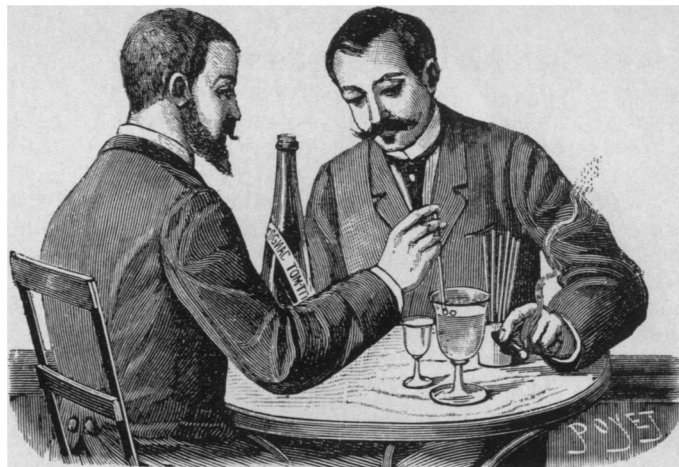


# Alcoholism's Elusive Genes

It runs in families and ruins lives, but is alcoholism inherited?



By BRUCE BOWER

**R**esearch into the genetics of alcoholism has taken off in the last 15 years, and with it has risen an air of inevitability. A dizzying array of data from around the world has led many people to think of this tragic disorder as a disease stemming from tainted genes.

This view received federal approval in 1985 with publication of a National Institute on Alcohol Abuse and Alcoholism (NIAAA) monograph titled "Alcoholism: An Inherited Disease." Recent research shows, according to the monograph, that heredity is a major contributing cause of alcoholism "in a large proportion of cases, and perhaps in nearly all cases."

Scientists involved in the inheritance investigations are far more cautious in interpreting the findings, however, and some fear that the NIAAA as well as many concerned individuals hold an oversimplified view of alcoholism's causes. Although these researchers search for genetic clues, they see alcoholism largely as a complex interaction of nature and nurture, with nature not necessarily being the dominant factor.

"It's easier to study the biology [of alcoholism]," says psychiatrist Marc A. Schuckit of the University of California at San Diego, who has identified several potential biological markers of alcoholism in the sons of alcoholics. "I know I'm only studying part of the pie, but there are no good environmental measures at this point."

Psychiatrist Donald W. Goodwin of the University of Kansas in Kansas City has found that children of alcoholics have an increased risk of becoming alcoholic even when brought up by adoptive parents, but he echoes Schuckit's caution. "The chances of a genetic factor playing an important role in some cases have increased sizably as a result of several adoption studies," he notes. "But these studies do not unequivocally prove that

the major cause of alcoholism is genetic."

Psychologist John S. Searles of the University of Pennsylvania in Philadelphia goes a step further. Investigations of the genetic legacy in alcoholism have been "readily and uncritically accepted" by many scientists and clinicians, he maintains in the May *JOURNAL OF ABNORMAL PSYCHOLOGY*. Twin, adoption and biological-marker studies have also injected new vigor into the long-running, acrimonious debate over whether alcoholism is a disease or a learned behavior. But ironically, says Searles, that same work highlights the need to identify critical environmental pressures driving alcoholics to the bottle.

If investigators do not heed the environmental implications of genetic studies, he argues, it will hinder efforts to identify and treat alcohol abusers as early as possible.

**A** case in point, says Searles, is an influential adoption study directed by psychiatrist C. Robert Cloninger of Washington University in St. Louis. Searles' reanalysis of the investigation suggests that as-yet-unspecified environmental pressures played a dominant role in determining alcohol abuse, not often-cited genetic factors.

Cloninger and his colleagues analyzed extensive government records in Sweden on 862 men and 913 women adopted at an early age, as well as background information on their biological and adoptive parents.

In 1981, they suggested there are two types of predisposition to alcoholism. Type 1, or "milieu-limited," alcoholism was found in three-quarters of the abusers. It occurred among men and women 25 years of age or older, and was linked to both a family history of alcoholism and four environmental influences: being reared by the biological

mother for more than six months, greater age at the time of adoptive placement, more time spent in the hospital prior to placement and lower occupational status of the adoptive father. Less common was Type 2, or "male-limited," alcoholism. This brand was largely unaffected by the environment. It often developed during adolescence and was accompanied by aggressive behavior and law breaking.

According to Cloninger, Type 1s are often highly anxious, emotionally dependent on others, shy and reflective. Type 2s, on the other hand, are impulsive, distractible and emotionally detached. Many alcohol abusers, he says, have some personality traits from both types.

Cloninger's discovery of two predictable types of alcoholism is "at best, preliminary and, at worst, unfounded," holds Searles. One problem with the Swedish study, he argues, was the lack of a non-adopted control group to test for the effects of being an adopted child. As in many adoption studies, Searles adds, it is not known whether biological mothers drank heavily during their pregnancies, possibly creating a constitutional (not genetic) risk for alcoholism in their unborn children. Furthermore, environmental measures were limited to what could be gleaned from official records and do not explore specific environmental influences on each adoptive child and his or her siblings.

To top it off, says Searles, alcohol abuse was defined in an unusual way — by the number of times each adoptee was registered with Sweden's county Temperance Boards for insobriety, usually after public intoxication, family violence or traffic offenses. There is no counterpart to this system in the United States.

In his review of Cloninger's data, Searles finds that almost half of the adoptees classified as alcohol abusers had neither a genetic predisposition nor

an environmental "releaser" linked closely to their drinking habits. Overall, he concludes, unidentified environmental pressures were probably more important in determining alcohol abuse than were genetic factors.

There is also reason to question Goodwin's Danish adoption studies, maintains Searles. Goodwin and his co-workers found that adopted boys with an alcoholic biological parent are four times more likely to become alcoholic than are counterparts without an alcoholic biological parent. But nearly half the adoptive parents in the study had psychiatric disorders, Searles says, which may have influenced the development of alcoholism. It is also unclear, he says, why Goodwin's study found an increased genetic influence among subjects diagnosed as alcoholic, but not among those given milder diagnoses such as problem drinkers or heavy drinkers.

The adoption studies nevertheless indicate an important genetic predisposition to alcoholism in men and women with an extensive family history of alcohol abuse, Goodwin says. Cloninger's male-only Type 2 alcoholism is actually a co-ed category, adds Goodwin. Female alcoholics, he explains, are less likely to be diagnosed by physicians or arrested for criminal behavior, thus leading to an underestimate of their numbers.

**A**t the least, in Searles' view, adoption studies must move beyond a reliance on government records to diagnose alcohol abuse. Some investigations, he says, have inaccurately lumped "problem drinkers" and "heavy drinkers" into the alcoholic category.

A better picture of genetic and environmental contributions to alcoholism, says Searles, may come from the Colorado Adoption Project, an extensive study incorporating measures of environmental influences on each sibling in an adopted child's family. This long-term investigation of 182 adopted infants and 165 control infants was launched in 1975 by psychologist Robert Plomin and his colleagues of the University of Colorado in Boulder; the children are still too young to be evaluated for alcoholism and alcohol abuse.

Another approach in determining the development of alcoholism involves tracking a large group over several decades. For example, in an analysis of a prospective 40-year study of 600 men begun in the 1940s by Harvard researchers, psychiatrist George Vaillant of Dartmouth University in Hanover, N.H., concluded in 1983 that the major risks for alcoholism were having an alcoholic parent and coming from an ethnic background that condones adult drunkenness. Antisocial behavior and emotional problems such as depression are usually the result of alcoholism, he reported, not its cause.

But several researchers, including psy-

## A problem of definition

**E**pidemiologists estimate there are about 10 million severe alcoholics and another 7 million alcohol abusers in the United States. At the extremes, alcohol abuse is easy to identify, but the distinction between heavy drinking and alcoholism is often murky.

The National Council on Alcoholism defines alcoholism as a "chronic, progressive and potentially fatal disease" marked by "repeated drinking that causes trouble in the drinker's personal, professional or family life. When they drink, alcoholics can't always predict when they'll stop, how much they'll drink or what the consequences of their drinking will be."

The recently revised manual of psychiatric disorders published by the American Psychiatric Association de-

scribes three patterns of alcohol abuse or dependence: regular daily drinking of large amounts, regular heavy drinking limited to weekends, and long periods of sobriety punctuated by heavy drinking binges lasting for weeks or months. "It is a mistake to associate one of these particular patterns exclusively with alcoholism," advises the manual.

The abuse of other drugs, including marijuana, cocaine, heroin, amphetamines and sedatives, often accompanies alcohol dependence, according to the manual.

However alcoholism is defined, it is clear that most alcohol is consumed by a small percentage of people. In the United States, 10 percent of the drinkers imbibe 50 percent of all alcohol consumed. — B. Bower

chologist Robert A. Zucker of Michigan State University in East Lansing, have reanalyzed Vaillant's data and found that adolescent antisocial behavior, including misbehavior at school and truancy, played an important role in stimulating later alcoholism. Moreover, critics charge that since Vaillant's study began when participants were teenagers, it neglected childhood influences on adult alcoholism.

In an effort to identify people with a genetic vulnerability to alcoholism, investigators have sought biological markers appearing exclusively among youngsters with a family history of alcohol dependence. Schuckit has reported that, compared with sons of nonalcoholics, sons of alcoholics feel less drunk, display a less intense hormonal reaction and exhibit less body sway after drinking (SN: 11/21/87, p.324). In addition, sons of alcoholics have a distinctive brain-wave pattern also found among abstinent alcoholics.

Children in these marker studies are being followed into adulthood, and researchers are attempting to chart important events and influences in their lives that might contribute to alcohol dependence.

**O**n the molecular level, scientists at the NIAAA are looking for associations between specific markers on DNA and drinking patterns among members of families with a history of alcoholism. Experiments with mice bred to prefer alcohol over water have revealed a potential gene position on chromosome 1 possibly involved in the control of alcohol intake. The function of the protein coded at the gene position is unknown.

These and other biological-marker studies are just beginning, says Schuckit. It remains to be seen if any biological markers exist in women or across ethnic groups, and how biological mechanisms responsible for reactions to alcohol might affect the development of alcoholism.

"It's clear from family history studies on alcoholism that something in addition to genetic transmission is going on," says psychiatrist and alcoholism researcher Theodore Reich of the Jewish Hospital of St. Louis. "That 'something' is a potent phenomenon."

He and his colleagues are developing measures of the extent to which youngsters resemble their alcoholic parents and their siblings in various behavioral and psychological characteristics. If siblings develop increasingly different susceptibilities to alcoholism as they age, says Reich, "the effect of aging on susceptibility is likely to be culturally based. Genetic effects are usually more stable."

Biologically inherited factors still may influence the transmission of alcoholism, notes Reich. Several genetic mechanisms, for instance, may be related to the process of becoming addicted to a variety of drugs. On the other hand, some people may inherit buffers to alcohol use. One such buffer is a genetically based enzyme deficiency found among many Asians that delays alcohol metabolism and causes facial flushing, queasiness and other unpleasant physiological reactions after ingestion of small amounts of alcohol.

Psychiatric disorders with a genetic legacy also may lead to alcoholism, Reich says. Alcoholics often have other psychi-

*Continued on p.79*

spectral energy is in the ultraviolet, it's not visible to the eye. But the wintergreen's fluorescence is in the visible part of the spectrum. So the more wintergreen there is, Sweeting found, the higher the proportion of sugar-lightning emissions that will be shifted to visible light.

Although she investigated the unexplained candy-flashing phenomenon

though it was triboluminescent, there was no sign of what might be energizing its glow. Microlightning, the most obvious explanation, was conspicuously absent.

Sweeting now says "the theoretical importance of the candy experiments is that it gives us a way to estimate how big the lightning would be, if it were there [in the substituted-anthracene case]." Using

*Continued from p.75*

atric diagnoses, including antisocial personality (marked by rebelliousness, family and social problems and law breaking), anxiety, depression and schizophrenia.

For now, though, a direct connection between heredity and alcoholism is a "missing link," says anthropologist Dwight B. Heath of Brown University in Providence, R.I. The question of who is at risk is a sticky one, notes Heath, who studies cultural and social influences on alcohol use. It may be true, he explains, that half of hospitalized alcoholics have alcoholic relatives and one out of four sons of alcoholics become alcoholics themselves, but this says nothing about any individual's risk of alcoholism.

"Certainly there are more sons of alcoholics who do not have drinking problems than who do, just as there are many problem drinkers who have no alcoholic relatives," says Heath. "No one is genetically predestined to become an alcoholic. Even if the genetic missing link were eventually found, the interaction of various environmental factors is certainly crucial if alcoholism is to occur in an individual." □

Next: Alcoholism as learned behavior



"just because it was there," Sweeting later realized her findings point toward "something that could be important"—what lies behind the triboluminescence of other perplexing crystals.

Many asymmetric crystals create an electrical voltage when squeezed, pressed or crushed. Ones that don't—and many are triboluminescent—interest Sweeting. "Substituted anthracene," a molecule with appendages of carbons and oxygens coming off its three rings, creates one such crystal. What particularly intrigued Sweeting was that al-

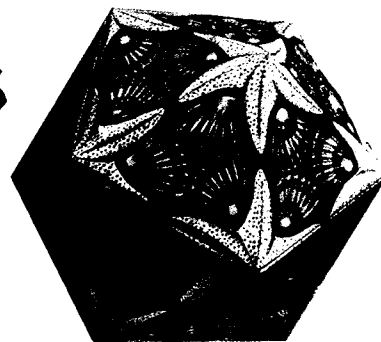
the formula she computed from the wintergreen candy as a gauge, she estimated the percentage of lightning that would have been needed to energize these anthracene-based compounds into glowing. And her calculations suggest it "would be on the order of 0.005 percent [of their triboluminescent display]—way too little to see with current technologies."

So the fact that she didn't see lightning in the substituted anthracene's triboluminescence no longer means it's not there. And that's sweet news to one who has been hunting it so long. □



# M.C. Escher Kaleidocycles

Doris Schattschneider Wallace Walker



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— Doris Schattschneider

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