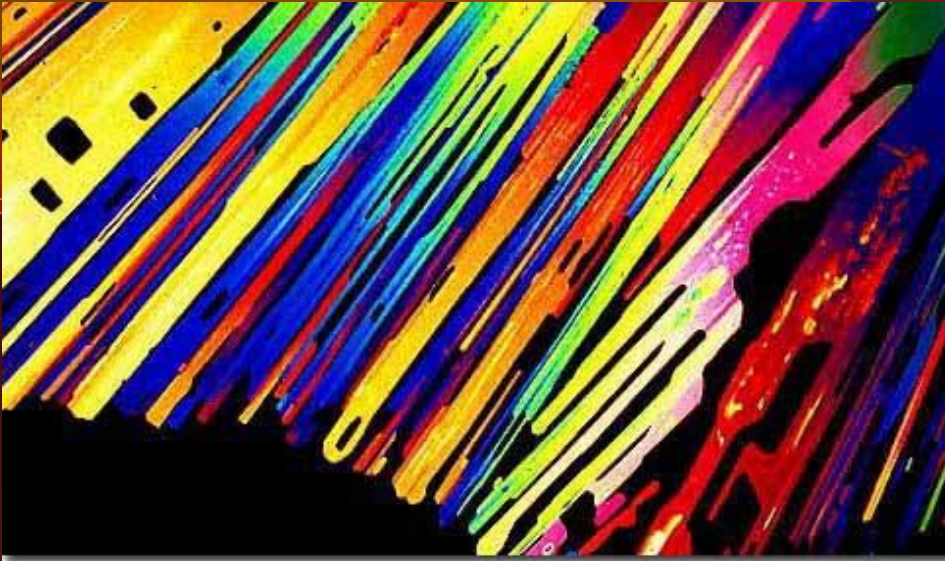


SYMPATHOMIMETICS

Dr. Tawfiq Almezeiny
MBBS, FRCPC (CCM)



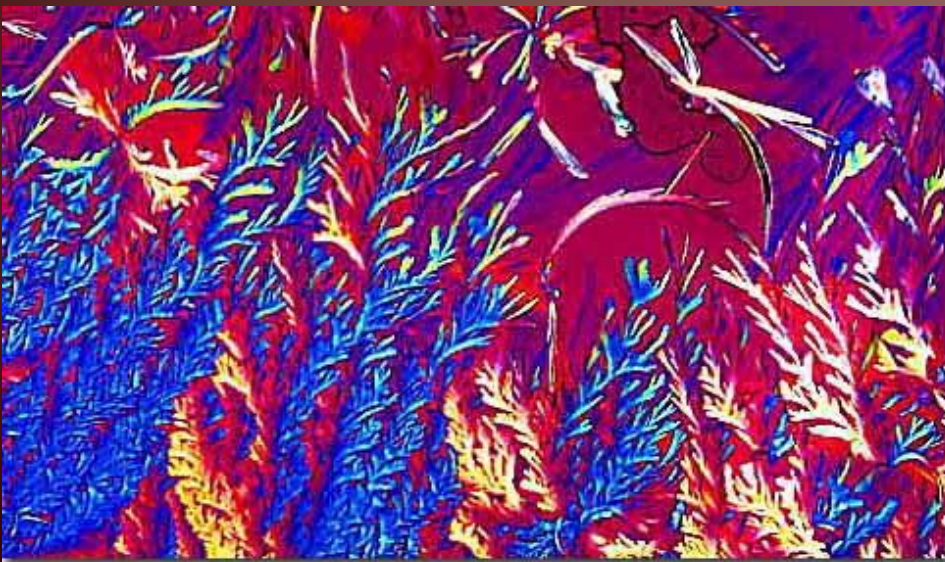
Cocaine



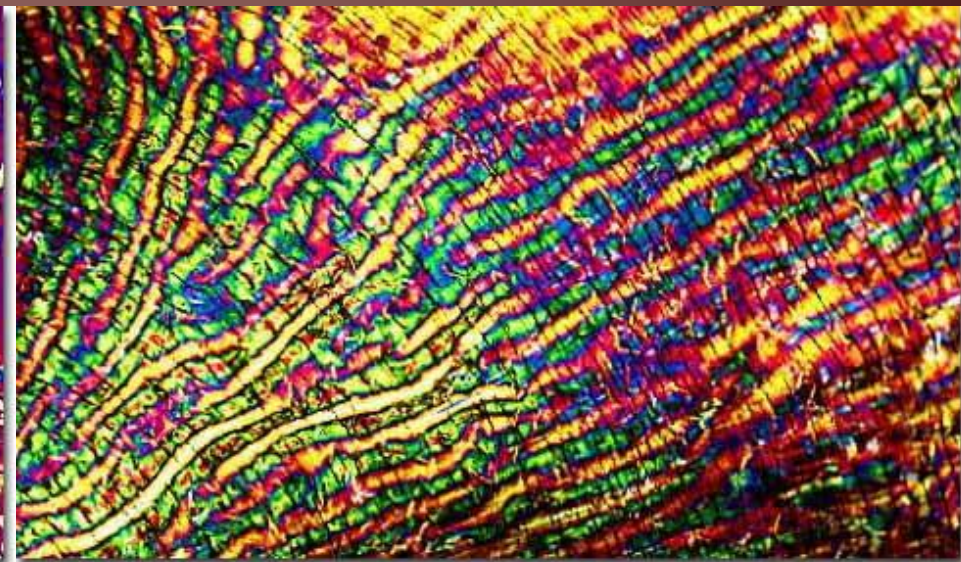
Ephedrine

Stimulants

Methamphetamine



Methylphenidate



CNS Stimulants

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

II. Amphetamines:

D-Amphetamine, Methamphetamine, methylphenidate (use to treat attention deficit disorders in children), phenmetrazine (Preludin) - used to treat obesity, (hallucinogens = MDA, MDMA, DOM; methylenedioxymethamphetamine, "ecstasy," dimethoxyamphetamine).

III. Khat: Cathinone, methcathinone.

IV. Methylxanthines: caffeine (coffee), theophylline (tea), theobromide (chocolate).

Cocaine Overview

- Alkaloid from *Erythroxylon coca*
- Indigenous to western South America
- Coca leaves used for religious, mystical, social, stimulant, and medicinal purposes
- Main stimulant uses: endurance, feeling of well-being, alleviate hunger
- Medical uses: local anesthetic, vasoconstrictor



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



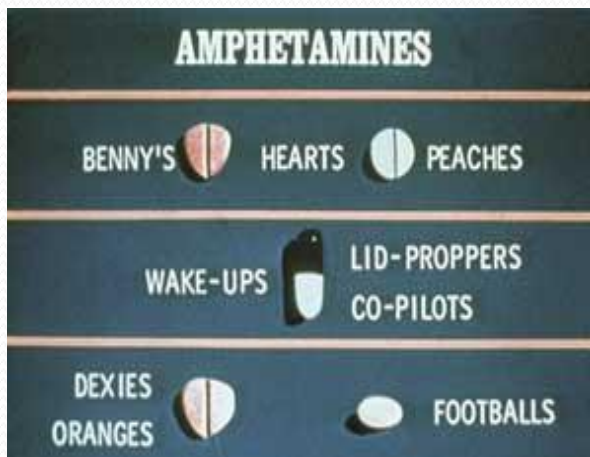


Amphetamine Overview

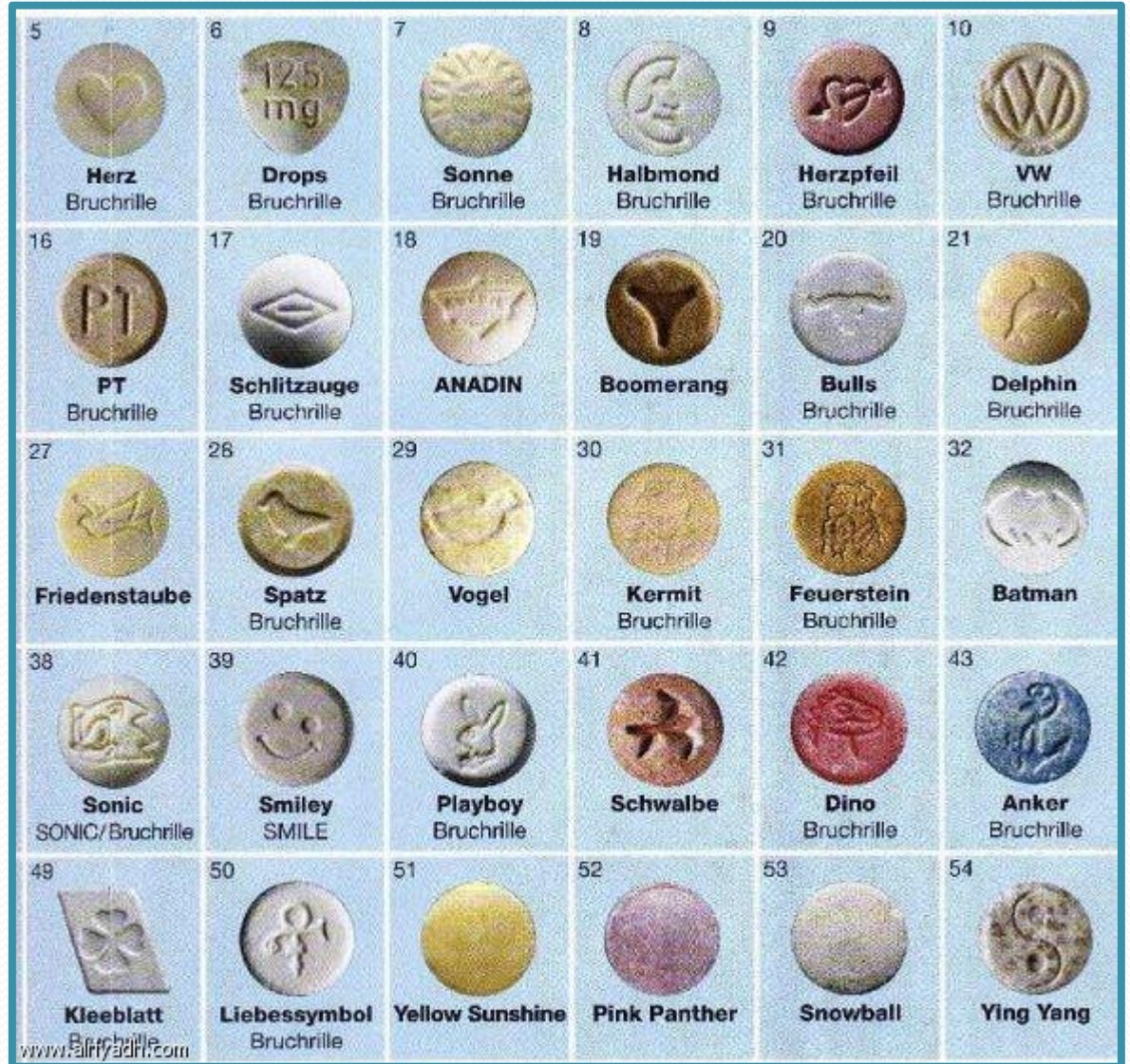
(poor man's cocaine, crystal meth, ice, glass, speed)



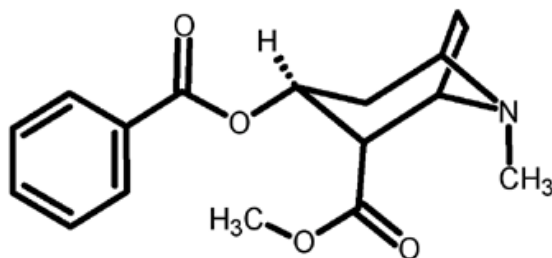
- Synthetic analog of ephedrine, active ingredient in mahuang
- Mahuang used in China for asthma
 - Chinese (Mandarin) *má huáng* : *má*, hemp + *huáng*, yellow
- Methamphetamine and Methylphenidate (Ritalin) are very similar
- Medical uses: obesity, ADHD, narcolepsy



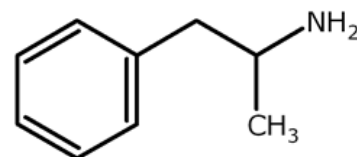
أبو ملف ، الأبيض ،
أبوداب ، قضم
،القشطة ، أبو قوسين ،
المتخفي،ابو وجه،
ابو زهرة، ابو مقص ،
ابو شمس، ابو استفهام
، ابو كرسي
و حديثا تسمى الليكزس
او في اكس ار



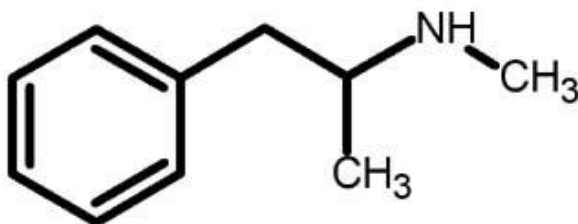
Chemical Structure of Stimulants



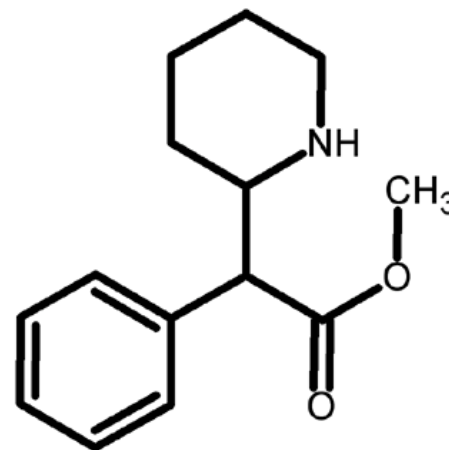
Cocaine (C₁₇H₂₁NO₄)
Image by Erowid, © 2001 Erowid.org



Amphetamine
Image by Erowid, © 2006 Erowid.org



Methamphetamine (C₁₀H₁₅N)
Image by Erowid, © 2001 Erowid.org



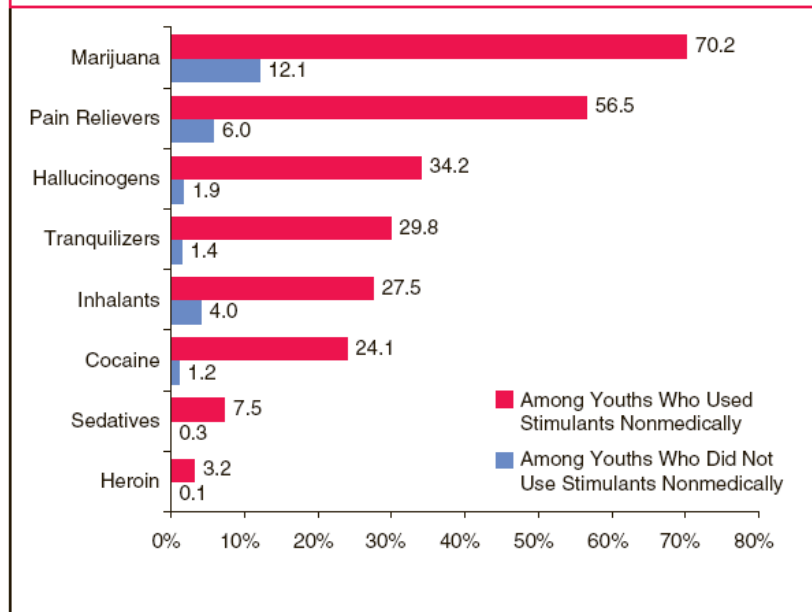
Methylphenidate (C₁₄H₁₉NO₂)
Image by Erowid, © 2001 Erowid.org





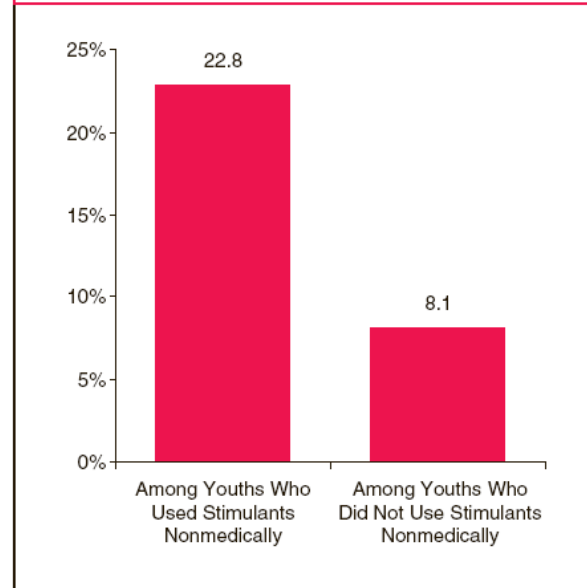
National Survey on Drug Use and Health

Figure 1. Percentages of Youths Aged 12 to 17 Using Illicit Drugs in the Past Year, by Past Year Nonmedical Stimulant Use: 2005 and 2006



Source: SAMHSA, 2005 and 2006 NSDUHs.

Figure 3. Percentages of Youths Aged 12 to 17 with Past Year Major Depressive Episode (MDE), by Past Year Nonmedical Stimulant Use: 2005 and 2006



Source: SAMHSA, 2005 and 2006 NSDUHs.

In 2009, 4.8 million Americans age 12 and older had abused cocaine at least once in the year.

Cocaine use peaked in 1985 at 5.7 million.

788K use non-cocaine prescription-like stimulants; 387K of them use methamphetamine.

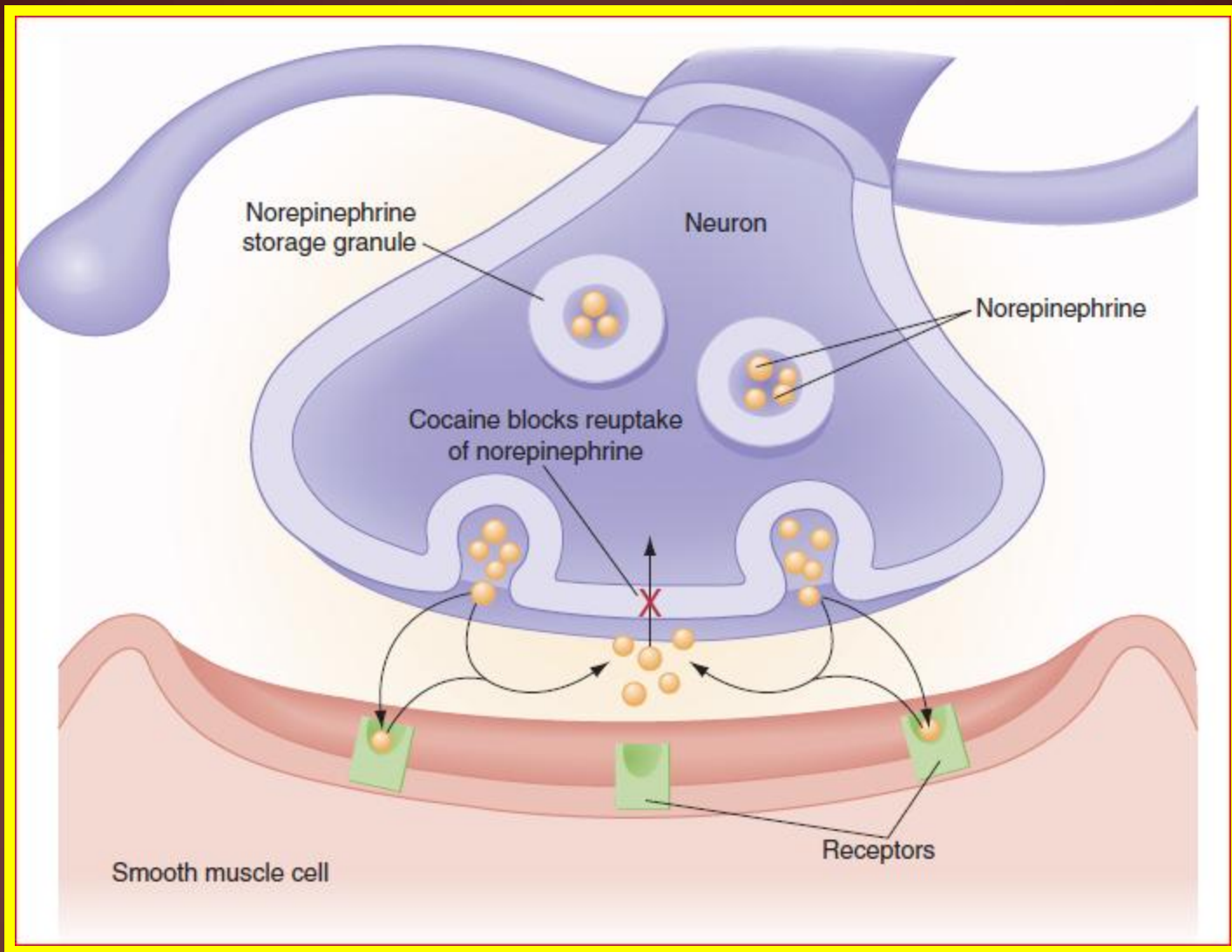


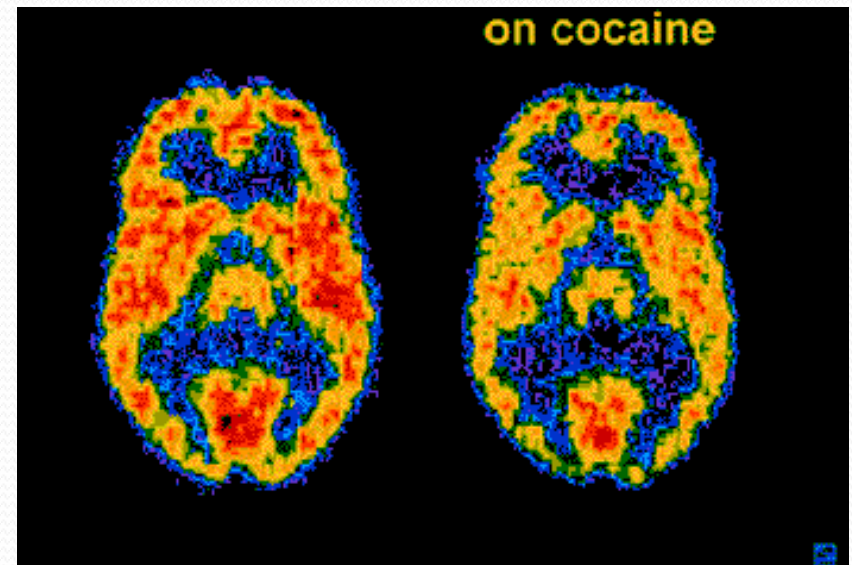
Table 152-1 Cocaine Pharmacology by Route of Administration

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

Effects on Mind, Brain, Behavior

- ↑ 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

London et al., 1999



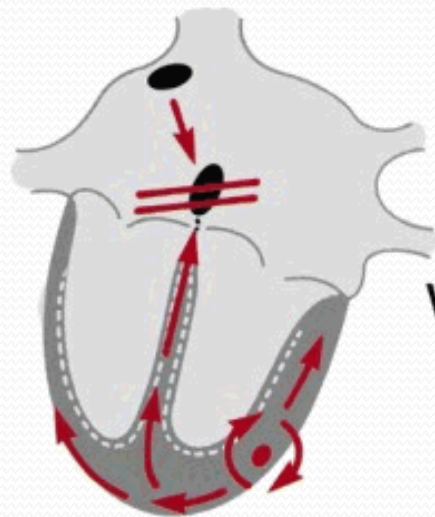
Effects on Mind, Brain, Behavior (cont.)

- ↑ sexual desire, but cocaine can ↓ performance
- ↑ anxiety, suspiciousness, paranoia
- ↑ convulsions, tremor, seizure
- ↑ psychosis, delirium
- ↑ locomotion at low/moderate doses
- ↑ ↑ reinforcement/addiction
- ↓ judgement, complex multi-tasking



Peripheral Effects (sympathomimetic)

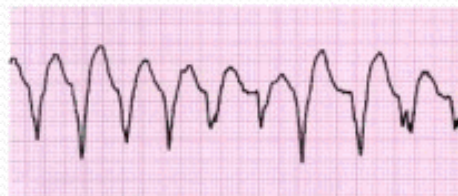
Fight/Flight/Fright Syndrome
(sympathetic nervous system arousal)



Normal Sinus Rhythm



Ventricular Tachycardia



↑ Blood pressure

↑ Blood sugar

↑ Heart rate

Irregular heart beat

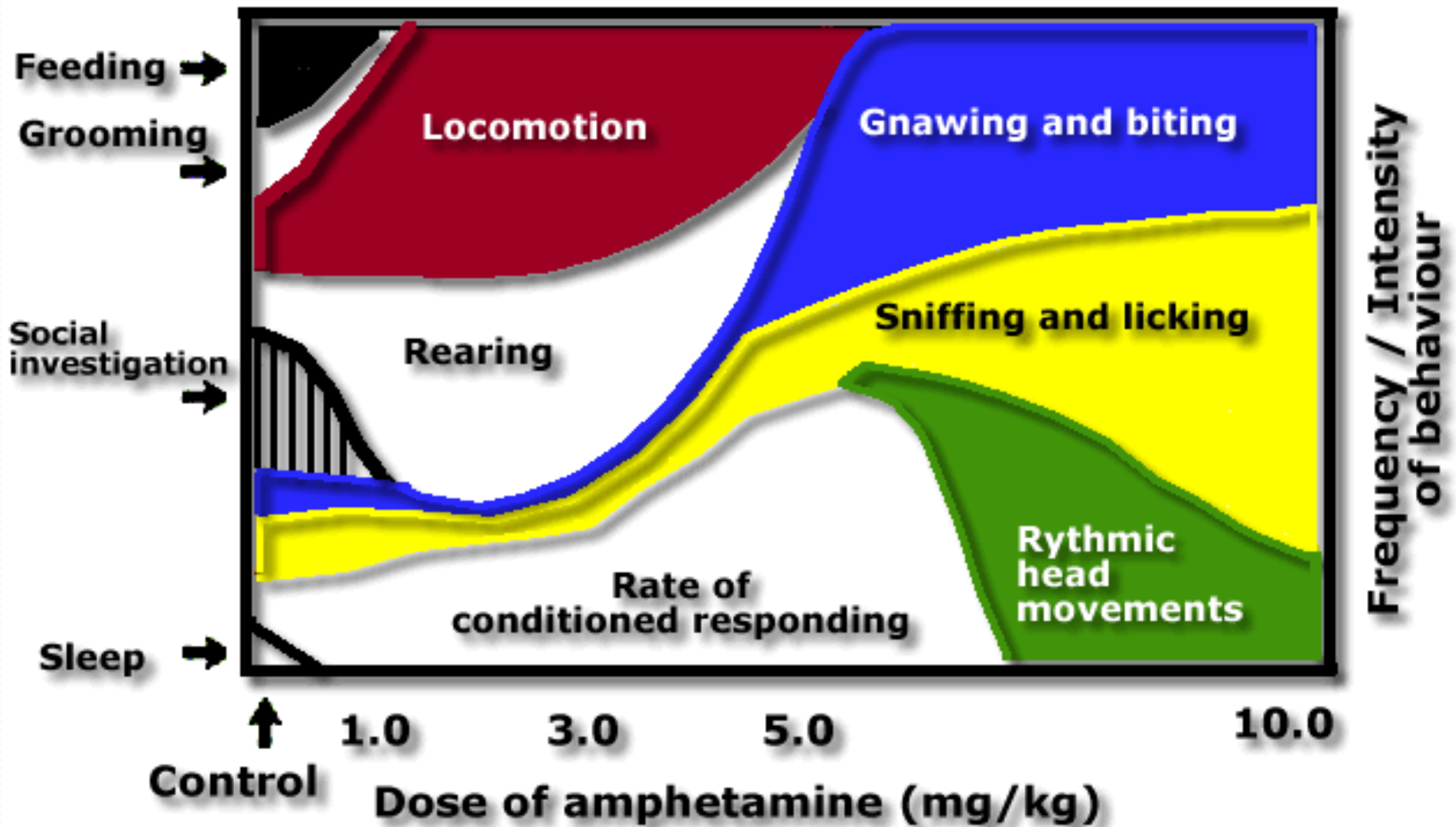
Vasoconstriction

↑ Body temperature

Bronchodilation

& Impaired breathing

Amph Effects on Rat Behavior



BOX 152-1

CLINICAL EFFECTS OF SYMPATHOMIMETICS

Hypertension

Hyperthermia

Tachycardia

Mydriasis

Diaphoresis

Central nervous system excitation







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







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(1500 m) in: 00:03:56.15 !





Busted: The first of the CT scans shows roughly 20 packages of drugs lodged in a man's colon

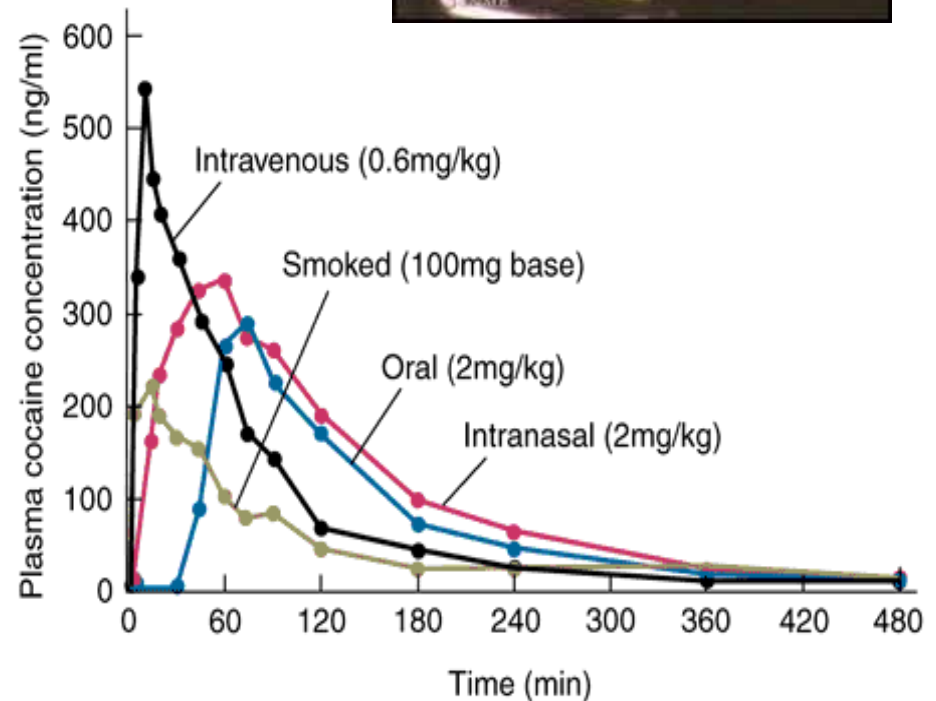




Cocaine Pharmacokinetics:

Absorption

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



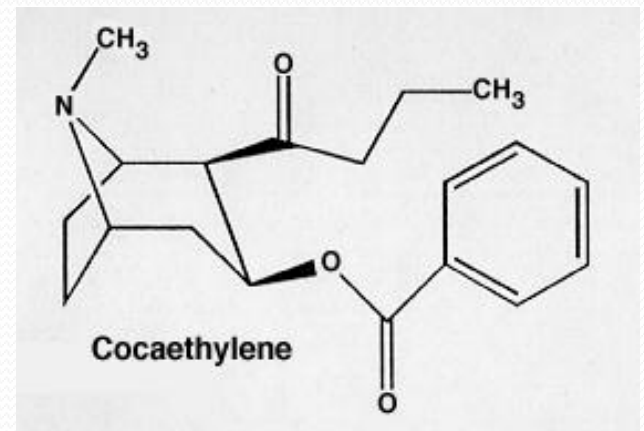
Pharmacokinetics:

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

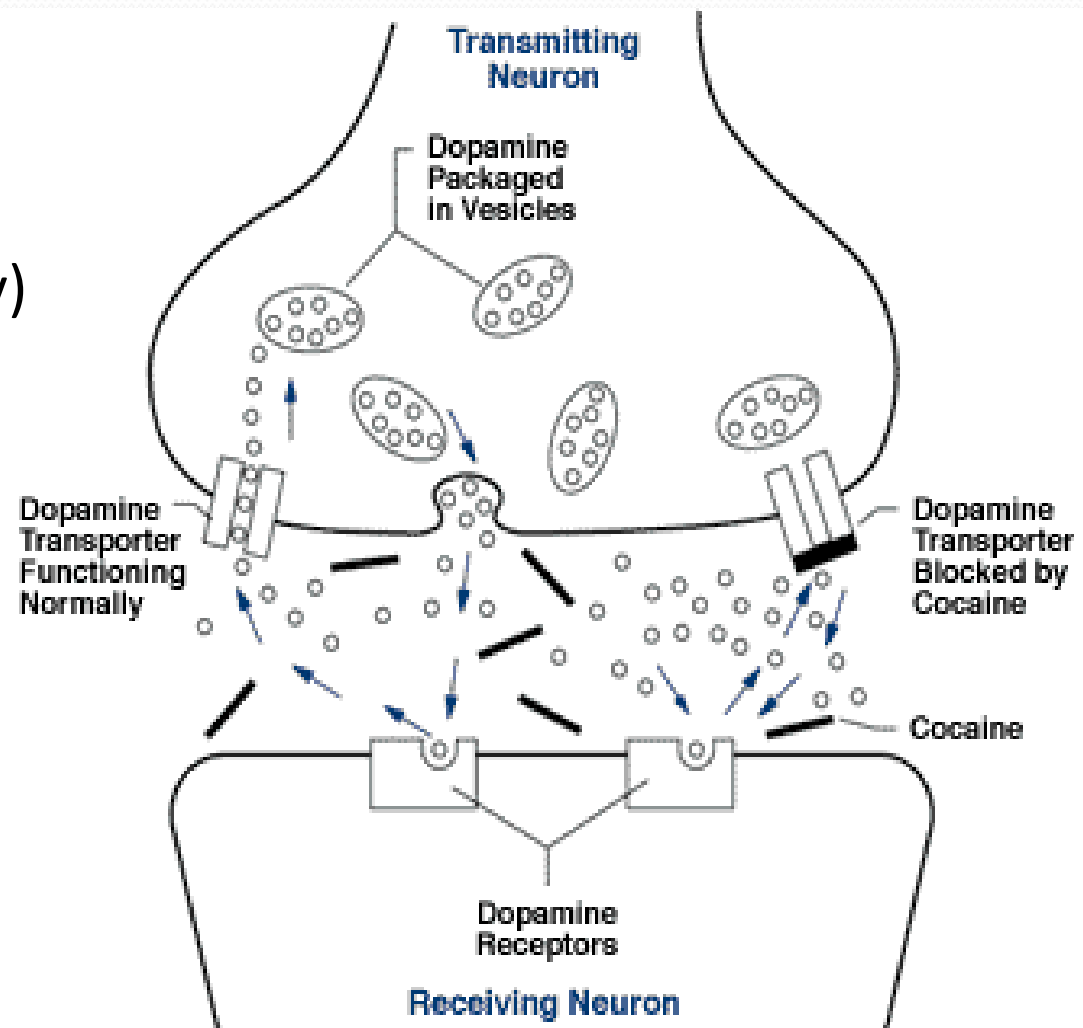
Cocaethylene

- Alcohol inhibits metabolism of cocaine
- Alcohol + cocaine chemically react to form **cocaethylene**
- 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 (high affinity)
 - NE (high affinity)
 - 5-HT (modest affinity)
- Mechanism:
 - Blocks monoamine reuptake



تعاطي الكبتاجون بأنواعه في المناسبات لا يمنع من أضراره التي أبرزها الوفاة المفاجئة
بعد الاختبارات ... حبة واحدة من «الأبيض» قد تجعل مستقبلك كله «أسود» !



شاب توفي اثر تعاطيه جرعة من المنشطات

Amphetamine Pharmacodynamics

- Indirect Agonist for
 - DA (high affinity)
 - NE (high affinity)
 - 5-HT (low affinity)
- Mechanisms:
 - Blocks monoamine reuptake
 - Inhibit vesicular storage
 - Inhibit MAO metabolism
 - Reverses reuptake

Tolerance, Withdrawal, Addiction

- High abuse potential
- Physical and psychological dependence
- Tolerance to euphoria, appetite suppression; sensitization to psychomotor
- Withdrawal
 - Physically mild to moderate (hunger, fatigue, anxiety, irritability, depression, panic attacks, dysphoric syndrome)
 - 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.
 - Anhedonia from biogenic amine depletion?
 - 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

- Foreign body aspiration

Cardiac chest pain

- Endocarditis

- Pericarditis

- Ischemia/infarction

 - During acute intoxication

 - After acute intoxication

- Coronary stent thrombosis

KHAT

Catha edulis



Pharmacotherapies

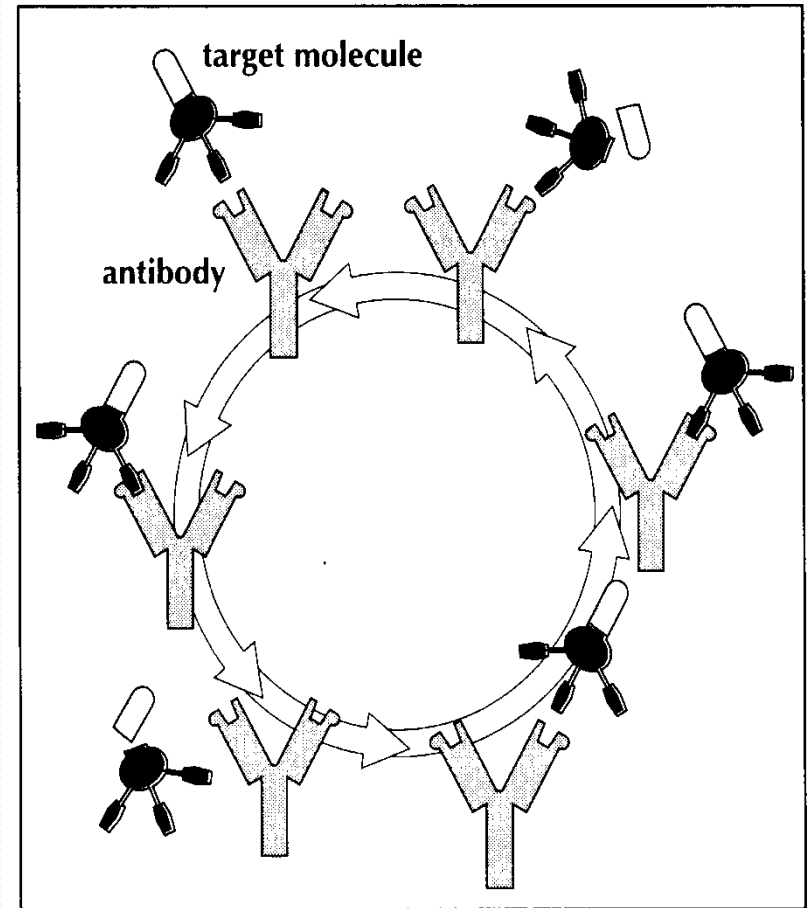
Treatment of withdrawal:

- Alpha-blockers
- Chlorpromazine: DA antagonist (also blocks alpha receptors)
- Haloperidol (antipsychotic – 50x more potent than chlorpromazine).
- Alprazolam (Xanax - benzodiazepine) for panic attacks.
- Antidepressants (fluoxetine or desipramine).
- Diazepam (Valium) for seizures - binds to benzodiazepene site of GABA_A receptor.

New Treatment Approaches

IMMUNOLOGICAL

- Antibodies made against cocaine, to break-down the molecule and stop its effects.
- Undergoing Phase III trials in US
- An inactive cholera toxin protein – attach inactivated cocaine
- Immune system makes antibodies against both
- When individual takes cocaine, antibodies bind to it and prevent it from reaching brain – high does not occur, patient loses interest



The top of the slide features several overlapping, wavy lines in shades of brown, tan, and gold, creating a decorative header.

THANKS