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EDITORIAL

Alcohol-attributable cancer: fact or fiction?

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The *International Journal of Wine Research* has published a number of articles related to wine and cancer, which have concluded that wine and its polyphenol components may have largely beneficial effects. Thus, a review of the role of wine in cancer concluded that regular and moderate wine consumption was associated with a decreased risk of mortality from certain cancers, and that the risk increased progressively with immoderate consumption.[1] The mechanisms invoked for the decreased risk included the effects of wine-derived polyphenolic compounds on the cell life cycle, most notably their ability to arrest cell division and induce mitochondrial apoptosis. The antiproliferative role of red wine flavonoids in reducing the membrane fluidity of tumor cells in vitro has recently been emphasized.[2] Furthermore, one of the more important red wine polyphenols, resveratrol, which is structurally a stilbene rather than a flavonoid, has been shown to decrease the incidence and multiplicity of intestinal tumors in rats in vivo significantly, as well as to inhibit proliferation and viability of human colonic adenocarcinoma cells in vitro.[3]

Therefore, it was somewhat surprising recently to read online in an authoritative journal that "In western Europe, an important proportion of cases of cancer can be attributable to alcohol consumption, especially consumption higher than the recommended upper limits".[4] This conclusion is based upon the multicenter, prospective cohort study known as European Prospective Investigation into Cancer and Nutrition (EPIC), which now has a mean follow-up of 8.8 years for more than 300,000 subjects covering eight European countries. Although the authors identify an increase in risk of cancers of many types from alcohol consumption, they give no data allowing the identification of a threshold of consumption beyond which risk is increased. As the International Scientific Forum on Alcohol Research rightly commented, "... the authors did not separate moderate consumption from heavy consumption for their main analyses, ignored the demonstrated benefits of moderate drinking on total mortality, and did not point out other environmental factors (eg, smoking, diet, obesity) that often have much larger effects on the risk of many cancers than does alcohol consumption".[5]

The International Scientific Forum on Alcohol Research suggests that the intentions of the authors in the preparation of the paper from this well performed analysis of a large data set with good follow-up seem to focus on indicting alcohol as a major cause of cancer, and cites a number of large studies that do demonstrate a lower risk of various cancers for frequent moderate drinking when compared with heavy drinking.[6–10] Two more recent publications on liver disease[11] and gastric cancer[12] have further emphasized the relationship between the level of alcohol consumption and risk. Although the EPIC

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analyses did not establish a J-shaped curve, whereby moderate drinking carries a lesser risk of cancer than heavy drinking or abstention, such curves are very common in other diseases, including cardiovascular disease,[13] stroke,[14] type 2 diabetes,[15] and dementia,[16] as well as overall mortality.[17,18]

From the perspective of the *International Journal of Wine Research*, failing to differentiate the type of alcoholic beverage is a major fault of the EPIC study. There are many indications that moderate and regular consumption of wine has greater beneficial effects than either beer or spirits on the risk of a variety of medical conditions.[16] Unlike beer and spirits, wine contains not only alcohol but also a variety of polyphenolic compounds which are extracted from the grapes during vinification, mostly in the form of members of the stilbene (eg, resveratrol) and flavonoid (eg, quercetin) chemical families and contained in grape tannins and anthocyanin pigments. These polyphenols can have profound physiological effects both in their own right, eg, resveratrol seems to activate cerebral blood flow upon cognitive demand in the human brain,[19,20] and in the form of wine, which can alter Alzheimer-like neuropathology and cognition in transgenic mouse models.[21]

In conclusion, we concur with the views of the International Scientific Forum on Alcohol Research that the EPIC study supports the well-known association between heavy drinking and an increased risk of upper aerodigestive and certain other cancers, but that it adds little information useful for the prevention of most types of cancer. The EPIC comment that alcohol has negative effects on total mortality studiously ignores the copious data available on the benefits of regular and moderate wine consumption, and indeed is heavily contradicted by most large-scale population-based studies. More research, please!

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