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NON-ALCOHOLIC
STEATOHEPATITIS
AND
FATTY
LIVER



Non Alcoholic Steatohepatitis and Fatty Liver

Liver
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WHAT IS FATTY LIVER AND WHAT IS NASH?

Fatty liver is presence of excess fat in the liver. If the fat is accompanied by inflammation (bruising) then it is called steatohepatitis (steato = fat and hepatitis = liver injury). The commonest recognised cause for steatohepatitis up until 10 yrs ago was alcohol. However with changes in lifestyle our population has become increasingly overweight and it is now recognised that steatohepatitis can occur in patients with obesity, diabetes, high levels of fat in the blood and hypertension, conditions associated with our so-called affluent society. Steatohepatitis occurring in such patients who do not appear to drink alcohol in excess is called Non Alcoholic Steatohepatitis or NASH for short. Based on information available so far we know that in the majority of patients with simple fatty liver, the liver remains stable over time. In contrast, patients with NASH are at a relatively high risk of worsening liver injury, with approximately 25% developing irreversible liver scarring or cirrhosis over 8-10 years. Recently the term NAFLD or non-alcoholic fatty liver disease has been coined to include the full spectrum of fatty liver disease from simple fat, through NASH to NASH with cirrhosis.

WHAT CAUSES FATTY LIVER /NASH?

Fatty liver and NASH are associated with the same risk factors and it appears that different individuals have different susceptibility to these factors. Common conditions associated with fatty liver and NASH include obesity, type 2 diabetes mellitus, the presence of high levels of triglyceride (fat) in the blood and high blood pressure. Rarely, fatty liver and NASH may be associated with severe chronic debilitating illnesses such as tuberculosis and cancer, obesity surgery and some drugs such as corticosteroids and amiodarone. Rapid weight loss in patients on rash diets can lead to worsening of liver function tests and the development of NASH in patients with simple fatty liver. Importantly, many patients with NAFLD are neither obese (overweight) nor diabetic. In some studies there is a suggestion that there may be an inherited tendency to the development of fatty liver.

HOW COMMON IS THIS CONDITION?

Fatty liver is more common than NASH. So far we do not have studies that tell us the precise prevalence of NAFLD in the British population as a whole, but studies in the United States suggest that up to 90% of obese individuals have fatty liver, with around a quarter of these patients having

NASH. Since the present prevalence of obesity in the UK is around 30%, the expected prevalence of NAFLD is probably somewhere between 20-27%. Furthermore, a recent study from the UK has shown that NAFLD is the diagnosis in two thirds of patients referred to liver clinics with abnormal liver blood tests not related to alcohol excess or viral hepatitis.

HOW IS FATTY LIVER / NASH IDENTIFIED?

Most patients with fatty liver do not have specific liver-related symptoms. They are often picked up incidentally whilst having their liver tests checked for another reason, such as attendance at a well-man clinic, medicals performed for life insurance purposes, or during investigation of other diseases. The liver blood tests are usually abnormal, but not invariably so. Perhaps somewhat surprisingly, the degree of derangement of the liver blood tests does not reliably predict the severity of NAFLD. When a patient is suspected of having NAFLD on the basis of clinical history, examination and blood tests, the next step in investigation is to image the liver. The commonest form of liver imaging is ultrasound examination. On ultrasound a fatty liver shows up as a brighter-than-normal image. Other ways of obtaining images of the liver include a CT or MRI scan. Both tests are, however, more expensive than ultrasound and do not provide any extra useful information. Unfortunately, neither the blood tests nor the ultrasound scan can reliably distinguish between simple fatty liver, NASH or NASH with cirrhosis. Accurate staging of the disease and exclusion of other conditions that cause abnormal liver enzymes, requires a sample of liver tissue to be examined under the microscope. This sample is obtained by liver biopsy. At present, liver biopsies are performed if there is evidence of persistent abnormal liver tests on more than two occasions at least 6-12 weeks apart. The risk of liver biopsy has to be weighed against the benefits of diagnosing the liver disease accurately. For these reasons physicians currently differ over if and when to perform liver biopsies in patients with suspected NAFLD.

WHAT IS THE NATURAL HISTORY OF NAFLD?

The natural history of simple fatty liver appears to very benign, with 2 studies showing a very low (less than 5%) risk of the disease progressing to NASH or fibrosis over a 8-15 year time period. In contrast, around 25% of patients with NASH will progress to cirrhosis over 8-10 years and around 1 in 10 will die from a liver-related cause.

Once cirrhosis occurs, patients are at risk of bleeding from oesophageal varices and the development of ascites, encephalopathy and liver cell cancer. The risk of these complications appears to be similar to that seen in patients with hepatitis C-related cirrhosis.

HOW DOES FAT GET INTO THE LIVER?

The exact mechanism(s) leading to fatty liver are not well established, although they appear to involve a combination of excessive delivery of fat to the liver from the body fat stores, impaired breakdown of fat in the liver, excessive synthesis of fat from carbohydrate within the liver and defects in the export of stored fat from the liver to the rest of the body. The mechanisms leading to the progression of fatty liver to NASH are even less well understood, but most probably involve the toxic effects of fat coming into the liver from fat (adipose) tissue in obese patients. Patients with type 2 diabetes have an even greater release of fat from adipose tissue than obese patients without diabetes, presumably accounting for their higher risk of NASH.

IS THERE A TREATMENT FOR FATTY LIVER?

The treatment of fatty liver is related to the underlying cause. In patients who are obese or have diabetes or high lipids, studies have shown that control of these underlying conditions may improve liver function as judged by blood tests and liver biopsy appearances. At present the best evidence of a beneficial role is for weight reduction achieved by diet and exercise. Diet and exercise should be carried out in a sensible manner with supervision, preferably by a trained dietician. No specific diets are recommended, however, it is important to remember that crash dieting or fad diets which result in an excessive and rapid amounts of weight loss (more than 2 pounds a week) can lead to worsening of liver function in the short-term, and should not, therefore be undertaken.

Control of diabetes has been shown to play an important role in preventing the progression of fatty liver disease, and there is some preliminary evidence that treatment with some anti-diabetic drugs may reduce the severity of fatty liver even in non-diabetic patients. Importantly some treatments used for lowering blood cholesterol (oral statins) can rarely lead to abnormal liver blood tests. However, in most patients the liver blood tests were abnormal prior to starting therapy due to pre-existing NAFLD and statin treatment should only be stopped if there is clear evidence that liver blood tests deteriorated after treatment was started. In most patients it is better to

continue with treatment in view of the proven beneficial effects of statins on the risks of cardiovascular diseases including heart attacks and strokes.

IS THERE A TREATMENT FOR NASH?

At present there is no specific treatment for NASH of definite proven benefit. Patients who are obese, diabetic and have high levels of fat in their blood are advised to lose weight on a programme of diet and exercise, control their blood sugars strictly and lower their fat levels with appropriate therapy. It is recommended that patients with NASH should avoid alcohol and other medications /substances, known to be harmful to the liver. Presently, research studies are in progress aimed at increasing our understanding of the precise causes of NASH and trials of new drugs based on this increased understanding are currently underway. As a result, it is hoped that in a few years time we will have specific therapies to treat or prevent the development of NASH and cirrhosis.

We have a more detailed booklet (No. 11 - Lifestyle and Your Liver, A guide to Non-Alcoholic Fatty Liver Disease). Please ask your consultant or email us for a copy.

CAN FATTY LIVER/NASH LEAD TO OTHER DISEASES?

Obesity and the resulting excess deposition of fat in the liver may increase the liver vulnerability to other causes of liver disease including excess alcohol intake and hepatitis viruses, particularly hepatitis C. Accordingly patients with all types of liver disease should be advised to maintain a normal body weight by sensible diet and exercise.

Acknowledgement:

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