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A Small Dose of Alcohol

Introduction



Viewed through the lens of toxicology, alcoholic beverages provide a fascinating window into our relationship with a substance that many of us consume because of its intoxicating properties. Our relationship with alcoholic beverages began over 10,000 years ago with the accidental fermentation of grain. But despite our great familiarity with the use of alcohol, it was not until the early 1970s that we realized that alcohol consumption during pregnancy severely affected the developing infant, with no apparent harm to the mother. Worldwide, 9.1 infants per 1000 are affected by Fetal Alcohol

Spectrum Disorder (FASD).

The word alcohol comes from the Arabic *al-kuhul* originally referring to a white powder of antimony used as eye makeup. It was not until the middle of the 18th century that alcohol took on its current meaning of the fermented and intoxicating ingredient found in many common beverages. Fermentation occurs when microorganisms such as yeast, fungi, or bacteria break down complex molecules to produce energy in the absence of oxygen. During fermentation, certain strains of yeast produce ethyl alcohol and carbon dioxide in their quest for energy from available sugars. Below is a list of common fermentation starting points and the end products either as a direct result of fermentation or from further distillation.

- Cereal grains -> Beers and whiskeys
- Honey -> Mead
- Grapes -> Wine and brandy
- Root vegetables -> Vodka
- Sugar cane -> Rum

Alcohol is also an excellent and widely used solvent, appearing in many products from gasoline to drugs. Industrially, it is produced by chemical reactions using acetaldehyde or petroleum byproducts and more recently from biomass, such as corn or sugar cane. In the United States, annual corn ethanol production

for use in fuel has grown from 175 million gallons in 1980 to nearly 9.3 billion gallons in 2008. Worldwide production is estimated at over 16 billion gallons and is expected to continue to grow.

Alcohol Case Studies

Fetal Alcohol Syndrome Disorder

Despite alcohol's long history of use, its effects on the developing fetus were not recognized until the early 1970s. Fetal Alcohol Syndrome Disorder (FASD) is the result of maternal consumption of alcohol during pregnancy and is one of the leading causes of permanent learning disabilities and physical growth deficiency. Some believe that 1% of the U.S. population may be affected and a greater percentage are affected worldwide (Wattendorf and Muenke, 2005). FAS is identified by characteristic changes in facial features, particularly around the mouth and eyes. A milder form without the facial deformities, but associated with learning disabilities and CNS dysfunction, is called Fetal Alcohol Effect (FAE) or Alcohol-Related Neurodevelopmental Disorder (ARND). In the US, it is estimated that between 4,000 and 12,000 infants suffer from FAS and 36,000 children have milder forms of alcohol-related disabilities. Worldwide, as many as three infants per 1,000 births have FAS, and an unknown number are afflicted with milder forms of disability related to maternal alcohol consumption. The effects of alcohol on the infant illustrate the sensitivity of the developing fetus to chemical exposure. The tragedy is two-fold: 1) the effects of alcohol on the fetus are preventable, and 2) the effects last a lifetime, robbing individuals of the opportunity to express their full genetic potential.

Alcohol and the Liver

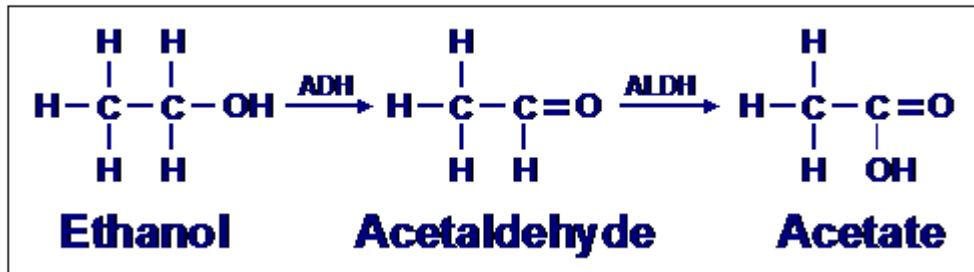
Alcohol has a range of effects in addition to the effects on the developing fetus: for some, desirable acute effects; and with long-term consumption, effects on the liver and other organs. In the US, over 2 million people experience alcohol-related liver disease. Effects of alcohol on the liver are dose related: the more consumed, the greater the effects. Early on there is an accumulation of fat in the liver as a result of the metabolism of alcohol. Metabolites of alcohol, produced by the liver, are toxic to liver cells. Some heavy drinkers develop an inflammation (alcoholic hepatitis) of the liver. As consumption continues, the liver becomes less functional and a process starts that can lead to cirrhosis, or scarring of the liver. Continued drinking can result in death, but if the drinking stops, functioning of the liver can improve; however, the underlying damage is not reversible.

Biological Properties of Alcohol

Alcohol is readily absorbed from the stomach and the intestine, and the highest blood level occurs about 30 minutes from the time of the last drink. Alcohol absorption is slowed by the presence of food in the stomach; however, once it reaches the small intestine, alcohol absorption is rapid. Alcohol vapors can be inhaled and absorbed by the lungs and can be a significant occupational hazard where used industrially. After consumption and absorption the majority of alcohol distributes into body water, and like most solvent and anesthetics some distributes into fat. It is excreted in the urine and breath, hence the utility of the taking breath samples to evaluate alcohol exposure. Your breath alcohol level is directly related to your blood alcohol level. The majority of alcohol in your body is metabolized in the liver. An enzyme, alcohol dehydrogenase (ADH), metabolizes alcohol to acetaldehyde. Acetaldehyde is toxic, with elevated

levels causing flushing, headache, nausea, and vomiting. Acetaldehyde is in turn quickly metabolized to the less toxic metabolite acetate by another enzyme acetaldehyde dehydrogenase (ALDH) (Figure 3.1).

Figure 3.1 Metabolism of Alcohol



Humans have varying amounts and types of ALDH which affects their ability to metabolize the toxic metabolite acetaldehyde. For example, approximately 50% of people of Asian heritage have a single base change in a gene that encodes for ALDH resulting in an inactive form of ALDH, which makes alcohol consumption very unpleasant. Antabuse (disulfiram), a common drug prescribed to discourage alcohol consumption, blocks ALDH and causes blood levels of acetaldehyde to rise. The subsequent toxic side effects discourage continued alcohol consumption. Disulfiram was a chemical originally used in the rubber industry. Workers inadvertently exposed to disulfiram accidentally discovered its effects when they became sick after drinking alcoholic beverages.

The metabolism of most drugs or chemicals is proportional to the concentration of the compound in the blood. This allows us to calculate the rate of metabolism or a half-life. However, ethanol is different; its metabolism is relatively constant over time and the rate of metabolism does not increase with rising blood concentrations. We also know that metabolism is proportional to body weight; thus the bigger you are, the higher the rate of metabolism, but on average, ethanol is metabolized at a rate of 120 mg/kg per hour or about 1 oz (30 ml) in 3 hours.

Ethanol is easily measured in the blood and reported as milligrams per milliliter (mg/ml) of blood. Current laws regulating driving after drinking specify specific blood alcohol concentration (BAC) as unacceptable when operating a motor vehicle. Most states set 0.08 or 0.1, which is equivalent to 80 mg/100 ml or 80 milligrams per deciliter (mg/dL) of blood. Alcohol content of exhaled breath is about 0.05% of the BAC.

Another factor that influences blood alcohol concentrations and thus the effects of alcohol is gender. Drink for drink, a female will have a higher BAC than a male. First, women tend to be smaller, so by body weight they receive a higher dose of alcohol. Second, women metabolize less alcohol in the intestine than men, which results in great absorption of alcohol and a higher BAC. Finally, women usually have a greater proportion of body fat per body weight, which results in lower volume of fluid by weight. An average male of medium weight (160-180 pounds) must consume almost four drinks in an hour to reach a BAC of 0.08, whereas an average female weighing 130 to 140 pounds requires only 3 drinks within one hour to reach a BAC of 0.08. The exact number of drinks to reach a BAC of 0.08 of course depends on many variables, not the least of which is the percent alcohol in the drink.

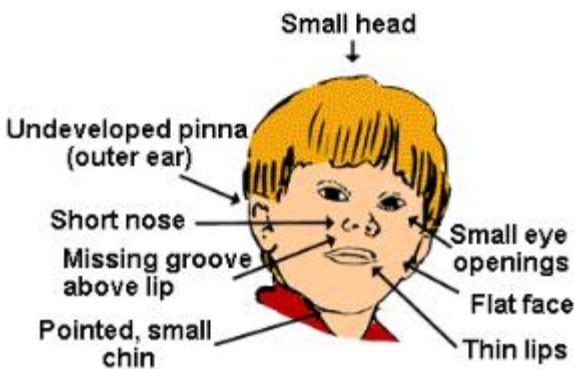
How alcohol affects the central nervous system is still not completely clear. For some time, researchers thought that the depressant affects of alcohol, like other anesthetic agents, was caused by the dissolving of cells' lipid membranes and the disruption of the function of various proteins. More recently, researchers have focused on specific receptors such as glutamate (excitatory) and GABA (inhibitory). Despite intensive research, the mechanism by which alcohol affects the developing fetus is still unknown.

Health Effects of Alcohol

By any measure, alcohol has an enormous impact on our society: it contributes to at least 100,000 premature deaths, and economic costs are estimated to be over \$275 billion a year, including medical expenses, lost worker productivity, automobile accidents, and crime. The toxic effects of alcohol have resulted in efforts and laws to control and regulate its consumption. While alcohol affects the individual consumer, two areas are of particular concern for the greater society: 1) the effects of alcohol on the developing infant from maternal alcohol consumption and 2) the death and injury caused by driving motor vehicles following drinking. This section is divided into the health effects of alcohol on children and adults to emphasize the sensitivity of fetal exposure to alcohol during pregnancy.

Before starting, it is necessary to define what a drink means. This is not as straightforward as it might seem given the wide range of beverages that contain varying concentrations of alcohol. One common definition of a drink is a beverage that contains 0.5 oz or 15 ml of ethanol.

Children



Despite alcohol's long history of use, the adverse effects of maternal alcohol consumption on the developing fetus wasn't described until 1968, by French researchers at the University of Nantes. In 1972, the cluster of effects was further described and named Fetal Alcohol Syndrome (FAS) by researchers at the University of Washington in Seattle, USA. FAS is characterized by physical and facial abnormalities (Figure 3.2), slow growth, central nervous system dysfunction, and other disabilities. The related brain damage can be

severe, leaving the child with serious learning and functional disabilities that have lifelong impacts. Another form of alcohol-related effects is Fetal Alcohol Effect (FAE), where children are born with learning or memory disabilities, but without the characteristic physical abnormalities. The disabilities associated with fetal alcohol exposure are now described as Fetal Alcohol Spectrum Disorder (FASD), which recognizes the range of effects alcohol has on development. In addition, alcohol consumption during pregnancy causes an increase in stillbirths and spontaneous abortions. It is extremely important to recognize that alcohol consumption during pregnancy results in the largest number of preventable mental disabilities in the world.

In 1981 the US Surgeon General first advised that women should not drink alcoholic beverages during pregnancy because of the risks to the infant. In 1989 warning labels were mandated on all alcoholic

beverages sold in the United States, and since 1990 the US government policy has clearly stated that women who are pregnant or planning to become pregnant should not drink alcohol.

It is difficult to determine exactly how many young children and subsequent adults are handicapped by fetal exposure to alcohol because the diagnosis of less severe forms of the disease is imprecise.

Worldwide, alcohol consumption affects between 1 and 3 out of 1,000 infants. In the United States, 4,000 to 12,000 infants per year are born with FAS and as many as three times of that with minor disabilities. Recent studies in the United States estimate that 14 to 22.5 percent of women report drinking some alcohol during pregnancy. An additional concern is that a woman is often not aware she is pregnant during the first few very vulnerable weeks of pregnancy.

The consequences of maternal alcohol consumption are tragic and last a lifetime for the exposed infant. In 1989, Michael Dorris described the life of his adopted son Able, who had FAS, as that of a drowning man, one "conceived in an ethanol bath" and unable to find the shore.

Adults

Alcohol, a toxic solvent, flows freely in our society. Because it is heavily advertised, easy to make, easy to purchase, and widely consumed across all ages because of its neuroactive properties, we struggle to address adverse health consequences of consumption. In the United States the legal drinking age is 21 years, but illicit consumption of alcoholic beverages often starts much earlier. In Europe and other parts of the world the legal drinking age is generally 18 and sometimes 16 years of age.

The acute effects of alcohol consumption are associated with mild nervous system effects such as relaxation and reduced inhibitions that many people find desirable. Additional consumption results in sleepiness and reduced motor and reaction time, which effects the ability to operate a motor vehicle or engage in complex tasks. Continued consumption can result in drunkenness, which is often associated with uncontrolled mood swings and emotional responses and sometimes violence. Excessive alcohol consumption can result in violence, spousal and child abuse, crime, motor vehicle accidents, workplace and home accidents, drowning, suicide, and accidental death. Rapid consumption of large quantities of alcohol sometimes seen on college campuses can result in respiratory depression, coma, and possibly death due to depressed respiration. Vasodilation also occurs especially in vessels near the skin, which gives the drinker false feeling of warmth. Contrary to popular belief, sexual function is decreased for both men and women after alcohol consumption.

The chronic effects of alcohol consumption include alcoholism, liver disease, various cancers, brain disorders, cardiovascular disease, absence from or loss of work, family dysfunction, and malnutrition. Chronic consumption of alcohol can result in a tolerance to its overt effects, but it still affects functional ability, such as that required to drive a vehicle. Tolerance can develop to such an extent that an individual can have very high alcohol levels (300 to 400 mg/dl) and still not appear to be physically affected. However, the ability to tolerate high blood alcohol levels does not change the level necessary to produce death from acute consumption.

Chronic excessive consumption of alcohol can result in physiological dependence or alcoholism. There is often a steady progress in the need to consume alcohol, so that the person starts drinking early in the day to maintain blood alcohol levels and avoid withdrawal effects. Alcoholism often results in a variety of organ system effects, some of which are related to accompanying malnutrition. Treatment for

alcoholism must address the withdrawal effects as well as associated vitamin deficiencies associated with any malnutrition.

Alcohol Withdrawal Effects:

- Tremor
- Nausea
- Irritability
- Agitation
- Tachycardia
- Hypertension
- Seizures
- Hallucinations

Alcohol affects a number of organs, but the liver is most commonly affected. Initially there is accumulation of fat in the liver. Cellular damage appears to be associated with increased levels of acetaldehyde. This in turn results in a scarring or hardening of the liver called cirrhosis. All these changes to the liver result in decreased ability to metabolize alcohol as well other drugs; the toxicity of some drugs, such as the pain reliever Tylenol (acetaminophen), is enhanced.

The International Agency for Research on Cancer (IARC) states that "alcoholic beverages are carcinogenic to humans (Group 1)" and concluded that "the occurrence of malignant tumors of the oral cavity, pharynx, larynx, esophagus, liver, colorectum, and female breast is causally related to alcohol consumption." Alcohol is also associated with a general increase in cancer of other organs and interacts synergistically with smoking, putting smokers who drink at a greater risk for developing cancer. There is increasing evidence that alcohol consumption by women increases the risk for breast cancer.

Regulatory Standards for Alcohol

Advice or regulation related to alcohol consumption during pregnancy was slow to arrive even following the documentation of fetal effects, and more needs to be done to discourage alcohol consumption during pregnancy.

- 1981 - US Surgeon General first advised that women should not drink alcoholic beverages during pregnancy.
- 1988 - US required warning labels on all alcoholic beverages sold in the United States.
- 1990 - US Dietary Guidelines stated that women who are pregnant or planning to become pregnant should not drink alcohol.
- 1998 - 19 states required the posting of alcohol health warning signs where alcoholic beverages are sold.

Recommendation and Conclusions for Alcohol

Reducing Exposure

Reducing exposure is easy in concept but is usually more difficult in practice. Most importantly, women who are planning on becoming pregnant or who are pregnant should not consume alcohol. Men need to

support and encourage women's avoidance of alcohol consumption during pregnancy. For many who consume alcohol, it is important to learn how to manage exposure. Food consumption slows alcohol absorption, so eat when drinking and do not to consume alcohol on an empty stomach. There is a great amount of variability in the percent of alcohol in drinks. It is a good practice to consume fewer drinks that have high alcohol content.

Conclusion

Alcohol is a readily available toxic chemical that can yield pleasurable experience or disastrous effects that can cause enormous suffering. The most tragic effects occur when a woman consumes alcohol during pregnancy, producing irreversible harm to the developing fetus. The consumption of alcohol during pregnancy is the single greatest cause of preventable birth defects and learning and performance disabilities. Alcohol is associated with motor vehicle accidents and a range of other detrimental effects. While government regulatory agencies and policy responses have worked to reduce the adverse health and societal effects, over \$1 billion is spent every year advertising the consumption of this chemical. In conclusion, consume with caution and beware of your individual sensitivity.

Alcohol Information and References

European, Asian, and International Agencies

- England - Department of Health (DOH) Alcohol Misuse Information. Online: <<http://www.dh.gov.uk/en/Publichealth/Healthimprovement/Alcoholmisuse/index.htm>> (accessed: 13 July 2008).

The DOH provides extensive information on the health effects of alcohol

- Nordic Council For Alcohol And Drug Research (NAD). Online: <<http://www.kaapeli.fi/nad/>> (accessed: 13 July 2008).
- International Council on Alcohol and Addictions (ICAA). Online: <<http://www.icaa.de/>> (accessed: 13 July 2008).

"ICAA is a non-governmental organization in consultative status (Category Special) with the Economic and Social Council of the United Nations and in official relations with the World Health Organization."

North American Agencies

- Health Canada - Fetal Alcohol Spectrum Disorder (FASD). Online: <<http://www.phac-aspc.gc.ca/fasd-etcaf/index-eng.php>> (accessed: 13 July 2008).

This site provides tools to reduce and manage the effects of fetal exposure to alcohol.

- U.S. Centers for Disease Control's "Fetal Alcohol Syndrome: Guidelines for Referral and Diagnosis". Online: <http://www.cdc.gov/ncbddd/fas/publications/FAS_guidelines_accessible.pdf> (accessed: 13 July 2008).
 - U.S. The Bureau of Alcohol, Tobacco, Firearms and Explosive (ATF), Department of Justice. Online: <<http://www.atf.gov/>> (accessed: 13 July 2008).
- ATF's unique responsibilities include protecting the public and reducing violent crime and enforce the Federal laws and regulations relating to alcohol and tobacco diversion, firearms, explosives, and arson.
- U.S. National Institute on Alcohol Abuse and Alcoholism (NIAAA). Online: <<http://www.niaaa.nih.gov/>> (accessed: 13 July 2008).

"The NIAAA supports and conducts biomedical and behavioral research on the causes, consequences, treatment, and prevention of alcoholism and alcohol-related problems."

- Alcohol - Center for the Evaluation of Risks to Human Reproduction (CERHR) - The National Toxicology Program. Online: < <http://cerhr.niehs.nih.gov/common/alcohol.html> > (accessed: 13 July 2008).

CERHR alcohol web site has information for parents about the effects of alcohol on reproduction and development.

- U.S. National Clearinghouse for Alcohol and Drug Information (NCADI). Online : <<http://www.health.org/>> (accessed: 13 July 2008).

"NCADI is the world's largest resource for current information and materials concerning substance abuse."

- U.S. Department Of Health And Human Services, Substance Abuse and Mental Health Services Administration (SAMHSA) Center for Substance Abuse Prevention .Online : <<http://www.samhsa.gov/>> (accessed: 13 May 2014).

"The CSAP mission is to decrease substance use and abuse by bringing effective prevention to every community."

Non-Government Organizations

- Alcoholics Anonymous (AA). Online: <<http://www.aa.org/>> (accessed: 13 July 2008).

An international organization dedicated to helping people with alcohol consumption concerns.

- Center for Science in the Public Interest (CSPI). Online: <<http://www.cspinet.org/>> (accessed: 13 July 2008).

"CSPI is an advocate for nutrition and health, food safety, alcohol policy, and sound science."

- Mothers Against Drunk Driving (MADD). Online: <<http://www.madd.org/>> (accessed: 13 July 2008).

"MADD's mission is to stop drunk driving, support the victims of this violent crime, and prevent underage drinking."

- National Council on Alcoholism and Drug Dependence, Inc. (NCADD). Online: <<http://www.ncadd.org/>> (accessed: 13 July 2008).

NCADD provides education, information, help and hope to the public and advocates prevention, intervention and treatment.

- Rutgers, The State University of New Jersey Center of Alcohol Studies (CAS). Online: <<http://alcoholstudies.rutgers.edu/>> (accessed: 13 July 2008).

The Center of Alcohol Studies (CAS) is a multidisciplinary institute dedicated to acquisition and dissemination of knowledge on psychoactive substance use and related phenomena with primary emphasis on alcohol use and consequences.

- FAS Bookshelf, Inc. Online: <<http://www.fasbookshelf.com/>> (accessed: 13 July 2008).

Web site devoted to providing resources on Fetal Alcohol Syndrome.

- National Organization on Fetal Alcohol Syndrome. Online: <<http://www.nofas.org/>> (accessed: 13 July 2008).

"NOFAS is dedicated to eliminating birth defects caused by alcohol consumption during pregnancy and improving the quality of life for those affected individuals and families."

- Alcohol and Drug History Society (ADHS). Online. : <<http://www.athg.org/>> (accessed: 13 July 2008).

ADHS, formerly Alcohol and Temperance History Group, the ADHS is an international group of alcohol, temperance, and drug history scholars founded to foster the exchange of ideas among scholars of all disciplines who are interested in any aspect of past alcohol use, abuse, production, and control within

given societies or countries and online home of The Social History of Alcohol and Drugs: An Interdisciplinary Journal (SHAD).

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- Fetal Alcohol Syndrome - Diagnosis, Epidemiology, Prevention, and Treatment. Kathleen Stratton, Cynthia Howe, and Frederick C. Battaglia, Editors; Committee to Study Fetal Alcohol Syndrome, Institute of Medicine, Washington, DC. 1996. The National Academy Press. Online: http://www.nap.edu/catalog.php?record_id=4991 (accessed: 13 July 2008).
- Global Status Report on Alcohol 2004. World Health Organization, 2004. Online: [http://whqlibdoc.who.int/publications/2004/9241562722_\(425KB\).pdf](http://whqlibdoc.who.int/publications/2004/9241562722_(425KB).pdf) (accessed: 13 July 2008).
- Wattendorf, D. J., and Muenke, M. (2005). Fetal alcohol spectrum disorders. American family physician 72, 279-82, 285. Open access: <http://www.aafp.org/afp/20050715/279.html> (accessed; 13 July 2008).