Non-alcoholic Fatty Liver Disease (NAFLD)

Non-alcoholic Fatty Liver Disease (NAFLD) Overview

Non-alcoholic fatty liver disease (NAFLD) is a very common disorder and refers to a group of conditions where there is accumulation of excess fat in the liver of people who drink little or no alcohol. The most common form of NAFLD is a non serious condition called fatty liver. In fatty liver, fat accumulates in the liver cells. Although having fat in the liver is not normal, by itself it probably does not damage the liver. A small group of people with NAFLD may have a more serious condition named non-alcoholic steatohepatitis (NASH). In NASH, fat accumulation is associated with liver cell inflammation and different degrees of scarring. NASH is a potentially serious condition that may lead to severe liver scarring and cirrhosis. Cirrhosis occurs when the liver sustains substantial damage, and the liver cells are gradually replaced by scar tissue (see figure), which results in the inability of the liver to work properly. Some patients who develop cirrhosis may eventually require a liver transplant (surgery to remove the damaged liver and replace it with a "new" liver).

Symptoms

The majority of individuals with NAFLD have no symptoms and a normal examination. Children may exhibit symptoms such as abdominal pain, which may be in the center or the right upper part of the abdomen, and sometimes fatigue. However, other causes of abdominal pain and fatigue should be considered. On physical examination the liver might be slightly enlarged and some children may have patchy, dark discoloration of the skin present (acanthosis nigricans) most commonly over the neck and the under arm area.

Causes of NAFLD/NASH

NAFLD is part of the metabolic syndrome characterized by diabetes, or pre-diabetes (insulin resistance), being overweight or obese, elevated blood lipids such as cholesterol and triglycerides, as well as high blood pressure. Not all patients have all the manifestations of the metabolic syndrome. Less is known about what causes NASH to develop. Researchers are focusing on several factors that may contribute to the development of NASH. These include:

- Oxidative stress (imbalance between pro-oxidant and anti-oxidant chemicals that lead to liver cell damage)
- Production and release of toxic inflammatory proteins (cytokines) by the patient's own inflammatory cells, liver cells, or fat cells
- Liver cell necrosis or death, called apoptosis
- Adipose tissue (fat tissue) inflammation and infiltration by white blood cells
- Gut microbiota (intestinal bacteria) which may play a role in liver inflammation

Risk Factors

NAFLD is a very common disorder affecting and may affect as many as one in three to one in five adults and around one in ten children in the United States. Obesity is thought to be the most common cause of fatty infiltration of the liver. Some experts estimate that about two thirds of obese adults and half of obese children may have fatty liver. About 2 to 5 percent of adult Americans and up to 20 percent of those who are obese may suffer from the more severe condition NASH. The number of children who have NASH is not known. The presence of type 2 diabetes and other conditions associated with insulin resistance, such as polycystic ovarian syndrome are know risk factors for the development of fatty liver and NASH.

Screening/Diagnosis

People with risk factors for fatty liver are often overweight or obese, and can have diabetes, or high levels of triglycerides/cholesterol in their blood. People with these risk factors should have their liver tests checked at least once per year. Those who are found to have elevated liver tests or possible fat in their liver on an abdominal ultrasound, or other imaging study, should be evaluated for possible fatty liver in addition to other causes of elevated liver tests. Once fat is identified in the liver, other causes of liver fat such as drinking too much alcohol, certain medications, and other liver diseases must be checked for before making a diagnosis of fatty liver.

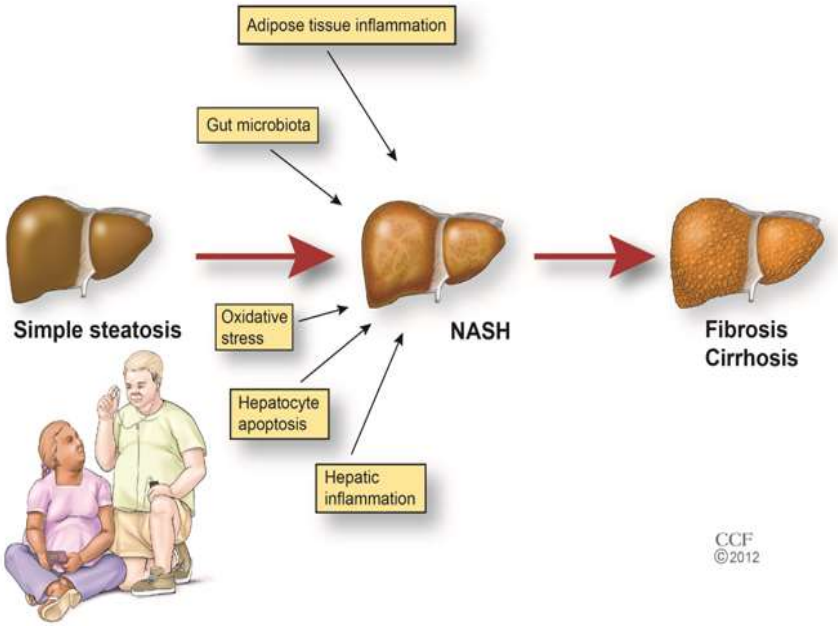
The next step is to determine whether the patient with fatty liver has only fat within their liver (also called steatosis), where scarring of the liver is rare or non-alcoholic steatohepatitis (NASH) with both fat and inflammation in the liver that over time can cause scarring in the liver. The most accurate way to figure this out is to perform a liver biopsy, a procedure where a small needle is inserted through the skin after numbing medicine is given to obtain a small piece of the liver for examination under a microscope. A pathologist then interprets the biopsy sample and determines whether NASH is present and, if so, whether any liver damage or scarring has taken place. There are a growing number of alternatives to liver biopsy that can also provide much of the same information without requiring needle insertion into the liver. These include measuring liver stiffness and fat content of the liver with elastography testing through the use of a specialized ultrasound (Fibroscan®)or MRI scan. Special blood tests or a combination of routine blood tests can also be used to evaluate for possible liver scarring in patients with NAFLD. Because none of these tests are perfect, patients with fatty liver are advised to discuss the risks and benefits of these tests with their doctor to decide which tests are best in their situation. In general, it is most beneficial to do a combination of tests to see if they all point to the same degree of fat in the liver and liver scarring. If the tests point to more significant scarring in the liver, your doctor may recommend a liver biopsy.

Treatment of NAFLD/NASH

In addition to good control of diabetes and high cholesterol/triglycerides when present, the most effective treatment for fatty liver, either NAFLD or NASH, involves changes in how you eat and live including weight loss, increasing your exercise, eating a balanced diet, and avoiding alcohol. Losing a small amount of body weight has been shown to improve liver biopsy results in those with NASH in addition to having a beneficial effect on blood sugars, blood pressure, and cholesterol levels. Various diets can lead to a reduction in liver fat, as long as there is a decrease in calories eaten in a day compared to a person's daily required calories to maintain their current weight, with a goal of 500 fewer calories daily. Individuals should try to exercise 30 minutes or greater per day at least 5 times a week. However, both losing weight and maintaining weight loss can be difficult for many patients to achieve with lifestyle changes alone. In these instances, a doctor may prescribe a type of weight loss medication or may refer patients for a weight loss procedure or surgery.

While there are currently no U.S. Food and Drug Administration (FDA) approved medications for treatment of NASH specifically, several are being studied and medicines to improve liver scarring in patients with NASH and fibrosis may soon be available to patients. In general, these experimental medications target different areas in the pathway of fat accumulation in the liver, associated inflammation, and scar tissue formation.

If inflammation from NASH continues for years, an extensive amount of liver scar tissue can form which eventually leads to liver cirrhosis (severe scarring of the liver that can be permanent). Patients who develop cirrhosis related to NASH are at risk for two major developments: hepatocellular carcinoma (liver cancer) and/or end-stage liver disease. Developing either complication of cirrhosis significantly impacts life expectancy, but certain patients can be cured by undergoing a liver transplant if they are evaluated and found to be a good candidate. For this reason, patients with NASH cirrhosis should see a GI or liver specialist regularly who will monitor their liver function and screen them for liver cancer with periodic liver ultrasounds or other scans, in addition to monitoring for other complications.



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Return to Top

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