National Collaborating Centre for Infectious Diseases
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Purple Paper

Volatile Substances Misuse: Epidemiology in North America, and Association with HIV and Other Sexually Transmitted and Bloodborne Infections

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NCCID Comments

Inhalation of widely available volatile substances for their unintended psychoactive effects is gaining prominence and is clearly a concern for public health practitioners and policy makers. But why and how is this issue relevant for the infectious disease/communicable disease community? This 2-part mini-series on solvent use and its association with HIV and other sexually transmitted and bloodborne infections (HIV/STBBIs) aims to shed some light on the topic.

This paper, the first issue of the mini-series, will present some epidemiological data on the prevalence of solvents use in Canada and the US, and evidence of an association between solvent use and HIV/STBBIs. The second paper will explore the biological mechanisms that may be contributing to the observed phenomena of increased susceptibility to and progression of HIV and HCV in solvent users.

Introduction

The inhalation of substances for the purposes of intoxication is a highly complex, and poorly understood phenomenon, despite being one of the oldest and most rudimentary forms of intoxication[1]. More modern forms of substance inhalation gained the Western world's attention in the latter half of the 19th century, with the prominence (both within, and outside of mainstream society) of inhalation of ether, nitrous oxide, petrol and other substances[1,2]. More recently, the term "glue-sniffing" became part of the common vernacular in North America with a newspaper account in 1959[2]. Despite this long history, only relatively recently has scientific attention been paid to this phenomenon[3-5].

Partially explaining this "hidden epidemic" is the literally hundreds of mostly unregulated and inexpensive substances which can be inhaled for their intoxicating effects[1,4]. Given this multitude and diversity, many different terms have been used, including: solvent/inhalant use, huffing, sniffing and volatile solvent use[4]. Adopting recent convention, the term "volatile substance misuse (VSM)" will be applied throughout this essay[4]. In 2005 an *ad hoc* international committee of experts offered this definition of volatile substances: "*… (they) contain volatile substances that are self-administered as gases or vapours to induce a psychoactive or mind-altering effect. These volatile substances are available in legal, relatively inexpensive and common household products, which can be gases, liquids, aerosols or, in some cases, solids*."[3, p. 879] Broadly speaking, volatile substances can be grouped into four classes: solvents (e.g. toluene, glues, gasoline), aerosols (e.g. hair/deodorant spray), gases (e.g. butane/propane fuels) and nitrites (e.g. "poppers", video head cleaner, room deodorizers)[4,6]. Although the above classification can be useful in many applications, it should be noted that due to the myriad substances available, any classification of substances is likely to be incomplete[3]. Additionally, there is not yet consensus on either the term VSM, or the inclusion/exclusion of specific substances.

Epidemiology of VSM in North America

Because a full review of the epidemiology of VSM is beyond the scope of this essay, the next section will focus only on the epidemiology of VSM in North America. The discussion will then move towards existing evidence surrounding the association between VSM and HIV/STBBIs. In order to understand the connection between VSM and HIV/STBBIs, this section will conclude with a discussion on the association between VSM and opiates and injection drug use.

Nationally-representative data on VSM in Canada are extremely sparse, with the most recent national-level data, the 2004 Canadian Addictions Survey (CAS), almost a decade old as of this writing[7]. This multi-stage randomized survey, administered to

13,909 individuals 15 years and over, found overall lifetime prevalence of VSM was 1%, with prevalence of 2% among males and 1% among females. Prevalence varied slightly across the provinces, with a low of 1% in Newfoundland and Labrador, to a high of 2% in Quebec. At 1.6%, prevalence was similar across Alberta, Saskatchewan and Manitoba. When examined by age group, prevalence was highest among 20-24 year olds and 25-34 year olds (2%). The lifetime prevalence of those aged 15-19 was 1%. Notably, the CAS found that two-thirds of individuals who used volatile substances first did so between the ages of 12 and 16, with 13% using before the age of 12[8].

Age of initiation has important implications on the type of volatile substances used, with older VSM initiates more likely to report using nitrites or nitrous oxide.

Several Canadian provinces have administered school-based surveys to assess the prevalence of substance use among school-aged adolescents. Although methodological differences limit direct comparisons, these surveys typically report higher rates of VSM, both in terms of lifetime and past year use. For example, results from the long-standing Ontario Student Drug Use and Health Survey found the past year prevalence of VSM among Ontario students was 5%, with the highest prevalence reported by those in grade 9 (9%)[9]. The reported 2007 prevalence of past year VSM was 4% in the Atlantic provinces, with prevalence varying by province, from a low of 3% in New Brunswick, to a high of 4% in Nova Scotia and Newfoundland/Labrador[10]. A 2007 survey of Manitoba found a past year prevalence of 2% in males and females, with the highest prevalence reported in Senior 3 (grade 11, 5%) for males and Senior 2 (grade 10, 3%) for females[11].

In comparison, probably the best information on VSM in the world is from the US, where three major nationally-representative surveys, the National Survey on Drug Use and Health (NSDUH), Youth Risk Behavior Survey (YRBS), and Monitoring the Future (MTF) have tracked trends in VSM for several years. Although differing in methodology and target populations, a consistently higher prevalence of VSM has been found among the US population, compared to Canadian results[2,12]. Among youth (those aged 12-17 years), the 2009 NSDUH and MTF estimated lifetime prevalence of VSM at 9%-14%, past year use at 4%-7% and past month use at 1%-3%, with MTF consistently reporting higher prevalence[13]. Among young adults (those aged 18-25 years) the lifetime prevalence of VSM was estimated at 8%-11%, past year use at 1%-2% and past month use at 0.2%-0.4%, with the NSDUH consistently reporting higher prevalence[13]. Of the approximately 3 million persons aged 12 years or over who initiated any illicit substance use in 2009, about 10% listed volatile substances as their first substance, ranking only behind marijuana (59%) and pain relievers (17%)[13]. Notably, initiates of VSM tended to be the youngest, at an average age of 16.9 years, compared to other substances such as marijuana. Estimates derived from the NSDUH suggest that more than half a million (593,000) adolescents between the age of 12 and 17 initiated VSM in the year prior to being surveyed[14]. These figures have remained fairly consistent over time[2]. Finally, it should be noted that in 2007, the YRBS estimated lifetime VSM among youth at 13%, trailing only lifetime (38%) and current (20%) marijuana use, and ahead of lifetime use of cocaine (7%), crystal methamphetamine (4%) and illegal steroid (4%)[2].

A unique feature of VSM is its association with late childhood or early adolescence[2,4,12,15]. VSM is unique because its prevalence appears to decrease with age[2,12]. For example, 2009 MTF results revealed that previous years' prevalence of volatile substance use was 8%, 6% and 3% among 8th, 10th and 12th graders, respectively[16]. Data from school-based surveys on this phenomenon should be interpreted with caution however, as those who continue to use volatile substances may be more likely to drop out of school. Other alternate explanations of the decline in use of volatile substances as youth age include the replacement of volatile substances by the other illicit and licit substances, the ability of the user to afford other substances, and increasing social biases against the use of a fairly unsophisticated substance[16,17].

Nevertheless, this pattern of usage suggests that there is heterogeneity in users of VSM, where broadly speaking, there may exist early experimenters, those that partake occasionally, and habitual users[8,12]. Age of initiation is of some interest, as some serious negative outcomes, such as continued use or high dependence has been associated with younger age of onset[18,19]. As will be discussed in more depth, relationships between early-onset VSM and subsequent heroin and injection drug use, antisocial behaviour, and other psychoactive drug use have also been established [13,20-22].

Compared to respondents [of the National Survey on Drug Use and Health] who did not report VSM, where HIV prevalence was 0.2%, HIV prevalence was 0.5%, 1.0% and 8% among those reporting VSM for ≤1year, 2-10 years, and ≥11 years, respectively.

On the issue of heterogeneity, there is a lack of data regarding types of substance used, with most information derived from the US. One US-based study of incarcerated youth found that gasoline (60%), permanent markers (40%) and computer duster sprayer (40%) were the most commonly inhaled substances; however, the types of substances inhaled differed by frequency of use[23]. According to the 2009 NSDUH, and among youth aged 12-15 years who initiated VSM in 2009, the three most common volatile substances inhaled were: glue, shoe polish, or toluene; spray paints; and gasoline or lighter fluid[14]. Age of initiation also has important implications on the type of volatile substances used, with older VSM initiates more likely to report using nitrites or nitrous oxide[14]. In fact, many researchers believe that the different demographic (e.g. older age) and reasons for use (e.g. sexual enhancement) may differentiate those whose preferences lean towards nitrites from those who prefer solvents or gases[16].

Association with HIV/STBBI Risk

A 2010 study using data from the NSDUH found an association between VSM and HIV/STBBIs among those aged 35-49 years[24]. In addition to linking VSM and HIV/STBBIs, duration of use strongly determined the strength of the association. For example, compared to respondents who did not report VSM, where HIV prevalence was 0.2%, HIV prevalence was 0.5%, 1.0% and 8% among those reporting VSM for ≤1year, 2-10 years, and ≥11 years, respectively.

A 2002 study conducted among street-involved individuals in Winnipeg, Canada suggested associations between lifetime VSM and viral hepatitis, but these associations were not statistically significant when other factors, such as age and injection drug use were accounted for[25]. However, the authors did not explicitly investigate the association between viral hepatitis and VSM *within* injection drug users. In a more recent study of Aboriginal IDU in Winnipeg, an increased risk for the hepatitis C virus (HCV) among IDU who used volatile substances was detected. In this cross-sectional study, prevalence of HCV was 81% among IDU who reported lifetime VSM, compared to a prevalence of 55% among those who did not[26]. Once adjusted for other factors, this translated to an over three-fold risk of HCV among IDU reporting lifetime VSM. In this same sample, HIV prevalence was 18% among IDU reporting VSM, compared to 8% among those that did not report VSM.

Although high frequency users of volatile substances have been linked to risky behaviours such as unprotected sex[2], and notwithstanding the use of nitrites as sexual enhancements[27], the as-yet unproven link between HCV and sexual transmission suggests other transmission routes[28,29], such as injection drug use. That VSM is associated with serious negative outcomes such as HIV/HCV infection, and the behaviours that lead to their acquisition and transmission has a long history. As far back as the late 1960s[30], studies have demonstrated an association between early VSM initiation and the progression to use of opiates through injection drug use (IDU)[20,21,30-35]. An early study found that over a quarter of heroin users in a treatment sample started their drug use with the inhalation of glue[35]; a subsequent longitudinal study found adolescents with a history of VSM prior to the

age of 16 were nine times more likely to progress to using heroin by the age of 32[33]. Finally, a 2005 study found that youth who started VSM before the age of 14 were over twice as likely to have initiated the use of opiates in young adulthood, compared to youth who never used volatile substances[20].

More recent evidence suggests that the *combination* of VSM and polydrug use (misuse of more than one substance) is likely a more robust predictor than a history of VSM alone. A 1994 study utilizing the NHSDA found that VSM was associated with an 11-fold increase in likelihood of injection drug use, when compared to those with no history of VSM[30]. When the sample was further stratified, researchers found those with a history of both marijuana use and VSM were over 80 times more likely to have reported the use of injection drugs. A 2007 study confirmed the greater likelihood of IDU in polydrug users: in a sample of over 8,000 youth, those that reported both VSM and marijuana use were almost three times more likely to have reported using injection drugs, compared to youth reporting only marijuana use[21].

Thus, VSM may lead to increased acquisition of HIV/STBBIs through its association with high risk behaviours. Absent biological reasons (explored further later), and because of the specific trajectory towards injection drug use those IDU reporting VSM have taken, this particular group may also be more vulnerable to HIV/STBBIs through especially high risk sexual and/or injection practices. Alternatively, VSM may stand as an index for unique social/sexual networks where pathogen prevalence tends to be higher, thus increasing the risk of acquisition[30]. Others have suggested that VSM itself might be better conceptualized as a proxy for some "susceptibility trait", which may explain both the young age of initiation and opiate use[20,21,36]. Research suggests that early VSM initiators, those who are polydrug users, and those who continue on towards chronic and frequent use of volatile substances are at the highest risk of HIV/STBBI acquisition.

Nonetheless, whether the association between VSM and HIV/STBBIs is due to factors that are biological, behavioural, or socio-cultural in nature, or some combination of the above, it is clear that VSM can be an important indicator of future negative outcomes, and thus has public health relevance. It should come as no surprise that with their relative affordability and ubiquity, VSM is associated with the most socio-economically disadvantaged[18,34,37-41]. Moreover, understanding why some individuals continue VSM, despite overwhelming social stigma against their use, may reveal important processes that govern the misuse of substances more broadly. It stands to reason then that VSM research itself is a means towards understanding those who are most marginalized, and who remain so, despite much public health intervention. Filling in some of the knowledge gaps, such as characterizing social and sexual networks, exploring the specific effects of individual substances, and validating biological pathways leading to increased pathogen risk may delineate the specific causal roles volatile substances may have in heightening HIV/STBBI risk, and the underlying vulnerabilities that predispose one to prolonged and continued use of volatile substances.

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Production of this document has been made possible through a financial contribution from the Public Health Agency of Canada. The views expressed herein do not necessarily represent the views of the Public Health Agency of Canada.