Haemochromatosis
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The British Liver Trust works to:

- support everyone affected by all kinds of liver disease
- improve knowledge and understanding of the liver and related health issues
- encourage and fund research into new treatments
- campaign for better services and improved patient care
- increase awareness of the risk factors of liver disease and promote earlier diagnosis

All our publications are reviewed by medical specialists and people living with liver disease. Our website provides information on all forms of adult liver disease and our Helpline gives advice and support on general and medical enquiries. Call the Helpline on 0800 652 7330, General enquiries on 01425 481320, or visit www.britishlivertrust.org.uk
The liver

Your liver is your body’s ‘factory’ carrying out hundreds of jobs that are vital to life. It is very tough and able to continue to function when most of it is damaged. It can also repair itself – even renewing large sections.

Your liver has around 500 different functions. Importantly it:

- fights infections and disease
- destroys and deals with poisons and drugs
- filters and cleans the blood
- controls the amount of cholesterol
- produces and maintains the balance of hormones
- produces chemicals – enzymes and other proteins – responsible for most of the chemical reactions in the body, for example, blood clotting and repairing tissue
- processes food once it has been digested
- produces bile to help break down food in the gut
- stores energy that can be used rapidly when the body needs it most
- stores sugars, vitamins and minerals, including iron
- repairs damage and renews itself.
How liver disease develops

Liver damage develops over time. Any inflammation of the liver is known as hepatitis, whether its cause is viral or not. A sudden inflammation of the liver is known as acute hepatitis. Where inflammation of the liver lasts longer than six months the condition is known as chronic hepatitis.

Fibrosis is where scar tissue is formed in the inflamed liver. Fibrosis can take a variable time to develop. Although scar tissue is present the liver keeps on functioning quite well. Treating the cause of the inflammation may prevent the formation of further liver damage and may reverse some or all of the scarring.
Cirrhosis is where inflammation and fibrosis has spread throughout the liver and disrupts the shape and function of the liver. With cirrhosis, the scarring is more widespread and can show up on an ultrasound scan. Even at this stage, people can have no signs or symptoms of liver disease. Where the working capacity of liver cells has been badly impaired and they are unable to repair or renew the liver, permanent damage occurs.

This permanent cell damage can lead to liver failure or liver cancer. All the chemicals and waste products that the liver has to deal with build up in the body. The liver is now so damaged that the whole body becomes poisoned by the waste products and this stage is known as end stage liver disease. In the final stages of liver disease the building up of waste products affects many organs. This is known as multiple organ failure. Where many organs are affected, death is likely to follow.
What is haemochromatosis?

Haemochromatosis is a medical condition caused by an overload of iron in your body.

There are several forms of haemochromatosis. This leaflet provides information about the most common form, known as hereditary or genetic haemochromatosis (GH), and looks very briefly at some more rare forms and other types of iron-overloading disorders.

In genetic haemochromatosis, inheritance of a faulty or abnormal gene is responsible for an increase in the amount of iron entering the body.

What is iron doing in my body?

Iron is a mineral that is essential to help your body grow. Some minerals, such as calcium, sodium and potassium, are required by your body in large amounts ("macrominerals"). Iron is a "trace mineral" which is needed in smaller amounts. Other trace minerals include zinc, copper and chromium.

As a nutrient, iron is important in your diet to help make haemoglobin, a vital protein in red blood cells. Haemoglobin gives red blood cells their colour and helps them carry oxygen around your body.

If you receive too little iron, you can become anaemic. In fact, a lack of iron in the body is the most common nutritional deficiency in the UK and throughout the world.
Iron enters the body when nutrients are taken in, or absorbed, by your small intestine following digestion. An overload of iron is caused by an increase in the absorption of iron from food.

About two thirds of the iron absorbed is incorporated into haemoglobin itself. Most of the rest is stored in your liver, with smaller amounts distributed to other organs and body tissue. Normally you should have around three to four grams (g) of iron in your body.

Iron storage is thought to be an evolutionary survival mechanism. When the body loses a large amount of blood, it replaces the lost blood cells more quickly than it can take on enough dietary iron to make haemoglobin. Over time, the body developed the ability to absorb and store extra iron in case it was required. Today, blood transfusions and infusion of iron intravenously can provide iron rapidly in a medical emergency.

When red blood cells die, the iron in the haemoglobin is rapidly released to make new haemoglobin and any excess returns to storage. Only small amounts of iron – around a milligram (mg) – are lost from the body each day, mostly in cells from the gut. Your body has no natural mechanism for getting rid of unwanted iron once it has been absorbed.

People with haemochromatosis absorb at least twice as much iron as normal. When more than five grams of iron has been absorbed, it will start to become deposited around the body. An excessive amount of iron can mean 20g or more.

The poisonous (toxic) effects of this extra iron mean that haemochromatosis is a potentially lethal condition, but it can be treated effectively if diagnosed early enough.
How will haemochromatosis affect me?

Haemochromatosis can cause a range of problems in your body, primarily in the liver.

It is thought that the extra iron causes damage by increasing the production of harmful oxygen molecules in your body cells. Known as ‘free radicals’, these molecules are linked to other diseases and understood to play a role in the body’s aging process. They can be toxic when there are too many and this is made worse by the presence of iron. Free radicals will interact with other molecules to damage cells, tissues and organs.

In the liver this takes the form of scarring, known as fibrosis. Additionally, your liver may become enlarged (hepatomegaly). With ongoing liver damage, fibrosis may progress to cirrhosis. If this happens, you are at greater risk of liver cancer, known as hepatocellular carcinoma, or HCC.

Haemochromatosis is likely to lead to serious problems in other organs. Pancreatic damage leading to diabetes and dysfunction in the sexual glands are common, as is the development of arthritis. Heart disease may also develop.

It will also increase your skin pigmentation (hyperpigmentation) so that your appearance develops a yellowish or bronzed effect.

Haemochromatosis is most commonly found in people of northern European descent. The highest frequencies of the disease are found in people
from the British Isles and Ireland. The most common form probably originated in a single individual in Europe at the end of the last ice age and spread as people moved into Northern and Western Europe.

It is more likely to occur in men than in women because women lose iron each month through menstruation.

In the UK the genetic condition is found in about one in 200 people. However, only about one person in 5000 people is ever diagnosed with haemochromatosis. The fact that there are no specific symptoms associated with haemochromatosis supports the view of disease specialists and related health organisations that it is under-diagnosed by doctors and that the disease prevalence is higher.

Other types of haemochromatosis

There are at least five other identified forms of the disease. These include neonatal and juvenile forms.

Neonatal haemochromatosis (NH) is a rare condition that occurs while a baby is developing in the mother’s womb. Toxic levels of iron accumulate in the liver and in other parts of the body. This is usually lethal to the baby before birth or in the early stages of life, although drug treatment and/or a liver transplant have helped some babies to survive the disease. It is not considered to be an inherited disorder. However, the risk of a woman having another baby with NH after her first is much higher.
When severe iron overload is detected in someone under the age of 30 it is called juvenile haemochromatosis (JH). Unlike genetic haemochromatosis, the condition affects both sexes equally. The effects of early iron overload are generally more severe and can lead to extensive organ damage in people aged between 15 and 30.

Juvenile haemochromatosis is inherited. Fortunately, both juvenile and neonatal forms of the disease are very rare.

Other inherited blood disorders such as thalassemia and sickle cell anaemia can cause iron overload. Here, overload occurs when the body accumulates iron in an attempt to counteract anaemia, and by blood transfusions. Transfusions are often a major part of therapy for these disorders, whether given occasionally during acute crises or as part of a regular treatment programme.

People with these diseases cannot be treated in the same way as for genetic haemochromatosis. Instead, they may need regular chelation therapy (the use of drugs which bind with metals in the body so that they can be excreted) and blood exchange rather than transfusions. You can discuss how to prevent iron overload in thalassemia and sickle cell disease with your haematologist.

Alcohol related liver disease can play a role in developing iron overload, as can hepatitis C and other liver problems. However, the degree of iron overload is mild.
How is haemochromatosis inherited?

Genetic haemochromatosis, as its name suggests, runs in families and is now recognised as one of the most common disorders of this type.

The disorder is caused by a gene. This is a segment of DNA containing the instructions for making up your body. Genes are packaged in a sequence on strands of DNA called chromosomes which are found in the nucleus of your body cells. All of us carry up to 30,000 individual genes.

All of your body cells should contain a gene inherited from your mother and one from your father. We generally carry the same genes as each other, but around 1% of genes will differ between people. These small differences are what contribute to each person’s unique physical traits.

The HFE gene mutation

Genes are responsible for managing the production of proteins that control the cells in your body.

The HFE gene contains instructions for producing a protein that helps with the digestion of food by managing the absorption of iron into your small intestine. When functioning normally this mechanism limits the amount of iron going into your body from your diet.
In 1996 changes in the HFE gene were found to be associated with haemochromatosis. A permanent change in the code of the DNA making up a gene or chromosome is known as a 'mutation'. This can alter the way a physical characteristic is expressed or cause some function in the body to occur differently. Sometimes the word 'variant' is used instead as many changes do not cause any disorder.

It is thought that mutations on the HFE gene restrict its ability to control iron intake. This is linked to a deficit of hepcidin, a peptide or small protein responsible for regulating iron in your body.

There are actually two known common variants in the HFE gene that have been associated with iron overload. These are called C282Y and H63D. The numbers 282 and 63 indicate where the mutations are found on the HFE gene. The mutations occur on a specific chromosome (chromosome six).

The C282Y mutation is the more severe. It is found only among people of northern European origin and may date back several thousand years (see pages 10, 11). In the UK about one in eight people carry one copy of the HFE gene with the C282Y mutation but such 'carriers' are not at risk from iron overload.

The H63D variant is associated with a milder disease and usually only when inherited with a copy of the HFE gene having the C282Y
To develop haemochromatosis that is linked to the HFE gene, both copies of the gene must be affected. For this reason it is known as a ‘recessive’ disorder, as opposed to a ‘dominant’ disorder where only one gene is required.

In over 90% of people diagnosed with the disorder, both genes have been found to be abnormal. A person who has only one abnormal gene is known as a ‘carrier’. They are not usually affected but can pass on the gene to their own children. On average, half the eggs or half the sperm of a carrier will contain the abnormal gene.

A person who inherits the mutation from both parents will carry the abnormal gene in all of their eggs and sperm.

Mutation. It is thought to be much older and is spread more widely throughout the world. In the UK one in four people carry one copy of the HFE gene with the H63D variant. They are not at risk from iron overload.

In the UK about 90% of people with haemochromatosis have two copies of the C282Y mutation. About 5% have one copy of each mutation (C282Y/H63D) and the remainder have only one copy of the C282Y or H63D variants or no copies. These people may have other changes in the HFE gene or changes in other genes causing iron overload.

Not all people with haemochromatosis will therefore have typical gene mutations.

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A person who inherits the mutation from both parents will carry the abnormal gene in all of their eggs and sperm.
People who inherit the same mutated gene from both of their parents (e.g. C282Y/C282Y) are termed 'homozygote'. Those who inherit one mutated gene only (carriers) are called 'heterozygote'. People who have two different forms of the mutated gene are called 'compound heterozygotes'.

Scientists still have some way to go to be able to answer important questions about how genetic haemochromatosis occurs. It is still not known how many people with the defective HFE gene will go on to develop symptoms or why some people develop symptoms and others do not.

However, using data based on the whole population it has been possible to work out the theoretical chance of a person inheriting the abnormal gene when one or both of their parents have it (see diagram on the next page).

When both parents are carriers for the abnormal gene there is a 25% chance of a child being homozygote. On average, 50% of the children from this relationship will be carriers and 25% will not carry the affected gene.

Where one parent is homozygote for the gene and the other is a carrier, 50% of the children will be homozygote and 50% will be carriers.

If one parent is homozygote and the other is unaffected, all of their children will be carriers.

In the rarest case, where both parents are homozygote, all of their children will also be homozygote and will be at risk of developing haemochromatosis.
What are the symptoms of haemochromatosis?

Although haemochromatosis is inherited, the build-up of iron in the body happens quite slowly and symptoms do not usually appear until a person is aged 30 or 40 years old. In women,
this is commonly closer to 50 years. Remember that for many homozygotes for C282Y the lifetime build-up of iron is quite small and does not cause clinical problems.

When symptoms do appear, they may include the following:
- tiredness, fatigue or lack of energy
- a feeling of weakness in your limbs
- pain in the joints, especially in the knuckles and in the joints of your first two fingers
- pain in your stomach or abdomen
- loss of libido (sex drive) and possibly impotence or early menopause
- evidence of liver damage from scarring (fibrosis) and cirrhosis
- cardiomyopathy (disease of the heart muscle)
- type 2 diabetes
- a yellowing or ‘bronzing’ of the skin.

Some people diagnosed with haemochromatosis report having mental confusion, mood swings and depression.

**Diagnosis**

Doctors may be required to investigate and rule out a range of other illnesses that share the same symptoms before haemochromatosis is suspected.

Abnormal iron levels are often the only sign of haemochromatosis. Therefore, the most important tests for detecting iron levels in the blood are the transferrin saturation and serum ferritin tests.
Transferrin saturation (TS)

Transferrin is a protein that binds iron in the blood serum and carries it around your body. This test measures the level of iron in your blood against the capacity of the blood iron binding protein (transferrin) to bind it. This is known as the Total Iron Binding Capacity or TIBC.

The transferrin saturation (TS) is the concentration of serum iron divided by the TIBC expressed as a percentage. A value over 55% in a man and over 50% in a woman may indicate an overload of iron. If this is the result you may be asked to provide another sample after an overnight fast so that a more accurate reading can be gained.

Serum ferritin (SF)

Ferritin is the protein that stores iron in the tissues. Small amounts of ferritin are found in the blood serum. As the amount of iron in your body increases, so do the levels of ferritin in the serum. Ferritin is measured in micrograms (mcg) per litre. The upper limit is set at 300 for men and 200 for women. Levels over this limit are seen as an indication of haemochromatosis. Usually both transferrin saturation and ferritin are measured when testing for haemochromatosis.

However, measurement of ferritin is not totally reliable as iron levels may increase when the liver is inflamed and can also increase in medical conditions other than haemochromatosis. Additionally, your ferritin levels may be within normal range during the early stages of haemochromatosis. The TS may be depressed in a patient who has inflammation (such as arthritis) or an infection.
Genetic test
Genetic testing is a recent development in haemochromatosis and is used to determine whether you have the HFE gene mutation. Doctors may use the test to identify the cause of high iron levels detected in the TS and SF tests.

Your blood cells will be examined for the HFE gene mutations C282Y and H63D by using a simple blood test. In some cases this may be a finger prick test in which a small drop of blood is applied to a card and taken away for examination.

If homozygosity for C282Y or compound heterozygosity for C282Y/H63D is found, the test is ‘positive’. Genetic testing is positive in over 90% of people with iron overload.

Liver function tests
If liver disease is suspected, liver function tests (LFTs) may also be used. These involve a number of separate examinations, each looking at different properties of your blood to gain an idea of how much your liver is inflamed or damaged in its ability to work properly.

In particular, doctors will be concerned to measure levels of the liver enzymes ALT and AST which are increased during liver inflammation (hepatitis).

Liver biopsy
The genetic test has reduced some of the need for liver biopsy to confirm haemochromatosis. However, if you have high serum ferritin (over 1000 mcg per
Magnetic Resonance Imaging (MRI) is a special tube scanner used to provide a detailed view of the liver. It creates powerful magnetic fields by releasing radio frequency energy to act on water molecules in your body. A type of radio signal is returned and picked up by the MRI equipment. This is relayed to a computer that can generate very detailed cross-sectioned images (or ‘slices’) of your liver area.

Diagnostic technology has been developed specifically for iron-overloading disease. ‘Ferriscan’ is a procedure that has been developed to analyze the MRI scans themselves in order to measure iron concentration.
Prevention

If you have a family history of haemochromatosis, you should see a medical professional as soon as you can.

Relatives may be at risk and need to be encouraged to be screened by genetic testing to find out whether they carry the HFE gene mutation (though children do not need to be tested until they reach adulthood and can decide for themselves). ‘Screening’ in this sense means testing people who have no symptoms but are considered to be at increased risk of a particular disorder.

It is very important that brothers and sisters are screened because they are more likely to carry both abnormal genes.

Genetics is a complex and fast changing area. Genetic counselling can help you to better understand the likely occurrence of haemochromatosis in your family or explain the implications of any diagnosis. Genetic counsellors are specially trained professionals, usually from a medical or nursing background, who have first-hand knowledge of genetic disease and its practical impact.

You may wish to talk to a counsellor to find out more about an inherited disorder in your family or you can be referred for counselling by a GP or hospital consultant following diagnosis.
**Screening for haemochromatosis**

Awareness of haemochromatosis among GPs is still emerging and it is still often mistakenly considered to be a rare disease.

Diagnosis is not easy because most symptoms are non-specific, meaning that they are usually caused by other conditions not related to haemochromatosis.

Symptoms can also take a long time to develop. As they often occur after the age of 40 they can be mistaken for, or coincide with, conditions that have a later onset such as diabetes and heart disease. This can mean that people are not referred for the correct diagnostic tests quickly enough.

In the UK the National Screening Committee has yet to recommend national screening for haemochromatosis despite the known benefit of early detection. This is due to major uncertainty about the chance of a person becoming ill as a result of inheriting genetic haemochromatosis.

Without national screening, the possibility of carrying out blood iron tests to screen age and ethnically-targeted people should be examined urgently.

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**Treatment**

Treatment of haemochromatosis is simply aimed at removing iron from your body. As the body has no natural method for getting rid of the extra iron, this done by regular bleeding known as phlebotomy.
During phlebotomy a unit of blood, usually 450 millitres (ml), is removed. This amount will contain 220mg of iron. Bleeding in this way will activate the remaining stored iron to make new red blood cells.

You will be required to have phlebotomy once a week, depending on the degree of your iron overload. This may continue for up to two years. Over this period doctors will monitor your serum ferritin levels until they fall to a safe level (generally 20 mcg per litre). Removing blood does not stop the iron building up.

**Phlebotomy**

Phlebotomy, also called venesection (or venepuncture), is much the same method as is used for blood donation. Blood is extracted by a person specially trained to do this, called a phlebotomist, or a doctor or nurse. It is normally an outpatient procedure.

To collect the blood a syringe with a needle is inserted into a vein on your inner arm. You should only feel a tiny pin-prick as this is done and the rest of the procedure should be painless.

It is possible that you may feel a little dizzy or nauseous during or after phlebotomy. You may be encouraged to rest for a short while following the procedure. Over the next 24 hours it will help to drink plenty of fluids and eat regularly to replace your lost blood cells.

After your course of treatment you will be required to have further phlebotomies two to four times a year for the rest of your life. Doctors will continue to monitor
transferrin saturation and serum ferritin levels (ideally maintained at 50% and 50 mcg per litre respectively) to assess when phlebotomy may be required. This is known as ‘maintenance therapy’.

**Who will be looking after me?**

In hospital it is likely you will be treated either by a specialist in liver disease called a hepatologist, a specialist in digestive disorders called a gastroenterologist, or a specialist in blood disorders called a haematologist.

Where you may have other conditions or problems caused by haemochromatosis, additional specialists may be involved in your care. These may include a cardiologist (heart), an endocrinologist (glands) or rheumatologist (joints).

**Can I return to normal?**

Some of the symptoms of haemochromatosis will go away and some will not. This is likely to depend on the stage at which your disease has been diagnosed.

Generally, any conditions that existed before your treatment for haemochromatosis was begun will not improve.

An enlarged liver may reduce in size but if cirrhosis has become advanced, improvement is unlikely. If you have cirrhosis, doctors may run blood tests and imaging tests at regular intervals (usually every six months). Having cirrhosis will put you at a much higher risk of developing hepatocellular carcinoma (HCC).

If this occurs, a liver transplant may be required. This is usually only recommended if other treatments are no longer helpful and your life is
threatened by end stage liver disease. It is a major operation and you will need to plan it carefully with your medical team, family and friends.

In diabetes, phlebotomy will not be able to repair damage to your pancreas. Other serious problems such as arthritis and sexual disorders arising from damage to the pituitary gland are unlikely to improve.

Symptoms such as tiredness and abdominal pain should lessen with recovery. The colour of your skin should return to normal.

If you have heart disease, such as cardiomyopathy, any improvement will be linked to the severity of any damage caused by haemochromatosis.

I am a Haemochromatotic

I was fit – a sportsman. I ran marathons. So why was my brother phoning me every Saturday, all the way from Australia, insisting I visit my GP for tests? After six weeks of resisting 5am phone calls, my wife said ‘enough is enough’. I made the appointment.

My brother’s persistence saved my life!

My GP took blood tests and referred me to hospital where I was told my ferritin level was nearly 2,700. This was twice that of my brother who is three years older. I started venesection (phlebotomy) treatment that day. Later, an ultrasound scan and a liver biopsy showed that I had a severely fibrotic liver. I stopped drinking alcohol immediately.
My treatment then consisted of weekly venesections. This lasted for 18 months and finally began to reduce my ferritin level. The weekly visits to hospital proved quite disruptive – an understanding employer is to be welcomed.

Like most people, I was ignorant of genetic haemochromatosis. So I joined the GH Society, not only to gain knowledge but to meet other haemochromatotics. I have found this to be very beneficial. Unfortunately, for some haemochromatotics, late diagnosis is to prove fatal. But it makes me realise how very lucky I have been and explains why no male member of our family, other than my father, had ever reached the age of 65.

Looking back, I had visited my GP and presented classic symptoms such as arthritis, chest pain and discomfort on my right side. Each was treated but never connected.

Other symptoms, such as extreme tiredness and mood swings, presented themselves before and during treatment. This certainly tested relationships. A supportive partner is essential.

I do have sympathy with GPs as the condition presents itself over an extended period. In many ways, my brother has totally different symptoms to my own. What I do question is, after 14 years, why are my brother and I still the only haemochromatotics in our respective surgeries? A national screening programme would help, but the NHS appears reactive rather than proactive in nature. As with all initiatives, cost is paramount.
I have found it invaluable to manage my own treatment. I have, during the last 14 years, met many nursing staff. I've been transferred from Haematology to Gastroenterology and back again. Simple things such as knowing the colour tube for a specific blood test can save time. Nursing staff change regularly. Keeping a record of when I need extra tests etc. has proved helpful.

Bringing things up to date, my treatment has reduced most of the symptoms mentioned earlier, apart from the arthritis. In fact, I write this as I recover from a total knee replacement.

A follow-up liver biopsy showed that my fibrosis is almost completely reversed. This demonstrates the benefit of reducing alcohol intake, especially during the ‘de-ironing’ phase. My life expectancy is now considered to be normal and, after recovery from my knee operation, I will be back in the gymnasium and leading an active lifestyle. I even take the odd glass of wine.

Yes, I am a very lucky haemochromatotic.

Looking after yourself

Medical staff may suggest that you regulate the amount of iron in your diet. Having haemochromatosis does not mean that you have to go out of your way to avoid iron. It is better that you try to balance your intake, as foods containing iron will also contain other nutrients that are essential for your general well-being.
How can I control the iron in my diet?
There are two different forms of dietary iron, known as haem and non-haem. Haem iron is found in animal tissues while non-haem iron exists in plant or vegetable material.

The amount of iron you absorb from eating foods made from various plant sources ranges from around 1% up to 10%.

Absorption from animal food sources is much higher, at between 10% and 20%.

You should avoid consumption of the following:
- vitamins or multivitamin supplements that contain iron
- Vitamin C in pill form as this increases absorption of non-haem iron. Vitamin C from fruit and vegetables does not need to be avoided
- breakfast cereals that are ‘fortified’ with iron
- shellfish such as oysters, mussels and clams as these contain a bacteria that may be fatal to people with iron overload.

Because of the increased absorption from animal foods you may wish to cut down on eating red meat. Offal (organs such as heart, liver, kidneys etc.) in particular is very iron-rich.

There are certain substances that should be included in your diet:
- calcium, as found in dairy foods, limits the absorption of haem iron (it is therefore helpful to consume dairy foods when you are eating meat)
- tannin, as found in tea, limits the absorption of iron.

It is a good idea to develop a habit of reading the package labelling on processed foods to find out their nutritional content. You may be surprised to learn that even certain breads may have too much iron for you.

While watching your diet is essential, it is important to note that it is very unlikely you will prevent the development of haemochromatosis or be able to avoid the need for phlebotomy by dietary means.

**Alcohol and haemochromatosis**

The relationship between excessive drinking and haemochromatosis remains the subject of much research. At one time, drinking too much alcohol was wrongly considered to be the cause of haemochromatosis.

Studies now show that the combination of alcohol and iron increases the way in which free radicals cause 'oxidative stress' in the body.

This means that drinking alcohol is likely to speed up and worsen the impact of the disease. If you have cirrhosis it is sensible to avoid alcohol completely.

**Exercise**

A common symptom of haemochromatosis is not having the energy to carry out physical tasks. This may improve with phlebotomy.

You should talk to your medical advisor before undertaking any strenuous activity.
Useful words

**Absorption** – process by which nutrient substances are taken in and processed by the small intestine before being moved into the blood stream to be used around your body.

**ALT** – alanine aminotransferase, a liver enzyme that enters the blood following liver damage. An increase in ALT levels, as measured in liver function tests, may indicate the presence of liver disease.

**Amino acids** – the compounds that make up proteins. Proteins in the human body are made of 20 different amino acids that are either manufactured by the body or absorbed from your diet.

**Anaemia** – a condition in which you have less than the normal amount of red blood cells or haemoglobin in your blood.

**AST** – aspartate aminotransferase, a liver enzyme but less specific to the liver than ALT (see above). A raised AST level may follow a heart attack, for example.

**Base sequence** – the order of the chemical units known as ‘nucleotide bases’ (adenine, thymine, cytosine and guanine) in DNA that forms the genetic code. The sequence of the bases will determine what protein is produced.

**Cell** – the most basic and smallest functioning unit or ‘building block’ of living things. Your body is made up of cells, each with its own unique functions and features. Within the outer skin (membrane) of each cell is a central compartment known as the cell ‘nucleus’ that contains your genetic material.
Chromosome – a single, long molecule of DNA that holds our genes, contained within the nucleus of a cell. A cell should contain 46 chromosomes in two pairs of 23. One set of 23 chromosomes is inherited from the egg of the biological mother and the other from the sperm of the biological father. Chromosomes are numbered from 1 to 22 (and known as ‘autosomes’) with the 23rd pair, the sex chromosomes, designated ‘X’ and ‘Y’.

DNA – deoxyribonucleic acid, the chemical compound of which chromosomes are made and which contains the genetic instructions for the making of proteins in your body. DNA molecules consist of two paired strands that twist to form a double helix. Each strand is made of four chemical units called ‘nucleotide bases’. These are adenine (A), thymine (T), guanine (G), and cytosine (C). They pair specifically with bases on opposite strands e.g. ‘A’ always with ‘T’, ‘C’ always with ‘G’ etc. and their order determines the meaning of the information encoded in that part of the DNA molecule.

Enzyme – a protein that speeds up a chemical reaction within a cell, without being changed or used up in the reaction.

Expression – the process where information encoded in a gene is converted into the structures and functions of a cell.

Ferritin – the protein that stores iron in your body. As the amount of iron increases, so do the levels of ferritin in the serum. Measuring ferritin levels is more accurate than measuring blood iron in the long run, as the latter may vary with diet.
**Free radical** – an unstable molecule created from the metabolism of oxygen in your body. Free radicals belong to a group known as ‘reactive oxygen species’. Although a by-product of normal cell function, when too many are generated they can become toxic and lead to cell damage.

**Gene** – a segment of a chromosome (or unit of DNA) that carries the instructions or code for making a specific protein or set of proteins responsible for, or contributing to, a specific physical trait or action.

**Genotype** – the genetic makeup encoded in your DNA.

**Haemoglobin** – an iron-containing protein (metalloprotein) contained in the red blood cells. Haemoglobin is responsible for transporting oxygen from the lungs to the rest of your body. It is also the pigment that provides the colour of red blood cells.

**Hepatocyte** – a liver cell.

**Inflammation** – the first response of the immune system to infection, commonly characterised by heat, swelling, pain and tenderness.

**Molecule** – the smallest component of a substance able to show the typical chemical properties of that substance. Molecules are made up of atoms that are held together by chemical bonds and make up all living and non-living things.

**Mutation** – an occurrence where a gene undergoes a change or variation in the base sequence of its DNA. Some mutations result in the gene no longer coding for the correct protein, or producing a reduced amount of the protein.
Nutrient – a substance required from our diet for growth and sustenance of life. Nutrients can be ‘organic’, such as carbohydrates, fats, proteins and vitamins, or ‘inorganic’. Inorganic nutrients are usually minerals such as water, oxygen or iron.

Oxygen – an odourless, colourless gas absorbed from the atmosphere through your lungs and into your blood. Oxygen is a major component of organic molecules and is necessary for most forms of life.

Peptide – a compound formed when two or more amino acids are joined.

Protein – the active molecule in cells that determines the physical structure of the organs and tissue that make up your body. Proteins also control the biological and chemical reactions within your body.

Serum – more than half of your blood is made of plasma, the substance which carries the circulating blood cells and platelets. Normally clear or yellowish, serum is the liquid that separates from blood when clotting occurs. Many chemical tests will carried out using serum.

Transferrin – a protein that binds iron in the blood serum and carries it around your body. The percentage of transferrin bound to iron is increased in haemochromatosis.

Variant – as in gene variant, a term that may be used in place of ‘mutation’ (see above) as many gene changes do not cause any disorder.
Special thanks

Professor Mark Worwood, Director of the Graduate School in Biomedical and Life Sciences, Department of Haematology, School of Medicine, Cardiff University

Peter Wells
Janet Fernau, Haemochromatosis Society

Further information

There are a number of other useful organisations that you may find helpful – the contact details of these can be found on our website.

The British Liver Trust publishes a large range of leaflets about the liver and liver problems written for the general public.

Leaflets that you may find particularly helpful include:

- Alcohol and liver disease
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