Lecture 7
cocaine and sympathomimetics

Color Index
Green: Doctor's note.

Editing File

CNS Stimulants

I. Cocaine, Crack (free base or hydrochloride=Powder).

II. Amphetamines:

D-Amphetamine, Methamphetamine, methylphenidate, phenmetrazine (Preludin) - used to treat obesity,

(hallucinogens = MDA, MDMA, DOM; methylenedioxymethamphetamine, "ecstasy,").

III. Khat: Cathinone, methcathinone.

IV. Methylxanthines: caffeine (coffee), Theophylline used to treat asthma in the past (tea), theobromide (chocolate).

Cocaine Overview

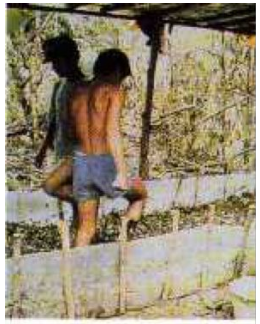
- Alkaloid from *Erythroxylon coca plant.*
- Indigenous to western South America
- Coca leaves used for religious, mystical, social, stimulant, and medicinal purposes
- Main stimulant uses: endurance (athletes), feeling of well-being (euphoria) , alleviate hunger (for weight loss porpuses)
- Medical uses: local anesthetic, vasoconstrictor (nasal congestion)

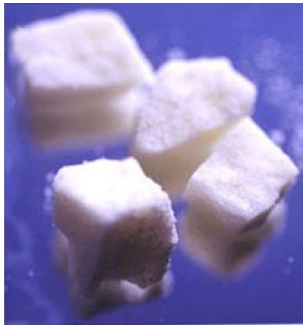
Cocaine Production

-Coca paste extracted from soaked and mashed leaves (60-80% cocaine)

-Cocaine powder made by mixing paste with hydrochloric acid (cocaine HCl)

-Freebase/crack extracted from powder with baking soda





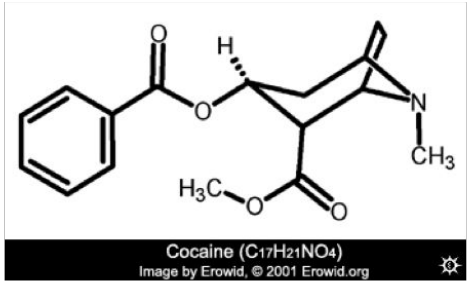
By inhalation or IV ingestion

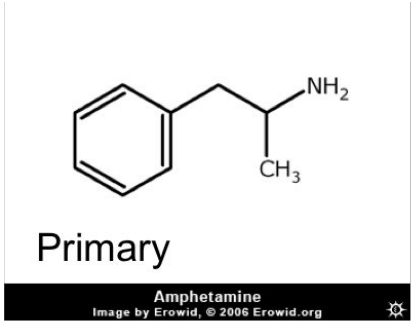
Amphetamine Overview

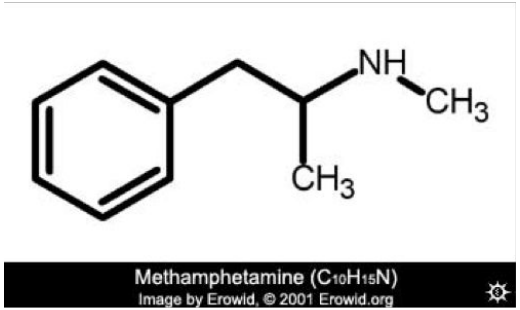
(poor man's cocaine bcs cheeper, crystal meth, ice, glass, speed)

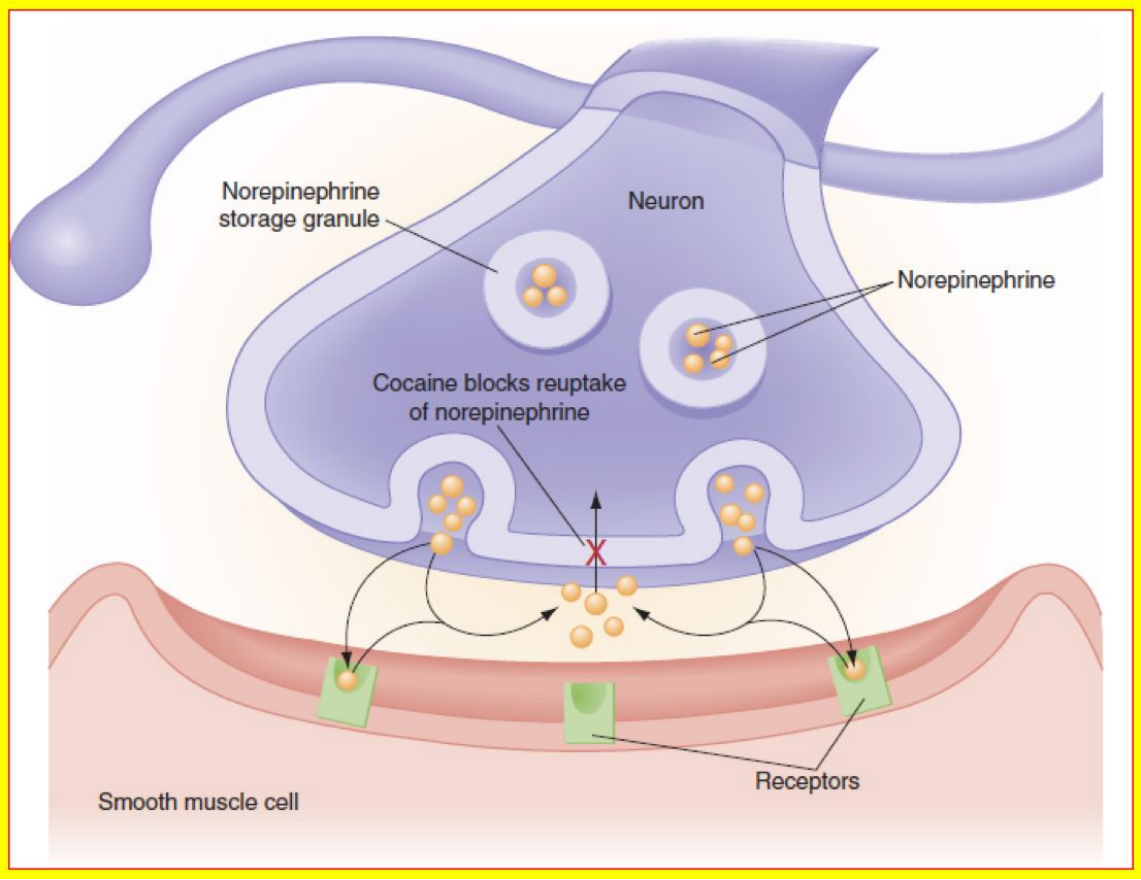
- Synthetic analog of ephedrine, active ingredient in mahuang
- Mahuang used in China for asthma
  - Chinese (Mandarin) *má huáng* : *má*, hemp + *huáng*, yellow
- Methamphetamine and Methylphenidate (Ritalin) are very similar
- Medical uses: obesity, ADHD, narcolepsy

Chemical Structure of Stimulants









Neurophysiology: cocaine blocks the reuptake of norepinephrine so they stay at synaptic membrane.

Table 152-1 Cocaine Pharmacology by Route of Administration

ROUTE	FORMULA	ONSET OF ACTION	PEAK EFFECT	DURATION
Inhalation	"Crack"	8 sec	2–5 min	10–20 min
Intranasal	Cocaine HCl	2–5 min	5–10 min	30 min
Intravenous	Cocaine HCl	Seconds	10–20 min	60–90 min
Oral	Cocaine HCl	30–60 min	60–90 min	Unknown
"Skin popping"	Cocaine HCl	Unknown	Unknown	Unknown

Subcutaneous, stays longer.

Effects on Mind, Brain, Behavior

Increase	Decrease
alertness/vigilance, concentration mental acuity, sensory awareness euphoria/elevated mood brain electrical activity self-confidence, grandiosity need for sleep (insomnia)	appetite brain blood flow, glucose metabolism

Effects on Mind, Brain, Behavior (cont.)

Increase	Decrease
anxiety, suspiciousness, paranoia. convulsions, tremor, seizure. psychosis, delirium. Locomotion (cant stay at one place) at low/moderate doses. Reinforcement/addiction.	judgment, complex multi-tasking (cant do it).

Peripheral Effects (sympathomimetic)

Fight/Flight/Fright Syndrome (sympathetic nervous system arousal)

-Cause of death is the heart because it affect AV node and cause Ventricular tachycardia
Mechanism: Na channel blocker (mainly cocaine) increase blood pressure, blood sugar, HR, Vasoconstriction, hyperthermic

Increase:

Blood pressure.

Blood sugar.

Heart rate.

Irregular heart beat.

Vasoconstriction.

Body temperature Bronchodialation.

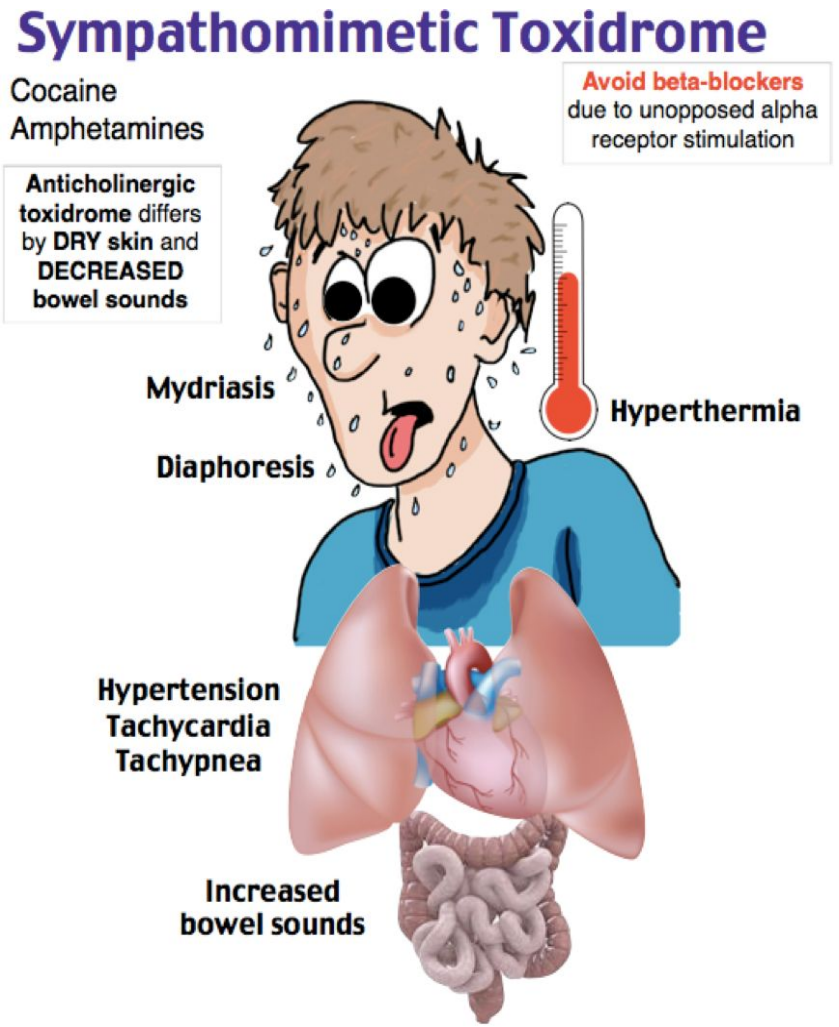
& Impaired breathing

-Avoid BB because sympathomimetic affect alpha and beta receptors, B receptor will be blocked and alpha will become worse, HTN will happen.

-Dry skin: anticholinergic.
-Sweaty: sympatho.

BOX 152-1 CLINICAL EFFECTS OF SYMPATHOMIMETICS

Hypertension
Hyperthermia
Tachycardia
Mydriasis
Diaphoresis
Central nervous system excitation



Cocaine Cardiac Features

- Cocaine dysrhythmias: Sodium and Potassium blockade.
- Supraventricular tachycardia (SVT),
- Wide or prolonged QRS is dangerous and might go to Vtach and die soon, for prevention give sodium bicarbonate subacute.
- Atrial fibrillation/flutter
- Wide complex tachycardia

Amph Effects on Rat Behavior same dose on humans.

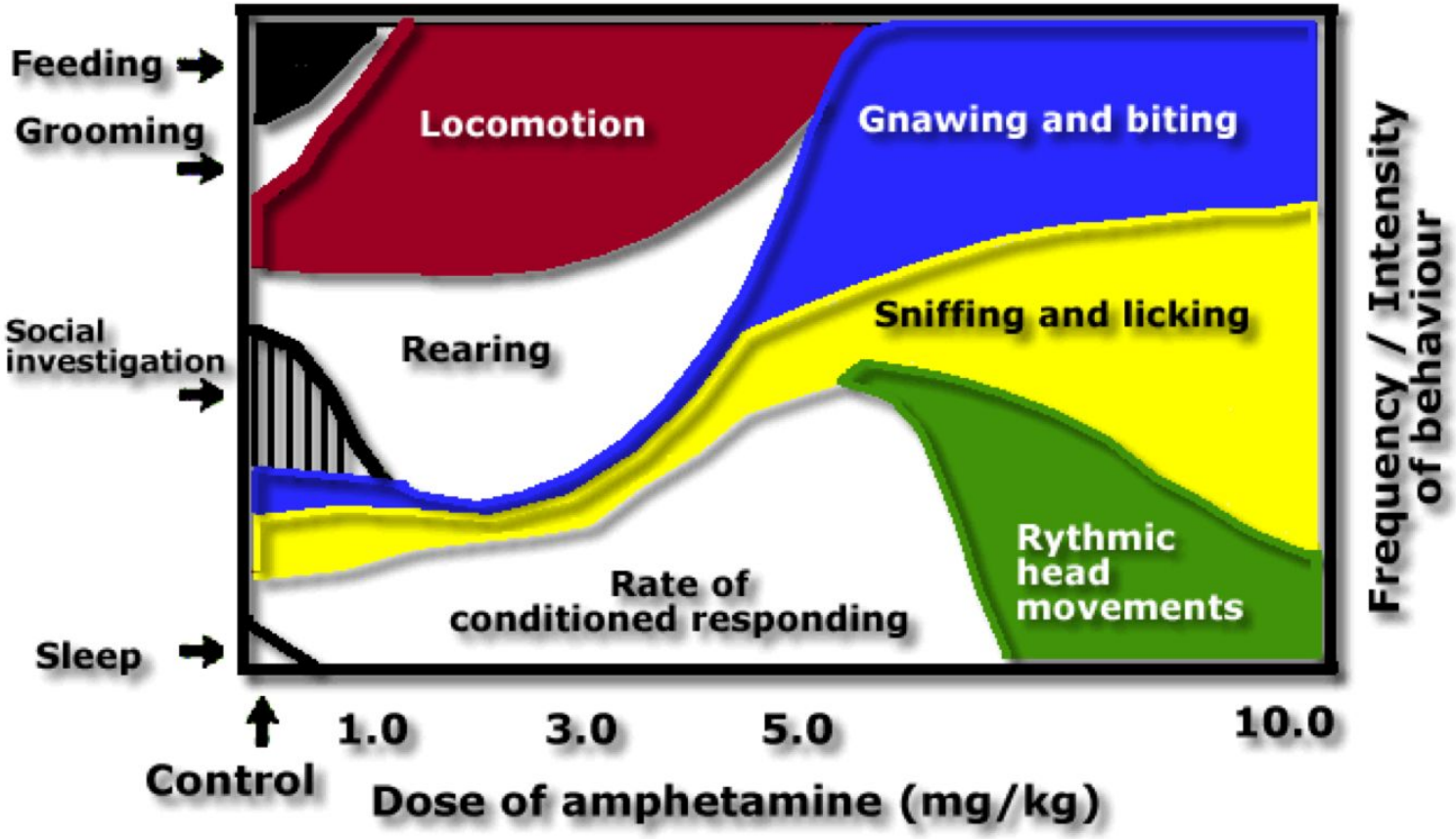


FIGURE 8: Granuloma (foreign body) along the venous path due to cocaine injection

Marks due to chloride.

If still suspecting and no marks on the hand go check the groin.

For weight loss and body building.

Body PACKER

↳ **"Packing a suitcase"** to go on a trip (to smuggle drugs)

Body STUFFER

↳ **"Stuffs"** everything down the mouth when caught by police

Cocaine Pharmacokinetics:

Absorption

- **Routes of administration**
  - Insufflated (snorted)
  - IV (mainlined)
  - Inhaled (freebased)
  - Oral

Pharmacokinetics: Distribution and Metabolism

- -Both cocaine and amphetamines penetrate BBB easily
- -Half-lives
  - Cocaine: ~ 50-90 min
  - Amphetamine: ~ 5-10 hours
  - Meth: ~ 12 hours
- -Metabolites include active and inactive compounds
- -Cocaine is unusual in that it "autometabolizes" in the blood in addition to normal liver metabolism.
  - Cocaine ----> norcocaine, ecgonine methyl ester, benzoylecgonine

Cocaethylene

- Alcohol inhibits metabolism of cocaine (Alcohol makes it accumulate and last longer)
- Alcohol + cocaine chemically react to form **cocaethylene**

ACTIVE

- Only known example where body forms new psychoactive compound from two others

•Cocaethylene

–Similar effects to cocaine

–Greater cardiac toxicity than cocaine

–3-5x the half-life of cocaine

–associated with seizures, liver damage, compromised immune system

Cocaine Pharmacodynamics

-**Indirect Agonist for**
- DA=dopamine (high affinity).
- NE= nore pinephrine(high affinity).
- 5-HT= seretonin(modest affinity).

-Mechanism:
Blocks monoamine reuptake.

Hyperthermia fatal due to hot weather

-In Saudi they take Amph more and die because of hyperthermia, CNS seizure.

Amphetamine Pharmacodynamics

- **Indirect Agonist for**
- DA (high affinity)
- NE (high affinity)
- 5-HT (low affinity) Unique feature in amphetamine.

Mechanisms:

–Blocks monoamine reuptake

–Inhibit vesicular storage

–Inhibit MAO metabolism

Reverses reuptake

Tolerance, Withdrawal, Addiction

- Withdrawal
  - Physically mild to moderate (hunger, fatigue, anxiety, irritability, depression, panic attacks, dysphoric syndrome may last up to 1 week)
    - Dysphoric syndrome (1-5 days after the crash): characterized by decreased activity, amotivation, intense boredom and anhedonia, intense "craving" for cocaine. May last 1-10 weeks.
  - Intense cravings
- Route of administration important to addiction risk

BOX 152-5 CAUSES OF STIMULANT-INDUCED CHEST PAIN

- Noncardiac
  - Pneumothorax
  - Pneumomediastinum
  - Pneumopericardium
  - Aortic dissection
  - Pulmonary infarction
  - Infection

  Due to inhalation injury by crystals and other toxic chemical
- Foreign body aspiration
- Cardiac chest pain
  - Endocarditis
  - Pericarditis
  - Ischemia/infarction Vasoconstriction my coronaries of heart, in Cath they will find spasm
    - During acute intoxication
    - After acute intoxication
- Coronary stent thrombosis

KHAT *Catha edulis*

Ingestion large amount will cause sympathomimetic affect, seizures and cardiac arrhythmias.

Addiction usually physologic.

Sympathomimetic Treatment:

- **Benzodiazepines: First line** (for any toxic case)
- Seizures: Benzodiazepines.... May use Propofol .
- β-blockers contraindicated (unopposed α-receptor stimulation) need to block both Alpha and beta so we can use phentolamine to block the alpha.
- Cocaine-induced wide complex tachycardia (Wide QRS) sodium bicarbonate Alprazolam (Xanax - benzodiazepine) for panic attacks.
- Hypertension unresponsive to benzodiazepines Phentoamine.
- Decontamination ? Do whole bowel irrigation or by opening the bowel and take it out if the amount absorbed is ALOT (a bag of cocaine)
- Prevention of toxicity from Amphetamine (pills) is by activated charcoal.