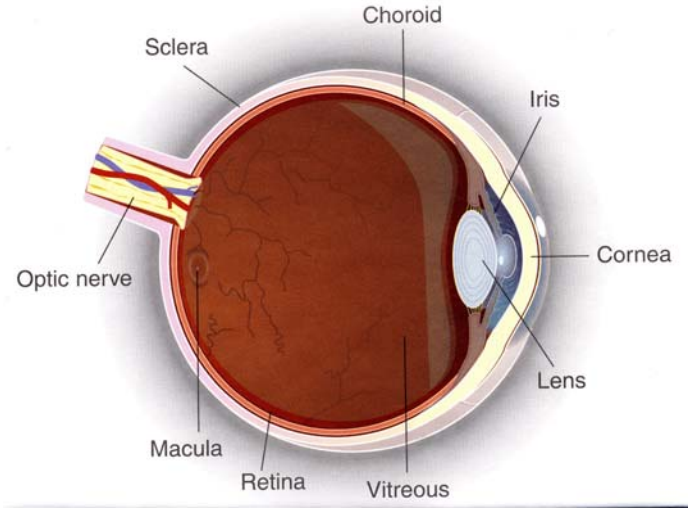
What You Should Know About Choroideremia

By David J. Browning, MD, PhD

Choroideremia is a rare disease of males causing night blindness and later visual field constriction and central vision loss. The affected tissues are the retina, the retinal pigment epithelium, and the choroid, all thin layers just inside the tough white scleral coat of the eye. The choroid is a layer of nutritive blood vessels. The retinal pigment epithelium is a layer of cells between the choroid and retina responsible for processing waste material made by the retina. The retina is a layer of nervous tissue that converts light into nerve impulses that travel to the brain. Figure 1 shows a diagram of the tissues involved. Figure 2 shows the appearance of a normal fundus. Figure 3 shows the fundus of a patient with advanced choroideremia. Since most of the retina and choroid are atrophied, one can see the white sclera abnormally clearly.

Figure 1. Anatomy of the Human Eye



What Causes Choroideremia?

Choroideremia is caused by a genetic mutation that occurs on the X chromosome. Since males have only one X chromosome, if they have the mutation, they show the disease. Females, on the other hand, have two X chromosomes, so that even if they have one mutated X chromosome, it is quite probable that the other X chromosome will not have this mutation. The female's normal copy of the choroideremia gene will protect her from developing severe disease, but her carrier state is usually evident because of a granular pigmentary change to the retina. Thus the mothers of males suspected of having choroideremia should have a dilated fundus examination by a knowledgeable ophthalmologist to confirm their status as carriers. If they are, they can be counseled that on average, half of future sons would be expected to possess the mutant gene and manifest the disease.

The choroideremia gene codes for an enzyme that attaches lipid groups to certain proteins inside the cell. The technical name for this protein is Rab escort protein–1 (REP-1). There is a related protein called Rab escort protein–2 which is similar to REP-1 and is normal in choroideremia. The rest of the body's cells seem to function quite well with REP-2. The cells of the retina, however, require the slightly different REP-1 protein, and if they do not have it, they die.

Figure 2. Normal Fundus

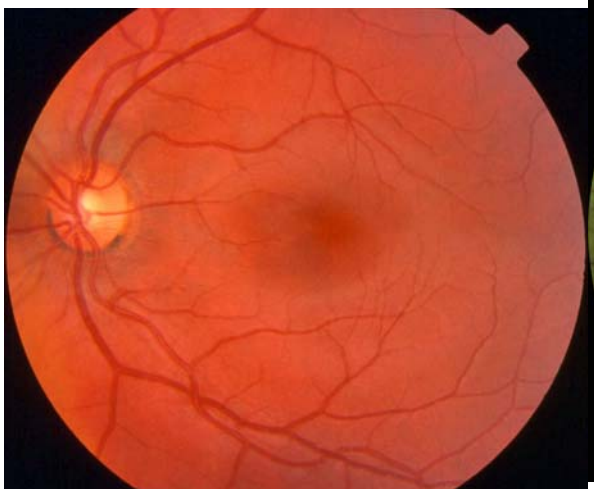
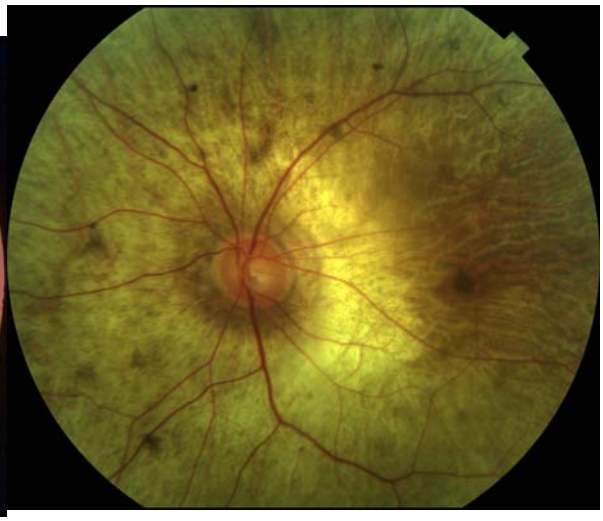


Figure 3. Fundus with Choroideremia



Are Other Organ Systems Affected?

In most cases, choroideremia is a disease of the eyes only. There are rare case reports of patients with other maladies, including mental deficiency, obesity, extra fingers, and skin abnormalities, but these are the exception.

Possible Diagnostic Confusion

Although the diagnosis of choroideremia is generally straightforward, it is occasionally difficult to distinguish this disease from several mimicking conditions. Ocular albinism may resemble a late case of choroideremia, but the electroretinogram in ocular albinism would not be depressed or absent. X linked retinitis pigmentosa can cause similar symptoms, but generally looks different with much less profound choriocapillaris atrophy. Gyrate atrophy can resemble choroideremia, but has an autosomal recessive inheritance pattern rather than the X linked recessive pattern of choroideremia. In addition, a check of serum ornithine will show an elevated level in gyrate atrophy, but not in choroideremia. Two definitive blood tests for choroideremia exist. One is a blood test in which the presence of REP-1 protein is sought. The other test looks for the DNA mutation on the X chromosome using DNA from the white blood cells.

Final Comments

Although the genetic basis of choroideremia has been discovered, no effective treatment or cure is forthcoming in the near future. Affected patients are given education and informed of visual aids that may help. Genetic counseling is provided to help with family planning of affected males and carrier females. Yearly eye exams are important to detect onset of cataracts and deal with problems of glare that can arise as the disease progresses. Sunglasses are the best solution for the glare that arises from the increased light scatter in the eyes of affected patients.

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