Designer Drugs: Untested and Dangerous

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Contact hours: 3

Course price: $29

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Course Summary

Designer drugs are synthetic compounds whose molecular structures have been modified based on chemically similar illicit drugs. The newly created substances can often be purchased legally because their modified chemical structures are not covered under existing drug laws. Since, in many cases, designer drugs are not yet illegal, they are inaccurately referred to as “legal highs” or “herbal highs.” This course gives an overview of the types of designer drugs and describes the challenges related to testing and assessment of designer drug use as wells as goals for treatment of designer drug addiction.

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Criteria for Successful Completions

80% or higher on the post test, a completed evaluation form, and payment where required. No partial credit will be awarded.

Course Objectives

1. Provide a definition of the term *designer drugs*.
2. Describe three key aspects of synthetic cathinones.
3. Explain three ways in which synthetic cannabinoids differ from cannabis.
4. List three clinical features of synthetic hallucinogen misuse.
5. Describe two challenges related to testing and assessment of designer drug use.
6. Explain two overall goals for the treatment of designer drug addiction.

Human Experiments Without Informed Consent

Synthetic designer drugs are basically human experiments without informed consent. Every drug we take that is prescribed by a physician has gone through the most rigorous testing: First in animals. . . and then in humans. And in humans it is done so carefully—you measure the doses, you first find out if there's any dose that becomes toxic. Then you go into trials with people who are sick to see if it helps them. In the case of designer drugs none of these precautions have been taken, none of the care has been taken.

> Chemists can make anything, anywhere in the world. Some can be poisonous, downright toxic, some can promote addiction, some can destroy brain cells—you don't know. You are simply walking into a cave without a flashlight, and you are hoping there aren't bears, or scorpions, or rabid bats, or chasms, or crevices that you can fall into. That is why I call it a human experiment without any knowledge on what these drugs can promote in your brain and to the rest of your body.
>
> Dr. Bertha Madras
> Harvard Medical School

Over the last decade, designer drugs have exploded onto the illicit drug scene. When their molecular structure is published, amateur and professional chemists reproduce these drugs, alter them to increase their potency, and flood the market with dangerous untested compounds that are undetectable by most known tests. Very little is known about the effects these drugs will have on the human nervous system because their chemical structure has been tweaked and modified so rapidly and so often that it is impossible for researchers and law enforcement to keep up with the changes.

Designer drugs are synthetic compounds whose molecular structures have been modified based on chemically similar illicit drugs. The newly created substances can often be purchased legally because their modified chemical structures are not covered under existing drug laws. Since, in many cases, designer drugs are not yet illegal, they are inaccurately referred to as "legal highs" or "herbal highs."

Designer drugs are characterized by the U.N. Office on Drugs and Crime as **novel* psychoactive substances (NPS)** and are defined 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" (UNODC, 2014a).

*Novel: Materials identified but never reported in scientific or patent literature—made by changing or modifying known materials.

Designer drugs can be placed into eight groups, although there is some overlap and there are differences in definitions among researchers, law enforcement, and clinicians. This course will focus on three of the groups: (1) synthetic cathinones (bath salts), (2) synthetic cannabinoids, and (3) synthetic hallucinogens, primarily NBOMe.

The other five groups are beyond the scope of this course, but they are listed briefly as follows:

1. **Aminoindanes**: similar to amphetamine; first developed in the 1970s for their analgesic and bronchodilation properties. Aminoindanes have a strong effect on the release and re-uptake of serotonin. This group of designer drugs includes

highly potent selective serotonin releasing agents such as MDAI and 5-IAI—and ETAI, which is an analogue of fenfluramine, a substance formerly marketed as an appetite suppressant. Street names of MDAI include MDAI gold, while 2-AI has been found in party pills known as pink champagnes (UNODC, 2014b).

2. **Ketamine and phencyclidine-type substances**: closely related to phencyclidine (also known as PCP or "angel dust"). Phencyclidine was originally investigated as an intravenous anesthetic in the 1950s but was later withdrawn due to undesired hallucinogenic and delirium effects. Following the withdrawal of phencyclidine, ketamine was synthesized as an anesthetic in 1962, and subsequently patented in Belgium and in the United States. In the early 1970s, ketamine was marketed as a medical alternative to phencyclidine. Ketamine and phencyclidine have similar modes of action, affecting a range of central neurotransmitters. Ketamine is frequently sold as ecstasy. Street names for ketamine include K, special K, kit kat, tac, tic, cat valium, cat tranquilizer, vitamin K, ket, and super K (UNODC, 2014b).
3. **Piperazines**: Although not derived from plants, piperazines are so named because of their chemical similarity to piperidine, a part of the chemical piperine, found in the black pepper plant. Some piperazines have been evaluated as potential therapeutic agents but never brought to market. One piperazine, BZP, was initially developed as a potential antidepressant but was found to have similar properties to amphetamine and therefore liable to abuse. In the 1980s, BZP was used in Hungary to manufacture piberaline, a substance marketed as an antidepressant, but later withdrawn (UNODC, 2014b).

   In the late 1990s, BZP emerged in New Zealand as a "legal alternative" for MDMA (ecstasy) and methamphetamine. In Europe its use was first reported in Sweden in 1999, but it only became widespread as a novel psychoactive substance from 2004 onward until controls over the substance were introduced by the European Union in 2008. Some of the generic names for these substances include pep pills, social tonics, or simply party pills (UNODC, 2014b). Piperazines are frequently sold as ecstasy and are also used in the manufacture of plastics, resins, pesticides, brake fluid, and other industrial materials.
4. **Plant-based substances** (khat, kratom, *salvia divinorum*): the khat shrub (*Catha edulis*) of the Celastraceae family is a plant native to the Horn of Africa and the Arabian Peninsula. Khat (pronounced "cot") chewing is a social custom there. The psychoactive effects result from the release of cathinone and cathine alkaloids when chewed. The khat shrub became known to Europeans in the late eighteenth century and the active constituents of the plant were isolated later; a "katin" alkaloid was identified in 1887, "cathine" in 1930, and "cathinone" in

1975. In Europe and North America, khat was traditionally used by migrant communities from Ethiopia, Kenya, Somalia, and Yemen, but in recent years its use has spread to Bahrain, Canada, Finland, Ireland, Italy, New Zealand, Norway, Oman, and the United States. Hong Kong reported that khat emerged on their markets in 2009, and it was the second most popular plant-based substance, after *salvia divinorum*, reported by Member States from 2009 to 2012. *Catha edulis* is not under international drug control, but cathinone and cathine are listed in Schedules I and III, respectively, of the 1971 Convention (UNODC, 2014b).

5. **Tryptamines**: while some naturally occurring tryptamines are neurotransmitters (serotonin, melatonin, and bufotenin), most are psychoactive hallucinogens found in plants, fungi, and animals. Naturally occurring psilocybin became widespread in the late 1950s in the United States, while synthetic tryptamines appeared on illicit drug markets in the 1990s. Recently, a group of synthetic tryptamines that are derived from DMT and other naturally occurring tryptamines have been reported as novel psychoactive substances. Street names for some tryptamines include foxy-methoxy, alpha-O, alpha, O-DMS, and 5-MEO. Natural tryptamines are available in preparations of dried or brewed mushrooms, while tryptamine derivatives are sold in capsule, tablet, powder, or liquid form (UNODC, 2014b).

Cathinones, Cannabinoids, and Hallucinogens

In the United States (and internationally) synthetic cathinones, synthetic cannabinoids, and synthetic hallucinogens are manufactured and distributed to circumvent drug laws and evade interdiction.* They are intentionally marketed and distributed for recreational use by exploiting inadequacies of existing controlled substance legislation (Weaver et al., 2015).

*Interdiction: A continuum of events focused on interrupting illegal drugs smuggled by air, sea, or land (U.S. Department of Defense).

These compounds (see table below) have evolved rapidly and have largely evaded legal regulation and detection by routine drug testing. Young adults are the primary users, but trends are changing rapidly and use has become popular among members of the military. Acute toxicity is common and multiple deaths have been reported with each of these types of designer drugs (Weaver et al., 2015).

Non-chemists can easily synthesize these compounds with readily available raw materials, or they can obtain the synthetic compounds directly. The chemicals are packaged with labels that do not accurately describe product contents, which may vary substantially regarding chemical content and concentration. Labels often include the phrase, “not for human consumption,” in an attempt to avoid legal risk (Weaver et al., 2015).

Cathinones, Synthetic Cannabinoids, and Synthetic Hallucinogens			
Drug class	Chemical name	Chemical origin	Slang names
Cathinone	Mephedrone	Cathinone	Bath salts (Ivory Wave, Vanilla Sky) meow-meow, M-Cat
	Methylone		
	Methylenedioxypyrovalerone (MDPV)		Sextacy
	Naphyrone		NRG-1
Cannabinoid	JWH-018; JWH-073; JWH-250	Laboratory of J.W. Huffman	Spice, K2, K9, Aroma, herbal highs, Scooby Snax
	CP 47,497; CP 47,497-C8; CP 59,540; cannabicyclohexanol	Pfizer laboratory	
	HU-210	Hebrew University laboratory	
	UR-144	CB2 receptor agonist	
	Oleamide	Fatty acid	
	XLR-11, AKB-48		
	AM-2201, AM-694		
Hallucinogen	25I-NBOMe	Free University of Berlin	N-bomb, Solaris, Smiles, Cimbi-5
	25B-NBOMe		
	25C-NBOMe		

Source: Weaver et al., 2015.

Although the emerging designer drug trend was initially recognized by increased calls to U.S. poison control centers, the incidence of designer drug problems in emergency departments, hospitals, and other medical settings is largely unknown. Only a small percentage of those using designer drugs will come into contact with the healthcare system, but consequences of use can be severe (Weaver et al., 2015).

The growing popularity of designer drugs relates to factors such as novelty, marketing, and accessibility. Designer drug packaging is colorful and attractive, with enticing names for the products to attract younger individuals. Designer drugs are sold without age restriction. Widespread availability, including purchase via the Internet, has contributed to expanded use (Weaver et al., 2015).

Colorful packaging attracts young users of designer drugs. Source: Drug Enforcement Administration.

Clinicians should keep designer drugs in mind when evaluating substance use in young adults or in anyone presenting with acute neuropsychiatric complaints. Treatment of acute intoxication involves supportive care targeting signs and symptoms. Long-term treatment of designer drug use disorder can be challenging and is complicated by a lack of evidence to guide treatment. Familiarity with designer drugs can help clinicians recognize common adverse reactions and life-threatening consequences (Weaver et al., 2015).

Designer drugs affect the brain in a number of ways. Bath salts—synthetic cathinones—act on transporters for the neurotransmitters dopamine, serotonin, and norepinephrine; cocaine, ecstasy, and amphetamines produce their psychoactive effects through these same transporters. Similarly, the synthetic cannabinoids mimic marijuana by activating the same cannabinoid receptors as THC (tetrahydrocannabinol), the main psychoactive component in marijuana (NIDA, 2015a).

Animal studies have shown that designer drugs cause behavioral effects that resemble the drugs of abuse whose mechanisms they share. However, slight differences in chemical structure cause some different effects. For example, the synthetic cathinone MDPV (discussed in the next module) acts on the dopamine transporter 50 times more strongly than cocaine. Synthetic cannabinoids also act on the nervous system differently than non-synthetic cannabis; they are shorter-lasting than THC and are metabolized differently, which could increase potential for abuse and for medication interactions and other toxic effects. Further understanding of both expected and unexpected effects of designer drugs is needed to address their growing availability and to better inform the public of health and safety risks associated with their use (NIDA, 2015a).

Epidemiology of Emerging Designer Drugs

> The appearance of new psychoactive substances (NPS) on the drugs market that are not controlled under international and national drug control laws is not a new phenomenon; many of the substances themselves were first synthesized years ago. The "cat and mouse game," whereby there is a continuous circumvention of existing legislation as new substances appear, can be traced back to the early years of the twentieth century with international attempts to control esters of morphine.
>
> In recent years, however, there has been an increasing commodification of the market in new substances. This has been fueled by entrepreneurs and increasingly organized crime groups who have exploited a growing manufacturing capacity in countries such as China and India and globalized trade. Here, the Internet has played a key role in both the advertisement and sale, allowing an open market to develop. This is reflected in the rapid rate of appearance of NPS, which in Europe over the past few years has averaged one new substance every 5–6 days.
>
> Brandt, King, & Evans-Brown, 2014

Designer drug use is most prevalent among young adults, primarily males in their mid-to-late twenties, but ranging from teens to adults 40 years of age. Those who use designer drugs tend to be single and have lower levels of education and income compared to the general population (Weaver et al., 2015).

Because it is so prevalent, synthetic cannabis has been studied more thoroughly than other designer drugs. Its use may be higher in select subpopulations, particularly regular cannabis users and college students. Among high school seniors, the annual prevalence of synthetic cannabis consumption was 11% in 2011 and 2012. Annual prevalence rates among high school seniors dropped to 8% in 2013, but remained more prevalent than any illicit drug except cannabis (annual use of cannabis remained unchanged) (Weaver et al., 2015).

A *Monitoring the Future* survey looked at synthetic cannabis use in a 2011 survey by asking twelfth graders about their use in the prior 12 months. Annual prevalence was 11.4%, making synthetic cannabis the second most widely used class of illicit drug after marijuana among twelfth graders. Despite the DEA's scheduling of synthetic cannabis as a Schedule I drug in 2011, use among twelfth graders remained unchanged in 2012 at 11.3%, which suggests either that compliance with the new scheduling had been limited or that producers of these products succeeded in continuing to change their chemical formulas to avoid using the ingredients that had been scheduled (Johnston et al., 2015).

In 2012, for the first time, eighth and tenth graders were asked about their use of synthetic cannabis; annual prevalence rates were 4.4% and 8.8%, respectively. Use in all three grades dropped in 2013, with a sharp and significant decline among twelfth graders. The declines continued into 2014 and were significant for both tenth and twelfth graders (Johnston et al., 2015).

All three grades were asked whether they associated great risk with trying synthetic cannabis once or twice. The level of perceived risk for experimental use was quite low (between 24% and 33%) but has been rising somewhat among twelfth graders. Likely the availability of these drugs over the counter has had the effect of communicating to teens that they must be safe, though they are not (Johnston et al., 2015).

Bath salt (synthetic cathinone) use is lower than that of synthetic cannabinoids. Overall use of hallucinogens remains very low in the United States, and the epidemiology of synthetic hallucinogens is not currently captured in national surveys (Weaver et al., 2015).

Data from the National Crime Survey for England and Wales in 2012 shows that 3.3% of adults aged 18 to 24 years had used mephedrone (a novel synthetic cathinone discussed in the next module) within the previous year. On an international level, data from the European Monitoring Centre for Drugs and Drug Addiction's early warning system currently receives a report relating to a newly identified substance about once every week (Smith & Robert, 2014).

Marketing designer drug products as "legal high" alternatives may contribute to the perception of greater safety or purity compared to traditional illicit drugs, which could promote increased consumption. Risk factors for adolescent experimentation with and problems resulting from designer drug use include parents with substance use disorders (SUDs), poor family relationships, poor discipline, or high family conflict; adolescents involved with foster care or the criminal justice system are also at risk (Weaver et al., 2015).

In response to rising designer drug use and its consequences, a series of state and federal initiatives have been enacted during the past several years prohibiting the manufacture, sale, and possession of many designer compounds. Although designer drug use has persisted despite regulatory efforts, there may be a national trend toward reduced consumption of some designer drugs. Use appears to be growing in some subpopulations—including the U.S. military—perhaps to evade detection by urine drug screening. Designer drug use is especially prevalent among those in the military who abuse other substances. Patients presenting for consequences of designer drug use are frequently using more than a single drug (Weaver et al., 2015).

Synthetic Cathinones (Bath Salts)

Cathinones are a loosely defined group of central nervous system stimulants that tend to increase alertness and cause agitation or excitation (NCBI, 2015). Common neurologic effects of cathinone use include anorexia, headache, hyperactivity, insomnia, and tremors as well as depression, panic attacks, and anxiety. Chronic use may result in paranoid psychosis. Cathinones may be addictive.

Catha edulis, a flowering plant native to the Horn of Africa and the Arabian Peninsula. Source: Wikipedia, public domain.

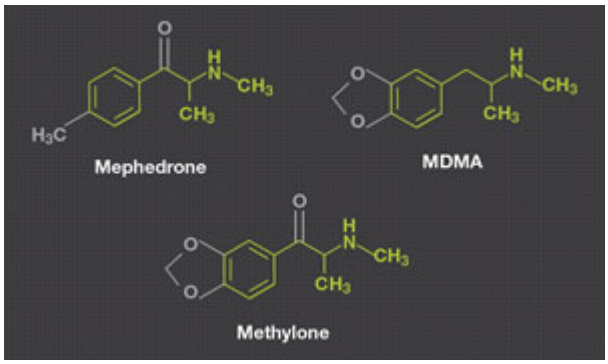
Bundles of khat. Source: Drug Enforcement Administration.

Synthetic cathinones, also referred to as bath salts, are artificially engineered drugs belonging to the phenethylamine* class. They are similar to amphetamine, ecstasy (MDMA), and cathinone structurally and pharmacologically, and all drugs in this category share certain structural similarities. Synthetic cathinone products are also marketed as plant food, fertilizer, insect repellant, pond-cleaner, and vacuum fresheners (Karch, 2015).

*Phenethylamine: a class of organic alkaloid chemicals known for their psychoactive and stimulant effects. Similar to amphetamine in its action at common biomolecular targets, releases norepinephrine and dopamine.

Many of the most common designer stimulants are derivatives of cathinone, the primary active alkaloid in the natural herbal stimulant khat (*Catha edulis*) (Weaver et al., 2015). Khat (pronounced "cot") has been utilized for centuries by indigenous peoples of the Horn of Africa and Arabian Peninsula for its stimulant properties (Watterson & Olive, 2014).

Synthetic Cathinones Are Chemically Related to MDMA (Ecstasy)



Mephedrone, methylone, and MDMA (ecstasy) all share the chemical structures shown in green. Source: NIDA, 2013.

Ecstasy tablets, which allegedly contain MDMA, but may contain adulterants. Source: Wikipedia.

Synthetic cathinones did not appear on the United States' illicit drug market until 2010, but they have been popular drugs of abuse in Europe since 2003 (Karch, 2015). The rise of synthetic cathinone use in the United States was alarmingly rapid, with poison control centers receiving 0, 304, and 6,156 reports of synthetic cathinone toxicity in the years 2009 to 2011, respectively (Watterson & Olive, 2014).

Synthetic Cathinones (Bath Salts) Drug Facts	
Street names	Blizzard, Bloom, Blue Bliss, Charge+, Cloud Nine, Cosmic Blast, Drone, Energy-1, Hurricane Charlie, Ivory Snow, Ivory Wave, Lunar Wave, Meow Meow, Ocean Burst, Pure Ivory, Purple Wave, Red Dove, Scarface, Silk, Snow Leopard, Stardust, Vanilla Sky, White Dove, White Knight, White Lightning, White Rush
Commercial names	No commercial uses for ingested "bath salts"
Common forms	White or brown crystalline powder sold in small plastic or foil packages labeled "not for human consumption" and sometimes sold as jewelry cleaner; tablet, capsule, liquid
Common ways taken	Swallowed, snorted, injected
DEA schedule	Schedule I, some formulations have been banned by the DEA

Source: National Institute on Drug Abuse, 2015b.

Cathinone Pharmacology

Synthetic cathinones (also referred to as "designer substituted cathinones") are part of the larger family of stimulants that includes amphetamine, methamphetamine, and MDMA (ecstasy) (Weaver et al., 2015). They work by stimulating release and inhibiting the re-uptake of norepinephrine, serotonin, and dopamine (Falgiani et al., 2012).

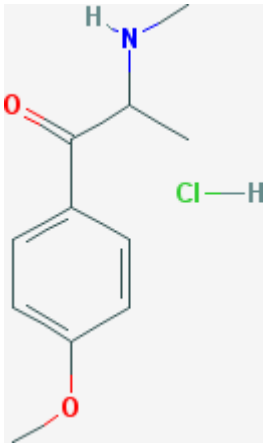
Synthetic cathinones are rapidly absorbed: the "high" is at its most intense 1.5 hours after oral consumption and lasts for 2 to 8 hours, depending on the substance (Hohmann et al., 2014). The pharmacology and product effects (such as increased alertness, tachycardia, and potential for psychosis) appear similar to stimulants such as amphetamines and cocaine (Weaver et al., 2015).

All drugs in this category share certain common structural similarities and yield a group of substances with cathinone as their core structure. Certain synthetic cathinones—methedrone, mephedrone, methylone, and MDVP—seem to be particularly widespread and problematic (Karch, 2015).

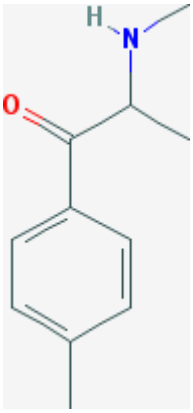
Methedrone, Mephedrone, Methylone, and MDPV

Methedrone, mephedrone, methylone, and MDVP are the most likely active agents found in most bath salts. Of these, mephedrone appears to be the most common synthetic cathinone sold on the recreational market (EMCDDA, 2015).

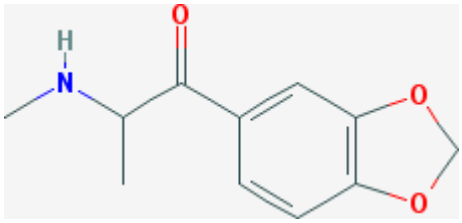
Methedrone, Mephedrone, Methylone, and MDPV



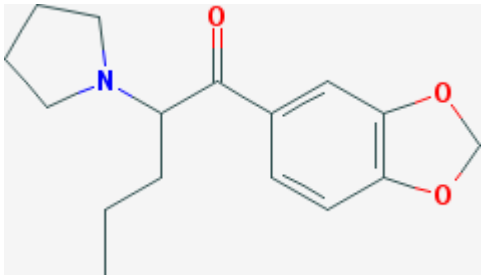
Methedrone



Mephedrone



Methylone



MDPV

Note the similar chemical structure of these four synthetic cathinones. Making a small chemical change alters the effects of the drug and creates a slightly different nervous system response. Source: PubChem, 2015.

Methedrone

Methedrone (meth-a-drone) is a synthetic cathinone first synthesized in 1933. Due to the ease with which synthetic cathinones can be chemically modified to create unique chemical entities, more than forty synthetic cathinones have been identified in clandestine drug markets, including "second generation" synthetic cathinones such as methedrone (Watterson & Olive, 2014).

Methedrone is closely related to methylone and mephedrone and has euphoric and stimulant properties. Very little research has been conducted on methedrone and little is known about its pharmacodynamics. Doses are reported by users to vary from 50 to 500 mg, with its effects lasting from 45 minutes to 2 hours. **Methedrone should not be confused with methadone**.

Mephedrone

Mephedrone (mef-a-drone) is a synthetic central nervous system stimulant that, in very small amounts, can produce psychoactive symptoms such as intense pleasure, feelings of happiness, light-headedness, a distorted sense of time, and reduced appetite, as well as paranoia, increased blood pressure, anxiety, nausea, vomiting, and convulsions. Overdose can lead to seizures, respiratory failure, and death. Based on its chemical structure, mephedrone likely works by blocking re-uptake of, and stimulating the release of, stimulant neurotransmitters such as serotonin, dopamine, and norepinephrine (NCBI, 2015).

Mephedrone was initially synthesized in 1928 but did not become a recreational drug until 2003. It first gained notoriety in Europe, especially in the United Kingdom, because of the remarkably high incidence of hospital admissions, even deaths, associated with its use. The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) reported that during the first quarter of 2010, mephedrone was detected in about twenty European Union Member States (Karch, 2015).

A sample of mephedrone that was confiscated in Oregon, 2009. Source: Drug Enforcement Administration.

The main routes of administration for mephedrone are snorting (nasal insufflation) and swallowing (oral ingestion), sometimes after dissolving with water. As mephedrone is primarily available in powder form, injecting use is reported but appears to be rare (NCBI, 2015).

Symptoms reported anecdotally by users of mephedrone include: numbness and lack of tactile sensitivity, loss of appetite, insomnia, increased mean body temperature ("mephedrone sweat"), decreased mean body temperature, bruxism, elevated heart rate and blood pressure, chest pain, nausea and vomiting, painful joints, discoloration of extremities and joints, abdominal pain, painful nasal drip with presence of blood, light-headedness and dizziness, tremors and convulsions, headaches, cravings, nightmares, loss of concentration and memory loss, anxiety, dysphoria, depression, hallucinations, paranoia, fatigue, and respiratory difficulties (NCBI, 2015).

Thirty-One Cases

Detailed data on 31 cases of acute toxicity associated with self-reported mephedrone use in London since January 2009 indicated the most common clinical symptoms/signs on presentation were:

- Agitation (51.6%)
- Palpitations (25.8%)
- Vomiting (19.4%)
- Self-limiting pre-hospital seizure (9%)
- Bruxism (3.4%)
- Headache (3.4%)

No patients had any skin discoloration or cool/cold peripheries. Twenty-five (80.6 %) patients were discharged either directly from the emergency department or the short-stay observation ward. These patients required either a period of observation prior to discharge and/or symptom control medications.

Four (12.9 %) patients required the use of benzodiazepines for the management of agitation on presentation to the hospital. Of the six patients who were admitted to hospital, four were admitted for observation and management on a general internal medicine ward and two (6.4% of all presentations) required admission to the intensive care unit. All patients survived to leave hospital with no long-term sequelae on discharge.

Source: NCBI, 2015

Methylone

Methylone (meth-a-lone) is an analogue of MDMA (ecstasy). It first appeared in The Netherlands, mixed with mCCP (meta-chlorophenylpiperazine) as the main component of a designer drug called "Explosion." According to United Nations drug monitors, Methylenedioxypyrovalerone (MDPV) and methylone are among the most popular synthetic cathinones. MDMA and mCCP are both semi-synthetic derivatives methcathinone (Karch, 2015).

Three containers of a liquid called "Explosion" sold in The Netherlands in 2004. Analysis identified the liquid to be methylone. Printing on the label reads "Room odorizer Vanilla. Do not ingest. Keep away from children. Never use more than one bottle." Source: Wikipedia, GNU Free Documentation License.

Very little is known about methylone pharmacokinetics but there are unsettling reports that when methylone is co-ingested with MDVP, bizarre behavior, including a number of suicides, deaths, highly violent crimes, and delirium have occurred. The pathophysiology of methylone-related deaths is also poorly understood, but some *in vitro* evidence is emerging, the results of which seem to explain the myriad of symptoms observed. Symptoms seem to fall on a scale somewhere between serotonin syndrome* and excited delirium. The greater the methylone concentration, the greater the agitation produced. Both the psychological and physiologic abnormalities appear to be dose-related (Karch, 2015).

*Serotonin syndrome: occurs when two drugs that affect the body's level of serotonin are taken at the same time. The drugs cause too much serotonin to be released or to remain in the brain area. Serotonin syndrome is more likely to occur when you first start or increase a drug.

Self-Reported Side Effects of Methylone (NCBI, 2015)	
Modest to moderate severity	Most severe
Increase in heart rate and blood pressure	Insomnia
General change in consciousness (as with most psychoactives)	Hyperthermia and sweating
Pupil dilation, can lead to blurred vision	Dizziness, confusion
Difficulty in focusing, restlessness	Depersonalization, hallucinations, paranoia, fear (with high doses)
Change in perception of time	Unwanted life-changing spiritual experiences
Slight increase in body temperature	Gastrointestinal discomfort, nausea and vomiting
Muscle tension and aching	Skin rashes common
Trismus and bruxism	Hangover may include exhaustion, depression, disorientation, headache, amnesia.

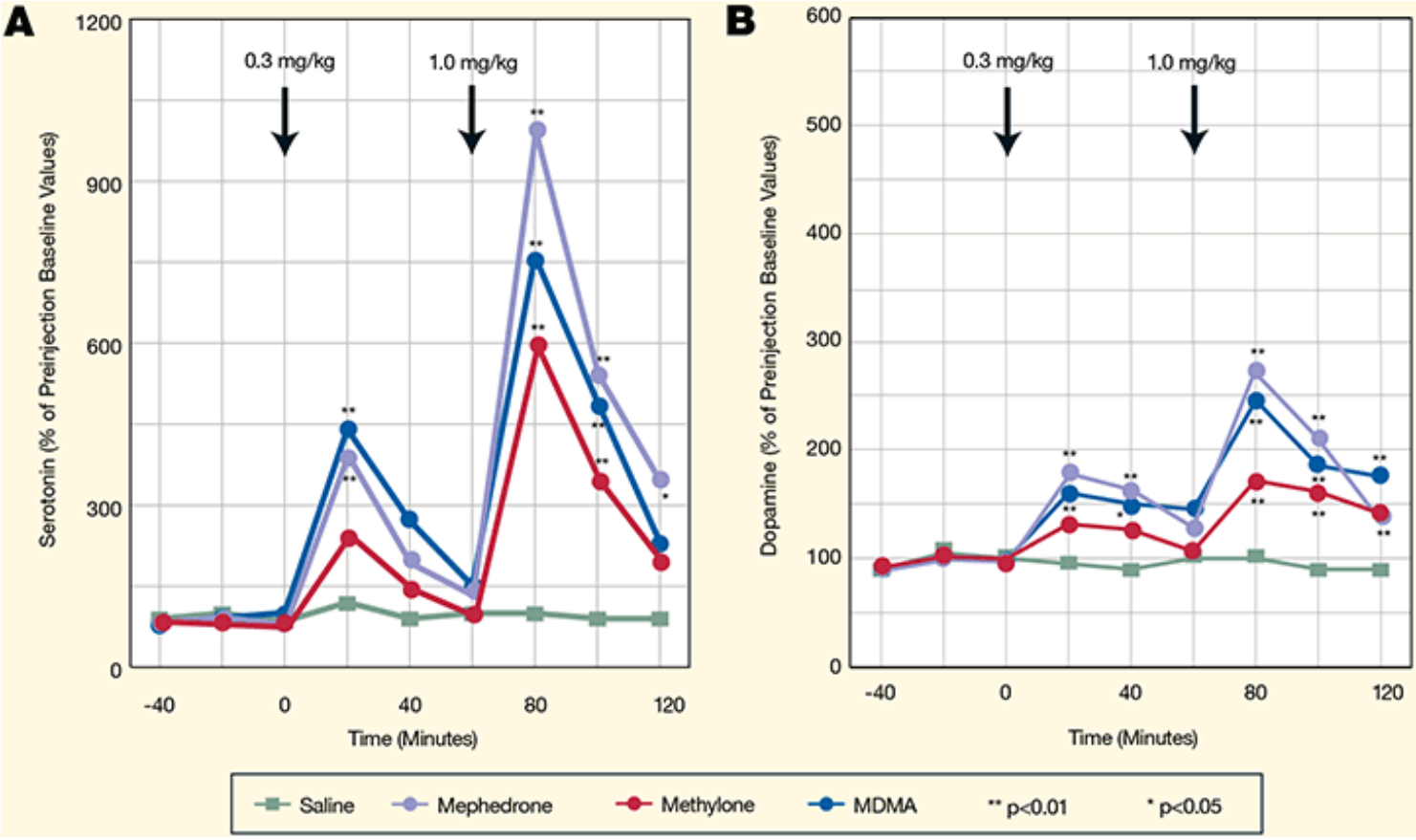
Case

A 22-year-old woman was brought to the emergency department following several episodes of tonicoclonic seizures a few hours after ingesting "legal ecstasy." The patient needed intubation for recurrent seizures and she was found to have severe hyponatremia (120 mmol/L) that was corrected with hypertonic saline. The patient's mental status improved rapidly, and she was extubated the day following her admission. However, she developed prolonged rhabdomyolysis (CK 34.537 U/L) that required a 6-day hospitalization.

The seizures and the hyponatremia may be explained by the MDMA-like characteristics of methylone that may induce inappropriate secretion of antidiuretic hormone mediated via the serotonin system. The combination of methylone and ethcatinone (both acting like serotonin re-uptake inhibitors) might have contributed to neurologic manifestations compatible with serotonin toxicity, although the patient never had autonomic instability. The patient had a prolonged period of rhabdomyolysis which may also be explained by excessive serotonin activity resulting in an increased motor hyperactivity.

Source: NCBI, 2015.

Mephedrone and Methylone Increase Extracellular Serotonin and Dopamine



Direct measurements of neurochemical release in the nucleus accumbens of living rats show that the higher the dose of mephedrone and methylone, the greater the increase in extracellular dopamine and serotonin levels. Like MDMA, the drugs produce a greater effect on serotonin (Figure 1A) than on dopamine (Figure 1B). Asterisks indicate a significant difference compared to saline-injected controls at a particular time point. Source: NIDA Notes, 2013.

MDPV: Methylenedioxypyrovalerone

Methylenedioxypyrovalerone (MDPV) is a derivative of pyrovalerone, which is a psychoactive drug that in the past was used to treat chronic lethargy and fatigue (Karch, 2015). As such, MDPV is one of many "failed" pharmaceuticals (substances originally developed as potential therapeutic agents, but never brought to market as licensed medicines). An important feature of the designer drug phenomenon has been the re-discovery of these agents as a potential source for commercial distribution on the illicit drug market (Brandt et al., 2014).

MDPV differs from other synthetic cathinones because it contains a pyrrolidine ring, which makes the drug a potent uptake blocker at dopamine and norepinephrine transporters, in much the same fashion as methylone. Although MDPV, mephedrone, and methylone are now controlled drugs, a group of MDPV derivatives remains legal (Karch, 2015).

The most frequently encountered MDVP derivatives are referred to as **pyrrolidinophenones**. Alpha-pyrrolidinovalerophenone (alpha-PVP) is the one most frequently encountered. In rats, alpha-PVP acts as a potent uptake blocker of dopamine and norepinephrine transporters, comparable in activity to MDPV; it is also a catecholamine* transporter blocker. This property may explain the hyperactivity that MDPV seems to induce. It may also explain why MDPV, and all of its analogs, induce stimulant effects at lower doses but bizarre behaviors at higher doses (Karch, 2015).

*Catecholamine: epinephrine (adrenaline), norepinephrine (noradrenaline) and dopamine; all of which are produced from phenylalanine and tyrosine. Release of the hormones epinephrine and norepinephrine from the adrenal medulla of the adrenal glands is part of the fight-or-flight response.

The acute side effects of MDPV include tachycardia, hypertension, vasoconstriction, and sweating. The duration of the subjective effects is about 3 to 4 hours and the side effects continue for a total of 6 to 8 hours after administration. Higher doses of MDPV have caused intense prolonged panic attacks in stimulant-intolerant users. Users have reported bouts of psychosis induced by sleep deprivation and becoming addicted after using higher doses or using at more frequent dosing intervals (NCBI, 2015).

Alpha-PVP is chemically similar to other synthetic cathinone drugs and takes the form of a white or pink foul-smelling crystal that can be eaten, snorted, injected, or vaporized in an e-cigarette or similar device. Vaporizing, which sends the drug very quickly into the bloodstream, may make it particularly easy to overdose. Like other drugs of this type, alpha-PVP can cause a condition called "excited delirium" that involves hyperstimulation, paranoia, and hallucinations that can lead to violent aggression and self-injury. The drug has been linked to deaths by suicide as well as heart attack. It can also dangerously raise body temperature and lead to kidney damage or kidney failure. A synthetic cathinone closely related to MDVP called alpha-pyrrolidinopentiophenone (alpha-PDP)—popularly known as "Flakka"—is surging in Florida and is also being reported in other parts of the country (NIDA, 2015c).

Acute Effects of Cathinone Use

Most designer stimulants are taken intranasally and the effects generally start about 10 to 20 minutes after dosing, peak at 45 to 90 minutes, last 2 to 3 hours, and then decrease over 6 to 12 hours. Users may consume multiple doses during a session to prolong the desired effects. Commonly reported effects—similar to cocaine, amphetamine, and MDMA—include increased energy, alertness, concentration, sexual stimulation, empathy, talkativeness, mood enhancement, euphoria, and decreased appetite (Weaver et al., 2015).

Confusing and misleading labeling add to the abuse of bath salts. Source: Drug Enforcement Administration.

Most synthetic cathinone users report intermittent adverse effects. Acute toxicity may be associated with larger binge consumption and exposure to multiple substances. Acute agitation is a hallmark of toxicity. Psychosis may be pronounced, with patients experiencing paranoia, hallucinations (primarily visual), and delusions (Weaver et al., 2015).

Repeated use of synthetic cathinones will likely lead to tolerance, which is indicated indirectly by the association between frequency of use and greater amount consumed. Binges have been reported with significant successive dosing of mephedrone. Withdrawal effects reported among chronic users include tiredness, insomnia, difficulty concentrating, irritability, depression, and nasal congestion. Some users experience a dependence syndrome with cravings and compulsive use (Weaver et al., 2015).

Sympathomimetic* toxicity is manifested by neurologic and cardiovascular clinical features. The use of bath salts has been associated with cardiac arrhythmias and myocarditis. Significant hyponatremia has been reported with mephedrone use (similar to that seen with MDMA), which is likely due to a combination of sweating, electrolyte loss, and antidiuretic hormone secretion. More serious renal impairment includes acidosis and acute renal failure associated with rhabdomyolysis. Deaths have been reported with mephedrone and MDPV (Weaver et al., 2015).

*Sympathomimetic: stimulant compounds that mimic the effects of agonists of the sympathetic nervous system such as the catecholamines (epinephrine, norepinephrine, dopamine, etc). Sympathomimetic drugs are used to treat cardiac arrest and low blood pressure, or even delay premature labor, among other things.

Bath salts were largely responsible for a doubling in annual stimulant or sympathomimetic-related toxicology cases reported, from 6% in 2010 to 12% in 2011. Commonly reported effects include diaphoresis, palpitations, muscle tension or spasms, and bruxism (jaw clenching). Most individuals exhibit autonomic hyperactivity on exam (eg, tachycardia, hypertension). Nasal-specific adverse effects include epistaxis and sore nasal passages, mouth, and throat (Weaver et al., 2015).

In addition to the cathinone effects, contaminants can play a role in adverse effects. Product analysis studies have found adulteration with benzocaine, lidocaine, procaine, caffeine, or even controlled drugs such as cocaine, amphetamine, ketamine, and piperazine compounds. Adulterants with stimulant properties could potentiate* the effects of bath salts and raise toxicity risk by increasing the sympathetic effects or chances of cardiac arrhythmias (Weaver et al., 2015).

*Potentiate: to intensify or increase the power or effect of a drug and increase the likelihood of a physiologic reaction.

Empirical or prospective data are limited regarding long-term adverse physiologic effects of synthetic cathinone use. However, neurotoxicity is plausible (eg, monoamine depletion, neuronal degradation) along with development of physiologic dependence among regular users, which is manifested by tolerance and a withdrawal syndrome (Weaver et al., 2015).

Bath Salts vs. Epsom Salts

The synthetic cathinone products marketed as "bath salts" to evade detection by authorities should not be confused with products such as Epsom salts that are sold for soaking and bathing. The latter have no psychoactive (drug-like) properties.

National Institute on Drug Abuse

Synthetic Cannabinoids (Spice, K2)

Synthetic cannabis (spice, K2) is a widely available, cheap, and increasingly popular type of designer drug. The synthetic cannabinoids have many features that mimic cannabis, but because key chemical components have been altered to avoid legal restrictions and increase potency they can cause seizures, vomiting, tachycardia, chest pain, and serotonin syndrome. Very little is known about management of acute intoxication or abuse of these drugs.

Synthetic cannabinoids are chemicals synthesized in laboratories to mimic the biologic effects of THC (delta-9-tetrahydrocannabinol), the main psychoactive ingredient in marijuana. A small number of these chemicals were initially developed in the 1980s for research purposes, primarily to investigate the biologic mechanisms of the cannabinoid system and to develop novel therapies for various clinical conditions. Additional synthetic cannabinoids were synthesized for research purposes in the mid-1990s to study drug-receptor interactions in the cannabinoid system (ODC, 2014).

Synthetic cannabinoids were marketed in several European countries as "herbal incense" before they were first encountered in the United States in late 2008. In 2009 their use began increasing in the United States with law enforcement encounters describing synthetic cannabinoids laced on plant material and being abused for their psychoactive properties. Forensic analysis identified multiple variations in both the type and amount of synthetic cannabinoid applied to the plant material (ODC, 2014).

K2 is typically sold in small, silvery plastic bags of dried leaves and marketed as incense that can be smoked. It is said to resemble potpourri. Source: Drug Enforcement Administration.

K2 synthetic cannabinoid. Source: National Institute on Drug Abuse.

Synthetic cannabinoids typically originate from foreign sources, including China and other countries in Southeast Asia. Bulk substances are smuggled into the United States and find their way to clandestine designer drug product manufacturing operations located in residential neighborhoods, garages, warehouses, and other similar destinations throughout the United States. The powder form of synthetic cannabinoids is typically dissolved in solvents (eg, acetone) before being applied to a green plant material or dissolved in a propellant intended for use in e-cigarette devices (ODC, 2014).

Did You Know . . .

Synthetic cannabinoids sometimes have a fragrance, which can include vanilla, potpourri, spice, blueberry, caramel, and strawberry.

The pharmacologically inactive vegetable matter onto which the synthetic cannabinoids are sprayed accounts for most of the bulk of "spice" by weight. These substances are supposedly derived from plants and are smoked by users. The ingredients listed on the package are generally incomplete or false. One gram of "spice" can contain varying amounts of synthetic cannabinoid, with high variability from one package to another. Consumers do not know what active substance they are using, or in what dose. Other ingredients often added to the vegetable matter are the β2-mimetic substance clenbuterol,* which may be responsible for the sympathomimetic manifestations of "spice" intoxication (tachycardia, hypokalemia), and large amounts of tocopherol (vitamin E), possibly added in order to prevent detection (Hohmann et al., 2014).

*Clenbuterol: a powerful bronchodilator used by sufferers of breathing disorders as a decongestant. It also has fat-burning properties and is widely used by athletes to quickly drop body fat.

Synthetic Cannabinoid Drug Facts	
Street names	K2, Spice, Aroma, Barely Legal, Black Mamba, Bliss, Bombay Blue, Bonsai, Dream, Fake Weed, Fake Pot, Fire, Fusion Galaxy, Genie, Gorilla, Incense, K3, Legal High, Moon Rocks, Pep Spice, Skunk, Smacked, Yucatan, Zohai, 50-state Legal
Commercial names	No commercial uses
Common forms	Dried, shredded plant material that looks like potpourri and is sometimes sold as “incense”
Common ways taken	Smoked, swallowed (brewed as tea)
DEA schedule	Schedule I

Source: National Institute on Drug Abuse, 2015b.

Pharmacology

The primary cannabinoid in cannabis is delta-9-tetrahydrocannabinol (Δ9-THC), a partial CB1 receptor agonist.* CB1 receptors are located throughout the human body, especially the central nervous system. Synthetic cannabinoids used recreationally may be full or partial CB1 agonists. Synthetic cannabinoid-containing products used recreationally include individual or mixtures of different synthetic cannabinoid compounds sprayed on psychoactively inert pulverized plant matter of virtually unknown content (Weaver et al., 2015). The active substance can be hundreds of times more potent than cannabis and, when used to lace herbal mixtures, can be extremely difficult to detect (Smith & Robert, 2014).

*Agonist: a chemical that binds to a receptor and activates the receptor to produce a biological response.

Synthetic cannabinoids include a diverse group of molecules with a nomenclature that can be confusing. Hundreds of compounds are in the JWH series (a series of analogues created in 1994 by Dr. John W. Huffman for studies of the cannabinoid receptors), although many have not yet been identified as drugs of abuse. Additionally, there are 43 JWH compounds of known toxicologic importance, along with 32 associated metabolites. Even within the JWH series there are different classifications including naphthoylindoles (eg, JWH-018), naphthylmethylindoles (eg, JWH-175), and phenylacetylindoles (eg, JWH-201). There are several other series of synthetic cannabinoids, including the AM, UR, RCS, and XLR series; some of these are closely related to compounds in the JWH series (Krasowski & Ekins, 2014).

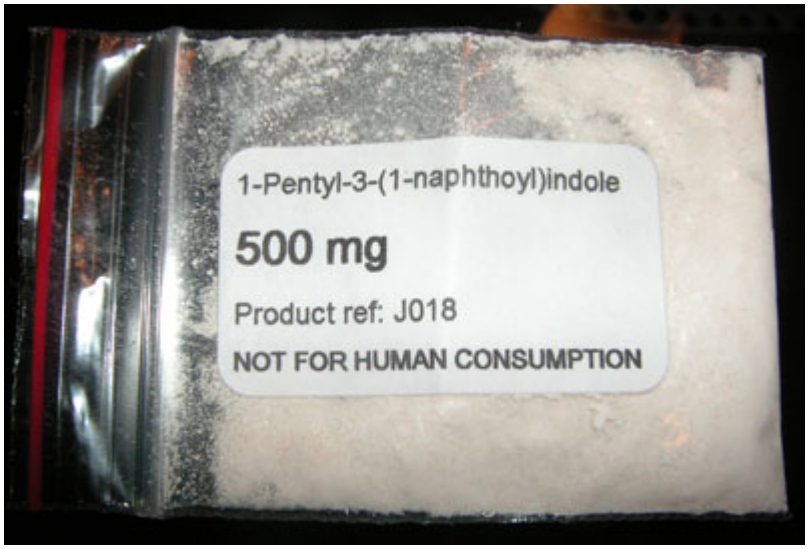
Though marketed as "natural" herbal blends, these products are usually adulterated with various synthetic cannabinoids, most of which are aminoalkylindoles* of the JWH family. They, along with other synthetic cannabinoids, such as CP-47,497, and HU-210, were first found in the "natural" herbal blends in 2008. One particular aminoalkylindoles, JWH-018, is prevalent across many different brands and batches of K2 products (Brents et al., 2011).

*Aminoalkylindoles (AAIs): a family of cannabinergic compounds that act as a cannabinoid receptor agonist. They were invented by pharmaceutical company Sterling-Winthrop in the early 1990s as potential nonsteroidal anti-inflammatory agents.

When these substances first appeared in Europe, they were accompanied by the claim that the drug's psychotropic effect was induced purely by natural botanical components. The real active substance was discovered in 2009 with the detection of undeclared synthetic cannabinoid receptor agonists by Volker Auwärter and colleagues at the University of Freiburg in Germany (Hohmann et al., 2014).

Cannabinoid receptor agonists are classified according to their chemical structure, as follows:

- Classic cannabinoids
  - delta-9-tetrahydrocannabinol (THC) from the cannabis plant (*Cannabis sativa*)
  - the approved anti-emetic nabilone, and
  - HU cannabinoids, which closely resemble THC
- Non-classic cannabinoids, such as the cyclohexylphenol (CP) cannabinoids
- Aminoalkylindoles: the JWH series, synthesized by the chemist J. W. Huffman, contains many CB ligands
- Eicosanoids, such as the endocannabinoid anandamide (Hohmann et al., 2014)



Half a gram of JWH-018. Source: Wikimedia Commons, public domain.

The term *Spice* is now generally applied to all products containing synthetic cannabinoids, regardless of branding. Compared to THC, synthetic cannabinoids are often more potent, are efficacious CB1 agonists, and may have a longer half-life, all of which may lead to greater cannabinomimetic* toxicity. There is substantial variability in product composition and wide concentration ranges for synthetic cannabinoid, which can also add to the risk of toxicity (Weaver et al., 2015).

*Cannabinomimetic: any substance that is a cannabinoid receptor type 1 (CB1 receptor) agonist as demonstrated by binding studies and functional assays.

Did You Know . . .

Synthetic cannabinoids were first developed to study the structure of the drugs and brain receptor activity. The aminoalkylindoles of the JWH family are named after Clemson University researcher John W. Huffman. JWH-018 and JWH-073 are two of the most common synthetic cannabinoids found in K2 products.
Source: Adams and Logan, Pharmacodynamics and Pharmacokinetics of Synthetic Cannabinoids.

Acute Effects of Cannabinoids

Synthetic cannabinoids are primarily smoked via a joint, bowl, or water pipe, although they can be consumed orally or intranasally. Acute effects are similar to cannabis, including alteration in mood, conjunctival injection,* and tachycardia. Effects are reported to start within 10 minutes after inhalation, and most effects appear to dissipate 2 to 6 hours after use (Weaver et al., 2015). Acute effects, however, can be associated with clinical symptoms atypical of marijuana use, including hypertension, agitation, hallucinations, psychosis, seizures, and panic attacks. In general, the severity of adverse effects associated with synthetic cannabis use is much greater than that of marijuana (Brents et al., 2011).

*Conjunctival injection: red eye, caused by dilation of the conjunctival vessels that overlie the sclera.

Chronic abuse of synthetic cannabis may result in a severe withdrawal and dependence syndrome. The use of synthetic cannabinoids has even been causally linked to at least one death by overdose and has been implicated for likely involvement in several other fatalities, resulting in over 2,500 calls to poison control centers in 2010 alone and numerous visits to emergency departments across the United States and Europe (Brents et al., 2011).

Adverse psychological effects are common and may include anxiety, trouble thinking clearly, agitation, paranoia, and delusions. Reports indicate that synthetic cannabinoids can provoke acute psychosis—which appears more likely in users with underlying biologic vulnerability due to family history of psychosis—as well as worsen pre-existing chronic psychotic disorders. Psychotic symptoms can persist for a significant time, from 1 week to 5 months in reported cases (Weaver et al., 2015).

Some regular users of cannabis may use synthetic cannabinoid as a substitute to relieve cannabis withdrawal symptoms, likely indicating cross-tolerance between synthetic cannabinoid and THC. Synthetic cannabinoids also appear to serve as a sufficient cannabis substitute, especially when cannabis is unavailable. Case reports have documented withdrawal symptoms after synthetic cannabinoid product use, as well as a dependence syndrome similar to those seen with cannabis (Weaver et al., 2015).

Physiologic side effects include dry mouth, lightheadedness, and headache. Other unwanted negative physiologic effects include diaphoresis, tremors, dystonia, and dyspnea. Tachycardia is common with synthetic cannabinoid use (similar in cannabis users), due potentially to reduced peripheral vascular resistance and the subsequent need to maintain cardiac output by increasing heart rate, rather than due to a direct sympathetic effect. The tachycardia may be severe, along with hypertension and chest pain. One case report of significant bradycardia with chest pain has also been reported (Weaver et al., 2015).

Several synthetic cannabinoid compounds (specifically JWH-018, JWH-073, and AM-2201) have been implicated as a cause of *cannabinoid hyperemesis syndrome*, which is a chronic disorder that was originally characterized among chronic cannabis users who experienced cyclic episodes of vomiting and abdominal pain relieved by bathing or showering with hot water. However, cannabis-related hyperemesis syndrome is rare. To the extent that synthetic cannabinoid might be more likely to cause nausea and vomiting, such symptoms could help to differentiate intoxication between the two (Weaver et al., 2015).

Severe synthetic cannabinoid-related toxicity requiring emergency treatment has included seizures, acute renal failure, and myocardial infarction. Deaths have been reported with synthetic cannabinoid due to a cardiac ischemic event and extreme anxiety resulting in suicide (Weaver et al., 2015).

There are no studies of the long-term effects of synthetic cannabinoids. Smoking synthetic cannabinoids typically involves inhalation of burned, unidentified plant material along with the synthetic cannabinoid, which may have adverse effects on the pulmonary system, so some sources recommend vaporization instead of smoking as a delivery method. Additionally, JWH-018 may be a carcinogen. Anecdotal data indicate the development of tolerance and a withdrawal syndrome with chronic use (Weaver et al., 2015).

These observations have garnered the attention of public health and legislative officials, and even moved the U.S. Drug Enforcement Administration (DEA) to use its emergency powers to categorize JWH-018 and four other synthetic cannabinoids as Schedule I substances for at least one year because ". . . they impose imminent hazard to public safety" (Brents et al., 2011). These compounds became permanent Schedule I substances on July 9, 2012, via passage of the Synthetic Drug Abuse Prevention Act of 2012 (DEA, 2013).

Regardless of proactive legislative movements, synthetic cannabinoids are still legal and available in most countries throughout the world. Clearly, the rapidly increased use of synthetic cannabinoids among youth, their current inability to be detected by standard drug urine tests, and the constant introduction of new structurally similar products of unknown content pose a significant risk to public health. The pharmacologic and toxicologic profiles of these products are virtually unknown, as are the mechanisms underlying the many adverse effects associated with the use of synthetic cannabinoids (Brents et al., 2011).

Synthetic Hallucinogens

Hallucinogens are drugs that distort a person's perception of reality. They occur in chemical form as well as in nature (eg, psilocybin mushrooms, peyote). These drugs can produce visual and auditory hallucinations, feelings of detachment from one's environment and oneself, and distortions in time and perception (SAMHSA, 2014). They can also cause an increase in blood pressure, heart rate, respiration, and body temperature, as well as confusion and loss of coordination.

Hallucinogenic compounds found in some plants and mushrooms (or their extracts) have been used during religious rituals for centuries. Almost all hallucinogens contain nitrogen and are classified as alkaloids. Many hallucinogens have chemical structures similar to those of natural neurotransmitters (acetylcholine-, serotonin-, or catecholamine-like). While the exact mechanisms by which hallucinogens exert their effects remain unclear, research suggests that these drugs work, at least in part, by temporarily interfering with neurotransmitter action or by binding to their receptor sites (NIDA, 2014).

Synthetic hallucinogens are derived from phenethylamine, which is altered in a laboratory to create effects that mimic those of natural hallucinogens. The molecular structures of all phenethylamines contain a phenyl ring, joined to an amino group via an ethyl side chain (phenyl-ethyl-amine).

One novel group of toxic phenethylamine derivatives called NBOMe has recently gained prominence. These compounds produce hallucinations through serotonergic stimulation (Weaver et al., 2015). They are sold as legal substitutes for lysergic acid diethylamide (LSD) or mescaline. Also called "N-bomb," "legal acid," "smiles," or "25I," they are generally found as powders, liquids, soaked into blotter paper, or laced on something edible. These chemicals act on serotonin receptors in the brain like other hallucinogens, but they are more powerful even than LSD. Extremely small amounts can cause seizures, heart attack or arrested breathing, and death.

In the last few years there has been a rapid increase in the recreational use and availability of synthetic hallucinogens. This new phenomenon represents not only an unprecedented challenge in the field of drug addiction, but also a fast-growing problem from social, cultural, legal, and political perspectives (Bersani et al., 2014).

Pharmacology

Synthetic designer hallucinogens gained popularity after the 1991 publication of Alexander Shulgin's book, *PIHKAL, A Chemical Love Story*. PIHKAL, an acronym for "Phenethylamines I Have Known and Loved," details the synthesis of over 200 psychedelic compounds. The "2C" series of hallucinogenic phenethylamines, first described by Shulgin, share a similar chemical structure; the term "2C" is derived from the two carbon molecules between the benzene ring and the amino group.

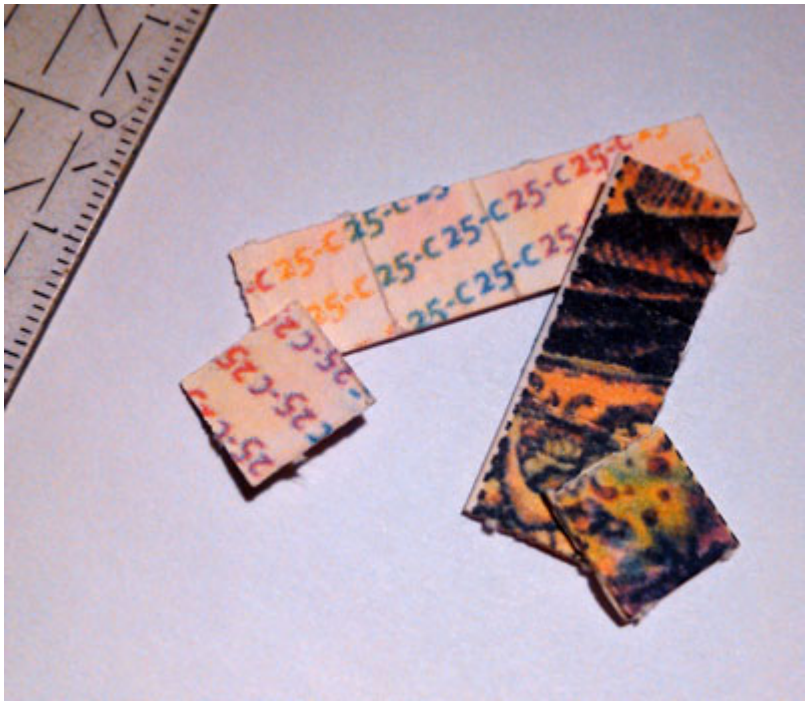
Alexander and Ann Shulgin, authors of *PIHKAL*, *A Chemical Love Story*, at December 2011 book signing in Oakland, CA. Source: Wikipedia.

There are more than 27 known 2C compounds, the most common being 2C-C, 2C-B, and 2C-I; these drugs are also referred to as *psychedelic phenethylamines*. One of the most common substances within this group is 25C-NBOMe (Bersani et al., 2014). NBOMe compounds are extremely potent and highly hallucinogenic at very low dosages—as low as 50µg.

Another compound, 25I-NBOMe, is a relatively new derivative of the 2C series of phenethylamines. 25I-NBOMe is one of several phenethylamines that have become popular since October 2011, when the DEA issued a temporary Schedule I status on many of the compounds marketed as bath salts. 25I-NBOMe is a highly potent, high-affinity agonist of the serotonin 2a (5HT2a) receptor that was originally synthesized for research on the serotonin receptor (Weaver et al., 2015).

25I-NBOMe has many potential routes of administration. In addition to liquid and powder form, other routes of administration include inhalation of vapor, nasal insufflation, oral ingestion, sublingual/buccal administration, and intravenous injection. The most common use is oral/sublingual/buccal, but nasal insufflation is not unusual. When administered by the oral/oral mucosal route, 25I-NBOMe is ingested as a pill or absorbed as powder or on blotter paper. Use of the drug generally occurs in a single administration of a small quantity or "cap" (about 0.1 gram). Clinical effects can occur rapidly after nasal use and generally peak in 20 minutes. A wide duration-of-action range of 3 to 13 hours has been reported. In reported cases of clinical toxicity, agitation persisted for several days (Weaver et al., 2015).

The reported effects of 25I-NBOMe are similar to those of typical serotonergic hallucinogens such as LSD or psilocybin. Users report hallucinations with a varying degree of stimulating effects. Depersonalization has been reported as well. In contrast to other serotonergic hallucinogens, 442 users responding to an Internet survey reported that 25I-NBOMe had greater "negative effects while high," but with more "value for money" (Weaver et al., 2015).



Blotter papers containing 1200 µg of 25C-NBOMe each. A dose as small as 200–500 µg can cause a significant hallucinogenic reaction. Source: Wikimedia, public domain.

Acute Effects of Synthetic Hallucinogens

As a result of NBOMe's recreational use, various episodes of acute intoxication and fatalities have been reported. While its general use poses a significant danger, a second danger is the accidental ingestion of NBOMe by individuals thinking they are ingesting LSD; according to anecdotal and media reports and scientific testing, in fact, LSD users may often unwittingly ingest the more dangerous 25C-NBOMe (Bersani et al., 2014).

In the following case, a user reports the effects of a 500 µg of 25C-NBOMe nasal insufflation (Bersani et al., 2014).

Case

The kitchen started to swirl around, everything became very colourful, the intensity increased exponentially. It became way, way more intense than I had expected very, very quickly. Panic started to take hold and no matter what I did I could not shake it off. I tried to reassure myself and tried to calm down but as my world started to become more and more chaotic and as I started to completely lose myself I found this impossible to do. Then things started to get really, really nasty. The thoughts in which the loop seemed to be wrecking peoples' lives were interlaced with the thoughts that somehow I was doing something so terrible, so humiliating and disgusting that the whole world thought I was a joke and that I did not deserve to live. I was completely dissociated and out of the room, I was on the ground outside being pelted with rubbish by hundreds of people. There were ambulances, police cars and my dad all whirling round. This image remained for a long time. However after a while it was as if people understood and whilst some still hated me others were rooting me on to make it through to the other side of this trip.

In addition to the anticipated visual and auditory hallucinations, many users experience psychiatric consequences, prompting them to access medical services. Some of these consequences include delirium, agitation, aggression, violence, paranoia, dysphoria, severe confusion, and self-harm. Some patients have presented with a serotonergic or sympathetic toxidrome* consisting of an "excited delirium" with severe agitation, aggression, and violence. In one case, a reportedly hallucinogen-naïve 19-year-old man died from a multiple-story fall after ingesting 25I-NBOMe and developing paranoid and bizarre behavior. In another fatal case, a 21-year-old male driver who ingested 25I-NBOMe developed sudden rage, pulled his car off the road, and began to destroy the inside of the vehicle before dying from an unknown cause (Weaver et al., 2015).

*Toxidrome: a clinical syndrome caused by dangerous levels of toxins in the body—often as a result of a drug overdose.

Tachycardia, hypertension, and mydriasis* are frequently described in the few clinical reports of 25I-NBOMe users. Hyperreflexia and clonus have also been reported in several cases. Seizures occurred in many of the cases that eventually required medical attention. Severe toxicity has included hyperthermia, pulmonary edema, and death from trauma. In one report of a fatal exposure, a 15-year-old girl became unresponsive after ingesting 25I-NBOMe outside a rave; on arrival at a local hospital she was in asystole with a rectal temperature of 39.9°C. Long-term physiologic effects are not known (Weaver et al., 2015).

*Mydriasis: prolonged or excessive dilation of the pupil.

Designer Drug Testing and Assessment

> An increase in use [of designer drugs] would not necessarily be relevant to acute healthcare professionals if these substances were not harmful. However, existing data shows that this is not the case. In 2012 alone, 52 deaths in England and Wales were directly attributable to novel psychoactive substances, with no other drugs listed on the death certificate. Many more deaths reference co-ingestion of these substances.
>
> Smith & Robert, 2014

Testing and assessment of patients admitted for designer drug use presents a number of challenges. Urine and other screening tests cannot yet identify or even detect specific designer drugs, particularly because their chemical structures are changed rapidly. Because of this, clinicians must be alert for signs and symptoms of designer drug use during the screening and assessment of new patients.

Testing Challenges

Urine or serum toxicology screens are unable to detect all of the designer drugs that have been synthesized, posing a major diagnostic and monitoring challenge for clinicians. Although laboratory testing is expanding, widespread standardized designer drug testing is not yet available in most clinical practice settings and laboratories. The analytical challenge is compounded by differences in designer drug product contents, concentration, and chemical constituents, all of which may vary between and within products (Weaver et al., 2015).

Illicit manufacturers have demonstrated remarkable flexibility in altering the psychoactive components of designer drugs to evade regulation and detection. It is common practice to modify functional groups, change substitutions, and alter moieties* of substances in a rapid and iterative process to evade legal restriction. This practice also poses significant challenges for detection of compounds or metabolites through urine drug screening (Weaver et al., 2015).

*Moiety: a part or a functional group of a molecule, part of a molecule.

Individuals frequently report that the lack of detection on standard urine drug screening tests is a reason for designer drug product use. For example, populations under criminal justice supervision may use designer drugs to evade detection by probation officers. Among the U.S. military, where most soldiers referred for addiction treatment are identified through urine drug screening, synthetic cannabinoids are consumed by those seeking cannabis-like mood-altering effects but with much lower risk of detection (Weaver et al., 2015).

Even though most emerging designer drugs will not be picked up on routine urine drug screening in a healthcare setting, collection of urine is still valuable clinically to test for unreported, co-occurring substance use. A general laboratory screening battery of urine or serum should be sent to screen for common drugs of abuse. This helps the clinician to be aware of potential toxicity due to drug interactions, and to the need for closer or prolonged monitoring due to the presence of other, non-designer substances. When comprehensive designer drug testing is unavailable or pending, familiarity with the most common designer drugs and other substances of abuse in a given locality can help clinicians rapidly recognize intoxication and begin management of serious complications (Weaver et al., 2015).

Michigan Department of Community Health Rapidly Identifies Presence of Toxic Bath Salts in Marquette County

On February 1, 2011, in response to multiple news reports, the Michigan Department of Community Health (MDCH) contacted the Children's Hospital of Michigan Poison Control Center regarding any reports of illness in the state caused by the use of recreational designer drugs sold as "bath salts." The poison control center told MDCH that, earlier in the day, they had learned that numerous persons had visited the local emergency department in Marquette County with cardiovascular and neurologic signs of acute intoxication. The subsequent investigation identified 35 persons who had ingested, inhaled, or injected "bath salts" and visited a Michigan ED during November 13, 2010–March 31, 2011.

Among the 35 patients, the most common signs and symptoms of toxicity were agitation (23 patients), tachycardia (22), and delusions/hallucinations (14). Seventeen patients were hospitalized, and one was dead upon arrival at the ED. The coordinated efforts of public health agencies, healthcare providers, poison control centers, and law enforcement agencies enabled rapid identification of this emerging health problem. Mitigation of the problem required the execution of an emergency public health order to remove the toxic "bath salts" from the marketplace. Lessons from the Michigan experience could have relevance to other areas of the United States experiencing similar problems.

Source: NCBI, 2015.

In the clinical and forensic toxicology settings, detection of designer stimulants and synthetic cannabinoids presents a complicated challenge. Detection of these designer drugs using mass spectrometry* is one method under investigation. Screening immunoassays** based on amphetamine, methamphetamine, or MDMA as the target molecules cross-react with only a small subset of designer amphetamine-like drugs and are thus unreliable for detection of designer amphetamine-like drugs (Krasowski & Ekins, 2014).

*Mass spectrometry: a technique that measures the mass or weight of atoms and molecules and uses this information to identify the amount and type of chemicals present in a sample.

**Screening immunoassays: a biochemical test that measures the presence or concentration of a macromolecule in a solution through the use of an antibody or immunoglobulin.

Immunoassays designed for THC metabolites generally do not cross-react with the synthetic cannabinoids that do not share the classic cannabinoid backbone found in THC. This suggests complexity in understanding how to detect and correctly identify whether a patient has taken a molecule of one class or another and it ultimately impacts clinical care. Recently, enzyme-linked immunosorbent assays (ELISAs)* for bath salts and synthetic cannabinoids have been developed and analyzed for cross-reactivity. The use of immunoassays such as ELISA for detection of designer drugs raises the question of how well such assays will detect a variety of compounds while avoiding false positives caused by cross-reactivity with unrelated compounds (Krasowski & Ekins, 2014).

*Enzyme-linked immunosorbent assay (ELISA): a test that uses antibodies and color change to identify a substance.

Clinical Assessment

Young adults are the most common demographic among those seeking emergency medical services related to designer drug use; hence, clinicians should consider direct inquiry about designer drug use, particularly among young adults presenting for acute medical care with signs or symptoms that could indicate substance-related toxicity (Weaver et al., 2015).

Since designer drugs are not detected by routine drug screens, healthcare providers relying solely on laboratory testing may be misled that illicit drugs have not been used. Conversely, the presence of routinely detectable illicit substances does not rule out the presence of designer drugs, since polysubstance use is typical in the population using designer drugs. Clinicians should be alert for inconsistencies between observed and expected intoxication syndrome from a self-reported or detected class of drugs. Such discrepancies could indicate recent designer drug use (Weaver et al., 2015).

Clinicians can be alert for clinical clues based on variations in patient presentation that may help identify designer drug use (see table below). Conjunctival injection is an indicator of synthetic cannabinoid intoxication as well as other cannabis products. Some patients presenting for emergency treatment may still have the package that contained the designer drug. This can be examined for possible identification of common brand names for a specific class of designer drug (see earlier table) and, potentially, any remaining content can be sent to a laboratory for analysis (Weaver et al., 2015).

Internet sites may be helpful for identification of specific substances ingested due to their rapidly changing appearance. However, the lack of research-based information on the adverse effects of designer drugs has led to the emergence of a range of websites that may or may not provide accurate information. The presence of paraphernalia such as a pipe for smoking could indicate designer drug or other smokable drug use, and a strong smell of perfume or cologne may be an attempt to mask the smell of recent smoking (Weaver et al., 2015).

Indicators of Designer Drug Use			
Body system	Finding	Medical indication	Drug(s)
General	Hyperthermia	Intoxication	Synthetic hallucinogens, bath salts
Head & neck	Conjunctival injection	Recent use	Synthetic cannabinoids
	Smoky chemical smell on breath	Recent smoking	Any smoked designer drug
	Epistaxis	Intranasal use	Bath salts, synthetic hallucinogens
	Nasal septal perforation	Intranasal use	Bath salts
	Poor dentition	Inadequate oral hygiene	Bath salts
	Jaw clenching, teeth grinding (bruxism)	Intoxication	Bath salts
Cardiac	Tachycardia	Recent use	Any designer drug
	Hypertension	Recent use	Any designer drug
	Chest pain	Cardiac ischemia, myocarditis	Bath salts, synthetic cannabinoids
Renal	Acute kidney injury	Recent use	Synthetic cannabinoids
Gastrointestinal	Nausea, vomiting	Recent use or withdrawal syndrome	Synthetic cannabinoids
	Enlarged and/or tender liver	Acute hepatitis	Any injected designer drug
Musculoskeletal	Muscle spasms	Intoxication	Bath salts

Indicators of Designer Drug Use			
Body system	Finding	Medical indication	Drug(s)
	Limb swelling and pain	Rhabdomyolysis	Bath salts, synthetic hallucinogens
Skin	Diaphoresis	Recent use	Bath salts
	Ecchymosis	Recent use or intoxication	Synthetic hallucinogens
	Fresh needle marks, track marks	Injection drug use	Any injected designer drug
Neurologic	Clonus	Recent use	Synthetic hallucinogens
	Seizures	Intoxication	Bath salts, synthetic hallucinogens, synthetic cannabinoids
Psychiatric	Agitation	Recent use	Any designer drug
	Hallucinations	Recent use	Any designer drug
	Psychosis	Intoxication	Any designer drug

Source: Weaver et al., 2015.

Routine inquiry about designer drug use is prudent, particularly among patients with a history of substance use disorder, those who are undergoing mandated urine testing (eg, criminal justice supervisees), or among those who have reported a history of designer drug use of a different chemical class. Different classes of designer drugs may be used concurrently, which could increase the incidence of adverse effects and toxicity (Weaver et al., 2015).

It is helpful for clinicians to ask about specific products by name, or perhaps "synthetics" in general, since patients may not be aware of designations used by medical personnel, or of different street names for similar products. For each affirmative response, followup questions should be asked about frequency, patterns of use, and subjective effects. Careful inquiry about subjective effects could help provide insight into the designer drug class, particularly when the brand–compound association is less well established and with wide variation in contents. Although our first table lists brand names along with the designer drug compound or class, the list is not comprehensive; there are likely thousands of different trade-name brands sold internationally (Weaver et al., 2015).

Further clinical inquiry should include specific questions about factors associated with designer drug use and the potential consequences, whether related to medical sequelae, interpersonal difficulties, or financial/legal problems. Chronic designer drug use may lead to physiologic dependence with tolerance and abstinence-related withdrawal, as well as a designer drug use disorder. Comprehensive inquiry about such factors regarding the patient's designer drug use helps the clinician make an initial determination about potential severity and provides insight into treatment needs (Weaver et al., 2015).

Among patients presenting for acute medical complications of designer drug use, routine laboratory testing should include—in addition to standardized urine drug testing—a complete blood cell count and complete metabolic panel. Cardiac enzymes should be obtained if cardiac symptoms are present. Creatine phosphokinase is helpful if rhabdomyolysis is suspected on the basis of severe muscle spasms, swelling and pain in the extremities, or severe seizures. Additional diagnostic studies may be selected on the basis of the initial presentation (Weaver et al., 2015).

Designer Drug Management and Treatment

Management of acute intoxication from designer drugs is especially difficult because no antidotes are available. Acute and long-term treatment is also a challenge and must rely heavily on counseling while encouraging young, impulsive patients to change their behavior.

Management of Acute Intoxication

No specific antidotes are available for designer drug toxicity. Activated charcoal is not useful unless there has been significant oral ingestion. Most non-psychiatric symptoms appear self-limited and resolve within one to several days with supportive treatment. Unpleasant psychological effects of acute intoxication, such as anxiety, agitation, or paranoia, may be managed with supportive treatment. Placing the distraught user in a quiet environment and maintaining gentle contact is often sufficient until the acute effects subside (Weaver et al., 2015).

Psychosis due to synthetic cannabinoid and 25I-NBOMe intoxication has been managed with monitored observation. For psychopathologic clinical features, benzodiazepines have been used to treat anxiety, agitation, and seizures. Antipsychotics are second-line agents for agitation, due to the lowered seizure threshold with use of cathinone and phenethylamine designer drugs. Sedation may be required if the patient is markedly agitated and at risk for harm to self or healthcare staff. Since some designer drug-associated psychosis may be severe and require prolonged inpatient treatment, psychiatric consultation is indicated, in particular for those with persistent symptoms (Weaver et al., 2015).

Abrupt discontinuation of stimulants or hallucinogens does not cause gross physiologic sequelae, so they are not tapered off or replaced with a cross-tolerant drug during medically supervised withdrawal. Abrupt discontinuation of synthetic cannabinoids could result in withdrawal symptoms such as nausea and irritability, similar to that with cannabis cessation: however, there is no indication for pharmacologic replacement (eg, dronabinol), since synthetic cannabinoid withdrawal is not life-threatening (Weaver et al., 2015).

Patients can be treated with supportive care by intravenous fluids and antiemetics if necessary. If marked psychiatric symptoms persist longer than one or more weeks after discontinuation, the patient should be evaluated carefully to determine whether there is a co-occurring primary psychiatric disorder, which then should be treated with specific therapy. Treatment of prolonged anxiety, depression, or psychosis is the same as when these conditions are not associated with recent designer drug use (Weaver et al., 2015).

For a significant number of patients, the high level of illness severity warrants admission to critical care. Intoxicated patients should be placed initially on continuous cardiac monitoring with pulse oximetry and frequent neurologic assessments. Adequate administration of intravenous fluids is encouraged to ensure good urine output, as these patients often are dehydrated. Fluid administration in the presence of rhabdomyolysis can help prevent acute renal failure. Intensive monitoring allows for early detection and intervention for serious consequences such as myocardial infarction (Weaver et al., 2015).

Patients may present with concurrent ingestion of drugs with different pharmacologic profiles, including both stimulant and depressant drugs. Clinicians should be alert for an unexpected response to a therapeutic intervention or to a change in patient presentation as one type of designer drug wears off and ongoing intoxication with another class of designer drug is revealed. This may require some flexibility in treatment due to changes in mental or cardiovascular status (Weaver et al., 2015).

Treatment of Designer Drug Addiction

Hospitalization for the adverse effects of designer drugs affords an excellent opportunity for advising patients to decrease their substance use and for engaging them in treatment. Healthcare provider awareness and patient education are cornerstones of public health initiatives to confront new challenges presented by designer drugs. Simple admonitions to stop are sometimes helpful if the diagnosis is made early, but in most cases are insufficient. Many patients who use designer drugs may be ambivalent about changing behavior, so the clinician should express empathy without confrontation, which shows respect for the patient's autonomy (Weaver et al., 2015).

Providing appropriate, accurate information about the potential risks of designer drugs and encouraging healthy choices can help patients make the best informed decision about changing behavior. Physicians should involve the patient proactively in the process of problem-solving, while reminding the patient of responsibility for all actions. The responsibility of the practitioner is to motivate the patient to seek recovery from designer drug use instead of blaming the patient for being unmotivated to change. Accurate information about the relative risks and unknown harms of these products helps a patient make an informed choice about continuing to use particular products, to make a quit attempt, or to seek more specific addiction treatment (Weaver et al., 2015).

Although prospective treatment data are limited, once a designer drug use disorder diagnosis is made, acute and long-term treatment is likely necessary. Recovery from substance use disorder in general is possible, and those who are treated have less disability than those who remain untreated. Long-term treatment of designer drug use disorders likely involves similar components to that of other types of addiction treatment, including behavioral components such as individual and group counseling with cognitive-behavioral therapy, motivational enhancement therapy, and 12-step self-help group facilitation. Family members should be considered as part of the treatment program, in particular when treating adolescents or young adults. Unfortunately, pharmacologic treatment data to guide management of those with designer drug use disorders are unavailable (Weaver et al., 2015).

Patients identified with substance use disorders in the ED or hospital inpatient setting should be provided with information linking them to local community addiction treatment resources. In the United States, physicians certified in the treatment of addictive disorders can be found through the American Society of Addiction Medicine or the American Academy of Addiction Psychiatry. At times, it may be more expedient and cost effective to refer the patient to a non-physician counselor, who can be found through the National Association for Alcohol and Drug Abuse Counselors' website. Substance abuse treatment services in the United States can also be located via the Substance Abuse and Mental Health Services Administration Behavioral Health Services Treatment Locator (Weaver et al., 2015).

Treatment of designer drug substance use disorders is challenging for several reasons. Designer drugs consist of several classes of substances, which vary in their psychological and physiologic effects. Treatment is often difficult due to the young age of most users and the possibility of concurrent polysubstance use. The pattern of use is usually intermittent in social settings, so it may be perceived as less of a problem. Clinicians should be knowledgeable and prepared to provide treatment for very different combinations, such as occurs with club drug use. A treatment environment with a supportive structure can be helpful. Addiction treatment is cost effective, and even multiple episodes of treatment are worthwhile. It can be rewarding for any healthcare practitioner to assist a patient who was impaired by addiction return to normal functioning in society (Weaver et al., 2015).

Concluding Remarks

Clinicians, both in emergency and other clinical settings, are increasingly faced with the challenge of identifying and treating patients who have used or abused substances of unknown origin and composition. This presents a difficult dilemma, forcing clinicians to rely largely on clinical assessment, experience, and intuition to treat an ever-expanding array of chemical substances created in illegal drug labs.

Bath salts, synthetic cannabinoids, and synthetic hallucinogens such as 25I-NBOMe are relatively new designer drugs that have become popular drugs of abuse, especially among young adults. Though chemically different, they are similar in that they are continually altered in order to avoid legal issues and detection on drug tests. They are also similar in that adverse reactions are common, especially clinically significant psychotic reactions (Weaver et al., 2015).

Detection of these drugs with urine tests is challenging, so when young adults present with agitation and psychosis clinicians should consider designer drugs as a causative factor. Treatment is primarily supportive, and benzodiazepines may be beneficial. When those who use designer drugs come into contact with the healthcare system, clinicians need to link their patients to specific treatment for substance use disorder (Weaver et al., 2015).

The growth and widespread use of synthetic designer drugs is truly, as Bertha Madras says, "human experiments without informed consent."

Resources and References

Resources

American Society of Addiction Medicine
http://www.asam.org

American Academy of Addiction Psychiatry
http://www.aaap.org/patient-resources/find-a-specialist/

National Association for Alcohol and Drug Abuse Counselors
http://www.naadac.org

Substance Abuse and Mental Health Services Administration
Behavioral Health Services Treatment Locator
https://findtreatment.samhsa.gov

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Post Test

Use the answer sheet following the test to record your answers.

1. Designer drugs are:

    a. Drugs designed to work along with prescription medications.

    b. Substances of abuse that are not controlled by the 1961 Single Convention on Narcotic Drugs or the 1971 Convention on Psychotropic Substances.

    c. Marketed and distributed solely for medical use and not considered substances of abuse by law enforcement agencies.

    d. Generally safe when taken in small amounts.

2. Designer drugs:

    a. Are not easy to synthesize and are easily detected by routine drug testing.

    b. Have labels that accurately indicate the contents of the drug.

    c. Rarely cause neuropsychiatric symptoms.

    d. Have evolved rapidly and have largely evaded legal regulation and detection by routine drug testing.

3. The use of designer drugs is most prevalent among:

    a. Older adults looking for a novel drug experience.

    b. Older adults looking for a novel drug experience.

    c. Young adults, primarily men in their mid to late 20s.

    d. Teenagers and adolescents.

4. Bath salts work by:

    a. Stimulating the release of adrenalin and suppressing the release of melatonin.

    b. Stimulating the release and inhibiting the reuptake of norepinephrine, serotonin, and dopamine.

    c. Producing hallucinations through serotonergic stimulation.

    d. Full or partially stimulating CB1 agonists.

5. Mephedrone is:

    a. A synthetic central nervous system stimulant that, in very small amounts, can produce psychoactive symptoms.

b. A synthetic central nervous system depressant that, in very small amounts, can cause intense depression.

c. A chemical synthesized in laboratories to mimic the biologic effects of delta-9-tetrahydrocannabinol (THC).

d. A hallucinogenic compound found in some plants and mushrooms (or their extracts).

6. A "failed pharmaceutical" is:

a. A substance that failed to work as expected once it was brought to market.

b. A potent uptake blocker at dopamine and norepinephrine transporters.

c. A drug that can dangerously raise body temperature and lead to kidney damage or kidney failure.

d. A substance originally developed as potential therapeutic agents, but never brought to market as licensed a medicine.

7. Repeated use of synthetic cathinones:

a. Is unlikely to lead to tolerance or abuse.

b. Will likely lead to tolerance.

c. Has been definitively shown to cause long-term brain damage.

d. Is completely safe.

8. Synthetic cannabinoids are:

a. Artificially engineered drugs belonging to the phenethylamine class.

b. Used in the manufacture of plastics, resins, pesticides, brake fluid, and other industrial materials.

c. Drugs that produce visual and auditory hallucinations, feelings of detachment from one's environment and oneself, and distortions in time and perception

d. Chemicals synthesized in laboratories to mimic the biological effects of THC, the main psychoactive ingredient in marijuana.

9. Synthetic cannabinoid-containing products:

a. Are made up of mixtures of different synthetic cannabinoid compounds sprayed on cannabis leaves.

b. Are herbal blends that are much weaker than non-synthetic cannabis.

c. Can be hundreds of times more potent than non-synthetic cannabis.

d. Are easy to detect when mixed with other herbal products.

10. Adverse physiologic effects of severe synthetic cannabinoids toxicity can include:

a. Acute agitation, pronounced psychosis, paranoia, hallucinations (primarily visual), and delusions.

b. Anorexia, headache, hyperactivity, insomnia, and tremors.

c. Seizures, severe anxiety, acute renal failure, and myocardial infarction.

d. Hyperthermia, pulmonary edema, and death from trauma.

11. Synthetic hallucinogens:

a. Are chemicals synthesized in laboratories to mimic the biological effects of THC.

b. Are derived from phenethylamine, which is altered in a laboratory to create effects that mimic those of natural hallucinogens.

c. Are compounds found in some plants and mushrooms (or their extracts).

d. Can be readily identified in standard urine tests.

12. A young man presents to your ER late on a Saturday night with what can only be described as "excited delirium." He is severely agitated and aggressive. During your assessment he grabs a chair and throws it across the room, grabs his head, and yells at you to stop staring at him. You suspect:

a. He has smoked marijuana.

b. He is high on heroin.

c. He has a head injury.

d. He has taken some sort synthetic hallucinogen.

13. Testing and analysis of designer drugs is particularly difficult because:

a. The drugs are usually fully metabolized before patients get to the emergency department or clinic.

b. Patients are usually so paranoid that they refuse to allow a blood draw.

c. Differences exist in contents, concentration, and chemical constituents, all of which may vary between and within products.

d. Most patients have taken so many drugs that they tend to mask one another.

14. When screening a patient for designer drug use, clinicians should:

a. Call in the police for assistance in case the patient has an acute psychotic episode.

b. Avoid asking about designer drug use, which may increase anxiety and confusion.

c. Wait for the results of a toxicology report before accusing someone of designer drug abuse.

d. Ask directly about designer drug use, particularly among young adults with signs or symptoms that indicate substance-related toxicity.

15. In the absence of significant oral ingestion, designer drug toxicity:

a. Is best treated with activated charcoal.

b. Is mostly self-limiting.

c. Usually resolves within one to several days with complete isolation.

d. Is best treated with intranasal naloxone.

16. Long-term treatment of designer drug use disorders likely involves:

a. Similar components to that of other types of addiction treatment.

b. A new approach because traditional treatment approaches have proven ineffective.

c. Is very successful because of the young age of most designer-drug users.

d. Consistent involvement of law enforcement to discourage further use.

Answer Sheet

Designer Drugs: Untested and Dangerous

Name (Please print your name): _____

Date: _____

Passing score is 80%

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____
7. _____
8. _____
9. _____
10. _____
11. _____
12. _____
13. _____
14. _____
15. _____
16. _____

Course Evaluation

Please use this scale for your course evaluation. Items with asterisks * are required.

- 5 = Strongly agree
- 4 = Agree
- 3 = Neutral
- 2 = Disagree
- 1 = Strongly disagree

* Upon completion of the course, I was able to:

a. Provide a definition of the term *designer drugs*.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

b. Describe three key aspects of synthetic cathinones.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

c. Explain three ways in which synthetic cannabinoids differ from cannabis.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

d. List three clinical features of synthetic hallucinogen misuse.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

e. Describe two challenges related to testing and assessment of designer drug use.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

f. Explain two overall goals for the treatment of designer drug addiction.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

* The author(s) are knowledgeable about the subject matter.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

* The author(s) cited evidence that supported the material presented.

○ 5 ○ 4 ○ 3 ○ 2 ○ 1

* This course contained no discriminatory or prejudicial language.

Yes No

* The course was free of commercial bias and product promotion.

Yes No

* As a result of what you have learned, do you intend to make any changes in your practice?

Yes No

If you answered Yes above, what changes do you intend to make? If you answered No, please explain why.

* Do you intend to return to ATrain for your ongoing CE needs?

- Yes, within the next 30 days.
- Yes, during my next renewal cycle.
- Maybe, not sure.
- No, I only needed this one course.

* Would you recommend ATrain Education to a friend, co-worker, or colleague?

- Yes, definitely.
- Possibly.
- No, not at this time.

* What is your overall satsfaction with this learning activity?

5 4 3 2 1

* Navigating the ATrain Education website was:

- Easy.
- Somewhat easy.

- ○ Not at all easy.

* How long did it take you to complete this course, posttest, and course evaluation?

- ○ 60 minutes (or more) per contact hour
- ○ 50-59 minutes per contact hour
- ○ 40-49 minutes per contact hour
- ○ 30-39 minutes per contact hour
- ○ Less than 30 minutes per contact hour

I heard about ATrain Education from:

- ○ Government or Department of Health website.
- ○ State board or professional association.
- ○ Searching the Internet.
- ○ A friend.
- ○ An advertisement.
- ○ I am a returning customer.
- ○ My employer.
- ○ Other
- ○ Social Media (FB, Twitter, LinkedIn, etc)

Please let us know your age group to help us meet your professional needs.

- ○ 18 to 30
- ○ 31 to 45
- ○ 46+

I completed this course on:

- ○ My own or a friend's computer.
- ○ A computer at work.
- ○ A library computer.
- ○ A tablet.
- ○ A cellphone.
- ○ A paper copy of the course.

Please enter your comments or suggestions here: _____

_____

_____

_____

Registration Form

Please print and answer all of the following questions (* required).

* Name: _____

* Email: _____

* Address: _____

* City: _____ * State: _____ * Zip: _____

* Country: _____

* Phone: _____

* Professional Credentials/Designations:

_____

Your name and credentials/designations will appear on your certificate.

* License Number and State: _____

* Please email my certificate:

○ Yes ○ No

(If you request an email certificate we will not send a copy of the certificate by US Mail.)

Payment Options

You may pay by credit card or by check.
Fill out this section only if you are **paying by credit card.**
3 contact hours: $29

Credit card information

* Name: _____

Address (if different from above): _____

* City: _____ * State: _____ * Zip: _____

* Card type:

○ Visa ○ Master Card ○ American Express ○ Discover

* Card number: _____

* CVS#: _____

* Expiration date: _____