Despite the pervasiveness of alcohol, its physiological effects are often overlooked or misunderstood. Discussion on the effects of alcohol often brings to mind drunk-driving and lowered inhibitions. However, the effects of alcohol on the body are much more subtle and comprehensive than impaired motor skills and judgement. In understanding the biological consequences of alcohol, better decisions can be made.

Chemistry

Beverages are considered alcoholic if they contain the chemical ethanol. Ethanol, C₂H₅O, is a polar molecule consisting of a two-carbon chain, and a hydroxyl (–OH) side group (Fig. 1). The non–polar covalent bonds between carbon and hydrogen and the polar covalent bonds between oxygen and hydrogen allow ethanol to be miscible in both hydrophobic (water–based) and hydrophilic (lipid–based) solutions. Moreover, the partial separation of charge between hydrogen and oxygen in the –OH group also permits hydrogen bonding with other substances.

Cellular Effects

In aqueous solutions, ethanol forms hydrogen bonds with water, disrupting the organization of the water molecules. Consequently, the presence of alcohol affects the hydrophilic interactions occurring on the cell membrane, including receptor and channel function. Normal ion flow is thus disrupted. This can cause cells to become dehydrated and eventually lyse. Active ion transporters also utilize additional adenosine triphosphate (ATP). In an attempt to maintain proper balance, increasing the energy demand of the cell. The hyper–metabolic state that ensues can induce tissue–wide hypoxia (lack of oxygen) and eventually necrosis (cell death). Due to its small size and lipid solubility, ethanol can also move through the membrane by passive diffusion. Once inside the cell, it can induce apoptosis, or programmed cell death, by activating enzymes called caspases. When broken down, ethanol also produces acetaldehyde, which can react irreversibly with both nucleic acids and proteins, compromising their function and successful repair (7). Free radicals are another potent by–product of ethanol metabolism that can cause oxidative stress, leading to lipid peroxidation and further damage to nucleic acids and proteins (Fig. 2) (10). In addition to its direct effects, ethanol can bind to specific neurotransmitter receptors, including NMDA, GABA, acetylcholine, and serotonin types, thus affecting nervous system activity.

Consumption

Before discussing the effects alcohol has on the different parts of the body, it is necessary to consider how alcohol is consumed. Additionally, the acute and chronic effects of drinking alcohol depend on the amount consumed per sitting. Ethanol is ingested through the mouth and absorbed through the stomach and intestinal lining, where it enters the bloodstream. Because ethanol can cross the blood–brain–barrier (BBB), it can affect virtually every cell in the body; however, it does not do so equally, as cell types are differentially sensitive. Finally, the alcohol is filtered out by the liver where it is broken down.

Mouth

Alcohol use is correlated with cancer of the mouth, a trend maintained for both moderate and heavy drinkers (4). This increased risk is facilitated in part by the activity of acetaldehyde, which impairs cellular DNA repair machinery (5). Consequently, mutations associated with cell division, which would normally be corrected, become permanent. Chronic alcohol abuse can also cause hypertrophy of the parotid gland, the largest salivary...
Ethanol also increases gastric transit time (how long food stays in the stomach). This allows for an early bacterial degradation of food, leading to feelings of fullness and abdominal discomfort. Chronic alcoholism decreases the gastric secretory capacity of the stomach, reducing its ability to destroy the bacteria in food. These deleterious effects can result in bacterial overgrowth and colonization of the duodenum, the upper small intestine.

Intestine

Ethanol decreases impeding wave motility, a process that retains food for further digestion in the small intestine and compaction in the large intestine. Reducing this movement causes diarrhea and a loss of nutrients. In addition, ethanol also inhibits nutrient absorption. Chronic alcoholism leads to decreased absorption of proteins, carbohydrates, fats, and some vitamins, which can contribute to malnutrition and weight loss (2). Ethanol also interferes with enzymes, including those involved in nutrient transport and digestion, like lactase. Heavy drinking can cause duodenal erosions and bleeding by damaging the intestinal mucosa and disturbing the integrity of the epithelium.

Ethanol also decreases prostaglandin synthesis and induces the release of cytokines, histamine, and leukotrienes. The ensuing inflammatory response can damage capillaries and lead to blood clotting and impaired transport of fluids. Consequently, fluid accumulates under the tips of villi causing their destruction. The resulting lesions increase intestinal permeability, allowing toxins into the bloodstream and lymphs, potentially harming other organs.

Pancreas

Alcohol elevates the synthesis of digestive enzymes in pancreatic acinar cells. Concomitant with this upregulation is an increase in the fragility of lysosomes (vesicles containing digestive enzymes) and zymogen granules (cellular packages containing enzyme precursors). This is due to the ethanol–induced accumulation of fatty acid ethyl esters (FAEEs) and reduced GP2 content of zymogen granule membranes. Consequently, these containers tend to lyse, causing auto–digestion of cells by trypsin and other enzymes. Chronic alcoholism can cause pancreatitis which is characterized by widespread tissue atrophy, fibrosis (tissue scarring), and calcification of the pancreas (8).

Circulatory System

Ethanol increases plasma high–density lipoprotein (HDL) levels, decreasing the risk for coronary artery disease (CAD) (3). Ethanol also reduces the chance of thrombosis (formation of a blood clot) by disrupting platelet function. This effect is facilitated by increased formation of prostacyclin, which inhibits platelet aggregation. Elevated levels of the enzyme plasmin also increase the rate of clot dissolution. As a result, there is a decreased risk for embolus (detached intravascular mass) formation, myocardial infarction (heart attack), and ischemic (restricted blood supply) stroke in moderate drinkers.

On the other hand, heavy drinking can cause dilated cardiomyopathy, which is characterized by low cardiac output and hypertrophy of the heart and can lead to congestive heart failure. This occurs because alcohol alters the permeability of the sarcoplasmic reticulum for Ca²⁺ ions, which are required for muscle contraction. In addition, ethanol decreases the synthesis of actin, myosin, and mitochondrial proteins. High blood alcohol content (BAC) also reduces the oxygen supply to cardiac muscle.

Chronic alcoholism can induce atrial fibrillation (irregular heart beat), premature beating, supraventricular tachycardia (rapid heart rhythm), and ventricular arrhythmias (abnormal heart rhythm originating in
the ventricles of the heart). In turn, these conditions can increase clot formation and the propagation of existing clots, which raises the risk for ischemic stroke. Additionally, Ethanol blocks the action of folate, which is used in red and white blood cell synthesis, lowering immune defense and blood health.

**Kidneys**

Acute ethanol consumption prevents kidney function by inhibiting the secretion of anti–diuretic hormone (ADH), or vasopressin, from the pituitary gland (1). As a result, diabetes insipidus (DI) can occur. DI is a condition in which water retention, which is normally regulated by ADH, is blocked, causing the body to become dehydrated. Chronic alcoholism can also cause permanent renal dysfunction, hypophosphatemia, hypomagnesaemia, hypokalemia, and aminoaciduria.

**Peripheral Nervous System**

Ethanol enhances the effects of GABA, an inhibitory neurotransmitter, by binding to its receptors. Consequently, intoxicated individuals experience decreased sensation in their peripheral nervous system (PNS).

Chronic alcoholism, however, can lead to a condition called alcoholic polyneuropathy. Alcoholic polyneuropathy is characterized by the degeneration of motor and sensory neuron axons in the PNS caused by the segmental thinning of myelin. This is especially harmful because the thinning myelin increases action potential leakage, producing further degeneration. These effects manifest themselves as pain, motor weakness, and eventually muscle atrophy.

**Liver**

The liver is the primary site of alcohol metabolism. As such, it is exposed to the acetaldehyde and free radicals that are produced by ethanol catabolism. Exposure to these molecules facilitates cell apoptosis.

The liver is also exposed to endotoxins. Endotoxins, which enter the bloodstream through lesions in the small intestine, bind to the CD14 receptor on Kupffer cells (immune cells which reside in the liver). Bound cells release cytokines and interleukins such as tumor necrosis factor (TNF), and radical oxygen species (9). These molecules induce an inflammatory response that damages the liver tissue.

Ethanol also increases the expression of iron transporter proteins, causing iron stores in the liver to expand. Because iron catalyzes the production of free radicals, this increased storage can be harmful.

By these mechanisms, chronic alcoholism can induce steatohepatitis. Steatohepatitis is a condition in which fat accumulates in the liver tissue. When combined with cell death, steatopatitls leads to hepatic fibrosis (scarring of the liver). The scar tissue that forms disrupts the structure of the liver, inhibiting the normal regeneration of hepatocytes (liver cells). From here, the pathology can progress to liver disease, cirrhosis of the liver, and cancer (Fig. 3) (6).

**Conclusion**

Alcohol can affect the body in a variety of harmful ways used in excess. On other hand, when consumed in limited amounts, alcohol can improve cardiovascular health, decreasing the risk for heart attack and stroke (Fig. 4). Like most things, moderation is key.

**References**