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 & codiene).
- **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).

Clinical presentation (Intoxication)	○ Euphoria, drowsiness, sedation, slurred speech, pinpoint pupils. ○ Depressed respiration, alteration in temp. regulation, hypovolemia. ○ ADH & constipation (due to increase sphincter tone).
Withdrawal symptoms	○ Tachycardia, high blood pressure, fever, chill. ○ Piloerection, mydriasis, lacrimation, runny nose, sweating. ○ Irritability, convulsion, tremor.
Investigations	For heroin: urine test looking for 6-MAM.
Management	1. ABCD. 2. Monitor the vital signs and cardiopulmonary status. 3. Opioid antidote: **naloxone** (opioid antagonist). 4. Maintenance (withdrawal treatment): ➢ **Methadone**: long-acting mu-opioid agonist of, preventing withdrawal symptoms for 24 hours or longer, reduce caving and euphoric effects. ➢ **Buprenorphine**: partial mu-opioid agonist. 5. Blood sample: risk of hepatitis & HIV.

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+ 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:

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

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2. Pesticides poisoning
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