Alcoholism Shows Its Youthful Side

A surprisingly large number of people who exhibit serious alcohol problems, including alcoholism, began imbibing during childhood or on the cusp of adolescence, a national survey finds.

Young people who take up alcohol drinking before age 15 are four times as likely to become alcohol-dependent—a diagnosis that corresponds to alcoholism—as those who begin drinking at age 21, according to psychiatric epidemiologists Bridget F. Grant and Deborah A. Dawson, both of the National Institute on Alcohol Abuse and Alcoholism (NIAAA) in Bethesda, Md. Small tastes or sips did not count as drinking.

The rate of alcohol abuse—a less severe but nonetheless disruptive condition—more than doubles in youngsters who start drinking before age 15, compared to those who first use booze as 21-year-olds, Grant and Dawson report in the January JOURNAL OF SUBSTANCE ABUSE.

"It was not previously known that alcohol dependence was influenced in such a dramatic way by early alcohol drinking," commented psychiatrist and NIAAA director Enoch Gordis at a press conference held in Washington, D.C., last week to announce the findings. Adolescent alcohol use has been linked to several troubling characteristics, however, including an increased risk of becoming depressed or violent.

It is not known whether the prevention of early alcohol drinking will, by itself, steer individuals away from alcoholism. "We don't know what causes this

extraordinary association between early drinking and later alcohol dependence," Gordis says.

Grant and Dawson examined interview responses of 27,616 current or former alcohol drinkers obtained by U.S. Census Bureau field-workers in 1992. The interviews focused mainly on symptoms of alcohol abuse and dependence.

The prevalence of alcohol dependence declined as the age of initial drinking rose, the researchers note. About 40 percent of those who began drinking before age 15 became alcohol-dependent at some later time, compared to 25 percent of those who began drinking at age 17 and 10 percent of those who first tried alcohol at ages 21 or 22.

Curiously, the prevalence of alcohol dependence rose for those who began drinking at ages 23 and 24—to around 15 percent and 14 percent, respectively. It then declined sharply for those whose alcohol initiation occurred after age 25.

Alcohol use that starts around 23 or 24, which is extremely late for U.S. residents, may signal the presence of emotional problems that contribute to a desire to drink excessively, the scientists suggest. A related study found better psychological health in teens who occasionally experimented with illicit drugs than in those who used drugs either frequently or not at all (SN: 5/1/93, p. 282).

Alcohol abuse also declined sharply among those who first imbibed at later ages, falling from 14 percent for those who started at age 14 to 2.5 percent for those who started at age 25 or older.

This pattern held for men and women, blacks and whites, and participants with and without alcoholic family members.

"I'm not surprised at these findings," says psychologist Rudy E. Vuchinich of Auburn (Ala.) University. Kids who begin drinking after age 15 may have had a chance to establish constructive habits and activities that discourage excessive alcohol use, he theorizes.

Further research is needed to determine whether early alcohol use induces brain changes that foster problems with alcohol later, Gordis adds. —*B. Bower*

Built-in drugs could target tissues

Instead of being packaged inside a pill, a special class of drugs can be stitched right into the fabric of a protein, a new study suggests. By choosing an appropriate protein as a delivery vehicle, scientists may be able to send these drugs to specific tissues or time their release in a new way.

Researchers at the Max Planck Institute for Biochemistry in Martinsried, Germany, demonstrated the feasibility of this idea by synthesizing a protein in which one amino acid was replaced with a non-natural, biologically active one. According to their scenario, the modified protein would travel inside the body like its normal counterpart and then deliver its drug—the nonstandard amino acid—to target cells. The team's report appears in the Jan. 20 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

"This is very nice work," says Peter G. Schultz of the University of California, Berkeley. "It's a novel application of the incorporation of amino acid analogs into proteins."

The researchers fed *Escherichia coli* bacteria with thiaproline, a version of the amino acid proline in which a sulfur atom replaces a carbon atom. About 20 years ago, thiaproline was heralded as a potential cancer treatment. "That euphoria calmed down a few years after," says study coauthor Nediljko Budisa, "mainly because of many toxic effects of thiaproline for other parts of the body."

Budisa and his coworkers had engineered the *E. coli* to make the human protein annexin V, "a good model protein, since its structure is well known and characterized, and purification is convenient and simple," Budisa says. Annexin V moves calcium ions across membranes, but its overall role in animals is not known.

The annexin V produced by *E. coli* incorporated thiaproline and retained its three-dimensional structure and biological function, but it was less stable when heated. Structurally familiar proteins should evade attack from the immune system while on their way to target cells, the authors reasoned. Once there, ordinary protein digestion should free up the altered amino acid to act as a drug.

Delivering pharmaceuticals in proteins could potentially reduce the amount of drug needed, suggests Budisa. Compared to the dose that achieves an effective overall concentration in the body, a much smaller amount of the compound could be escorted by a protein directly to appropriate tissues, where it would act, he says.

Amino acid substitution also provides a way to study how proteins fold and function. For example, scientists can deduce from the substitution of sulfur for carbon, an "atomic mutation," how that small difference affects annexin V.

This method comes with a catch, however. Bacterial synthesis produces a lot of protein, but the amino acids insert themselves randomly at many locations. Although that may be fine for drug delivery, protein studies require changes at a single location. Scientists would need to make the protein in a test tube, but then "you're limited to submilligram quantities," explains Schultz. To get around this obstacle, he and his colleagues are engineering a bacterium that can insert a non-natural amino acid only in specified locations. —*C. Wu*