education

ART OF MEDICINE

I am not a checklist

Medical school and residency training provided me with the skills to diagnose and treat patients, but it was one particular patient during my training who taught me how to be a doctor.

She was in her early 70s with hypertension and a history of cardiac stents. I only had 20 minutes to spend with her at our first meeting and had a lot of ground to cover. I asked about current symptoms, medical and surgical history, drug regimen, etc. I also discussed a treatment plan and reviewed her medical records. I was proud of myself for accomplishing these tasks in the allotted time.

At her next appointment, I started to inquire about interval history, etc. About a minute into our appointment, she asked, "Doc, do you know anything about me as a person? You haven't asked a single question about me." I turned red in embarrassment.

Before I could muster a response, she continued, "I know you are a new doctor. Let me share some advice. Get to know your patients as unique individuals. I have high blood pressure and heart problems, but I am different from the next patient with the same complaints. We are more than a checklist of symptoms."

She was right. No two patients with identical complaints are the same. They come from diverse backgrounds and have their own views about their illness and treatment. As such, they can respond differently to the same treatment. Even asking one personal question can let our patients know that we don't view them as simply a label.

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We welcome contributions to this column via our online editorial office: https://mc.manuscriptcentral.com/bmj

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PRACTICE UPDATES

Diagnosing and treating tuberculosis

A NICE quality standard on tuberculosis recommends that the following groups should be tested for latent TB: people aged 16-35 years who have arrived in this country within the past five years from areas with a high incidence of TB; and adults <65 years old with HIV infection. It also recommends people with active TB from under-served groups are offered directly observed therapy; people with features suggestive of active TB are assessed within one working day; and homeless people with active pulmonary TB are offered accommodation for the duration of their treatment.

http://bit.ly/NICETB

Learning disabilities and mental health

Young people and adults with learning disabilities should have an annual health check that includes a review of mental health problems, says a new quality standard. Any referral for a mental health assessment should be to a professional with expertise in mental health problems in people with learning disabilities. People with a serious mental illness should have a key worker to coordinate their care, and those taking antipsychotics should have annual documentation of the reasons for this prescription.

http://bit.ly/LDmentalhealth

If you would like to write a Case Review for Endgames (see page 167), please see our author guidelines at http://bit.ly/29HCBAL and submit online at http://bit.ly/29yyGSx

FAST FACT—WELLS CRITERIA FOR DVT

To apply the Wells criteria to assess the risk of deep vein thrombosis (DVT), there should be a clinical suspicion of acute leg DVT, and patients should:

- Be symptomatic within the preceding 72 hours
- Not be pregnant or in the postpartum period
- Not be taking a treatment dose of anticoagulant (including vitamin K antagonist, low molecular weight heparin, or direct oral anticoagulant).

If these conditions are not met, you should consider definitive imaging as a first line investigation.

For more information visit BMJ Learning (http://bit.ly/DVTWells)

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CLINICAL UPDATE

CPD READING LEARNING MODULE

0.5 HOURS

Novel psychoactive substances: types, mechanisms of action, and effects

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This is an edited version; the full version is on bmj.com

thebmj.com

Read more about drug policy, including *The BMJ*'s stance at bmj.com/war-on-drugs

In 2016 the Psychoactive Substances Bill banned trading but not possession of all current and future novel psychoactive substances (NPS), sometimes incorrectly called "legal highs," in an attempt to overcome rapid proliferation of these compounds. Over 560 substances are currently monitored by the European Monitoring Centre for Drugs and Drug Addiction, with 100 new agents identified in 2015 alone. Stimulants and synthetic cannabinoids account for the vast majority and are the types most commonly clinically encountered.[1] Online purchases are increasing according to the 2016 Global Drug Survey,[2] potentially in response to legislative changes, as is overall NPS use: lifetime consumption was reported by 8% of younger individuals in 2015, up from 5% in 2011, with figures relatively similar between sexes and different countries.[3]

Professionals report feeling less confident about managing NPS compared with established recreational drugs.[4] Information on NPS primarily stems from case reports and case series. However, there is evidence that risks associated with NPS are often different from those seen with established recreational drugs. This article classifies NPS into their major groupings and provides information on the desired effects of these compounds, their pharmacology, and the risks associated with their use. The linked Practice article[7] provides advice on what to ask and do when consulting with a patient who may be using NPS.

WHAT YOU NEED TO KNOW

- Novel psychoactive substances (NPS, "legal highs") are compounds designed to mimic existing established recreational drugs.
- Legislation regarding NPS varies internationally. In the UK it is now illegal to distribute or sell NPS, but possession is not a criminal offence
- NPS should not be regarded as safer than established recreational drugs
- The most commonly clinically encountered NPS are stimulants (such as mephedrone) and cannabinoids (such as "spice")
- Psychiatric and rehabilitation units, prisons, and schools face particular challenges in detecting and preventing use

HOW PATIENTS WERE INVOLVED IN THE PRODUCTION OF THIS ARTICLE

A patient with long term harmful use of NPS, including associated mental ill health, was involved in the initial design of this article. This particularly helped frame the discussion on the potential harms of these compounds. The patient wishes to remain anonymous.

INFORMATION FOR PATIENTS WHO ASK ABOUT NPS

- In the UK the Psychoactive Substances Bill states that individuals will be prosecuted for trading, but not possession, of NPS. It is uncertain how monitoring and enforcing will work in practice, but one effect is that supply chains will move away from high street "head shops"
- NPS do not seem to be safer than established recreational drugs, either in the short or longer term, though there is considerable variation in risks between individual NPS and classes of NPS
- If using a novel substance, as with any drug, start with a very small dose and increase to obtain desired effects
- Individuals can have different responses to the same drug, and combining with other recreational, prescription, or over the counter drugs or alcohol can increase risks
- Seek urgent medical help if you or a friend feel unwell after using an NPS (as with any recreational drug). Call 999 for an ambulance; take the compound or any information on it with you if possible

Cannabinoid NPS

Synthetic cannabinoid receptor agonists (SCRAs)

"Spice" "Noids" "Black mamba"

"Clockwork Orange" "Pandora's Box"

Typically full agonists of cannabinoid receptors, producing a pleasant state of relaxation and of feeling "stoned"

Smoked after being sprayed on to herbal mixtures

Inhaled using e-cigarettes and vapourisers

Short term risks:

Psychosis · Agitation · Confusion · Slurred speech · Cognitive impairment · Renal failure · Tachycardia · Hypertension · Myocardial infarction · Pulmonary damage · Seizures

Long term risks:

Psychological dependency · Addictive potential · Psychotic illnesses

Psychological withdrawal effects likely after cessation

Depressant NPS

Opioids

AH-7921 MT-45

Novel fentanyls

Similar to established recreational opioids, but with the potential for much longer durations of action

Benzodiazepines

Diclazepam

Flubromazepam

Sedative, anxiolytic, hypnotic, and anticonvulsant properties–some with long duration of action

Smoked

Swallowed Pills / tablets

Injected

Nasal

Short term risks:

Overdose · Confusional states · Seizures after withdrawal

Novel opioids may need more naloxone than traditional opioids

Long term risks:

Addiction · Impaired cognition

Potential for withdrawal effects after cessation

Stimulant NPS

Cathinone family, such as mephedrone (M-cat)

"Bath salts" "Plant food"

Increase synaptic levels of serotonin, dopamine, and/or noradrenaline to produce a sense of euphoria and wellbeing—a "high"

Commonly: Swallowed "Bombing"/pills · Nasal "Snorting"

Less commonly: Injected "Slamming" · Rectal "Plugging"

Short term risks:

Agitation · Psychotic symptoms · Hyperthermia · Anxiety · Hypervigilance · Cardiovascular toxicity · Seizures · Renal / respiratory failure · Delirium · Serotonin syndrome · Stroke

Long term risks:

Impulsive behaviour · Dependency · Depression · Cognitive impairments · Psychosis

Psychological withdrawal effects common after cessation

Hallucinogenic NPS

Psychedelics

5-MeO-DALT

NBOMe-series

2C-series

Produce perceptual alterations and quasi-mystical experiences. Some have stimulant properties

Dissociatives

Methoxetamine (mexxy)

Similar to ketamine and phencyclidine

Produce a euphoric, dissociated state, with a perception of disconnection from physical body

Swallowed Paper/capsules/liquid

Swallowed "Bombing"/pills · Nasal "Snorting"

Injected

Short term risks:

Accidents / trauma · Aggressive / psychotic states · Acute cerebellar toxicity · Cardiovascular toxicity · Respiratory failure

Long term risks:

Addiction · Problems with mood / memory · Cardiovascular problems · Abdominal pain · Kidney / bladder / urinary tract damage

(ketamine/methoxetamine)

What are NPS and how do they work?

NPS are compounds designed to mimic existing established recreational drugs such as "ecstasy" (MDMA) and cannabis. Before changes in the law, manufacturers would tweak the pharmacological structure of existing compounds to create a new "legal" substance, which earned them their familiar name "legal highs." There is no universally agreed way to categorise NPS. However, they can be broken down into four, somewhat overlapping, main categories: stimulants, cannabinoids, hallucinogens, and depressants (see infographic).

Competing interests: None declared.

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Find the full version with references at http://dx.doi.org/10.1136/bmj.i6848

PRACTICE, p 160

Cannabinoid NPS

Cannabis is the most widely used established recreational drug.[1] NPS variants are the synthetic cannabinoid receptor agonists (SCRAs), and there are over 150 different SCRAs available, usually sold having been sprayed onto herbal mixtures that are smoked. They are sometimes referred to as "spice" or "noids." Liquid SCRAs also exist for use in electronic cigarettes and vapourisers. They produce a pleasant state of relaxation and of feeling "stoned."

The major psychoactive component of cannabis is tetrahydrocannabinol, a partial agonist at cannabinoid receptors that ordinarily have roles in neuronal homeostasis and immune functioning.[27] However, SCRAs are typically full agonists of, and bind in a different pattern to, cannabinoid receptor subtypes. SCRAs also lack cannabidiol, an antipsychotic and anxiolytic compound found in cannabis that dampens some of the effects of tetrahydrocannabinol. These pharmacological differences may explain the variation in the subjective and physiological effects of SCRAs compared with cannabis.[28-30]

Risks

As well as a subjective effect of feeling stoned, cannabis and SCRAs can be both stimulating and sedating, anxiogenic and anxiolytic.[27 31] Both can cause anxiety, paranoia, and psychotic symptoms.[32 33]

Side effects have been reported more frequently with SCRAs than with cannabis,[28] and, as they are most commonly sprayed onto compounds for smoking, their strength and effects can be less predictable. Some highly potent agents can induce considerably agitated states.[31]Unlike cannabis, some produce a "hangover" state.[34] Emergency department case reports describe additional features with SCRA use not typically seen with cannabis, such as confusion and cognitive impairment, slurred speech, and excessive sweating, as well as symptoms of stimulant toxicity (hypertension, tachycardia),[32 35] renal failure, pulmonary damage, myocardial infarction, seizures, and stroke.[32-38]

In the longer term, cannabis is not traditionally considered to produce physical dependency, though individuals can demonstrate a psychological dependency.[39] Case reports and user discussion forums suggest that SCRAs have a higher potential for addiction and withdrawal effects.[40-42]

Depressant NPS

Depressant NPS subcategories—benzodiazepines and opioids—seem to carry a similar picture for acute emergency presentations but differ in their mental health implications. They are generally sold and consumed in pill or powder form. They are perhaps the least understood of the NPS. This may be because they are so similar to established recreational drugs that clinicians may not be aware that an individual has used an NPS version. NPS benzodiazepines include diclazepam and flubromazepam. Fewer NPS opioids have appeared in isolation, but they may be sold as part of NPS cannabinoid smoking mixtures, as has been reported for AH-7921.[62]

Benzodiazepines

These are positive allosteric modulators of the GABA receptor, enhancing inhibitory signalling in the central nervous system.[10] Alcohol has a similar pharmacodynamic mechanism and can potentiate their effects.[10] Acutely, NPS benzodiazepines have similar clinical effects to those of established compounds such as diazepam, with sedative, anxiolytic, hypnotic, and anticonvulsant properties. Some users of NPS benzodiazepines report that they have much longer durations of actions and effects than established agents, and several compounds have long half lives (flubromazepam, for example, having a half life of 100 hours[63]). While this reduces dependency potential, unwanted effects can persist for a long time and there are greater risks of accidental overdose. There are reports of NPS benzodiazepine induced confusional states lasting several days.[64] Acute withdrawal may cause seizures.[65] Long term use is associated with risk of addiction and impaired cognition,[66] physiological and mental health sequelae consistent with traditional benzodiazepines.[65]

Opioid NPS

Little is known about any specific subjective effects of NPS opioids to differentiate them from established recreational opioids. However, self experimentation reports suggest that some can have much longer durations of action.[67 68] They exert their euphoric effects through presynaptic μ-opioid receptors. Novel agents such as AH-7921, MT-45, and novel fentanyls seem to have similar mechanisms of action.[67 69]

Case reports of NPS overdoses are congruent with those of traditional opioids, though animal data suggest AH-7921 has a higher overdose risk than morphine.[67] Both human case series and animal studies have shown that naloxone can reverse the toxicity seen with novel opioids, although the doses of naloxone required may be higher than for traditional opioids, particularly in cases of novel fentanyl toxicity.[67-71] There have been reports of unusual toxicity related to the use of MT-45, including short-to-medium term hearing loss.[71]

No long term NPS risk data exist, though animal models have shown AH-7921 to be similar to morphine in addictive potential and withdrawal effects,[67] and MT-45 and novel fentanyls are probably similar.

Stimulant NPS

Stimulants are taken to produce a sense of euphoria and wellbeing, or "a high." This is one of the largest NPS groups, typically sold as powders or pills. Mephedrone is the most commonly available variant. They are structurally related to MDMA (ecstasy), cocaine, and amphetamines and can be swallowed (users often talk about "bombing," when the drugs are swallowed wrapped in paper), inhaled ("snorting"), and, less commonly, injected or administered rectally.

Stimulants increase synaptic levels of serotonin, dopamine, and/or noradrenaline. Agents act as neuronal reuptake pump inhibitors or as active releasers, and each has an unique effect on neurotransmitter concentrations.[8 9] Neurotransmitter releasers are associated with greater addiction and neurotoxicity.[10 11] NPS variants, such as the large cathinone family, are commonly associated with enhanced neurotoxicity compared with traditional stimulants.[9 12]

The ratio of serotonin to dopamine activation is important in achieving the desired effects. The more serotonergic drugs, similar to ecstasy, produce more empathy and emotional openness.[13 14] More dopaminergic drugs, similar to cocaine, produce more euphoric and mania-like experiences.[15] Some NPS stimulants, such as the NBOMe- and 2C-series, also produce psychedelic or hallucinogenic experiences.[16 17]

Risks

Acute adverse presentations are most commonly associated with agitation, anxiety, psychotic symptoms, hypervigilance, cardiovascular toxicity (arrhythmias and hypertension), and hyperthermia. Case reports also describe seizures, delirium, and renal and respiratory failure following ingestion.[18-21] Serotonin syndrome—autonomic instability, confusion, and neuromuscular problems—can be life threatening and is particularly associated with use of multiple serotonergic recreational drugs, or concomitant use of serotonergic prescription medication or over the counter medicines such as St John's wort.[15 22]

Long term, traditional stimulants are associated with impulsive behaviour, abuse, and dependency,[15] and NPS stimulants seem no different.[23] Depression and cognitive impairments are recognised sequelae,[24] and there are case reports of psychoses.[25 26] Cessation can lead to a psychological withdrawal syndrome of fatigue, insomnia, lethargy, flu-like symptoms, impaired concentration, and lability of mood.[23] There is considerable variation between individuals, but such outcomes are more commonly associated with longer term and more regular drug use.

Hallucinogenic NPS

Hallucinogens fall into two subcategories—dissociatives and psychedelics (or classical hallucinogens). Dissociatives are particularly associated with harmful side effects.

Dissociatives

Dissociatives produce a unique euphoric "dissociated" state, with a perception of an absence of time, weightlessness, and disconnection from the physical body. They can be inhaled, swallowed, or injected. The first agents in this class, ketamine and phencyclidine (PCP), were originally used as general anaesthetics, but they have generally been discontinued because of postoperative dissociative side effects. The spectrum of NPS dissociatives runs between some milder than ketamine to others as strong as phencyclidine.[10] The common variant methoxetamine (sometimes called "mexxy") is generally reported to produce more intense and longer lasting dissociative effects than ketamine.[43] In extremis, users may enter an "m hole" (similar to a "k hole" with ketamine), a state of profound dissociation that some people find highly pleasurable and others unpleasant.[10-47] They primarily act as uncompetitive antagonists at glutamatergic NMDA receptors,[48] but also bind at opioid and monoaminergic receptors.[10]

Risks

Most risk data come from the parent compounds ketamine and phencyclidine, though the evidence emerging from NPS case studies literature fits with these.[46 47] Deaths are primarily accidental, through impulsive and careless behaviours,[10] although there are reports of fatalities directly linked to methoxetamine toxicity.[49 50] Consistent with ketamine and phencyclidine, there are case reports of aggressive, psychotic, and catatonic states with dissociative NPS use, acute cerebellar toxicity, cardiovascular incidents, and renal and acute respiratory failure.[10-51] Methoxetamine was anecdotally sold as a physically safer alternative to ketamine, but there is limited evidence to support this currently.[50]

Longer term, dissociatives often produce considerable cravings and binge consumption patterns, although there is some evidence that methoxetamine may be less addictive than ketamine.[50] Long term sequelae of use can include neurocognitive deficits and deterioration in mood.[52 53] Physical health complications include abdominal pain ("M cramps"), nausea, vomiting, and diarrhoea; cardiovascular problems of arrhythmias and blackouts[10]; and severe ulcerative cystitis and renal damage.[54]

Psychedelics

These agents typically do not produce true hallucinations, but are associated with a range of "psychedelic" effects, including perceptual alterations and quasi-mystical experiences sometimes categorised under the headings of "oceanic boundlessness" and "anxious ego dissolution."[55 56]

These exert their effects primarily as an agonist at the 5-HT_{2A} receptor. There is some evidence they may also act on 5-HT_{1A} and heteromer receptor complexes.[56] Traditional agents include LSD and psilocybin; most NPS psychedelics, such as 5-MeO-DALT and the NBOMe- or 2C-series, also have stimulant effects.[10-58]

Risks

Psychedelics generally have a low risk-profile compared with both other established recreational drugs and NPS. Consumers seldom present acutely to clinical services, though acute intoxication may contribute to adverse mood reactions.[56] Unlike established recreational psychedelics, some NPS hallucinogens also have stimulant properties, and these have increased risk of acute toxicity, including agitation, hallucinations, tachycardia, hypertension, hyperthermia, rhabdomyolysis, serotonin syndrome, and seizures.[57-61] There is currently little evidence of longer term health risks or addiction.[56]

PRACTICE POINTER

CPD READING LEARNING MODULE
0.5 HOURS

Novel psychoactive substances: acute and chronic use

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Identifying and managing acute drug related harms and problematic substance misuse cuts across medical specialties. 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.

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.

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 were 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.

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

Exploring NPS use

A sensitive, non-judgmental approach is essential. 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 for 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 whether 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[16]: 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

Box 1 | Case scenario 1: emergency presentation

A 29 year old man is bought 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 hyper-reflexia in his lower limbs, and 5-6 beats of inducible ankle clonus. His friends told paramedics he had taken a "white powder" that he bought as a legal high on the internet.

Spotting acute use

A 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)[2]—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.[3-5] 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 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) causes a similar picture, so it is important to ask about prescribed medications and other medical and psychiatric problems. Finally, certain 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.[6 7]

The most commonly reported clinical features of mephedrone toxity are agitation or aggression, tachycardia, and hypertension

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.[3-13] Some case series report concomitant use of other drugs, and thus some of the symptoms reported may relate to these rather than to mephedrone.[11]

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.[14]

Management includes preventing further exposure to serotonergic drugs (including prescribed medications) and treating the stimulant clinical features.

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.[15]

Avoid the use of pejorative terms or labels such as "addict" and ensure a supportive 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 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.

Avoid the use of perjorative terms or labels such as "addict" and ensure a supportive approach to discussions

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

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

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

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

A*dvice* Straightforward advice on how drug use can be changed

M*enu* Provide the individual with their therapeutic options, and facilitate their decision making

E*mpathy* Have a non-judgmental and warm clinical approach

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

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[17] is a well 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.

Competing interests: None declared.

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Find the full version with references at http://dx.doi.org/10.1136/bmj.6814

CLINICAL UPDATES, p 156

The FRAMES approach is a well established model used in many substance misuse services and can be a useful strategy

RESOURCES FOR HEALTHCARE PROFESSIONALS

- **UK National Poisons Information Service and its clinical toxicology database TOXBASE** If you need advice or information that is not available on TOXBASE then call NPIS for clinical support (www.npis.org; www.toxbase.org)
- **NEPTUNE** (novel psychoactive treatment: UK network) Comprehensive clinical guidance on party drugs (http://neptune-clinical-guidance.co.uk)
- **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
- **New Psychoactive Substances (NPS) resource pack** UK Home Office NPS resource pack for "informal educators and frontline practitioners" (www.gov.uk/government/publications/new-psychoactive-substances-nps-resource-pack)
- **EMCDDA.** Guide to the European illicit drugs' market (www.emcdda.europa.eu/start/2016/drug-markets)

RESOURCES FOR DRUG CONSUMERS AND THE PUBLIC

- **FRANK** UK based general information guide offering friendly, confidential advice to patients and the lay public (www.talktofrank.com)
- **EROWID** Non-profit, international, drug-consumer-led website providing non-judgmental advice and guidance (www.erowid.org)
- **Rise Above** Website by NHS England for children and adolescents about substance misuse, mental health, and other social issues (http://riseabove.org.uk/tag/drinking-smoking-drugs/)
- **Bowden-Jones O.** *The Drug Conversation: How to talk to your child about drugs*. Royal College of Psychiatrists, 2016
- **Global Drug Survey** Information for, and international survey of, NPS consumers (www.globaldrugsurvey.com)
- **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/)—Guide to legislative changes in the UK

CASE REVIEW

Tiredness in a patient treated with itraconazole

A 72 year old woman with allergic bronchopulmonary aspergillosis and asthma presented to the emergency department with a two week history of increasing tiredness and shortness of breath. She had no headache, visual disturbance, abdominal pain, nausea, vomiting, or collapse. Her medication included Seretide 250 Evohaler (fluticasone 250 µg and salmeterol 25 µg) one puff twice daily for four years and inhaled Salbutamol. She had been treated with itraconazole 200 mg daily for two years, after unsuccessful attempts to stop this medication due to recurrence of the disease. She had never required treatment with oral corticosteroids. There was no family history of autoimmune disorders.

Observations were stable on admission, specifically no postural hypotension. General physical examination was unremarkable. There was no hyperpigmentation, and no visual field defects or clinical features of Cushing's syndrome. Full blood count, serum glucose, renal, and liver function tests were within normal limits. Random serum cortisol (1300 hours) was 4 nmol/L (9 am cortisol range, 138-635). Pituitary profile tests including TSH, FSH, LH, prolactin, and IGF-1 were within normal limits for the patient's age. Adrenocorticotrophic hormone was less than 10 ng/L (7-51) and adrenal autoantibodies were negative. Chest radiograph and magnetic resonance imaging of pituitary showed no abnormal findings.

1 What is the most likely diagnosis based on the hormone profile?
2 What is the likely cause of the diagnosis in this case?
3 How would you manage and follow up with this patient?

Submitted by Preethi Nalla, Thomas Alexander Dacruz, and Kofi Obuobie

Patient consent obtained.

Cite this as: *BMJ* 2017;356:i6819

If you would like to write a Case Review for Endgames, please see our author guidelines at http://bit.ly/29HCBAL and submit online at http://bit.ly/29yyGSx

SPOT DIAGNOSIS

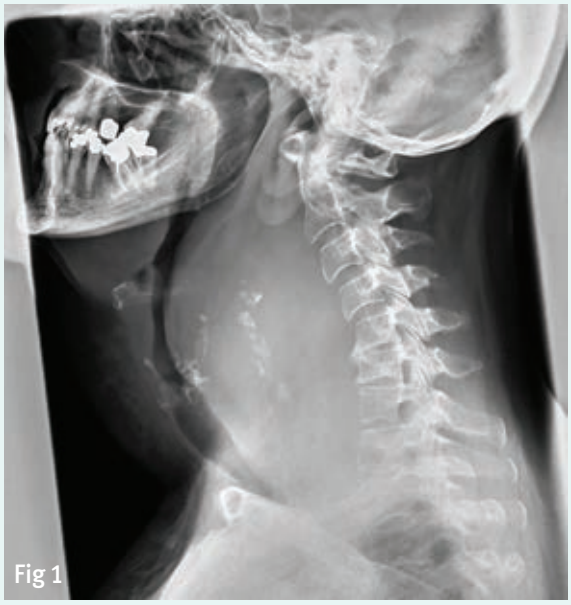


Fig 1

Management of subacute airway emergency after blunt neck trauma

A 60 year old woman was admitted after a fall, where she sustained a direct trauma to the anterior neck. She had a progressively worsening hoarse voice, difficulty swallowing, and pain with neck movement. The neck was visibly swollen with bruising tracking onto the anterior chest wall. There was no tenderness on palpation of the cervical spine. A lateral radiograph was taken (fig 1). What does the image show?

Submitted by Emily Lowe and Sachin Patil

Patient consent obtained.

Cite this as: *BMJ* 2017;356:j141

answers

CASE REVIEW

Tiredness in a patient treated with itraconazole

1 The hormone profile indicates secondary adrenal insufficiency. This explains the symptoms of tiredness and shortness of breath coupled with a very low serum cortisol (4 nmol/L) and a supressed adrenocorticotrophic hormone level.
2 Iatrogenic—it is likely that the interaction between oral itraconazole and inhaled fluticasone caused suppression of the hypothalamic-pituitary-adrenal axis.
3 Ensuring haemodynamic stability, replacement of intravenous fluids, and glucocorticoids are the mainstays of acute management. Chronic management includes timely assessment of hypothalamic-pituitary-adrenal axis function and considering the withdrawal of the medication causing adrenal insufficiency.

SPOT DIAGNOSIS

Management of subacute airway emergency after blunt neck trauma

The radiograph shows a massive retropharyngeal haematoma, with distortion of the upper aerodigestive tract and loss of normal cervical lordosis. The patient underwent awake flexible bronchoscopic intubation before emergency surgical tracheostomy and drainage of the haematoma. Fig 2 shows a postoperative computed tomography scan.

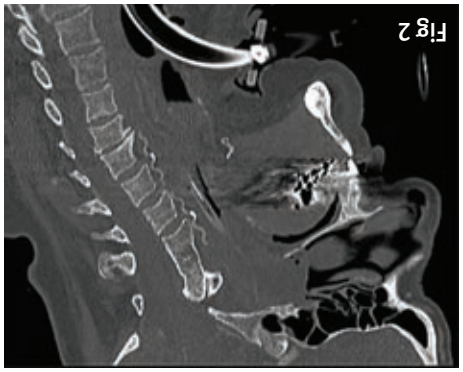


Fig 2

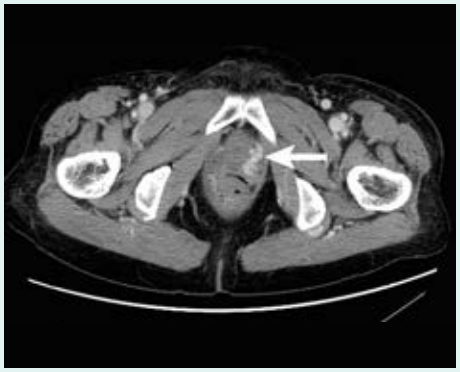
Vulvar varicosity

A 60 year old woman presented with the sensation of a swelling in the left vulvovaginal area after prolonged standing. Visual examination showed no abnormalities; however, a non-tender compressible mass in the left labia majora was palpable, suggesting vulvar varicosity. Most vulvar varicosities occur in pregnant women and regress spontaneously, and they are rare in non-pregnant women. We suspected a pelvic tumour was compressing the intrapelvic veins draining the vulvar veins. Contrast enhanced computed tomography (figure) showed dilated vaginal venous plexus and a left ovarian tumour; a high grade serous adenocarcinoma. Elderly onset pelvic congestion syndrome can be a rare sign for ovarian cancer, which is often asymptomatic until its advanced stage.

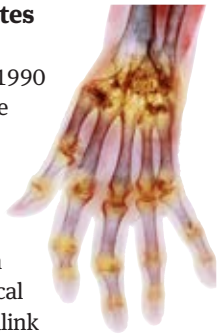
Takeshi Kondo (reds_liverpool_2005@yahoo.co.jp); Takanori Uehara; Kazutaka Noda; Yoshiyuki Ohira; Masatomi Ikusaka, Department of General Medicine, Chiba University Hospital, Chiba City, Chiba, Japan

Patient consent obtained.

Cite this as: *BMJ* 2017;356:i6332



UK rheumatoid rates are falling



During the years from 1990 to 2014, the prevalence of rheumatoid arthritis in the UK first rose a little up to 2005, and is now slowly falling, according to an analysis from the Clinical Practice Research Datalink (*Rheumatology* doi: 10.1093/rheumatology/kew468). This was driven by a 1.6% decrease in the annual incidence of rheumatoid arthritis throughout that period. But the "middle east" of England remains disproportionately affected, with incidence remaining highest in East Midlands, Yorkshire, and Humber.

Listeria and proton pump inhibitors

Systemic infection with food-borne *Listeria monocytogenes* is rare, but comes with a case-fatality rate of 20% or higher. A case-control study based on the whole population of Denmark identified 721 cases of listeriosis in people aged 45 and over, and compared them with 34 800 matched controls (*Clin Infect Dis* doi: 10.1093/cid/ciw860). People who got infected were nearly three times more likely to have been taking proton pump inhibitors. Maybe a bit of hydrochloric acid in the stomach does frazzle up some bad germs.

Underbreathing and listeria

Listeria hysteria is the name given to sporadic inflammation of the news media when it gets worked up about these nasty germs. But whereas hysteria usually causes hyperventilation, brain infection with listeria is more likely to cause hypoventilation. A woman who suffered from *Listeria monocytogenes* rhombencephalitis in 1977 was later found to have central sleep apnoea and daytime hypoxaemia (*Thorax* doi:10.1136/thoraxjnl-2016-208786). Extensive investigation in a French hospital clinic confirmed that this was a result of her earlier infection, but it was not until 2012 that she finally accepted treatment with nocturnal ventilation.

Type 2 diabetes and life expectancy

The epidemiology of type 2 diabetes in the UK gives little cause for comfort, but there is one subgroup who seem to do well despite running blood sugars above the defining threshold—older people of South Asian origin. A study based on the Clinical Practice Research Datalink shows that beyond the age of 65 years, South Asians with diabetes have up to 1.1 years' longer life expectancy than South Asians without diabetes (*Diabetes Care* doi: 10.2337/dc16-1616). On the other hand, developing diabetes at 40 knocks five years off life expectancy for men and six for women.

Repairing the drum of war

Tympanic membrane perforation is the most common primary blast injury, occurring in 8% to 16% of those wounded by explosives. Nearly all the American servicemen who suffered ear drum damage in the wars in Iraq and Afghanistan ended up being treated by a single neurotologist in Washington DC, and he has published his five year results in (*Otolaryngol Head Neck Surg* doi: 10.1177/0194599816677693). The overall success for grafting was 77% and was highest in soldiers under age 34. Timing to surgery did not appear to affect outcomes.

Patients rate care for serious illness

A new tool is designed to help patients rate their care through the course of serious illness (*BMC Palliative Care* doi: 10.1186/s12904-016-0172-x). "When administered earlier in the chronic illness trajectory, a new patient experience scale focused on care teams across settings, communication, and care goals, displayed strong reliability and performed well psychometrically." Sounds promising for clinical as well as research settings.

Zapping your brain at home

Transcranial direct current stimulators, below, designed for home use (pictured) are not a new phenomenon. Electricity was first used on patients in the Middlesex hospital in 1767, and an article in (*Brain Stimul* doi: 10.1016/j.brs.2016.11.081) describes how the late 19th and early 20th centuries saw a proliferation of electrical stimulation devices ("medical batteries") used to alleviate depression, anxiety, and neurasthenia. Minerva contents herself with lightning on Mount Olympus.

Cite this as: *BMJ* 2017;356:j327