# Best disease (Best vitelliform macular dystrophy)

Best disease is a genetic condition you are born with. It doesn’t usually start to affect your vision until later in life. Best disease affects the macula, which is the central part of your retina at the back of your eye. There is no treatment for Best disease at present, although research into gene therapy is on-going, which may lead to a treatment in the future.

## What is Best disease?

Best disease is a type of macular dystrophy and is also called “Best vitelliform macular dystrophy”. Macular dystrophies are inherited eye conditions, meaning they are caused by a fault in a gene. Best disease can affect both men and women. It usually occurs in both eyes, but one eye may be more affected than the other. Sometimes it only affects one eye. Best disease can start to cause changes at the macula between the ages of three to 15, although it does not usually affect vision until later in life.

Best disease only affects the macula. This means it causes problems with your central vision but does not lead to total loss of sight.

Best disease only affects the eyes. It is not caused by, or linked to, a problem or disease in any other part of the body.

The sight loss caused by Best disease can take many years to develop and some people with the condition can continue to read standard sized print into their forties, fifties or well beyond.

## How does the eye work?

When light enters your eye, it is focused onto your retina at the back of your eye. The retina includes a number of layers, but the most important for vision is a layer made up of photoreceptor cells. Photoreceptors are cells which are sensitive to light.

The macula is the central area of the retina that contains photoreceptor cells called cone cells. Cone cells work best in bright light levels and allow you to see fine detail for activities such as reading, writing, and recognising colours. Best disease causes your macula to stop working as well as it should.

Away from the central macula is the peripheral retina, composed mostly of the other type of photoreceptor cells, called rod cells. Rod cells enable us to see when light is dim and provide peripheral vision outside of the main line of sight.

Peripheral vision is the sight you have out of the corner of your eye when looking straight ahead. Best disease does not affect the peripheral retina so does not normally affect peripheral vision.



Diagram shows cross section of an eye with the following labels: cornea, iris, pupil, lens, vitreous gel, retina, macula, fovea, optic nerve.

## How does Best disease affect vision?

The symptoms of Best disease vary from person to person, but usually the first problems people notice are with their ability to see detail. You may have problems reading small print, or it may seem that there’s a slight smudge or a small, blurred area in the centre of your vision. Straight lines may look distorted, wavy, or as if there's a little bump in them. People may only notice these changes in one eye.

Some people with Best disease experience light sensitivity (photophobia). Light sensitivity may cause discomfort. You can find more information about light sensitivity on our website contacting our Helpline.

Best disease does not usually affect peripheral vision. As we use our peripheral vision for moving around, most people with Best disease can usually continue to get out and about on their own. For example, someone with Best disease may be able to get to the local bus stop and see a bus coming but find it difficult to see the number on the bus.

You should have your eyes examined by an optometrist (optician) if:

* you notice any difficulty with reading small print (with your reading glasses if you need them)
* straight lines start to look wavy or distorted
* your vision isn't as clear as it used to be.

The optometrist will be able to measure any changes in your vision and examine the back of your eye. If they detect any changes to your macula, they will refer you to an ophthalmologist (hospital eye doctor) for further tests.

## What causes Best disease?

Best disease is a genetic condition. This means it is caused by an altered or ‘faulty’ gene that was inherited from a parent or from a gene fault that developed after conception.

Best disease can be caused by a fault in a gene known as BEST1 (also known as VMD2). Normally, the BEST1 gene provides instructions for making a protein in the retinal pigment epithelium (RPE) layer of cells in the retina. The RPE supports and nourishes the retina, and the protein made by the BEST1 gene acts as a funnel to allow transport of fluid in and out of the RPE cells to keep them working properly.

If there is a fault in your copy of BEST1, these protein funnels don’t work as they should, which causes damage to the RPE cells and a build-up of cell waste material. With damage to the RPE, the cells of the retina start to die as they are no longer supported or nourished in the same way.

Researchers have identified hundreds of different faults within this one gene which can lead to several macular dystrophies, collectively known as bestrophinopathies. These include:

* Best vitelliform macular dystrophy (Best disease)
* Adult-onset vitelliform macular dystrophy
* Autosomal recessive bestrophinopathy
* Autosomal dominant vitreoretinochoroidopathy
* Retinitis pigmentosa (RP)

### Adult onset vitelliform macular dystrophy

Adult-onset vitelliform macular dystrophy is slightly different to Best disease because in adult-onset vitelliform macular dystrophy there are fewer changes at the back of the eye; the changes begin much later in life and they do not progress in the same way. Adult-onset vitelliform macular dystrophy usually begins around the age of 30 to 50 with mild or moderate changes in vision. The change to vision can be so small that often it’s detected by chance through a routine eye examination. In general, adult-onset vitelliform dystrophy has less impact on vision than Best disease.

In most cases of the adult-onset form of vitelliform macular dystrophy, the cause is unknown. However, in some cases, faults can be found in either the BEST1 or in other identified genes including PRPH2, IMPG1 or IMPG2. Many people with adult-onset vitelliform macular dystrophy do not have a fault in any of these genes and the cause remains unknown.

The inheritance pattern of adult onset vitelliform macular dystrophy is not yet clear. Not everyone who has the condition has a family history and not everyone who inherits a faulty gene develops symptoms. The symptoms are blurred or distorted central vision. The condition progresses very slowly, and many people may retain good vision into later life.

#### How are genes inherited?

All genes come in pairs. You inherit one copy of the gene from each of your parents to make a pair. Your genes give the cells in your body the instructions they need to work well and stay healthy. When a gene is faulty, the genes do not give their instructions correctly to the cells and the cells then don’t develop or work as they should.

There are several ways a faulty gene can be passed down from parents. These are known as patterns of inheritance.

### Autosomal dominant inheritance

Best disease is inherited in a dominant pattern.

Dominant inheritance means that a condition is inherited from a faulty gene from only one of your parents. A faulty gene paired with a normal gene from your other parent, will be enough to ‘switch on’ the trait or condition. This is because the faulty gene is dominant over the normal gene in the gene pair.

This means, if a person has one faulty copy and one healthy copy of the gene, they will have Best disease and will have a 50 per cent chance of passing the faulty gene on to each child they have. If a child doesn’t inherit the faulty Best disease gene, they cannot pass it on to their children.

### Autosomal recessive inheritance

More recently researchers have discovered that some faults in the BEST1 gene can be inherited in a recessive pattern. This means that you need to inherit two copies of the faulty gene (one from each of your parents) to be affected by the condition. This is a rarer type of macular dystrophy, known as autosomal recessive bestrophinopathy.

#### Genetic testing and counselling

If there is Best disease in your family, you may find it helpful to speak with a genetic counsellor, a consultant geneticist, or an ophthalmologist with a specialist interest in genetics.

Genetic testing can help to confirm the gene responsible for Best disease and how it has been inherited. Genetic counselling can help you understand how Best disease has been passed through your family and the chances of passing it on to future children.

Genetic counselling is a free NHS service. You can ask your GP or your ophthalmologist to refer you to your local genetic service.

## How does Best disease affect the eye?

Early signs of Best disease usually develop between the ages of three to 15. In these early stages, Best disease doesn’t always have much effect on vision, so a child may not notice a sight problem. Sometimes these early changes are picked up at an eye examination by an optometrist.

Even though someone may have changes to their macula because of Best disease at an early age, they may not develop vision problems until much later in life - often over the age of 40.

### The five stages of Best disease

There are five stages to Best disease which can be seen by the optometrist or ophthalmologist when they look at the macula. None of these stages cause eye pain.

**Stage 1.** At this stage your macula looks healthy, although there may be subtle changes to a layer underneath the macula, there is generally no effect on vision.

**Stage 2.** This stage is called the vitelliform stage. At this stage, there is a blister on your macula area which looks like an egg yolk. Although the optometrist or ophthalmologist can see these changes, often there is no effect on vision or only very slight changes to vision. Usually, this stage occurs between the ages of three and 15 years.

**Stage 3.** This stage is called the pseudohypopyon stage. With this stage, some of the yellow matter which causes the egg yolk-like blister can breakthrough a layer under your retina. This leads to a cyst forming under the retina. Again, there may be little change to your vision. This stage is usually seen in the teenage years.

**Stage 4.** This stage is called the vitelliruptive stage. In this stage, the blister begins to break up and can cause damage to some of the cells in the layers of your retina. At this point, you may start to notice that straight lines look wavy, or you have problems with reading small print.

**Stage 5.** This is the final stage of Best disease. It is called the atrophic stage. The yellow matter which caused the blister begins to disappear. However, it leaves behind scarring and damaged cells on your retina. At this stage, your sight is affected more, and you may find reading difficult.

Not everybody will pass through all these five stages and your condition may remain stable in any one of these stages.

Some people also develop another stage called choroidal neovascularisation (CNV). During this stage, the eye tries to fix the damage to the macula by growing new blood vessels. Unfortunately, these new blood vessels are very leaky and bleed easily, which can lead to scar tissue forming and further reduction in sight. However, most people with Best disease do not experience CNV. If you have any sudden change in your vision, you should be seen urgently by an ophthalmologist to ensure you do not have CNV. CNV can be treated if detected at an early stage.

You can have Best disease for a long time without having any sight difficulties. Your sight is not normally affected until stage 4 or 5 which may not develop until over the age of 40, although it can occur as early as in your late 20s. It is not possible to know exactly when or how much your sight will be affected as it can vary from person to person.

Not everyone with Best disease has the same kind of progression or sight problems. Some people will not progress beyond the early stages of the condition and so maintain good vision. Many people will have good vision until they reach their 50s and some people will retain reading vision in one eye throughout life. Vision loss is usually extremely slow in people before the age of 40.

## How is Best disease diagnosed?

If an optometrist detects any changes at the macula which could be Best disease, they would refer you to an ophthalmologist for further tests and diagnosis.

The ophthalmologist will examine your retina. Your vision will be checked, and your pupils dilated to allow the ophthalmologist to look at the macula and see any changes Best disease may have caused.

Sometimes the ophthalmologist can tell you if they think you have Best disease from this examination. However, your ophthalmologist may suggest further tests which may include the following:

## Fluorescein angiogram

The ophthalmologist can usually see the damage to your retina by looking at the back of your eyes, but they can't see the network of blood vessels underneath it. A fluorescein angiogram is a way of taking pictures of these blood vessels which allows the ophthalmologist to see if there are any changes which could be causing problems.

Before a series of pictures is taken, a yellow dye called fluorescein is injected into your arm which then travels through your bloodstream to your eye. This usually isn't painful but can make some people feel sick. This dye makes the blood vessels visible in the pictures taken.

Once the dye has been injected, you will be asked to look at a special machine. The machine takes pictures of the back of your eye as the dye is travelling through the blood vessels. You'll experience a series of flashing lights as the pictures are taken, but the test is not painful. It usually takes about 10 minutes.

It is a very common test and very few people have any serious side effects. Fluorescein dye may give your skin a slightly yellow tinge, but it’s soon removed from the body by passing into your urine. This may appear a darker yellow than normal for up to three days, but often it fades quicker than that.

## Optical Coherence Tomography (OCT)

OCT allows photos to be taken of the back of your eye which provide your ophthalmologist with cross-sectional images of the retina, a bit like a 3D image of the inside of your eye. Quite often, a fluorescein angiogram and OCT are both used to obtain a thorough picture of the retina.

## Optical Coherence Tomography Angiogram (OCT-A)

OCT-A is similar to an OCT image, but it can also show the health of the blood vessels in the retina without a dye being injected into the body. It can sometimes be used instead of a fluorescein angiogram.

## Electrodiagnostic tests

Electrodiagnostic tests can tell your ophthalmologist how well your retina is working. They check how your retinal cells respond to patterns and different lighting conditions.

## Electroretinography (ERG):

An electroretinogram (ERG) looks at how well the retinal rod and cone cells are working. The ERG tests the whole of your retina, but the pattern electroretinogram (PERG) uses a checkerboard pattern to test how your macula is working.

During an ERG test you are asked to look at a screen which displays patterns of lights including flashes and checkerboard patterns. Your pupils are dilated with eye drops and anaesthetic drops will also be put into your eyes to numb them so that you don’t feel any pain. You’ll have a small electrode placed on or near the front of your eyes. This can be a bit like placing a contact lens in your eye. Another electrode is placed on the skin near your eyes. The electrodes measure your retina's response to the light patterns and are recorded on an electrical trace or plot.

## Electro-oculography (EOG):

The EOG test measures how the rods and cones and the retinal pigment epithelium behind them are working. Electrode pads are placed on your skin near to the nasal (nose) side of your eye and on the temporal (outer side), of your eye. The electrodes are not placed in or on your eye.

You will be asked to look at different lights when they light up. Often this means you are looking back and forth between illuminated targets. The lights will alternate back and forth at different speeds whilst your eyes follow them. Some of this test will take place with the overhead room light dimmed or off, and some of the test will be performed with the overhead room lights on. The EOG can be particularly useful to diagnose Best disease.

## Is there any treatment for Best disease?

Unfortunately, there is no treatment for Best disease at the moment. Although many advances are being made in identifying genes responsible for Best disease, this hasn’t yet led to a treatment.

A small minority of people with Best disease may develop new blood vessels on or under their macula, medically called choroidal neovascularisation (CNV). There is treatment for CNV which aims to prevent further sight loss.

New blood vessels can be treated with an anti-VEGF drug injection. Although treating new blood vessels may not lead to a great improvement in sight, it often helps to prevent further damage to the macula and to sight.

Anti-vascular endothelial growth factor medications (Anti-VEGFs) are drugs which stop or reduce the growth of new blood vessels. This can slow their leakage and slow down vision loss. Anti-VEGFs are not yet automatically available on the NHS for people with vitelliform macular dystrophy related CNV, but your ophthalmologist is best placed to decide what treatment is needed in your individual case.

Gene therapy is currently being researched as a possible treatment for different types of inherited macular dystrophies. Gene therapy aims to replace the faulty gene with a new gene that works properly. Normal genes are injected into the retina using a harmless virus to carry the genetic material. The hope is that the affected retinal cells begin to work properly, and the damage is either stopped or reversed. Gene therapy is in its early stages in the hope of finding future treatments. No gene therapy treatment is currently available for Best disease. At the moment, one gene therapy treatment is available for a specific type of inherited retinal dystrophy (caused by faults in a gene called RPE65). This gives hope that in the future, a similar successful gene therapy treatment could be developed for other inherited retinal eye conditions such as Best Disease.

There is currently no research to show that diet can help to slow down the progression of Best disease. However, a good diet full of fresh fruit and vegetables can help with eye health in general. Smoking is known to accelerate other forms of macular disease so it would be sensible to stop smoking, as this may help delay progression of Best disease also.

## Looking after your sight

Even though there is no treatment for Best disease, it is very important you receive long-term follow-up care to monitor your condition and its progression. Having regular checks with the hospital or optometrist will ensure that if there are any signs of CNV, this can be detected and treated as early as possible.

If you notice a sudden change in vision in either of your eyes, you should see your optometrist or let your eye clinic know straight away so that your risk of developing CNV can be assessed, as sight saving treatment may be possible.

The risk of developing CNV may be increased by head trauma. Therefore, it makes sense to take extra precaution in situations where you might get a bang on the head, for example, by avoiding contact sports or wearing a bicycle helmet when cycling.

Even if you have only slight changes in your vision, you should arrange for an eye examination with your optometrist. They are trained to detect any eye problems and, if necessary, can refer you to an ophthalmologist at the hospital.

People with Best disease have a much higher chance of being long-sighted. Long-sightedness means your eyes have difficulty focusing close up. Long-sightedness can be easily corrected with glasses.

Although glasses or contact lenses cannot correct vision problems caused by Best disease, your optometrist might be able to improve your long-sightedness or short-sightedness with glasses to help give you the best vision possible. Your optometrist will check your glasses prescription at your regular eye examination to make sure your glasses, if needed, are the right strength for you.

**It is important to remember that many young people who have Best disease may have good vision for a long time and may only need help when and if their Best disease progresses to the later stages.**

## Help to see things better

Best disease can cause problems with your central vision. However, most people with Best disease have some vision they can use every day and using your vision won't make your Best disease worse.

There are lots of things that you can do to make the most of the vision you have. This may mean making things bigger, using brighter lighting, or using colour to make things easier to see. We have a series of leaflets with helpful information on living with sight loss, including how to make the most of your sight. You can find out more about our range of titles by contacting our Helpline.

You can ask your ophthalmologist, optometrist or GP about low vision aids and having a low vision assessment. During this assessment you’ll be able to discuss the use of magnifiers and aids to help you see things more clearly.

Local social services should also be able to offer you information on staying safe in your home and getting out and about safely. They should also be able to offer you some practical mobility training to give you more confidence when you are out.

Depending on how much of a person’s sight is affected by Best disease, they may be eligible to be registered as sight impaired (partially sighted) or severely sight impaired (blind). An ophthalmologist would be able to tell you if you are eligible. Registration can act as a passport to help and sometimes to financial concessions, but a lot of this support is still available to people who are not registered.

## Coping

If you have been diagnosed with Best disease, it’s normal to find yourself worrying about the future and how you will manage with a change in your vision.

It can sometimes be helpful to talk about these feelings with someone outside your circle of friends or family. At RNIB, we can help with our telephone Helpline and our Counselling and Wellbeing team. Your GP or social worker may also find a counsellor if you feel this might help.

The Macular Society runs local groups which meet throughout the country, they also offer a telephone counselling service. Sometimes it can help to talk about your feelings or share with people who may have had similar experiences.

Your eye clinic may also have an Eye Care Liaison Officer (ECLO), who can be on hand to provide you with further practical and emotional support about your child’s or your own eye condition.

## Sources of support

### RNIB Helpline

If you need someone who understands sight loss, call our Helpline on **0303 123 9999**, say "**Alexa, call RNIB Helpline**" to an Alexa-enabled device, or email **helpline@rnib.org.uk**. Our opening hours are weekdays from 8am – 8pm and Saturdays from 9am – 1pm

You can also get in touch by post or by visiting our website:

**RNIB**

Grimaldi Building

154a Pentonville Rd

London N1 9JE

**rnib.org.uk**

### Sight Advice FAQ

Ask the Sight Advice FAQ website your questions about sight loss and get helpful answers: **sightadvicefaq.org.uk**

### Connect with others

You can meet or connect with others who are blind or partially sighted online, by phone or in your community to share interests, experiences and support for each other. From book clubs and social groups to sport and volunteering, our friendly, helpful and knowledgeable team can link you up with opportunities to suit you. Visit **rnib.org.uk/connect** or call our Helpline.

## Other useful organisations

Macular Society

PO Box 1870

Andover SP10 9AD

Tel: **0300 3030 111**

Email: **help@macularsociety.org**

Web: **macularsociety.org**

Genetic Alliance UK

Creative Works

7 Blackhorse Lane

London E17 6DS

Email: **contactus@geneticalliance.org.uk**

Web: **geneticalliance.org.uk**

Gene Vision

A resource on rare genetic eye disorders for everyone. Visit **gene.vision**

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Send your comments to us by emailing us at **eyehealth@rnib.org.uk** or by writing to the Eye Health Information Service, RNIB, Grimaldi Building,154a Pentonville Road, London N1 9JE.

## Information sources

This factsheet has been written by the RNIB Eye Health Information service. Our factsheets have been produced with the assistance of patient and carer input and up-to-date reliable sources of evidence. The accuracy of medical information has been checked by medical specialists. If you would like a list of references for any of our factsheets, please contact us at **eyehealth@rnib.org.uk**.

Our factsheets are available in a range of formats including print, audio, and braille.

RNIB is a member of the Patient Information Forum (PIF) and have been certified under the PIF TICK quality mark scheme.



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