Alcoholics Offer Surprises in Long Run

Depressed people rarely resort to uncontrolled alcohol use, but alcoholics often get depressed. Alcoholism, like obesity or hypertension, usually reaches a stable plateau rather than getting progressively worse, like AIDS or multiple sclerosis. Compared with moderate alcohol abusers, hard-core alcoholics stand a better chance both of giving up the bottle and of dying young.

These and other results of a 50-year prospective study of two groups of men, one poor and the other privileged, provide a sobering jolt to some widespread assumptions about alcoholism.

"Alcoholics often feel that they began drinking to alleviate depression, and researchers often accept that view," asserts George E. Vaillant, a psychiatrist at Brigham and Women's Hospital in Boston. "But that is as wrong as thinking that the world is flat."

Vaillant presented his findings at the annual meeting of the American Psychiatric Association in Washington, D.C., last week.

One group in his study consists of 456 men recruited between 1940 and 1943, when they were in their early teens. The men, from some of the poorest parts of Boston, originally served as controls in a study of juvenile delinquency. The other group consists of 268 men selected between 1940 and 1942 as Harvard University sophomores to participate in a study of physical health.

Vaillant analyzed early prospective data on these men gathered by other researchers and, starting in 1977, coordinated regular physical and psychological follow-ups. At the time of the most recent follow-up, in 1992, participants were between 60 and 70 years old.

Over the 50-year study, about one-third of the city sample and one-fifth of the college sample developed alcohol dependence — heavy, uncontrolled alcohol consumption on a regular basis.

City men tended to descend into alcoholism between age 21 and 30 and often developed severe forms of the disorder with wide-ranging effects on their lives. College men more often developed alcoholism between age 41 and 50 and generally displayed more moderate symptoms than their city counterparts.

By age 60, only one alcoholic in five still abused alcohol.

Alcoholics in both groups died at three times the rate of nonalcoholics, and alcoholics who smoked cigarettes stood the greatest chance of dying during the study period, Vaillant says. Smokers who stopped drinking displayed increased mortality because they usually smoked more cigarettes to compensate for the loss of liquor, he adds.

Ironically, the heaviest abusers of alcohol both died and recovered most often. For many alcoholics, fundamental change may require the dire consequences of "hitting rock bottom," Vaillant holds.

After five years of abstinence, alcoholics almost always avoided any further alcohol abuse. Those with shorter periods of abstinence often resumed heavy alcohol consumption.

A small minority of men drank alcohol for up to one year in a "controlled" fashion that fell short of alcohol abuse. But most then returned to their previous level of alcoholism.

"Trying to return to controlled drinking is a bit like driving without a spare tire," Vaillant contends.

Depression often coexisted with alcoholism, but alcoholism usually began first, according to Vaillant.

About one-third of all the men received hospital treatment for alcoholism at some time, but treatment did not affect the long-term course of their disorder, Vaillant argues. Around 40 percent attended Alcoholics Anonymous regularly.

Hospital treatment for alcoholics usually lasts about a month and offers important short-term help, Vaillant says. But clinicians must develop ways to help people abstain for five years following hospitalization to change the long-term course of the disease, he contends.

Vaillant's data also challenge a popular theory that men with a strong genetic predisposition to alcoholism experience an extreme version of the illness by young adulthood, whereas alcoholism occurs later and with fewer problems among men who respond mainly to environmental influences.

In Vaillant's study, a family history of alcoholism — indicating a genetic contribution of some kind — characterized both early- and late-onset alcoholics. However, alcoholism in close relatives, combined with a troubled family life while growing up, frequently led to early alcoholism in study participants.

"Prospective follow-up suggests that alcoholic heredity affects *whether* someone develops alcoholism and a chaotic family life affects *when* someone develops alcoholism," Vaillant asserts. — *B. Bower*

Cancer risk linked to increased DNA mix-ups

Genomic instability — the tendency of DNA to get mixed up and for genes to mutate — underlies evolutionary change and makes possible varied immune responses against infections. But this tendency can also get cells in trouble and ultimately lead to cancer.

An analysis of genetic activity in people with an inherited defect that predisposes them to malignant tumors now strongly supports this notion. Also, a new test may make it possible to assess DNA mix-ups in large groups of people.

"If we can measure genetic instability, then we might be able to gain insight into the risk of that individual or that population to develop cancer," says Ilan Kirsch of the National Cancer Institute-Navy Oncology Branch in Bethesda, Md.

Finally, evidence is building that problems concerning the tumor-suppressor gene p53 (SN: 5/16/92, p.324) may exacerbate this instability and predispose a cell to uncontrolled division.

The cancer-predisposing genetic disease, called ataxia-telangiectasia (A-T), leads not only to tumors but also to problems with nerves and the immune system. This presumably results because genes fail to rearrange and generate a diverse array of antibodies, says M. Stephen Meyn, a clinical geneticist at Yale University School of Medicine. Cells in people with A-T are also very susceptible to ionizing radiation.

But Meyn's study shows that genes within chromosomes of people with A-T play molecular musical chairs — moving around at rates 30 to 200 times higher than those of normal cells, he says.

Unlike previous investigators, who evaluated rearrangements in free-floating DNA inserted into cells and saw little increase in these rearrangements, Meyn waited until that DNA became incorporated into the cell's own chromosomes. In one experiment, the DNA insert contained two defective copies of a gene that, when repaired, enables cells to resist the killing effects of an antibiotic. In another, the insert contained two defective copies of a gene that, if repaired, makes cells blue. The large number of surviving cells or the number of blue cells revealed the high frequency of mix-ups, he reports in the May 28 SCIENCE.

"In these high rates of recombination, one finds a ready explanation for why A-T patients get cancer," Meyn concludes.

The high rate of DNA mix-ups seen by Meyn parallels observations by Kirsch and his colleagues, who use a very different measure of genomic instability. These researchers focus on mix-ups that occur between two pieces of chromosome 7, whose DNA is active in white blood cells. The mix-up causes the cells to make a hybrid molecule consisting of parts of