

# Non-alcohol related fatty liver disease



Pioneering Liver Health

# Non-alcohol related fatty liver disease

This publication is for people diagnosed with non-alcohol related fatty liver disease (NAFLD), which is characterised by infiltrations in the liver not caused by alcohol. It is also for those who would like to better understand the condition, associated risk factors and how to help prevent the development of the condition.

The British Liver Trust works to:

- support people with, and affected by, 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 and our Helpline gives advice and support on enquiries about liver health. Call the Helpline on **0800 652 7330**, general enquires on **01425 481320**, or visit **[britishlivertrust.org.uk](http://britishlivertrust.org.uk)**

For the latest updates to this information, please refer to our website **[britishlivertrust.org.uk](http://britishlivertrust.org.uk)**

A list of reference sources for this information is available on our website, or by contacting **[info@britishlivertrust.org.uk](mailto:info@britishlivertrust.org.uk)**

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## The liver

Your liver is your body's 'factory' carrying out hundreds of jobs that are vital to life. It is able to repair itself (even renewing large sections). **However, the liver's ability to repair itself is limited and continuous harm can lead to permanent scarring.** Your liver is very tough and able to function even when some of it is damaged, which means you may not notice any symptoms until your disease is quite advanced and noticeably affecting your health.

Your liver performs hundreds of functions. Importantly it:

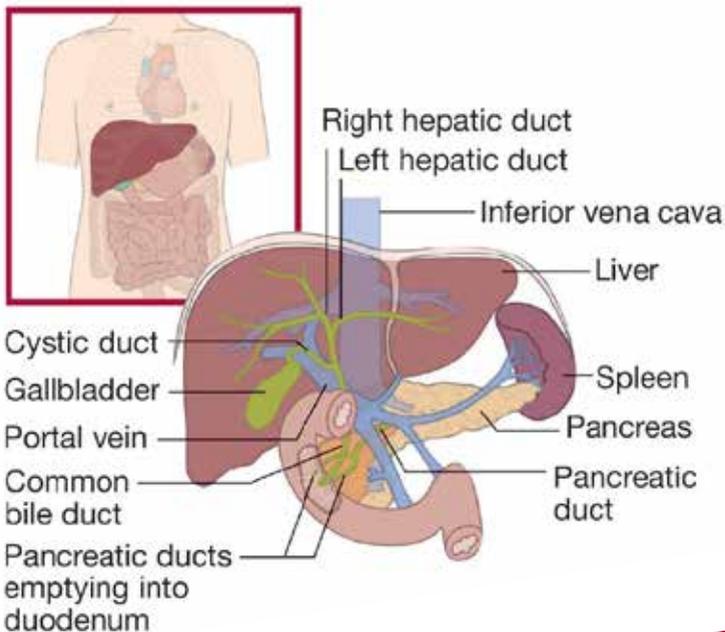
- filters and cleans the blood
- fights infections and disease
- deals with and destroys poisons and drugs
- makes vital proteins which make your blood clot when you cut yourself
- produces bile to help break down food in the gut
- processes food once it has been digested
- stores energy that can be used rapidly when the body needs it most
- regulates fat breakdown and distribution in the bloodstream
- stores sugars, vitamins and minerals, including iron
- gets rid of waste substances from the body
- produces and maintains the balance of some hormones
- produces chemicals – enzymes and other proteins – responsible for most of the chemical reactions in the body, for example repairing tissue
- repairs damage and renews itself (up to a point).

## How liver disease develops

Your liver responds to harm by becoming inflamed. Any inflammation of the liver is known as hepatitis, whatever its cause. Sudden inflammation of the liver is known as acute hepatitis. When inflammation of the liver lasts longer than six months, it is known as chronic hepatitis.

Inflammation is part of the process of repairing damaged tissue. In a similar way to a scab forming over a skin wound, a temporary fibrous 'scaffold' forms while new liver cells regenerate. If your liver is repeatedly harmed, new liver cells cannot regenerate fast enough and the fibrous scaffold remains as a scar. This is called fibrosis, and can take a variable amount of time to develop.

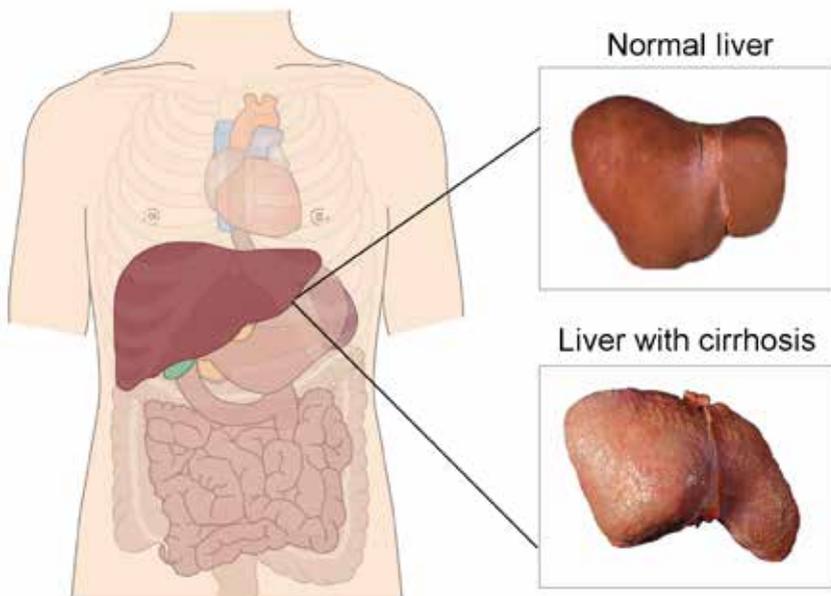
When fibrosis is present, your liver may be able to keep functioning quite well. Removing or treating the cause of the inflammation may reverse some, or all, of the fibrosis and prevent further liver damage.



If the harm to your liver continues, the inflammation and fibrosis can spread throughout your liver, changing its shape and affecting how well your liver cells work. This is known as **compensated** cirrhosis. Even at this stage, people can have no obvious signs or symptoms.

The scar tissue in cirrhosis interrupts the blood flow through the liver. As a result, the blood pressure in the veins in your abdomen is increased and may result in bleeding. Scar tissue in cirrhosis is difficult to remove and may be permanent. However, further progression can be halted and your cirrhosis stabilised, if the cause of the liver damage is removed.

Cirrhosis increases your risk of liver cancer and can lead to liver failure. If damage to your liver continues, it will become unable to function sufficiently (**decompensated** cirrhosis) and start to fail; this is sometimes referred to as 'end stage liver disease'. At this stage chemicals and waste products can build up in the body, commonly causing jaundice, ascites (a build-up of fluid in the abdomen) and hepatic encephalopathy (confusion and memory loss). In the final stages of liver disease the build-up of waste products may lead to multiple organ failure and loss of life.



## What is fatty liver?

Fatty liver is the name given to a condition in which you have too much fat in your liver<sup>14</sup>. There should be little or no fat in a healthy liver. For most people, carrying a little fat in the liver causes no problems.

Too much fat in your liver is caused by the build-up of fats called triglycerides. These are the most common fats in our bodies. They belong to a group of fatty, waxy substances called lipids, which your body needs for energy and growth. We get triglycerides from our diets. Foods high in fat and sugar contain high amounts of triglycerides. They can also be made in the liver from sugars and proteins.

The liver processes triglycerides and controls their release. The triglycerides are combined with special proteins to form tiny spheres called lipoproteins which are sent into the bloodstream to circulate among the cells of your body. When the release or 'secretion' of lipoproteins from the liver is interrupted, or the flow of triglycerides to the liver is increased, there will be a build-up of fat in your liver cells<sup>15</sup>.

### Acute Fatty Liver Disease

It is important to differentiate NAFLD and NASH from acute fatty liver disease, which may occur during pregnancy or with certain drugs or toxins (poisons).

This condition is very rare and may lead rapidly to liver failure. More information is available on the British Liver Trust website.

Consuming too much alcohol can cause an accumulation of fat in the liver and can spur the liver to make triglycerides. If alcohol is the cause of fatty liver disease it is called alcoholic liver disease (see our 'Alcohol and liver disease' publication).

Fatty liver that is not caused by alcohol is known as non-alcohol related fatty liver disease (NAFLD), which can then lead to non-alcoholic steatohepatitis (NASH).

Until recently NAFLD was considered to be rare and relatively harmless. It was not thought to progress to chronic (long-term) or serious liver disease. For most people, a fatty liver can remain free of inflammation<sup>16</sup> and they will experience few symptoms.

However, for an increasing number of people, the effects of having fat in their liver, over a long period, may lead to inflammation causing scarring (fibrosis)<sup>15</sup>. In some people this can progress to a potentially life-threatening condition known as cirrhosis.

Today, NAFLD is recognised as one of the most common forms of liver disease worldwide and one that can progress to advanced liver damage.

## How does NAFLD affect my liver?

### **Non-alcohol related fatty liver disease (NAFLD)**

NAFLD is characterised by the build-up of excess fat in the liver of people who do not drink more than recommended guideline amounts<sup>17</sup> of alcohol.

The first stage is fatty liver, or steatosis. This is where fat accumulates in the liver cells without any inflammation or scarring. For many people, the condition will not advance and a serious liver condition will not develop, but for some, NAFLD can progress on to NASH.

NASH is a more significant condition, as it may cause scarring to the liver, and can progress to cirrhosis. Cirrhosis causes irreversible damage to the liver and is the most severe stage of NAFLD<sup>18</sup>.

It may be easiest to think of NAFLD as having the following stages:

1. Non-alcohol related fatty liver or steatosis
2. Non-alcohol related steatohepatitis (NASH)
3. NASH with fibrosis
4. Cirrhosis

### **How common is NAFLD?**

NAFLD can affect a wide range of people. In general, the more overweight you are, the more chance there is that you may have the condition. NAFLD is typically seen in people aged around 50 and more commonly in men than women<sup>19</sup>.

It is hard to be precise about how many people have NAFLD but it is estimated that one in five people (20%) in the UK are in the early stages of the condition<sup>20,21</sup>.

NASH is a more aggressive form of NAFLD where there is inflammation in and around the fatty liver cells. This may cause swelling of your liver and discomfort around it. If you place your right hand over the lower right side of your ribs, it will cover the area of your liver.

Over a long period of time, ongoing inflammation leads to a build-up of scar tissue in your liver. This process is known as fibrosis and can lead to cirrhosis.

NASH is now considered to be one of the main causes of cirrhosis; many cases of cryptogenic (of unknown origin) cirrhosis are now being recognised as being caused by NASH.

Cirrhosis is usually the result of long-term, continuous damage to the liver. This is where irregular bumps, known as nodules, replace the smooth liver tissue and the liver becomes harder<sup>22</sup>. The effect of this, together with continued scarring from fibrosis, means that the liver will run out of healthy cells to support normal functions. This can lead to complete liver failure (please see our 'Cirrhosis' publication for more information).

### **Jez's story**

Jez is a 35 year old marketing exec. He isn't much of a drinker and until he injured his knee, he used to play football on the weekends. He now watches DVDs instead. Jez has started to feel exhausted at work and is aware that he has recently put on some weight. He has put this down to no longer playing football.

On seeing his GP, Jez learns he has high blood pressure and is shocked to find out he is three stone overweight. With a BMI of 29, Jez is almost clinically obese. The doctor runs some blood tests, including LFTs (liver function tests); the results come back showing abnormalities. Jez is referred to his local hospital for an ultrasound scan, which reveals that he has excess fat in his liver and is diagnosed with NAFLD.

Jez's GP explains that he can slow down the NAFLD's progression and even stop it, but he will need to make some lifestyle changes. Jez agrees to eat a healthy well-balanced diet and to increase the amount of exercise he does.

Because Jez can no longer play football, he looked for other forms of exercise he would enjoy. He has taken up swimming and something completely new to him, yoga (see page 28 for more information on exercise). He cuts down on the fatty foods he likes and finds planning his meals helps with this; he even takes his own lunch to work.

Six months after Jez made these changes, he has lost three stone and his blood tests have almost returned to normal. Jez's GP tells him that his change in lifestyle has stopped him from progressing to more serious liver disease, but he must continue to eat a well-balanced diet, maintain a healthy weight and take regular exercise if he would like to remain well.

## What are the causes of NAFLD?

Clinical knowledge about NAFLD is still developing. However, known common risk factors are obesity, lack of physical exercise, insulin resistance, and other features of metabolic syndrome (also known as syndrome X)<sup>21</sup>.

People most at risk are those who:

- are overweight or obese
- have a poor diet and do little or no exercise
- smoke
- have insulin resistance
- have type 2 diabetes
- have hypertension (high blood pressure)
- have hyperlipidaemia (too much cholesterol and triglyceride in their blood)
- have polycystic ovaries
- have hepatitis B
- have hepatitis C
- are taking certain drugs prescribed for other conditions.

It is likely there are other factors which contribute to the disease as not everyone with NAFLD exhibits these risk factors.

## **Non-alcoholic steatohepatitis (NASH)**

Metabolic syndrome is defined by the presence of several risk factors associated with an increased risk of cardiovascular disease (CVD); these include insulin resistance, type 2 diabetes, high blood pressure, high triglycerides, low HDL cholesterol and an increased waist circumference (above 102 cm in men and 88cm in women<sup>23</sup>).

Very rapid weight loss can also lead to fat building up in the liver<sup>21</sup>. It is thought this may result from the sudden, massive release of free fatty acids into the bloodstream following the breakdown of fat stored in fat cells. This can sometimes follow surgery to reduce obesity, such as a gastric bypass.

More rarely, fatty liver can be associated with other causes such as rare genetic conditions, prolonged fasting, some drug treatments, total parenteral nutrition (intravenous feeding)<sup>24</sup>, polycystic ovaries and hepatitis B and C.

The exact cause of progression from NAFLD to NASH and cirrhosis is still unknown.

### **Fatty liver and obesity**

Not everyone who is overweight or obese will develop a fatty liver and not everyone who has a fatty liver is overweight. However, the majority of people with NAFLD are overweight.

As tall people are generally heavier than short people, a person's weight alone is not particularly useful in assessing their risk of developing a fatty liver or metabolic syndrome. The ratio between height and weight, known as the body mass index (BMI), is a more useful measurement.

Calculating BMI is now the accepted method for working out whether you are a healthy weight, overweight or obese. The terms 'overweight' and 'obese' describe the two BMI categories above what is considered a healthy body size<sup>25</sup>.

A healthy BMI is regarded as being between 18.5 and 25kg/m<sup>2</sup>. A BMI between 25 and 30kg/m<sup>2</sup> is defined as overweight. If your BMI is over 30kg/m<sup>2</sup> then you qualify as obese<sup>25</sup>.

Obesity can also be defined according to the distribution of fat in your body. This either subcutaneous fat (fat under the skin) or visceral fat (intra-abdominal fat)<sup>26</sup>. Increased visceral fat is more of a risk factor for NAFLD.

Women have a higher proportion of body fat (about a fifth of their body weight) than men. However, men usually have more visceral fat than women. If you have an 'apple' body shape, you will have more fat around your abdomen causing a high release of fatty acids into your circulation. A continued high release of fatty acids can cause insulin resistance and other metabolic complications.

In men, a low-risk waist circumference is 94cm (37.6 inches) or below, and high-risk abdominal obesity is defined in a waist circumference greater than 102cm (40 inches). In women, the equivalent values are a waist circumference lower than 80cm (31.5 inches) and greater than 88 cm (35 inches)<sup>25</sup>.

There is evidence that people of South Asian origin have a more centralised distribution of body fat (leading to a higher risk of chronic diseases and mortality) even when their waist circumference and BMI are lower than that of their European counterparts. Therefore, a revised BMI range has been recommended for the South Asian population by WHO (World Health Organization) and the South Asian Health Foundation. If you are South Asian, a BMI above 23kg/m<sup>2</sup> is considered to increase your risk of NAFLD.

Similarly, a recommendation has been made to reduce the healthy waist circumference range for men, from 94cm to 90cm. No change from 80cm has been recommended for women<sup>27</sup>.

There are more overweight and obese people in the UK than any other country in Europe but not as many as in the US. For the majority, the root causes of becoming overweight or obese are:

- eating more calories in a day than you use (eating too many fatty foods which are particularly high in calories)
- drinking too much alcohol
- not doing enough exercise (using fewer calories than you consume).

In England more than half (61.3%) of the adult population (aged 16 years or over), and over a quarter (28.3%) of children, between two and 10 years old, are now defined as overweight or obese<sup>28</sup>.

As more and more people in the UK lead inactive lives and carry extra weight so the number of cases of fatty liver, in particular NASH, is rising<sup>29</sup>. For more information about diet and exercise see our 'Looking after yourself' section, page 27.

<b>Risk of associated disease according to BMI and waist size</b>			
BMI	Weight Category	Waist less than or equal to 40in/102cm (men), 35in/88cm (women)	Waist greater than 40in/102cm (men), 35in/88cm (women)
18.49 or less	Underweight	Low	N/A
18.5 – 24.9	Normal	Low	N/A
25.0 – 29.9	Overweight	Increased	High
30.0 – 34.9	Obese	High	Very High
35.0 – 39.9	Obese	Very High	Very High
40 or greater	Extremely Obese	Extremely High	Extremely High

### **Fatty liver and diabetes**

Type 2 diabetes usually develops in men and women over 40 years of age, although it is now being seen in overweight children<sup>30</sup>.

Type 2 diabetes is a condition that occurs when your body cannot regulate the amount of glucose in your blood. Glucose is a sugar, produced when you digest your food; it passes through the gut wall into your blood stream.

Blood glucose levels are regulated by insulin, a hormone produced by your pancreas.

Insulin stimulates the cells in your body to absorb the glucose from your bloodstream. Your cells use some of the absorbed glucose for energy, and the rest is converted into glycogen or fat and stored by your liver and muscles ready to be released when the body needs energy quickly<sup>30</sup>.

Problems start when you do not produce enough insulin for your body's needs (type 1), or if your muscles, liver or fat cells do not respond normally to insulin (insulin resistance type 2), or a combination of these, leading to high levels of glucose in the blood (hyperglycemia), which is harmful.

Insulin also helps your liver to metabolise (process) fats and to release them into the blood. While fats are a necessary source of energy, too much fat in the blood is bad for you. It is now thought that insulin resistance interferes with this process and causes an accumulation of triglyceride fats in the liver cells.

### **Fatty liver and hyperlipidemia**

Having too many lipids or fat chemicals (also known as triglycerides and cholesterol), in the bloodstream is known as hyperlipidaemia. Like triglycerides, cholesterol is taken in from our diet and is also produced by the liver.

Cholesterol is carried in the blood in particles called lipoproteins. There are different types of lipoproteins but the most relevant to cholesterol are:

- high levels of LDL cholesterol (low density lipoprotein cholesterol), also known as 'bad cholesterol', as it can build up in the artery walls and can lead to heart disease
- HDL (high density lipoprotein cholesterol), also known as 'good' cholesterol, removes the excess LDL cholesterol and gets rid of it through the liver.

Generally the higher the LDL cholesterol level and the lower the HDL cholesterol level, the greater the health risks.

Cholesterol levels in your blood are most accurately measured by taking a blood sample after you have fasted for nine to 12 hours. This may be done as part of a 'lipid profile' which will measure levels of total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides. Levels are recorded in millimoles per litre (mmol/L)<sup>31</sup>.

The 'target levels' your doctor may recommend for you will be based on the risk to your health from factors such as age, weight, family history, lifestyle or any existing medical condition(s).

Below are guidelines to what your results or 'numbers' may mean.

<b>Total cholesterol</b>	
Less than 5 mmol/L	Normal
5 mmol/L to 6.5 mmol/L	Borderline high
More than 6.5 mmol/L	High
<b>LDL (bad) cholesterol</b>	
Less than 3 mmol/L	Normal <sup>32</sup>
3.5 mmol/L to 4 mmol/L	Borderline
4 mmol/L and higher	High
<b>HDL (good) cholesterol</b>	
Less than 1.1 mmol/L	Increased risk
1.1 mmol/L to 1.2 mmol/L	Borderline
1.2 mmol/L or higher	Healthy <sup>32</sup>
<b>Triglycerides</b>	
Less than 2.2 mmol/L	Healthy
2.2 mmol/L to 4.4 mmol/L	Increased risk
4.4 mmol/L and higher	High

You may be given your ideal TC (total cholesterol) / HDL ratio by your GP; this is measured by dividing your total cholesterol by your HDL. For example, 5mmol/L divided by 1.2mmol/L gives you a ratio score of 4.16.

A TC/HDL ratio of 4.5 or less is recommended<sup>32</sup>.

## **Fatty liver and hypertension (high blood pressure)**

Blood pressure refers to the pressure of blood in your arteries; the higher your blood pressure, the greater the risk of cardiovascular disease. It is measured in millimetres of mercury (mmHg) and is recorded as two figures. The first number is the systolic pressure; the pressure in the arteries when the heart contracts. The second number is the diastolic pressure; the pressure in the arteries when the heart rests between each heartbeat, for example 130/100 mmHg.

If you have a continuous blood pressure of 140/90 mmHg or above each time it is taken, you have high blood pressure. High blood pressure is diagnosed if you have:

- a continuous high systolic reading
- a continuous high diastolic reading
- or both continuous high systolic and diastolic readings.

## **Other causes of fatty liver**

In addition to the common causes of NAFLD and its progression to NASH, there are a number of other causes of excess fat in the liver. These causes are far less common and are not typically associated with NASH. Unlike the other causes, once they are recognised and removed, the liver usually totally recovers.

### **Total parenteral nutrition (TPN), fasting and rapid weight loss**

TPN is a procedure that provides patients with the nutrients they need by intravenous feeding. You may have this procedure if you are malnourished (unable to eat enough to sustain your body's nutritional needs). TPN can be used to reverse or prevent malnutrition.

Patients prescribed TPN long term are at risk of developing liver dysfunction, acute cholecystitis (a painful inflammation of the gallbladder) and fatty liver. Fatty liver is usually a long-term complication of TPN and is fairly common. The reasons for this are still unknown.

Very rapid weight loss caused by some gastrointestinal operations (e.g. bariatric surgery) for obesity, and fasting for long periods of time, are further risk factors for developing a fatty liver. In these cases, the accumulation of liver fat is due to the release of fatty acids from fat tissue that swamp the liver.

## Medications associated with fatty liver

A number of drugs prescribed for other conditions have been linked with fatty liver. In some cases this liver damage is related to high doses of the drug. With other drugs, fatty liver only occurs in a small minority of people. This is known as an 'idiosyncratic drug reaction.'

The drugs most commonly associated with causing fatty liver in this way are:

- prednisolone and hydrocortisone<sup>33</sup>, used to treat inflammation
- premarin and ortho-est (synthetic oestrogen), for menopause<sup>34</sup>
- amiodarone, used to treat heart arrhythmia<sup>35</sup>
- tamoxifen, used to treat breast cancer<sup>36</sup>
- diltiazem, used to treat high blood pressure<sup>37</sup>
- methotrexate, used to treat rheumatoid arthritis<sup>38</sup>
- sulfasalazine, used to treat Crohn's disease and ulcerative colitis<sup>39</sup>.

## Polycystic ovary syndrome (PCOS)

You may be diagnosed with PCOS if you have two or more of the following:

- having 12 or more follicles (tiny cysts) develop in your ovaries, detected by an ultrasound scan
- your balance of hormones is altered, in particular your ovaries are making more testosterone than normal. This may be detected by a blood test or you may have symptoms of excess testosterone.
- you do not ovulate regularly or at all. If you do not ovulate then you may have infrequent or absent periods.

The cause of PCOS is largely unknown and several factors seem to be important. For example, women with PCOS may have resistance to insulin<sup>40</sup>. A raised level of insulin in the bloodstream is thought to cause your ovaries to produce too much testosterone. High levels of insulin and testosterone in the body leads to the development of follicles.

Some women with PCOS develop diabetes type 2 (about one in ten), hypertension, hyperlipidemia and are overweight or obese<sup>41</sup>, causing them to be at a higher risk of developing fatty liver disease.

## Lysosomal acid lipase (LAL) deficiency

Lysosomal acid lipase (LAL) deficiency, also known as cholesterol ester storage disease (CESD) or Wolman disease, is a rare genetic condition which belongs to a family of conditions known as lysosomal storage disorders. Like other genetic diseases it is an inherited condition. If both parents are carriers there is a one in four chance that their child will be born without the ability to process LAL enzymes.

The LAL enzyme is what allows your body to break down fats. If you are LAL deficient, fats start to build up in your liver, gut, blood vessels and other organs. A build-up of these fats in your liver can lead to NASH, cirrhosis and chronic liver failure.

## What are the symptoms?

Most people who have mild NAFLD will not notice any symptoms because the amount of fat build-up is not enough to damage the liver.

A few people complain of tiredness and may feel some discomfort in the area around the liver (on the right side of the body, under the ribs)<sup>24</sup>. The pain may be a sign that the extra fat has made the liver expand. This stretches the liver's outer covering and may cause discomfort.

For people who go on to develop NASH, fibrosis and cirrhosis, it may be many years before symptoms develop.

The following symptoms may indicate a serious development in your liver condition. Patients with a liver condition who develop any of these symptoms should seek urgent medical attention:

- yellowness of the eyes and skin (jaundice)
- bruising easily
- dark urine
- swelling of the lower tummy area (ascites)
- vomiting blood (haematemesis)
- dark black, tarry faeces (melena)
- periods of confusion or poor memory (encephalopathy)
- itching skin (pruritus).

## Diagnosis

In most cases, people only find out they have fatty liver when a routine blood sample (usually liver function tests) shows there may be a problem. If this happens to you, your doctor may ask a lot of questions about your lifestyle, such as any drugs you are taking (including over-the-counter medication and nutritional supplements), your diet, how much exercise you do and the amount of alcohol you drink.

### Helping the doctors to help you

There is no specific laboratory test for NAFLD, making it difficult to diagnose. It is important that you answer questions about your lifestyle as accurately as you can. It is not easy for doctors to tell the difference between alcoholic liver disease and NAFLD, so it is important that you are honest about the amount of alcohol you drink.

NAFLD is almost the same as alcoholic liver disease (ALD) and shares the same stages. In practical terms the only difference between the two conditions – NAFLD and ALD – is that the latter is caused by drinking too much and the former by other causes.

Liver disease can have no or few symptoms and doctors have to consider a number of conditions that could be affecting you. The clearer the picture of your general health you can provide, the better the chances will be that the doctors can pin down your illness and help you recover.

Liver blood tests, sometimes referred to as liver function tests (LFTs), measure various proteins and chemicals in the blood made or cleared by the liver. An abnormal result indicates a problem with the liver, and may help to identify the cause. Further tests may be needed to clarify the cause of the liver problem.

As the liver performs its various functions it makes chemicals that pass into the bloodstream and bile. Various liver disorders alter the blood level of these chemicals<sup>42</sup>.

The tests are used to help diagnose liver disorders; the pattern of the blood results may help to determine which disorder is causing the problem. For example, the levels of liver enzymes and proteins in your blood can increase during liver inflammation (hepatitis).

Further blood tests will then be done to exclude other possible illnesses, such as viral hepatitis, autoimmune hepatitis, diabetes (fasting glucose levels) and other causes of liver disease.

If these results are negative for any of the above, you will then be referred for a non-invasive test such as an ultrasound scan, a CT or CAT scan (computed (axial) tomography) or an MRI scan (magnetic resonance imaging) to confirm the diagnosis.

Certain risk factors for NAFLD should be assessed, along with more extensive analysis of the LFTs, to determine whether there is significant fibrosis<sup>43</sup>.

### **Liver Blood Test (LFT) results**

Do not be alarmed by 'abnormal' liver blood test results. Strange as it sounds, abnormal liver blood tests are not uncommon. In some people, results may often fall outside normal range and doctors may consider that increases or decreases of certain enzymes and proteins in your blood are not an indication of serious liver disease.

However, the British Liver Trust encourages all people with any form of liver disease to take an active interest in their healthcare. If you feel you require more information about your abnormal liver blood test results, you should feel confident to ask for further advice from medical staff.

### **Ultrasound**

An ultrasound scan is a routine procedure; the same technology is used in pregnancy to examine the unborn baby. It is usually performed in the X-ray department of the hospital or in an outpatient clinic. The procedure is very safe and should not be painful, but it may take 10 to 15 minutes to complete.

You will be asked to uncover the top of the right half of your abdomen (below your ribs) and lie on your back. Gel will be applied to your skin which may feel slightly cold. A probe will be moved across the surface of your skin. The gel helps to make this movement easier and makes sure that sound waves can be directed through your skin as the probe passes over your liver area. Anything solid will cause the sound wave to be reflected back via the probe and will be turned into an image that can be seen on a screen. Sometimes you may be asked to move into a different position so that your liver can be clearly seen on the screen.

For further information please refer to our 'Liver disease tests explained' publication.

### **Fibroscan**

This is a non-invasive scan, very similar to an ultrasound scan and is increasingly being used to assess the levels of fibrosis in a patient. The scan measures the stiffness of the liver. The stiffer the liver, the greater the degree of fibrosis; this is helpful in assessing the severity of NAFLD<sup>44</sup>.

### **CT or CAT scan (computed (axial) tomography)**

A CT or CAT scan is performed in a large ring-shaped machine. You will be asked to lie on a couch and the couch will then move backwards and forwards through the ring. A series of images will be taken using a scanner, which rotates in small movements inside the machine. The scan will take 10 to 30 minutes and is not painful<sup>45</sup>.

### **MRI (magnetic resonance imaging) scan**

MRI scans use a strong magnetic field and radio waves to create an image of your liver.

MRI is performed in a tunnel about 1.5 metres long, surrounded by a large circular magnet. You will be asked to lie on a couch and the couch will then move into the tunnel and a series of images will be taken. The scan will take 15 to 40 minutes and is not painful<sup>46</sup>.

Scanning your liver with imaging equipment such as ultrasound, CT or MRI may reveal significant deposits of fat in your liver<sup>24</sup>. Once a diagnosis of NAFLD is confirmed, you may then be sent to see a liver specialist (hepatologist) or a digestive disease specialist (gastroenterologist), for further tests to establish what stage of fatty liver you have, and what follow-up you require.

## Liver biopsy

During a liver biopsy, a tiny piece of the liver is taken for study. This usually involves a fine hollow needle being passed through the skin into the liver and a small sample of tissue being withdrawn.

The test is usually done under local anaesthetic and most people will be allowed home later the same day, although for some it may mean an overnight stay in hospital. As the test can be uncomfortable and there is a very small risk of internal bleeding or bile leakage, a stay in bed of at least six hours after the procedure is required. Ask your doctor for more information on this.

The results of your biopsy are graded and staged according to the degree of liver inflammation and scarring.

## Prevention

Maintaining a healthy weight through eating a well-balanced diet and being active is the best way to prevent NAFLD. The health risks from being overweight or obese can impact on your physical, social and emotional well-being. People with NAFLD who go on to develop cirrhosis are at higher risk of liver failure.

It is not always possible to avoid NAFLD, as some factors such as genetics, cannot be prevented. However, you can significantly reduce your risk by exercising as much as you are able to, and eating healthily to control your weight (see our 'Diet and liver disease' publication).

Better control of existing medical conditions, such as glucose levels in diabetes, can also help prevent the development and progression of NAFLD and NASH.

## Treatment

There is no specific treatment for NAFLD that all doctors agree on.

However, if your NAFLD is linked to being overweight, then you will be advised to make various lifestyle changes including losing weight gradually and taking

sensible exercise. There is good evidence that gradual weight loss coupled with increased exercise can reduce the amount of fat in your liver<sup>47</sup>.

In mild cases of NAFLD doctors may concentrate on treating associated conditions, such as obesity and diabetes, which can cause fat to build up. They will also treat disorders such as high blood pressure and high cholesterol as these are often associated with NAFLD. If you are active and eat a healthy diet but find you are unable to lose weight, you may be tested for an underactive thyroid.

Maintaining good control of existing health conditions, such as diabetes, thyroid problems, obesity and metabolic syndrome is important as this will improve your health, reduce your risk of a premature death and can also improve your NAFLD. On the other hand, poor control can speed up the progression of NAFLD to cirrhosis. If your NAFLD is linked to diabetes, high blood pressure or high cholesterol then you will need to watch your diet and your weight, and may also need to take medication.

Some medications used to treat diabetes, hypertension and hyperlipidaemia can be beneficial to the liver. These work by lowering your lipid levels and increasing you cell's sensitivity to insulin. For this reason, if you are diagnosed with NAFLD and you have one of these conditions, your medication may be changed to one which could potentially be more beneficial to your liver. However, as yet there is no sufficient evidence for the use of these medications for patients with NAFLD in the absence of an associated condition.

### **Treatments under investigation**

There are no specific medications available for the prevention or treatment of NAFLD but a number of areas are being explored, principally drugs that reduce appetite, lower blood fats and increase insulin sensitivity. Many of these drugs have been developed to treat other conditions.

These include statins, a class of drug used to treat cardiovascular disease. Statins decrease the production of bad cholesterol in your body and it is thought that this may have a benefit in treating NASH. In the past there have been concerns about the use of statins in patients with liver disease but it is now clear that patients with fatty liver disease and NASH can take these drugs as safely as any other patient. However, there are few studies proving their effectiveness in the prevention or treatment of fatty liver disease<sup>48</sup>.

Statins can cause some side effects. These are usually mild, easy to recognise, reversible and rarely dangerous. You should tell your GP if your symptoms are getting worse or you develop any new symptoms. Before you start taking statins, you will have a blood test to check your liver function (LFTs). You will have a follow-up blood test after a few months to check your statin dose. If you are taking statins you may be advised to avoid eating grapefruit and drinking grapefruit juice as this can increase your risk of side effects<sup>49</sup>.

As the majority of patients with NASH have insulin resistance, it is thought medications that make the body more sensitive to insulin, such as metformin and thiazolidinediones, may reduce liver damage in people with NASH<sup>50</sup>. However, it has not been proven to be an effective treatment for NAFLD patients without diabetes. These medications are not widely used for the treatment of NAFLD as, like all medications, they can have side effects and are not proven to have a lasting effect once stopped.

Dietary supplements are being evaluated. These include the role of fat-soluble antioxidants, such as vitamin E, which have been shown to be effective in a large clinical trial of non-diabetic patients with NAFLD. Antioxidants are considered helpful in reducing levels of bad cholesterol (LDL) in the arteries<sup>51</sup>.

Omega-3 fatty acids, extracted from fish oil, may be effective in decreasing triglycerides and raising HDL<sup>52</sup>.

## **Clinical trials**

Doctors are always trying to find better ways of treating people. Medical staff may talk to you about the possibility of taking part in a clinical trial. This may involve treatment with new drugs or new ways of using drugs.

You do not have to take part in clinical trials and your care will not be affected if you do not. If you do take part, you may receive extra monitoring which may be beneficial to your treatment. The doctor involved in the research will give you specific information about any clinical trials.

## **What are the long term effects?**

What will happen largely depends on what stage of NAFLD you have when you are diagnosed with the condition. Most people who have a fatty liver (steatosis) should not have any long-term ill effects.

Very few people<sup>53</sup> will go on to develop NASH. Of those who do develop NASH approximately 12% go on to develop cirrhosis<sup>17</sup>, and fewer than one in ten (10%) die from a liver-related problem<sup>16</sup>. Unfortunately, there is no reliable way to predict who will develop these serious later stages of NAFLD.

For this reason, if you have been diagnosed with NAFLD, most doctors recommend some form of monitoring (usually a blood test every six months or so) to make sure the condition is not getting worse.

If you have cirrhosis, you are at a higher risk of liver cancer or liver failure, both of which are potentially fatal. The risk of further damage can be reduced enormously if the cause of the cirrhosis is removed. However, if progression can be halted and the liver is still compensating you can potentially continue to lead a normal life.

If the cause of the cirrhosis is not removed or the damage to your liver has become severe, your liver may fail completely, and a liver transplant may be the only option.

A liver transplant 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 is not undertaken lightly. You will need to plan it carefully with your medical team, family and friends. Unfortunately, increasing numbers of people are being listed for a transplant due to NASH. Not all of the patients listed will have a transplant, due to the increasing need for liver donors.

## **Liver Transplant**

A liver transplantation is not a guaranteed success and you will need to take medication for the rest of your life in order to stop your body rejecting your donor liver. If the cause for the transplant is not removed (for example, you do not maintain a healthy weight or drink alcohol) you will also damage your donor liver.

After a successful transplant you can make a full recovery and lead a normal active life. However, you may have an increased cardiovascular risk and you will need to be checked regularly by your doctor as the cause of your fatty liver will still be present. Medical conditions such as diabetes, obesity, metabolic syndrome and psychological issues will need to be managed to prevent recurrence of NASH in your new liver.

## Fiona's story

Weighing 17 stone and standing little over five feet tall, Fiona feels tired all the time and is usually asleep on the sofa by 9pm. Her doctor has classed her as obese and, because she has high blood glucose levels, Fiona has been diagnosed with type 2 diabetes.

Following a series of blood tests Fiona is referred to hospital where doctors diagnose non-alcoholic steatohepatitis (NASH). Her liver has become enlarged and unable to function properly, explaining some of her extreme fatigue and exhaustion.

Fiona is put on a balanced diet and is given tablets for her diabetes. Fiona starts going to the gym and takes spinning classes. Unfortunately further tests reveal that Fiona is actually suffering from cirrhosis and not NASH. Her liver is so badly scarred that her hepatologist suggests she should be put on a transplant list for a new liver.

Fiona is distraught but even more determined to continue to lose weight. She cuts alcohol from her diet completely, even though she only drinks three or four glasses a week, and increases the amount of exercise she does by going to the gym more regularly. Over a four month period Fiona steadily loses four stone, she continues to eat healthily and to exercise regularly.

Fiona's boyfriend proposes to her and within six months of her lifestyle changes, she continues to steadily reduce her weight by maintaining healthy changes to her diet and increasing her exercise levels.

Two weeks before she is due to get married Fiona visits her specialist again. The news is good – Fiona's gradual weight loss has taken the pressure off her liver, allowing it to regenerate itself to such a degree that Fiona is removed from the transplant list. Fiona will need to continue to maintain a healthy weight and keep exercising, to maintain a healthy liver and prevent her liver from becoming seriously damaged again.

# Looking after yourself

## Diet

For most people there is no special diet, however, eating a good, balanced diet is one of the most important things you can do to keep yourself well. As the blood fats associated with NAFLD (triglycerides and cholesterol) are partly absorbed from your food intake<sup>54</sup>, it is essential that you watch what you eat.

Regular low-calorie meals containing protein (such as lean meat, fish or beans), starch (such as bread, potatoes or rice) and vitamins (in fruit and vegetables) are the best approach (for more information see our 'Diet and liver disease' publication).

The following will help:

- eating plenty of fruit and vegetables: aim for five portions a day
- avoiding salty foods
- eating plenty of high-fibre foods such as brown rice, wholemeal bread and pasta
- avoiding foods high in saturated fats such as full-fat milk, yoghurt and cheeses
- eating small amounts and choosing low-fat versions
- choosing lean cuts of meat
- eating a low-cholesterol diet
- eating carbohydrate foods (such as pasta, potatoes, wholemeal bread and rice) rather than fat-rich foods
- trying to grill, bake or poach food rather than frying
- avoiding crash diets and rapid weight-loss programmes.

If you have any questions about your diet, talk to your GP or hospital consultant. You can ask to be referred to an NHS registered dietitian for a specialist diet consultation.

## Alcohol and smoking

Alcohol is processed by your liver and, as a result, it can be dangerous for anyone with liver problems. Check with your doctor whether it is safe for you to drink any alcohol, and if so, how much.

If you have alcohol-related liver disease it is important that you stop drinking and remain abstinent for life.

Alcohol can accelerate the rate of liver damage in those with hepatitis B and C, and can limit the effectiveness of anti-viral treatment<sup>55</sup>. It can also accelerate the rate of liver damage in those with NASH (non-alcoholic steatohepatitis)<sup>56,66</sup> therefore, it is recommended to avoid alcohol in these circumstances.

Smoking is dangerous to everyone's health<sup>57,58,59</sup> and can increase the severity of liver damage<sup>60</sup>. People with liver disease are more vulnerable to infection and to general poor health, so smoking or exposure to passive smoking is not advisable. If you smoke, speak to your doctor about what help is available with cutting down and giving up.

### **Exercise**

Exercise will help you to maintain a healthy weight.

The Department of Health recommends adults should try to be active daily. Over a week, activity should add up to at least 2½ hours or 150 minutes of moderate intensity activity (such as walking quickly or cycling) in bouts of 10 minutes or more. One way to approach this is to do 30 minutes on at least 5 days a week. Alternatively, comparable benefits can be achieved through 75 minutes of vigorous intensity activity (such as running or playing football) spread across the week or combinations of moderate and vigorous intensity activity. You should also undertake physical activity to improve muscle strength on at least two days a week. Try to also minimise the amount of time spent being sedentary (sitting) for extended periods.

If you are overweight, the amount of exercise you do may need to be increased to help you to lose weight. Try to find an exercise that you enjoy – for example some people love playing a sport with friends or dancing.

If you are overweight, speak to your doctor about losing weight safely. Avoid crash diets and rapid weight loss as these rarely work and you are unlikely to maintain weight loss. They can also be dangerous and increase the risk of malnutrition and gallstones. A safe weekly rate of weight loss is between 0.5kg and 1kg (1-2lb).<sup>22</sup>

## Complementary and alternative medicines

There is a great deal of information on the internet about diets and many people offering dietary advice. If you have liver disease it is important to seek advice from your doctor and ask to be referred to a dietitian. Registered dietitians are regulated, whereas other professionals such as Chinese herbalists are currently not.

Many of the complementary and alternative medicines available suggest they can ease the symptoms of liver disease. Before taking any medicine you should check with your doctor that it is safe to do so, because most are processed by the liver, they can be toxic to people with liver problems<sup>62</sup>. Some can damage the liver and make you more severely ill. At present, healthcare professionals are not clear on the role and place of some complementary medicines in managing liver disease; more research is needed.

Licensing has been introduced for some traditional herbal medicines<sup>63</sup> however, many herbal products are not classified as a medicine so there is no regulation of the product. This means you cannot be sure how much of the active ingredient you are getting or how pure it is. Unregulated products are not monitored or assessed for how effective or safe they are. Some remedies can damage the liver and make you more severely ill.

It is wise to be cautious about the claims made for herbal remedies, particularly those advertised on the internet, as they can offer false hope. **It is important to discuss the use of these remedies with your doctor before taking them.**

Some people choose to use complementary therapies alongside their conventional medical treatment, both to ease symptoms and boost emotional wellbeing. Such therapies may include massage, aromatherapy, meditation or acupuncture.

To ensure your chosen therapy does not adversely affect your health or medical treatment, you should discuss any therapies you are thinking of using with your doctor. Make sure your practitioner is registered with an accredited body; your doctor may be able to refer you to a locally recommended practitioner. Always inform your practitioner of your medical conditions as these may impact on the type of therapies that are safe for you.

## Useful words

**Acute** – a short sharp illness that may be severe but from which most people will recover in a few weeks without lasting effects.

**Alanine aminotransferase (ALT)** – a liver enzyme, it enters the blood following liver trauma or infection. An ALT test is used to monitor and assess the amount of this enzyme in the blood and is a marker of liver irritation and inflammation.

**Ascites** - accumulation of fluid in the abdomen (peritoneal cavity) which surrounds the bowel, leading to enlarged, swollen and tender abdomen.

**Aspartate aminotransferase (AST)** – is a liver enzyme, but it is less specific to the liver than ALT (see above). A raised AST level may also indicate muscle damage elsewhere in the body.

**Autoimmune disease** – a type of disease where the immune system loses the ability to distinguish between its own material and foreign material, causing mistaken attacks on parts of the body.

**Balanced diet** – a diet that contains all the different substances your body needs, in the right amounts, to keep you healthy.

**Bilirubin** – a yellow pigment and waste product from the breakdown of haemoglobin. Increases of bilirubin in your blood can indicate liver disease, especially disease of the bile ducts (see jaundice).

**Calories** – units of energy, sometimes written as kilocalories (kcal) or kilojoules (kJ).

**Carbohydrate** – a substance that provides energy or fuel for your body. ‘Simple’ carbohydrates are sugars as found in fruit, honey and jam. ‘Complex’ carbohydrates are starches, as found in bread, rice and potatoes.

**Cholesterol** – a type of fat (lipid) that is made by the liver and also comes from the food you eat. Cholesterol is found in all the cells of your body and is necessary to help them function. However, a high cholesterol level in the blood causes an increased risk of heart disease and stroke.

**Chronic** – an illness that lasts more than six months, possibly for the rest of a person’s life.

**Encephalopathy** - disturbed brain function, leading to mental confusion and memory loss. Hepatic encephalopathy occurs when the liver is severely damaged and is unable to process toxins, as in the development of cirrhosis.

**Enzyme** - a protein that speeds up a chemical reaction within a cell without being changed or used up in the reaction. Each enzyme has a specific job and there are many types of enzymes for the various different reactions.

**Free fatty acids** - organic acids that circulate in the bloodstream.

**Gastroenterologist** - a doctor who specialises in diseases of the gullet, stomach, bowel and their associated organs, the pancreas, liver and spleen.

**Glycogen** - once eaten, carbohydrates break down into smaller sugars (glucose, fructose and galactose) that get absorbed and used as energy. Any glucose not needed right away gets stored in the muscles and the liver in the form of glycogen.

**Hepatic** - anything relating to the liver.

**Hepatitis** - 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.

**Hepatocyte** - a liver cell.

**Hepatologist** - a doctor who specialises in liver diseases.

**Jaundice** - a condition in which the whites of the eyes go yellow and in more severe cases the skin does too. This is caused by a rise of bilirubin (containing yellow pigment), a waste product which is normally disposed of by the liver.

**Lipids** - a group of organic fats or fat like substances, inclusive of triglycerides, cholesterol and fatty acids. They are insoluble in water. Lipids are important as they are stored by your body for energy.

**Lipoprotein** – a combination of fat and protein made by the liver and transported around the body in the bloodstream.

**Lysosomes** – structures within cells which contain enzymes responsible for breaking down foreign substances in the cell.

**Metabolism** – the physical and chemical processes by which food is transformed into energy. This occurs by absorbing substances and using them in the body or by removing toxins and disposing of them from the body as waste products.

**Triglycerides** – a lipid or neutral fat (the form in which fat is stored in the body), it is produced by the liver and found in certain foods and alcohol. Its name reflects its construction: three ('tri') molecules of fatty acid combined with a glycerol ('glyceride') molecule.

## Further information

Please refer to the Trust website for details of patient organisations and support groups specialising in specific liver conditions, that you may find helpful.

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:

- Acute fatty liver of pregnancy (available for download only)
- Alcohol and liver disease
- Cirrhosis of the liver
- Diet and liver disease
- Hepatitis B
- Hepatitis C
- Liver cancer
- Liver disease tests explained
- Liver transplantation
- Gallstones

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This leaflet is for information only. Professional, medical or other advice should be obtained before acting on anything contained in the leaflet as no responsibility can be accepted by the British Liver Trust as a result of action taken or not taken because of the contents.

## Special thanks

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## We hope you have found this publication helpful

All our publications are reviewed by medical experts and people living with liver disease. If you have any feedback on this publication please email the Trust at **info@britishlivertrust.org.uk**

The British Liver Trust is proud to be recognised as a provider of expert liver health information, but to do this we must depend on the kind donations of our supporters. The Trust receives no government aid, yet strives to fill the growing need for liver health information in the UK.

### **We are a small charity, and your donation can make an important difference.**

A gift of £5 could help us answer patient calls to our helpline

A gift of £20 could help us set up a new patient support group

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Please consider supporting The British Liver Trust today.

#### **If you have questions about making a donation,**

please call **01425 481320** or email **fundraising@britishlivertrust.org.uk**

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