The genetics of autosomal recessive conditions

Mikey H, Year 7

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1. Autosomal recessive inheritance

We inherit traits (physical characteristics) or conditions (diseases or disorders) from our parents. This happens through the DNA in our genes, which are found on the chromosomes in all our cells.

Autosomal traits or conditions are passed down through the 22 non-sex chromosomes, and these are the subject of this investigation. However, some other traits or conditions are passed down through the sex chromosomes, and these will be mentioned in the final section.

A gene is made up of two different alleles - one dominant (or expressed) and one recessive (or masked), and we inherit one allele from each of our parents. Through the genetic studies of Mendel we know how these work. A very useful diagram for this is the Punnett square (see below) - the dominant allele is given an upper-case letter (e.g. R) and the recessive allele is given a lower-case letter (e.g. r).

In the study of recessive conditions, we look at the specific case of an abnormal condition, usually caused by a mutation (unwanted change) in the recessive allele, with both parents being carriers for the condition (see illustration below). This means that the parents both have one dominant and one recessive allele (Rr). The dominant one prevails, so that the parents do
not actually exhibit the abnormal condition. As the Punnett square shows, though, any of their children has a 25% chance of being double-recessive (rr) which means that they will exhibit the condition.

So, for a child born to parents who both carry the abnormal allele but do not have signs of the condition, i.e. who are Rr, the expectation for each child is:

A 25% chance that the child is born with two normal R alleles (RR);
A 50% chance that the child is born with one normal R and one abnormal r allele (so is a carrier, without signs of the condition, like the parents: Rr);
A 25% chance that the child is born with two abnormal r alleles (having, or certainly at risk for, the condition: rr).
2. A table of well-known recessive traits

These traits are just physical characteristics which are interesting but don't give rise to any medical problems. In most cases, they follow the genetics of the diagrams above.

<table>
<thead>
<tr>
<th>DOMINANT allele</th>
<th>RECESSIVE allele</th>
</tr>
</thead>
<tbody>
<tr>
<td>brown eyes</td>
<td>blue/green eyes</td>
</tr>
<tr>
<td>(involves more than one allele)</td>
<td>(involves more than one allele)</td>
</tr>
<tr>
<td>farsightedness</td>
<td>nearsightedness</td>
</tr>
<tr>
<td>dark, thick, curly hair</td>
<td>light, thin, straight hair</td>
</tr>
<tr>
<td>oval face shape</td>
<td>square face shape</td>
</tr>
<tr>
<td>cleft chin</td>
<td>non-cleft chin</td>
</tr>
<tr>
<td>thick lips</td>
<td>thin lips</td>
</tr>
<tr>
<td>dimples and/or freckles</td>
<td>no dimples and/or freckles</td>
</tr>
<tr>
<td>good hearing</td>
<td>prone to deafness</td>
</tr>
<tr>
<td>prone to tone-deafness</td>
<td>good tone hearing</td>
</tr>
<tr>
<td>detached/free/dangling earlobes</td>
<td>attached earlobes</td>
</tr>
<tr>
<td>can roll tongue</td>
<td>can't roll tongue</td>
</tr>
<tr>
<td>can't fold tongue</td>
<td>can fold tongue</td>
</tr>
<tr>
<td>much body hair</td>
<td>little body hair</td>
</tr>
<tr>
<td>straight thumb</td>
<td>curved/hooked thumb</td>
</tr>
<tr>
<td>fold arms right first</td>
<td>fold arms left first</td>
</tr>
<tr>
<td>second toe longer than first toe</td>
<td>second toe shorter than first toe</td>
</tr>
<tr>
<td>Rhesus factor (+) in blood</td>
<td>no Rhesus factor (-) in blood</td>
</tr>
</tbody>
</table>
3. A survey of autosomal recessive conditions

In each case, there is no cure, but the condition can be treated in various ways to allow the sufferer to have a longer and more pain-free life.

(i) Cystic fibrosis

Cystic fibrosis (CF) is caused by a mutation in the 7th chromosome, which prevents a special protein, which moves salt in and out of cells, from working properly. As a result, the CF sufferer has problems with their lungs, pancreas, intestine and sweat glands, and may not live for very long. CF can be treated by lung and pancreas therapy, antibiotics and gene therapy.

(ii) Sickle-cell anaemia

Sickle-cell anaemia (SCA) is caused by a mutation in the 11th chromosome, and affects the type of haemoglobin a person makes in their red blood cells. Haemoglobin is very important because it carries oxygen from the lungs to the rest of the body. Anaemia is the state of tiredness and faintness which is the result of lack of proper haemoglobin.

In a sufferer, the shapes of the red blood cells are distorted from being smooth and doughnut-like to being spiky and ragged (i.e. shaped like a sickle or scythe - hence the name of the condition). It can be treated by drugs e.g. hydroxycarbamide.

(iii) Huntington's disease

Huntington's disease is caused by a mutation in the 4th chromosome, and it damages certain nerve cells in the brain. This brain damage gets
progressively worse over time and can affect movement, behaviour, and cognition (perception, awareness, thinking, judgement).

Huntington's disease was originally called Huntington's chorea ("chorea" is the Greek word for dancing) or St. Vitus' Dance. This is because the involuntary movements associated with the condition can look like jerky dancing. It can be treated with the drug xenazine and various forms of therapy.

(iv) MCADD

MCADD (medium-chain acyl-CoA dehydrogenase deficiency) is a rare genetic condition where a person has problems breaking down fat to use for energy. It is caused by a mutation in the 1st chromosome. MCADD is a potentially serious condition that can be life-threatening if not recognised quickly and treated appropriately. However, most cases are picked up soon after birth and can be managed quite easily.

If someone with MCADD becomes unwell and is unable to eat or tolerate food, they appear tired and sluggish, they are sick, sweat a lot, and breathe rapidly, possibly having seizures (fits). Left untreated, more serious and potentially life-threatening problems can develop, including coma and brain damage. Treatment involves drugs connected with certain foods and diets.

(v) Beta thalassaemia

Thalassaemia is a group of inherited blood disorders where haemoglobin in the blood is abnormal, like sickle-cell anaemia (above). It is caused by a mutation in the 16th chromosome. If left untreated, the most serious types of thalassaemia can cause other complications, including organ damage, restricted growth, liver disease, heart failure and death.
There are two types, alpha and beta, with beta being the more severe form of the condition. People with beta thalassaemia will require blood transfusions for the rest of their lives.

(vi) PKU

Phenylketonuria (PKU) is a rare condition caused by a mutation in the 12th chromosome. The body is unable to break down a substance called phenylalanine, which builds up in the blood, and can damage the brain.

PKU is treated with a special low-protein diet, which reduces the levels of phenylalanine in the body and prevents brain damage. If PKU isn't treated, damage to the brain and nervous system can lead to learning disabilities, behavioural problems, and epilepsy.

(vii) Tay-Sachs disease

Tay-Sachs disease is a rare and usually fatal genetic disorder, caused by a mutation in the HEXA gene on the 15th chromosome. It causes progressive damage to the nervous system. Symptoms usually begin before a baby is six months old. Their development slows down and they gradually lose their ability to move. Most children with the condition die before they're four years old.

(viii) Bloom's disease

This is a rare condition, caused by a mutation in the BLM gene on the 15th chromosome. People who exhibit the condition have short stature and may suffer from cancer.
X-linked recessive inheritance

unaffected father

unaffected son

unaffected daughter

carrier daughter

affected son

carrier mother

unaffected

carrier

affected
4. Sex-linked recessive inheritance: haemophilia

Sex-linked recessive inheritance is not quite the same as the autosomal type. The genetics are similar but more complicated. It involves the sex chromosomes X and Y: normal females have two X chromosomes (so are \textbf{XX}) and normal males have an X and a Y chromosome (so are \textbf{XY}). The recessive condition is passed down via the X chromosome. The main points are that only males actually exhibit the condition, and a carrier mother can give birth to a son who exhibits the condition. The diagram on the previous page shows how this happens.

\*

The most important of these conditions is \textbf{haemophilia}, where blood does not clot properly, and the man suffers bleeding from cuts and haemorrhages (internal bleeding), so this is a life-threatening disease. The male traits of baldness and colour-blindness have similar genetics, but are not a problem medically.

In the late nineteenth century, the Royal family suffered from haemophilia: Queen Victoria was a carrier, and her son Prince Leopold exhibited the condition. In those days, haemophilia was sometimes known as the "Royal disease".

(1400 words)