The Pathology of Alcohol Use and Abuse

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ABSTRACT

Alcohol is the most widely abused substance in the United States and its pathology is responsible for more pathological conditions than all other forms of drug use combined.[1] Alcohol dependence is associated with a number of adverse individual and societal consequences[2,3] and high rates of morbidity and mortality.[4] Alcohol use and abuse have a significant pathological effect on the brain, fetus, liver, heart, pancreas, and immune system.[2] Cancer risks have also been attributed to alcohol use and abuse.[5] Assessing acute and chronic alcohol consumption is critical to effective treatment but unfortunately currently available clinical laboratory testing procedures lack the ability to inform alcohol treatment providers about use and abuse.[6]

ABBREVIATIONS: DSM-IV-Diagnostic and Statistical Manual of Mental Disorders, FAS-fetal alcohol syndrome, HDL-high density lipoprotein

INDEX TERMS: Abuse, Addiction, Alcohol Dependence, Pathology, Use.

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INTRODUCTION

Many cultures around the world use alcohol to celebrate special occasions, to socialize, and to self-medicate during trying times.[7] While alcohol is legal in the United States, the abuse of alcohol has health, social and legal implications. Alcohol abuse can have serious health effects including weakening of the immune system, contributing to cancers, and damage to internal organs.[2] Alcohol is known to affect people in different ways due to genetics, an individual's environment and diet which all culminate in the effect of alcohol on an individual and in alcohol related diseases.[4]

Alcohol consumption is measured by what is referred to as a "standard drink" and this measurement helps assess the risks an individual undertakes per given time period.[7] One standard drink contains 0.6 fluid ounces or 14 grams of pure alcohol (ethanol). Another way of viewing this is as follows:

- 12 fluid ounces of beer (about 5% alcohol)
- 8 to 9 fluid ounces of malt liquor (about 7% alcohol)
- 5 fluid ounces of table wine (about 12% alcohol)
- 1.5 fluid ounces of hard liquor (about 40% alcohol).

Using this definition, research has shown that "low-risk" drinking levels for males are four or less drinks on any single day and no more than 14 drinks per week. For females, it is three or less drinks in any single day and no more than 7 drinks per week.[7] Individuals over the age of 65 should consume no more than 3 drinks per day or 7 drinks per week.[8] It is recommended that people who should abstain from alcohol completely include those who:

- Plan to drive a vehicle or operate machinery;
- Are pregnant or trying to become pregnant;
- Take medications that interact with alcohol; and
- Have a medical condition aggravated by alcohol.[8]

Alcohol use is categorized into three categories.[10] These are use, abuse, and addiction (DSM-IV uses the word dependence instead of addiction). The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) is a coding manual published by the American Psychiatric Association that includes all currently recognized mental health disorders. Use is defined as the consumption of alcohol in a social manner that does not create problems for the user. Abuse is the misuse of alcohol that leads to intoxication and/or behavior that is counterproductive for the individual. Addiction on the

other hand is a state where the individual becomes dependent on alcohol and feels a need to consume alcohol which often leads to tissue destruction.

Alcohol Effects on Health

The brain is an elaborate network of connections that drive the physical and psychological processes. Alcohol causes a disruption that can have long lasting consequences by changing the way the brain works which results in an array of assorted problems.[11] The structure of the brain is complex and it includes multiple systems that interact to support the body's functions including cognition, breathing, and muscle movement.[12] The multiple brain structures communicate with each other through over a trillion nerve cells termed neurons.[12] Neurons in the brain transform information into electrical and chemical signals the brain can understand.[12]

Chemicals termed neurotransmitters carry messages between neurons.[12] The brain is constantly balancing the neurotransmitters that speed things up and the ones that slow things down to create stability.[12] Alcohol can alter the tempo of communication between neurotransmitters in the brain.[4] Heavy alcohol consumption (even on a single occasion) can disrupt the delicate balance of neurotransmitters.[11] Acute alcohol intake can cause sluggish neurotransmitter relays causing extreme drowsiness, trigger mood and behavioral changes, including depression, agitation, memory loss, seizures and loss of executive control.[11]

There still is much that is not understood about the brain's working mechanisms and how alcohol affects those mechanisms. Researchers are constantly developing a better understanding about how alcohol interrupts communication pathways in the brain and changes the brain's structure, as well as the resulting effects on behavior and functioning.[12] Using brain imaging and psychological tests, researchers have identified the regions of the brain most vulnerable to alcohol's effects.[13] These include:

- **CEREBELLUM** – This portion of the brain controls motor coordination. Damage to the cerebellum results in a loss of balance and may affect cognitive functions such as memory and emotional response.
- **LIMBIC SYSTEM** – This system is a complex one that orchestrates a variety of tasks such as memory and emotion. Damage to the limbic system impairs the orchestration of these functions.
- **CEREBRAL CORTEX** – This region of the brain directs our abilities to think, plan, behave intelligently, and interact socially. This area also connects the brain to the rest of the nervous system. Damage to the cerebral cortex may impair memory, the ability to solve problems, and to learn.

Long-term, heavy drinking causes changes in the actual neurons including reductions in the size of brain cells.[11] As a result brain mass shrinks and the brain's inner cavity grows bigger.[12] These changes often affect a wide range of abilities, such as motor coordination; temperature regulation; sleep; mood; and various cognitive functions, including learning and memory. One neurotransmitter particularly susceptible to even small amounts of alcohol is the glutamate which affects memory.[14] Researchers believe that alcohol interferes with glutamate action, resulting in temporary "black outs," or forgetting much of what happened during a night of heavy drinking.[14] This mechanism also accounts for gradual loss of other cognitive functions.

The brain tries to compensate for these disruptions by having the neurotransmitters adapt to the presence of alcohol.[14] Unfortunately, these adaptations can have negative results, including alcohol tolerance, developing alcohol dependence, and experiencing alcohol withdrawal symptoms.[14]

Liver Damage that Affects the Brain

Liver disease due to alcohol abuse also damages the brain.[15] This is because the liver breaks down alcohol and its associated toxins. During this process, alcohol's byproducts damage liver cells so they no longer function as well as they should they then allow toxic substances (ammonia and manganese in particular) to travel to the brain.[15] These substances cause a serious and potentially fatal brain disorder known as hepatic encephalopathy.[16] Hepatic encephalopathy causes a range of problems including:[16]

- Sleep disturbances;
- Mood and personality changes;
- Anxiety;
- Depression;
- Shortened attention span;

- Coordination problems, including asterixis, which results in hand shaking or flapping;
- Coma; and
- Death.

Hepatic encephalopathy can be treated with compounds that lower blood ammonia concentrations and medical devices that remove harmful toxins from the blood.[16] In severe cases, patients suffering from hepatic encephalopathy require a liver transplant.[16]

Fetal Alcohol Spectrum Disorders

Alcohol can affect the brain at any stage of development including during fetal growth. Fetal alcohol spectrum disorders include the full range of physical, learning, and behavioral problems, and other birth defects.[17] The most serious of these disorders is the fetal alcohol syndrome (FAS), which is characterized by abnormal facial features and is associated with severe reductions in brain function and overall growth.[17] The Centers for Disease Control report that FAS is the leading preventable birth defect associated with mental and behavioral impairment in the United States today.[18]

The brains of children born with FAS are smaller than normal and contain fewer cells and neurons.[19] Current research is studying whether the brain function of children and adults with FAS can be enhanced with complex rehabilitative training, dietary supplements, or medications.

Effects on the Heart

Alcoholic Cardiomyopathy - Long-term heavy drinking will weaken the heart muscle, resulting in a condition called alcoholic cardiomyopathy.[20] A weakened heart droops and stretches and it is therefore unable to contract effectively.[20] As a result, the heart cannot pump enough blood to sufficiently nourish the organs causing severe damage to organs and tissues. Symptoms of cardiomyopathy include shortness of breath and other respiratory issues, fatigue, swollen legs and feet, and an irregular heartbeat that can lead to absolute heart failure.[20]

Arrhythmias – Even binge drinking can affect the pace at which a heart beats.[21] The heart's internal pacemaker keeps the heart pumping consistently and at the appropriate speed. Often alcohol disrupts the pacemaker causing the heart to beat rapidly or irregularly.[21] These heart rate abnormalities are referred to as arrhythmias. The two types of alcohol related arrhythmias are:[21]

- **ATRIAL FIBRILLATION** – During this arrhythmia, the heart's upper, or atrial, chambers shudder weakly but do not contract as they should. Blood can pool and/or clot in the upper chambers. If a blood clot does develop and travels to the brain, a stroke occurs. Should the clot travel to other organs such as the lungs, an embolism occurs.

- **VENTRICULAR TACHYCARDIA** –This arrhythmia occurs in the heart's lower, or ventricular, chambers. Electrical signals travel through the heart's muscles, prompting contractions that keep blood flowing. Alcohol-induced damage to heart muscle may cause electrical impulses to loop through the ventricle too many times, causing excessive contractions. As a result the chambers do not fill up with sufficient blood between each beat. In turn the rest of the body does not get enough blood causing dizziness, lightheadedness, unconsciousness, cardiac arrest or sudden death.

Strokes

When blood cannot reach the brain a stroke occurs. About 80 percent of strokes are the result of a blood clot preventing blood flow to the brain.[22] These are termed ischemic strokes. Another reason for a stroke is blood accumulating in the brain or in the spaces surrounding the brain and these are termed hemorrhagic strokes.[22]

Clinicians attribute binge drinking or long-term heavy drinking to strokes regardless of a history of coronary heart disease.[23] Recent studies show that those who binge drink are 56% more likely than persons who never binge drink to experience an ischemic stroke.[23] Binge drinkers also are about 39% percent more likely to suffer any type of stroke when compared to people who never binge drink.[23] It should be noted that alcohol exacerbates the problems associated with strokes such as hypertension, arrhythmias, and cardiomyopathy.[23]

Hypertension

Chronic alcohol use, as well as binge drinking, can lead to hypertension.[23] A healthy blood vessel is elastic in nature, stretching as the heart pumps blood through the vessel. Hypertension occurs when the blood vessels stiffen, making them less flexible, thus increasing the pressure within the vessels. Adding to this event heavy alcohol consumption prompts the release of certain stress hormones that constrict blood vessels.[23]

Research shows that healthy people who drink moderate amounts of alcohol may have a lower risk of developing coronary heart disease than nondrinkers.[5] This research defines moderate drinking as no more than two drinks in a given day for men and one drink per day for women who are not pregnant or trying to conceive.

Other recent studies show that moderate drinking helps inhibit and reduce the build-up of fat in the arteries.[24] It can also raise the levels of HDL in the blood, which help prevent heart disease. Moderate drinking can help safeguard against heart attack and stroke by averting blood clots from forming and by dissolving blood clots that do develop.[24] Drinking moderately has also been shown to help keep blood pressure levels in check.[24]

Careful consideration must be given to these benefits because they may not apply to people with existing medical conditions, or who take certain medications. An important note is that researchers discourage people from initiating moderate drinking simply for the health benefits.[24]

Biliary Effects

Morbidity and mortality statistics show that liver disease is one of the leading causes of illness and death in the United States.[25] Alcohol abuse is attributed to more than 2 million Americans suffering from liver disease.[25] For the most part liver disease strikes people who abuse alcohol over many years.

Risk factors tend to be individualistic and include gender, genetics, alcohol accessibility, social customs pertaining to drinking, cigarette smoking, obesity and poor diet.[26,27] These can affect a person's susceptibility to alcoholic liver disease. Research shows that about one in five heavy drinkers will develop alcoholic hepatitis, while one in four will develop cirrhosis.[27]

One of the foremost functions of the liver is to store energy and nutrients.[26] The liver also produces proteins and enzymes that thwart disease.[26] Perhaps the best known function of the liver is to rid the body of dangerous substances such as toxins. The liver recognizes alcohol as a harmful substance and breaks most of it down.[26] Unfortunately, the process of breaking down alcohol generates toxins yet more harmful than alcohol itself.[26] The resulting toxins damage liver cells, promote inflammation, and weaken the body's natural resilience.[27] Ultimately, these problems will disrupt the body's metabolism and impair the utility of other organs.[27] Because the liver plays such a vital role in alcohol detoxification, it is particularly vulnerable to impairment from excessive alcohol.

One cause for fat build up in the liver is heavy drinking (even if for just a few days).[28] The result of fat building up in the liver is referred to as steatosis, or more commonly known as a fatty liver. This is the earliest stage of alcoholic liver disease.[28] The excessive fat is grueling for liver functioning and heartens the development of dangerous inflammations, such as alcoholic hepatitis.[28] Interestingly alcoholic hepatitis does not present obvious symptoms for some individuals. However, for others alcoholic hepatitis presents symptoms of fever, nausea, appetite loss, abdominal pain, and mental confusion.[28] As the severity of alcoholic hepatitis increases, the liver becomes dangerously enlarged, resulting in jaundice, excessive bleeding, and clotting complications.[28]

Fibrosis is a liver condition where scar tissue builds up in the liver as a result of heavy drinking.[26] The chemicals in the liver that are needed to break down and remove this scar tissue are altered by alcohol resulting in diminished liver function.[26] Continued consumption of alcohol promotes excessive scar tissue build up resulting in a condition called cirrhosis, which can be thought of as a slow deterioration of the liver. Complications such as jaundice, insulin resistance and type 2 diabetes, and liver cancer, may result as cirrhosis diminishes liver function.[26]

A variety of lifestyle changes can aid in addressing alcoholic liver disease. The first and most effective change is abstinence from all alcohol.[28] Abstinence from alcohol will prevent further injury to the liver. However, when cirrhosis becomes severe, a liver transplant may be the principal treatment option.[26,27]

Pancreatic Considerations

Many people who suffer from problems of the pancreas are also heavy drinkers. Pancreatitis is often caused by habitual and excessive drinking which damages the pancreas.[29] The risk of developing pancreatitis increases as excessive drinking continues over time, but only about 5% of people with alcohol dependence will develop pancreatitis.[31] For unknown reasons some people are more susceptible to the disease than others, but researchers have not yet identified what factors (e.g. genetic, environmental) contribute to the disparity.[31]

The pancreas is vital in food digestion and its conversion into fuel for the body. The pancreas delivers enzymes into the small intestine that digest carbohydrates, proteins, and fat.[30] The pancreas also secretes insulin and glucagon, two hormones that regulate the process of utilizing glucose and controlling glucose levels.[30] Alcohol consumption damages pancreatic cells and impacts the metabolic processes involving insulin.[29,30] This often leads to pancreatic inflammations.

A healthy pancreas secretes enzymes to the small intestine for the metabolizing of food. Alcohol interferes with this process by causing the pancreas to secrete its enzymes internally, rather than sending them to the small intestine.[29] These enzymes (as well as acetaldehyde) are harmful to the pancreas.[29] The process can cause inflammation, as well as swelling of pancreatic tissues and blood vessels. This inflammation is called pancreatitis, and it prevents the pancreas from functioning properly. Pancreatitis occurs as a sudden attack, and is referred to as acute pancreatitis.[29] If excessive drinking continues, the inflammation can become constant and worsen.[30] When this happens the condition is known as chronic pancreatitis.

Pancreatitis is also a known risk factor for pancreatic cancer.[31] Someone who is a heavy drinker may not detect pancreatic damage until they experience an attack. An acute pancreatic attack may consist of the following symptoms:

- Abdominal pain, which may radiate up the back;
- Diarrhea;
- Fever;
- Nausea and vomiting;
- Rapid heart rate; and
- Sweating.[31]

Chronic pancreatitis may trigger these same symptoms as well as blood sugar problems.[30] Chronic pancreatitis will slowly destroy the pancreas leading to diabetes or possibly death.[30]

Abstinence from alcohol can slow the progression of pancreatitis and at the same time reduce its painful symptoms.[29] A low-fat diet often helps and it is also imperative to guard against infections.[31] Treatment options are limited but include enzyme-replacement therapy and insulin, so as to improve pancreatic function.[30] Surgery is necessary to relieve pain, clear blockages, and reduce attacks in some patients.[30,31] In short, the effects of alcoholic pancreatitis can be managed, but rarely reversed.

Cancer risks

Cancer risks can be attributable to genetics, the environment, and lifestyle behaviors.[32] Effecting change to our genes and our environment is limited however, lifestyle behaviors offer an opportunity for change.

Alcohol abuse is one lifestyle behavior that can increase the risk of developing certain cancers.[32] While the risk is increased it does not mean that everyone abusing alcohol will develop cancer. Numerous studies do show the more a person drinks, the greater the risk of developing certain types of cancer.[32] For example, Italian research scientists conducted a meta-analysis on 200 studies reporting alcohol's impact on cancer risk.[33] The results show that as alcohol consumption increases, the risk for developing a variety of cancers also increases. The National Cancer Institute has identified alcohol as a risk factor for the following types of cancer:

- Breast;
- Esophagus;
- Larynx;
- Liver;
- Mouth; and
- Pharynx.[34]

Epidemiology reports show that 7 out of 10 people diagnosed with mouth cancer are heavy drinkers. Individuals who consume five or more drinks per day have risks that are associated with colon and rectal

cancers.[34] In fact, summary from the World Cancer Research Fund report indicate that women who drink five standard alcohol drinks per day have about 1.2 times the risk of developing colon or rectal cancer when compared to women who do not drink at all.[35]

Research has found that people who drink are also more likely to smoke, and the combined effect increases the risk of cancer significantly.[36] It is well documented that smoking alone is a risk factor for some cancers, but when combined with alcohol the risk intensifies the cancer-causing properties of each substance.[33]

Because alcohol and tobacco both come in direct contact with the mouth and throat, the risk of oral cancer is greater. People who drink and smoke are 15 times more prone to develop cancers of the mouth and throat than non-drinkers and non-smokers.[33,34,36] Research studies estimate that when alcohol and tobacco are used together they are responsible for:

- 80% of throat and mouth cancers in men;
- 65% of throat and mouth cancers in women;
- 80% of esophageal squamous cell carcinoma (a type of esophagus cancer); and
- 25 to 30% of all liver cancers.[34]

Alcohol effects on the immune system

The immune system is designed to protect the body from foreign substances that cause illness. The immune system is often conceptualized as a military unit because it defends the body from infection and disease. The skin as well as the mucous that lines the respiratory and gastrointestinal tracts help prevents foreign substances from entering or staying in the body. Should foreign substances somehow make it through these barriers, the immune system triggers two defensive systems; the innate and adaptive systems.[37]

The innate system exists in the body prior to any exposure to foreign substances such as bacteria, viruses, fungi, or parasites (referred to as antigens). The components of the innate system include:

- **WHITE BLOOD CELLS** – White blood cells are the first line of defense against infection. They surround and swallow foreign bodies quickly.
- **NATURAL KILLER (NK) CELLS** – Natural Killers are a specialized white blood cell that detect and destroy cells infected with cancer or viruses.
- **CYTOKINES** – White blood cells produce and direct these chemical messengers directly to an infected site. Cytokines then trigger an inflammatory response, such as dilating blood vessels and increasing blood flow to the affected area. These chemical messengers also attract more white blood cells to an infected area.[37]

The adaptive system is engaged after the initial exposure to an infection. In subsequent infections, the adaptive system is employed to attack the antigen faster and more efficiently than occurred during the first exposure.[37] The components of the adaptive system include:

- **T-LYMPHOCYTE CELLS** – T-cells reinforce the work of white blood cells by targeting individual foreign substances. The strength of T-cells is that they can identify and destroy a vast array of bacteria and viruses. They can also kill infected cells and secrete cytokines.
- **B-LYMPHOCYTE CELLS** – B-cells produce antibodies that fight off harmful substances by sticking to them and making them jut out to other immune cells.
- **ANTIBODIES** – After B-cells encounter antigens, they produce antibodies. These proteins target specific antigens and then remember how to combat the antigen.[37]

Drinking too much alcohol weakens the immune system by suppressing both the innate and the adaptive immune systems. Chronic alcohol use reduces the ability of white blood cells to effectively engulf and destroy harmful bacteria.[38] Excessive drinking also disrupts cytokines production, resulting in either excessive or insufficient amounts of chemical messengers.[38] An abundance of cytokines often cause damage to tissues, whereas a lack of cytokines increases the opportunity for infection.[38] Chronic alcohol use also suppresses the development of T-cells and may impair the ability of NK cells to assault tumor cells.[38] This reduced function makes the body more vulnerable to bacteria and viruses, and less capable of destroying cancerous cells.[38]

With a compromised immune system, chronic alcohol drinkers are more prone to contract diseases (e.g. pneumonia, tuberculosis) than people who do not drink.[39] There is also research data showing an association between alcohol's damage to the immune system with an increased susceptibility to contracting HIV.[39] It appears HIV progresses faster in chronic drinkers when compared to non-drinkers.[39] Drinking excessively on a single occasion (such as binge drinking) can also compromise the immune system.[37] Drinking to intoxication slows the body's ability to produce cytokines which produce inflammations that ward off infections.[37] Without these inflammatory responses, the body's ability to defend itself against bacteria is significantly reduced. A recent study demonstrates that slower inflammatory cytokine production can reduce the body's ability to fight off infections for up to 24 hours after intoxication.[39]

It is not known if abstinence, reduced drinking, or other measures will reverse the effects of alcohol (either partially or completely) on the immune system. Nevertheless, it is notable to remember that avoiding drinking alcohol minimizes the burden on the immune system, especially when fighting a viral or bacterial infection.

DISCUSSION

Alcohol use has a two-edge sword. It contributes to social functions and used in moderation can have health benefits. On the other hand alcohol can be destructive to the physiological systems within the human body and affecting a person's quality of life. Alcohol can cause measurable pathology in one system of the body or it can simultaneously affect multiple systems. Some of these effects, such as cancer, can be life threatening. Because alcohol is a legal drug, communicating its dangers and effecting behavioral changes has been a challenge to clinicians and public health officials.

Organizations such as the National Institute of Alcohol Abuse and Alcoholism, Mothers Against Drunk Drivers, Alcoholics Anonymous (AA), and law enforcement agencies have all undertaken efforts to educate the public to the dangers of alcohol use and abuse however the problem persists. Binge drinking on college campuses is a common problem as is drinking and driving which cause untold carnage on highways.

Behavioral treatment programs have been developed in most locations and aim to treat individuals who abuse alcohol or have become dependent. Because alcohol dependence is a chronic disease success rates vary among programs. One of the challenges the treatment programs face is the measurement of alcohol use. Most currently available clinical laboratory tests for alcohol do not offer the sensitivity and specificity required by treatment providers, so they must rely on patient self-reports which often are not accurate or truthful. More research into the development of alcohol testing (both acute and chronic) by clinical laboratory methods is needed to advance the treatment of patients with alcohol problems so as to minimize its pathology.

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