SUBSTANCE MISUSE FACT SHEETS

CATEGORY III – NOVEL PSYCHOACTIVE SUBSTANCES (NPS)

1.0 Introduction

This factsheet includes information on emerging and re-emerging psychoactive drugs known as novel psychoactive substances (NPS), which are colloquially called "legal highs" and "designer drugs".

2.0 What are NPS?

Novel psychoactive substances (NPS) are often called 'designer drugs' or 'legal highs' in the media, with specific variants known as 'herbal highs' or 'bath salts'.

The United Nations Office on Drugs and Crime (UNODC) uses the term 'new psychoactive substances' (NPS) which they define as "substances of abuse, either in a pure form or a preparation, that are not controlled by the 1961 Single Convention on Narcotic Drugs or the 1971 Convention on Psychotropic Substances, but which may pose a public health threat". It is important to note that the term 'new' does not necessarily mean a new chemical invention (some NPS were actually first synthesised around 40 years ago) but rather to substances that have recently emerged on the market and are now controlled under the Psychoactive Substances Act 2016. This UK Act restricts the production, sale and supply.

LEARNING OBJECTIVES

Medical students will gain an understanding of:

1. The rapidly changing nature of the recreational drug scene, trends in substance abuse, current usage patterns and the ease with which new psychoactive substances can be obtained.
2. The need to ask patients about the use of 'legal highs' and the potential effects of such substances as well as the need to treat the presenting symptoms without access to confirmatory laboratory analysis or other information.

Vignette

A previously well 35-year-old male, with no past medical or psychiatric history presented to A&E with agitation and visual hallucinations. He was admitted with suspected viral encephalitis, however a CT head scan, lumbar puncture and serology were all normal. His symptoms subsided within a week, and he was reviewed one month later. An EEG and HIV serology were normal, whilst an MRI head scan revealed a suspected benign lipoma, however this was not investigated further.

The same individual presented a further four times with episodes of psychotic symptoms requiring various medical interventions including treatment with sedatives and anti-psychotics, all subsiding completely within a week. Symptoms included auditory and visual hallucinations such as being shot at; passivity of volition; prosopagnosia; depersonalisation; derealisation; and tactile hallucinations including feeling metal objects being thrown at him.

After the fifth presentation, he finally disclosed that each episode was associated with the use of NRG-3 purchased online. This NPS was thought to contain synthetic cathinones (including mephedrone) however recent testing suggests it may contain benzofuran (a compound of the phenethylamine and amphetamine classes). Both mephedrone and the benzofurans are now banned.

Summary of: Transient psychoactive episodes following recreational use of NRG-3 (Kihara and Day, 2014): http://onlinelibrary.wiley.com/doi/10.1002/pnp.331/pdf

2.1 Recent NPS trends

In recent years, NPS have become increasingly available, particularly via the internet and in 'head-shops' (retail outlets that often sell smoking and drug-related paraphernalia). Deaths related to their consumption have also increased (Claridge & Goodair 2015).

Many NPS are manufactured to mimic the effects of the more 'traditional' drugs, such as cocaine, MDMA and cannabis. NPS are now illegal, however, consumers may still believe them to be safe to consume, despite the lack of data on the pharmacology, toxicology and safety profiles of these substances. Health professionals should therefore be aware of the ever-changing nature of recreational drug use and the potential mental and physical health issues that may be caused by the consumption of new psychoactive molecules.

The rapid and increasing creation of new substances in an attempt to stay ahead of legal frameworks is demonstrated by figures published by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). The EMCDDA are currently monitoring more than 450 NPS, with 101 of these newly-reported in 2014 alone, compared to 41 in 2010 (EMCDDA 2015). The rapidity of development of new drugs poses significant challenges to Emergency Departments, due to the limited data available on the health risks associated with new substances, either through acute exposure and/or chronic use.

The UK's Advisory Council on Misuse of Drugs (ACMD) has a working group on New Psychoactive Substances that monitors developments and provides information and

advice to Ministers on potential emergent issues. The EMCDDA and Europol also have a network of early warning systems in place to report instances of new substances and annual updates are reported on-line.

There are several types of sources regarding keeping track of changes in substance use and the emergence of new drugs. General household surveys such as the British Crime Survey are good at revealing changes over time in terms of prevalence in the general population of commonly abused substances, and are only reported once a year. Music magazines, especially "Mixmag", may have reviews of new substances appearing on the club scene. "Mixmag" conducts an on-line survey once a year and publishes the results in the following Spring. Internet chat rooms and user fora are useful sources of information on what is available and its subjective effects. Commercial websites offer psychoactive substances for sale. The EC-funded EU –Madness Project- http://www.eumadness.eu/about-eu-madness/ and I Trend http://www.i-trend.eu/index.htm a research project which aims to help prevent health and social harms associated with New/Novel Psychoactive Substances (NPS), or 'New Synthetic Drugs'.

2.2 Examples of NPS and their reported effects

Group	Potential effects	Examples of substances
Phenethylamines Whilst phenethylamine can be found in the mammalian CNS and other organisms, phenethylamine derivatives are referred to as 'phenethylamines', and include psychedelics, hypnotics, entactogens and empathogens, amongst others.	Arousal and euphoria accompanied by sweating, agitation, vasoconstriction, cold extremities, chest pain, difficulty passing urine, headache, nausea, tachycardia, anorexia, anxiety, paranoia and insomnia.	4-Methylamphetamine (4-MA) Methiopropamine (MPA)
Piperidines Commonly used in the synthesis of organic compounds including pharmaceuticals and recreational drugs.	Euphoria, empathy, intensification of sensory experience, mood enhancement. Toxicity effects may include agitation, vomiting, excessive sweating, hypertension, tachycardia, palpitations, seizures and cardiotoxicty.	2-Methoxphenidine Ethylphenidate
Substituted tryptamines Whilst tryptamine can be found in animals, fungi and plants, the tryptamine chemical structure provides the basis for compounds including psychedelic drugs, which are collectively called 'substituted tryptamines'.	Powerful hallucinations may occur even at low dosage, with other effects including agitation, restlessness, confusion, lethargy, vomiting, pupil dilation, jaw clenching, increased heart rate, increased blood pressure, increased temperature and respiratory rate.	5-MeO-DALT 5-MeO-DiPT α-Methyltryptamine (AMT)
Synthetic cannabinoids These bear no relation to the cannabis plant except in that the chemicals which are blended into the plant matter are sold as acting on the brain in a similar way to cannabis; however this is often not the case.	May make the user feel happy, talkative, hungry and drowsy, with mood and perception changes, with concentration and co-ordination possibly difficult. Toxicity effects may include tachycardia, hypertension, ECG changes, muscle jerking, vomiting, hypokalaemia, hallucinations, seizures and psychosis.	5F-AKB-48 5F-PB-22 AB-FUBINACA AKB-48 AKB-48F AM-2233 STS-135
Synthetic cathinones The effects of these drugs replicate across the range, those encountered with amphetamine and MDMA. The majority of synthetic cathinones are now banned and thus not technically NPS, however many are still regarded as NPS (e.g. mephedrone) and are still causing deaths across the UK and elsewhere.	The effects are often reported to be similar to MDMA, with stimulant properties. Side effects may include agitation, increased heart rate and hypertension, with toxic effects including chest pains and convulsions.	Mephedrone (4-MMC) 4-Methylethcathinone (4-MEC) Methylone (bk-MDMA) Methylenedioxypyrovalerone (MDPV)

3.0 NPS-related primary care presentations

Individuals often present to emergency services experiencing acute toxicity or with symptoms related to side effects or adverse effects of taking the substance either on its own or in combination with other substances or alcohol. Presentation may include overdose and temporary psychotic states and unpredictable behaviours as well as suicidal ideation when the effects of the substances wear off (come – down) and the individual feels low in mood/depressed.

Due to the lack of detailed scientific knowledge on the pharmacological, metabolic, toxicological and pathological aspects of new substances when they initially appear, it is important that clinicians and other health professionals dealing with emergency presentations treat the symptoms presented and patients should be asked about their use of "legal highs", as well as other substances abused. If confirmatory witnesses or other evidence is available about what has been consumed, that may be of assistance but should not be the sole basis for decision-making. Patients and witnesses may not in reality know what was in the products consumed, for if the substances were sold under a brand-name, often the contents and active ingredients are not listed and therefore consumers do not know what they are taking. Even if a substance is advertised using its chemical name, due to these products being unregulated, there is no guarantee that what is displayed on the packet is what is actually contained within.

Acute health issues are not the only concern when dealing with NPS-related health harms, as their use is also associated with longer term health issues including:

- Increase in mental health issues including psychosis, paranoia, anxiety, 'psychiatric complications'
- Depression
- Physical and psychological dependence which develops quite rapidly after a relatively short period – which can be within weeks - of intense use

3.1 Practice points:

- Keep informed about the emergent drugs especially in the locality in which you are practising, and keep channels of communication open with the relevant specialists e.g. toxicologists, forensic experts, police.
- Have a high index of suspicion especially if there are any hints of atypical and subtle presentations which may alert you and reflect the use of novel substances perhaps combined with the 'classical' drugs of misuse.
- Undertake a comprehensive history and clinical examination including necessary investigations according to the usual protocol.
- Attempt to obtain as much information as possible from multiple sources about the drug use of the individual who may not be aware themselves that they might have taken one of these new substances.
- Attempt to obtain toxicological assessment of the individual as soon as possible.
- Monitor the clinical state frequently as appropriate for the environment e.g. whether patient is assessed in the Emergency department or in an inpatient service or a community service.

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