DRUGS OF ABUSE

Marijuana toxicity

- **Marijuana consists of the leaves and flowering parts of the plant *Cannabis sativa*. It usually is smoked in or pipes or added to food (usually cookies, brownies, or tea). Resin from the plant may be dried and compressed into blocks called hashish. Marijuana contains a number of cannabinoids; the primary psychoactive one is delta-9-tetrahydrocannabinol (THC).**

Marijuana toxicity

- **Tetrahydrocannanbinol (THC) is the most psychoactive cannabinoid, producing euphoria, relaxation, diminished pain, and difficulties with memory and concentration.**
- **THC is used medically as an appetite stimulant for patients with such AIDS-related anorexia; it also is used as treatment for vomiting associated with cancer chemotherapy, for chronic pain and other disorders.**

- **Cannabinoid antagonists include rimonabant (a CB_1 selective antagonist) which was developed as medication to reduce appetite and weight, and also for smoking cessation. It was marketed briefly in Europe and then withdrawn due to psychiatric side effects, particularly depression and suicidal ideation.**

Absorption

- **The route of administration determines the absorption of the cannabis product .**
- **Smoking – Onset of action is rapid (within minutes); it results in 10-35% absorption of the available THC; peak plasma concentrations occur within 8 minutes.**
- **Ingestion – Onset occurs within 1-3 hours; 5-20% is absorbed due to stomach acid content effect and metabolism; peak plasma levels occur 2-6 hours after ingestion .**

Pathophysiology

- In the early 1990s, the specific cannabinoid receptors were discovered, CB1 and CB2.
- The CB1 receptors are predominantly located in the brain areas responsible for anxiety, pain, sensory perception, motor coordination, memory, movement and endocrine function. This distribution is consistent with the clinical effects obtained by cannabinoids .

Pathophysiology

- **The CB_2 receptor, is located peripherally. Specifically, it is involved in the immune system (macrophages, T and B lymphocytes), peripheral nerves .**
- **Both the CB_1 and CB_2 receptors inhibit adenylate cyclase and stimulate potassium channels. As a result, the CR_1 receptors inhibit the release of several neurotransmitters, including acetylcholine, glutamate, norepinephrine, dopamine, serotonin, and gamma–aminobutyric acid (GABA). CR_2 receptor signaling is involved in immune and inflammatory reactions .**

Toxic dose

- **Toxicity is dose related, but there is individual variability such as degree of tolerance.**
- **Typical marijuana cigarettes contain 1–4% THC, but more potent varieties may contain up to 25% THC.**
- **Hashish contains 3–6% and hashish oil 30–50% THC.**
- **Dronabinol is available in 2.5-, 5-, and 10-mg capsules.**

Signs and symptoms

- **Smoking a marijuana cigarette cause euphoria, palpitations, increasing sensory awareness, and altered time perception, followed by sedation after 30 minutes.**
- **More severe intoxication may result in anxiety, impaired short-term memory, visual hallucinations, and acute paranoid psychosis.**
- **Cannabis use may precipitate or exacerbate psychosis in individuals with schizophrenia or bipolar disorder.**
- **Acute cannabis intoxication may result in impaired driving and motor vehicle accidents.**

Signs and symptoms

- **Cannabis dependence, both behavioral and physical, occurs in 5–10% of users. A cannabis withdrawal syndrome is seen after stopping use in heavy chronic users, consisting of irritability, anxiety, fatigue, sleep disturbance often with abnormal dreams, and depression.**

- **Physical findings include tachycardia, orthostatic hypotension, conjunctival injection, incoordination, slurred speech, and ataxia.**

Signs and symptoms

- **Marijuana use has been associated with precipitation of acute myocardial infarction, usually in people with underlying coronary disease.**

- **Salmonellosis and pulmonary aspergillosis are reported from use of contaminated marijuana. Marijuana may be contaminated by paraquat, but paraquat is destroyed by pyrolysis, and there have been no reports of paraquat toxicity from smoking marijuana.**

Treatment

- **1. Most psychological disturbances can be managed by simple reassurance, possibly with adjunctive use of lorazepam, diazepam, or midazolam.**
- **2. Sinus tachycardia usually does not require treatment but, if necessary, may be controlled with beta blockers.**
- **3. Orthostatic hypotension responds to head-down position and IV fluids.**
- **4. Gastric decontamination may be considered with an acute ingestion less than 2 hours prior to presentation..**
- **5. Enhanced elimination. These procedures are not effective owing to the large volume of distribution of cannabinoids.**

Cocaine

- Cocaine is one of the most popular drugs of abuse. Powerfully Addictive Stimulant made from leaves of the coca plant which are most commonly found in South America.
- Purest form is a white pearly product In a powder form it looks identical to salt.

Mechanism of toxicity

- The primary actions of cocaine are local anesthetic effects, CNS stimulation, and inhibition of neuronal uptake of catecholamines.
- **A.** Central nervous system stimulation and inhibition of catecholamine uptake result in a state of generalized sympathetic stimulation very similar to that of amphetamine intoxication.
- **B.** Cardiovascular effects of high doses of cocaine related to blockade of cardiac cell sodium channels, include depression of conduction and contractility resulting in QT prolongation.

Pharmacokinetics

- Cocaine is well absorbed from all routes, and toxicity has been described after mucosal application as a local anesthetic.
- Smoking and IV injection produce maximum effects within 1–2 minutes, whereas oral or mucosal absorption may take up to 20–30 minutes.
- Once absorbed, cocaine is eliminated by metabolism and hydrolysis, with a half-life of about 60 minutes. In the presence of ethanol, cocaine is trans-esterified to **cocaethylene,** which has similar pharmacologic effects and a longer half-life than cocaine.

Toxic dose

- **The toxic dose is highly variable and depends on individual tolerance, the route of administration, and the presence of other drugs.**
- **Rapid IV injection or smoking may produce transiently high brain and heart levels, resulting in convulsions or cardiac arrhythmias, whereas the same dose swallowed or snorted may produce only euphoria.**

Clinical presentation

- **A. CNS manifestations of toxicity occur within minutes after smoking or IV injection or may be delayed for 30–60 minutes after snorting, mucosal application, or oral ingestion.**
- **Initial euphoria may be followed by anxiety, agitation, delirium, psychosis, muscle rigidity or hyperactivity, and seizures. High doses may cause respiratory arrest.**
- **Coma may be caused by a postictal state, hyperthermia, or intracranial hemorrhage resulting from cocaine-induced hypertension.**

- **B. Cardiovascular toxicity occur rapidly after smoking or IV injection and is mediated by sympathetic overactivity.**
- **Fatal ventricular tachycardia or fibrillation may occur. QRS-interval prolongation similar to that seen with tricyclic antidepressants may occur.**
- **Severe hypertension may cause hemorrhagic stroke or aortic dissection. Diffuse myocardial necrosis similar to catecholamine myocarditis and chronic cardiomyopathy have been described.**

- **Death** is usually caused by a sudden fatal arrhythmia, status epilepticus, intracranial hemorrhage, or hyperthermia. Hyperthermia is usually caused by seizures, muscular hyperactivity, or rigidity and typically is associated with rhabdomyolysis, myoglobinuric renal failure, coagulopathy, and multiple-organ failure. Severe hyperthermia is more common when the environmental temperature is high, particularly when a high ambient temperature is combined with physical hyperactivity.

Management

- **The general objectives of pharmacotherapeutic intervention in cocaine toxicity are to reduce the CNS and cardiovascular effects of the drug by using benzodiazepines initially and then to control clinically significant tachycardia and hypertension while simultaneously attempting to limit deleterious drug interactions.**
- **Hyperthermia may be treated with convection cooling, which involves spraying the patient's body with water. Rapid fluid resuscitation promotes urine output.**

Lysergic acid diethylamide (LSD) toxicity

- **Lysergic acid diethylamide (LSD) is one of the most potent psychoactive compounds known (LSD was used as a psychotherapy in 1950's).**
- **An oral dose of 25 µg is capable of producing potential psychological effects. The drug is odorless, colorless, and slightly bitter tasting and water-soluble substance.**
- **It is usually taken by mouth and rapidly absorbed by the gastrointestinal (GI) tract.LSD toxicity can lead to respiratory arrest, coma, emesis, hyperthermia, autonomic instability, and bleeding disorders .**

Psychoactive effects

- **LSD causes changes in thought, mood, and perception, with minimal effects on memory and orientation. The drug primarily produces pseudohallucinations.**
- **True hallucinations occur as well; visual hallucinations are the most common .In general, hallucinogens can intensify the patient's current mood; pleasant feelings can be augmented to euphoric ones, with an expanded consciousness.**
- **Negative feelings or depressive symptoms can be amplified to a dysphoric experience. Changes produced in consciousness lead to loss of boundaries between the patient and the environment .**

Pathophysiology

- Lysergic acid diethylamide (LSD) is one of the most potent psychoactive compounds known. It is usually taken by mouth and rapidly absorbed by the gastrointestinal (GI) tract .LSD toxicity can lead to respiratory arrest, coma, emesis, hyperthermia, and bleeding disorders .An oral dose of 25 µg is capable of producing potential psychological effects.

Mechanism of toxicity

- **The hallucinogenic effects of LSD are thought to be mediated by 5-HT2 receptor activation (which plays a major role in the modulation of sensory signals and is predominantly found in pyramidal neurons of the prefrontal cerebral cortex). Central and peripheral sympathetic stimulation may account for some of the side effects, such as anxiety, agitation, psychosis, dilated pupils, tachycardia, and hyperthermia.**

Signs and symptoms

- LSD causes changes in thought, mood, and perception, with minimal effects on memory and orientation. The drug primarily produces visual hallucinations. In general pleasant feelings can be augmented to euphoric ones.
- Changes produced in consciousness lead to loss of boundaries between the patient and the environment .

Management

- **The basic rule of management is reassurance in a safe, calm and stress-free environment. Rarely, patients need to be either sedated or physically restrained.**
- **Benzodiazepines can safely be given to treat agitation .**
- **Massive ingestions of LSD should be treated with supportive care, including respiratory support and endotracheal intubation if needed. The following should be treated symptomatically :Hyperthermia, Hypotension - Should be treated initially with fluids and subsequently with pressors if required**