

# CHEMICAL DEPENDENCY CONTINUING EDUCATION ARTICLE FOR 2009

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Your answers must be received no later than January 31, 2010. If you have any questions, call the Concerned Dental Professionals Program Director, Dr. Wayne McElhiney, at 615-628-3200.

## Genetics and the Disease of Chemical Dependency

David R. Sain, D.D.S., M.S., • Edward D. Eastham, M.D.

### Introduction – Effects on our society, our patients, our families and ourselves

The social impact of chemical dependency is obvious with only a quick review of the data. According to the National Institute of Health, substance abuse costs more than \$484 billion per year (Fig. 1). This is more than diabetes and cancer combined. A study also reveals that Americans think drug abuse is leading the list of “very serious problems” in the United States. (Fig. 2)<sup>1</sup>

In 1956, the American Medical Association identified alcoholism as a disease.<sup>2</sup> David Dodd, M.D., certified by the Board of Addiction Medicine, describes chemical dependency as a primary disease that is chronic, progressive, relapsing, and fatal. According to Roland Gray, M.D., the current director of the Tennessee Physicians’ Wellness Program, 10-15 percent of dentists, physicians, and the general population will suffer from the disease of chemical dependency sometime in their lifetime. Obviously, when a condition affects 10-15 percent of the population, dentists are going to see chemically dependent patients on a regular basis. Therefore, we know this disease is very serious (fatal), and that we will come into contact with patients with this disease frequently.

Over one-half of American adults have a close family member who has chemical dependency.<sup>3</sup> When one realizes the parents, spouses, and children of the



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chemically dependent person are also impacted, it is obvious that the majority of our patients and other dental professionals



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are being affected by this disease at some level.

At a local dental meeting where 50 dentists might gather, there may be five or more of us that have the disease of chemical dependency. Some have argued there will be as many as eight or more.<sup>4-6</sup> As a dentist and therefore a highly skilled, well-paid professional, we often times assume we are immune to many of society’s problems. The disease of chemical dependency is not one of them. In their book, Inaba and Cohen state, “Intelligence is not a guaranteed protection against addiction. Members of MENSA, a high-IQ society, also have a relatively high rate of addiction, as do gifted high school students. Members of the American clergy also have a higher than average rate of alcoholism. Even nuns have a problem with prescription drug abuse. If people use psychoactive substances, they are liable to addictive disease no matter what race, class, or region of the country they live in. Addiction is an equal opportunity disease.”<sup>7</sup>

There are a number of different paths researchers have explored examining the inheritability of the disease of chemical dependency. In fact, recent research shows that some genes can even afford us some protection from the disease of chemical dependency.<sup>8</sup>

### Environmentally Controlled Animal Studies

Experiments on animals have

become, in many ways, a preferred avenue in research. This gives scientists strong evidence of expected results in humans. Because of the multifactorial nature of chemical dependency, experimental animal models are helpful. Experimentation can be carried out on relatively large samples, in a number of generations, and over a relatively short period of time while having control over mating. This reduces the number of variables making it more likely to discover any relationship between a specific genetic make-up (genotype) and a specific physical or behavioral trait (phenotype).<sup>9</sup> Mice have proven especially useful in studying alcohol addiction because mice and humans react to alcohol in a similar way and share most of their genes.<sup>10</sup>

A number of years ago, it was discovered that certain strains of mice would consume large quantities of alcohol when given the choice of 75% alcohol or water. In contrast, another strain demonstrated extreme alcohol avoidance given a choice of as low as 2% alcohol or water (Fig. 3).<sup>11, 12</sup>

The researchers started with these two strains of mice. When the mice that liked alcohol had all the alcohol they could drink made available to them, they became alcohol addicted and drank themselves to death (Fig 3a). These addicted mice, when subjected to electrical shock that was meant to discourage their drinking, would still drink even when the electrical shock became nearly fatal.<sup>7</sup>

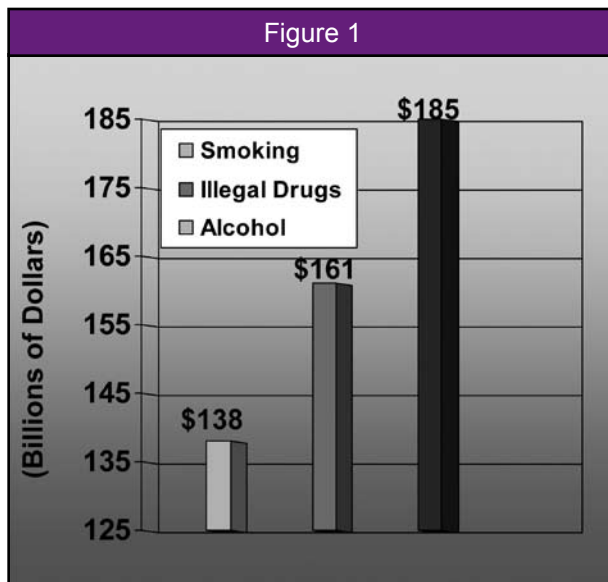
The group of mice that genetically disliked alcohol was injected with alcohol. Each mouse was injected with an amount of alcohol to mimic what might be consumed by a human if he was a heavy drinker. Before long, the mice that originally disliked alcohol now preferred alcohol and would drink themselves to death (Fig 3b).

The researchers took another group of alcohol disliking mice and stressed them by confining them, intermittently, in close quarters. Over time, these mice started consuming more and more alcohol instead of water (Fig. 3c).

Another researcher limited the vitamin B in a group of mice that disliked alcohol. This nutritionally insufficient diet led to

an increase in alcohol consumption (Fig 3d).

A number of observations need to be made about these experiments. The first point addresses the question, "Did the mice return to their genetic predisposition after the significant experimental conditions were discontinued?" As expected, the mice that genetically liked alcohol continued to drink alcohol when they had the opportunity after the experimental conditions were halted. All the mice that genetically disliked alcohol but were injected with it, stressed by close



Graph adapted from NIDA website. *Drug Abuse and Addiction: One of America's Most Challenging Public Health Problems.*

confinement, or were fed a nutritionally deficient diet continued to use alcohol addictively when given the opportunity after these experimental conditions were concluded.

Second, the strain of mice that liked alcohol had a neurotransmitter imbalance before the experiment started. The mice that disliked alcohol had a normal neurochemical balance. After the experiment, all groups of mice showed neurochemical imbalances that made them prefer alcohol.

These results demonstrate that addiction was the outcome whether it was brought on by a genetic factor (mice that liked alcohol), the chemical itself (mice that were injected with alcohol), stress (mice that were confined), or nutritional deficiency (mice that were fed a nutritionally insufficient diet). Of course, there would have been no alcohol addiction if none of the mice were

exposed to alcohol.<sup>7, 11-15</sup>

## Human Studies

The assumption that alcohol abuse and addiction runs in families is not new.<sup>16-18</sup> This assumption has been shown to be true.<sup>19</sup> Studies suggest that close relatives of alcoholics have a three to seven times greater risk of developing an alcohol addiction.<sup>20</sup> It has also been shown that other chemical addictions run in families.<sup>21</sup>

While this information is interesting and useful, we could assume this observation is due to some family members simply learning this behavior from other family members. If this behavior is simply a learned behavior, then it would not be a genetic trait passed from one generation to the next.

One way of distinguishing the difference between environmental influences versus genetic traits is studying sons that had been adopted at birth. This allows one set of parents to furnish the genetic material and another to supply the environment. Sons of alcohol addicted fathers that were adopted and therefore received no environmental influence from their genetic parents had an increased alcohol addiction rate.<sup>18</sup>

Another way of separating the genetic influences from the environmental influences in chemical dependency is twin

studies. Twin studies have been useful in identifying the role of genetics in chemical dependency. There have been two approaches used. One compares the rate of chemical dependency in identical (monozygotic) twins to fraternal (dizygotic) twins. Monozygotic twins are genetically identical. Dizygotic twins share only one half of their genes. If chemical dependency has an important genetic component, we would expect the same trait to be expressed more often in the monozygotic twins than in the dizygotic twins.

An additional technique, which has been useful in twin studies, is when twins have been separated at birth. If they come from a chemically dependent parent, we would expect to find a higher incidence of chemical dependency in them regardless of the environment of the adoptive parents if chemical dependency is indeed an

(Continued on Page 12)

inheritable trait.

The human twin studies suggest genetic factors have a dramatic role in chemical dependency. Inheritability represents a 50% impact on the disease of chemical dependency.<sup>17, 22-27</sup>

Three other findings from human studies are worthy of attention. First, studies have shown that young men from alcoholic pedigrees, with little experience with alcohol, tend to be affected less by alcohol. That is, when they drank, they felt less intoxicated; their electrical brain activity was less affected. Also, their walking and speaking seemed to be impacted to a lesser extent.<sup>28, 29</sup>

Second, it seems family history might be the best predictor of alcohol addiction as an adult. However, family history is not as good a predictor of adolescent drinking as the drinking behavior of an adolescent's peer group.<sup>30-32</sup>

Third, Kendler and others in their twin studies could find no inherited trait toward the preference of one chemically addictive substance over another. While they confirmed the genetic tendency to become chemically dependent, there seems to be no genetic influence passing along a specific preference for one type of mood altering chemical over another.<sup>33</sup>

**Molecular Genetic Studies**

The Human Genome Project was a 13 year project that ended in 2003. Its goal was to identify all of the approximately 25,000 genes in the human DNA. It is expected this project will have a major impact on all health care professionals in the future. The Collaborative Study on the Genetics of Alcoholism is a study to identify genes that affect the risk of alcohol addiction. This is a large scale study comprising six different sites and involving thousands of families. Alcohol addiction is assumed to be a complex genetic disorder with multiple gene involvement (genotype) producing many different behaviors and physical characteristics (phenotype).<sup>21, 34-36</sup>

At this point, particular regions on at least genes 1, 2, 3, and 7 seem to be involved and may increase a person's

risk of alcoholism. Genes related to the inheritance of the disease of chemical dependency may involve the neurotransmitter-receptor systems of GABA and acetylcholine; the dopamine receptor; the opioid receptors  $\mu$  (*mu*),  $\kappa$  (*kappa*), and  $\delta$  (*delta*); and the serotonin transporter.<sup>35</sup> An in-depth review of these complex molecular genetic studies is beyond the scope of this article, but one example of a site found on gene 4 might be instructive.

flushing, tachycardia, headaches, and nausea. This defective gene is more common in Asian populations than in Caucasians. Disulfiram, a medication used in some cases to help treat alcohol addictions, produces the same adverse reaction by blocking the metabolism of acetaldehyde. The aversion produced by this adverse reaction may help an alcohol addict reduce his drinking.<sup>8, 10, 37</sup>

As one might expect, alcohol addiction is less common in people with this gene variation. While it is less common, there are people with this genotype that have developed the phenotype of alcohol addiction.

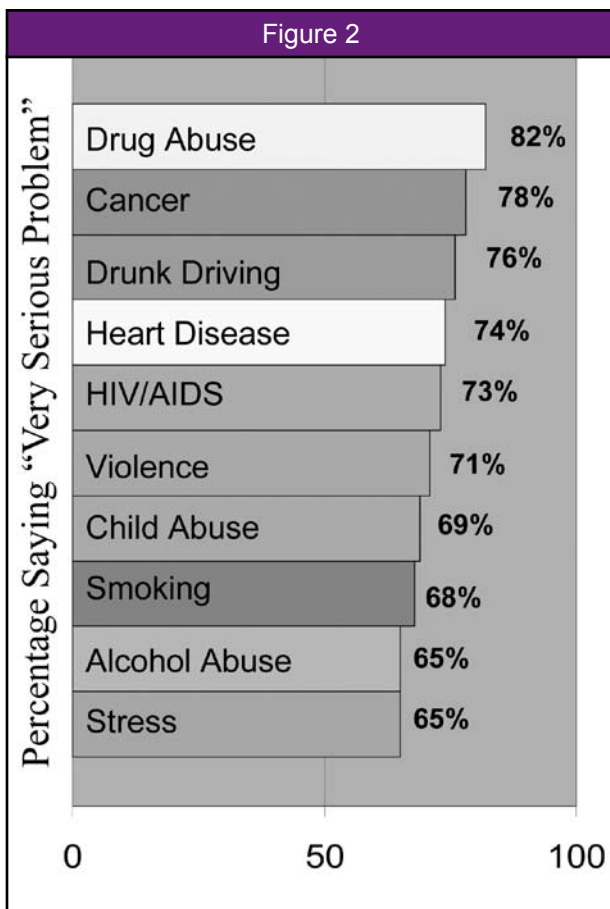
**Conclusions**

The disease of chemical dependency has a significant impact on our society and our patients. While environmental influences are a factor, it is apparent that genetics play a major role. This disease seems to be much like diabetes or other complex, polygenetic inherited disorders. No one gene makes a person chemically dependent. Hope exists that many of these complex genetic diseases will be better understood in the future with the completion of the Human Genome Project and ongoing research like the Collaborative Study on the Genetics of Alcoholism.

While one may not have the inherited trait to become chemically dependent, it is important to realize that no one may be immune to this disease. As discussed above, the mice that disliked alcohol and were injected became addicted. Also, some humans that had the "protective gene" developed chemical

dependency.

Considering the inheritability of chemical dependency, a thorough history, including a family history of this disease, seems to be in order for all of our patients. If a patient has a positive family history, the risks of prescribing mood altering chemicals should be recognized by the dentist and explained to the patient. It seems prudent to recommend that patients with a positive family history of chemical dependency refrain from mood altering



Graph adapted from NIDA website. Drug Abuse and Addiction: One of America's Most Challenging Public Health Problems.

There seems to be a "defective gene" in some people for the encoding of aldehyde dehydrogenase. Aldehyde dehydrogenase is an important enzyme in the metabolism of alcohol. The people that have this defective gene cannot metabolize alcohol as effectively as people with the more commonly found gene. Therefore, in people with this defective gene, acetaldehyde builds up, and they experience very uncomfortable symptoms. These symptoms include

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chemicals, both legal and illegal, except for appropriate medical/dental use. Beyond a thorough history and informing the patient about the disease when a patient presents in our office with the disease, we are responsible for treating this patient in an informed and appropriate manner.

Kimberly Bullock, M. D., recommends dentists perform interventions on chemically dependent patients. She writes, "Brief intervention therapy has been shown to be just as effective as a structured, intensive treatment plan and is easy for the dental provider to accomplish."<sup>38</sup> Being prepared to do an intervention not only requires a dentist to be familiar with the influence of genetic factors on chemical dependency, but he must also have the suitable educational materials available. He must also be familiar with the treatment professionals in his area to make an appropriate referral.

Because no one is immune to this disorder, an in-depth understanding of chemical dependence will help us deal with the potential risk of the disease in our patients, our family, as well as ourselves. Additionally, an appreciation for the disease will, hopefully, help us interact appropriately with other members of our profession that have this illness.

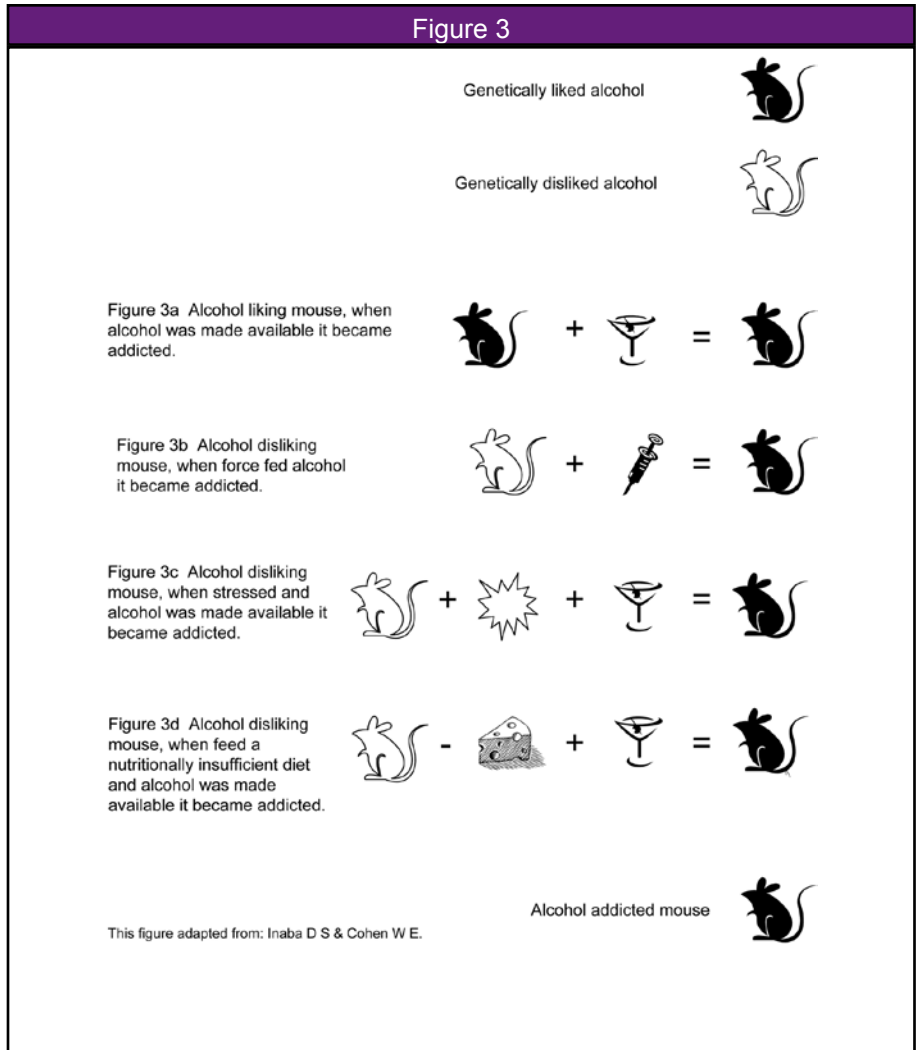
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Two strains of mice have been bred. One genetically liked alcohol and one genetically disliked alcohol. This figure adapted from Inaba D S & Cohen W E.

Complete the Chemical Dependency exam on page 17 and submit with payment to the TDA Executive Office. The exam page may be duplicated for use by multiple individuals.

# Exam for 2009 Chemical Dependency CE Article

1. According to the National Institute on Drug Abuse (NIDA) America's most challenging public health problem is:
  - a. Heart disease
  - b. Smoking
  - c. Drug abuse
  - d. Cancer
2. Aldehyde Dehydrogenase is an important enzyme in the metabolism of:
  - a. Hydrocodone
  - b. Alcohol
  - c. Cocaine
  - d. Emerol
3. Intelligence is a guaranteed protection against addiction:
  - a. True
  - b. False
4. The genetic role of the disease of chemical dependency seems to be:
  - a. From one specific gene
  - b. One specific strain of DNA
  - c. A polygenetic inherited disorder
  - d. No genetic implications
5. According to human twin studies, inheritability represents a \_\_\_\_\_ percent impact on the disease of chemical dependency:
  - a. 50%
  - b. 60%
  - c. 43%
  - d. 71%
6. Alcohol addiction is a complex genetic disorder with multiple gene involvement producing:
  - a. Increased members of the clergy
  - b. "Rock" stars
  - c. Professional athletes
  - d. Different behaviors and physical characteristics
7. Human studies have shown that young men from alcoholic pedigrees and little experience with alcohol:
  - a. Become more intoxicated when they drink
  - b. Show increased electrical brain activity
  - c. Walking and speaking seemed to be impacted to a greater extent
  - d. Tend to be affected less by alcohol
8. Kendler and others found an inherited trait for which addictive substance:
  - a. No trait toward the preference of one substance over another was found
  - b. Cocaine
  - c. Alcohol
  - d. THC
9. What seems to be the best predictor of alcohol addiction as an adult:
  - a. Beer parties in college
  - b. Family history
  - c. Rave parties
  - d. Smoking
10. According to the National Institute of Health, substance abuse in America costs:
  - a. Less than the cost of diabetes
  - b. Same as cancer
  - c. \$484 billion per year
  - d. Same as cancer and diabetes combined
11. A report from the Collaborative Study on Genetics of Alcoholism, Archives of General Psychiatry, alcohol was the only substance that was shown to have familial transmission:
  - a. True
  - b. False
12. Which of the following statements are true according to researchers studying the effects of alcohol on mice:
  - a. Mice that liked alcohol had a neurotransmitter imbalance before the experiment
  - b. Mice that disliked alcohol had a normal neurochemical balance before the experiment
  - c. Both groups of mice showed neurochemical imbalances after the experiment
  - d. All statements are true

1. Circle the correct answer on the exam and complete the form below;

2. Mail, along with your check or credit card payment, to: Tennessee Dental Association, 660 Bakers Bridge Ave., Suite 300, Franklin, TN 37067, prior to January 31, 2010.

Date: \_\_\_\_\_ (Credit is granted, upon successful completion of the exam, in the year materials are read and the exam submitted.)

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