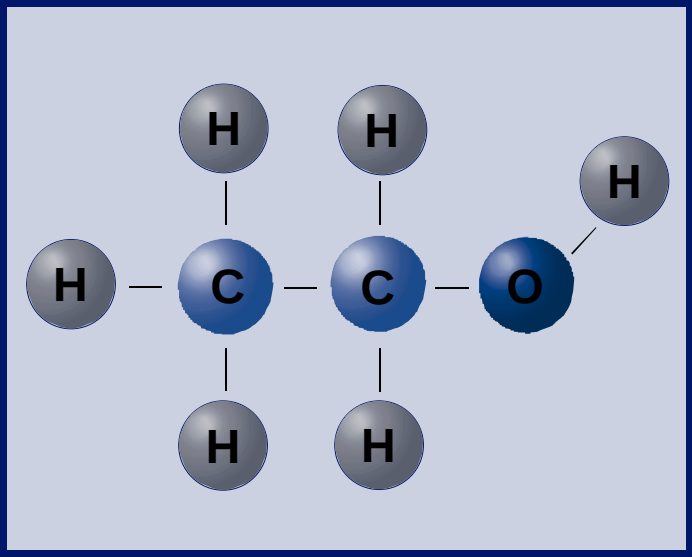
ILSI EUROPE CONCISE MONOGRAPH SERIES



ALCOHOL

HEALTH ISSUES RELATED TO ALCOHOL CONSUMPTION

Second edition

ILSI
International Life Sciences INSTITUTE

ALCOHOL
HEALTH ISSUES RELATED TO ALCOHOL CONSUMPTION

by Michael Gurr

Second edition

ILSI Europe

ILSI EUROPE CONCISE MONOGRAPHS

This booklet is one in a series of ILSI Europe concise monographs. These are written for those with a general background in the life sciences. However, the style and content of the concise monographs will also appeal to a wider audience who seek up-to-date and authoritative reviews on a variety of important topics relating to nutrition, health and food safety.

Concise monographs present an overview of a particular scientific topic and are usually based on the proceedings of scientific meetings. The text of each concise monograph is peer reviewed by academic scientists of high standing. The concise monographs make important results and conclusions widely available.

Titles of concise monographs in preparation include:

- Healthy Lifestyles
- Microwave Ovens
- Nutritional Epidemiology, Possibilities and Limitations.

Current and newly published concise monographs are:

- Starches and Sugars: A Comparison of Their Metabolism in Man
- A Simple Guide to Understanding and Applying the Hazard Analysis Critical Control Point Concept
- Dietary Fibre
- Food Allergy and Other Adverse Reactions to Food
- Sweetness – The Biological, Behavioural and Social Aspects
- Oxidants, Antioxidants, and Disease Prevention
- Caries Preventive Strategies
- Nutritional and Health Aspects of Sugars – Evaluation of New Findings
- Food Biotechnology – An Introduction
- Dietary Fat – Some Aspects of Nutrition and Health and Product Development.

INTERNATIONAL LIFE SCIENCES INSTITUTE AND ILSI EUROPE

The International Life Sciences Institute (ILSI) is a worldwide, public, non-profit scientific foundation headquartered in Washington, DC, USA, with branches in Argentina, Australasia, Brazil, Europe, Japan, Korea, Mexico, North America, Southeast Asia, and Thailand, with a focal point in China.

ILSI is affiliated with the World Health Organization as a non-governmental organization (NGO) and has specialised consultative status with the Food and Agriculture Organization of the United Nations.

ILSI Europe was established in 1986 to provide a neutral forum through which members of industry and experts from academic, medical and public institutions can address topics related to health, nutrition and food safety throughout Europe in order to advance the understanding and resolution of scientific issues in these areas. ILSI Europe is active in the fields of nutrition, toxicology and food microbiology. It sponsors research, conferences, workshops and publications.

For more information about its programmes and activities, please contact:

ILSI Europe
Avenue E. Mounier 83, Box 6
B-1200 BRUSSELS
Belgium
Telephone (+32) 2 771 00 14
Telefax (+32) 2 762 00 44

ILSI Press
1126 Sixteenth Street, N.W.
Washington, DC 20036-4810
USA
Telephone: (+1) 202 659 0074
Telefax: (+1) 202 659 8654

ILSI Europe
Avenue E. Mounier 83, Box 6
B-1200 Brussels
Belgium
Telephone: (+32) 2 771 00 14
Telefax: (+32) 2 762 00 44

Printed in Belgium

ISBN 0-944398-88-X

FOREWORD

For millennia the consumption of alcoholic beverages has been part of many cultures in the world. Their wide diversity in the form of beers, wines, spirits and liqueurs contributes to the pleasure of eating and drinking as well as to social interactions. Most are obtained by fermentation of extracts of fruits and grains in which carbohydrates are transformed into alcohol. This simple natural organic compound is both a source of metabolic energy and also has physiological and psychotropic effects depending on the level of intake. Among drinkers, most people consume alcoholic beverages responsibly and in moderation. However, excessive drinking of alcoholic products has been recognized throughout the ages as presenting serious health and social risks and the problems of misuse have led to controversy about the appropriate place of alcoholic beverages in society.

Although alcoholic beverages have been consumed since the beginning of civilization, and alcohol has been one of the most studied and researched substances consumed by man, most of the scientific and academic attention has focused on excessive rather than moderate consumption.

This concise monograph written by Professor Michael Gurr is based on an extensive critical scientific review of the biomedical literature which was published by ILSI Europe in a book entitled "Health Issues Related to Alcohol Consumption" (Ed. P.M. Verschuren, ILSI Press, 1993). More than thirty eminent medical experts from Europe and the U.S.A. have contributed to the review of nine topics of human health with a particular focus on the moderate consumption of alcoholic beverages.

The results of this review have been presented to the European Commission's Directorate General V.

Author: Michael Gurr
Scientific Editor: Ian Macdonald
Scientific Referees: Ambroise Martin and Timothy J. Peters
Series Editor: Nicholas J. Jardine

CONTENTS

THE PLACE OF ALCOHOL IN HUMAN CULTURE

Alcohol is a naturally occurring substance formed during the fermentation by yeasts of a number of sugar-containing foods. As such it has been consumed by human beings, mainly in the form of alcoholic beverages, for millennia. As a constituent of foods and beverages, and because it provides a source of metabolic energy, alcohol might be considered a nutrient. However, social and scientific interest in alcohol generally lies in the fact that it has potentially powerful effects on the central nervous system. For this reason, alcoholic drinks have been prized by many and shunned by others.

In human society, there is a consumption continuum ranging from complete abstinence, to normal social use of alcohol, to harmful misuse, to alcohol abuse and dependency. This concise monograph deliberately focuses on moderate drinking. Scientific publications on the health effects of moderate alcohol consumption are sparse; most have been concerned with the effects of overconsumption.

There is no doubt that taken in excess, alcohol can have devastating effects on the body that can lead to addiction and total breakdown of bodily function and personality. Extremes of intake can lead to alcoholism, which can be defined as "the extreme dependence on excessive amounts of alcohol associated with a cumulative pattern of deviant behaviours".

Extremes of alcohol consumption and alcoholism are outside the scope of this monograph, but it will be helpful on occasion to draw distinctions between "moderate" and "excessive" consumption in terms of their measurable effects on organs of the body. A brief summary of what is known of the genetics of alcoholism will also be given.

This concise monograph is based on a full-length monograph with the same title written by international experts whose remit was to review scientific studies on many aspects of moderate alcohol consumption. In reading this brief digest of that work, one should realize that whereas experimental studies with animals have been performed with pure alcohol (ethanol), human studies have been concerned with the consumption of alcoholic beverages. It may be possible to conclude that the effects observed in animals and people were unequivocally due to alcohol, but sometimes constituents of the beverage other than alcohol, which may have been generated during the fermentation process, could also have been responsible for the observed effects.

MEASURING ALCOHOL CONSUMPTION

A recurring problem, which was emphasized by authors of chapters of the book on which this concise monograph is based, is the difficulty of measuring alcohol consumption accurately. This is partly due to the social stigma of excessive drinking in many societies. Many methods for estimating intake of foods and drinks rely on records kept by subjects in epidemiologic studies. Such methods are notoriously prone to errors. It is worth noting that many epidemiologic studies have recorded only 40–60% of the intake expected from alcohol sales records. It may be easier to measure changes in consumption than absolute consumption.

Anonymous questionnaires are more reliable than individual records or interviews. Theoretically, biochemical markers of alcohol intake, which provide data on levels of alcohol in blood, urine or breath, should be more objective, but individual differences in rates and pathways of metabolism (see the section on Metabolism) make it difficult to relate these measurements to actual consumption. Altered liver metabolism that results from excessive alcohol consumption causes damage leading to leakage of enzymes into the blood, which can act as a type of marker. However, this is not relevant to the moderate alcohol consumption that is the principal subject of this concise monograph.

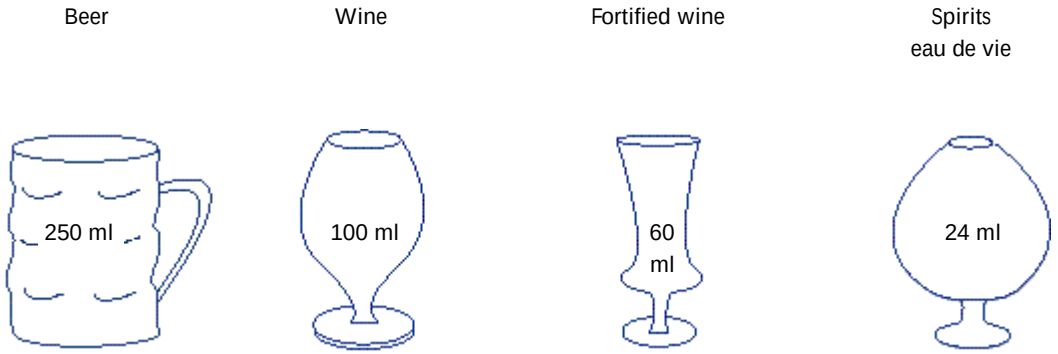
There are no universally accepted definitions of what constitutes "light", "moderate", or "excessive" drinking, and definitions of how much alcohol constitutes a "drink" or "unit" differ to some extent (Figure 1). For example, in the United States, one "drink" contains 12 g of alcohol, in Australia 10 g and in the United Kingdom, 8 g. For the purposes of this monograph, "light" and "moderate" consumption will be regarded as being up to 10 g and between 10 and 30 g per day for women, and up to 15 g and between 15 and 40 g for men. Chronic consumption above these ranges could be regarded as "excessive" consumption.

Drinking habits vary widely between and within populations. Nations differ in their preferences for types of alcoholic drinks (beers, spirits, wines, etc.) and the amounts consumed also differ considerably among nations, between the sexes and in different age groups.

The unreliability of estimates of consumption and the lack of generally accepted definitions of what constitutes moderate consumption must be borne in mind when reading the parts of this concise monograph that deal with alcohol and disease. Further research is needed to develop methods for the more accurate assessment of alcohol intake.

FIGURE 1

What constitutes a drink?

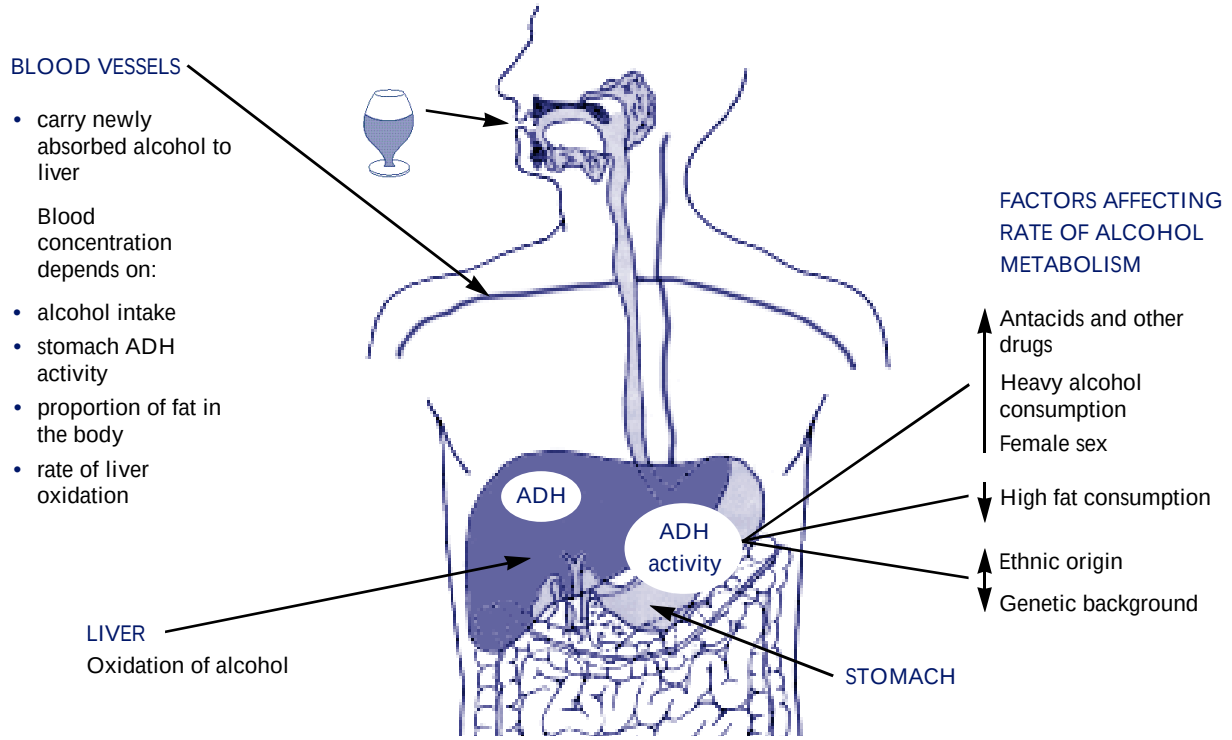


METABOLISM OF ALCOHOL

Normally, alcohol is rapidly absorbed into the body and metabolized. The appearance of alcohol in the blood is not related in a simple way to the amount consumed, because some is metabolized in the stomach by the enzyme alcohol dehydrogenase (ADH) before absorption. The quantitative role of ADH in alcohol metabolism is controversial. Factors that reduce the activity of stomach ADH (e.g., antacid drugs, heavy alcohol consumption) tend to result in a greater than normal rise in blood alcohol concentration in response to alcohol consumption. Women have less gastric ADH activity than men, and there are marked ethnic variations. High fat intake prior to consumption of an alcoholic drink reduces the effects of alcohol by slowing absorption and stimulating gastric metabolism (Figure 2).

FIGURE 2

The fate of alcohol in the human body



ADH

Alcohol dehydrogenase converts alcohol into acetaldehyde

Once absorbed, alcohol quickly spreads throughout the body's water space. The greater the proportion of fat in the body, the greater the rise in concentration in the blood. On average, a man weighing about 65 kg and consuming about 8 g of alcohol can expect to experience a rise in blood alcohol of 150 mg/l within the first hour, whereas a woman weighing 55 kg might expect a rise of about 200 mg/l. Healthy people clear this alcohol, mainly by metabolism in the liver, at a constant rate of about 150 mg/l blood per hour. There are marked differences among individuals and races, and the rate of metabolism is markedly affected by many commonly taken drugs.

The principal route by which the liver metabolizes alcohol is via the enzyme ADH (Figure 3, a), although at least three other pathways have been described (as illustrated in Figure 3, b–d).

The second important pathway for alcohol metabolism (Figure 3, b) is via the microsomal ethanol oxidizing system (MEOS). The activity of this enzyme system is not normally detected in liver cells but is "induced" (see the caption to Figure 3 for an explanation) in response to exposure of the membranes of the endoplasmic reticulum to alcohol. In alcoholism, where exposure to alcohol is more or less continuous, MEOS is permanently induced.

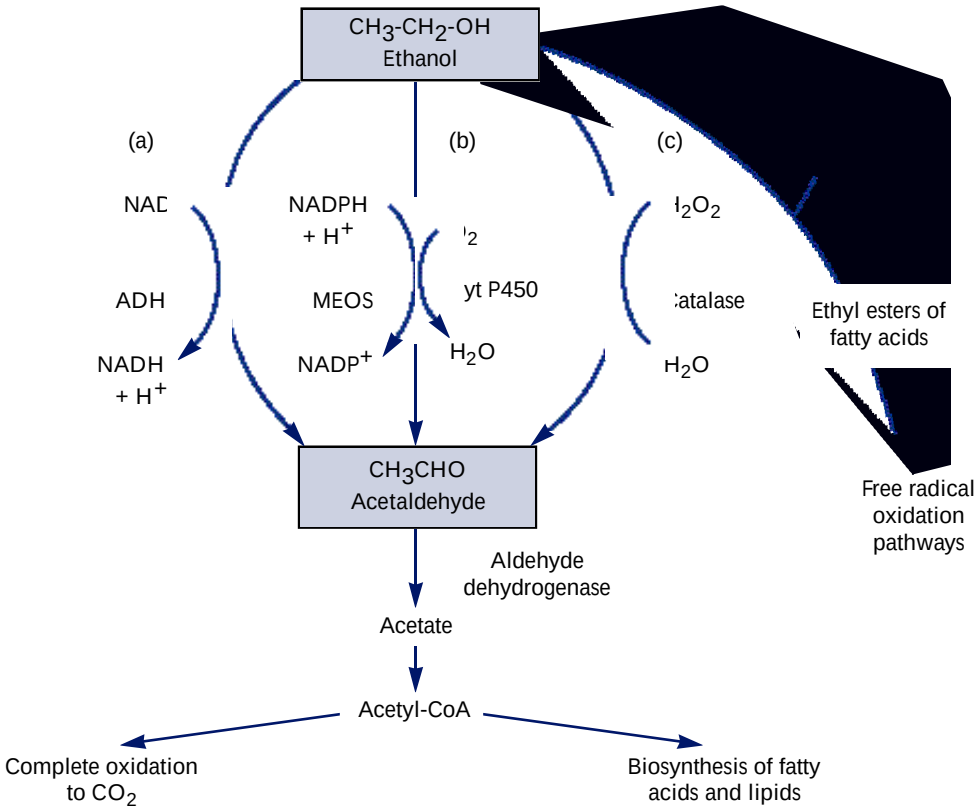
The third pathway, which is probably a minor one, is indirectly via the enzyme catalase (Figure 3, c), which is ubiquitous in cells. If alcohol is present, the breakdown of hydrogen peroxide by catalase can result in the oxidation of alcohol.

Acetaldehyde is the first product of the metabolism of alcohol by each of these pathways (Figure 3, a–c). Because acetaldehyde is toxic, it is normally cleared rapidly by conversion first into acetate and then into acetyl-CoA (the biochemically active form of acetate) in the mitochondria. Therefore, acetaldehyde dehydrogenase, which disposes of acetaldehyde, is a key enzyme in alcohol metabolism and detoxification. Acetyl-CoA can be oxidized completely to carbon dioxide or can serve as the starting point for the biosynthesis of fatty acids and lipids.

Finally, alcohol can also form ethyl esters with fatty acids (Figure 3, d), which can then be disposed of by oxidation reactions, but the quantitative significance of this pathway is unclear.

FIGURE 3

Metabolic pathways for disposal of alcohol



Enzymes

ADH: alcohol dehydrogenase, a normal constituent of liver tissue. MEOS: microsomal ethanol oxidizing system. The activity of the MEOS enzymes is not normally detectable; the presence of alcohol sends signals to the cell to produce more enzyme protein to catalyse the oxidation of alcohol. In biochemistry, this process is known as enzyme induction.

Cofactors and Intermediates

NAD^+: oxidized nicotinamide adenine dinucleotide. NADH: reduced nicotinamide adenine dinucleotide. $NADP^+$ and NADPH: the corresponding phosphorylated derivatives of NAD^+ and NADH. These contain nicotinamide which belongs to the B family of vitamins. H_2O_2: hydrogen peroxide; Cyt P450: Cytochrome P450, an inducible family of proteins involved in oxidation reactions.

INHERITED FACTORS INFLUENCING RESPONSE TO ALCOHOL

Familial nature of alcoholism

Most scientific studies of the inheritance of factors influencing responses to alcohol have been concerned with individuals with alcoholism. This is a disease involving extreme dependence on excessive amounts of alcohol resulting in deviant behaviours. It is uncertain to what extent genetic factors are concerned in less severe alcohol-related problems.

As long ago as the time of Aristotle, it was observed that alcoholism often runs in families. Many scientifically well-conducted studies have since confirmed this observation. That a condition is "familial", however, does not necessarily imply that it is inherited. Environmental factors are also involved in the development of the alcoholic condition, and members of families tend to be exposed to similar surroundings as well as having similar genes.

Interactions between genes and the environment

One of the most active aspects of modern nutrition research is the growing understanding that dietary components, other environmental factors and genetics all interact to determine human health. Some well-known diseases are the result of a defect in a single gene. Good examples are cystic fibrosis and sickle cell anaemia. It is unlikely that there is a single "alcoholism" gene; indeed, recent research confirms that susceptibility to the adverse effects of alcohol results from many different genes (so-called polygenic inheritance) interacting with a wide variety of environmental conditions.

The evidence on which these conclusions are based comes mainly from research with specifically bred laboratory animals and from human twin and adoption studies.

Animal studies

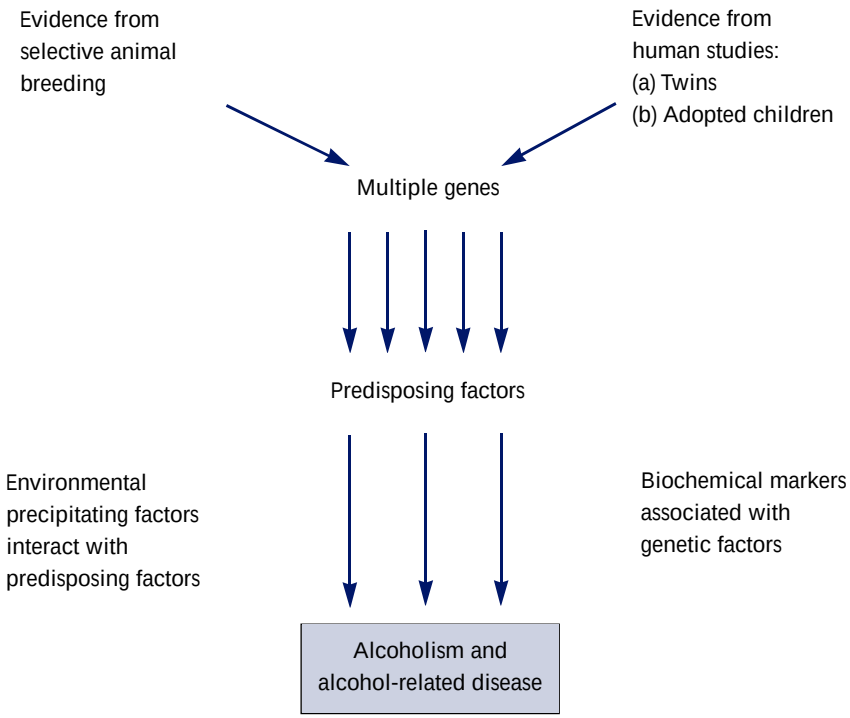
The observation that some animals presented with the choice of water or an alcohol solution prefer alcohol has stimulated the use of selective breeding to produce strains of animals that voluntarily drink quantities of alcohol or choose water to the exclusion of alcohol. The results of these selection programmes clearly indicate that genetic factors influence the drinking of alcohol by animals. Thus, individual susceptibility to the effects of alcohol, the capacity to develop tolerance, the likelihood of developing physical dependence and the severity of the state of "withdrawal" when alcohol consumption ceases after chronic ingestion can all be studied using animals.

Human twin and adoption studies

If a trait such as susceptibility to the effects of alcohol is under strong genetic control, identical twins will be more likely to share problems resulting from exposure to alcohol than will non-identical twins or siblings born at different times. Another way to distinguish genetic and environmental factors is to study adopted children whose biological parents were either alcoholics or non-alcoholics.

Geneticists use the term heritability to assess the degree to which a condition is genetically determined. A heritability index of 0 implies no genetic basis for an observed characteristic, whereas an index of 1 implies that the characteristic is entirely determined by genes. Identical twin studies have generally revealed heritabilities of 0.3 and 0.6 for the amount and frequency of alcohol consumption. Genetic influences seem to be particularly important in young men, and

FIGURE 4
Genes and alcohol-related disease



environmental factors increasingly influence drinking habits as a person gets older.

Twin and adoption studies are not perfect, and many biases can be introduced. Nevertheless, from research with animals and human beings, the evidence for a strong genetic component in alcoholism is compelling (Figure 4).

The search for biological markers

A prime reason why the genetic component of susceptibility to alcohol is so difficult to unravel is that multiple genes are undoubtedly involved. Thus, single mutations at different points on an individual's genes may result in clinically indistinguishable disease states and any number of environmental factors may interact

with any one of these gene mutations to predispose to disease. Because each gene mutation affects the synthesis of a specific protein resulting in some identifiable biochemical change, it should be possible to identify biological markers that are capable of identifying individuals at risk of alcohol-related disease.

These markers currently include characteristic patterns of electrical activity in the brain, changes in specific enzymes and even changes in certain genes themselves. In the next few years, sets of markers may be available that are related to a particular type of alcohol-related disease and that are sufficiently accurate to warrant general practical use, although complete determination of the full genetic profile may not be possible.

ALCOHOL AND THE ALIMENTARY TRACT

Early findings

All substances ingested with, or as, food and drink pass through the alimentary tract from the mouth until they are either metabolized in the gut itself, absorbed into the body or eliminated in the faeces. There is opportunity, therefore, for ingested substances to affect tissues lining the alimentary tract at a wide range of locations.

The principal adverse effects of alcohol that have been studied in any detail in these tissues have to do with the development of cancers. A statistical association between heavy consumption of alcohol and the development of cancer of the oesophagus was recognized early in the 20th century, but detailed understanding of the link had to await the development of epidemiologic techniques for investigating non-infectious diseases and animal experiments that could distinguish the effects of alcohol from many other possible confounding factors.

Epidemiology

The epidemiologic approach (the main aspects of which are outlined in the Epidemiological techniques box) has shown that cancers of the mouth, oesophagus and larynx are associated with alcohol consumption and that the risk increases in a dose-related manner. Smoking multiplies this risk substantially. In the absence of smoking, the risk of cancers resulting from alcohol consumption in developed countries is very small except in very heavy drinkers. It is not known whether other constituents of alcoholic beverages exacerbate the effects of alcohol itself.

BOX 1

Epidemiological techniques for studying associations between alcohol consumption and health and disease

Epidemiologists make observations on existing disease patterns and their statistical associations with environmental factors.

In a case-control study, patients ("cases") with a specified disease are compared with respect to their alcohol consumption with "control" subjects. Controls do not have the disease but are matched with cases for as many other characteristics as possible to see how their exposures to potential causative factors may have differed.

In a prospective (or cohort) study, certain characteristics, including alcohol consumption, are measured at a chosen time in a defined population of people who do not have the disease under investigation. The subjects are then followed for a long time and aspects of the chosen disease (e.g., the occurrence of heart attacks) are recorded. The epidemiologist then examines the strength of the statistical association between alcohol consumption and the disease characteristics along with the influences of other lifestyle characteristics on that association.

Intervention studies impose an experimental treatment (e.g., reduction or cessation of normal alcohol consumption) on a group of subjects for a period of time and compare the outcome of interest (e.g., blood pressure) with a group of controls, who maintain normal alcohol consumption. In animal studies, conditions can be carefully controlled and the effects of pure alcohol can be studied. In human studies, ethical considerations preclude imposing additional alcohol intake, so the effects of a reduction in the consumption of alcoholic beverages are normally studied in intervention studies.

In contrast, the results of 18 prospective and 37 case-control studies provide no evidence that alcohol consumption is involved in the development of stomach cancer. Likewise, prospective studies give no indication that pancreatic cancer is associated with alcohol consumption. Most prospective and case-control studies have noted an association between alcohol consumption and cancers of the colon and rectum. However, the overall risk is acknowledged to be very small, and it cannot be ruled out that some differences in diet between alcohol drinkers and non-drinkers could account for the association. Further research is needed on possible confounding by dietary habits. Sometimes a moderate association in epidemiology can be produced by the selective publication of positive results.

Animal studies

A substance that induces the development of tumours that rarely or never occur spontaneously is said to be a carcinogen. Alcohol is not a carcinogen, but animal experiments have shown that it can in some circumstances behave as a co-carcinogen: it may enhance the carcinogenic process without itself having initiating capacity. One study, for example, found that cancer of the oesophagus induced in rats by giving a well known carcinogen was enhanced only when alcohol was administered after the tumours had been initiated by the carcinogen. When alcohol was given before or during initiation by the carcinogen, the incidence of tumours decreased.

Not all studies have demonstrated positive effects on the oesophagus, and conflicting results may be explained by differences in the design of experiments, for example, whether the alcohol was given in drinking water, as part of the diet or by intubation. The amount, concentration and duration of alcohol treatment are also important, as are the type of carcinogen used and the manner of its administration.

ALCOHOL AND THE LIVER

The liver's central role in removing alcohol

There is no doubt that excessive alcohol consumption by human beings increases the risk of developing several diseases of the liver. These are principally "fatty liver", hepatitis and cirrhosis. The existence of a link with liver cancer is less certain. These conditions are important only in people whose alcohol consumption is excessive and long term. Moreover, because only a relatively small proportion of even heavy drinkers develop the severest forms of liver damage, it is probable that other factors are also involved.

The liver is the principal organ in the body in which alcohol is metabolized (Figures 2 and 3). Acetaldehyde, a major product of alcohol metabolism, is thought to be the principal toxic agent in the development of liver disease induced by alcohol, but its true role still needs to be clearly defined.

Fatty liver

An early sign of liver damage induced by alcohol is the accumulation of large amounts of fat in liver cells, so-called fatty liver. The oxidation of fatty acids is inhibited by alcohol, and the formation of triacylglycerols is enhanced. Protein damage by acetaldehyde may also reduce the availability of the apoproteins needed to carry fat from the liver into the blood in the form of very low density lipoproteins. This further reinforces the accumulation of fat within the liver.

Damage to membranes and membrane enzymes

Alcohol also directly affects the membranes of liver cells. It can make the membranes more fluid than they would normally be. With moderate alcohol exposure, membranes adapt by subtle alterations in their chemical composition, but chronic heavy alcohol consumption may overwhelm the adaptive mechanisms.

Lipid peroxidation

Another way in which alcohol may cause liver damage is by promotion of the process known as lipid peroxidation. During the oxidation of alcohol, highly reactive chemicals known as free radicals are generated. These react with polyunsaturated fatty acids in the lipids of cell membranes to initiate the formation of lipid peroxides and related compounds that can cause cellular damage. Such oxidative damage is normally kept under control by a variety of antioxidants in cells.

However, one of the effects of excessive alcohol exposure is to reduce the activity of some of these antioxidants so that cells are no longer able to defend themselves adequately, even when later exposed to only small acute doses of alcohol.

Types of liver disease

Although fatty liver is probably the first condition to develop in response to excessive consumption of alcohol, no symptoms are evident. Fibrosis, in which an abnormal accumulation of the connective tissue protein collagen occurs around the liver cells, is also generally without symptoms in the early stages. In alcoholic hepatitis, parts of the liver tissue die and are invaded by cells belonging to the immune system. Some people are without symptoms, but some may develop gastro-intestinal bleeding, and in a proportion of people the liver fails to function. In cirrhosis, general degeneration of the liver tissue occurs, and the disease has many of the characteristics of fatty liver, hepatitis and fibrosis. Alcohol is only one of a number of factors that can lead to the development of cirrhosis. Malnutrition, which is itself associated with chronic alcohol consumption (see below), can also precipitate cirrhosis. It must be stressed that these conditions occur only in people with long-term excessive alcohol consumption and are not relevant to moderate consumption.

A major difficulty in drawing firm conclusions about the effect of alcohol consumption on the liver is in distinguishing the direct effects of alcohol from the indirect effects of poor nutrition. Animal experiments have been useful in exploring mechanisms by which alcohol may exert its effects on the animal's physiology, but caution is required when relating the results to humans in studies in which up to 50% of dietary energy came from alcohol. In these cases, nutritional deficiencies must also have played a part. In human studies, alcoholics with cirrhosis have lower energy and nutrient (especially protein) intakes than those without cirrhosis, but it is not clear whether the poor nutrition resulted from the cirrhosis or contributed to its development. Liver damage is known to be more likely to occur in those who are severely overweight, but again, it is not clear whether this is due to the excessive adipose tissue itself or to the high fat consumption that is often associated with overweight.

Much still needs to be learned about nutrient intakes and nutritional status in those with moderate alcohol intakes.

ALCOHOL AND THE CARDIOVASCULAR SYSTEM

Alcohol affects a variety of functions of the blood and the blood vessels that ultimately influence the susceptibility to diseases such as stroke and coronary heart disease.

Hypertension

An association between alcohol intake and blood pressure was noted in 1915. Since that time, epidemiologic studies and experiments in which alcohol consumption has been systematically changed have led to the firm conclusion that chronic ingestion of more than about 30 g of alcohol per day results in raised blood pressure in men and women.

Above the threshold of 30 g/day, increments of 10 g/day raise blood pressure about 1–1.5% on average. About 7–11% of hypertension in Western industrialized countries is thought to be due to alcohol intakes exceeding 40 g/day. Thus, alcohol consumption is a major environmental, as distinct from genetic, determinant of hypertension.

Conclusions from epidemiologic studies are likely to be influenced by other environmental factors (or inherited characteristics, see earlier section) that confound the results. Allowance needs to be made for the effects of age, sex and body weight, as well as for dietary variables such as sodium, potassium or magnesium intakes, all of which influence blood pressure. It has also been confirmed that people who regularly consume alcohol tend to smoke more cigarettes. To add to the complexity, alcohol intake is notoriously difficult to measure reliably, and the potential for misclassification is considerable.

Nevertheless, after all these potential problems have been accounted for, the alcohol–blood pressure association is strong above intakes of about 30 g/day, which is supported by the results of intervention studies (see Box 1). These show that the magnitude of the fall in blood pressure with reduced alcohol intake under experimentally controlled conditions is similar to that which would be predicted from the observational association if this represented a causal effect.

Stroke

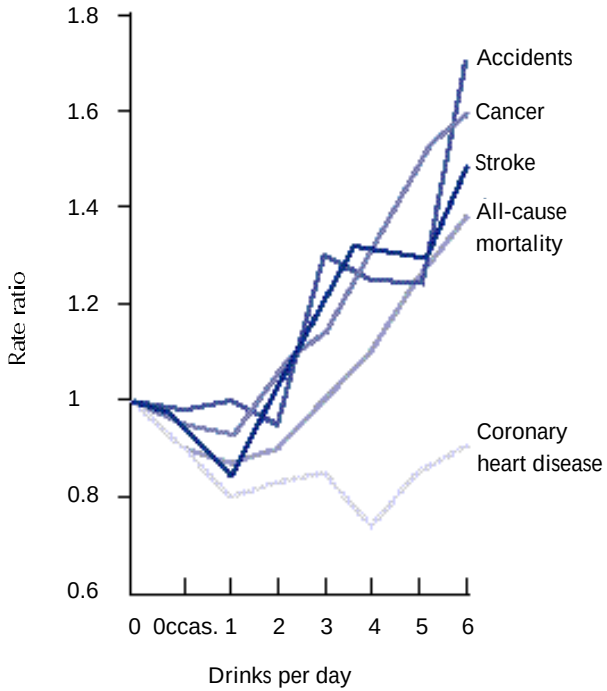
There are two types of stroke: ischaemic, making up 85% of all strokes, in which an artery supplying part of the brain is blocked, cutting off the supply of blood and therefore oxygen; and haemorrhagic, 15% of all strokes, in which profuse bleeding occurs inside the brain. They are differently influenced by alcohol. However, because many studies have not distinguished the two, these results are not very informative.

Prospective epidemiologic studies (providing nearly 2 million person-years of observations) find no strong association between alcohol intake and total stroke. There may be some increased risk at higher levels of intake, but there is no consensus about how much alcohol is required. More than three regular alcoholic drinks per day over a long period are probably needed. Studies focused only on ischaemic stroke also found no association. Haemorrhagic stroke, by contrast, seems to be strongly correlated with alcohol consumption, with typically about a threefold increase in risk at the higher levels of consumption. It has been suggested that "binge drinking" – when people have intermittent bouts of excessive consumption rather than steady high or moderate intake – may explain the link, and this proposal needs further research.

There is some debate among scientists about whether moderate drinking decreases the risk of ischaemic stroke. Only a few studies have addressed the question

FIGURE 5

Alcohol consumption and mortality rates



Source: R. Curtis Ellison, Cheers, Epidemiology, Sept. 1990, Vol.1, 337-339.

of moderate or light drinking, and several problems associated with epidemiologic methods, discussed elsewhere in this monograph, have reduced the sensitivity of those studies.

Coronary heart disease

Results of case-control and prospective studies (see the Epidemiological techniques box) and of international comparisons are unanimous in supporting the conclusion that moderate consumption of alcohol, whether taken as beer, wine or spirits, is associated with a reduced incidence of coronary heart disease (CHD) and fatalities from the disease. This conclusion applies to men and women, both young and old. The mortality from CHD is significantly less in people who consume about 10-20 g of alcohol per day than in nondrinkers of alcohol, but at higher levels of intake the risk of CHD increases (Figure 5).

CHD is generally regarded as beginning with the development of atherosclerosis (thickening and loss of elasticity of arterial walls) over many decades. When the atherosclerotic deposits rupture, a clot or thrombus may be formed that blocks a major artery supplying the heart. The resultant restriction in the supply of blood and oxygen causes the heart muscle to cease functioning, precipitating a heart attack (see the Alcohol and CHD box).

The protection afforded by moderate alcohol consumption is in part due to its effect on atherosclerosis. One effect of alcohol ingestion is to increase the concentration of particles in the blood called high-density lipoproteins. Among their several functions may be the removal of cholesterol from arterial deposits, thus reducing the extent of atherosclerosis. Another beneficial effect of alcohol seems to be to reduce the tendency of the blood to form a thrombus (Box 2), and it may even stimulate the removal of small thrombi once formed. Alcohol acts, therefore, by reducing thrombosis and thus heart attacks.

It may be important to distinguish between effects that can be attributable directly to alcohol and those that may result from other constituents of alcoholic drinks. Thus, there is currently much research interest in the antioxidant properties of some constituents of red wine, which, it has been proposed, may protect against the development of CHD (see the Alcohol and CHD box).

The discovery that moderate drinking protects against heart disease poses a dilemma for those concerned with making public health recommendations. Many authorities are unwilling to recommend even mild consumption of alcohol in view of the known addictive effects of this substance and the harm that could be done by insidious increases in alcohol consumption generally.

ALCOHOL AND ASPECTS OF REPRODUCTION

Pregnancy

Heavy alcohol consumption can reduce the growth and development of the foetus in experimental animals, and the effect is related to the dose of alcohol consumed and the time of exposure. Similar foetal abnormalities occur in pregnant women who are alcohol dependent. This is a condition known as foetal alcohol syndrome. It is associated with serious dysfunction of the nervous system as well as with abnormalities in body growth and development. Foetal alcohol syndrome, like so many other clinical conditions involving alcohol, is complex and involves various aspects of human life, including poverty, poor maternal health and diet, past obstetric difficulties, heavy smoking and drug abuse.

These remarks apply almost entirely to women whose alcohol consumption is so heavy that they have become addicted. There is little evidence that low to moderate drinking has adverse effects. While researchers have been unable to define a clear-cut association with maternal alcohol consumption, there is evidence of a threshold below which adverse effects cannot be detected. There is evidence, too, that in many cases of foetal alcohol syndrome the father is also a heavy drinker. Thus the possibility that some of the effects result from damage to the sperm induced by alcohol cannot be ruled out.

Breast cancer

The accumulated evidence from some 40 epidemiological studies reveals only a weak and inconsistent association between alcohol consumption and the likelihood of developing breast cancer.

BOX 2

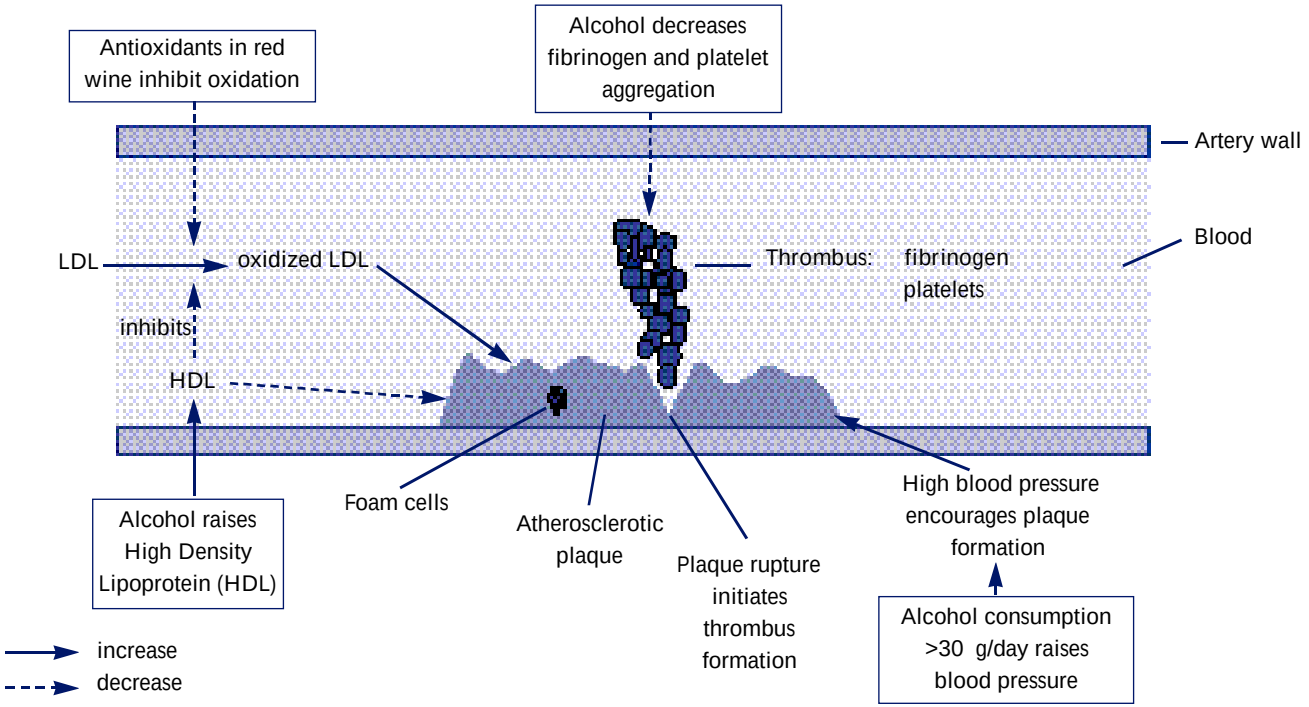
Alcohol and coronary heart disease

In simple terms, coronary heart disease (CHD) develops in two stages:

Atherosclerosis. Deposits (atherosclerotic plaque) build up on the wall of the artery over a long period of time, narrowing the vessel. Among many constituents of plaque are oxidized lipids originating from low-density lipoproteins (LDL) in the blood.

Thrombosis. A thrombus forms at places where the atherosclerotic plaque ruptures. This includes aggregates of blood platelets and a matrix of fibrin formed from the protein fibrinogen in blood.

Many factors influence plaque and thrombus formation, including the lipoproteins that carry lipids in the blood. LDL particles may become oxidized and are then entrapped in "foam cells" which are cholesterol-rich consituents of the plaque. The role of high-density lipoproteins (HDL) is to remove cholesterol for disposal by the liver.



Epidemiological studies cannot demonstrate causality and it is entirely probable that the observed weak association was due to factors related to alcohol consumption that are as yet unrecognized or poorly understood.

A considerable barrier to progress has been the lack of a supportable hypothesis about the causes of breast cancer, although many factors have been discussed. In any epidemiologic study there are many unrecognized factors that could confound the association. Thus dietary fat has often been implicated in the development of breast cancer, and studies on the role of alcohol need to take this into account. Moreover, breast cancer is a disease that develops slowly, so that dietary factors that influenced current cancer would have been operating some time in the past. The accuracy with which intakes of dietary components consumed many years ago can be recalled is poor, making the assessment of confounding factors difficult and unreliable.

Only when there is better knowledge about the primary risk factors for breast cancer will it be possible to design studies of the role of alcohol that reliably account for confounding factors. Meanwhile, present understanding is that there is currently insufficient evidence to support any general causative relationship between alcohol and breast cancer.

ALCOHOL AND OVERWEIGHT

People are described as overweight when they accumulate excessive adipose tissue. Their body mass index, defined as their weight in kilograms divided by the square of their height in metres, would be in the range of 25–30. Overweight arises when energy expenditure is exceeded by intake over time. A major difficulty in studying the underlying causes of overweight is that so many factors influence its development: nutrition, exercise patterns, and psychological and social factors. Regarding nutrition, the total amount of energy consumed is clearly important but whether excess energy supplied as fat has a greater tendency to promote weight gain than has energy supplied as carbohydrate is still a matter of intense research activity. A discussion of the relative fattening effects of sugars and fats can be found in the ILSI Europe concise monograph on Nutritional and Health Aspects of Sugars.

One gram of alcohol supplies about 29 kJ of energy compared with 17 kJ from sugars and 38 kJ from fats. On the basis of its ability to supply dietary energy, therefore, over-consumption of alcohol might be expected to lead to overweight if energy expenditure is fairly low. Indeed, public perception is that alcohol consumption does lead to overweight as exemplified by the so-called "beer belly" profile. However, it has been difficult to demonstrate a clear association between alcohol intake and body fat content in epidemiologic surveys, because the results have been conflicting.

What contributes to this confusion is the multitude of uncontrolled variables that exist in many studies, including personality, level of education, physical activity, socioeconomic status, other dietary factors and smoking habits. Those who consume the most alcohol

also tend to be the heaviest smokers; however, the heaviest smokers also tend to have the lowest body weight. Confusion is bound to arise if alcohol is studied without taking these variables into consideration.

Alcohol is not consumed as pure alcohol, so the type of alcoholic drink may be important. In some studies, for example, body mass index was inversely related to the consumption of spirits but directly related to the consumption of beer or wine. Some differences in the pattern of consumption of other nutrients occur in drinkers compared with abstainers. For example, there seems to be an inverse association between alcohol intake and sugar consumption, but this effect is modest. Minor differences in vitamins and fats have been noted in some studies but not in others. In general, it appears that alcohol tends to supplement rather than displace dietary energy intake from fats and carbohydrates.

Thus, on average, drinkers probably consume more energy than abstainers. Nevertheless, an interpretation (although controversial) of much of the research on this subject is that the body neither uses nor stores most of the 29 kJ/gram of alcohol consumed. There is a small increase in the basal metabolic rate when alcohol is consumed, but this seems inadequate to account for all the energy ingested from this source. The question of what the body does with this energy is one that is currently occupying many researchers. Detailed metabolic studies, rather than more epidemiologic surveys, will be required to discover the fate of this "lost energy" and these will need to be conducted over extended time periods, since weight changes are likely to be small.

SUMMARY

Alcohol is formed during the fermentation of carbohydrates by yeasts and has been consumed in the form of alcoholic beverages by human beings for millennia. It is metabolized in the body to yield energy. Many people enjoy small quantities of alcoholic drinks for example with meals and in social situations. When consumed in large quantities, however, it can become addictive, toxic, and the cause of ill health and widespread social problems. Although research has now demonstrated that there is a genetic contribution to the disease of alcoholism, it is unclear to what extent genetic factors are involved in less severe alcohol-related problems.

Much of our knowledge of the effects of alcohol consumption on health comes from epidemiologic surveys. For these studies to be of value, a prime consideration is the accurate assessment of alcohol consumption, but this is recognized as being extremely difficult.

Alcohol is rapidly absorbed into the body from the small intestine, but some may already have undergone metabolism in the stomach. Healthy people clear alcohol from the body relatively quickly. Most is metabolized in the liver, mainly through the action of the enzyme alcohol dehydrogenase, which catalyses conversion into acetaldehyde. Because the latter compound is toxic in its own right, it must also be metabolized by the enzyme aldehyde dehydrogenase to acetic acid, which is then converted into acetyl-CoA, the biochemically "active" form of acetic acid. This can be completely oxidized to carbon dioxide or used to form fats. Two other metabolic pathways convert alcohol into acetaldehyde. One of these is important in that it is "inducible". In other words, its activity is normally too low to be detected, but it becomes induced to high activity when the liver is confronted with a high dose of alcohol. Such a mechanism enables the body to adapt quickly to changes in alcohol intake.

In this concise monograph, the possible ill effects of consumption of alcohol have been classified broadly as cancers of the alimentary tract, diseases of the liver, influences on the cardiovascular and reproductive systems and effects on body weight. Knowledge has come mainly from epidemiologic studies of three types:

- simple comparisons between different races, countries or communities;
- comparisons between people with a defined disease (cases) and healthy people (controls), who are otherwise matched for other life-style factors that might confuse the interpretation of the results; and
- prospective studies in which a large group of people with known drinking habits is followed over a long period and specific disease outcomes recorded.

It has sometimes been possible to compare these findings with results of experiments with laboratory animals, which can be useful in elucidating basic mechanisms by which alcohol might exert its effects.

Epidemiologic evidence shows that the consumption of alcohol increases the risk of developing cancers of the mouth, oesophagus and larynx. Smoking multiplies this risk substantially. In the absence of smoking, the risk of developing these cancers is small except in heavy drinkers. There is little evidence that alcohol has any influence on the development of stomach or pancreatic cancers. The overall risk of colon cancer owing to alcohol is small.

Excessive, but not moderate, alcohol consumption increases the risk of developing fatty liver, hepatitis and cirrhosis. Whether alcohol can be associated with the development of liver cancers is unclear. Liver

deterioration owing to chronic alcohol consumption may show no clinical signs until the liver becomes seriously damaged. This can make it difficult to draw firm conclusions about alcohol's precise effect. Another difficulty is in distinguishing the effects of alcohol itself from the concomitant effects of poor nutrition, which are frequently associated with overindulgence in alcohol. Alcohol may cause damage through a direct effect on cell membrane structure, through its stimulation of lipid peroxidation or indirectly via the toxic effects of acetaldehyde.

Epidemiology has found a strong association between alcohol consumption and high blood pressure. Reducing alcohol intake experimentally brings about a fall in blood pressure similar to that predicted from observational studies. Alcohol consumption increases the risk of haemorrhagic stroke but has no effect on ischaemic stroke and only modest effects on stroke overall. It is now clearly established that there is a "J-shaped" association between alcohol consumption and coronary heart disease. Lifelong abstainers appear to be at higher risk than light or moderate consumers, but the risk of coronary heart disease increases at higher levels of consumption. Alcohol may act metabolically by promoting increased concentrations of high-density lipoproteins in the blood and, by reducing the tendency of the blood to clot, i.e., by influencing thrombosis.

The risk of developing breast cancer is only weakly related to alcohol consumption. Women whose drinking is excessive may produce deformed foetuses, but there is no clear-cut evidence that light drinking has any ill effect.

Even though alcohol has an energy value of 29 kJ/gram (intermediate between carbohydrate and fat), it has been difficult to demonstrate a clear association between alcohol consumption and overweight in epidemiologic surveys. This is mainly because a wide variety of other lifestyle factors influence overweight, many of which were not controlled in the published studies. Alcohol seems to be consumed in addition to normal energy intakes rather than replacing fat or carbohydrate energy. There is little experimental evidence that the energy from alcohol is stored or used in the body and the fate of the "lost alcohol energy" is the focus of current research.

Much of the uncertainty about the effects of alcohol will need to be resolved by improvements in techniques for assessing alcohol intake and by controlling potential confounding factors. The discovery that moderate drinking may protect against heart disease poses a problem for those in public health education, since few are willing to recommend even mild consumption of alcohol in view of its known addictive properties.

GLOSSARY

Acetaldehyde: The primary product of alcohol metabolism in the body. It is toxic and must itself be removed rapidly from tissues.

Alcohol: The common name for the substance with the chemical names ethyl alcohol or ethanol. Produced during fermentation of sugars, it is the characteristic component of alcoholic beverages.

Alcohol dehydrogenase: The enzyme, present in most tissues of the body, that catalyses the oxidation of alcohol to acetaldehyde. There are several genetically determined forms of the enzyme, whose pattern differs among individuals.

Carcinogen: A substance that induces the development of malignant tumours that rarely or never occur spontaneously. The chemical causes a change in the structure of cellular DNA, which programmes cell growth.

Case-control study: A study design in which persons with a disease (cases) are compared with those without the disease (controls) to see how their exposures to causative factors may have differed.

Cirrhosis: A chronic degenerative disease of the liver. Fat infiltration occurs, the cells degenerate, the liver architecture is destroyed by fibrous tissue, blood supply is reduced and liver function deteriorates.

Co-carcinogen: A chemical substance that enhances the action of a carcinogen but does not itself initiate cancer.

Coronary heart disease (CHD): A condition in which the main (coronary) arteries supplying the heart are blocked or restricted and are no longer able to supply blood, and therefore oxygen, to the heart muscle (myocardium), which may then quickly die. The main cause of reduced blood flow is the accumulation of plaques in the arterial walls, a disease known as atherosclerosis. The blockage of an already narrowed artery is thrombosis.

Epidemiology: The study of the distribution and determinants of disease in human populations and the application of this study to control health problems.

Ethanol: A chemical name for alcohol.

Fatty liver: An abnormal accumulation of fat in the liver associated, in extreme cases, with abdominal discomfort. It often precedes other liver diseases such as cirrhosis.

Foetal alcohol syndrome: Defects in the growth and development of the foetus resulting from excessive consumption of alcohol by the mother or possibly even the father.

Fibrosis: A condition in which there is a proliferation of fibrous or connective tissue. It is often associated with the formation of scar tissue following an injury or infection.

Free radical: A highly reactive chemical species that normally exists for a relatively short time. Some free radicals are formed in the body during processes of oxidation and may be useful, e.g., in killing infectious organisms. Free radicals are also capable of doing extensive damage to tissues unless kept in check by antioxidants. The latter can be enzymes or chemicals, many of which are vitamins obtained from the diet (e.g., vitamins C and E).

Hepatitis: Inflammation of the liver, generally accompanied by abdominal discomfort. There may be many causes, including bacterial or viral infections and various drugs, including alcohol.

Hypertension: A disorder in which blood pressure is raised above the normal range, persistently exceeding 140/90 mm Hg. There may be no visible signs, but the condition poses an increased risk for several diseases such as stroke and coronary heart disease.

Lipid peroxidation: A process in which unsaturated fat-soluble substances (lipids) are oxidized to form very reactive products, some of which are free radicals and therefore capable of causing extensive tissue damage. The polyunsaturated fatty acid components of lipids are particularly prone to oxidation in this way. The process can occur in foods before they are eaten or can take place in the body.

MEOS: An abbreviation for the microsomal ethanol oxidizing system, an enzyme system, mainly in the liver, that metabolizes alcohol. MEOS is normally present at a low level and is enhanced upon exposure to a large influx of alcohol.

Prospective (cohort) study: A study in which the study population is characterized at the start of the study and followed into the future. A population of people who do not (yet) have the disease under investigation is identified, and information is collected on the subjects' exposure to risk factors generally including nutritional factors. The frequency of the disease among subjects exposed to a particular risk factor during the follow-up period is compared with the frequency among those who were not exposed.

Stroke: A layman's term for a cerebrovascular accident in which the blood supply to part of the brain is reduced, with clinical consequences.

Other ILSI Europe Publications Available from ILSI Press

Caries Preventive Strategies
1995. 24 pp.. ISBN 0-944398-63-4 Order code: 398634

Dietary Fat – Some Aspects of Nutrition and Health and Product Development
1995. 37 pp.. ISBN 0-944398-74-X Order code: 39874X

Dietary Fibre
1994. 23 pp.. ISBN 0-944398-24-3 Order code: 398243

Food Allergy and Other Adverse Reactions to Food
1994. 24 pp.. ISBN 0-944398-19-7 Order code: 398197

Food Biotechnology – An Introduction
1995. 40 pp.. ISBN 0-944398-62-6 Order code: 398626

Health Issues Related to Alcohol Consumption
1993. 329 pp.. ISBN 0-944398-17-0 Order code: 398170

Light Foods – An Assessment of Their Psychological, Sociocultural, Physiological, Nutritional and Safety Aspects
1995. 98 pp. ISBN 0-944398-44-8 Order code: 398448

Nutritional and Health Aspects of Sugars – Evaluation of New Findings
1995. 24 pp.. ISBN 0-944398-65-0 Order code: 398650

Oxidants, Antioxidants and Disease Prevention
1995. 24 pp.. ISBN 0-944398-52-9 Order code: 398529

A Simple Guide to Understanding and Applying the Hazard Analysis Critical Control Point Concept
1993. 12 pp. ISBN 0-944398-18-9 Order code: 398189

Starches and Sugars: A Comparison of their Metabolism in Man
1991. 20 pp. ISBN 0-944398-70-7 Order code: 398707

Sweetness – The Biological, Behavioural and Social Aspects
1995. 24 pp. ISBN 0-944398-51-0 Order code: 398510