

# Ocular Manifestations of Systemic Disease

## **Diabetes Mellitus**

The factors thought to be important in the development of diabetic retinopathy include:

- duration of time that the patient has had diabetes
- diabetic control
- coexisting disease particularly hypertension
- smoking

The longer a patient has had diabetes, the greater the likelihood of developing retinopathy. Approximately 5 years after diagnosis, 23% of patients with Type I diabetes have retinopathy, and after 15 years, 80% have retinopathy. Type II diabetics have a similar but slightly lower incidence of retinopathy. Retinopathy is a leading cause of new blindness in those aged 20-74.

Blindness is defined as visual acuity  $< 20/200$  or field of vision  $< 20^\circ$

## **Stages of Diabetic Retinopathy**

### **No Retinopathy**

There are no abnormal signs present on the retina. Vision is normal

### **Background Retinopathy**

Signs of microvascular leakage (hemorrhage and exudates) away from the macula. Vision is normal

### **Maculopathy**

Exudates and hemorrhages within the macula region, and/or evidence of retinal edema, and/or evidence of retinal ischemia. Vision may be reduced, sight threatening.

### **Preproliferative**

Evidence of occlusion (cotton wool spots). The veins become irregular and may show loops. Vision is normal.

## **Proliferative**

Occlusive changes have led to the release of vasoproliferative substances from the retina resulting in neovascularization of the disc or elsewhere on the retina. Neovascularization may also occur on the iris (rubeosis iridis), causing severe glaucoma. Vision is normal, sight threatening.

## **Advanced**

Proliferative changes result in bleeding into the vitreous or between the vitreous and retina. The retina may also be pulled away from its underlying pigment epithelium by a fibrous proliferation associated with the growth of the new vessels. Vision is reduced, often acutely with vitreous hemorrhage, sight threatening.

The detection error of diabetic retinopathy in non-ophthalmologists is 50%. Eighty percent of untreated individuals in the proliferative category will experience some form of visual loss in 5 years. Laser photocoagulation to areas of leaking blood vessels has been shown to reduce visual loss by 50%. Those patients with poorer glycemic control have a more rapid progression of retinopathy. Pregnant patients with Type I diabetes should be examined by an ophthalmologist during the first trimester and every 3 months thereafter until completion of the pregnancy.

## **Hypertension**

Prolonged systemic hypertension accelerates the normal aging process of arterioles which includes thickening and sclerosis. Arteriosclerosis can be visualized in the eye as an attenuation of the retinal arterial vessels (copper and silver wiring) and by the presence of nipping of the retinal vein where it is crossed by an arteriole.

Normally eye retinal arterioles are transparent in nature which reflect light from the convex surface of the arteriole. Progression of arteriolar sclerosis causes thickening and fibrosis of the vessel wall so as to increase the thickness of the reflected light from the arteriole. At this point the vessel is called copper wiring. As fibrosis progresses, the light reflex is completely obscured and arterioles appear whitish. The vessel is called silver wiring at this point.

Arterio-venous crossing changes are most noticeable at or beyond the second bifurcation of the arteriole which is about 1 disc diameter distal to the optic nerve head. These crossing changes may result in elevation or depression of the vein or even abrupt right-angle changes in severe cases. The size of the vein might also change due to constriction at the crossing leading to dilation of the distal portion of the vein.

## **Elevated Blood Pressure**

Moderate increases in blood pressure result in arteriolar constriction. Severe rises in blood pressure (diastolic >120mmHg) cause fibrinoid necrosis of the vessel wall leading to exudates, cotton-wool spots, flame-shaped hemorrhages and sometimes whitish swelling and edema of large portions of the retina. In malignant hypertension, the disc is swollen(similar in appearance to papilledema) and there are retinal hemorrhages and exudates.

It is easier to identify changes due to hypertension in previously normal arterioles rather than in those affected by prolonged hypertension leading to arteriolar thickening and fibrosis. The most sensitive ophthalmoscopic signs of hypertension include attenuation of the retinal arterioles, focal narrowing, and A/V crossing changes.

## **Thyroid Disease**

A common sequelae of thyroid disease is exophthalmos with retraction of the upper and lower eyelids. This may result in cornea drying leading to tearing and foreign-body sensation which may be relieved by frequent application of lubricating medications.

## **Sarcoidosis and Inflammatory Conditions**

The ocular manifestations of sarcoidosis include focal noncaseating granulomas. The disease is more common in African-American women aged 20-40. Laboratory findings include elevated serum calcium, decreased energy, elevated angiotensin-converting enzyme, and abnormal results on chest x-ray. The most frequent location containing ocular granulomas is the lacrimal gland. Sarcoidosis may also cause anterior or posterior uveitis (inflammation of the iris and choroid respectively). Systemic corticosteroids are required to prevent complications such as glaucoma, cataract, and adhesions to the lens

Juvenile rheumatoid arthritis can have serious ocular manifestations. Approximately 10% of all juvenile rheumatoid arthritis patients have iritis, but the inflammation is more common with the pauciarticular form and less common in the polyarticular form of the disease. If left unrecognized, serious complications such as cataract, glaucoma, and calcification of the cornea may result.

## **Acquired Immunodeficiency Syndrome**

The most common ophthalmic manifestations are cotton-wool spots, CMV retinitis, and Kaposi's sarcoma affecting the eyelids. Patients may also develop microvascular occlusion causing retinal hemorrhages and cotton wool spots (infarcted areas of the nerve fibre layer of the retina). These occlusions are thought to be due to microthrombi from antigen-antibody complexes and fibrin. Cytomegalovirus (CMV) retinitis occurs in more than 25% of patients and is the leading cause of visual loss in patients with AIDS.

## **Systemic Infection**

The most common systemic infections aside from AIDS include candidiasis and herpes zoster. The patient with candidiasis requires systemic therapy with amphotericin B. Herpes Zoster Ophthalmicus is usually preceded by the appearance of vesicles in the distribution of the ophthalmic division of the trigeminal nerve. Ocular problems are more likely if the naso-ciliary branch of the nerve is involved (vesicles at the root of the nose). Oral antiviral treatment (acyclovir) is effective in reducing post-infective neuralgia (a severe chronic pain in the area of the rash) if given within 3 days of the skin vesicles erupting. The most important side-effect of herpes zoster is anterior uveitis. Both simplex and zoster cause anesthesia of the cornea. This combination of anterior uveitis and corneal anesthesia is a serious vision-threatening effect. Cornea infiltration with the virus leads to disruption of the normal epithelium and thus may be identified by fluorescein staining and slit-lamp examination.