

# *Lupus and the Eye*

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The immune system protects the body from microorganisms such as bacteria and viruses, but in lupus its ability to distinguish between foreign material and its own tissues is defective. Inflammation follows immune attack on body tissues. At its onset, lupus may involve only one organ system. Lupus most commonly affects joints, the skin and the kidneys but the eye may also be involved. Autoantibodies and immune complexes damage tissues and cells. The cause of lupus is unknown.

## **Ocular Symptoms and Signs**

Ocular findings in lupus are the consequence of:

- \* Manifestations of lupus
- \* Manifestations of complications of lupus
- \* Toxicity of drug treatment for lupus or its complications

## **Ocular Manifestations of Lupus**

Dry eye symptoms of discomfort, itching, gritty sensation and reflex watering may occur when the lacrimal glands that supply tears become involved. This may occur as part of Sjogren's syndrome or sicca syndrome, where the salivary glands are also damaged, with dry eyes and a dry mouth. Symptoms are generally controlled with over-the-counter tear substitutes, control of ambient humidity, and barriers to evaporation of tears (glasses, side shields, goggles) and the loss of tears (minor lid surgery.) Although there is no specific treatment, there is a study on the use of cyclosporine in the treatment of dry eye. DHEA has also been the subject of investigation.

The skin around the eyes, including the eyelids, may be involved with the cutaneous changes of lupus. A rare but severe generalized skin eruption called erythema multiforme can occur. This causes severe inflammation of the conjunctiva that is the membrane that covers the sclera (white of the eye) and lines of the eyelids. Resultant scarring can lead to danger of exposure of the cornea (the clear window of the eye).

Other external abnormalities include a red eye resulting from inflammation of the conjunctiva and episclera (deeper blood vessels) generally without significant pain, or of the sclera (white coat of the eye) with aching pain. If not self-limiting, these generally respond to anti-inflammatory drugs. These are seen commonly as isolated conditions without underlying disease but occur in other collagen vascular diseases. Corneal ulceration can also occur.

Intraocular problems may result from retinal vasculitis. Retinal vasculitis is an inflammation of the blood vessels that damages and may occlude the small vessels of the retina (microangiopathy). It is a potentially serious manifestation. Since the retina is the tissue that lines the posterior cavity of the globe and is the light-sensing layer analogous to the film in a camera, damage resulting from occlusion of its blood supply can lead to loss of vision. Although it can be progressive over a few days, necessitating aggressive immunosuppression to prevent

blindness, it appears to be uncommon. Examination shows narrow white (sheathed) retinal vessels and “cotton wool spots” (white patches in the retina) from localized temporary swelling. These changes may be present in the absence of any symptoms. Ophthalmic examination of patients with lupus-like syndromes or in seronegative cases of lupus may assist in diagnostic clarification of such patients.

## **Ocular Manifestations of Complications of Lupus**

### **Renal**

Renal disease may cause fluid retention and swelling of the eyelids. “Puffiness” of the eyelids may be an early sign of relapse. Renal hypertension, where it results in hypertensive retinopathy, may show visible retinal changes similar to those seen with lupus microangiopathy but which respond to control of the blood pressure.

### **Neurological**

An increase in the pressure of the cerebrospinal fluid that bathes the central nervous system may mimic an intracranial tumor (pseudotumor) and may cause swelling of the optic nerves (pseudopapilledema). These changes may have no symptoms. Undetected and untreated, they may lead to loss of vision with symptoms only occurring late in the disease process.

When the brain is involved in lupus there are sometimes ocular manifestations that help to identify the location of neurologic involvement. Optic neuritis that impairs vision is uncommon and may mimic multiple sclerosis. Cranial nerve palsies can result in double vision (diplopia). These findings are also uncommon and often transitory in lupus.

Other problems such as cerebellar dysfunction may have eye manifestations that are subordinate to the overall clinical picture. Deficits resulting from large strokes result in lost areas in the field of vision (peripheral vision) as part of the overall presentation.

### **Vascular**

Occlusion of a vessel may occur from problems in its wall (e.g., vasculitis), its lining (e.g., atherosclerosis), and its lumen (e.g., coagulation). There is evidence that antibodies against phospholipids (lupus anticoagulant, anticardiolipin) may be associated with coagulation and blockage of retinal vessels. Anticoagulation in these patients aims to reduce the risk of similar future events.

Lupus endocarditis may rarely be a source of embolism or rarely become infected. Retinal signs of infected endocarditis such as white-centered hemorrhages as well as emboli in the retinal circulation can be identified if present at the time of examination.

### **Hematologic**

Anemia (chronic disease, hemolysis, cytotoxic drugs) if severe may produce a retinopathy with retinal hemorrhages. Low platelets (thrombocytopenia) could increase bleeding during eye surgery but a bleeding tendency, unless very severe, is not usually a problem for routine eye operations such as cataract surgery.

Low white cells (leukopenia) could, hypothetically, increase susceptibility to postoperative infection and may increase the predisposition to opportunistic infections of the retina in the context of severe immunosuppression and illness. Patients on immunosuppression after renal transplantation could be similarly at risk.

### **Gastrointestinal**

Acute pancreatitis (from active lupus, corticosteroids or azathioprine) is known to cause Purtscher's retinopathy, a multifocal vascular injury with profuse white patches in the retina (cotton wool spots). Vision is variably affected and tends to recover.

### **Musculoskeletal**

Children with antinuclear antibodies and pauciarticular arthritis (arthritis in few joints) may suffer severe loss of vision from an associated chronic uveitis (inflammation of iris tissue) without treatment.

## **Ocular Complications of Drugs in Lupus**

### **Corticosteroids**

Nonsteroid anti-inflammatory drugs very rarely have serious ocular side effects but corticosteroids do. Serious ocular complications of chronic corticosteroid therapy include cataracts (clouding of the lens of the eye) and glaucoma (a specific form of optic nerve injury most often related to abnormal intraocular pressure). Cataracts are treated in most cases successfully with surgery. Risk of cataract would not ordinarily be an indication to withhold steroid treatment if it is necessary. Likewise patients who develop glaucoma have drugs, laser treatment and surgery available to reduce their intraocular pressure. Since glaucoma is a silent disease until almost all vision is lost and the advanced damage irreversible, it is important that any patient considered for long-term treatment with steroids be under the care of an ophthalmologist. Steroids may also cause or aggravate existing diabetes mellitus which also may cause loss of vision in the longer term.

In general, risks of complications of corticosteroids increase with higher doses and extended periods of treatment.

### ***Antimalarial Drugs***

Antimalarial drugs have been effective in the treatment of lupus. Hydroxychloroquine (Plaquenil) is now the most commonly used. Chloroquine (Aralen) has been associated with more toxicity. At the beginning of treatment, there may be mild blurring of vision that clears spontaneously. Antimalarial drugs may damage the macula (the most sensitive area of the retina) and cause loss of vision. The ophthalmologist will look for retinal pigmentation that indicates early damage from antimalarial drugs. The risk of this complication is low with the lower doses of antimalarial drugs that are now used. There are varying opinions on what constitutes appropriate follow-up. There is a trend toward less frequent monitoring since the doses currently used to treat lupus are rarely associated with retinal damage. Damage due to antimalarial drugs is dose-related. Most cases of retinal damage occurred in patients who had received more than 400 mg of Plaquenil or more than 250 mg of Aralen daily. Early minimal retinal damage from Plaquenil is reported to be reversible if the drug is stopped. However,

pigmentary changes, classically a bull's eye appearance of the macula, are irreversible. Based on lean body weight, doses of Plaquenil below 6.5 mg/kg/day for less than six years were not reported to be associated with retinal toxicity in a series of nearly a thousand patients. There have been insufficient data to advise on a maximum safe dose of chloroquine.

Standard of care at present would be a dilated eye examination before treatment is initiated and at least annually in the absence of problems with documentation and evaluation of any existing pigmentary abnormalities in the macula. This may include photographic documentation. Patients can also monitor themselves with a grid of lines (Amsler grid). This may facilitate the detection of early symptoms from retinal damage. In addition and dependent on other findings, tests of color vision and visual fields might be appropriate.

### **Cytotoxic Drugs**

Undesirable side effects of cytotoxic drugs (cyclophosphamide, azathioprine) include an increased risk of infection with opportunistic organisms such as herpes. Herpes zoster may affect the ophthalmic branch of the fifth cranial nerve and damage several structures of the eye.

### ***In Summary***

Ocular damage in lupus may occur from the disease or its treatment. Fortunately blindness is uncommon. Eye examination may reveal unsuspected complications such as glaucoma from steroids, macular damage from antimalarial drugs, pseudotumor and pseudopapilledema from lupus, uveitis in pauciarticular childhood arthritis, all of which without intervention may result in irreversible loss of vision. Changes in vision should be reported immediately to a physician because early intervention may be sight saving.

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