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Alcohol Consumption: The Good, The Bad, and The Indifferent

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Abstract Dietary ethanol (alcohol) is the most widely consumed drug worldwide. High levels of mortality, morbidity, and social malaise are associated with abuse of alcohol, and increasing numbers of women and youth are abusing alcohol. However, strong epidemiological data demonstrate a U- or J-shaped relationship between volume of alcohol consumed and all-cause mortality or disease burden. Moderate alcohol consumption is associated with a lower risk of all-cause mortality and disease burden than are abstinence and immoderate drinking. A brief review of the absorption, distribution, metabolism, and excretion of ethanol is provided with a discussion of the impact of gender differences. Potential mechanisms by which ethanol, ethanol metabolites, and (or) phytochemicals, as associated with different types of ethanol-containing beverages, are discussed in regards to the beneficial and detrimental impacts they may have on physiological system functioning and mortality or disease burden. Per capita consumption of ethanol-containing beverages varies across geo-political regions worldwide. A more recent research focus is the impact of consumption patterns on consumption volumes as they relate to disease and mortality. Certain drinking patterns moderate overall volume of ethanol consumption. Thus, an emerging approach to the study of alcohol consumption in populations is to consider both the volume and pattern of consumption as they relate to mortality and disease burden. Alcohol consumption patterns among athletes are discussed; physiological implications of alcohol abuse in this population are outlined. Current guidelines for the consumption of alcohol are reviewed. Alcohol consumption guidelines reflect the current scientific understanding of both the benefits of moderate alcohol consumption and the detriments of immoderate alcohol consumption.

Keywords alcohol, moderation, consumption patterns, gender differences, guidelines, oxidative stress

INTRODUCTION

Dietary ethanol (ETOH) is a physiologically non-essential, energy-yielding (29 $kJ \cdot g^{-1}$) molecule in humans, produced by the yeast-driven fermentation of pyruvate from plant products with high carbohydrate content. Trace amounts of ethanol, or alcohol as it is commonly called, are produced by the mammalian gastrointestinal flora and also occur naturally in some foods. The principal source of alcohol in the diet, however, is that derived from beverages processed by alcoholic fermentation, such as beer, distilled spirits, and wine.

Current conversations about ETOH range from the beneficial effects associated with moderate intakes to the deleterious effects associated with excessive intakes; research investigations have followed similar lines of inquiry. Alcohol, like all drugs, can be considered both a tonic and a toxin; the difference apparently lies in the dose.

Indeed, epidemiological data from more than 100 studies across 25 countries have rather consistently demonstrated that there is an inverse association between moderate ETOH consumption and coronary heart disease (Goldberg et al. 2001). Positive effects of alcohol or wine intake on several metabolic syndrome factors have been demonstrated in the literature, such as blood triglycerides, lipoprotein profiles, and blood pressure (Djousse et al. 2004), as well as on several cardiovascular disease risk factors such as oxidative stress (Zima et al. 2001), insulin sensitivity and diabetes mellitus (Koppes et al. 2005), anthropometric parameters (Bobak et al. 2003), hemostasis (Booyse et al. 2007), inflammation (Szabo 2007), endothelial function (Hoffmeister et al. 2003), and cancer (McPherson 2007).

Nationally, however, ETOH consumption is also accountable for high levels of mortality, morbidity, and social malaise in Canada (Adlaf et al. 2005). Worldwide, alcohol abuse is expected to take an increasing toll on lives and communities. Consumption volumes and patterns of ETOH

across the world are increasingly more harmful and risky, and more young people and women are adopting these patterns (Mancinelli et al. 2006).

WORLDWIDE CONSUMPTION PATTERNS: PER CAPITA

Worldwide per capita consumption of pure ETOH by adults varies across countries (Rehm et al. 2003a; Rehm and Monteiro 2005). Germany, France, and Spain each consume over 10 $L \cdot y^{-1}$ total across the 3 categories of alcoholic beverage; the USA, Canada, and Italy each consume more than 7 $L \cdot y^{-1}$, but less than 10 $L \cdot y^{-1}$; the Republic of China's per capita consumption is less than 6 $L \cdot y^{-1}$. The World Health Organization (WHO) designated Eastern Mediterranean region B and parts of Southeast Asia region D, including India, demonstrate a low volume consumption (1.3 $L \cdot y^{-1}$ and 2.0 $L \cdot y^{-1}$, respectively), for example. Worldwide average per capita consumption of ETOH across the 3 categories of alcoholic beverage is 5.8 $L \cdot y^{-1}$, a population-weighted average value, with distilled spirits accounting for the majority of the alcohol consumed (Rehm et al. 2003a; Rehm and Monteiro 2005). The highest volume of ETOH consumption occurs in the established market economies in Western Europe and in the former socialist countries such as Russia and surrounding countries (12.9 $L \cdot y^{-1}$ and 13.9 $L \cdot y^{-1}$, respectively). The lowest volume of ETOH consumption occurs in pockets of the WHO designated regions, specifically in the mostly Islamic regions of Eastern Mediterranean D and B (0.6 $L \cdot y^{-1}$ and 1.3 $L \cdot y^{-1}$, respectively).

In the Americas, the Federal Republic of Brazil and the countries of North America (Canada, United Mexican States, and the USA) each consume per capita almost twice the world average at approximately 9 $L \cdot y^{-1}$, with beer providing the majority of the ETOH consumed (Rehm and Monteiro 2005). Not surprisingly, heavy drinking is a major cause of preventable death in these countries (Rehm et al. 2003b). Consumption of ETOH in the US is documented through alcohol tax records. After Prohibition in 1935, alcohol sales in the US slowly increased and peaked in the 1980s at approximately 10 $L \cdot y^{-1}$ pure ETOH consumed per capita. Thereafter, consumption declined to current levels. Consumption of ETOH in Canada is documented in surveys such as the Canadian Addiction Survey (CAS) and its ancestors the National Alcohol and Other Drugs Survey 1989 (NADS) and Canada's Alcohol and Other Drugs Survey 1994 (CADS), and confirmed by alcohol sales records (Adlaf et al. 2005). In Canada, the data indicate that the percentage of drinkers declined from 1989 to 1994, but has since risen to a new high in 2004, at the time of the CAS, a monitoring and surveillance initiative focused on alcohol and other drug use in Canada. In 2001, 7.6% and 3.5% of all deaths in Canada among men and women under the age of 70 y, respectively, could be attributed to ETOH (Rehm et al. 2006). Nonetheless, the results in Canada can be summarized to say that the protective effects of moderate ETOH consumption on diabetes mellitus and cardiovascular outcomes outweigh the detrimental effects on mortality.

The highest per capita consumption of alcohol in the Americas occurs in Argentina at 16.3 $L \cdot y^{-1}$, and the lowest occurs in Trinidad and Tobago at 2.4 $L \cdot y^{-1}$ (Rehm and Monteiro 2005). The Andean region of South America has a regional per capita consumption of ETOH (mostly in the form of distilled spirits) of 5.1 $L \cdot y^{-1}$, a level slightly lower than the worldwide average. The mainland Central American countries also consume less alcohol per capita than the worldwide average, at 4.8 $L \cdot y^{-1}$ (Rehm and Monteiro 2005).

ABSORPTION, DISTRIBUTION, METABOLISM, AND EXCRETION

Alcohol, consumed in the form of beverages, does not require mechanical or enzymatic digestion in the gastrointestinal tract. The intact ETOH molecule — that which is not metabolized in the gastric mucosa by alcohol dehydrogenase (ADH) — is quickly and completely absorbed by passive diffusion in the stomach and proximal

small intestines, and subsequently enters the portal circulation. Factors that influence the rate of absorption of alcohol include the presence of sugar (Wu et al. 2006), presence of carbonation (Roberts and Robinson 2007), and gastric contents such as food (Gentry 2000; Levitt 2002; Ramchandani et al. 2001a). Although ETOH does not require enzymatic digestion in the gastrointestinal tract, a small portion of ingested ETOH (approximately 2%) undergoes gastric first-pass metabolism by gastric ADH (Levitt 2002; Levitt et al. 1997). Gastric first-pass metabolism decreases ETOH bioavailability in healthy young men to a greater extent than in healthy young women; these gender differences are not seen in the elderly, as gastric ADH activity in the elderly is significantly lower, especially in aged men (Pozzato et al. 1995). Recent advances in the study of ETOH pharmacokinetics using the alcohol-clamp methodology allows for the study of elimination kinetics independent of variation in alcohol absorption (Ramchandani and O'Connor 2006). Its application will undoubtedly clarify many of the determinants of alcohol absorption, distribution, and elimination in humans (Ramchandani et al. 2001b), such as gender differences in the expression of molecular forms of ADH (Baraona et al. 2001).

The alcohol molecule is intriguing in that it is amphipathic; it has both lipophilic and hydrophilic characteristics. The lipophilic qualities of alcohol facilitate the capacity of the molecule to diffuse across cell membranes. The hydrophilic qualities of alcohol are explained through hydrogen bonding. The attraction between water and the hydroxyl group of the alcohol molecules is strong enough to solubilize ETOH, but not so strong that alcohol is irrevocably bound to water. As ETOH is a small polar molecule completely soluble in water, its volume of distribution throughout the body is comparable with total body water (Ramchandani et al. 2001a). Thus, approximately 70% of the body's mass is ETOH accessible (Koolman and Röhm 2005). These characteristics have important implications for both understanding physiological responses to ETOH, and subsequent policy-making (e.g., definition of moderate drinking across genders).

Maximal blood alcohol concentrations (BACs) are reached approximately 75 min post-consumption (Jones et al. 1991). Ethanol is quickly distributed across all water compartments of the body, which is approximately 70% of body mass. Therefore, BACs are dependent in part upon body composition. For example, as women generally have a lower skeletal muscle mass and a higher fat mass than men, BAC will be higher in women than in men upon consumption of an equal volume of ETOH (Ramchandani et al. 2001a). This observation is largely due to a lower tissue mass in women within which ETOH can be diffused away from the bloodstream before hepatic metabolism. Compartmental pharmacokinetic models for ETOH quantify alcohol concentrations in the body using compartments with combinations of zero-order kinetics, first-order kinetics, and Michaelis–Menten kinetics. However, they do not quantitatively characterize the ETOH pharmacokinetics in terms of physiologically based body compartments as do the emerging "physiologically based pharmacokinetic models" (PBPKs) (Ramchandani et al. 2001a). Future research should clarify the distributional behavior of ETOH using appropriate models to describe ETOH absorption, distribution, and elimination in the body (Ramchandani and O'Connor 2006).

The primary site of ETOH metabolism is in the hepatocyte (Koolman and Röhm 2005). Alcohol dehydrogenase (ADH), a non-inducible cytoplasmic enzyme, oxidizes alcohol to acetaldehyde, capturing reducing equivalents as $NADH + H^+$ by the coenzyme NAD^+. This is the rate-limiting step in the cytoplasmic series of ADH reactions. Alternatively, ETOH can be oxidized in the smooth endoplasmic reticulum of the hepatocyte by the non-specific, inducible cytochrome P450 monooxygenase (MOX) (Lieber 1997). This enzyme, which uses reducing equivalents from $FADH_2$, catalyzes the hydroxylation of ETOH and concomitant reduction of molecular oxygen to form acetaldehyde, water, and FADH. Monooxygenases catalyze what are known as phase 1 inter-conversion reactions to prepare polar or weakly polar substances such as

ETOH for renal excretion as more strongly polar metabolites (Koolman and Röhm 2005).

Regardless of the path used to oxidize ETOH, acetaldehyde is a reactive compound even more toxic than alcohol (it can form covalent complexes with biomolecules such as proteins and nucleic acids). It is oxidized in the mitochondria by acetaldehyde dehydrogenase using the coenzyme NAD^+, forming acetate and NADH + H^+. In the cytosol, acetate is converted to acetyl CoA by acetate CoA ligase. Acetyl CoA is a key intermediate in the amphibolic pathways of intermediary metabolism; as such, it represents the site of entry of metabolic products of ETOH degradation into intermediary anabolism and catabolism (Koolman and Röhm 2005).

Alcohol dehydrogenase and aldehyde dehydrogenase both use NAD^+ as a coenzyme. As NAD^+ is found in limited supply in the liver and must be regenerated, this places a limit on the detoxification rate to approximately one standard drink per hour (about 15 g ETOH). Induction of the MOX enzymes increases the reaction velocity for ETOH metabolism, but not without consequence. Induction of the non-specific MOX enzymes will also enhance metabolism of other weakly polar and non-polar compounds in the body (Lullmann et al. 2000), potentially leading to situations ranging from vitamin deficiency (e.g., retinol), drug interactions and amplifications due to co-metabolism, and reactive oxygen species (ROS) formation.

Hepatic elimination of ETOH obeys a linear time course (zero-order kinetics), as ADH achieves half-saturation at low blood alcohol concentrations of 0.008% (e.g., 80 $mg \cdot L^{-1}$) (Lullmann et al. 2000). Thus, unlike many other drugs that obey exponential kinetics, the amount of ETOH that can be metabolized by the liver per unit of time remains constant at BAC above 0.02%, which represents the plateau of the reaction velocity.

Ethanol has characteristics of both a drug and a nutrient. A nutrient is a chemical substance that is used by the body to provide energy, to build or repair tissues, and (or) to regulate life processes, and is usually obtained in a food or beverage form (Lagua and Claudio 2004). Drugs are non-nutritive chemical substances used for the diagnosis, treatment, or prevention of a disease or as a component of pharmacotherapy (Houghton Mifflin Company 2007). Ethanol is one of the worlds' most widely consumed drugs. Thus, like all drugs, it has the potential for therapeutic and toxic capacities in dose-dependent fashion.

CONSUMPTION PATTERNS: THE GOOD

Retrospective epidemiological studies throughout the world have demonstrated that there is a J-shaped relationship between intake of ETOH and mortality from all causes, and that there may be differences in the strength of this relationship across the 3 main categories of alcoholic beverages (beer, distilled spirits, and wine) (Gronbaek 2007). Prospective population studies, however, have shown that all 3 categories of alcoholic beverages have protective effects on mortality from myocardial infarction (Mukamal et al. 2003), and that it may be a daily moderate habit that confers the protection, regardless of the type of alcoholic beverage. In general, abstainers and light drinkers of alcohol have a higher risk of all-cause mortality, coronary heart disease, and cancer than do moderate drinkers. Compared with light drinkers and moderate drinkers, heavy drinkers have a higher risk of all-cause mortality, coronary heart disease, and cancer. Moderate drinkers demonstrate a reduced risk of peripheral vascular disease, myocardial infarction, ischemic stroke, and mortality from cardiovascular disease (Goldberg et al. 2001).

Of the 3 main classes of alcoholic beverages, wine is commonly believed to confer the most protection against all-cause and coronary heart disease mortality. Beer is believed to confer protection equal to or at a level somewhat below that conferred by wine. Distilled spirits are believed to confer the weakest protection. However, these are hypotheses that remain to be conclusively demonstrated by the scientific process, and the current evidence suggests that the major protective agent appears to be ETOH itself regardless of source (Mukamal et al. 2003). Lifestyle factors and other confounders that contribute to health benefits, such as diet and exercise habits,

as well as socioeconomic status, must be adequately accounted for in research designed to elucidate the effects of various alcoholic beverages on health (Gronbaek 2007).

Drugs are often delivered to the body as relatively isolated chemical substances, and an example of this would be ETOH consumed as distilled spirits (approximately 50% pure ETOH per volume of 100 proof liquor). Thus, distilled spirits are notably absent of vitamins and phytochemicals commonly associated with plant foods and plant food products. However, drugs can also be delivered in a "food matrix". Consider, for example, the consumption of dried herb preparations of yesteryear (the word "drug" is etymologically derived from the Old French word "drogue", which means dried herb (Houghton Mifflin Company 2007)). Through the delivery of such preparations (e.g., herbal infusion), one hoped to obtain enough of the desired therapeutic molecule(s). In somewhat similar fashion, ETOH is usually delivered in a liquid "food matrix" (e.g., beer and wine) that may be rich in some nutrients such as vitamins, minerals, and important non-nutritive phytochemicals. Both ETOH and bioactive molecules, such as secondary phytochemicals, have been implicated in conferring health benefits through disease mitigation when alcoholic beverages are consumed in moderation.

Oxidative stress is implicated in the pathology of many lifestyle-related diseases (Ames and Gold 1991; Salonen et al. 1997; Zima et al. 2001) such as cancer, cardiovascular disease, and diabetes mellitus. Oxidative stress refers to the acute and chronic effects of ROS and other radical species formed through chemical intoxication, radiation, and metabolism. These reactive molecules are characterized by having an unstable, unpaired electron configuration. In the process of scavenging electrons to stabilize the unpaired electron, reactive species oxidize body proteins, lipids, and nucleic acids. Anti-oxidant molecules, either endogenous (e.g., superoxide dismutase) or exogenous, (e.g., vitamins C and E and phytochemicals such as carotenoids), can act as protectors of our biomolecules by allowing themselves to donate electrons to the reactive species, by scavenging free radicals, or through anti-mutagenesis. Epidemiological studies demonstrate a correlation between increased consumption of antioxidant-rich, plant-derived food products and reduced risk of cardiovascular disease (Ignarro et al. 2007) and certain cancers (Williams and Hord 2005).

Secondary phytochemicals are plant chemicals that have defense, pigment, scent, color, and growth-regulating functions in the secondary metabolism of plants. When consumed in the form of plant-derived foods and food products, these phytochemicals may continue to have bioactive properties that have physiological importance in the mammalian body. However, as we do not have a physiological requirement for any one of these thousands of plant molecules, they are non-nutritive. These bioactive molecules are classified according to their basic structure.

Polyphenols are among the most widely distributed and numerous of plant compounds; flavanoids are the largest polyphenol sub-group comprising thousands of compounds. Polyphenols contribute astringency and bitterness to foods and beverages, and are especially plentiful in commonly consumed erva mate (*Ilex paraguariensis*), tea (*Camellia sinensis*), coffee (*Coffea arabica*), fruits and vegetables, and hops (*Humulus lupulus*). The average intake of polyphenols is ~200 $mg \cdot d^{-1}$, and the human absorption and metabolism of both free and conjugated forms of phenolic acids has been demonstrated for both foods and beverages, including beer (Nardini et al. 2006).

Recently, a variety of alcoholic and non-alcoholic beverages were assessed for polyphenol content and anti-oxidant capacities (i.e., fruits, tea, carrots, wines (red and white), and beers (lager and dark)) (Lugasi and Hovari 2003). Polyphenols were found most plentiful in elderberry juice (approximately 5700 $mg \cdot L^{-1}$), high in red wines and fruit juices (approximately 1000 $mg \cdot L^{-1}$), and lower in beers and white wines (approximately 400 $mg \cdot L^{-1}$). In vitro anti-oxidant activity in all tested beverages was commensurate with the total polyphenol content.

There are recent claims that the in vivo anti-oxidant capacities of beer and red wine are simi-

lar despite different concentrations of total polyphenols, possibly due to superior absorption of the beer phenolics as compared with those in red wine (Kondo 2004; Nardini et al. 2006). Thus, although beer contains twice the antioxidant content as white wine and half that of red wine (Suter 2001), the red wine antioxidants may be larger molecules that are not as readily absorbed as smaller beer antioxidant molecules. Research shows that beer antioxidants are readily absorbed and bioavailable (Ghiselli et al. 2000). This hypothesis regarding possible differential absorption across matrix delivery systems warrants further investigation (Nigdikar et al. 1998).

An alternative hypothesis worthy of exploration is that the differential polyphenolic profiles that occur across foods and beverages (e.g., wine vs. beer) are responsible for the different in vitro and in vivo observations of anti-oxidant capacities. For example, hops are a rich source of isohumulones in beer (Kondo 2004), whereas red wine is rich in other polyphenols (e.g., resveratrol) as compared with those found in white wine (Nigdikar et al. 1998). However, it must be emphasized that the research evidence supporting the protective effects of moderate drinking on the heart, and against many other conditions, cannot be tied assuredly to particular types of alcoholic beverages at this time.

Finally, this brief discussion on the known benefits of ETOH should make mention of the under-emphasized topic of the psychotherapeutic value of moderate alcohol consumption upon health. Although experts may tacitly acknowledge positive psychological benefits associated with moderate alcohol consumption, the scientific literature appears to be preoccupied with the ills associated with excessive drinking (Heath 2007). It has been pointed out that the majority of the ETOH literature ignores 2/3 of the WHO's definition of health: "...mental and social well being...." (Heath 2007). This forgotten dimension in alcohol research lies in striking contrast to the reality that ETOH has important social consequences in most societies by way of celebration, stress reduction, appetite enhancement, social interaction enhancement, and feelings of well-being (Peele and Brodsky 2000). These psychosocial aspects of the benefits of alcohol should be regarded and further explored via the scientific process as potential health benefits associated with moderate ETOH consumption (Meister et al. 2000).

CONSUMPTION PATTERNS: THE BAD

The overall consumption of alcohol (e.g., per capita intake) has been the typical expression of exposure to ETOH as it relates to disease in the literature (Rehm et al. 2003a; Rehm and Monteiro 2005). However, there is emerging evidence that the pattern of drinking (e.g., drinking in moderation with meals; abstention, followed by binge drinking) moderates the impact of the overall consumption of alcohol (e.g., average intake) on disease and mortality. Increasing numbers of investigations are attempting to consider the joint impact of average ETOH intake, as well as pattern of drinking (of average alcohol intake) in epidemiological studies.

In the 2000 WHO study on the Global Burden of Disease, a continuation, refinement, and update of the global epidemiological study of the average volume of alcohol consumed as related to disease burden was presented (Meloni and Laranjeira 2004). In general, with increasing average volume of ETOH consumed, an increased occurrence of health problems was observed. A novel attempt was also made to describe by a summary score the patterns of global drinking, as related to disease burden, which are independent of the average volume consumed (Rehm et al. 2003a; Rehm and Monteiro 2005). That is to say, two countries that present with a similar adult per capita consumption of ETOH may present with different burdens of disease outcomes due to different patterns of alcohol consumption. Although the process of qualifiying and quantifiying risk relations between ETOH consumption and disease as affected by consumption pattern is a work in progress, some illuminating and alarming statistics emerged from the effort.

Through the use of key informant surveys on WHO regions, available survey data, and factor analysis, countries were classified into four (1, 2, 3, 4) score categories reflecting the risk for mor-

tality and burden of disease associated with different volumes of ETOH intake, as follows: 1, least-risky drinking pattern (characterized by light to moderate drinking with meals and without irregular heavy drinking bouts, and associated with a lower burden of disease and mortality); 4, most-risky drinking pattern (characterized by the highest level of irregular drinking, and associated with a higher burden of disease and mortality) (Rehm and Monteiro 2005). Although not specifically quantified, the least-risky patterns (1, 2) were associated with the drinking of more wine and beer, whereas the most-risky patterns (3, 4) were associated with the drinking of more distilled spirits.

As detailed earlier, the volume of ETOH consumed was found to be highest in Western Europe, the former Socialist economies in Eastern Europe, and in North America. The lowest volume of consumption was observed in parts of Southeast Asia and the Eastern Mediterranean region. However, when considering the drinking pattern scores of individual countries and (or) geopolitical regions, it was found that a drinking pattern score of 1 was only found in Europe, Australia, and Japan (Rehm et al. 2003a; Rehm and Monteiro 2005), such that no American country had a drinking pattern score of 1. In the Americas, the only countries with a drinking pattern score of 2 were Canada, the USA, Argentina, and the Caribbean countries. Other regional countries with an average score of 2 include the predominantly Muslim countries of Iran and Saudi Arabia, and countries of the Western Pacific region such as China, Philippines, and Viet Nam.

In the Americas, the Central American countries most frequently had a drinking pattern score of 4 (Belize, El Salvador, Guatemala, Honduras, Nicaragua, and also Mexico from North America), and many countries in Central and South America have a drinking pattern score of 3 (Bolivia, Brazil, Chile, Colombia, Costa Rica, Ecuador, Guyana, Paraguay, Peru, Suriname, Uruguay, and Venezuela) (Rehm and Monteiro 2005). Other WHO regions with an average drinking pattern score of 3 or greater include countries of Africa E (e.g., Ethiopia, South Africa), Europe B (e.g., Bulgaria, Poland, Turkey), Europe C (e.g., Russian Federation, Ukraine), America B (e.g., Brazil) (Meloni and Laranjeira 2004), and Southeast Asia D (e.g., Bangladesh, India) (Rehm et al. 2003a; Rehm and Monteiro 2005). Thus, in Guatemala and Nicaragua (for example), an isovolumic intake of ETOH is related to a greater burden of disease and mortality than in the other American countries, as per the inherent characteristics of the drinking pattern score of 4 (Rehm et al. 2003a; Rehm and Monteiro 2005).

Alcohol has been found to be a major risk factor for disease burden throughout the world. In the Americas, lifestyle-related risk factors predominated; ETOH was found to be the risk factor that confers the greatest burden of disease, followed by smoking, and then by undernutrition (when broken down into American subregions, smoking is the first risk factor that confers the greatest burden of disease in Anglophone North America (Canada and the US)). Thus, prevention interventions are warranted that address the overall volume of ETOH consumption (decrease to a moderate intake), the consumption pattern should be addressed (decrease irregular bouts of heavy drinking and, if alcohol is consumed, it should be consumed in moderation and with meals) and perhaps also the types of alcoholic beverages chosen. It has been demonstrated that among females, the primary determinant of the inverse association between drinking ETOH and risk of heart disease may be the simple intake of alcohol, and not the frequency of consumption (Tolstrup et al. 2006). Among the men studied, the frequency of ETOH appears to be more important; specifically, the lowest risk of coronary heart disease was observed among the men who drank daily (Tolstrup et al. 2006).

ALCOHOL AND ATHLETICS: CONSUMPTION PATTERNS AND HEALTH AND PERFORMANCE ISSUES

Alcohol has also been found to be a major health risk among athletes and habitual exercisers, as ETOH is the most frequently consumed drug in this population. Alcohol abuse is one of the biggest problems on college and university campus-

es (El-Sayed et al. 2005). It is currently recognized that the abuse of ETOH among university students is a public health concern, and that intercollegiate athletics is recognized to be a subpopulation of the campus community at higher risk for excessive drinking practices specifically (Martens et al. 2006), and immoderate drinking practices generally. In the arena of one of the world's most popular sports, football (soccer), it is not currently clear if the volume and pattern of ETOH consumption among footballers differs from that of other competitive athletes. However, it is clear that footballers engage in binge drinking, as do other athletes (Maughan 2006). Binge drinking is defined by the International Center for Alcohol Policies as the consumption of 5+ standard drinks on one occasion (of unspecified duration) by men or 4+ standard drinks on one occasion (of unspecified duration) by women (International Center for Alcohol Policies 2003). The general health and performance consequences of immoderate drinking have some ramifications of special concern to athletes.

Dietary ETOH, with a density of 0.79 g/mL, is an energy-yielding molecule without requirement by mammalian physiology. Alcohol has a high energy density at 29 $kJ \cdot g^{-1}$, and can readily displace nutrient-dense foods in the diet while contributing excess dietary energy. This can impact energy balance, as well as macronutrient balance in the body, potentially interfering with glycogen re-synthesis through displacement of carbohydrate in the diet and non-adherence to sport nutrition guidelines (El-Sayed et al. 2005; Shirreffs and Maughan 2006)

Micronutrients (vitamins and minerals) are displaced along with the dietary intake of foods when excess ETOH is consumed; additionally, the requirements for certain micronutrients are likely increased through the metabolism of alcohol (van den Berg et al. 2002). Hepatic metabolism of ETOH requires increased use of the NAD^+ and FAD cofactors of several enzymes used in alcohol metabolism (of which vitamins B3 and B2 are components, respectively), as well as vitamins B1 (used in pyruvate dehydrogenase reaction), B5 (a component of acetyl CoA, which accumulates and leads to increased fatty acid synthesis), and B6 (involved in transamination reactions and glycogenolysis).

Ethanol is a drug capable of producing toxic effects in a dose-dependent manner, especially when taken in doses greater than what the liver can process per hour (approximately 15 g ETOH). The implications of the toxic chemical effects of ETOH and acetaldehyde can be considered from the moment of ingestion or production upon all points of contact with body tissues thereafter (until metabolism). For example, alterations in mucosal lining in the gastrointestinal tract due to chemical damage can subsequently lead to malabsorption of nutrients (Rajendram and Preedy 2005). Another example is that the toxic effects of alcohol and acetaldehyde may partially explain the atrophy of types I, IIa, and IIb myofibers, decreased capillarity, and altered metabolism observed in skeletal muscle tissue in exercisers (El-Sayed et al. 2005).

ROS, such as the hydroxyl radical, are known to be generated in response to ETOH and acetaldehyde metabolism (Dahchour et al. 2005). Oxidative stress occurs when there is an imbalance between anti-oxidant defense systems and the production of ROS. Metabolism of ETOH generates ROS both in the mitochondrial electron transport chain and by MOX (Albano 2006), and oxidative stress is attributed to alcoholic liver disease (Albano 2006) and alcohol myopathy (Lang et al. 2005). Thus, several metal co-factors (e.g., zinc, manganese, copper, iron, and selenium) likely have increased rates of recycling owing to up-regulation of endogenous anti-oxidant systems such as superoxide dismutase, catalase, and glutathione peroxidase in response to alcohol metabolism-derived production of ROS such as the hydroxyl radical. Exogenous anti-oxidants, such as vitamin E (particularly in the central nervous system), vitamin C, and β-carotene may also require dietary attention due to increased use in the face of alcohol-induced oxidative stress.

Immoderate intakes of alcohol exceed the capacity of the ADH system to metabolize ETOH, leading to hepatic MOX induction. Exercise performance also enhances the metabolism of ETOH by the microsomal system (El-Sayed et al. 2005). These observations should raise a red flag

regarding the potential for oxidative stress due to both exercise and ETOH consumption (both chemically induced and as a result of ROS formation). However, it has also been shown that exercise training mitigates alcohol-induced oxidative damage (El-Sayed et al. 2005), suggesting a need for further research in this area.

Ethanol provides a powerful diuresis effect that is well recognized; it acts as a diuretic via suppression of the release of anti-diuretic hormone from the pituitary. This presents important considerations for athletes who either consume alcohol in moderate or immoderate doses. It has been estimated that the kidney will produce excess urine on the order of 10 mL/g ETOH ingested (Shirreffs and Maughan 2006). So, one drink of approximately 14 g ETOH will result in diuresis of 140 mL urine above and beyond normal output. This can lead to negative hydration balance.

Other notable effects of ETOH include effects upon the thermoregulatory system and on wake–sleep patterns. Ethanol depresses the thermoregulatory center in the brain, allowing cooling of the body to dangerous levels if the ambient temperature is sufficiently low (Shirreffs and Maughan 2006). Sedating substances such as ETOH can lead to daytime periods of sleepiness and interrupt the nocturnal sleep period (Roehrs and Roth 2001), especially if the person is taking other medications that have a synergistic interaction with ETOH.

Gender differences in alcohol consumption and metabolism are important to mention, as they may relate to exercise. The overall burden of disease and injury due to ETOH consumption is less in women than in men both throughout the world (15.3%) and in the Americas (16.7%) (Rehm and Monteiro 2005). This may be explained, in part, as a result of the overall significant gender differences in the proportion of drinkers throughout the world. Only in the WHO regions Europe A, Europe C, and Western Pacific A are the proportion of female drinkers within 10% of the proportion of male drinkers (Rehm et al. 2003a; Rehm and Monteiro 2005). In anglophone North America (e.g., Canada, the US), the proportion of female drinkers is within 15% of the proportion of male drinkers, as compared with 22% of the WHO region Americas B (e.g., Brazil, Mexico). Women's consumption rate and pattern of immoderate ETOH intake is rapidly increasing, both in the Americas and throughout the world (Mancinelli et al. 2006). The age of first use is dramatically decreasing, and the drinking rate among female teenagers is quite similar to the drinking rate of their male peers (Mancinelli et al. 2006).

In a systematic review of college student–athlete drinking, it has been reported that the prevalence rates of ETOH consumption were consistently lower among female athletes than among male athletes (Martens et al. 2006). However, it was also reported that drinking rates were consistently higher among female athletes than among female non-athletes across the following categories: heavy episodic drinking in the past 2 weeks, frequent heavy episodic drinking in the past 2 weeks, and number of drinks per week (Martens et al. 2006). The brief discussion provided earlier regarding female metabolism of ETOH highlighted gender differences in BAC due to body composition and gender differences in gastric first-pass metabolism (Frezza et al. 1990). Additionally, there are also suggested gender differences in ADH activity, effects of hormonal profiles on ETOH metabolism, and other gender differences related to ETOH metabolism that warrant further research (Mancinelli et al. 2006; Muller 2006). Especially notable is the relative paucity of alcohol-related research in female athletes, given the clear indication of the rising rates of use and abuse in this population and the aforementioned gender differences in metabolism.

Although discussing the acute effects of excess ETOH consumption are outside the scope of this review, it is important to at least comment upon the possible aftereffects of immoderate and binge drinking on next-day training and practice endeavors by athletes. First, it has been documented that BAC can remain above the legal limit of driving a car the morning after a binge-drinking bout (Maughan 2006). This would result in an athlete showing up for practice or a game still under the influence of alcohol. Alternatively,

BAC may have returned to normal the day after the binge drinking bout, but the athlete may present with a hangover at practice or competition. The symptoms of hangovers are believed to be due to dehydration, aberrations in acid–base balance, macronutrient metabolism disruption, cardiovascular changes (increased heart rate, decreased left ventricular performance, and increased blood pressure), and immune defense suppression (Maughan 2006). Any of the above possible aftereffects of excess alcohol consumption are sufficient to merit discouragement of immoderate ETOH use by athletes for health and performance reasons. The reader is referred to the American College of Sports Medicine (1982) position stand on the use of alcohol in sports for an older, comprehensive review on the topic.

MODERATE CONSUMPTION GUIDELINES

The International Center for Alcohol Policies (ICAP) has compiled international guidelines for ETOH consumption. These are guidelines designed to alter alcohol consumption behavior in target populations. The reader is referred to ICAP report 14 for the compendium (International Center for Alcohol Policies 2003). It is noteworthy that the recommendations across many countries are quite disparate, despite the readily available current scientific literature. This may be partly attributable to differences in intended outcome: decrease ETOH misuse vs. promote moderate use (Harding and Stockley 2007).

In Canada, the Centre for Addiction and Mental Health defines a standard alcoholic drink as one containing 13.6 g ETOH. Women and men are both advised not to exceed 27.2 $g \cdot d^{-1}$ ETOH (2 standard drinks). In the US, one standard drink is considered to provide on average 14 g ETOH: 355 mL (12 fl. oz) beer, 150 mL (5 fl. oz) wine, or 45 mL (1 fl. oz) distilled spirits. According to the United States Department of Agriculture (USDA) and the Department of Health and Human Services (DHHS) in the US, women should consume no more than one standard drink per day, and men should consume no more than two standard drinks per day.

SUMMARY

Current literature shows both the promise and peril of alcohol consumption; it appears that the tonic becomes a toxin in a dose-dependent fashion. The balancing act is perturbed by alarming statistics demonstrating the devastating potential of one the world's most consumed drugs in excess — especially among the young, women, and athletes — and is assuaged by statistics demonstrating reduced risk of all-cause mortality and coronary heart disease mortality among moderate drinkers. It is important to have a clear understanding of both the benefits and risks of ETOH consumption. It is imperative to communicate our current understanding of the scientific literature on alcohol research to our target populations. We can do this through refinement and promulgation of the official guidelines for the moderate consumption of alcoholic beverages. In so doing, we can provide both individuals and populations with a consistent message for guidance regarding the use of ETOH that is reflective of the evidence regarding both the detrimental effects of excessive consumption and the beneficial effects of moderate consumption.

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