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Leber Congenital Amaurosis / Early-Onset Severe Retinal Dystrophy Overview

Synonyms: EOSRD, LCA

Neruban Kumaran, BSc, MBBS, FRCOphth,[1] Mark E Pennesi, MD, PhD,[2] Paul Yang, MD, PhD,[2] Karmen M Trzupek, MS, CGC,[3] Catherine Schlechter, MS, MBI, CGC,[4] Anthony T Moore, MA, BM BCh, FRCS, FRCOphth, FMedSci,[5,6] Richard G Weleber, MD, DABMG, FACMG,[4] and Michel Michaelides, BSc, MBBS, MD(Res), FRCOphth, FACS[1]

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Summary

The purpose of this overview is to increase the clinician's awareness of Leber congenital amaurosis (LCA) / early-onset severe retinal dystrophy (EOSRD) and its clinical phenotypes, genetic causes, and management. The following are the goals of this overview.

Goal 1

Describe the clinical characteristics of LCA/EOSRD.

Goal 2

Review the genetic causes of LCA/EOSRD.

Goal 3

Provide an evaluation strategy to identify the genetic cause of LCA/EOSRD in a proband (when possible).

Goal 4

Inform (when possible) medical management of LCA/EOSRD based on genetic cause.

Author Affiliations: 1 UCL Institute of Ophthalmology, University College London, Moorfields Eye Hospital, London, United Kingdom; Email: n.kumaran@ucl.ac.uk; Email: michel.michaelides@ucl.ac.uk. 2 Casey Eye Institute, Oregon Health Sciences University, Portland, Oregon; Email: pennesim@ohsu.edu; Email: yangp@ohsu.edu. 3 InformedDNA, St Petersburg, Florida; Email: ktrzupek@informeddna.com. 4 Ophthalmic Genetics Clinic, Casey Eye Institute, Oregon Health Sciences University, Portland, Oregon; Email: beattie@ohsu.edu; Email: weleberr@ohsu.edu. 5 University of California San Francisco, San Francisco, California; Email: tony.moore@ucsf.edu. 6 UCL Institute of Ophthalmology, University College London, London, United Kingdom; Email: tony.moore@ucsf.edu.

Goal 5

Inform genetic counseling for LCA/EOSRD.

1. Clinical Characteristics of Leber Congenital Amaurosis / Early-Onset Severe Retinal Dystrophy

Leber congenital amaurosis (LCA) / early-onset severe retinal dystrophy (EOSRD) comprises a spectrum of inherited retinal disorders that ranges from LCA at the severe end to EOSRD at the milder end.

LCA is characterized by severe visual impairment from birth or the first few months of life, roving eye movements or nystagmus, poor pupillary light responses, oculodigital sign (poking, rubbing, and/or pressing of the eyes), and undetectable or severely abnormal full-field electroretinogram (ERG).

EOSRD is characterized by the onset of visual impairment typically after infancy but before age five years, with variably preserved visual acuity and minimally preserved full-field ERG [Kumaran et al 2017].

The fundus in LCA/EOSRD can appear normal at presentation or show a variety of retinal abnormalities including pigmentary retinopathy, white deposits at the level of the retinal pigment epithelium, vascular attenuation, or pseudopapilledema and macular atrophy. Those with a normal fundus appearance at birth usually develop pigmentary retinopathy, optic disc pallor, and vascular attenuation with time. Other late changes include optic disc drusen, keratoconus, and lens opacities. Some genetic subtypes have a characteristic retinal phenotype.

The rate of visual loss varies, and some genes have been associated with faster progression (see Table 2). Infants with severe visual impairment may also have delays or difficulties with speech, social skills, and behavior, highlighting the importance of early involvement by a developmental pediatric specialist.

Persons with LCA/EOSRD usually present with isolated ocular signs and symptoms and have manifestations that remain confined to the eye. Some infants who present with visual impairment may later develop other systemic issues, particularly kidney disease. Nephronophthisis with subsequent end-stage kidney disease can be seen with certain genetic subtypes of LCA/EOSRD (e.g., *IQCB1*-, *IFT140*-, and *CEP290*-associated LCA) as part of syndromes including Senior-Loken syndrome and Joubert syndrome (see Table 2). Early molecular diagnosis can help identify individuals who require systemic investigations.

Differential Diagnosis

Table 1. Retinal Disorders to be Considered in the Differential Diagnosis of LCA/EOSRD

Disorder		Gene(s)	MOI	Distinguishing Clinical Features / Assessments
Nonsyndromic	Achromatopsia	*CNGB3* *CNGA3* *GNAT2* *PDE6C* *ATF6* *PDE6H*	AR	In achromatopsia: • Absent / markedly reduced cone responses w/normal rod ERG responses • Stationary natural history In LCA/EOSRD: • Non-recordable / markedly reduced full-field ERGs • Progressive disease

Table 1. continued from previous page.

Disorder		Gene(s)	MOI	Distinguishing Clinical Features / Assessments
	Congenital stationary night blindness (See X-Linked Congenital Stationary Night Blindness.)	>10 genes [1]	XL AR AD	Can be differentiated by ERG phenotype & natural history
	Ocular (OMIM 300500) & oculocutaneous (OMIM PS203100) albinism (See OCA Type 4 and OCA and OA Overview.)	>10 genes [2]	XL AR	• Clinical exam (hypopigmentation of skin, hair, eyebrows/eyelashes, iris, retina) • Retinal imaging (OCT & FAF); OCT can highlight foveal hypoplasia • Normal ERG & chiasmal misrouting on VEP
Syndromic	Neuronal ceroid lipofuscinoses (NCL) (OMIM PS256730)	13 genes [3]	AR AD [4]	• Infantile NCL presents w/ congenital or early-onset (age <6 mos) blindness. • Late-infantile & juvenile-onset NCL present at ages 2-4 & ≥6 yrs, respectively. • ERG can show a negative waveform. • NCL is assoc w/neurocognitive decline & epilepsy.
	Joubert syndrome	>30 genes [5]	AR XL [6]	• Presents w/severe visual impairment, ocular motor abnormalities • Characteristic MRI appearance incl "molar tooth sign" • Nephronophthisis in later childhood
	Zellweger spectrum disorder	13 genes [7]	AR	Assoc features: • Sensorineural deafness • Dysmorphic features • Developmental delay • Hepatomegaly • Early death
	Alström syndrome	*ALMS1*	AR	Presenting features: • Infantile-onset nystagmus • Photophobia • Cone-rod dystrophy Other systemic features: • Childhood obesity • Hyperinsulinemia • Type 2 diabetes mellitus • Hepatic dysfunction • Heart failure • Sensorineural hearing loss • Kidney failure

Table 1. continued from previous page.

Disorder		Gene(s)	MOI	Distinguishing Clinical Features / Assessments
	Cobalamin C deficiency (See Disorders of Intracellular Cobalamin Metabolism.)	*MMACHC*	AR	Variable phenotype. Severely affected persons have progressive, infantile-onset, metabolic, neurologic, & ophthalmic manifestations: • Infantile nystagmus • Bull's-eye maculopathy • ↓ responses on ERG

Adapted from Kumaran et al [2017] (Table 2)
AD = autosomal dominant; AR = autosomal recessive; EOSRD = early-onset severe retinal dystrophy; ERG = electroretinography; FAF = fundus autofluorescence; LCA = Leber congenital amaurosis; MOI = mode of inheritance; OA = ocular albinism; OCA = oculocutaneous albinism; OCT = optical coherence tomography; VEP = visual evoked potentials; XL = X-linked
1. See OMIM Phenotypic Series: Night Blindness, Congenital Stationary for a list of genes associated with this phenotype.
2. X-linked ocular albinism is caused by pathogenic variants in *GPR143*. See OMIM Phenotypic Series: Oculocutaneous Albinism for a list of genes associated with oculocutaneous albinism.
3. Pathogenic variants in *PPT1*, *TPP1*, *CLN3*, *CLN5*, *CLN6*, *MFSD8*, *CLN8*, *CTSD*, *DNAJC5*, *CTSF*, *ATP13A2*, *GRN*, and *KCTD7* are known to cause NCL.
4. The NCLs are inherited in an autosomal recessive manner; adult-onset NCL can also be inherited in an autosomal dominant manner.
5. Pathogenic variants in *ARL13B*, *B9D1*, *B9D2*, *C2CD3*, *C5orf42*, *CC2D2A*, *CEP41*, *CEP104*, *CEP120*, *CEP290*, *CSPP1*, *IFT172*, *INPP5E*, *KATNIP* (*KIAA0556*), *KIAA0586*, *KIF7*, *MKS1*, *NPHP1*, *OFD1*, *PDE6D*, *POC1B*, *RPGRIP1L*, *TCTN1*, *TCTN2*, *TCTN3*, *TMEM67*, *TMEM107*, *TMEM138*, *TMEM216*, *TMEM231*, *TMEM237*, *TTC21B*, and *ZNF423* are known to cause Joubert syndrome.
6. Joubert syndrome is predominantly inherited in an autosomal recessive manner. Joubert syndrome caused by pathogenic variants in *OFD1* is inherited in an X-linked manner. Digenic inheritance has been reported.
7. Pathogenic variants in *PEX1*, *PEX6*, *PEX12*, *PEX26*, *PEX10*, *PEX2*, *PEX5*, *PEX13*, *PEX16*, *PEX3*, *PEX19*, *PEX14*, and *PEX11β are* known to cause Zellweger spectrum disorder.

2. Causes of Leber Congenital Amaurosis / Early-Onset Severe Retinal Dystrophy

To date, mutation of 24 genes accounts for 70%-80% of individuals with Leber congenital amaurosis (LCA) / early-onset severe retinal dystrophy (EOSRD) (Table 2).

Table 2. Leber Congenital Amaurosis (LCA) / Early-Onset Severe Retinal Dystrophy (EOSRD): Genes and Distinguishing Clinical Features

Gene [1]	% of All LCA/ EOSRD	Distinguishing Clinical Features		Other	References	
		Visual function	Fundus appearance		OMIM	Selected citations
ALMS1	?				606844	
AIPL1	<5%	LCA: early profound visual loss	Can be relatively normal in infancy	On OCT: • Relative preservation of outer retinal structure before age 4 yrs • Progressive loss from birth to total macular atrophy	604393	Aboshiha et al [2015]

Table 2. continued from previous page.

Gene [1]	% of All LCA/ EOSRD	Distinguishing Clinical Features		Other	References	
		Visual function	Fundus appearance		OMIM	Selected citations
CABP4	?				608965	Aldahmesh et al [2010]
CEP290	15%-20%	LCA: • Significant variability; severe VA loss in most • No clear progression in 1st decade	Can be relatively normal in infancy	• On OCT: residual outer retinal structure often present until 4th decade • Assoc w/ nephronophthisis, Joubert syndrome	611755	
CLUAP1	?				616787	Soens et al [2016]
CRB1	10%	• Phenotypes: LCA/ EOSRD, RP, & others [2] • Severity & rate of progression vary significantly.	Variably present: • Nummular pigmentation • Maculopathy • Relative preservation of para-arteriolar RPE	On OCT: retinal thickening & loss of lamination reported	613835	
CRX	1%				613829	Jacobson et al [1998]
DTHD1	?				616979	Abu-Safieh et al [2013]
GDF6	?				615360	
GUCY2D	10%-20%	LCA: • Early profound visual loss • Lack of color perception • Significant photophobia • Substantial residual rod-driven visual function	Relatively normal		204000	Jacobson et al [2013]
IFT140	?			Assoc w/nephronophthisis, Joubert syndrome	614620	Xu et al [2015]
IMPDH1	5%				613837	
IQCB1	?			Assoc w/nephronophthisis, Joubert syndrome	609237	Estrada-Cuzcano et al [2011]
KCNJ13	?				614186	
LCA5	1%-2%				604537	

Table 2. continued from previous page.

Gene [1]	% of All LCA/ EOSRD	Distinguishing Clinical Features		Other	References	
		Visual function	Fundus appearance		OMIM	Selected citations
LRAT	<1%	EOSRD: similar to *RPE65*-LCA			613341	
NMNAT1	?	LCA/EOSRD: • Majority have early-onset profound vision loss & extensive maculopathy. • Minority have milder phenotype.	Marked maculopathy		608553	Kumaran et al [2021]
OTX2	?				600037	Henderson et al [2009]
RD3	<1%				610612	
RDH12	10%	LCA phenotype	• Early, widespread RPE & retinal atrophy • Minimal intraretinal pigmentation in early childhood • Dense intraretinal bone-spicule pigmentation developing over time • Early progressive macular atrophy	• On OCT: macular excavation • On FAF: loss of autofluorescence	612712	Mackay et al [2011]
RPE65	5%-10%	EOSRD: • Profound night blindness from birth • Minimal nystagmus • Poor color discrimination • Residual cone-mediated vision in 1st 3 decades w/ progressive visual field loss	May show blonde fundus w/peripheral, white, punctate lesions	FDA-approved gene therapy available (See *RPE65*-Related LCA/EOSRD.)	204100	Kumaran et al [2018a], Kumaran et al [2018b]
RPGRIP1	5%	Initial rapid decline in vision followed by lack of progression			613826	

Table 2. continued from previous page.

Gene [1]	% of All LCA/ EOSRD	Distinguishing Clinical Features		Other	References	
		Visual function	Fundus appearance		OMIM	Selected citations
PRPH2	?				608133	
SPATA7	3%				604232	
TULP1	<1%		Maculopathy		613843	

Adapted from Kumaran et al [2017]
? = unknown; FAF = fundus autofluorescence; OCT = optical coherence tomography; RP = retinitis pigmentosa; RPE = retinal pigment epithelium; VA = visual acuity
1. Genes are listed alphabetically.
2. Retinitis pigmentosa may or may not be accompanied by Coats-like vasculopathy, later-onset macular dystrophy, and isolated autosomal recessive foveal retinoschisis.

3. Evaluation Strategies to Identify the Genetic Cause of Leber Congenital Amaurosis / Early-Onset Severe Retinal Dystrophy in a Proband

Establishing a specific genetic cause of Leber congenital amaurosis (LCA) / early-onset severe retinal dystrophy (EOSRD):

- Can aid in discussions of prognosis (which are beyond the scope of this *GeneReview*) and genetic counseling and management (see Section 5);
- Usually involves a medical history, physical examination, laboratory testing, family history, and genomic/ genetic testing.

Medical history. See Table 2.

Physical examination and other studies. See Table 2.

Family history. A three-generation family history should be taken, with attention to relatives with manifestations of LCA/EOSRD and consanguinity. Document relevant findings in relatives through direct examination or review of medical records, including results of molecular genetic testing.

Molecular genetic testing. Because LCA/EOSRD is both genetically heterogeneous and indistinguishable from many other inherited retinal dystrophies, recommended molecular genetic testing approaches include either gene-targeted testing (multigene panel) or comprehensive genomic testing (exome/genome sequencing). Gene-targeted testing, typically done using multigene panel tests, requires prior characterization of the causative gene as a "retinal dystrophy gene." Genomic testing enables the clinician to explore genes not previously known to be associated with retinal dystrophy.

Note: (1) Single-gene testing (sequence analysis of a given gene, followed by gene-targeted deletion/duplication analysis) is rarely useful and typically NOT recommended. (2) Single-gene sequence analysis and/or targeted deletion/duplication analysis MAY be considered if previous testing has identified a heterozygous pathogenic variant in a recessive LCA-associated gene. Of note, large deletions, insertions, and duplications very rarely account for the presumed second variant.

- **A multigene panel** that includes some or all of the genes listed in Table 2 is most likely to identify the genetic cause of LCA/EOSRD while limiting identification of variants of uncertain significance and pathogenic variants in genes that do not explain the underlying phenotype. Note: (1) The genes included

in the panel and the diagnostic sensitivity of the testing used for each gene vary by laboratory and are likely to change over time. (2) Some multigene panels may include genes not associated with the condition discussed in this *GeneReview*. Of note, given the rarity of some of the genes associated with LCA/EOSRD some panels may not include all known LCA/EOSRD genes listed in Table 2. (3) In some laboratories, panel options may include a custom laboratory-designed panel and/or custom phenotype-focused exome analysis that includes genes specified by the clinician. (4) Methods used in a panel may include sequence analysis, deletion/duplication analysis, and/or other non-sequencing-based tests.

For an introduction to multigene panels click here. More detailed information for clinicians ordering genetic tests can be found here.

- **Comprehensive genomic testing** (which does not require the clinician to determine which gene[s] are likely involved) may be considered. **Exome sequencing** is most commonly used; **genome sequencing** is increasingly possible. If exome sequencing is not diagnostic, exome array (when clinically available) may be considered to detect (multi)exon deletions or duplications that cannot be detected by sequence analysis.

  Note: Unlike exome sequencing, genome sequencing can identify noncoding variants. Although most confirmed pathogenic variants identified by genome sequencing are within exons [Taylor et al 2015], likely pathogenic variants have been detected in noncoding regions of *CRB1*, *GUCY2D*, and *IFT140* in individuals with inherited retinal dystrophies [Daich Varela et al 2023].

  For an introduction to comprehensive genomic testing click here. More detailed information for clinicians ordering genomic testing can be found here.

4. Medical Management of Leber Congenital Amaurosis / Early-Onset Severe Retinal Dystrophy Based on Genetic Cause

Management of most forms of Leber congenital amaurosis (LCA) / early-onset severe retinal dystrophy (EOSRD) is symptomatic. The only form of LCA/EOSRD for which specific therapy (gene replacement therapy) is available is *RPE65*-LCA. See *RPE65*-Related Leber Congenital Amaurosis / Early-Onset Severe Retinal Dystrophy.

Visual Impairment

Symptomatic management. Affected children benefit from correction of refractive error, use of low vision aids when possible, and optimal access to educational and work-related opportunities.

Children and their parents should be referred to programs for visually impaired children within their state or locality.

Gene therapy for LCA/EOSRD. In the case of LCA, gene supplementation therapy compensates for loss-of-function variants by providing a healthy copy of the gene to cells where it is required [Kumaran et al 2018c]. Viral vectors, or more specifically recombinant adeno-associated virus (AAV) vectors, have been used in LCA clinical trials.

Subretinal gene therapy administration for LCA has been investigated most extensively in ***RPE65*-associated LCA** [Kumaran et al 2018b]. A total of five Phase I/II trials [Bainbridge et al 2008, Hauswirth et al 2008, Maguire et al 2008, Weleber et al 2016, Le Meur et al 2018] and one Phase III trial [Russell et al 2017] have shown that subretinal injection of a recombinant AAV vector containing the *RPE65* cDNA can improve retinal function:

- The Phase I/II clinical trials identified varied improvements in aspects of sight [Testa et al 2013, Bainbridge et al 2015, Jacobson et al 2015, Le Meur et al 2018, Pennesi et al 2018].

- The Phase III trial of subretinal administration of an AAV2/2 vector has reported benefit at one year, reaching its primary end point for efficacy with improved performance on a novel test of multiluminance mobility [Russell et al 2017]. This product, voretingene neparvovec (Luxturna™, Spark Therapeutics Inc) has been approved by the FDA for the treatment of *RPE65*-associated retinopathy.

Following successful gene supplementation therapy in experimental models of *AIPL1*-, *RDH12*-, *GUCY2D*-, and *RPGRIP*-associated LCA, clinical trials in these subsets of LCA are likely in the future. A different technique of gene therapy utilizing antisense oligonucleotide-mediated exon skipping to abrogate the disease-causing variant has resulted in a clinical trial investigating the safety and tolerability of intravitreal injections of this type of gene therapy (ClinicalTrials.gov identifier: NCT03140969) for *CEP290*-associated LCA.

Developmental Delay / Intellectual Disability Management Issues

Children with LCA/EOSRD who have developmental delay should be referred to a developmental pediatrician and enrolled in a continuing program of care and support.

Advice on developmental delay / intellectual disability management issues will vary from country to country, or even region to region within a country, depending on support services available. Overarching principles should include the following:

- Involving child development and educational specialists at the earliest available opportunity, often with specialist teachers / schools for the visually impaired
- Early referral to low vision services to access low visual aids, especially with improving technologies, such as the refreshable braille display
- As affected individuals grow older, identifying further assistance (including financial or employment assistance), which in some countries is available through certification/registration processes

Some countries have registration services to record population data on the causes and effects of visual impairment.

Note: The following information represents typical management recommendations for individuals with developmental delay / intellectual disability management issues in the United States.

Motor Dysfunction

Gross motor dysfunction

- Physical therapy is recommended to maximize mobility.
- Consider use of durable medical equipment as needed (e.g., wheelchairs, walkers, bath chairs, orthotics, adaptive strollers).

Fine motor dysfunction. Occupational therapy is recommended for difficulty with fine motor skills that affect adaptive function such as feeding, grooming, dressing, and writing.

Oral motor dysfunction. Assuming that the individual is safe to eat by mouth, feeding therapy (typically from an occupational or speech therapist) is recommended for affected individuals who have difficulty feeding due to poor oral motor control.

Communication issues. Consider evaluation for alternative means of communication (e.g., augmentative and alternative communication [AAC]) for individuals who have expressive language difficulties.

Social/Behavioral Concerns

Children may qualify for and benefit from interventions used in treatment of autism spectrum disorder, including applied behavior analysis (ABA). ABA therapy is targeted to the individual child's behavioral, social, and adaptive strengths and weaknesses and is typically performed one on one with a board-certified behavior analyst.

Consultation with a developmental pediatrician may be helpful in guiding parents through appropriate behavior management strategies or providing prescription medications (e.g., to treat attention-deficit/hyperactivity disorder) when necessary.

5. Genetic Counseling for Leber Congenital Amaurosis / Early-Onset Severe Retinal Dystrophy

Genetic counseling is the process of providing individuals and families with information on the nature, mode(s) of inheritance, and implications of genetic disorders to help them make informed medical and personal decisions. The following section deals with genetic risk assessment and the use of family history and genetic testing to clarify genetic status for family members; it is not meant to address all personal, cultural, or ethical issues that may arise or to substitute for consultation with a genetics professional. —ED.

Mode of Inheritance

Leber congenital amaurosis (LCA) / early-onset severe retinal dystrophy (EOSRD) is typically inherited in an autosomal recessive manner.

Rarely, LCA/EOSRD is inherited in an autosomal dominant manner as a result of a heterozygous pathogenic variant in *CRX*, *OTX2*, or *IMPDH1*.

Note: In the estimated 30% of individuals with LCA/EOSRD in whom no molecular diagnosis is found, the mode of inheritance is most likely autosomal recessive with a small likelihood of autosomal dominant inheritance resulting from a *de novo* pathogenic variant.

Autosomal Recessive Inheritance – Risk to Family Members

Parents of a proband

- The parents of an affected child are obligate heterozygotes (i.e., carriers of one LCA/EOSRD-causing allelic variant).
- Heterozygotes (carriers) are asymptomatic and are not at risk of developing the disorder.

Sibs of a proband

- At conception, each sib of an affected individual has a 25% chance of being affected, a 50% chance of being an asymptomatic carrier, and a 25% chance of being unaffected and not a carrier.
- Heterozygotes (carriers) are asymptomatic and are not at risk of developing the disorder.

Offspring of a proband. The offspring of an individual with autosomal recessive LCA/EOSRD are obligate heterozygotes (carriers) for an LCA/EOSRD-causing allelic variant.

Other family members. Each sib of the proband's parents is at a 50% risk of being a carrier of an LCA/EOSRD-causing allelic variant.

Carrier detection. Carrier testing for at-risk relatives requires prior identification of the LCA/EOSRD-causing allelic variants in the family.

Autosomal Dominant Inheritance – Risk to Family Members

Parents of a proband

- Some children diagnosed with autosomal dominant LCA/EOSRD have an affected parent.
- Most children diagnosed with autosomal dominant LCA/EOSRD have the disorder as the result of a *de novo CRX*, *OTX2*, or *IMPDH1* pathogenic variant [Jacobson et al 1998, Sohocki et al 1998, Swaroop et al 1999, Rivolta et al 2001, Perrault et al 2003].
- Molecular genetic testing is recommended for the parents of a proband with an apparent *de novo* pathogenic variant.

Sibs of a proband. The risk to sibs of the proband depends on the clinical/genetic status of the proband's parents:

- If a parent of the proband is affected and/or is known to have the pathogenic variant identified in the proband, the risk to the sibs is 50%.
- If the proband has a known LCA/EOSRD-causing allelic variant that cannot be detected in the leukocyte DNA of either parent, the recurrence risk to sibs is estimated to be 1% because of the theoretic possibility of parental germline mosaicism [Rahbari et al 2016].
- If the parents have not been tested for the LCA/EOSRD-causing allelic variant but are clinically unaffected, the risk to the sibs of a proband appears to be low.

Offspring of a proband. Each child of an individual with LCA/EOSRD has a 50% chance of inheriting the LCA/EOSRD-causing allelic variant.

Other family members. The risk to other family members depends on the status of the proband's parents: if a parent is affected, the parent's family members are at risk.

Prenatal Testing and Preimplantation Genetic Testing

Once the LCA/EOSRD-causing allelic variant(s) have been identified in an affected family member, prenatal and preimplantation genetic testing are possible.

Resources

GeneReviews staff has selected the following disease-specific and/or umbrella support organizations and/or registries for the benefit of individuals with this disorder and their families. GeneReviews is not responsible for the information provided by other organizations. For information on selection criteria, click here.

- **American Council of the Blind (ACB)**
  2200 Wilson Boulevard
  Suite 650
  Arlington VA 22201
  Phone: 800-424-8666 (toll-free); 202-467-5081
  Fax: 202-467-5085
  Email: info@acb.org
  www.acb.org

- **Foundation Fighting Blindness**
  7168 Columbia Gateway Drive
  Suite 100
  Columbia MD 21046

Phone: 800-683-5555 (toll-free); 800-683-5551 (toll-free TDD); 410-423-0600
Email: info@fightblindness.org
www.fightingblindness.org

- **National Federation of the Blind**
  Phone: 410-659-9314
  Email: nfb@nfb.org
  www.nfb.org
- **Retina International**
  Ireland
  Phone: 353 1 961 9259
  Email: info@retina-International.org
  www.retina-international.org

Chapter Notes

Author Notes

UCL Gene and Cell Therapy Group website

Casey Eye Institute Ophthalmic Genetics Service website

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Revision History

- 23 March 2023 (aa/gm) Revision: Daich Varela et al [2023] and information about likely pathogenic variants in noncoding regions detected by genome sequencing added to Evaluation Strategies to Identify the Genetic Cause of LCA/EOSRD in a Proband
- 4 October 2018 (bp) Overview posted live
- 13 December 2017 (mm,nk) Original submission

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