Cocaine

Psychology 472
Pharmacology of Psychoactive Drugs

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Cocaine – Background Info

- From the leaves of Erythroxylan coca
- Used for centuries (maybe 5,000 years) in South America: Peru, Bolivia, Ecuador
- Used for
  - Religious
  - Social
  - Euphoriant
  - Medicinal

History

- Used to reduce hunger and increase energy.
- Under Inca rulers it was sacred; restricted to priests and aristocrats.
- Spanish conquerors first tried to ban it, but then realized it would improve work capacity of the Indians.
- 1749: Samples sent to Europe. Linnaeus gave the plant its own family and Lamarck named most important species in 1786 (Erythroxylon coca)

More History

- Robert Louis Stevenson reportedly wrote “The strange case of Dr. Jekyll and Mr. Hyde” with cocaine use in mind.
- Sherlock Holmes’ keen powers of observation were due to his 7 percent solution of cocaine.
- Paranoia of Holmes being pursued by criminal Professor Moriati resembles cocaine paranoia.

Medicine

- Proven to be one of the 1st local anesthetics for surgery
- Sigmund Freud obtained and studied cocaine's psychological effects
  - Advocated its use and prescribed cocaine for depression and chronic fatigue.
  - Later he realized its adverse side effects

Medicine Cont.

- Cocaine incorporated into numerous medicines and beverages
- Physicians thought it might be antidote to alcohol and opiate addiction
  - Produced effects opposite to CNS depression
Other Products

- Used in:
  - Lozenges and pastilles,
  - Elixirs
  - Pills.

More History

- Angelo Mariani patented a wine containing coca and became wealthy.
  - Cocaine praised by Edison, Czar of Russia, Prince of Wales, Jules Verne, Emile Zola, Henrik Ibsen, the Pope, others

Coca-Cola

- Originally had 60 mg / 8 oz.
- John Styth Pemberton made his version of Mariani wine drink in 1881.
  - He was moderately successful,
- 1885, Atlanta bans the sale of alcohol.
- Pemberton took out the alcohol
  - Sold his new drink under the name Coca-Cola.
  - Profits were good, but not great.
- Disillusioned he sold the entire operation to Asa Griggs Candler for $2,300.
- Rest is history

Included in Harrison Narcotic Act (1914)

- Banned its use
- Drove it underground until around the 1960s.
- By the 1920’s,
  - Limited to cultural “avant-garde.”
  - Was expensive and glamorous.
- Recreational use increased dramatically in the late 1960’s
- Inexpensive “crack” cocaine use spread in the late 1970’s
- Later use decreased and replaced with amphetamines

Cocaine in Medicine

- Was the 1st local anesthetic (topical, regional and spinal.
- Toxicity was marked with regional blocks.
- Still occasionally used, primarily in nasal surgery.

Statistics

- Use peaked in 1980’s
- Decreased in 1990’s
- Currently increasing
  - 2 million users
  - 22-25 million used at least once
  - Males are more likely to use than females
  - 0.7 million new male users each year
  - 0.5 million new females each year.
  - > 400,000 infants born addicted to cocaine each year.
Forms of Cocaine
- E. coca contains about 0.5-1.0% cocaine
- Leaves are soaked in kerosene and gasoline and mashed
- Cocaine extracted in the form of coca paste
- Paste approx 50-60% purity

Cocaine Hydrochloride
- Paste is treated with numerous chemicals to oxidize and purify the paste to form the water soluble cocaine hydrochloride powder.
- Can be close to 100% pure
- Can be injected, inhaled as powder, or ingested orally
- Cannot be smoked

Freebase Form
- Crack Cocaine
- Similar to the unpurified insoluble coca paste.
- Made by reversing the oxidation process
- Cannot be inhaled (as powder) or injected because it is not water soluble
- Forms a stable vapor when heated and inhaled (smoked)

Pharmacokinetics
- Absorbed from all sites of application
  - Mucous membranes, lungs, stomach
- Potent Vasoconstrictor
  - crosses mucosal membrane poorly
- Peak plasma levels in 30-60 minutes
- Inhalation causes slow absorption
  - Prolongs effects
Pharmacokinetics
- IV injection
  - Bypasses all barriers to absorption
  - Total dosage goes into blood stream and eventually the brain
- Smoking Cocaine Base
  - Absorption is rapid and complete at the lungs
  - Effects onset in seconds, peaks in 5 minutes and lasts about 30 minutes

Pharmacokinetics
- Distribution
  - Penetrates brain rapidly
  - Brain concentrations far exceed plasma levels
  - Freely crosses the placental barrier

Pharmacokinetics
- Metabolism & Excretion
  - Half-life 30-90 min.
  - Metabolized by enzymes in both plasma and liver to benzoylecgonine
  - Slowly removed from brain
  - Positive urine tests for 12 hours

Use With Alcohol
- In the presence of ethanol a different metabolite is produced – cocaethylene
  - Cocaethylene has the same physiological effect on the brain as cocaine but more toxic

Alcohol + Cocaine = Cocaethylene
- Active metabolite of cocaine
- Produced in liver when cocaine and alcohol used together.
- Half-life is about 2.5 hours
- Is a indirect dopamine agonist like cocaine
  1. Alcohol inhibits cocaine metabolism
  2. Resulting in production of cocaethylene,
  3. Further inhibits hepatic metabolism
  4. Further increases cocaethylene levels
- Is longer lasting and more toxic than cocaine.

Cocaethylene
- Euphoric effects last longer
  - Increases risk of dual dependency
  - Increases severity of withdrawal
  - Probably the reason 85-90% of cocaine users are alcohol dependent
- Alcohol/Cocaine is the largest two drug combination resulting in death
Pharmacodynamics
- Attaches to and blocks presynaptic dopamine reuptake transport proteins
- Result - Dopamine stays in the synapse longer
- Potentiates the synaptic actions of dopamine, norepinephrine and serotonin

Blocks Dopamine Reuptake Transport

Reinforcing Action
- Increases the sensitivity of D3 dopamine receptors in MFB
  - Increased density of D3 receptors
  - More Dopamine in synaptic cleft
  - Get Down Regulation
  - Responsible for craving

Psychological Effects
- Immediate euphoria
- Giddiness
- Enhanced self-consciousness
- Forceful boastfulness
- These last approx 30 min.

More Effects
- Increased alertness
- Motor hyperactivity
- Tachycardia
- Pupils dilate
- Increased glucose availability
- Shifts of blood flow from internal organs to muscles
- Numerous cardiovascular complications can occur with prolonged or single use

Effects in the CNS
- Depletion of Oxygen
- Cerebral Atrophy
- Seizures
- Others
Effects of Short Term Use

- Moderate euphoria lasts for 60-90 min
- A state of anxiety lasts for hours
- Thoughts race, rapid speech
- Sleep delayed
- Appetite suppressed
- A depressive state follows

Physiological Responses

- Responses are exaggerated
  - Anxiety, sleep deprivation, hypervigilance, suspicious/paranoiac, fearful
  - Develop an altered perception of reality
  - Can become aggressive or homicidal in response to imagined persecution
  - Toxic paranoid psychosis

Cocaine: Urine Testing

- Urine can test positive for cocaine for up to 12 hours.
- Benzoylecgonine can be detected for up to 48 hours; even to a week or more in chronic users.
- Therefore, urine presence of metabolite is not an indicator of recent use; nor does it "prove" that one was under the influence of cocaine at the time of commission of a crime.
- Cocaethylene is also tested for in urine.

Tolerance and Sensitization

- Tolerance occurs due to downregulation
  - Get sensitization of the anesthetic and convulsant effects
  - Explains deaths after low doses

Medical Complications

- Many cardiovascular effects
  - Heart attacks
  - Irregular heart rhythm
  - Respiratory failure
  - Seizures

Cocaine and Pregnancy

- Many indirect effects from the vasoconstriction of mothers blood vessels
  - Decreased blood flow and oxygen to Uterus
  - Associated with
    - Placental detachment
    - Preterm labor
    - Stillbirth
    - Low birth weight
    - Others
Kids Effects from Cocaine

- Direct effects from cocaine in the fetus
  - Neonatal neurological syndrome
  - Abnormal sleep patterns, tremors, seizures
  - Increased incidence of SIDS
- Some problems
  - Difficulty developing attachments
  - Difficulty dealing with multiple stimuli
  - Often behave aggressively
  - High incidence of ADHD

Cocaine Today

- Use will be determined by price and availability.
  - Today methamphetamine is cheaper and more available.
  - As we stop methamphetamine, cocaine may return.

Treatment

- No consensus on a generally accepted successful pharmacological treatment.
- Three problems that complicate therapy
  1. Intensity of the drug effect and reinforcing action
  2. Pronounced tendency toward relapse
  3. Most addicts have a coexisting disorder

Summary

- Very powerful drug
- Use is increasing again
  - Can cause death the first time using it.