Preconception Substance Use: A Call to Raise Awareness of Potential Adverse Effects

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Although a great deal of behaviour change still needs to occur, North American society shows signs that there is a growing realization and acceptance of the knowledge that substance use during pregnancy can cause irreversible brain damage and harm to the fetus. However, the general public does not seem to be aware of the research suggesting that one's life history of substance use prior to conception may also adversely affect one's future children, grandchildren, and great-grandchildren [1-3]. For example, most women do not stop using alcohol until they know they are pregnant [4,5] and a Canadian study examining women's beliefs about the preconception period suggested that only 38% of respondents believed that women should stop alcohol use in the preconception period and only 28% believed that men should do the same [6]. In this paper we take the position that there is a serious need to "raise the bar" in terms of the education and practical recommendations provided to the public about preconception substance use (PSU) in both men and women.

There is emerging evidence that our life history of exposure to alcohol, drugs, and other toxins can affect the physical, psychological, and neurological health of our children and future generations. Thus, everything that future mothers and fathers are exposed to prior to conceiving a child (e.g., diet, stress hormones, toxins, and drugs) has the potential to affect future offspring. Animal research has suggested this possibility as far back as 1913 [7]. However, more recent research in the field of epigenetics provides even stronger evidence of transgenerational effects of paternal and maternal exposure to drugs and toxins. Epigenetic changes that occur due to substance use can be explained as changes to DNA that alter gene transcription without changing the underlying code. Given evidence of transgenerational effects of paternal nutritional and toxicological exposure on disease risk and behavior, the epigenetic marks appear heritable [1].

The research linking fathers' preconception substance use to offspring health and behavior is compelling. In humans, studies have found associations between male preconception use of some substances (i.e., cigarettes and alcohol) and outcomes such as greater body mass index, reduced birth weight, hyperactivity, and reduced cognitive performance [8-11]. Laboratory studies on paternal preconception exposure to alcohol in mice have found many effects on offspring, including: reduced litter size; reduced birth weight; developmental retardation; increased mortality; decreased immunity; changes in adult hormone levels; reduced avoidance learning; deficits in spatial ability; and changes in aggressive, risk taking, and anxiety-like behaviour [8,12-19]. Paternal preconception exposure to other drugs (e.g., cocaine, opiates) has been linked with reduced visuospatial attention, spatial working memory, and spontaneous alternation; reduced cerebral volume; and developmental and behavioral impairments in mice [20-22]. These findings suggest that both men and women should consider alcohol abstinence or reduced consumption during the preconception period.

One of the best ways to prevent substance abuse and addiction is to increase the likelihood that one never takes or tries the substance. Research suggests that providing knowledge, education, and brief interventions about drug effects may reduce use or increase the likelihood of abstinence [23]. Given evidence that substance exposure can affect future response to that particular drug and to other drugs, and may sensitize one to addictive effects by inducing genes after initial use [24], it is important that fetal exposure to all non-nutritive substances be minimized or avoided. Furthermore, early education about the possible long-term effects of substance use on future offspring could have many positive effects on the physical, psychological, and neurological health and well-being of both individuals and society.

Raising awareness about potential adverse effects of using drugs and alcohol prior to conceiving one's children may have at least three beneficial effects. First, there is the potential for a direct effect of a reduction in drug effects on offspring and future generations (i.e., FASDs (Fetal Alcohol Spectrum Disorders), fetal alcohol effects, or fetal drug effects) by reducing use during both the preconception and prenatal periods. Second, there could be an indirect effect of reduced use or abstinence in children, teens, and young adults as young people will be better informed about the potential effects of their substance use on their future offspring. For each individual there may be one piece of information that causes a "tipping point" to be reached, whereby they develop a belief or attitude that tips them into a resolution of abstinence. Given that young children often report a desire to have children in the future; the knowledge that substance use during their teens may affect future offspring may increase their likelihood of adopting a resolution of abstinence prior to being confronted with opportunities to try a particular drug. This information could be the difference between use and non-use in some young people. Third, increasing public awareness about the possible effects of preconception substance use could help to ensure that individuals living with FASDs, fetal alcohol effects, fetal drug effects, and preconception substance effects are identified, assessed, and diagnosed. This is important given evidence that early diagnosis of FASDs improves long-term outcome [25].

Educating the public about the importance of "clean living" during the preconception period also has the potential to move towards equalizing the gender imbalance in terms of responsibility for future offspring health. In addition to the above-noted direct effects of reduced paternal perinatal substance use on offspring health, there would be at least three benefits to such a change. First, there would be potential benefits for men's health (risk of injury and future disease) by reducing substance use to levels considered low or moderate [26]. Second, there would be a psychological benefit for women by having

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shared responsibility, as blame (frequently self-blame) is most often currently placed on women when children are not optimally healthy [27]. Third, making both partners responsible for offspring health during the preconception period should increase the likelihood of each individual having success with abstinence or use reduction. This is based on evidence that one's exposure to substance-related cues or triggers (e.g., sight or smell of the substance; substance user friends) [28] and a partner's substance use [29-31] both affect one's likelihood of abstinence or use reduction. Thus, providing the same substance use recommendations to both partners during the preconception period may increase gender equality in responsibility, improve abstinence rates, and reduce teratogenic effects on future offspring.

Most individuals and couples would welcome strong specific recommendations that could maximize the health of any future children and facilitate optimal brain health over the lifespan if implemented. Given the potential harm of preconception substance use, it is shocking that the public is not better informed and one may wonder why this is the case. It may be that there is concern about scaring the public by focusing on data from animal studies (human experimental studies cannot be done for obvious ethical reasons). However, this is not a unique paradigm as many human models of disease are drawn from animal research. Perhaps there is concern about emphasizing findings where the effect sizes are small, or concern about instilling a sense of guilt in the majority of parents and grandparents who have used alcohol or other drugs prior to having children. The transmission of knowledge about preconception risks may also be hindered partly by studies on specific diseases or outcomes that suggest some long-term benefits for consumers of low doses of alcohol [26]. However, it is important to recognize that studies on potential health benefits of low alcohol use do not typically take into account the potential for adverse epigenetic effects of alcohol on future generations. Furthermore, it is possible that the high public awareness of studies on alcohol’s beneficial effects and the lack of specific recommendations about a period of preconception abstinence (i.e., a number of months or years) may be partly related to the fact that we live in a society that accepts, or embraces the normalcy of alcohol use. In keeping with the pace of attitudinal changes in society, public health recommendations seem to take into consideration the perspective of the majority of the persons living within it and the value systems that serve to define it. One could argue that alcohol-related recommendations made to the public are partly based on the alcohol-embracing nature of our current society and the low likelihood of getting most people to engage in alternate ideal healthy behaviours such as daily exercise, stress reduction techniques, and eating healthy foods. However, it is critical for public and individual health that we recognize that alcohol use is not part of an ideal healthy lifestyle. We must also consider whether any real harm would be caused by sharing the findings and possible implications of the preconception substance exposure research if it were to turn out that the effects on future offspring are only of statistical significance and not of any real clinical significance. As detailed above, the positive indirect effects of educating the general public are all compelling reasons to ensure that the public (particularly children and youth) is kept fully informed of all new epigenetic research findings related to the effects of substance use on future offspring.

Guidelines about alcohol use often define “low risk drinking” as 0 to 2 drinks per day for women and 0 to 3 drinks per day for men [32] and no mention is typically made of epigenetic or transgenerational research. While guidelines do typically recommend abstinence “if pregnant or planning to be pregnant”, no mention is made of men during the preconception period, and the wording used to describe the preconception period for women is vague enough to suggest it refers to someone who is attempting to conceive within the next 12 to 24 hours. Thus, it appears that recent research on epigenetics and transgenerational effects of substance use is not being considered in most reports on the overall relative risks and benefits of alcohol use.

Currently, most individuals are not aware of the information necessary to maximize the health and success of their future offspring. Thus, we have four recommendations.

**Recommendations**

1.1. Public education programs should be implemented to focus on ensuring that the general public is fully informed about the potential effects of alcohol and other substance use by both sexes on future children and future generations. Programs should include a school based education preventative component to teach children about the possible long-term effects of their environment (e.g., nutrition, alcohol use, and drug use) during preconception years on future offspring health.

1.2. Recommendations regarding preconception substance use should be provided to men and women who are planning on trying to conceive a baby. At a minimum, it should be strongly recommended that such individuals abstain from substance use and exposure while trying to conceive. Studies have shown that abstaining from alcohol use after pregnancy is confirmed may be too late to prevent adverse effects on the fetus as most major organ systems have started to develop [33]. The recommendation to abstain from substance use starting 1 to 3 months prior to an attempted conception should be provided. This latter time frame is not based on any specific research finding and could be changed if there are any specific relevant data. While it would of course be ideal to recommend a longer “detox” period prior to conception, the above guideline would be a good starting point as no current official recommendations seem to exist to guide couples in their preconception planning. At the risk of being perceived as extreme, the public should also be provided with the recommendation to strongly consider abstaining from, or at least limiting, substance use during the preconception years.

1.3. Funding and research needs to be directed toward further examining the issue of preconception substance use. An emphasis should be placed on funding retrospective or longitudinal studies examining the effects of preconception alcohol use on children, adolescents, and adults.

1.4. Future publication of research findings or guidelines that contain recommendations regarding low risk, safe, or “healthy” drinking levels should, at the very least, mention the body of research suggesting that substance use prior to having children has the potential to affect one’s offspring and future generations. Providing this information in the context of research on the healthy benefits of alcohol use would provide the public with a more balanced view of all of the potential risks and benefits of preconception use.

Educating the public about the potential adverse effects of preconception substance use is more important than: being cautious about the clinical significance of research findings; than protecting the conscience of an alcohol-embracing society from guilt; or than considering whether it is likely that people will succeed in meeting “ideal” recommendations within our alcohol-embracing society. The above recommendations are provided given our position that it is the right of all individuals to be made fully aware of the risks their current or future behaviour may impart to their prospective children. Given
evidence that initial exposure to a substance may affect one's response to it in the future [24], information about preconception substance use needs to be provided early in life, at a time when one still has maximal control over future choices and the health and well-being of future offspring.

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