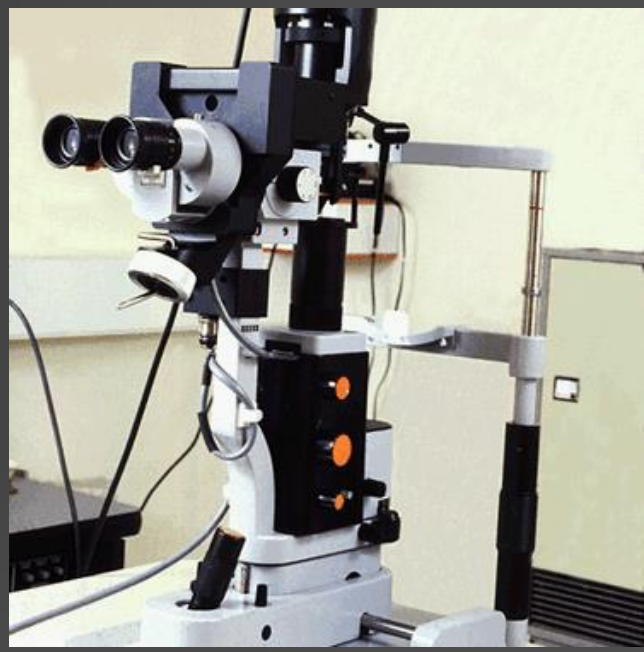
- Light Amplification by Stimulated Emission of Radiation

CHARACTERISTICS

- monochromatic light

  (only 1 wavelength)
- spatial coherence

  (energy change at same instant → corresponding waves)
- high density of electrons



LASER

PARAMETERS

Number of Spots (N)
Spot-size (D = µm)
Energy (E = mW)
Time (T = ms)

Energy-density = E / µm²
Power = E / ms

MODES of DELIVERY

Slit lamp (+ contactglas)

HIO

Endoprobes

Transscleral
(e.g. diode / NdYAG)

PHOTOCOAGULATION

XENON ARC	historical (i.o. tumours?)
LASER e.g. • Argon green • Frequency doubled NdYAG • Krypton • Diode	WAVELENGTH: ➢ 514 nm ➢ 532 nm ➢ 647 nm ➢ 810 nm

LASER (absorption)

ABSORBING PIGMENTS IN THE EYE:

- MELANIN — in the RPE
- XANTHOPHYLL — in the fovea
- HAEMOGLOBIN — within RBC
- MELANOCYTES — in choroid & sclera
- LIPOFUSCIN — in ageing retina

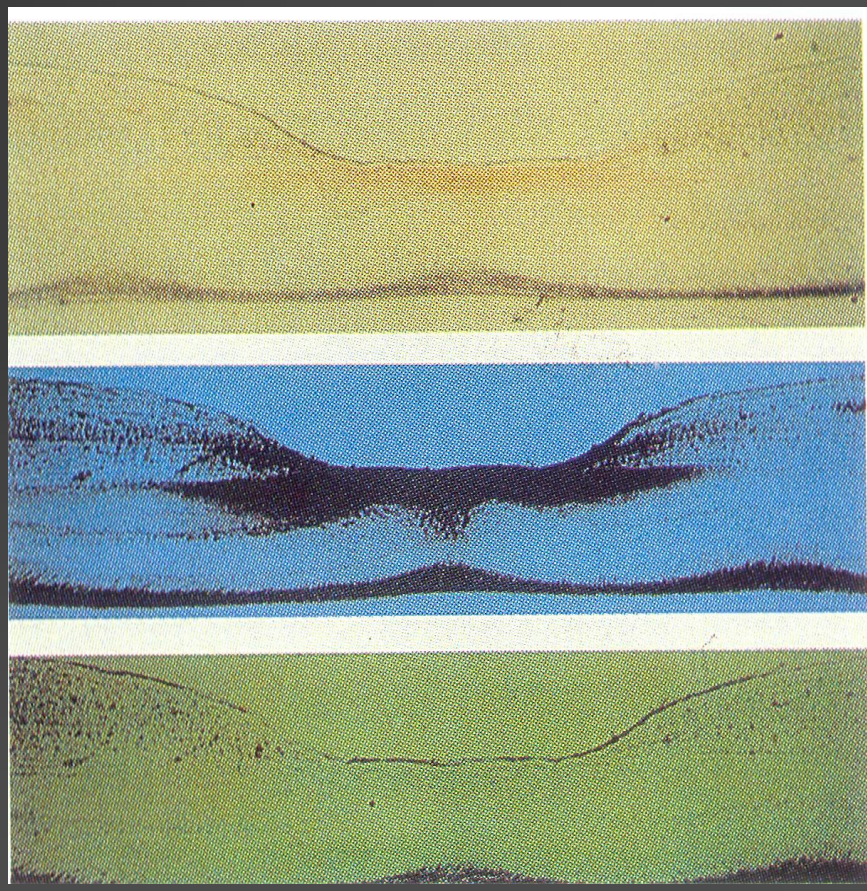
LASER	nm	RPE	HAEMOGLOBIN	XANTHOPHYLL
Argon (blue)	488	++++	++	++
Argon (green)	514	++++	++	+
FD NdYAG	532	++++	++	(+)
Dye (y / o)	577	+++	++	-
Dye (o / r)	630	++	-	-
Krypton	647	++	-	-
Diode	810	+	-	-

LASER (central absorption)

XANTHOPHYLL (macula):

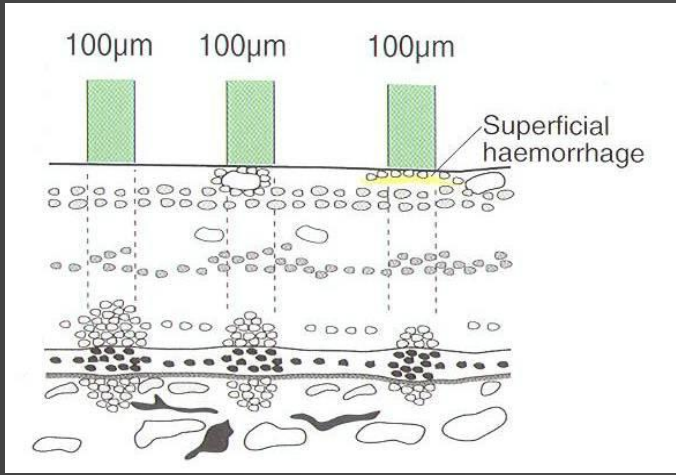
- white light
- blue light
- green light

➢ **Xanthophyll absorbs blue light!**



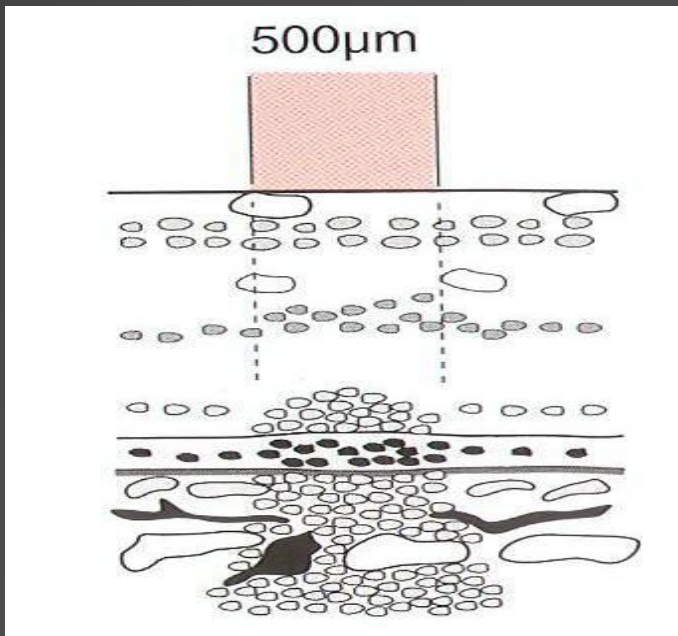
LASER (absorption)

ENERGY ABSORBTION & HEAT TRANSMISSION



FD-NdYAG & ARGON LASER:

- right: RPE (ca. 60%)
- middle: retinal blood vessel
- left: superficial haemorrhage



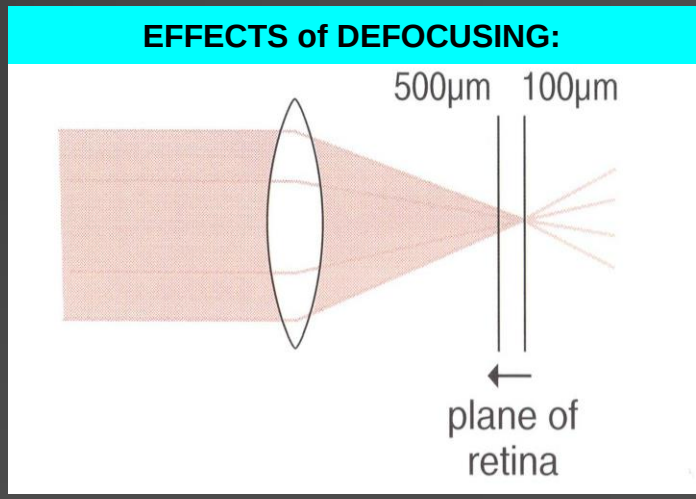
DIODE LASER:

- RPE (ca. 8%)
- greater transmission of light
- greater absorption by melanocytes of choroid

LASER PARAMETERS

SPOT SIZE (µm)

- 50 - 500 µm (central - panretinal)
- Laser glass
  - Volk Area Centralis (ca. 1:1)
  - Volk Quadraspheric (> 1:2)
- Focus (most glasses)
  - anterior shift ▸ increases spot size
  - posterior shift ▸ decreases spot size
- Energy
  - high energy ▸ increases spot size
  - low energy ▸ decreases spot size



LASER PARAMETERS

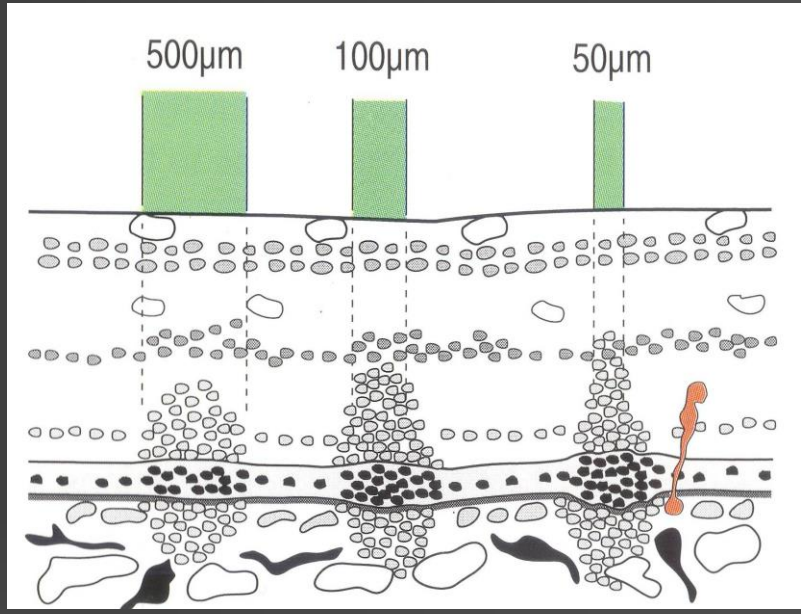
ENERGY (mW)

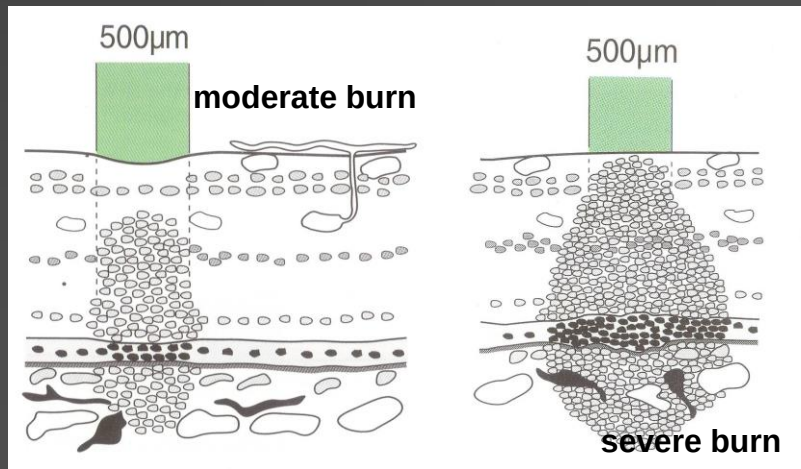
Spot size
- E-density changes!
- Power = E / µm²

Threshold
- RPE & PR

Suprathreshold
- damage ↑

- Bruch's membrane
- Choroidal haemorrhage
- Neurosensory retina (horizontal connections / ganglion cell layer)

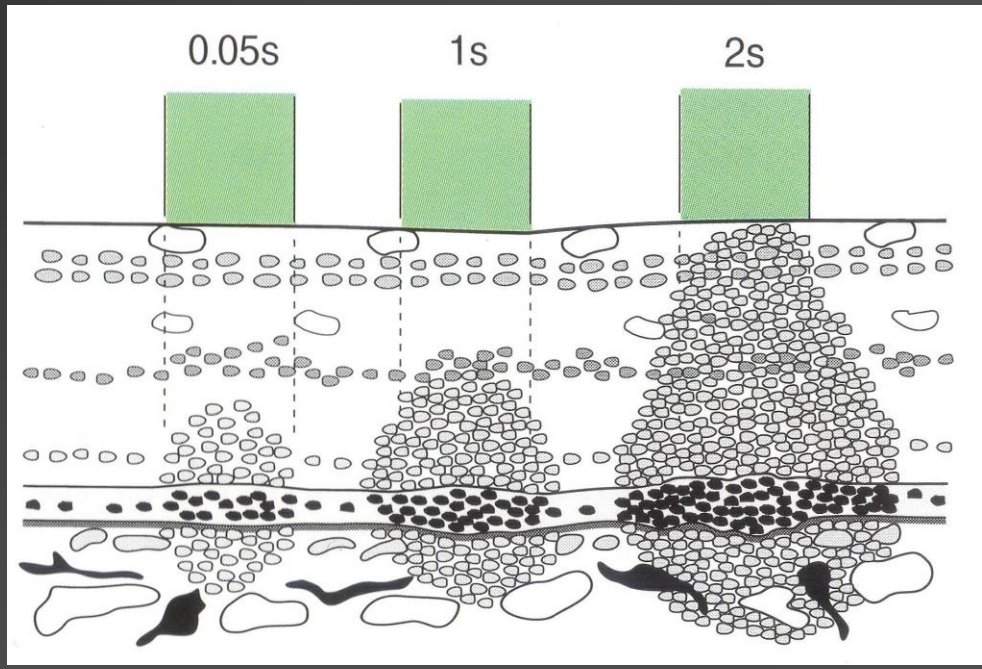




LASER PARAMETERS

TIME (ms) - DURATION

- Spot-size & damage
- Power = E / ms



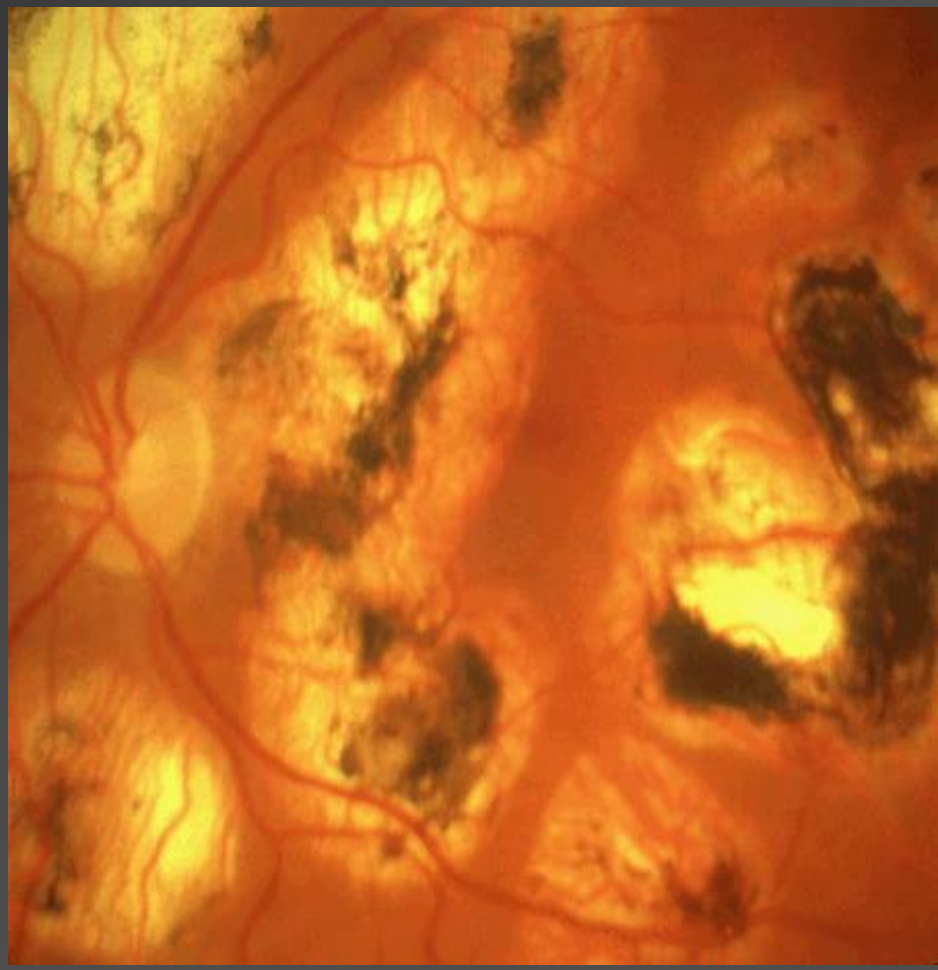
- Longer duration
  - more energy / damage
- Shorter duration
  - less energy / damage

LASER (spots & scars)

SPACING:

Full scatter (≥ 1200 spots)

- spacing ≤ 1 spot size
- spots appear larger later! (healing processes / scaring)



AREA TREATED:

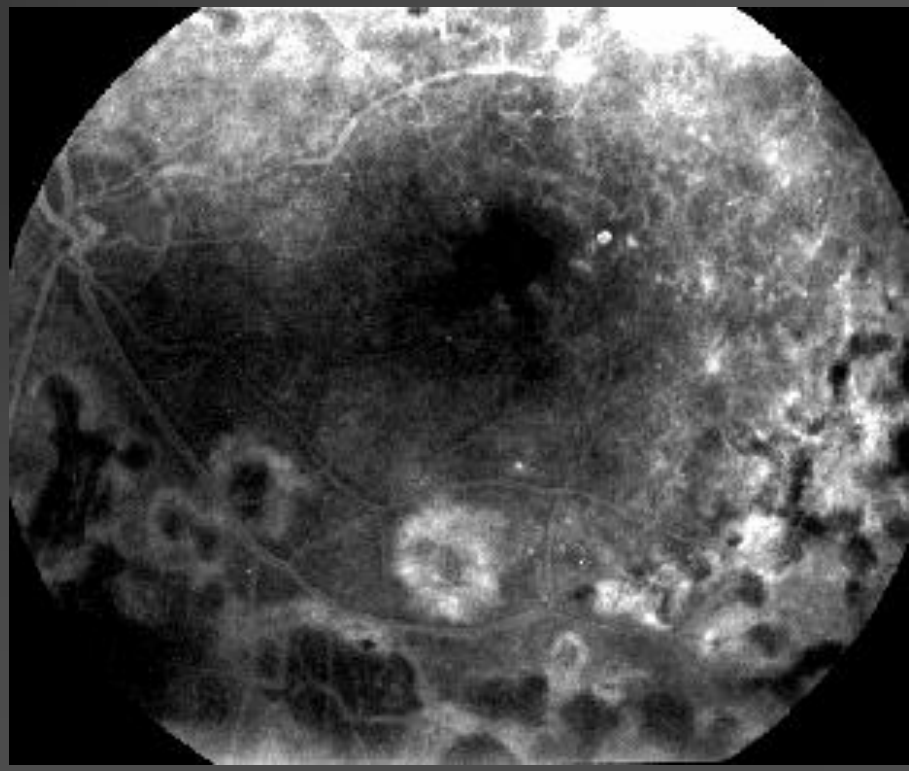
Retinal Area ≈ 1500 mm²

- prLC (500µm = 0.5mm)
- area of each burn = πr^2
  - 22/7 x 0.25 mm = 0.196 mm² per spot
  - N = 4000: 4000 x 0.196 mm² = 785.7 mm²
  - 785.7 mm² / 1500 mm² = 52% of retina!

LASER INDICATIONS

NUMERICAL DOMINANCE OF TYPE 2 DM

- **Previously:**
  late NPDR & PDR
  - prLC
- **Today:**
  moderate NPDR & csME
  - central laser



LASER PATTERN

FOCAL pattern	**centre (periphery)**
GRID pattern	**centre**
PANRETINAL pattern (prLC) • mild scatter (arcades – equator) • full scatter (arcades – equator – beyond)	**periphery** • 600 - 1200 spots • ≥ 1200 spots …

CENTRAL LASER

Timely central laser reduces risk for severe VI by 50-75% (ETDRS)

INDICATIONS:

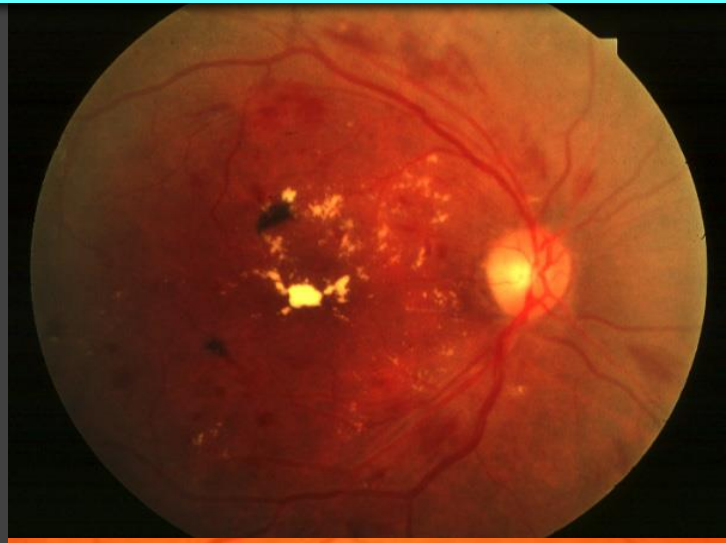
- csME
- at any VA?

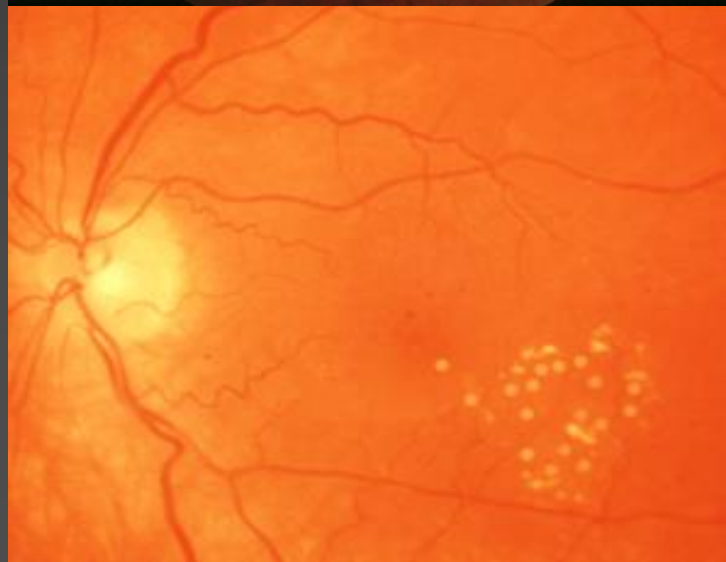
BEST PROGNOSIS:

- VA ≥ 6/24
- age < 60 years

VISUAL ACUITY:

- stabilization (long-term)!
- initial drop (temporary)?
- may improve (e.g. focal csME)





CENTRAL LASER

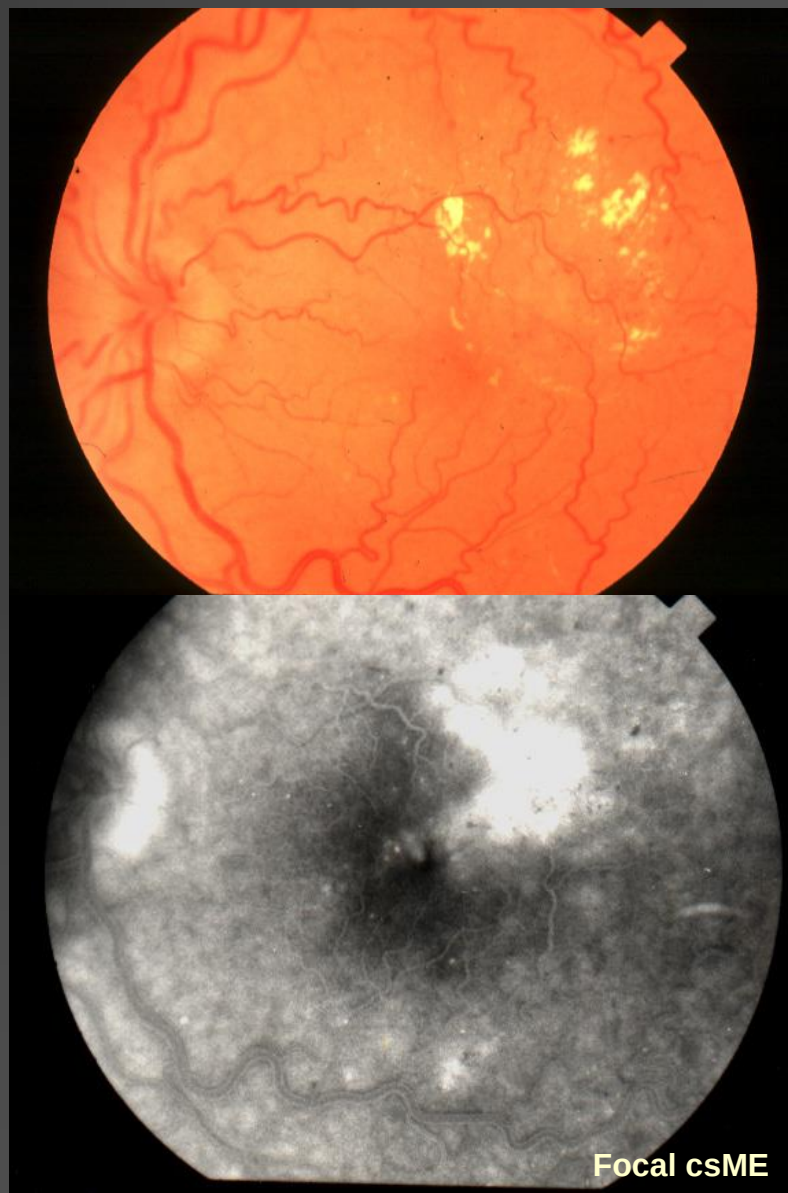
CLINICAL COURSE AFTER CENTRAL LASER:

EXSUDATE

- increase initially?
- decrease slowly (3-6 months or longer)
- no indication for more laser!

OEDEMA

- RELEVANT PARAMETER!
- should decrease over 3 months (Fd / FLA?)



CENTRAL LASER

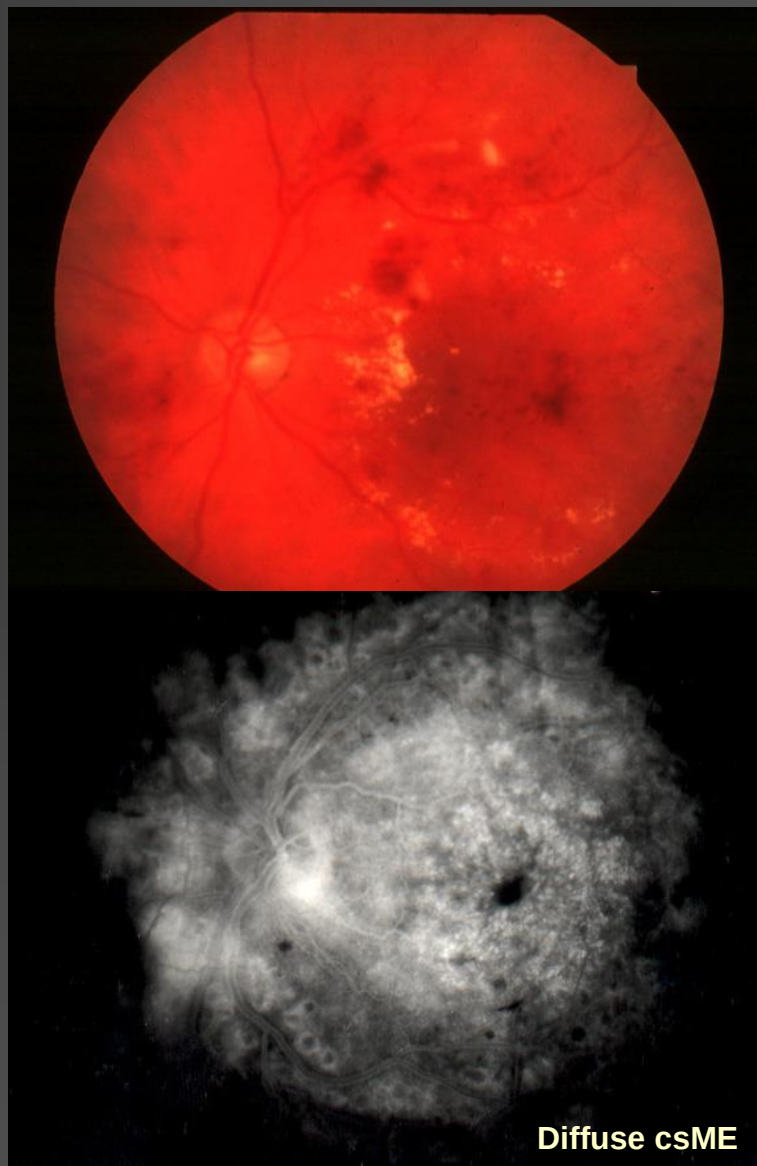
FOLLW UP:

AFTER 3 MONTHS (Fd / FLA?)

- no csME ▸ observe
- regression ▸ TCA 3/12
- no regression ▸ LC – 2?

AFTER 6 MONTHS (Fd / FLA?)

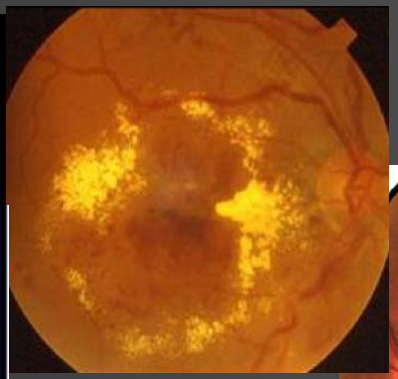
- no csME ▸ observe
- still csME ▸ LC - 2

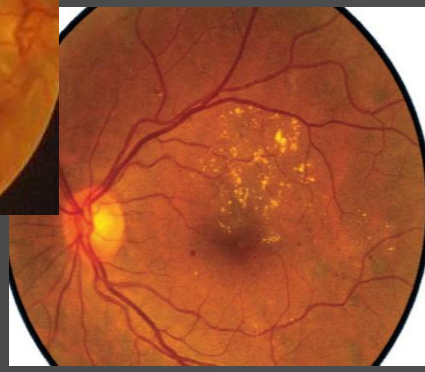


Diffuse csME

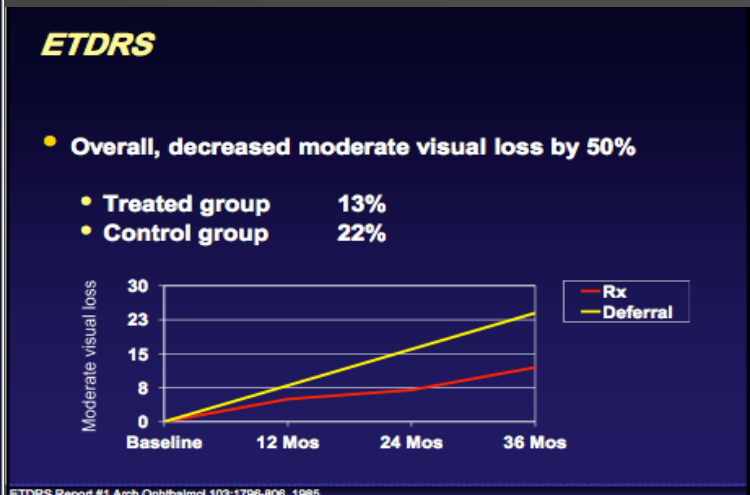
ETDRS – STUDY FINDINGS

- **Laser photocoagulation reduced the rate of moderate vision loss by 50% in eyes with CSME**





- 35% of patients in laser-treated group continued to have DME after 1 year
  - 24% at 3 years
  - 12% of treated eyes still lost 15 or more ETDRS letters at 3 years
- 40% of patients required retreatment within 1 year
- Only 3% had > 3 lines of improvement
- Only 17% had any improvement in vision after 5 years



TREATMENT TECHNIQUES

Modified ETDRS

- Direct treatment to microaneurysms and grid to thickened areas only

Mild Macular Grid Laser Technique

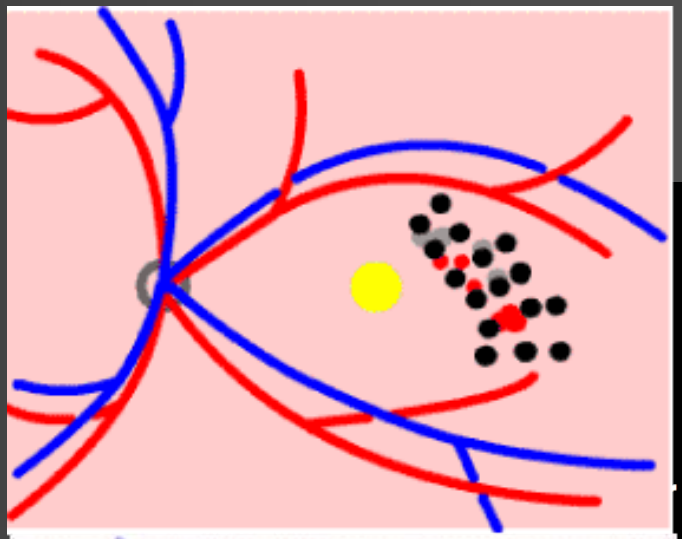
- Diffuse widespread area of grid treatment to macula in thick and non-thick areas
- No treatment of microaneurysm

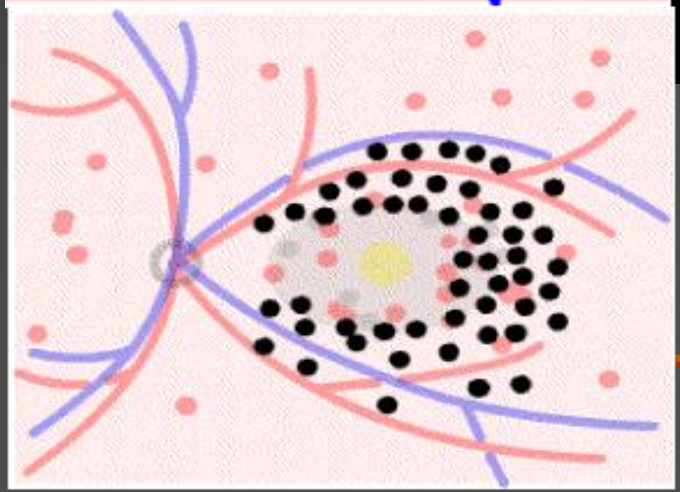
Focal/Grid Photocoagulation Treatment

DRCR.net technique:

Burn Size	50 microns
Burn Duration	0.05 - 0.1 seconds
Wavelength	Green to yellow
Intensity	Barely visible (light gray)
Grid Treatment	Cover areas of diffuse retinal thickening or nonperfusion 2 burn widths apart*
Direct treatment of microaneurysms	All microaneurysms are treated directly, but only in areas of retinal thickening
Placement of laser treatment	Retina thickening 500 - 3000 microns from center of fovea

*Cover areas of retinal thickening not judged to be due to microaneurysms 2 burn widths apart. If a fluorescein angiogram is obtained, cover areas of retinal thickening 2 burn widths apart within areas on angiography of diffuse leakage from retinal telangiectasis and consider covering areas of non-perfusion.



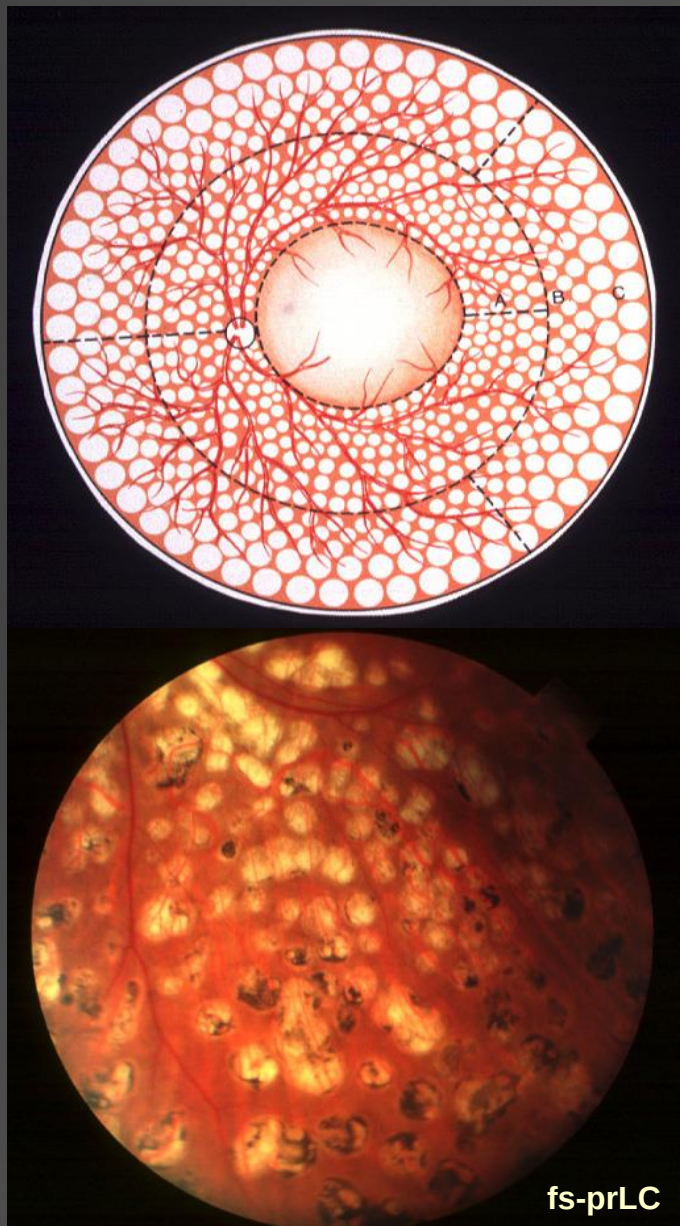


PANRETINAL LASER

DEFINITIONS (prLC):

disseminated laser coagulation (arcades ≥ equator)

- **mild scatter (fs):**
  - 600 – 1200 spots (initially)
  - spot distance ≥ 1 spot diameter
- **full scatter (ms):**
  - 1200-2000 spots (initially)
  - spot distance < 1 spot diameter
- **persistent PDR (Type 1 > Type 2):**
  - significantly more spots!
  - almost no distance between spots!



PANRETINAL LASER

APPROACH:

CAUTIOUS

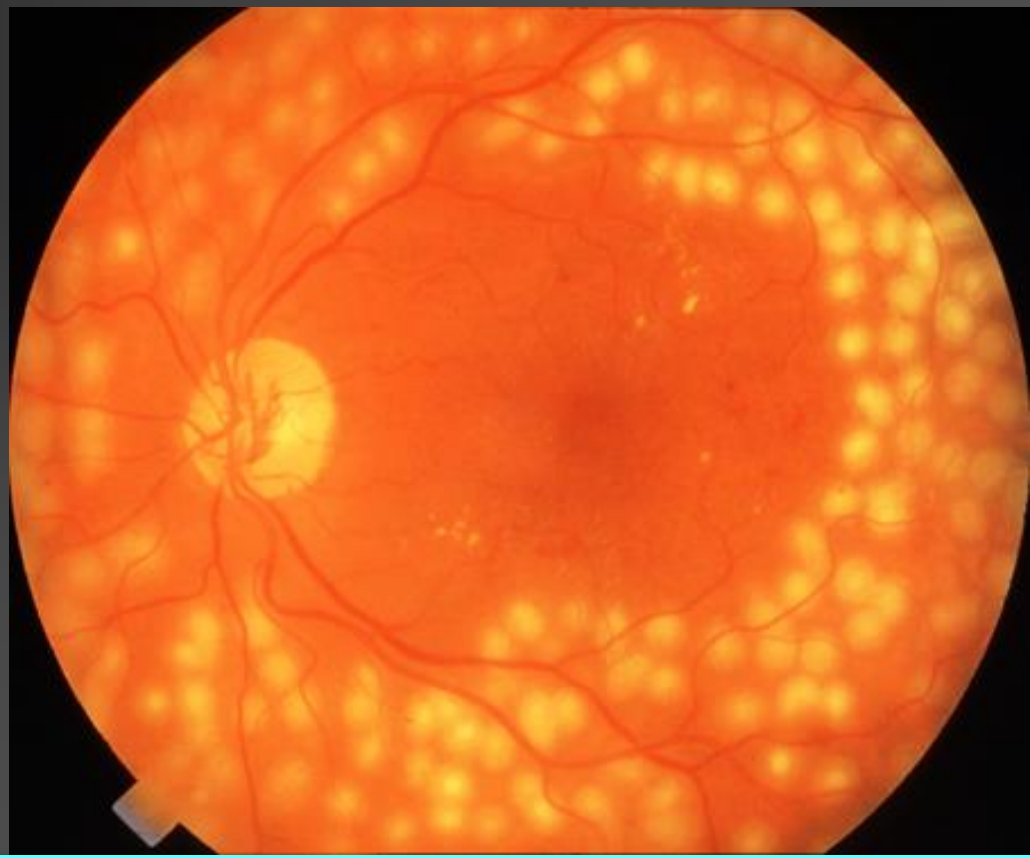
< 1000 spots / session

- **ME?**
- **fractioning?**

AGGRESSIVE

≥ 1000 spots / session

- **faster fibrosis (NV)**
- **NO more side-effects?**



Timely prLC reduces risk of blindness by 90% (DRS 1976)

PANRETINAL LASER

"HARD" INDICATIONS

(HR – PDR: NVD / NVE & epiretinal / vitreous haemorrhage)

TYPE 1 DM	• csME less extensive • Reacts less disastrous to prLC ➢ aggressive approach! ➢ full scatter (initially ≈ 1200 spots) ➢ csME (first central LC & fast prLC / simultaneously)
TYPE 2 DM	• Approach (extend of PDR & follow up?) • Avoid prLC without HR-PDR (▸ csME↑)! ➢ csME (always first central LC ▸ prLC after 3/12?) ➢ moderate HR-PDR (CL ▸ mild scatter prLC) ➢ extensive HR-PDR (CL ▸ full scatter prLC) ➢ very extensive HR-PDR (CL & fs-prLC)

PANRETINAL LASER

"SOFT" INDICATIONS

(Type 1 > Type 2)

Severe NPDR	**extensive IRMA & venous beading in 4 Quadrants** • **ischemia** • **progression to PDR?** ➢ **follow up?**
Non-HR-PDR	**No NVD / NVE & epiretinal / vitreous haemorrhage** • **csME ▸ VA?** ➢ **follow up?**

PANRETINAL LASER

FOLLOW UP (after 4 – 6 weeks)

"Stop / Regression of NV?"

YES:	➢ observe
NO: • mild scatter LC • full scatter LC	 ➢ fill in ➢ fill in & extension (periphery)

PANRETINAL LASER

MANAGEMENT

(progressive HR-PDR)

Laser	➢ several thousand spots (fs-prLC + fill in + periphery) ➢ almost no distance between spots • VFD • Dark adaptation ↓ • Colour vision ↓
ppV	➢ early?

LASER PARAMETER

DEPEND ON:

- Laser type
- Laser glass
- Extend of oedema (20% ↑ E in csME?)
- Optical media
  - Energy
  - Spot size
  - Time

Shorter exposure time preferable:

- heat conduction ↓
- (but energy ↑)

LASER MARKS:

- Mild bleaching (RPE)
- NO benefits from stronger marks!
- Avoid:
  - damage of inner retina (NFBD)
  - damage of Bruch's membrane (SRNVM)
  - choroidal effusion
  - serous RD
  - haemorrhages
  - epiretinal gliosis & traction (VA!)
  - pain

LASER PARAMETER
(FD NdYAG 532 & Argon)

LASER	GLAS	PARAMETER
Central - focal	**Area centralis** (ca. 1: 1)	• **N**? • **T** = 100 – 150 ms • **D** = 50 – 100 µm • **E** = 50 – 100 mW …
Central - grid	**Area centralis** (ca. 1 : 1)	• **N**? • **T** = 100 – 150 ms • **D** = 100 – 200 µm • **E** = 50 – 100 mW …
Panretinal	**Quadraspheric** (ca. 1 : 2)	• ms: **N** = 600-1200 • fs: **N** = ≥ 1200 • **T** = 100 - 200 ms • **D** = 200 – 300 µm (x 2) • **E** = 100 – 400 mW …

ADVERSE EFFECTS (LASER)

ILUMINATION (SL & Microscope)	AIMING BEAM	LASER BEAM
Photic damage (e.g. blue light) ➢ transient & permanent ➢ diseased / treated / elderly retina ➢ duration of exposure ▸ avoid excessive illumination (macula!)	**Blue-cone damage (Argon laser)** ➢ patient's retina ➢ observer's retina (reflection off contact glass) ▸ red coaxial beam ▸ blue-green protective filter	**Unintended absorption** ➢ iris, synechiae, cataract, haemorrhage **Inadvertent laser** ➢ fovea (eye movement, 3 mirror glass) ➢ large vessels (temporary occlusion, haemorrhage) **Scatter of beam** ➢ opacities, vitreous haemorrhage, ME ➢ myopic eyes (sensitive!) ▸ longer wavelength

LASER SIDE - EFFECTS

TRANSIENT	MEDIUM TERM	PERSISTENT
Blurring of Vision ➢ mydriasis, pigment, iris? **Choroidal Detachment** ➢ myopic shift / ACG? ➢ recovery over 10 days **Macula Oedema** ➢ BRB disruption (e.g. parafoveal & large areas) ➢ BRB (for 7 – 10d) ▸ VA↑ 4 weeks (Type 1 DM) ▸ permanent (Type 2 DM)? **Axoplasmatic Flow↓** ➢ NFL-defects (laser of Ma) **Headache (24 hrs)** ➢ anxiety?	**Macula Oedema** ➢ parafoveal & prLC ➢ pre-existing ME ➢ diffuse ME ➢ may persist up to 3 months with permanent drop of VA ➢ VA may drop to CF (severity does NOT correlate strictly with final outcome) ➢ Type 1 DM: mostly recovery to pre-OP VA ➢ Type 2 DM: ME may persist with permanent loss of VA! ➢ strict indication for prLC in elderly Type 2 patients & BP ➢ central laser (first / same time?)	**Loss of VA (1-2 lines)** ➢ prLC (photochemical?) ➢ may improve (18/12)? **Accommodation↓** ➢ long cilliary nerve damage **Dimness** ➢ dose related (> 2000 spots) **Nyctalopia (rods)** ➢ prLC (rods / others?) ➢ prolonged adaptation time **Colour Vision↓ (cones)** ➢ direct damage / scatter **Photophobia (RPE)** ➢ dose related, fair skin, PSC **Loss of VF (rods & cones)** ➢ dose related (fs + fill in)

LASER COMPLICATIONS

PATIENT	SURGEON	OBSERVER
Anaesthesia (rare)	**Accidental Exposure**	**Accidental Exposure**
Anterior Segment (rare) ➢ burns (cornea / lens) ➢ transient iritis (accid. laser)	➢ mechanical shutter failure ➢ reflected laser light (CG)	➢ reflected laser light (CG)
Raised IOP (rare) ➢ ACG / pigment dispersion / steroids / rubeosis iridis	➢ blue colour vision loss (Argon / aiming beam)	
PVD (therapeutic!) ➢ RD / haemorrhage		
Retina ➢ fovea (movement / orient.) ➢ haemorrhage (sr / re / chor) ➢ CNV (Bruch's membrane))	➢ fixed protective filters	➢ at least 1 m distance ➢ protective goggles (correct wave-length?) ➢ laser room protection (signed & lock)
Hard Exudates (1 / 52)		
Enlargements of Burns		
Choroidal NV ➢ long wave-length / high E		

PROBLEMS & DIFFICULTIES

ANXIETY	PAIN	SMALL PUPIL	CATARACT	MYOPIA	OBESITY
Explanation Reassurance Success Medication?	Anterior: e.g. 3-6-9-12 o'clock Long nm High mW Pigment↓ Medication? pb / rb?	DM? Synechiae? Opacities? 90 D non-contact glass Mydriatics? Surgical dilatation?	Axial CG Long nm Surgery? (CR / ppV)	Thin RPE & prominent choroidal vessels FLA (NV?) High energy necessary ("burns") Risk of: · CNV · choroidal haemorrhage · pain	Limited patient access (SL) Low SL & move chair far from laser HIO-Laser?

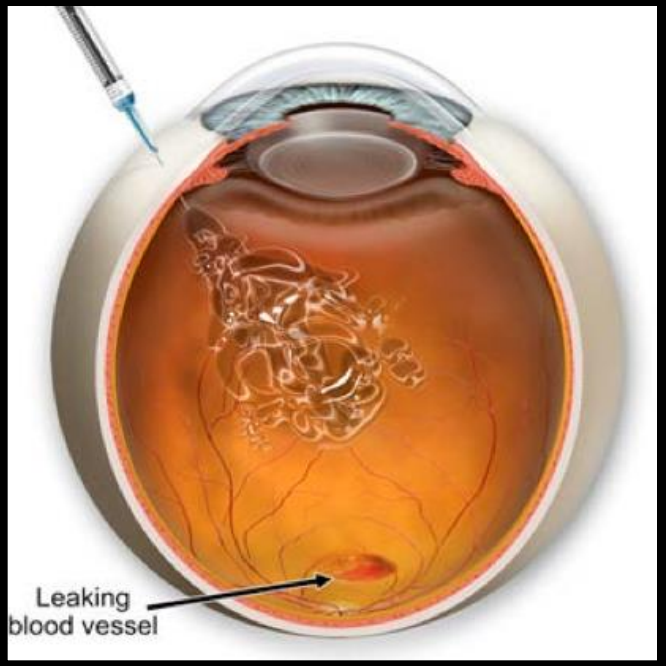
DIABETIC MACULOPATHY (management)

BEFORE LASER:

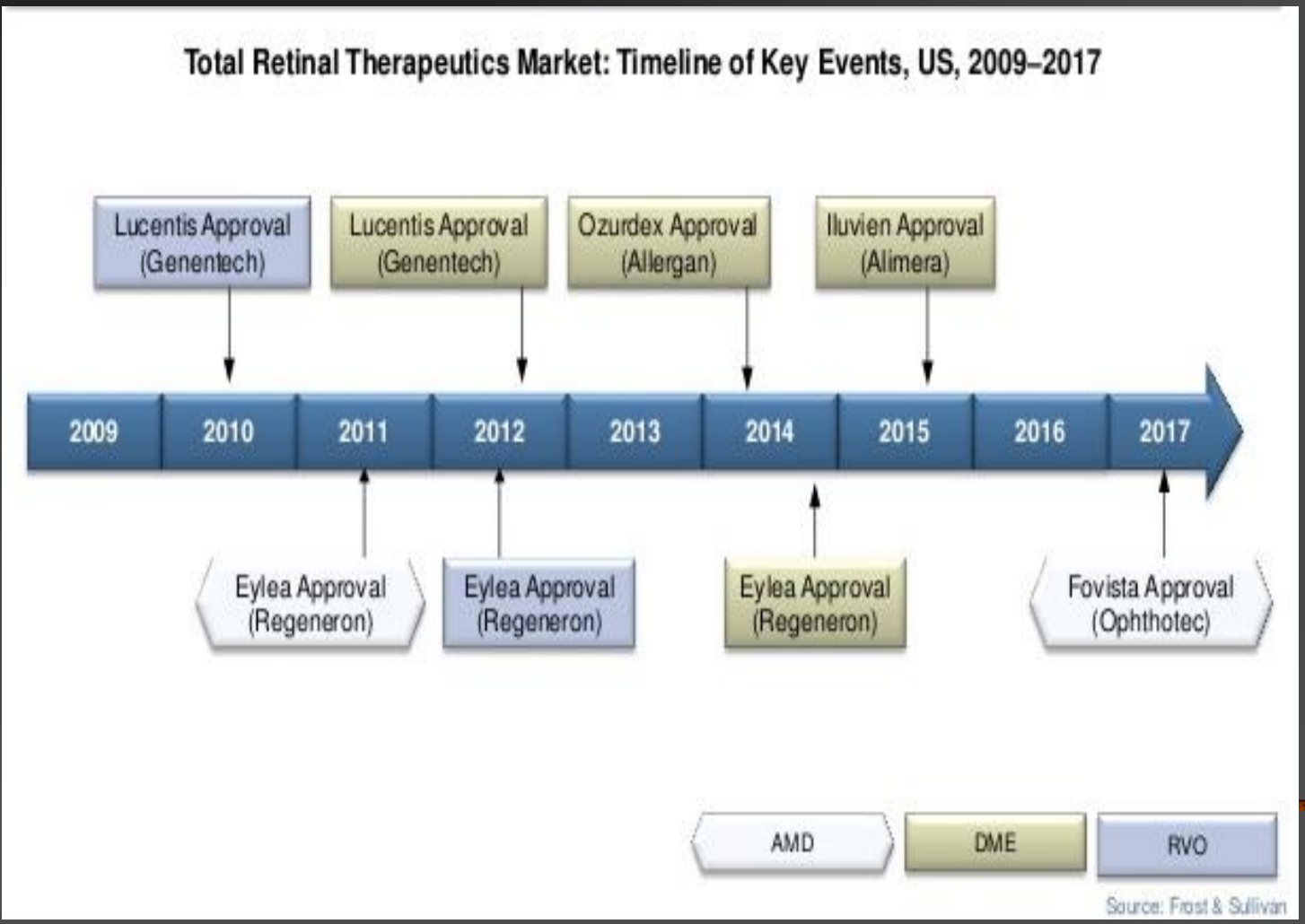
- Regulate BS, BP & Lipids
- Stabilise cardio-pulmonar & renal situation

ISCHEMIC	FOCAL EXSUDATIVE	DIFFUSE EXSUDATIVE	CYSTOID
FLA ➢ perfusion? RISK (laser) ➢ damage of remaining peri-foveolar capillaries? VA ↓	focal LC ➢ visible aneurysms? grid LC ➢ areas of thickened retina	grid LC ➢ entire thickened retina	often irreversible! ➢ therapeutic trial with e.g. (?) • grid LC • Triamcinolone • Diamox

MANAGEMENT – PHARMACOTHERAPY



MEDICAL – FDA TIMELINE APPROVALS



DIABETIC RETINOPATHY TREATMENT NEWER DEVELOPMENTS:

- The use of anti-vascular endothelial growth factor antibodies has been shown to be useful in the treatment of DR
- Anti-VEGF antibody treatment appears to be useful for both macular edema and proliferative retinopathy
- Studies to determine the exact role of anti-VEGF treatment in relation to laser treatment in specific situations are underway.

PRINCIPLE OF DRCR.net DME TREATMENT Intravitral Anti-VEGF

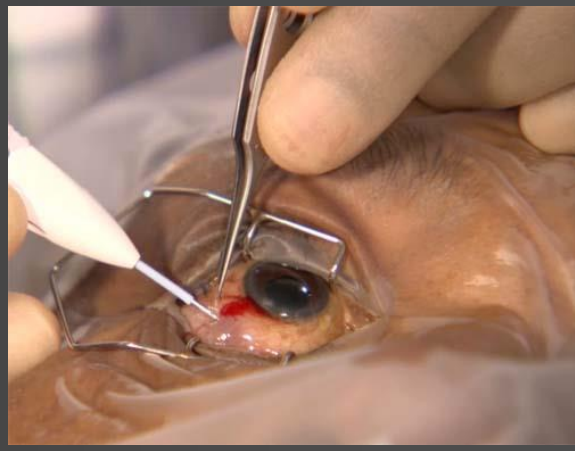
- **Improving on OCT or VA ⟶ Inject**

  Improving = OCT CST decreased by ≥ 10% or VS letter Score improve by ≥ 5

- **Worsening on OCT or VA ⟶ Inject**

  Worsening = OCT CST increased by > 10% or VA letter score decrease > 5

- **Stable: Not Improving or Worsening on OCT or VA**
  - **Inject unless stable since last 2 injection which case inject only if before 24 weeks visit when OCT >250nm and VA 6/6**



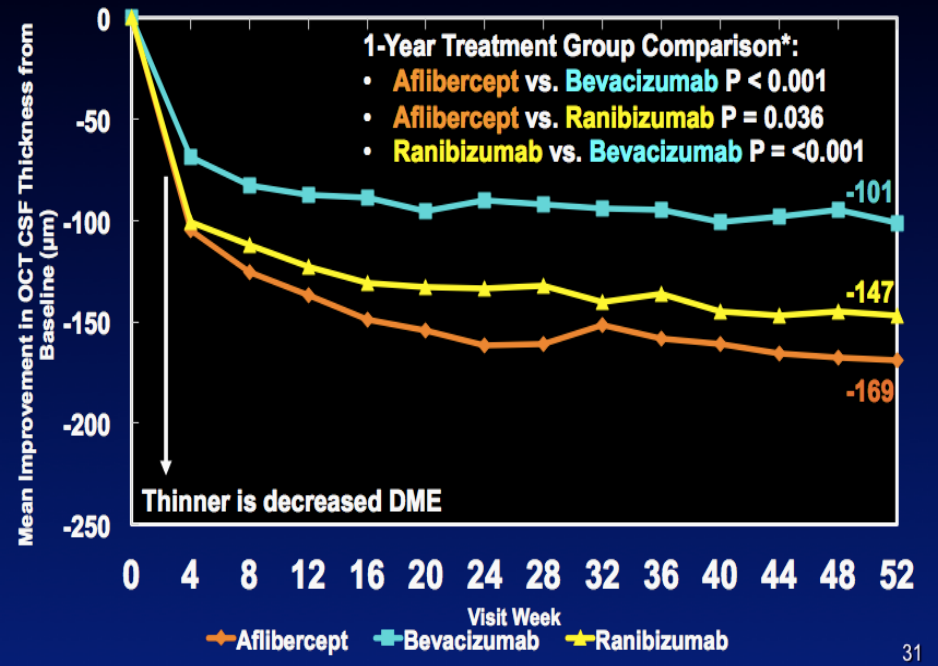
OTHER INTRAVITRAL ANTI-VEGF RETREATMENT STRATEGIES

- **RESTORE: 0.5 mg ranibizumab**
  - 3 consecutive monthly injections, then retreat if visual acuity not stable, regardless of OCT – once stable, withhold injection and resume if worsen until stability again
- **RIDE/RISE: 0.5 mg or 0.3 mg ranibizumab**
  - Monthly treatments for 36 months (36 injections)
- **VIVID/VISTA: 2 mg aflibercept**
  - 5 consecutive monthly injections, then every other month through 36 months (21 injections)
- **Anything you like? – ok if outcomes mirror DRCR.net visual acuity outcomes (mean change from baseline of 10 letters) and frequency of injections (median of 15 through 36 months, median of 16 through 5 years)**

Mitchell P, et al. *JAMA Ophthalmol* . 2013;131(10):1339-47; Brown DM, et al. *Ophthalmology* . 2013;120(10):2013-22; Korobelnik JF, et al. *Ophthalmology* . 2014 Jul 8. [Epub ahead of print]

COMPARATIVE EFFECTIVENESS STUDY OF AFLIBERCEPT, BEVACIZUMAB, OR RANIBIZUMAB FOR DME

Overall Mean (μm) Change in OCT CST Over Time



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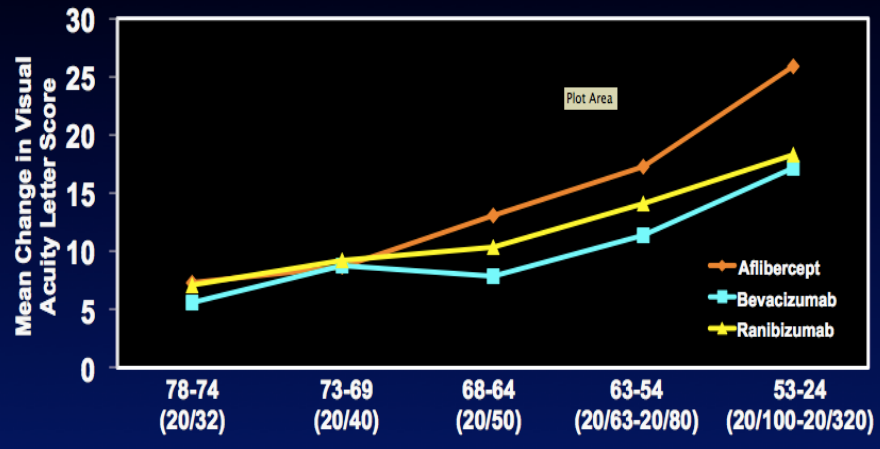
* *P*-values adjusted for baseline visual acuity, OCT central subfield thickness, and multiple comparisons

Visual Acuity Mean Change: Baseline to 1 Year

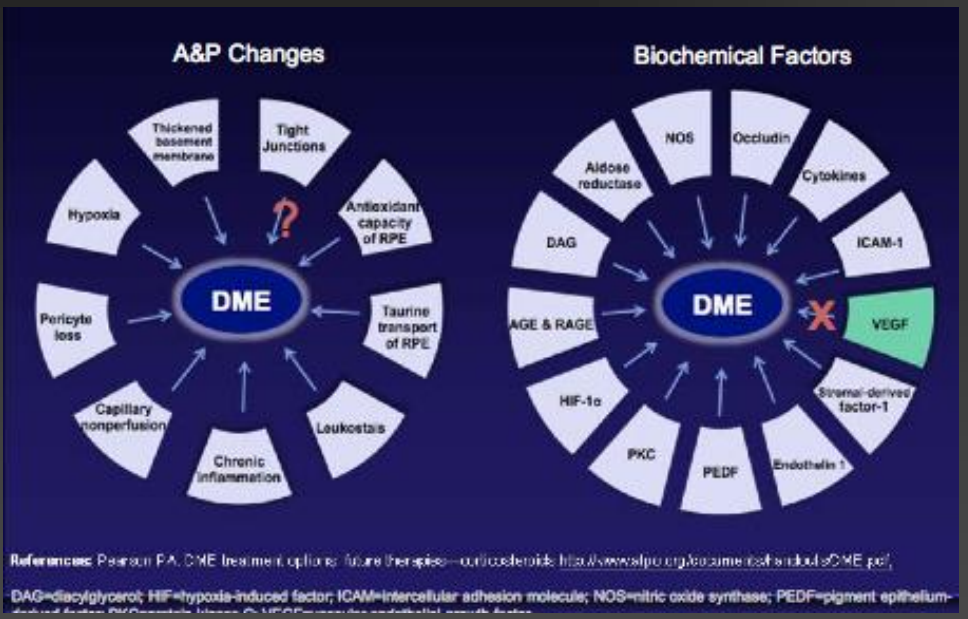


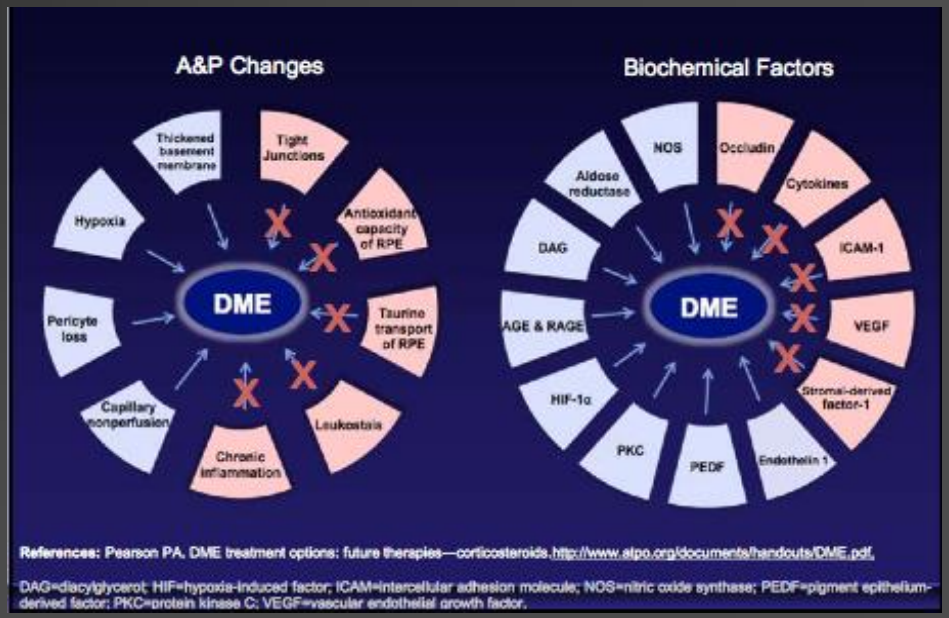
N =					
Aflibercept	54	52	36	29	37
Bevacizumab	41	63	35	38	29
Ranibizumab	46	59	32	37	32

- All three anti-VEGF agents are effective treatments for DME causing vision impairment.
- When initial visual acuity loss is mild, on average there is little difference in visual acuity at 1-year.
- At worse levels of initial visual acuity aflibercept is more effective at improving vision.

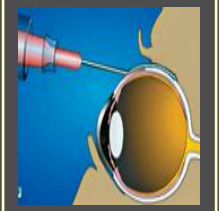
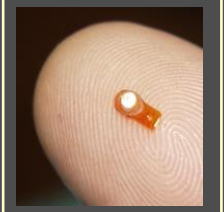
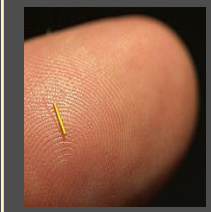
STERIODS IN DME - PATHOPHYSIOLOGY

Early focal leakage is primarily VEGF-driven, but when it advances to diffuse leakage, leading to fibrosis, pigmentary alterations, and loss of PRs, the equation changes. The process is now primarily inflammation driven,





STERIODS – INTRAOCULAR DEVELOPMENT

	NOVA63 035 NVG	Posurdex (Ozudex) Allergan	Kenalog BMS	I-Vation SurModics	Retaane Alcon	Retisert B&L	Medidur Alimera
							
API	Dexamethasone palmitate	Dexamethasone	Triamcinolone acetonide	Triamcinolone	Anecortave acetate	Fluocinolone acetonide	Fluocinolone acetonide
Administration	Injectable emulsion	Injectable implant (DDS)	Injectable suspension	Implant (DDS)	Juxtascleral injection	Implant	Injectable implant
Duration	6-9 months	1-3 months	1-3 months	12 months	6 months	30 months	18-36 months
Indication / Dev	DME Phase I	DME Phase III	All Off label	DME Phase I, III	ARMD Phase III	DME, Phase 2b/3	DME Phase III
Comment	Reduction of side effects ?		Toxic excipients			$ 18,250	

STERIOD – (Intravitreal)*

Advantages of Steroid

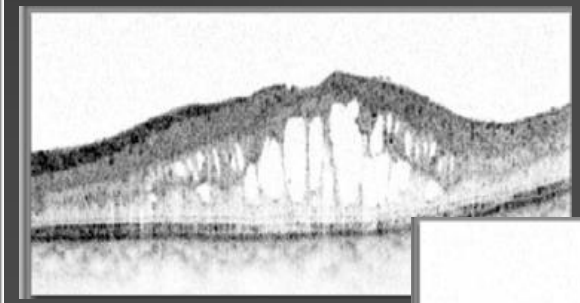
- Less Frequent Dosing
- Treat Inflammatory Component
- Okay in Pregnancy
- No Systemic Risk
- Some Patients Respond Dramatically, Even if No Response to Anti-VEGF Agent
- Ozurdex Helpful in Vitrectomized Patient

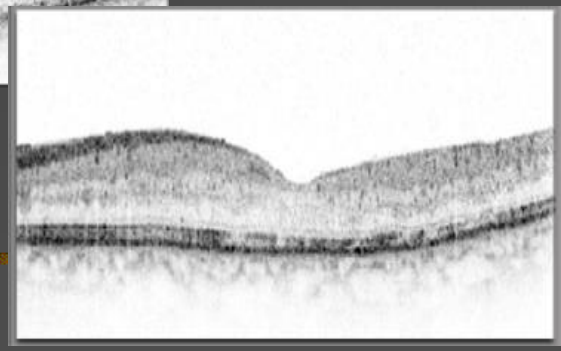
Consider Intraocular Steroid

- Anti-VEGF Failure
  - Significant Edema and Poor Vision after 6 Injections and Laser
  - Pseudophakic, not Severe Glaucoma
- Recent Cataract Surgery (CME Component)
- Chronic Edema
- Systemic Factors
  - Stroke, Heart Attack, Non-healing Wound, Pregnancy

Disadvantages of Steroid

- Cataract
  - Virtually 100%, Significant Problem Within One Year
- Glaucoma
  - 40% Require Therapy (60 % Do Not)
  - Filter or Surgical Removal of Steroid Can be Necessary





Diffuse diabetic maculopathy

* G.E. Lang: Ophthalmologe 2004; 101/12 (1165-1170)

SUMMARY FOR DME

QUESTIONS TO CONSIDER

1. What is the Vision
2. Is the Centre of The Fovea Involved
3. Ocular Risk Factors: Lens, Glaucoma, Steriod Responder, PDR
4. Systemic Risk Factors: Stroke, Heart Attacks, Surgery, Ulcers
5. Ability to Foillw Up
6. Who is Paying

INTRAVITRAL ANTI-VEGF INJECTION

- Centre Involving Edema
- Decreased Vision 6/9 or Worse
- First Line – begin with Anti VEFG Agent (Less Side Effect)
- Consider the various Option – DRCR.net, Restore, Rise and Ride, Vista and Vi

FOCAL LASER

Edema Threatening but not Involving the Central Macular

- Prior to PRP, Cataract Surgery or Worsening Vision

Poor Compliance

Uncertain Follow up

Cost Burden

CONSIDER INTRAOCULAR STEROIDS

Anti-VEGF Failure

- Significant Edema (Chronic) and the Poor Vision after 6 injection and Laser
- Pseudophakic or Planed Lens extraxtion, Severe Glaucoma

Recent Cataract Surgery (CME Component)

Chronic Edema (Diffuse Edema)

Systemi Side Effect – Stroke, Heart Attacks, Surgery, Non healing Wound, Pregnancy

Focal or Multifocal Macular Edema

Metabolic control and risk factor assessment

OCT

No traction

Traction (and functional loss)

ME of well-defined origin, treatable with laser photocoagulation

ME with central involvement, not treatable with laser photocoagulation

Vitreoretinal surgery with hyaloidectomy +/- ILM peeling

Laser photocoagulation ETDRS guidelines

Improvement

No improvement

Periodic Control

Anti-VEGF therapy*

Anti-VEGF therapy* then laser photocoagulation or not / IVT corticoids** then laser photocoagulation in pseudophakic eyes

Improvement

No improvement

Periodic Control

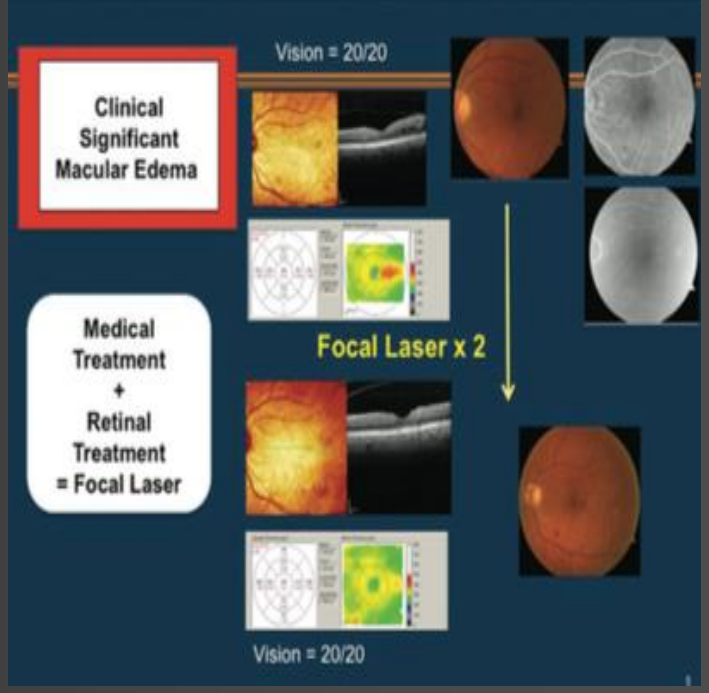
PPV optional

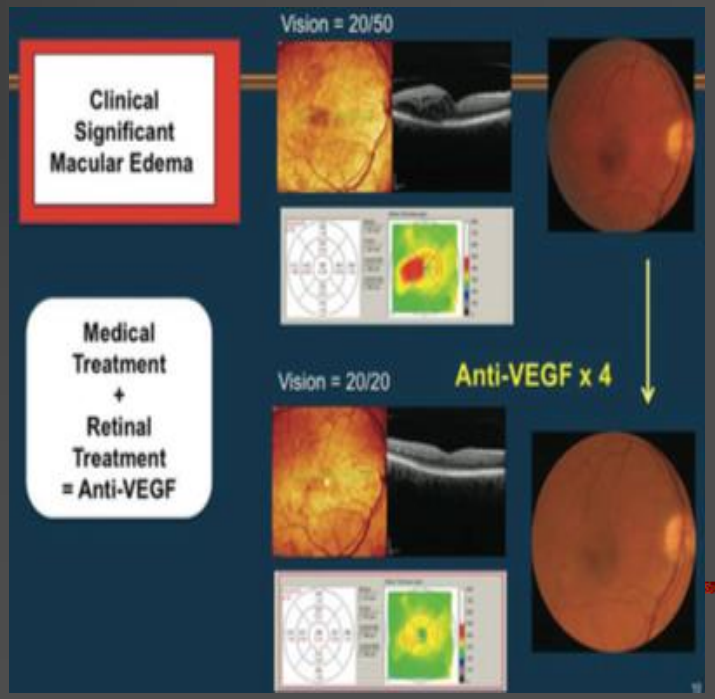
Improvement

No improvement

Periodic Control

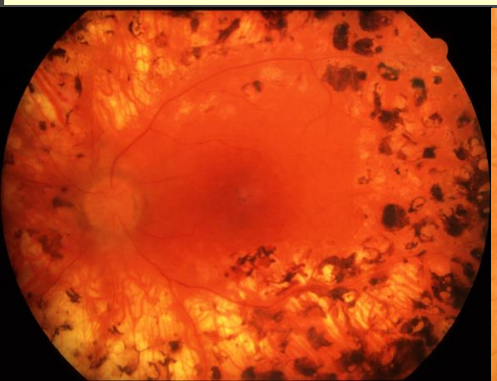
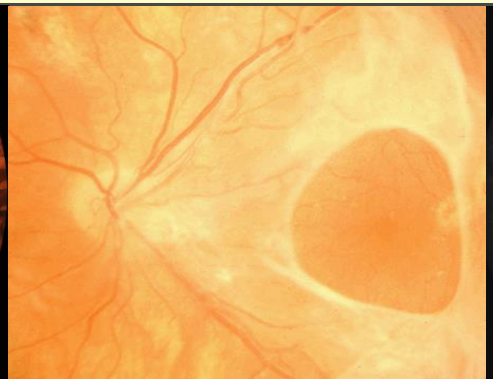
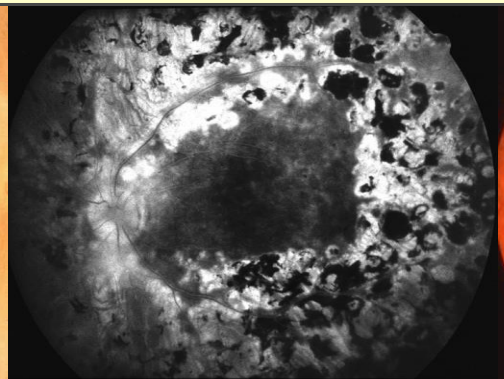
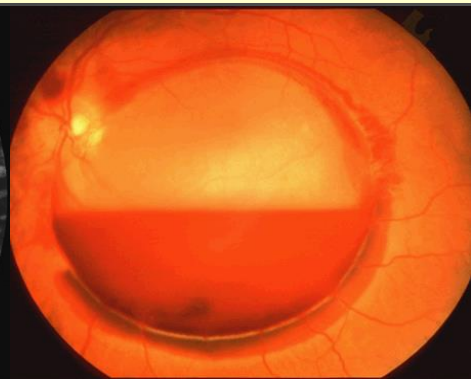
Treat as with non-tractional ME



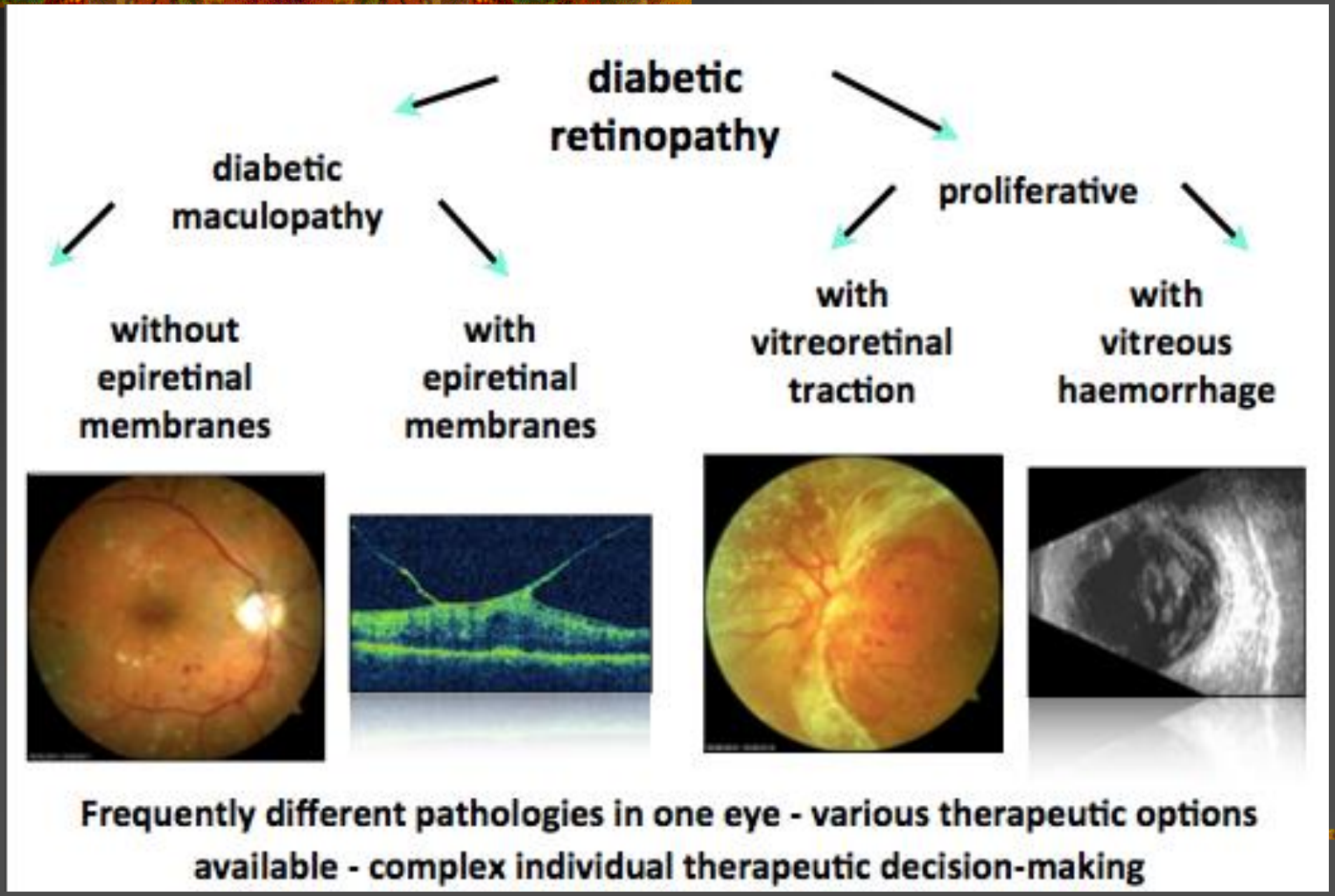


SUMARY LOCAL TREATMENT (PDR)

DIAGNOSIS	TREATMENT
PDR (HR)	pan retinal laser coagulation
vitreous haemorrhage	ppV
retinal detachment	ppV / RD-surgery
tractional csME	ppV & mp
non-responsive PDR	ppV & endolaser

VITRECTOMY in DR*



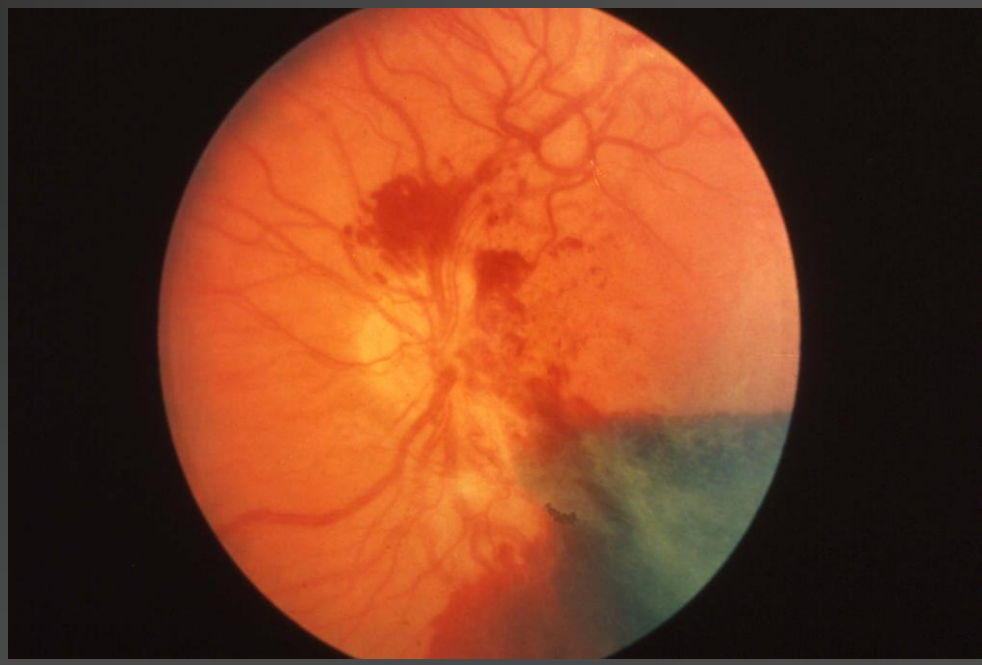
Frequently different pathologies in one eye - various therapeutic options available - complex individual therapeutic decision-making

MANAGEMENT - HIGHLIGHTS

- **Strict blood-sugar control** is the single most important factor to prevent visual loss (early)
- **A poly-pragmatic "vasoprotective" approach** significantly reduces cardio-vascular mortality and diabetic retinopathy
- **Early laser treatment** (csME) reduces severe visual loss by 50-75%
- **Timely treatment of PDR** (prLC / ppV) reduces severe visual loss by 65-75% & blindness by 90%
- **Effective bi-directional communication and cooperation** between diabetologists and ophthalmologists is essential for the complex management of diabetics

PLANING

VISION 2020



NATIONAL DEVELOPMENT PLAN

GHANA

(NPBWG / K.H.M. Kollmann)

INTERVENTION STRATEGIES

(≥ 5-10% or more blindness due to DR?)

COMMUNITY

- awareness (DM & blindness)
- change of behaviour

MEDICAL STAFF

- systemic control (BS, BP…)
- communication & co-operation

SCREENING

- on Dx & annually

DR - CENTRES

- laser (& ppV), training
- communication & co-operation

SCREENING

WHO?

Ophthalmologist
OCO
Optometrist / Optician / ON / OA ... ?
GP ... ?

HOW?

Fundoscopy (dilated!)
Stereoscopic SL-Biomicroscopy
Fundus photography?

WHEN?

Dx / annually / findings:

TYPE 1 (puberty / 5 years DM)
TYPE 2 (on Dx of DM!)

DIABETIC RETINOPATHY (SUMMERY)

DIABETIC RETINOPATHY:

- Major cause of **avoidable blindness** (increasing world-wide)
- **NOT a late manifestation** of DM
- Early & sensitive indicator for **cardio-vascular risk**
- Assists in **precise categorisation** of vascular high-risk patient
- Chronic **Hyperglycaemia** & **Hypertension** are most important risk factors

DIABETIC RETINOPATHY (SUMMERY)

MANAGEMENT:

- **Poly-pragmatic vasoprotective approach** is efficient & cost-effective
- Need to promote **evidence based management** (DM & DR)
- Effective **bi-directional communication and co-operation** between diabetologists & ophthalmologists essential
- **Research** & appropriate **national planning** important to address epidemic dimension of DM & DR

DIABETIC RETINOPATHY

(Photos & Diagrams)

- American Academy of Ophthalmology: Diabetic retinopathy 1992
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- RGM Michels: Vitreous Surgery 1982
- HMA Towler, JA Patterson, S Lightman: Diabetes and the eye, ULC, 1998 (2nd ed.)


THANK
YOU!