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, jejun-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

![Image of fatty liver tissue](http://en.wikipedia.org/wiki/Fatty_liver)
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. The diagnosis of steatosis is made when fat in the liver exceeds 5–10% by weight.

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. 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 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.
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[13]

<table>
<thead>
<tr>
<th>Elevated liver enzyme</th>
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<td>Serology to exclude viral hepatitis</td>
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<td>Imaging study showing fatty infiltrate</td>
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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. 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.