

POPPERS

This *Making it Count* briefing sheet provides an overview on the recreational drug poppers for sexual health promoters working with gay men, bisexual men and other men that have sex with men (MSM). Poppers (nitrite inhalants) are substances with a long and contested history of links with HIV infection, immune suppression and AIDS. This briefing presents an overview of the evidence for links between HIV transmission and the use of poppers.

WHAT ARE POPPERS?

Poppers is the name for a range of chemical compounds belonging to the alkyl nitrite family. Available as a clear or yellow liquid in small bottles, poppers are usually inhaled through the nose. They have a sickly sweet odour and are flammable. Poppers are sometimes known as 'aromas' or 'liquid incense' and are sold under a variety of sexualised brand names (Rush, Locker Room, Bolt, Ram, Liquid Gold etc.).

A number of different chemicals have been sold as poppers at various times: amyl nitrite, butyl nitrite, isobutyl nitrite and isopropyl nitrite.

The use of amyl nitrite to relieve symptoms of angina pectoris was described in *The Lancet* in 1867. The drug came in glass ampoules wrapped in gauze mesh which made a popping sound when crushed between the fingers prior to use, hence the name 'poppers'.

When amyl nitrite became a prescription-only medicine, poppers manufacturers replaced amyl nitrite with other formulations. Until recently, most contained butyl nitrite or isobutyl nitrite. European law on the sale of these compounds was tightened in 2007, and manufacturers have now switched to isopropyl nitrite.

The chemicals in poppers are sometimes incorrectly referred to as 'nitrates' whereas the correct term is nitrite. *Nitrates* are a related compound used in prescription medicines (usually in tablet form) to treat heart conditions.

WHAT DO POPPERS DO?

Poppers act as a vasodilator – they open (dilate) blood vessels, increasing blood flow. They do this by relaxing the smooth muscle that the walls of blood vessels are made of. Smooth muscle is also found in other parts of the body that need to have an elastic quality, such as the bladder, digestive tract, vagina and anal sphincter.

As poppers cause blood vessels to relax and expand, this creates an inflow of extra blood, blood pressure drops and the heart must beat faster to maintain circulation. Because of the drop in blood pressure some men find poppers interfere with erections.

Short-term side effects of this drop in blood pressure last a few minutes and include:

- increased heartbeat,
- flushing of the face and chest,
- very occasionally, dizziness or fainting,
- sense of (sexual) excitement,
- detachment and disinhibition,
- headache sometime after use.

A degree of tolerance builds to the drug but sensitivity returns after a few days of not using them. Poppers have no effect on pain receptors, but because of the drug's effect on relaxing the anal sphincter, are used to ease discomfort during penetration, in particular anal intercourse and fisting.

WHO USES POPPERS?

Widespread use of poppers as a recreational drug dates back to the 1970s. They are usually used as either as an adjunct to sex or on the dance floor to boost the effects of music, lights or other recreational drugs.

The *Gay Men's Sex Survey* has shown around half of MSM in the UK use poppers at least once a year, making it the most widely used drug after alcohol and on a par with tobacco. Use is common across all demographic and behavioural groups, but especially in men with diagnosed HIV, men with more sexual partners, men with a higher annual income, men of white ethnicity and men in their thirties and forties. The majority of men who had used poppers in the last year, had done so during sex.

Moreover, it is thought that the specific act of an HIV-negative man using poppers during receptive unprotected anal intercourse increases his risk of acquiring

HIV if his partner has HIV (see *Poppers and HIV infection*, below). In GMSS 2008, just under one third of untested or HIV-negative men who had had receptive unprotected anal intercourse had used poppers while doing so.

In the general population, 1.1% (around 350,000 people) use poppers at least once a year. This makes them the fourth most popular drug after cannabis, cocaine and ecstasy (excluding alcohol and tobacco).

WHAT IMPACT DO POPPERS HAVE ON HEALTH?

Poppers are a very widely used drug and most users do not report any harms. However a number of side effects have been reported.

Because they cause blood pressure to drop and heart rate to rise, use of poppers is not advised for people with glaucoma (high blood pressure in the eye) or breathing, heart and blood pressure irregularities. Extremely high doses can also cause the potentially fatal methaemoglobinaemia (excess of the protein methaemoglobin in the blood).

The use of poppers after taking erection drugs such as Viagra is contraindicated by the regulatory authorities and the manufacturers of erection drugs. As *nitrites* used for treating heart-conditions can cause a fatal drop in blood pressure when taken with erection drugs, it is thought that *nitrites* could have a similar effect.

Poppers can burn the skin if not washed off immediately, although a 'poppers burn' (usually seen around the nostril) lasts only a few days and leaves no scar. If swallowed, poppers can kill as they interfere with heart function. There are case studies in which use of poppers has been linked to loss of vision, over a period of months; this side effect may be more common with the most recent formulation of poppers (isopropyl nitrite).

A long-term cancer-causing effect in humans has not been demonstrated, but isobutyl nitrite is considered a human carcinogen by European regulators (see Legal status).

There have been a range of claims that poppers weaken the immune system, but very little robust evidence for this effect. The majority of studies of this hypothesis have involved animal, not human subjects, and much of this research is open to criticism for weak methodology. In studies suggesting a negative impact on immunity, there appears to be a modest suppression of CD4 cells (in mice) or natural killer cells (in humans) for 4-7 days following poppers use. However, many factors affect immune function or CD4 count, including diet, exercise, smoking and time of day.

There is research suggesting poppers have no significant lasting effect on the human immune system, and certainly no conclusive research shows any significant impact on human

LEGAL STATUS

The legal status of poppers is not clear cut and depends on which chemical substance the bottle contains. Because of legal restrictions on selling poppers as a medicine or a drug, manufacturers have frequently marketed their poppers as products not intended for human consumption such as 'leather cleaners', 'room odourisers' or 'tape head cleaners'. Some poppers' labelling carries warnings stating they are harmful if inhaled.

In March 2010, the Advisory Council on the Misuse of Drugs said that they would be gathering evidence on the harms associated with poppers. However when this body has looked into the issue in the past (in 1984, 1987 and 1991) their enquiries have found insufficient evidence of harm to the individual or society to warrant restricting the use of poppers under the *Misuse of Drugs Act*, which is the legislation used to control other recreational drugs.

Instead, when poppers have been the focus of legal proceedings it has been in connection with the *Medicines Act*. Since 1997, amyl nitrite has been a prescription-only drug under the act. Although possession of amyl nitrite without a prescription is legal, supply is an offence.

Whether poppers made of butyl nitrite, isobutyl nitrite or isopropyl nitrite are covered by the *Medicines Act* is less clear. None of these have any medical use so it has often been thought they do not come under the control of the act. However the Medicines and Healthcare Products Regulatory Agency (which administers the *Medicines Act*) consider that that any substance on sale with a psychoactive or mood-altering effect could be classed as a medicine, so these products would be covered.

In 1994 the Royal Pharmaceutical Society (RPS) investigated poppers, under pressure from Positively Healthy, a gay health rights group concerned about a link between poppers and Kaposi's sarcoma. In 1996 the RPS took a case under the *Medicines Act* against a North London shopkeeper for selling poppers. It is likely that most of the poppers in this case were butyl or isobutyl nitrite but the RPS argued that all poppers should be treated in law as if they were amyl nitrite. The case was not contested and the retailer was fined £100. A further prosecution in 2001 involving butyl and isobutyl nitrite failed.

Until August 2007 isobutyl nitrite, for many years the most common chemical compound used in poppers, was freely on sale. However it came under tighter control following a 2006 European Union directive which classed it as a Class 2 carcinogen (a cancer-causing substance), making its sale prohibited.

Within weeks poppers made of isopropyl nitrite appeared on the shelves. Advertisements appeared in the gay press drawing attention to the change in law regarding isobutyl nitrite and the introduction of isopropyl nitrite. The new formulation was marketed as stronger (although anecdotal reports claim its effects are actually weaker). Some manufacturers even promoted isopropyl nitrite poppers as 'safer'. In the UK this formulation remains widely available from sex shops, bars, nightclubs and online.

MAKING IT COUNT

Making it Count is the strategic planning framework that guides HIV prevention with men who have sex with men across the CHAPS partnership. Due to the link between using poppers during receptive anal intercourse and HIV acquisition, it is a population target of *Making it Count* to reduce the frequency with which men use poppers during unprotected receptive anal intercourse.

However, *Making it Count* does not advocate efforts to reduce men's access to poppers (for example, restrictions on their sale) as this would involve restricting men's own choices. Instead it proposes that an increase in knowledge of the risks associated with poppers, will lead to men changing their behaviour.

immunity. In fact, inhaled nitrites break down easily and quickly leave the body.

Although users cannot become physically addicted, it has been suggested that they may become psychologically dependent.

POPPERS AND HIV INFECTION

In the early 1980s, before HIV was identified as the infectious agent responsible for AIDS, poppers were suspected of causing the syndrome. This was based on widely reported use of poppers in the gay men who made up the bulk of early AIDS cases. After the identification of HIV, credible opinion dismissed poppers as the cause of AIDS although some who deny HIV causes AIDS continue to present poppers as a cause, or a co-factor in immune system damage.

In the mid 1980s poppers were also linked to the AIDS-related skin cancer Kaposi's sarcoma (KS), again because a large proportion of those developing KS used poppers. However, in 1994 infection with a previously unknown herpes virus (HHV-8) was identified as the cause of KS in people with weakened immune systems. The false link between poppers use and KS is an example of concluding a causal link between one thing and another, when they commonly occur in the same people.

Although poppers use in itself was not shown to cause KS, doubts remain over whether the drug plays a role as a co-factor in acquiring HHV-8 and / or developing KS among the immune-suppressed. Studies are inconclusive. It may be that poppers use acts as a marker for other factors linked to the development of KS. However, it may be possible that among people already infected with HIV and HHV-8, poppers use may increase the likelihood of developing KS.

As a consequence of these debates, over the last two decades very many studies have sought to investigate whether there is a link between using poppers and acquiring HIV, including studies which have asked specifically about poppers use during unprotected anal intercourse. Increasingly studies have attempted to take into account other factors that might also play a role in acquiring HIV. By controlling for these confounding factors using multivariate

analysis (looking at several statistical variables at a time) the role played by poppers in acquiring HIV has become clearer.

INSIGHT was a three year research project conducted in the UK to investigate new seroconversions among gay men. A major finding was that poppers use during receptive unprotected anal intercourse was a key risk factor for acquiring HIV.

After multivariate analysis had taken into account such factors as men's sexual behaviour (eg. unprotected anal intercourse), poppers were the only drug men took that was associated with an additional risk of sero-conversion. 80% of men who tested HIV positive used poppers compared to 58% who remained HIV negative. Of men who had receptive anal intercourse without a condom with someone they did not know was HIV negative, 61% of those who acquired HIV had sniffed poppers during sex, compared to 32% of those who had stayed HIV negative.

The disinhibiting effect of poppers is unlikely to be the explanation for greater HIV transmission to poppers users in studies. Many other drugs with similar or stronger disinhibiting effects do not emerge as significant risk factors in studies. Moreover, several studies have found no association between poppers use and not using condoms.

It is believed that the physiological effect of nitrite inhalants on the blood vessels of the rectum accounts for the observed increase in HIV transmission. As a vasodilator, nitrite inhalants increase blood flow to the rectum and engorge blood vessels. As the walls of these expand this may provide a larger and a thinner surface area through which HIV might pass. It has also been suggested that this might also result in a higher likelihood of blood vessels breaking during anal penetration, leading to anal bleeding and an easier way for HIV to enter the bloodstream.

Poppers use may also be associated with longer or rougher intercourse, being fisted and use of sex toys, and therefore increased friction and trauma, which will make HIV transmission more likely when HIV exposure occurs.

CHAPS CAMPAIGN

Although CHAPS health promotion materials and early editions of *Making it Count* had considered whether poppers might make HIV transmission more likely, the issue became much more prominent after the first release of the INSIGHT findings in 2007.

In response, in December 2007 the CHAPS partnership launched a mass media campaign educating gay men about the role of poppers in HIV transmission, as part of its ongoing programme of work on the biology of HIV transmission.

During the summer of 2008, men completing the *Gay Men's Sex Survey* were asked about their awareness of the increased risk of HIV acquisition if sniffing poppers during unprotected receptive anal intercourse. Forty two per cent already had this information, with the rest not knowing or not being sure about it. The campaign was updated and re-run from April to June 2011.



FIVE KEY POINTS

- Poppers are recreational drugs which are inhaled, usually through the nose.
- Poppers are one of the most widely used recreational drugs by men who have sex with men.
- The chemical composition of poppers has changed a number of times; the most common current formulation contains isopropyl nitrite.
- There is no good evidence for poppers causing immune suppression, KS or AIDS.
- An HIV-negative man who uses poppers during unprotected receptive anal intercourse with an HIV-positive man has an increased risk of acquiring HIV.

FURTHER READING

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