

The Inheritance of Ichthyosis

Introduction

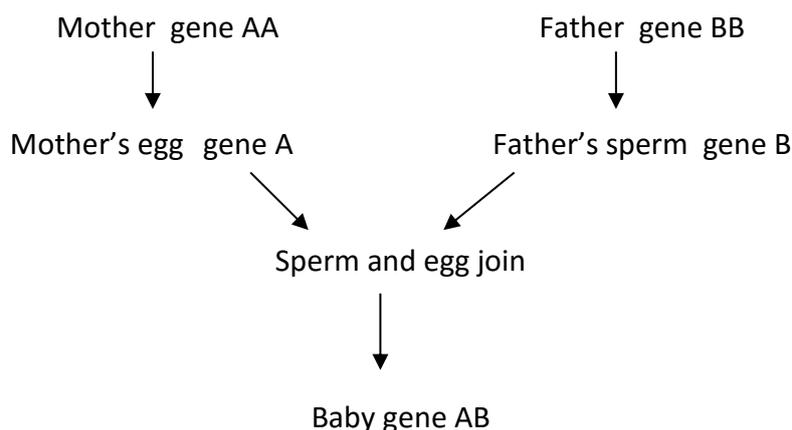
There are many different types of ichthyosis. None of them are catching or contagious but they all depend on a small genetic mistake which has often been inherited from ones parents. There are 3 basic patterns of inheritance but a basic understanding of genetics is needed to understand how this occurs.

- 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 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:



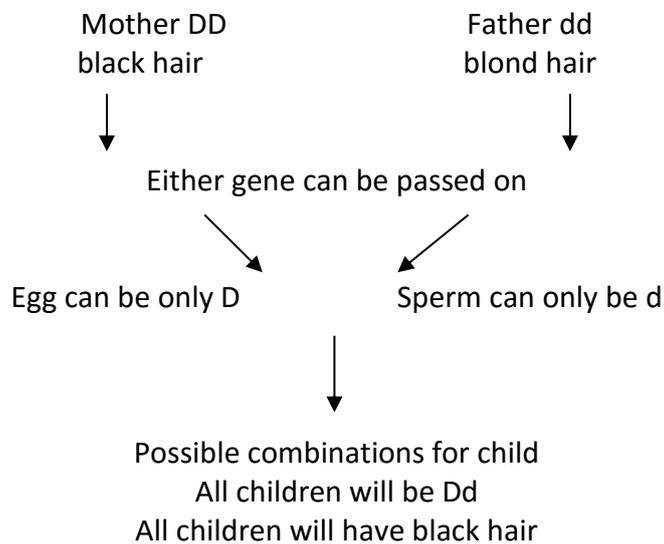
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Dominant and recessive genes

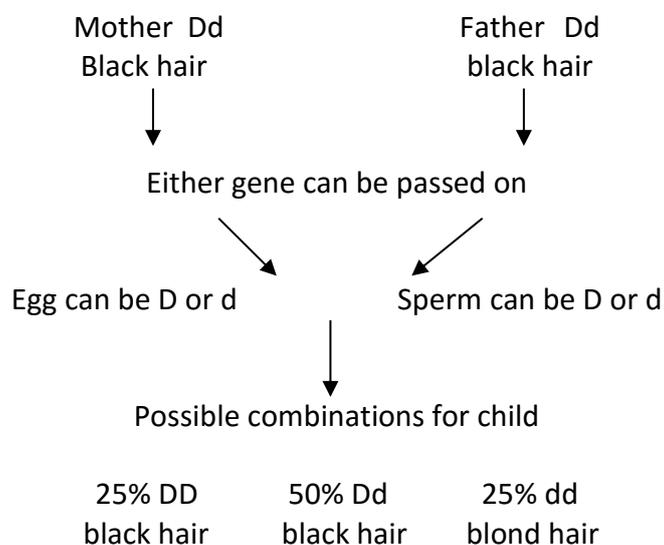
As we have mentioned genes come in pairs. These may be identical genes (eg DD or dd) or non-identical genes eg (Dd). Let's say that this gene causes hair colour. For example gene D may cause black hair and gene d blond hair.

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



Example 2



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Autosomal dominant disease (eg ichthyosis vulgaris)

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

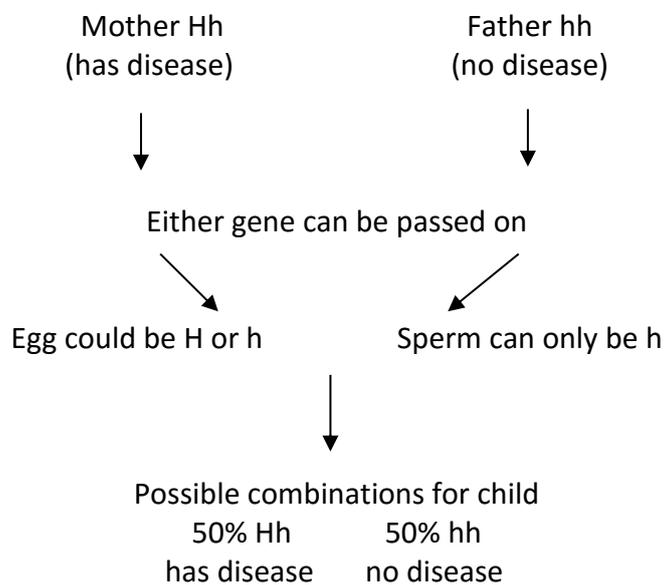
Say gene h is a normal gene. Gene H is an abnormal gene with a small mistake that stops it from working normally.

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.

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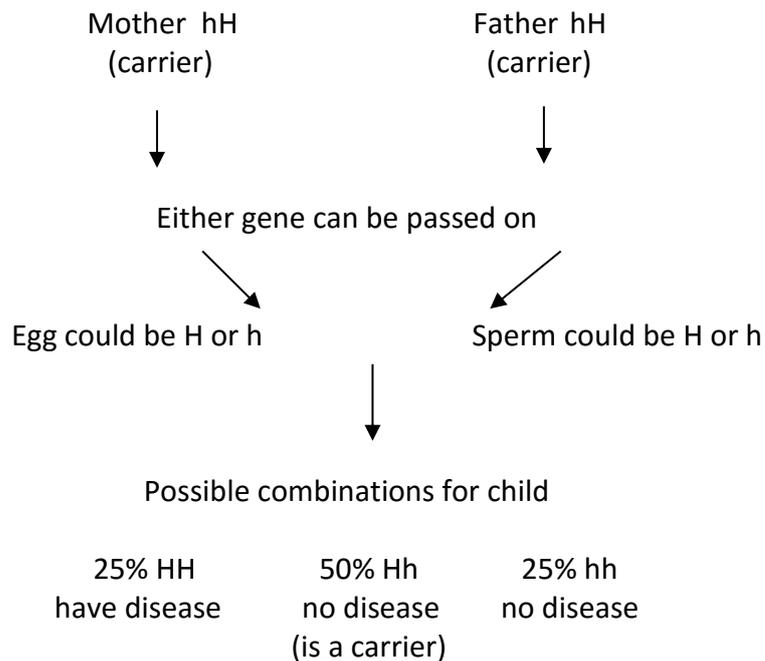
Autosomal recessive disease (eg lamellar ichthyosis)

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.



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 carry 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 (eg a first cousin) increases your chances of your few abnormal genes being the same as your partners and thus increase the chances of producing autosomal recessive disease.

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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).

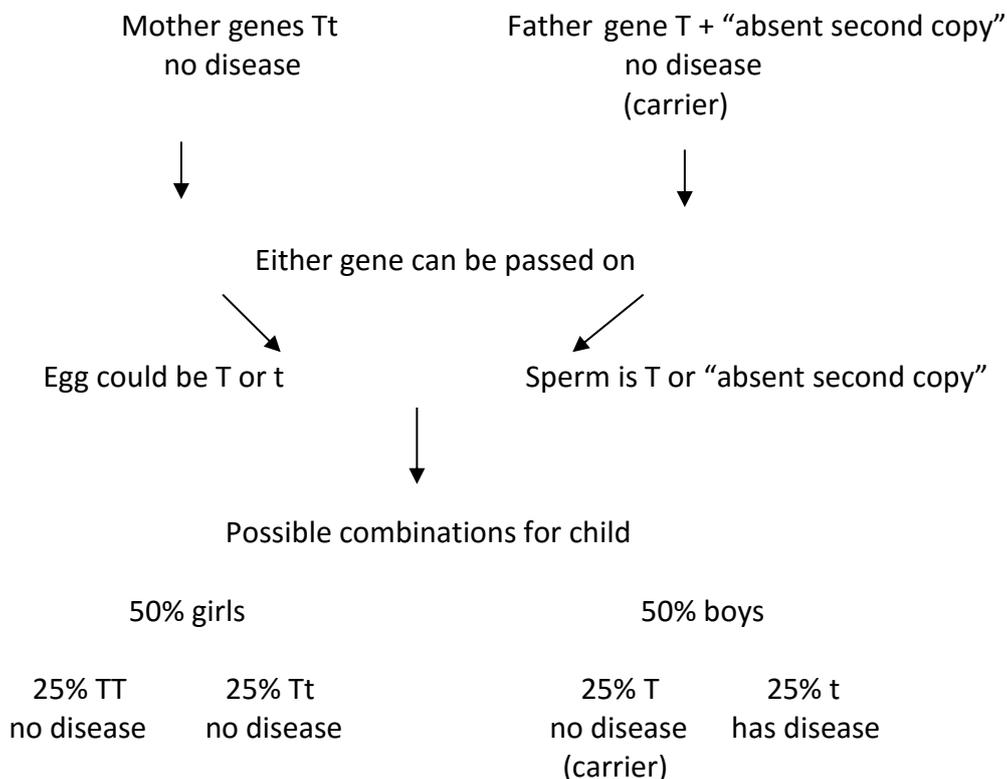
Females have 2 X-chromosomes which carry the sex genes. However, males only have 1 X-chromosome and 1 Y-chromosome. Therefore they do not have 2 copies of the X-chromosome genes. This is important if a male has an abnormal gene on the X-chromosome. Even if this gene is recessive he will have the disease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



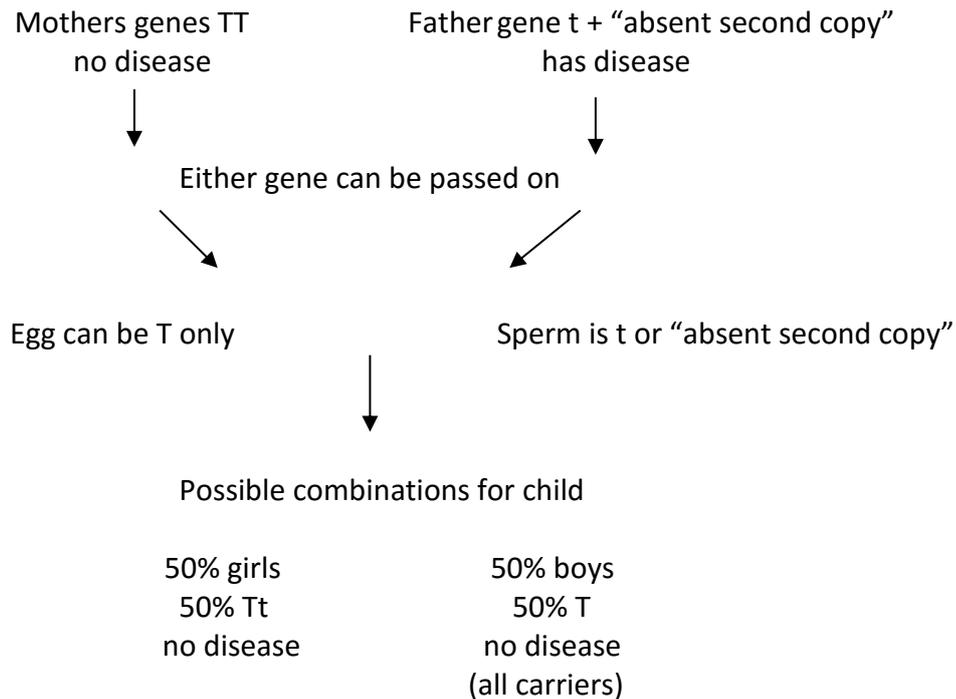
So for X-linked recessive conditions females are normal or carriers whereas males are normal or have the disease. This is why X-linked ichthyosis only occurs in males. Interestingly if an affected male has children none will be affected so it appears to “skip” a generation. In fact all his daughters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

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X-linked dominant disease (eg 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.



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
- KID syndrome

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)

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People who care about ichthyosis

X-linked recessive

X-linked ichthyosis

X-linked dominant

Conradi-Hünemann syndrome

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

Conditions can appear in a child when neither parent is affected. This is usually because the disease gene is newly created (new mutation) 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 low. However the affected child has a chance of passing the condition on to their offspring when they are older depending on the affected gene. This sounds complicated but all this really means it that a genetic mistake has to start somewhere.

Further help

There are a number of online forums about Ichthyosis where individuals can share their experiences and detail their own treatment recommendations. Not everything will work for everyone but these forums are a good place both to receive and offer support.

Contact the Ichthyosis Support Group for information, advice, details on useful products, and to be connected with other people to share experiences and helpful advice.

To find out more about the ISG or become a member please get in touch in one of the following ways:

By Phone or Fax:

Tel: **0845 602 9202** Fax: **0560 343 8046** (on request)

By Email:

isg@ichthyosis.org.uk

By Post:

Ichthyosis Support Group

PO Box 1242, Yateley GU47 7FL

Facebook:

facebook.com/ichthyosissupportgroup

Twitter:

twitter.com/ISG_Charity