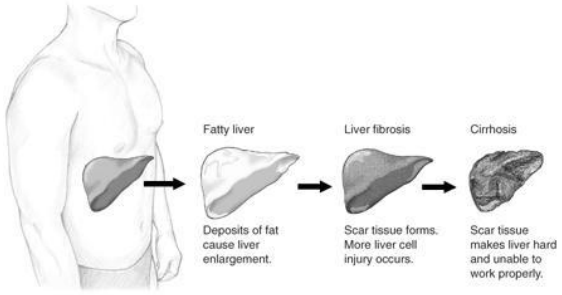
Fatty liver

Not to be confused with foie gras.

Fatty liver, also known as **fatty liver disease** (**FLD**), is a reversible condition wherein large vacuoles of triglyceride fat accumulate in liver cells via the process of steatosis (i.e., abnormal retention of lipids within a cell). Despite having multiple causes, fatty liver can be considered a single disease that occurs worldwide in those with excessive alcohol intake and the obese (with or without effects of insulin resistance). The condition is also associated with other diseases that influence fat metabolism.[1] When this process of fat metabolism is disrupted, the fat can accumulate in the liver in excessive amounts, thus resulting in a fatty liver.[2] It is difficult to distinguish alcoholic FLD from nonalcoholic FLD, and both show microvesicular and macrovesicular fatty changes at different stages.

Accumulation of fat may also be accompanied by a progressive inflammation of the liver (hepatitis), called steatohepatitis. By considering the contribution by alcohol, fatty liver may be termed alcoholic steatosis or nonalcoholic fatty liver disease (NAFLD), and the more severe forms as alcoholic steatohepatitis (part of alcoholic liver disease) and non-alcoholic steatohepatitis (NASH).

1 Causes



Different stages of liver damage

Fatty liver (FL) is commonly associated with alcohol or metabolic syndrome (diabetes, hypertension, obesity, and dyslipidemia), but can also be due to any one of many causes:[3][4]

Metabolic abetalipoproteinemia, glycogen storage diseases, Weber-Christian disease, acute fatty liver of pregnancy, lipodystrophy

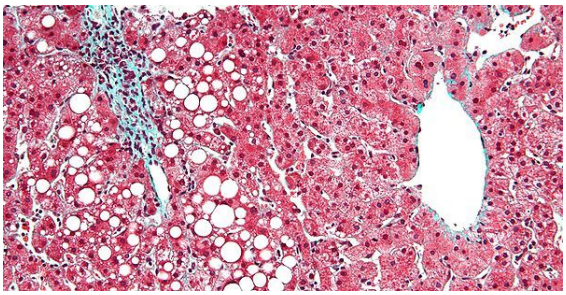
Nutritional malnutrition, total parenteral nutrition, severe weight loss, refeeding syndrome, jejunoileal bypass, gastric bypass, jejunal diverticulosis with bacterial overgrowth

Drugs and toxins amiodarone, methotrexate, diltiazem, expired tetracycline, highly active antiretroviral therapy, glucocorticoids, tamoxifen, environmental hepatotoxins (e.g., phosphorus, mushroom poisoning)

Alcoholic Alcoholism is one of the major cause of fatty liver due to production of toxic metabolites like aldehydes during metabolism of alcohol in the liver. This phenomenon most commonly occurs with chronic alcoholism.

Other inflammatory bowel disease, HIV, hepatitis C (especially genotype 3), and alpha 1-antitrypsin deficiency[5]

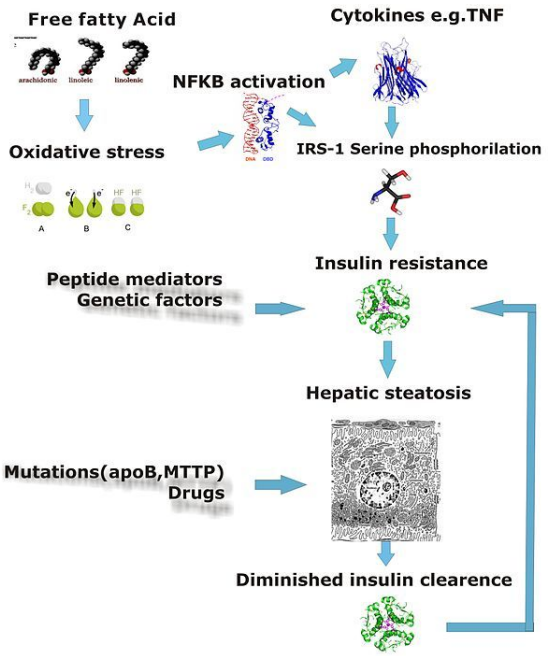
2 Pathology



Micrograph of periportal hepatic steatosis, as may be seen due to steroid use, trichrome stain

Fatty change represents the intracytoplasmatic accumulation of triglycerides (neutral fats). At the beginning, the hepatocytes present small fat vacuoles (liposomes) around the nucleus (microvesicular fatty change). In this stage, liver cells are filled with multiple fat droplets that do not displace the centrally located nucleus. In the late stages, the size of the vacuoles increases, pushing the nucleus to the periphery of the cell, giving characteristic signet ring appearance (macrovesicular fatty change). These vesicles are well-delineated and optically "empty" because fats dissolve during tissue processing. Large vacuoles may coalesce and produce fatty cysts, which are irreversible lesions. Macrovesicular steatosis is the most common form and is typically associated with alcohol,

diabetes, obesity, and corticosteroids. Acute fatty liver of pregnancy and Reye's syndrome are examples of severe liver disease caused by microvesicular fatty change.[6] The diagnosis of steatosis is made when fat in the liver exceeds 5–10% by weight.[1][7][8]

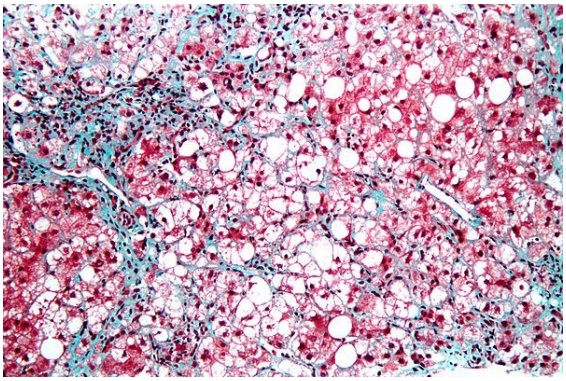


Mechanism leading to hepatic steatosis

Defects in fatty acid metabolism are responsible for pathogenesis of FLD, which may be due to imbalance in energy consumption and its combustion, resulting in lipid storage, or can be a consequence of peripheral resistance to insulin, whereby the transport of fatty acids from adipose tissue to the liver is increased.[1][9] Impairment or inhibition of receptor molecules (PPAR-α, PPAR-γ and SREBP1) that control the enzymes responsible for the oxidation and synthesis of fatty acids appears to contribute to fat accumulation. In addition, alcoholism is known to damage mitochondria and other cellular structures, further impairing cellular energy mechanism. On the other hand, nonalcoholic FLD may begin as excess of unmetabolised energy in liver cells. Hepatic steatosis is considered reversible and to some extent nonprogressive if the underlying cause is reduced or removed.

Severe fatty liver is sometimes accompanied by inflammation, a situation referred to as steatohepatitis. Progression to alcoholic steatohepatitis (ASH) or Non-alcoholic steatohepatitis (NASH) depends on the persistence or severity of the inciting cause. Pathological lesions in both conditions are similar. However, the extent of inflammatory response varies widely and does not always correlate with degree of fat accumulation. Steatosis (retention of lipid) and onset of steatohepatitis may represent successive stages in FLD progression.[10]

Liver disease with extensive inflammation and a high degree of steatosis often progresses to more severe forms

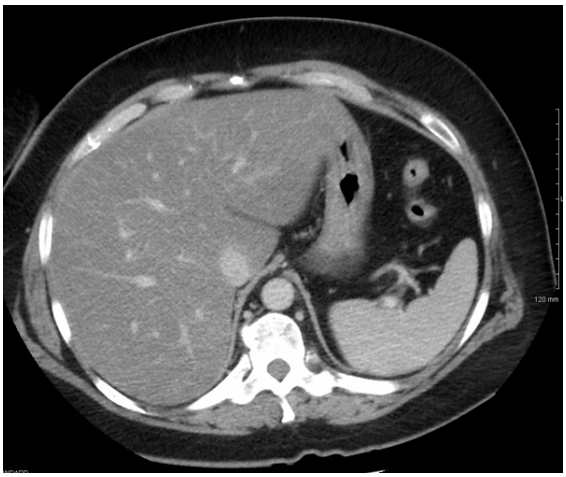


Micrograph of inflamed fatty liver (steatohepatitis)

of the disease.[11] Hepatocyte ballooning and necrosis of varying degrees are often present at this stage. Liver cell death and inflammatory responses lead to the activation of stellate cells, which play a pivotal role in hepatic fibrosis. The extent of fibrosis varies widely. Perisinusoidal fibrosis is most common, especially in adults, and predominates in zone 3 around the terminal hepatic veins.[12]

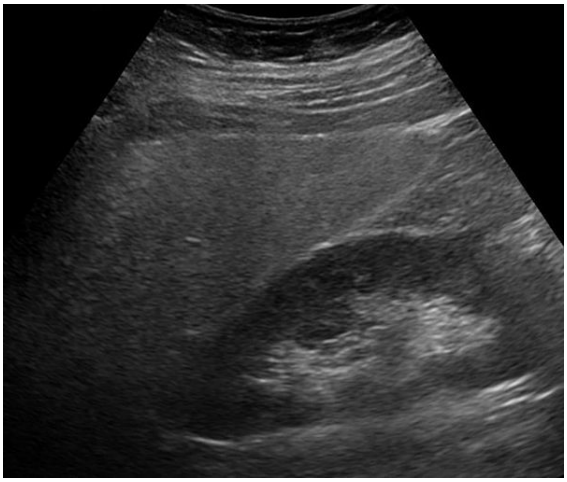
The progression to cirrhosis may be influenced by the amount of fat and degree of steatohepatitis and by a variety of other sensitizing factors. In alcoholic FLD, the transition to cirrhosis related to continued alcohol consumption is well-documented, but the process involved in nonalcoholic FLD is less clear.

3 Diagnosis



Liver steatosis (fatty liver disease) as seen on CT

Most individuals are asymptomatic and are usually discovered incidentally because of abnormal liver function tests or hepatomegaly noted in unrelated medical conditions. Elevated liver biochemistry is found in 50% of patients with simple steatosis.[14] The serum alanine transaminase level usually is greater than the aspartate



Ultrasound showing diffuse increased echogenicity of the liver.

transaminase level in the nonalcoholic variant and the opposite in alcoholic FLD (AST:ALT more than 2:1).

Imaging studies are often obtained during the evaluation process. Ultrasonography reveals a "bright" liver with increased echogenicity. Medical imaging can aid in diagnosis of fatty liver; fatty livers have lower density than spleens on computed tomography (CT), and fat appears bright in T1-weighted magnetic resonance images (MRIs). No medical imagery, however, is able to distinguish simple steatosis from advanced NASH. Histological diagnosis by liver biopsy is sought when assessment of severity is indicated.

4 Treatment

The treatment of fatty liver depends on its cause, and, in general, treating the underlying cause will reverse the process of steatosis if implemented at an early stage. Two known causes of fatty liver disease are an excess consumption of alcohol and a prolonged diet containing foods with a high proportion of calories coming from lipids.[15] For the patients with non-alcoholic fatty liver disease with pure steatosis and no evidence of inflammation, a gradual weight loss is often the only recommendation.[3] In more serious cases, medications that decrease insulin resistance, hyperlipidemia, and those that induce weight loss have been shown to improve liver function.[4]

For advanced patients with non-alcoholic steatohepatitis (NASH), there are no currently available therapies.

Up to 10% of people with cirrhotic alcoholic FLD will develop hepatocellular carcinoma. The overall incidence of liver cancer in nonalcoholic FLD has not yet been quantified, but the association is well-established.[16]

5 Epidemiology

The prevalence of FLD in the general population ranges from 10% to 24% in various countries.[3] However, the condition is observed in up to 75% of obese people, 35% of whom progressing to NAFLD,[17] despite no evidence of excessive alcohol consumption. FLD is the most common cause of abnormal liver function tests in the United States.[3] "Fatty livers occur in 33% of European-Americans, 45% of Hispanic-Americans, and 24% of African-Americans."[18]

6 See also

- Steatosis
- Steatohepatitis
- Alcoholic liver disease
- Non-alcoholic fatty liver disease
- Metabolic syndrome
- Cirrhosis
- Focal fatty liver
- Acute fatty liver of pregnancy
- Feline hepatic lipidosis

7 References

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8 External links

- American Association for the Study of Liver Diseases
- American Liver Foundation
- Fatty Liver Disease, Canadian Liver Foundation
- *00474* at CHORUS
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- Healthdirect

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