

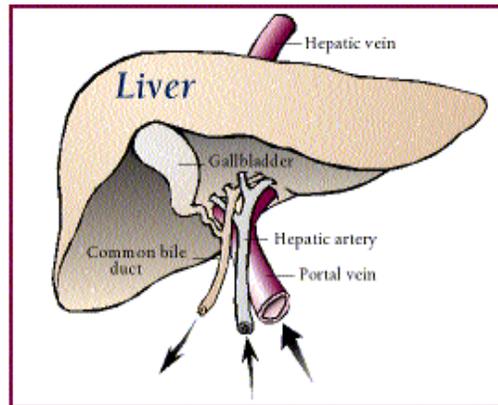
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**NONALCOHOLIC FATTY LIVER DISEASE  
AND  
NONALCOHOLIC STEATOHEPATITIS**

**What is NAFLD?**

Nonalcoholic fatty liver disease or NAFLD is a common, often "silent" liver disease. It resembles alcoholic liver disease, but occurs in people who drink little or no alcohol. The major feature in NAFLD is fat in the liver. Nonalcoholic steatohepatitis (NASH) is present if there is also inflammation and damage to the liver. Most people with NAFLD feel well and are not aware that they have a liver problem.

**How common is NAFLD?**

10 to 20 percent of Americans have simple fatty liver, with fat in their liver, but no inflammation or liver damage. Although having fat in the liver is not normal, by itself it probably causes little harm or permanent damage. NASH, on the other hand, affects 2 to 5 percent of Americans. It can be severe and can lead to cirrhosis, in which the liver is permanently damaged and scarred and no longer able to work properly. Most affected people are between the ages of 40 and 60 years, although the condition can also occur in children over the age of 10 years. NASH is diagnosed more often in women than in men.

Both NASH and NAFLD are becoming more common, possibly because of the greater number of Americans with obesity. In the past 10 years, the rate of obesity has doubled in adults and tripled in children. Obesity also contributes to diabetes and high blood cholesterol, which can further complicate the health of someone with NASH. Diabetes and high blood cholesterol are also becoming more common among Americans.

**What causes fatty liver?**

Fat may accumulate in the liver with extreme weight gain or diabetes mellitus. Fatty liver can also occur with poor diet and certain illnesses, such as tuberculosis, intestinal bypass surgery for obesity, and certain drugs such as corticosteroids, or in the setting of heavy alcohol use. A patient has fatty liver when the fat makes up at least 10% of the liver. Eating fatty food by itself does not produce a fatty liver. Simple fatty liver is not associated with any other liver abnormalities such as scarring or inflammation. It is a common finding in patients who are very overweight or have diabetes mellitus. Alcoholism can also result in inflammation of the liver (alcoholic hepatitis) and/or scarring (alcoholic cirrhosis) and needs to be differentiated from NASH by patient history. Possible explanations for fatty liver include the transfer of fat from other parts of the body, or an increase in the extraction of fat presented to the liver from the intestine. Another explanation is that the fat accumulates because the liver is unable to change it into a form that can be eliminated.

**What causes NASH?**

Although NASH has become more common, its underlying cause is still not clear. It most often occurs in persons who are middle-aged and overweight or obese. Many patients with NASH have elevated blood lipids, such as cholesterol and triglycerides, and many have diabetes or pre-diabetes, but not every obese person or every patient with diabetes has NASH. Furthermore, some patients with NASH are not obese, do not have diabetes, and have normal blood cholesterol and lipids. NASH can occur without any apparent risk factor and can even occur in children. Thus, NASH is not simply obesity that affects the liver.

## **How is NAFLD diagnosed?**

NAFLD is usually first suspected in a person who is found to have elevations in liver tests that are included in routine blood test panels, such as alanine aminotransferase (ALT) or aspartate aminotransferase (AST). When further evaluation shows no apparent reason for liver disease (such as medications, viral hepatitis, or excessive use of alcohol) and when X-rays or imaging studies of the liver show fat, NAFLD is suspected. The physician will first search for other possible causes of chronic liver disease, especially alcohol abuse. Images of the liver obtained by an ultrasound test, a computed tomography (CT) scan, or a magnetic resonance imaging (MRI) scan, can suggest the presence of a fatty liver. In the ultrasound test, a fatty liver will produce a bright image in a ripple pattern. A CT scan will show a liver that is less dense than normal. The only means of proving a diagnosis of NASH and separating it from simple fatty liver is a liver biopsy. For a liver biopsy, a needle is inserted through the skin to remove a small piece of the liver, which is then examined under a microscope. If there is fat without inflammation and damage, simple fatty liver or steatosis, is diagnosed. An important piece of information learned from the biopsy is whether scar tissue has developed in the liver. Currently, no blood tests or scans can reliably provide this information.

## **How is NASH treated?**

At this time, there are no treatments that cure NASH. The main goal of treatment is to control the conditions that are associated with NASH, such as obesity, diabetes and hyperlipidemia. The most important recommendations given to persons with this disease are to reduce their weight (if obese or overweight), follow a balanced and healthy diet, increase physical activity, avoid alcohol and avoid unnecessary medications.

Experimental approaches under evaluation in patients with NASH include ursodeoxycholic acid (UDCA) and antioxidants, such as vitamin E, selenium, and betaine. Antioxidants may be of benefit by acting to reduce the oxidative stress that appears to increase inside the liver in patients with NASH. Whether these substances actually help treat the disease is not known, but the results of clinical trials should become available in the next few years.

Another experimental approach to treating NASH is the use of newer antidiabetic medications—even in persons without diabetes. Most patients with NASH have insulin resistance, meaning that the insulin normally present in the bloodstream is less effective for them in controlling blood glucose and fatty acids in the blood than it is for people who do not have NASH. The newer antidiabetic medications make the body more sensitive to insulin and may help reduce liver injury in patients with NASH. Studies of these medications—including metformin, rosiglitazone, and pioglitazone—are being sponsored by the National Institutes of Health and may answer the question of whether these medications are beneficial in NASH.

## **What is the prognosis for patients with NASH?**

The typical course of NASH is still being studied. Very few factors have been useful in predicting the course of this condition, although specific features in the liver biopsy can be helpful. The good news is that in most people, NASH appears to be a stable medical condition. The results of one study showed that people with NASH live just as long as people without this condition. Furthermore, the results of liver function tests remain the same over time in most people with NASH.

On the other hand, NASH can progress in some people. Studies that tracked liver damage in people with NASH who underwent several liver biopsies over time showed that the liver damage improved in about 3 percent of people, remained stable in 54 percent of people, and worsened in 43 percent of people.

Progressive liver damage can eventually lead to cirrhosis. Over a seven-year period, about 8 to 26 percent of people with NASH develop cirrhosis. Older diabetic women may be at increased risk. People who have developed cirrhosis are at risk for eventually developing complications of cirrhosis (such as internal bleeding, fluid accumulation in the legs and abdomen, mental confusion, and jaundice), that may ultimately require liver transplantation.

## **Where can you get more information?**

Your doctor is the best resource for finding out important information related to your particular case. Not all patients with NASH are alike, and it is important that your situation is evaluated by someone who knows you as a whole person. However, you can obtain more information from:

### **American Liver Foundation (ALF)**

75 Maiden Lane, Suite 603  
New York, NY 10038-4810  
Phone: 1-800-GO-LIVER (465-4837),  
1-888-4HEP-USA (443-7872),  
or 212-668-1000  
Fax: 212-483-8179