

OVERVIEW OF THE HEALTH ISSUES RELATED TO ALCOHOL CONSUMPTION



EXECUTIVE SUMMARY OF THE BOOK "HEALTH ISSUES
RELATED TO ALCOHOL CONSUMPTION", 2ND EDITION

Prepared under the responsibility of
the ILSI Europe Alcohol Task Force

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SEPTEMBER 1999

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INTRODUCTION

The role of beverages containing alcohol has been a prominent feature of life in many societies. For as long as alcohol has been consumed, and that is millennia, the relationships between drinking and various aspects of health have been explored.

Under the auspices of the International Life Sciences Institute-ILSI Europe, leading scientists were invited in 1992 to review critically and objectively the state of information available on the relationship between alcohol consumption and nine important health issues: hypertension, stroke, coronary heart disease, digestive tract cancers, liver disease, breast cancer, pregnancy, overweight, and genetics. This group of scientists included epidemiologists, clinicians, toxicologists, and other biomedical researchers. The task assigned was to appraise what we know and, equally important, what we do not know about alcohol and especially moderate consumption, as it pertains to a wide range of biomedical considerations. The result was the publication of the book "Health Issues Related to Alcohol Consumption" ILSI Press 1993.

Recently it was determined to update the project with this new edition, which includes additional new topics and combines some of the topics from the original book. Again, nine panels were formed, each with its own chairperson. Each panel was asked to address the relationship between alcohol consumption and one of the following areas: moderate drinking, assessment of intake, genetics, body weight, the cardiovascular system, pregnancy, breast cancer, bone, and the central nervous system. All panels were asked the following:

- To list possible associations between specific biomedical conditions and the consumption of alcohol.
- For each possible association or hypothesis, to assess the progress reached in achieving a scientific consensus, including whether a consensus exists, the specific content of the consensus, and the body of research that allows the consensus to form. The panels were also asked to address whether the consensus reached far enough to cover a relationship between biomedical consequences and a particular dose or range of dosage, and whether the intakes are consistent across the population.
- To identify issues where a scientific consensus does not exist and, in such cases, to identify the gaps in knowledge or contradictory results that preclude such a consensus, and to specify research tasks necessary for shifting each possibility to a consensus, confirmation, or dismissal.
- To determine whether there are cases:
 - where a hypothesis is supported by epidemiological findings that demonstrate a relationship between alcohol consumption and a biomedical effect, but where a causal relationship cannot be confirmed because of the absence of clinical, laboratory or animal research defining a mechanism;
 - where the findings are too dependent on a particular piece of research to permit consensus; or
 - where it is recommended that increased attention be paid to contrary evidence.

Also included as appendices to this book are two chapters from the first edition, Alcohol and Liver Diseases and Cancers of the Digestive Tract and Larynx. The panel chairmen considered that so few new findings have been reported since the 1993 edition that an update on these subjects was not necessary.

This overview is intended to summarise the reports of the nine panels plus the appendices; readers interested in the details can refer to the full chapters.

The reader will note that different panels have used differing measurements of the amounts of alcohol consumed by subjects in medical research. This reflects differences in the measurements employed in the studies themselves. A number of the panel reports measure consumption in grams of pure ethanol consumed. In most countries, a standard serving of beer, wine, or spirits varies between 8 to 12 g of ethanol.

Moreover, several of the panels have noted serious methodological problems in the consumption measurements employed in the currently available studies reviewed by the panels, especially those of the non-experimental observational studies. Measurement of alcohol intake in the studies is usually based on self-reporting by the subjects of the study, and this can result in recall errors. Specifically, people in general, and heavy drinkers in particular, often underreport their intake. In other words, subjects may not recall (or wish to admit) precisely how many grams or millilitres they drank per day or what proportion of a mixed drink consumed consisted of alcohol. Because of this underreporting, the threshold amounts of alcohol consumption associated with certain health risks may in fact be higher than those indicated in the existing studies. Alternatively, persons reporting as teetotallers may have been former heavy drinkers, and indeed self-styled abstainers have been found to have alcohol in their urine. Here again, such misclassification may cast doubt on the precise consumption figures shown in the research literature.

Additional methodological problems include a number of “confounding factors”, such as age, sex, body mass index, diet, physical activity, smoking, coffee consumption, educational attainment, Type A/B behaviour, socioeconomic status and medical history, that may be factors in particular health problems in persons who have been the subjects of the reported studies. For example, a generally poor nutritional condition could possibly play a significant role in various health problems associated with heavy drinking. In most of the investigations, adjustments could be made for many of these confounding factors, but for some this was not possible because the relevant information was not available or assessment was too difficult.

It is worth noting that the ILSI Europe panels did not address every aspect of alcohol and health or every system of the human body. The panels were charged with considering or updating nine specific issues, with an emphasis on the health effects of moderate consumption. Some topics involving the neuropathological consequences of alcohol use, such as the psychiatric effects of alcohol abuse and injuries from drinking and driving, have not been addressed by the panels.

MODERATE DRINKING: CONCEPTS, DEFINITIONS AND PUBLIC HEALTH SIGNIFICANCE

The term “moderate”, when referring to the amount of alcohol ingested, can be used in at least five senses. The oldest sense is “non-intoxicating” but it is also used as “statistically normal”, “non-injurious”, “problem-free” and “optimal”. However, regardless of definition it is difficult to specify moderate intake quantitatively because intakes are still frequently expressed in “units” or “drinks” and there is no uniform international definition of a standard drink.

The idea of an “optimal” level of alcohol intake is based on the demonstration that overall mortality in a population, or mortality or morbidity due to certain specific causes, is lower among those who drink lightly than those who drink more heavily or who do not drink at all. For those diseases which do not show such a “J-shaped” or “U-shaped” relation between degree of risk and level of alcohol intake, it is not possible to talk of an optimal level.

In a review of 28 scientific papers the lower limit of moderate intake ranged from 4.5 to 50 g/day and the upper limit range was 24–80 g/day. Contributing to this wide scatter is the variability arising from the relatively low level of accuracy in estimating alcohol intake.

It is not possible to give any exact advice on moderate drinking. Estimates based on epidemiological studies (because they are under-evaluations, a notable safety margin is included) suggest that for an average adult man the optimal level is about 10–19 g/day and the non-injurious level is about 30–40 g/day. For an average woman the respective levels are <10 g/day and about 10–20 g/day. These estimates of the optimal and non-injurious levels of alcohol intake are valid only for the average adult. Variation in body size and composition has a marked influence on the blood alcohol concentrations produced by the same amount of alcohol and must be taken into account. Differences in individual drinking patterns also introduce additional variation in the degree of health risk associated with any given daily intake of alcohol.

The wise drinker will bear in mind the words of Aristotle “The temperate man keeps a middle course in these matters ... such pleasures as conduce to health and fitness he will try to obtain in a moderate and right degree; as also other pleasures so far as they are not detrimental to health and fitness, and not ignoble, nor beyond his means.”

ASSESSMENT OF ALCOHOL CONSUMPTION

It is well known that assessment of dietary intake is prone to errors. However, assessment of alcohol intake poses a larger problem because, for example, alcohol is not considered as a normal food substance, it has a highly symbolic value and drinking is influenced by cultural differences and social norms.

Methods used to assess alcohol consumption may be divided into those that use official data such as sales statistics, and those in which the individual is aware of the investigation, such as self-reporting. An important disadvantage of sales statistics is that they do not provide information about the manner and amount of alcohol consumption of specific groups or individuals.

Self-reporting includes face-to-face interviews, telephone interviews and self-administered questionnaires. The major types of self-reporting ask for a summary of drinking, for example, the quantity-frequency method and lifetime drinking history, or for current drinking, for example, diaries and recalls. In general, data collected from self-reports are sufficiently reliable for ranking subjects according to intake and can be used for associations in epidemiological studies but are unreliable for assessing actual individual intakes. Common errors in assessing alcohol intake in surveys include selection bias, non-response, under- or overestimation of portion size and recall bias.

Biological markers can be important for assessing objective intake but currently their sensitivity and specificity are relatively low.

It is not easy to state which method is the closest to real intake because a gold standard is lacking, but the quantity/frequency method and the prospective diary are probably the closest to real intake, provided they cover the different types of alcoholic beverage and deal with the problem of standard units.

ALCOHOL AND GENETICS

It has long been observed that alcoholism runs in families and more recently epidemiological and experimental studies have provided substantial evidence for the role of heredity in alcoholism and also in disease in organs resulting from alcohol. It is now widely accepted that the genetic predisposition to develop alcoholism is, unlike, for example, cystic fibrosis, dependent on the interaction of these genetic factors with environmentally determined precipitating factors. Alcoholism is thus a complex disorder.

Studies on ethanol intake in animals and the development of animal models are made possible by the fact that a variety of animals voluntarily consume ethanol. Breeding experiments with animals differing in their preference to consume alcohol voluntarily and new statistical methods (including a technique called Quantitative Trait Loci) has greatly extended the understanding and identification of the genes involved. The development of genetic engineering techniques has also allowed progress to be made in identifying specific genes in alcoholism. At present the risk and the protective genes influencing ethanol-related traits in animals have not been specifically extrapolated to humans.

In man, a very large collaborative study (Collaborative Study on the Genetics of Alcoholism) has been implemented whose purpose is to identify genes which predispose to the development of alcoholism.

Candidates considered for genetic involvement in alcoholism that have been studied include the dopamine receptor in the brain, monoamine oxidase activity in blood platelets, lymphocyte and platelet adenylate cyclase activity, serotonin transporter and receptor mechanisms, as well as alcohol and acetaldehyde metabolism.

Turning to end organ effects of alcoholism, the fact that only 20-30% of chronic alcoholics develop liver cirrhosis, has led to a search for the genotypes of this and other alcohol-related organ injuries. So far studies have produced no convincing results.

The ability to genetically predict a person's reaction to alcohol and the use of molecular biology in therapy are important goals yet to be achieved.

ALCOHOL AND BODY WEIGHT

Nation-wide studies indicate that 10–30 g of alcohol daily is the average per capita consumption which is 3–9% of daily energy intake in the Western diet. However, there is no consensus on the relationship between moderate drinking and body weight and epidemiological studies are almost equally divided between those which show a positive correlation, those which show a negative correlation and those which show no correlation.

In recent years there have been several studies that have looked at the possible reasons for this discrepancy in epidemiological findings on the relationship between alcohol and body weight. One possibility is that alcohol influences the amount of food eaten and, despite the errors arising from dietary studies in free-living people, in 11 out of 12 studies alcohol use was associated with a raised total energy intake in both men and women. For social drinkers the mean increment in energy intake would be close to 10% but for heavy drinkers it can reach over 30%. In most of these studies the non-alcohol food energy remained constant irrespective of drinking level.

Studies carried out in the laboratory on the “aperitif” effect of alcohol, which is supposed to increase appetite, have been few and inconclusive either showing an increase in food intake or changes in the subjective feelings of hunger or fullness or, in one study, showing no effects. In free-living people drinkers tend to consume more energy than non-drinkers and among the drinkers energy intake is higher on days when alcohol is drunk. This, however, may be due to the fact that alcohol consumption often occurs at special meals and in company.

Does alcohol affect the body’s expenditure of energy? The gross energy of alcohol is 7.1 kcal/g or 29.7 kJ/g and after consumption very little is lost in breath, urine or sweat, it cannot be stored and it is principally metabolised in the liver. This metabolic handling of alcohol has a cost in terms of energy and several studies have reported figures of around 17% for the energy of the ingested alcohol used in its metabolism to carbon dioxide and water. So a large increase in heat dissipation after ethanol intake is not an explanation for the apparent lack of weight gain when excess energy as alcohol is consumed. The general conclusion is that no mysterious loss of energy results from moderate alcohol intake in healthy subjects.

Laboratory studies on energy and nutrient balances show that ethanol is a nutrient that the body utilises with an efficiency close to that of carbohydrates and that alcohol calories do count. Thus, all these studies do not explain the epidemiological evidence of no clear correlation between alcohol use and body weight. Controlled metabolic experiments show that habitual alcohol use in excess of energy needs favours lipid storage. Thus, ethanol acts as a preferred fuel.

Possible explanations for this discrepancy include the possibility that alcohol could be associated with or induce a higher level of physical activity. Also there are suggestions that the increase in heat production after alcohol ingestion could be higher in thin individuals than in fat subjects because thin persons lose heat easier. Furthermore, subjects who are overweight systematically underscore energy intake more than lean subjects. Thus, the expected positive relation between alcohol intake and body weight could be due to under-reporting in subjects who are overweight. Also, a negative correlation between alcohol use and body weight, as often observed in women, could be due to a high degree of under-reporting in this sex.

The mechanism(s) behind the relation between alcohol consumption and the maintenance of energy balance is for future research.

ALCOHOL AND THE CARDIOVASCULAR SYSTEM

There is abundant epidemiological and clinical evidence to show that light to moderate drinking is associated with a reduced risk of coronary heart disease, total and ischaemic stroke and total mortality in middle-age and elderly men and women. There is little basis to expect one particular beverage to be more effective in reducing risk than another and the effect appears to be due to alcohol itself, though the discussion continues.

The evidence suggests that there is a U-shaped relation between alcohol and coronary heart disease and the threshold at which the right side of the U begins to increase could be as few as 2 or as many as 6 drinks/day. Though vascular disease takes a long time to develop it is not known how long alcohol needs to be consumed, in light to moderate quantities, in order to have an effect on reducing the manifestations of vascular disease.

There is considerable evidence to support the suggestion that moderate drinking reduces the risk of coronary heart disease both by inhibiting the formation of atheroma and decreasing the rate of blood coagulation.

Observational and interventional studies provide strong support for the view that alcohol use is an important lifestyle factor in raising the blood pressure and that a causal association exists between the use of 30–60g/day and blood pressure elevation in men and women.

The two subtypes of stroke are (1) where there is a blockage (ischaemia) of a cerebral artery (75–85% of all strokes) and (2) cerebral haemorrhage. Light and moderate habitual drinkers have a slightly lower risk of ischaemic stroke, whereas heavy drinking, both regular and short-term, is an independent risk factor for haemorrhagic stroke. Binge drinking is associated with an increased risk of both ischaemic and haemorrhagic stroke.

Alcohol use in moderation appears to promote cardiovascular health and guidelines adopted in the USA and UK suggest that individuals may achieve some benefit if daily consumption is limited to 2–3 drinks.

ALCOHOL AND PREGNANCY

Considerable advances in the understanding of the Foetal Alcohol Syndrome (FAS) and related abnormalities resulting from prenatal alcohol exposure have been made since 1993. As it is over 35 years since the first scientific reports were published, it is possible to study potential prenatal alcohol-related harm in older children and adults. In 1996, a new diagnostic paradigm was developed in which maternal alcohol exposure was more clearly stated to be part of the diagnosis (although certain features of FAS can occur without a history of maternal alcohol use).

Changes have also been made in the diagnosis of Foetal Alcohol Effects (FAE). As there is no single anomaly of the foetus specific to, or consistently associated with, lower levels of maternal alcohol use during pregnancy, there may be a tendency to over-diagnose FAE.

The level and, in particular, the pattern of maternal drinking has received further attention but no consistent picture of alcohol-related foetal harm has emerged in relation to lower levels of maternal drinking. However, there are critical periods during gestation, for example early pregnancy, when heavy maternal drinking is particularly risky.

There is no consistent evidence for a clear-cut relationship between the adverse effects in pregnancy on the foetus or on the child and lower levels of maternal alcohol use. Information is insufficient to state where exactly this threshold lies but it may be around 30–40 g/day, a level well above that defined as moderate drinking for non-pregnant women. On the other hand, no level of maternal drinking can be established that is absolutely safe for the foetus.

FAS is related to a variety of adverse influences other than heavy maternal drinking. These include the mother's socioeconomic status, her nutritional status, the extent of prenatal care, lifestyle, age, smoking and drug use, as well as her genetic make-up. The general health of alcohol-dependent women is often poor with immune deficiency and liver damage increasing the risk of a poor outcome to the pregnancy.

Follow-up studies of children born to mothers drinking "light to moderate" amounts during pregnancy tend to show no lasting impairment. Some studies have found behavioural or school problems in these groups. Even so, it is difficult to show that this is necessarily attributable to maternal drinking during pregnancy rather than to environmental or other factors.

Experimental data have shown that ethanol can interfere with all stages of brain development and that the effects are dose-dependent. The effects are also dependent on the time in pregnancy the drinking occurs; for example, exposure to high levels during the early formation of the embryo produces significant changes. Binge drinking and heavier drinking during the foetal "brain growth spurt" in the last three months of pregnancy may induce functional deficits in specific areas of the brain.

Animal models have provided evidence that foetal alcohol effects are dose-dependent and have clearly demonstrated that the peak maternal blood alcohol concentration and the pattern of drinking (e.g. bingeing) are the most important determinants of the magnitude of alcohol-related birth defects. Different aspects of development may be sensitive to different levels of alcohol.

The search for the underlying mechanisms of foetal alcohol damage goes on. Possible factors include acetaldehyde toxicity, placenta dysfunction, impaired foetal nutrition, foetal hypoxia, abnormal prostaglandin metabolism and free radical formation.

ALCOHOL AND BREAST CANCER

Some 70 studies investigating if there is a causative association between alcohol and the risk of breast cancer are reviewed and the accumulated evidence suggests the possibility of a weak association between alcohol use and breast cancer. The most likely causative relationship exists for large amounts of consumption. Since the evidence for an association between alcohol intake and breast cancer is all non-experimental and since the cause of this tumour remains largely unexplained, the interpretation of the evidence is necessarily problematic.

Considering first the epidemiological evidence, the findings are of limited value because of the many possible confounding variables that cannot be or were not adequately measured. Also the exact measurement and timing of the alcohol intake, the accuracy of the recall of the intake of alcohol some 20–30 years ago, the type of drink (wine, beer, spirits) were often poorly recorded. Psychological stress, the use of oral contraceptives, socioeconomic status, tobacco use and body mass as well as many important dietary factors are possible confounders.

The combination of several individual epidemiological studies (meta-analysis) shows a considerable variation between some of them, in the estimated relative risks of alcohol consumption and breast cancer. Most of these estimates are not significant and are certainly not consistent at any drinking level.

Some investigators have reported that the risk of breast cancer is associated with a specific type of drink, such as wine or beer, whereas others did not find such a specific association.

Concerning the quantity of alcohol consumed, it is probably not possible for anyone to provide exact quantitative data and in addition there is much under-reporting, so it is not possible to demonstrate a strong and consistent relationship, based on epidemiological evidence, between the risk of breast cancer and a particular dose of alcohol.

In spite of intensive investigation, evidence for a casual relationship between moderate or “social” drinking among women and breast cancer is lacking. Even a causal link at higher levels of consumption is most likely to be seriously compromised by unknown confounders. Any recommendations that women should limit their alcohol use to reduce the risk of breast cancer can only be supported in terms of reduction from excessive drinking.

ALCOHOL AND BONE

The incidence of osteoporosis, leading to hip fracture, has increased in most industrial countries in recent years. It is a disease with a significant morbidity, mortality and economic impact. Many factors connected with lifestyle and nutrition have been held responsible, among them alcohol.

The effects of alcohol on bone differ depending on the dose and duration of its use. Different effects are observed as a result of moderate consumption, of acute heavy drinking and of alcohol abuse.

Acute alcohol intoxication enhances urinary excretion of calcium with a drop in the blood calcium level. Both blood magnesium and its urinary excretion are increased after alcohol ingestion, and these alcohol-induced changes in mineral metabolism are dose-dependent. Bone formation is depressed.

With the exception of a few studies, the overall conclusion is that moderate drinking is not likely to have adverse effects on bone density. In some studies a positive association has been observed between moderate alcohol use and the risk of hip and forearm fracture, and there is some indication that age may play a role, particularly in women. Moderate drinking does not change serum calcium, magnesium, phosphate or their urinary excretion. The levels of vitamin D and the absorption of calcium remain unchanged.

Although the evidence suggests that chronic alcohol abuse adversely affects bone mineral density, it may well be that clinical effects only become apparent after a long period of abuse. Nevertheless, chronic alcohol abuse seems to be associated with an increased risk of fractures. Chronic alcohol abuse brings about profound changes in mineral metabolism such as low serum calcium and phosphate levels and magnesium deficiency. These lead to deranged bone quality and may adversely affect bone quality. There is evidence that the physiological response of the parathyroid glands to produce parathyroid hormone is impaired by alcohol.

In summary, acute alcohol intoxication has a short-term effect on bone metabolism, moderate drinking does not derange mineral metabolism and abuse easily leads to fracture.

ALCOHOL AND THE CENTRAL NERVOUS SYSTEM

The effects of alcohol on the central nervous system include a reduction in anxiety, feelings of pleasure, sedation, muscular incoordination, aggression, alterations in cognition as well as changes in social interaction. Beverage alcohol has a relatively simple structure, and in order to see physiological and behavioural effects, considerably higher blood alcohol concentrations (BACs) are required as compared to other psychoactive drugs. These comparative differences in chemical structure and dose indicate that alcohol's mode of action in the brain is inherently different from that of psychoactive compounds. Specific receptors in the brain are utilised by psychoactive drugs to initiate actions but no such receptors have been identified for alcohol. The mode of action of alcohol seems to be that of a modulator of certain neurotransmitter systems in the brain.

Individuals differ extensively in their responses to alcohol and these differences in response are affected by genetic factors, the environment and by previous experience. The character, intensity and duration of alcohol's actions are also affected by its rate of absorption, its distribution in the body and the rate of its metabolism so that, for example, the question "what dose of alcohol impairs motor performance?" will not be a single number but a range of values and will, furthermore, also be determined by the complexity of the task.

Alcohol increases social interaction and conversation whereas the same dose decreases performance of a non-verbal task. The reinforcing effects of alcohol, such as an increase in speech, are restricted to the rising limb of the BAC curve. Certain individuals find even low doses of alcohol aversive and a significant proportion of the population choose not to drink even when alcohol is freely available. The aversive and rewarding properties of alcohol are probably mediated by different neural mechanisms, and it is the balance between these two properties that affects alcohol intake.

Turning to the biochemical and electrophysiological effects in the brain of alcohol, at the cellular level, signalling by the major excitatory and inhibitory systems of the brain seem to be the target of alcohol's action, and within these systems there is differential sensitivity. Alcohol also alters the release of transmitter substances in particular areas of the brain. These transmitter substances may have a direct effect on the excitability of neurons (ionotropic effect) or may stimulate the production of molecules known as "second messengers", which then trigger a cascade of reactions within neurones (metabotropic effect). Some of these neural systems affected by alcohol, adapt during periods of chronic alcohol ingestion and this may generate tolerance, physical dependence and craving.

There is clearly much to be learned about the effects of alcohol on the central nervous system, both in the context of "social" drinking and in the generation of physical dependence.

ALCOHOLIC BEVERAGES AND CANCERS OF THE DIGESTIVE TRACT AND LARYNX

Ethanol is not a carcinogen by standard laboratory tests. Animal experiments suggest, however, that, given by mouth, it may act as a co-carcinogen in the production of cancers in the oesophagus and possibly also in the non-glandular (fore)stomach, but not in the glandular stomach or pancreas. The evidence relating to the production of colorectal cancer is conflicting, and no conclusion can be drawn from it.

Epidemiological evidence shows that the consumption of alcoholic beverages increases the risk of developing cancers of the mouth (other than the salivary glands), pharynx (other than the nasopharynx), and larynx; that the risks are principally due to the presence of ethanol and increase with the amount consumed; that the risks are increased by increased smoking, each agent approximately multiplying the effect of the other; and that, in the absence of smoking, the risks in developed countries are small unless consumption is exceptionally heavy. The risks may be diminished by a diet rich in fruit and green vegetables, but the evidence is inconclusive. Whether the co-carcinogenic effects of different alcoholic beverages depend solely on the presence of ethanol and are unaffected by its concentration or by the presence of congeners (other constituents in alcoholic beverages) is uncertain.

The epidemiological evidence also suggests that there may be some direct relationship between the consumption of alcohol and colorectal cancer. The apparent relationship is quantitatively moderate, and even with heavy consumption a doubling of the relative risk can be excluded. No apparent difference exists between the susceptibility of men and women or of the two sites (colon and rectum), or between the effect of different types of alcoholic beverage. The nature of the observed relationship remains in doubt: it may be causal, it may be due to confounding between the consumption of alcoholic beverages and some other dietary factor that increases the risk of the disease, and it may be due, at least in part, to the selective publication of positive results. Research aimed at discovering whether the association can be explained by confounding with dietary habits should be encouraged.

The balance of the evidence suggests that alcoholic beverages do not cause cancers of the stomach or pancreas, but it does not rule out the possibility altogether. Alcohol may contribute specifically to the production of cancer of the gastric cardia and, indirectly through the production of chronic (calcifying) pancreatitis, to cancer of the pancreas; but the evidence is insufficient for any conclusion to be reached.

ALCOHOL AND LIVER DISEASE

There is strong evidence for a direct relationship between the toxicity of alcohol and liver damage. The liver plays a major role in the metabolism of alcohol. By the action of alcohol dehydrogenase, alcohol is transformed to acetaldehyde, which in turn is rapidly oxidized in the liver to acetate by aldehyde dehydrogenase. Acetaldehyde is a very potent and reactive compound, and it has been suggested that it is one of the major factors in the pathogenesis of alcoholic liver disease.

There is a firm consensus about the association between chronic excessive drinking and the development of fatty liver, perivenular fibrosis, acute alcoholic hepatitis and liver cirrhosis. The potential for developing these conditions is higher in individuals who, for a period of time, have had a daily excessive intake of alcohol. Whereas the consensus about the qualitative association between excessive drinking and the development of the above-mentioned hepatic lesions is well established, there is much uncertainty about the dose-effect relationship.

The key mechanism in the genesis of fatty liver is due to the alcohol-induced change in the redox state of the liver. Excessive alcohol intake may produce liver damage by other mechanisms, such as promotion of lipid peroxidation and toxicity associated with an activation of the microsomal alcohol-oxidizing system. Although there is some evidence that both mechanisms may play a role in the development of alcohol-induced injury to the liver, further studies are required to reach a definite consensus. Nutritional studies have also been implicated, but data are insufficient to establish a critical role.

It is considered that chronic alcoholism constitutes a significant public health problem. Four prospective studies have assessed the relationship between daily alcohol use reported at the start of the study and subsequent cirrhosis mortality during long-term follow-up. In one study it was found that, among subjects reporting drinking at least 50 g/day, the number of those who developed cirrhosis after 10–15 years was about 2% per year. Many studies have demonstrated a very close correlation between total alcohol use in populations and mortality from cirrhosis. Although the incidence of heavy drinkers is higher among men, women are more sensitive to the development of liver injury. Individuals drinking intermittently had a lower incidence of liver damage. Abstinence will reverse, improve or delay progression of alcoholic liver disease depending on the stage of the lesion, which also indicates that alcohol is responsible for the liver damage.

The fact that only a minor proportion of alcohol abusers develop the most severe forms of liver damage, cirrhosis in particular, indicates that other causal factors may be involved. Despite years of research, no consensus has been reached on any one such factor. Current research focuses on genetic factors, viral infections and specific nutritional disturbances.

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