New Drugs of Abuse

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Drugs of Abuse

- New York State at a Glance (2008) [14]
  - One of the top ten states for drug use rates in several categories:
    - Marijuana use among young adults age 18-25
    - Cocaine use among persons age 12 and older
  - Approximately 9% of residents reported past-month use of illicit drugs;
  - National average was 8.8%.
- Heroin is the most commonly cited drug among primary drug treatment admissions
  - 3.54 percent of residents reported using an illicit drug other than marijuana in the past month
- Drug-Induced Deaths
  - As a direct consequence of drug use, 1,909 persons died (2007)
    - Persons in who died from motor vehicle accidents (1,478)
    - Firearms (985) in the same year.

Introduction

- Drug Users/Makers
  - Seeking new highs
  - Using old drugs in new ways
  - Creating designer drugs
  - Legal
  - Less expensive
  - Less contaminated
  - More readily available
  - More desirable physiologic effects

Case 1

- A 35 year old male, who usually only uses marijuana, presents to the ED after smoking something "new".
  - He says his dealer was recently arrested, so instead he bought something from a "friend" who had gotten something from a local tobacco shop.
  - After smoking it, he felt nauseous, had palpitations, he felt "high" but not a good high, and thought his dead grandmother was telling him to "run into the forest and not come back".
  - He became frightened and came to the ED

"Spice"

Known as “herbal highs” [16-19]
  - Sold
    - Internet
    - Head Shops
    - Tobacco Shops
  - Available
    - Since 2006
    - In 2008
    - Became widely available via internet, smoke shops
    - $25-40 for a 3g packet [18]

Spice

- Known as
  - Spice
  - Herbal Essence
  - K2
  - Lava Red
  - Aroma
  - Dream
  - TaiFun
- Advertised as [16]
  - Room Odors
  - Herbal Incense
  - Animal feed
  - Plant fertilizer
  - Collectibles
  - Not for human consumption
Spice
- Said to contain natural plant products
  - Baybean, Blue Lotus, Lion's Tail, Lousewort, Indian Warrior, Dwarf Skullcap, Macochea Brava, Pink Lotus, Marshmallow, Red Clover, Rose, Siberian Motherwort, Vanilla and Honey.
- Psychoactive? Stimulant?
- Synthetic Cannabinoids [16-19]
  - JWH-018 / JWH-073 / JWH-122
  - HU-210
  - CP-47,497 homologues

Synthetic Cannabinoid
- JWH-018
  - 1-naphthalenyl(1-pentyl-1H-indol-3-yl)methanone
- Clemson University
  - “potential development of new pharmaceutical products and an exploration of the geometry of both the cannabinoid brain (CB1) and peripheral (CB2) receptors”

Pharmacology
- Synthetic Cannabinoids [16]
  - Possess higher affinity for CB1 and CB2 receptors than THC
  - May have up to 10x greater affinity
  - Higher potency
  - Lower doses cause clinical effects
  - HU-210
    - Reported to have 100x the potency of THC

Difficult to know how much synthetic product per use
- Tens to hundreds of mg/sample
- Many preparations/types

Variations [16]
- Among the same product
  - No reliable similarities of type of synthetic cannabinoid
  - Leads to confusion by user
- Type of synthetic cannabinoid depended on flavor

Similarity based on Flavor? [16]

Flavor
- Vanilla
  - Cannabicyclohexanol
- Cherry
  - JWH-018
- Blackberry
  - Cannabicyclohexanol
- Natural Smoke Flavor
  - JWH-073
Clinical Effects

- Tachycardia
- Xerostomia
- Hypertension
- Hallucinations
- Seizure
- Psychosis
- Weakness
- Coma
- Dependence
- Withdrawal

Management

- Decontamination
  - GI
    - Limited value
- Benzodiazepines
  - Agitation
  - Seizures
- UDS
  - Will be negative for THC

Supportive Care

- CK levels - beware rhabdo
- EKG if chest pain
- Fluids
- Temperature control
- Seizure precautions

On November 24, 2010, the DEA announced that it would make JWH-018, JWH-073, JWH-200, CP-47,497 and cannabicyclohexanol illegal using emergency powers. The ban will make the sale and possession of synthetic cannabinoids illegal. The temporary ban, for at least a year, came into effect on March 1, 2011. (20-21)

Case 1 conclusion

- Patient received PO diazepam, and was admitted where his symptoms resolved
- He admitted to using something called “Blonde”

Case 2

Two male patients present to ED after a Phish Concert. They both are highly agitated and altered. Both have heart rates greater than 120 b/m.

- Patient 1
  - Becomes highly agitated and violent, and requires seven security guards to hold him down.
- Patient 2
  - Not as agitated, but has periods of yelling, and has noticeable horizontal nystagmus.

Phencyclidine

- PCP
  - Initially used as a general anesthetic
  - 10-30% incidence of post-op psychosis & dysphoria
  - 1967: exclusive veterinary use
  - 1960s' and 70s' gained popularity as drug of abuse
  - 1970 ketamine introduced as anesthetic
  - ~ 5x the potency as PCP
Phencyclidine (22)

- Common names: angel dust, embalming fluid, sherms
  - Powder, liquid, tablets, leaf mixtures, rock crystal
  - Mixed with THC: wet, fry, crystal joint, supergrass, embalming fluid
  - Often referred to as ‘smoking wets’
- Onset of action
  - Highly Lipid Soluble - IV/Inhalational: 2 – 5 minutes
- Duration of activity
  - Acute toxicity: 4 - 6 hours
  - Resolution: 24 – 48 hours
- UDS: metabolites may be present seven days after exposure

How does it work?

- Not completely understood (22)
  - Block NMDA receptors in cortex and limbic structures
  - May be contributory to PCP induced psychosis
  - Antagonize amine re-uptake complexes
  - Sympathomimetic
  - Psychomotor agitation
  - Also said to bind nicotinic, opioid, and muscarinic receptors

Clinical Manifestations (22-23)

- Superhuman strength
- Horizontal, Vertical, Rotary nystagmus
- Ataxia/Altered gait
- Dysarthria
- Miosis
- Myoclonus, dystonia, hypertonia
  - Usually not apparent unless unconscious

Management

- Supportive care
  - Temperature
  - CK levels
- Psychobehavioral symptoms
  - Quiet, non-stimulating environment
- Psychomotor symptoms
  - Physical/chemical restraints
  - Benzodiazepines to effect

PCP and the UDS

- Phencyclidine
  - Many cross-reactant can give false positives (22)
  - Dextromethorphan
  - Diphenhydramine
  - Ketamine
  - Venlafaxine
  - Venlafaxine

- Dextromethorphan
- Dextromethorphan
- Dextromethorphan
- Venlafaxine
- Ketamine
Case 2 conclusion
- Both patients required high doses of benzodiazepines
  - Patient 1 received nearly 200mg IV diazepam
  - Patient 2 received 180mg IV diazepam
- Deplete Emergency Room supply
- Tachycardia resolved
- Both patients did well overnight and discharged without sequelae

Case #3
- A 35 year old Cornell graduate student was overheard by neighbors screaming and called the campus police when they heard his apartment being “trashed” shortly thereafter
  - The police found a man with a bloody face
  - His apartment was in disarray with broken walls and overturned furniture
  - EMS was called, and the patient had a seizure for which he was given midazolam
- In the ED, the patient was highly agitated, but not violent
  - HR = 150

Legal Highs
- Type of Legal High
  - Neither
  - Controlled by governmental acts/policies
  - Licensed for legal use
  - Legal to possess and supply
  - Not sold for human consumption
  - Mixed with plant extracts or synthetic chemicals
    - Sold via internet or Head shops
      - “bath salts”
      - “research chemicals”
      - “plant food”
      - “hoover freshener”
      - “for botanical research”

Bath Salts
- Generic Term
  - Collective group of agents
    - Local tobacco shops
    - Truck stops
    - Mini-marts
    - Internet
- Surge in use since November 2010
  - NPDS Data:
    - ~1500 exposures reported nationally since 9/10
    - 31,100 exposures since Jan 2011
Bath Salts

- Cathinones
  - Constituent of the Khat plant
  - Leaves chewed for stimulant effect
  - Flowering plant native to tropical East Africa and the Arabian Peninsula.
- Synthetic Cathinones
  - Common Ingredients
    - Mephedrone (4-methylmethcathinone)
    - Meow-Meow
    - Bubbles
    - MDPV (3,4 methylenedioxypyrovalerone)
    - Methylone (3,4-methylenedioxymethcathinone)

Pharmacology

- Structurally Similar
  - Amphetamines
    - CNS stimulant
    - Peripheral Stimulant
      - Increasing release and inhibition of neurotransmitters
      - Norepinephrine
      - Dopamine
      - Serotonin
  - Phenylethylamine

Structures

Formulations and Routes

- Most are powder
  - Insufflation
  - Onset within minutes
  - Peak < 30 min
  - Rapid decline
- Ingestion
  - Longer onset of action
- Rectal
- IV
  - Has been combined with heroin
- Dose
  - Mephedrone
    - 90 mg
  - MDPV
    - 5 mg

Clinical Manifestations

- Symptoms
  - Agitation (53.3%)
  - Tachycardia (40%)
  - Hypertension (20%)
  - Seizures (20%)
  - Palpitations (13.3%)
  - Hallucinations/delusions
  - Suicidal ideation
  - Symptoms persisted for
    - more than 24h in 45%
    - More than 48h in 30% of cases
**Prolonged Symptoms?**

- The Times-Picayune
  - 21 yo male used Cloud 9
  - For several days he had paranoid delusions of the police coming to arrest and shoot him
  - Took a butcher knife and cut his throat
  - Was stitched and sent home
  - A day later, was found dead with a self inflicted gun shot wound

- WNDU – Indiana
  - 36 yo M, father
  - 2 months of abusing bath salts
  - Believed to have gotten from mini-marts
  - Lost 50 lbs
  - Had a fixed delusion that the FBI was after him
  - Killed himself by vehicle carbon monoxide

46% of bath salt abusers had a history of mental illness (bipolar, schizophrenia, or depression [10]).

**Management**

- Decontamination
  - GI
    - Limited value
    - Unless taken orally
  - Non-water soluble jelly
    - For insufflation
  - Benzodiazepines
    - Agitation
    - Seizures

- Supportive Care
  - CK levels – beware rhabdo
  - EKG if chest pain
  - Fluids
  - Temperature control
  - Seizure precautions

**Legal Status**

- May 23rd, 2011
  - NY State banned: mephedrone and 1,4-methylenedioxypyrovalerone (MDPV)

- July 15, 2011
  - Cuomo signed bill to ban "bath salts"

**Case 3 conclusion**

- Lab work
  - CK = 156,000 IU/L
  - Urine myoglobin
  - Alkalization with bicarbonate
  - Fractured nasal bones
  - Received benzodiazepines for agitation

- Patient eventually felt better
- Pulse decreased to 100 b/m
- He admitted to using bath salts and remembered a face in his wall (hallucination?) telling him to smash his head into everything in his apartment

**Case 4**

- 17 year old girl was partying all night
- Next morning she was found unresponsive behind her parents' couch
- Patient had seizures in ED
- Uncontrolled with IV benzodiazepines
- Intubated, sedated with propofol

**Molly**

- Recreational use
  - First reported in California in 1990's
  - Since 2004, widely used
  - Piperazines, as well as many other drugs
  - Sold as "Bliss"
  - "Purest ecstasy"
  - Charge
  - Bliss
  - Mash
Molly

- Traditionally marketed as “Purest Ecstasy”

Piperazines

- Molly -TFMPP (1,3 Trifluoromethylphenyl piperazine)
- Other piperazines
  - Not closely related to any familiar recreational drugs
  - No examples found in nature
    - Fully synthetic
  - Developed as anti-helminthic in 1950s
  - Evaluated as anti-depressant in 1970s
  - Terminated shortly thereafter

Pharmacology

- TFMPP (p)
  - Post synaptic serotonin agonist
  - Pre-synaptic serotonin release
  - Inhibition of re-uptake inhibitor
  - Little to no affect at dopamine and noradrenaline transport (q)
  - Sometimes combined with BZP (r)(benzylpiperazine)
  - Amphetamine like properties
  - TFMPP + BZP
  - MDMA affect?

Symptoms - Molly

- If TFMPP
  - Serotonergic Toxicity
    - Nausea
    - Migraines
    - Anxiety attacks
    - Serotonin syndrome
    - Seizure
    - Hyponatremia
  - If TFMPP + BZP
    - Agitation
    - Anxiety
    - Hallucinations
    - Vomiting
    - Insomnia

- Ecstasy (s)
  - Entactogen
    - A strong sense of inner
    - Diminished aggression, hostility, and jealousy
    - Diminished fear
euphoria
  - Feelings of intimacy and love for others
  - An intensification of all of the bodily senses (hearing, touch, smell, vision, taste)

Treatment

- Symptomatic
- Benzodiazepines
- Agitation
- Anxiety
- Consider serotonin syndrome
- Pay close attention to electrolytes
- Bottom line
  - Conflicting reports as to what it actually contains!
  - Treat the patient
Case 4 conclusion

- Serum sodium was 115 mEq/L
- Patient was intubated for almost a week
- Complications included aspiration pneumonia
- Further intermittent seizure activity
- Several episodes of hemodynamic instability
- Finally extubated
- Eventually discharged home
- Anoxic brain injury
- Difficulties with activities of daily living

Even Newer Drugs of Abuse!? 

- The Upstate PCC
  - Received a call
    - 20 year old female who used "Pond Cleaner" or "Pond Scum" for several days in a row
    - Last ingestion was 3 days ago
    - She presents with shakiness, confusion, and ataxia
  - 5-Iodo-2-aminoindane (5-IAI)
    - Little information available
    - Thought to be agonists of dopamine and act similarly to amphetamine

Conclusion

- Drug abuse remains a significant public health concern
- The "old" drugs of abuse are still very popular
- But the "new kids on the block" are emerging as dangerous alternatives