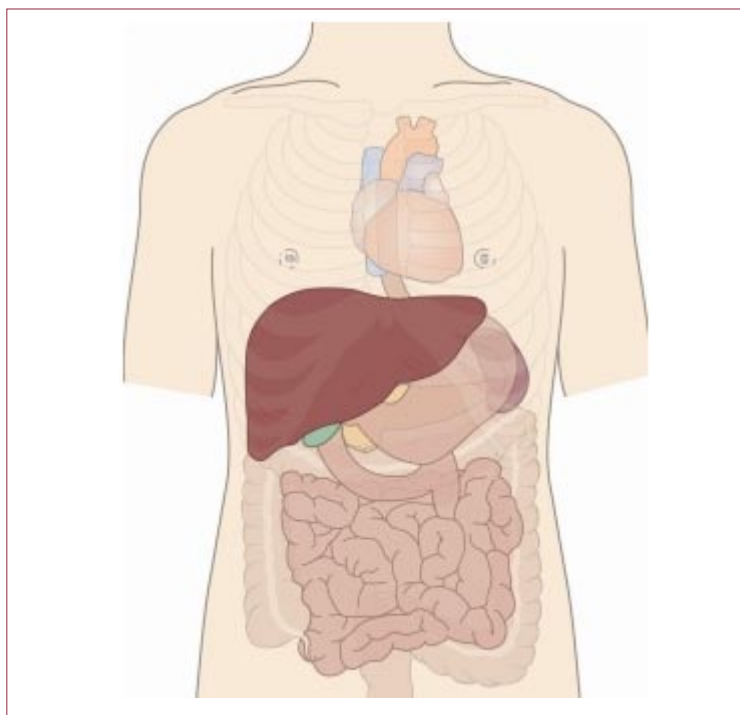


The liver - a complex diagnosis by Helena Conibear

Ask a lay person about the effect of heavy drinking on the body and they will invariably reply cirrhosis of the liver.

The liver is a vital organ, involved in the processing of fats, sugars, proteins and vitamins and in the regulation of blood clotting. It plays a central role in the body's defences, filtering toxins and microbes from the blood and marshalling an array of responses to trauma, stress or inflammation. The liver also has a remarkable capacity to regenerate and repair itself.



The liver is your largest internal organ. If you place your right hand over the area under the ribs on the right side of your body it will just about cover the area of your liver. The liver is the largest gland, and the largest solid organ in the body, weighing an average 1.8 kgs in men and 1.3 kgs in women. It holds approximately 13% (about one pint or 0.57 litres) of your total blood supply at any given moment and is estimated to have over 500 functions. One of the many jobs it has to deal with is breaking down, or 'metabolising', the alcohol you drink, first to the toxic substance acetaldehyde, then into harmless substances (carbon dioxide and water). The liver has become known as 'the canary of drinking' i.e. it becomes damaged if you drink excessively. Due to its huge functional reserve, fatty liver or cirrhosis can often be advanced before

any symptoms arise - hence liver disease is known as 'a silent disease'.

Drinking too much alcohol over a long period harms the liver and makes it very fatty, with the liver cells becoming bloated. This can result in swelling and inflammation of the liver - known as alcoholic hepatitis or alcoholic steatohepatitis - and can lead to scarring, known as fibrosis. Extensive scarring, combined with development of nodules, is known as cirrhosis (affecting between 10 and 20% of excessive drinkers) - a disease we have all come to associate with heavy long term drinking of alcohol - to such an extent, that any liver related illness is presumed by consumers to be due to excessive drinking - is this accurate or fair?

How does the liver break down alcohol?

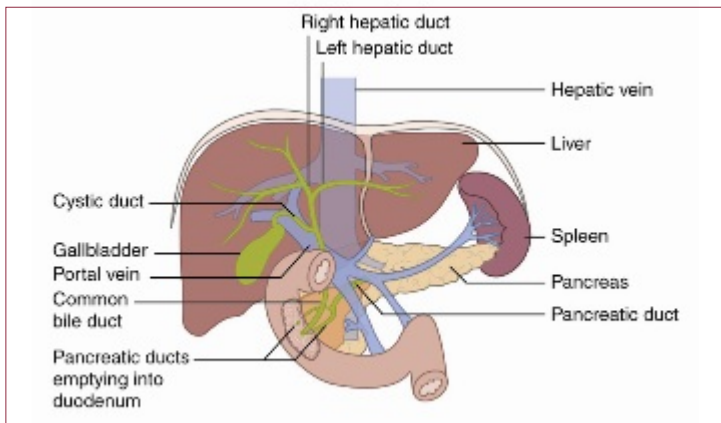
Alcohol is quickly soaked up through the lining of the stomach and the upper part of the gut (intestine) and into your blood stream. The higher the concentration of alcohol, the faster it will be absorbed. From there, the alcohol is carried to your liver as well as other organs and body tissue. Your brain is affected by the flow of alcohol which acts on the central nervous system, altering your physical coordination and mental judgement as you drink more.

Your liver cannot store alcohol. It metabolises about 90 per cent of the alcohol you drink to eliminate it from your body (the rest is excreted through your urine and sweat). Your liver can process about 10g - or a small drink an hour, any remaining alcohol circulates in your blood until it can be broken down - this is what is measured to assess 'blood alcohol concentration' for drink drive limits for example. Your liver needs water to do its job, as alcohol acts as a diuretic (makes you pass urine), it dehydrates you. When the liver is processing alcohol it produces a toxic substance called acetaldehyde. Acetaldehyde is subsequently broken down into a harmless chemical called acetate, which is broken down further into carbon dioxide and water, which are excreted via the normal route! Regular heavy drinking over time can strain or disrupt this process, leading to alcoholic liver disease.

What does your liver do?

The liver;

- processes digested food from the intestine
- controls levels of fats, amino acids and glucose in the blood
- combats infections in the body - the liver plays a vital role in fighting infections by mobilising part of your body's defence mechanism called the macrophage system. The liver contains over half of the body's supply of macrophages, known as Kupffer cells, which literally destroy any bacteria that they come into contact with.
- neutralises and destroys drugs and toxins
- manufactures bile
- stores iron, vitamins and other essential chemicals
- breaks down food and turns it into energy
- manufactures, breaks down and regulates numerous hormones including sex hormones
- makes enzymes and proteins which are responsible for most chemical reactions in the body, for example, those involved in blood clotting and repair of damaged tissues.



The liver is dark reddish brown in colour and is divided into two main lobes (the much larger right and the smaller left) which are further subdivided into approximately 100,000 small lobes, or lobules. About 60% of the liver is made up of liver cells called hepatocytes which absorb nutrients and detoxify and remove harmful substances from the blood. A hepatocyte has an average lifespan of 150 days. There are approximately 202,000 in every milligram of your liver tissue. Two-thirds of the body of your liver is the parenchyma, which contains the hepatocytes, and the remainder is the biliary tract. It receives its blood supply via the hepatic artery and portal vein (which transports nutrients from your intestine, or gut).

What is liver disease?

As the liver is such a complex organ, performing over 500 functions, it is not surprising that liver function can be damaged in a number of ways, through viral infection - Acute viral hepatitis A and Chronic viral hepatitis B and C in particular, through illegal drug use, legal drug overuse especially paracetamol or acetaminophen.

What many do not realise is that there are many types of cirrhosis including autoimmune, biliary, cryptogenic, post hepatic. There are also congenital liver diseases. The majority of liver cancer can be linked to cirrhosis of the liver. Many liver diseases eventually cause cirrhosis, most notably hepatitis B and C.

When is alcohol implicated?

Fatty Liver

Fatty liver is a condition in which too much fat builds up in the liver. You are more at risk of this if you tend to put on weight around your middle – ‘apple-shaped’ as opposed to ‘pear-shaped’. Fatty liver is also associated with high blood fat hyperlipidemia and diabetes

irrespective of any alcohol use. You can get a fatty liver without drinking. This is called ‘non-alcoholic fatty liver disease’ (NAFLD). NAFLD is a very common type of liver disease that may be present in up to one-third of Americans (associated with obesity and metabolic syndrome).

So, if you cut down on fatty foods and lose weight you will also lose fat from the liver. For the majority of people in the Western world, the root causes of becoming overweight are down to:

- eating too much, especially too much fatty food
- not doing enough exercise.

Research is increasingly proving a link between an increased risk of liver disease with obesity. Body weight determines the serum level of liver enzymes. Furthermore obesity is thought to slow intestinal motility, enabling bacterial overgrowth and other noxious factors in the intestine.

There should be little or no fat in a healthy liver. Too much of this fat can build up if you drink more than the liver can cope with, leading to fatty liver disease.

It is thought that if you are overweight and drinking too much, you increase the chances of damaging your liver. Alcoholic Fatty livers should return to normal if you drink within the sensible limit. If you carry on drinking above that limit you are running the risk of more serious damage.

Alcoholic hepatitis

If you have a fatty liver and continue to drink, you have up to a one in four chance of getting alcoholic hepatitis. This is a condition where your liver becomes puffy, swollen and tender. Alcoholic hepatitis can happen to you at an early stage or after many years of excessive drinking. Up to 35% of heavy drinkers develop alcoholic hepatitis. Symptoms may include loss of appetite, nausea, vomiting, abdominal pain and tenderness, fever and jaundice. The damage may be reversible if you stop drinking. In its severe form, the disease may occur suddenly and it can quickly lead to life-threatening complications.

Alcoholic Cirrhosis

The final stage of alcoholic liver disease is cirrhosis. This is usually the result of long-term, continuous damage to the liver. Irregular bumps, known as nodules, replace the smooth liver tissue and the liver becomes harder. The effect of this, together with continued scarring from fibrosis, means that the liver will run out of healthy cells to support normal functions. This can lead to complete liver failure.

Between 10 and 20% of heavy drinkers develop cirrhosis, usually after 10 or more years of high levels of drinking, but may be much less. Symptoms of cirrhosis are completely silent. The damage from cirrhosis is not reversible, but patients who stop drinking can live near normal lives.

Many heavy drinkers will progress from fatty liver to alcoholic hepatitis and finally to alcoholic cirrhosis, though the progression may vary from patient to patient. The risk of developing cirrhosis is particularly high for people who drink heavily and have another chronic liver disease such as viral hepatitis C. Those with cirrhosis of the liver of any cause are also at higher risk of development of liver cancer, nearly always fatal. In addition to causing liver damage by excess, alcohol, at least when abused, inhibits liver regeneration

(healing) from any damage, by viral hepatitis, toxin, medication overdose (acetaminophen), hemochromatosis (hereditary iron overload), or alcohol itself.

Deaths from liver disease

It is very important to keep the important issue of liver disease death in proportion with mortality from other causes. The most recent UK figures show that 81 women per million died from any kind of liver disease in the UK (2005) and 156 men, this relates to 1205 heart related deaths (IHD and CVD) per million women and 2019 per million men. According to data from the U.S. Acute Liver Failure Study Group registry of more than 700 patients with acute liver failure across the US, acetaminophen (paracetamol) poisoning (over the counter pain killers) are implicated in nearly 50% of all acute liver failure in the US.

The American Liver Foundation ALF warns that an estimated 16,780 Americans will die of liver cancer in 2008 – an increase of 580 deaths from the disease since 2006. Over four million Americans have been infected with the hepatitis C virus and another 1.4 million have chronic hepatitis B. It is further estimated that 10-20% of all Americans have fatty liver disease. *“The increase in liver cancer is due to the near epidemic rates of many liver diseases. The hepatitis C virus, for example, is the fourth leading cause of liver cancer-related deaths in the U.S”* according to the ALF.

Hence, to conclude, like the liver itself, reasons for rises in liver disease in countries such as the UK and US are complex and due to a variety of causes. There is no doubt that if you drink heavily you increase your risk, not only of alcoholic liver disease, but for many cancers and all cause mortality. If you combine heavy drinking with obesity, poor diet and a sedentary lifestyle, the risks increase further. The message, as ever, is to enjoy drinking in moderation, and if you believe you are drinking too heavily, cut back, and with care, your liver can recover.

Thanks to Marsha Morgan, Reader in Medicine and Honorary Consultant Physician, The Centre for Hepatology, Royal Free & University College Medical School, for her help in the editing of this article.

Advice from the experts:

“Our manuscript’s findings lend support to the growing scientific interest in the role of drinking patterns on many health and social outcomes. Our findings may also have important public-health implications for the kind of advice given to both the population at large and to women in particular. The suggestion is, if you drink, drink in moderation and with food, and spread the consumption over a long period of time, rather than a short period such as a weekend.”

Source: Stranges, S et al, Differential Effects of Alcohol Drinking Pattern on Liver Enzymes in Men and Women. *Alcoholism: Clinical & Experimental Research*. 28(6): 2004.

‘It is important to highlight, that if you have been abusing your liver through excessive eating and drinking, that it has a great ability to heal itself - Transient and isolated over-indulgence may irritate the liver, but, with its enormous regenerative capacity, it quickly heals. Repetitive major insults over the years, however, are likely to lead to lasting damage, in sequential order of gravity: fatty liver (hepatic steatosis) inflammation (alcoholic hepatitis), and, finally, cirrhosis. In each case, structural abnormalities are accompanied by disorder of the vital almost unimaginable complex of liver functions. While the degree of damage is in general proportional to the quantity of alcohol imbibed, there are wide individual differences in susceptibility’. Harvey Finkel M.D.

(Dr. Finkel is clinical professor of medicine at Boston University Medical Center. He writes and lectures- internationally on the influences of wine upon health. He is a member of AIM Council).

‘The factors determining why fewer than 20% of heavy drinkers develop advanced alcoholic liver disease remain largely unknown. There is a weak relationship between disease risk and the dose and pattern of alcohol consumed. The risk of all stages of alcoholic liver disease is increased by obesity, probably reflecting the role of steatosis in the pathogenesis of more advanced disease. Compared with men, women develop disease at a lower intake due in part to their lower volume of distribution for alcohol, but also potentially to increased gut permeability to endotoxin. Recent studies suggest a non-gender-linked genetic component to disease susceptibility and recent case-control studies have suggested that polymorphisms of genes encoding cytokines and other immuno-regulatory molecules may exert a significant effect. The pattern of polymorphisms associated with risk suggests that antibody-mediated mechanisms play a role in disease pathogenesis. This has implications for treatment and for identifying high risk individuals at an early age’.

Source: Day CP. Who gets alcoholic liver disease: nature or nurture? *Ctr Liver Res, J R Coll Physicians Lond* 2000; 34:557-62

Age-standardised mortality rates by cause and sex, England and Wales, 1991-2005, rates per million population

Males – all ages	Oesoph cancer	Lung cancer	Prostate cancer	IHD	CVD	Pneumonia	Bronchitis, etc	Liver diseases
1991	117	842	302	2,984	940	391	606	76
2005	132	513	255	1,466	553	351	367	156

Females – all ages	Oesoph cancer	Lung cancer	Breast cancer	Ovarian cancer	IHD	CVD	Pneumonia	Bronchitis, etc	Liver diseases
1991	50	300	401	118	1,407	812	325	211	49
2005	48	290	284	102	686	519	298	224	81

