RARE resources ENGLAND

1 Genetic, rare and undiagnosed conditions explained

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Rare Resources is a collection of information guides for families who have recently received a diagnosis of a genetic or rare condition, are on the journey to a diagnosis, or have been told their child's condition is so rare they might not get a diagnosis.

The Rare Resources guides have been developed in collaboration between Genetic Alliance UK and families in the UK. The guides provide links to reliable sources of information and support, and contain 'top tips' from other families.

Rare Resources contains the following guides:

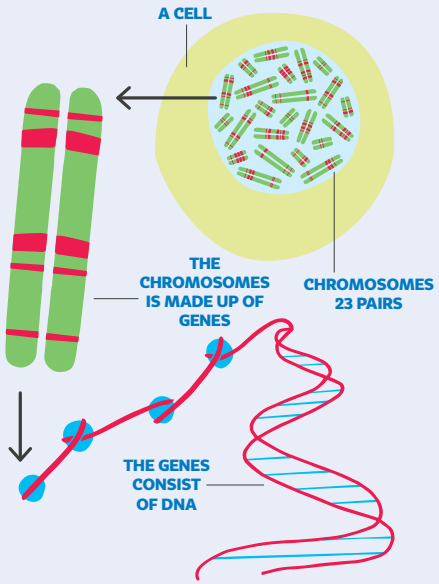
1. Genetic, rare and undiagnosed conditions explained
2. The journey to diagnosis
3. Using NHS England
4. Support and information for parents and carers
5. Support and information for your child
6. Information directory detailing support services available in England

The Rare Resources guides can be downloaded from geneticalliance.org.uk/rr

To request a hard copy of any of the Rare Resources guides, please contact Genetic Alliance UK on 0300 124 0441 or contactus@geneticalliance.org.uk

GENETIC ALLIANCE UK

1.1 What are genetic, rare or undiagnosed conditions?



Genetic, rare and undiagnosed conditions cover a broad range of health conditions that will also vary in their severity and the impact they have. To understand what genetic, rare and undiagnosed conditions are, first we must understand the role of genes and chromosomes.

Genes and chromosomes

Our bodies are made up of millions of cells. Most cells contain a complete set of genes. Genes act like a set of instructions, controlling our growth and how our bodies work.

They are also responsible for many of our characteristics, such as our eye colour, blood type and height. We have thousands of genes.

Genes are located on small thread-like structures called chromosomes. Usually we have 46 chromosomes in most cells. We inherit one set of 23 chromosomes from our mother and one set of 23 chromosomes from our father. So we have two sets of 23 chromosomes, or 23 pairs.

Because the chromosomes are made up of genes, we inherit two copies of most genes, one copy from each parent. This is the reason we often have similar characteristics to our parents. The chromosomes, and therefore the genes, are made up of a chemical substance called DNA.

The chromosomes numbered one to 22 look the same in males and females. These are called the autosomes.

Pair number 23 is different in males and females and they are called the sex chromosomes. There are two kinds of sex chromosomes, the X chromosome and the Y chromosome.

Females normally have two X chromosomes (XX). A female inherits one X chromosome from her mother and one X chromosome from her father. Males normally have an X and a Y chromosome (XY). A male inherits an X chromosome from his mother and a Y chromosome from his father.

It is important that we have the correct amount of chromosome material, as the genes (that instruct the cells in our body) are found on the chromosomes.

Genetic conditions

A genetic condition is caused by changes in an individual's DNA sequence. We all have lots of changes in our DNA sequence and often these don't have any impact.

Sometimes however these changes can result in learning disabilities, developmental delay or other health problems. Genetic conditions can be divided into three different categories: single gene, chromosomal or complex disorders.

Single gene disorders are caused by changes in one particular gene.

There are over 10,000 human disorders caused by a change in a single gene. Individually, single gene disorders are each very rare, but as a whole, they affect about one percent of the population.

Since only a single gene is involved, these disorders can often be easily tracked through families, and geneticists can predict the risk of them occurring in later generations. Single gene disorders can be divided into different categories: dominant, recessive and X-linked.

Examples of single gene disorders include cystic fibrosis, sickle cell disease, fragile X syndrome, muscular dystrophy and Huntington's disease.

Chromosomal disorders result from changes in the number or structure of the chromosomes.

Changes in the number of chromosomes happen when there are more or fewer copies of a particular chromosome than usual. Changes in chromosome structure happens when the material in an individual chromosome is disrupted or rearranged in some way. This may involve the addition or loss of parts of a chromosome.

Examples of chromosomal disorders include Down's syndrome or trisomy 21, Cri du chat syndrome, Turner syndrome and Wolf-Hirschhorn syndrome.

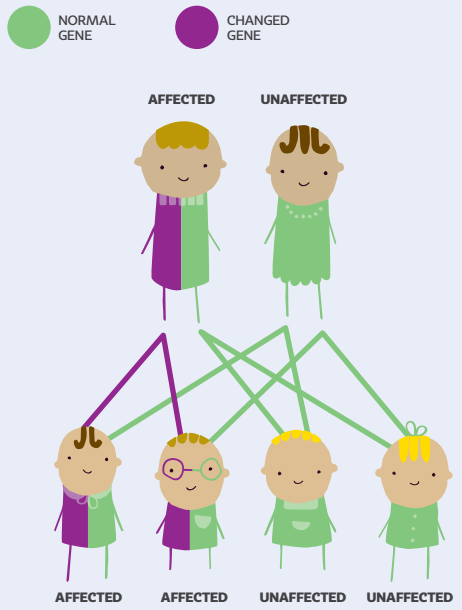
Complex disorders (also known as multifactorial or polygenic) are those that are caused by the simultaneous effect of many different genes, often in complex interaction with environmental and lifestyle factors such as diet.

Many of the common diseases of adult life, such as diabetes mellitus, hypertension, and most common developmental abnormalities, such as cleft lip and congenital heart defects, have a strong genetic component and are caused by more than one genetic change.

Because polygenic diseases involve more than one gene, inheritance patterns are diverse and complex. If a parent has a disease, it does not necessarily mean a child will develop the same disease. On the other hand, an individual may not be born with a disease but may be at a higher risk of developing it. This is known as genetic predisposition or susceptibility.

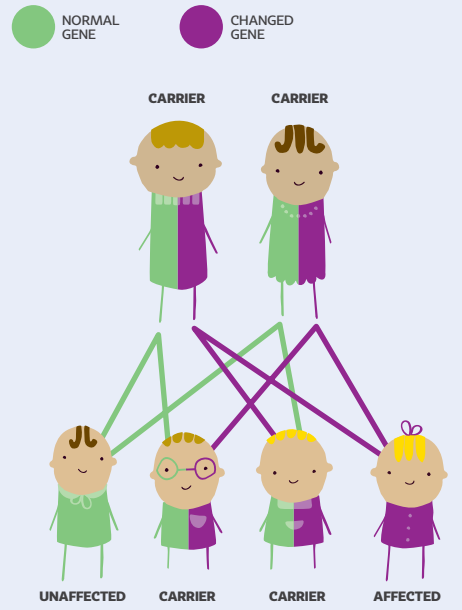
HOW ARE DOMINANT CONDITIONS INHERITED?

How dominant conditions are passed on from parent to child.

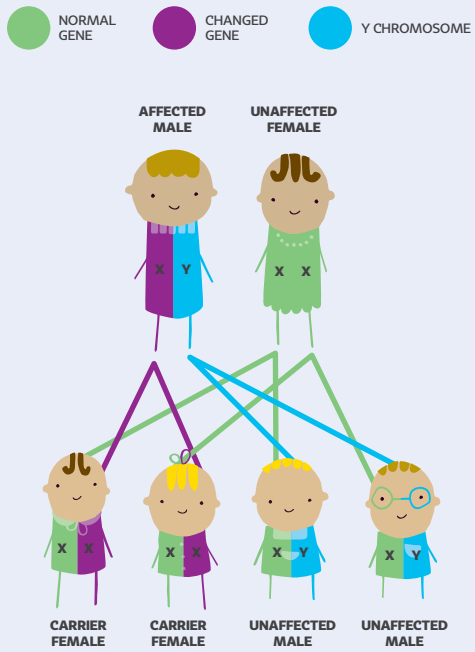


HOW ARE RECESSIVE CONDITIONS INHERITED?

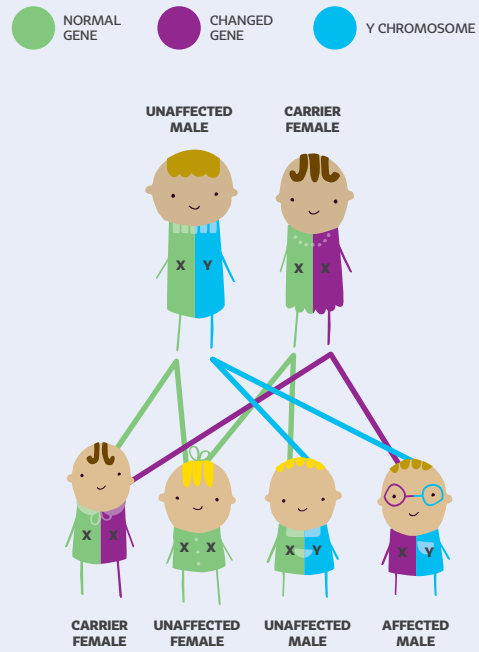
How recessive conditions are passed on from parent to child.



HOW X LINKED RECESSIVE CONDITIONS ARE PASSED ON BY AFFECTED MALES



HOW X LINKED RECESSIVE CONDITIONS ARE PASSED ON BY FEMALE CARRIERS



Rare conditions

A rare condition is any condition that affects less than 1 in 2,000 people. There are over 6,000 rare conditions.

1 in 17 people will be affected by a rare condition at some point in their lives. This equates to approximately 3.5 million people across the UK. Most rare conditions are also genetic conditions (so the result of a change in an individual's DNA sequence).

Rare conditions include rare cancers such as childhood cancers and some other well known conditions, such as cystic fibrosis and Huntington's disease.

'When we were given the diagnosis our geneticist didn't know much about the condition as there are only 65 known cases worldwide.'
Workshop participant

Undiagnosed conditions

Sometimes a child or young person may be suspected to have a genetic condition, but genetic testing has so far failed to identify the change in their DNA that has caused it. Sometimes this is because the change is so rare it has never been seen before and so isn't tested for in the usual tests available in NHS clinics. On other occasions, a change may be found in the child or young person's DNA sequence but it is not possible to confirm if this is the change that has caused their condition. These changes are called 'variants of unknown significance' (VUS).

Sometimes undiagnosed genetic conditions are called 'syndromes without a name', or SWAN for short.

Children affected by a syndrome without a name can have a range of different symptoms and each child is likely to be affected differently. Some children affected by a syndrome without a name might be described as having global developmental delay or failure to thrive. They might have learning disabilities and/or physical disabilities.

They can sometimes have complex medical needs and may have epilepsy. Some children may not have any learning difficulties but may be physically disabled whilst others are physically unaffected but have learning disabilities.

Your **Notes**

1.2 What does it mean to have a genetic, rare or undiagnosed condition?

The effects of having a genetic, rare or undiagnosed condition can be very varied and can affect many aspects of family life.

How it affects your family will depend on a number of factors but it is not uncommon for families of children and young people with genetic, rare and undiagnosed conditions to experience similar challenges.

These often include:

- A long journey to diagnosis.
- Uncertainty about the future.
- Poorly coordinated care, lots of different healthcare professionals involved and lots of appointments.
- Difficulties in accessing information and support from an expert, or patient group, for their child's condition.

You can find out more about how to obtain a diagnosis for a genetic, rare or undiagnosed condition in **2 Rare Resources: The journey to diagnosis** guide.

Further information about genetic, rare and undiagnosed conditions

Genetic Alliance UK provides information about genetics, genetic services and living with a genetic condition. geneticalliance.org.uk

Genetic Alliance UK provides information resource explaining the different types of inheritance: Dominant, recessive and X-linked inheritance.
geneticalliance.org.uk/about-genetics

Rare Disease UK is the national campaign for people living with rare conditions.
geneticalliance.org.uk/rarediseaseuk

SWAN UK (syndromes without a name) is the only dedicated support network available for families of children and young adults with undiagnosed genetic conditions in the UK. It is run by the charity Genetic Alliance UK.
geneticalliance.org.uk/swanuk

Your Genome is a website providing information and education resources explaining genetics.
yourgenome.org

Contact is a charity providing information and advice for families with disabled children.
contact.org.uk/

Orphanet is a European website providing information about rare conditions and a searchable rare condition database.
orpha.net

Your **Notes**

GENETIC ALLIANCE UK

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