This fact sheet describes how genes affect our health when they follow a well understood pattern of genetic inheritance known as autosomal dominant.

In summary

- **Genes contain the instructions for growth and development. Some gene changes make the gene faulty so that the message is not read correctly or is not read at all by the cell. A variation in a gene that makes it faulty is called a *mutation***
- **If a genetic condition occurs when only one copy of the gene is changed, this is called a *dominant mutation***
- **An autosomal gene is a gene located on a numbered chromosome and usually affects males and females in the same way.**

CHROMOSOMES, GENES AND DNA

In all the cells of our body, our genes are found on chromosomes (long strings of genes). We have many thousands of genes that provide information for our body to grow, develop and remain healthy. The gene sends messages to the cell to make important chemical products such as proteins.

There are usually 46 chromosomes in each cell that are arranged into 23 pairs. One of each pair is passed on to us from our mother and the other from our father. 22 of these chromosome pairs are numbered. These numbered pairs are known as the autosomal chromosomes. The 23rd pair is made up of the sex chromosomes called X and Y. Males have an X and a Y chromosome and females have two copies of the X chromosome.

Since the chromosomes come in pairs, there are also two copies of each of the genes. The exception to this rule applies to the genes carried on the sex chromosomes called X and Y. A variation in a gene that creates a fault is called a **pathogenic variant** or **mutation**. Genes are sections of DNA that code for the proteins our body needs to function. A mutation in a gene will affect the body differently depending on how much it changes the resulting protein, how critical that protein is to the body and how much of that protein is needed in the body.

If a DNA change occurs in only one of the pair of genes and this causes a health condition, it is called a **dominant mutation**. If a health condition only occurs when both copies of the gene are changed, this is called a **recessive mutation**.

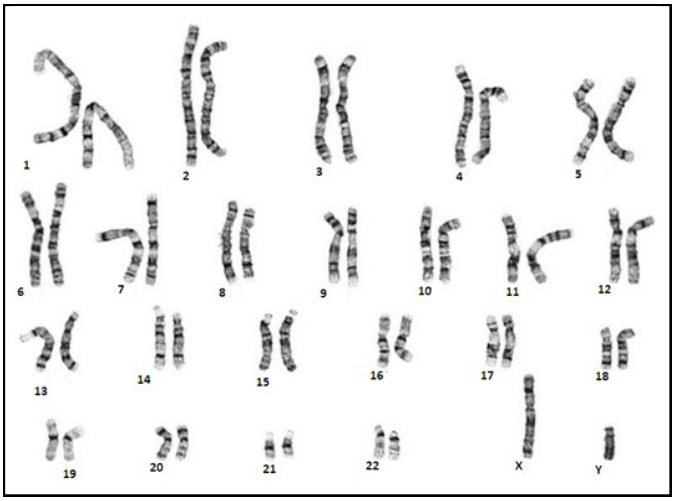

Figure 8.1: *Chromosome picture (karyotype) from a male 46,XY.*

An **autosomal** gene is a gene located on a numbered chromosome and usually affects males and females in the same way.

An **X-linked** gene is located on the X or Y chromosome and affects males and females differently.

A CLOSE LOOK AT AUTOSOMAL DOMINANT INHERITANCE

This type of inheritance refers to the inheritance of a **dominant** gene mutation on an autosome (one of the chromosomes numbered 1-22). See *Figure 8.1*.

There are two copies of every autosomal gene. Both copies of the gene send a message to the cells to produce a particular product such as a protein.

Individuals who have a dominant mutation on one gene, and a working copy of that gene on the other partner chromosome, will be affected by that condition despite the working copy.

Therefore although one of the gene copies is correctly sending the instructions to make the gene product, the other copy with the dominant mutation is not sending the correct message and overrides the action of the working gene.

WHAT DOES IT MEAN IF YOU HAVE AN AUTOSOMAL DOMINANT GENE MUTATION?

If a person has an autosomal dominant gene mutation, they do not have the ability to make enough of the correct gene product and will have symptoms of the genetic condition from birth or be predisposed to developing the condition later in life (depending on the gene involved).

HOW ARE AUTOSOMAL DOMINANT GENE MUTATIONS PASSED DOWN THROUGH THE FAMILY?

Humans need two copies of each gene in order to have the correct balance of DNA (with the exception of the sex-chromosome genes).

One copy of each gene is passed to a child from their mother and the other from the father. The possible gene combinations a parent may have for a dominant gene are represented by the individuals in *Figure 8.2*.

If one parent has an autosomal dominant gene mutation

One parent would have the genetic make-up of the person in *Figure 8.2A* and the other would have the genetic make-up of the person in *Figure 8.2B*.

The outcomes for each pregnancy are the same whether it is the father who has the dominant gene mutation (as in *Figure 8.3*) or the mother.

A		• Affected by or predisposed to a genetic condition • This person has the gene pair Dd. This means that one copy of the gene is working and producing the correct gene product however the other copy (D) is not working. They may develop symptoms of the genetic condition because for this gene, you need both copies to be working • When this person has a child, there is a 50% chance they will pass on a working d gene to each of their children and a 50% chance they will pass on the gene mutation which is not working (D)
B		• Unaffected person • This person has the gene pair dd. This means that both copies of the gene are working and they are able to produce the gene product. They will not develop symptoms of the genetic condition caused by this gene • When this person has a child, they will only pass on the working gene copy (d)
C		• Affected by or predisposed to a genetic condition • This person has the gene pair DD. This means that both copies of the gene are not working and none of the correct gene product is being made • This person has a double copy of a dominant mutation and is often more severely affected by the condition than someone with just one dominant mutation (Dd)

Figure 8.2: *Where an autosomal dominant gene mutation is represented by 'D' and the working gene copy by 'd', There are three possible combinations a person could have. This is regardless of whether the person is a male or female.*

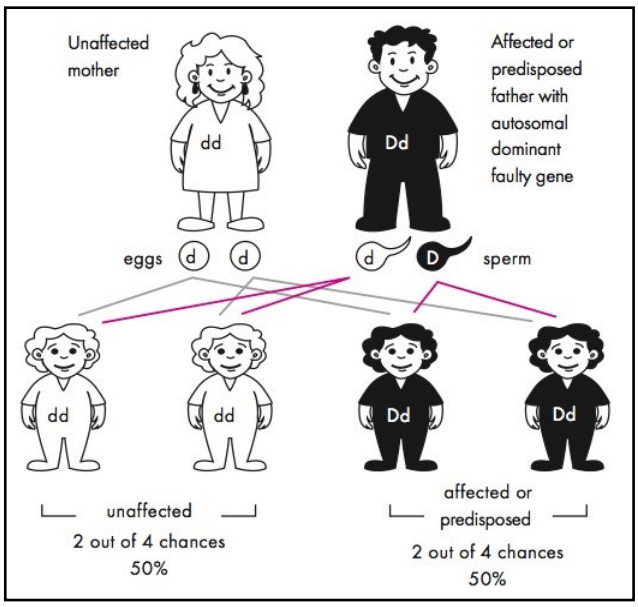

Figure 8.3 *Autosomal dominant inheritance when one parent carries the autosomal dominant faulty gene copy. The autosomal dominant faulty gene copy is represented by 'D'; the working copy of the gene by 'd'.*

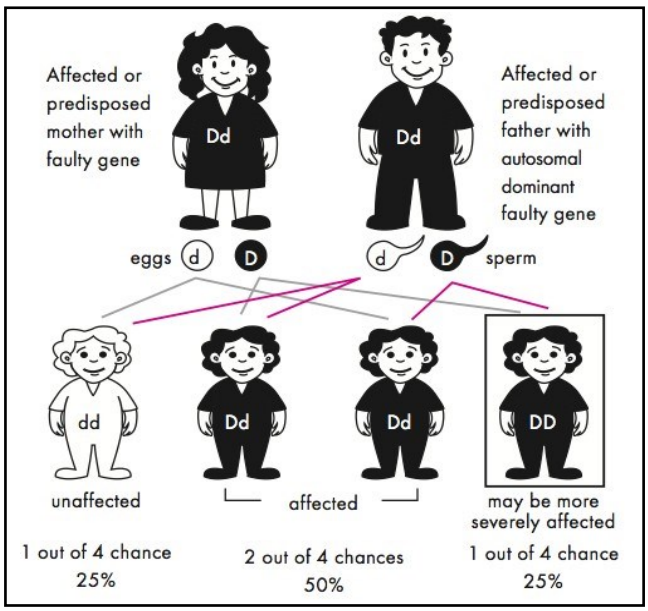

Figure 8.4 *Autosomal dominant inheritance when both parents carry the autosomal dominant faulty gene copy. The autosomal dominant faulty gene copy is represented by 'D'; the working copy of the gene by 'd'.*

This means that in every pregnancy there is:

- 1 chance in 2 (2 chances in 4 or 50% chance) that they will have a child who inherits **both copies of the working gene** from his/her parents. In this case, the child will be unaffected by the condition
- 1 chance in 2 (2 chances in 4 or 50% chance) that their child will inherit the **dominant gene mutation and the working copy of the gene** from the parents and he/she will be affected or predisposed to developing the condition caused by the gene mutation.

If both parents have the autosomal dominant gene mutation

Both parents would have the genetic make-up of the person in *Figure 8.2A*.

This means that in every pregnancy there is:

- 1 chance in 4 (25% chance) that they will have a child who inherits **both copies of the working gene** from his/her parents. In this case, the child will be unaffected by the condition
- 1 chance in 2 (2 chances in 4 or 50% chance) that their child will inherit the **dominant gene mutation and the working copy of the gene** from the parents and he/she will be affected or predisposed to developing the condition caused by the gene mutation, like their parents
- 1 chance in 4 (25% chance) that they will have a child who inherits **both copies of the dominant gene mutation** from his/her parents. Depending on the condition, the child may be more severely affected than their parents, or may not even survive, and/or have a younger age of onset for conditions that develop later in life.

WHAT GENETIC CONDITIONS ARE CAUSED BY AN AUTOSOMAL DOMINANT GENE MUTATION?

A number of conditions follow this pattern of inheritance in families. While some are obvious at birth, in other cases the symptoms do not appear until much later in life. Neurofibromatosis type 1, achondroplasia, Huntington disease, inherited predisposition to breast, ovarian and bowel cancers and familial hypercholesterolaemia all follow a pattern of autosomal dominant inheritance.