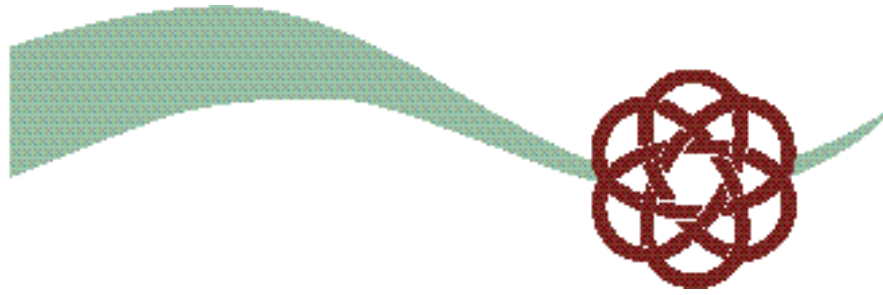


# 30

## Les intoxications à la cocaïne



**Vendredi**  
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8 h

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### I. History

- 1200 1553 Inca Empire. Coca declared gift of Sun God, divine plant
- 1580 Coca leaves arrive in Europe
- 1859 Alkaloid cocaine characterized, anesthetic properties recognized
- 1884 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
- 1886 Pemberton invents "Coca-cola"
- 1890 Sherlock Holmes uses cocaine in The Sign of the Four
- 1891 Death from oral cocaine first reported in medical literature
- 1906 Congress passes pure food and drug act to control cocaine  
Cocaine removed from "Coca-cola"
- 1914 Narcotic Act labeled cocaine as a narcotic with penalties and restrictions like heroin

### 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.

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## IV. Metabolism

Stewart: *Clin.Pharmacol.Ther.* 1979;25:464-468

Cocaine has three metabolites. Ecgonine 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.

Hoffman *Ann Emerg Med* 1992;21:247-253

Benzoylecgonine is formed by nonenzymatic hydrolysis, urine tox screening looks for this.

Norcocaine 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

Goldfrank, Hoffman: *Ann Emerg Med* 1991;20:165-175  
Hollander, Hoffman: *J Emerg Med* 1992;10:169-177

#### 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
- Moliterno, Lange: *Am J Med* 1994;96:492-496
- 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

##### e. Increased myocardial oxygen demand

##### f. Left ventricular hypertrophy

##### g. Hypertension and tachycardia

#### 2. MYOCARDIAL INFARCTION

##### a. 6% incidence in cocaine users with chest pain

(Hollander: *Acad Emerg Med* 1994;1:330-339)

(Zimmerman *Ann Emerg Med* 1991;20:611-615)

(Gitter: *Ann Intern Med* 1991;115:277-282)

##### 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%  
*Acad Emerg Med* 1994;1:330-339

##### f. Chemical Markers for cardiac disease

1. Creatine kinase elevated:  
agitation, hyperthermia, muscle injury  
a. MB fraction difficult to interpret
2. Troponin I  
a. Need studies

#### 3. MYOCARDITIS

#### 4. ENDOCARDITIS

#### 5. CARDIOMYOPATHY

*Wiener Am J Med* 1986;81:699-700

#### 6. GREAT VESSELS

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- a. Dissecting aortic aneurysm  
*Barth Am J Cardiol 1986;57:496*
- b. Vasculitis

## 7. VEINS

- a. Deep venous thrombosis
- b. Septic thrombophlebitis
- c. Superficial thrombophlebitis

## 8. CEREBRAL VASCULATURE

*Levine: NEJM 1990;323:699-704*

- a. Subarachnoid hemorrhage  
*Wojak: Stroke 1987;18:712-715*
- b. Intracranial hemorrhage
- c. Cerebral infarction  
*Seaman: Ann Emerg Med 1990;19:34-37*
- d. Headache
- e. Seizure  
*Myers: Neurology 1984;34:675-676*  
*Holland: Ann Emerg Med 1992;21:772-776*
- f. Cerebral vasculitis  
*Kaye: JAMA 1987;258:2104-2106*
- g. Brain abscess  
*Rao: NY State J Med Oct, 1988; 548-550*

## 9. PULMONARY

*Ettinger: Amer J Med 1989;87:664-668*

- a. Alveolar hemorrhage
- b. Pulmonary infarction
- c. Pulmonary edema
- d. Pneumomediastinum

## 10. MUSCLE

- a. Rhabdomyolysis  
*Roth: NEJM 1988;319:673-677*

## 11. HEPATIC

- a. Hepatonecrosis  
*Perino: Gastroenterology 1987;93:176-180*

## 12. URETEROPLACENTAL / FETAL

*Volpe: 1992;327:399-407*

- a. Abruptio  
*Acker: Am J Obstet gynecol 1983;146:220-221*
- b. Teratogenic effects  
*Chasnoff: NEJM 1985;313:666-669*

## 13. INTESTINAL

- a. Mesenteric ischemia / infarction  
*Nalbandian Surgery 1985;97:374-376*
- b. Intestinal obstruction in body packers

## 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. HYPERTHERMIA

1. Sedate and cool
  - a. Benzodiazepines for sedation
  - b. No haloperidol or phenothiazines  
*Catavas: 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  
*Derlet: J Emerg Med 1989;7:633-637*

### C. SEIZURES

1. Benzodiazepines  
*Derlet Ann Emerg Med 1989;18:542-546*
2. Barbiturates
3. Observe for complications

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## 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  
(*Catrasvas: J Pharmacol Exp Ther* 1981; 217:350-356.)

1. Labetolol
  - a. Combined alpha-beta antagonist
  - b. 7: 1 Beta blockade to alpha blockade effect when given IV
  - c. In pheochromocytoma, unopposed alpha effects
  - d. Increases seizure activity and mortality in animals  
(*Spivey: Ann Emerg Med* 1990;19:467)
  - e. No effect on cocaine coronary vasospasm in humans  
(*Boehrer: Am J Med* 1993;94:608)

## 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  
*Derlet Ann Emerg Med* 1991;20:135-138
  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?