Non-alcoholic Fatty Liver Disease (NAFLD)

Overview

Non-alcoholic fatty liver disease (NAFLD) is a very common disorder and 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).

Symptoms

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

Causes of 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. Less 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
- Adipose tissue (fat tissue) inflammation and infiltration by white blood cells
- Gut microbiota (intestinal bacteria) which may play a role in liver inflammation

Risk Factors

NAFLD is a very common disorder affecting and may affect as many as one in three to one in five adults and around one in ten children in the United States. 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. The presence of type 2 diabetes and other conditions associated with insulin resistance, such as polycystic ovarian syndrome are know risk factors for the development of fatty liver and NASH.

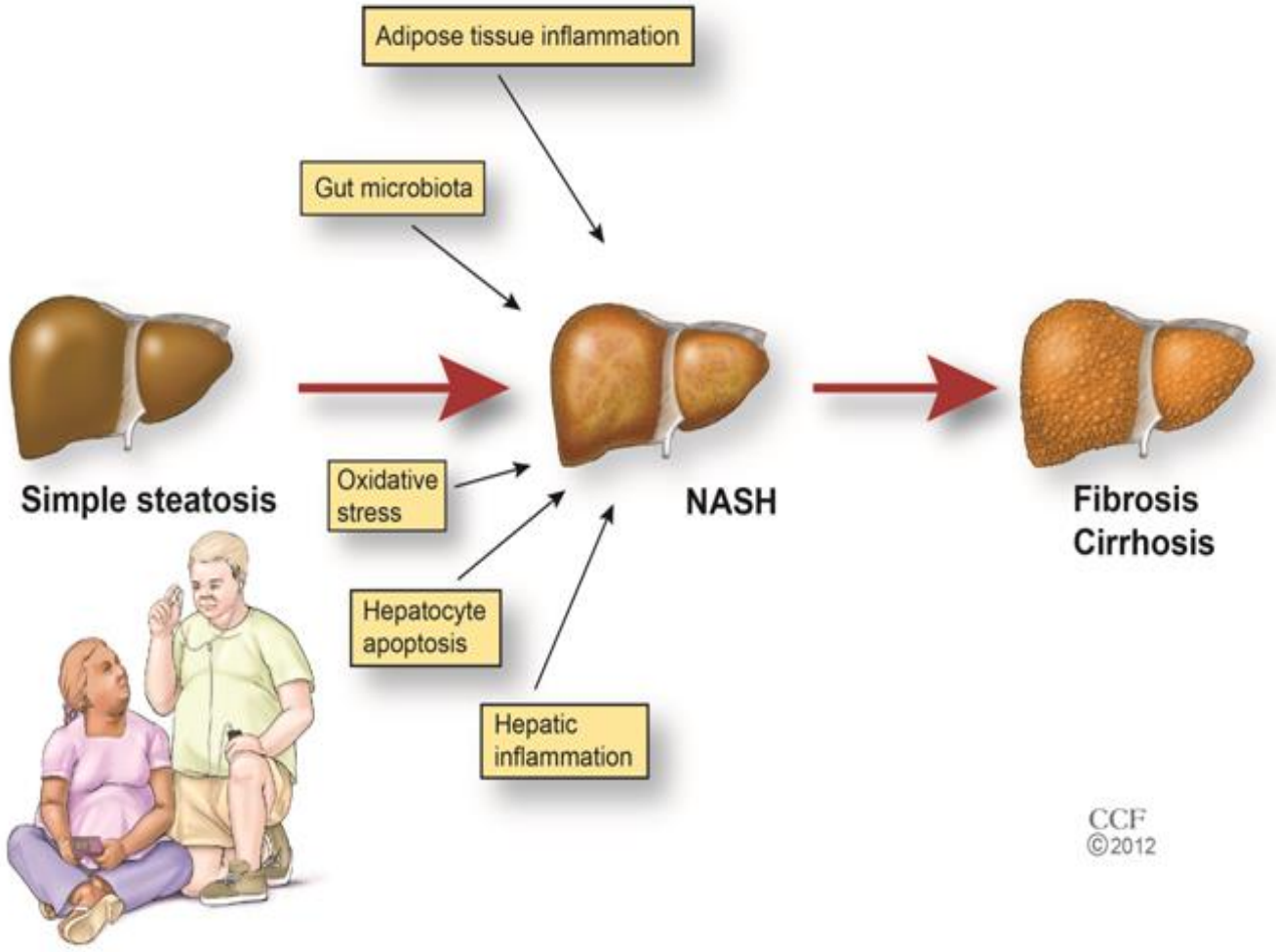
Screening/Diagnosis

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 or incidentally detected on radiologic investigations such as abdominal ultrasound or CT scan. 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.

Treatment of NAFLD/NASH

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. New evidence suggests that Mediterranean diet (rich in monounsaturated fatty acids) may be more beneficial than low fat diet. Drinking coffee seems to decrease the risk of having fatty liver in large cohort studies. 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 NAFD and NASH is an area of intense research. Recent trials in adult and children have shown that vitamin E (an anti-oxidant) could help improve NASH in non-diabetic patients. Strategies currently being evaluated by physicians and scientists to decrease the amount of fat/ inflammation 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



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