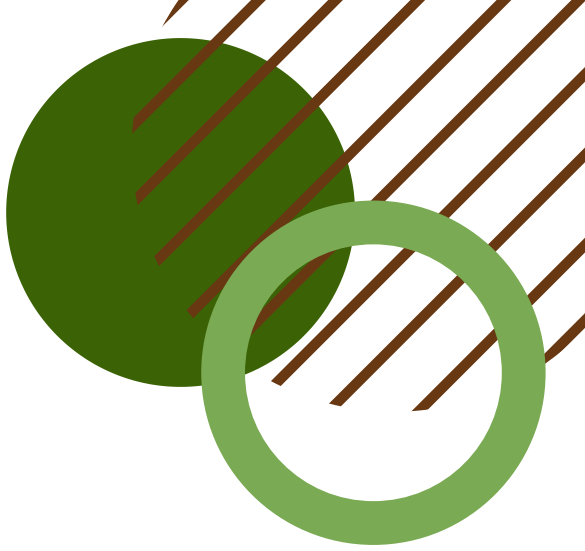


A Forensic Medicine Perspective





CANNABIS

What is Cannabis?

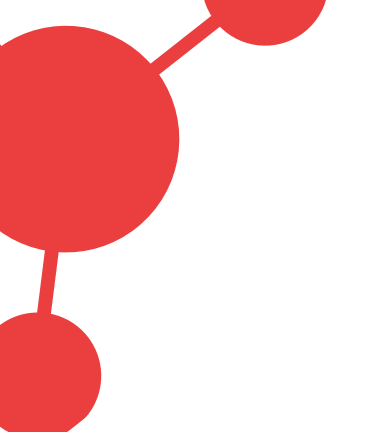
- Source: Belonging to the Cannabaceae family
 - ◆ Genus: Cannabis.
 - ◆ Species: sativa, indica, ruderalis
 - ◆ It is characterized by dense, sticky flowers
 - ◆ It is one of the most popular psychoactive substances globally, particularly among teenagers
- Active Compounds:
 - **Delta-9-Tetrahydrocannabinol (THC):** The Primary Psychoactive Component.
 - **Cannabidiol (CBD):** Non-impairing, with potential therapeutic effects.
- Route of Administration:

1-smoking: Using implements such as bongs and pipes, The most common route.

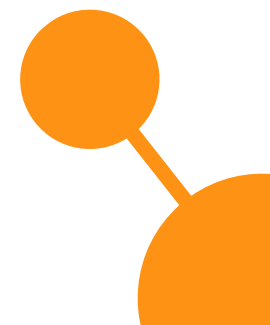
2-Vaporizer: Heats herbal cannabis to 85 –100 °C (185 –210 °F), which causes the active ingredients to evaporate into a gas without burning the plant material

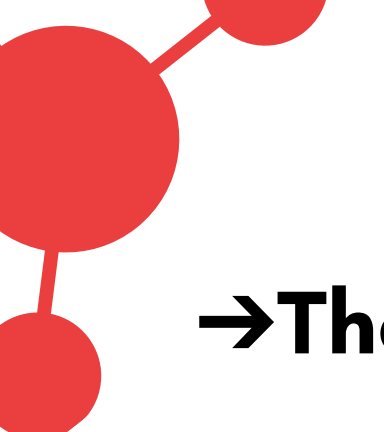
3-Ingestion (oral)





Mechanism of action

- The Delta-9-Tetrahydrocannabinol (**THC**) works as an Agonist at Cannabinoid (CB1 and CB2) receptors in the brain, **modulating neurotransmitter release**.
 - Both of CB1 and CB2 receptors are G-Protein coupled receptors.
 - CB1 receptors: regulate glutamate and GABA neurotransmission (located in CNS and peripheral tissues)
 - CB2 receptors: regulate pain and emesis (located in immune cells & peripheral tissue)
 - Upon binding to CB receptors, THC triggers a cascade of cellular events, leading to changes in the activity of various enzymes and ion channels.
- 

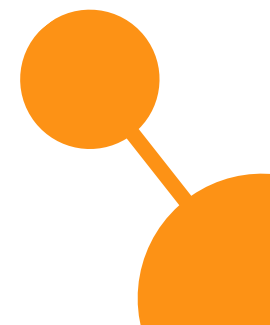


→ **The specific effects of THC depend on the location of the activated cannabinoid receptor**

◆ **Adenylyl Cyclase Inhibition:** This will affect various cellular functions like **gene transcription** and **ion channel activity**.

◆ **Ion Channel Modulation:** Directly interacts with ion channels (like calcium and potassium channels) modifying their activity. This alters the flow of ions into and out of the cell, affecting neuron excitability and neurotransmitter release.

◆ **MAPK Activation:** The beta-gamma subunits can stimulate the mitogen activated protein kinase (MAPK) pathway, **a cascade of proteins involved in cell growth, proliferation and differentiation**



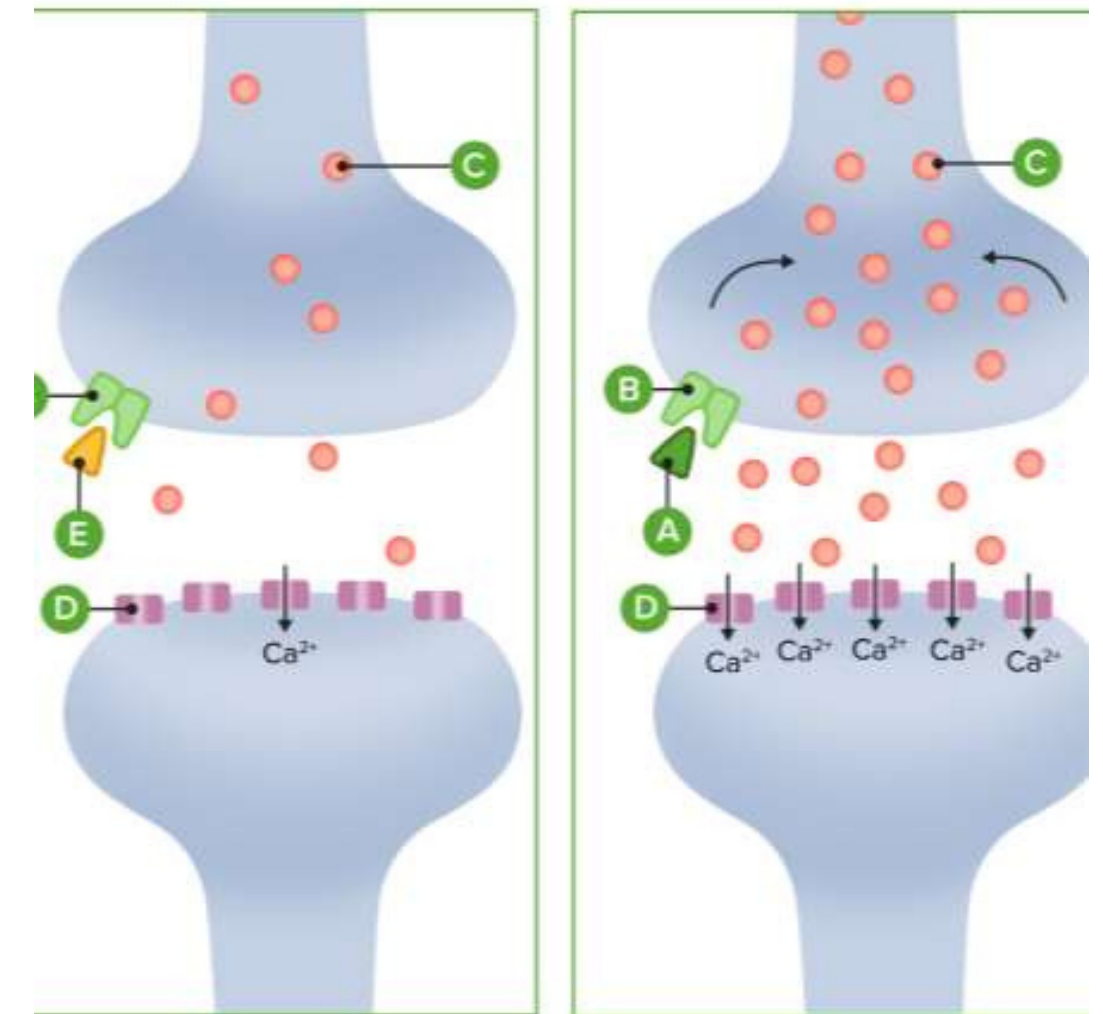
→The specific effects of THC depend on the location of the activated cannabinoid receptor

→Neurotransmitters (including dopamine) flood into the synaptic cleft, causing calcium to be pumped into the postsynaptic neuron **at higher levels than observed in healthy natural stimuli.**

- The higher amount of neurotransmitters gives the “high” associated with cannabis.

→Acting through cannabinoid receptors:

- THC activates the reward system of the brain.
- Tetrahydrocannabinol (THC) also disrupts functioning of the cerebellum and basal ganglia.



A: THC / B: CB1 receptors / C: neurotransmitters / D: postsynaptic receptors / E: cannabinoid

WATCH THIS VIDEO



Cannabis Effects

◦ 1. Increased Dopamine Release:

- This neurotransmitter plays a key role in the reward system, contributing to feelings of **euphoria, pleasure, and relaxation**.

◦ 2. Decreased Glutamate Release:

- This excitatory neurotransmitter **is involved in learning and memory**, and its reduction by THC might explain the **memory impairment** associated with cannabis use.

◦ 3. Modulation of Other Neurotransmitters:

- THC can also influence the activity of other neurotransmitters, such as GABA (inhibitory) and serotonin (mood regulation).
 - This contributes to various effects like **sedation, altered sensory perception, and mood swing**
- 

Effects on The Central Nervous System:

- Euphoria (Pleasurable sensation & Distorted reception)
 - relaxation
 - altered time perception (Unawareness of time passage)
 - Poor coordination
 - anxiety
 - paranoia
 - psychosis: Delusions, Increased laughing,... (in high doses or predisposed individuals).
-
- Long-term psychological effects have suggested a 6x increase in the incidence of schizophrenia.

Marijuana Side Effects

Physical Effects Are:

- Conjunctival injection ("red eyes")
- tachycardia
- Dry mouth (Thirst) & Dry eyes
- increased appetite (Hunger)
- Recurrent chest infections Injury of the trachea and major bronchitis.



Paranoia



Impaired Memory



Fatigue



Delusions



Psychosis



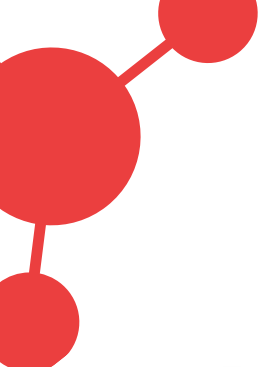
Impaired Motor Skills



Tachycardia



Increased Appetite



Cannabis Metabolism & Excretion

→ About 80% of THC is eliminated **by the feces**.

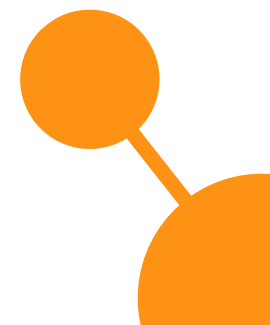
→ Less than **2-5%** of an oral dose of THC is excreted as an **unchanged drug**.

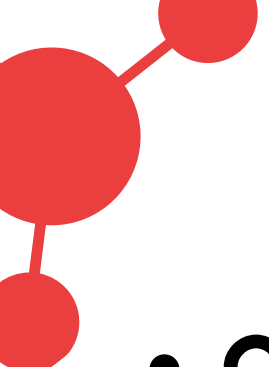
→ A pronounced entero-hepatic recirculation for THC and metabolites does contribute to slow elimination, but most of the THC (around 50 - 90%) is excreted within the first 4 - 5 days.

✦ While entero-hepatic recirculation does occur, meaning some THC and metabolites re-enter the bloodstream after excretion in the bile, the majority (80 - 90%) is eliminated within the first few days.

→ The THC metabolites have been found in the urine of users for up to 80 days after the last dose, and the dominant urinary metabolite is THC-COOH (11-nor-9-carboxy-THC).

✦ While THC-COOH exists in the body as a conjugate with glucuronic acid, it's the THC-COOH molecule itself that is typically detected in urine tests

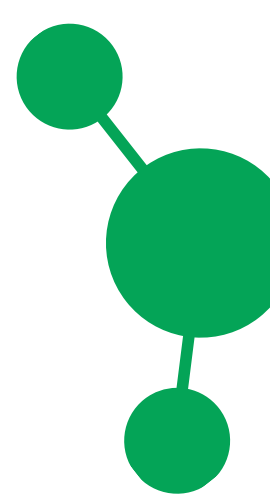


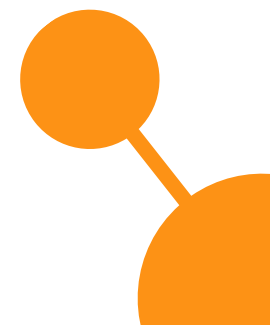


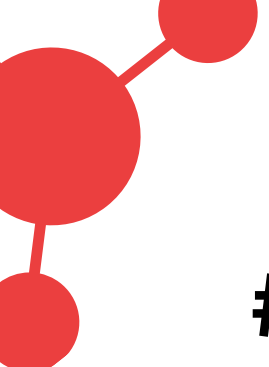
Cannabis Treatment

- Our approach in treating people who use cannabis is :
 - **Supportive** mostly for the Signs & Symptoms and their consequences and complications.
 - **Psychiatric** reassurance.
 - Psychosis is usually transient and manageable with **benzodiazepines**

Cannabis Medical uses



- Cannabidiol (Medical Cannabis) is used medically for:
 - Antiemetic effect
 - Stimulation of hunger in chemotherapy and AIDS patients
 - Lowered intraocular eye pressure
 - General analgesic effects
- 



Cannabis in forensic medicine

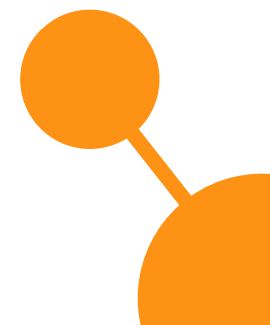
Key Forensic Issue: IMPAIRMENT

- Impacts: motor coordination, reaction time, and cognitive function.
- **Major concern for Driving Under the Influence of Drugs (DUID).**
- Cannabis is a widely used depressant/hallucinogen with **low direct lethality**, but **immense forensic importance regarding impairment** (Driving, workplace accidents) and its evolving legal status.

- Crucial Point: There are **NO specific pathognomonic autopsy findings** directly attributable to a cannabis overdose death.

- **Death solely from cannabis is considered extremely rare.**

- The forensic role is to:

1. Exclude other causes of death (trauma, other toxins, natural disease).
 2. Document circumstantial evidence: (pipes, rolling papers) at the scene.
 3. Recognize indirect deaths: e.g., traumatic accidents (MVA, falls) **while impaired**.
- 

COCAINE

What is Cocaine?

→ Cocaine (Benzoylmethylecgonine):

is a crystalline alkaloid and **stimulant drug** primarily obtained from the leaves of the *Erythroxylum coca* plant. It is commonly used as a recreational drug for its stimulating effects, although it can also produce euphoria.

→ **Highly addictive:** It is one of the most addictive drugs known, with a strong potential for dependence and abuse.

→ **Street names:** Coke, Crack, Nose Candy, Snow, White lady, Blow, and White dust

→ Cocaine comes in several forms, including:

- ◆ A fine White powder (snorted, injected) with a bitter taste (Common).
- ◆ A rock crystal "Freebase" form known as crack cocaine (smoked)



Coca Leaf (> 2% Cocaine)



Cocaine Hydrochloride
(Powder)



Crack Freebase (Rock Cocaine)



Freebase

Route of Administration

1. Smoking (Inhalation of vapor from heated foil or pipe)

- ◆ Absorbed through lungs.
- ◆ Onset of Action: 7 seconds, Duration of Action: 20 minutes.
- ◆ Example: Crack & Freebase.



2. Intravenous Injection

- ◆ Directly by blood.
- ◆ Onset of Action: 15 seconds, Duration of Action: 22–30 minutes.
- ◆ Example: Cocaine hydrochloride.



3. Insufflation (Snorting)

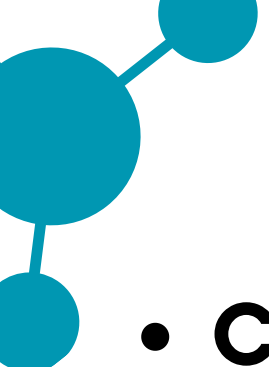
- ◆ Rapidly absorbed through mucous membranes.
- ◆ Onset of Action: 3 minutes, Duration of Action: 45–90 minutes.
- ◆ Example: Cocaine Hydrochloride (Powder).



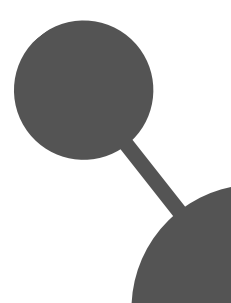
4. Ingestion (Oral)

- ◆ Inactivated by stomach, metabolized by liver – cause VC to capillaries in mouth and esophagus, which makes it harder for the body to absorb.
- ◆ Weak bases like cocaine, will be mostly charged or ionized (Polar) at low pH in stomach.
- ◆ Onset of Action: 10 minutes, Duration of Action: 60 minutes.
- ◆ Example: Coca leaves.

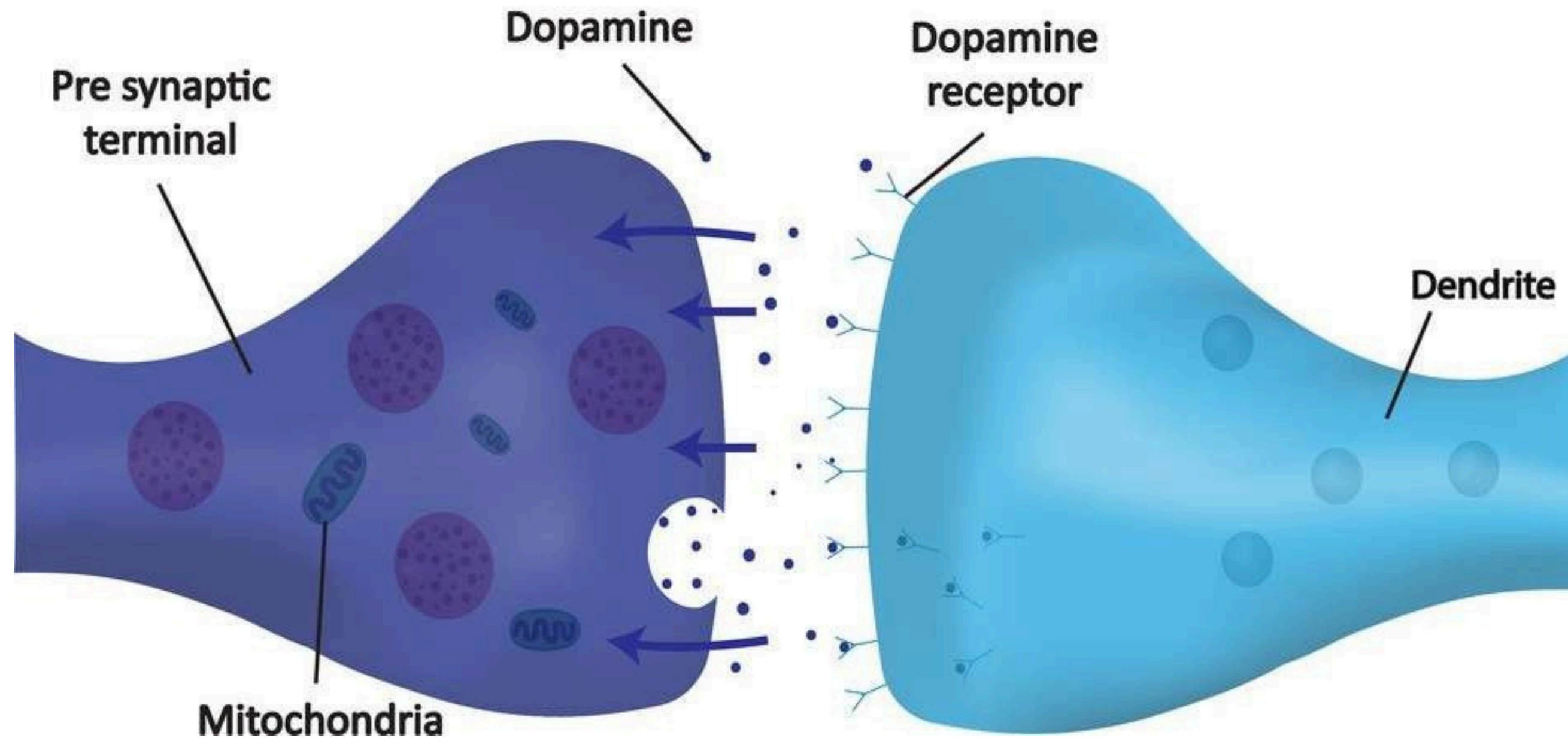




Mechanism of Action

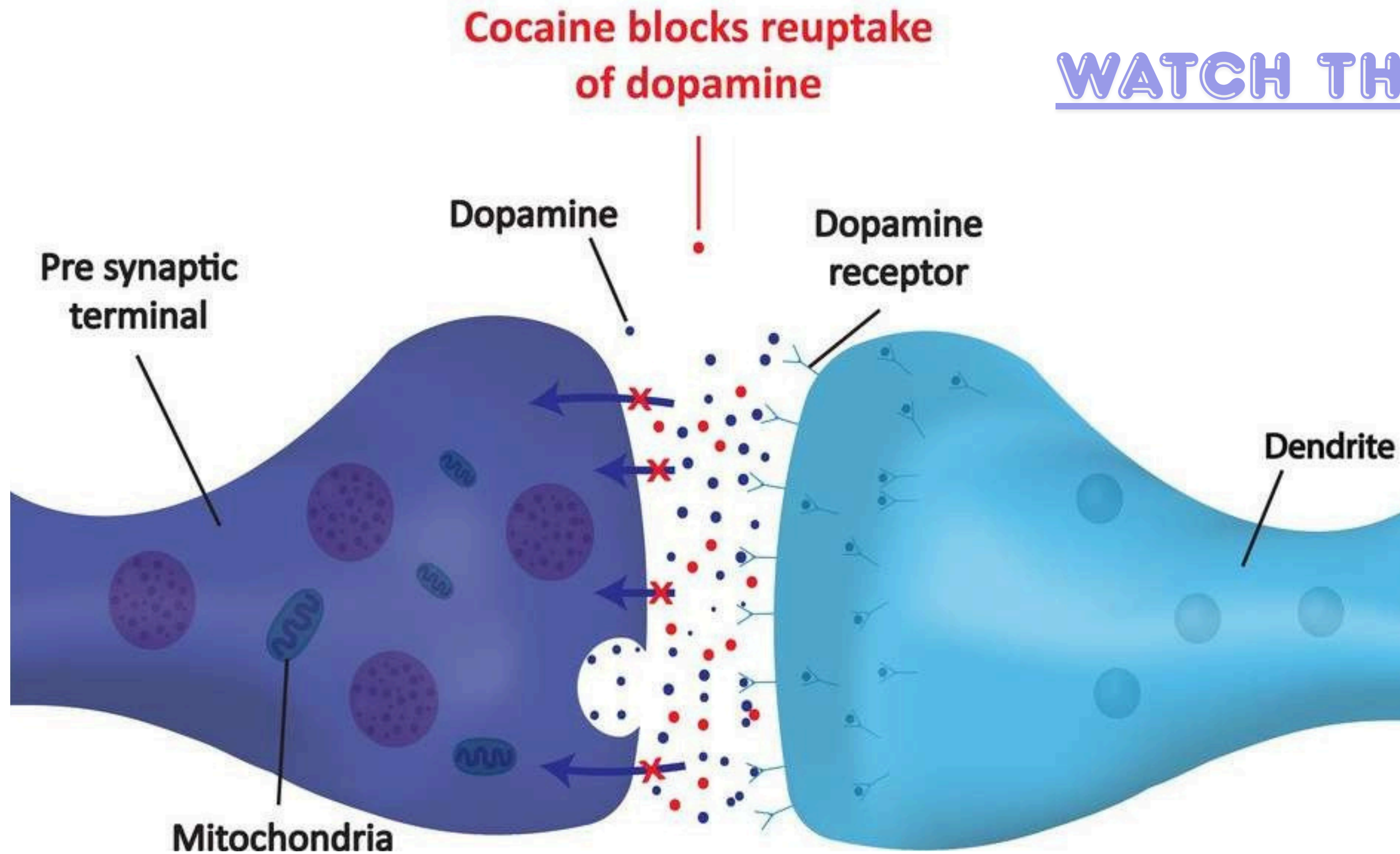
- Cocaine is **a Potent sympathomimetic**. Blocks reuptake of dopamine, norepinephrine, and serotonin.
 - Normally, electrical signals, or action potentials, travel down the axon to the axon terminal, where they trigger the release of neurotransmitters from synaptic vesicles into the synapse.
 - The neurotransmitters travel across the synapse and bind to receptors on the postsynaptic neuron, where they give the cell a message.
 - After the neurotransmitters have done their job, they unbind from the receptors, and can just diffuse away, get degraded by enzymes, or get picked up by proteins and returned to their release site in a process called reuptake.
 - **Cocaine** increases the release of certain neurotransmitters, but **it's biggest effect is blocking reuptake receptors** on presynaptic axon terminals.
 - Both of these actions **keep** neurotransmitters like **dopamine, norepinephrine, and serotonin** in the synapse **longer**, increasing their effects.
- 

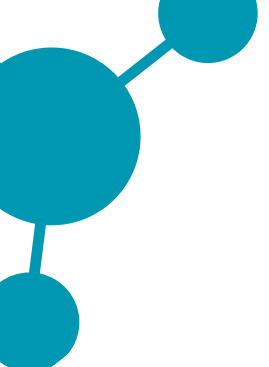
Normal Synapse



Synapse with Cocaine

[WATCH THIS VIDEO](#)





Cocaine Effects

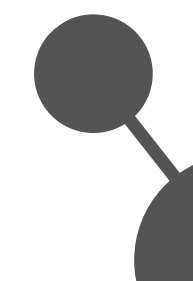
1 Dopamine:

- ◆ Increased concentrations of dopamine in the brain's reward pathway.
- ◆ Intense feelings of **euphoria**, **pleasure**, and **the emotional "high"** associated with cocaine.

2 Norepinephrine:

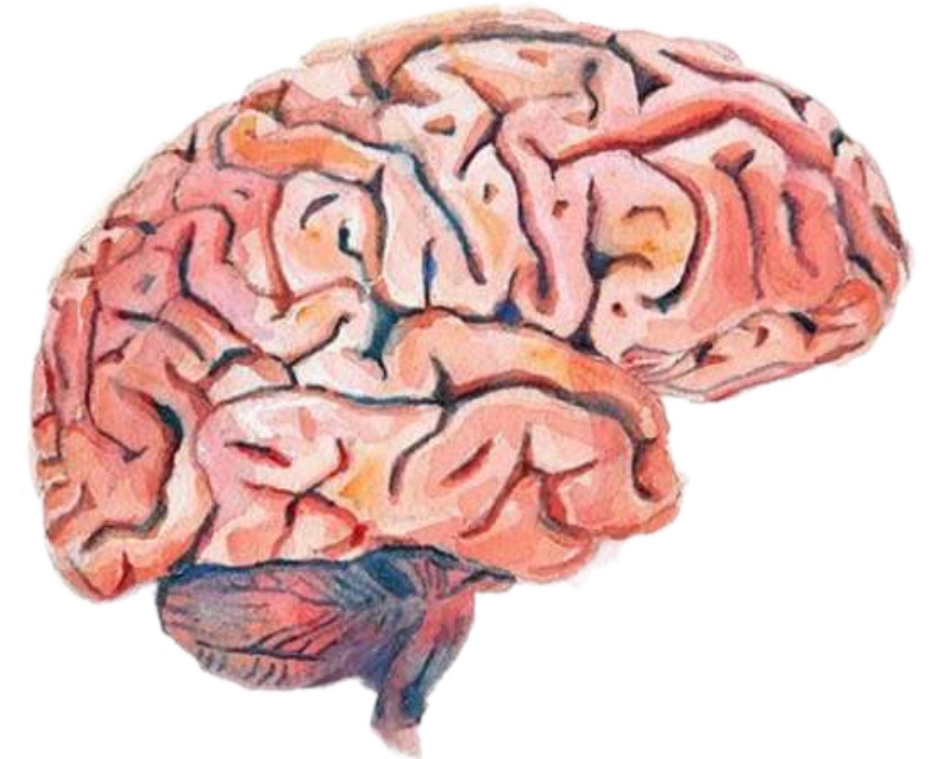
- ◆ Increased norepinephrine concentrations throughout the brain.
- ◆ **Physical "high"** or feeling of hyper-stimulation & **Vertigo**.
- ◆ Increased energy, constricted blood vessels, dilated pupils, increased body temperature, increased heart rate, and increased blood pressure (**sympathomimetic effects**)

3 Serotonin:

- ◆ Higher levels of serotonin are associated with **greater confidence**.
Includes the nucleus accumbens, ventral tegmentum, and prefrontal cortex.
- 

Actions on Nervous System

- Cocaine illects the following actions on the central nervous system:
 - ◆ Acutely **increases mental awareness**.
 - ◆ Hallucinations.
 - ◆ Produces a feeling of **wellbeing & Euphoria**.
 - ◆ **Increases motor activity**.
- Cocaine at high doses can cause:
 - ◆ **Tremors**.
 - ◆ Convulsions.
 - ◆ Followed by **respiratory and vasomotor depression**.
- For the sympathetic NS, it potentiates the action of norepinephrine, and produces the “fight or flight” syndrome which is associated with:
 - ◆ Tachycardia.
 - ◆ Hypertension.
 - ◆ Pupillary dilation (Mydriasis).
 - ◆ Peripheral vasoconstriction.



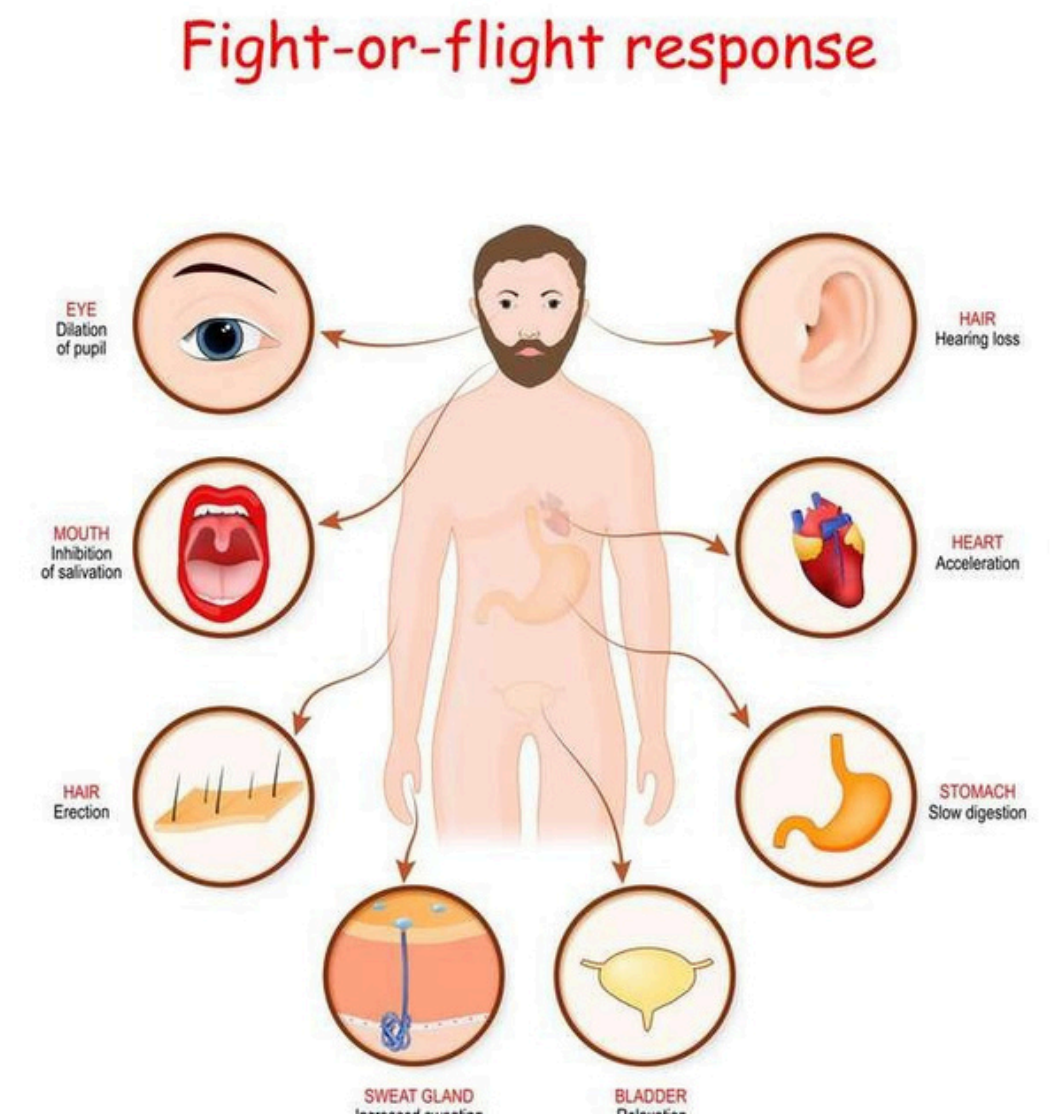
Actions on CVS

→ Cardiopulmonary symptoms are the most frequent complaints in cocaine users who seek medical help, with **chest pain being the most frequent symptom**.

→ Cocaine increases Heart Rate, Blood Pressure, & Peripheral Vascular Resistance, by **increasing adrenergic activity in the heart**, and indirectly via the CNS.

→ Chronic use is associated with:

- ◆ Left ventricular hypertrophy.
- ◆ Cardiomyopathy.
- ◆ Myocardial fibrosis and myocarditis.



Actions on RS

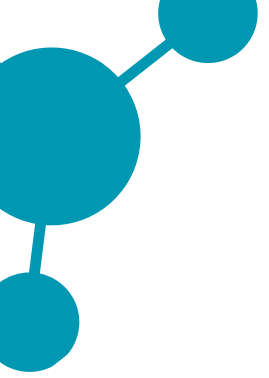
The effects of cocaine on the respiratory system depend on the route of administration.

Intranasal cocaine (Snorting) may cause **chronic rhinitis**, **perforation of the nasal septum**, **oropharyngeal ulcers**, due to vasoconstriction and resulting ischemic necrosis.

Smoked cocaine produces **acute respiratory symptoms in up to half of users.** These effects are probably due to direct damage to the alveolar-capillary membrane by cocaine or inhaled micro particles. These symptoms can be:

- ◆ Productive cough.
- ◆ Shortness of breath.
- ◆ Chest pain.
- ◆ Hemoptysis.
- ◆ Wheezing.
- ◆ Exacerbation of asthma.





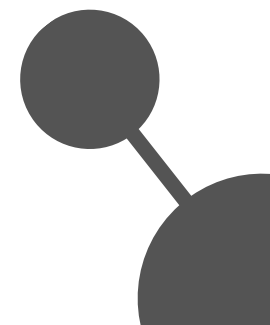
Medical Uses

→ As a **local anesthetic** action, applied topically during surgeries to:

1. Eye. 2. Ear. 3. Nose. 4. Throat.

→ Cocaine **constricts blood vessels**:

This property helps reduce bleeding and swelling during surgery.

- The use of Cocaine has significantly decreased due to:
 - ◆ High potential for addiction and abuse.
 - ◆ Availability of safer and equally effective alternatives.
 - ◆ Stricter regulations.
- 

Metabolism & Excretion

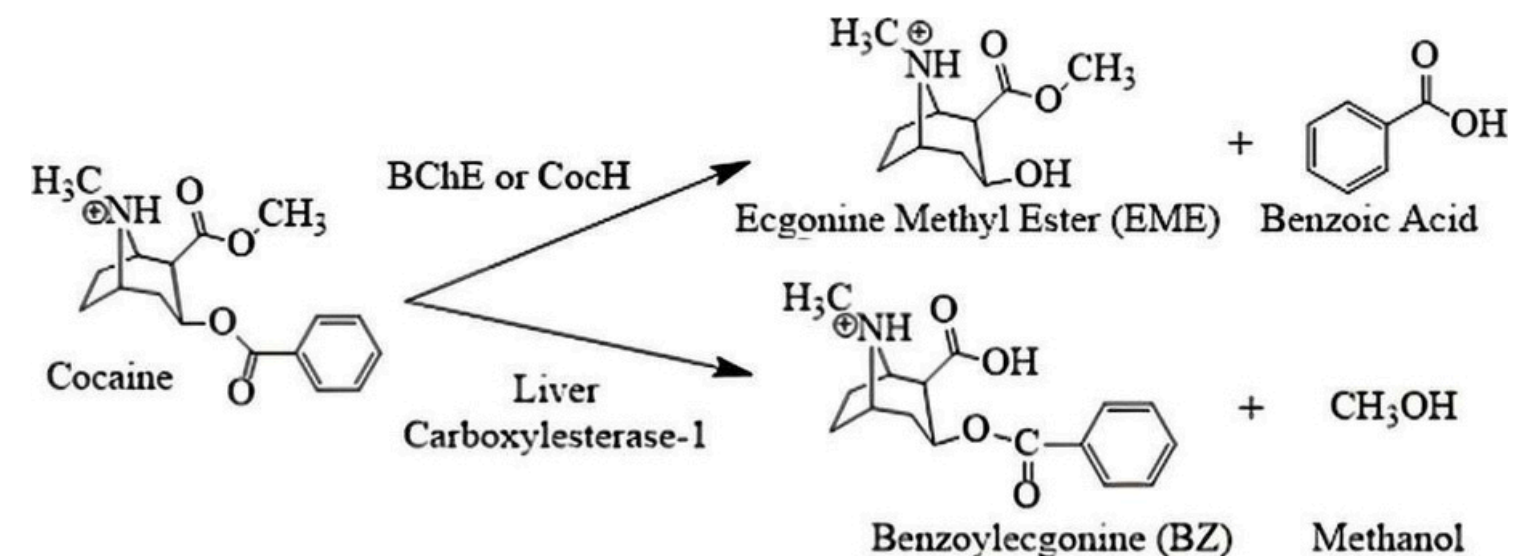
→ Cocaine undergoes extensive metabolism, primarily in the liver through a combination of processes, including **hydrolysis by esterases** and **oxidation by the Cytochrome P450 system**. Only a tiny fraction (around 1%) is excreted unchanged in the urine.

→ The metabolism is dominated by hydrolytic ester cleavage, so the eliminated metabolites consist mostly of benzoylecgonine (BE), major metabolite, and other metabolites in lesser amounts such as ecgonine methyl ester (EME) and ecgonine.

→ Benzoylecgonine can typically be detected in urine **within 4 to 8 hours of cocaine use**.

Positive blood cocaine/BE indicates recent use.

There is no absolute "fatal level"; context is critical.



Response to Drug

1. Dependence

◆ Once the abused drug is no longer available, signs of withdrawal become apparent, which defines Dependence.

2. Tolerance

◆ It is said to develop when **the response to the same dose of a drug decreases with repeated use.**

3. Withdrawal Symptoms

◆ Cocaine is **one of the most addictive drugs ever known**. Those who use cocaine heavily or regularly find it **extremely difficult to stop** and often suffer through serious withdrawal symptoms such as:

- ◆ Severe **irritability** & **Excessive sleep**.
- ◆ Insomnia & **Paranoia** (Feeling of risk).
- ◆ **Loss of sex drive** & **Chronic depression**.
- ◆ **Eating disorders** & **Diarrhea**.
- ◆ **Nausea & Vomiting**.
- ◆ Muscle & Nerve **aches**.

The term "physical dependence" is now denoted dependence, while "psychological dependence" is called Addiction

WITHDRAWAL SYMPTOMS

MILD SYMPTOMS

MOSTLY PSYCHOLOGICAL

DEPRESSION

ANXIETY

FATIGUE

REDUCED

CONCENTRATION

CRAVINGS

TIREDNESS

INCREASED APPETITE

EXCESSIVE SLEEPING

VIVID DREAMING

(↑ REM)



WORST SYMPTOMS

AFTER HABITUAL USE

"CRASH"

SUICIDAL IDEATION

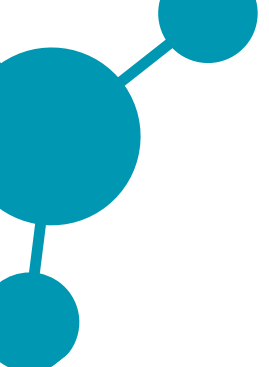
NAUSEA

VOMITING

SENSATION ^{of}

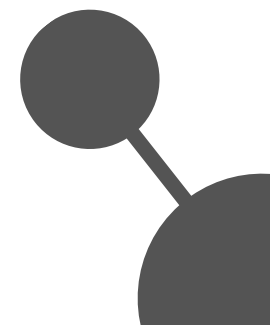
INSECTS ^{on}

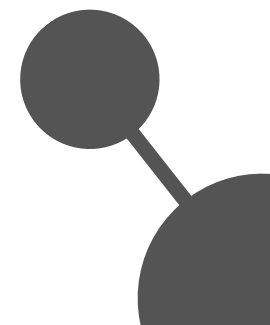
SKIN

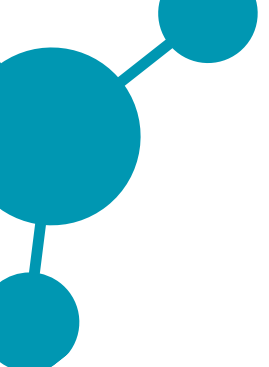


Complications of Chronic Drug Abuse

In general, chronic drug abuse is associated with:

- 1. Malignancies (Cancers).**
 - 2. Lung disease (Like Pneumonia).**
 - 3. Heart diseases (Like MI, & Heart attack).**
 - 4. Mental illnesses (Like Depression, Anxiety, & Suicide).**
 - 5. Infectious disease.**
 - 6. Addiction (psychological dependence).**
 - 7. Kidney failure, Liver failure, & Risk of collapsed veins.**
- 

- 
- The use of needles by sharing amongst addicts is the cause of life-threatening infections like: **HIV, Hepatitis**.
 - **Lack of hygiene**, or using **subcutaneous route** for injecting drugs produces infection on the site of injection: ♦ **Cellulitis**. ♦ **Abscess**.
 - Infection like **endocarditis**, **infarction** of skin and muscle, **renal failure** and **shock** are common among cocaine drug users.
 - **Lack of appetite** which causes unhealthy weight loss & malnourishment.
 - **Ulceration of the nasal septum** (It is always recorded as a complication of long-term nasal abuse of cocaine but this is, in fact a rare phenomenon) & **tears in the GIT** related to decreased blood flow.
 - Movement disorders as **Parkinson's disease**.
 - **Intracranial Hemorrhage**, and Increased risk of **stroke** & **aortic rupture**.
 - Unlike opioids, there are **few physical withdrawal symptoms**.
- 



Diagnosis of Chronic Cocaine Toxicity

Cocaine toxicity diagnosis relies on a combination of factors:

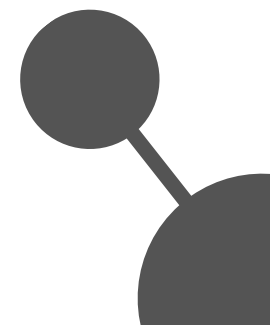
→ History of Cocaine Use:

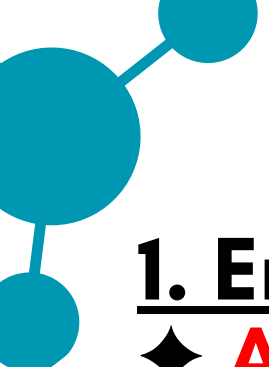
- ◆ Self-reported cocaine use.
- ◆ Witness reports.

→ Physical Examination:

- ◆ Symptoms (Typical features of **sympathomimetic intoxication**, Mentioned before).
- ◆ Findings similar to **external autopsy findings** (Discussed Later).

→ Investigations:

- ◆ Chest pain with ECG **evidence of ischemia or infarction:**
Especially in a young and healthy individual, **strongly suggests cocaine use**, as it can constrict blood vessels & increase the risk of heart attack.
- 



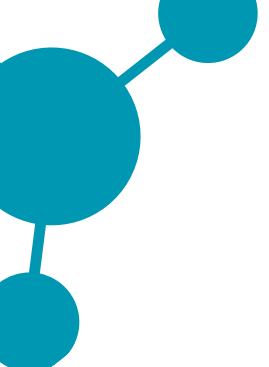
Treatment of Chronic Cocaine Toxicity

1. Emergency and Supportive Measures

- ◆ **ABCs** and Secure two large-bore IV cannulas.
- ◆ Administering a **Benzodiazepine**, such as diazepam (Valium) to prevent seizures.
- ◆ **Physical cooling** (Ice, cold blankets, etc...) and **paracetamol** may be used to treat hyperthermia.
- ◆ **In a cardiac arrest, vasopressin** may offer considerable advantage over epinephrine.
- ◆ **Hypotension** may compound the patient's status; if present, **norepinephrine** may be required.
- ◆ **Monitor vital signs and ECG** for several hours.

2. Specific Drugs and Antidotes

- ◆ **There is NO** officially approved **specific antidote** for cocaine overdose.
- ◆ **Propranolol** was previously recommended as the drug of choice for treatment of **cocaine-induced HTN**. It may in fact produce paradoxical worsening of hypertension because of blockade of beta-2-mediated vasodilation. **Cardioselective beta-blockers** may be **used alone for treatment of tachyarrhythmias**.



Treatment of Chronic Cocaine Toxicity

Decontamination (NOT necessary after smoking, snorting, or IV, but used after ingestion)

◆ **Prehospital:**

- Administer **activated charcoal** if available.
- **Do not induce vomiting**, because of the risk of abrupt onset of seizures.

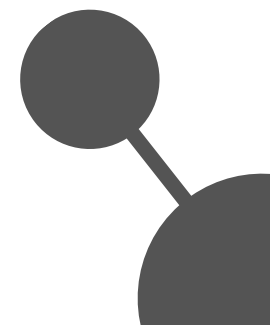
◆ **Hospital:**

- Administer **activated charcoal**.
- **Gastric emptying is NOT necessary** if activated charcoal can be given promptly.

◆ **For ingestion of cocaine-filled packets:**

- Give **repeated doses of activated charcoal**.
- **Consider whole-bowel irrigation** (Wash out GIT by osmotically balanced macrogol solution "laxative").

If large ingested packets (ie, Ziploc™ bags) are not removed by these procedures, **laparotomy and **surgical removal** may be necessary.**

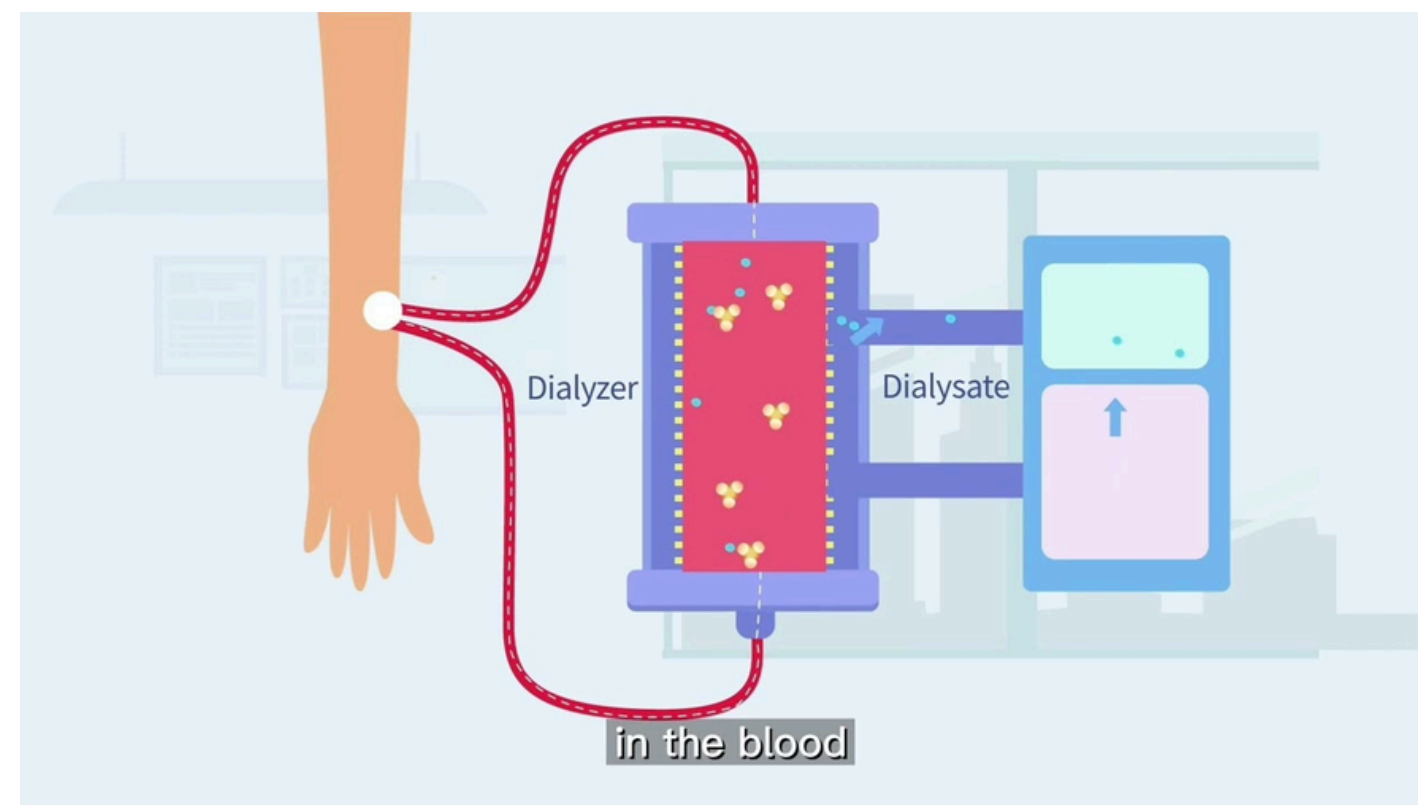


Treatment of Chronic Cocaine Toxicity



Enhanced Elimination (Not used due to inefficacy)

- ✦ Enhanced elimination techniques serve to **increase the rate of removal of an agent from the body** with the aim of reducing the severity and duration of clinical intoxication.
- ✦ Cocaine is **extensively distributed to tissues** and **rapidly metabolized**.
- ✦ Because of that, Dialysis and Hemoperfusion procedures are not effective.



Medico-Legal Spot Considerations

We must consider the total circumstances of the case including:

→ **History & Physical Examination** (Discussed before).

→ **Complete Toxicological Analysis:**

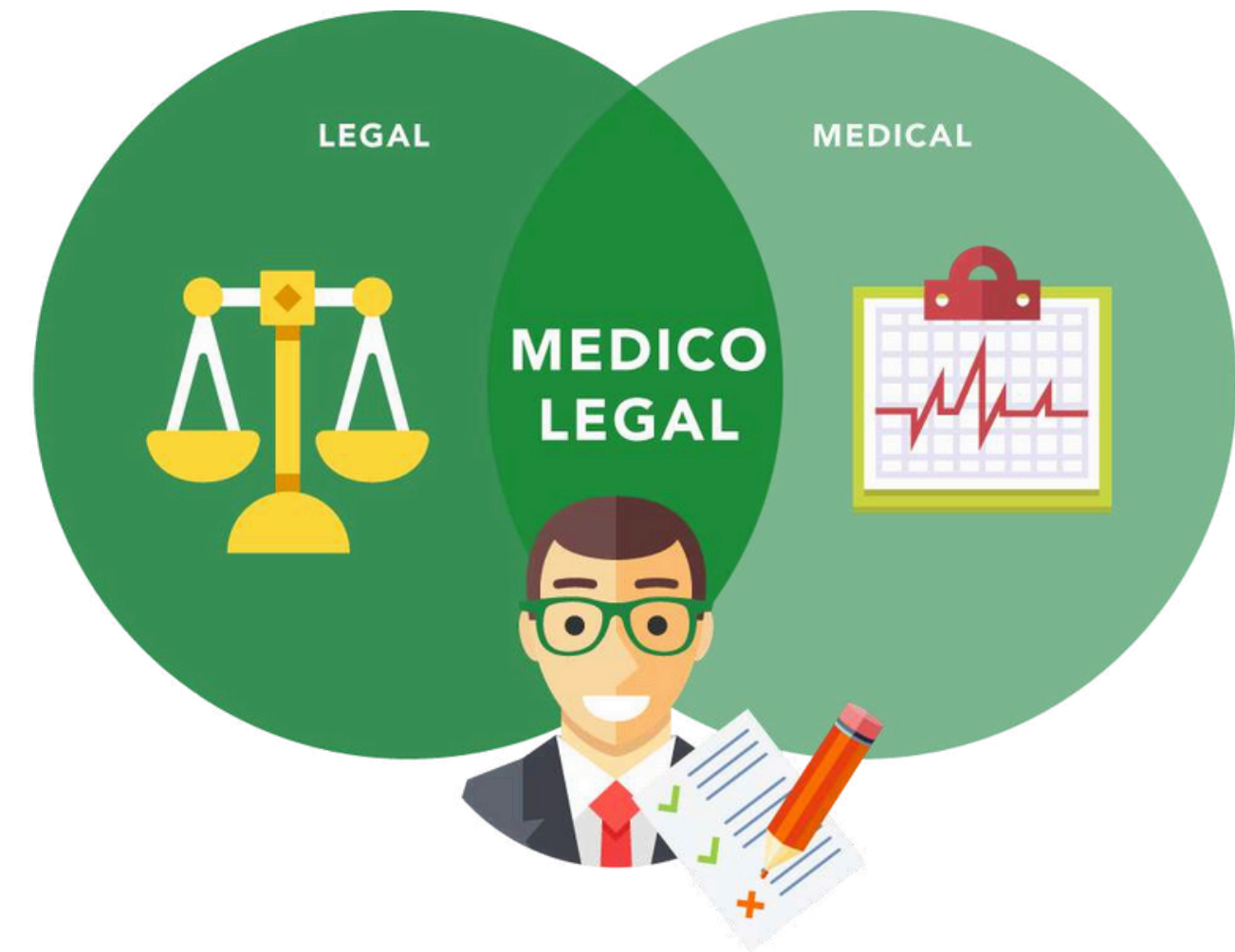
- ◆ Cocaine and its **metabolites** in Blood.
- ◆ Cocaine and its metabolites in Saliva.
- ◆ Cocaine and its metabolites in Human breast milk.
- ◆ Cocaine and its metabolites in Urine.
- ◆ Cocaine and its metabolites in Hair.

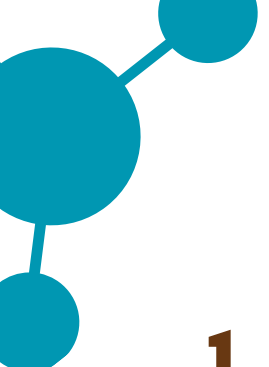
→ **Autopsy Findings:**

- ◆ Signs suggestive of intravenous use.
- ◆ Signs suggestive of crack use.

→ **Lethal Dose of Cocaine & Causes of Death.**

- ◆ Signs suggestive of intranasal use.
- ◆ Internal Findings.





Complete Toxicological Analysis

1. Blood Cocaine Levels:

- ◆ They are **not routinely available** and do not assist in emergency management.

2. Cocaine and its metabolites in Urine:

- ◆ **Cocaine** and its metabolite **Benzoylecgonine** are easily detected in the urine. It provide qualitative confirmation of cocaine use.
- ◆ **Benzoylecgonine** is the major metabolite that **can be found in the urine for 2 - 5 days** after a binge.

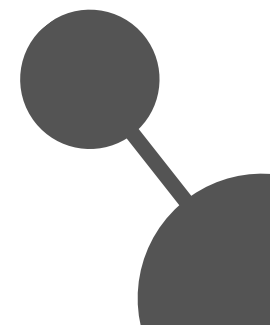
3. Cocaine and its metabolites in Saliva:

- ◆ Saliva can be used to detect any **recent use.**

4. Cocaine and its metabolites in Hair:

- ◆ They **can be found** in hair, **longer than in the urine**, where we find more cocaine than its metabolites.

5. Cocaine and its metabolites in Human breast milk:

- ◆ Cocaine also may be **secreted in significant concentrations in human breast milk**, which put infants at risk of cocaine exposure and its toxic effects.
- 

Autopsy: External Findings

1. Signs suggestive of intravenous use:

- ◆ Fresh needle tracks.
- ◆ Shallow cutaneous ulcers.
- ◆ Fresh injection sites.
- ◆ Round / oval scars.
- ◆ Pyogenic infections are most common, with phlebitis and distant embolic abscesses occurring.



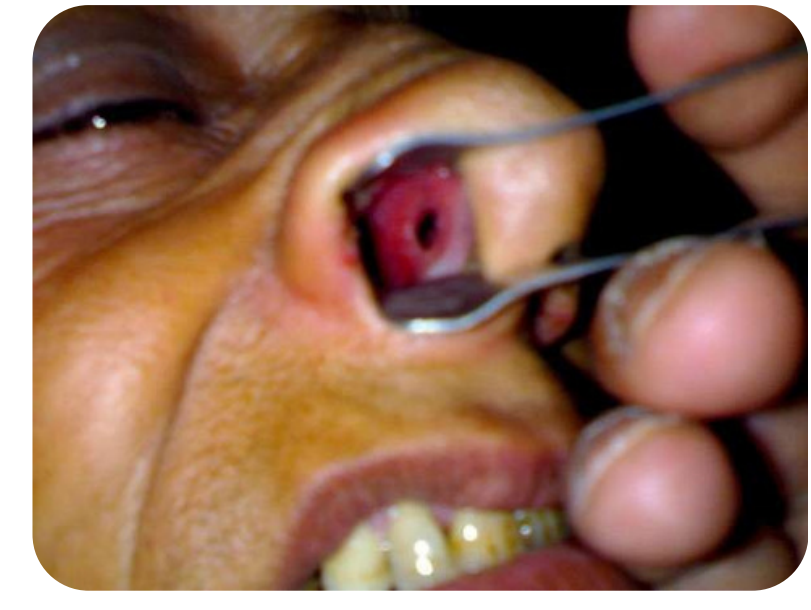
Autopsy: External Findings

2. Signs suggestive of crack use:

- ◆ Crack callus (on the ulnar aspect of the thumb) from repeated activation of a flint-lighter.

3. Signs suggestive of intranasal use:

- ◆ Perforation of the nasal septum.
- ◆ Collapse ("Saddle nose" deformity, Rare).
- ◆ Positive nasal swab.

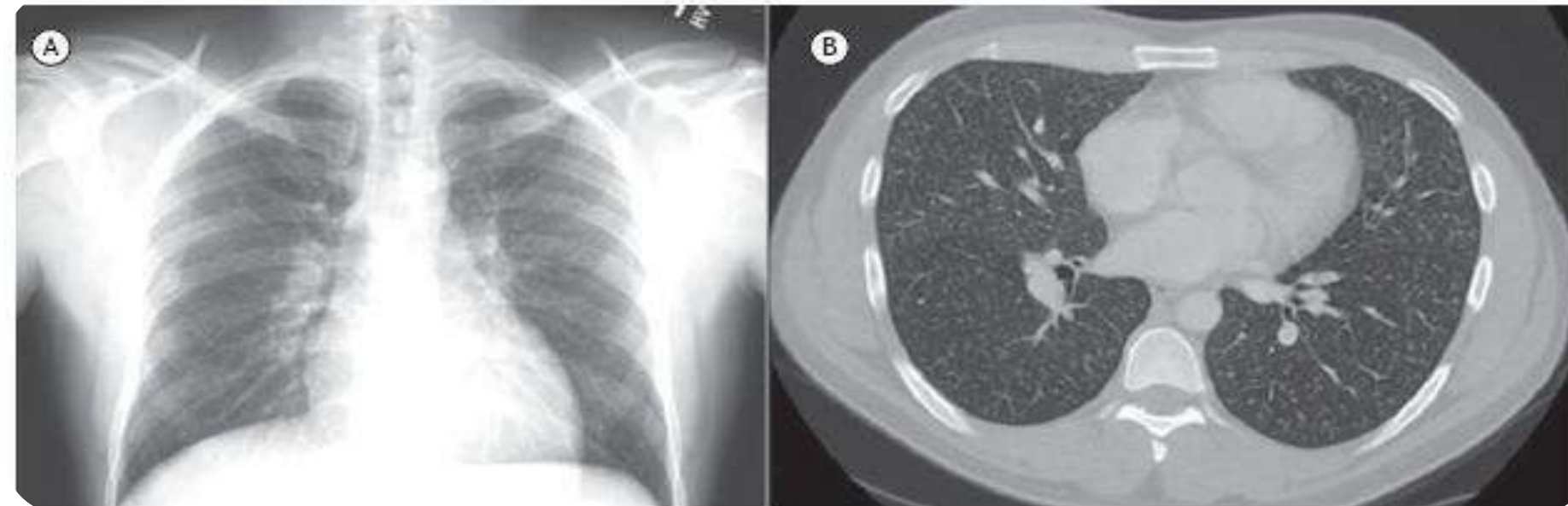
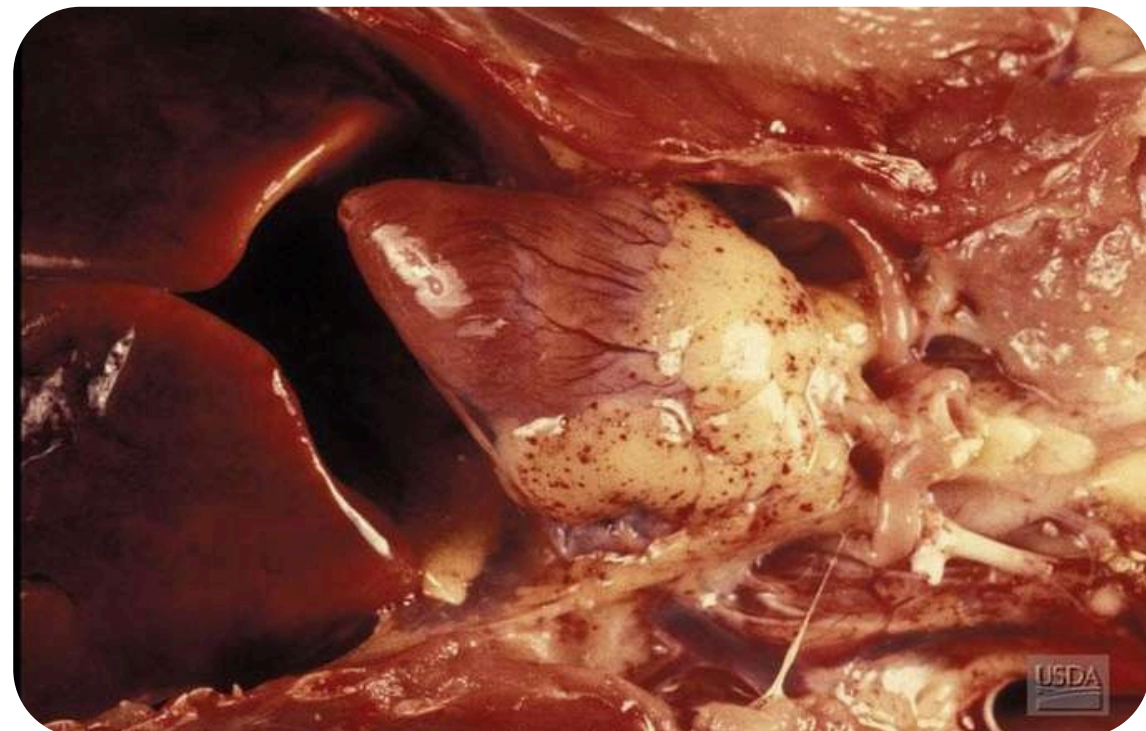


Autopsy: Internal Findings

→ Visceral congestion.

→ Serosal petechiae.

→ Any drug used intravenously if it has particulate matter admixed, such as starch or talc, may cause foreign-body granulomas in the lungs.



Autopsy: Internal Findings

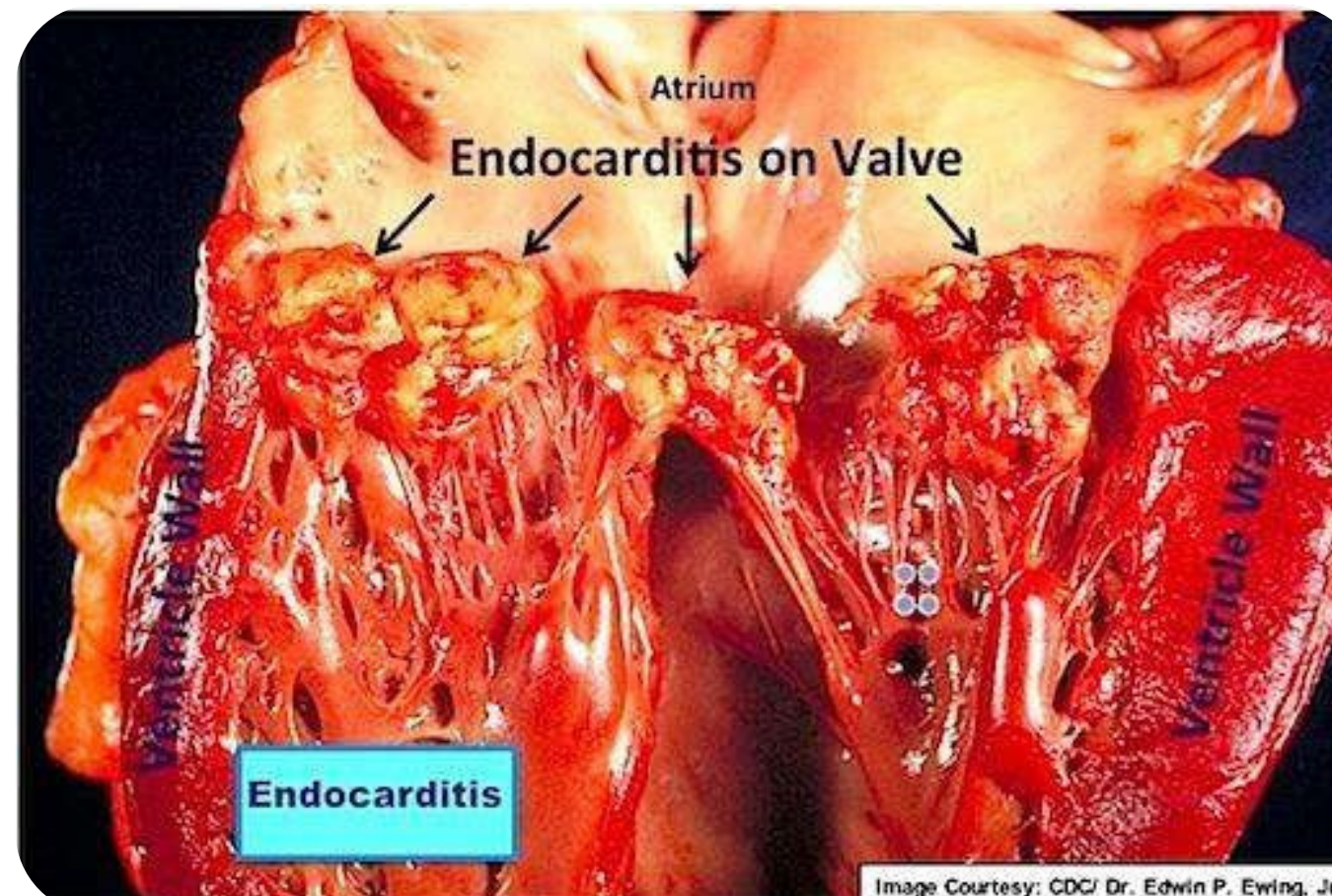
Signs of terminal convulsions (Bite marks on the tongue, and lower lip).

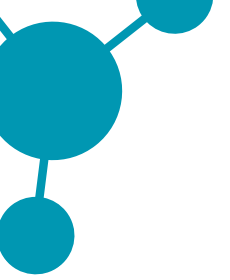
→ **The diluent (talc, starch, quinine, lactose and dextrose)** used in 'cutting' the drug for street sale may be found in the injection sites, the regional lymph nodes, in the lungs and in other organs.

→ **Particles of cocaine itself may also be found as microemboli.**

→ **Regional lymphadenitis.**

→ **Endocarditis.**





Lethal Dose & Causes of Death

→ There is **NO minimum specific fatal level** for cocaine, but **the range is 20 mg IV - 500 mg ingested orally**.

→ **Lethal dose is dependant on the tolerance** of the patient especially in chronic uses.

→ Cocaine causes sudden death by two mechanisms:

◆ **Cardiac arrhythmia** caused by the direct action of the cocaine on the myocardium.

◆ **Cardiopulmonary arrest** induced by the CNS action of the drug. (Overdose will lead to Overstimulation of the CNS).

→ **Death** may occur with considerable rapidity **in cocaine overdose** or **hypersensitivity**. It may be quite sudden, **from cardiac arrest**, in first-time users.



Thank You 