Gene G. Ryerson, M.D.

I have no conflicts of interest with the topics that I am going to discuss..
Inhaled drugs of abuse

Objectives

• Discuss the pulmonary effects of inhaled marijuana smoke.
• Discuss the pulmonary complications of smoked cocaine.
• List the chronic effects and overdose manifestations of methcathinones.
• List the physical and mental signs of overdose of Phencyclidine.
Route of Drugs and onset of brain effects

<table>
<thead>
<tr>
<th>Route</th>
<th>Time to Brain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>7 – 10 Seconds</td>
</tr>
<tr>
<td>Ingesting</td>
<td>20 – 30 Minutes</td>
</tr>
<tr>
<td>Injecting</td>
<td>15 – 30 Seconds if injected into vein</td>
</tr>
<tr>
<td></td>
<td>3 – 5 Minutes if injected into muscle</td>
</tr>
<tr>
<td>Snorting</td>
<td>3 – 5 Minutes</td>
</tr>
</tbody>
</table>
# Marijuana: Basics

<table>
<thead>
<tr>
<th>Type of drug</th>
<th>Hallucinogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>How taken</td>
<td>Smoked, Ingested, inhaled with vaporizer</td>
</tr>
<tr>
<td>Duration of effect</td>
<td>2 to 8 Hours</td>
</tr>
<tr>
<td>Addiction potential</td>
<td>Low</td>
</tr>
<tr>
<td>Physical danger</td>
<td>Low</td>
</tr>
<tr>
<td>Death from overdose from smoking</td>
<td>none</td>
</tr>
</tbody>
</table>
# Marijuana: Superweed

<table>
<thead>
<tr>
<th>Marijuana and crack cocaine</th>
<th>Buda, cocktail</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana and formaldehyde</td>
<td>Amp, wet sticks</td>
</tr>
<tr>
<td>Marijuana and heroin</td>
<td>Atom bomb</td>
</tr>
<tr>
<td>Marijuana and PCP (Angel Dust)</td>
<td>Happy sticks, superweed</td>
</tr>
</tbody>
</table>
Marijuana: Chemical Characteristics as the plant matures

**Cannabinoids**

- Cannabidiolic acid
- Cannabidiol (CBD)
- Tetrahydrocannabinol (THC)
- Cannabinol (CBN)
Marijuana: Sinsemilla

- Used in India since prehistoric times
- Potency increase by selecting small leaves and bracts from female plants - ganja
- Female plants raised in isolation from male plants - no seeds formed
- 85% of US production: 10-17% THC
Marijuana - Hashish

- Dried resin from flower tops
- 10 – 20% THC
- Hand-rubbing of plants
- Compressed to cakes
- Smoked in pipes
- Developed in Middle East
Marijuana: Psychoactive Effects

- Not water soluble, therefore must smoked or ingested (after heating)
- Peak effects: 15 – 45 min, diminish 2 to 6 Hr.
- Effects: euphoria, relaxed inhibitions, increased appetite, increased visual and auditory awareness
- Impaired- concentration, learning, perception, fine motor skills
Marijuana: Effects of regular use alone in comparison with nonsmokers

Chronic Symptoms

- Increased chronic cough
  sputum
  wheezing
- Increased incidence of acute bronchitic episodes
- Increased clinic visits for acute respiratory illness

Tashkin, 2013
Marijuana: systemic effects

- Eyes:
  - Reddening
  - Decreased intra-ocular pressure

- Mouth:
  - Dryness

- Skin:
  - Sensation of heat or cold

- Heart:
  - Increased heart rate

- Muscles:
  - Relaxation
## Eye signs of drugs of abuse

<table>
<thead>
<tr>
<th></th>
<th>Marijuana</th>
<th>Alcohol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal-sized pupil</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Slow or no reaction of pupil to light</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Nonconvergence</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Redness of sclera</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Glazing of cornea</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Nystagmus</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Swollen eyelids with watering</td>
<td>x</td>
<td></td>
</tr>
</tbody>
</table>
Marijuana: Effects of regular use alone in comparison with nonsmokers

Lung Function

• No difference in FEV1 or FVC (3)
• Increase FVC (3), Increase (1)
• Decrease FEV1/FVC (2)
• Lung volumes: Increased (1), No difference (2)
• No difference in Dlco (3)

Tashkin 2013
Marijuana: Effects on Alveolar Macrophages

• Bronchial alveolar lavage
  – 14 marijuana only smokers (MS)
  – 16 tobacco only smokers (TS)
  – 16 both tobacco and marijuana smokers (TS-MS)
  – 19 non-smokers

• Threefold increase in Alveolar Macrophages (MS)

• Six fold in TS-MS

• Significant functional impairment of fungicidal activity (MS and TS)

• Significant functional impairment of Phagocytic and bactericidal activity (MS)
Does Marijuana Smoking Increase the Risk of Lower Respiratory Tract Infection?

• Case reports of aspergillosis in immunocompromised patients
• Case report of cluster tuberculosis- sharing waterpipe
• Older study suggests increased risk of bacterial pneumonia in HIV patients
• Multicenter AIDS study- no association with progression of HIV or opportunistic pneumonia
Inhaled Marijuana smoke

• Carcinogens compared with unfiltered tobacco
  – 50% more Benzopyrene
  – 75% more benzanthracene

• Higher levels of ammonia and hydrogen cyanide

• Prolonged and deeper inhalation

• Smoked to a shorter butt length

• Higher combustion temperature

• 5X carbon monoxide concentration

• 3X tar with greater retention in airways

Moir  Chem Research in Toxicology 2008
Is regular smoking of marijuana a risk factor for respiratory cancer?

**Lung cancer-Upper Airway Cancer**

- Mixed studies
- Increased risk only in heavy marijuana smokers (>10.5 joint years) (small numbers)
- Studies mixed with tobacco users
Possible Associations of Marijuana with Barotrauma and Lung Bullae

• Case reports of pneumothorax and pneumomediastinum
• Case reports of lung bullae associated with marijuana smoking
Marijuana – Drug Testing

- Urine drug test: immunoassay or gas chromatography/mass spectroscopy
- Cutoff value- 15ng/mL
- Stored and accumulate fatty tissue
- Half-life 18-48 hours
- First time smoker- “Positive” from up to 3 days
- Frequent smoker- “Positive” for 4 weeks after last used
Synthetic Marijuana: K2/Spice

- Mixture of herbs and spices, sprayed with synthetic compounds similar to THC
- Common herb: Darmiana from Central America
- Street names: Bliss, black mamba, fake weed
- Usually smoked in pipes or joints or as tea
Synthetic Marijuana: K2/Spice

- Psychological effects: similar marijuana
  - Paranoia, panic attacks and jovial behavior
- Physiological effects: HR and BP
- Reports of life threatening toxicity: seizures, renal failure, psychosis, severe agitation
COCAIN TOOTHACHE DROPS
Instantaneous Cure!
PRICE 15 CENTS.
Prepared by the
LLOYD MANUFACTURING CO.
219 HUDSON AVE., ALBANY, N. Y.
For sale by all Druggists.
(Registered March 1885.)
See other side.
Erythroxylon coca leaves (chewed)  
(< 2% cocaine)  

Kerosene, sulfuric acid, alkali  

Coca paste (occasionally smoked)  
(20%-85% cocaine sulfate)  

Hydrochloric acid  

Cocaine hydrochloride (snorted, used parenterally) (90% cocaine)  

Baking soda  

Volatile organic solvent  

'Crack' (smoked) (95% cocaine)  

Freebase cocaine (smoked) (95% cocaine)
# Forms of Cocaine

<table>
<thead>
<tr>
<th>Property</th>
<th>Hydrochloride</th>
<th>Free Base Crack</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melting Point</td>
<td>About 200 C</td>
<td>About 100 C</td>
</tr>
<tr>
<td>Solubility</td>
<td>Water</td>
<td>Fat</td>
</tr>
<tr>
<td>Pyrolysis</td>
<td>yes</td>
<td>No</td>
</tr>
<tr>
<td>Vaporizes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Route</td>
<td>Intravenous</td>
<td>Inhalation</td>
</tr>
</tbody>
</table>
Cocaine

- Plasma Cholinesterase
  - 32-49%
  - Nonenzyme Hydrolysis

- Mixed Oxidase
  - 2.6-6.2%
  - N-demethylation

- Ecgonine Methyl Ester
  - Inactive Metabolite

- Benzoylcegonine
  - Inactive Metabolite

- Norcocaine
  - Active Metabolite
Cocaine Metabolism

Plasma Conc. (ng/ml)

Dose → $C_1V$

Slope = $-k$

Time (hours)

$T_{1/2}$

$k$

$C_1$

$V$

$5$

$10$

$100$

$50$

$20$

$10$

$5$

$2$

$1$

$1$

$2$

$3$

$4$

$5$

$6$

$7$

$1$

$2$

$3$

$4$

$5$

$6$

$7$

$8$

$9$

$10$

$11$

$12$

$13$

$14$

$15$

$16$

$17$

$18$

$19$

$20$

$21$

$22$

$23$

$24$

$25$

$26$

$27$

$28$

$29$

$30$

$31$

$32$

$33$

$34$

$35$

$36$

$37$

$38$

$39$

$40$

$41$

$42$

$43$

$44$

$45$

$46$

$47$

$48$

$49$

$50$

$51$

$52$

$53$

$54$

$55$

$56$

$57$

$58$

$59$

$60$

$61$

$62$

$63$

$64$

$65$

$66$

$67$

$68$

$69$

$70$

$71$

$72$

$73$

$74$

$75$

$76$

$77$

$78$

$79$

$80$

$81$

$82$

$83$

$84$

$85$

$86$

$87$

$88$

$89$

$90$

$91$

$92$

$93$

$94$

$95$

$96$

$97$

$98$

$99$

$100$
Cocaine: Terms of Abuse

• Run: continuous use for several days
• Crash – dysphonia after euphoric effects
  – Hours to days
• Cocaine Blues – Depression after crash
  – Days to weeks
• Reverse tolerance – “Kindling Phenomena”
Cocaine Toxicity
Kindling Phenomena

- Repetitive subthreshold electrical stimulation of limbic system

  - Convulsions with single small dose
  - Reverse Tolerance
The Acute Cocaine Reaction
(Casey Jones)
Early Stimulation

- Euphoria
- Mydriasis
- Tremor/jerks
- Bruxism
- Cold sweats

- Emotionally unstable
- Possible cocaine bugs
- Visual lights
- Core body temp rises
The Acute Cocaine Reaction (Casey Jones)

Advanced Stimulation

- Decreased responsiveness
- Convulsions
  - Flaccid paralysis
  - Coma
  - Respiratory failure
  - Pulmonary edema
REPORTS OF COCAINE-ASSOCIATED PULMONARY COMPLICATIONS

- NONCARDIOGENIC PULMONARY EDEMA
- BRONCHIOLITIS OBLITERANS WITH ORGANIZING PNEUMONIA
- DIFFUSE ALVEolar HEMORRHAGE
- INTERSTITIAL INFLAMMATION WITH EOSINOPHILS
- TRANSIENT PULMONARY INFILTRATES
- PULMONARY ARTERY HYPERTENSION (?)
Acute pulmonary symptoms associated with heavy, habitual cocaine smoking

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency of occurrence (%)</th>
<th>Prevalence (%)</th>
<th>Occasional</th>
<th>Most of time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough with black sputum</td>
<td></td>
<td>44</td>
<td>34</td>
<td>10</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td></td>
<td>6</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Chest Pain</td>
<td></td>
<td>38</td>
<td>31</td>
<td>7</td>
</tr>
</tbody>
</table>
Cocaine Toxicity
Chronic Effects

- Depression
- Insomnia
- Anorexia
- Impotence

- Perceptual changes - Magnan’s sign (Cocaine bugs)
- Paranoid psychosis
- Chronic upper respiratory symptoms
- Violent outbursts
COCAINE TOXICITY

MANAGEMENT OF ACUTE TOXICITY

• AVOID HALOPERIDOL
• BENZODIAZEPINES FOR SEDATION
• SEIZURES – DIAZEPAM
• AVOID BETA BLOCKERS-
• HYPERTENSION – NITROPRUSSIDE, POSSIBLE PHENTOLAMINE
• CONSIDER NALOXONE (HEROINE USE WITH COCAINE)
Cathinones
## Cathinones-Basics

<table>
<thead>
<tr>
<th>Type of drug</th>
<th>Stimulant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cathinone (Khat, Abyssinian tea)</td>
<td>Smoked, ingested, chewed</td>
</tr>
<tr>
<td>Methcathinone (Bathtub speed, Cat)</td>
<td>Smoked, Ingested, snorted, injected</td>
</tr>
<tr>
<td>Duration of effect</td>
<td>Up to 6 days</td>
</tr>
<tr>
<td>Physical danger</td>
<td>Moderate</td>
</tr>
<tr>
<td>Addiction Potential</td>
<td>High</td>
</tr>
</tbody>
</table>
What is Khat?

• Flowering evergreen shrub
• Two active ingredients: cathine, cathinone
• Origin: East Africa, Arabian Peninsula
• Sold for leaves, tender twigs, shoots
What are the acute effects of Khat?

• Induces manic behavior
• Grandiose delusions, paranoia, nightmares, hallucinations and hyperactivity, insomnia
• Immediate increase in blood pressure and HR
Methcathinone

• Patented wholly synthetic drug by Parke-Davis in 1957.
• Parke-Davis did not market due to side effects
• Soviet chemists discovered formula-called ephedrone
• Synthesized like methamphetamine
• 1982-cooked throughout Russia
• 1993- US Schedule 1 controlled substance
• More potent and addictive the cathinone
Methcathinone: Contaminants and Adulterants

• Illegally manufactured methcathinone
  – Ephedrine
  – Sodium dichromate
  – Sulfuric acid
  – Sodium hydroxide
  – Epsom salts
  – Toluene
  – Muriatic acid
  – Acetone

• Adulterants: caffeine. laxatives
Cathinones: Chronic Health Effects

• Similar chronic amphetamine use

• Common:
  – Loss of personal hygiene
  – Anorexia
  – Muscle wasting
  – Antisocial behavior
  – Parkinsonian symptoms
  – Anxiety and disorientation → paranoid psychosis
  – Violence and suicidal depression
  – Disagreeable body odor
Methcathinone Overdose

<table>
<thead>
<tr>
<th>Physical signs</th>
<th>Mental signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hyperthermia</td>
<td>• Confusion</td>
</tr>
<tr>
<td>• Tachycardia</td>
<td>• Agitation</td>
</tr>
<tr>
<td>• Hypotension</td>
<td>• Paranoia</td>
</tr>
<tr>
<td>• Mydiasis</td>
<td>• Visual and auditory hallucinations</td>
</tr>
<tr>
<td>• Sweating</td>
<td>• Unresponsive coma</td>
</tr>
<tr>
<td>• Tremors</td>
<td></td>
</tr>
</tbody>
</table>
Cathinone and Methcathinone Withdrawal Signs

• Abrupt withdrawal
  – Fatigue
  – Irritability
  – Miosis
  – Rhinorrhea
  – Muscle aches and spasms
# Phencyclidine/PCP/Angel Dust Basics

<table>
<thead>
<tr>
<th>Type of Drug</th>
<th>Stimulant, Hallucinogen Schedule II Controlled Substance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Routes</strong></td>
<td>Smoked, ingested, snorted, injected</td>
</tr>
<tr>
<td><strong>Duration of effect</strong></td>
<td>About 8 hours</td>
</tr>
<tr>
<td><strong>Physical danger</strong></td>
<td>Moderate</td>
</tr>
<tr>
<td><strong>Addiction potential</strong></td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Other Names</td>
</tr>
<tr>
<td>------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>Phencyclidine/PCP</td>
<td>Blue madman</td>
</tr>
<tr>
<td></td>
<td>Zombie dust</td>
</tr>
<tr>
<td></td>
<td>Aurora borealis</td>
</tr>
<tr>
<td>PCP</td>
<td></td>
</tr>
<tr>
<td>PCP mixed with crack</td>
<td>Beam me up Scottie</td>
</tr>
<tr>
<td>PCP mixed with marijuana</td>
<td>Crystal joints Killer weed</td>
</tr>
<tr>
<td>PCP mixed with heroin</td>
<td>Alien sex weed</td>
</tr>
</tbody>
</table>
PCP: History

- 1926 - First synthesized
- 1952 - Patented by Park-Davis Pharm Co.
- 1957 - Marketed as general anesthetic under name - Sernyl.
- Patients c/o delirium, delusions, visual disturbances, psychotic behavior
- 1965 - Withdrawn from medical use
- 1967 - Reintroduced as veterinary drug
Phencyclidine/PCP/Angel Dust Effects

MNEMONIC : RED DANES

- Rage                              Delusions
- Erythema                          Amnesia
- Dilated pupils                    Nystagmus
                                      Excitation
                                      Skin dryness
Phencyclidine/PCP/Angel Dust Effects

- Drunken behavior with drowsiness
- Slurred speech and poor coordination
- Less sensitive to pain
- Sense of strength and invulnerability
- Some: Impending doom, paranoia
- Violent hostility with risky behavior
Phencycline/PCP/Angel Dust- Signs of overdose

• Catatonic state: blank stare, inability to speak
• Violent behavior
• Fever, tachycardia, increase BP
• Drooling
• Muscle rigidity
• Panic and paranoia
Inhaled drugs of abuse

Objectives

• Discuss the pulmonary effects of inhaled marijuana smoke.
• Discuss the pulmonary complications of smoked cocaine.
• List the chronic effects and overdose manifestations of methcathinones.
• List the physical and mental signs of overdose of Phencyclidine.