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Annotation: Alcohol and Longevity

There are more old wine drinkers than old doctors.

—German proverb

Although epidemiologically unsound, this bit of folklore suggests a general public awareness that drinking alcoholic beverages may contribute to longevity; it also suggests skepticism about medical advice. Social and medical harm from heavier drinking has always been evident, but the concept of a safe limit has also been accepted. For example, in 1861 Anstie's Rule advised a daily limit of 45 mL of alcohol (about three drinks)¹; more recently, the Royal Colleges of General Practitioners, Psychiatrists, and Physicians advised a "sensible" weekly limit of 21 small drinks for men and 14 for women.² Modern epidemiologic population studies of alcohol and mortality risk confirm increased risk at three or more

drinks per day, with yet higher risk at very heavy drinking levels.³⁻¹³ The same studies validate the folk wisdom about the benefits of drinking by showing lowered mortality risk for light to moderate drinkers. Thus, there is a J-shaped alcohol-mortality curve, with the lowest risk among drinkers who take less than three drinks daily. Numerous conditions contribute to the higher risk of heavier drinkers, including liver cirrhosis, pancreatitis, gastritis, trauma, suicide, certain cancers, cardiomyopathy, hypertension, cardiac arrhythmia, hemorrhagic stroke, and degenerative nervous system conditions. The lower risk of lighter drinkers is due almost entirely to less coronary heart disease, with smaller contributions from ischemic stroke and gallstones.

The first population study showing lower mortality in moderate drinkers than

in abstainers was published in 1926 by Raymond Pearl.¹⁴ In this study of working-class Baltimore residents, no specific causes of death were analyzed. With no explanation, Pearl avoided attributing any benefit to lighter drinking in those Prohibition days, but he did conclude that such drinking was probably not harmful. He also suggested the possibility that earlier death among abstainers might, in some cases, be attributable to "constitutional" weakness systematically related to a tendency to abstain from alcohol.

Epidemiological studies in recent years have consistently shown that alcohol drinkers have a lower risk of fatal³⁻¹³ and nonfatal^{5,9,11,15} coronary heart disease events. The studies show that this relation-

Editor's Note. See related article by Carmelli et al. (p 99) in this issue.

ship is independent from numerous potential confounders, including age, sex, ethnicity, cigarette smoking, education, adiposity, dietary habits, and physical exercise. With respect to coronary heart disease mortality, the risk of heavier drinkers is greater than that of lighter drinkers, so that the alcohol–coronary heart disease mortality relation is U-shaped. Some earlier studies were unable to separate ex-drinkers from lifelong abstainers or to control for baseline coronary heart disease risk. This problem was highlighted by Shaper, whose study showed little alcohol–coronary heart disease relation among persons free of baseline disease.¹⁶ This led to the speculation that prior movement of high-risk persons into the nondrinking reference group explained the U-shaped curve (the “sick quitter” hypothesis). However, a number of studies^{3,8–12,17} that separated ex-drinkers from lifelong abstainers, controlled for baseline coronary heart disease risk, or both have also shown that drinkers have lower coronary heart disease risk than do abstainers and thus refute the sick quitter hypothesis.^{3,8–12,17} Plausible biological mechanisms for a protective effect of alcohol against coronary heart disease have been found, including higher levels of high-density lipoprotein cholesterol in drinkers^{18–20} and an antithrombotic effect of alcohol.^{21–28} All things considered, a causal protective effect of alcohol against coronary heart disease is robustly supported by the data.

Previous studies cannot rule out a genetic or lifelong environmental predilection to earlier death of abstainers. Light drinkers have an approximately 30% to 40% lower coronary heart disease mortality risk and about a 10% lower total mortality risk. These differences are not large enough to preclude the possibility of indirect explanation. The constitutional hypothesis is one such explanation, although it is not clear why such an explanation should be relatively specific for coronary heart disease and not for other conditions.

The study in this issue of the Journal by Carmelli et al²⁹ uses a large twin registry to test the constitutional hypothesis. The data show lower mortality risk in alcohol drinkers than in abstainers within alcohol-discordant twin pairs. This trend was similar in nonsmoking and smoking twin pairs but stronger and statistically significant only for nonsmokers. Cigarette smoking and drinking are strongly related habits.^{30,31} Since smoking is a strong predictor of coronary heart disease, the usual problem in epidemiologic studies

not fully controlled for smoking is that the inverse alcohol–coronary heart disease relationship is weakened. Although not all effects of the smoking–drinking interaction upon coronary heart disease are clear, the existence of an inverse alcohol–coronary heart disease relation in lifelong nonsmokers is presumably free of any smoking–drinking interaction. Thus, the Carmelli et al. study refutes the genetic constitutional hypothesis and strengthens the case that light drinking reduces coronary heart disease mortality and total mortality.

The major public health problems of heavier drinking remain of paramount concern. Nothing in the literature justifies heavier drinking, and since increased medical risks predominate, all heavier drinkers should reduce their intake or abstain. Although it seems unlikely that heavier drinkers drink to improve their health, there is some concern that making public the health benefits of lighter drinking would encourage some people to indulge in heavier drinking. This concern makes it inappropriate to indiscriminately advise nondrinkers to start drinking alcohol for its health benefits. Most people do not drink alcohol for health reasons at all, but many do want advice about the health risks and benefits. This advice is best individualized because many people, including those at high risk of alcohol addiction, should abstain.^{32,33}

Some of the considerations pertinent to individual counseling by health practitioners include age, sex, personal and family history of problem drinking, and risk of coronary heart disease, certain cancers, or other illnesses. However, now that the case for the benefits of lighter drinking has become compelling, we agree with Pearson and Terry³³ that it might be as inadvisable for public health officials to promote general abstinence as to advise the entire population to drink. We can no longer indulge in an oversimplified message to the public that will not be believed. □

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Editorial: Drug Regulation and Drug Information—Who Should Do What to Whom?

As modern medical practice and education obsessively prune the tree of knowledge of all but the branches of high technology and basic science, the ancient growth being cut most drastically is an understanding of our origins, particularly the historical evolution of present assumptions, practices, and traditions in medical care. Loss of humility is perhaps our most significant disability that results from such cultivated narrowness. Almost as significant is our losing the historical perspective that might have helped us confront a number of recurring issues. The health care system collectively behaves like a patient with a dementing illness: in coping with current realities, we are disabled by loss of memory of past events.

This situation is typical of the regulation of chemical substances in the United States, which is described by Marks¹ in this issue of the Journal. He reminds us that the notion of "prescription drug" is not an immutable category in natural science as are quarks and dinosaurs. Instead, this notion is a social construct—a culturally and legally sanctioned convention in which members of a given society agree that some ingested chemicals are to be thought of as foods, some as legal recreational substances, some as illegal recreational substances, others as remedies available without restriction, and still others as medications available only on authorization by a physician.

Every day, headlines remind us of the impermanence of these distinctions. Medications such as nonsteroidal anti-

inflammatory drugs and histamine antagonists are being converted from prescription-only to over-the-counter status at an accelerating pace. We recently rediscovered that cigarettes function more as a drug delivery system than as mere recreation and thus have more in common with patient-controlled analgesia and sublingual nitroglycerin than with pepperoni pizzas and video games. We are more willing to think of occasional marijuana use and heavy alcohol intake as being neither evil, as is the case with marijuana, nor as socially acceptable, as is the case with alcohol, as we have traditionally thought.

These reassessments of the social characterization of drugs are less disorienting if viewed in light of the evolution of our perspectives during the course of this century. Marks' analysis focuses on the period surrounding World War II, although the modern redefinition of what a "drug" is extends back at least as far as the progressive era at the beginning of the century. Before it became the drug of choice for inner-city desperadoes and bored yuppies, cocaine was a popular and legal food additive and diversion, hardwired into the mainstream culture through such icons as Coca-Cola and Sherlock Holmes. Heroin, promoted by Bayer Co at the beginning of the century as its new cough remedy, was as freely available to the public as another new Bayer invention of that day, aspirin. At another end of today's spectrum, the increasingly blurred distinction between foods and drugs has

given rise to such hybrid terms as "pharmaceuticals" and "nutriceuticals": should a manufacturer of oat bran be held to the same standards of evidence as a drug manufacturer in describing its product's health benefits?

In the middle of the century, the period Marks covers in his article, the United States again tried to distinguish among ingested chemicals to reconcile the demands of public health, the needs of specific patients, the authority of physicians, and the profits of industry—not necessarily in that order. History may repeat itself as tragedy or farce, but in health care, history often seems simply to repeat itself, period. Boredom is relieved somewhat because, as in a Bach fugue, the theme is replayed each time against a novel counterpoint. In our time, the struggle to redefine the regulatory status of ingested chemicals is occurring against the counterpoint of the ubiquitous, inevitable, eats-through-anything medical cost containment movement. In earlier decades, the professional sovereignty of physicians required that they be the sole source of access to topical hydrocortisone, antihistamines, nonsteroidal anti-inflammatory drugs, and remedies for vaginal candidiasis. Before these chemicals were converted to over-the-counter status, pharmacists could lose their licenses for dispensing such substances to patients who did not have a prescription. Now

Editor's Note. See related article by Marks (p 109) in this issue.