by Lauri O. Byerley and Roger Clemens

# How Much Alcohol Is Safe?

Alcohol, particularly ethanol, is a component in numerous beverages. In fact, humans have been drinking alcoholic beverages for thousands of years. It has been an influential part of our lives and involved in shaping our modern culture. Interestingly, the 1980 Dietary Guidelines for Americans cautioned consumers to drink alcoholic beverages in moderation due to adverse health effects. Even the latest iteration of the Dietary Guidelines for Americans (2015–2020) noted that alcohol consumption may contribute to excess calorie intake and lead to health challenges, particularly for those who are taking prescription medications, those who have certain medical conditions, and women who are pregnant or lactating.

An article from *National Geographic* explored the anthropological data and discussed the hypothesis that alcohol might be the driver behind the movement from hunters/gatherers to an agrarian-based society (Curry 2017). By throwing a good party, replete with alcoholic beverages, ambitious individuals could cultivate alliances with potential defense partners, seal beneficial marriage deals, and rise to prominence within burgeoning communities. Agricultural development would obviously be driven by the demand for fermentable grains. It is intriguing that the anthropological record illustrates adaptive sociocultural functions around alcohol consumption.

In contrast to the positive spin suggested by the anthropological and archaeological record, the latest information from the National Institute on Alcohol Abuse and Alcoholism raises a number of health and societal concerns associated with alcohol consumption (NIH 2018). As many contemporary consumers raise concerns about food safety, they typically fail to realize that alcohol is at least indirectly toxic to liver and brain function and challenges one's detoxification system, which is also modulated by our genetic makeup. Thus, it is interesting to explore the question: What amount of alcohol is safe? It seems like an easy question, and the Centers for Disease Control (CDC) has recommendations for those who drink (CDC 2016). If you don't drink alcohol, the CDC does not recommend starting, but if you do drink alcohol, it recommends no more than one drink per day for women and no more than two drinks a day for men. The CDC considers this level of alcohol drinking moderate.

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The guideline is specific that one serving contains 15 g of alcohol or 5 oz of wine at 12% alcohol, 12 oz beer at 5% alcohol, and 1.5 oz spirits or "hard liquor" at 40% alcohol. These drink sizes are based on averages. Buyer beware because many wines, beers, and spirits contain more or less than the CDC's moderate guidelines. For example, the alcohol content of wine can range from 5%–14%, beer ranges from 4%–12%, and distilled spirits range from 28%–60% (AAC 2018). So, one serving of beer, wine, or liquor could contain more or less than the average amount used by the CDC to compile its moderate alcohol drinking recommendations, and manufacturers are experimenting with ways to increase the alcohol content (Bryner 2010).

In the 1990s, the "French Paradox" was introduced, based on the observation that the French drank a lot of wine but had low rates of cardiovascular disease (Rifler 2018). Red wine, a source of polyphenols such as resveratrol, was connected with purported health benefits. People now incorrectly associate the health benefit with all types of alcohol. In fact, epidemiologic studies have shown a U-shaped curve; that is, there is a lower mortality rate among people who drink moderate amounts of alcohol than among those who do not drink. This observation has come under scrutiny because the nondrinkers included those who were not well and stopped drinking because of poor health, which may or may not be related to their prior alcohol consumption. This effect has been called the "sick quitter" (Rehm, Irving, Ye, et al. 2008) (Shaper, Wannamethee, and Walker 1988).

In 2018, a large study was published that suggested the currently recommended levels of alcohol may not be as safe as previously thought (Wood, Kaptoge, Butterworth, et al. 2018). Using prospective epidemiologic studies and not clinical evidence, the risk for all-cause mortality and cardiovascular disease was studied among 599,912 current drinkers without previous cardiovascular disease. Drinkers were divided into eight groups based on their weekly consumption of alcohol. The dose varied from as little as less than 25 g alcohol/week to more than 350 g alcohol/week. The study found that drinking

more than 100 g alcohol/week increased the risk of cardiovascular disease subtypes other than myocardial infarction. This dichotomy with myocardial infarction was attributed to HDL-C associated pathways, observed in those who drank more alcohol. Troublesome was the lower life expectancy observed as early as age 40; drinking more than 100 g alcohol/week reduced life expectancy by 6 months compared with those who drank less than 100 g alcohol/week.

The study was not without flaws. Although the data were corrected for variables like age, sex, and history of diabetes and smoking status, it did not consider other confounders like race and lifestyle, or possible genetic variations and transcriptional profiles. We are reminded that the comprehensive genetic network for alcohol-related phenotypes involves brain transformation; neurotransmitter biosynthesis and signaling and signal transduction; growth factor signaling; and metabolism of inositol 1,4,5-triphosphate, which is another signal transducer (Morozova, Mackay, and Anholt 2014).

In a subgroup analysis of the study, beer and liquor drinkers appeared to have a higher risk of death from cardiovascular disease than wine drinkers. Beer and/or liquor drinkers were more likely to be of a lower socioeconomic class, smoked more, and exercised less compared to wine drinkers. Despite these shortcomings, the study does remind us that alcohol may have serious side effects regardless of the amount consumed, especially when paired with other factors such as sedentary lifestyle, poor nutritional status, family history, and psychiatric status. These points were emphasized in a follow-up article that advocated further reduction of the apparent 100 g alcohol/week threshold (Connor and Hall 2018).

So what level of alcohol is safe and will keep one from developing heart disease, high blood pressure, stroke, dependency issues, and memory and mental health problems that are associated with alcohol? For now, that amount is unknown but may be less than the current moderation levels set by the CDC. A recent commentary opined that "state-of-the-art epidemiology" demonstrates that alcohol-related harm pervades virtually every aspect of life (Burton and Sheron 2018).

It will be interesting to learn if the 2020–2025 Dietary Guidelines Advisory Committee considers this topic, particularly since the three areas at risk from alcohol intake involve the health of infants and children, pregnant and lactating women, and seniors. This arena of alcohol and health is an illustration of the perennial struggle to understand the complexity of human metabolism: A large dose of humility with an appropriately moderate dose of alcohol is recommended. **FT**

*References cited are available via hyperlinks in the digital version of this column.*

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