Division of Human Genetics
University of Cape Town

CONE ROD DYSTROPHY

WHAT IS CONE–ROD DYSTROPHY

Cone-Rod Retinal Dystrophy [CRD] is a progressive retinal degenerative condition that involves both Cone and Rod photoreceptors. An initial loss of colour vision and of visual acuity is followed by nyctalopia (night blindness), a loss of peripheral visual fields and Chorioretinal atrophy. CRD may be accompanied by skin pigmentation, teeth abnormality [amelogenesis imperfecta], Nystagmus [involuntary movements of the eye] and light sensitivity.

Without a genetic diagnosis it is very difficult to distinguish between Cone and Cone Rod Dystrophy, particularly in the early stages of the condition.

INHERITANCE

CRD can be inherited as either an autosomal dominant, autosomal recessive or X- linked trait. In its most common form, however, it is usually inherited as an autosomal recessive trait. It is inherited when both parents, called carriers, have one changed (mutated) copy of the disease-causing gene paired with one normal copy of the disease associated gene. Each child has a 25% chance of inheriting the two copies of the CRD causing gene (one from each parent). Carrier parents are unaffected because they have only one copy of the faulty gene.

There are numerous genetic mutations that are associated with Autosomal Recessive Cone-Rod Dystrophy (arCRD) and the ABCA4 gene is one of ten genes associated with this condition.

In the Autosomal Dominant form one parent will be affected and there is a 50% chance, on each pregnancy, that the child will inherit the gene and the condition from this parent. More than ten genes have been associated with Autosomal Dominant Cone or Cone-Rod Dystrophy.

In the X-Linked form the mother carries a single copy of the mutated gene on one of her X Chromosomes. As she has another working copy of the gene she is normally unaffected. She may pass the defective gene to her daughters, who will in turn be carriers or to her sons, who will be affected. There is a 50% chance on each pregnancy that the defective gene will be inherited. There are two genes that have been associated with X-Linked Cone or Cone- Rod Dystrophy.

Genetic counsellors are excellent resources for discussing inheritability, family planning, genetic testing, and other related issues. Genetic testing is available through Retina South Africa to help people define their condition and the risk of other family members or future offspring being affected.

DIFFERENTIATING BETWEEN CONE AND CONE- ROD DYSTROPHY

Cremers et al at the Erasmus Medical Center, Rotterdam, have published data on the clinical course, genetics and visual prognosis in patients with Cone Dystrophy (CD) and Cone-Rod Dystrophy (CRD). The mean age onset for CD was 16 years and 12 years for CRD. The pattern of inheritance was mostly recessive [AR] in both. Ten years after diagnosis, 35% of CD and 51% of CRD had a Bull's Eye Maculopathy; 70% of CRD showed absolute peripheral visual field defects and 37% of CD developed rod involvement on Electroretinagram (ERG). ABCA4 mutations were found in 9% of AR-CD, and in 26% of AR-CRD. Other mutations detected were the CNGB3 gene [3%], KCNV2 gene [4%], and in the PDE6C gene [1%]. The RPGR gene was mutated in both the X-linked CD patients studied and in 80% of the X-linked CRD patients. ABCA4 mutations as well as age of onset [less than 20 years old] were significantly associated with a faster rate of degeneration. The researchers hope that this data may serve as an aid in counselling patients with progressive cone disorders.

PREVALENCE

The prevalence is estimated to be in the range of one in 10,000 to one in 100,000.

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DIAGNOSIS

The earliest symptom of cone-rod dystrophy is decreased visual acuity. However, the diagnosis of CRD is usually established with loss of the peripheral visual fields. CRD must be distinguished from Retinitis Pigmentosa (RP). In CRD, rods and cones are lost at approximately the same rate. It is further distinguished from RP by the absence of night blindness as a presenting symptom.

TREATMENT AND MANAGEMENT

As of 2001, there are no known treatments or cures for CRD. It has been suggested, however, that people with CRD may be able to slow the progression of their blindness by wearing sunglasses and avoiding bright light.

PROGNOSIS

Studies of individuals thought to have CRD reveal that central vision loss begins in the first decade of life with the onset of night blindness occurring sometime after age 20. Little visual function remains after the age of 50. There is no cure for this syndrome.

TREATMENT AND MANAGEMENT

There are at present no treatments or cures for CRD. It has been suggested, however, that people with CRD may be able to slow the progression of their vision loss by wearing sunglasses and avoiding bright light. Due to the high frequency of the ABCA4 gene in CRD, patients are advised not to take supplements containing Vitamin A or beta-carotene.

Clinical trials to replace the entire ABCA4 gene in Stargardt Dystrophy have begun and this gene therapy will also benefit CRD patients with this genetic mutation.

SOUTH AFRICAN RESEARCH

The University of Cape Town, in partnership with Retina South Africa [RSA], is conducting a genetics research project to investigate the genes causing retinal degeneration in South African families. In addition, a gene-testing service is offered by Retina South Africa. A co-payment plan is available to members of RSA who wish to find their specific genetic mutation. Only people who have a genetic diagnosis will be eligible for upcoming gene-specific therapy trials and treatments.

BOOKS

McKusick, Victor A. Mendelian Inheritance in Man: A Catalog of Human Genes and Genetic Disorders. 12th ed. Baltimore: Johns Hopkins University Press, 1998.

Yanoff, Myron, and Jay S. Duker. Ophthalmology. St. Louis: Mosby, 2000.

PERIODICALS

Downes, Susan M., et al. "Autosomal Dominant Cone and Cone-Rod Dystrophy With Mutations in the Guanylate Cyclase Activator 1A Gene-Encoding Guanylate Cyclase Activating Protein-1." Archives of Ophthalmology 119, no. 1 (2001): 96–105.

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ORGANIZATIONS

American Academy of Ophthalmology. PO Box 7424, San Francisco, CA 94120-7424. (415) 561-8500.

http://www.eyenet.org

Association for Macular Diseases, Inc. 210 East 64th St., New York, NY 10021. (212) 605-3719. 2020@nei.nih.gov.
http://www.macula@macula.org

Foundation Fighting Blindness. Executive Plaza 1, 11350 McCormick Rd, Suite 800, Hunt Valley, MD 21031. (888) 394-3937. jchader@blindness.org
http://www.blindness.org>

National Eye Institute. 31 Center Dr., Bldg. 31, Rm 6A32, MSC 2510, Bethesda, MD 20892-2510. (301) 496-5248. 2020@nei.nih.gov.
http://www.nei.nih.gov

Retinitis Pigmentosa International. 23241 Ventura Blvd., Suite 117, Woodland Hills, CA 91364. (818) 992-0500 or (800) 344-4877. rpint@pacbell.net.

http://www.rpinternational.org

WEBSITES

Foundation Fighting Blindness:
http://www.blindness.org/html/science/wcord2.html

Retina Foundation of the Southwest.
http://www.retinafoundation.org/eyeinfo2.html

Southeastern Eye Center.
http://www.southeasterneyecenter.com/cases/bulls_eye.htm

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Who do I contact for more information regarding testing?

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