### I. History

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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<tbody>
<tr>
<td>1200</td>
<td>Inca Empire. Coca declared gift of Sun God, divine plant</td>
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<tr>
<td>1580</td>
<td>Coca leaves arrive in Europe</td>
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<td>1859</td>
<td>Alkaloid cocaine characterized, anesthetic properties recognized</td>
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<td>1884</td>
<td>Freud wrote enthusiastically of cocaine’s ability to relieve depression and cure morphine addiction. Robert Louis Stevenson wrote “Dr. Jekyll and Mr. Hyde” while being treated with cocaine for tuberculosis</td>
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<td>1886</td>
<td>Pemberton invents “Coca-cola”</td>
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<tr>
<td>1890</td>
<td>Sherlock Holmes uses cocaine in The Sign of the Four</td>
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<tr>
<td>1891</td>
<td>Death from oral cocaine first reported in medical literature</td>
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<td>1906</td>
<td>Congress passes pure food and drug act to control cocaine</td>
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<tr>
<td>1914</td>
<td>Narcotic Act labeled cocaine as a narcotic with penalties and restrictions like heroin</td>
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### II. Epidemiology

- 1980's most frequently used illicit drug in ED patients
- 23 million Americans have used cocaine at some time
- 30% of people in US age 18-25 have used cocaine
- Intranasal cocaine primary route in early 1980's
- Intravenous use in middle 1980's, now smoking alkaloid "crack" most common

### III. Pharmacology

Cocaine is benzoylmethylecgonine, a naturally occurring plant alkaloid from Erythroxylon coca plant. Leaves are crushed, mixed with hydrocarbon solvent, alkaloid extracted with sulfuric acid. White crystalline powder formed after purification. This white crystalline powder is well absorbed from all sites (Mucous membranes, GI tract, respiratory tree).

Cocaine hydrochloride dissolved in alkaline solution and extracted with ether yields the pure alkaloidal form of cocaine called free base. Free base is called crack because of sound crystals make when heated. Crack is not destroyed by heating and vaporizes at high temperatures, therefore suitable for smoking.
Les intoxications à la cocaïne (suite)

IV. Metabolism
Cocaine has three metabolites. Ecgoline methyl ester is inactive, and is formed primarily by plasma pseudocholinesterase.
Decreased plasma cholinesterase activity is associated with increased risk of life-threatening cocaine toxicity.
Benzoylcegonine is formed by nonenzymatic hydrolysis, urine tox screening looks for this.
Norocaine is formed by N-demethylation, an active metabolite.
Inhibits the reuptake of epinephrine and norepinephrine while stimulating the presynaptic release of norepinephrine. In the CNS, cocaine may also block neuronal reuptake of dopamine and excitatory amino acids.

V. Complications of cocaine use
Cregler: NEJM 1986;315:1495-1500
A. CARDIAC
1. MYOCARDIAL ISCHEMIA
(Hollander:NEJM 333:1267-1272)
   a. Coronary artery vasoconstriction
      • Worse in diseased areas of vessels
      • Cigarette smoking synergistic for coronary vasoconstriction
   b. Thrombus formation
      • Plasminogen-activator inhibitor is increased
      • Thrombus formation occurs even without underlying coronary artery disease
   c. Platelet aggregation
      • Alpha-adrenergic mediated
      • Aggregation induced by adenosine diphosphate is enhanced
   d. Accelerated atherosclerosis
      • Demonstrated in animals and autopsy studies of young cocaine users
      • Increased myocardial oxygen demand
      • Left ventricular hypertrophy
      • Hypertension and tachycardia

2. MYOCARDIAL INFARCTION
   a. 6% incidence in cocaine users with chest pain
   b. Location, duration and quality, associated symptoms: None predictive
   c. Usually within 24 hours of use, but may be longer
   d. Cocaine withdrawal may cause ischemia
   e. Electrocardiogram interpretation
      1. Abnormal in 56 to 84% with cocaine chest pain
      2. J-point elevation and ST-segment elevation common
      3. Left ventricular hypertrophy findings
      4. 43% without infarction may meet criteria for thrombolytics
      5. Infarction occurs in some with normal EKGs
      Sensitivity of EKG for infarction 36%
      Specificity 90%
      Positive predictive value 18%
      Negative predictive value 96%
   f. Chemical Markers for cardiac disease
      1. Creatine kinase elevated:
         a. MB fraction difficult to interpret
      2. Troponin I
         a. Need studies
   g. Hypothesis, pathophysiology of myocardial injury

3. MYOCARDITIS
4. ENDOCARDITIS
5. CARIDOMYOPATHY
6. GREAT VESSELS
14. **DERMATOLOGIC**
   a. Ischemia
   b. Skin popping
   c. Formication

15. **MISCELLANEOUS**
   a. Intranasal cocaine use:
      1. Loss of smell
      2. Atrophy of nasal mucosa
      3. Perforation of septum
   b. Smoking
   c. Keratitis
   d. Conjunctivitis

VI. **Management of cocaine intoxication**

A. **AGITATED DELIRIUM**
   1. Consider all causes
      a. Anticholinergics
      b. Sedative hypnotic withdrawal
      c. Infection
      d. Hypoglycemia
      e. CNS trauma
   2. If due to cocaine:
      a. Due to block of reuptake of catecholamines
      b. Increase in excitatory amino acids
      c. Hypoperfusion of some areas of brain
      d. Seizure or intracranial bleeding?

B. **HYPERTERMIA**
   1. Sedate and cool
      a. Benzodiazepines for sedation
      b. No haloperidol or phenothiazines
         Catravas: Arch Int Pharmacodyn Ther 1978;235:328-340
      1. Blocks dopamine receptors
      2. Interferes with thermoregulation
      3. Lowers seizure threshold
      4. Induces dystonias
      5. Not protective in animal models

C. **SEIZURES**
   1. Benzodiazepines
   2. Barbiturates
   3. Observe for complications
D. HYPERTENSION
1. Secondary to agitated state
2. Sedate the CNS and hypertension will be controlled
3. B-blockers are contraindicated

E. CHEST PAIN
(Hollander: NEJM 333:1267-1272)
1. Benzodiazepines
   a. Reduce heart rate and blood pressure
   b. Decrease myocardial oxygen demand
   c. Decrease anxiety
2. Aspirin
   a. Prevent thrombus formation (no data in cocaine chest pain)
3. Nitroglycerin
   a. Limits size of infarct
   b. Reduces infarct complications
   c. Sublingual reverses cocaine induced coronary artery vasoconstriction
4. Phentolamine
   a. Alpha-adrenergic blocker
   b. Reverses cocaine-induced coronary vasoconstriction
   (Lange NEJM 1989;321:1557-1562)
5. Calcium channel blockers
   a. Prevent malignant arrhythmias
   b. Blunt negative inotropic effects
   c. Limit increases in systemic vascular resistance
   d. Protect against MI
   e. Verapamil reverses cocaine coronary vasoconstriction
   (Am J Cardiol 1994;73:510-513.)
6. Beta-adrenergic antagonists
   Contraindicated in Cocaine Myocardial Ischemia
   (Lange:NEJM 1989;321:1557-1561)
   (Lange Ann Int Med 1990;112:897-903)
   a. Enhance cocaine coronary vasoconstriction
   b. Increase blood pressure
   c. Heart rate not controlled
   d. Increases seizures
   e. Decrease survival
   (Catravas J Pharmacol Exp Ther 1981; 217:350-356.)
7. Thrombolytics
   a. Major complications 2.8%
   (Hollander NEJM 1992;327:361)
   b. One patient died with CNS bleed
   c. Limitations to use:
      1. Benefit in cocaine not proven
      2. Cocaine chest pain patients with lots of early repolarization abnormalities
      3. Mortality low in cocaine chest pain patients
8. Lidocaine
   a. Conflicting data
   1. Sodium bicarbonate for arrhythmias safer

F. CARDIAC ISCHEMIA
1. Uncommon
2. Soon after arrival within 12 hours
3. Ventricular arrhythmias 4-12%
4. Congestive heart failure 5-7%

G. CARDIAC ARRHYTHMIAS
1. Sedate the CNS
2. Wide complex: Sodium bicarbonate, Lidocaine
3. Consider Hyperkalemia as cause (from Rhabdomyolysis)

H. FUTURE THERAPY
1. Plasma cholinesterase administration?