

Alcohol and the Liver

Mark Thursz

Professor of Hepatology, Imperial College London

Data from the Office for National Statistics shows that liver disease has risen to fifth place in the list of causes of mortality in the United Kingdom. However, unlike the top four causes which include coronary artery disease, cerebrovascular disease, respiratory disease and cancer, liver disease mortality is rising rather than falling. In the majority of liver related deaths alcohol is either the primary cause or a major contributory factor. The reason for the increasing mortality from alcoholic liver disease is clear; we as a society are consuming more alcohol. However, the relationship between alcohol consumption and liver disease is not straightforward; not everyone who consumes excessive amounts of alcohol will develop significant liver disease. It is estimated that only 10-15% of alcoholics will develop alcoholic hepatitis and/or cirrhosis (Mann 2003). The risk of developing alcoholic liver disease is related to the blood alcohol concentration and the duration of raised blood alcohol concentration. These parameters are determined by the pattern of drinking (daily versus binge) and total alcohol consumption (quantity and frequency). There are large inter-individual variations in the rate of alcohol elimination (Li 2001) which indicate that blood alcohol concentrations and risk of developing alcoholic liver disease are influenced by genetic variation in the alcohol metabolising enzymes.

Patterns of alcohol consumption affect the risk of developing liver disease. The term 'binge drinking', currently beloved and misused by the media, is formally defined as consumption of 5 or more units (50g) of alcohol in 2 hours in males and 4 or more units (40g) in 2 hours in females. Binge drinking is undoubtedly a marker of an alcohol use disorder and may be associated with violent behaviour, risky sexual behaviour and emergency hospital admissions. However, it is frequent heavy drinking which results in alcoholic liver disease rather than binge drinking. Nevertheless early binge drinking in teenagers may progress to frequent heavy drinking and subsequently to alcoholic liver disease.

The amount of alcohol required to induce liver disease is controversial. There is some evidence to support the concept of a threshold level of alcohol consumption at around 30g/day (Kamper-Jorgensen 2004). Above this level, the risk of developing significant liver disease rises in proportion to consumption levels; an individual who consumes 50g/day increases the risk of cirrhosis 5 times above the population average and in someone who consumes 100g/day the risk increases to 25 times the population average.

The liver is the main site for alcohol metabolism and therefore the main focus of alcohol induced damage. Alcohol is converted to acetaldehyde primarily by the enzyme alcohol dehydrogenase. Acetaldehyde is a highly reactive molecule which binds to cellular proteins, inhibits protein functions and incites an immune response. When alcohol is present in excess, alcohol is metabolised to acetaldehyde through two additional pathways; the cytochrome P450 oxidation pathway and the catalase pathway. Metabolism through either of these pathways generates excess amounts of oxygen-derived free radicals which injure the liver cells by damage to cell membranes, proteins and DNA. Cell damage activates immune and inflammatory responses which, in turn, stimulate wound healing processes resulting in the deposition of fibrous scar tissue within the liver. Accumulation of fibrous tissue eventually results in cirrhosis where islands of normal liver cells are surrounded by bands of scar tissue. Further cell damage may then lead to liver failure or liver cancer. Acetaldehyde is metabolised by the enzyme acetaldehyde dehydrogenase to produce acetate which is used as an energy source within the cell. The excess calories generated by alcohol consumption are converted to triglycerides and stored as lipid droplets in liver cells which is relatively benign for the liver.

There are a number of ways in which people who drink to excess may present to medical services. Blood tests performed either in acknowledgement

of an alcohol use disorder or for other medical indications may reveal derangements in the liver biochemical tests. Evaluation by a specialist at this stage will exclude other causes of liver disease and determine the extent of liver damage. Control of alcohol consumption at any stage of the disease will improve the prognosis and if alcohol is withdrawn prior to the development of cirrhosis the liver will return to normal. There is therefore a valid argument to use liver biochemical tests to screen for liver disease as interventions to control alcohol abuse are highly effective (Crawford 2004).

Alcoholic hepatitis is a more dramatic presentation of alcoholic liver disease where there is an overwhelming inflammatory response to alcohol induced cell damage and the patient is often deeply jaundiced. The mortality rate from alcoholic hepatitis is greater than 20% but with care in specialist hepatology units the outcomes may be substantially improved.

The third presentation of alcoholic liver disease is with the complications of cirrhosis. Scar tissue in the liver interrupts the normal blood flow from the intestines through the liver and back to the heart causing an increase in pressure in the blood vessels in the abdomen known as portal hypertension. With portal hypertension there may be an accumulation of fluid in the abdominal cavity, known as ascites, which causes abdominal distension. A second consequence of portal hypertension is dilated veins in the lower oesophagus (oesophageal varices) where blood flow from the intestine finds an alternative route back to the heart. Oesophageal varices may rupture and bleed profusely with a mortality rate of 20% associated with each hospital admission. Cirrhosis may also present with hepatic encephalopathy, a cause of confusion and coma resulting from liver failure, where toxins absorbed by the gut are not removed by the liver. Whilst alcoholic liver disease is also a cause of liver cancer, it is not particularly common for patients to present with this condition.

In addition to being a direct cause of liver injury alcohol is now recognised as a major contributory factor in other causes of liver disease. The prognoses of hepatitis C virus infection, hepatitis B virus infection and haemochromatosis are all worse in

patients who consume excess alcohol. It should be noted, however, that liver disease is not the only physical consequence of excess alcohol consumption. Alcohol causes a range of neurological disorders, ranging from peripheral neuropathy to dementia. Chronic pancreatitis, muscle damage and cardiac damage are caused by alcohol and may develop independently or coexist with liver damage.

In conclusion it is important to recognise the range of diseases to which alcohol contributes and the extent of morbidity and mortality attributable to this recreational drug. It

is estimated that £2.9 billion a year of NHS resources are spent on alcohol related disorders but these statistics hide a much greater burden of social and emotional costs (Royal College of Physicians 2001). Effective action to control alcohol consumption is therefore urgently required.

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Health equity in a generation? Time to address the social determinants of health

Professor Sir Michael Marmot and Dr Sharon Friel

Commission on the Social Determinants of Health, Department of Epidemiology & Public Health, University College London

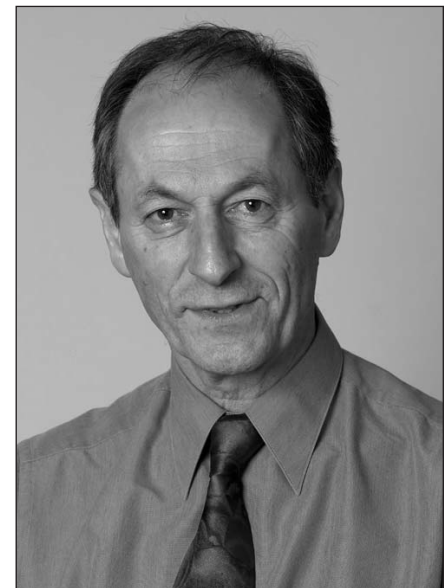
Health inequity and its social causes

Our children have dramatically different life chances depending on where they were born. In Japan or Sweden they can expect to live more than 80 years; in Brazil, 72 years; India, 63 years; and in one of several African countries, fewer than 50 years. And within countries, the differences in life chances are dramatic and are seen worldwide. The poorest of the poor have high levels of illness and premature mortality. But poor health is not confined to those worst off. In countries at all levels of income, health and illness follow a social gradient: the lower the socioeconomic position, the worse the health.

The Commission on Social Determinants of Health, set up by the World Health Organisation to marshal

the evidence on what can be done to promote health equity and to foster a global movement to achieve it, is a global collaboration of policy-makers, researchers, and civil society led by Commissioners with a unique blend of political, academic, and advocacy experience. Importantly, the focus of attention embraces countries at all levels of income and development: the global South and North.

The Commission takes a holistic view of social determinants of health. The poor health of the poor, the social gradient in health within countries, and the marked health inequities between countries are caused by the unequal distribution of power, income, goods, and services, globally and nationally, the consequent unfairness in the immediate, visible circumstances of people's lives – their access to health care, schools, and



education, their conditions of work and leisure, their homes, communities, towns, or cities – and their chances of leading a flourishing life. This unequal distribution of health-damaging experiences is not in any sense a 'natural' phenomenon but is the result of a toxic combination of poor social policies and programmes, unfair economic arrangements, and bad politics. Together, the structural determinants and conditions of daily life constitute the social determinants of health and are responsible for a major part of health inequities between and within countries.

A new approach to development

Health and health equity may not be the aim of all social policies but they