CARE FOR KIDS
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Playing with the Devil: Designer Drugs and its Dangers

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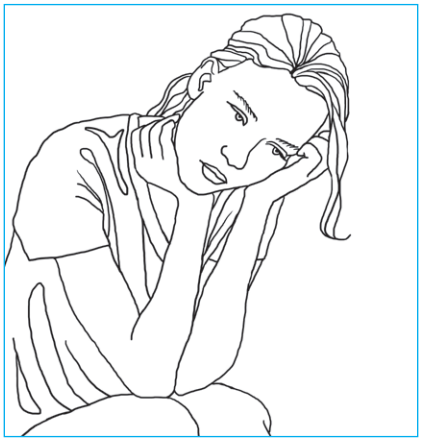
An Iowa teenager shot and killed himself after suffering a panic attack. A university basketball player collapsed while participating in a preseason workout and later died. The son of a physician slit his own throat, and three days later shot and killed himself after suffering continuous hallucinations. An 11-year-old boy died after hanging himself, and a woman attacked and killed her sleeping mother with a machete. What do all of these tragic events have in common? They were all triggered by the use of "designer drugs." These are just a sample of the growing number of horrible tragedies that have occurred because of the use of these agents.



"Designer drugs" is the term used to describe drugs that are synthetically derived from federally controlled substances or naturally derived to create new psychoactive agents. The molecular structures of existing drugs are slightly modified and produced in clandestine laboratories for illicit, recreational use. The intent of designer drugs is to circumvent the law and test the bounds of new chemicals, frequently with deadly results. Part of the problem is that these new products keep changing. Illicit drug makers use this tactic to stay one step ahead of law enforcement agencies. If law enforcement identifies a new compound and classifies it as an illegal drug, then clandestine laboratories react by altering the composition slightly in order to produce a new, technically legal, drug.

Banning these substances is a time-consuming administrative and scientific process that can take months to accomplish for each drug. The U.S. Drug Enforcement Agency (DEA) has recently banned some

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compounds, but they have identified 60 new synthetic compounds just in the last two years that are generally legal. To date, there are more than 250 different compounds that are considered new psychoactive substances.

Widespread Availability and Use

Designer drugs are sold in small packages in head shops, convenience stores, gas stations, and all over the Internet. Drug makers bypass current laws by placing the phrase "not for human consumption" on the labels, which is code language meant to imply the opposite. These psychoactive agents are frequently legal to possess, easy to obtain, heavily marketed as producing "legal highs" similar to illegal drugs, and are perceived to be "safer." Pop culture also plays a role in the increased use of these drugs. For example, teen pop idol Miley Cyrus and rappers Kanye West and Lil Wayne have all made reference to the designer drug "Molly," which is a newer analog of the stimulant ecstasy. Miley Cyrus admitted to making reference to this drug in her new song, "We Can't Stop."

An urgent need exists for health care providers worldwide to be familiar with the adverse effects of these novel psychoactive designer drugs. The goal of this article is to describe the pharmacology, clinical effects, and treatment of two important classes of these psychoactive designer drugs. This article will discuss synthetic cathinones ("Bath Salts") and synthetic cannabinoids ("Spice," "K2").

Synthetic Cathinones (a.k.a."bath salts")

This category of designer drugs has nothing to do with the bath salts used as a bath additive. Instead, this innocent looking name is the term given to a category of compounds that mimic certain illicit drugs, like cocaine, ecstasy, and methamphetamine. Cathinone is a naturally occurring beta-ketone amphetamine analogue found in the leaves of the Khat (*Catha edulis*) plant. Its euphoric effects were first described 1,000 years ago. Synthetic cathinones are newer derivatives of this compound. The key ingredients that have most often been used to make "bath salts" are the synthetic compounds MDPV (3,4-methylenedioxypyrovalerone), mephedrone, pyrovalerone, and methylone. Many other ingredients have also been used in addition to, or in place of, these compounds. For instance, extremely high levels of caffeine have been found in many of the "bath salts." In 2011, the DEA classified the three most common chemicals used to make "bath salts" as Schedule I controlled substances. Unfortunately, they are still easily obtained as illegal substances and as newly modified "legal" substances.

These products are given innocent-looking and enticing names to lure consumers and to disguise its true identities. They are sold as a fine white powder and are usually taken by nasal insufflation, oral ingestion, intravenous/intramuscular injection, or rectal insertion. Based on information collected from the increased numbers of calls to poison control centers, young men account for approximately 70% of bath salt users. Roughly 18% of users are less than 19 years old, and its use is highest in the 20-29-year-old range (43%).

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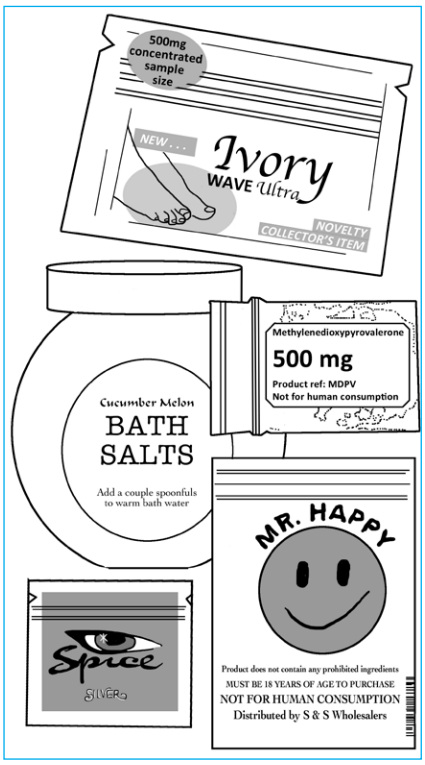

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Common Names for Synthetic Cathinones

Cat
Drone
Bubbles
Blizzard
Stardust
Bath Salts
Pure Ivory
Plant Food
Red Rocket
Vanilla Sky
Ivory Wave
Cloud Nine
Hookah Pipe Cleaner
White Lightning
Bonsai Fertilizer
Jewelry Cleaner
Snow Leopard
Meow Meow
White Knight
White Dove
Purple Wave
Lunar Wave
Ocean Burst
Ocean Snow

Pharmacology and Effects

Similar to other psychomotor stimulants, these agents target plasma membrane transporters for dopamine, norepinephrine, and serotonin. Users of synthetic cathinones describe euphoria, increased energy, heightened alertness, talkativeness, and increased libido, with effects typically lasting two to eight hours. Users frequently describe a compulsion to repeatedly redose to prolong the drug's effect, with sessions lasting several hours to several days. Like amphetamines, these drugs are capable of inducing tolerance, addiction, and dependence. Many recent reports and first-hand accounts by physicians, drug counselors, and law enforcement officers describe severely aggressive and psychotic behavior by people who have used bath salts. Often this aggressive behavior is coupled with phenomenal physical strength, similar to that seen in phencyclidine (PCP) intoxication. Reports of self-mutilation, suicide, and persistent paranoid psychosis are becoming common across the U.S. Interestingly, users themselves describe persistent paresthesias and mood changes lasting from days to weeks after using these drugs.

Physical signs of synthetic cathinones intoxication are consistent with sympathomimetic toxicity and include tachycardia, hypertension, hyperthermia, dehydration, agitation, combative behavior, psychosis, and seizures. In addition, hyponatremia, myocardial infarction, myocarditis, rhabdomyolysis, stroke, and death have been reported. The most commonly reported adverse symptoms include headache, chest pain, palpitations, paranoia, insomnia, tremors, trismus (clenching of the jaw), and bruxism (grinding of the teeth). Studies have demonstrated long-term neuronal toxic effects of these drugs, similar to those seen with methamphetamine.

Detection/Treatment

Currently none of the synthetic cathinones are detected on routine urine drug screening for amphetamines. However, they may cause a false positive methamphetamine result. Blood and urine specimens can be analyzed by gas and liquid chromatography and mass spectrometry, but these assays have not yet been accepted into routine clinical practice, thus are unlikely to give timely results.

No specific antidote exists, so treatment of exposures to these drugs is primarily supportive. Given the similarities to amphetamines and cocaine, similar management strategies based on treating the sympathomimetic effects are useful. Sympathomimetic toxidrome symptoms, including tachycardia, agitation, psychosis, hypertension, and seizures, should be treated with benzodiazepines. High doses of benzodiazepines may be necessary to sedate these patients effectively. Persistent hypertension can be treated with vasodilators (i.e., nitroglycerin or sodium nitroprusside). Beta blockers should be avoided in these patients, due to potential hypertension exacerbation that may result from unopposed alpha-adrenergic stimulation. Hyperthermia should be treated with aggressive cooling. In the case of severe psychiatric symptoms, proper restraints should be used to

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prevent harm to self or others. The use of antipsychotic medications to treat psychosis may decrease the seizure threshold, placing the patient at an even greater risk of seizures. When appropriate, physicians should test for rhabdomyolysis, hemolysis, and coagulopathies. Patients should be closely monitored until resolution of symptoms and normalization of vital signs.

Synthetic Cannabinoids (a.k.a. "Spice," "K2")

Synthetic cannabinoids are not structurally similar to tetrahydrocannabinol (THC), the active ingredient in marijuana. However, they are agonists of the cannabinoid receptors (CB_1 and CB_2). Synthetic cannabinoids are also referred to as synthetic marijuana or Herbal Marijuana Alternatives (HMAs). These products are sold as alternatives to marijuana, because they provide similar effects but are not detectable by traditional marijuana screening methods. Synthetic cannabinoids were originally designed in the 1960s by scientists who were searching for cannabinoid receptor agonists that had the same analgesic and anti-inflammatory properties of THC, but without the psychotropic effects. These agents are now best described as herbal blends adulterated with synthetic cannabinoid compounds. These blends often contain 10 or more different herbal additives, each of which is difficult or impossible to identify. Additionally, hundreds of different synthetic cannabinoid compounds could be incorporated into HMAs, making them extremely difficult to control. The most frequently identified synthetic cannabinoid compounds present in

HMAs are JWH-018, JWH-073, JWH-200, CP 47-497, and CP 47-497C8. The compound JWH-018 has a much greater affinity for cannabinoid receptors (four times higher for CB_1 and 10 times higher for CB_2), than does THC. This greater receptor affinity may partly explain the higher number of adverse effects caused by synthetic cannabinoids, compared to THC. Even more worrisome is the fact that the synthetic cannabinoid HU-210 is 100-800 times more potent than THC. In 2011, the DEA classified the five most common chemicals used to make HMAs as Schedule I controlled substances. Unfortunately, they are still easily obtained as illegal substances and as newly modified "legal" substances with marketing claiming that they contain no banned substances.

These drugs are given enticing names and flashy packaging that usually state such claims as "legal high" or "herbal high." These drugs are typically sold in small, silvery plastic bags of dried leaves and marketed as incense or potpourri. The actual contents are rarely listed on the packaging, and brand names and ingredients vary widely. Although these products are usually smoked, some users make them into tea. Much like bath salts, data gathered by poison control centers found that young men account for approximately 75% of synthetic cannabinoid users. Almost 50% of users are 13-19-years-old, and most of the remainder of users are 20-29-year-olds.

Common Names for Synthetic Marijuana

K2	*Spice Diamond*
K3	*Clover Spring*
Zen	*Red Merkury*
Nice	*Arctic Spice*
Bliss	*Spice Gold*
Black	*Fake Weed*
Aztec	*Chill Zone*
Zohai	*Zen Ultra*
Silver	*Thunder*
Spice	*Dream*
Genie	*Incense*
Smoke	*Mamba*

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2014 Early & Periodic Screening, Diagnosis, and Treatment (EPSDT)

Care for Kids Newsletter Survey

Please assist us in making the EPSDT newsletter more valuable to you by filling out the postage-paid survey below. Mailing instructions are on the reverse side. *Thank you.*

1. My profession is:

a. ❑ Family physician
b. ❑ Pediatrician
c. ❑ Physician, other specialty: _____
d. ❑ Health care office manager
e. ❑ Nurse
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g. ❑ Nurse, public health
h. ❑ Physician assistant
i. ❑ Dietitian
j. ❑ Psychologist
k. ❑ HeadStart provider
l. ❑ School nurse
m. ❑ Social worker
n. ❑ Teacher or other educator
o. ❑ Other: _____

2. Topics that interest me

	Most	Some	Least
a. ❑ Well-child care			
b. ❑ Health issues: Children birth to age 5 years			
c. ❑ Heath issues: Children age 5 to 12 years			
d. ❑ Health issues: Adolescents age 12 to 18 years			
e. ❑ Health issues: Children with special needs			
f. ❑ Health issues: Family			
g. ❑ Preventive health care			
h. ❑ Updates: Recommended clinical protocols			
i. ❑ Updates: State and federal programs			
j. ❑ Referral information: Community resources			
k. ❑ Care coordination			
l. ❑ Handouts I can provide to families			
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Additional comments or suggestions on newsletter content:

3. I would like each issue of this newsletter to:

	Always	Sometimes	Never
a. ❑ Focus on single topic			
b. ❑ Cover a range of topics			
c. ❑ Have fewer articles of greater depth			
d. ❑ Have more short articles with references on how to find more information			
e. ❑ Provide information in a more clinical way			

4. When the *EPSDT Care for Kids Newsletter* comes, I usually *(please check all that apply):*

a. ❑ Read all of it
b. ❑ Read some articles
c. ❑ Scan the headlines
d. ❑ Look for the handouts
e. ❑ Put it aside to read later
f. ❑ Route the newsletter to others in my workplace
g. ❑ Share it with families
h. ❑ Talk about it with others
i. ❑ File it for future reference
j. ❑ File some articles for future reference

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g. ❑ Nurse, public health
h. ❑ Physician assistant
i. ❑ Dietitian
j. ❑ Psychologist
k. ❑ Public health nurse
l. ❑ Head Start provider
m. ❑ School nurse
n. ❑ Social worker
o. ❑ Teacher or other educator
p. ❑ Other: _____

6. Please profide the following about the population your practice serves:

a. ____% Children
b. ____% Adults

7. The community in which we provide services has a population of:

a. ❑ Less than 1,000
b. ❑ 1,000 to 2,000
c. ❑ 2,000 to 5.000
d. ❑ 5,000 to 10,000
e. ❑ 10,000 to 20,000
f. ❑ 20,000 to 30,000
g. ❑ 30,000 to 50,000
h. ❑ 50,000-100,000
i. ❑ 100,000 to 250,000
j. ❑ 250,000 or more

8. Our services are provided through:

a. ❑ Private practice
b. ❑ Hospital-based service
c. ❑ County health department
d. ❑ Child Health Specialty Clinic
e. ❑ School
f. ❑ Child care provider
g. ❑ Other, please describe _____

Fold here first

9. I prefer to get this newsletter:

a. ❑ In print, by regular mail
b. ❑ Via email link to online newsletter
c. ❑ Twice per year
d. ❑ Three times per year
e. ❑ Four times per year

10. I have read this newsletter online or downloaded articles from it. ❑ Yes ❑ No

11. In my opinion, the most significant health concern of the children and their families I serve is:

12. Please provide the email address(es) where you, or your clinic, would be interested in receiving future communications regarding ithe EPSDT newsletter:

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Pharmacology and Effects

The pharmacologic effects of HMAs are likely due to both the synthetic cannabinoids and the herbal ingredients. Many herbs have been identified in these products, but there is very little medical information available to guide health care professionals regarding its effects and toxicities. Additionally, the wide variety of synthetic cannabinoids present in these products makes it even more difficult to predict the symptoms and outcomes for specific patients. Typically, after use, there is a rapid onset of effects that last between one-half and two hours. The desired effect of HMAs is euphoria. However, many users report that their experiences with these drugs are not pleasant and are unlike their experiences with THC. Drug therapists in addiction centers report that users universally state that the effects were extremely unpleasant and that they wanted to stop, but were unable to do so. The most common adverse effects of HMAs include dry mouth, tachycardia, diaphoresis, nausea, vomiting, loss of concentration, tremors, and feelings of alienation/disassociation. Other adverse effects include panic attacks, agitation, paranoia, delusions, psychosis, hallucinations, seizures, coronary ischemic events, and suicide.

Detection/Treatment

Traditional laboratory assays for delta-9-THC do not detect synthetic cannabinoids. Liquid chromatography and mass spectrometry methods have sometimes detected specific metabolites of synthetic cannabinoids in blood and urine specimens. Encouraging progress has been made by some independent companies that have developed commercial tests for the detection of synthetic cannabinoids in blood and urine. However, these assays are limited to testing for specific metabolites of known compounds typically in synthetic cannabinoids. It must be stressed that, since there are many different possible metabolites, depending on the synthetic cannabinoid product used, it is not currently possible to definitively rule out synthetic cannabinoid use on the basis of a negative test result. It is not known how long parent compounds and its metabolites persist in the urine following an exposure, but it is estimated to range from 48-72 hours.

There is no antidote for synthetic cannabinoid exposures, so treatment consists of supportive care. Benzodiazepines should be administered to control agitation, anxiety, tachycardia, and seizures, which are all symptoms not typically seen with regular marijuana. The use of antipsychotic medications to treat psychosis may decrease the seizure threshold, placing the patient at an even greater risk of seizures. Appropriate patient restraints should be used if there is risk of harm to self or others. All exposed patients should be closely observed until abnormal vital signs, vomiting, and psychiatric symptoms have resolved.

General Advice

Health care professionals must become aware of the intense consequences and adverse effects that may result from the use of designer drugs. It is essential that all possible exposures be reported to regional poison control centers (800-222-1222) in order to better track and manage the use of designer drugs in the U.S.

Resources

www.drugfree.org

http://www.justice.gov/dea/docs/drugs_of_abuse_2011.pdf Drugs of Abuse. 2011 Edition. A DEA Resource Guide.

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