Is Abstinence from Red Wine Hazardous to Your Health?

By Arthur L Klatsky, MD

A Very Public Message

Hardly a month goes by without the appearance of a research finding suggesting that drinking red wine is good for you. The media publicity is never nuanced or subtle, so the headlines blare. Here are several recent ones: "Procyanidinrich red wines reduce heart attack and mortality," "Resveratrol, a redwine ingredient, improves health and survival in mice on a high-fat diet," and "Cabernet sauvignon red wine reduces the risk of Alzheimer's disease." With the hint of greater longevity what non-red wine drinker wouldn't feel pressure to start a red wine habit? What person over age 65 years wouldn't consider a lifestyle change that promised a lower chance of Alzheimer's? The public has heard the implied message. A 60 Minutes TV broadcast (CBS: 1991 Nov 17) attributed lower heart attack risk in France partially to red wine. This explanation of the "French Paradox" (low coronary disease death rate despite relatively unfavorable lifestyle habits) has become widely known. Red wine sales in the US skyrocketed in the 1990s and remain high. In a recent Kaiser Permanente (KP) survey, 80% of those interviewed had heard of presumed benefit from alcohol and half of these volunteered that this was true only of red wine.1

Alcohol and Risk of **Coronary Disease** Social and medical harm from heavier drinking has been evident for millennia, but the concept of a safe drinking limit was also accepted. Perhaps better than "safe" is the word "sensible," since no level is absolutely safe for all persons. Modern population cohort studies² confirm the increased risks of heavy drinking, defined as ≥3 standard-sized drinks/ day. The same studies show that light to moderate drinkers have lower risks of coronary artery disease (CAD), ischemic stroke, and type 2 diabetes mellitus. Thus, for total mortality, the composite is a J-shaped curve, with lowest risk among drinkers who take < 3 drinks per day, and highest risk from numerous conditions among heavy drinkers. The lower mortality risk of lighter drinkers is due mostly to less CAD.

Light drinkers have about 30% lower CAD mortality risk and an approximately 10% lower total mortality risk.3 Consistency in studies, relative specificity of benefit for CAD and plausible biological mechanisms for protection by alcohol against CAD, support a causal protective effect. Some earlier studies were unable to separate exdrinkers from lifelong abstainers or to control for baseline CAD risk. Skeptics have repeatedly cited this problem as the explanation of spurious benefit really due to prior

movement of high-risk persons into the nondrinking reference group.⁴⁻⁵ This "sick quitter" hypothesis has been refuted by a number of studies, 3,6 including KP analyses.7-8 Studies that separate exdrinkers from lifelong abstainers or controlled for baseline CAD risk also consistently show that drinkers have lower CAD risk than lifelong abstainers. Although there have been no randomized, controlled trials of CAD outcome events, many epidemiologists now feel that there is little doubt that alcohol exerts a protective effect against CAD.

Plausible biological mechanisms for CAD protection by alcohol start with higher levels of protective highdensity-lipoprotein (HDL) cholesterol in drinkers.9 The evidence for this effect of alcohol is compelling. Several analyses in different cohorts show that HDL effect explains about 50% of the alcohol-CAD benefit. This is an effect of alcohol, without specificity for wine. Antithrombotic effects, less specifically an alcohol effect, are also supported by substantial data. 10 Less established mechanisms for CAD benefit of alcohol include improved endothelial function and reduced insulin resistance. The evidence that mechanisms of benefit have to do with ethyl alcohol means that any nonalcohol-related benefit from a specific beverage type, such as red wine, would be additional to that from alcohol.

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Is Red Wine Better?

Support for the hypothesis that wine may be more beneficial than liquor or beer is of two major types. The first consists of international comparisons showing lower CAD mortality in wine-drinking countries (eg, France) than in countries where beer or distilled spirits are the preponderant alcoholic beverages.3,11 Called ecological studies, these analyses relate mean consumption data to aggregate mortality. Since traits of individuals are not involved, these ecological studies are not well controlled for confounding explanations. The second type of evidence, the type frequently receiving media hyperbole, is the presence of potentially beneficial nonalcohol compounds in wine. 11,12 Found usually more concentrated in red wine, these substances are mostly phenolic compounds with antioxidant and antithrombotic properties. Since oxidation of lowdensity-lipoprotein (LDL) cholesterol is an integral part of development of atherosclerotic plaques, it follows that antioxidant compounds in the diet represent an appealing hypothesis for benefit. Diets rich in natural antioxidants seem to be associated with better health outcomes, although trials of antioxidant supplementation have been disappointing. Many feel that red wine could be considered a fermented food beverage with beneficial antioxidant ingredients.

Epidemiologic studies with data about specific beverage types are fewer in number than those that deal with total alcohol consumption. They do not consistently and convincingly support specific additional benefit from wine. ^{3,8,11} Important in this regard are good studies in beer-drinking populations showing apparent substantial CAD protection by that beverage. ¹³ A series of studies

in Denmark show that wine drinkers have lower risk of total mortality, cancer, and stroke, but the Danish investigators point out that, compared to beer/liquor drinkers, wine drinkers have a healthier drinking amount and pattern.14 The Danish wine drinkers smoke less, exercise more, eat healthier diets, have higher socioeconomic status, and score higher on intelligence tests. It is well known that in epidemiologic studies "healthy" traits tend to cluster in the same individuals. In observational studies there may be residual confounding by uncontrolled or incompletely controlled traits. KP studies show evidence of CAD benefit from each major beverage type, with apparent benefit greatest for wine, next for beer, and least for spirits.8,15 Importantly, the apparent effect was the same for white wine as for red wine. As in Denmark, our California wine drinkers had the healthiest lifestyle habits.

Wine has been called the "beverage of moderation."16 To some extent this seems true in Denmark and in California, both of which include substantial numbers of persons that drink each beverage type. Yet in countries in which wine drinking preponderates most heavy drinkers drink the prevalent, usually inexpensive beverage. Resultant wine-induced pathologies include liver cirrhosis, systemic hypertension, cardiomyopathy, and peripheral neuropathy.17 Organ damage from chronic heavy drinking is related primarily to lifetime ethyl alcohol intake, not beverage choice. In the appropriate cultural milieu, some wine drinkers readily progress to heavy drinking. In the US, for low cost some alcoholics choose wine. The pejorative term "wino" arose because a proportion of down-and-out alcoholics drink cheap fortified wine or jug wine.

The acceptance of the specific

benefits of red wine for CAD involves interpretive stretching of the data. For example, the truly fascinating resveratrol—longevity story involves up-regulation of a genetic system (the sirtuin genes) that influence metabolic processes promoting longevity.18 Resveratrol has this effect and has shown the ability to increase longevity in several species. Extrapolation from the doses used in the mouse study to humans indicates that a comparable human resveratrol dose from drinking red wine would involve >1000 glasses per day, hardly a practical proposition. In the oligomeric procyanidins (OPC) report¹⁹ correlations were done between OPC content of wines and longevity in several areas, with the finding that both were highest in certain areas of France and Sardinia. Found largely in grape seeds, the OPC's are said by the authors to be the wine polyphenols with the strongest endothelial relaxant effect. These analyses were not controlled for other potential confounders; in the view of this commentator these data do not suggest that wine drinkers would do well by switching to Sardinian wines. The Alzheimer's report20 was another mouse study.

Problems When Giving Advice

In view of the major health problems of heavier drinking, there are legitimate concerns about any medical advice that encourages drinking. Although it is likely that few heavy imbibers drink to improve their health, the concerns are based on the fear that some persons might not be able to handle the knowledge of benefit responsibly, and deliberately or inadvertently indulge in heavier drinking. Advice to persons already heavy drinkers needs no risk/benefit individualization. Since nothing ... our
California
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in the medical literature justifies heavier drinking and increased risks predominate, all heavier drinkers should reduce intake or abstain.

The advice problem can be ameliorated by individualization of advice to light drinkers and abstainers,21 taking into account risk/benefit factors like age, sex, personal and family history of problem drinking, and risk of CAD, certain cancers or other illnesses. Advice to drink must be weighed very carefully for nondrinkers. Abstainers usually have a valid reason for abstinence. Alcohol drinking is not at or near the top of the list of ways to reduce CAD risk; it comes well after smoking avoidance, proper diet and exercise, and attention to lipids, hypertension, diabetes and obesity. However, the case that lighter drinking in a healthy pattern has health benefits has become compelling. Thus it is as inappropriate for public health officials to promote general abstinence as to advise the entire population to drink. Most adults already are established light-moderate drinkers. Except for special reasons an established lightmoderate drinker at average or greater than average CAD risk should not be advised to abstain. Studies have shown that this applies to those with and without pre-existent CAD, hypertension, and diabetes. Most medication-alcohol interactions are documented only with heavy alcohol intake; this should not be too readily generalized to a prohibition of all alcohol for these patients.

Conclusion

But what about the abstinence from red wine issue in the title? The short answer is that the question of additional benefit from nonalcohol ingredients is unresolved. Red wine is obviously fine for the light-moderate drinker who prefers it, but the scientific knowledge offers insufficient basis for urging the man or woman who prefers another beverage to switch. Most of the CAD benefit derives from ethyl alcohol. If small amounts are taken in the optimal pattern, slowly and with food, it is likely that beer, liquor, white wine, and red wine would have fairly similar benefit. Most moderate drinkers are more interested in the sensory pleasures and relaxing effect than in health benefit. One hopes that the number of people who drink red wine when they would prefer something else is not too large. �

References

- Klatsky AL, Armstrong MA, Landy C, Udaltsova N. The effect of coronary disease on changes in drinking in an older population. Alcohol Research 2003;8:211-3.
- Corrao G, Bagnardi V, Zambon A, La Vecchia C. A meta-analysis of alcohol consumption and the risk of 15 diseases. Prev Med 2004 May;38(5):613-9.
- 3. Klatsky, AL. Drink to your health? Sci Am 2003 Feb;288(2):74-81.
- 4. Shaper AG, Wannamethee G, Walker M. Alcohol and mortality in British men: explaining the U-shaped curve. Lancet 1988 Dec 3;2(8623):1267-73.
- Fillmore KM, Kerr WC, Stockwell T, et al. Moderate alcohol use and reduced mortality risk: systematic error in prospective studies. Addiction Research and Theory 2006;14:1-1-132.
- 6. Klatsky, AL. Errors in Selection of "Error-Free" Studies. Addiction Research and Theory 2007;15:1 (In
- Klatsky AL, Armstrong MA, Friedman GD. Alcohol and mortality. Ann Intern Med 1992;117:646-54.
- 8. Klatsky AL, Friedman GD, Armstrong MA, Kipp H. Wine, liquor, beer, and mortality. Am J Epidemiol 2003 Sep 15;158(6):585-95.
- Dreon DM, Krauss RM. Alcohol, lipids and lipoproteins. Chapter 20 in National Institute of Health. Alcohol and the cardiovascular system. Eds

- Zakhari S, Wassef M. Research Monograph 1997;1:369-91.
- Zakhari S. Molecular mechanisms underlying alcohol-induced cardioprotection: contribution of hemostatic components. Alcohol Clin Exp Res 1999 Jun;23(6):1108-10.
- Rimm EB, Klatsky AL, Grobbee D, Stampfer MJ. Review of moderate alcohol consumption and reduced risk of coronary heart disease: is the effect due to beer, wine, or spirits? BMJ 1996 Mar 23;312(7033):731-6.
- Booyse FM, Parks DA. Moderate wine and alcohol consumption: Beneficial effects on cardiovascular disease. Thromb Haemost 2001 Aug;86(2):517-28.
- Keil U, Chambless LE, Doring A, Filipiak B, Stieber J. The relation of alcohol intake to coronary heart disease and all-cause mortality in a beer-drinking population. Epidemiology 1997 Mar;8(2):150-6.
- Gronbaek M. Wine, alcohol and cardiovascular risk: open issue. Is wine better than alcohol? J Thromb Haemost 2004 Nov;2(11):2041–8.
- 15. Klatsky AL, Armstrong MA, Friedman GD. Red wine, white wine, liquor, beer, and risk for coronary artery disease hospitalization. Am J Cardiol 1997 Aug 15; 80(4):416-20.
- Stockwell TR, Lang E, Lewis PN. Is wine the drink of moderation? Med J Aust 1995;162:578, 580-1.
- 17. Klatsky AL. Where have all the winos gone? Epidemiology 2002 Mar;13(2):120-2.
- Baur JA, Pearson KJ, Price NL, et al. Resveratrol improves health and survival of mice on a high-calorie diet. Nature 2006 Nov 16;444(7117):337-42.
- Corder R, Mullen W, Khan SC, et al. Oenology: red wine procyanidins and vascular health. Nature 2006 Nov 30;444(7119):566-72.
- Wang J, Ho L, Zhao Z, et al. Moderate consumption of Cabernet Sauvignon attenuates Abeta neuropathology in a mouse model of Alzheimer's disease. FASEB J 2006 Nov;20(13):2313-20.
- 21. Klatsky AL. Should patients with heart disease drink alcohol? JAMA 2001 Apr 18;285(15):2004-06.