

Source: http://en.wikipedia.org/wiki/Fatty_liver

1.Fatty liver, also known as **fatty liver disease (FLD)**, is a reversible condition where 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 those who are obese (with or without effects of [insulin resistance](#)). The condition is also associated with other diseases that influence fat [metabolism](#).^[1] Morphologically it is difficult to distinguish alcoholic FLD from non alcoholic FLD and both show micro-[vesicular](#) 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 [non-alcoholic fatty liver disease](#) (NAFLD), and the more severe forms as alcoholic steatohepatitis (part of [alcoholic liver disease](#)) and [non-alcoholic steatohepatitis](#) (NASH).

Fatty liver is commonly associated with [alcohol](#) or [metabolic syndrome](#) ([diabetes](#), [hypertension](#), [obesity](#) and [dyslipidemia](#)) but can also be due to any one of many causes^{[2][3]}:

Metabolic

[Abetalipoproteinemia](#), [glycogen storage diseases](#), [Weber-Christian disease](#), [acute fatty liver of pregnancy](#), [lipodystrophy](#)

Nutritional

[Malnutrition](#), [total parenteral nutrition](#), severe [weight loss](#), [refeeding syndrome](#), [jejuno-ileal bypass](#), [gastric bypass](#), jejunal [diverticulosis](#) with [bacterial overgrowth](#)

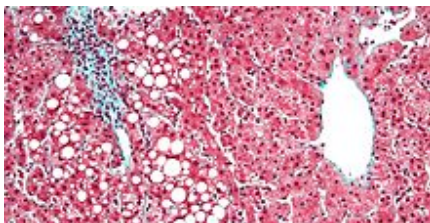
Drugs and toxins

[Amiodarone](#), [methotrexate](#), [diltiazem](#), expired [Tetracycline](#), [highly active antiretroviral therapy](#), [glucocorticoids](#), [tamoxifen](#), environmental [hepatotoxins](#) (e.g., [phosphorus](#), [mushroom poisoning](#))

Other

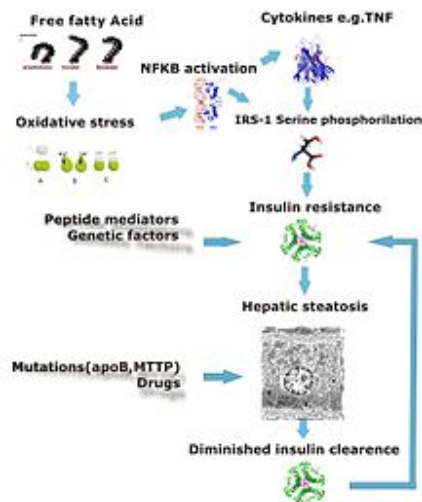
[Inflammatory bowel disease](#), [HIV](#), Hepatitis C especially genotype 3, and Alpha 1-antitrypsin deficiency^[4]


[\[edit\]](#) Pathology



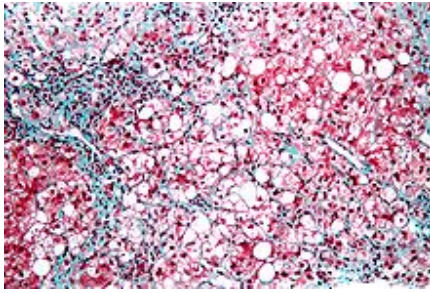
[Micrograph](#) of [periportal hepatic](#) steatosis, as may be seen due to [steroid](#) use. [Trichrome stain](#).

Fatty change represents the intra-[cytoplasmic](#) accumulation of triglyceride (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 increase 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.^[5] The diagnosis of steatosis is made when fat in the liver exceeds 5–10% by weight.^{[1][6][7]}



 Mechanism leading to hepatic steatosis

Defects in [fat 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][8]} Impairment or inhibition of receptor molecules ([PPAR- \$\alpha\$](#) , [PPAR- \$\gamma\$](#) and [SREBP1](#)) that control the enzymes responsible for the oxidation and synthesis of fatty acids appears to contribute towards fat accumulation. In addition, alcoholism is known to damage mitochondria and other cellular structure further impairing cellular energy mechanism. On the other hand non alcoholic FLD may begin as excess of unmetabolised energy in liver cells. Hepatic steatosis is considered reversible and to some extent nonprogressive if there is cessation or removal of underlying cause.



Micrograph of inflamed fatty liver ([steatohepatitis](#)).

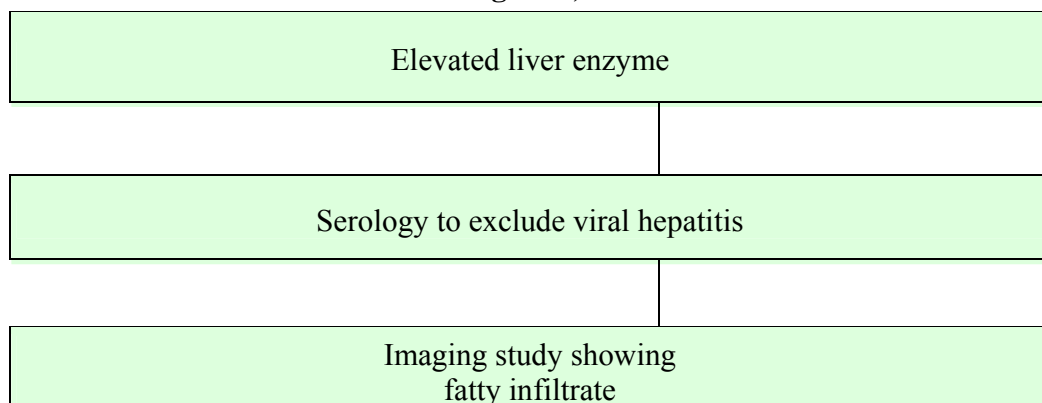
Severe fatty liver is sometimes accompanied by [inflammation](#), a situation that is referred to as [steatohepatitis](#). Progression to alcoholic [steatohepatitis](#) (ASH) or [non-alcoholic steatohepatitis](#) (NASH) depend on persistence or severity of inciting cause. [Pathological](#) lesions in 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.^[9]

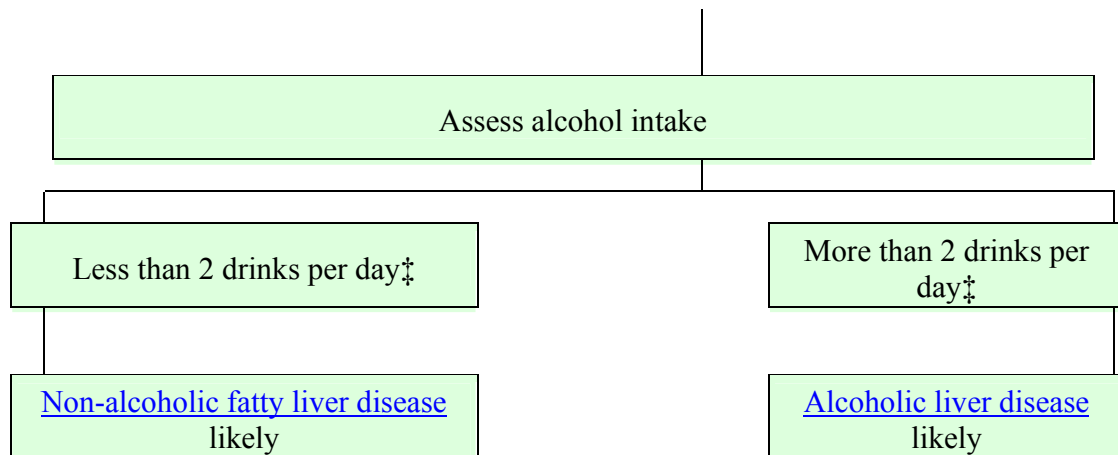
Liver with extensive inflammation and high degree of steatosis often progresses to more severe forms of the disease.^[10] [Hepatocyte](#) ballooning and hepatocyte [necrosis](#) of varying degree are often present at this stage. Liver cell death and inflammatory responses lead to the activation of [stellate 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](#).^[11]

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 non-alcoholic FLD is less clear.

[\[edit\]](#) **Diagnosis**

Flow chart for diagnosis, modified from^[3]





‡ Criteria for nonalcoholic fatty liver disease:
consumption of ethanol less than 20g/day for woman and 30g/day for man^[12]

Most individuals are asymptomatic and are usually discovered incidentally because of abnormal liver function tests or hepatomegaly noted in unrelated medical condition. Elevated liver biochemistry is found in 50% of patients with simple steatosis.^[13] The serum [ALT](#) level usually is greater than the [AST](#) level in non-alcoholic variant and the opposite in alcoholic FLD (AST:ALT more than 2:1).

Imaging studies are often obtained during 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 [spleen](#) 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.

[\[edit\]](#) Treatment

The treatment of fatty liver depends on what is causing it, and generally, treating the underlying cause will reverse the process of steatosis if implemented at early stage.

[\[edit\]](#) Complication

Up to 10% of cirrhotic alcoholic FLD will develop [hepatocellular carcinoma](#). Overall incidence of liver cancer in non-alcoholic FLD has not yet been quantified, but the association is well established.^[14]