This technical brief reviews the patterns and consequences of psychostimulant use. The physiological, medical and psychological consequences of low- or high-dose as well as short- or long-term amphetamine use are described. Amphetamine dependence and the risks for HIV and hepatitis infections are also described.

A. Background

Amphetamine-type stimulants (ATS) are drugs that belong to the stimulant class of drugs and, as such, they excite or speed up the nervous system and produce effects similar to adrenaline. Methamphetamine and amphetamine are now the major forms of ATS available worldwide and the most widely consumed synthetic stimulants. Unlike cocaine, a stimulant that is derived from the naturally occurring coca plant, ATS were initially synthesized from ephedrine in 1919, and were legal experimental substances used in medical practice as a stimulant and performance enhancer for the military in World War II. Subsequently, they were widely prescribed for weight control and treatment of attention deficit disorders. However, since the 1970s, amphetamines have been manufactured in clandestine laboratories and increasingly used as recreational drugs. Because of their high potential for abuse, amphetamines became a Schedule 2 controlled drug following the 1971 Convention on Psychotropic Substances.1

In 2009–10, it was estimated that between 13.7 and 52.9 million people used substances belonging to the amphetamines group at least once in the preceding year.2 Data for East and South-East Asia suggest that between 4.4 and 37.9 million people have used amphetamines in the past year, no estimates were available for South Asia. Amphetamines are attractive to users because they are perceived as enhancing performance and communication and, in some circles, have come to embody modern and fashionable lifestyles. Furthermore, they are not only affordable but perceived as being less harmful than other drugs, as their health risks are frequently underestimated.2 In Asia, the Philippines and Thailand have the highest numbers of amphetamine users per capita, but use is increasing in most Asian countries. Globally, amphetamine is associated with significant public health, social and security problems.

The information presented in this brief refers to both amphetamine and methamphetamine. Both are used by a wide cross-section of society and their use is not limited to any particular population group. The major difference between methamphetamine and amphetamine is the manufacturing process and potency. Methamphetamine is water-soluble and can be smoked, snorted or – especially in its crystalline form – injected, and is more quickly absorbed by the body than non-methylated amphetamine and is thus generally more potent. Otherwise, there is no difference between the two. In fact, methamphetamine breaks down into amphetamine once it is ingested. Overall, methamphetamines are considerably more potent than amphetamines.

The similarities between methamphetamine and cocaine are noteworthy, since both belong to the class of drugs referred to as psychostimulants. The immediate and long-term effects of both are similar, as are treatment outcomes. However, the two drugs also have significant differences; the effects of methamphetamine last longer and are more severe than those of cocaine. The cocaine “high” generally lasts for 15–30 minutes, while the methamphetamine “high” may last for 8–12 hours. Cocaine-induced paranoia may last for just 4–8 hours following cessation of drug use but methamphetamine-induced paranoia may continue for up to 7–14 days. Psychosis appears to be more profound with ATS than with cocaine.

B. Who uses amphetamine/methamphetamine?

There is no definitive profile of a “typical” user. ATS are used for many reasons. For example, sports persons may use ATS to enhance their performance, long-distance truck drivers may use it to keep awake on long journeys, labourers and porters engaged in heavy physical activities may take ATS to make them feel stronger, and students may use it to help them stay awake and study. Another group of ATS users comprises those who take ATS for social reasons such as at parties, nightclubs or gatherings of friends and acquaintances. Some are heavy and regular users who smoke or inject potent forms of methamphetamine and also use a variety of other drugs. They are thus likely to experience poor mental and physical health and may become dependent on amphetamines. However, the majority of non-medical use is by young people who use low-potency ATS, swallow or snort the drug, do not inject and are not dependent.

To summarize:

- The usual age of first methamphetamine use appears to be mid-adolescence and metamphetamine is most typically used by boys.
- The rate and frequency of methamphetamine use tends to increase from early adolescence to early adulthood and then gradually diminishes.
- Those who are viewed as being especially vulnerable to experimentation with ATS include:
  - working/homeless children;
  - incarcerated and institutionalized youth;
  - sexually abused children;
  - unemployed youth;
  - sex workers and other workers in the entertainment/hospitality industry (e.g. clubs and casinos);
  - young people frequenting places of entertainment such as clubs and discothèques; and
  - men who have sex with men (MSM), lesbian, bisexual and transgender youth, who have higher rates of drug use including ATS than the rest of the community.

C. Patterns and consequences of amphetamine/methamphetamine use

Amphetamine may be ingested, snorted or smoked and, less commonly, injected. In powder form, methamphetamine is generally swallowed or snorted. The crystalline form of methamphetamine, which looks like glass and is often referred to as “ice”, is typically smoked. When smoked or injected, ice reaches the brain rapidly and is associated with a high risk of dependence. There is growing evidence

---

that smoking crystal methamphetamine has more harmful psychological effects and a higher addictive potential than other forms of methamphetamine.7,8 Furthermore, methamphetamine is sometimes mixed with other drugs and sold as “ecstasy” 3,4 (methylene dioxy methamphetamine – MDMA), a drug with hallucinogenic properties that is frequently used in clubs and entertainment venues.

C.1 Patterns of use

Within the dependence/harmful use continuum, there are several discernable patterns of use. None are without potential risks though it is not clear whether occasional use inevitably leads to regular or dependent use. These include a pattern of experimental occasional use, usually with friends and in social settings. The pattern of intermittent heavy binge use is more serious; it generally occurs on weekends and is precipitated by party-going and the desire to stay awake. Such binge use may be occasional with large gaps between binges. Some people use ATS regularly – daily or almost daily – and such use may be accompanied by physical and psychological dependence. In addition, polydrug use is very common among methamphetamine users. Alcohol, cannabis and other psychostimulant drugs (such as ecstasy) are the most frequently used drugs.9

C.2 Consequences of amphetamine use

A range of harms is associated with amphetamine use. Some are predominantly dose related and others are a combination of dose and length of use.

<table>
<thead>
<tr>
<th>Physical consequences of low-dose use</th>
<th>Physical consequences of high-dose use</th>
<th>Physical consequences of short-term use</th>
<th>Physical consequences of long-term use</th>
<th>Physical consequences of ATS use</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Sweating</td>
<td>- Overdose</td>
<td>- Intoxication</td>
<td>- Drug dependence</td>
<td>- Precipitates psychiatric problems</td>
</tr>
<tr>
<td>- Intoxication</td>
<td>- Intoxication</td>
<td>- Dehydration</td>
<td>- Poor nutrition</td>
<td>- Exacerbates existing problems</td>
</tr>
<tr>
<td>- Palpitation</td>
<td>- High blood pressure</td>
<td>- Cardiovascular problems (i.e. rapid heart rate, irregular heartbeat and increased blood pressure and death from a cardiac event)</td>
<td>- Poor sleep</td>
<td>- Mood disorders: confusion, paranoia, anxiety, depression, suicidal ideation, panic attacks, obsession, psychosis</td>
</tr>
<tr>
<td>- Chest pain</td>
<td>- Seizures</td>
<td>- Overdose</td>
<td>- Susceptibility to illness including cardiovascular problems</td>
<td>- Cognitive impairment</td>
</tr>
<tr>
<td>- Headache</td>
<td>- Nausea</td>
<td>- Hyperthermia and convulsions</td>
<td>- Potential death from arrhythmias or myocardial infarction or stroke</td>
<td>- Sleep disorders, fatigue</td>
</tr>
<tr>
<td>- Hot and cold flushes</td>
<td>- Vomiting</td>
<td>- Decreased appetite and weight loss</td>
<td>- Agitation</td>
<td>- Agitation</td>
</tr>
<tr>
<td>- Reduced appetite</td>
<td>- Cerebral haemorrhage and death</td>
<td>- Skin and teeth problems</td>
<td>- Increased impulsivity</td>
<td>- Increased impulsivity</td>
</tr>
<tr>
<td>- Increase in blood pressure</td>
<td></td>
<td>- Sleep disorders</td>
<td>- Aggression and violence</td>
<td>- Aggression and violence</td>
</tr>
<tr>
<td>- Euphoria</td>
<td></td>
<td>- Feelings of invincibility while intoxicated</td>
<td>- Social and family disruption/breakdown</td>
<td>- Social and family disruption/breakdown</td>
</tr>
<tr>
<td>- Alertness</td>
<td></td>
<td>- Increased high-risk behaviours such as unsafe sex</td>
<td>- Unemployment</td>
<td>- Unemployment</td>
</tr>
<tr>
<td>- Reduction of fatigue</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Talkativeness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Improved physical performance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: Adapted from the Australian ATS strategy10


C.3 Consequences of amphetamine use in the context of polydrug use

Methamphetamine toxicity is increased when taken in combination with alcohol, cocaine or opiates.\textsuperscript{11,12}

\begin{itemize}
  \item Use of alcohol and methamphetamine in tandem can be dangerous – it increases the blood pressure, placing a greater burden on the heart. Methamphetamine can also disguise the effects of alcohol, which may increase the risk of alcohol poisoning and accidents due to a false sense of feeling sober and in control.
  \item Use of cannabis and methamphetamine in tandem has been shown to increase psychotic symptoms in some users.
  \item Heroin and methamphetamine used together can cause respiratory depression which may induce cardiac failure. Methamphetamine can also increase the risk of heroin overdose.
  \item The combination of methamphetamine and cocaine has been shown to substantially increase the cardiotoxic effects of both drugs.\textsuperscript{12}
\end{itemize}

C.4 ATS dependence\textsuperscript{11}

Dependence on ATS is characterized by increasing tolerance to the drug, occurrence of withdrawal symptoms, a preoccupation with the drug and an inability to reduce ATS use despite significant negative social, health or psychological consequences and impairment.

\begin{itemize}
  \item Tolerance can sometimes be observed when ATS users transit from non-injecting to injecting as they begin to use higher doses of ATS per episode.
  \item Withdrawal from ATS is marked by fatigue, lethargy, sleep disturbances, appetite disturbances, depression, irritability, psychomotor retardation or agitation and strong craving.
\end{itemize}

The degree of methamphetamine dependence is strongly related to the route of administration: the highest number of dependent users is among those who inject.

C.5 Methamphetamine use and risks for acquiring HIV\textsuperscript{13}

There have been conflicting findings with respect to the association of ATS injection and HIV infection largely because of the coexistence of high-risk sexual and injecting behaviours among users. Reported associations are related to a number of factors, including the higher prevalence of HIV in the general population in which ATS users live, as well as the characteristics and behaviour of the users themselves, particularly sharing of injection equipment and binge use. ATS use has become associated with a culture of risky sexual behaviour, both among MSM and heterosexual populations, as is evidenced by high rates of sexually transmitted infections (STI) among ATS users.\textsuperscript{14} This link may be due to the fact that methamphetamine increases libido although,

\begin{flushleft}
\end{flushleft}
paradoxically, long-term methamphetamine use is sometimes associated with decreased sexual functioning, at least in men.15

Both methamphetamine use and HIV infection cause changes in brain chemistry and these changes may be associated with impaired cognitive functions. Concurrent methamphetamine use and HIV infection appear to result in greater impairment than each condition alone.16 Research to examine whether methamphetamine was associated with increased HIV replication suggested that methamphetamine use was associated with increased viral loads even among those taking antiretroviral medication.17 Although data are limited, methamphetamine use has been associated with decreased adherence to antiretroviral medication, especially during methamphetamine binging episodes.18 However, the prevalence of drug resistance among methamphetamine users with HIV remains unknown.15,19

As noted above, ATS use has significant consequences. Most of the potential harms are the result of methamphetamine use. However, it is important to note that because of the widespread use of ATS, dependence on methamphetamine is more common than cocaine and heroin dependence combined, and ending dependence on amphetamines can be as difficult as it is for cocaine and heroin.20 Serious harms from amphetamine are usually the result of heavy, long-term and “dependent” use. However, all users of ATS, whether dependent or not, whether regular or recreational, are vulnerable to a range of harms.

Summary

Overall, the public perception of the risks of ATS use are both underestimated and overestimated. Attempts to totally eliminate the drug problem by stringent law enforcement and compulsory treatment can be seen as an example of overreaction – where even modest occasional use is regarded as dangerous and criminal. Elsewhere, notions prevail that recreational use causes no long-lasting harms, and is likely to be simply discontinued by the users of their own accord without the need for outside interventions. The truth lies somewhere in the middle.

17 Ellis RJ et al. Increased human immunodeficiency virus loads in active methamphetamine users are explained by reduced effectiveness of antiretroviral therapy. Journal of Infectious Diseases, 2003, 188:1820–1826.
The four Technical Briefs on Amphetamine-type Stimulants were designed by the WHO Regional Office for the Western Pacific in response to the demand from Member States and civil society organizations working with people who use drugs in the Region. They are intended to provide guidance and technical assistance.

WHO is grateful to Ms Edna Oppenheimer, a senior consultant, who compiled the available literature for the content and drafted the original; and for the coordination and inputs received from Dr Fabio Mesquita and Ms Nina Rehn-Mendoza from the Regional Office of the Western Pacific.

WHO also appreciates the intense collaboration of Mr Graham Shaw from WHO Cambodia, and Ms Annette Verster and Dr Nicholas Clark from WHO Headquarters towards a better final product.

Technical editing was done by Bandana Malhotra.