



## PRACTICE

## PRACTICE POINTER

# Novel psychoactive substances: identifying and managing acute and chronic harmful use

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Identifying and managing acute drug related harms and problematic substance misuse cuts across medical specialities. Data suggest that clinicians are seeking readily accessible information on novel psychoactive substances (NPS), incorrectly known as “legal highs.” Clinicians may encounter acutely disturbed or unwell patients, individuals with harm or dependency related to chronic NPS use, and those reporting incidental consumption that might require psychoeducation and monitoring. Such assessments will have more successful and meaningful outcomes if clinicians are aware of the spectrum of NPS available and how they might affect their patient.

The linked clinical update<sup>1</sup> describes the different classes of NPS and their effects. This article provides practical advice to the non-specialist on how to approach an assessment of individuals using NPS, including examples of acute and chronic use.

## Exploring NPS use

A sensitive, non-judgmental approach is essential. Key aspects of the history are applicable in all scenarios. Boxes 1 and 2 cover specific issues relevant to emergency and longer term presentations. Patients may be concerned about being criticised for using drugs, and they might be uncertain of, but worried about, the potential harms and available services for those using NPS. Individuals can also be fearful of legal consequences of disclosure, and the principle and limits of confidentiality should be discussed. Adopt an empathic line of questioning, such as “I can imagine it might be difficult or worrying to talk about drug/NPS use. My role is to try understand any problems you are having, and to see how I can help.”

Include a history, mental state, and physical examination (particularly blood pressure, heart rate, temperature, and level of consciousness) in the initial assessment. Explore the type of drug or NPS used and the method and frequency of consumption, and ask about acute and chronic harms associated

with use (box 3). Unlike established recreational drugs such as cannabis, heroin, or cocaine, most standard urinary drug tests have limited sensitivity and specificity to NPS. Nevertheless, a urinary drug test can prove useful in helping to establish if other drugs are being used.

Consider whether there are relevant social and environmental issues that might precipitate or perpetuate substance misuse. The National Drug Treatment Monitoring System identified specific factors associated with longer term, harmful use in those under 18 years old<sup>16</sup>: early onset (<15 years old) and poly-drug use, antisocial behaviour, being affected by others' drug use or domestic violence, and being a child in need of or on a protection plan.

## Evaluating motivation to change

There are no well evidenced screening tools for identifying problematic NPS use. Not everyone who uses NPS, or any other established recreational drug, necessarily needs or wants professional help. However, if a patient discloses use of NPS, view this as an opportunity to provide information and discuss potential risks in a non-judgmental manner. Also consider whether to signpost the patient to relevant specialist healthcare services such as substance misuse, sexual health, and mental health teams.

Motivational interviewing is a goal-oriented technique to engage individuals and reduce their ambivalence to change behaviour. Rather than tackle drug use “head on” with (at least perceived) messages of just stopping, which can be challenging and may provoke disengagement, motivational interviewing encourages individuals to focus on their own goals and how they might plan for them. For example, “It sounds as if things have been difficult for a while. Have you thought about aspects of life that might be holding you back from where you would like to be, or what you would like to achieve?” The FRAMES approach<sup>17</sup> is a well

**What you need to know**

- Most standard urinary drug tests have limited sensitivity and specificity to novel psychoactive substances (NPS)
- Discuss risks and encourage reduction in the frequency and quantity of harmful NPS use, but be cautious with benzodiazepines or opioids where sudden discontinuation can lead to physical withdrawal
- Offer referral to drug and alcohol treatment services or other professionals, such as psychiatry, sexual health, or social services when appropriate

**Box 1: Case scenario 1: emergency presentation**

A 29 year old man is brought into the emergency department by ambulance after acting erratically with staff at a nightclub. On arrival, he is pacing, agitated, and mildly aggressive. On examination, his heart rate is 130 bpm, blood pressure 160/95 mm Hg, temperature 38.5 °C, and he has dilated pupils, increased tone and hyperreflexia in his lower limbs, and 5-6 beats of inducible ankle clonus. His friends told paramedics he had taken a 'white powder' which he bought as a legal high on the internet.

*Spotting acute use*

A more direct line of questioning is required in acute presentations. The clinical presentation in this example is consistent with use of a serotonergic drug (either an established recreational drug or NPS variant) and serotonin syndrome (toxicity)<sup>2</sup>—characterised as a triad of mental status changes, autonomic hyperactivity, and neuromuscular abnormalities, although clinical features are not always consistent.

In terms of NPS, mephedrone is commonly implicated given its high reported prevalence of use and availability.<sup>3-5</sup> From a treating clinician's perspective, although knowing the precise drug(s) used helps provide better informed patient advice before discharge, management of acute stimulant toxicity is broadly similar regardless of whether an individual has taken an NPS or an established recreational drug. Accidental or intentional overdose of selective serotonin reuptake inhibitors (SSRIs) cause a similar picture, so it is important to ask about prescribed medications and other medical and psychiatric problems. Finally, certain medical conditions may present with similar clinical features (such as severe sepsis or encephalitis).

*Assessment and management of mephedrone toxicity*

Although broadly similar to that for established recreational stimulants, the full clinical picture associated with acute toxicity of mephedrone remains incompletely understood.<sup>6,7</sup> However, signs and symptoms associated with use have been described in user self reports, surveys, and cases confirmed by toxicology. The most commonly reported clinical features are agitation or aggression, tachycardia, and hypertension (>25% of users). Others include (in 10-25% of cases) palpitations, insomnia, hallucinations, paranoia, nausea, vomiting, chest pain, paraesthesia, confusion, and anxiety; and in <10% of cases, seizures, headache, hyperpyrexia, cold or blue extremities, tremor, and reduced level of consciousness.<sup>8-13</sup> Some case series report concomitant use of other drugs, and thus some of the symptoms reported may relate to these rather than mephedrone.<sup>11</sup>

Some reports indicate that the acute toxicity of mephedrone and other NPS stimulants is more prolonged than that seen with established recreational stimulants. For example, the UK National Poisons Information Service reported 45% of patients had symptoms for more than 24 hours after use of mephedrone, and 30% had symptoms for more than 48 hours.<sup>14</sup>

Management includes preventing further exposure to serotonergic drugs (including prescribed medications) and treating the stimulant clinical features. Benzodiazepines may be used to help reduce sympathomimetic toxicity (agitation, hypertension, tachycardia), in the same way that they are used for patients with toxicity after harmful use of MDMA, cocaine, and amphetamines. The oral 5-HT<sub>2A</sub> antagonist cyproheptadine helps directly reduce the effects of the excess serotonin concentrations seen in such instances.

Hyperpyrexia (core temperature of >39 °C) is a medical emergency, and the patient's temperature needs to be reduced rapidly. Initial measures include cold intravenous fluids, removing excess clothing, use of benzodiazepines and cyproheptadine; the most effective method for reducing temperature seems to be packing the patient in ice, with very rapid temperature decreases reported. If clinicians are unsure how to manage a patient, or the patient has severe toxicity (such as hyperpyrexia), they are advised to seek advice from their local toxicology service.

**Box 2: Case scenario 2: chronic use**

A 24 year old woman presents to her GP with low mood and feeling "up and down." She admits she is concerned about her use of "spice," which she has been smoking regularly for several years, but she is not sure she wants professional help with this at the moment. She says that most of her friends use similar drugs, and she does not think she would discontinue use completely.

*Exploring harmful use and dependency*

This case presents a pattern of chronic novel psychoactive substance (NPS) use. Diagnostically, "harmful use" typically involves an intermittent binge pattern of use that can be damaging to an individual's physical or mental health. Dependency is a more complex syndrome of behavioural, cognitive, and physiological symptoms that can accompany repeated use. Three of the following six criteria are required for a diagnosis of dependency on any drug: (a) desiring the substance; (b) difficulty controlling the amount consumed; (c) tolerance to its effects; (d) withdrawal effects; (e) giving primacy to use of the substance and neglecting alternatives; and (f) persisting use despite these difficulties.<sup>15</sup>

Avoid the use of pejorative terms or labels such as "addict" and ensure a supportive motivational approach to discussions. In instances of both harmful use and dependency, agreeable individuals can be referred to substance misuse services, though the management of dependency can be more complex. In the case of benzodiazepine and opioid dependency, this will usually involve stabilisation on suitable replacement therapy, followed by detoxification ("detox") on a staggered reduction regimen. Care may be provided in community or inpatient settings, depending upon individuals' requirements and locally available services, and is sometimes followed by a period of psychosocial rehabilitation ("rehab"). Various specialist psychosocial interventions are available for patients with dependency or harmful use who wish to modify their behaviour.

**Box 3: Areas to explore and document in a history of novel psychoactive substance (NPS) use**

*Drug class(es)*—Stimulant, cannabinoid, hallucinogen (dissociatives and psychedelics), depressant (opioids and benzodiazepines)

*Method(s) of use*—Oral ingestion, nasal insufflation ("snorting"), intravenous injection, rectal insertion

*Drug consumption patterns*—Quantity, frequency; concomitant consumption of prescribed or over-the-counter medication or alcohol or other recreational drugs. Use of cigarettes

*Acute and chronic harmful effects*—Physical and psychological sequelae, risks from impulsive behaviour, including sexual health. Impact on mental health and social functioning. Identification of individual vulnerabilities, risk of exploitation by others, and potential safeguarding issues towards others

established model used in many substance misuse services and can be a useful strategy in this regard (box 4).

## Harm minimisation

Harm reduction begins with encouraging decreasing the frequency and quantity of NPS use, but care must be taken in the case of novel benzodiazepines or opioids because sudden discontinuation can lead to physical withdrawal. Where relevant, discuss risks associated with injecting drugs, signpost to a needle exchange or injecting service, and offer referral for HIV and hepatitis testing. Anecdotally, there have been reports of an increase in intravenous NPS use in “chem sex” parties and that some new drug users have poor injection technique, with associated increased risk of thrombosis and abscesses and other infections.

## When to refer

Consider harm in a wider social context. Assessment and support from social services may be required for individuals, or their families, who may be vulnerable or at risk of harm from or towards others.

Offer interventions within the limits of expertise and clinical setting, and recommend referral to drug and alcohol treatment services or other healthcare professionals, such as psychiatry, when appropriate.

A “strengths based approach” should help highlight positive environmental factors and aspects of personal resilience that will help individuals through recovery. For example, inquire into, and highlight back to the patient, relevant social factors such as good family and relationship support, and individuals’ desire and motivation to change their life.

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- 1 Tracy DK, Wood DM, Baumeister D. Novel psychoactive substances: types, mechanisms of action, and effects. *BMJ* 2017;356:i6848. doi:10.1136/bmj.i6848.
- 2 Boyer EW, Shannon M. The serotonin syndrome. *N Engl J Med* 2005;356:1112-20. doi:10.1056/NEJMr041867 pmid:15784664.
- 3 Wood DM, Measham F, Dargan PI. ‘Our favourite drug’: prevalence of use and preference for mephedrone in the London night-time economy 1 year after control. *J Subst Use* 2012;356:91-7. doi:10.3109/14659891.2012.661025.
- 4 Dargan PI, Sedefov R, Gallegos A, Wood DM. The pharmacology and toxicology of the synthetic cathinone mephedrone (4-methylmethcathinone). *Drug Test Anal* 2011;356:454-63. doi:10.1002/dta.312 pmid:21755604.
- 5 Hockenfull J, Murphy KG, Paterson S. Mephedrone use is increasing in London. *Lancet* 2016;356:1719-20. doi:10.1016/S0140-6736(16)30258-6 pmid:27116276.
- 6 Wood DM, Dargan PI. Mephedrone (4-methylmethcathinone): what is new in our understanding of its use and toxicity. *Prog Neuropsychopharmacol Biol Psychiatry* 2012;356:227-33. doi:10.1016/j.pnpbp.2012.04.020 pmid:22564711.
- 7 Wood DM, Dargan PI. Understanding how data triangulation identifies acute toxicity of novel psychoactive drugs. *J Med Toxicol* 2012;356:300-3. doi:10.1007/s13181-012-0241-3 pmid:22581465.
- 8 James D, Adams RD, Spears R, et al. National Poisons Information Service. Clinical characteristics of mephedrone toxicity reported to the U.K. National Poisons Information Service. *Emerg Med J* 2011;356:686-9. doi:10.1136/emj.2010.096636 pmid:20798084.
- 9 EMCDDA. Europol. EU drug markets report. 2016. www.emcdda.europa.eu/start/2016/drug-markets.
- 10 Regan L, Mitchelson M, Macdonald C. Mephedrone toxicity in a Scottish emergency department. *Emerg Med J* 2011;356:1055-8. doi:10.1136/emj.2010.103093 pmid:21183522.
- 11 Wood DM, Davies S, Greene SL, et al. Case series of individuals with analytically confirmed acute mephedrone toxicity. *Clin Toxicol (Phila)* 2010;356:924-7. doi:10.3109/15563650.2010.531021 pmid:21171849.
- 12 Wood DM, Greene SL, Dargan PI. Clinical pattern of toxicity associated with the novel synthetic cathinone mephedrone. *Emerg Med J* 2011;356:280-2. doi:10.1136/emj.2010.092288 pmid:20581379.
- 13 Dargan PI, Albert S, Wood DM. Mephedrone use and associated adverse effects in school and college/university students before the UK legislation change. *QJM* 2010;356:875-9. doi:10.1093/qjmed/hcq134 pmid:20675396.
- 14 National Poisons Information Service, Public Health England. National Poisons Information Service Report 2014/15. 2015. www.npis.org/NPISAnnualReport2014-15.pdf
- 15 World Health Organization. *International classification of diseases*. WHO, 2016.
- 16 Public Health England. Adult substance misuse statistics from the National Drug Treatment Monitoring System (NDTMS). 2015. www.nta.nhs.uk/uploads/adult-statistics-from-the-national-drug-treatment-monitoring-system-2014-2015.pdf
- 17 Hester RK, Miller WR. *Handbook of alcoholism treatment approaches*. 2nd ed. Allyn and Bacon, 1995.

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**Box 4: The FRAMES motivational interviewing model for encouraging engagement and self responsibility with drug use**

**Feedback**—Discuss the potential adverse outcomes of drug use, individualised to the person's pattern of use, and listen to their responses

**Responsibility**—Emphasise that it is up to the individual to decide if they wish to change their behaviour

**Advice**—Straightforward advice on how drug use can be changed

**Menu**—Provide the individual with their therapeutic options, and facilitate their decision making

**Empathy**—Have a non-judgmental and warm clinical approach

**Self efficacy**—Project optimism that they have the ability to positively change their life if they so wish

**Resources for healthcare professionals**

- UK National Poisons Information Service ([www.npis.org](http://www.npis.org)) and its clinical toxicology database TOXBASE ([www.toxbase.org](http://www.toxbase.org))—If you need advice or information that is not available on TOXBASE then call NPIS for clinical support
- NEPTUNE (novel psychoactive treatment: UK network) (<http://neptune-clinical-guidance.co.uk>)—Comprehensive clinical guidance on party drugs
- Wood DM, Dargan PI. Understanding how data triangulation identifies acute toxicity of novel psychoactive drugs. *J Med Toxicol* 2012;8:300-3
- Baumeister D, Tojo LM, Tracy DK. Legal highs: staying on top of the flood of novel psychoactive substances. *Ther Adv Psychopharmacol* 2015;5:97-132—Review of the neurobiology of NPS
- GOV.UK. New Psychoactive Substances (NPS) resource pack ([www.gov.uk/government/publications/new-psychoactive-substances-nps-resource-pack](http://www.gov.uk/government/publications/new-psychoactive-substances-nps-resource-pack))—UK Home Office NPS resource pack for "informal educators and frontline practitioners"
- EMCDDA. EU drug markets report ([www.emcdda.europa.eu/start/2016/drug-markets](http://www.emcdda.europa.eu/start/2016/drug-markets))—Guide to the European illicit drugs' market

**Resources for drug consumers and the public**

- FRANK (friendly confidential drugs advice). Legal highs ([www.talktofrank.com/legalhighs](http://www.talktofrank.com/legalhighs))—UK based general information guide for patients and the lay public
- EROWID ([www.erowid.org](http://www.erowid.org))—Non-profit, international, drug-consumer-led website providing non-judgmental advice and guidance
- Rise Above (<http://riseabove.org.uk/tag/drinking-smoking-drugs/>)—Website by NHS England for children and adolescents about substance misuse, mental health, and other social issues
- Bowden-Jones O. *The Drug Conversation: How to talk to your child about drugs*. Royal College of Psychiatrists, 2016
- Global Drug Survey ([www.globaldrugsurvey.com](http://www.globaldrugsurvey.com))—Information for, and international survey of, NPS consumers
- Sumnall H, Atkinson A. The new Psychoactive Substances Bill—a quick introduction. ([www.cph.org.uk/blog/the-new-psychoactive-substances-bill-a-quick-introduction/](http://www.cph.org.uk/blog/the-new-psychoactive-substances-bill-a-quick-introduction/))—Guide to legislative changes in the UK

**How patients were involved in the creation of this article**

An individual receiving residential care for mental health issues related to chronic "spice" use was interviewed in the preparation of this paper. The proposal and plan of the papers was discussed with him, and he wished to remain anonymous in the production of this work. His input particularly helped highlight the need to emphasise individuals' strengths and supports in any assessment of substance misuse.