The Biochemical and Pathophysiological Effects of Alcohol Consumption

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Abstract

While the stance of some conservative Christian (and other) groups advocating abstinence from alcohol intake may not be popular, contemporary research into alcohol and its effects on the body may lend weight to such a position. The consumption of alcohol, coupled with its addictive properties, can lead to a wide variety of societal problems that are not only costly in medical terms but also in terms of domestic violence, accidents and antisocial behaviour.

Alcohol is metabolised by the liver and this organ may be consequently damaged resulting in serious impairment of normal hepatic structure and function. Nearly all the physiological systems of the body are adversely affected by alcohol to varying degrees and the behavioural effects observed with intoxication are associated with compromised neurotransmitter functions in the brain and altered brain structure in the long term. Adverse consequences of alcohol intake may be evident in other systems including the cardiovascular, gastrointestinal, reproductive and immunological systems. There is an increased risk of atherosclerosis, cancers of the oral cavity, pancreatitis and immune system disturbances associated with prolonged alcohol intake. In pregnant women alcohol metabolism is reduced and as the developing foetus has lowered ability to metabolise blood alcohol compared to an adult there is an elevated risk of serious consequences associated with foetal alcohol syndrome. Despite the nearly overwhelming negative consequences of alcohol intake, the beneficial effects of drinking red wine linked to lowered heart disease despite a high fat diet (the 'French Paradox') may be associated with the antioxidants and other polyphenols also found in non-alcoholic red grape juice. Serious consideration of the effects of alcohol on the body should inform decisions on the intake of alcohol.

INTRODUCTION

Conservative Christian denominations and associated temperance groups have often advocated total abstinence from alcohol consumption. Various reasons have been given in support of this view that range from the prevention of alcohol related social disruption, increased accidents and impairment of family life to the Christian responsibility of honouring the body

as the temple of the Holy Spirit. Such positions have often been viewed in a negative sense by not only secular society but also other more liberal Christian groups. There is no doubt that alcohol is a significant contributing factor for many problems in society, a fact supported by contemporary sociological and scientific research. Such research may lend significant support to the arguments of temperance groups.

In 2004, 83 percent of Australians reported drinking alcohol, and one in five of these reported drinking at levels associated with a high risk of harm at least once a month[1]. Considering the contribution of alcohol consumption to a range of societal problems including serious systemic disease, domestic violence and road accidents, this behaviour appears to be uninformed given the accumulation of a large body of literature documenting the harmful effects of alcohol on the body. The wide range of serious medical problems associated with alcohol consumption relates to the fact that nearly all the body's physiological systems are adversely affected. This also results in diverse psychosocial problems which are of great cost to society in general, families and individuals specifically. This paper examines some of the biochemical and pathophysiological effects associated with alcohol consumption beginning with how the body metabolises or processes alcohol.

THE ROLE OF THE LIVER IN METABOLISM

The human body is continuously subject to a wide variety of environmental chemicals[2]. While many of these chemicals are of benefit, there are those that are very harmful[2]. The food we eat, the air we breathe, our occupations, the very environment that surrounds us on this planet consists of a massive reservoir of such chemicals. Chemical compounds from the environment (both beneficial and harmful) may gain entry (deliberately or otherwise) to the body through the lungs, gastrointestinal tract and the skin. The liver is the major metabolic organ of the body not only processing nutrient molecules from the gastrointestinal tract but also detoxifying harmful chemicals by transforming them into more water soluble forms so that they may be more easily excreted from the body (often through the urinary system)[2]. Unfortunately the detoxification process can result in liver damage, either directly from exposure to the harmful molecules themselves or from subsequent metabolites formed during the detoxification.

The liver is the second largest organ of the body and weighs about 1.4 kilograms in an average adult. The main functional cell of the liver is the hepatocyte which is relatively large when compared to the average body somatic cell[3]. Hepatocytes are metabolically very active, continuously processing and storing nutrients, manufacturing proteins and carrying out detoxification reactions[2].

Kupffer cells are also present in the sinusoids of the liver. They are active phagocytic cells and effectively remove pathogens or other unwanted substances from the blood filtering through this organ. Both of these cell types are affected by high concentrations of alcohol which can lead to a decrease in their ability to act in disease prevention[3].

METABOLISM OF ALCOHOL

Although most ingested alcohol is metabolised in the liver, between two and ten percent escapes metabolic activity and is directly excreted through the lungs, or in the urine or perspiration[4]. The excretion of alcohol from the lungs forms the basis of breath testing for intoxication levels. In humans there are two main enzymes that are involved in the metabolic oxidation of ethanol[5]. These reactions mostly occur within the hepatocytes of the liver and involve the enzymes alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH). The presence of ADH is essential in dealing with different types of alcohols resulting from normal cellular metabolism or even the low levels occurring in ripe fruit etc. Such alcohols derive from metabolites such as lactate, hydroxybutyrate, sorbitol, and glycerol phosphate[5].

These enzymes participate in a simple two step oxidative pathway that ultimately converts ethanol (CH_3CH_2OH) into acetate ($CH_3CO_2^-$)[5].

1. $CH_3CH_2OH + NAD^+ \xrightarrow{ADH} CH_3CHO + NADH + H^+$
2. $CH_3CHO + NAD^+ \xrightarrow{ALDH} CH_3CO_2^- + NADH + H^+$

Acetaldehyde (CH_3CHO), produced by the action of ADH on ethanol is a very reactive molecule being quickly converted to acetate by ALDH[6]. Acetaldehyde is capable of binding to proteins forming harmful modifications which can cause serious damage in brain and liver tissue[6].

The final product of this two step reaction is the much less harmful acetate, which is a naturally occurring metabolite[5]. However the formation of excess acetate can have a damaging caloric effect along with any sugar or other nutrient molecules added to alcoholic beverages. Acetate can also be a reactive molecule when present in higher concentrations that may result from alcohol metabolism. It can depress the central nervous system and detrimentally affect various other metabolic processes[6].

PATHOPHYSIOLOGICAL EFFECTS OF ALCOHOL

The harmful effects of alcohol on different organs of the body are quite diverse. Some of the more common pathological problems associated with alcohol consumption are now considered.

Liver

As the liver is the main site of alcohol metabolism, it is particularly susceptible to the harmful effects of alcohol. There are three main stages of alcoholic liver disease: fatty liver, alcoholic hepatitis, and alcoholic cirrhosis.

Fatty Liver

The metabolic breakdown of alcohol to acetaldehyde is an oxidation reaction that changes the chemical redox state of the hepatocyte, favouring the accumulation of the coenzyme NADH[7]. This change affects several elements of liver metabolism. Gluconeogenesis (the metabolic production of glucose from non-carbohydrate sources) is prevented by the accumulation of fatty acids resulting from accelerated fatty acid synthesis[7]. This leads to fat being deposited in the liver, and can eventually lead to the condition known as fatty liver. This condition does not show clinical effects until the late stages, and may be reversible if the individual abstains from alcohol[8].

Alcoholic Hepatitis

The next stage in liver disease is hepatitis characterised by widespread hepatic inflammation and subsequent development of necrosis and subsequent scar tissue formation[9]. The inflammation is a result of overproduction of inflammatory mediators by activated Kupffer cells (liver macrophages) in response to tissue damage[7]. Long term consumption of alcohol stimulates liver cells to produce collagen, the basis of scar tissue[7]. Scar tissue is non-functional tissue and as it progressively replaces healthy liver tissue liver functionality is lost.

Cirrhosis

The final stage of liver disease is cirrhosis. This is characterised by fibrosis of the liver to such an extent that it stiffens blood vessels passing through the liver, and seriously alters liver structure and function[9]. In cirrhotic livers blood flow is directed around rather than through damaged areas of hepatic tissue thereby leaving toxins in the blood to affect other organs[8]. In cirrhosis there is the vicious circle of increased alcohol intake causing increased liver damage but the liver becomes less and less able to metabolise the alcohol, thus worsening and prolonging the damaging effects of alcohol. Cirrhosis has a high mortality rate, although death is usually from secondary causes, such as kidney failure[8]. It is estimated that ten to fifteen percent of alcoholics will develop alcoholic cirrhosis[10]. The potential to prevent this condition was clearly demonstrated during the period of Prohibition in the United States when the mortality rates from cirrhosis halved for the next twenty years[11].

Brain and Central Nervous System

The typical behaviour associated with intoxication (slurred speech, impaired reflexes and reaction times, unsteadiness, disorientation, confusion and emotional disturbances) is caused by

the action of alcohol on the brain and central nervous system (CNS)[12].

Neurotransmitters

Information is relayed throughout the brain by electrochemical signalling processes where activated neurons release neurotransmitters that bind to receptors on other neurons. Electrical signals travelling down neurons cause the release of neurotransmitters that cross the synaptic junctions between nerve cells in order to carry signals through the complex neural networks of the brain. According to some neurologists there are well over 100 different types of neurotransmitters and hundreds of different respective target receptors[13]. Any chemical interference with neurotransmitters can manifest in motor and behavioural changes evident in an intoxicated individual[12]. Alcohol induces alterations in many different neurotransmitters and their interactions with receptors. The main neurotransmitter systems affected are the glutamate, gamma-amino-butyric acid (GABA), dopamine, serotonin and opioid peptide systems.

Glutamate System

Glutamate is a major excitatory neurotransmitter in the brain and has numerous different receptors in the nervous system[14]. One such target is the N-methyl-D-aspartate (NMDA) receptor and is most sensitive to alcohol exposure even at low doses[12].

NMDA receptors mediate enhanced signal transmission referred to as long-term potentiation (LTP) associated with learning and memory[13]. Alcohol inhibits glutamate activity at NMDA receptors which can cause memory loss during intoxication (memory blackouts) and over time reduce learning ability. It is believed that this may contribute to the memory impairing effects of alcohol[12]. Spatial memory is also affected as the amount of glutamate released in the hippocampus of the brain is decreased. Due to inhibited glutamate activity, chronic alcohol use can cause more NMDA receptors to form particularly in the hippocampus, thalamus and the cerebral cortex[15]. Following episodes of alcohol consumption the amount of glutamate released then increases which can lead to hyperexcitabilty, seizures, cell death and possibly irreversible alcohol-induced neuronal damage during alcohol withdrawal[14].

Gamma-Amino-Butyric Acid (GABA) System

Gamma-amino-butyric acid (GABA) is a major inhibitory neurotransmitter in the CNS mediating fast synaptic inhibition throughout the brain[12]. GABA is sensitive to the effects of alcohol, causing enhancement of the function of $GABA_A$ receptors on postsynaptic neurones. This means that alcohol can bind to different sites on $GABA_A$ receptors to that of GABA improving the efficiency of receptor activation[12]. There is uncertainty as to which $GABA_A$ subtypes are affected by alcohol because the specific binding site has not yet been identified[14]. However, the effects of

alcohol have been observed at very low consumption levels, for example the alcohol from a single drink binds to $GABA_A$ receptors enhancing their function[13]. Alcohol has the ability to act on presynaptic neurons which causes an increase in the release of GABA in some synaptic junctions in the brain. This appears to cause some of the characteristic signs of intoxication such as a lack of motor coordination, reduced anxiety and sedation[12]. Chronic alcoholism causes alterations to the subunits on $GABA_A$ receptors which can in turn alter the effectiveness and timing of inhibitory synaptic transmissions. However the most noticeable effects can occur during alcohol withdrawal as the brain can become hyperexcitable, triggering seizures and anxiety[12].

Dopamine

Dopamine is a neurotransmitter that is part of the brain's mesolimbic system also known as the pleasure or reward centre[13]. The dopaminergic (dopamine activated) mesolimbic system is believed to be involved in functions such as the brain's mechanisms of reward, evaluation of environmental stimuli and general behavioural activity levels. Dopamine has a significant effect on brain function even though it is only produced by a limited number of brain cells and only acts on specific brain regions[12]. There are at least five different types of dopamine receptors and two of these classes have separate and in some cases opposing or synergistic effects on neuronal physiology. Alcohol acts on this system by increasing dopamine release. This has a stimulating and energising effect and the accompanying pleasurable sensations are mostly experienced during the first twenty minutes of alcohol exposure[13]. The elevation in dopaminergic transmission increases the firing rate of dopaminergic neurons thus increasing the amount of dopamine released in the mesolimbic system[14]. This appears to raise the extracellular dopamine levels in other regions of the brain connected by these neurones. Altered dopamine levels in other major brain structures have also been observed[12]. Furthermore, it is believed that dopamine plays a key role in alcohol addiction. As dopamine levels are decreased during alcohol withdrawal there is a reduction in neural firing causing melancholic feelings including depression and anxiety[14]. This can account for the typical feeling of needing to drink again to restore levels of dopamine and experience the associated pleasurable feelings.

Serotonin

The neurotransmitter serotonin (also known as 5-hydroxytryptamine or 5-HT) is involved in the regulation of mood, eating, arousal, sleep, pain perception and perception of other environmental stimuli[14]. It is a close chemical relative of dopamine. Serotonin is produced by small distinct clusters of neurons located at the base of the brain which are connected to other neurons throughout the CNS including those in the cerebral cortex

and other forebrain structures[12].

The consumption of alcohol acts to increase the amount of serotonin that is released, even after a single drink. This affects behaviours such as emotion, mood and cognitive thought in individuals[14]. In the presence of alcohol, each type of serotonin receptor produces different effects related to intoxication such as the perceived rewarding effects of alcohol as well as withdrawal symptoms. Serotonin can also stimulate an increase in dopamine production causing increased emotional behaviour and it may also affect the GABA system influencing decision making[14].

Opioid Peptide Systems

Certain protein peptides are able to function as neurotransmitters and are referred to as neuropeptides[12]. The three major types of opioid peptide include endorphins, dynorphins and enkephalins which contribute to the regulating of pain, mood, appetite, reinforcement and response to stress[14]. Alcohol enhances the activity of endogenous opioids by increasing their release in the brain, particularly from the pituitary and hypothalamus[16]. Alcohol also alters endogenous opioid peptide receptors[12]. However, it is not known how these effects contribute to intoxication. On the other hand chronic alcohol use can lead to reduced endorphin levels accounting for some of the negative emotional effects that are experienced during withdrawal[14].

Effects of Alcohol on Brain Structures

Alcohol not only affects chemical neurotransmitters but also brain structure itself. It has been demonstrated that alcohol can damage many regions of the brain and this damage may be either temporary or permanent. The degree of damage usually depends upon the age and gender of the individual, the period of time in which they have been drinking and the level of alcohol consumption. Damage to the brain due to alcohol intake occurs at lower consumption levels in women than men. Women may attain higher blood alcohol concentrations than men due to their smaller body size and lower concentrations of alcohol dehydrogenase in the liver. Therefore they reach the threshold for brain damage at lower levels of alcohol consumption compared to their male counterparts[17]. Research has also shown that with increasing age the brain becomes more vulnerable to the effects of alcohol consumption[18].

Brain Atrophy

Brain atrophy, or shrivelling of the brain, is characterised by the loss of neurons and connections between them[19]. This results in impaired functioning of activities that the damaged regions of the brain control. Furthermore, the consumption of alcohol has been linked with whole brain atrophy as well as atrophy of only certain regions of the brain. For example, in males aged 60-64 years of age, greater cortical atrophy in the frontal

and midtemporal lobes which is indicated by larger lateral ventricles and less grey and white matter, has been observed[17].

Neuroplasticity

Neuroplasticity refers to the brain's ability to change and reorganise itself throughout life by forming new connections between nerve cells and altering the activities of existing neurons. This is important as it allows the brain to compensate for injuries and to adjust to new experiences, situations and changes in the environment. The plasticity of neurons is often decreased by the presence of alcohol in the brain which is significant as it affects the interaction between neurotransmitters and their receptors, damaging brain function[16].

Hippocampus and Amygdala

Magnetic resonance imaging (MRI) studies indicate that alcoholics have decreased activation of neural centres such as the hippocampus and amygdala[20]. There is also reduced neuronal plasticity in these regions of the brain[21]. This appears to cause emotional and cognitive abnormalities which results in difficulty in detecting the emotional expressions of other people[21]. The amygdala is involved in responding to facial expressions, while the hippocampus remembers them. This has the potential to interfere with interpersonal relationships and can cause miscommunications which may lead to conflict or criminal behaviour. Diminished hippocampus and amygdala activity also provides an explanation for abnormal behaviour such as angry outbursts, emotional flatness and sensitivity[22]. Another contributor to this change in behaviour may be due to a reduction in the volume of the hippocampus observed in both alcoholic men and women[18].

Prefrontal Cortex

The prefrontal cortex is the part of the brain which decides whether an individual should take action or not[23]. A percentage blood alcohol level of about 0.08 has been shown to alter the function of NMDA receptor ion channels. This inhibition affects the ability of neurons to carry out their functions and in the prefrontal cortex it results in an inability to assess the consequences of an individual's reactions. This may contribute to poor decisions being made and uncontrolled behaviour by those consuming alcohol. In addition, it may be one of the reasons why alcoholics have difficulty controlling their drinking habits[23].

Cerebellum

The cerebellum is one of the main areas of the brain involved with motor control and coordination. It is adversely affected by alcohol, decreasing in size due to the shrinkage of large neurons in the anterior superior vermis[24]. Alcohol consumption also damages the granule cells and Purkinje cells that make up the cerebellar cortex. Purkinje cells are found throughout the cerebellum and are packed tightly into a single celled layer[2]. They are the

most abundant nerve cells found in the cerebellum and it has been found that chronic alcoholism has degenerative effects on these cells. This explains why chronic alcoholics often exhibit general co-ordination problems[2]. Thus, alcohol related damage to the cerebellum results in body and lower limb motor deficits which are seen as a lack of coordination and degraded sense of equilibrium, slurred speech, visual problems, as well as diminished higher order functions such as problem solving and memory. These effects are irreversible after chronic alcohol consumption[15].

Grey Matter and White Matter

MRI measurements have shown that the consumption of alcohol causes a reduction in cortical grey matter as well as grey matter in the superior frontal and parietal lobes[17]. Alcohol use also decreases the grey matter volume in the cerebral cortex which is the folded outer layer of the brain[24]. Alcohol can cause changes in white matter which are referred to as white matter hyperintensities (WHMs). WHMs are associated with brain atrophy, poor physical health and with cognitive, balance and gait deficits[17]. A decrease in white matter volume has been observed in those who consume alcohol compared to those who do not. This reduction in white matter may be explained by demyelination or changes in axonal integrity caused by alcohol[17]. Studies have also shown signs of fibre tract degradation, particularly of myelin in the frontal and superior brain regions of alcoholics and women display higher levels of degradation than men[24]. A reduction in white matter of the frontal and temporal lobes has been observed in those who consume alcohol compared to those who do not[24]. Therefore, there is a clear link between alcohol consumption and decreased total white matter volume.

Long term alcohol use has been shown to result in changes in the morphology, proliferation and survival of neurons. Furthermore, many studies have revealed that in alcoholics many brain structures have reduced volume compared to non-alcoholics. This has particularly been observed in the prefrontal cortex responsible for decision making, the amygdala, the corpus callosum and the cerebellum[25]. Studies have demonstrated that some of the structural and functional effects of alcohol on the brain may be reversed over time during a period of sobriety as the brain is able to regenerate some regions, thus improving cognitive, sensory and motor functions. This may occur through remyelination, cellular revoluming and neurogenesis[24]. However, some changes are permanent. Recovering chronic alcoholics particularly have impaired complex cognitive processes such as visuospatial abilities, psychomotor speed, gait, balance and executive functions like working memory, problem solving, temporal ordering and response inhibition[24]. Although the consumption of alcohol results in the impairment

of many functions it has been found that alcoholics sometimes are still able to achieve normal levels of performance as the brain compensates for the damage by using regions of the brain that are not usually used for the task. This has been termed "processing inefficiency" and although they may successfully carry out the task with accuracy it takes a lot longer to complete it than normal[24].

Despite the negative effects of alcohol, research suggests that a low intake of alcohol in certain specific population groups has a limited positive effect on brain health. For example it is believed that one drink a day may be neuroprotective which means that it allows individuals to experience less age-related brain atrophy[17]. It has also been suggested that low doses decrease the occurrence of WMHs and reduce the risk of cerebral infarction[17].

OTHER BODY SYSTEMS AFFECTED BY ALCOHOL

In addition to compromising the liver and CNS alcohol has numerous other detrimental systemic effects. It has serious negative effects on the cardiovascular system, the immune system, the gastrointestinal tract, the reproductive system, the bones, the pancreas and the blood.

Heart

When consumed in large quantities, alcohol can cause irregular heartbeat (arrhythmia), and even smaller doses of alcohol can increase heart rate (tachycardia)[26]. Heart irregularities have been linked to sudden death occurring among alcoholics[26]. In a study of sudden death in individuals between the ages of twenty and fifty, one remarkable autopsy finding indicated excessive fat in the liver[26]. This observation often normally correlates with high consumption of alcohol. However, these individuals did not have high concentrations of alcohol in their blood at the time of death, so while there is a definite link between alcohol and sudden death, the exact cause is more complicated than just arrhythmia or tachycardia caused by high levels of alcohol[26]. Another potentially serious cardiovascular effect is increasing blood pressure[27]. Long term heavy drinking also has negative effects on the heart muscle, causing enlargement of the heart and a loss of some contractility resulting in insufficient blood flow to the rest of the body[28]. Alcohol may also cause an increase in the amount of triglycerides found in the blood[29]. Increased triglyceride levels are associated with hypertension and coronary artery disease[29].

Blood

Alcohol also has several negative effects on blood. It has direct toxic effects on bone marrow where the blood cells are produced, the precursor cells that blood cells derive from, and on the mature blood cells themselves[30]. It also has indirect effects, through nutritional deficiencies and other metabolic problems[30]. There are also effects on blood biochemistry and enzymic reactions.

Combined, these direct and indirect effects can result in decreased production of red and white blood cells, as well as platelets[30]. Alteration of the structure and metabolic function of the red blood cells can also result[30]. In alcoholics large fluid filled vacuoles are found in cellular precursors to red and white blood cells and are an indicator of recent heavy drinking[30]. The resulting appearance of macrocytes (enlarged red blood cells) is common among heavy drinkers and this can be used as a relatively reliable method for identifying people who drink to excess[30]. Alcohol abuse also causes several types of anaemia by interfering with the production of red blood cells in such a way that they are structurally defective and are consequently destroyed more rapidly than normal healthy cells[30]. Alcohol also decreases the numbers of platelets in the blood decreasing the ability of the blood to stop bleeding.

Gastrointestinal Tract

There are many different ways in which alcohol can negatively affect the gastrointestinal tract as it comes into contact with the alcohol in its most concentrated form. Alcohol is absorbed into the blood stream by simple diffusion through the walls of the stomach and small intestines[31]. Alcohol can directly impair the function of the oesophageal muscles, leading to heartburn[31]. Alcohol increases the permeability of the walls of the small intestine to toxins which can lead to liver damage during detoxifying processes[31]. Alcohol also inhibits the absorption of nutrients in the small intestine possibly leading to weight loss and also malnutrition[31].

The mouth and throat are the first parts of the body to come into contact with alcohol. There is a definite link between alcohol consumption and cancers of the mouth, tongue and throat[31]. The risk of oesophageal cancer is increased by damage caused by alcohol to the mucosal lining of the oesophagus[31]. There is also a stronger cancer risk for individuals who both drink and smoke, as the alcohol solubilises the carcinogens found in the cigarettes and increases membrane permeability thus increasing carcinogenicity[31].

Pancreas

Alcohol has two important negative effects on the pancreas. Firstly, as liver cells break down alcohol, the breakdown products exert toxic effects on pancreatic cells, and can lead to acute pancreatitis . When the pancreas becomes inflamed, the digestive enzymes that it normally produces leak out, and begin to digest the pancreas itself[32]. This leads to chronic pancreatitis, which causes destruction of the pancreas that is irreversible[32]. The major cause of chronic pancreatitis is the excessive use of alcohol[32].

Reproductive System

There have been several studies investigating whether alcohol has any effect on fertility and the ability of women to conceive. It was found that among women who drank moderately

their chances of falling pregnant were greatly decreased by their alcohol intake[33]. It was also found that there was a much higher risk of menstrual disturbance, abortion and miscarriage among alcoholic women[34]. These studies would suggest that women aiming to fall pregnant abstain from drinking all alcoholic beverages[33].

Immune system

Acute bacterial infections are found to be more common among alcoholics suggesting that alcohol has a detrimental effect on some components of the immune system[30]. Normally when an individual has a bacterial infection, the numbers of neutrophils (white blood cells) in the blood are found to be increased[30]. In alcoholics the numbers of neutrophils are decreased contributing to suppression of the immune system and the reduced ability to deal with infections effectively[30]. In the presence of alcohol the movement of neutrophils to the site of an infection is slowed quite considerably[28]. This indicates that even individuals who drink only moderately are compromising their immune systems by doing so.

Bones

There appears to be a well documented link between heavy drinking and osteoporosis. These effects are more pronounced in older individuals, however heavy drinking during the teen years increases the risk of osteoporosis later in life[28]. This osteoporosis risk seems to be due to the fact that heavy alcohol use weakens the bones, making them more fragile by decreasing their density[35]. Studies have also shown that there is increased risk of bone fracture for alcoholics[28].

Mother-Foetal Metabolism of Alcohol

In a pregnant woman, the metabolic breakdown of alcohol occurs a lot slower and with less efficiency when compared to a woman who is not pregnant[28]. This is due to the presence of oestrogens in the mother's blood. Oestrogens (particularly oestradiol) inhibit the functioning of ADH and ALDH resulting in a slower metabolism of alcohol by the liver. The levels of oestrogen in the blood are raised 10-100 times in the first stages of pregnancy, and this increases to 100-1000 times in the last half of pregnancy[28].

The metabolism of alcohol in the body has no feedback mechanism, thus the body is unable to increase or decrease the rate at which alcohol is broken down. The rate at which the liver breaks down alcohol is about 7 grams per hour[28]. However, as the metabolism of alcohol is less efficient in a pregnant woman's body, this rate is decreased by one and a half times[28]. Therefore, it will take 1.5 times longer for the mother to completely metabolise a glass of alcohol compared to a non-pregnant woman. A foetus has very limited ability to metabolise alcohol as the foetal liver only produces small amounts of ADH from the middle of the third month onwards[28].

Although the production of ADH in the foetal liver steadily increases over the pregnancy in a linear fashion, the amount is insignificant compared to the levels produced by the mother's liver. Consequently alcohol passing into the circulatory system of the foetus is largely unmetabolised. This has harmful effects on the foetus as half of the alcohol in the mother's blood (or more if she has a compromised liver) crosses the placental wall and directly enters the foetal circulatory system.

Foetal Alcohol Syndrome and Teratogenicity of Alcohol

Foetal alcohol syndrome (FAS) manifests as birth defects primarily affecting the developing brain. The cause of FAS is exposure of the foetus to alcohol during pregnancy with the most dangerous period being the first trimester[36]. The effects of the FAS endure throughout the lifetime of the individual; however the effects may change as the person ages[37]. Common characteristics of FAS include growth retardation of the foetus in utero, postnatal growth retardation, underweight during childhood and microcephaly (smaller head than normal due to poor development of brain)[38], mental retardation, hyperactivity, underdeveloped muscles, typical facial features such as a rounded forehead, and improper development of other organs such as the heart and genitals[36]. There are also increased risks of miscarriage, stillbirths, neonatal morbidity, neonatal death and much reduced longevity.

Alcohol is also classified as a teratogen, meaning that it is able to impair normal development and cause birth defects in the offspring due to exposure during pregnancy[37]. Teratogens may cause four main types of complications in offspring, including death, disfigurement or malformed body parts, stunted growth, and problems in systemic functions. These four complications are all commonly associated with FAS.

There is a dose-response relationship where the alcohol dose directly relates to effects on the offspring. With respect to FAS the more the mother drinks during her pregnancy, the more likely it is that there will be adverse neonatal complications and birth defects in the baby[39]. The timing of when the mother drinks is also important, as the alcohol will only affect the tissues that are developing at that time. If the mother drinks early on in the pregnancy during embryonic formation the baby will have a greatly increased risk of structural defects and malformations[37]. However if the mother only drinks in the last trimester when the foetus is mostly growing in size, the baby will be born smaller than usual. Additionally, since the brain is developing throughout the duration of pregnancy, the brain will be affected by alcohol at any stage[37]. The drinking pattern of the mother is also very important in relation to how the foetus develops. Occasionally binge drinking will affect the foetus differently to regular light exposure[37].

Alcohol has a direct toxic effect on the foetal brain (as in the adult brain) promoting cell death. The foetal hippocampus, cerebellum, corpus callosum (which coordinates left and right side activity), and cortex are specific areas of the brain targeted by alcohol. In the developing brain alcohol also impairs the transport of amino acids and glucose and may reduce the amount of oxygen available to the foetus by affecting placental blood flow. Alcohol may also impact the endocrinal and chemical systems in the body which regulate the development of nerve cells in the brain[37].

Positive Effects of Alcohol? Red Wine vs Grape Juice

It is observed that French population groups have considerably lower mortality rates related to coronary heart disease despite their diet containing foods that are high in fat. This has become known as the 'French Paradox' and is thought to be associated with the regular consumption of red wine[40]. It has been demonstrated that it is not only the consumption of red wine that is associated with a reduced risk for cardiovascular disease, but also the consumption of grapes and grape juice[41]. There is significant evidence suggesting that such health benefits are associated with the antioxidant properties of polyphenols found in grapes rather than the alcohol content of the wine itself.

Polyphenols help prevent the oxidation of low-density lipoproteins (LDL - also known as 'bad cholesterol') which is associated with the formation of atherosclerotic plaques on arterial walls leading to coronary heart disease[42]. These plaques contribute to blockages in coronary arteries and are also associated with blood clot formation. Polyphenols found in purple grape juice act to reduce adhesion of blood platelets and the subsequent clot formation associated with acute coronary events such as heart attacks[43]. Further, consumption of purple grape juice is also associated with arterial vasodilatation[44]. Arterial vasodilatation leads to better blood flow in coronary arteries which also contributes to a lowered risk of cardiovascular disease.

Thus evidence would suggest that the health benefits of red wine intake observed in the French Paradox are associated with grape polyphenols and are independent of the alcohol content of the red wine. The intake of purple grape juice has the obvious benefit of reducing cardiovascular disease risk without the increased systemic health risks associated with alcohol consumption.

CONCLUSION

The consumption of alcohol not only affects physical structures of the body such as the liver and brain, but also physiological processes and behaviour. These effects may be permanent if alcohol consumption is continued over a prolonged period of time or may be partly reversible if consumption is

ceased. While the body does have the capacity to metabolise alcohol through hepatic metabolic pathways these processes may eventually function inefficiently as the tissues involved with alcohol metabolism become damaged. The consequences of short and long term interference with brain neurotransmitters and altered brain structure argue strongly against alcohol consumption. The Christian would consider the intellect and the ability to make intelligent and informed decisions a part of being created in the image of God. Thus any chemical interference with brain structure or neurotransmitter function would work against this concept. Impaired immune system function renders the body more susceptible to infectious disease. The development of atherosclerosis with associated cardiovascular complications is accelerated with alcohol intake. With respect to cardiovascular disease, the benefits observed in the 'French Paradox' appear to be associated with the ingestion of antioxidants found in red grape juice.

The decision to drink alcohol should be informed by contemporary research into its short and long term effects. Deciding to ingest alcohol as an individual may have ramifications for not only individual health and well being but may have ramifications for others as well. Antisocial behaviour, implications for marriage and family, risk of accident and injury should also be considered. The consequences of alcohol consumption are rarely restricted to the individual. Possibly the most serious consequence of alcohol consumption is that imposed on the foetus in pregnant women who decide to drink. The risk of foetal alcohol syndrome for the unborn is a serious matter and due consideration should be given to the fact that the foetus has no choice in its exposure to alcohol. The long term consequences of foetal alcohol syndrome need to be weighed.

Perhaps Christian temperance movements may appear restrictive in terms of free will choices. The free will choices of individuals should be respected in all aspects of life, including the decision to consume alcohol. However, any decision that has serious consequences for the individual and those with whom they associate (and especially with respect to foetal development) should be as informed as possible. Given the wealth of material now available reporting on the negative effects of alcohol consumption it is possible to be intelligently informed regarding the choice of whether to consume alcohol or not. There is certainly sufficient evidence to suggest that abstinence from alcohol consumption, while appearing unpopular to some, may be an intelligently informed and respected option to alcohol consumption.

DISCUSSION QUESTIONS:

1. Where does Christian responsibility lie with respect to personal decisions regarding the use of alcohol and other recreational drugs?

2. What could be done to enhance public discussion regarding the problems of alcohol in society?

3. Discuss the unique health benefits associated with the 'French Paradox'. What other lifestyle choices have direct effects on health? Consider the Mediteranean and Okinawa diets.

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