

## NONALCOHOLIC STEATOHEPATITIS

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**ABSTRACT:** Nonalcoholic steatohepatitis (NASH) is a hepatic disorder with histologic features of alcohol-induced liver disease that occurs in individuals who do not consume significant alcohol. NASH is believed to be one of the most common explanations for abnormal liver chemistries in American adults. Risk factors for NASH include obesity, type II diabetes, hyperlipidemia, total parenteral nutrition, jejuno-ileal bypass surgery, and the use of certain drugs. However, some patients with NASH have no identifiable risk factors for the disease. Clinically, NASH is a diagnosis of exclusion that should be suspected as a cause of chronic hepatitis in patients who deny significant alcohol consumption and have negative serologic tests for congenital and other acquired causes of liver diseases. The identification of fatty liver on imaging studies supports the diagnosis of NASH, which can be established definitively by liver biopsy. The latter also provides useful prognostic information since most patients with simple steatosis follow an indolent clinical course, whereas those with steatohepatitis, fibrosis, or cirrhosis are more likely to develop clinically significant complications of liver disease. Weight reduction and treatment of confounding medical conditions are the mainstays of therapy for NASH. However, there is a little evidence that any of the current treatments prevent progression to more histologically advanced stages of NASH. Several experimental therapies, including treatment with bile acids, antibiotics, nutritional supplements, and antioxidants, have had anecdotal success in selected patients, but improved understanding of the pathogenesis and natural history of NASH will be required to develop generally effective therapy for the disorder.

**KEY WORDS:** fatty liver, alcohol-like hepatitis, steatonecrosis

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Nonalcoholic steatohepatitis (NASH) is a form of chronic hepatitis with histologic features of alcohol-induced liver disease that occurs in individuals who do not consume significant amounts of alcohol. Several other terms have been used to refer to this entity, including pseudoalcoholic liver disease, alcohol-like hepatitis, fatty liver hepatitis, diabetic hepatitis, nonalcoholic Laennec's, and steatonecrosis. A number of retrospective studies have suggested that this is an uncommon disorder that occurs most often in middle-aged obese women. Hyperglycemia and/or hyperlipidemia are commonly associated with NASH and are thought to be predisposing conditions. Other identified risk factors include total parenteral nutrition, protein-calorie malnutrition, jejunoileal bypass, and the use of certain drugs. Recent reports suggest that NASH may be much more

common than originally suspected and that many afflicted individuals lack typical risk factors for the disorder. The clinical implications of NASH have not been clearly defined. Although progression to cirrhosis has been documented, and some patients develop clinical manifestations of portal hypertension and hepatic failure, many others appear to have an indolent course. Lack of information about the natural history of NASH has generated controversy about the wisdom of recommending invasive diagnostic tests or attempting to develop specific therapies for patients with this disease. Efforts to prevent or improve NASH have also been limited by our poor understanding of its pathogenesis. Careful epidemiologic studies and basic investigation are needed to provide new data that can be used to guide the management of patients with NASH.

#### CLINICAL FEATURES

The clinical features of NASH are summarized in Table 1.

#### SYMPTOMS AND SIGNS

Like most patients with other types of chronic liver disease, most patients with NASH are asymptomatic.

TABLE 1. CLINICAL FEATURES OF NASH

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Symptoms
Variable
Vague (fatigue, malaise, right upper quadrant discomfort)
Mostly absent
Signs
Hepatomegaly common
Splenomegaly in some
Portal HTN unusual
Laboratory Values
Increased AST, ALT typical
+/- increased alk. phos., GGT
Increased cholesterol, triglycerides common
Increased glucose common
Viral markers (-)
Autoantibodies (-)
Iron studies abnormal sometimes
Imaging
Fatty liver

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Hence, NASH is often diagnosed after abnormalities are noted during "routine" laboratory testing. Fatigue, malaise, and vague right upper quadrant abdominal discomfort bring some patients

with NASH to medical attention. In a recent article by Bacon et al, these symptoms antedated the diagnosis of NASH in about a third of patients. Although many patients deny symptoms of liver disease, hepatomegaly is frequently noted in most published series, occurring in up to three-fourths of patients in several studies. Stigmata of portal hypertension appear to occur much less frequently, although splenomegaly was noted at the time of diagnosis in about 25% of the patients in one recent series.

In contrast to most patients with NASH, some patients with certain types of drug-induced fatty liver (steatosis) present dramatically, with the rapid evolution of severe hepatic failure. For example, fulminant liver failure and death have been reported in patients treated with certain nucleoside analogues, antimetabolic agents, or tetracycline. In other patients with inborn error of metabolism, such as tyrosinemia, steatosis appears to progress rapidly to cirrhosis and commonly leads to death from various liver-related complications, including hepatocellular carcinoma.

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