

# FORENSIC & TOXICOLOGY SUMMARY

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## Toxicology summary

### Lecture 5: CNS depressants

Problems of substance abuse: toxicity, physiological & psychological dependence, tolerance & withdrawal.

#### Opioids (narcotics)

- ❖ **Opioids:** natural or synthetic substances that act on opioid receptors (mu, kappa, delta).
- ❖ **Opiate:** natural opioid that derived from *Papaver Somniferum* (morphine & codeine).
- ❖ **Heroin:** semi-synthetic opioid derived from morphine, the most commonly use.
  - Its chemical name is diacetylmorphine.
  - Half-life: 30 minutes.
  - Duration of action: 4-5 hours.
  - Active metabolite: **6-monoacetylmorphine (6-MAM)**, detectable on urine testing.
  - More lipid soluble than others, penetrate BBB within 15-20 seconds.
  - Heroin withdrawal starts within 6-12 hours after the last dose, and peaks within 1-3 days and gradually subsides over 5-7 days.
- ❖ **Endorphins:** natural endogenous peptides for pain & stress relief (enkephalins, endorphins).

<b>Clinical presentation (Intoxication)</b>	<ul style="list-style-type: none"><li>○ Euphoria, drowsiness, sedation, slurred speech, pinpoint pupils.</li><li>○ Depressed respiration, alteration in temp. regulation, hypovolemia.</li><li>○ ADH &amp; constipation (due to increase sphincter tone).</li></ul>
<b>Withdrawal symptoms</b>	<ul style="list-style-type: none"><li>○ Tachycardia, high blood pressure, fever, chill.</li><li>○ Piloerection, mydriasis, lacrimation, runny nose, sweating.</li><li>○ Irritability, convulsion, tremor.</li></ul>
<b>Investigations</b>	For heroin: urine test looking for 6-MAM.
<b>Management</b>	<ol style="list-style-type: none"><li>1. ABCD.</li><li>2. Monitor the vital signs and cardiopulmonary status.</li><li>3. Opioid antidote: <b>naloxone</b> (opioid antagonist).</li><li>4. Maintenance (withdrawal treatment):<ul style="list-style-type: none"><li>➤ <b>Methadone:</b> long-acting mu-opioid agonist of, preventing withdrawal symptoms for 24 hours or longer, reduce craving and euphoric effects.</li><li>➤ <b>Buprenorphine:</b> partial mu-opioid agonist.</li></ul></li><li>5. Blood sample: risk of hepatitis &amp; HIV.</li></ol>

## Lecture 6: CNS stimulants

### General clinical symptoms:

- Elevated mood, increased alertness, increased energy, insomnia, anorexia.
- Chest pain, tachypnea, nausea, abdominal pain, headaches.
- Long-term: tolerance, weight loss, irritability, aggression, impulsivity, hallucinations, delusion.
- MDMA intoxication may include restlessness, anxiety, trismus, grinding teeth, impaired memory.
- Increased BP & HR, arrhythmia, hyperthermia, pupil dilation, itching.
- MI, AKI, rhabdomyolysis, hemorrhagic stroke.

### General withdrawal symptoms:

- Sedation, depressed, fatigue, impaired memory, decreased attention, suicidal behaviors.

### Cocaine

- ❖ Source: leaves of the *Erythroxylum coca* plant.
- ❖ Forms:
  1. Cocaine base ("crack," "freebase"): smoked, difficult to dissolve in injection, water insoluble.
  2. Cocaine salt: injected or insufflated ("snorted"), easily dissolve in injection, water soluble.
- ❖ Mechanism of action:
  - Enhances monoamine neurotransmitter (dopamine, NE, and serotonin) activity in the by blocking its presynaptic reuptake.
  - Enhancement of brain dopamine activity, especially in the corticomesolimbic dopamine reward circuit >> positive psychological symptoms.
  - Has local anesthetic effect due to blockage of voltage-gated membrane Na<sup>+</sup> channels.
- ❖ Distribution: Rapidly taken up into most body organs.
- ❖ Metabolism: metabolized by hydrolysis to **benzoylecgonine** and to ecgonine methylester.
- ❖ Elimination: largely eliminated in the urine. Benzoylecgonine found in highest concentration in urine.
- ❖ Cocaine intoxication:

<b>CVS</b>	Arterial & coronary vasoconstriction, HTN, tachycardia, enhance thrombus formation >> cardiac ischemia. At high dose: -ve inotropic effects & left ventricular function depression >> HF.
<b>CNS</b>	Psychomotor agitation, seizures, coma, headache, intracranial hemorrhage, stroke, and focal neurologic symptoms.
<b>RS</b>	Angioedema, pharyngeal burns, pneumothorax, pneumomediastinum, pneumopericardium, exacerbations of reversible airway disease and bronchospasm, shortness of breath, hemoptysis, wheezing.
<b>GI</b>	Reduces salivary secretions, gastric motility and delays gastric emptying. Induced vasoconstriction and ischemia may result in gastrointestinal ulceration, infarction, perforation and ischemic colitis.
<b>Skin</b>	Pseudovasculitic lesions.

- ❖ **Investigation:** urine test looking for benzoylecgonine.

- ❖ Management:
  1. ABCD
  2. Control cardiac complications, arrhythmia, hypertension, hyperthermia, convulsion, agitation, irritability, nutritional status.
  3. **No antidote.**
  4. **Benzos to control convulsions** & antipyretic for hyperthermia

### *Amphetamines*

- ❖ Examples: Methamphetamine, Methylphenidate, MDMA.
- ❖ Mechanism of action: Stimulation of alpha and beta adrenergic receptor (sympathomimetic).
- ❖ Methamphetamine:
  - Used clinically for treatment of ADHD & adult narcolepsy.
  - After cannabis, it is the most widely abused drug worldwide.
  - MOA: it lacks direct adrenergic effects but is instead an indirect neurotransmitter by increase their release in the synaptic cleft & inactivates neurotransmitter reuptake transporter systems.
- ❖ Management:
  5. ABCD
  6. Control cardiac complications, arrhythmia, hypertension, hyperthermia, convulsion, agitation, irritability, nutritional status.
  7. **No antidote.**
  8. **Benzos to control convulsions** & antipyretic for hyperthermia.
  9. **Acidify urine to induce elimination (ammonium chloride)**
  10. **Give charcoal for gastric decontamination.**

## Lecture 7: hallucinogen

### Cannabis (tetrahydrocannabinol)

- ❖ Source: cannabis sativa.
- ❖ 2 major forms: Marijuana & hashish.
- ❖ Routes:
  1. Inhalation (most common):
    - Onset: few minutes.
    - Duration: 2-3 hours.
  2. Ingestion:
    - Onset: 30 minutes.
    - Duration: 5-8 hours.
    - Plasma half-life: 18 hours - 4 days.
- ❖ Highly lipid soluble >> storage in fatty tissue for a period of time.
- ❖ Mechanism of action:
  - **Delta-9-tetrahydrocannabinol (THC) is the major psychoactive component of cannabis that activate cannabinoid receptor 1 or 2 or both.**
  - Stimulation of these receptors causes monoamine and amino acid neurotransmitters (Dopamine) to be released.
- ❖ Clinical features:
  - Low dose: relaxation, euphoria, hallucinations.
  - Moderate dose: disruption of thoughts, ataxia, short-term memory impairment.
  - High dose: paranoia, depersonalization, disorientation, tachycardia, sensory disturbances, loss of libido.
  - May cause hypotension, pulmonary edema, AKI, DIC.
  - No loss of consciousness.
- ❖ **No physical dependence but cause psychological dependence.**
- ❖ Withdrawal symptoms:
  - 1 week after cessation.
  - At least 3 of the following: Irritability, nervousness, anxiety, restlessness, sleep disturbance, appetite and weight loss, depressed mood.
  - At least 1 of the following: abdominal pain, tremors, sweating, fever, chills, headache.
- ❖ Investigation:
  - **Urine test: Cannabinoids can be detected in the urine for as many as 21 days after use in persons chronically using marijuana.**
  - Blood test: measuring the quantitative level of THC can distinguish between recent use and residual excretion.