ADS Position Statements

1996

Diabetes and the Eye

Retinopathy Sub-committee of Australian Diabetes Society
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DIABETES AND THE EYE

The information contained in the practice guidelines has been prepared by the Diabetic Retinopathy Sub-committee of the Australian Diabetes Society and has been endorsed by R.A.C.0, R.A.C.P and R.A.C.G.P.

CURRENT RECOMMENDATIONS (SUMMARY)

For retinal examination, pupil dilatation and an adequate magnified view of the fundus is essential using either detailed direct opthalmoscopy, indirect opthalmoscopy, slit-lamp biomicroscopy or the fundus camera. For epidemiological purposes or early detection programs, fundus photography using a non-mydriatic camera is acceptable.

For insulin-dependent diabetic patients diagnosed before age 30, the first retinal examination should occur no later than after 5 years diabetes duration or at 30 years of age.

In patients diagnosed at or after age 30, the first retinal examination should be made at the time of diagnosis to detect those patients who already have significant retinopathy.

Subsequently examination in both groups is recommended at least every 2 years if no retinopathy is found.

Once any retinopathy lesions are detected, the eyes should be reviewed every 12 months or more frequently if the signs indicate significant capillary closure or any threat to macular function.

Where possible, patients should be encouraged to improve blood glucose control to reduce the risk of retinopathy developing or progressing.

As retinopathy may progress during pregnancy, all women with diabetes be examined prior to commencing a pregnancy and re-examined at three monthly intervals during the pregnancy particularly if retinopathy is detected at the preliminary examination.

Patients should be advised to seek an ophthalmic review if they report any decrease in vision.

If these measures are fully implemented, the risk of blindness from diabetic retinopathy should be reduced by up to 95%.

INTRODUCTION

Almost all people with diabetes will eventually develop diabetic retinopathy. [1,2] Diabetic retinopathy is the commonest cause of legal blindness up to age 65.[3] It was previously shown to cause 10 to 12% of blindness in Australia. [4] In 1988, diabetic retinopathy was found to be the cause of blindness in 3 to 4% of registrations. The rate of blindness in diabetic patients is 25 times that of non-diabetic patients.[5] Diabetic retinopathy is the most frequent chronic complication associated with diabetes.[6]

The Diabetes Control and Complications Trial (DCCT)[7] demonstrated that intensive treatment and very tight control of blood glucose levels dramatically reduced the development and progression of diabetic retinopathy in insulin dependent patients. It is likely that the results can be extrapolated to non-insulin dependent diabetes.

In the last 20 years laser photocoagulation treatment has been shown to be extremely effective in preventing visual loss due to diabetic retinopathy. [8 9 ' 41] Currently diabetic retinopathy is the most preventable cause of blindness. [8,10] This treatment success has been demonstrated in a number of well-designed, randomised multicentre trials conducted in the USA and the UK for treatment of both proliferative retinopathy and macular oedema. [8,9, 12,13,14,32,33]

It is clear from these trials that treatment is more successful if it is carried out before visual loss and irreversible changes have occurred. There is, therefore, a significant need to diagnose and consider patients with retinopathy for treatment before any visual loss occurs.

EPIDEMIOLOGY

The 1989-90 National Health Survey of the Australian Bureau of Statistics indicated that more than 300,000 people are known to have diabetes. A similar number are likely to have undiagnosed diabetes or impaired glucose tolerance [15,16] to give a total of in excess of 600,000. Epidomiological studies in the USA (using glucose tolerance tests) show that almost 50% of persons age 65 or older with diabetes are not diagnosed .[17] The non-insulin dependent patients may have diabetes for four to seven years before clinical diagnosis.[18]

Population-based surveys show that, at any one time, around one-third of people with known diabetes have retinopathy and that approximately one third of these i.e. 10% of the total number, have vision-threatening retinopathy. [19,20,21]

In this position statement the term Type 1 (insulin-dependent diabetes mellitus - IDDM) refers to patients who require permanent insulin therapy to sustain life. Most require insulin shortly after diagnosis, and most are diagnosed in childhood or adolescence. Type 2 (non-insulin dependent diabetes mellitus - NIDDM) refers to patients who are insulin resistant and whose diabetes can be controlled initially with diet and/or oral medication, but who may require insulin for blood glucose control later in the course of disease.

Type 2 diabetes is usually diagnosed in adulthood. In Australia, there are approximately five times as many people with Type 2 Diabetes as those with Type 1 Diabetes.[22]

In terms of diabetic retinopathy, the type of diabetes is important. In those with IDDIVI, diabetic retinopathy is not present at the time of diagnosis, and is unlikely to occur during the next five years. [20,23] In the NIDDM group, up to 13% will have non-proliferative diabetic retinopathy (NPDR) at time of diagnosis. [49]

Diabetic retinopathy is found in almost 100% of patients if they have had IDDM for 20 years or more. At the end of that period, the majority will have non-proliferative diabetic retinopathy and 20% will have proliferative diabetic retinopathy and 20% will have proliferative retinopathy with the proportion rising to 65-86% after more than 30 years. [1,2,21]

In the NIDDIV1 group, approximately 70% will have signs of retinopathy after 20 years of diabetes, with a similar proportion (25-30%) having vision-threatening retinopathy. [2,21] In this group, the problems with vision are predominantly due to macular oedema. Nevertheless, because of the large number of NIDDIV1 patients, they still form the majority of patients with proliferative retinopathy.

Overall for both IDDM and NIDDM diabetic patients, 8% without retinopathy will develop it each year. On average retinopathy develops in 8% of diabetics without retinopathy per year, so that after 3 years, around 1 in 4 patients would be expected to have some signs of early background retinopathy. 7% of those with background retinopathy will progress to develop vision-threatening retinopathy each year. [21]

RISK FACTORS FOR DIABETIC RETINOPATHY

The two major determinants for the development of diabetic retinopathy are the duration and control of diabetes but other factors may also contribute.

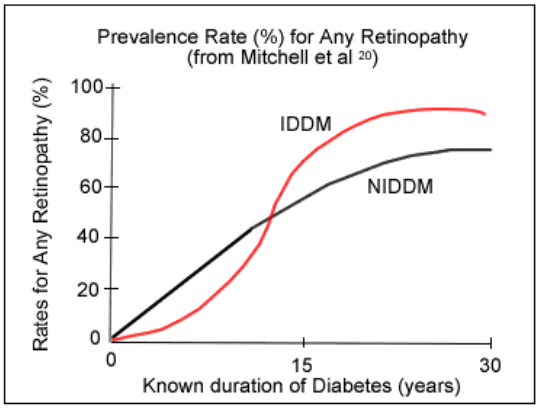
1. *Duration Of Diabetes*

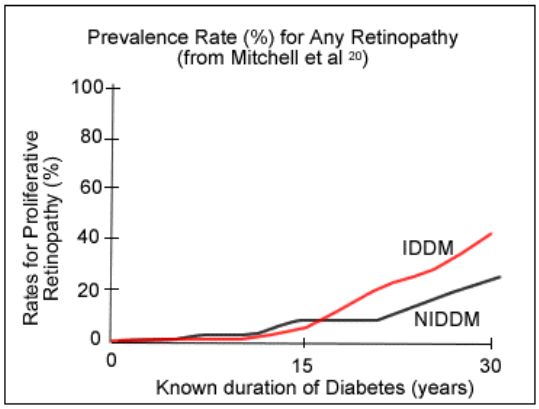
The duration of diabetes is the primary risk factor for the development of retinopathy. In the IDDM group, the risk of retinopathy rises after the first five years. The prevalence rate increases from 25% after 10 years to around 90% after 20 years' duration . [2,21] The risk of retinopathy in this group in the first five years after diagnosis and before puberty is very low or negligible.

The rate of proliferative disease in the IDDM group rises from 0% - 4% after 10 years to 27% - 50% after 20 years' duration. [1,21] Maculopathy also increases with duration - 12% after 10-14 years and 26% after 30 years. [21]

In the NIDDM group there is also a rise in the prevalence of retinopathy with increasing duration. With less than five years of diabetes, there is an 18% prevalence of retinopathy which rises to 76% after 30 or more years of retinopathy. In this group, 13% have retinopathy at initial diagnosis of diabetes, and 3% of patients have clinically significant macular oedema or high-risk proliferative retinopathy. [21]

The rate of proliferative disease also rises with duration in this group - up to 26% after 30 or more years - but it is less prevalent for any given period (except within the first 5 years) than in the IDDM group. On the other hand, maculopathy occurs frequently with increasing duration in the NIDDM. The prevalence of maculopathy in NIDDM is more than twice as frequent as in IDDM. [21]





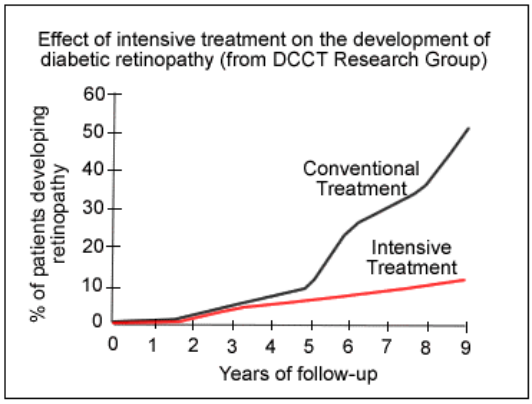
2. Diabetic Control

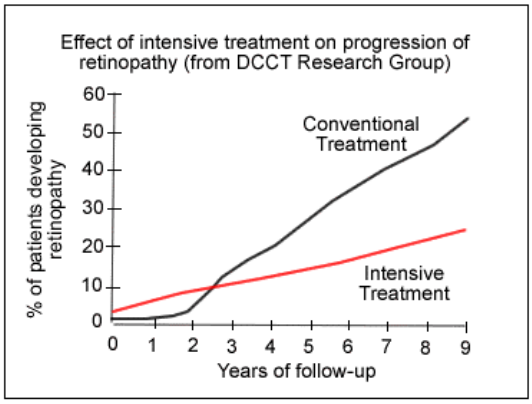
The Diabetes Control and Complications Trial (DCCT)[7] studied 1441 insulin-dependent diabetic patients and compared the effect of conventional control to intensive therapy.

The results of the DCCT were published in 1993 and established that optimal blood glucose levels or good diabetic control can reduce the development and progression of retinopathy. In this prospective, randomised study, patients were given intensive therapy (3 or more insulin injections daily or insulin pumps and frequent blood glucose monitoring) or standard therapy (1 or 2 daily injections and 3-monthly reviews). Two groups of patients were studied:- a cohort with no retinopathy at entry to the trial, and a cohort with mild background retinopathy at entry. Only IDDM patients were included in the study.

Over an average period of 6.5 years only 10% of the intensive therapy group without pre-existing retinopathy developed retinopathy whereas 60% of the conventional group developed diabetic retinopathy.

Among people with pre-existing retinopathy, the progression of retinopathy and the development of severe non proliferative or proliferative retinopathy were approximately halved over the time of the study by intensive treatment and control. Estimates of the long term efficacy of intensive therapy suggest a risk reduction for the progression of retinopathy of 80% or more.





Intensive treatment produced a slight worsening of retinopathy over the conventional therapy group in the first two years however thereafter the prognosis for the development and progression was clearly better in the intensive treatment group. This initial deterioration of retinopathy was not vision-threatening and manifested as a temporary increase of cotton-wool spots and intraretinal microvascular changes. The incidence of vision threatening complications, such as macula oedema and neovascularistion, was reduced dramatically by intensive insulin therapy. [57]

The incidence of severe hypoglycaemia was three times higher in the intensive therapy group.

3. *Type Of Diabetes (i.e. IDDM vs NIDDM)*
After the first decade, the rate of retinopathy in IDDM patients exceeds that in the NIDDIV1 group. There is a steep rise in the second decade from 25% at the beginning of that period to 88% at the end. [21]

4. *Renal Disease*
IDDM patients with proteinuria have a three times higher prevalence of macular oedema and proliferative retinopathy than those without proteinuria.

Patients nearly always present with retinopathy before signs of overt renal disease and most patients with diabetic renal failure will already have had treatment for proliferative diabetic retinopathy. The onset of renal failure may herald the rapid onset of proliferative changes. [23]

5. *Pregnancy*
There is an increased risk of development and progression of retinopathy with pregnancy. [25] A 2.3 times increase in progression of retinopathy has been found in pregnant previously diagnosed diabetic women when compared to non-pregnant women. [26] Women commencing a pregnancy without retinopathy have a 10% risk of developing background changes during pregnancy. If background retinopathy is already present then there is a 4% risk of progressing to proliferative retinopathy.

Diabetic retinopathy does not occur in gestational diabetes.

6. *Smoking*
Smoking has been found in recent incident studies to be associated with visual loss in IDDM27 , but previously was found not to be associated with retinopathy in the cross-sectional data from the Wisconsin Epidemiology Study of Diabetic Retinopathy. [50]

7. *Hypertension*
Hypertension is now considered a much less important risk factor for the development and progression of diabetic retinopathy than diabetic control. [24] Severe hypertension may produce similar microvascular disease features in the fundus (haemorrhages, lipid exudates and retinal oedema) as occur in diabetes.

Antihypertensive drugs reduce severity of diabetic retinopathy in experimental models by actions other than just reducing blood pressure.

8. *Other Medical Factors*

a) cataract surgery
There is an increased risk of visual loss from diabetic retinopathy following uncomplicated cataract surgery. [30,31] Any retinopathy should be completely assessed prior to surgery. Fluorescein angiography can be particularly useful if lens opacities make clinical assessment difficult. If fundus examination is possible through the lens and retinopathy requiring treatment is found, either at the macula or in the peripheral retina, then laser treatment should be carried out at least two or three months prior to surgery if possible.

If the fundus is not visible through the cataract then assessment and treatment of retinopathy should be carried out in the early post-operative period.

b) anticoagulants
Aspirin - use in patients with diabetic retinopathy was studied in the Early Treatment Diabetic Retinopathy Study (ETDRS). There was no evidence that aspirin altered the course of retinopathy. There was no increased risk of vitreous haemorrhage in proliferative retinopathy. It did not prevent the development of high-risk proliferative retinopathy. [28] There is no contraindication to the use of aspirin in patients with diabetic retinopathy when it is required for other medical conditions.

Anticoagulant agents such as Warfarin and Streptokinase are not contraindicated, however they should be used with caution in patients with untreated high-risk proliferative retinopathy, because of the risk of vitreous and preretinal haemorrhage. All efforts should be made to treat proliferative retinopathy prior to the use of anticoagulants.

c) carotid artery disease
There is an increased likelihood that patients with diabetes will have carotid artery disease and ischaemic heart disease.

A significant unilateral carotid artery obstruction may produce marked asymmetry of diabetic retinopathy with more or less signs of retinopathy on the side of the obstruction. This may be related to reduced ocular vascular perfusion on that side.[29]

Generalised ocular ischaemia may develop in cases of severe carotid artery obstruction.

PREVENTING VISUAL LOSS

1. *Visual Loss In Diabetes*
Visual loss in diabetes may occur from:-

a) maculopathy
- macular oedema/exudates
- macular ischaemia

b) proliferative retinopathy
- vitreous/pre-retinal haemorrhage
- traction retinal detachment

c) generalised ocular ischaemia
- iris new vessels producing neovascular glaucoma
- lowered choroidal perfusion
- optic nerve infarction anterior ischaemic optic neuropathy)
- cataract

d) lens opacities (cataract)
- specific diabetic cataract is extremely rare and only found in very poorly-controlled young diabetics. There is a significant increased risk of age-related cortical cataract and posterior subcapsular cataract in diabetes.

e) diabetic papillopathy
- acute optic disc swelling in insulin-dependent diabetic patients, often bilateral with usually mild reversible visual loss. [34,35,36]

2. *Preventing Development And Progression Of Diabetic Retinopathy*
Results from the DCCT demonstrate that monitoring and management of risk factors for diabetic retinopathy will help reduce both the incidence of developing diabetic retinopathy and the rate of progression of existing changes.

3. *Prevention Of Visual Loss From Diabetic Retinopathy*
The key measures employed to prevent visual loss from diabetic retinopathy are:-

a) early detection of retinopathy and monitoring of existing retinopathy with regular and appropriately timed fundus examinations together with

b) effective appropriately timed laser treatment.

The rationale for early detection and continued follow-up is threefold. First, significant vision-threatening retinopathy may develop before visual symptoms appear. Second, laser treatment to the retina is an effective therapy for both diabetic maculopathy and proliferative disease. Third, laser treatment for diabetic maculopathy is most effective in preventing visual loss when it is used before visual loss has occurred. Similarly regression of neovascular tissue is more readily achieved by panretinal laser if treatment is carried out in the early stages of neovascular development.

4. *The Importance Of Education*
It is recognised that visual loss from retinopathy can be reduced further by education of the professional, the patient and the public. To this end, it is considered that all messages should convey the same points:

1 . People can develop vision threatening diabetic retinopathy even in the absence of eye symptoms.

2. Severe eye disease may occur in all diabetic patients, even those who are controlled on diet alone.

3. The duration of diabetes in all age groups is the most important risk factor for the development of diabetic retinopathy.

4. Regular and repeated examinations for diabetic eye disease are essential for early detection and referral.

5. Prompt referral and appropriate treatment can prevent almost all severe visual loss due to diabetes.

TREATMENT OF DIABETIC RETINOPATHY

1. *Early Detection And Monitoring Of Diabetic Retinopathy*
Referral to an ophthalmologist for assessment and treatment is indicated if:

- any retinopathy or retinal abnormality is detected
- visual acuity less than 616 in either eye
- unable to obtain a clear view of the retina
- declining visual acuity is detected at subsequent examinations

Methods of early detection and monitoring include:-

a) Direct Ophthalmoscopy
Direct ophthalmoscopy is the method most commonly advocated for use by general practitioners and physicians. It is the most accessible method of examination by non-ophthalmologists however it is the least sensitive in detecting retinopathy especially if used through an undilated pupil. The sensitivity improves to 60% with the pupils dilated. [52] Repeated examinations will partially compensate for the low sensitivity. [5]

b) Indirect Opthalmoscopy
Indirect ophthalmoscopy has a sensitivity of approximately 85% and is mostly the technique of ophthalmologists. When it is used in conjunction with slit lamp biomicroscopy techniques, the sensitivity of the fundus examination is improved further. The examination is performed through a dilated pupil.

c) Non-Mydriatic Fundus Photography
Non-mydriatic fundus photography of the retina through an undilated pupil. These photographs have a 45' field and a sensitivity of approximately 80% . [54] This sensitivity is improved further if the pupils are dilated. The most appropriate role for a non-mydriatic camera is in a setting where ophthalmic examination is not readily available. The main disadvantage is the number of unreadable photographs particularly in older patients due to small pupils and media opacity such as cataract. The proportion of ungradable photographs is approximately 10%.[56] However these patients may have required an ophthalmic referral for their cataracts or other co-existent ocular problems. In approximately 15% of cases, significant proliferative retinopathy may occur outside the 45º field.[54] These patients are still likely to be referred as there is usually co-existent pathology at the posterior pole within the 45º field.

d) Fundus Photography & Fluorescein Angiography
Colour fundus photography through dilated pupils is recommended in the documentation of retinopathy. Examination of stereo colour photographs, particularly of the seven standard 30º fields, is the most sensitive method of diagnosis of retinopathy. This degree of sensitivity however is not required in early detection programs.

Clinically significant macular oedema (CSME) and proliferative diabetic retinopathy (PDR) can usually be diagnosed clinically.

Fluorescein angiography is not useful in evaluating patients with early non-proliferative diabetic retinopathy (NPDR) and is not useful or appropriate for early detection.

Fluorescein angiography can assist in management of more advanced diabetic retinopathy:-

- to demonstrate macular ischaemia and define the area of macular oedema and capillary bed leak
- to monitor or direct laser treatment both for macular ischaemia or oedema and proliferative retinopathy
- to locate early new vessels not seen ophthalmoscopically, when significant pre-proliferative signs are present

- to assist in the investigation of unexplained visual loss
- to document the extent of significant retinopathy particularly prior to treatment of new patients

2. Treatment Of Vision- Threatening Diabetic Retinopathy

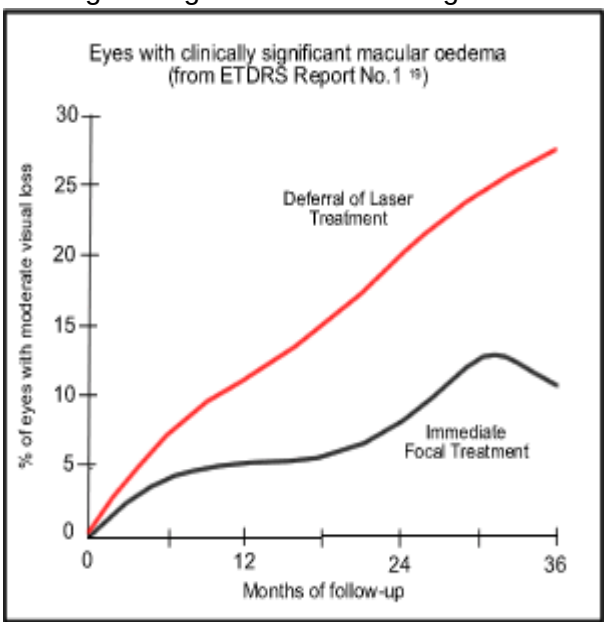
The treatment of vision-threatening retinopathy has been studied in two large, randomised, multicentre trials, the Diabetic Retinopathy Study (DRS) and the Early Treatment Diabetic Retinopathy Study (ETDRS). These studies have provided protocols for management of macular disease and proliferative retinopathy with laser photocoagulation surgery.

a) Treatment Of Macular Oedema (CSME)

Focal and grid laser treatment of clinically significant macular oedema (CSME) reduced the likelihood of moderate visual loss (defined as a double of the visual angle) by 50% or more. Treated eyes were twice as likely to have a visual improvement as untreated eyes. There was no advantage found for treatment of non CSME[9]. The laser treatment of diabetic maculopathy was studied as part of the ETDRS.

i) focal treatment

- laser treatment is directed to microaneurysms or other sources of focal leakage thought to be contributing to macular oedema. [42]



ii) grid treatment

- mild 100 - 200 micron laser burns are placed in a grid pattern across diffusely thickened or oedematous areas of the macula remaining at least 500 microns from the centre of the macula. [42]

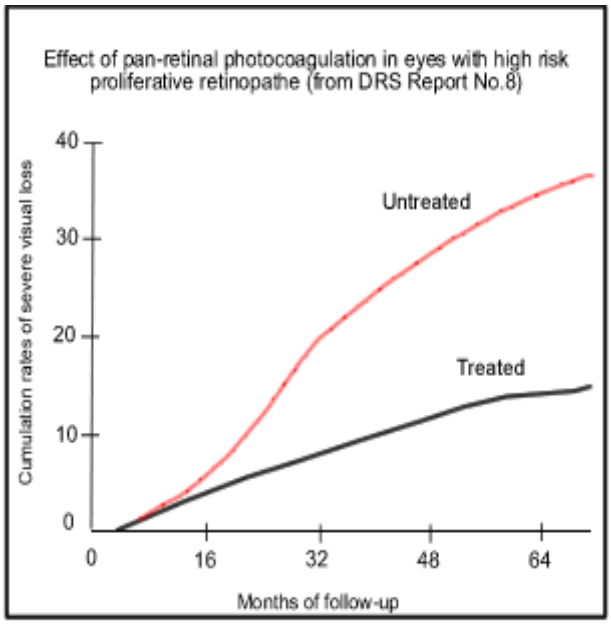
b) Treatment Of Proliferative Retinopathy (PDR)

Pan-retinal (scatter) laser photocoagulation applied to the peripheral retina reduced the risk of severe visual loss by greater than 50%. [41]

Eyes with high-risk proliferative retinopathy are at particularly high risk of severe visual loss if untreated. The high-risk characteristics, as defined by the DRS, are proliferative retinopathy with viticoms/preretinal haemorrhage or disc new vessels greater than one third to one fourth in disc area[8].

Pan-retinal (scatter) laser photocoagulation as used by the DRS consists of 500 micron burns applied across all quadrants of the peripheral retina and remaining outside the temporal vascular arcades. Application of 1200 burns comprises full scatter treatment. Clinical experience indicates that many patients often require more treatment than this to induce regression of new 42 vessels. Treatment is usually better tolerated if applied in several sessions .

By two years of the DRS, 16% of untreated eyes had developed severe visual loss compared to 6.4% in the treated group. (over 6 years, 37% vs. 17%) Over the same period of time, untreated eyes with high-risk characteristics had a 26% risk of severe visual loss and a 11 % risk if treated. [14]



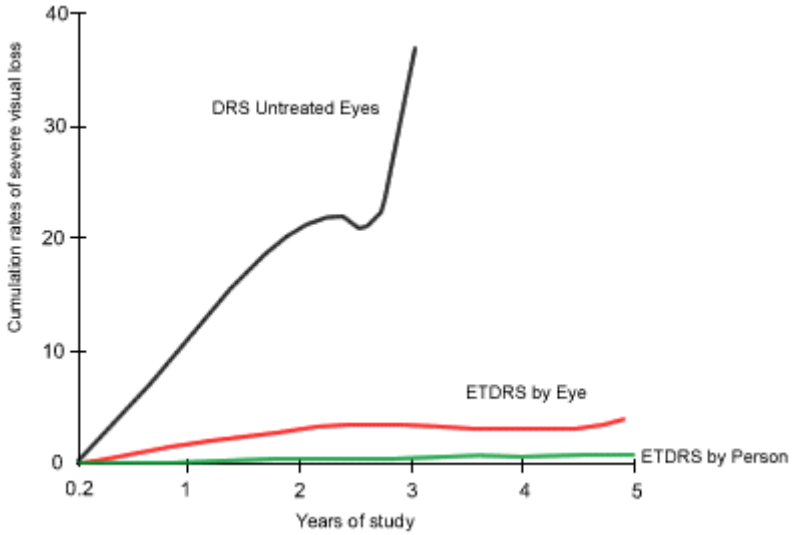
The ETDRS examined whether panretinal treatment was indicated in cases of non-high risk proliferative retinopathy or eyes with severe NPIDR. Risk of visual loss in eyes with non-high risk proliferative retinopathy or severe NPIDR is low whether eyes are treated or untreated (2-year risk for visual loss in PDR eyes without high-risk features was 7% if untreated vs 3% if treated). However eyes with severe NPIDR are at high risk of developing "high risk characteristics" (50% in 12-18 months).[10]

The difference in visual outcome in eyes with PDR is more striking when untreated eyes from the DRS are compared to treated eyes from the ETDRS. Untreated eyes from the DRS have a 30% risk of severe visual loss at three years and a probable risk of 50% at five years. Severe visual loss is reduced

by 95% in treated eyes with PDR from the ETDRS and reduced by 98% in treated patients over the same five year period.[11]

The eyes studied in the DRS may have had more retinopathy at baseline examination than eyes in the ETDRS.

Proportion of untreated eyes with Proliferative Diabetic Retinopathy (PDR) from the Diabetic Retinopathy Study (DRS) developing severe visual loss (VA<5/200) compared with rates in treated eyes and patients with PDR from Early Treatment DR Study (ETDRS)[11].



3. *Recommendations From DRS And ETDRS*

From the DRS and ETDRS studies, several treatment recommendations can now be made:

1 Prompt panretinal laser is recommended in all eyes with PDR with high risk characteristics to prevent severe visual loss.

2. Eyes with less severe PDR or advanced NPDR should either be followed until high risk characteristics occur or should be considered for panretinal laser treatment if adequate follow-up examinations are not possible or not likely.

3. Focal photocoagulation should be considered for eyes with clinically significant macular oedema (CSME). This does not mean that all such eyes need to be treated. If the centre of the macula is not involved, it may be appropriate to defer treatment and follow the patient closely, particularly if the principal leaking areas are.near the centre of macula where treatment carries a somewhat greater risk. Visual acuity is not relevant when deciding whether CSME is present or not.

4. Pan-retinal treatment is not indicated in eyes with mild or moderate NPDR.
5. In cases with both CSME and PDR, treatment should first be directed at controlling the macular oedema then followed by pan-retinal laser for the proliferative changes. Pan-retina] laser may exacerbate pre-existing maculopathy. The delay between the macular and panretinal treatment should be influenced by the severity of the proliferative disease. If advanced PDR is present, there should be only a minimum delay.

In all studies, there is agreement that treatment is most effective in subjects before significant visual loss occurs. Treatment of maculopathy does not, as a rule, lead to recovery of visual acuity if it is already impaired, however stability of residual vision is the desired aim of treatment. Laser treatment is not indicated for macular ischaemia, although if focal capillary leak is present, this can be treated according to protocols from the ETDTRS. Adequate treatment may take several months to cause recompensation of the retinal vasculature and visual acuity may continue to deteriorate during that time. It needs to be stressed that some diabetic patients may still go blind despite laser treatment especially if treatment is not initiated early enough. Complications of panretinal laser may occur and include a mild reduction in peripheral visual field and night vision, an early onset of presbyopia and a worsening of maculopathy which is usually temporary.

4. *The Role Of Vitrectomy (From The Diabetic Retinopathy Vitrectomy Study (DRVS))*

Vitrectomy is an intraocular microsurgical procedure designed to remove the vitreous and allow access to the retina. It has been shown to be of benefit for:

1 . Non-clearing vitreous haemorrhage

2. Recent macular traction retina] detachment

3. Eyes with florid retina] neovascularisation where laser has failed to produce regression or where persistent vitreous haemorrhage has prevented adequate laser treatment.

The Diabetic Retinopathy Vitrectomy Study (DRVS) was established to investigate the role of early vitrectomy versus conventional treatment in eyes with severe proliferative retinopathy.

Conventional treatment consisted of follow-up without vitrectomy unless retinal detachment occurred involving the macula, or vitreous or preretinal haemorrhage did not clear after twelve months.

Early intervention was defined as vitrectomy performed between one and six months duration of vitreous haemorrhage. A clear benefit was found for eyes that had early vitrectomy with severe vitreous haemorrhage in IDDM patients. [44,45] Early vitrectomy in severe PDR with good vision was found to be useful, with the advantage increasing with more severe new vessels. [46] The incidence of complication is slightly higher in the early intervention group. [46]

The application of laser may be limited by pre-retinal or vitreous haemorrhage, however as much panretinal laser as possible should be applied before surgery.

In both conventional and early treatment groups, the outcome was improved if panretinal photocoagulation had been performed prior to surgery. [46]

5. *Cost-Benefit Of Early Detection And Treatment Of Diabetic Retinopathy*

Recent studies in the USA have examined the economic benefit of detection and appropriate treatment of retinopathy in IDDM and NIDDM .[58, 59] Treatment recommendations and treatment efficacy data were taken from the DRS and ETDRS studies. In both IDDM and NIDDM a clear cost benefit was demonstrated by comparing estimated cost of treatment with cost of social security disability payments to the visually disabled.

Australian parameters are currently being applied to similar study of cost - effectiveness. It is likely that, using similar strategies of early detection, monitoring and treatment, the same cost benefits exist.

CURRENT RECOMMENDATIONS FOR THE DETECTION AND MONITORING OF DIABETIC RETINOPATHY

For retinal examination, pupil dilation and an adequate magnified view of the fundus is essential using either detailed direct ophthalmoscopy, indirect ophthalmoscopy, slit-lamp biomicroscopy of fundus camera. For epidemiological purposes or early detection programs, fundus photography using a non-mydriatic camera is acceptable.

For insulin-dependent diabetic patients diagnosed before age 30, the first retinal examination should occur no later than after 5 years diabetes duration or at 30 years of age.

There is no risk of developing retinopathy prior to puberty and only minimal risk up to 5 years after diagnosis of diabetes.

In patients diagnosed at or after age 30, the first retinal examination should be made at the time of diagnosis to detect those patients who already have significant retinopathy.

In both groups subsequent examination is recommended at least every 2 years if no retinopathy is found.

Once any retinopathy lesions are detected, then referral to an ophthalmologist is indicated and the eyes should be reviewed every 12 months or more frequently if the retinopathy demonstrates more than mild changes or any threat to macular function.

Where possible, patients should be encouraged to improve blood glucose control to reduce the risk of retinopathy developing and progressing.

As retinopathy may progress during pregnancy, all women with diabetes be examined prior to commencing a pregnancy and re-examined at three monthly intervals during the pregnancy particularly if retinopathy is detected at the preliminary examination.

Patients should be advised to seek an ophthalmic review if they report any decrease in vision.

High risk groups (patients with nephropathy or prolonged poor diabetic control) may need closer follow up.

With these measures, we could expect to prevent or reduce a large proportion of the visual loss and blindness from diabetic retinopathy in Australia.

APPENDIX A

PATHOPHYSIOLOGY

Two basic pathophysiologic mechanisms underlie the clinical manifestations of retinopathy - increased capillary permeability and closure of retina[capillaries. These changes produce vascular leakage - causing retina] oedema and the accumulation of lipid seen as hard exudate in the retina -and retinal ischaemia.

Microscopic changes include thickening of the capillary basement membrane, loss of capillary intramural pericytes, capillary microaneurysms, capillary acellularity and breakdown of the blood-retinal barrier at the level of the capillary endothelial cells and/or the retinal pigment epithelium.

APPENDIX B

GLOSSARY

These terms, used to describe the features of the various stages of retinopathy, were developed to produce a consistent language for diabetic retinopathy. They are based on a system of photographic grading which requires comparison with a standard set of photographs showing different features and stages of retinopathy. The terminology is employed in the trials that define the current management of vision-threatening retinopathy, the DRS and the ETDRS.

"Background" retinopathy is now referred to as "mild to moderate nonproliferative" retinopathy. "Pre-proliferative" retinopathy is now termed “severe non-proliferative" retinopathy.

Microaneurysms
- are saccular or fusiform dilatations in the retinal capillary wall. They are red dots up to 75-100 microns in size and may thrombose and regress with time. They may be a site of vascular leakage.

Intraretinal Haemorrhages
-are found at the sites of capillary wall rupture. Dot and blot-shaped haemorrhages are found in the deeper layers of the retina. Linear or flame shaped haemorrhages are found in the more superficial nerve fibre layer..

Hard Exudates
-are well-defined yellowish deposits found in the retina. They consist of lipoproteins that have leaked from abnormally permeable microaneurysms or capillaries. They may be single or multiple or in a circinate (ring-like) pattern. The lipoproteins tend to aggregate at the margin between oedematous and non-oedematous retina. They are commonly found in the macular area and, if they are deposited centrally at the fovea, they may cause dramatic reduction of vision.

Retinal Oedema
- appears when abnormally permeable capillaries and microaneurysms allow oedema fluid to escape into retinal tissue.

Macular Oedema
- is defined as retina[oedema located within two disc diameters of the centre of the macula.

Clinically Significant Macular Oedema (CSME)
- is defined as thickening and oedema of the retina at or within 500 microns of the centre of the macula and/or hard exudate at or within 500 microns of the centre of the macula if associated with oedema of the adjacent retina. Also included in the definition is retinal thickening or oedema one disc diameter or larger in size, any part of which is within a disc diameter of the centre of the macula - (defined as retinal thickening or oedema that involves or threatens the centre of the macula even if visual acuity is not yet reduced).

Macular oedema is the most frequent cause of visual impairment in patients with diabetic retinopathy. In the long-term it may cause cystoid or permanent retinal pigmentary degenerative changes at the macula.

Cotton-Wool Spots
(nerve fibre layer infarcts - previously termed soft exudates) - are white superficial retinal lesions with ill-defined edges. Infarction is produced by capillary closure in the nerve fibre layer. Isolated cotton-wool spots, with only minimal retinopathy elsewhere, may be consistent with mild to moderate NPDR.

Retinal Haemorrhages
-large and blot-shaped, are typically found in advanced non-proliferative retinopathy, especially temporal to the macula.

Venous Beading
-describes irregular calibre changes in the veins. It is a non-specific sign of retinal ischaemia. Other venous changes seen at this stage include tortuosity, venous loops and generalised dilatation of venules.

Intraretinal Microvascular Abnormalities (IRMA)
- are enlarged hypercellular capillaries that function as shunt vessels around or adjacent to areas of capillary occlusion. They may be similar in appearance to new vessels but display only mild fluorescein leakage on angiography and occur within the retina only.

New Vessels
-are new abnormal vessels that arise from the retina[surface (not intraretinal). They may extend along the retinal surface or into the vitreous cavity. If new vessels appear on or within one disc diameter of the disc margin, they are known as new vessels on the disc (NVD). In any other location on the retina they are referred to as new vessels elsewhere (NVE).

Fibrous Glial Proliferation
- growth of new vessels is accompanied by a proliferation of fibrous tissue between the posterior vitreous surface and the internal limiting membrane. This tissue is derived from retinal glial cells and fibrocytes. Contraction of the vitreous can produce traction retinal detachment via these fibrous connections between the retina and vitreous.

APPENDIX C

CLASSIFICATION OF DIABETIC RETINOPATHY
(from American Academy of Ophthalmology - Focal Points: Diabetic Retinopathy.)

This classification is derived from the ETDIRS and defines retinopathy as nonproliferative (NPDR) or proliferative (PDR). Macular oedema can be present at any level of retinopathy.

Minimal NPDR
- microaneurysms only

Mild NPDR
- microaneurysms with one or more of the following:-
    - retina] haemorrhage
    - hard exudate
    - nerve fibre layer infarct

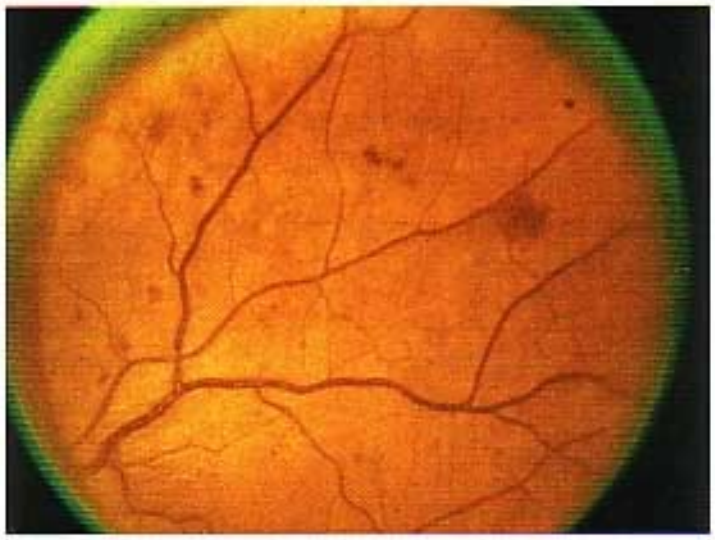
    but does not meet definition for moderate NPDR

Moderate NPDR

-haemorrhages and microaneurysms > standard photograph 2A in at least one quadrant and one or more of the following:-

- nerve fibre layer infarct
- venous beading
- IRMA

But does not meet definition for severe NPDR



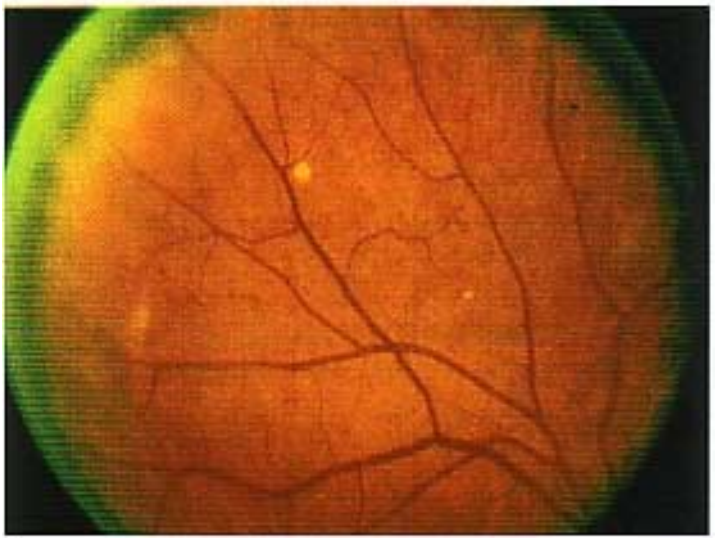
ETDRS Standard Photograph 2A

Severe NPDR

- one of the following:-

- haemorrhages and microaneurysms > standard photograph 2A in all four quadrants
- IRMA > standard photograph 8A in at least one quadrant
- Venous beading in at least two quadrants

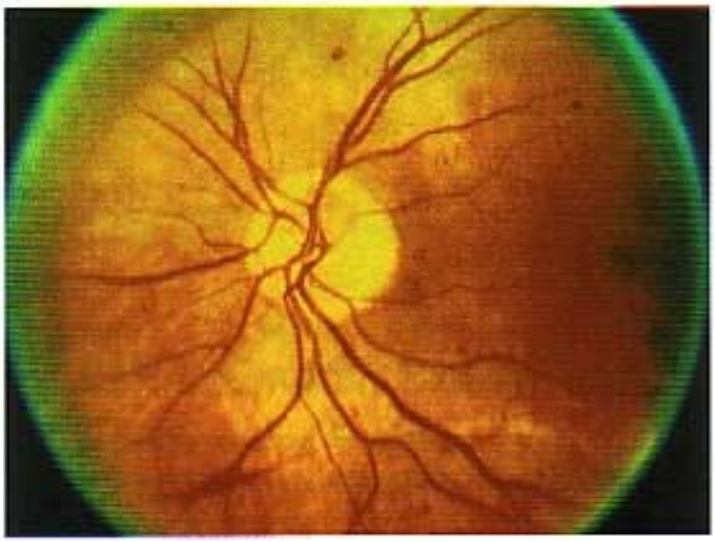
- from severe NPDR 50% of patients will progress to PDR in one year and 17% will progress to high-risk PDR.



ETDRS Standard Photograph 8A

PDR
-one or more of the following:-

- NVE
- NVD < standard photograph 10A
- NVE < fi disc area without NVD or vitreous/preretinal haemorrhage



ETDRS Standard Photograph 10A

High Risk PDR
-one or more of the following:-

- NVD >/- 1 third disc area
- NVD with vitreous or preretinal haemorrhage
- NVE > fi disc area with vitreous or preretinal haemorrhage

-severe visual loss (VA <5/200) develops in 25% - 40% within two years if untreated.

Advanced PDR
- high risk PDR with tractional detachment involving macula or vitreous haemorrhage obscuring ability to grade NVD and NVE.

APPENDIX D

ILLUSTRATED STAGES OF DIABETIC RETINOPATHY

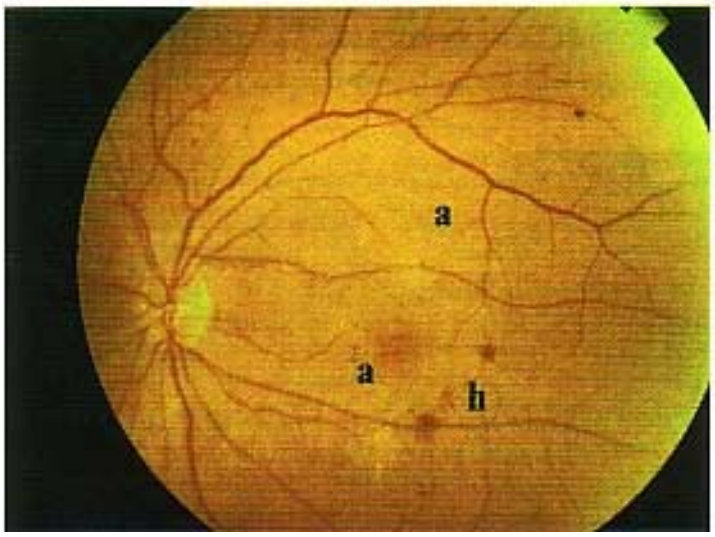


Figure 1. Mild non-proliferative diabetic retinopathy with a few scattered microaneurysms (a) and dot haemorrhages (h).

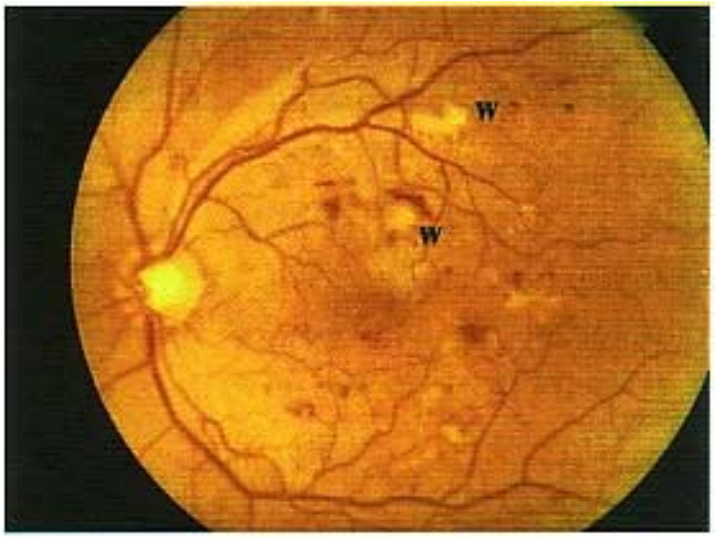


Figure 2. Mild non-proliferative diabetic retinopathy with cotton-wool spots (w), more retinal haemorrhages and microaneurysms.

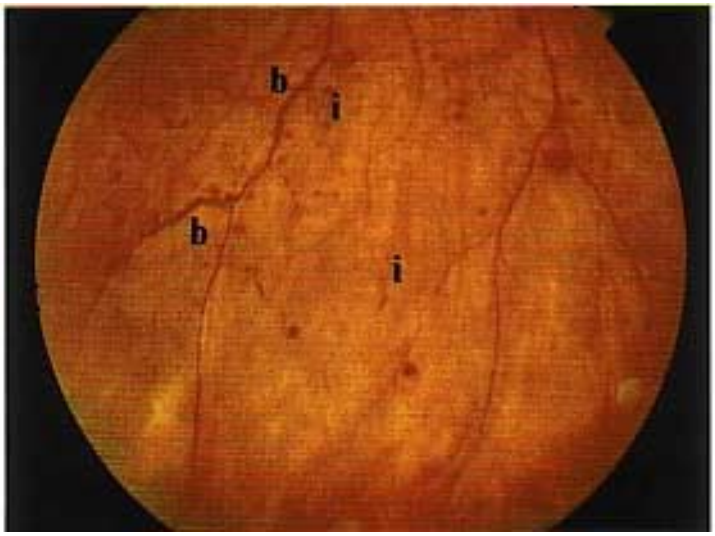


Figure 3. Severe non-proliferative diabetic retinopathy
Displaying venous beading (b), intraretinal
Microvascular abnormalities or IRMA (i) and
multiple retinal haemorrhages.

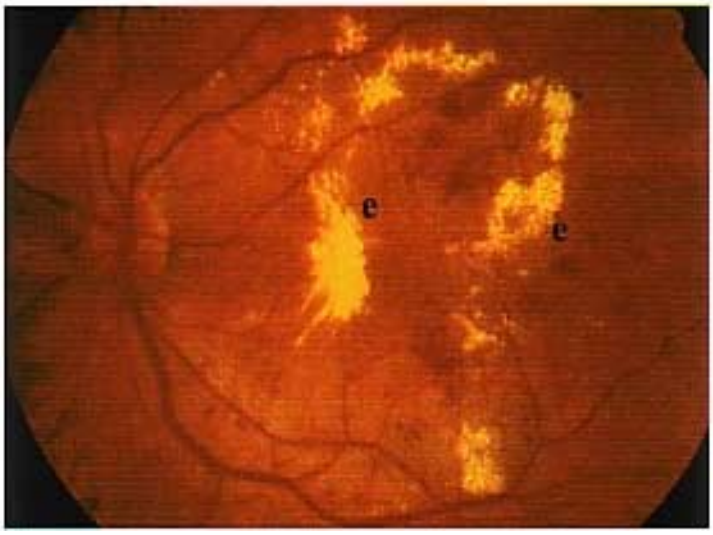


Figure 4. Clinically significant mascular oedema with a localised area of retinal thickening surrounded by lipid exudate (e) extending to the macula.

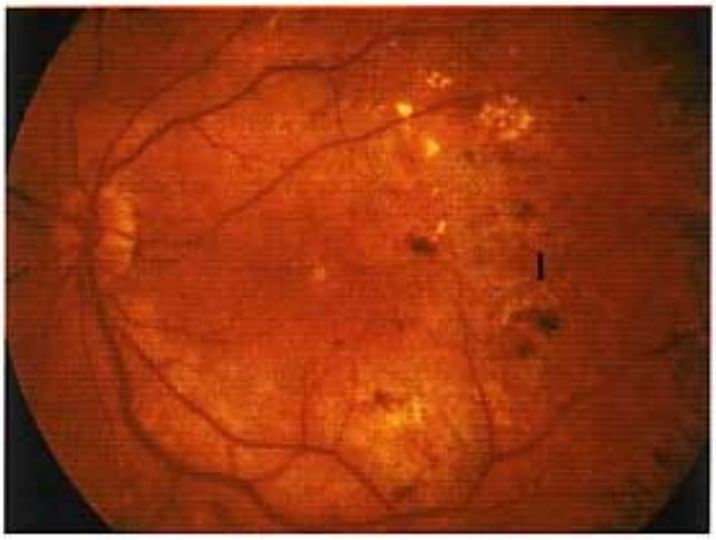


Figure 5. Clinically significant mascular oedema post focal laser treatment. The lipid exudate has resolved. Laser scars (1) are visible temporal to the macula.

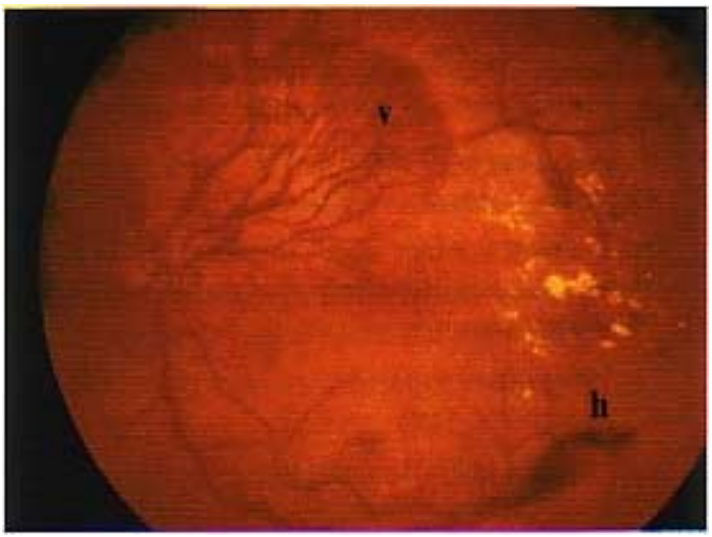


Figure 6. Proliferative diabetic retinopathy with a large Frond of a new vessel s (v) extending from the disc and a small amount of preretinal haemorrhage (h).

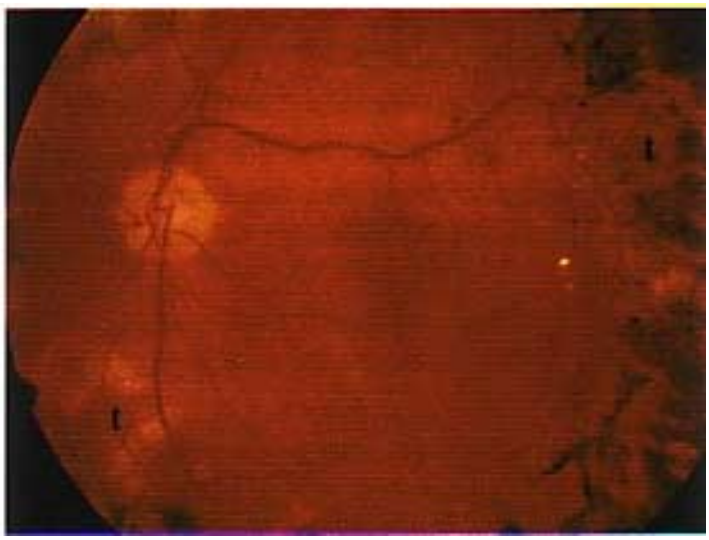


Figure 7. Resolution of new vessels after pan-retinal laser treatement.

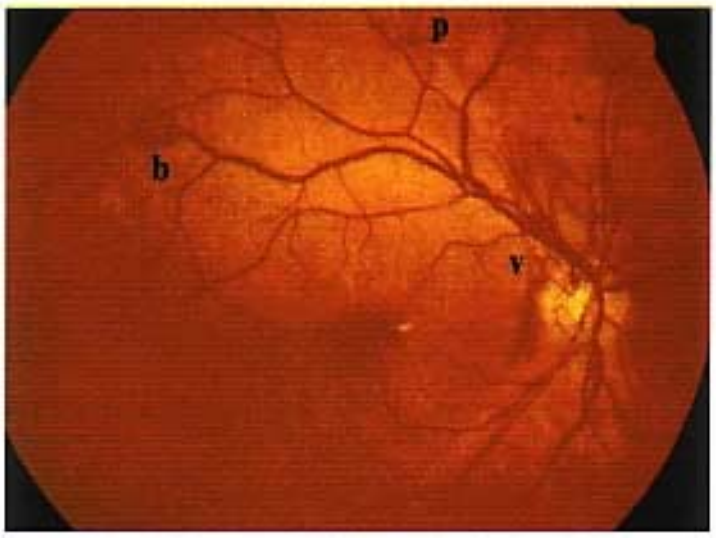


Figure 8. PDR with disc new vessels (v), peripheral new vessels (p) and venous beading (b).

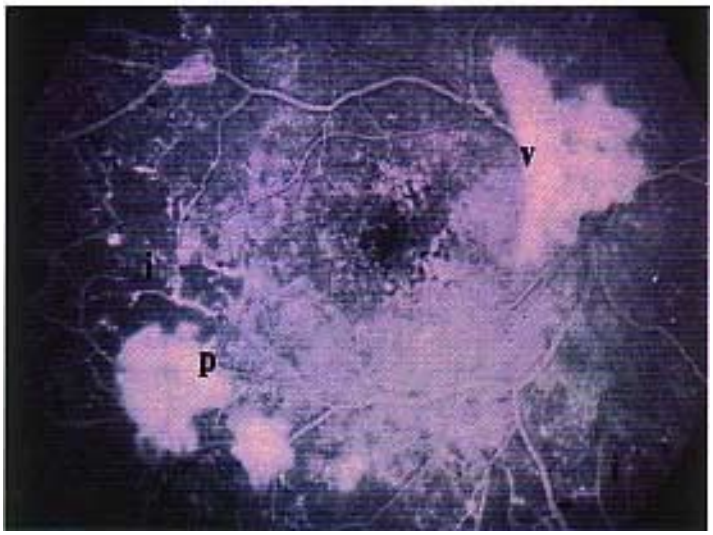


Figure 9. Fluorescein angiogram of Fig. 8 displays disc new vessels (v) with fluorescein lead at disc and peripheral new vessels (p). There is marked capillary closure and retinal ischaemia in the temporal and inferior retina (i).

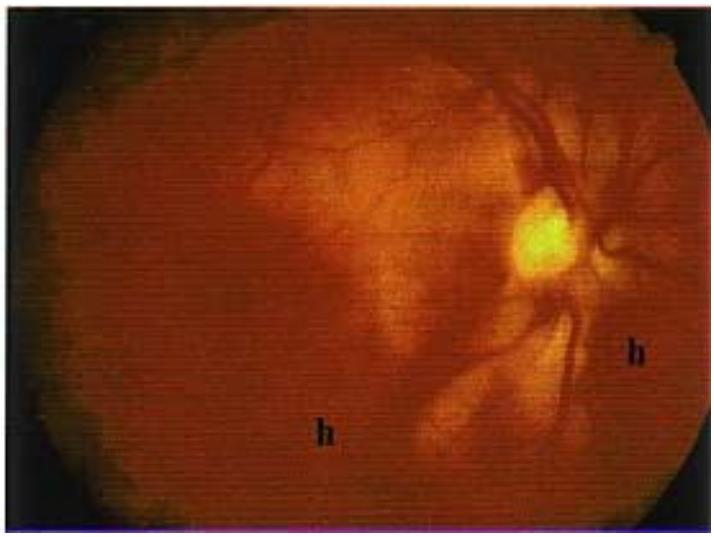


Figure 10. Advanced proliferative diabetic retinopathy with vitreous haemorrhage (h) obscuring fundus detail.

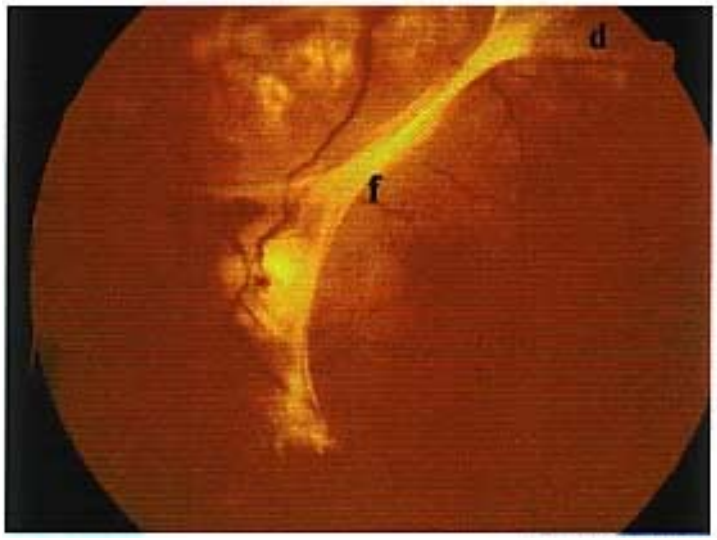


Figure 11. Advanced proliferative diabetic retinopathy with vitreous haemorrhage obscuring fundus detail and a preretinal fibrous brand (f) producing localised traction detachment (d).

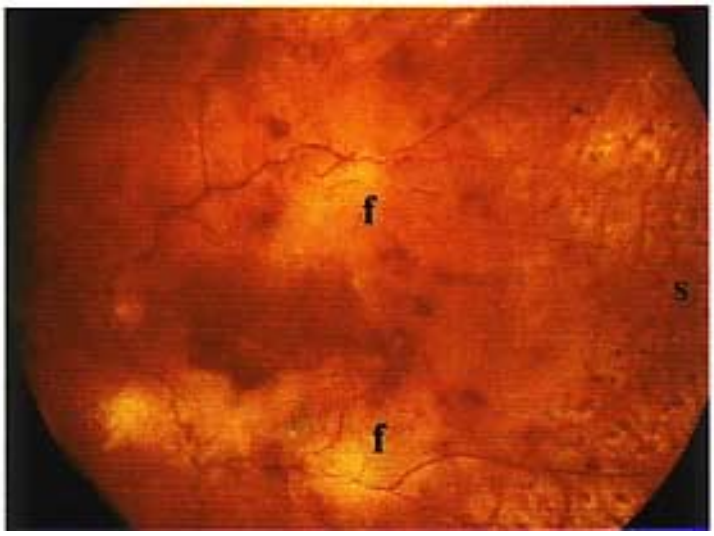


Figure 12. Advanced proliferative diabetic retinopathy with multiple areas of preretinal fibrosis (f) producing traction on the underlying retina. Pan-retinal photocoagulation scars (s) are seen temporally.

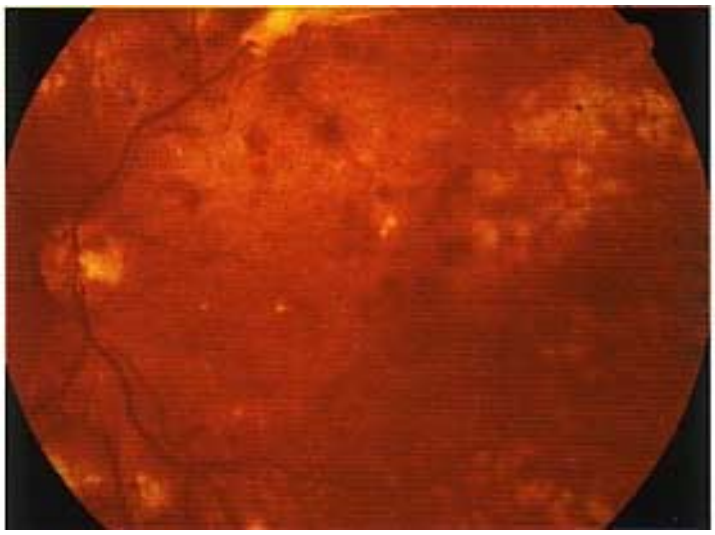


Figure 13. Figure 12 after vitrectomy with removal of preretinal fibrosis.

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