Is it all in the genes? Nature and nurture

The characteristics of an organism, such as its height, shape, blood group or sex, are known as its **phenotype**. Differences in phenotype between the members of a population are caused by differences in:

- genetic make-up or **genotype**
- the environment in which an individual develops.

Some characteristics are controlled almost completely by the organism’s genotype, with the environment having little or no effect. For example, a person’s blood group (group A, B, AB or O) is controlled by the genes they inherit. The genes code for protein antigens on the surface of their red blood cells. A person’s blood group is not affected by the environment in which they develop. Such characteristics are controlled by genes at a single locus and show **discontinuous variation**. They have phenotypes that fall into discrete groups with no overlap (Figure 3.45A). In garden peas, unlike humans, height also shows discontinuous variation.

Characteristics that are affected by both genotype and environment often show **continuous variation**. Human height is a characteristic showing continuous variation. This means that a person can be any height within the human range. The most common height will be somewhere mid-way between the extremes of the range. If a graph is drawn showing the frequency distribution of the different height categories it will be bell-shaped (Figure 3.45B). Characteristics that show continuous variation are controlled by genes at many loci, known as polygenic inheritance, and also by the environment, either directly or by influencing gene expression.

**Figure 3.45 A** Human blood groups show discontinuous variation. **B** Height in humans is an example of continuous variation.
Key biological principle: Polygenic inheritance

1. In monohybrid inheritance, each locus is responsible for a different heritable feature. For example, one gene might be coding for the colour of a flower with another gene coding for the shape of the petals. However, inheritance of most characteristics does not follow simple Mendelian rules of inheritance, but involves interaction of alleles at many loci. When a number of genes are involved in the inheritance of a characteristic, rather than just one, we call the pattern of inheritance polygenic.

2. In many human characteristics that show polygenic inheritance, such as height and skin colour, the alleles clearly have additive effects. With conditions such as diabetes, coronary heart disease, Alzheimer’s disease, schizophrenia and some cancers, several genes may confer a susceptibility to the condition, with environmental factors also contributing. Two people who inherit the same susceptibility may not both develop the illness; it will depend on environmental factors such as diet, exposure to toxins and stress. Such factors act as triggers to bring about the symptoms of disease. Conditions where several genetic and one or more environmental factors are involved are said to be multifactorial.

3. The degree of similarity between identical twins is a measure of the influence of the genes on that characteristic. 99% of identical twins have the same eye colour, and 95% the same fingerprint ridge count. Where the environment has a greater effect, the similarity fails. One study found that if you are an identical twin and you have Alzheimer’s disease, your twin sibling (brother or sister) has a 40% chance of having Alzheimer’s disease. However, if you have Alzheimer’s disease as a non-identical twin, your sibling has only a 10% chance of having Alzheimer’s disease. This suggests that there is a significant but not inescapable genetic basis to Alzheimer’s disease. Both genes and the environment influence the development of the disease.

4. How polygenic inheritance works
In any introductory course on genetics, it is common for eye colour to be used as an example of monohybrid inheritance – a single locus with brown dominant to blue. This is not entirely the case. Eye colour is an example of polygenic inheritance; alleles at several loci control eye colour. Eye colour ranges from blue to brown, depending on the amount of pigment in the iris. The pigment absorbs light so brown eyes appear dark. Blue eyes have little pigment, so light reflects off the iris.

Let us say three loci are involved in the inheritance of this characteristic, each with alleles B and b. B adds pigment to the iris and b does not. If all three loci were homozygous for the allele B, the person’s genotype would be BB BB BB. The additive effect would produce a dark brown iris, whereas bb bb bb would add no pigment to the iris, making it pale blue. A range of possible genotypes and phenotypes are possible between these two extremes, according to how many alleles add brown pigment, as shown below.

<table>
<thead>
<tr>
<th>Number of alleles adding brown pigment</th>
<th>Example of genotype</th>
<th>Eye colour</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>BB BB BB</td>
<td>very dark brown</td>
</tr>
<tr>
<td>5</td>
<td>BB BB Bb</td>
<td>dark brown</td>
</tr>
<tr>
<td>4</td>
<td>BB BB bb</td>
<td>medium brown</td>
</tr>
<tr>
<td>3</td>
<td>BB Bb bb</td>
<td>light brown</td>
</tr>
<tr>
<td>2</td>
<td>BB bb bb</td>
<td>deep blue</td>
</tr>
<tr>
<td>1</td>
<td>Bb bb bb</td>
<td>medium blue</td>
</tr>
<tr>
<td>0</td>
<td>bb bb bb</td>
<td>pale blue</td>
</tr>
</tbody>
</table>

Table 3.2 Eye colour is a polygenic characteristic

The greater the number of loci involved, the greater the number of possible shades.

If a pale blue-eyed woman has children with a very dark brown-eyed man they will have light brown-eyed children as shown below.

**Parental phenotypes**
- Mother: Pale blue
- Father: Very dark brown

**Parental genotypes**
- Mother: bb bb bb
- Father: BB BB BB

**Gametes**
- Mother: bbb
- Father: BBB

**Offspring genotypes**
- Bb Bb Bb

**Offspring phenotype**
- Light brown

Q3.18 A deep blue-eyed woman (BB bb bb) has a child with light brown eyes. Her medium blue-eyed partner (Bb bb Bb) suspects that he is not the father. Copy and complete the Punnett square below and describe how you would use it to explain to him that he could be the father.

**Parental phenotypes**
- Mother: Deep blue
- Father: Medium blue

**Parental genotypes**
- Mother: Bb bb Bb
- Father: Bb bb bb

**Possible gametes**
- Bbb, BBB, bbb, bBB

**Gametes from the father**
- Bbb
- bbb

**Gametes from the mother**

<table>
<thead>
<tr>
<th>Gametes from the mother</th>
</tr>
</thead>
<tbody>
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</tbody>
</table>

>209.2
Gene and environment interactions

There are countless examples of genes and environment interacting to produce an organism’s phenotype. Some are very familiar, such as skin and hair colour; others are less so. We will take a detailed look at four examples:

- height
- hair colour
- MAOA
- causes of cancer.

Height

Have you noticed that each human generation seems to be a bit taller than the last (Figure 3.46)? The average human height in industrialised countries has risen each generation over the past 150 years. People in the UK now average about 8 cm taller than they did in 1850. How can this be explained?

Before reading on, list as many reasons as you can for the increase in human height over recent generations.

Activity

In Activity 3.16 discover how many genes can affect a single characteristic.

A3.16S
The following are some possible answers. You may have thought of others.

1. There is some evidence that taller men have more children, which would result in a gradual change in the genetic make-up of the population.
2. Greater movements of people have resulted in less inbreeding, leading to taller people.
3. Better nutrition, especially increased protein, has resulted in greater growth of children.
4. Improved health, with a reduction in infectious diseases, has occurred through improved sanitation, clean water supplies, vaccination and antibiotics.
5. The end of child labour has allowed more energy to go into growth.
6. Better heating of houses and better quality clothing reduces the amount of energy needed to heat the body, so again more energy can go into growth.

Q3.20 Which of these reasons for change in height are due to the environment and which are the result of genotype?

It is widely accepted that a person’s height is determined by an interaction between the effects of their genes for height and environmental influences, such as diet. A person may have genes for being tall, but not achieve his or her full potential height because of malnutrition. We do not know for certain which of the possible reasons for change in height is the most important. However, most people think that better diet is the most significant factor.

Hair colour

Differences in hair colour are largely genetically determined, due to variation in the amount and type of pigment the hair contains. But the environment can influence hair colour in some cases.

Making melanin

The dark pigment in skin and hair is called melanin. Melanin is made in special cells, melanocytes, found in the skin and at the root of the hair in the follicle. These are activated by melanocyte-stimulating hormone (MSH). There are receptors for MSH on the surface of the melanocyte cells. The melanocytes place melanin into organelles called melanosomes. The melanosomes are transferred to nearby skin and hair cells where they collect around the nucleus, protecting the DNA from harmful UV light. People with more receptors have darker skin and hair; they have more protection against sunburn. Ultraviolet (UV) light increases the amount of MSH and also of MSH receptors, making the melanocytes more active (Figure 3.47) and causing the skin to darken. Hair does not appear darker because although more melanin is produced, UV light causes chemical and physical changes to melanin and other proteins in hair cells. Hair lightens due to destruction of the melanin by UV light.
Seasonal colour change

Arctic foxes have brown fur in summer and white fur in winter (Figure 3.48). They must have the genes for making brown fur (which contains melanin) all the time, so how can white fur be made?

The white winter coat is actually grown during the summer. It grows under the brown summer coat and is revealed when the summer coat is moulted in autumn. The foxes produce fewer MSH receptors in the summer. Without these receptors, MSH has no effect and no melanin is made in the hair follicles.

Q3.21 Explain why MSH has no effect on the developing hairs in summer, meaning that the coat grows white.

Q3.22 Explain why it is surprising that white fur is able to grow in the summer.

Figure 3.48 How does the arctic fox change colour?
White with dark tips
To make melanin, animals use an enzyme called tyrosinase. Tyrosinase catalyses the first step along a chemical pathway, changing the amino acid tyrosine into melanin. Some animals, such as Himalayan rabbits and Siamese cats, have mutant alleles for tyrosinase. The enzyme is made but it is unstable and is inactivated at normal body temperature. However, the tips of their tail, paws and ears are much darker than the rest of their bodies (Figure 3.49).

Figure 3.49 Only the ears, paws and tail of this Himalayan rabbit are dark.

Q3.23 Suggest how the environment and genotype are interacting to produce the distinct colouring at the tail, paws and ear tips in Figure 3.49.

Q3.24 There are rare cases in humans in which hair in the armpits is white, but hair on places such as the legs is dark. Suggest how this happens.

MAOA
Monoamine oxidase A is an enzyme that catalyses the breakdown of a neurotransmitter in the brain involved in the regulation of behaviour, including the response to stress. It was found that some individuals have a rare mutation in the MAOA gene and produce no enzyme. They exhibit aggressive and sometimes violent behaviour. Genetically modified mice which lack the MAOA gene are also aggressive. These observations led scientists to suggest there might be a connection between the gene and violent behaviour but studies did not show a clear link.

Researchers at King's College in London revealed an interaction between MAOA genotype, mistreatment in childhood and antisocial behaviour in later life. They used the results of a study that had followed the health and social development of over 1000 children in Dunedin, New Zealand, for over 20 years. There are two alleles for the MAOA gene. One results in the production of high levels of the enzyme, the other is linked with low level production of the enzyme. The researchers focused on the boys in the study because the MAOA gene occurs on the X chromosome so males have only one allele.

Childhood maltreatment was associated with more antisocial behaviour as adults. No direct link was found between MAOA levels and subsequent antisocial behaviour. However, maltreated children with high levels of MAOA were less likely to exhibit violent behaviour than maltreated children with low MAOA. 12% of the males had low MAOA and had been maltreated, but they committed 44% of the violent crimes recorded for the whole group. Further studies have supported this complex interaction between childhood environment and MAOA genotype.

Cancer
What causes cancer?
One in three people in the UK will suffer from cancer at some stage in their life and, at present, one in four people dies from the disease. If we could understand the way our genetic make-up and our environment combine to cause cancer, we would be on the way to finding means of prevention and cure.

Cancers occur when the rate of cell multiplication is faster than the rate of cell death. This causes the growth of a tumour, often in tissues with a high rate of mitosis, such as the lung, bowel, gut or bone marrow. Cancers are caused by damage to DNA. DNA is easily damaged by physical factors such as UV light or asbestos. It can also be damaged by chemicals, known as carcinogens, which may be in the environment or can be
produced by cell metabolism. Mutations can also occur when cells divide (see Topic 2, Section 2.5). If DNA is copied incorrectly in gamete formation, an inherited form of cancer can result.

Q3.25 Explain why cancers are more likely to occur in tissues with a high rate of mitosis.

Q3.26 Explain why damage to the DNA in an embryo can result in inherited cancer.

Telling cells what to do

Cells go through a fixed sequence of events during the cell cycle – G1, S, G2 and mitosis (M) – as shown in Section 3.2. The progression from one phase to the next is controlled. During each stage of the cycle, proteins are produced that stimulate the next stage in the cycle. Cells also produce proteins that stop the cell cycle, preventing progress from one stage to the next. These proteins activate or inhibit enzymes that initiate the reactions in the next stage of the cycle.

Cancer cells do not respond to the control mechanisms. Two types of gene have a role in control of the cell cycle and play a part in triggering cancer. These are:

- oncosenes
- tumour suppressor genes.

Oncogenes code for the proteins that stimulate the transition from one stage in the cell cycle to the next. Mutations in these genes can lead to the cell cycle being continually active. This may cause excessive cell division, resulting in a tumour.

Tumour suppressor genes produce suppressor proteins that stop the cycle. Mutations inactivating these genes mean there is no brake on the cell cycle. One example of a tumour suppressor protein is p53. This protein stops the cell cycle by inhibiting the enzymes at the G1/S transition, preventing the cell from copying its DNA. In cancer cells a lack of p53 means the cell cannot stop entry into the S phase. Such cells have lost the control of the cell cycle. Loss of tumour suppressor proteins has been linked to skin, colon, bladder and breast cancers.

There is a very complex network of signals and inhibitors that interact to control the cell cycle. There needs to be damage to more than one part of the cell control system for cancer to occur. This makes cancer very unlikely in any particular cell, but because the body contains so many cells dividing and changing over a lifetime, cancers will occasionally occur. Cancers are more likely in older people as they have accumulated more mutations.

In some people one of two alleles for the tumour suppressor protein p53 is damaged. The damaged allele is recessive to the normal allele. Explain why such people are more susceptible to environmentally induced cancer than people with two normal alleles for p53.

Inherited cancer

Most common cancers occur more frequently in close relatives of cancer patients, suggesting an inherited component. Many gene defects have been identified that predispose people to cancers including bowel cancer, ovarian cancer, prostate cancer, retinal cancer and some types of leukaemia.

For example, mutations in the gene BRCA1 predispose a person to breast cancer. The functioning BRCA1 gene produces a protein used to repair DNA. A child who inherits one defective BRCA1 allele may get cancer later in life if the other allele becomes
damaged in breast tissue cells. Having a single defective BRCA1 allele does not therefore mean that breast cancer is inevitable. It simply means that such individuals are more susceptible to cancer through environmental DNA damage. Women who inherit a single BRCA1 mutation have about a 60% chance of developing breast cancer by the age of 50 compared with only a 2% chance for those who inherit two normal BRCA1 alleles. The mutation confers a high risk but is relatively rare, accounting for only 5% of breast cancer cases.

Environment and cancer

You will have noticed that newspapers and magazines are full of suggestions for living a healthy life and reducing cancer risk. How useful are these suggestions?

Damage from the environment can be either chemical or physical. The greatest chemical risk of all is from smoking. Smoking increases the likelihood of many forms of cancer, especially lung cancer, through the action of carcinogens in tar. Tar lodges in the bronchi and causes damage to DNA in the surrounding epithelial cells.

Ultraviolet light (UV) physically damages DNA in skin cells. Sometimes, a mole which has been affected by UV light may start to grow bigger, and can develop into a tumour (Figure 3.50). If a tumour is not removed, cancer cells sometimes spread to other parts of the body, carried in the blood and lymphatic systems. New cancers may then form in other organs.

Diet is also linked to cause and prevention of cancer, though the connections are not always clear. A diet with plenty of fresh fruit and vegetables provides antioxidants which destroy radicals (see Topic 1). Radicals are chemicals from the diet, from environmental factors such as smoke and UV, or produced by the cell’s own metabolism, which contribute to ageing and cancer through DNA damage.

Several cancers are triggered by virus infection. For example, liver cancer can follow some types of hepatitis, and cervical cancer can follow infection by the papilloma (genital wart) virus. A virus’s RNA may even contain an oncogene, which it has picked up from one of its hosts and then transfers to the cells it infects.

Q3.28 Explain why chemotherapy and radiotherapy are often unsuccessful in tumours where the cause of the cancer is damage to the protein p53.

Did you know?

Combating cancer

One way of treating cancer is to use surgery to physically remove the tumour. Another is to destroy the cells in the tumours. In chemotherapy powerful chemicals are used to do this, and in radiotherapy X-rays or other radiation are directed at the tumour. The difficulty is to target the tumour cells without damaging nearby healthy tissues.

It used to be thought that chemotherapy and radiotherapy work by preferentially killing dividing cells in the tumour. It is now believed that these treatments actually work by inducing cells to carry out cell suicide. Chemotherapy and radiotherapy cause some DNA damage, but not enough to kill tumour cells. However, the DNA damage causes the release of the protein p53, so the cancer cells stop dividing.