



A MESSAGE FROM PRESIDENT DAVID NEWHOUSE

On behalf of the society I wish to thank Gulshan Bhatia for an outstanding year as President. Dr. Bhatia planned a wonderful year of events, which were greatly enjoyed by all the members who participated. With sophistication and wit she more than met the challenges of a demanding year.

It is a great honor and pleasure for me to begin the 64th year as president of the society. My goal is to preserve the traditions of the society while embracing a progressive spirit that will insure our societies strength and longevity. We will continue to improve our use of the internet and make our web site appealing and accessible.

Please join me in welcoming our new Executive Secretary Susan Guerguy. Susan is a consummate wine and food expert with an in-depth knowledge of classical cuisine and restaurant management. A graduate of the Lausanne Hotel School, Susan speaks three languages, English, French, and German. She has managed fine ho-

tels in Switzerland and the Bahamas, and was owner and proprietor of the Le Marquis Restaurant in Lafayette.

I wish to encourage the participation of our members in all the activities of the society. One of the most enjoyable activities are the trial dinners that precede the membership dinners. This is your opportunity to actively participate in the creation of a successful and enjoyable membership dinner. Not only are these dinners an opportunity to develop an appreciation for the finer aspects of food and wine but they are often a source of stimulating repartee as our members often agree to disagree. To volunteer for any of these events simply contact the executive secretary or feel free to contact me via phone mail or email.

Sincerely,

David Newhouse MD, MPH

Calendar of Events for 2003 - 2004

Wed., April 30	221st Quarterly Dinner
Wed., May 28	Board of Governors Dinner
Sat., June 28	222nd Quarterly Dinner (Social)
Sat/Sun., October 4/5	60th Annual Vintage Tour of Carmel Valley
Wed., November 5	223rd Quarterly Dinner
Wed., January 28, 2004	65th Annual Dinner

WINE AND HEART HEALTH

J. Bruce German Ph.D.,

Department of Food Science,
University of California at Davis

Lecture delivered at the 63rd annual Meeting, Jan 31st. 2002 at the Concordia - Argonaut, San Francisco

INTRODUCTION

The role of non-essential nutrients in influencing health has been compellingly made by the moderate consumption of wine. The potential influence of wine was first identified in modern terms by Serge Renaud and his identification of the French paradox in which the French, suffered from mortality from heart disease significantly less than predicted in spite of consuming diets normally linked to high rates of heart disease and exhibiting blood cholesterol levels consistent with that elevated risk. While Serge Renaud noted that “the quality of alcohol” in red wine was “superior” to other forms of alcohol in preventing ASCVD death, it was workers in California and Israel that asserted that it was red wine’s polyphenolic content and resultant antioxidant effects that conferred this superiority; predicting that these same compounds would be active against other oxidant-linked chronic diseases (Frankel, 1993, Kinsella 1993). These predictions and provision of plausible and testable mechanisms for observed epidemiological relationships prompted a large number of researchers to address the issue of wine and health.

Establishing the nutritional impact of wine remains a major scientific challenge. Challenge comes not only from trying to document the biological activities of the more than 200 individual phenolic compounds found in wine, but also from its stratified consumption within society and its alcohol content. Even the amount of wine that constitutes moderate intake remains debated. Moderate daily intakes have been defined as 1 drink per day for most women and 2 drinks per day for men. Others defined a serving as 150 mL (Paganga, 1999). Since there are no reliable biomarkers for moderate ethanol intake, and “moderate daily intake values” rely upon self-reported consumption data it is still not clear at the level of population epidemiology how much wine is consumed nor what its dose-dependent effects are. Nevertheless, statistical analyses of the data that are obtainable are revealing. Beneficial effects of alcohol consumption on plasma lipid parameters and CHD mortality were observed in populations where moderate ethanol intakes were defined as 30-50 g/day (Rimm 1996).

Why is wine consumption beneficial to heart disease?

The mechanisms proposed to account for wine’s reported ability to reduce coronary disease for the most part predict that various vascular diseases should be lower par-

ticularly those of occlusive and aggregatory origin. While not as well studied, reports have now addressed the consumption of wine and its relationship to incidence of stroke, both ischemic and hemorrhagic, and peripheral hypertension.

Resolving the various hypotheses advanced to date much less those that emerge in the future will require a strict mechanistic understanding of the biological effects of consuming wine and the various molecules within it. To date literally dozens of different mechanisms have been advanced to explain the benefits of wine apart from the mere presence of alcohol. The steps necessary to resolve competing hypotheses requires several stages of investigation. The specific biological action of a molecule must be tested mechanistically, usually in an in vitro model in which the essential biological or chemical principles against which the molecule should act in vivo, are present. If a mechanistic principle is validated, that is, that the mechanism of action of the molecule(s) from wine is shown to be true, and further that the dose dependency of that action is achievable through normal consumption of the components in wine, many more steps are needed to resolve that this effect is of actual benefit in vivo. It is necessary to show that the active molecule(s) are absorbed and delivered to the tissue or site of action after consuming wine. It is necessary to demonstrate that the mechanism of action identified in vitro persists in vivo.

Finally it is necessary to demonstrate in humans or appropriate animal models that the consumption of this active molecule(s) in levels consistent with their abundance in wine, translates into a genuine improvement in the final endpoint of disease relative to true controls which differ only by the absence of the active molecules. To date, none of the mechanisms proposed has been rigorously demonstrated in humans however several hypothesized actions, that would genuinely improve the risk of disease were they true, have been tested.

Antioxidant Effects:

The hypothesis that wine is beneficial due to the presence of antioxidants has been advanced. The oxidation hypothesis of heart disease and the role of oxidized LDL in promoting the disease was a key rationale underlying the hypothesis that antioxidants in wine could alleviate heart

disease. The original observations of Renaud and the paradoxically low incidence of cardiovascular disease in the French would ostensibly require a protective mechanism that did not act through altering lipoprotein profiles in as much as the typically high lipid profiles predictive of high rates of heart disease were exhibited by normal French populations. The oxidation hypothesis of atherosclerosis has been well reviewed and an important supportive evidence for the importance of oxidation in the atherosclerosis process has been the ability of antioxidant nutrients to slow the rate of heart disease in animals and humans.

The oxidation of polyunsaturated fatty acids in lipoproteins follows a well described chemistry in which an initiating free radical reaction starts an autocatalytic chain reaction. In the absence of redox scavenging antioxidants this chain reaction accelerates inexorably, consuming polyunsaturated fatty acids and yielding hydroperoxides. Since the tendency of the lipids in LDL to oxidize is a simple chemical fact, and it is generally agreed that oxidation of LDL is a contributing process in artery disease hence the only true issue of importance to artery disease are whether the compounds in wines especially red wines are capable of interrupting or slowing that progress *in vivo*. The basic chemistry of this question has been answered. Phenolic molecules including flavonoids are increasingly well described redox active antioxidants that in a host of chemical models are able to interrupt autocatalytic chain reactions of polyunsaturated lipids chemically by trapping the autocatalytic free radical as a stable phenoxyl radical. Many of the compounds in wine are redox active and many of these have been very well established to slow oxidation of LDL *in vitro*. The chemistry of this relationship is quite sound. Catechins alone in wine are present in sufficient quantities and possess sufficient antioxidant activity to protect LDL *in vivo*, if they are biologically available. The biological activity of the flavonoids of wine has thus become the most important question with respect to whether these compounds actually provide protection *in vivo*. Unfortunately, there is a very large difference between the well described chemistry of oxidation *in vitro* and the frankly poorly understood processes of oxidation *in vivo*. Evidence that has been advanced to address this question comes from several perspectives, none of which are satisfactory. The ability of plasma isolated from humans who have consumed wine or grape phenolics to slow a free radical reaction has been measured by a variety of methods. Many of these studies have indeed resolved a difference between plasma from subjects after consuming wine relative to consuming control beverages. However, the methods that have been used in these studies are non-specific, use artificial free radical donors and measure the oxidation of non-physiological targets. Perhaps even more important, such methods are attempting to assess the effects of the presence of very low microgram quantities of redox antioxidants within plasma that already contains 100's of micromolar equivalents of other redox active constituents normally present.

Cell Signaling

Cells communicate via chemical signals and their alteration is thought to be an important problem in the development of cardiovascular and other chronic diseases. Indeed, modifying cellular communication has been a widely successful pharmacologic strategy for preventing and reversing these diseases. The potential to alter cell signaling has been tested on cells or similar assay systems *in vitro*. Phenolics and other compounds from wine have been shown to affect various properties of endothelial cells, platelets, lymphocytes, macrophages, intestinal cells and smooth muscle cells. However, even when found to exert positive effects using *in vitro* assays, several additional steps are necessary before it can be concluded that such a mechanism of action in such a cell type is important to wine and health. Many of the processes that mediate cellular responses and especially those that mobilize the cell's appropriate response to stress are actuated through redox active molecules. The ability to generate signal molecules through energy liberating reactions such as oxidation or hydrolysis is an obvious advantage to the response to acute stress. This does not mean that altering any destructive chemistry confers a health benefit. Compounds must be shown to be effective, via the mechanism described *in vitro*, using an accepted *in vivo* model of the signaling process and the disease that its modification is proposed to benefit. A strong case has been developed for the ability of compounds in grapes that are retained in an apparently active form in wine to slow the processes of platelet aggregation. Studies have been performed largely *in vivo*, have yet to identify a clear mechanism but the consistency of effects and the variety of models in which they are effective, even extending to humans (consuming admittedly large quantities of grape juice or wine in acute studies) are compelling evidence that the non-alcohol components in grapes exert significant and potentially cardio-protective benefits. John Folts has shown that the effects of wine and grapes are similar in action to aspirin (acetylsalicylic acid) and concluded that their benefits to heart disease could be similar as well (Folts et al 1997).

Lipoprotein Biology

Lipoproteins are highly specialized transporters of lipids and lipophilic compounds within the body. Intimately involved in energy distribution and exquisitely responsive to diet, the number and subtle variation in the molecular mechanisms that orchestrate lipid disposition within the body continue to be revealed. Triglyceride-rich lipoproteins are secreted predominantly from the intestine and liver, and circulate in blood undergoing continuous metabolism and remodeling until they are removed by specific receptors. During this circulation and metabolism, triglyceride-rich lipoproteins are depleted of triglyceride and become smaller, more dense and enriched in cholesterol. In fasting humans most of the cholesterol in plasma is present within the particles characterized as low density lipoproteins (LDL), which are derived from the metabolism exclusively of hepatic (ApoB-100) triglyceride-rich lipoproteins (VLDL). Less but

still significant proportions of cholesterol circulate as high density lipoproteins (HDL) made by quite different mechanisms in the peripheral tissues. HDL participate in the processes of reverse cholesterol transport facilitating the return of cholesterol from peripheral tissues to the liver for disposal primarily in bile. There is significant exchange of lipid molecules between ApoB-based lipoproteins and HDL facilitated by lipoprotein remodeling enzymes that also circulate in the blood. Thus as the triglyceride core of larger diameter triglyceride-rich lipoproteins such as chylomicrons, VLDL and IDL are hydrolyzed, the resulting excess surface phospholipid and cholesterol is transferred to Apo-AI containing HDL. Lecithin-cholesterol acyl transferase (LCAT) present on HDL can act on these lipids to form cholesteryl esters that are carried within the core of HDL or exchanged for triglyceride within ApoB-based particles by cholesterol ester transfer protein (CETP). The negative correlation between plasma HDL cholesterol and CHD mortality has resulted in HDL cholesterol being dubbed "good cholesterol." Similarly, the positive correlation between LDL-cholesterol and CHD mortality has earned it the name "bad cholesterol."

The correlation between plasma total cholesterol and CHD mortality is well described for middle-aged males living in the United States. The association between plasma total cholesterol and CHD mortality is not just linear but risk actually accelerates with increasing plasma total cholesterol leading to a disproportionate increase in risk for CHD mortality. The value of plasma total cholesterol in predicting CHD mortality has rendered this single measurement the most widely used clinical index for the treatment of CHD.

The reasons why circulating plasma cholesterol is so predictive of disease are still emerging from mechanistic studies into plaque formation. CHD develops as inflamed lipid engorged artery tissue over long periods of time. Artery lesions contain lipid desposits, cholesterol and cholesteryl ester. Both as an initial cause and a subsequent consequence inflammation, and fibroproliferative responses continue within the vessel wall. Myocardial infarction occurs when the endothelial surface no longer prevents but instead promotes platelet aggregation and thrombosis. While the source of arterial cholesterol deposits were traced to plasma LDL, neither macrophage nor arterial smooth muscle cells took up native LDL even when presented with high concentrations of this lipoprotein (Goldstein et al., 1979). Goldstein et al noted that chemical modification of LDL to a non-native form, caused macrophages to take up the particles by a receptor that was ultimately shown to be scavenger receptor, type A, or SRA (Kodama et al., 1990). Following the efforts of many workers it was recognized that the most plausible modification to LDL was the oxidative modification of lipids (Steinberg et al., 1999) that the endothelial cells themselves were likely responsible for LDL oxidative modification and that the presence of oxidized lipids, particularly arachidonyl-containing phosphotidyl choline (Navab et al., 1996) caused a variety of effects that ac-

celerated lesion formation. In later stages of atherosclerotic lesion formation altered endothelial metabolism and function, inflammation and necrotic changes are all exacerbated by the generation of reactive oxygen species (ROS), lipid peroxides and damaged proteins.

Because elevated plasma total or LDL cholesterol are due to an impairment in lipoprotein metabolism and a delay in removal from the blood vasculature (Brown et al., 1983) it was suggested that it was in fact this prolonged exposure of circulating LDL to the subendothelial compartment and its high concentration of oxidants that lead to the oxidation of LDL. Experiments on an animal model demonstrated that indeed, prolonged residence time *in vivo* did render apoB-containing lipoproteins susceptible to oxidation (Walzem et al., 1995). This established a link between high circulating plasma ApoB cholesterol and increased oxidative susceptibility. Furthermore it was predicted that various biological and nutritional factors acting on the amount of time that an LDL spent in circulation, the amount of oxidative stress it was exposed to and the quantity of antioxidant protection would all influence the tendency for an LDL to become oxidized and lead finally to the development of heart disease (Walzem, 1995).

The interrelations that derived from this interpretation of lipoprotein metabolism and oxidative damage provide a conceptual framework to view the actions of wine phenolic and flavonoids on heart disease (German et al., 1997). To date the greatest amount of effort has been described the simple chemical protection of the lipid moieties of isolated LDL or VLDL using both native lipoproteins and model liposomal systems. The relationships are well understood for parent flavonoids. Far less well understood are flavonoid effects on other elements of the cardiovascular system. However, to date flavonoids found in wine have been shown to modify the ability of endothelial cells to oxidize lipoproteins to promote vasorelaxation and alter platelet aggregability (reviewed in German and Walzem 2000).

FUTURE DIRECTIONS FOR RESEARCH ON WINE AND HEALTH

1. Improve the understanding of alcohol's effects within "moderate range."
2. Enhance current epidemiological studies to resolve if life-long moderate wine intakes by women influence post-menopausal morbidity and mortality.
3. Improve the understanding of the bioavailability, metabolism and elimination of individual phenolic compounds and identify the chemical species that circulate *in vivo*.
4. Expand the understanding of the multiple actions of phenolic compounds in relation to mechanisms of pathogenesis.

REFERENCES

- Brown MS, Goldstein JL. 1983. Lipoprotein metabolism in the macrophage: implications for cholesterol deposition in atherosclerosis. *Annu. Rev. Biochem.* 52:223–61
- Folts JD, Begolli B, Shanmuganayagam D, Osman H, Maalej N. 1997. Inhibition of platelet activity with red wine and grape products. *Biofactors* 6:411–14
- Frankel EN, Kanner J, German JB, Parks E, Kinsella JE. 1993. Inhibition of oxidation of human low-density lipoprotein by phenolic substances in red wine. *Lancet* 341:454–57
- German J, Frankel E, Waterhouse A, Hansen R, Walzem R. 1997. Wine phenolics and targets of chronic diseases. In *Wine: Nutritional and Therapeutic Benefits*, ed. T Watkins, pp. 196–214. Washington, DC: Am. Chem. Soc. 284 pp
- German J.B. and Walzem RL. 2000 Health Benefits of Wine *Annu. Rev. Nutr.* 20:561-593
- Goldstein JL, Ho YK, Basu SK, Brown MS. 1979. Binding site on macrophages that mediates uptake and degradation of acetylated low density lipoprotein, producing massive cholesterol deposition. *Proc. Natl. Acad. Sci. USA* 76:333–37
- Kinsella J, Frankel E, German J. 1993. Possible mechanisms for the protective role of antioxidant in wine and plant foods. *Food Technol.* 47:85–89
- Kodama T, Freeman M, Rohrer L, Zabrecky J, Matsudaira P, Krieger M. 1990. Type I macrophage scavenger receptor contains alpha-helical and collagen-like coiled coils. *Nature* 343:531–35
- Navab M, Berliner JA, Watson AD, Hama SY, Territo MC, et al. 1996. The Yin and Yang of oxidation in the development of the fatty streak. *Arterioscler. Thromb. Vasc. Biol.* 16:831–42
- Paganga G, Miller N, Rice-Evans CA. 1999. The polyphenolic content of fruit and vegetables and their antioxidant activities. What does a serving constitute? *Free Radic. Res.* 30:153–62
- Rimm EB. 1996. Alcohol consumption and coronary heart disease: Good habits may be more important than just good wine. *Am. J. Epidemiol.* 143:1094–98
- Steinberg D, Witztum J. 1999. Lipoproteins, lipoprotein oxidation and atherogenesis *Am. J. Med.* 94pp. 458–76
- Walzem RL, Watkins S, Frankel EN, Hansen RJ, German JB. 1995. Older plasma lipoproteins are more susceptible to oxidation: a linking mechanism for the lipid and oxidation theories of atherosclerotic cardiovascular disease. *Proc. Natl. Acad. Sci. USA* 92:7460–64



“The object of the Society of Medical Friends of Wine is to stimulate scientific research on wine, develop an understanding of its beneficial effects, and encourage an appreciation of the conviviality and good fellowship that are a part of the relaxed and deliberate manner of living that follows its proper use”



The Mystery of Zinfandel

Charles L Sullivan
Wine Historian

Lecture delivered at the 217th Quarterly Dinner, April 24th, 2002 at 231 Ellsworth, San Mateo

Years ago people might ask me why the interest in the history of Zinfandel. I never hear such queries today. The wine from that wonderful grape has become so popular, in its many forms, that Zinfandel, as a topic of discussion is unquestioned. What I'll try to do tonight is to show how two great mysteries about the history of Zinfandel have been cleared up in the last thirty years.

These mysteries were:

1. *How did the grape get to North America from Europe and thence to California?*
2. *What is the varietal's provenance. That is, what are its vinifera ancestors in Europe?*

The Zinfandel first came to North America in the late 1820s, imported by George Gibbs, a Long Island nurseryman. He acquired it and several other varieties from the Austrian imperial horticultural collection at the Schönbrunn Palace in Vienna. Gibbs shared the vine with William Prince, whose great Long Island nursery was the finest in America at that time. The next year they took the vine to show at the annual meeting of the Massachusetts Horticultural Society in Boston. We don't know what name, if any, it had in the Austrian collection, but by the early 1830s it was being called the *Zinfindal* in New England. And, like the other vinifera grapes grown there and on Long Island, it was considered a table grape. By 1840 it had become fairly popular, grown in hot houses and forced so that ripe grapes were available in the local markets as early as May. The *Zinfindal* was one of more than a dozen vinifera varieties so employed in New England until the 1870s.

The vine came to California in the early 1850s, brought here by several nurserymen and importers from Boston, and thought at first useful strictly for eating purposes. But Californians were willing to try any grapes for winemaking, since the local Mission variety, left over from the Spanish/Mexican period, was of little use in making good table wine. It is also worth noting that the *Zinfindal* also arrived here from Boston under the name Black St. Peters. It was later discovered that the two varieties were the same. Although several persons brought the vine from New England, two are especially noteworthy. One was Frederick Macondray, a New England sea captain and also a member of the Massachusetts Horticultural Society. The other was San Jose nurseryman Antoine Delmas, who also made the first importation of good French

wine varieties to California in 1852. These included the Cabernet Sauvignon and the Merlot.

Macondray supplied vines to his fellow New Englander, Joseph Osborne, who planted them on his Oak Knoll estate north of Napa. In 1859 William Boggs, as secretary of the Sonoma Horticultural Society, bought two wagon loads of vine cuttings from Osborne and hauled them to the site of the Society's new vineyard. But the winter was cruel and only the Zinfandel vines survived. By 1862 there were enough grapes to make a little wine, but Boggs, from Missouri, had no idea then what good red table wine tasted like. He thought this stuff too tart and bitter. So he took it over to Victor Fauré, General Vallejo's French-born winemaker, to make it into vinegar. Fauré immediately recognized a delicious claret-style red wine, and the word spread. By 1865 there was a rising demand for *Zinfindal* cuttings in the Sonoma area.

The same sort of discovery was made by Delmas at San Jose in 1859 when his Black St. Peters wine won first prize at the State Fair. The judges were surprised at so fine a wine from grapes "selected more as table fruit than for winemaking." In later years the Black St. Peters vineyards in the Santa Clara Valley became **Zinfandel** vineyards, when that variety's popularity was soaring. Note the new spelling which had gradually caught on by the early 1870s.

There was, however, no rush to plant any kind of grapes through much of the 1870s, for the nation was plunged into a great economic depression, which was particularly severe in most areas of agriculture. But by the time that good times returned, after 1878, there was a rush to plant vines in California to take advantage of the rising demand for wine on the East Coast. The number one vine in the planting binge was the Zinfandel, which was now accepted as the best red wine grape here because of its good quality and high yield. Wine men knew about the high quality of Cabernet wine, but growers were turned off by its low yield.

The 1890s was a time of suffering for the wine industry. Another depression choked off demand and the phylloxera root louse destroyed northern California's vineyards. In 1890 Napa had about 20,000 acres of vines. By 1898 less than 4000 were still alive.

But when the economy improved after 1897 there again was a rush to plant vines, and again Zinfandel was a leader, used mostly to produce California claret, often blended with other varieties. Note that varietal names for wines were rarely seen in those days.

When Prohibition came Americans were still allowed to produce 200 gallons of home made wine per household. Thus millions of tons of grapes headed east from California between 1919 and 1933. And Zinfandel was one of the leading varieties shipped. As the years went by the tons of Zin hauled out of the state tended to decline as more and more of these grapes stayed home to serve the needs of California home winemakers. It was in these years that most of today's really "old-vine" Zinfandel vines were planted.

When Repeal came in 1933 Zinfandel again took its place in the production of generic blended red table wine. But the American sweet tooth made dessert wine the chief product of the California wine industry. And huge amounts of Zinfandels went into the production of California port wine. huge amounts of Zinfandels went into the production of California port wine.

The great wine revolution in America began in the 1960s and when many of the newcomers to wine production looked around for good grapes, the old-timers showed them their excellent Zinfandels to drink, and pointed out the fine old vineyards whose grapes could be had for a song. Thus such pioneers as David Bruce, the Ridge partners, Joseph Swan, Lee Stewart, and Robert Mondavi were proud to bring out

well extracted, rich, tasty varietal Zinfandels and in the 1970s there was a Zin-boom. But there was a decline in interest in such powerful, perhaps too powerful, wines in the 1980s, as red Zinfandel actually took a back seat to White Zinfandel (really pink).

We all know how that trend changed in the 1990s and in the new century. I can make the point most tellingly by pointing out that the price of Zinfandel grapes in Napa/Sonoma in 2001 was higher than that for Cabernet Sauvignon grapes there two years earlier.

The solution to the second mystery is quickly explained, although it has taken more than thirty years to get it straight.

Two European varieties have been shown to be genetically identical to the Zinfandel. One is the Primitivo grape grown in Puglia at the top of the heel of the Italian boot. The other is also grown in the Adriatic area, along the Dalmatian coast of what is today Croatia. This variety is the Crljenak, a close relative of the Plavac Mali, which was earlier thought to be the same as Zinfandel, but is not. These discoveries were made by Professor Carole Meredith and her team of DNA specialists at the University of California (Davis).

Of course, these discoveries do not show the ultimate source of the variety. But it is clear that the Adriatic marks the route of its entry into modern winegrowing areas of Europe. But from where? My informed historical guess, for which I have no historical smoking gun, is Crete or Cyprus.



*The discovery of a wine is of greater moment
than the discovery of a constellation.
The universe is full of stars.*

Brillat Savarin



Podea or Unhand the Maiden, Sirrah!

Randall Graham

Winemaker Bonny Doon Vineyard

Lecture delivered at 218th Quarterly dinner, June 26th, 2002 at Uncle Yu's, San Ramon

I am deeply passionate about *syrah* and have been toasted head over heels for the grape and for the wine for quite some time now. But with the anxiety of any lover comes the fear that I may, *we* may soon be losing her to a bigger, stronger rival, in this case, the stalwart and bold Antipodean stylists - Rugbyers to a man, who talk loudly, ameliorate liberally and carry a big *schtick*. In fact, *she - la syrah* is unique in being one of the very few named red *vinifera* grape varieties which takes the feminine article in French, in contrast to *le virile petite verdot* or *le manly mourvèdre - she* is really not mine to lose. But I find that she is lately changing in ways that I don't really understand. She has taken on a different style, one that is brash, saucy and frankly a little over-the-top. She's changed her perfume and is wearing way too much make-up. I can barely recognize the elegant lady; tarted up (better living through acid-base chemistry), the lady is a tramp. And while she may be unchaste, observing the proliferation of floor stacks of brightly colored labels, with their all too piquant nomenclature, she is certainly not unchased.

Let's put the fancy romantic palaver aside and talk about the lady in red herself, that is to say, *la syrah*. There has been a lot of discussion lately of *syrah* becoming "the next *merlot*" and frankly, that prospect fills me with a significant sense of foreboding. I believe that *syrah* has great potential for California but I am equally persuaded that, as with *merlot*, indeed with virtually all of the vinous *nouvelles vagues* that have swept our trend-conscious state, given half an opportunity to muck it up¹, we inevitably will.

How will the New World stuff up *syrah*? How could a grape variety, which has a history of 2000 years in a single location, that was praised by Pliny for its unique fragrance of violets, be in clear and present danger? Cue the Antipodeans.

Syrah, proper *syrah*, is a remarkably complex, seductive wine and a superb harmonizer with modern fusion cuisine. But I worry that too few American palates will now ever bother to learn what real *syrah* actually tastes like. The Australian stylistic paradigm of *syrah - "shiraz"* as it is so piquantly called in Antipodea, has quietly become the dominant one. Why? First guess is that American critics tend to reward ultra-ripe wines that taste like *bombas de fruta*. In fact, I have a pet theory, utterly unproved or unprovable that we, as primates, heck, even as

mammals, likely have a genetic predisposition to the flavors of ultra-ripe fruit, whether it is a banana, a mango or a grape. And it's not the sugar in the grape that I'm talking about; I think it really has more to do with the perception of a softer tannin that one finds in seeds that have been given a longer time to ripen. The fact that the wine smells like mom's kitchen after she has put up some raspberry jam doesn't hurt either. California winemakers have even taken to calling their *syrah shiraz*. Can bright yellow and/or orange labels be too far behind? On very grumpy days I conceive of *shiraz* as a pernicious weed, crowding out the strange, rare and beautiful *syrah* specimens found in such corners as the rock walled terraces of Cote Rotie.

They seem so disarmingly benign with their "G'days" and "No worries, mates." But beneath their apparently artless geniality and *bonhomie*, they are very cool and calculating customers indeed. The Aussies have been waging a hugely successful war for the hearts, minds, palates and wallets of the Anglo-Saxon consumer with their *shiraz*, so-called, a wine made from a grape that is genetically identical to *syrah*, but having little to do with the sublime Old World exemplars. They have clearly shown that nurture wins out over nature, at least at the cash register, and have been fiendishly efficient in producing a wine with a taste and texture profile that is somehow greatly resonant with the Anglo-Saxon palate. Or maybe it's the cute mammals and the orange labels.

So, in the interest of understanding what we are truly up against and to perhaps outline a course correction to the broken guard-rail, seriously off-road walk-about towards which we are careering headlong, I have prepared a little primer outlining the salient differences between *shiraz* from Antipodea and proper *syrah* from what I call *Podea*, which is to say, anti-Antipodea. Doris Day once sang a tune that went something like, "*Que syrah, sera*" but we cannot afford to be so *laissez-faire*.

PS: Proper (Podean) Syrah

AS: Antipodean Shiraz

PS: Nomenclature of wine usually determined by geographical situation of the vineyard.

AS: Nomenclature of wine is determined by the following formula: Cute or piquant animal name + geographical feature + name of grape

(Eg. Wallaby Ridge, Roo's Leap, Madfish Bay, Wombat Gorge, &c Shiraz.)

If this formula is not rigorously employed, then a reference to an obscure WW 1 cavalry regiment or a pernicious vine pathology will also suffice.

PS: Fundamental expression of the wine is elegant, feminine, and stylistically closely allied with Burgundy.

AS: Stylistically allied with raspberry motor oil.

PS: Primary growing area rich in cultural history, dating back to Roman times.

AS: Region settled primarily by ex-convict population.

PS: Grape variety: *la syrah*, sometimes called *petite syrah* or *serine* in *Côte Rôtie*, though no relation (of course) to *petite sirah* in California.

AS: Grape variety: *shiraz*², mate. And assigning a gender to a bloody grape? Sounds a bit left-handed, if you ask me. I don't have to worry about you pitching for the other side now, do I, mate?

PS: The greatest *syrah* vineyards are located in close proximity to Lyon, arguably the locus of French gastronomy. The wine is also eminently suitable to so-called bistro cuisine, *i.e.* gristle and *frites*.

AS: Throw another road-kill emu on the barbie.

PS: Alcohol typically 12.0-12.5%.

AS: Do not open bottle in presence of open flame.

PS: Eminently sippable and drinkable.

AS: Typically gulped though but truth be told, one glass'll do you, mate.

PS: Capable of expressing *terroir* for a French person.

AS: Capable of instilling terror *in* a French person.

PS: Seduces with its elegant perfume.

AS: Rapes and pillages the palate.

PS: Often find detectable presence of minerality

AS: Marked lack of minerality, substituted by palpable presence of big tits, sorry, that would be big *chips*.

AS: *Parfum de chène*

PS: *Parfum de chiens*

AS: Parker friendly

PS: *Par coeur* friendly

PS: Reductive style - bring in da funk

AS: "International" style - fruit-driven, accessible

PS: Hard tannins

AS: Generally soft tannins

PS: Cynical sugar additions

AS: Cynical tannin and acid additions

PS: *Brettanomyces* science experiment

AS: "Fruit driven"

PS: pH in double digits.

AS: pH in high single digits (would be in double digits were it not for the acid out of the bag).

PS: Primary flavors: white pepper, anise, smoked meat, bacon fat and licorice.

AS: Primary flavors: raspberry sundae and American oak.

AS: Clever, infernally effective marketing to Anglo-Saxon markets

PS: Can't be bothered with such a *bourgeois* preoccupation. Instead have declared cultural war on the Anglo-Saxon, McDo-imbibing running dogs and *A bas!* to the British *rosbif*

PS: Appellation difficult to pronounce and impossible to remember. Labeling requirements: dull gray or matte color, obscure or Gothic typography.

AS: Name of wine related to cute mammal. Color of label: bright orange or yellow, information readily readable, though often on a diagonal.

PS: The wine celebrates the unique characteristics of the vintage.

AS: The wine is usually palatable every goddamn year.

AS: Commercially successful. Who can resist charming marsupials and/or brightly colored labels?

PS: Commercially iffy. Who can pronounce the names of the appellations, much less remember which years are the "good" ones, which ones the dicey ones?

PS: No gobs of fruit in your face but often more depth of flavor, just requires some digging.

AS: Heaps of gobs of sensual fruit in your face. You can easily find yourself in a wine porno video.

I know what you are all thinking. How can I throw some money into one of the companies of those very clever and stalwart young men? Wrong, wrong, wrong. We're here to help prevent the further degradation and abasement of the distressed maiden. While she may have temporarily lost her way, one can only hope that she will find her way back to the righteous path, perhaps with bells on her toes: To the sweet cheat, *La Syrah: Salut!*



²There is no gender assigned to our nouns in English, of course, but that being said, shiraz is a wine that one would pour for oneself, having returned from a long day of wrestling alligators, no, make that crocodiles.

Alcohol Ambivalence

What is it and can anything be done about it?

Gene Ford

Lecture delivered at the 219th Quarterly Dinner, Oct 18th, 2002, The Olympic club, Lake Side, SF

*We must recall that nature's laws
Are generally sound.
And everywhere, for some good cause,
Some alcohol is found.
There's alcohol in plant and tree.
It must be nature's plan,
That there should be in fair degree,
Some Alcohol in man.*

Alan Herbert (1800's)

Thirty some years ago, I represented the Christian Brothers Winery in Washington and Montana, control states which had opened their retail shelves to wines. I had a moral dilemma: Having known alcoholism in my own family, I had concerns not about drinking but about the propriety of *selling* wine and brandy. So, I embarked upon a research and writing avocation concentrating specifically on the good news about drinking. These efforts opened up a fascinating world of research that remains largely under wraps in this nation. Plenty of ink about alcohol problems. Little comprehensive coverage of several dozen benefits.

This has led me to some unique insights to the topic of the day - alcohol ambivalence.

Early on, Salvatore Lucia, a president of this Society and science advisor to the Wine Appreciation Board, prophesied that science would define a positive role for responsible drinking. A colleague, Stepto from the University of Chicago in 1968 recommended: *Young physicians should be encouraged to explore the scientific mysteries of alcohol and wine. These explorations will open new vistas to them and make them better physicians and better citizens.* Lucia's books, Leake and Silverman's *Alcoholic Beverages in Clinical Medicine*, and the series of symposia staged by the Wine Institute, had already established a credible research base in support of responsible drinking.

There are indeed real risks in drinking for a minority in any society, but the *presumed risks* to health for everyone who drinks - the "drinking is risk-taking" myth - is the most formidable legacy of the Prohibition era. This fear has morphed into a cultural artifact - an ambivalence.

My goal today is to explore briefly the roots of alcohol ambivalence, to present examples of its debilitating impact on medical communication, and to suggest a *medical* antidote.

In 1916, joining the prohibitionary juggernaut, federal health officials removed alcohol from the *Pharmacopoeia of the U.S.* On June 6, 1917, the House of Delegates to the American Medical Association followed suit by enacting the following resolution:

WHEREAS, WE BELIEVE THAT THE USE OF ALCOHOL AS A BEVERAGE IS DETRIMENTAL TO THE HUMAN ECONOMY, AND WHEREAS, ITS USE IN THERAPEUTICS, AS A TONIC OR AS A STIMULANT, OR AS A FOOD HAS NO SCIENTIFIC BASIS, THEREFORE, BE IT RESOLVED, THAT THE AMERICAN MEDICAL ASSOCIATION OPPOSES THE USE OF ALCOHOL AS A BEVERAGE, AND BE IT FURTHER RESOLVED, THAT THE USE OF ALCOHOL AS A THERAPEUTIC AGENT SHOULD BE DISCOURAGED.

Contemporary medical ambivalence remains firmly rooted in this prohibitionary rhetoric. Its assumptions support a range of anti-drinking policies within American medicine.

Curt Ellison presented to this society in October 1999, "Should doctors prescribe wine?" *"By failing to give patients scientifically sound, balanced advice about the potential health benefits of moderate use, as well as the adverse effects of excessive or inappropriate use, physicians may be doing their patients a disservice."* In the September 28, 1994 issue of JAMA, an editorial titled "The Clinician's Conundrum" reinforced that dilemma by speculating that nationwide abstinence would cause as many as 135,884 additional heart disease deaths annually. The federal goal today of reducing per capita consumption seeks to remove acknowledged health protection from current drinkers.

A drinking survey in 1890 reported that 20 percent of adult males abstained, 5 percent were intemperate and 75 percent engaged in occasional or moderate drinking. A century later, only 65 percent of adults drink. A drop of 15 percent despite much favorable epidemiology.

During the 1990s, my own publications and reach were considerable and were distributed to Congress, state legislatures, wineries, breweries and distilleries and to key media. I guest lectured often. My impact in raising public awareness of healthy drinking and neoprohibition was mini-

mal. The Department of Health and Human Services' linkages in 1987 of drinking with tobacco and street drugs effectively short-circuited any group interest in responsible drinking.

In 1998, the Wine Appreciation Guild and the University of California press came to me interested in a definitive book on drinking and health. This led to my new book, "Healthy Drinking," which substantially broadens the benefit horizon with over 600 direct quotes from the literature for thirty different health conditions. It contrasts these positive findings with medical publication updates which ignore or downgrade the science. It provides findings from other disciplines - anthropology, social science and economics - which debunk the six major lingering prohibitory myths which support ambivalence.

Noteworthy neglect of the issue is noted in my chapter on diabetes research. An article, "Five Keys to Diabetes Control," appears in Johns Hopkins *Health After 50* February 1998 issue, which fails to cite any favorable drinking research. It over refers to a Johns Hopkins 70 page monograph, *Diabetes Mellitus*, where there is a single paragraph about drinking. It states diabetics can drink moderately but concludes with: *Small to moderate amounts of alcohol have been shown to reduce the risk of CHD, although not specifically in people with diabetes, and may reduce the risk of developing Type 2 diabetes.* No medical references provided, and yet ignores Launder's 1996 evidence of lower risk for poor cognition among diabetic drinkers, Forsham's 1981 data on mood elevation, Facchini's 1994 report of enhanced insulin-mediated glucose uptake, Rimm's 1995 reduced risk of diabetes among moderate drinkers, Conigrave's 2001 finding of the lowest risk of Type 2 diabetes among moderate drinkers, which concurs with Hu's 2001 finding of lowered female risk for Type 2 among drinkers. When the positive findings are thus shielded from the practicing physician, both the doctor and the patient are shortchanged by the medical communication system. Clinical care is corrupted because of the politics of alcohol ambivalence.

The preceding is a common protocol in medical school and clinic publications. The February 1998, *Mayo Clinic Health Letter* included an eight page supplement titled "Diabetes." One short paragraph about drinking notes: *Alcohol prevents the release of glucose from the liver and can increase the risk of your blood sugar falling too low. If you drink alcoholic beverages, do so only in moderation, and eat food before you have a drink. Food helps moderate the effects of alcohol.* Good general advice but, again, no positive drinking findings. *The New England Journal's Health News* offered "You can Prevent Type 2 Diabetes" on June 2001 with no mention of favorable research.

The failure is compounded by overblown references to drinking risks: *Consume alcohol moderately, if at*

all . . . says American Heart Association which is well aware of hundreds of positive studies. *If you currently don't drink, don't start . . .* warns *Health After 50*. *Few if any, medical experts advise non-drinkers to start drinking for health reasons. . .* opines *Mayo Clinic Health Letter*. *But even moderate drinking can place you at increased risk for conditions such as breast cancer, hip fracture and possibly colon cancer, and it can interfere with your reproductive ability. . .* from *Harvard Women's Health Watch*. The editors forgot hangnail! Alcohol ambivalence is not the most important issue in medicine today, but it impacts over 130 million people adversely.

Ambivalence is also responsible for the inexplicable absence of drinks in American nutritional literature. Six percent of the American diet calories derives from drinks, up to twenty percent among daily drinkers. Four prestigious new books illustrate this shameful convention. Willet in *The Harvard Medical School Guide to Healthy Eating*, Perry and Schacht in *The American Medical Association's Complete Guide to Men's Health* and Margen in both the *Wellness Encyclopedia of Food and Nutrition* and *Wellness Foods from A to Z* from UC Berkeley. They all ignore Lucia's outline forty years ago of parts per million of calories, vitamins and minerals supplied by wines. They ignore Bert Grant's laboratory analysis of his Scotch Ale which contains the following RDA's in a single bottle of beer: calories 5.4%, pyroxin 13.9%, protein 4%, riboflavin (B²) 4-6%, niacin 14.6%, folacin 62.5%, pyroxin 13.9% and B¹² 170%. How many practicing physicians are aware of these data? No one in medicine, public health or the beverage industries supported Grant when the feds told him to remove the RDA sticker or lose his license to brew. For displaying the same information required of most other foods. Our goal must be to re-establish drinks as nutritious foods.

You will recall that in 1990 the American Heart Association broke into the Physicians Health Study to release the dramatic finding that an aspirin every other day reduced the risk of heart attack by 47 percent compared to placebo takers. Every media outlet in America trumpeted the finding and every medical institution promotes it today. Compare this with the thunderous silence about a similar finding in another Heart Association study - conducted by the same lead researcher, Charles Hennekens of Harvard Medical School. Two months earlier, Hennekens reported that people who drink moderately - the equivalent of two beers or wines or one mixed drink - had a 49 percent lower risk of a heart attack - two points better than the aspirin and a whole lot more tasty and nutritious. Withholding this finding deprives American drinkers of health information that could reduce morbidity and extend life. The generally receptive popular media also suffers from medical censorship.

Now for some good news.

Recall the stunning impact of the 1991 discussion of the French paradox on the CBS-TV *60 Minutes* show. In less than fifteen minutes, Curt Ellison and Serge Reynaud convinced a majority of the estimated twenty million viewers that red wine consumption facilitates heart health. Thousands of non-wine drinking viewers rushed to retail stores the next day to purchase red wines. Red sales have been escalating ever since. Such is the power of drinking science when it is calmly presented by competent medical authority.

William Dickerson in his speech to Oregon's new Society of Physicians for Wine and Health reported that eighty-three percent of American adults approve of "moderate and responsible consumption of wine and food" and that seventy-seven percent of the American physicians polled are drinkers. A majority of private citizens and physicians already favor moderate drinking. What an unheralded opportunity to expand the philosophy of the Society of Medical Friends of Wine by simply bringing the research to public attention.

These failed lines of communication are the prime responsibility of those who have the moral authority, the professional standing and the de facto responsibility of delivering health care for our entire society - docs and moms. My new book's strategy targets clinical physicians, alternative caregivers and health-informed mothers. (It asks them to demand fair and unbiased coverage of drinking science both in the medical and popular media).

Here's the problem. A recent *Seattle Times* article employed 56 words to recount a Dutch study reporting less dementia and Alzheimer's among daily moderate drinkers and another 43 words warning of the ill effects of drinking. This is typical dry obfuscation. Consider how the *Time* editors might edit future articles if one hundred Seattle physicians had written or e-mailed providing other positive citations and noting that such gratuitous warnings had the effect of diluting an important research message.

Will harried doctors and hassled moms rise to this challenge? Frankly, I don't know. They know that there's a lot of positive data in the research domain, as the recent de Lorimier survey in your Bulletin demonstrates. When the full story gains currency in the media, alcohol therapy will return to the clinical armamentarium. Physicians will feel free to discuss options with their patients. Ambivalence will fade gradually into history. Fortunately the good news can be accessed, downloaded and e-mailed to editors from any physician's desk computer. Excellent web sources include:

✓ *The Wine Institute*

www.wineinstitute.com

✓ *The Society of medical Friends of Wine*

www.medicalfriendsofwine.org

✓ American Wine Alliance for Research and Education

www.alcohol-aware.com

✓ *David Hanson's Alcohol: Problems and Solutions*

www2.potsdam.edu/alcohol-info/,

✓ *Alcohol in Moderation*

www.AIM-digest.com

✓ *International Center for Alcohol Policies*

www.icap.org

But first, a critical mass of clinical physicians must be updated on the research and the extent of the communication problem. Eye-opener books include, *To Your Health: Two Physicians Explore the Health Benefits of Wine*, by Whitten and Lipp; *To Your Good Health The Wine Drinker's Guide* by Stuttaford from London, and my own *The Science of Health Drinking*. In chapters of from two to ten pages, my book provides docs and moms sufficient motivation to justify personal action. Whole chapters can be photocopied and sent on. Informed mothers also can be extraordinarily effective. Imagine the impact of 50,000 mothers taking copies of my book to doctor appointments wondering why they hadn't been informed of findings pertinent to their family's problems.

On November 11, 1958, twenty years after your formation, Leon Adams spoke to a quarterly meeting suggesting that informed physicians should assume some responsibility for educating the public. Other speakers have echoed this plea - David Whitten, Martin Lipp, Lew Perdue, Keith Marton, John De Luca, Curt Ellison and now me. Adams argued in 1958: *The public today has no information - other than folklore - concerning the health values in wine. He then asked whether this Society: . . . may wish to express itself as to whether it is time for some public education on reasons to use wine. I hope that you, the members, your governors and officers will give this some consideration and perhaps do something about it.*

Will physicians and women rise to this challenge? The opportunity is monumental. If medical practitioners don't rise to the occasion, I confidently predict that the federal dry bureaucracies will expand and press the linkage of alcohol with tobacco and street drugs. The internal public health consortium and the U.S. Alcohol Policy Conference of dries last year agreed upon this goal (cosponsored by the AMA).

My plan will work because of its simplicity. It requires no laws, regulations or votes. It relies totally on exposure of the mass of valid, peer-reviewed science. Can anyone show me the scientific rationale for the exclusion of wines and beers from UC Berkeley's encyclopedias of food and nutrition? There is none, aside from alcohol ambivalence. When drinks are once again accepted and discussed as good foods, they will be seen as the healthiest foods of all since they impact so many health conditions.

With their familiarity with this research, members of this society could form an international vanguard in medicine by urging the major newsletters - Berkeley Wellness Letters, Harvard's Men's Health and Women's Health and Hopkins Health After 50, etc. - to publish all aspects of healthy drinking science in a comprehensive, unbiased manner. It's an achievable plan.

Informed doctors and health-informed women can regain for wines and other drinks a dignified presence on the American dinner table and in popular culture. Lucia and Adams had absolute faith that informed Americans would choose moderate use over abuse.

Valid health science is one, perhaps the only, card that can trump the lingering myths and misperceptions of alcohol ambivalence. I close with two literary allusions:

*Wine puts life into a man,
If he drinks in moderation.
What is life to a man deprived of wine?
Was it not created to warm men's hearts?
Wine brings gaiety and high spirits,
If a man knows when to drink and when to stop.
But wine in excess makes for bitter feelings
And leads to offense and retaliation.*
Ecclesiastes 31:27-29

The second is a more gentle reminder of the foibles and frailties of the eternal human condition.

*God made man, frail as a bubble.
God made love. Love made trouble.
God made the vine.
Was it a sin that man made wine
To drown trouble in?*

T.L. Peacock



*As our speakers will clearly define,
Every sickness will surely decline
If, when treatment's obtuse,
One will only make use
Of the medical friendship of wine.*

Phil O. Sofer, Jr.



Wine and Health Abstracts

Bv Alfred A. de Lorimier MD

Alcohol Intake and Incidence of Type 2 Diabetes in Men
Wei M, Gibbons L.W, Mitchell T.L, Kampert J.B, Blair S.N.
Diabetes Care 23: 18-22, 2000

This prospective study, from the Cooper Institute, Dallas, Texas, followed 8633 men, age 30-79 years, between 1970 and 1995 for an average of 6 years. More than 97% were Caucasian and had a white-collar or professional occupation. Excluded were those with abnormal resting or exercise electrocardiograms or a history of diabetes, heart attack, stroke or cancer at first examination, and those with less than one year of follow-up. All participants recorded personal and family health histories, had complete physical examination, anthropometrics, EKG, blood chemistry, blood pressure and maximal exercise test on a motor-driven treadmill. Type 2 diabetes was defined as having a fasting plasma glucose greater than 126 mg/dl, a history of diabetes, or being treated for diabetes with insulin. Patients who had diabetes by these criteria at baseline were excluded from the study. These patients responded to a questionnaire asking: "How many 12-ounce drinks of beer, 3-5 ounce drinks of wine, and/or 1.5-ounce drinks of hard liquor do you consume per week?" The alcohol content was estimated as 1.1 g for 1 ounce of beer, 2.7 g for 1 ounce of wine, and 15.1 for 1 ounce of liquor. The incidence rates of diabetes were calculated by dividing the number of incident cases during the study period (the interval between the baseline and last follow-up examinations) by the number of person-years of observation. Five categories of alcohol intake were defined: non-drinkers, drinkers in quartile 1 consumed 1-61.8 g/week, quartile 2 consumed 61.9-122.7 g/week, quartile 3 consumed 122.8-276.6 g/week and quartile 4 had intakes greater than 276.6 g/week. Systolic blood pressure, HDL cholesterol, and cigarette smoking showed a linear trend related to alcohol intake. During the average 6 years of follow-up 149 subjects developed type 2 diabetes. Risk of diabetes was calculated by multivariable-adjusted odds ratios. There was a U-shaped curve of risk for developing Type 2 diabetes and alcohol intake. The lowest incidence was in those with an intake between 61.9 and 122.7 g/week (Q2), followed by intakes between 1-61.8 g/week (Q1). The risk of diabetes in non-drinkers was 1.8 fold, and those whose intakes exceeded 122.8 g/week (Q3 & Q4) had a 2.2-2.3-fold risk compared to the moderate drinkers. The authors cite literature indicating that large amounts of alcohol result in decreased glucose tolerance and a possible toxic effect of alcohol on the pancreatic islet cells. Ethanol and its metabolites are potent inhibitors of insulin-stimulated adipocyte metabolism. However light to moderate alcohol intake has been shown to be associated with enhanced insulin sensitivity.

Alcohol Consumption and Risk of Type 2 Diabetes Mellitus Among US Male Physicians
Ajani U.A, Hennekens C.H, Spelsberg A, Manson J.
Arch. Intern. Med. 160:1025-1030, 2000

This study is an average 12.1 year follow-up of 20,951 male participants in the Physicians' Health Study who were between the ages of 40-84 years. Excluded from this study were those with missing baseline data on alcohol consumption, and those who reported a baseline history of diabetes prior to or within 2 years of the study, any history of cardiovascular disease, or cancer. At the time of entry participants were asked, "How often do you usually consume alcoholic beverages?: rarely/never, 1-3/month, 1/week, 2-4/week, 5-6/week, daily, and 2+/day." Every year in follow-up these physicians were mailed a questionnaire inquiring about their health, including the development of diabetes. During the 12 years of follow-up 766 became newly diagnosed cases of diabetes. Incidence rates of diabetes were calculated by dividing the number of incident cases by person-years in each category of alcohol consumption. Cox proportional hazard models were used to assess the contribution of alcohol consumption to the risk of diabetes, and this was adjusted for smoking status, body mass index, physical activity, hypertension, high cholesterol level, and parental history of diabetes. This population of physicians were very moderate drinkers, in that only 3% of them consumed more than an average of 1 drink/day. Compared to physicians who rarely or never drink, the relative risk of diabetes was 0.95 for those consuming 1 drink/week, 0.73 for consumers of 2-4 drinks/week, 0.64 with 5-6 drinks/week, and 0.58 with one or more drinks/day. No significant changes occurred adjusting for hypertension, high cholesterol level, parental history of myocardial infarction before age 60 years, and there was no effect of body mass index, smoking, physical activity or family history. There were not enough heavy drinkers to assess this group. This study corroborates that of a number of other articles, where a similar inverse association between alcohol consumption and diabetes, as follows.

The Nurses Health Study of 85,000 women: *Stampfer, MJ, Colditz, GA, Willett, WC, et al: A prospective study of moderate alcohol drinking and risk of diabetes in women. Am. J. Epidemiol.* 128:549, 1988;

The Health Professionals' Follow-up Study of over 41,000 men: *Rimm, E, Chan, J, Stampfer, MJ, et al Prospective study of cigarette smoking, alcohol use and the risk of diabetes in men. BMJ* 310:555-559, 1995),

The British Regional Heart Study *Perry, IJ, Wannamethee, SG, Walker, MK, et al: Prospective study*

of risk factors for development of non-insulin-dependent diabetes in middle-aged British men. BMJ 310:560-564, 1995)

Solomon C.G, Hu F.B, Stampfer M.J, et al:
Moderate Alcohol Consumption and Risk of Coronary Heart Disease Among Women with Type 2 Diabetes Mellitus.

Circulation 201: 494-499, 2000

The Nurses' Health Study is a prospective cohort study of 121,700 female nurses aged 30-55 years at the study inception in 1976. This article is an analysis of 5,103 women who reported a physician diagnosis of diabetes mellitus from baseline through 1992, had no myocardial infarction, angina, or coronary revascularization, stroke or cancer before the 1980 questionnaire, and who provided alcohol consumption. The participants answered a biennial food and beverage questionnaire, which included details about beer, wine and spirits consumption. The total alcohol intake was calculated in grams, assuming that 12 ounce beer was 12.8 g, 14 ounce glass of wine was 11 g, and a standard drink of spirits was 14 g. There was a high correlation of each individual's consumption between the reports of 1980, 1984 and 1990. Incidence rates and relative risks for diabetes were calculated for: no alcohol intake; consumption of 0.1-4.9 g/day (1/3-1/2 drink/day); and consumption greater than 5 g/day. Adjustments were made for confounders for: age, cigarette smoking, body mass index, menopausal status/postmenopausal hormone use, multivitamin and vitamin E supplement, and aspirin use, and regular vigorous exercise at once/week. Women taking medications for control of hyperglycemia were analyzed as a subgroup. During 39,092 person-years of follow-up from 1980 to 1994 there were 295 coronary heart disease events—194 nonfatal and 101 fatal cases of myocardial infarction. With adjustment for age and for multivariate confounders, and non-drinkers having a relative risk (RR) of 1, consumption of 0.1-4.9 g/day was associated with a RR of 0.72-0.79, and the RR for those consuming more than 5 g/day was 0.43-0.48—highly significant differences. The differences were essentially the same when analyzed separately for cigarette smoking, body mass index, hypertension, a family history of myocardial infarction, the duration of diabetes, and for a history of insulin or sulfonylurea treatment. It should be noted that the RR reduction for moderate alcohol consumption in this cohort is comparable to that reported for the entire 85,881 nurses analyzed in the Nurses' Health Study, with and without diabetes, where the relative risk of stroke and/or myocardial infarction was 0.6 for alcohol consumption between 5 and 25 g/day. (Stampfer, MJ, Graham, A, Colditz, MB, et al: A Prospective Study of Moderate Alcohol Consumption and the Risk of Coronary Disease and Stroke in Women. N. Engl. J. Med. 319:267-273,1988). Furthermore, analysis from the Nurses' Health Study has indicated that moderate alcohol consumption is inversely associated with the risk of the development of diabetes. (Stampfer, MJ, Colditz, GA,

Willett, WC, et al: A Prospective Study of Moderate Alcohol drinking and Risk of Diabetes in Women. Am. J. Epidemiol. 128:594-598. 1988)

Association Between Alcohol Consumption and Mortality, Myocardial Infarction, and Stroke in 25 year follow up of 49,618 young Swedish Men.

Romelsjo A, and Leifman A.

BMJ 319:821-822 1999

This is a 25-year follow-up of the 49,618 Swedish men conscripted between July 1969 and June 1970 and born between 1949 and 1952. Each was given a questionnaire covering social background, behavior, and alcohol and tobacco use. They all met with a psychologist for assessment. Non-responders were less than 2%. Using the Swedish personal identification number the questionnaire data were linked to the Swedish register of causes of death, and to the national inpatient care register for 1970-1995. Total mortality was 1473. Myocardial infarctions occurred in 279, and 38 were fatal. Stroke occurred in 233, and 30 were fatal. Social, psychosocial, and behavioral variables were used as confounders. Alcohol consumption was calculated as the number of grams of 100% alcohol consumed per day. All of this is based upon the data collected at conscription, without regard to changes that might have occurred in these variables with these individuals over the 25-year interval.

The authors state that, compared with abstainers, alcohol consumers had higher unadjusted relative risks for all three outcomes, and the risks were significantly higher with consumption of 15 or more grams of ethanol/day. To a considerable extent, the increased mortality with high alcohol consumption was due to an association with smoking. However they found a clear relationship between the level of alcohol use at conscription and risk of subsequent hospitalization or death with a diagnosis of alcoholism, alcohol psychosis, or alcohol intoxication, with a relative risk of 5.71 for consumption greater than 15 g/day. However, the results also show a cardio protective effect of alcohol when consumption begins in young men. The authors conclude: "Calculations of the attributable proportions clearly indicated that alcohol consumption had a negative net effect on the subjects' health up the age of 45. The results support a restrictive alcohol policy and recommendation for little or no alcohol consumption by young men."

Endothelin-1

Endothelin-1 is a 21 amino acid, paracrine hormone secreted by the endothelium which acts directly on vascular smooth muscle promoting vasoconstriction. Stimulators of endothelin-1 production include: Angiotensin II, catecholamines, insulin, oxidized LDL, shear stress, and thrombin. Inhibitors of endothelin-1 production are nitric oxide (NO), atrial natriuretic peptide, prostacyclin and prostaglandin E₂. Endothelin-1 contracts venous and arterial vascular smooth

muscle, has positive inotropic and chronotropic myocardial function, but it produces intense coronary arterial constriction. It also increases plasma atrial natriuretic peptide, renin, aldosterone, and catecholamines.

Corder R, Douthwaite J.A, Lees D.M, Khan N.Q, Dos Santos A.C.V, Wood E.G, Carrier M.J.

Endothelin-1 Synthesis Reduced by Red Wine.
Nature 414: 863, 2001.

These authors indicate that endothelin-1 overproduction is a factor in the development of atherosclerosis, and they cite experimental models whereby endothelin-1 antagonists prevent endothelial dysfunction. The authors were curious to find whether the favorable effects of wine on cardiovascular disease could be related to an influence on endothelin-1 production. They used cultured bovine aortic endothelial cells to measure the production of endothelin-1 when exposed to red wine, ethanol-free extract from 23 red wines, four white wines, one rose and one grape juice. The wines were from France, Spain, Italy, Australia and South America and they represented by Cabernet sauvignon, Shiraz, Merlot, Pinot noir, and others. They measured the concentration of each wine which would cause a 50% reduction in the basal endothelin-1 synthesis from the cultured aortic endothelial cells. Inhibition of endothelin-1 synthesis was directly proportional to the polyphenols concentration. Red-grape juice was much less potent than red wine. The rose wine made from cabernet sauvignon and white wines had no effect. This indicates that the active substance resides in the grape skins or other grape components during wine making.

Homocysteine

An abnormal elevation of the amino acid homocysteine in the serum is considered a risk factor for arterial and venous thrombosis, myocardial infarction and stroke. High levels are toxic to the endothelial lining of arteries. Vitamins B12, B6 and folic acid are important in the metabolism of homocysteine, and there is an inverse relationship between these vitamin levels and homocysteine concentrations in the blood. van der Gaag, et al (Effect of consumption of red wine, spirits and beer on serum homocysteine, Lancet 355: 1522, 2000) report that, in people without alcohol dependency, serum homocysteine increases after moderate consumption of red wine and spirits, but not after moderate consumption of beer. Hyperhomocysteinemia is known to be associated with chronic alcoholism.

Bleich, S., et al: Red wine, spirits, beer and serum homocysteine. Lancet correspondence 35:512, 2000.

Bleich, et al respond and differ from van der Gaag et al by stating that homocysteine levels are related to blood alcohol concentrations, rather than the type of alcohol consumed.

In their experience beer drinkers admitted to hospital always presented with much lower blood alcohol concentrations and lower homocysteine levels compared to spirits and wine drinkers. They have also noted that serum levels of vitamins B6, B12, and folate in these hyperhomocysteine patients are normal. The hyperhomocysteine levels decreased rapidly over the 3-5 day course of withdrawal therapy. All patients with alcohol intoxication, who were not alcohol-dependent, had completely normal serum homocysteine concentrations. They speculate that alcohol withdrawal syndromes, such as seizures, may be due to direct neurotoxicity of homocysteine by activating the N-methyl-D-aspartate subtype of the glutamate receptor. Stroke and brain damage associated with alcohol toxicity, could be mediated by excessive stimulation of these receptors in the presence of focal ischemia. Hyperhomocysteinemia would explain the increased incidence of cardiovascular complications related to high alcohol consumption.

Alcohol consumption and risk of coronary heart disease by diabetes status

Ajani U.A, Gaziano J.M, Lotufo P.A, Liu S, Hennekens C.H, Buring J.E, Manson J.E.

Circulation 102: 500-505, 2000

This was a prospective analysis from the Physicians Health Study of 87,938 male physicians followed up to 12 yrs. who responded to serial initial and follow-up questionnaires about their age, health status, level of alcohol consumption, amount of cigarette smoking, use of antihypertensive medications, blood pressure, cholesterol level, use of cholesterol-lowering medications, frequency of vigorous exercise, history of angina pectoris, and diabetes. The subjects had no history of myocardial infarction, stroke, cancer or liver disease at baseline. 3.2% had diabetes at the time of enrollment. Deaths were identified by searches of the National Death Index and by review of death certificates to determine the cause of death.

Conclusion: Light to moderate alcohol consumption is associated with similar risk reductions in CHD among diabetic and nondiabetic men.

Alcohol Consumption and Multivariate adjusted Relative Risk of Cardiac Mortality				
	Rarely or Never	Monthly	Weekly	Daily
Non-diabetic	17	11%	46%	26%
Relative risk	1	1.02	0.82	0.61
Diabetics	29%	14%	35%	22%
Relative risk	1	1.11	0.67	0.42

The Society of Medical Friends of Wine

www.medicalfriendsofwine.org

511 Jones Place
Walnut Creek, CA 94597

Tel: 925 933 9691, Fax: 925 939 5224
Email: o:marq@inreach.com” marq@inreach.com

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