Macular conditions – Genes and genetic testing

The chance of developing a particular condition often depends on both environmental and genetic factors. For some conditions, it's mainly environmental. For some, such as juvenile macular dystrophy, it's mainly genetic and for others, such as age-related macular degeneration (AMD), the chance is more evenly split between genetics and environment.

Genes and inheritance

Genes are segments of DNA, arranged on chromosomes. We all have about 20,000 genes. They act like recipes, making proteins that influence how our bodies grow and function. If genes are altered or damaged, they may not work properly, just like a recipe with a missing ingredient. These alterations can influence our risk of getting particular conditions.

Genes act in pairs and we get one copy of each gene from

each of our parents. The way in which a disease is passed from one generation to another is called the pattern of inheritance. There are three main inheritance patterns known as dominant, recessive and X-linked inheritance.

Dominant inheritance: When an alteration in only one copy of a gene causes a genetic condition, the inheritance pattern is said to be dominant. People with a dominant condition have usually inherited the condition from a parent. They will have a 50% chance (1 in 2) of passing the altered gene onto each child they have. Most people with the altered gene will develop visual problems.

Recessive inheritance: When alterations in both copies of a gene are needed to cause a genetic condition, the inheritance pattern is said to be recessive. An altered gene will have been inherited from both parents. They may not have the condition themselves but are “carriers” of an altered copy of the gene. This means that they have one altered copy of the gene but also another working copy. When both parents are carriers they will have a 25%

chance (1 in 4) of passing the condition on to each child they have.

Dominant and recessive conditions affect both sexes equally.

X-linked inheritance: Some genetic conditions are caused by altered genes on the X chromosome. They usually affect males only. This is because males have only one X chromosome and so only one copy of all the genes on that chromosome. If that copy is altered, there is no working copy of the gene. Females have two X chromosomes. If one copy of a gene is altered, they have another, working copy in reserve and will usually not be affected.

Your eye doctor may spend some time asking about other family members to work out the pattern of inheritance. In some families the condition may have been present for several generations but in others there may be no other affected family members.

Genetic testing

Genetic testing involves looking for altered genes in a sample of DNA taken from a person's blood or, sometimes, saliva. A positive test result means that an altered gene has been identified. Genetic testing for eye disease is becoming more common. Testing may help provide or confirm the diagnosis or the pattern of inheritance.

It may also explain the reason for an eye problem and provide a better idea of future vision. Less commonly it may be used to help couples plan their families or to identify people who are likely to develop eye disease as they get older. In the future, it is hoped that genetic testing may also help to identify new treatments.

There can also be some downsides to genetic testing. Testing often takes several months and, even then, the results may be inconclusive or provide a different diagnosis or inheritance pattern from what was expected. Parents can feel guilty that they have passed a condition onto their children and some people can find explaining the implications of test results to other family members difficult. At present, insurance companies in the UK do not

routinely ask for the results of genetic testing. Given the potential benefits and risks, the decision about whether to seek genetic testing is a personal one. After discussing the options with your eye doctor or a genetic counsellor, you may need some time to make a decision. It is also usually best to discuss the potential implications with your partner and family before going ahead with any testing.

Genetic testing can often be arranged by your local eye or genetic clinic and the samples are analysed through accredited NHS laboratories. A small number of genetic tests are also available over the internet. You need to pay for these tests yourself and usually send a cheek swab directly to a laboratory. Although this testing is designed to help you understand the genetic risk of particular conditions, the results may only provide part of the answer. It can help to discuss any plans for this type of testing with your doctor.

At present several hundred genes causing macular and other retinal dystrophies have already been identified. Genetic research is ongoing in the UK and other countries

to identify the remaining genes. You may be invited to take part in this research by giving a sample of your DNA for analysis in a research laboratory.

AMD - genes and environment: With a history of AMD in the family, a person is 3 times more likely to develop AMD in later life than someone without any affected relatives. Much of this added risk is genetic. The most important genetic factor is having either one or two altered copies of a particular gene, Complement Factor H (CFH).

The environmental factor most strongly associated with AMD is tobacco smoking. Current smokers have 4 times the risk of ex-smokers or people who have never smoked. However, the risk in smokers falls for each year that they don't smoke.

Written by Martin McKibbin,

Consultant Ophthalmologist, Leeds Teaching Hospitals NHS Trust.

Macular Society

Further information:

www.geneticalliance.org.uk Genetic Alliance UK is a national charity of 150 patient organisations supporting those affected by genetic conditions

www.rpfightingblindness.org.uk information about other inherited retinal conditions and genetics

