Update in Toxicology 2014

- Designer Drugs
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Update in Toxicology 2014

- Goal
  - Increase knowledge in management of the poisoned patient

- Objectives
  - Demonstrate an organized approach to the poisoned patient
  - Describe manifestations & management of the stimulant syndrome
  - List new designer drugs, their mechanisms, & their sources

Designer Drugs

Tox Update 2012
MINNEAPOLIS (KMSP) - Jun 06, 2013

The Twin Cities metro is experiencing a dramatic increase in heroin overdose deaths and emergency room admissions for overdoses.

Hidden America: Heroin Use Has Doubled, Spreading to Suburbs - ABC News Jul 31, 2013

Heroin-Related Deaths Spike In DuPage County (Chicago) July 18, 2013

Kentucky drug deaths decline slightly in 2012, but heroin deaths up sharply - Jul 26, 2013

Washington heroin use, deaths increase, especially among young people Associated Press June 12, 2013

Heroin and prescription overdoses rise throughout N.J.; skyrocket in Ocean County - Jun 11, 2013

The Law of Unintended Consequences

- Has the Crackdown on Prescription Opiates Shifted Abuse to Heroin?
  - Kentucky - HB#1 (Pill mill bill)
    - 10.4% decrease in Rx's in 6 mo (2011)
    - Heroin OD deaths - 3.2% in 2011
    - 19.5 % in 2012, 26% in 2013
    - FL, CA, MA, NY, OR, WA, OH

Poisoning Case

- A 47 year-old female presents to the ED with a "necrotic" rash of her legs.
- She has a past history of cocaine & heroin use, but denies any recent use.
- She is awake, alert, with normal vital signs & no fever.
- She has several "craters" of her lower legs
- The treatment team is concerned about possible use of "krokodil"
**Krokodil?**
- deadly 'cannibal heroin' that 'eats' addicts alive:

Designer Drugs
Levamisole

- Anti-helminthic
  - Used to treat parasitic worm infections
  - Also studied as chemotherapy agent
- Agranulocytosis (WBC depletion)
  - Still used to deworm cattle & for roundworms in aquarium fish
- Common in cocaine (over 80%)

Levamisole in Cocaine

- Levamisole contaminated cocaine induced cutaneous vasculitis syndrome.
- Levamisole-induced occlusive necrotizing vasculitis of the ears after use of cocaine contaminated with levamisole
- Why?
Levamisole

- Aminorex
  - Metabolite of levamisole
  - Amphetamine effect at monoamine receptors
- Hofmaier T, et al.
  Neurochem Int. 2013 Dec 1 (epub)

Poisoning Case

- A 23 year-old female presents to the ED after a seizure.
- She has no significant past history of seizures.
- She is sleeping, but awaken to verbal stimuli
- Her vital signs 99.8-128-12 96/60
- She reports using "Molly" at a concert the previous night.
- The treatment team is confused by her negative urine toxicological screen & wonders how they should evaluate her.

Molly?
“Molly” – 2010’s

- Variety of ecstasy-like substances in crystal or powder form (in bulk or in capsules)
  - As likely methylene as MDMA
  - Also ethylone, cocaine, 4-MEC, MDA, ethcathinone, methamphetamine, and BK-MBDB sold as “molly”.
  - A powder or chemical containing a euphoric stimulant or stimulant, with the implication of purity

Poisoning Case

- EMS is called to a local veterinary clinic
- A 22 year-old male is found confused after a 1 minute tonic-clonic seizure
- He has no significant past medical history, but brought his dog to the clinic for seizures
- Awake, answers questions only with “I’m cold”
- Tachycardic, hypertensive, hot, & diaphoretic
  - (P 106, RR 24, BP 167/102)
- How would you manage this encounter?

22 Year Old Male Confused after Seizure

- Mental Status
  - A – Open & Protected ?
  - B – Ventilating & Oxygenating ?
  - C – Rhythm, Perfusion ?
  - D - Disability / Seizures
    - Decontamination, Dextrose ?
  - E – Exposure, Elimination ?
    - Poison Center 1-800-222-1222

Designer Drugs
Initial Management

- Airway
- Breathing
- Circulation
  - 80% of poisonings
- Disability/Decontamination
  - 90% of poisonings
- Exposure/Elimination
  - Antidotes
  - 100% of poisonings

WA Poison Center
1-800-222-1222
1-800-709-0911

22 Year Old Male
Confused after Seizure

- Now complaining of nausea
- A – Open with intact gag reflex
- B – RR 24 / minute, clear lungs
- C - Tachycardic (Sinus - 110’s)
  Hypertensive (167/102)
- D - Seizure, Glucose 176
  Decontamination?
- E – Elimination?

Poisoning Management

- ABCDE
- Safety Net
  - IV, Monitors (ECG & O2)
- Focused History
  - What, when, why, what has been done?
  - What else is available?
- Focused Physical Examination
  - Toxicologic Syndrome?
### Poisoning Case

- A 22 year-old male
- Tachycardic, hypertensive, warm, & wet
  - (P 110, BP 170/100)
- Synthetic marijuana?

### Physical Examination

**Stimulant Syndrome**

<table>
<thead>
<tr>
<th>Vital Signs</th>
<th>Mental Status</th>
<th>Pupils</th>
<th>Mucus membranes</th>
<th>Respiratory</th>
<th>Gastrointestinal</th>
<th>Skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>T, P, R, BP</td>
<td>Seizures</td>
<td>Dilated &amp; reactive</td>
<td>Moist</td>
<td>Rate, depth</td>
<td>Motility</td>
<td>Pink, warm, moist</td>
</tr>
</tbody>
</table>
Spice Case

- Roomate produces packets of incense purchased at a local "head shop."

Georgia Department of Public Health Warning 26 August, 2013

- Dangerous, potentially lethal substance in convenience stores & smoke shops
- Ingested or inhaled neurotoxin can render a person motionless and/or unconscious and cause severe cardiac problems.
- In 24 hours, 8 hospitalized, 2 intubated.
Georgia Department of Public Health (DPH) Warning 26 August, 2013

- DPH working closely with Georgia Bureau of Investigation testing to identify the toxins
- Clinicians are advised to treat symptomatically
- Crazy Clown, Herbal Madness Incense
  - display a clown or “joker face”
  - and/or "5X" in product labeling

Designer Drugs

EViLDed's Mario Madness Herbal Incense is a brand new aromatic potpourri or herbal incense, if you will. This blend of aromatic potpourri is engineered to ease the stresses of work, school, home, etc. Powerful enough to easily blow your hair back. The recent ban on certain compounds does not affect our scents at all, and they also use the freshest and highest quality ingredients to create an uplifting fulfillment that is only a few clicks away.

Designer Drugs

Stimulant Agents - ?

Designer Drugs
Stimulant Agents

- Cocaine
- Amphetamines
  - Methamphetamine, Ecstasy, methylphenidate, phentermine
- Decongestants
  - Ephedrine, Pseudo-ephedrine
- Beta Stimulators
  - Albuterol, caffeine, theophylline
- Withdrawal States
  - EtOH, benzodiazepine, GHB

Designer Drugs

Cannabinoids

Our K2 blends are 100% legal!

View our entire collection as low as $7/gram

BUY NOW!

THE STRONGEST K2 INCENSE EVER MADE
Cannabinoids

- Spice products - Europe in 2004
- "Herbal smoking blend"
- "Not for Human Consumption"
- Synthetic agents, created to simulate effects of cannabis
  - CNS cannabinoid receptors
  - Derived from cathinones ("Khat")

Designer Drugs

Plant & Herbal Blends

- Marketed as incense
- Desire for 'legal high'
- Ability to avoid detection on drugs-of-abuse testing (THC)

Designer Drugs

Cannabinoids

- Heterogeneous structured compounds
  - Agonize endogenous cannabinoid receptors
  - Include phytocannabinoids derived from Cannabis sativa (delta 9-THC)
  - Endogenous cannabinoids
  - Synthetics

Designer Drugs
U.S. DEA Activity

- March, 2011
- Temporary Schedule I
  - unsafe, highly abused, no medical usage
- Five synthetic cannabinoids
  - JWH-018, JWH-073, JWH-200
  - CP-47,497 & Cannabicyclohexanol
  - HU-210 all ready Schedule I

Designer Drugs

Synthetic Cannabinoids 2010

- JWH – 250: 13%
- JWH – 73: 11%
- JWH – 18: 67%

U.S. DEA, Office of Diversion Control

Synthetic Cannabinoids 2011

- JWH – 250: 12%
- AM-2201: 28%
- JWH – 210: 9%
- JWH-122: 12%
- JWH-18: 14%

U.S. DEA, Office of Diversion Control
Synthetic Drug Abuse Prevention Act of 2012

- Signed into law July 9, 2012
- Adds certain classes of synthetic cannabinoids & two substituted cathinones—mephedrone and MDPV—to the federal controlled substances act.

Stimulant Agents

- Cocaine
- Amphetamines
- Decongestants
- Beta Stimulators
- Withdrawal States
- Cannabinoids
  - JWH-018, JWH-073, JWH-200
  - CP-47,497, Cannabicyclohexanol
  - HU-210

Stimulant Toxicity Clinical Management

- Central inhibition of catecholamine reuptake
  - Benzodiazepines (GABA receptor agonists)
    - 0.1-0.2 mg/kg Diazepam IV (5-10 mg)
    - 0.05 mg/kg Lorazepam or Midazolam IV or IM (2-5 mg)
    - Repeat every 5-10 minutes for seizures, every 10 minutes until calm
  - Neuroleptics (monitor the QT interval)
    - 2-5 mg IM or slow IV Haloperidol or Droperidol
Stimulant Toxicity Management

- Peripheral stimulation of alpha & beta receptors
  - Benzodiazepines (cardiac receptors)
  - Vasodilators; phentolamine, nitroprusside
  - Cardiac monitoring
- Additional effects
  - Benzodiazepines
  - Hydration, Cooling, Neuromuscular paralysis

Renal Injury with Cannabinoids

- 16 cases of AKI after synthetic cannabinoid use in six states
  - Oregon (6), Wyoming (4), New York (2), Oklahoma (2), Rhode Island (1), Kansas (1)
  - XLR-11 fluorinated-derivative of UR-144

Spice Case

- A 22 year-old Male
  - "confused after seizure"
- Tachycardic, hypertensive, warm, & wet
  - Midazolam 5 mg IM
- ED – Agitated & fighting
  - RSI
  - Urine reddish brown
  - IV ½ NS with 2 amps NaHCO₃
Spice Case

- CT head negative
- Urine Tox negative
- Admitted ICU
- Wakes next morning
  - “Crazy Monkey”
  - 3 cans/ day
  - Peak CPK 12,000
  - No renal failure
  - Discharged home intact
day #3

Designer Drugs

‘I’m a eat you’: Crazed naked man high on bath salts threatens to eat police officers as they try to arrest him on golf course Liburn, GA 3 July 2012

Police: Naked Man High On Bath Salts Chases Down Car Altoona, PA March 11, 2013

A naked stalker may have been high on bath salts when he came after a 3-year-old girl on a playground Designer drug thought to be behind face-chewing attack last month Miami, FL 12 June 2012

Designer Drugs

‘Smoking Bath Salts’

- 20 y.o. male – agitated & confused
- Ran from police
- Restrained
- “Tazed”
- Seizure
- EMS Called

Designer Drugs
**Smoking ‘Bath Salts’**

- 20 y.o. male – Seizing
- Per Roomate - Smoking ‘Bolivian Bath Salts’

**20 Year Old Male Seizing**

- Management?

**‘Bath Salts’ Case**

- Seizure stops
- Agitated
- No trauma
- Pupils 6 mm
- P 160 BP 120/60
- Diaphoretic & Hot Temp 39.6
“Bath Salts”

- $20 packets from convenience stores, truck stops & via Internet

“Bath Salts” - Compounds

- Very similar to amphetamines
- Side effects largely the same we see with amphetamines in large dose
  - Jeffrey Baldwin, University of Nebraska Medical Center
- Typically snorted, smoked, injected
- Can be mixed with water as a beverage

Snorting & Smoking Bath Salts
“Bath Salts” - Contents

- Mephedrone
- MDPV (3,4-methylenedioxypyrovalerone)

Mephedrone - Europe

- Cathinone derivative
- Marketed as ‘plant feeder’ ‘not for human consumption’
- Potentially addictive &
- Increasingly popular legal substitute for cocaine & ecstasy

MDPV - 3,4 methylenedioxypyrovalerone

- Epinephrine & Nor-epinephrine re-uptake inhibitor
**MDPV - 3,4 methylenedioxy pyrovalerone**

- Epinephrine & Norepinephrine re-uptake inhibitor
- Beta ketone 'research chemical'
- Intake (Dose 5-15 mg);
  - Oral (capsule, 'bombing,' beverage)
  - Rectal, Insufflation, Smoking, IV
  - Onset 1 hr, Peak 1.5 hr, Duration 3-12 hrs

**MDPV Toxicity - ?**

**“Bath Salts” Toxicity**

- 35 patients, Michigan ED's
- Agitation - 23 patients (66%)
- Tachycardia - 22 (63%)
- Delusions/hallucinations - 14 (40%)
- 17 patients hospitalized, 1 DOA
  - MDPV Identified
    - MMWR / May 20, 2011 / Vol. 60 / No. 19
‘Bath Salts’ Case

- Treated with paralysis & cooling (ice packs)
- Developed DIC
- Became pulseless
- Died 8 hours after arrival
- MDPV on toxicology

Cannabinoids & Bath Salts 2010 - 2011


Stimulant Agents

- Cocaine
- Amphetamines
- Decongestants
- Beta Stimulators
- Withdrawal States
- Cannabinoids
- ‘Bath Salts’
  - Mephedrone
  - MDPV
‘Dropping 25I’

- 26 y.o. female – agitated & confused
- Using 25I at Folk Life Festival
- Dropper
  - “1, 2, or 3”
- Restrained
- EMS Called

New “Rave” (2 C agents)

- Minneapolis, MN 17 March 2011
  - Eleven hospitalized (16-21 y.o.)
  - 2 critical, 1 dead
- Konawa, OK 7 May 2011
  - Seven hospitalized (19-20 y.o.)
  - 2 critical, 1 dead
- 2,5-dimethoxy-4-ethyl-phenethylamine

2, 5, 1-NBOMe Deaths Erowid.org (Extracts)

- March 2012 – Adult male South Australia
  - 2C-I-NBOMe & 2C-B-NBOMe (MVC)
- June 2012 – 17 & 18 yo males MN
  - Mixed 25i with chocolate candy
- July 2012 - 25 yo female, NC
  - 25i pills, died >12 hours after ingestion
25I-NBOMe (2C-I-NBOMe)

- Derived from 2C-I in 2003
  - Substituted phenethylamine psychedelic
  - First full agonist of 5-HT2A receptor
- Inactive orally
  - Readily absorbed
    - Mucous membranes
  - Common admin
    - Sublingual, buccal, nasal

Potent & active in sub-milligram doses
- Common dose 600–1,200 µg
- Difficult or impossible to measure as powder (do not snort - erowid.org)
- Duration 6–10 hours (sublingual, buccal)
- Up to 12 hours if insufflated in high dose

2 Ci Blotter Paper
### Designer Drugs

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Street Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>3,4,5-trimethoxy-phenethylamine</td>
<td>Mescaline</td>
</tr>
<tr>
<td>2C-E 2,5-dimethoxy-4-ethyl-phenethylamine</td>
<td>Europa</td>
</tr>
<tr>
<td>2C-B 2,5-dimethoxy-4-bromo-phenethylamine</td>
<td>Bees, Bromo, Bromo mescaline, Nexus, Spectrum, Toonies, Venus</td>
</tr>
<tr>
<td>2C-I 2,5-dimethoxy-4-iodo-phenethylamine</td>
<td>N-Bomb</td>
</tr>
<tr>
<td>2C-T7 2,5-dimethoxy-4-propythio-phenethylamine</td>
<td>Blue Mystic, Vanilla Aroma</td>
</tr>
</tbody>
</table>
Phenethylamines

- Agonist/antagonist 5-HT receptor
  - Hallucinations
  - Over-stimulation & agitation (amphetamines)
- Multiple forms
  - Tablets, capsules, powder for insufflation
- Kinetics
  - Onset 20 min, peak 2 hrs, duration 6-12 hrs

Designer Drugs

Phenethylamines

Clinical Effects

- Hallucinations, agitation, seizures
- Hyperthermia, tachycardia, hypertension, tachypnea
- Extreme/rapid cycling emotions
- Mydriasis, flushing, diaphoresis
- Nausea, vomiting,
- Facial dystonia (teeth grinding, grimacing)
- Rhabdomyolysis

Designer Drugs
Phenethylamines (cont)

- Insufflation - immediate pain nasal mucosa
- Law enforcement officers
  - Phenethylamine laboratories
  - Mucous membrane & respiratory symptoms

Designer Drugs

Phenethylamines

- Legal control
  - Nov 15, 2013 - DEA
  - 25I-, 25C-, 25B-NBOMe Schedule I
  - controlled substance analogs
- “Bad trips” alleviated by SSRIs?
  - Not studied nor recommended

Designer Drugs

25I Case
(26 y.o. female)

- Restrained & sedated
  - 24 mg Lorazepam
- Managed in ED
  - 36 hours
  - Progressive improvement
  - Ataxia
- “Want to try it again”

Designer Drugs
Stimulant Agents

- Cocaine
- Amphetamines
- Decongestants
- Beta Stimulators
- Withdrawal States
- Cannabinoids
- ‘Bath Salts’
- Phenethylamines
  - 2 CE & 2 CI

Stimulant Agents
Mechanisms of Action

- Central inhibition of catecholamine reuptake
  - Epinephrine, norepinephrine
- Peripheral stimulation of alpha & beta receptors
- Additional effects (nuances)
  - Na channel / local anesthetic (cocaine)
  - Serotonin reuptake inhibition (MDMA)

Poisoning Management

- ABCDE – Poison Center (1-800-222-1222)
- Safety Net
  - IV, Monitors (ECG & O2)
- Focused History
  - What, when, why, what has been done?
  - What else is available?
- Focused Physical Examination
  - Toxicologic Syndrome?
- Laboratory Studies?
"New designer drugs"

- "Smart Shops" in Poland
  - GC-MS 539 pills & 403 "plant-derived substances"
  - Piperazines (BZP, MPMP, TFMP)
  - Cathinones (ethylone, methylene, flephedrone)
  - Pyrovalerones (MDPV, naphyrone)
  - Synthetic cannabinoids
    - AM-694, JWH-019, 073, 081, 122, 200, 250)

- Bath Salts and Stimulants Designer Drugs - Expanded, Urine Test (8756U)
  - Methamphetamine, Amphetamine, O-Desmethylytramadol
  - MDMA, MDEA, MDA, DOM
  - Mephedrone, MDPV, Pyrovalerone,, Ethylone, Flephedrone, Buphedrone, Methedrone, Methyllone, Cathinone, Methcathinone
  - 2C-B 2C-C 2C-E 2C-H 2C-I 2C-N 2C-P 2C-T-2 2C-T-7

- Synthetic Cannabinoid Metabolites Screen - Expanded, Urine (Forensic) Test (9562U)

Tox Update 2012

Stimulant Toxicity - Key Points

- Central & Peripheral catecholamine surge
  - Characteristic clinical toxicological syndrome

- Specific agents
  - Cocaine, amphetamines, decongestants, cannabinoids, Mephedrone, MDPV, phenethylamines
  - Often unavailable for decontamination & detection
  - Treat the patient, not the agent

- Importance - reduce severity of poisoning (avoid complications)
  - Benzodiazepines & Hyperthermia management

Designer Drugs
“Spice” References


“Bath Salts” - References


Phenethylamine References

Update in Toxicology 2014

Goal
- Increase knowledge in management of the poisoned patient

Objectives
- Describe manifestations & management of the stimulant syndrome
- List new designer drugs, their mechanisms, & their sources

Designer Drugs

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