Non-alcoholic Fatty Liver Disease

Non-alcoholic fatty liver disease describes a range of conditions caused by a build-up of fat within liver cells. It is very common and in many cases is linked to being obese or overweight. Most people with non-alcoholic fatty liver disease do not develop serious liver problems. In some people, the build-up of fat in the liver can lead to serious liver disease. However, all people with non-alcoholic fatty liver disease have an increased risk of developing cardiovascular problems such as heart attacks and stroke.

If you are obese or overweight, a main treatment advised for non-alcoholic fatty liver disease is usually gradual weight loss and regular exercise. This not only helps with non-alcoholic fatty liver disease but will help reduce your risk of developing cardiovascular problems. Other treatment methods are discussed below.

What does the liver do?

The liver is in the upper right part of the tummy (abdomen). Its functions include:

- Storing fuel for the body. Much of the food we eat is broken down by the body into a type of sugar called glucose. This is what our bodies use for energy. Glucose can't be stored so it is turned into a storage version called glycogen. This is kept in the liver and, when we need energy, it releases it in the form of glucose. The liver also stores iron and vitamins.
- Making proteins that are essential for blood to clot (clotting factors).
- Helping to remove or process alcohol, medicines and poisons from the body.
- Making a type of fat called cholesterol. This is needed in the body, although too much of it causes harm.
- Making a juice called bile, which digests fat. This passes from the liver to the gut down the bile duct. Bile breaks down the fats in food so that they can be absorbed from the bowel.

What is non-alcoholic fatty liver disease (NAFLD)?

NAFLD describes a range of conditions caused by a build-up of fat within liver cells. It is helpful to divide NAFLD into four stages:

- **Simple fatty liver (hepatic steatosis).** Normally, very little fat is stored in liver cells. Simple fatty liver means that excess fat builds up (accumulates) in liver cells. For most people, simple fatty liver does not cause any harm or problems to the liver. However, in some people it can progress to more severe forms of NAFLD.
- **Non-alcoholic steatohepatitis (NASH).** In this condition the excess fat in the liver cells is associated with, or may cause, inflammation of the liver. (‘Steato’ means fat, and ‘hepatitis’ means inflammation of the liver). This is much less common than simple fatty liver.
• **Fibrosis.** Any form of persistent hepatitis, including steatohepatitis, may eventually cause scar tissue (fibrosis) to form within the liver. When fibrosis first develops often there are many liver cells that continue to function quite well.

• **Cirrhosis.** This is a serious condition where normal liver tissue is replaced by a lot of fibrosis. The structure and function of the liver are badly disrupted. It is, in effect, like a severe form of liver fibrosis. Many liver conditions can lead to cirrhosis, including NAFLD. Severe cirrhosis can lead to liver failure. See separate leaflet called Cirrhosis for more details.

NAFLD occurs in people who do not drink excessive amounts of alcohol and so alcohol is not the cause. Most people with NAFLD have simple fatty liver. Only a minority will progress to develop NASH. And, only a minority of people with NASH will progress to develop cirrhosis. It is not clear why some people with simple fatty liver progress to the more severe forms of NAFLD, and most do not.

**Other forms of fatty liver**
A condition similar to NAFLD can affect people who do drink a lot of alcohol. See separate leaflet called Alcohol and Liver Disease for more details. Another fatty liver condition called fatty liver of pregnancy is a rare but serious condition of pregnancy. In this condition a lot of fat builds up in the liver cells and causes damage quite quickly. The cause is not known. Symptoms include being sick (vomiting), tummy (abdominal) pain and jaundice. Jaundice is a condition caused by a build-up in the body of a chemical called bilirubin, where your skin and other body parts turn a yellow colour.

The rest of this leaflet is only about NAFLD.

**Who develops non-alcoholic fatty liver disease (NAFLD)?**
NAFLD is the most common persistent (chronic) liver disorder in western countries such as the UK. It is thought to occur in about 1 in 5 adults in the UK and in up to 4 in 5 adults who are obese. (However, most of these people have 'simple fatty liver' and not the more serious types of NAFLD.)

The risk factors for developing NAFLD include:

• Obesity. Most people with NAFLD are obese or overweight. However, the relationship between body fat and NAFLD, and factors that determine which people with obesity will develop NAFLD, are not clear. So, for example, some people who are only mildly overweight develop NAFLD. On the other hand, some people who are very obese do not develop NAFLD.

• Diabetes. People with type 2 diabetes have an increased risk of developing NAFLD. However, there is no increased risk for those with type 1 diabetes.

• Age. NAFLD is more common in people aged over 50 years. It is also more common in men.

• High blood pressure (hypertension). People with hypertension are at a greater risk of developing NAFLD.

• High level of blood fats (hyperlipidaemia). If you have high level of cholesterol and/or triglycerides in your blood then you have a higher risk of developing NAFLD.

• Very rapid weight loss. For example, NAFLD develops in some people following surgery to reduce obesity. This may be due to rapid changes of fats and fatty acids in the blood that occur when weight loss is rapid.

• Medicines (for example, methotrexate and tamoxifen) can, rarely, cause NAFLD.

People with NAFLD have a higher chance of developing type 2 diabetes and cardiovascular disease (this includes heart attacks and strokes). Also, as NAFLD is common, some people with NAFLD also have another liver disorder. NAFLD can make the other liver disorder worse.

**What are the symptoms of non-alcoholic fatty liver disease (NAFLD)?**
Most people with simple fatty liver or non-alcoholic steatohepatitis (NASH) have no symptoms. However, some people with simple fatty liver or NASH have a nagging persistent pain in the upper right part of the tummy (abdomen), over an enlarged liver. You may feel generally tired if you have NASH. As most people do not have symptoms, the diagnosis is often first suspected when an abnormal blood test result occurs.
A small proportion of people with NAFLD develop cirrhosis. Cirrhosis is a condition where normal liver tissue is replaced by a lot of scar tissue (fibrosis).

How is non-alcoholic fatty liver disease (NAFLD) diagnosed?

There is no simple test that can confirm NAFLD. Blood tests called liver function tests (LFTs) measure the blood levels of certain chemicals (enzymes) made by the liver cells. An abnormal pattern of LFTs may suggest that you have NAFLD. However, many other liver conditions can cause abnormal LFTs. Therefore, if you have abnormal LFTs, a doctor will usually then do various other blood tests to rule out other causes of liver problems. For example, blood tests to detect various germs (viruses) and other liver-related chemicals.

LFTs are tests that are done for various reasons. Therefore, NAFLD is often first suspected when an abnormal result occurs when the tests are done for an unrelated reason.

A scan of the liver can be helpful. For example, an ultrasound scan, CT scan or MRI scan. The scan can show an enlarged liver compatible with the diagnosis of NAFLD. However, a scan cannot definitely diagnose NAFLD.

The diagnosis of NAFLD is usually based on the abnormal LFTs and scan being compatible with NAFLD, and ruling out other causes of liver problems. If there is doubt about the diagnosis, a specialist may arrange a small sample (biopsy) to be taken from your liver. This can be looked at under the microscope and can show the extent of any fatty accumulation, inflammation, scarring, etc, in the liver. See separate leaflet called Liver Biopsy for more details.

However, a liver biopsy is not routinely done when simple fatty liver or non-alcoholic steatohepatitis (NASH) is the likely diagnosis, as there is some risk involved when doing a liver biopsy. A liver biopsy is mainly done if the diagnosis is in doubt, or if there is concern that cirrhosis has developed.

What is the treatment for non-alcoholic fatty liver disease (NAFLD)?

Weight reduction
Most cases of NAFLD are linked to being obese or overweight. There is good evidence that a programme of gradual weight loss and regular exercise can reduce the amount of fat in your liver. So, if you have simple fatty liver or mild NASH, this may prevent or delay the progression of NAFLD. It may reduce your chance of developing cirrhosis - a condition where normal liver tissue is replaced by a lot of scar tissue (fibrosis).

In some people who are very obese, obesity surgery may be considered, as studies have shown that this may help to improve NASH.

Treatment of linked conditions and risk factors
As mentioned, having NAFLD increases your risk of developing cardiovascular disease. In fact, people with NAFLD are actually more likely to become ill and die from cardiovascular diseases such as heart attacks than from a liver problem. Therefore, your doctor is likely to stress the importance of reducing any 'lifestyle' risk factors that increase the risk of developing cardiovascular disease. For example, not smoking, keeping your weight in check, taking regular exercise and eating a healthy balanced diet. See separate leaflet called Preventing Cardiovascular Diseases for more details. Also, to treat high blood pressure (hypertension) and a high cholesterol level (hyperlipidaemia), if appropriate.

If you have diabetes, good control of your blood sugar (glucose) level is thought to help reduce the risk of NAFLD becoming worse.

It is also advised that you do not drink any alcohol. NAFLD (by definition) is not caused by alcohol. However, even modest amounts of alcohol may make NAFLD worse.

Medication that affects the liver itself
Various medicines have been suggested as possible treatments for NAFLD. However, there is little research evidence to say that any medicine works very well. For example, for NASH, no treatment has been proved to stop or reverse the inflammation. Various medicines are being trialled in different studies. One or more medicines may emerge as treatments in the future.
What is the outlook (prognosis)?

For most people with non-alcoholic fatty liver disease (NAFLD), the condition does not progress beyond simple fatty liver or non-alcoholic steatohepatitis (NASH). Cirrhosis - a condition where normal liver tissue is replaced by a lot of scar tissue (fibrosis) - and serious liver problems do not develop in most cases. The condition may reverse and even go away by weight loss (if you are overweight or obese) or with good control of diabetes (if diabetes is the cause).

However, fatty liver does progress to NASH in some people and NASH progresses to cirrhosis in some people. It is not clear why some people with NASH (and not others) progress to cirrhosis. Cirrhosis is very serious, can lead to liver failure and be fatal.

It is estimated that, on average:

- About 2 in 100 people with simple fatty liver progress to cirrhosis over 15-20 years.
- About 12 in 100 people with NASH progress to cirrhosis over about eight years.

So, most people with NAFLD do not develop serious liver disease. However, because NAFLD has become very common in recent years (probably because of the epidemic in obesity), NAFLD has become a common cause of cirrhosis.

However, also remember that cardiovascular disease is the most common cause of illness and death in people with NAFLD. Perhaps the most important ‘take home message’ if you are diagnosed with NAFLD is not to focus too much on your liver. Rather, concentrate on reducing any risk factors for developing cardiovascular problems. This is mainly lifestyle changes - in particular, diet, weight loss and exercise for most people and giving up smoking if you smoke.

Further reading & references

- EASL–EASD–EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease; European Association for the Study of the Liver (2016)
- Non-alcoholic fatty liver disease (NAFLD) - assessment and management; NICE Guidance (July 2016)
- Anstee QM, McPherson S, Day CP; How big a problem is non-alcoholic fatty liver disease? BMJ. 2011 Jul 18;343:d3897. doi: 10.1136/bmj.d3897.

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