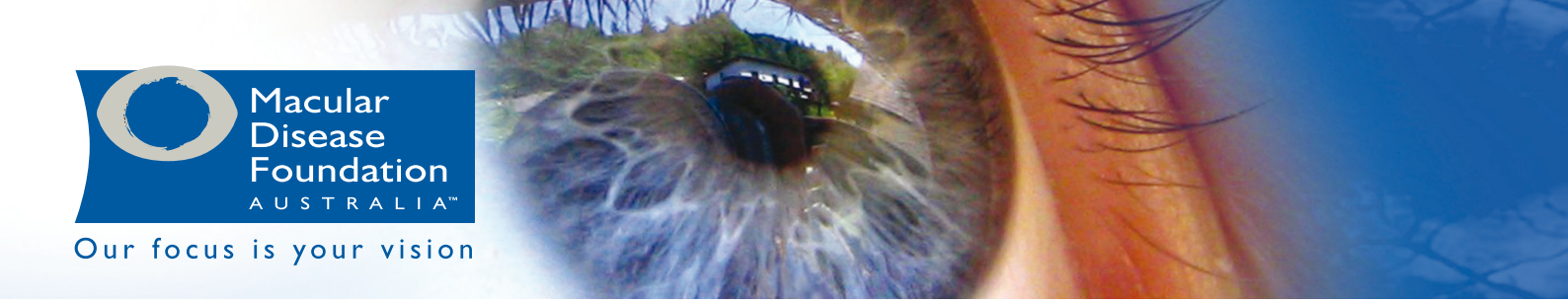

Macular Disease Foundation AUSTRALIA™

Our focus is your vision

# Vitelliform macular dystrophy (Best's disease)

Vitelliform macular dystrophy is a genetic eye disorder that can cause progressive vision loss. This disorder affects the retinal pigment epithelium (RPE) layer underneath the light sensitive cells (photoreceptors) of the macula at the back of the eye. Sight loss can be variable and can affect central vision in one or both eyes.

## How the eye works

Light passes through the cornea at the front of your eye, and is focused by the lens onto your retina. The retina is a delicate tissue that lines the inside of your eye. The retina converts the light into electrical signals that travel along the optic nerve to your brain. The brain interprets these signals to "see" the world around you.

Light from the object you are looking at directly is focused onto a tiny area of the retina called the macula at the back of the eye. The macula is about 4mm across and is responsible for detailed central vision and most colour vision. It provides the vision you need to read, recognise faces, drive a car, see colours clearly, and any other activity that requires detailed, fine vision. The rest of the retina gives you side vision (peripheral vision).

## Progression of vitelliform macular dystrophy

Vitelliform macular dystrophy causes a fatty yellow pigment (lipofuscin) to build up in the RPE layer, forming a lesion that has the appearance of an egg yolk (vitelliform means looking like an egg yolk). Over time, the abnormal accumulation of this substance can damage cells that are critical for clear central vision. As a result, people with this disorder often lose their central vision, and their sight may become blurry or distorted. Vitelliform macular dystrophy typically does not affect side (peripheral) vision or the ability to see at night.

There are two forms of vitelliform macular dystrophy with similar features. The early-onset form (known as Best's disease, named after Franz Best who first identified the disease in 1905), usually appears in childhood; the onset of symptoms and the severity of vision loss vary widely. The adult-onset form usually begins in mid-adulthood, and generally causes relatively mild vision loss that worsens slowly over time. The two forms of vitelliform macular dystrophy each have characteristic changes in the macula that can be detected during an eye examination. Electro-oculogram tests, which assess the electrical response of the retina when stimulated by light, can be part of the testing used to identify people with the problem.

# Genetics of vitelliform macular dystrophy

## Genetic inheritance

Genes are basically the body's set of instructions on how the body should develop. We all inherit two sets of genes, one set from each of our parents, and we each pass on one of those sets of genes to our children. These sets of genes 'lie' in pairs (one from each parent) and they determine our traits - the many things which make us individuals, such as hair or eye colour, or whether we get certain genetic conditions. There are two ways a trait can be passed through genes to children - by a dominant pattern or a recessive pattern.

## Difference between dominant and recessive traits

A dominant trait only needs to be inherited from one parent. With this type of inheritance, only one copy of the gene is needed. When a dominant gene from one parent is paired with a recessive gene from the other parent, the dominant gene 'switches on' the trait. It is 'dominant' over the other (recessive) gene inherited from the other parent and the child will have that dominant trait.

With recessive traits, two copies of the gene are needed, meaning both parents have to carry and pass on a copy of the recessive gene. When this happens, the recessive trait will be 'switched on' and the child will have that recessive trait.

## How vitelliform macular dystrophy fits into these patterns

Vitelliform macular dystrophy is inherited in an autosomal dominant pattern which means children of an affected parent have a 50% chance of receiving the gene.

The early onset form (Best's disease) is caused by mutations in the BEST1 gene. In most cases of the adult-onset form, the cause is unknown, although in about a quarter of cases, mutations can be found in either the BEST1 or PRPH2 gene.

The BEST1 gene provides instructions for making a protein called bestrophin. This protein acts as a channel that controls the movement of charged chlorine atoms (chloride ions) into or out of cells in the retina. Mutations in the BEST1 gene probably lead to the production of an abnormally shaped channel that cannot properly regulate the flow of chloride. Researchers have not yet determined how these malfunctioning channels are related to the build up of lipofuscin in the macula and progressive vision loss.

The PRPH2 gene provides instructions for making a protein called peripherin2. This protein is essential for the normal function of light-sensing (photoreceptor) cells in the retina. Mutations in the PRPH2 gene cause vision loss by disrupting structures in these cells that contain light-sensing pigments. It is unclear why PRPH2 mutations affect only central vision in people with adult-onset vitelliform macular dystrophy.

As with other autosomal dominant conditions, it is likely that there would be several affected individuals in successive generations but Best's can be erratic and may miss a generation.

Further information and genetic counselling will be available from a specialist clinic and your GP will be able to advise you about local genetic services. Tests are available to determine which gene mutation is causing the disease in most cases. People with Best's disease/vitelliform macular dystrophy may also wish to be entered onto the Australian Inherited Retinal Disease Register and DNA Bank - phone (08) 6457 2866, located at Sir Charles Gairdner Hospital in Perth.

## Stages of vitelliform macular dystrophy

The appearance of the vitelliform lesions is generally grouped into 6 stages:

- Stage I (Previtelliform): normal vision, normal or only subtle RPE changes with abnormal electro-oculogram. Often not detected at this stage.
- Stage II (Vitelliform): usually between 10 and 25 years of age. Classic "egg-yolk" lesion. 30% have ectopic lesions (away from the macula). Normal vision or mild vision loss.
- Stage III (Pseudohypopyon): layering of lipofuscin. Vision similar to stage II.
- Stage IV (Vitelliruptive): breakup of material gives a "scrambled egg" appearance. Vision may be similar or mildly decreased from stage I/II.
- Stage V (Atrophic): Central RPE and retinal atrophy. Vision may range from 6/9 – 6/60.
- Stage VI (Choroidal neovascularisation or CNV): This complication occurs in about 20% of patients. Vision often decreased to 6/60 or worse (legal blindness). May be treatable with anti-VEGF injections.

## Treatment

There is currently no effective treatment for vitelliform macular dystrophy, but scientific research, both traditional and genetic, may provide useful treatments for the future.

In some people, usually during the later stages of the disease, new, leaky blood vessels may form under the retina, in a process called neovascularisation. This is similar to what happens with the 'wet' form of age-related macular degeneration. This can lead to a rapid loss of central vision, however it can now be treated very effectively in most cases with a series of injections of an anti-VEGF drug into the eye. Since this treatment is most effective when given soon after the formation of the new blood vessels, it is recommended that people with vitelliform macular dystrophy should self-monitor their vision, one eye at a time, using an Amsler grid. Any sudden changes in the appearance of the Amsler grid (e.g. distortion, blurry or blank patches) should be checked by the ophthalmologist immediately as this may be a sign of neovascularisation.

There is no specific evidence regarding the effect of diet on the progression of vitelliform macular dystrophy, but the adoption of an eye-health diet, as recommended for age-related macular degeneration, may be beneficial. This includes the

consumption of fish two to three times a week, daily leafy greens and other fruit and vegetables, a handful of nuts a week, and where possible, eating low glycemic index (GI) carbohydrates in preference to high GI.

## Managing vision loss

When managing vision loss, a key priority is maintaining quality of life and independence. Contacting a low vision organisation can be helpful as they can work with you to assess your individual needs and determine which aids and technologies can help. There are many excellent solutions to help you live well with low vision.

## Macular Disease Foundation Australia Resources

Macular Disease Foundation Australia has developed a comprehensive range of publications on macular degeneration, diabetic eye disease and other macular diseases. Information and advice on living well with vision loss is also available. Call the Foundation for a free information kit or to register to receive newsletters and invitations to attend education sessions and events.

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July 2015