NORTHWEST AIDS EDUCATION AND TRAINING CENTER

The New Club Drugs: Designer Drugs & Legal Highs Synthetic Cannabinoids and Cathinones

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Club drugs

- **Who uses club drugs?**
  - Survey of gay male circuit party attenders in SF (1)
    - 80% used ecstasy, 66% ketamine, 43% methamphetamine (MA), 29% GHB, 14% Viagra and 12% poppers during their most recent party. 53% used 4+ drugs.
  - Study of rave attenders in Chicago (2)
    - 48.9% used club drugs, 29.8% used LSD, 27.7% ecstasy & 8.5% MA. Also used club drugs with other drugs such as marijuana (87%), alcohol (65.2%) and cocaine/crack (26.1%).

(1) Colfax GN, Mansergh G, et al. J of Acquired Immune Deficiency Syndromes 2001;28:373-379.
(2) Fendrich M, Wislar JS et al. Addiction 2003;98:1693-1703

Club drug use among MSM and heterosexuals

- ↓inhibitions, impair judgment, ↑sexual endurance & ↑sexual risk-taking.
- Sexual risk taking among club drug users: high rates of unprotected anal intercourse (UAI) & high no. partners w/ unknown HIV status(1).
- In one study(2), HIV- heterosexual MA users reported
  - 9.4 sex partners over 2 mo.
  - Unprotected sexual acts in 2 mo: 21.5 for vaginal sex, 6.3 for anal sex and 41.7 for oral sex.
  - Most users (86%) reported engaging in “marathon sex” while high on MA. 37% of users reported injecting, almost half had shared or borrowed needles

(1) Clatts MC, Goldsmat LA, Yi H. Subs Use & Misuse 2005;40(9-10):1317-30
(2) Semple SJ, Patterson TL, Grant I. Addictive Behavior 2004;29:807-810.

The “old” club drugs

- Methamphetamine
- Ecstasy
- LSD
- GHB/GBL
- Amyl nitrite “poppers”
- Cocaine
- Ketamine
- Viagra
- Rohypnol

Newer club drugs

- Designer drugs: belong to a group of legally or illegally produced substances that are structurally and pharmacologically very similar to an illicit substance (e.g. amphetamines, Ecstasy, LSD)
  - "Spice", "K2", "Incense"
  - "Bath Salts", "Research Chemicals""Plant Food"

- Salvia Divinorum, "Diviner's Sage, Magic Mint"
- Kratom

Spice, K2 or "herbal incense": Synthetic Cannabinoids

- Psychoactively inert material sprayed with SC compounds.
- Sold on the Internet, “head shops” & smoke shops under the disguise of herbal blends, incense, or air fresheners. **Package labels indicate “not for human consumption”**
- Reasons for use: potent psychoactivity, legality, ready availability & non-detection in drug testing as reasons for its popularity.
- Abuse potential led to Drug Enforcement Agency (DEA) control of several SCs under the Controlled Substances Act.

Every-Palmer S. Drug Alcohol Depend 2011; Sep 1;117(2-3):152-7.

Spice & K2 “Incense”: Synthetic Cannabinoids

Cannabinomimetic Compounds

- Designed as research tools to study cannabinoid system.
- Bind to both the brain cannabinoid receptor CB1 and the peripheral cannabinoid receptor CB2 with higher affinity than Δ9-THC.

- CP 47,497 and homologues
- HU-210
- JWH-018: 1-Pentyl-3-(1-naphthoyl)indole
- JWH-073: 1-Butyl-3-(1-naphthoyl)indole

Every-Palmer S. Drug Alcohol Depend 2011; Sep 1;117(2-3):152-7.

Synthetic cannabinoid use: recognition and management

- Clinicians should suspect synthetic cannabinoid use if a patient:
  - Presents w/ signs & symptoms consistent w/ cannabis use.
  - Has negative routine urine toxicology screens.
  - Is in a situation in which his or her urine is being routinely monitored for illicit substance use.
  - Presents with otherwise unexplained sudden onset psychosis.

To make the diagnosis, clinicians should become familiar with the effects of synthetic cannabinoid use and have a high index of suspicion.

Castellanos D, Thornton G. J Psychiatr Pract. 2012; Mar;18(2):86-93.

“Bath crystals” & “Plant food”: Synthetic cathinones

- Sold in “head shops”, & via internet.
- Cost $25-50/50mg
- Packaging usually includes the disclaimer, “not for human consumption” to evade the authorities and avoid regulation
- Names: Blue Silk, Charge+, Ivory Snow, Ivory Wave, Ocean Burst, Pure Ivory, Purple Wave, Snow Leopard, Stardust, Vanilla Sky, White Knight, and White Lightening
- July 2012: DEA placed 2 of the 3 drugs and SCs under schedule I

Fass JA et al. Ann Pharmacother 2012;46:436-41.

“Bath crystals” & “Plant food”: Synthetic cathinones

- Cathinone: alkaloid found in *Catha edulis.*
- Substituted cathinones: designer drugs in the phenethylamine class, w/ 5-HT, NE & DA reuptake inhibition.
- Pharmacologically similar to methamphetamine and Ecstasy (methylenedioxymethamphetamine (MDMA)) and produce similar adverse effects.
- Most common active ingredients contained in “Bath Crystals”:
  - mephedrone (4-methylmethcathinone)
  - methylone
  - methylenedioxypyrovalerone (MDPV)

Fass JA et al. Ann Pharmacother 2012;46:436-41.

Mephedrone

- Clinical effects: euphoria, alertness, empathogenic effects, & mild sexual stimulation.
- Most frequent adverse effects
  - Tachycardia
  - Hypertension
  - Tremor
  - Loss of appetite
  - Hypertension
  - Hypertension
  - Trismus, bruxism
  - ↑ sweating (“mephedrone sweat”)
- Acute toxicity reports: CNS hyperstimulation, cardiovascular compromise, & serotonin syndrome
- Hallucinations, paranoia, seizures, & delusions
- High & frequent use: craving & tolerance

Fass JA et al. Ann Pharmacother 2012;46:436-41.

Methylenedioxypyrovalerone (MDVP)

- ↑release & reuptake inhibition of the monoamine neurotransmitters.
- Desired psychoactive effects: increased sociability, energy, sexual performance, euphoria.
- Adverse effects: panic attacks, tremor, agitation, insomnia, headache, tinnitus, confusion, suicidal thoughts, anhedonia, depression, psychosis, risk of tolerance and dependence.
- Acute toxicity: neurological, cardiovascular & psychopathological symptoms such as: tachycardia & S-T segment changes, hypertension, hyperthermia, mydriasis, tremors, psychomotor agitation, motor automatisms, parkinsonism, delusions, hallucinations, paranoid psychosis, long term changes in cognition and emotional stability, rhabdomyolysis, abdominal pain, renal damage

Coppola M & Mondola R. Toxicology Letters 2012; 208: 12–15

Methylone (3,4-methylenedioxy-*N-methylcathinone)*

- Structural analogue of MDMA. Inhibits DA, NE, 5-HT reuptake & stimulates release.
- Not scheduled substance in USA. Illegal in Sweden since 2007 & in UK since April 2010.
- Sold in powder, liquid & tablet form via Internet and in head shops.
- Reported to produce calm euphoria, alertness, restlessness, & strong sense of empathy with mild stimulation.
- Somatic adverse effects include tachycardia, hypertension, hyperthermia, sweating, mydriasis, nystagmus, nausea, vomiting, trismus, and bruxism. Psychiatric adverse effects include anorexia, anxiety, derealisation/depersonalisation, impaired short-term memory, psychosis, hallucinations & suicidal ideations.

Karila & Reynaud, Drug Test Anal. 2011; Sep;3(9):552-9.

Other analogs of cathinones and MDMA

- **Methedrone:** Stimulant w/ ↑sociability, euphoria, disinhibition, & energy. Mydriasis, polypnea, and hyperthermia are the main physiological responses. Deaths reported. Under control in Sweden and in Romania.
- **Flephedrone:** 4-fluoromethcathinone (4-FMC) along w/ structural isomer (3-FMC) sold as party drug by Internet-based companies. Has weaker stimulant effects & is often an ingredient in Ecstasy tablets
- **4-MEC (4´-methylethcathinone)**
- **MDAI** (5,6-Methylenedioxy-2-aminoindane) MDMA analogue
- **Butylone** [ß-keto-N-methyl-1-(3,4-methylenedioxyphenyl) -2-butanamine (ßk-MBDB)] Homologue of MDMA, also known as Methyl-J and Eden, metabolism is similar to MDMA.

Gunderson EW et al. American Journal on Addictions 2012; 21: 320–326.

Methoxetamine (MXE)

- Dissociative drug class, NMDA antagonist. Analog of ketamine; shares structural similarity with phencyclidine (PCP).
- Popular in UK via internet sales.
- ***Clinical Presentation*** (limited to self-report & advertising)**:** Euphoric & hallucinogenic effects.
    - Adverse effects: respiratory depression, vomiting, diarrhea, agitation, anxiety, and paranoia.
    - Like with ketamine: stupor, nystagmus, ataxia can be observed.
    - Not detectable via GC-MS
- ***Patient Management:*** **Similar to ketamine, PCP intoxication**. Suggested strategies include supportive care, IV fluid resuscitation, bzds for agitation, & respiratory support

Rosenbaum CD, et al. Drug Test Anal 2011; Jul-Aug;3(7-8):404-16

Piperazine Derivatives

- **Piperazine**: antihelminthic w/ stimulant properties. (eg, **BZP**, CPP, MBZP, MeBP, MeOPP, MeP, & TFMPP). Often sold as pills or powders containing a mixture of multiple drugs.
- ***Who Is Most at Risk?*** Young adults, especially in club culture, may be most attracted to this designer "party pill," or **"legal ecstasy**." Piperazine abuse is seen in Europe & New Zealand among young males. Used for amphetamine / stimulant-like effects, especially when attending dance clubs.
- Available on Internet, popularity will likely spread to the US & to demographics beyond just the "club scene."
- Illegal in N. Zealand since 2008.

Rosenbaum CD, et al. Drug Test Anal. 2011; Jul-Aug;3(7-8):404-16

Salvia Divinorum (Diviners Sage)

- **Hallucinogenic herb, mint/sage family, contains the hallucinogen Salvinorin A (Kappa Opioid Agonist).**
- ***Who Is Most at Risk****?* Young adults, adolescents w/ Internet access & interested in avoiding drug detection via this "legal high".
- ***Clinical Presentation:*** **Potent hallucinogenic effects.** It does not have serotonergic activity. Affinity for the **kappa opioid receptor** may cause sedation, analgesia, GI hypomotility, dysphoria & depression.
- ***Drug Screen Availability****:* not detected by standard immunoassays. Can be detected in urine and saliva using GC-MS.
- **Management:** Supportive care. Salvinorin A acts at kappa opioid receptors, in theory should not cause respiratory depression.

Rosenbaum CD, et al. Drug Test Anal. 2011; Jul-Aug;3(7-8):404-16

Kratom (*Mitragynia speciosa korth)* *

- Medicinal herb indigenous to SE Asia w/ analgesic, euphoric & antitussive effects via high affinity agonist activity at mu & kappa opioid receptors.
- Efficacy/adverse effects are poorly understood. Illegal in Thailand, Malaysia, Myanmar, South Korea & Australia; but remains legal & uncontrolled in UK & USA, & easily available via Internet
- Dependence is reported w/ withdrawal symptoms of anxiety, restlessness, tremor, sweating & cravings.
- Purchased online by Americans w/ chronic pain to self-manage opioid withdrawal.
- **Krypton**: available via internet. Consists of powdered Kratom leaves plus another mu-receptor agonist- O-desmethyltramadol added (active metabolite of tramadol).

Boyer EW et al. Addiction 2008;103(6):1048-50