
DIABETIC RETINOPATHY

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angiography, microaneurysms frequently leak dye, implying a focal breakdown in the blood-retinal barrier.

Capillary occlusion is another hallmark of diabetic retinopathy. These include the hemorrhological abnormalities commonly found in diabetic persons, such as increased fibrinogen concentration, increased platelet adhesion and aggregation increased erythrocyte aggregation, increased whole blood viscosity, and possible abnormalities in leukocyte-capillary endothelial cell interactions. When a focal area of capillaries loses perfusion, the overlying retina suffers acute ischemic changes. The ophthalmoscopically visible signs of these occlusions are cotton wool spots, which are caused by the accumulation of axoplasmic debris in the nerve fiber layer of the ischemic retina. Microvascular dilatation is often found near areas of capillary obliteration and is called intraretinal microvascular abnormality (IRMA).

Mild-to-Moderate Nonproliferative Diabetic Retinopathy.

An early sign is the microaneurysm, which appears to derive from focal capillary endothelial proliferation.

Intraretinal hemorrhages are a result of rupture of microaneurysms, capillaries, or venules. The location of the hemorrhage reflects the shape of the hemorrhage; for instance, hemorrhages residing in the nerve fiber layer have a feathery, flame-shaped appearance, whereas hemorrhages deep in the retina such as the outer plexiform layer will have a fuzzy, bolt-shaped appearance.

Hard exudates glisten and can appear in streaks, clusters, or circinate rings surrounding a group of microaneurysms. The exudate is made up of lipoproteins that leak through the abnormally hyperpermeable capillary walls. They have a particular predilection to congregate in the macula where they are often associated with retinal thickening.

Macular edema may be a result of abnormal permeability of the retinal vascular endothelial cells of capillaries, microaneurysms and IRMA. Macular

It will not surprise to know that we have the largest number of diabetics in the world; this is just one more of our dubious disease distinctions. More alarming, the majority of those affected are not even aware they have the killer disease. Twenty-five million Indians are diabetic, with the maximum number in the age group 20-40. Indians are genetically more prone to the condition, perhaps owing to a syndrome that makes them vulnerable to risk factors like hypertension, insulin resistance and abdominal obesity. Most Indians also suffer from impaired glucose tolerance which means that they contract diabetes at an early age. A dangerous recent trend is the spread of the disease among urban children.

As a people, we tend to be careless about what we eat; in fact, prosperity in India is equated with an unhealthy fatty diet and sedentary lifestyle.

The importance of recognizing the clinical features of diabetic retinopathy lies in the epidemiology of the disease. It is estimated that 12 million Americans have diabetes today. Diabetic retinopathy is the leading cause of blindness in working Americans aged 20 to 74 years, constituting up to 12% of new cases of blindness in the United States each year. It is necessary to recognize the features of diabetic retinopathy, the indications for treatment, and the recommendations for follow-up.

Clinical Features

Nonproliferative Diabetic Retinopathy.

The retinal findings that occur in diabetic retinopathy are a consequence of retinal microangiopathy. The two main results of the microangiopathic abnormalities are increased vascular permeability resulting in macular edema and vascular occlusive changes resulting in fibrovascular proliferation, hemorrhage, and scarring. The goal of our management is to identify the features of retinopathy that are associated with progression and to interrupt with appropriate treatment its natural progression to the scarring phase.

Focal proliferations of capillary endothelial cells occur and are known as microaneurysms. During fluorescein

pulling on the friable new vessels. Contraction of the neovascular tissue along the detaching posterior hyaloid may be seen to exert additional traction along the points adherent to the retina and create tractional detachment of the retina. The majority of detachment will remain extramacular. Progressive macular detachment will occur in up to 14% in 1 year and up to 23% in 3 years.

Blood can also break through the posterior hyaloid into the vitreous cavity, with a subsequent vitreous hemorrhage.

The natural course of this tangle of new vessels, hemorrhage and traction is fibrosis and eventual replacement by a vascular scar tissue, referred to as involutional, end-stage, or burnt out retinopathy.

Review of National Diabetic Studies.

The DRS was a multicenter national prospective clinical trial designed to evaluate whether photocoagulation could prevent the development of severe visual loss in eyes with proliferative retinopathy.

The DRS identified four retinopathy risk or new vessel vitreous hemorrhage risk factors. These were (1) the presence of new vessels; (2) the location of new vessels on or within one disk diameter of the optic disk (NVD) (3) the severity of new vessels defined for NVD as greater than one fourth to one third disk area in extent; and for NVE equal to or greater than one half disk area; and (4) presence of vitreous or preretinal hemorrhage.

The DRS recommended that all eyes with three or four retinopathy risk factors were at the highest risk for the development of severe visual loss and should be treated with photocoagulation promptly.

ETDRS recommended grading retinopathy by looking for the following features (1) four quadrants of severe microaneurysms or intraretinal hemorrhages; (2) two quadrants of venous beading; or (3) one quadrant of a least moderately severe IRMA. Very severe retinopathy consists of eyes with at least two of the above three characteristics; these eyes were found to be at significantly greater risk for developing proliferative disease in 1 year, even higher than those eyes with early proliferative disease. Severe retinopathy consists of eyes with at least one of these characteristics. This grading system has been called the 4-2-1 rule since over 50% of eyes with certain

edema is described in two distinct forms, either focal or diffuse. The diagnosis of macular edema is made on the clinical finding of retinal thickening on slitlamp biomicroscopy.

Moderate - to - Severe Nonproliferative Diabetic Retinopathy.

As the retina becomes more severely damaged by increasing vascular occlusion and abnormal permeability, retinopathy worsens and can be further subdivided into moderate - to - severe, and very severe nonproliferative diabetic retinopathy.

Venous beading represents focal areas of venous dilation and thinning of the venous walls. Venous beading is most easily seen as alterations in the vascular caliber of the veins of the vascular arcades. There may also be looping or reduplication of venous segments, in addition to venous sheathing and focal narrowing. These changes are all related to progressive capillary nonperfusion and retinal ischemia and are also markers of an increased risk of progressing to proliferative disease. The ETDRS found that the presence of severe intraretinal hemorrhages venous beading, and IRMA were much more statistically predictive of developing proliferative disease. Venous beading was found to be the most powerful single predictor for the development of proliferative disease when compared with all of the other individual factors.

Proliferative Diabetic Retinopathy.

Proliferative diabetic retinopathy is characterized by neovascularization, new blood vessels that arise from the retinal and optic disk vessels and proliferate along the retinal surface or into the vitreous with or without a fibrous component. Neovascularization of the disk (NVD) appears as fine wisps or loops of blood vessels seeming to bud off other disk vessels. All other neovascularization is referred to as neovascularization elsewhere (NVE).

Neovascularization elsewhere is seen as a fine network of vessels appearing like cartwheels or lace, usually arising from the retinal veins, venules, or capillaries and bridging between the arterial and venous circulations.

Neovascular vessels are often adherent to the posterior hyaloid. Vitreous and preretinal hemorrhages will occur as a patient undergoes a vitreoretinal separation

For eyes with severe, very severe nonproliferative and early proliferative retinopathy, early photocoagulation should be considered.

Color fundus photography is useful in cases of eyes with greater than moderate nonproliferative disease as these may be used to document or confirm progression of the retinopathy. Certain circumstances, however warrant early treatment. The monocular patient, the pregnant patient the patient with impending cataract surgery or impending yttriumaluminum garnet capsulotomy and the patient with imminent renal failure should all be considered for early photo coagulation rather than for follow-up. Each of these situations has been associated with an accelerated progression or retinopathy.

Management of Diabetic Macular Edema

Macular edema can accompany any stage of retinopathy and has been found to be directly correlated to the duration and severity of retinopathy.

Once the decision has been made to offer treatment, a fluorescein angiogram is obtained in an effort to delineate the macular perfusion and guide the treatment pattern planned. In clinical practice it is sometimes acceptable to follow a 20/20 eye. The treatment itself depends on the type of leakage found on the angiogram, often a combination of both focal and diffuse fluorescein leakage.

Wavelengths consistent with argon green or krypton red are generally used in macular treatments. Focal treatment is applied to individual leaking microaneurysms as delineated on the angiogram. Fifty to 100 μ spot sized burns are used at 0.1 seconds duration with the minimum power needed to achieve a light white burns; in general treatment should start at 100 mw of power with gradual increments should start of 10 to 20 mw to reach this goal.

All lesions that are located at least 500 from the center of the fovea should be treated. Gird treatment is applied to areas of diffuse leakage or segments of parafoveal capillary nonperfusion as seen on the fluorescein angiogram.

Areas of diffuse leakage are treated with light gird treatment almost upto the edge but not within the foveal avascular zone. Discrete focal points of leakage outside the areas of diffuse leakage are treated with light gird treatment almost up to the edge but not

characteristics of 4-2-1 rule, namely those eyes than 50% chance of developing highrisk disease, these eyes need particularly close attention with frequent serial dilated examinations, if not early treatment.

The ETDRS states that eyes with less than high-risk proliferative disease and those with greater than severe nonproliferative disease can be considered for early photocoagulation, although it is not necessarily recommended, given the known side effects of peripheral visual field constriction and subtle color vision changes. If both eyes are approaching the high-risk stage, a prudent approach would be to initiate early treatment in at least one eye. If high-risk retinopathy is seen immediate panretinal photocoagulation is recommended.

The initial reports of the ETDRS studied the role of photocoagulation in the treatment of diabetic macular edema. The ETDRS found that macular laser photocoagulation substantially reduced the risk of moderate visual loss in treated patients when compared with untreated control subjects .

The results of the ETDRS shows that focal photocoagulation reduced the risk of moderate visual loss by 50% in eyes with clinically significant diabetic macular edema. This beneficial effect was seen in all eyes regardless of initial entry visual acuity; alongwith visual loss in the study was significantly reduced by treatment, cisual gain was minimal.

The ETDRS found that there is no ophthalmic contraindication to the use of aspirin when needed for cardiovascular or other medical reasons, even in patients with high-risk retinopathy.

Management of Nonproliferatives Diabetic Retionopathy

The American Academy of ophthalmology recommended that patients with juvenile onset diabetic be first examined at 5 years after diagnosis since retinopathy is rarely found before 5 years in this group. Patients with adult-onset diabetes are recommended to be examined at the time of diagnosis since significant retinopathy may be present at the time of initial diagnosis. Patients with minimal to no retinopathy should be examined annually.

Eyes with mild-to-moderate retinopathy without macular edema should be evaluated at 6 to 12 month intervals.

increased gradually to achieve an endpoint of a white burn.

In general panretinal treatment is given in divided sessions at 10 day to 5 week intervals. 800 to 1000 burns are placed in the inferior half of the retina followed by a second session to complete the superior half with another 800 to 1000 laser burns. This allows for treatment to have been performed in the inferior quadrants if the eye undergoes vitreous or preretinal hemorrhage between sessions, which will usually settle to the inferior periphery precluding treatment of that inferior retina covered by blood. Local treatment of flat surface NVE can be performed with confluent overlapping 500 burns if located in the peripheral retina. NVE that is elevated or located within the posterior pole should not be treated in this fashion and NVD is never treated directly with laser photocoagulation.

Postoperatively, patients are given a mild oral nonprescriptive agent such as acetaminophen. Patients are told that there should be minimal discomfort following the treatment session and instructed to return immediately if severe pain occurs. The first follow-up visit is scheduled for 4 to 8 weeks following the completion of the panretinal treatment.

Complete scatter panretinal treatment is usually considered to be from 1500 to 2000 burns. If very advanced proliferative disease is being treated an initial plan of three sessions is reasonable for an anticipated treatment plan of 2000 to 3000 burns. Treatment at any given sitting of more than 1000 burns is not recommended since it appears that greater numbers of burns delivered at a single session are associated with a higher risk for the iatrogenic development of choroidal effusion, exudative retinal detachment and angle closure.

As long as there has been a response to treatment, small wisps of neovascularization that appear to be residual new vessels can generally be followed. Supplemental treatment is also indicated if a patient has shown good regression of disease and, in the course of follow-up shows new neovascularization.

Skipped areas and spaces between the previously placed burns are treated.

If the patient has already received several thousand burns and appears to have floridly advancing proliferative disease early vitrectomy may be indicated.

within the foveal avascular zone. Discrete focal points of leakage outside the areas of diffuse leakage are treated with focal laser burns at the same session. Supplemental treatment is performed at 3 to 4 months after the initial treatment if residual central thickening involving the foveal avascular zone is noted on follow-up clinical examination.

Patients should be followed at 3-4 month intervals and receive supplemental treatment until the central retinal thickening resolves.

Patients with large irregular foveal avascular zones signaling a high degree of macular ischemia may not benefit, and actually may be harmed by macular laser these advanced cases are often followed without treatment for their macular edema. The patient should be told that the laser treatment will be done in stages, and that future touch-ups will be necessary.

The most important adverse effects of macular laser treatment are inadvertent foveal burn and secondary choroidal neovascularization.

Management of Proliferative Retinopathy

As stated by the DRS, all patients with high risk proliferative disease or three of the retinopathy risks factors as described in prior section should be offered prompt photocoagulation. Patients who have rubeotic vessels should be evaluated for immediate panretinal photocoagulation.

The prevalence of proliferative diabetic retinopathy is directly related to the duration of the disease with 0% seen in patients with younger onset insulin dependent diabetes of under 5 years duration, to 4% in patients with 10 years of diabetes to 26% in patients with 15 years of diabetes and 56% in patients with diabetes of 20 years or more.

Treatment Guidelines

Panretinal photocoagulation is performed with either argon green or krypton red wavelengths. Quadraspheric lens is applied to the eye with a coupling solution such as methylcellulose. With these lenses the treating ophthalmologist must remember that the view is inverted and reversed.

A spot size is chosen to, deliver a laser burn of approximately 500 μ m. on the retina. A duration of 0.1 to 0.2 seconds is set on the laser. Typically, a low power of approximately 200 mw is set initially and

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Vitrectomy removes the scaffolding for a neovascular growth and also removes possible stimuli for new vessel growth such as disintegrating blood products.

Vitrectomy is also indicated for tractional detachments involving the macula. Extramacular detachment, as stated earlier can be followed with frequent serial dilated examinations, if the tractional detachment progresses, causes significant visual distortion or threatens to involve the fovea, vitrectomy may be indicated.

An uncommon and unfortunate complication of panretinal photocoagulation, particularly in a patient with vitreous hemorrhage and preexisting fibrosis, is the acceleration or production of a tractional detachment by the laser treatment. Some of these patients are considered for early vitrectomy. In most cases it is preferable to attempt panretinal photocoagulation, because the more laser patient has previtrectomy, the better he or she usually does after vitrectomy.

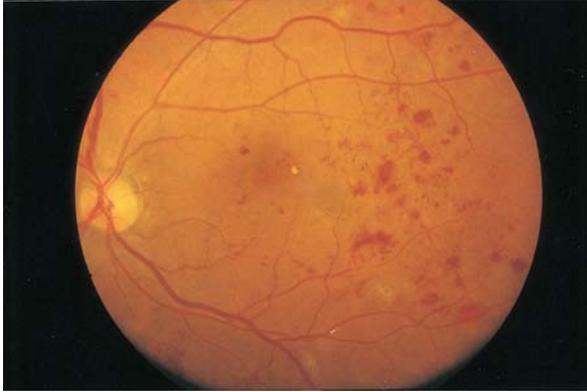
Systemic Considerations

The diabetes Control and Complication Trial found that the development of retinopathy and the progression of retinopathy already present were significantly reduced in patients with insulin dependent juvenile onset diabetes who maintained tight control of their blood sugar levels with intensive frequent treatment, in comparison with those who underwent conventional once or twice-daily insulin injections. Control of hypertension and cessation of smoking may help prevent ocular and systemic complications of diabetes. Close integration of the ophthalmologist in the central care of the diabetic patient is necessary to optimize treatment.

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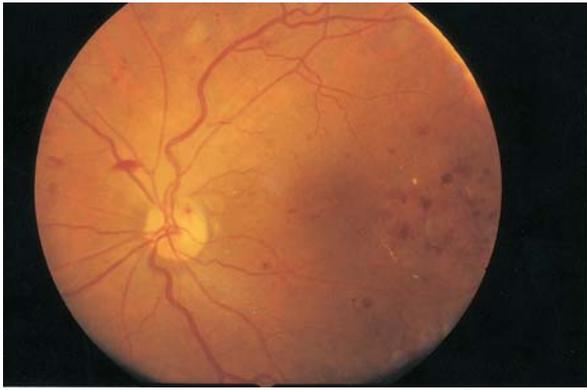
Diabetic Retinopathy



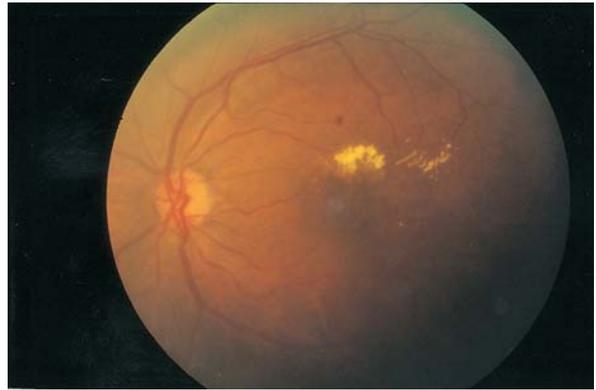
Severe Non Proliferative Diabetic Retinopathy



Mild Non Proliferative Diabetic Retinopathy with Maculopathy



Moderate Non Proliferative Diabetic Retinopathy with Maculopathy



Diabetic Macular Edema with Hard exudates



Macular Edema