

Amyl Nitrites: A Review of History, Epidemiology, and Behavioral Usage

David Cheng

This paper looked into the abuse of inhalable nitrites, mainly amyl nitrites, commonly known by the street name of poppers. This paper compiled several studies of nitrite inhalant abuse and the risk associated with the sexual practices that may concur. The paper explores first, the history and true intentions of nitrite inhalants, then the increasing abuse mainly within the homosexual community, and the legitimacy of the link of nitrites and the HIV/AIDS epidemic. Various studies discussed in the paper will show that there is no legitimate link between poppers increasing the chance of HIV/AIDS but it is the unsafe sexual practices that occur with poppers that lead to various sexually transmitted diseases. The dangers of inhalable nitrites come from legal loopholes, use with other drugs such as Viagra, and the nature of unsafe sexual practices mostly within the homosexual community.

Keywords: Drugs; Inhalants; Sex; Homosexual

BASIC FACTS OF AMYL NITRITES

$C_5H_{11}ONO$ is the chemical formula of amyl nitrite; there are several isomers but they all feature amyl groups with a nitrite group attached. Amyl nitrites falls into a group of drugs which is more commonly known by the street name 'poppers'. Popper is a slang term to describe the various alkyl nitrites such as isopropyl nitrite, isobutyl nitrite, butyl and amyl nitrites inhaled for recreational purposes. Unlike most other inhalants the effects of poppers don't last very long and don't create the same 'high' as other inhalants (Meyer, 2005). The name popper comes from the sound of the small glass ampoules that were crushed to release the inhalants. The substance itself is a clear, yellowish liquid that has a peculiar ethereal, fruity odor and is highly volatile ("Data sheet: Amyl nitrite," 2000). All of these compounds are based upon the chemical structure R-ONO. The most commonly used products for abuse are air freshener, video head cleaner, and finger nail polish remover. Nitrites relax smooth muscle tissue such as the anus, iris and dilate blood vessels which cause a drop in blood pressure (Cohen, 1979). Poppers are almost always inhaled for recreational use producing a sense of warmth, mild euphoria, and sometimes visual distortions (Kuhn, 2003). Often the intention of popper users is to increase sexual pleasure often among the homosexual population due to the smooth muscle relaxation effects of the drug. As will be seen, poppers have been the subject of several studies attempting to link nitrite abuse with sexual behavior (Colfax, 2001; Haverkos, 1988; Kennedy, 1988). The medically intended uses of nitrites was to relieve heart pain by dilating arteries allowing more blood flow to the heart and as an antidote to cyanide poisoning by producing methemoglobin in the blood stream which binds to and neutralizes the cyanide.

HISTORY

The drug is popular among the club and rave scene and nitrites as a chemical compound has been around since

the 1850s. Amyl nitrite was originally created by Antoine Jerome Balard, a French chemist known for the discovery of bromine. However it was not until the late 1850s that Sir Thomas Lauder Brunton used amyl nitrite as a treatment for angina pectoris (chest pain). Doctors discovered that amyl nitrites helped to relax smooth muscle allowing increased blood flow to reach the chest. It was particularly effective in the treatment of heart and chest pain. However, doctors noticed that the drug was unreliable at times with the effects disappearing too rapidly to have any long term health benefits. Amyl nitrite is still inhaled however when rapid absorption is required for some heart problems. It was also found that amyl nitrites was an effective cyanide poisoning antidote and EMTs today still carry amyl nitrite antidote kits. In 1960, the FDA approved nitrites as an over the counter drug without the need for a prescription. One short year later, the FDA instated a prescription requirement and only amyl nitrites were approved for use in humans. The popper craze began in the 1970s and by 1979; over 5 million people in the United States used poppers more than once a week (Haverkos, 1988). Academic research into nitrites began in the 1970s with mixed conclusions over the correlation of AIDs, HIV, and Kaposi's sarcoma and abuse of inhaled nitrites. Politically in the United States, politicians in Washington were advised over the years that nitrite inhalation posed no significant risk and that no further federal action was needed (Kennedy, 1987). Despite this, lawmakers banned the sale of nitrites for human consumption. Illicit use began with adolescents in 1960 that purchased nitrites as recreational inhalants. Popper abuse really began to take off in the 1970s as the disco club scene began to take over. TIME magazine reported that popper abuse (legal at the time) was a fabrication of the homosexual population as a way to enhance sex (Nation: Rushing to a New High, 1978). Poppers quickly spread to heterosexual couples and continued into the rave and club scenes of the future. Poppers contain nitrites that are synthesized from alcohols and sodium nitrite in a solution of sulfuric acid. The solution is mixed and decomposes slowly at room temperature and is bottled into small ampoules for use.

EPIDEMIOLOGY

The Monitoring the Future Survey found that through 2007 to 2010 among 8th, 10th, and 12th graders, lifetime use of inhalants is on the decline. However, short term month to month use appears to be on the rise; from 2007 to 2008 use rose from 2.1 percent to 2.2 percent among 10th graders. Also past year use appears to be increasing among all three grade levels (Monitoring the Future, 2010). The National Survey on Drug Abuse and Health also shows that the majority of users are adolescents between the ages of 12 – 17 and about 67 percent of users were less than 18 when they first used inhalants. (Substance Abuse & Mental Health Services Administration, 2011). Below is a chart from the National Survey of Drugs and Health showing specific types of inhalants abused by users aged 12 to 17 from 2002 to 2007. A 1988 study found that 69% of men who had sex with other men in the Baltimore/DC area used poppers (Lange, 1988). When compared to other abused drugs, a more recent report of 736 homosexual men in San Francisco, found poppers to be the most widely abused substance when compared to cocaine and methamphetamines (Colfax, 2005). Although dated, it is positive to see a 1987 survey commissioned by the US Senate that found only 3% of Americans had even used poppers (Kennedy, 1987). Also interesting, about 20% of the teenage population in the United Kingdom (UK) abuses nitrites due to it being legal in the UK. Nitrite abuse among users was more frequently reported among the white population relative to blacks or Hispanics and more often abused by men than women (Haverkos, 1988). Although amyl nitrite abuse isn't as high as other inhalants it still poses an inherent risk to abusers and data indicates that nitrite abuse is on the rise. This may be caused by a perception that inhalants aren't as dangerous as other types of drugs such as cocaine or heroin.

PHYSIOLOGICAL IMPACT

Like many inhalants, the route of administration is nasal. The inhaled nitrites quickly reach the lungs and diffuse through the pulmonary alveoli and into the capillaries full of oxygen rich blood on its way to the heart. The heart then quickly distributes the nitrites to tissues in the body allowing an effect to be felt quickly. Average times for the onset of effects are about thirty seconds and the effects last anywhere from three to five minutes (Wolters Kluwers Health, 2009). Not enough research has been done to confirm the metabolism but it is believed that nitrites are metabolized by hydrolytic denitration and about a third of the drug is excreted through urine (Baxter Healthcare, 2000). The pharmacodynamics are not known for sure but the acute effects of volatile inhalants like nitrites often produce effects similar to alcohol intoxication (Meyer & Quenzner, 2005). The effects are very consistent and users can expect headaches, flushing of the skin, dizziness, weakness, and in very high doses can cause anesthesia, loss of consciousness and even comas (Kuhn, 2003). Users report that they get a feeling of warmth, pounding hearts, and a loss of inhibitions. The ocular organs also have increased intraocular pressure and supraorbital pain. Inhaled nitrites also appear to be able to interact with endogenous trivalent nitrogen compounds that

produce nitrosamines that are known to be carcinogens (Haverkos, 1988).

It is widely believed that there is a correlation between nitrite abuse and AIDS/HIV however there are multiple studies that suggested there is no correlation between the two (Kennedy, 1988). Amyl nitrites are abused mainly for their muscle relaxing effects for easier anal and vaginal sex. Users claim that poppers help prolong erections and increase libido. The real value is the effect of the "relaxation of rectal smooth muscle and anal sphincter tone, thus facilitating intromission" (Haverkos, 1988). In other words the relaxation of the anus helps reduce the pain and increase the ease of penetration. Haverkos (1988) also states that the illicit usefulness of amyl nitrites has allowed it to pass into every corner of gay life. The issues of poppers are that when they are abused for sex, questionable and unsafe sexual behavior can occur and many believe poppers are a contributing factor towards the Acquired Immunodeficiency Syndrome (AIDS) and Human Immunodeficiency Virus (HIV) epidemic. According to Colfax (2001), amyl nitrite abuse is the third highest risk indicator of having unprotected anal sex behind Viagra and crystal meth. This is significant considering the ease of availability of poppers that can be purchased online with just a credit card. According to Schwarcz (2007), a study conducted on homosexual and bisexual men in San Francisco found that 29.1 percent of HIV positive men used amyl nitrites. It is interesting to note that the same study showed that 87.2 percent of HIV positive and 78.9 percent of HIV negative men had intercourse with a male compared to only 2.3 and 9.6 percent of the HIV positive and negative groups saying they had intercourse with a female. Based off of this data, it could be concluded that amyl nitrite abuse is most common among the homo and bisexual male population. The only drug that was used more than amyl nitrites in the Schwarcz (2007) study was Viagra and that remained constant in both the HIV positive and negative community. The Schwarcz (2007) study found that 44.2 and 22.4 percent of the HIV positive and negative groups used Viagra and because amyl nitrites are the most used drug after Viagra, this can be alarming. Amyl nitrites are contraindicative with other vasodilators like Viagra and, when used in combination, can cause a serious decrease in blood pressure that can lead to fainting, strokes, and heart attacks. The link between Viagra use and popper use could be because the side effects of amyl nitrites can cause erectile problems prompting the use of Viagra. Haverkos (1998) also found that individuals that used poppers frequently had almost two times more partners a week than those who never used nitrites. Occasional users had about one and a half times more partners than those who never used.

Nutt (2007) suggests that nitrites as a group have the second least addictive potential and is the third least harmful among the twenty most commonly abused drugs. Despite this, there are still a variety of other health problems associated with nitrites that are particularly dangerous. Only amyl nitrite is produced for legitimate medical use in humans and is approved by the FDA. This means other nitrites commonly found in poppers such as butyl nitrite and alkyl nitrites are industrial chemicals and could be harmful. The major problem is when nitrites are swallowed instead of inhaled. By ingesting nitrites, a person runs the risk of methemoglobinemia, a condition in which the nitrites

interfere with the way oxygen bonds with hemoglobin in the blood. Ingesting nitrites has the similar effects of cyanide poisoning but to a slower degree. Awareness of the negative effects of nitrite abuse was being raised in the early 1970s because of the growing concern over AIDs. The belief that nitrite inhalation was a factor in AIDs was well warranted as the first five homosexual men with AIDs that were reported to the Centers for Disease and Control (CDC) all abused nitrite inhalants (Centers for Disease and Control, 1981).

Another risk that was believed was an effect of poppers early in the AIDS epidemic was the development of Kaposi's sarcoma. Kaposi's sarcoma is a kind of skin cancer that is one of the most common symptoms of AIDs. It was also another public perception that poppers were the cause of Kaposi's sarcoma however several subsequent research into the matter showed that it was the sexual "actions" that were responsible for obtaining the AIDs related skin cancer (Beral, 1992). Actions such as fisting and rimming are thought to be the main causes and that the faecal-oral contact are the main routes of transmission of Kaposi's sarcoma in homosexual and bisexual men with AIDs. It could be said that the poppers ability to relax the anus can be blamed for some of the actions that could be associated with Kaposi's sarcoma and the sexual behavior associated with Kaposi's sarcoma but Beral (1992) claims the cases of Kaposi's sarcoma was somewhat rare prior to the outbreak of AIDs, suggesting that AIDs is the main factor. Another study also theorized that a history of Syphilis, not the use of poppers, was the underlying cause for Kaposi's sarcoma. Haverkos (1988) compiled data showing that patients with a history of Syphilis are two times more likely to contract Kaposi's sarcoma.

An idea that has been presented about the association between HIV/AIDS and nitrite usage is that nitrites suppress the immune system. A study done on eighteen male volunteers found that nitrite inhalation did indeed suppress the immune system. The number of T - lymphocytes, the site of attack of HIV and AIDs, temporarily decreased (but not to a dangerous degree) during inhalation and returned to normal levels after about a week (Dax, 1991). Nitrite inhalation causes a little more vulnerability to HIV and AIDs as suggested by the investigation but there is not a significant long term risk unless the drug is heavily abused. It is conceivable that popper users could use them several times over the course of a day or weekend which makes it a very interesting suggestion of how HIV and AIDs could spread. However, this is really only limited to the sexually active population with access to the drug which is mainly in industrialized Western countries.

There has also been concern over possible eye damage in habitual popper users. In a report of six patients who abused poppers, doctors noted that all patients experienced progressive bilateral vision loss (Audo, 2011). Doctors believed that the repeated use of poppers causes vision loss due to disruption of the foveal cone but also suggested that the damage may heal itself if popper use is stopped. Some other side effects include burns if the nitrites are spilled on skin and can cause lipoid pneumonia if accidentally swallowed into the lungs. Lipoid pneumonia is when oils enters into, and inflames, the lungs.

Users can develop a tolerance to the drug and there are symptoms from withdrawal. The most common problems with withdrawal are cardiac and circulatory problems and

patients are usually prescribed nitroglycerin patches (Kuhn, 2003). The issue is the tolerance that has been built up by use of poppers that reduce the effectiveness of nitroglycerin patches and the cardiac problems that accompany with this.

Another health issue is a possibility of cancer. Inhaling nitrites interact with endogenous trivalent nitrogen compounds to produce nitrosamines. Nitrosamines are well established carcinogens in animal studies with increased nitrites in diets leading to liver cancer (Newell, 1985). Although no direct studies on humans have been conducted, it is thought that nitrosamines can cause gastric cancer (Hill, 1973). Although there may be evidence linking nitrite inhalants and cancer, one would probably have to be a habitual user of nitrite inhalants to significantly increase the chance of cancer.

LEGALITY

It is important to discuss the legal aspects of poppers because of the unique situation of being a medically approved product but also an industrial chemical agent. Amyl nitrite requires a prescription after wide spread abuse in the 1960s. Other nitrites such as alkyl nitrites were banned by the United States in the Anti - Drug Abuse Act of 1988. Interestingly, the law was only for human consumption and granted an exception for products with commercial purpose. Basically, this means that as long as a manufacturer claims the product is not intended for human consumption, it is legal. This allows poppers to be legally sold, usually in sex shops, as video head cleaner, polish remover, and room air refreshers as industrial products intended for uses other than human consumption. It is easy to see however that these products are truly intended for human consumption and what is more ironic is that they are not regulated by the FDA because, technically, this is an industrial product. This legal loophole, although beneficial to manufactures, can be harmful to the consumer because of unregulated production practices. By claiming nitrite poppers are deodorizers and video head cleaners, this completely bypasses the safety tests that each drug must go through in order to be sold to the population. It is also incredibly ironic that labels warning against the dangers of inhalation are on the ampules of poppers such as Rush, however the intention is for the nitrite to be inhaled. In the early 1990s, most Western nations outlawed the sale and importation of alkyl nitrites for inhalant uses. Poppers however remain legal in many countries like the United Kingdom and China and are easily purchased by adolescents.

CONCLUSION

In conclusion, nitrite poppers are most often used in the homosexual male population for sexual pleasure. However, there should be done more to control the use and sale of poppers. It can be argued that nitrites should be banned due to its role in the AIDs and HIV epidemic. But this is only because of the unsafe sex practiced under the influence of poppers. Studies such as Kennedy (1988) have found no link between HIV/AIDS and popper use. However, it is uncertain if there is correlation or causal relation between popper use and HIV/AIDS due to numerous underlying factors and the difficulty of conducting a true experiment. No studies also have been conducted on the long term health effects of

repeated popper abuse either. Also, nitrite inhalants do not significantly decrease immune function enough to contract HIV/AIDS commonly (Dax, 1991). The immune systems studied also returned to normal health fairly quickly so there isn't a long term immune function decrease. The effect of poppers on sexual behavior is very large especially in the homosexual community. The health risks associated with poppers cannot be denied as diseases such as Kaposi's sarcoma and AIDS are much more common among homosexual populations and unsafe sex practices are to blame. Poppers do not necessarily lead to sexually transmitted disease but it is the unsafe sex practices stemming from popper use. More sex education should be provided to the population detailing the dangers of poppers and ways to safely use them. Further the legal loophole that allows for inhalable nitrites to exist without medical prescription needs to be closed. If the loophole is not addressed then nitrite inhalants should be classified as a drug and undergo the safety testing that they currently avoid by being labeled as deodorizers. Amyl nitrites should only be used for its medically intended functions, not for its purposes in the homosexual universe.

ACKNOWLEDGEMENTS

The author wishes to express sincere appreciation to Willamette University, the psychology department for their support, and especially to Professor Brian J. Piper for his patience and knowledge. An earlier version of this review was completed as part of a course, Neuropharmacology and Behavior, by Brian J. Piper, PhD.

References

- Audo, I., El, S. M., Morin, A., Sahel, J.-A., Paques, M., Vignal-Clermont, C., Gocho-Nakashima, K., ... Goureau, O. (2011). Foveal damage in habitual poppers users. *Archives of Ophthalmology*, 129, 6, 703-708.
- Baxter Healthcare Ltd., New Zealand Medicine and Medical Devices Safety Authority. (2000). *Data sheet: amyl nitrite*. Retrieved from Baxter Healthcare Ltd. website: http://www.medsafe.govt.nz/profs/datasheet/a/Amyl_nitrateinh.pdf
- Beral, V., Bull, D., Darby, S., Weller, I., Carne, C., Beecham, M., & Jaffe, H. (1992). Risk of Kaposi's sarcoma and sexual practices associated with faecal contact in homosexual or bisexual men with AIDS. *Lancet*, 339, 8794, 632-5.
- Cohen, S. (January 01, 1979). The volatile nitrites. *Jama : the Journal of the American Medical Association*, 241, 19, 2077-8.
- Colfax, G., Coates, T., Husnik, M., Huang, Y., Buchbinder, S., Koblin, B., Chesney, M., & Vittinghoff, E. (2005). *Longitudinal patterns of methamphetamine, popper (amyl nitrite), and cocaine use and high-risk sexual behavior among a cohort of San Francisco men who have sex with men*. Manuscript submitted for publication, Oxford University Press, Oxford University, New York, NY.
- Colfax, G., Mansergh, G., Guzman, R., Vittinghoff, E., Marks, G., Rader, M., & Buchbinder, S. (2001). Drug use and sexual risk behavior among gay and bisexual men who attend circuit parties: A venue-based comparison. *Journal of Acquired Immune Deficiency Syndromes*, 28, 373-379.
- Dax, E. M., Adler, W. H., Nagel, J. E., Lange, W. R., & Jaffe, J. H. (1991). Amyl nitrite alters human in vitro immune function. *Immunopharmacology & Immunotoxicology*, 13, 4, 577-87.
- Department of Health, Centers for Disease and Control. (1981). *Pneumocystis pneumonia --- Los Angeles*. Retrieved from CDC website: http://www.cdc.gov/mmwr/preview/mmwrhtml/june_5.htm
- DrugScope. (2012). *Nitrites*. Retrieved from <http://www.drugscope.org.uk/resources/drugsearch/drugsearchpages/nitrites>
- Haverkos, H. W., Dougherty, J. A., & National Institute on Drug Abuse. (1988). *Health hazards of nitrite inhalants*. Rockville, MD: U.S. Dept. of Health and Human Services, Public Health Service, Alcohol, Drug Abuse, and Mental Health Administration, National Institute on Drug Abuse ; Washington, DC : For sale by the Supt. of Docs., U.S. G.P.O.
- Hill, M. J., Hawksworth, G., & Tattersall, G. (January 01, 1973). Bacteria, nitrosamines and cancer of the stomach. *British Journal of Cancer*, 28, 6, 562-7.
- Inhalants*. Bethesda, MD: National Institute on Drug Abuse. DOI: www.drugabuse.gov/drugs-abuse/inhalants
- Kennedy, Edward, U.S. Senate, Chair Committee on Labor and Human Resources. "REPORT of the Committee on Labor and Human Resources." Comprehensive Alcohol Abuse, Drug Abuse, and Mental Health Amendments of 1988. Section 4015. 1988.
- Kuhn, C., Swartzwelder, S., & Wilson, W. (2003). Buzzed: The straight facts about the most used and abused drugs from alcohol to ecstasy. New York: W.W. Norton.
- Lange, W. R., Haertzen, C. A., Hickey, J. E., Snyder, F. R., Dax, E. M., & Jaffe, J. H. (1988). Nitrite inhalants: patterns of abuse in Baltimore and Washington, D.C. *The American Journal of Drug and Alcohol Abuse*, 14, 1, 29-39.
- Meyer, J. S., & Quenzer, L. F. (2005). *Psychopharmacology: Drugs, the brain, and behavior*. Sunderland, Mass: Sinauer Associates, Publishers.
- National Survey on Drug Use and Health, Substance Abuse & Mental Health Services Administration. (2009). *Trends in adolescent inhalant use: 2002 to 2007*. Retrieved from website: http://www.samhsa.gov/data/NSDUH/2k10MH_Finding/2k10MHRResults.htm
- Nation: Rushing to a new high. (1978, July 17). Retrieved from <http://www.time.com/time/magazine/article/0,9171,916269,00.html>
- Newell, G. R., Mansell, P. W., Spitz, M. R., Reuben, J. M., & Hersh, E. M. (1985). Volatile nitrites. Use and adverse effects related to the current epidemic of the

- acquired immune deficiency syndrome. *The American Journal of Medicine*, 78, 5, 811-6.
- Nutt, D., King, L. A., Saulsbury, W., & Blakemore, C. (2007). Development of a rational scale to assess the harm of drugs of potential misuse. *The Lancet*, 369, 9566, 1047-1053.
- O'Connor, P. (2008, July). *Volatile nitrites*. Retrieved from http://www.merckmanuals.com/professional/special_subjects/drug_use_and_dependence/volatile_nitrites.html?qt=&sc=&alt=
- Schwarcz, S., Scheer, S., McFarland, W., Katz, M., Valleroy, L., Chen, S., & Catania, J. (2007). Prevalence of HIV infection and predictors of high-transmission sexual risk behaviors among men who have sex with men. *American Journal of Public Health*, 97, 6, 1067-75.
- Substance Abuse and Mental Health Services Administration, *Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings*, NSDUH Series H-41, HHS Publication No. (SMA) 11-4658. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2011.
- University of Michigan, National Institute on Drug Abuse. (2010). *Monitoring the future study: Trends in prevalence of various drugs*. Retrieved from website: <http://www.drugabuse.gov/related-topics/trends-statistics/monitoring-future/trends-in-prevalence-various-drugs>
- Wolters Kluwers Health. (2009). *Amyl nitrite*. Retrieved from <http://www.drugs.com/ppa/amyl-nitrite.html>