Nonalcoholic steatohepatitis (NASH)

Nonalcoholic steatohepatitis (NASH) is a condition characterized by inflammation and the accumulation of fat and fibrous tissue in the liver. Although similar findings can be seen in patients who abuse alcohol, NASH occurs in those who do drink little to no alcohol. The exact cause of NASH is unknown.

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 seen more often in women than in men.

It is difficult to predict the natural course of NASH in individual patients.Most people with this condition will not develop serious liver problems. However, the condition can lead to progressive scarring and cirrhosis in a small number of patients. Cirrhosis is the term used to describe a severely scarred liver.

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 patients for progression.

CONDITIONS ASSOCIATED WITH NASH

Although the cause of NASH is unknown, it is most frequently seen in persons with a number of other conditions.

Obesity

More than 70 % of people with NASH are obese. Most obese people with NASH are between 10 and 40 % heavier than their ideal body weight.

Diabetes mellitus

Up to 75 % of people with NASH have diabetes mellitus.

Hyperlipidemia

About 20 to 80 % of people with NASH have hyperlipidemia (high blood triglyceride levels and/or high blood cholesterol levels).

Insulin resistance

Insulin resistance refers to a state in which the body does not respond adequately to insulin. In addition to causing diabetes mellitus, insulin resistance is also often associated with obesity and hyperlipidemia, a constellation of findings encompassed under the general term insulin resistance or metabolic syndrome.

Factors that affect metabolism

A variety of factors that alter metabolism have been linked to NASH. These factors include total parenteral nutrition , rapid weight loss, sudden starvation, and intravenous glucose therapy in people with terminal conditions.

Abdominal surgery

Several types of abdominal operations have been linked to NASH. These include surgical removal of large portions of the small intestine, surgery of the stomach to treat severe obesity, surgery of the gall bladder and pancreas, and surgery used to bypass parts of the small intestine.

Drugs and toxins

Several drugs used to treat medical conditions have been linked to NASH, including amiodarone , tamoxifen , perhexilene maleate , steroids (eg, prednisone, hydrocortisone), and synthetic estrogens. Pesticides that are toxic to cells have also been linked to NASH.

Other conditions

Certain other medical conditions have also been linked to NASH. These conditions include Wilson's disease , Weber-Christian disease , abetalipoproteinemia , and diverticula of the small intestine.

SYMPTOMS

Most people with NASH have no symptoms. Very rarely, NASH is diagnosed after patients consult their doctor because of fatigue, a general feeling of being unwell, and vague discomfort in their upper right abdomen, although the relationship of these symptoms to NASH is unclear.

DIAGNOSIS

NASH is most often discovered during routine laboratory testing and proven by a liver biopsy. Additional tests help confirm the presence of NASH and rule out other types of liver disease.

Medical history

A medical history may reveal conditions or events that have been associated with NASH, such as diabetes or abdominal surgery. In addition, a clinician may ask about risk factors for other forms of liver disease such as viral, drug-induced, or alcoholic hepatitis.

Physical examination

A physical examination may reveal an enlarged liver, but it is usually normal.

Liver function tests

Liver function tests determine blood levels of substances produced or metabolized by the liver. They can be helpful for diagnosing NASH and for differentiating NASH from alcoholic hepatitis. Levels of two liver enzymes (AST and ALT) are elevated in about 90 % 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.

Imaging test

Imaging tests (such as ultrasound, CT scan, or magnetic resonance imaging) may reveal fat accumulation in the liver. Imaging tests are not used to diagnose NASH since they cannot differentiate it from other causes of liver disease that have a similar appearance.

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. Sometimes, doctors will recommend gradual weight loss and watchful waiting for six months to one year before a liver biopsy; abnormal liver function tests return to normal after losing weight in some people.

TREATMENT

At this time, there is no treatment to cure NASH. Treatment aims to control the conditions that are associated with NASH, such as obesity, diabetes, and hyperlipidemia. Several experimental treatments with drugs that treat insulin resistance are being studied.

Weight loss

Weight reduction may be helpful but should be done gradually since, since rapid weight loss has been associated with worsening of liver disease. Your doctor can help provide a customized weight loss program for you.

Treatment of insulin resistance

Several drugs are available for persons with insulin resistance, including rosiglitazone , pioglitazone and metformin . These are being studied in patients with NASH; improvement in ALT and AST levels and liver histology has been seen in one and two year studies. Long-term studies are still in progress

Miscellaneous drugs

Several new drugs are being tested in patients with NASH but none has yet proven to be beneficial in large studies. Many drugs that initially showed promised later turned out to be of no benefit . For example, ursodeoxycholic acid was used for patients with NASH based upon initial studies that found that it improved liver blood tests. However, later studies found no benefit.

Vitamin E was used in NASH because of earlier reports suggesting it may reduce liver blood tests, but these results were not confirmed in later studies. Long-term vitamin E may also be associated with an increased risk for heart disease.

PROGNOSIS

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 that NASH is a stable medical condition in most people.

However, NASH can progress in some people. One study that tracked liver damage over time showed that it improved in about 3 % of people, remained stable in 54 % of people, and worsened in 43 % of people .

Progressive liver damage can eventually lead to cirrhosis. Over a seven-year period, between 8 and 26 % 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