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The Inheritance of Ichthyosis

Introduction

There are many different types of ichthyosis. None of them are catching or contagious but they all depend on a small genetic mistake which has often been inherited from one's parents. There are 3 basic patterns of inheritance but a basic understanding of genetics is needed to understand how this occurs.

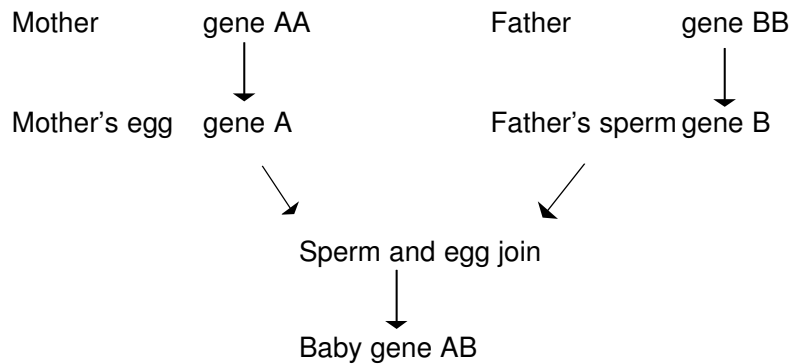
- We all have billions of genes. Each gene has a specific function such as to make a protein or fat within the body.
- Each gene is made up of tens of thousands of building blocks called nucleotides.
- When these complicated genes replicate it is not uncommon for there to be very small mistakes. A single nucleotide (out of many thousands) may be changed or in the wrong position in the gene. Often this causes no problem or disease at all as the gene can still function.
- However if the mistake is in a crucial position in the gene – it may make the gene malfunction so that it can't produce, for example, a skin protein, and this may lead to a disease such as ichthyosis.
- In practice most human beings have a number of small genetic mistakes and these do not cause disease. Only when these mistakes stop a gene from working normally does a disease arise.

How do we inherit genes from our parents?

Every human being has 2 copies of each gene. However the father's sperm and the mother's egg have only 1 copy of each gene. This means that when the egg and sperm join to make a new baby, the baby will have 2 copies of each gene just like its parents. So on average half your genes come from your mother and half from your father.



An example of the blood group genes illustrates this:

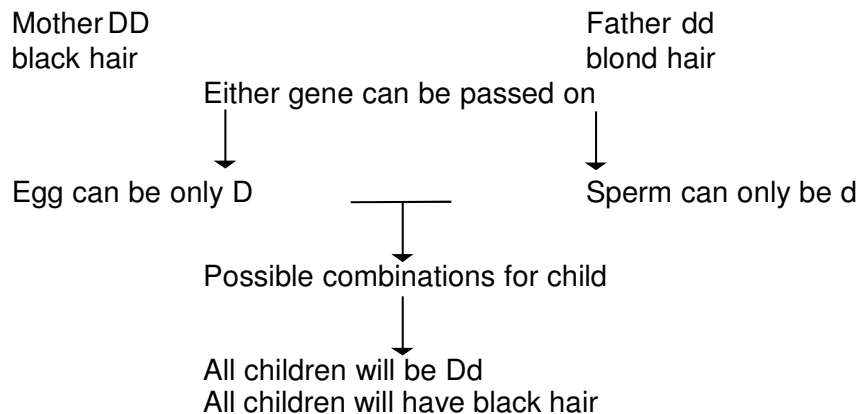


Dominant and recessive genes

As we have mentioned genes come in pairs. These may be identical genes (e.g. DD or dd) or non-identical genes (e.g. Dd). Let's say that this gene causes hair colour. For example gene D may cause black hair and gene d blond hair.

If gene D is said to be a dominant gene it will dominate over gene d. This means that anyone with the gene combination DD or Dd would have black hair. Only those individuals with gene combination dd would have blond hair. Therefore gene d is called a recessive gene. 2 copies of a recessive gene must be present before it can express itself.

Example 1



So how do we apply this to ichthyosis?

The first step is for your doctor to diagnose which type of ichthyosis you have. Once this is achieved he will explain how this condition is inherited.

- **Autosomal dominant conditions**

Ichthyosis vulgaris
Bullous ichthyosiform erythroderma

- **Autosomal recessive**

Non-bullous ichthyosiform erythroderma
Lamellar ichthyosis
"Limited" lamellar ichthyosis
Sjögren Larsson syndrome
Netherton's syndrome
Harlequin ichthyosis
Refsum's disease
Trichothiodystrophies (IDIDS syndrome)

- **X-linked recessive**

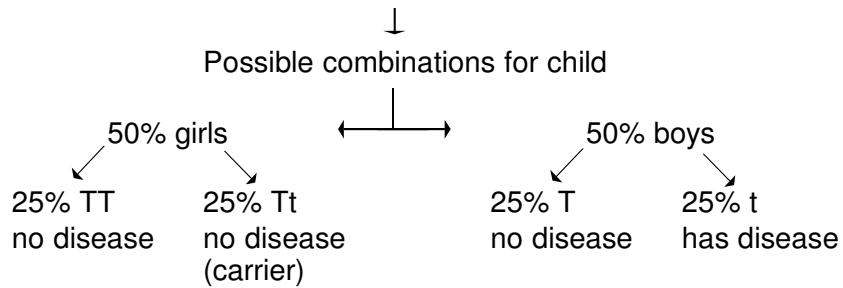
X-linked ichthyosis

- **X-linked dominant**

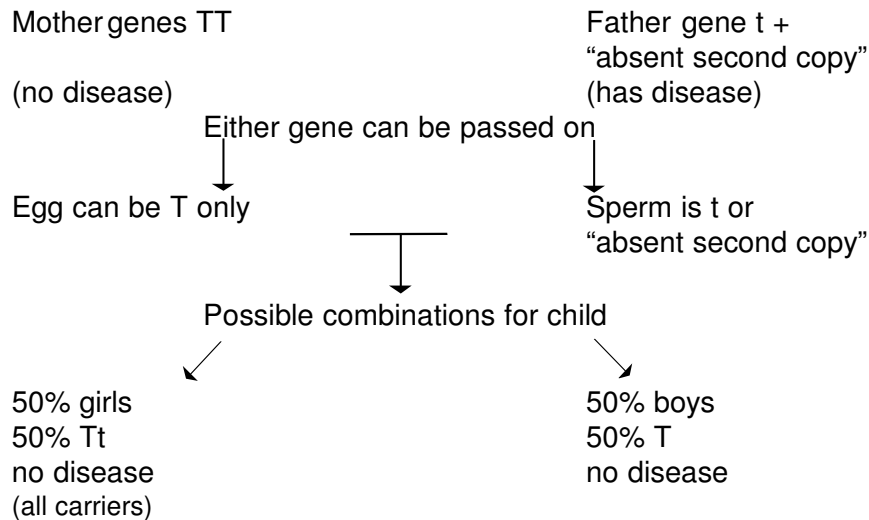
Conradi-Hünemann syndrome
(also called X-linked dominant ichthyosis, Happle syndrome and chondrodyplasia punctata)

- **Unclear**

KID syndrome - ? autosomal dominant



So for X-linked recessive conditions, females are normal or carriers whereas males are normal or have the disease. This is why X-linked ichthyosis only occurs in males. Interestingly if an affected male has children none will be affected so it appears to “skip” a generation. In fact all his daughters are carriers and all his sons will be normal.

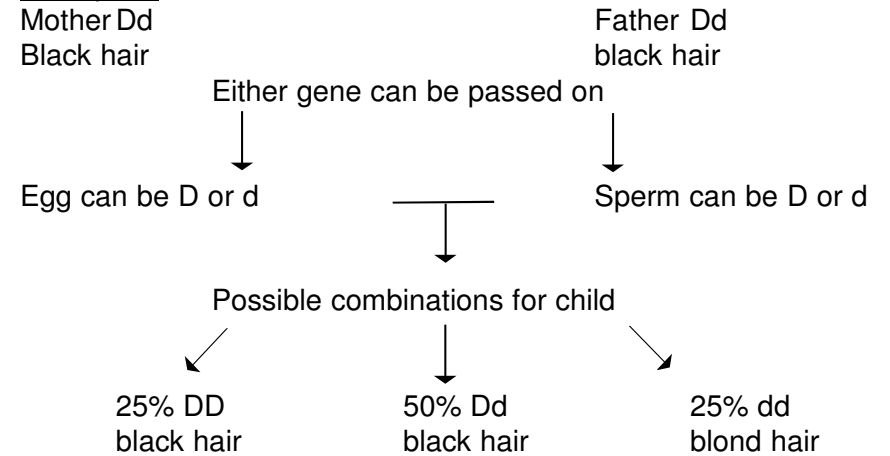


X-linked dominant disease (e.g. Conradi-Hünemann syndrome)

This is extremely rare.

Here the abnormal gene on the X-chromosome dominates the normal copy. This causes disease in females and there is a 50% chance of passing this on to their daughters. This abnormal gene is so severe in males who have no second copy that it appears to be incompatible with life. Therefore X-linked dominant ichthyosis is not seen in males.

Example 2



Autosomal dominant disease (e.g. ichthyosis vulgaris)

Let’s take the above a step further to see how this fits with disease.

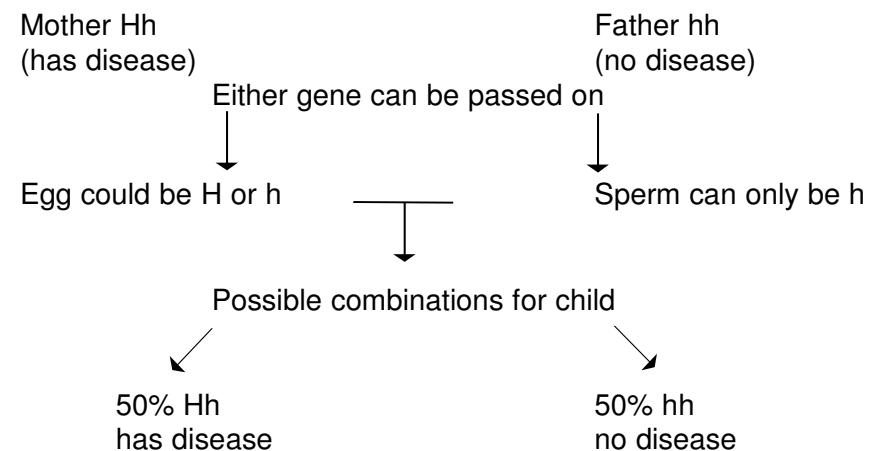
Say gene h is a normal gene. Gene H is an abnormal gene with a small mistake that stops it from working normally.

Example

Disease gene H is dominant.

All individuals with Hh or HH will have the disease.

Individuals with hh will be normal.



This pattern of inheritance is called autosomal dominant. It means if one parent is affected there is a 50% chance of a child being affected.

Special situation – Occasionally an autosomal dominant condition can appear in a child when neither parent is affected. This is usually because the disease gene is newly created and may have occurred when the sperm or egg were produced. As the mistake is not present in the parents the risks of them having a further affected child are very low indeed. However the affected child has a 50% chance of passing the condition on to their offspring when they are older. This sounds complicated but all this really means is that a genetic mistake has to start somewhere.

Autosomal recessive disease (e.g. lamellar ichthyosis)

Example

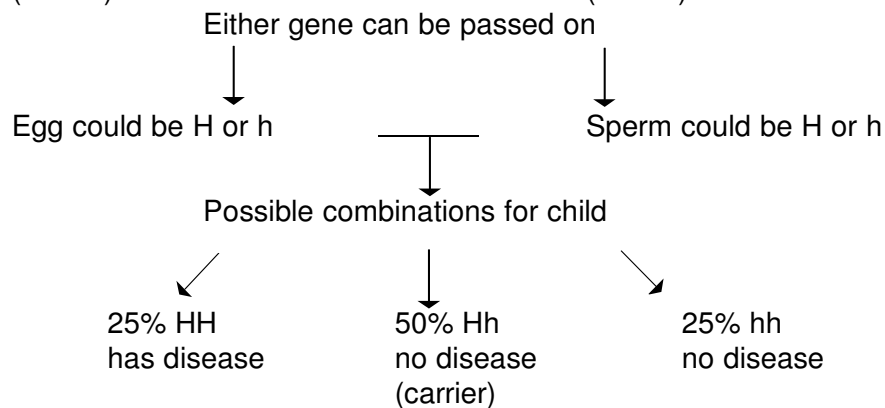
Disease gene H is recessive (Normal gene h is dominant)

Only individuals with HH will have the disease.

All individuals with hh or hH will be normal, however hH individuals will be carriers for the disease.

Mother hH
(carrier)

Father hH
(carrier)



This pattern of inheritance is called autosomal recessive. Neither parents are affected but both are carriers. On average 25% of their children will be affected, 25% normal and 50% will be unaffected carriers.

So how do I know if I am a carrier for a recessive gene?

You don't because a carrier does not have the disease. In fact most people are carriers for a number of recessive genes. Let's say you were a carrier for 5 different diseases. This is only 5 genes out of the many millions of genes that you have. If each individual only carries 5 abnormal recessive genes it is very, very unlikely that your partner would have mistakes in the exact genes. It is therefore extremely unlucky when you have children with somebody who is a carrier for the same condition as this can produce a child with a disease.

Marrying within your own family (e.g. a first cousin) increases your chances of your few abnormal genes being the same as your partners and thus increases the chances of producing autosomal recessive disease.

Sex-linked recessive disease (also called X-linked disease)

We have already mentioned that all humans carry 2 copies of their genes. There is one partial exception to this and this involves the sex genes (or sex determining genes).

Females have 2 X-chromosomes which carry the sex genes. However, males have 1 X-chromosome and 1 Y-chromosome. Therefore they do not have 2 copies of the X-chromosome genes. This is important if a male has an abnormal gene on the X-chromosome. Even if this gene is recessive he will have the disease as he doesn't have a second copy to override this.

Example (X-linked ichthyosis)

Normal gene T is dominant

Disease gene t is recessive

Remember males only have 1 X-chromosome

Mother genes Tt

Father gene T +
"absent second copy"

no disease
(carrier)

no disease

