

Important points

- Mosaicism refers to the situation where individuals have in their bodies a mixture of cells containing different genetic information
- Some cells may contain the correct genetic information while others contain faulty genetic information. Also cells may contain the correct chromosome complement while others contain a change in chromosome number or structure
- Without studying every cell in the body (which is impossible), we cannot exclude the possibility that an individual could be mosaic for a chromosome change or a faulty gene
- When the chromosome change the faulty gene(s) is/are in only some of a woman's egg cells or a man's sperm cells, this is described as **germline mosaicism** as the egg and sperm cells are referred to as **germ cells**. This situation is also referred to as **gonadal mosaicism** (since the egg and sperm are produced in the **gonads**)
- In a situation where a couple has more than one child affected with a condition that is due to a 'dominant' faulty gene, we would normally expect one of the parents to also be affected. When neither are affected, germ line mosaicism is possible
 - The possibility of mosaicism is frequently the reason that parents cannot be completely reassured a condition affecting their child "will never happen again" in their family
- Genetic counselling will assist in enabling a couple to make an informed decision with the most up-to-date information

Understanding the patterns of inheritance of genetic conditions in families is becoming increasingly complex (See Genetics Fact Sheet 2).

Complex patterns of inheritance

The cells of the body contain the genes or set of instructions for the cell to make all the necessary proteins (chemicals) for our bodies to grow and work normally (see Genetics Fact Sheet 1).

Variation in a gene causes the gene to not work properly, the gene is described as being faulty (ie. there is a *gene mutation* present). The product of the faulty gene is impaired, or is not produced in the right amounts (see Genetics Fact Sheets 4 & 5).

The traditional patterns of inheritance apply to the inheritance of conditions due to changes in a single gene, located on the chromosomes in the nucleus (see Genetics Fact Sheets 8, 9 & 10). Estimating the chance of developing a genetic condition when someone carries a faulty gene is generally straightforward in these individuals.

In some cases, interactions between a person's genetic make-up and the environment means that despite the presence of a faulty gene, the condition does not always develop.

For example, not all women with a faulty breast cancer gene will develop breast cancer (see Genetics Fact Sheet 48). This is described as *incomplete penetrance* of the faulty gene: the gene is present but will not be expressed unless other environmental factors, or changes in other genes, are also present (see Genetics Fact Sheet 11). It is therefore more complex to determine the pattern of inheritance and to estimate the chance for a genetic condition to occur, if a faulty gene is present.

Another example of complex inheritance patterns is the situation where the faulty gene is located in small compartments in the cell called the *mitochondria*, rather than on a chromosome in the cell's nucleus. The pattern of inheritance of conditions due to faulty mitochondrial genes is also known as maternal inheritance and is discussed in Genetics Fact Sheet 12.

This Fact Sheet discusses another example of complex patterns of inheritance, where the genetic change is not present in all the cells of the individual. Instead, they have a mixture of cells containing the correct genetic information, and cells containing the changed information. This situation is referred to as *mosaicism*.

Mosaicism

A person can have some cells in their body in which the chromosome number is different from other cells. The concept of **mosaicism in relation to chromosomes** is discussed in Genetics Fact Sheet 6.

For most people, the genes in **all** the cells in their body will contain the same information, whether they are blood cells, skin cells or sperm (in men) and egg cells (in women). Where a parent has a gene variation which makes the gene faulty, a child who inherits the faulty gene will usually have the faulty gene copy in all the cells of their body (see *Figure 13.1*).

Some people, however, will have a mixture of cells in their body in relation to their genetic information. Some cells in some body tissues or organs will have the correct information in a particular gene(s), and other cells in the same or other tissues or organs will have the gene variation(s) (*Figure 13.2*). Just as mosaic tiles on a floor have a mixture of patterns, someone with a mixture of cells containing different genetic information in a particular gene(s) is said to be mosaic for that gene change/ those gene changes.

When the faulty gene(s) is/are in only some of a woman's egg cells or a man's sperm cells, this is described as **germline mosaicism** as the egg and sperm cells are referred to as **germ cells** (*Figure 13.2*). This situation is also described as **gonadal mosaicism** since the egg and sperm are produced in the **gonads**.

Without studying the genes in every cell in the body (which is impossible), we cannot always be certain that someone is not mosaic for a gene variation.

What are the indications that a person is mosaic for a faulty gene?

All of the genes are contained in every cell but only the genes that produced proteins necessary for the cell will be switched on (See Genetics Fact Sheet 14). For a faulty gene to cause a problem, its product must have an impact on the cells of the tissue or organ in which it is present.

A person may have a faulty gene detected in their blood cells but not have the condition associated with it. For example, a faulty gene that would usually impact on brain development may be found in the blood of a normally functioning person. This means that the blood cells contain the faulty gene but the brain cells contain only the working copy of the gene.

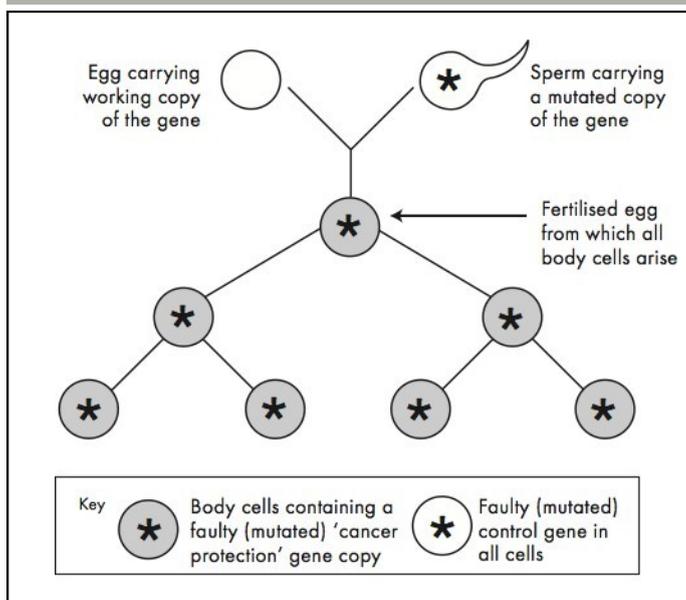


Figure 13.1: A faulty gene will usually be present in all the cells arising from the fertilised egg

This person is a mixture (mosaic) of cells in his/her body containing the faulty gene copy and the working copy.

In rare cases, mosaicism may explain the variability of symptoms in people with the same genetic condition. It is, however, impossible to study the genes in every cell in the body, and so we cannot always be certain if someone is mosaic for a faulty gene.

Germline mosaicism (mosaicism in sperm cells and egg cells)

A faulty gene may not be present in the blood cells, but is in the germ cells (egg or sperm cells). An indication that this is possible is when a couple have several children with a condition that is due to a 'dominant' faulty gene located on one of the numbered chromosomes (an autosome) but neither parent is affected with the condition (see Genetics Fact Sheet 9 for more information about autosomal dominant inheritance).

- When parents have one child with a condition that is due to an autosomal 'dominant' faulty gene but neither parent has the faulty gene on a blood test, it is usually assumed that the gene variation in the child occurred due to a new or spontaneous change in the egg or sperm at, or shortly after conception
- If they have a second child with the same condition, the chance of the condition occurring again because of another spontaneous variation in the same gene is highly unlikely
- The explanation may be that one of the parents is mosaic for the faulty gene in their egg (the mother) or the sperm (the father)

What can be done if there are indications that one of the parents is mosaic for a faulty gene in their egg or sperm cells (germline mosaicism)?

A number of genetic conditions have been described, where a variation that makes the gene faulty occurs in the germ cells i.e. the egg cells of a woman or the sperm cells of a man.

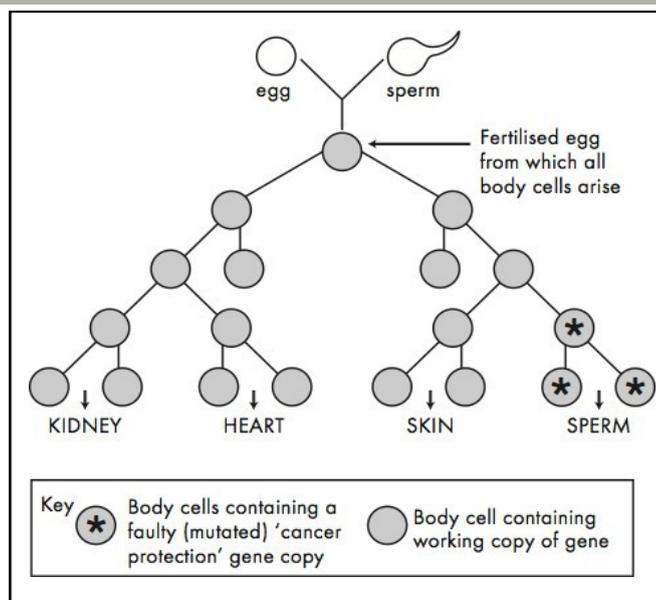


Figure 13.2: The faulty gene copy is only in the sperm cells. The man is mosaic for the faulty gene. Since the sperm cells are the 'germ cells', the man has germline mosaicism for the faulty gene.

If one parent has an autosomal dominant condition (See Genetics Fact Sheet 9) it would be expected that on average half (50%) of their egg (or sperm) cells would contain the working copy, and half (50%) the faulty gene copy. There is therefore 1 in 2 chance (50% chance) of passing on either the faulty copy, or the working copy of the gene to each of his/her children

- On the other hand, if a woman has mosaicism for the faulty gene in her egg cells, it would be likely that **less** than 50% of her egg cells would carry the faulty gene. In other words, the chance of passing on the faulty gene to a child is less than 50%. This is lower than the chance of a woman affected with the condition passing on the faulty gene copy but it is not possible to provide a more accurate risk assessment
- These chances would also apply if the father had mosaicism for the faulty gene in his sperm. Neurofibromatosis type 2 (NF2) is an example of a condition where germ line mosaicism has been found (See Genetics Fact Sheet 52)

Testing in pregnancy to determine the presence of the faulty gene may be possible. For more information about prenatal testing options see Genetics Fact Sheet 17C. Testing of the embryo in association with assisted reproductive technologies (ART) including *in vitro* fertilisation (IVF) may also be possible (see Genetics Fact Sheet 18).

Genetic counselling may be helpful in assisting a couple with making an informed decision with the most up-to-date information available (see Genetics Fact Sheet 3).

Other Genetics Fact Sheets referred to in this Fact Sheet: 1, 2, 3, 4, 5, 6, 8, 9, 11, 12, 17C, 18, 48, 52

Information in this Fact Sheet is sourced from:

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Edit history

April 2012

Author/s: A/Prof Kristine Barlow-Stewart

Previous editions: 2007, 2004, 2002, 2000, 1998, 1996, 1994, 1993

Acknowledgements previous editions: Gayathri Parasivam; Dr Anne Turner