Case studies

The following case scenarios were written to provide examples of the types of conditions that could looked for in the Newborn Genomes Programme, if they meet our principles.

They are not based on a single family's experience; the Newborn Genomes Programme team have written these with the aim of highlighting how parents might experience finding out about results in the context of newborn screening.

Familial hypercholesterolaemia (FH)

Eli and Susan's second child, Amy, is born with mild jaundice but has otherwise been well. They have an older son, Ethan, who is 6 years of age and also healthy. The couple receive a telephone call from Jordan, a specialist nurse who explains that Amy's newborn screening test was positive for a condition called familial hypercholesterolaemia (FH). Jordan explains that no urgent action is needed, but would like to arrange an appointment for the family to meet along with a doctor who specialises in this condition.

At the appointment, Jordan takes a family history and explains that individuals with FH have very high cholesterol which causes an increased risk of heart disease and heart attacks. Eli and Susan are told that although the risk of heart disease is primarily in adulthood, treatment would need to start earlier in childhood. Treatment involves taking medication (called statins) which lowers cholesterol levels. This treatment is usually started between the ages of 5 and 10. Jordan also discusses the importance of maintaining a healthy diet, regular exercise, and not smoking.

Jordan also explains that if Amy is confirmed to have this condition, then it is likely that she inherited this from either Eli or Susan. If the test indicates they have FH, treatment using statins could begin immediately, and other relatives in the family could also be tested. They are provided with information from the British Heart Foundation and are surprised to learn that this condition is relatively common, affecting 1 in 250 people.

Where can I learn more?

- British Heart Foundation: www.bhf.org.uk/informationsupport/conditions/familial-hypercholesterolaemia
- Health Education England: https://www.genomicseducation.hee.nhs.uk/documents/familial-hypercholesterolaemia/

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Hereditary fructose intolerance

Morgan is a single parent to a newborn called Tim, who was born after an emergency C-section. Morgan receives a call from Louise, a metabolic specialist nurse, who explains that Tim's newborn screen test showed that he may have hereditary fructose intolerance. Louise briefly explains that this condition could cause problems when Tim starts eating fruit and drinking juices or other formulas which could include fructose. Louise offers an appointment to discuss the condition further.

At the appointment, Morgan is told that the condition is caused by a gene that affects how fructose, a sugar found in many foods, is processed. When children with this condition consume fructose, they can get tired, have diarrhoea or vomit, or experience more serious issues such as seizures, organ damage, or coma. Morgan asks how they know for sure that Tim has this condition, as he looks perfectly healthy and well. Louise reviews Tim's genetic result (showing alterations in a gene called *ALDOB*). She explains that a liver biopsy could be done to look at the protein that wouldn't be processing fructose properly to confirm the diagnosis, but notes that this is an invasive procedure. She explains that if Tim avoids any formulas or foods that contain fructose (and gives Morgan a list of what this includes), this should not have any impact on his quality of life.

Where can I learn more?

- MedlinePlus (US): https://medlineplus.gov/genetics/condition/hereditary-fructose-intolerance/
- National Library of Medicine (US): https://www.ncbi.nlm.nih.gov/books/NBK333439/

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Immunodeficiency 41

Alex and Daniel have three heathy children and have just welcomed their fourth child, Arya. They are contacted by Dr Jackson who explains that Arya's newborn screen test suggests that she has an immune deficiency condition, where she is at greater risk of having multiple infections. Dr Jackson explains that newborns with this condition can develop infections quite early on in life which could cause a number of complications and be life threatening, so he would like to see the family in clinic to discuss this further. She reassures the family that this is a very rare condition but there are interventions available to help manage this.

A couple of days later, Alex, Daniel, and Arya travel to a specialist centre for an appointment with Dr Jackson, who describes in greater detail that there are different medications that can be provided to Arya to manage infections, but that a more permanent treatment would involve a bone marrow transplant. Dr Jackson acknowledges that a bone marrow transplant is a significant procedure and includes its own short- and long-term risks that would be discussed with the family in more depth. She also explains that this condition is caused by changes to a gene, where Alex and Daniel are expected to be carriers. They can provide blood samples to confirm this, and if they are carriers any future children would have a 25% chance of having this condition as well.

Where can I learn more?

- OMIM Catalogue: https://www.omim.org/entry/606367
- Immunodeficiency UK: http://www.immunodeficiencyuk.org/whatarepids/basics

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RPE65-associated retinal dystrophy

Sana and Amal have had two previous miscarriages, and have now given birth to a son, Zain. They are contacted by Dr Jones when Zain is a few weeks old, who explains that the result of Zain's newborn screen test indicates that he has a condition that would affect his sight. Sana and Amal report that they haven't noticed any issues yet with Zain tracking light.

Amal and Sana bring Zain to an appointment with Dr Jones and a genetic counsellor, Sarah, who conduct some eye tests and describe the condition. They explain that two alterations were found in a gene called *RPE65*, causing a type of eye condition called retinal dystrophy which causes significant vision loss in early childhood. Vision loss typically develops before age 5, although it is difficult to determine exactly when this would happen for each individual child.

Dr Jones and Sarah explain that there is a new therapy specific to individuals that have changes in the RPE65 gene. The therapy replaces the non-working copy of the gene and is administered through injection into the eyes. They explain that they need to conduct some further checks to ensure Zain would be able to receive this treatment, and note that there are possible side effects and uncertainties. However they highlight that the therapy could improve Zain's vision and his ability to carry out future activities that depend on vision.

Amal and Sana are told that they are likely carriers for this condition - a blood test could be done to confirm this - which would mean that each of their future children would have a 25% chance of having this condition as well.

Where can I learn more?

- RetinaUK: https://retinauk.org.uk/information-support/luxturna/
- US National Library of Medicine: www.ncbi.nlm.nih.gov/books/NBK549574/
- Medline Plus: https://medlineplus.gov/genetics/gene/rpe65/

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Propionic acidemia

Lorenzo and Stella have just given birth to their first child, Laura. They receive a phone call from Pam, who explains she is a metabolic advanced practice nurse who has news about Laura's newborn screening test. Pam explains that the test suggests Laura has a rare condition called propionic acidemia. Lorenzo and Stella report that Laura has been healthy so far, but Pam explains that this condition can lead to serious health problems and asks that they come into hospital the following day.

The family meet with Pam and a metabolic consultant who describe how they will run some further blood and urine tests to confirm Laura has this condition, as well as scan her heart. They tell Lorenzo and Sarah that there are a number of dietary changes and medications that would need to be put in place as soon as possible to prevent any problems that could occur. Lorenzo and Stella ask what the outlook could be for Laura. They are told that most cases of propionic acidemia cause problems in the first few days of life, with poor feeding, weak muscle tone, tiredness and potentially life-threatening issues. However, less commonly, individuals with the condition can present at a later point, in childhood or adulthood, especially after having had another infection or period without food. They explain that there are a number of other issues that individuals with this condition could develop, including heart problems, delayed development, or seizures - but it is difficult to predict what the outcome would be in each person.

The team make a plan with the family regarding next steps including offering a referral to speak with a genetic counsellor, and provide information about the condition and a UK support group.

Where can I learn more?

- Organic Acidemia Association: https://www.oaanews.org/pa.html
- US National Library of Medicine: www.ncbi.nlm.nih.gov/books/NBK92946/
- Medline Plus: https://medlineplus.gov/genetics/condition/propionic-acidemia/

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