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Patient information: Nonalcoholic steatohepatitis (NASH)

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INTRODUCTION — Nonalcoholic steatohepatitis (NASH) is a condition that causes inflammation and accumulation of fat and fibrous tissue in the liver (<u>figure 1</u>). Although a similar condition can occur in people who abuse alcohol, NASH occurs in those who do drink little to no alcohol. The exact cause of NASH is unknown. However, it is seen more frequently in people with certain medical conditions such as diabetes, obesity, and insulin resistance.

It is not clear how many people have NASH because it causes no symptoms. However, NASH is diagnosed in about 7 to 9 percent of people in the United States who have a liver biopsy. Most 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 seen more often in women than in men.

The cause of NASH is not clear, although research is ongoing in an attempt to find effective treatments. At the present time, treatment of NASH focuses on controlling some of the medical conditions associated with it (such as diabetes and obesity) and monitoring for progression.

CONDITIONS ASSOCIATED WITH NONALCOHOLIC STEATOHEPATITIS — Although the cause of NASH is unknown, it is most frequently seen in people with one of more of the following conditions.

- Obesity More than 70 percent of people with NASH are obese. Most obese people with NASH are between 10 and 40 percent heavier than their ideal body weight.
- Diabetes Up to 75 percent of people with NASH have type 2 diabetes. (See <u>"Patient information: Diabetes mellitus type 2: Overview"</u>.)
- Hyperlipidemia About 20 to 80 percent of people with NASH have hyperlipidemia (high blood triglyceride levels and/or high blood cholesterol levels). (See <u>"Patient information:</u> High cholesterol and lipids (hyperlipidemia)".)
- Insulin resistance Insulin resistance refers to a state in which the body does not respond adequately to insulin. Insulin resistance often occurs in people with hyperlipidemia who are obese; this group of symptoms is known as the metabolic syndrome and is frequently seen in people with NASH. (See <u>"Patient information: Diabetes mellitus type 2: Overview"</u>.)
- Drugs and toxins Several drugs used to treat medical conditions have been linked to

NASH, including <u>amiodarone</u> (Corderone®, Pacerone®), <u>tamoxifen</u> (Nolvadex®, Tamone®), perhexiline maleate (Pexhid®), steroids (eg, <u>prednisone</u>, <u>hydrocortisone</u>), and synthetic estrogens. Pesticides that are toxic to cells have also been linked to NASH.

NONALCOHOLIC STEATOHEPATITIS SYMPTOMS — Most people with NASH have no symptoms. Rarely, NASH is diagnosed in people with fatigue, a general feeling of being unwell, and a vague discomfort in their upper right abdomen, although it is not clear if these symptoms are related to NASH.

NONALCOHOLIC STEATOHEPATITIS DIAGNOSIS — NASH is most often discovered during routine laboratory testing. Additional tests help confirm the presence of NASH and rule out other types of liver disease. Imaging tests (such as ultrasound, CT scan, or magnetic resonance imaging) may reveal fat accumulation in the liver but cannot differentiate NASH from other causes of liver disease that have a similar appearance. A liver biopsy is required to confirm NASH.

Liver function tests — Blood tests to measure the liver function measure levels of substances produced or metabolized by the liver. These levels can help to diagnose NASH and differentiate NASH from alcoholic hepatitis. Levels of two liver enzymes (aspartate aminotransferase [AST] and alanine aminotransferase [ALT]) are elevated in about 90 percent of people with NASH.

Other blood tests — Additional blood tests are useful for ruling out other causes of liver disease. These usually include tests for viral hepatitis (hepatitis A, B, or C), and may include tests for less common cause of liver disease. (See <u>"Patient information: Hepatitis A"</u> and <u>"Patient information: Hepatitis B"</u> and <u>"Patient information: Hepatitis C"</u>.)

Liver biopsy — Although other tests may suggest a diagnosis of NASH, liver biopsy is required to confirm it. A liver biopsy is also helpful for determining the severity of NASH and may provide clues about the future course of the condition. The procedure involves collecting a small sample of liver tissue, which is sent to a laboratory for microscopic examination and biochemical testing. More detailed information about liver biopsies is available in a separate topic review. (See "Patient information: Liver biopsy".)

NONALCOHOLIC STEATOHEPATITIS TREATMENT — There is no cure for NASH. Treatment aims to control the conditions that are associated with NASH, such as obesity, diabetes, and hyperlipidemia. Several experimental treatments are being studied with drugs that treat insulin resistance.

Weight loss — Weight reduction can help to reduce levels of liver enzymes, insulin, and can improve quality of life. Weight loss should be gradual (no more than 3.5 lbs or 1.6 kg per week) since rapid weight loss has been associated with worsening of liver disease. A healthcare provider or nutritionist can provide an individualized weight loss plan. (See "Patient information: Weight loss treatments".)

Treatment of insulin resistance — Several drugs are available for people with insulin resistance, and they are being studied in patients with NASH. Their role is not yet proven.

More information about treatments for insulin resistance is available in a separate topic review. (See "Patient information: Diabetes mellitus type 2: Treatment", section on 'Thiazolidinediones'.)

Miscellaneous drugs — Several new drugs are being tested in patients with NASH but none has yet proven to be beneficial in large, long-term studies.

NONALCOHOLIC STEATOHEPATITIS PROGNOSIS — NASH is typically a chronic condition (ie, it persists for many years). It is difficult to predict the course of NASH in an individual. Few factors have been useful in predicting the course of this condition, although features in the liver biopsy can

be helpful.

The good news is most people with NASH will not develop serious liver problems. One study showed that most people with NASH live as long as those without it. Furthermore, liver function tests are stable over time in most people with NASH.

However, NASH can progress in some people. One study that tracked liver damage over time showed that the condition improved in about 3 percent of people, remained stable in 54 percent of people, and worsened in 43 percent of people [1].

The most serious complication of NASH is cirrhosis, which occurs when the liver becomes severely scarred. In one study, between 8 and 26 percent of people with NASH developed cirrhosis $[\underline{1}]$. Older diabetic women may be at increased risk. (See "Patient information: Cirrhosis".)

WHERE TO GET MORE INFORMATION — Your healthcare provider is the best source of information for questions and concerns related to your medical problem.

This article will be updated as needed every four months on our web site (www.uptodate.com/patients).

Related topics for patients, as well as selected articles written for healthcare professionals, are also available. Some of the most relevant are listed below.

Patient Level Information:

Patient information: Diabetes mellitus type 2: Overview

Patient information: High cholesterol and lipids (hyperlipidemia)

Patient information: Hepatitis A
Patient information: Hepatitis B
Patient information: Hepatitis C
Patient information: Liver biopsy

Patient information: Weight loss treatments

Patient information: Diabetes mellitus type 2: Treatment

Patient information: Cirrhosis

Professional Level Information:

Immunizations for patients with chronic liver disease

Natural history and treatment of nonalcoholic steatohepatitis

Pathogenesis of nonalcoholic fatty liver disease

Epidemiology, clinical features, and diagnosis of nonalcoholic steatohepatitis

The following organizations also provide reliable health information.

National Library of Medicine

(www.nlm.nih.gov/medlineplus/healthtopics.html)

National Institute of Diabetes and Digestive and Kidney Diseases

(www.niddk.nih.gov)

The American Association for the Study of Liver Diseases

(www.aasld.org)

• The American Liver Foundation

(<u>www.liverfoundation.org</u>)

[1-4]

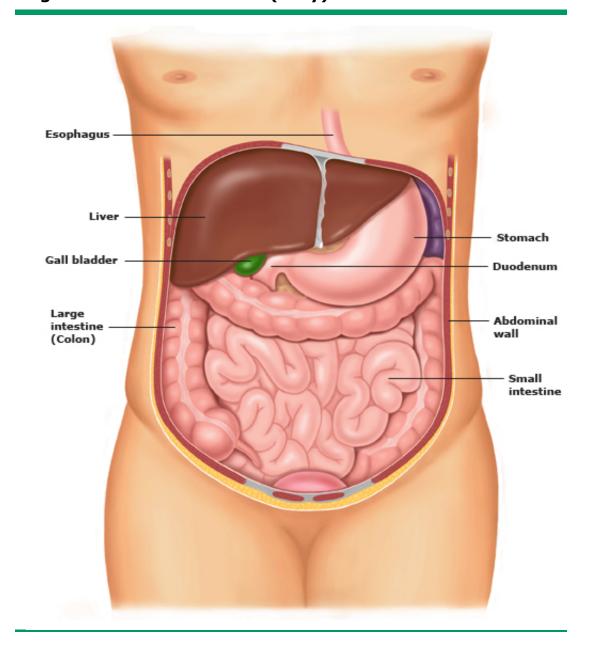
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- 3. Angelico F, Burattin M, Alessandri C, et al. Drugs improving insulin resistance for non-alcoholic fatty liver disease and/or non-alcoholic steatohepatitis. Cochrane Database Syst Rev 2007; :CD005166.
- 4. Musso G, Gambino R, Cassader M, Pagano G. A meta-analysis of randomized trials for the treatment of nonalcoholic fatty liver disease. Hepatology 2010; 52:79.

GRAPHICS

Organs inside the abdomen (belly)



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