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FEATURE

YOU ARE WHAT YOU EAT *AND* DRINK: NEW RESEARCH FOCUSES ON ALCOHOL AND NUTRITION

More and more researchers are investigating how alcohol and nutrition interact to impact our biology, our behavior, and our health. In addition to dependence, alcohol can trigger a host of health problems, including certain cancers, cardiovascular disease, liver

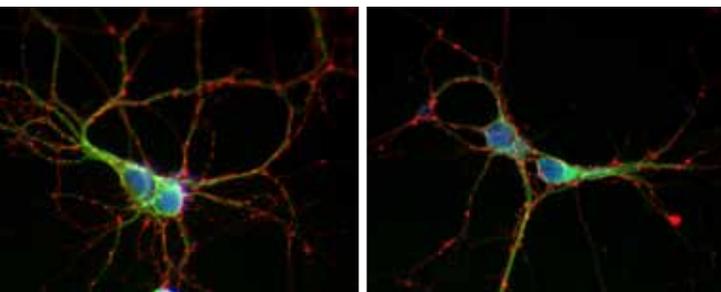
intake, and how do various patterns of alcohol and food consumption together influence the risk of chronic disease?" said Dr. Rosalind Breslow, an epidemiologist in NIAAA's Division of Epidemiology and Prevention Research.

Dr. Breslow recently collaborated with researchers at the National Cancer Institute (NCI) and the U.S. Department of Agriculture (USDA) to investigate some of the connections between alcohol and diet. She led a team that analyzed data collected from participants in the National Health and Nutrition Examination Survey (NHANES) and from scores on the Healthy Eating

Index-2005 (HEI). NHANES is a survey of nationally representative samples of the U.S. population that the U.S. Department of Health and Human Services' Centers for Disease Control and Prevention conducts on an ongoing basis. The USDA created HEI to measure how healthy our diets are based on how closely they conform to the 2005 U.S. dietary guidelines for Americans.

disease, and fetal alcohol syndrome. Researchers are interested in what role nutrition can play in preventing and treating these alcohol-related health outcomes.

"When you think about alcohol as part of your overall diet—a food like any other that you consume with other foods, it leads to lots of questions—like does alcohol consumption change food intake, does food intake change alcohol



These images compare the synapse formation (appears in red) in the neurons from two mouse fetuses. The one on the left is from the fetus that had sufficient DHA during gestation while the one on the right is from the fetus that did not. The neurons derived from the DHA-deficient mouse fetus show 50 percent fewer synapses. The inhibited synapse formation due to DHA-deficiency may have significant implication in developing depression and alcohol dependence.

Photo courtesy of Dr. Hee-Yong Kim, NIAAA intramural program of (Journal of Neurochemistry. 2009 Oct;111(2):510-21).

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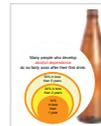


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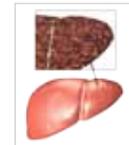
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Dr. Breslow and her team found that heavier drinkers tend to eat less fruit and consume more calories from a combination of alcoholic beverages and foods high in unhealthy fats and added sugars. Men in particular who consumed a lot of calories from alcohol also ate less whole grains, an important source of dietary fiber, and less low-fat dairy products, including milk, yogurt, cheese, and soy beverages, important sources of calcium and other nutrients. Women who drank too much also had lower HEI-2005 scores.

Overall, the researchers found that as a study participant's average daily number of drinks went up, their HEI-2005 score went down. This may be one reason why heavy drinkers are more susceptible to alcohol's negative health effects, including certain cancers, liver cirrhosis, and heart disease.

People who drink more also consume less omega-3 fatty acids, which are fats that help compose our brain and are critical for brain function. These fats are found in fish like salmon, sardines, and tuna. What's more, alcohol actively depletes omega-3s from the brain.

"We can only get omega-3 fatty acids through our diets. Alcoholics have very little omega-3s going in and a lot of them going out," said Joseph Hibbeln, M.D., a psychiatrist and acting chief, Section on Nutritional Neurosciences

at NIAAA and captain, U.S. Public Health Service.

Alcohol can deplete one particular type of omega-3 fatty acid in the brain, docosahexaenoic acid, or DHA, by half.

Dr. Hibbeln's research is moving toward understanding the consequences of this DHA deficiency for everyone, including alcoholics. For example, low DHA levels can result in depression, aggression, and impulsivity. As Hibbeln stated, "My more than 20 years of research indicates that people who eat little fish are at much greater risk of depression."

A lack of DHA in the brain can also run down dopamine levels. "It is well known that chronic addicted states are characterized by dopamine depletion," explained Hibbeln. Diets deficient in omega-3s can lower dopamine levels by half. A recent study introduced mice with a diet low in omega-3s to low levels of amphetamines. The mice released dopamine at levels similar to a chronically addicted animal. Hibbeln attributes this dopamine deficiency to their "bad diet."

Insufficient omega-3s can also link directly to a cycle of addiction. Too little omega-3s, coupled with too many omega-6 fatty acids, which are fats in abundance in the typical American diet, can lead to excess food intake, excess

alcohol intake, and an inability to feel satiated. This imbalance increases the craving for alcohol, and causes those who are susceptible to drink too much.

One recent study illustrates the potential for positively impacting alcohol dependence by increasing omega-3s in the diet.

Dr. Hibbeln offered 2 grams of omega-3s to 96 alcoholics in early recovery. He verified that participants were taking the omega-3s by measuring the levels of fatty acids in their spinal fluid. Over the 90 days of the study, alcoholics who took omega-3s had an average of about 3.2 drinking days compared to the 17.5 drinking days in the placebo group.

"This study of 96 alcoholics provides promising pilot data for potential benefits of ensuring adequate brain nutrition among alcoholics in recovery," Hibbeln said.

Hibbeln plans to focus future studies on evaluating whether these results can be replicated.

Hibbeln's and Breslow's work are just two examples of the research investigating the connections between alcohol and nutrition.

As Breslow said, "It's a very exciting area, with implications for both public health and basic research."

FEATURE

ALCOHOL'S HEALTH EFFECTS GO BEYOND HANGOVERS

Alcohol is part of our culture—we use it to celebrate and socialize, and it is part of many of our religious ceremonies.

But drinking too much—on a single occasion or over time—can have serious consequences for our health. These consequences go far beyond having a headache and a hangover that

make us uncomfortable, but go away relatively quickly.

Most people recognize that excessive drinking can lead to accidents and dependence, and even liver disease. But that's only part of the story. Unlike other drugs, alcohol disperses in all body tissues and therefore has the potential to harm many organ systems.

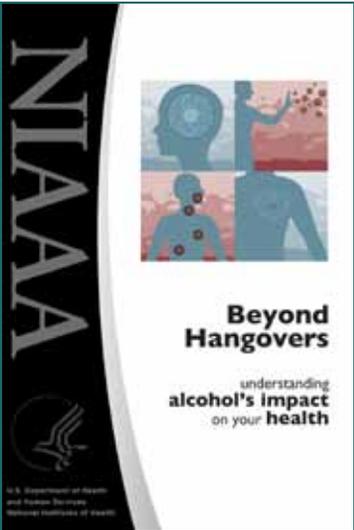
Alcohol abuse can damage organs, weaken the immune system, and contribute to cancers.

Plus, much like smoking, alcohol affects different people differently. Genes, environment, and even diet can play a role in whether you develop an alcohol-related disease.

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On the flip side, some people may actually benefit from drinking alcohol in small quantities.

Alcohol's effect on your heart is the best example of alcohol's dual effects.



Drinking a lot over a long time or too much on a single occasion can cause heart problems including high blood pressure, strokes, arrhythmia, and cardiomyopathy, a condition that causes your heart muscle to weaken and droop. But research also shows that

healthy people who drink moderate amounts of alcohol may have a lower risk of developing coronary artery

disease than people who never drink at all.

While drinking in moderation may not affect the health of your liver, heavy drinking can definitely take its toll. Your liver helps rid your body of substances that can be dangerous—including alcohol. By breaking down alcohol, your liver produces toxic byproducts that damage liver cells, promote inflammation, and weaken the body's natural defenses. This can make conditions ripe for disorders like steatosis, fibrosis, and cirrhosis, and dangerous inflammations like hepatitis to develop.

Pancreatic inflammations can also develop in response to drinking too much. Alcohol causes the pancreas to produce toxic substances that can eventually cause inflammation and swelling in tissues in blood vessels. This inflammation, called pancreatitis, prevents the pancreas from digesting food and converting it into fuel to power your body.

Aside from damaging your organs, drinking too much alcohol can also increase your risk of developing certain cancers, including those of the mouth, esophagus, pharynx, larynx, liver, and breast.

Alcohol also can weaken your immune system, making your body a much easier target for disease. Drinking a lot on a single occasion slows your body's ability to ward off infections—even up to 24 hours after getting drunk. Chronic drinkers are more likely to contract diseases like pneumonia and tuberculosis than people who do not drink too much.

To learn more about the health effects of alcohol, please download NIAAA's newest publication, *Beyond Hangovers: Understanding Alcohol's Impact on Your Health*. <http://pubs.niaaa.nih.gov/publications/Hangovers/beyondHangovers.htm>

CHARTICLE

HOW LONG DOES IT TAKE ALCOHOL DEPENDENCE TO DEVELOP?

About 1 in 7 adults who have had alcohol dependence, commonly known as alcoholism, developed it less than a year after having their first drink, according to a nationwide survey of U.S. adults aged 18 or older.¹ About a quarter of people who have had alcohol dependence developed it less than 2 years after their first drink, about a third in less than 3 years, and about half in less than 5 years.¹

In the United States, most people have had their first drink by the time they leave high school.² This fact, combined with the relatively rapid onset of dependence in many drinkers, helps to explain why alcohol dependence is found most commonly in young adults. About 1 in 9 people aged 18–24 have alcohol dependence, more than twice the proportion of any other age group.³



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The survey also shows that alcohol dependence occurs only rarely among drinkers who always stay within these limits: for men, no more than 4 drinks on any single day and 14 per week; for women, no more than 3 drinks on any day and 7 per week.⁴

- (1) Unpublished data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC).
- (2) Faden VF. Trends in initiation of alcohol use in the United States 1975-2003. *Alcoholism: Clinical and Experimental Research*. 2006 June;30(6):1011-22.
- (3) Unpublished data from the NESARC.
- (4) Dawson DA, et al. Quantifying the risks associated with exceeding recommended drinking limits. *Alcoholism: Clinical and Experimental Research*. 2005 May;29(5):902-8.

IN THE LINE OF DUTY: HOW THE LIVER BECOMES DAMAGED AS IT DEGRADES ALCOHOL

There probably isn't a more vital—yet underappreciated—organ in the human body than the liver. While we may recognize, in the most general terms, the role that the liver plays, many of us don't fully understand its many functions or vulnerabilities, particularly with regard to alcohol. And yet the alcohol-liver connection is critical, as more than 2 million Americans suffer from liver disease caused by alcohol.

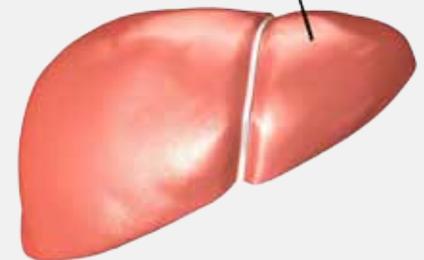
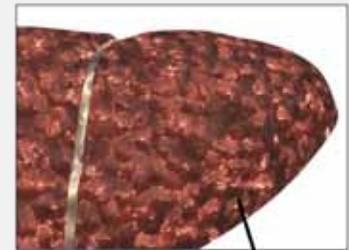
By performing more than 500 different functions, the liver is essential to our health. Its primary role is to filter all the blood in our bodies by breaking down and eliminating toxins and storing excess blood sugar. It also produces enzymes that break down fats, manufactures proteins that regulate blood clotting, and stores a number of essential vitamins and minerals. All told, the liver keeps us alive by enabling us to digest food, absorb nutrients, control infections, and get rid of toxic substances in our bodies.

While liver problems can be inherited, or developed in response to certain viruses or chemicals, excessive alcohol use plays a major role. To the human body, alcohol is a toxin that is broken down by

the liver as the body begins the process of getting rid of these foreign components. However, chronic heavy drinking causes the liver to become fatty. This condition makes the liver more vulnerable to dangerous inflammation, such as alcoholic hepatitis, and its associated complications. With continued drinking, persistent inflammation causes the liver to be fibrotic, which prevents the necessary blood supply from reaching the liver cells. Without the oxygen and other nutrients supplied by this blood, the liver cells eventually die and are replaced with scar tissue, creating a condition known as cirrhosis. In mild cases, the liver can actually make repairs and continue to function. However, advanced cirrhosis causes continued deterioration and liver failure.

In some cases, lifestyle changes can help treat alcohol-liver problems. Abstinence from alcohol, along with better nutrition and quitting smoking, can help prevent further injury and keep liver diseases in check. In extreme cases, however, a liver transplant may be the primary treatment option.

PHOTO ESSAY



Insert shows a portion of a liver scarred by cirrhosis, in comparison with a healthy liver.

For more information about the effects of alcohol on the liver and other organs, please see the new NIAAA booklet, *Beyond Hangovers: Understanding Alcohol's Impact on Your Health*. <http://pubs.niaaa.nih.gov/publications/Hangovers/beyondHangovers.htm>

MODERATE DRINKERS MAY LIVE LONGER THAN NON-DRINKERS

When compared to abstainers or heavy drinkers, moderate drinkers have the lowest mortality risk.

A new study published online in *Alcoholism: Clinical and Experimental Research* has shown that moderate drinking among older adults is



associated with lower mortality rates than those observed in adults who did not drink at all. What makes this study different from previous studies with similar findings was that the

researchers controlled for additional factors, most notably non-drinkers who previously drank problematically. In similar studies that do not control for the health problems caused by previous heavy drinking, the interpretation of findings regarding the potential benefit of moderate drinking is more difficult.

The study, led by Charles J. Holahan, Ph.D., of the University of Texas at Austin, included 1,824 adults between the ages of 55 and 65, and controlled for former problem drinking status, existing health problems, and important sociodemographic and social-behavioral factors. When controlled for these factors, the data showed that non-drinkers had a 45 percent increased mortality risk over moderate drinkers. Additionally, heavy

drinkers showed a 51 percent greater mortality risk than moderate drinkers.

The authors note that, “The apparent health-protective effects of moderate alcohol consumption compared to abstention may be related to reductions in cardiovascular illness.” The authors caution, however, that these health-protective effects “appear to be limited to regular moderate drinking. Heavy episodic drinking—even when average consumption remains moderate—is associated with increased cardiovascular risk.”

The article abstract can be found here:

Late-Life Alcohol Consumption and 20-Year Mortality. <http://www.ncbi.nlm.nih.gov/pubmed/20735372>

MORE ADULTS DRINKING...AND IN WAYS THAT INCREASE RISK

Studies reveal a significant increase in the proportion of men and women who drink.

A recent analysis of changes from the NIAAA’s 1992 National Longitudinal Alcohol Epidemiologic Survey (NLAES) to the 2002 National Epidemiologic Survey of Alcohol and Related Conditions (NESARC) shows that a larger proportion of U.S. adults of all ethnicities (White, Black, and Hispanic) and both sexes were current drinkers in 2002, with little change in the average number of drinks per month. Noting increases in adult males who drink five or more drinks a day at least once a month (Whites, Blacks, and Hispanics) or drink to intoxication (Whites and Blacks), the study suggests a “liberalization” of attitudes

toward alcohol and drinking practices linked to risk for alcohol use disorder and other consequences.

In addition to examining the 1992 to 2002 trends, Raul Caetano and co-authors at the University of Texas School of Public Health and the University of North Texas Health Science Center also looked at sociodemographic factors that might influence them. Their analysis was posted online in the journal *Alcoholism: Clinical and Experimental Research* and will appear in its October 2010 issue.



NEWS FROM THE FIELD: *More Adults Drinking. . . Continued from page 5*

Among the findings:

- Adult men who were current drinkers increased from about 53 percent in 1992 to 59 percent (64 percent of White men, 60 percent of Hispanic men, and 53 percent of Black men) in 2002.
- About 36 percent of adult women (47 percent of White women, 32 percent of Hispanic women, and 30 percent of Black women) were current drinkers in 2002, an increase from 28 percent in 1992.
- Two indicators of at-risk drinking rose among men who reported those patterns at least once a month:

drinking five or more drinks/day increased among White, Black, and Hispanic men, and drinking to intoxication increased among White and Black men.

- As in earlier studies, male gender, single status or living alone, U.S. birth, lower educational level, and unemployment were associated with higher drinking levels.

Although the study controlled for age, marital status, education, and income, unknown sociodemographic factors may have contributed to the results. “Understanding the complex reasons for ethnic and gender differences will

require continuous monitoring and further analyses,” says Dr. Caetano. “Such monitoring is essential for targeted prevention and meaningful public policy.”

The article abstract can be found here:

Sociodemographic Predictors of Pattern and Volume of Alcohol Consumption Across Hispanics, Blacks, and Whites: 10-Year Trend (1992–2002). <http://www.ncbi.nlm.nih.gov/pubmed/20645935>

NEWS FROM THE FIELD

NEW COMPOUND IMPROVES OBESITY-RELATED HEALTH COMPLICATIONS

A compound developed by a trans-NIH team and others may block endocannabinoid activity without causing mental health problems.

An experimental compound appears to improve metabolic abnormalities associated with obesity, according to a preliminary study led by researchers at NIAAA. A report of the study appeared in the August 2010 issue of the *Journal of Clinical Investigation*.

Previous studies have shown that compounds that block the activity of endocannabinoids—chemical messengers in the body that help regulate many biological functions—can lead to weight loss and improve metabolic complications of obesity such as diabetes and insulin resistance, changes in blood lipid composition, and fatty liver. However, the clinical advancement of such compounds has been stymied by behavioral side effects associated with their use, such as anxiety, depression, and suicidal thoughts.

George Kunos, M.D., Ph.D., NIAAA scientific director and the study’s senior author, and first author Joseph Tam, D.D.S., Ph.D., of the NIAAA Laboratory of Physiologic Studies, collaborated with a team of scientists within and outside NIH to investigate a compound designed to avoid those side effects while preserving the beneficial effects of blocking endocannabinoid activity.

Dr. Kunos explained that endocannabinoid receptors are present in the brain as well as in peripheral tissues, including the liver, skeletal muscles, pancreas, and fatty tissues. Activation of peripheral endocannabinoid receptors contributes to obesity-related metabolic and hormonal abnormalities.

The researchers reasoned that a compound that is unable to get into the brain would selectively block the activity of endocannabinoid receptors in peripheral tissues, and therefore might alleviate metabolic and hormonal problems related to obesity while avoiding the behavioral problems that

result from blocking endocannabinoid receptors in the brain. They developed such a compound, tested it in obese mice, and found that such mice showed improvements in glucose regulation, fatty liver, and plasma lipid profiles. They also found that the compound did not affect behavioral responses that are mediated by endocannabinoid receptors in the brain.

“These preliminary findings are very encouraging and warrant further testing of this compound as a potential pharmacotherapy for the metabolic syndrome associated with obesity,” said Dr. Tam.

The article abstract can be found here:

Peripheral CB1 Cannabinoid Receptor Blockade Improves Cardiometabolic Risk in Mouse Models of Obesity. <http://www.ncbi.nlm.nih.gov/pubmed/20664173> Free full text of the article is available at: <http://www.jci.org/articles/view/42551>

NEWS FROM THE FIELD

HALF-HOUR INTERVENTIONS CAN HELP REDUCE PEER VIOLENCE AND ALCOHOL CONSEQUENCES AMONG TEENS

Six months after receiving a brief intervention in the emergency department, participants maintain reduction in alcohol consequences.



Researchers affiliated with the University of Michigan have found that a brief intervention in an emergency department (ED) setting can help reduce peer violence and the consequences of alcohol use in adolescents. The researchers screened patients between ages 14 and 18 to determine their use of alcohol and experience with peer aggression both as perpetrator and victim. Those who had experienced

both aggression and alcohol use were randomized to receive a 35-minute intervention delivered either by a computer or a therapist. A control group received a brochure. The brief intervention included review of goals, tailored feedback, decisional balance exercise, role plays, and referrals. Their findings were published in the August 4, 2010, issue of the *Journal of the American Medical Association*.

The researchers followed up with participants 3 months and 6 months later. At the 3-month followup, they found that participants who received the brief intervention from a therapist were less likely to report severe peer aggression, experience of peer violence, and violence consequences when compared with the control group. At the 6-month followup, those in both the therapist and computer intervention groups showed reductions in alcohol

consequences compared with those in the control group.

Many adolescents seek care in the ED, particularly un- or under-insured individuals and those who believe they are too old for pediatric care but who have not sought out regular adult medical care. Because violence is a leading cause of morbidity and mortality in this age group, the authors believe that, “adolescents seeking care in the ED are an important population for injury prevention based on increased risk of problems related to alcohol and violence.”

The article abstract can be found here:

Effects of a Brief Intervention for Reducing Violence and Alcohol Misuse Among Adolescents: A Randomized Controlled Trial.
<http://www.ncbi.nlm.nih.gov/pubmed/20682932>

5 QUESTIONS WITH...



SAM ZAKHARI, PH.D.

Dr. Zakhari is the director of the NIAAA Division of Metabolism and Health Effects

1. In general, do you believe that Americans truly appreciate all of the ways that alcohol can impact their health?

Generally, no. We seem to understand, at least in general terms, the dangers of drinking and driving, and the effects of chronic drinking on the liver and the risk of dependence. But those are only part of the full picture; our research shows that alcohol’s effects are wide ranging, affecting every organ from the brain (cognitive and behavioral deficits)

to the heart (cardiomyopathy and hypertension), and from pancreatitis to suppression of the immune system, and even to cancer risk. For example, it might surprise people to know that people who drink heavily on holidays develop what is called “holiday heart syndrome” where the heart beats irregularly (known as arrhythmias)—this condition can be fatal. Drinking too much on an empty stomach after fasting changes the chemistry of the blood, causing what is called lactacidosis and ketoacidosis (especially in diabetics) and can earn you a trip to the emergency room.

In addition, it’s important to know that alcohol affects different people differently, depending on genes, environment, and even diet. For example, half of the population of Asian descent has a defective enzyme that metabolizes acetaldehyde, the first product of alcohol breakdown, leading to the accumulation of acetaldehyde, which causes them to flush, have nausea and fast heart rate, sweat, and simply feel miserable. This is not a bad thing because, in most cases, this is a protective mechanism from developing alcoholism.

Alcohol can even damage innocent fetuses, who do not drink voluntarily. When a pregnant mother drinks, alcohol could cause morphological, structural, and functional damage to the brain and other organs of the unborn. The most severe case is called fetal alcohol syndrome, where the child has small physical and brain size and a multitude of cognitive and behavioral deficits that may put him or her in conflict with the law.

Overall, I think we know quite a lot about alcohol and health, but we need to go beyond the current understanding so we can make informed decisions about our drinking.

2. What are some things we need to consider about alcohol as we age?

That's an important question, because different alcohol issues seem to take precedence at different stages across the lifespan. For youth and young adults, the consequences of binge drinking are prominent. It is not true at all that the young are invincible to alcohol's effects—just look at the almost 2,000 lives lost annually on college campuses across the Nation due to unbridled drinking. Those who are lucky enough not to succumb may cause damage to their endocrine system, resulting in irregular or absent menstrual cycle in women and a decrease in sperm count in men. It's also the time that many people begin to develop dependence; those who start drinking at the young age of 18 to early twenties have a high risk of developing alcohol dependence.

As we age, other issues begin to emerge. For example, after a long, hard day of work, people tend to drink to unwind and relax and to relieve stress. Interestingly, alcohol's physiological effects on the stress axis (hypothalamic-pituitary-adrenal axis) mimic stress. So, not only does alcohol not relieve stress, but consumed in high amounts, alcohol can rob the body of important vitamins and minerals that are essential for enzymatic activities. In addition, people who tend to treat a hangover with acetaminophen can cause irreparable damage to their liver.

Seniors not only metabolize alcohol at a slower rate than young adults but invariably are more likely to take one or more medications that interact with alcohol. Excessive alcohol consumption may increase the toxicity of some medications (e.g., antihistamines, antidepressants, anxiolytics) or decrease the efficacy of others (e.g., antidiabetics, antihypertensives). Furthermore, drinking too much can impair gait and may result in falls and breaking of brittle bones.

3. We're learning more about gender differences as well. Are there any specific issues that women should consider?

Yes. In general, women are more susceptible to alcohol-induced tissue damage than men. Imagine a 120-pound woman sitting next to a 350-pound linebacker at a bar, and both have a drink. The alcohol level in her blood will be higher because of her size and lower water content of her body. As a result, women are more susceptible to alcohol-induced damage to the brain, heart, and liver. Moderate drinking, therefore, is defined as no more than one drink a day for a woman and no more than two drinks a day for a man.

In addition, women who are pregnant or trying to conceive should abstain from drinking since that could harm the fetus. It could result in fetal alcohol syndrome or a milder form of behavioral and cognitive dysfunction. Alcohol also

increases the risk of breast cancer, especially in susceptible women.

4. There has always been much debate about the potential health benefits of moderate drinking. Can you shed any light on this issue?

Numerous epidemiological studies have shown that moderate drinking decreases the risk of coronary artery disease and ischemic stroke, protects against congestive heart failure and type-2 diabetes, reduces mortality after myocardial infarction, and enhances cognition. However, these effects are manifested on an individual basis, and not everyone may have the same benefits. I would urge individuals to consult with their physician before drinking, since people with a family history of alcoholism may be at higher risk for developing alcoholism.

5. Your background is in pharmacology. If you weren't in this research field, what other career path might you have chosen?

When I was in high school my passion was in math and physics. However, due to circumstances out of my control, I ended up in the medical field. That was great because it helped me deal with various medical situations in the family, and heightened my awareness of healthy food. I very much enjoy gourmet cooking and, after retirement, I am looking forward to using this talent to have family and friends enjoy moderate drinking with special meals!

ABOUT US

NIAAA Spectrum is NIAAA's first-ever webzine. With engaging feature articles, short news updates, and colorful graphics, *NIAAA Spectrum* offers accessible and relevant information on NIAAA and the alcohol research field for a wide range of audiences. Each issue includes feature-length stories, news updates from the field, charticles and photo essays, and an interview with an NIAAA staff member or alcohol researcher. *NIAAA Spectrum* is published three times a year.

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