All babies born in the UK, and other developed countries, are routinely screened for high phenylalanine levels. This is done using the 'heel prick test' carried out during the first week of a baby's life. A blood sample is taken from the baby's heel to test for a number of rare but serious conditions, including PKU. If phenylketonuria is detected, further tests will be arranged to confirm the diagnosis.

As long as a person with PKU sticks to a low-protein diet throughout childhood and their phenylalanine levels stay within certain limits, they will remain well and their natural intelligence will be unaffected.

Further background information can be found at:

- http://www.nspku.org/
- http://www.nhsinform.co.uk/screening/overview/leaflets/~/media/nhsinform/screeningzone/leaflets/newborn _ july2014.ashx (PKU page 13)

## Pre-implantation genetic diagnosis

It is now possible to tissue type embryos which have been created using in vitro fertilisation (IVF). In pre-implantation genetic diagnosis (PGD) one or two cells from 3-day old IVF embryos are removed and genetically tested. Particular embryos can then be chosen for implantation in the uterus.

One of the things such testing allows is the identification of a potential tissue match for a child who has already been born with a life threatening disease such as severe combined immunodeficiency syndrome. Those embryos which show the greatest likelihood of tissue matching are then implanted into the womb. When the child is born, stem cells may be taken from its umbilical cord, or in some cases from bone marrow, and used to treat their sibling.

PGD can be used to test for virtually any genetic condition where a specific gene is known to cause that condition. In the UK, screening is currently allowed for over 250 genetic conditions: http://guide.hfea.gov.uk/pgd/. Screening for a condition which has not been approved, requires application to the Human Fertilisation and Embryology Authority (HFEA). For approval to be granted the HFEA must, by law, agree that the condition meets certain criteria.

Further background information can be found at:

- http://www.hfea.gov.uk/preimplantation-genetic-diagnosis.html
- http://www.geneticalliance.org.uk/aboutpgd.htm
- http://thetechnologicalcitizen.com/?p=1022

HFEA 'saviour sibling' data can be found at:

- http://www.hfea.gov.uk/8562.html

*These resources were developed by SSERC, supported by the SQA.*



# Human genetic dilemmas

## Background information

### Huntington's disease

Huntington's disease (HD) is a dominant single-gene, late-onset condition. In the UK about one in 10,000 people have the disease. Affected individuals develop the condition in middle age. If either parent has the allele then each son or daughter has a 50% chance of inheriting HD. Because of late-onset of the disease, children are often born before their parents know that they themselves have the disease.

Early signs of the disease are usually behavioural; people become depressed or moody, become easily angry or they have unusual movements, often being described as clumsy.

Over the years symptoms become more severe, walking becomes difficult and the person suffers from dementia. Following diagnosis sufferers typically survive for 10-20 years. No treatment is currently available.

Further background information can be found at:

- http://www.hda.org.uk/
- http://www.nhs.uk/conditions/huntingtons-disease/Pages/Diagnosis.aspx
- http://en.hdbuzz.net/041

Data on a specific aspect of Huntington's disease can be found at:

- http://path.upmc.edu/cases/case669/dx.html

### Achondroplasia

Achondroplasia is an autosomal, dominant condition which is caused by a single gene mutation on chromosome 4. Achondroplastic individuals are heterozygous for the affected gene (babies with two copies of the mutant gene do not normally survive longer than a few months). The condition is passed from one generation to the next by one of two routes. Firstly, affected individuals (i.e. those who are achondroplastic) may pass on the condition to their offspring. Secondly, the condition may be passed on as a result of a mutation which occurs in development of either the sperm or ova from parents who themselves show no sign of the condition in their own DNA. Nine out of ten achondroplastic children have parents who are not themselves achondroplastic.

People with achondroplasia are short in stature and this is particularly noticeable in the upper arms and thighs. Other signs are a prominent forehead and a flat area at the base of the nose. People who have achondroplasia often also suffer from ear infections, dental problems and orthopaedic conditions. Intelligence is not affected in individuals with the condition. A couple, one of whom is achondroplastic, has a 50% chance of having a heterozygous achondroplastic child, and a 50% chance of having a non-achondroplastic child. If both parents are achondroplastic they have a 50% chance of having an achondroplastic child, a 25% chance of having a non-achondroplastic child and a 25% chance of having a child with 2 copies of the gene (i.e. homozygous for the achondroplasia gene).

Further background information can be found at:

- http://www.restrictedgrowth.co.uk/Achondroplasia.html
- http://www.medicinenet.com/achondroplasia/article.htm
- http://www.visionproject.org/images/img _ magazine/pdfs/achondroplasia.pdf

## Cystic fibrosis

Cystic fibrosis (CF) is an autosomal recessive disorder caused by a large number of different mutations mostly localised on chromosome 7. CF is relatively common in people of European origin affecting about 1 in 2000 births in the UK. Roughly 1 in 25 people carry one copy of the CF gene. People with CF are affected to different degrees. The most common symptoms are respiratory because thick mucus is produced in the lungs. Infections are common and each infection causes the lungs to become more damaged and consequently the person's health progressively deteriorates. Digestive problems due to lack of digestive enzymes are common and males with CF are often infertile.

If both parents are carriers then their children have a 25% chance of having CF; a 50% chance of having children who are carriers and a 25% chance of having children free of the condition. Carriers show no symptoms of the disease. Various treatments for CF are now available including gene therapy and, in general, CF patients are now living longer and IVF treatment is possible to treat infertility for some male sufferers.

Further background information can be found at:

- http://www.cysticfibrosis.com/
- http://www.nhs.uk/Conditions/Cystic-fibrosis/Pages/Introduction.aspx
- http://www.cf-europe.eu/

Data on the changes in life expectancy of people suffering from cystic fibrosis can be found at:

- http://www.disabled-world.com/health/respiratory/cystic-fibrosis/life-expectancy.php

## Tay-Sach's

Tay-Sach's is an autosomal, recessive genetic disorder which affects the central nervous system. The condition is common among Ashkenazim Jews (from Eastern Europe) and most carriers of the gene are related. Within certain orthodox Jewish New York communities, one person in 18 carries the gene compared with one in 300 in the USA as a whole. Children born with Tay-Sach's do not thrive well. The condition causes progressive destruction of nerve cells by the build up of poisonous waste products leading to early death.

Carriers of Tay-Sach's show no signs of the disease. There is a 25% chance that a child born to two carriers would have the condition. The gene which causes Tay-Sachs has been identified and a test is available to identify carriers.

Further background information can be found at:

- http://www.tay-sachs.org/taysachs _ disease.php
- http://www.nhs.uk/Conditions/tay-sachs-disease/Pages/introduction.aspx
- http://jama.jamanetwork.com/article.aspx?articleid=369230

## Familial hypercholesterolaemia

Familial hypercholesterolaemia (FH) is an inherited condition that causes high levels of LDL (low density lipoprotein). These high cholesterol levels begin at birth, and heart attacks can occur at an early age. FH is an autosomal dominant inherited condition. A parent who carries an altered gene for the condition has a 1 in 2 chance of passing it on to each of his or her children. The gene mutation that causes FH is located on chromosome 19. One in 500 individuals has FH. These individuals are usually heterozygous for the condition. More rarely individuals can be homozygous and have a much more severe form of hypercholesterolaemia, with heart attack and death often occurring before age 30.

Men with FH can have heart attacks in their 40's to 50's, and 85 percent of men with the disorder have a heart attack by age 60. Women with FH also have an increased risk of heart attack, but these usually happen in their 50's or 60's. Sufferers are offered medication to help bring their cholesterol level down. The usual medication to start with is a statin and affected children usually start statin medication in late childhood or early adolescence. Some children may need apheresis, a treatment which filters LDL cholesterol out of the blood. Apheresis is offered to those who have the greatest risk of developing problems - in particular, those with the rare homozygous form of FH. The outlook for people with heterozygous FH is usually good if they maintain a healthy lifestyle, have regular checks and take their medication without fail. The outlook for those with the more severe (homozygous) form of the condition is less good.

Further background information can be found at:

- http://www.patient.co.uk/health/familial-hypercholesterolaemia
- http://www.genome.gov/25520184
- https://www.bhf.org.uk/heart-matters-magazine/medical/familialhypercholesterolaemia

Data on specific aspects of treatment of high cholesterol can be found at:

- http://www.nice.org.uk/guidance/CG181/chapter/Introduction (follow Appendix A)

## Phenylketonuria

Phenylketonuria (PKU) is a rare congenital (present from birth) genetic condition. People with PKU are unable to break down an amino-acid called phenylalanine due to the lack of the appropriate enzyme, phenylalanine hydroxylase. Phenylalanine then builds up in the blood and brain. High levels of phenylalanine can damage the brain. PKU is treated with a special low-protein diet, which reduces the levels of phenylalanine in the body and prevents brain damage. PKU doesn't usually cause any symptoms if treatment is started early. If PKU isn't treated, damage to the brain and nervous system can lead to:

- learning disabilities
- behavioural difficulties
- epilepsy

Phenylalanine is an amino acid present in high-protein foods, such as:

- meat
- fish
- eggs
- cheese
- milk