Alcohol is consumed by millions of Americans annually and poses a major health problem. Alcohol-related problems plague an estimated 18 million adult Americans, of whom 10.6 million suffer from alcoholism. Experts estimate that 20-50% of all general hospital admissions, up to 50% of emergency room admissions, and 15% of office visits are alcohol-related and that alcohol is a factor in nearly 50% of all accidental deaths, suicides, and homicides. One in every 10 deaths is alcohol-related, and 200,000 Americans die of alcoholism annually. The economic cost of alcohol abuse and alcoholism was $117 billion in 1983 and is projected to rise to $136 billion in 1990 and $150 billion in 1995.7

Alcohol has long been recognized for its damaging effects to major organ systems. The ravages of alcohol on the liver, pancreas, gastrointestinal tract, heart, and developing fetus are well known to physicians. In addition, alcohol has been linked to various cancers, to hypertension, to male sexual dysfunction, and to bone disease.8-15

Perhaps the most noticeable adverse effects of alcohol are those on the nervous system.16,17 The clinical manifestations of acute alcohol intoxication reflect widespread cerebral depression and include varying degrees of excitational and disinhibited behavior, impaired coordination and motor performance, dulled cognitive abilities, and eventually stupor and coma. With chronic alcohol abuse there are abstinence syndromes, neurological deficits, and disorders consequent to hepatic dysfunction. While the incidence of these disorders in the community may not be well defined, municipal hospital experience has taught us that alcohol-related seizures, hallucinosis, delirium tremens, Wernicke-Korsakoff syndrome, cerebellar degeneration, and peripheral neuropathy are relatively common.16 Although alcohol is associated with a broad spectrum of neurologic complications, only recently has stroke been emphasized as a sequel.18

Alcohol was recognized as a possible risk factor for stroke as early as 1725.19,20 The association between alcohol and stroke was infrequently emphasized until more than 225 years later, when Pakkenberg21 and Balow et al22 proposed that alcohol ingestion might predispose to thromboembolic stroke, especially in young adults. By the late 1970s and early 1980s the relation between alcohol and stroke became the focus of intense epidemiologic scrutiny, and a spate of research reports linking alcohol consumption to stroke in young and middle-aged adults captured the public health community’s attention.23-30 By 1984 the Stroke Council’s Subcommittee on Risk Factors and Stroke listed alcohol as a “less well-documented” risk factor for stroke.31 More recent epidemiologic evidence has further sharpened our focus on alcohol as a potential risk factor for cerebrovascular disease.

In this issue of Stroke, Camargo32 shares with us a comprehensive and provocative treatise on the relation between moderate alcohol consumption and stroke. His synthesis of the observational epidemiologic data is prefaced by a discussion of the methodologic limitations and caveats that must be addressed before one can be persuaded that a firm relation between alcohol use and stroke exists. First, while alcohol consumption may be expressed as a dichotomous variable (drinker vs. nondrinker), it is preferable to estimate customary or typical drinking frequency and amount consumed. As no biologic marker presently exists to accurately quantify the amount or frequency of chronic alcohol use, ascertainment of customary or typical alcohol consumption relies on direct inquiry and self-reported information, parameters that may be subject to recall bias, poor recall, or obscure variability as might occur during alcohol “binges.” A second problem facing alcohol research is the lack of a...
reference standard against which to validate self-reported drinking. For example, if the respondent overestimates or underestimates the amount of alcohol consumed and even if the response error affects all respondents similarly, relative risks will achieve only rank-order validity. A third problem is that studies that fail to differentiate lifelong abstainers from former drinkers in the referent group may underestimate the relative risk at all levels of alcohol consumption. Finally, an operational epidemiologic definition of “light,” “moderate,” and “heavy” alcohol consumption must be developed. Cultural differences and underreporting of alcohol use must be considered when developing these operational definitions. To accommodate these factors, Camargo has chosen a liberal cutoff for the definition of “moderate” alcohol consumption (<5 standard drinks or 60 g ethanol per day).

Camargo’s analysis focuses on 62 international epidemiologic studies. To facilitate comparison, he has grouped the studies by stroke subtype (total stroke, ischemic stroke, and hemorrhagic stroke) and by alcohol consumption pattern (customary drinking and recent alcohol use). Camargo’s synthesis of the data reveals several interesting epidemiologic patterns. For ischemic stroke, a J-shaped curve describes the relation between moderate customary alcohol consumption and the relative risk of stroke among predominantly white populations whereas little if any association is found among Japanese and possibly among black populations. For hemorrhagic stroke (intracerebral hemorrhage or subarachnoid hemorrhage), a positive linear association with alcohol consumption and liver dysfunction appears to differ by population, and the latter mechanism remains controversial as alcohol might contribute to intracranial hemorrhage and increased blood viscosity, promoting vasocstriction, and hastening atherogenesis of the cerebral or coronary arteries.

The mechanism by which alcohol exerts its protective effect against ischemic stroke yet increases the risk of intraparenchymous and subarachnoid hemorrhage could be explained in the following ways: Following moderate doses of ethanol, prostacyclin levels have been shown to increase. Prostacyclin, a potent vasodilator and inhibitor of platelet aggregation, could exert protective effects through these mechanisms. Furthermore, alcohol-induced elevation of prostacyclin concentration could counterbalance the decrease in prostacyclin formation observed in atherosclerotic vascular tissue. Lower levels of prostacyclin predispose to intravascular thrombus formation and atherogenesis mediated by platelet mitogenic and chemotactic factors. Alternatively, the protective effects of moderate alcohol consumption could be mediated by augmenting the activity of the fibrinolytic system (enhanced vascular plasminogen activator secretion) or by depressing the concentration of low density lipoproteins and elevating the concentration of “protective” high density lipoproteins (HDLs) to achieve a less favorable milieu for atheroma formation. The latter mechanism remains controversial as alcohol may not elevate concentrations of the protective HDL2 subfraction.

The pathophysiologic mechanisms by which alcohol might contribute to intracranial hemorrhage include decreased circulating levels of clotting factors produced by the liver, excessive fibrinolysis, qualitatively abnormal fibrinogens, and disseminated intravascular coagulation. With moderate alcohol consumption, prolongation of the bleeding time and impairment of platelet function have been observed without involvement of coagulation parameters or fibrinolysis. In addition, hypertension, a recognized risk factor for intraparenchymous and subarachnoid hemorrhage, may be more prevalent among drinkers. It has been hypothesized that an abrupt significant elevation of systemic blood pressure with an increase in cerebral blood flow, as could occur with activation of the adrenergic system following alcohol ingestion or withdrawal, might be an important factor in the pathogenesis of intracerebral hemorrhage. Clinical experience suggests that intraparenchymous hemorrhage associated with alcohol consumption and liver dysfunction may be more massive than nonalcohol-related brain hemorrhage. This may reflect an interplay of hematologic abnormalities and possibly blood pres-
sure elevation associated with alcohol ingestion. Beyond the obvious relation between alcohol consumption, hypertension, and disordered coagulation it is unclear by what additional mechanism(s) alcohol could potentiate aneurysm rupture or formation.57,58

While many questions remain to be answered about the relation between alcohol use and stroke,22 our present epidemiologic focus has sharpened. The weight of the evidence suggests that excess alcohol consumption is a risk factor for both ischemic and hemorrhagic cerebrovascular disease, whereas moderate alcohol consumption may exert a protective effect similar to that proposed for coronary artery disease. As we expand our focus to include additional carefully designed epidemiologic studies of diverse populations,59-62 further answers will be forthcoming. Although the attributable risk of stroke due to alcohol consumption may be small in a given population, in view of the consistency of the available data, the high incidence of stroke and coronary artery disease, and the discretionary nature of this risk factor, the recommendation to restrict alcohol intake to no more than "modest" levels may bear rewards. Assessment of individual risk for other diseases that may be linked to alcohol consumption must be factored into the decision analysis as well.11

Furthermore, as the toll of heavy alcohol use is substantial, this recommendation should not be construed as a prescription extolling wholesale alcohol consumption.

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