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## WHAT IS NONALCOHOLIC FATTY LIVER DISEASE (NAFLD) / NONALCOHOLIC STEATOHEPATITIS (NASH)?

NAFLD 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).

## HOW COMMON IS NAFLD / NASH?

NAFLD is a very common disorder. It is estimated that NAFLD affects up to 20 percent of adults and nearly 5 percent of children. 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. In the past ten years the rate of obesity in our country has doubled in adults and tripled in children and teenagers, which may explain why NAFLD and NASH are becoming more common.

## WHAT CAUSES 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. Little 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

## WHAT ARE SIGNS AND SYMPTOMS OF NAFLD / NASH?

The majority of individuals with NAFLD have no symptoms and a normal examination. Children may exhibit symptoms such as abdominal pain, which maybe 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.

## HOW IS NAFLD / NASH DIAGNOSED?

The diagnosis of NAFLD is usually first suspected in an overweight or obese person who is found to have mild elevations in their liver tests during a routine blood testing. Some experts are now recommending that every obese child or adolescent should

have these liver enzymes checked. However NAFLD can be present with normal liver blood tests. The diagnosis of NAFLD is confirmed by imaging studies, most commonly a liver ultrasound, showing accumulation of fat in the liver. Fat accumulation in the liver can also be caused by excess alcohol intake, certain medications, viral hepatitis, autoimmune liver disease, and metabolic or inherited liver disease. These need to be excluded as causes of fatty liver disease in order to confirm the diagnosis of NAFLD. Currently, the only reliable way of telling whether a person has NASH or simple fatty liver is by a liver biopsy. In this procedure, a small needle is inserted through the skin after local anesthesia is given to obtain a small piece of the liver for microscopic evaluation. NASH is diagnosed when examination of this piece of liver under the microscope shows fatty infiltration of the liver, in addition to inflammation and different degrees of scarring. If only fat is present, then the diagnosis of simple fatty liver is made. The liver biopsy provides essential information regarding the degree of scarring within the liver, which would not be apparent on a blood test, ultrasound, or an x-ray alone. Liver biopsy rarely can be associated with serious risks including bleeding and patients should discuss the risks and benefits of the procedure with their physician.

#### WHAT ARE THE RISKS OF HAVING NAFLD /NASH?

Most people with NAFLD, especially those with simple fatty liver with no inflammation, have little or no problems from the condition. In contrast, about a quarter of people with NASH may have scarring of the liver that gets worse with time. In general, the progression of scarring is slow and can take years and even decades to occur. In some patients the scarring can stabilize and in persons who have lost significant amounts of weight there are cases where scarring has been shown to reverse. In others, the progression continues with scar tissue accumulating in the liver, leading to cirrhosis. NASH is an increasingly common reason for liver transplantation in the United States.

#### HOW IS NAFLD / NASH TREATED?

There is currently no medical treatment that reverses fatty liver disease and causes fat within the liver to resolve. As mentioned, a few studies have suggested that weight loss may be associated with regression of fat within the liver. Therefore, the most important recommendations for people with fatty liver are to lose weight if they are overweight or obese, increase their physical activity, follow a balanced diet and avoid alcohol and unnecessary medications. In patients with NASH, the more severe form of NAFLD, these same recommendations may be helpful. It is also important to control diabetes and treat elevated cholesterol levels when appropriate. Development of medications that could treat NAFLD and NASH is an area of intense research. Factors currently being evaluated by physicians and scientists to decrease the amount of fat in the liver include:

- Weight reduction (diet + exercise, medications, surgery)
- Lipid lowering medications
- Insulin sensitizers (medications)
- Decrease the amount of liver inflammation by administering anti-oxidant medications, anti-apoptotic medications and anti-cytokine medications

