Alcohol Consumption in Israel: A Public Health and Medical Problem

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In this publication, Jaworowski et al. present alcohol-screening findings from a sample of patients (aged 14 years and older) in a university-affiliated hospital in Israel [1]. Using the four-item CAGE questionnaire [2] with a cutoff of two or more positive responses, 22% of 178 patients referred for psychiatric consultation (95% confidence interval 17–29%, calculated), and 13% of 105 randomly recruited emergency room patients (CI 8–21%), were classified as having an alcohol use disorder. Extrapolation from data presented in Table 3 of their report reveals a particularly high positive CAGE result among divorced/separated/widowed patients (43%) and among those born in the Former Soviet Union/Russia (37%).

In a recent survey of women in three hospital maternity wards in Israel (N=3815), 14% reported having consumed alcohol during their pregnancy, and 26 women were identified as being at high risk for hazardous alcohol consumption (based on the T-ACE screening tool, a modified CAGE questionnaire designed to screen pregnant women for alcohol use) [3]. According to these results, the authors estimated that over 1000 babies are born annually in Israel at high risk for fetal alcohol spectrum disorder.

Tenenbaum and colleagues [4] investigated a high risk pediatric population of 100 infants referred to the Hadassah University Hospital's Medical Adoption Unit for clinical manifestations of FASD. Four children met FASD criteria: two exhibited fetal alcohol syndrome in the absence of a known history of maternal alcohol exposure, and two exhibited partial FAS with confirmed (self-reported) maternal alcohol consumption [5]. Another 11 were classified as “highly likely to receive a FASD diagnosis.” The authors maintain that the prevalence of FASD is likely to be higher as most of these infants had not yet reached one year of age when FASD becomes more apparent. They estimate that 22 to 225 FASD “at-risk” babies are born annually in Israel. Yet, during the 10 year period 1998–2007, only 4 FASD cases were recorded in 17 Israeli hospitals and 6 cases were diagnosed at the primary care level [6]. This discrepancy may be due to insufficient knowledge and awareness among health care professionals, as reported by the heads of all (but one) of the 43 child development centers and genetic counseling clinics in Israel [6], who estimated that there are “tens” of undiagnosed FASD cases, and some put the number at “hundreds.”

Regardless of the actual numbers of high risk drinkers and FASD cases, it is clear that physicians and other health professionals, particularly those who serve the adolescent population – those most vulnerable to alcohol-related harms – should be playing a more central role in the prevention, diagnosis, treatment, as well as research, of harmful drinking and alcohol-related disorders. There is ample evidence of effectiveness for brief behavioral counseling interventions for harmful alcohol use among adolescent and adult primary care patients [7,8]. Yet, these programs are rarely implemented, and general practitioners and other health care providers, owing to numerous clinical and administrative barriers, often fail to identify, counsel and refer patients who misuse alcohol [9]. Perhaps paramount among these barriers are lack of training, time constraints, and in some settings reimbursement issues [10]. Recent initiatives by the Ministry of Health in addiction medicine teaching for physicians will hopefully overcome the barrier posed by the limited training received by medical and paramedical students.

Having said that, we must be careful, however, not to confuse screening tests with diagnostic tests. Screening tests are designed to identify persons who are likely to have the condition being screened for, and who should then be referred for diagnostic confirmation and appropriate treatment when necessary. While the CAGE is a highly sensitive test (i.e., nearly all persons with alcohol dependence will have a positive CAGE result), the positive predictive value of the CAGE (using a 2+ cutoff) has consistently been shown to be about 85% among hospital-based and other high risk samples. This means that of the 54 patients identified by Jaworowski et al. [1] with a positive CAGE score, 46 can be expected to actually have an alcohol use disorder. Unlike sensitivity and specificity, the PPV of a screening test – and thus, its efficacy as...
a screening tool – is largely influenced by the underlying prevalence of the condition in the population. Application of the CAGE screening tool to the general adult population of Israel, where the prevalence of an alcohol-related disorder is about 4% [11], would produce a large number of false positives who might be unnecessarily referred for diagnostic assessment and/or treatment.

Epidemiological findings and anecdotal evidence suggest that Israeli society, long known to be relatively sober (and drug-free) by western standards, is no longer immune to the deleterious outcomes of alcohol (and drug) misuse. In recent years drinking has become a central element of entertainment and nightlife among Israeli adolescents and adults alike, with a concomitant growth in the number of drinking sites, and a burgeoning phenomenon of youthful drinking and harmful drinking. Indeed, the impression one gets from Israeli internet news is that Israel is drowning in alcohol: “Experts say Israel is now among world leaders in per capita consumption of vodka…” [Ynet, 2/17/08]; “Alcohol is killing Israel” [Ynet, 11/11/09]; “Alcohol abuse at Israel’s military bases is spiraling out of control” [Ynet, 12/29/11].

The available epidemiological evidence is almost equally alarming. Findings from the HBSC 2005/2006 survey of 5350 Israeli school-attending youth in grades 6, 8 and 10 rank Israel second out of 40 countries (behind only Ukraine) in the percent of youth who report drinking alcohol at least once a week – 19% and 8% of 11 year old Israeli boys and girls, respectively [12]. In the latest national school survey (grades 7–12) conducted in 2009 by the Israel Anti-Drug Authority, about 40% of adolescents reported drinking alcohol in the past month (apart from religious ceremonies), and one-third had gotten drunk at least once in the past year [13]. Relatively high rates of binge drinking and getting drunk were noted among Arab respondents, long believed to be immune to excessive drinking due to religious and cultural restrictions. IADA survey results also show that school-going youth who drink are much more likely than non-drinkers to smoke (36% vs. 5%), and to use illicit drugs (17% vs. 3%), inhalants (22% vs. 9%) and non-prescription medications (10% vs. 2%). In turn, a history of harmful alcohol consumption patterns (drunkenness and binge drinking) and drug use strongly predicts violence among Israeli adolescents, particularly among Arab girls [14].

Particularly troubling patterns of alcohol consumption are seen among immigrant youth from the Former Soviet Union [15] and Ethiopia [16] for whom the challenges of acculturation and integration into Israeli society, coupled with typical adolescent turmoil, contribute to a greater likelihood of social maladjustment and the development of risk-taking behavior patterns [17].

Perhaps most worrisome is the finding that nearly one-quarter (22%) of school-going youth surveyed by the IADA in 2005 believed there is little or no danger in drinking alcohol several times a week [18]. Similarly, approximately 70% of Israeli college/university students nationwide perceive drinking as carrying no harm or only minor harm, despite 35% admitting to drink-driving and 20% admitting that they had driven while they knew they were too drunk to do so [19].

In the IADA 2009 national household survey of 18–40 year old adults, just over half (53%) reported any post-month drinking (this has remained virtually unchanged over the past two decades); however, one-quarter reported having gotten drunk at least once in the past year, and 21% had at least one episode of binge drinking (5+ drinks within a few hours) [13]. While none of these sources address drink-driving or drug-driving directly, the findings certainly describe a culture in which dangerous drinking patterns are common among adolescents (including pre-teens) and adults, and clearly suggest the likelihood of the dangerous mix between alcohol, drugs and driving. Indeed, evidence from various sources suggests that the proportion of alcohol-related road accidents is growing [20].

Harmful patterns of drinking and drug use and associated behaviors such as drink-driving, particularly among young adults, pose a potential serious social threat and a real challenge for public health practitioners, health service providers and public policy makers. The consequences of such behavior are increasingly felt in many spheres of life at the level of the individual, the family and society as a whole.

Physicians, epidemiologists and public health professionals in Israel should be playing a more prominent role in the prevention, diagnosis, treatment as well as research of harmful drinking and alcohol-related disorders. The medical community must become more active in bringing their collective clinical experience regarding alcohol (and the misuse of other psychoactive drugs) to policy makers, health educators and the general public.

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References

HBSC = Health Behaviour in School-Aged Children
IADA = Israel Anti-Drug Authority

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**Capsule**

**The Cancer Cell Line Encyclopedia enables predictive modeling of anticancer drug sensitivity**

The systematic translation of cancer genomic data into knowledge of tumor biology and therapeutic possibilities remains challenging. Such efforts should be greatly aided by robust preclinical model systems that reflect the genomic diversity of human cancers and for which detailed genetic and pharmacological annotation is available. Barretina et al. describe the Cancer Cell Line Encyclopedia (CCLE): a compilation of gene expression, chromosomal copy number and massively parallel sequencing data from 947 human cancer cell lines. When coupled with pharmacological profiles for 24 anticancer drugs across 479 of the cell lines, this collection allowed identification of genetic, lineage, and gene expression-based predictors of drug sensitivity. In addition to known predictors, we found that plasma cell lineage correlated with sensitivity to IGF1 receptor inhibitors; AHR expression was associated with MEK inhibitor efficacy in NRAS-mutant lines; and SLF11 expression predicted sensitivity to topoisomerase inhibitors. Together, these results indicate that large, annotated cell-line collections may help to enable preclinical stratification schemes for anticancer agents. The generation of genetic predictions of drug response in the preclinical setting and their incorporation into cancer clinical trial design could speed the emergence of “personalized” therapeutic regimens.

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**Capsule**

**Atg7 modulates p53 activity to regulate cell cycle and survival during metabolic stress**

Withdrawal of nutrients triggers an exit from the cell division cycle, the induction of autophagy, and eventually the activation of cell death pathways. The relation, if any, among these events is not well characterized. Lee et al. found that starved mouse embryonic fibroblasts lacking the essential autophagy gene product Atg7 failed to undergo cell cycle arrest. Independent of its E1-like enzymatic activity, Atg7 could bind to the tumor suppressor p53 to regulate the transcription of the gene encoding the cell cycle inhibitor p21CDKN1A. With prolonged metabolic stress, the absence of Atg7 resulted in augmented DNA damage with increased p53-dependent apoptosis. Inhibition of the DNA damage response by deletion of the protein kinase Chk2 partially rescued postnatal lethality in Atg7−/− mice. Thus, when nutrients are limited, Atg7 regulates p53-dependent cell cycle and cell death pathways.

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