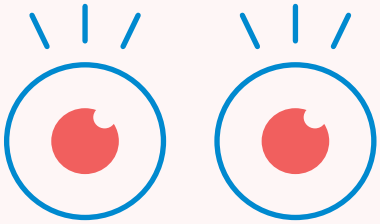
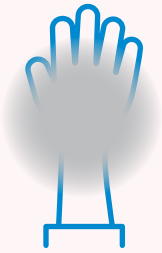
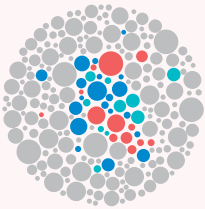
SingHealth DukeNUS
ACADEMIC MEDICAL CENTRE

Genomic
Medicine Centre

Inherited Retinal Diseases







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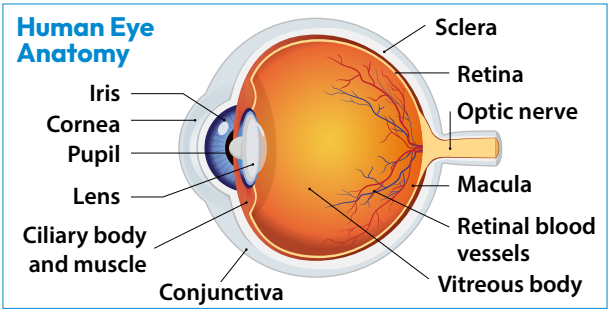
What are inherited retinal diseases?

Inherited retinal diseases, also known as IRDs, refer to a group of rare genetic disorders affecting the retina, the light-sensitive nerve layer at the back of the eye.

IRDs damage the rod and/or cone photoreceptor cells in the retina. Generally, rods help us see in dim light, while cones help with colour and central vision. There are many types of IRDs, such as retinitis pigmentosa (RP), cone-rod dystrophies (CRD) and macular dystrophies.



How common are IRDs in Singapore?

A study of the Singaporean population showed that between **one in 1,000 to 2,000 Singaporeans** are affected by IRDs.

What are the symptoms of IRDs?

The symptoms experienced by individuals differ depending on the type of photoreceptors affected.

- **Retinitis pigmentosa (RP)** causes difficulties with vision in dim light ('night blindness') and constriction of visual fields. As it progresses, central vision may become affected, with severe cases resulting in complete or nearly complete blindness.

- **Macular dystrophies** cause problems with central vision. However, there is a large amount of variability, with some IRD patients remaining asymptomatic until late in life.

Do IRDs only affect the eyes?

IRDs refer to a large group of genetic disorders that affect the retina. In most cases, the inherited gene defect only affects the eyes.

Sometimes, other parts of the body are also affected, and this is called **syndromic RP**. An example of syndromic RP is Usher syndrome, which causes both RP and hearing loss. Other examples include Refsum, Alström and Laurence-Moon-Bardet-Biedl (LMBB) syndromes.

How are IRD patients treated?

The general eye specialist you see initially will refer you to a retinal specialist with expertise in IRDs.

Diagnosis

The retina specialist will assess your visual function and arrange for a series of clinic-based tests to confirm the diagnosis of IRD. These tests include electrophysiology, highly specialised imaging or scans and visual field testing.

Genetic testing

Following the diagnosis of IRD, most patients will undergo genetic testing by sending a blood sample or mouth swab to a laboratory to determine which genetic changes are responsible for your IRD.

In some cases, confirmation of your genetic diagnosis may require other members of your family to also undergo genetic testing.

Monitoring and treatment

Following the initial diagnosis and genetic testing, IRD patients are monitored regularly for progression of the condition and the development of any complications, such as

swelling of the retina, by a retinal specialist or paediatric ophthalmologist.

Patients with syndromic RP may additionally require monitoring and treatment by other specialists, such as an ear, nose and throat (ENT) doctor and genetics doctor.

What causes IRDs?

IRDs can be caused by one of many possible genetic changes, but they all result in a similar set of symptoms related to vision. Researchers have identified hundreds of different genetic changes that can each cause IRDs, although most IRD cases are caused by changes to one of a small number of commonly affected genes.

How are IRDs diagnosed?

IRDs are diagnosed based on:

- The patient's symptoms
- Family history
- Clinical examination of the eye
- Several special tests of the retina that are conducted by an ophthalmologist and ophthalmic technician, including electrophysiology, highly specialised imaging and visual field testing

There are many different varieties of IRDs, each caused by specific changes in a patient's DNA. As a result, the definitive diagnosis of the type of IRD for each patient requires a blood test to check which DNA change is responsible for the condition.

How are IRDs inherited?

Genes are instructions for cells to make proteins in the body. Everyone carries two copies of each gene, one inherited from each parent. IRDs are the result of a change (mutation) in the relevant gene.

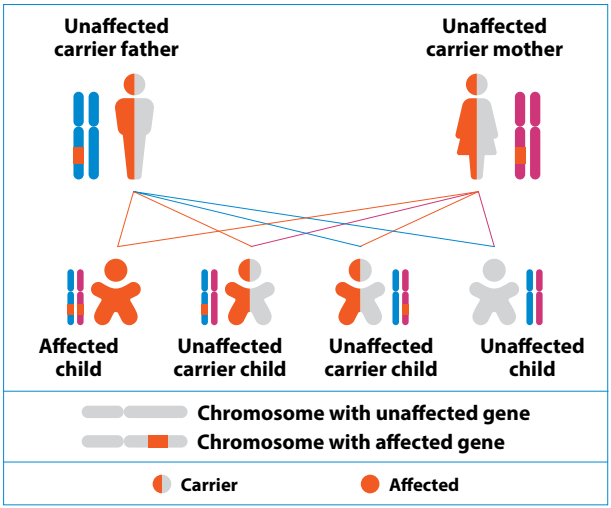
IRDs usually run in families, but the way it is passed from parents to their children varies depending on the specific genetic changes responsible for a person's IRD.

Autosomal recessive IRDs

Autosomal recessive IRDs occur when there are two faulty copies of the involved gene, one from each parent. Most IRD cases are inherited in an autosomal recessive pattern.

- Both males and females are equally affected
- There might be no known history of IRD in either family

Autosomal recessive IRDs tend to produce signs and symptoms between 30 and 40 years of age and usually cause more severe sight loss.

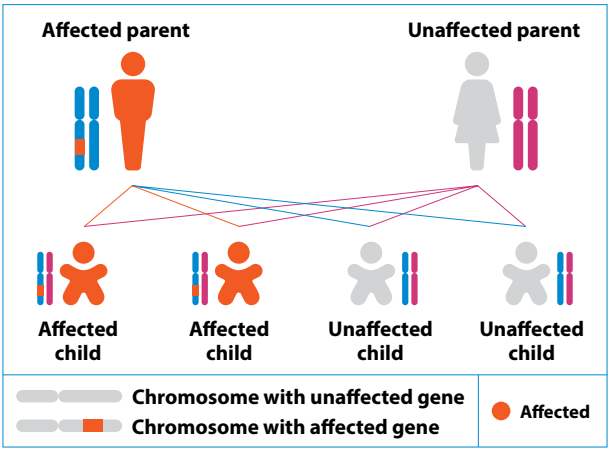


Autosomal dominant IRDs

Autosomal dominant IRDs occur when there is one faulty copy of the involved gene.

- It affects males and females equally
- There is usually a known history of the condition in the family

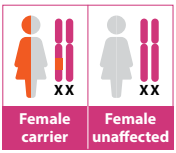
Autosomal dominant IRDs are generally less severe than other forms of IRD and usually result in symptoms from around 30 years of age.



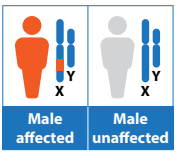
X-linked IRD

In diseases with X-linked inheritance, the affected gene is located on the X chromosome. Typically, females have two X chromosomes, whilst males have one X and one Y chromosome.

Females with one affected copy and one normal copy are known as carriers.



As males only have one copy of the X chromosome gene, males with one affected copy do not have a second working copy and are therefore affected with the genetic disorder.



- X-linked IRDs affect mostly men
- Females who are carriers of the faulty gene may be symptomatic but seldom as severely as affected males

X-linked IRDs can result in severe vision loss, often with blindness or near-blindness by the age of 40.

Many cases of IRDs occur in people without any known family history. Parents may have passed the genetic changes onto their offspring but did not develop symptoms themselves. In these cases, it may not be possible to determine how the IRD is inherited.

Why do I need genetic testing?

Up until recently, genetic testing for IRDs was done mainly to determine inheritance patterns, and for genetic counselling and research purposes. More recently, however, genetic testing has become much more important.

An accurate genetic diagnosis will enable your retinal specialist to determine if you or other members of your family are eligible for treatment with special gene-based therapies that can slow the progression of the IRDs and reduce vision loss.

These therapies may be offered as a normal clinical service, or as part of a clinical research trial.

Support Groups / Resources

iC2 PrepHouse
iC2 PrepHouse supports and empowers children with RP and other visual impairments by helping children with low vision stay in mainstream schools, and teaching them coping skills in everyday living.
Tel: 6790 1802
Email: admin@ic2.com.sg
www.ic2.com.sg

Guide Dogs Singapore (GDS)
Tel: 6339 7900
www.guidedogs.org.sg

Singapore Association of the Visually Handicapped (SAVH)
Tel: 6251 4331 / 6252 9116
www.savh.org.sg

Enabling Village
Tel: 1800 8585 885
Email: hello@ev.sg
www.enablingvillage.sg

Acknowledgements

Dr Chan Choi Mun, Singapore National Eye Centre

Medical Retina Department, Singapore National Eye Centre

Genetics Service, KK Women's and Children's Hospital

Information contributed by:

SingHealth DukeNUS ACADEMIC MEDICAL CENTRE

Genomic Medicine Centre

KK Women's and Children's Hospital
6294 4050
www.kkh.com.sg

Singapore General Hospital
6321 4377
www.sgh.com.sg

Changi General Hospital
6850 3333
www.cgh.com.sg

Sengkang General Hospital
6930 6000
www.skh.com.sg

National Cancer Centre Singapore
6436 8088
www.nccs.com.sg

National Heart Centre Singapore
6704 2000
www.nhcs.com.sg

National Neuroscience Institute
6321 4377 (SGH Campus)
6330 6363 (TTSH Campus)
www.nni.com.sg

Singapore National Eye Centre
6227 7266
www.snec.com.sg

Find out more about the Centre at:
www.singhealth.com.sg/genomic-medicine-centre

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Reg. No.: 200002698Z
Information correct as at February 2023

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