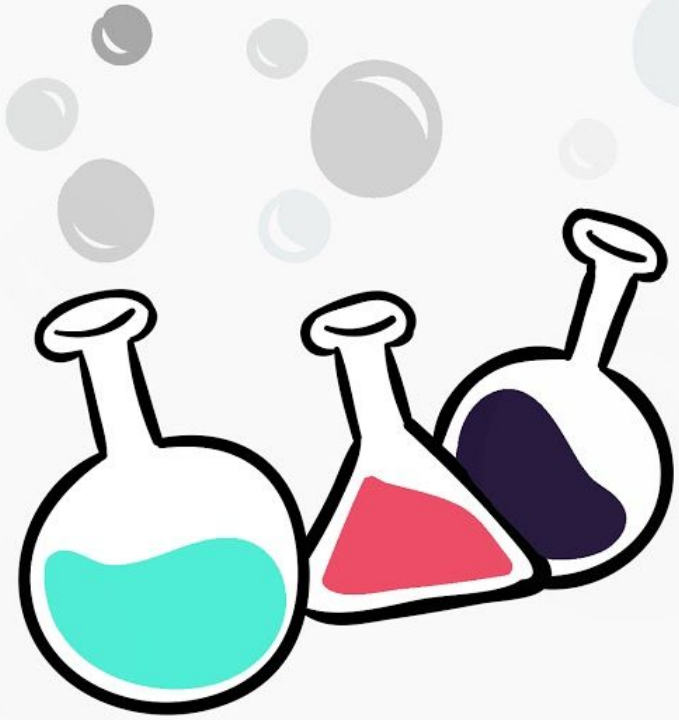

Cocaine and Sympathomimetics

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Objectives:

- Not given

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[Color index : Important | Notes | Extra | Editing file]

Perspective

- **Cocaine, amphetamines, and derivatives of amphetamines are called sympathomimetics.**
- **These agents cause central nervous system (CNS) stimulation and a cascade of physiologic effects.**

Clinical effects of Sympathomimetics:

The first three manifestations are the ones the might kill the patient

- **Hypertension** aortic dissection - pulmonary edema
- **Hyperthermia** this one will lead to DIC and kill the patient if untreated!
- **Tachycardia** Wide QRS Complex, Torsades de pointes and V tach
- **Mydriasis**
- **Diaphoresis**
- **CNS excitation**

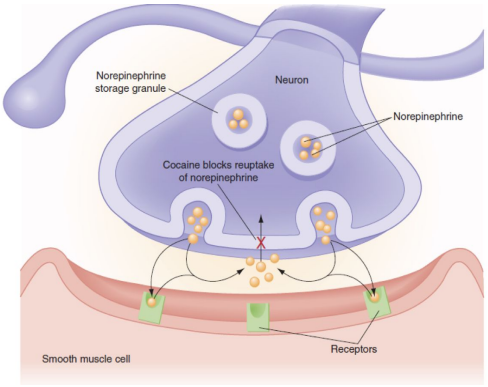
- Excitation of the sympathetic nervous system.
- Patients with moderate toxicity are alert and awake but may have diaphoresis, tachycardia, mydriasis, and hypertension without organ damage.
- A more severely intoxicated patient may present agitated, combative عنده استعداد يتخانق مع ذبان وجهه , and hyperthermic.
- Signs and symptoms of end-organ damage may be present, including acute hypertensive emergencies.
- Patients may present with focal, acute pain syndromes; circulatory abnormalities; delirium; or seizures.
- The clinical presentation depends on the dose, route of administration, and time to presentation after drug use.
- Patients who are "speed-balling[1]," using IV heroin and cocaine together, may be initially sedated, and administration of naloxone may reveal the underlying cocaine intoxication and the patient may go through seizure because cocaine is unopposed. Treat Cocaine symptoms first then you can intubate for Heroin
- Mortality is high with temperatures greater than 41.1°C.

These points are illustrating the 6 features above

Cocaine

Pathophysiology

- Acute cocaine use causes release of dopamine, epinephrine, norepinephrine, and serotonin.
- Most important effects are **adrenergic stimulation** by norepinephrine and epinephrine.
  - Norepinephrine causes peripheral **vasoconstriction** by stimulating **alpha-adrenergic** receptors on vascular smooth muscle.
  - Epinephrine increases **myocardial contractility** and heart rate through stimulation of **beta1-adrenergic receptors**. So it will give us tachycardia and hypertension



- In addition to causing catecholamine release, the reuptake of these stimulatory neurotransmitters from synaptic clefts is inhibited, **altering the normal balance between excitatory and inhibitory tone in the CNS**.
- Sodium channel blockade across myocardial cells, similar to the class IA antidysrhythmic agents, is responsible for the occasional conduction abnormality with acute cocaine toxicity.

- The use of **ethanol with cocaine** may form **coca ethylene**, a metabolite that may potentiate the drug's stimulatory effects.

[1] حركات بيسووها الحريفة (Speedball is a mix of cocaine with heroin or morphine taken intravenously or by insufflation (they oppose each other

Pharmacidiameics	Cocaine metabolism occurs in the liver and the plasma. ➔ In the liver, primarily to the active metabolite norcocaine, which potentiates the parent drug. ➔ In the plasma it transfers to **ecgonine methyl ester** via pseudocholinesterase (plasma cholinesterase) ◆ **Ecgonine methyl ester** may be protective because it is a vasodilator.
Other uses of cocaine	➔ Cocaine also is a local **anesthetic agent**, slowing nerve impulses from neuronal pain fibers by blocking the inward movement of sodium across cell membranes (**phase 0 of the action potential**).

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

DIAGNOSTIC STRATEGIES Diagnosis is **clinical**, don't wait for labs

- **Urine drug screening**

What do we look for in tox screen? Benzoyl ecgonine is a metabolite found in the plasma and is the metabolite identified by urine **toxicology screens**.

➔ Used to:
- ◆ Document possible abuse
- ◆ Confirm cocaine as the unknown substance in body packers
- ◆ Differentiate paranoia from drug-induced or psychiatric causes.

➔ Urine drug screening is unlikely to change treatment because it measures a cocaine metabolite (**Benzoyl ecgonine**) that is typically present for **3 days** after last use

- **ECG**

➔ Sinus tachycardia, wide complex tachycardia give them sodium bicarbonate if they have wide QRS

➔ Cyclic antidepressants and cocaine share class Ia antiarrhythmic effects. "Lidocaine" may cause seizures, so always combine with benzodiazepine

➔ Accurate diagnosis of chest pain is problematic. ST segment elevation is confounded by the presence of early repolarization. Patients with STEMI + and HTN must not receive fibrinolytics

➔ Serial ECGs may be helpful

- **Serum enzymes**

➔ Serum CK-MB fraction, troponin I, and troponin T are more specific in patients with atherogenic coronary disease.

- **Others:**

➔ Severe, persistent headache despite normalization of blood pressure may occur with a SAH (Subarachnoid hemorrhage) and warrants head CT and, if the scan is negative, lumbar puncture.

➔ **Urinalysis** should be checked for myoglobin, which indicates rhabdomyolysis.

Initial assessment and treatment:

Initial assessment and treatment should focus on rapidly fatal complications: زي ما قلنا أهم شي نهتم بالثلاث أشياء اللي ممكن تقتل المريض

1. Hyperthermia
2. Hypertensive emergencies
3. Cardiac dysrhythmias.
4. Seizure

Key points in management:

- After initial airway assessment
- Rapid assessment of vital signs especially core temperature.
- Physical restraints to obtain complete vital signs and to secure IV access.
- Rule out hypoxia and hypoglycemia
- Empirical therapy with **IV dextrose and thiamine** or assessment with a bedside blood glucose monitor.
- IV benzodiazepines may be necessary MAIN STEP OF COCAINE MANAGEMENT

❖ **Pharmacologic Sedation**

➢ In adults, IV diazepam can be administered in increments of 10 mg every 5 minutes until sedation is achieved.

➢ In wildly agitated patients in whom 20 to 30 mg of diazepam has no notable effect, the increments may be increased carefully by 20 mg each subsequent dose with close monitoring.

Assessment		
Hyperthermia	**Hypertensive Emergencies**	**Cardiac Dysrhythmias**
- Agitation with delirium increases the risk of hyperthermia. - Vasoconstriction and dehydration can compromise cooling, resulting in life-threatening hyperthermia with core temperatures exceeding 106 F (**41.1 C**). - Delay in recognition result in death. - Increased motor tone can release intramuscular (**CK**) with **rhabdomyolysis** and renal and electrolyte complications. So we always start with **benzodiazepine** to reduce muscle contractions - when you have a patient who's competitive first ربطه so you can take the IV line then sedate him. why ? competitive (moves a lot)→ vigorous virtus muscle exercise→ heat production you can't control temperature (hyperthermia) release of myoglobin → the patient will end up with Rhabdomyolysis + acute renal failure + hyperkalemia .	**Sequelae (Complications) include:** • Aortic dissection • Pulmonary edema • Myocardial ischemia & infarction • Intracranial hemorrhage, strokes • Infarction of the anterior spinal artery. - Vasospasm can compromise perfusion to various organs. - **Intestinal infarctions and mesenteric ischemia** can occur, particularly in **body packers** with large oral ingestions. - Other local ischemic events include retinal vasospasm, renal infarctions, and placental insufficiency and infarction in the gravid uterus.	- May not be noted until cardiac output abruptly diminishes, and the patient suddenly loses consciousness. - Sinus tachycardia is most common -Atrial fibrillation and other supraventricular tachycardias - **Torsades de pointes or wide-complex tachycardias** from blockade of fast sodium channels on the myocardium may deteriorate into poorly perfusing or fatal ventricular rhythms. - Hyperkalemia from rhabdomyolysis and myocardial ischemia can also cause dysrhythmias. treat with insulin and D50

Treatment

Hyperthermia

- **Rapid cooling.** Patients who sustain elevated core temperatures greater than (41 C) for more than 20 minutes are likely to stabilize transiently, then develop fatal multisystem organ failure, **often heralded by DIC**.

- It is crucial to reduce core temperature to (38.8? C) within 20 minutes.

- Cooling blankets are insufficient. Ice water, wet sheets with large fans, and packing the entire body in ice with continuous monitoring of core temperature can be used.

- Aggressive **fluid resuscitation**.

Patients should have continuous monitoring of core temperature with **a rectal probe**.

Early identification of elevated core temperature
Large-bore intravenous access with rapid infusion of crystalloid
Sedation and muscle relaxation with benzodiazepines
Rapid cooling within 20 min*
Foley catheterization to monitor output
Laboratory analysis for organ function
Serum chemistries/creatinine/CK
Liver function
PT/PTT/fibrin split products
Bacterial cultures†
Urinalysis for myoglobinuria
Paralysis and intubation if necessary

*Ideally with ice water immersion.
†Consider lumbar puncture or antibiotic therapy, especially in injection drug users.
CK, creatine kinase; PT, prothrombin time; PTT, partial thromboplastin time.

Hypertensive Emergencies

- **Benzodiazepines:** restore the CNS inhibitory tone on the peripheral nervous system.

- **IV Nitroglycerin or Nitroprusside:** can be used with evidence of end-organ damage.

- **Phentolamine:** a direct a-adrenergic antagonist, is the antihypertensive of choice.

  - It can be titrated slowly using repeat IV doses of 1 to 5 mg with blood pressure monitoring.

- **Beta Blockers** may cause paradoxical hypertension with cocaine. (Beta Blockers use in cocaine-related chest pain syndromes should be avoided)

Cardiac Dysrhythmias

- A-Fib and supraventricular tachycardias are likely due to sympathetic stimulation and often **respond to benzodiazepines**.

- **Sodium bicarbonate:** When the cause of a wide-complex tachycardia from cocaine is unknown. (Treats sodium channel blockade and potential cardiotoxicity from hyperkalemia.)

- **Lidocaine:** may increase **seizure risk** and mortality and is therefore reserved for patients with ventricular dysrhythmias for **whom bicarbonate therapy has failed** and who have already received benzodiazepines

  - Most useful for ventricular dysrhythmias with cocaine-associated MI.

- **Amiodarone**: is not well studied, but may be beneficial for ventricular dysrhythmias

- **Beta-adrenergic antagonists** should be **avoided**.

Other complications

- ❑ People who binge with continuous use causes catecholamine depletion, dehydration, and poor nutrition.
- ❑ After the acute effects of cocaine have subsided, these patients with "cocaine washout" are profoundly sleepy but arousable and oriented, with normal vital signs or a mild sinus bradycardia.
- ❑ "Crack dancing," a transient choreoathetoid movement disorder
- ❑ DVT is reported with cocaine use, probably secondary to effects on coagulation.
- ❑ Oropharyngeal burns from the high temperature required to volatilize the drug.
- ❑ Pneumothorax, pneumopericardium, and pneumomediastinum occur from inhalational barotrauma.
- ❑ Intranasal cocaine use is associated with sinusitis and nasopalatine necrosis or perforation.
- ❑ Transdermal injection of cocaine, or "skin popping," has similar types of complications.
- ❑ Intravenous users have a high risk of infection with blood-borne viruses, local abscesses, and systemic bacterial infections, including botulism, and endocarditis.

Differential Diagnosis

- Sedative-hypnotic withdrawal
- Amphetamines and its derivatives
- Heatstroke.
- Infection should be considered in all hyperthermic patients.

Metabolic causes
Electrolyte abnormalities
Hypoglycemia
Hypoxia
Uremia/hyperammonemia
Structural lesions of the CNS
Trauma
Stroke
Hemorrhage
Mass
Endocrine disease
Thyrotoxicosis
Infections
Bacterial/viral meningitis/encephalitis
Toxicologic causes
Sympathomimetic/stimulants
Cocaine
Amphetamines and derivatives
Caffeine
Phencyclidine/ketamine
Anticholinergics
Serotonin syndrome
Sedative-hypnotic withdrawal
Heatstroke
Postictal state

CNS, central nervous system.

Cocaine-Related Chest Pain

Pathophysiology:

- Cocaine induces coronary vasoconstriction and increase myocardial **oxygen demand**.
- Platelet aggregation is enhanced through **prothrombogenic** and **antifibrinolytic pathways**
- Fever and shortness of breath should prompt consideration of pneumonia, pulmonary infarction, or endocarditis with septic pulmonary emboli in IV drug abuse.

CAUSES OF STIMULANT-INDUCED CHEST PAIN:

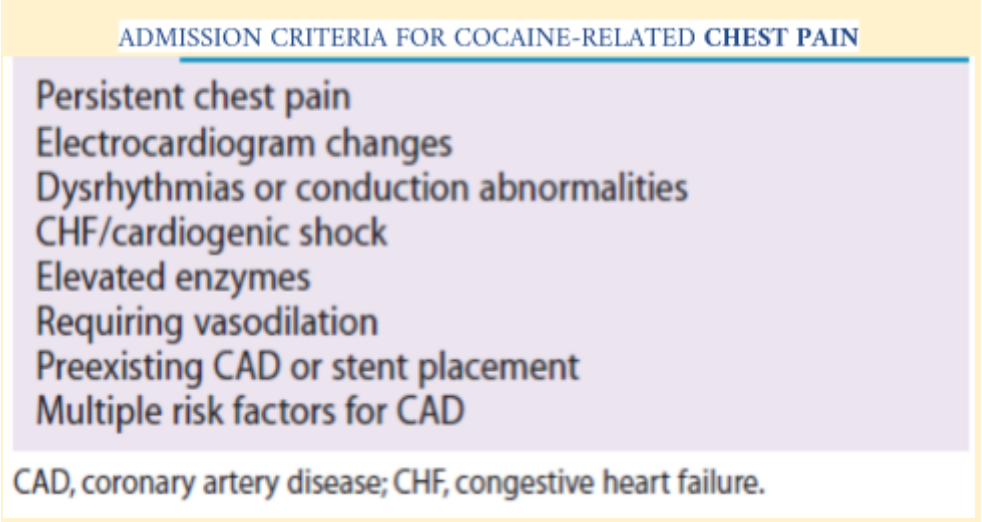
Non-Cardiac	Foreign Body Aspiration	Cardiac Chest Pain	Coronary Stent Thrombosis
- Pneumothorax - Pneumomediastinum - Pneumopericardium - Aortic dissection - Pulmonary infarction - Infection		- Endocarditis - Pericarditis - Ischemia/Infarction: • During/after acute intoxication	Patients with a history of coronary stent placement are at a high risk of thrombosis with cocaine use.

Investigations:

- **Chest radiograph to identify:**
  - Aspirated foreign bodies
  - Pneumothorax or pneumomediastinum from inhalational barotrauma.
- Patients with positive serum enzymes for MI have significant angiographic stenosis
- 18% still have significant disease by angiogram.
- **Elevated cholesterol** and prior diagnosis of coronary disease or **MI** are predictors of significant disease in this group.
- Patients with cocaine-related chest pain without other risk factors who have normal ECGs and cardiac enzymes are at low risk for myocardial infarction.

Management

Benzodiazepines	Used to decrease myocardial oxygen demand by limiting peripheral stimulation and should be given early
Aspirin and nitrates	Should be administered in patients meeting ECG criteria for MI with persistent chest pain and hypertension and a clear history of acute cocaine intoxication.
IV phentolamine	To achieve coronary vasodilation, should be considered.
Morphine sulfate	Used to treat the pain.
PCI	Patients with persistent chest pain and ST segments strongly suggestive of MI can be considered for percutaneous intervention in the catheterization laboratory or thrombolytic therapy, assuming there are no contraindications such as uncontrolled severe hypertension
Beta-adrenergic antagonists (including. labetalol), are absolutely **CONTRAINDICATED** during acute cocaine toxicity	



Body Packers and Body Stuffers

Body packers:

- Before crossing international borders, "body packers" **ingest cocaine** that has been wrapped tightly into condoms or other latex products and sometimes coated in wax.
  - Each packet can contain approximately 10 g of cocaine, and packers may **swallow as many as 150 packets**.
  - Body packers are likely to know the exact number of packets they ingested.
- A body packer may present without symptoms to the ED.
- The body packer should be placed immediately on continuous cardiac monitoring, with large-bore IV access.
- An abdominal radiograph may confirm foreign bodies
- When uncertainty persists, a contrast study is warranted.
  - CT and contrast abdominal radiographs may fail to detect isolated packets that contain potentially fatal quantities of cocaine.
- When evidence of **cocaine toxicity** is manifest, **rapid transportation to the operating room** may be the only way to save these patients.
- Benzodiazepines, neuromuscular blockade, or sodium bicarbonate administration may be required en route.
- **Endoscopic retrieval is discouraged** because of concern over packet rupture during the procedure.

Body Stuffers:

- ❖ A **"body stuffer"** is an individual who attempts to conceal evidence of cocaine possession by **swallowing the drug** while pursued by law enforcement officials.
- ❖ These are usually unplanned events with generally small quantities of drug intended for personal use.
- ❖ Can be discharged after the acute intoxication resolves. These patients may be extremely sleepy from catecholamine depletion, and it is best to discharge them with a responsible adult.
- ❖ Patients who develop complications should be admitted to the intensive care unit for further treatment.

Disposition:

- ❑ After a 12-hour monitored observation period, patients with a benign clinical course and **negative serum enzyme markers** can be discharged.
- ❑ Body packers need to be observed until all packets have passed.
- ❑ Ideally, these patients have had **three packet-free stools**, a reliable packet count consistent with the ingestion, and a negative contrast radiographic study.

Other stimulants: Amphetamines

- ➔ Enhance release of catecholamines from presynaptic nerve terminals
- ➔ Usually taken as pills, but occasionally are crushed and injected.
- ➔ CNS stimulation results in nearly identical sympathomimetic effects to those from cocaine, but not with the same frequency or intensity.
- ➔ Do not block sodium channels (no wide QRS) and only minimally affect presynaptic reuptake of catecholamines.

كبتاجون، مشهور عندنا مره. "حبوب لكسز" ➔

Patients are at risk for:

- **Hyperthermia**
- **Hypertensive emergencies**
- **Dysrhythmias**
- **Hyperkalemia associated with rhabdomyolysis**
- **Myocardial ischemia**

Screening	Management
Although urine drug screens can identify amphetamines, they are of little utility in treating an intoxicated patient.	The management follows the same guidelines as for cocaine, although the duration of toxicity tends to be longer for amphetamines.

Methylenedioxymethamphetamine "MDMA": Ecstasy, XTC or Adam

It's a chemically modified amphetamine originally taken orally at all-night dance parties, or "raves." Patients describe the euphoria allowing "**closeness to others**," so it is sometimes called the "**love drug**."

Clinical Manifestations:

- life-threatening hyponatremia
- May alter release of endogenous stores of vasopressin.
- Urine samples with a relatively **high urine sodium** level, similar to SAIDH.
- Unless seizures or other neurologic events are present, patients can be treated supportively with fluid restriction.
- In contrast to other amphetamines, chronic MDMA use causes potentially irreversible neurologic damage to serotonergic neurons.

Management:

- Normal saline or other crystalloids may worsen the hyponatremia because these patients are likely to retain more free water than sodium.
- **Their fluid intake should be restricted** unless severe hypovolemia exists, and they should be treated with hypertonic saline for neurologic impairment.

Methamphetamine:

- Methamphetamine, known as "crank" and "**crystal meth**," is a fat-soluble, smokable, designer amphetamine.
- Complications from methamphetamine use are similar to those from other sympathomimetics
- The duration of action can be significantly longer, however, with some paranoid delusions persisting for 15 hours.

KEY CONCEPTS

- Rapid sedation with an IV benzodiazepine is the key for most symptoms from cocaine and other stimulants.
- Hyperthermia is a high-risk sign, and body temperature must be reduced rapidly.
- Beta-adrenergic blockade may cause paradoxical hypertension and increase coronary vasoconstriction and is generally contraindicated.
- Wide-complex rhythms secondary to cocaine may respond to IV bicarbonate therapy.
- Cocaine body packers who become symptomatic need immediate surgery.
- Amphetamine symptoms and effects last longer than those produced by cocaine.

MCQs

1) which one of the examples is a stimulant drug ?

A. Barbiturate
B. Marijuana
C. Morphine
D. cocaine

2) cocaine metabolized in which of the following ?

A. Lung .
B. Kidney .
C. Pancreas .
D. Liver & Plasma .

3) 20 year old patient present to you with sweating, agitation, tachycardia and mydriasis .
This presentation can be caused by which of the following ?
A. Depressant drugs .
B. opioid .
C. cannabis.
D. Amphetamine .

4) 30 years old patient come to you after ingestion of large amount of cocaine with tachycardia and hypertension .you perform ECG which shows wide complex tachycardia . which of the following will be your first line medication to be given ?
A. Sodium bicarbonate .
B. Amipdarone .
C. procainamide .
D. lidocaine .

5) which one of the following is a fatal complication of simulant toxicity ?
A. Hyperthermia
B. Hypothermia
C. Hypokalemia
D. Bradycardia

6) You are treating a young patient with cocaine overdose, which of the following drugs you should avoid while treating such patients?
A- Benzodiazepines
B- Beta blockers
C- Alpha blockers
D- Sodium bicarbonate

7) 29-year-old male is brought to the emergency department after using amphetamine in a party. Which of the following complications may occur in this patient?
a. Convulsions
b. Hypothermia
c. Hypotension
d. Bradycardia

Answer: 1-D , 2-D , 3-D , 4-A , 5-A , 6-B , 7-A