Designer Drugs for Modern Times

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“I've never had a problem with drugs. I've had problems with the police.”

Keith Richards
Contemporary Drugs of Abuse

- Easily synthesized
- Widely used in past 15-20 years
- Designer drugs are structural modifications of illicit drugs
- Unscheduled for many years until they gained popularity
- Designer Drug Drug Act of 1986
Contemporary Drugs of Abuse

- Central Nervous System Stimulants
  - Amphetamines and Derivatives
  - Piperazines
  - Arylhexamines
  - Tryptamines

- Central Nervous System Depressants
  - GHB, GBL, BD
  - Inhalants
CNS Stimulants

- Cause the release of endogenous catecholamines and serotonin
- Patients present with sympathomimetic toxidrome:
  - Tachycardia
  - Diaphoresis
  - Mydriasis
  - Hyperthermia
  - Agitation
  - Seizures
CNS Stimulants

- Deaths from: hyperthermia, dysrhythmia, intracerebral hemorrhage
- Differential Diagnosis
  - Hypoglycemia
  - Hypo/hyperthermia
  - SAH
Amphetamines

- Amphetamine is the model CNS stimulant.
- FDA approval for ADD, weight loss, narcolepsy.
- Also refers to non-catecholamine sympathomimetics of the phenylethylamine family.
Amphetamines

- 1887: first synthesized in Germany
- 1932: sold as oral nasal decongestants
  - Benzedrine
  - Removed from market due to abuse
Amphetamines

- April 18, 2002
- Friendly fire incident
- Pilots had been using “go pills” to stay awake
- Said judgment was impaired when they dropped the bomb, killing 4 Canadians
Amphetamines

Street Names:
- Speed
- Pep pills
- wake-ups
- eye openers
- co-pilots
- coast-to-coast
- cartwheels
- A’s
- black beauties
Amphetamines

- Can be taken orally, snorted, injected
- Toxic dose: variable
  - LD 50 in humans is 20-25 mg/kg
- Metabolized by liver, excreted in the urine.
- Duration of effect can last up to 30 hours.
Amphetamines – Clinical Effects

- CNS: agitation, confusion, psychosis, coma
- CV: ischemia, hypertension, tachycardia, dysrhythmia, MI, vasculitis (chronic)
- Hyperthermia secondary to increased metabolism and agitation
- Rhabdomyolysis
- Dehydration
Amphetamines Mechanism

Amphetamine transported in by NE reuptake pump

Amphetamines cause leak of NE into cytoplasm

NE transported by Na+ dependent pump into synapse
Amphetamines Mechanism

- ↑ DOPAMINE = changes in mood, excitation, motor movements
- ↑ SEROTONIN = hallucinations
Treatment

- Supportive care; fluids
- Rapid external cooling
- Control of agitation: DIAZEPAM
Amphetamine Derivatives

Methamphetamine
Buzz killer.
He's tweaking. His heart is racing, he's grinding his teeth, he's talking really fast and not making much sense. He thinks he's sexy and popular. And he's bumped up his risk of getting HIV by 400%.

Don't mess with crystal.
For help, visit crystalmess.net

This message brought to you by SF Dept. of Public Health HIV Prevention Program
KAIZEN®
Pharmaceutical Grade
Ephedrin™
Bronchodilator*
Dietary Supplement
60 Tablets

Sudafed Dual Relief
Non-Drowsy
Clears Stuffy Nasal Congestion
Fast Acting relief from Sinus Pain
16 Capsules
Methamphetamine

- Much greater CNS potency than other amphetamines
- Staves off fatigue, improves cognitive and athletic performance
- Lasts up to 15 hours, infrequent dosing needed
- Treatment with restraint and benzodiazepines for sedation
MDMA

- Street names: Ecstasy, E, X, XTC, Adam, M&M, Tweety
- First synthesized in 1912; rediscovered in 1965
- Used therapeutically by psychiatrists in 1980s to enhance psychotherapy
- Recent popularity started in 1980s in NYC and London clubs
MDMA

- Controlled Substances Analogue Enforcement Act passed in response to MDMA in 1986
- Currently one of the most widely abused amphetamines by college students and teenagers
MDMA Mechanism of Action

Ecstasy blocks serotonin reuptake pump allowing more serotonin to accumulate in synapse
MDMA

- Mostly used PO
- Typical dose: 50-100 mg
- 1-2 pills/party
- Effects seen within 15-60 minutes
- Lasts 1-6 hours
MDMA Negative effects

- Jaw clenching, tooth grinding
- Muscular tension
- Restless movement of the legs
- Headache
- Insomnia
- Loss of appetite
MDMA – Negative effects

- Hyponatremia
  - $\uparrow$serotonin = $\uparrow$ADH
  - $\uparrow$ free water intake
  - $\uparrow$ Na$^+$ loss (dancing)
  - = seizures

- Treatment –
  - Fluid restriction if euvolemic
  - NS if volume depleted
  - Hypertonic saline if symptomatic
MDMA – Negative effects

- Serotonin syndrome by adding another serotonergic agent or an SSRI
- Also see those complications seen with amphetamines:
  - Hyperthermia
  - Dysrhythmias
  - Rhabdomyolysis
Paramethoxyamphetamine

- More hallucinogenic than MDMA
- More toxic than MDMA
  - MAOI effects – may be cause of enhanced toxicity
  - Greater frequency of hyperthermia, coma, seizures, arrhythmia, death than MDMA
Cathinone

- Naturally occurring psychoactive compound in the leaves of the Catha edulis plant.
- Sold openly on Somali streets.
- Made famous by book *Blackhawk Down*.
- Aidid’s soldiers used frequently.
Cathinone

- Increasingly intercepted by DEA & customs.
- Imported as fresh plant.
- Leaves are “chewed” as a wad in the cheek or put into teas.
Methcathionine

- Cat, Khat, Jeff
- Synthetic derivative of cathinone
- Synthesized from ephedrine
- Popular in Russia since 1970s; increased use in US in past decade
- Effects similar to methamphetamine (agitation, hallucinations)
Ephedrine

- Active substance in:
  - “Mormon’s tea”
  - Chinese herbal medicine “ma-huang”
  - “Herbal Ecstasy”
- Abused for its stimulant effect
- Marketed as a “safe and natural alternative to amphetamines”
  - weight loss
  - “natural high”
Ephedrine

- Similar toxicity to amphetamines
- Peripheral effects more pronounced
- Need to take much more to achieve CNS stimulation
- Linked to numerous deaths
Ephedrine

- FDA announced prohibition of sales of dietary supplements containing ephedra in 2003
- Beware of “Ephedra-free” products containing stimulants derived from other plants
Piperazines

- Amphetamine derivative – sold as ecstasy
- BZP (benzylpiperazine)
- TFMPP (1-3-trifluoromethylphenyl piperazine)
- Originally used as worming agents and as industrial chemicals.
- CNS stimulants when benzyl chloride is added to the core piperazine.
- NE and DOPA release enhanced.
BromoDragonFLY

- Amphetamine derivative
- 5HT 2a & 2c agonist
- Case reports of prolonged vasoconstriction and delayed sz

Treatment:
  - Sedation, cooling, vasodilators
Methylenedioxypyrovalerone

- Bath Salts, Ivory Wave, Vanilla Sky
- Norepi/Dopamine reuptake inhibitor
- Prolonged duration of action
- Tachycardia, dyspnea, hallucinations
- Treatment –
  - Supportive care
  - Benzos
  - Cooling
SYNTHETIC CANNABINOID

- Analogs of Δ9-tetrahydrocannabinol (THC)
- First developed in the 1960s!
- Agonists at cannabinoid receptors CB1 and CB2
- **JWH Series**
  - Act at receptor but are structurally different than THC

2006: First appearance of “Spice”

2008: Multiple reports in Germany

2009: Prominent in the United States
Clinical Presentation

Neuro
- Agitated
- Delirious
- Seizures
- Tremors

Cardiac
- Tachycardia/bradycardia
- Hypertensive
- STEMI

GI
- Nausea and Vomiting

Eye
- Injected conjunctivae

Young A, Schwarz E. Cardiotoxicity assoc w/the synth cannabinoid, k9, w/lab confirmation. AJEM 2011: in press
Treatment

- Supportive Care
- Sedation
- Cooling
Kratom

- Used to treat opioid addiction
- Derived from *Mitragyna speciosa*
- Top 5 legal highs in the UK
- Low doses stimulant
- High doses opioid
- 13 times more potent than morphine

http://www.thefix.com/content/never-heard-kratom-you-will
Arylhexamines

- Amphetamine derivatives
- Includes phencyclidine (PCP), ketamine, dextromethorphan
- Legitimate use as anesthetic agents
- Illegitimate use to alter sensory perception
Phenylcyclidine

- Prototype agent
- Causes altered sensory perception
- No LOC or pain
- First used as an IV anesthetic “Sernyl”
- Withdrawn in 1963 due to adverse reactions on emergence from anesthesia
- Available for veterinary use until 1973
NMDA RECEPTOR

Mg+
PCP
PCP

- Agonist at the sigma receptor
  - Dysphoria and hallucinations
- Inhibits reuptake of NE and DOPA
  - Sympathomimetic effects
- In OD associated with coma
- Lethal doses stimulate nicotinic, opioid and muscarinic receptors
PCP - Clinical Findings

- Nystagmus can be rotatory, vertical or horizontal
- Decrease in all sensory modalities (pain, proprioception, hearing, vision)
- Tachycardia, hypertension, hyperthermia
- Agitation, hallucinations
PCP – Clinical Findings

- Dissociative effects
  - “lights on, nobody home”
    - Consciousness, sensory perception and motor activity are dissociated in the brain – may result in violent behavior

- No Loss of consciousness

Delusion of superhuman strength and invulnerability
PCP

- Angel dust, elephant tranquilizer, hog, rocket fuel, mist, peace pill
- Available as powder, liquid, tablets, rock crystal
- PO, IV, snorted and smoked
PCP

- “illy” or “wet” when cigarettes or joints are dipped in PCP liquid and smoked
- “killer weed” when mixed with marijuana and smoked
Ketamine

- Ketalar synthesized in response to the dissatisfaction with phencyclidine as a surgical anesthetic
- Street ketamine is usually veterinary grade
- Emergence reactions
Ketamine

“Special K”, “K”, “Vitamin K”, “Fort Dodge”, “Super K”

- Effects similar to PCP
- Popularity in club scene comparable to MDMA (ecstasy)
Ketamine

- Liquid ketamine is dried leaving white crystalline material that is taken PO or insufflated.
- Clinical effects in minutes; lasts 15-45 min.
Ketamine

- Overdose is common – most users have experienced a “K-hole”
- Dysphoria, severe hallucinations, introspection lasts several minutes to an hour
Dextromethorphan

- Cough preparations
- “DM”, “Robo”, “Robo shots”
- Chemical structure to phencyclidine – may turn urine screen (+)
Dextromethorphan

- Complex receptor pharmacology
- Metabolite dextrophan interacts with sigma receptor
  - PCP-like dysphoria
- Binds to opioid receptors
  - Miosis, CNS/respiratory depression
- Blocks NMDA receptor
  - Sedation
- Blocks serotonin reuptake
  - Serotonin syndrome when mixed with MAOIs
- May alter DOPA transmission
  - Dystonia-like movements
Dextromethorphan

- Sedation with benzodiazepines
- Temperature control
- “Chemical restraint” preferred over physical restraint to avoid agitation induced rhabdomyolysis and hyperthermia
- Urine acidification not recommended – increases risk of renal failure from rhabdo
Tryptamines

- N,N-dimethyl-tryptamine (DMT)
- 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT)
- 5-methoxy-N,N-dipropyltryptamine (5-MeO-DPT, Foxy, Foxy Methoxy)
- N,N-dipropyltryptamine (DPT)
- Alpha-methyltryptamine (AMT)
Tryptamines

- Present in species of South American plants – long history of use there
- Usually smoked, but may be taken orally, injected or snorted
Tryptamines

- Potent serotonergic effects
- Sudden onset
- Intense hallucinations similar to LSD
- Physical exam is normal
- Internet sites promote use of MAOIs to enhance serotonergic effects
  - Risk of Serotonin Syndrome
Tryptamines

- DMT has a rapid onset (10-60 seconds) and short duration of action (5-20 minutes)
  - Businessman’s lunch
CNS Depressants

- Sedative-hypnotic agents
  - Benzodiazepines
  - Ethanol
  - Barbiturates
- Sedative-hypnotic/Short-term anesthetics
  - GHB, GBL, BD
  - Inhalants
- Opioids
GHB

- Resembles GABA – the inhibitory neurotransmitter in the brain
- Quickly crosses the Blood Brain Barrier
- Interacts with GABA$_B$ and opioid receptors
GHB

- Originally developed as an anesthetic; used legally to treat ethanol & opioid withdrawal; used to treat narcolepsy
- Gained popularity for its mood-altering effects and as a muscle-enhancing agent (thought to ↑ release of GH)
GHB

- FDA banned sale of GHB in 1991 because of abuse
- Chemical analogues to GHB were quickly popularized and are also illegal: gamma-butyrolactone (GBL) and butanediol (BD)
  - These were banned in 2001
- FDA approved use again in 2002 for cataplexy – a sudden loss of muscle tone associated with narcolepsy
  - Sodium oxybate (Xyrem)
GHB

- Very narrow “therapeutic window”
- Depending on dose, symptoms include: amnesia, deep hypnosis, somnolence, dizziness, euphoria, coma, seizures
  - ¼ teaspoonful can produce symptoms
  - 1 teaspoonful can produce coma
  - 3-4 teaspoonfuls can produce seizure-like activity
GHB

- Deaths reported from CNS depression, respiratory depression, bradycardia
- Overdoses are characterized by episodes of combativeness interspersed with episodes of obtundation
  - Commonly see random myoclonic motion of extremities and face with deep sedation
- Flumazenil and naloxone not consistently effective
GHB

- Supportive care
- Airway protection
- Most patients recover without sequelae within 6 hours
GHB withdrawal

- Seen most commonly in body-builders who are regular users
- Seizures, tachycardia, hypertension
- Benzodiazepines are mainstays of treatment for seizure activity
Inhalants

- Most commonly abused in 12-17 year-olds
- Products are widely available, inexpensive and legal to buy
- 991,000 new inhalant abusers in 1998
Inhalants

- Sniffing: direct inhalation of the vaporized substance from an open container
Inhalants

- Huffing: achieved by soaking a cloth with the volatile substance and then placing the cloth either over the nose and mouth or directly into the mouth while deeply inhaling
Inhalants

- Bagging: emptying the volatile substance into a paper or plastic bag and inhaling the bag’s contents through the opening or placing one’s head in the bag.
Inhalants

- Mechanism of CNS euphoria not clear
- May interact with GABA, nicotinic Acetylcholine, and glycine receptors
- May inhibit transmission at excitatory receptors such as the NMDA receptor
  - Causes post-synaptic inhibition
Inhalants

- Onset of symptoms is within seconds
- Euphoria, slurred speech lethargy, visual hallucinations, ataxia, headache, dizziness
- Severe toxicity may cause seizures and respiratory depression
Toluene

- Rubber cement, gasoline, paint thinner and stripper
- Metabolized to hippuric acid that produces a normal anion gap acidosis that may result in distal RTA and severe hypokalemia
Halogenated Hydrocarbons

- Correction fluid, dry cleaning agents, refrigerants
- Sudden Sniffing Death: prolongation of the QTc interval causes ventricular arrhythmias
  - Caused by any adrenergic stimulus following inhalation of the volatile substance
Amyl nitrite/Isobutyl Nitrite

- “Poppers”
- Amyl nitrite: part of CN kit
- Isobutyl nitrite: found in air fresheners
- Euphoria, floating sensation, ↑skin perception to light touch
- Vasodilation causes hypotension, reflex tachycardia
- Methemoglobinemia
Nitrous Oxide

- Whippits”, “nanging”
- Available in metal bulb whipped cream chargers
- Contents inhaled directly or from inflated balloons
- Euphoria, slurred speech, confusion, ataxia
Inhalants Treatment

- Supportive care
- Remove patient from source
- Decontamination of solvent-soiled clothing and skin
- Treat arrhythmias according to ACLS protocol, but avoid epinephrine in those induced by hydrocarbons to avoid dysrhythmia
  - β-blockers, Amiodarone if dysrhythmia in this setting
References

- Atwood BK et al. JWH018, a common constituent of “Spice” herbal blends is a potent and efficacious cannabinoid CB1 receptor agonist. British Journal of Pharmacology. 2010 160; (3);585-593.
- www.erowid.org