

Drug abuse

Prof. Omar
Shaheen



Drugs of Abuse

- Nonmedical use of drugs includes experimental use, in which a person tries a drug out of curiosity; recreational use, when moderate amounts are used to get “high”; and situational use,
- when drugs are used in specific circumstances, for example, amphetamines to stay alert. Sometimes these patterns can lead to more frequent use and dependence.



Definitions

- **Drug abuse** The use, usually by self-administration, of any drug in a manner that deviates from the approved medical or social patterns within a culture.
- **Drug misuse** Inappropriate use of a drug
- **Compulsive drug use or compulsive drug abuse** Continued self-administration of a drug despite the fact that the user may be suffering adverse social or medical consequences. In compulsive drug use, the user feels the drug is needed for his or her well-being. There is a continuum of compulsive drug use, from a simple desire to have more drug to a craving and preoccupation with procurement of the drug.



Drug addiction

- According to the World Health Organization, drug addiction is a behavioral pattern of drug use that is characterized by overwhelming involvement with the use of a drug and overwhelming involvement with securing a supply.
- Along with this, there is a high tendency to relapse after withdrawal.
- There is some overlap in the definitions of compulsive use and addiction, and it is not always clear when compulsive use becomes addiction.



Definitions

- **Tolerance:** Decreased responsiveness to a drug with repeated or continued dosing. Crosstolerance may occur between drugs or between drug classes.
- **Dependence :** Continued use of that drug is required to prevent withdrawal.
- **Withdrawal:** Withdrawal may consist of physical and/or psychological signs and symptoms that occur upon abstinence from a drug.
- * There is a difference between addiction and dependence. It is possible for a person to exhibit signs of dependence following withdrawal of a drug, yet not crave the drug.



Detoxification

- Detoxification is the same for all drugs that produce physical dependence. It involves substituting a longer-acting, orally effective, pharmacologically equivalent drug for the abused drug.
- The patient is stabilized on the substitute, and then it is gradually withdrawn. There is a high recidivism rate among drug abusers. Currently, there are many psychotherapeutic programs after detoxification, but these programs have success rates varying from 10% to perhaps a maximum of 50%.



Opioids

- Morphine, Diamorphine (Heroin), Codeine, Meperidine, and Methadone
- **Effects.** The effects of opioids on performance include mental clouding, faulty judgment, and a reduced ability to concentrate. Physical signs of abuse include miosis (pupillary constriction), depression, and apathy.



Heroin

- (it's also known as di acetyl morphine)
- This compound isn't natural occurring, it's highly addictive analgesic and hypnotic semi synthetic derivative. Heroin cause euphoria
- It's obtain from morphine but the difference between them is in 2 hydroxyl gp in morphine while in heroine 2 hydroxyl in morphine gps are replaced with acetate function gps (named so as diacetyl bond).
- - Morphine too is addicting from the first dose.
- Heroin is more addictive and each time the body need a higher dose than the previous one (has tolerance)



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Tolerance, dependence, and withdrawal

- . Tolerance, dependence, and withdrawal are characteristic of opioid use.
- — Pain relief may be less effective as tolerance develops, even after a single dose.
- Tolerance develops more slowly to meperidine than morphine.
- Withdrawal from an opioid is generally not life-threatening, although it is almost unbearable.
- The intensity of the withdrawal symptoms will be in proportion to the amount of drug being used and the duration of the abuse.
- Withdrawal will be more intense and of a shorter duration after use or abuse of more potent, shorter-acting agents. Likewise, it will be less intense but more prolonged with less potent, longer-acting agents.



Opioid withdrawal symptoms

Early symptoms
(10–12 h after withdrawal)

Rhinorrhea (runny nose), perspiration, lacrimation (secretion of tears), and yawning

Intermediate symptoms
(18–24 h after withdrawal)

Mydriasis, piloerection, anorexia, and muscular tremors

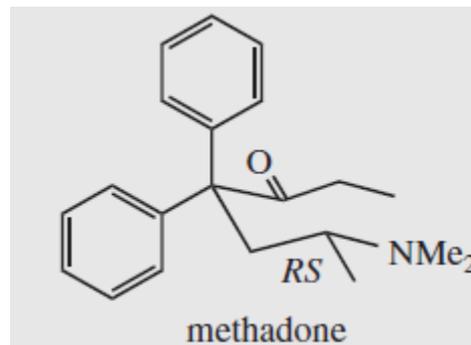
Peak symptoms
(36–72 h after withdrawal)

Restlessness, hot flashes alternating with chills, an increase in both blood pressure and heart rate, an increase in the rate and depth of respiration, fever of 1°C or more, nausea, retching, vomiting, and diarrhea

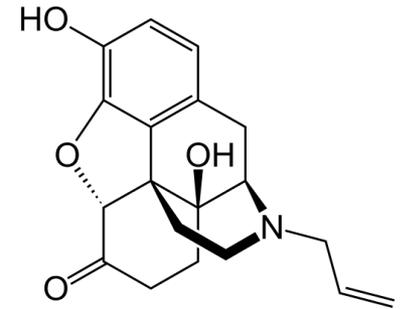


Methadone:

- *Methadone is orally active, has similar activity to morphine, but is less euphorogenic and has a longer duration of action. Although it is as potentially addictive as morphine, **the withdrawal symptoms are different and much less severe** than with other drugs such as heroin, so that methadone and **Buprenorphine** (a semi-synthetic derivative of thebaine) are widely used for the **treatment and rehabilitation of heroin addicts**.
- Ex: withdrawal symptoms with methadone don't appear before 48 hours but in morphine or heroin a second urgent dose needed within the next 24 hours.



Naloxone



- **Naloxone** is pure antagonists especially in [overdose](#).
- **Naloxone**, sold under the brand name **Narcan**
- Administration to opioid-dependent individuals may cause symptoms of opioid withdrawal, including restlessness, agitation, nausea, vomiting, a fast heart rate and sweating. To prevent this, small doses every few minutes can be given until the desired effect is reached.
- Naloxone is a pure [opioid antagonist](#). It works by reversing the depression of the central nervous system and respiratory system caused by opioids.¹
- The drug was approved for opioid overdose by the [Food and Drug Administration](#) in 1971.



Alcohol/Ethanol Toxicology

- Alcohol is rapidly absorbed from the gastrointestinal (GI) tract after oral administration. Its acute effects appear within minutes of ingestion.
- Ethanol is metabolized in the liver, primarily by alcohol dehydrogenase to acetaldehyde, then by acetaldehyde dehydrogenase to acetate.
- This metabolism follows zero-order kinetics, which means that a constant amount of ethanol is metabolized per unit of time. The implication of this is that as more ethanol is ingested, the degree of intoxication increases rapidly, as well as the time for the blood level to drop to a nonintoxicating level.



Effects of Acute intoxication with Ethanol

System/Tissue	Effects
Acute Intoxication	
CNS	Progressive CNS depression is correlated in time with blood concentrations of ethanol and may include vision and judgment impairments, decreased inhibitions, and muscular incoordination, progressing to staggering gait, slurred speech, and possible coma and death at higher doses.
GI system	Increased salivary and gastric secretions, direct irritation to gastric and buccal mucosa, emesis due to a central effect on the chemoreceptor trigger zone, and irritation of the gastric mucosa. Prolonged use also leads to decreased absorption of folates.
Other	Suppression of antidiuretic hormone (ADH, vasopressin) secretion Increased adrenocorticotropin hormone (ACTH), cortisol, and catecholamine secretion Diuresis due to decreased antidiuretic hormone release Increased consumption of fluids Hypothermia



Effects of Chronic intoxication with Ethanol

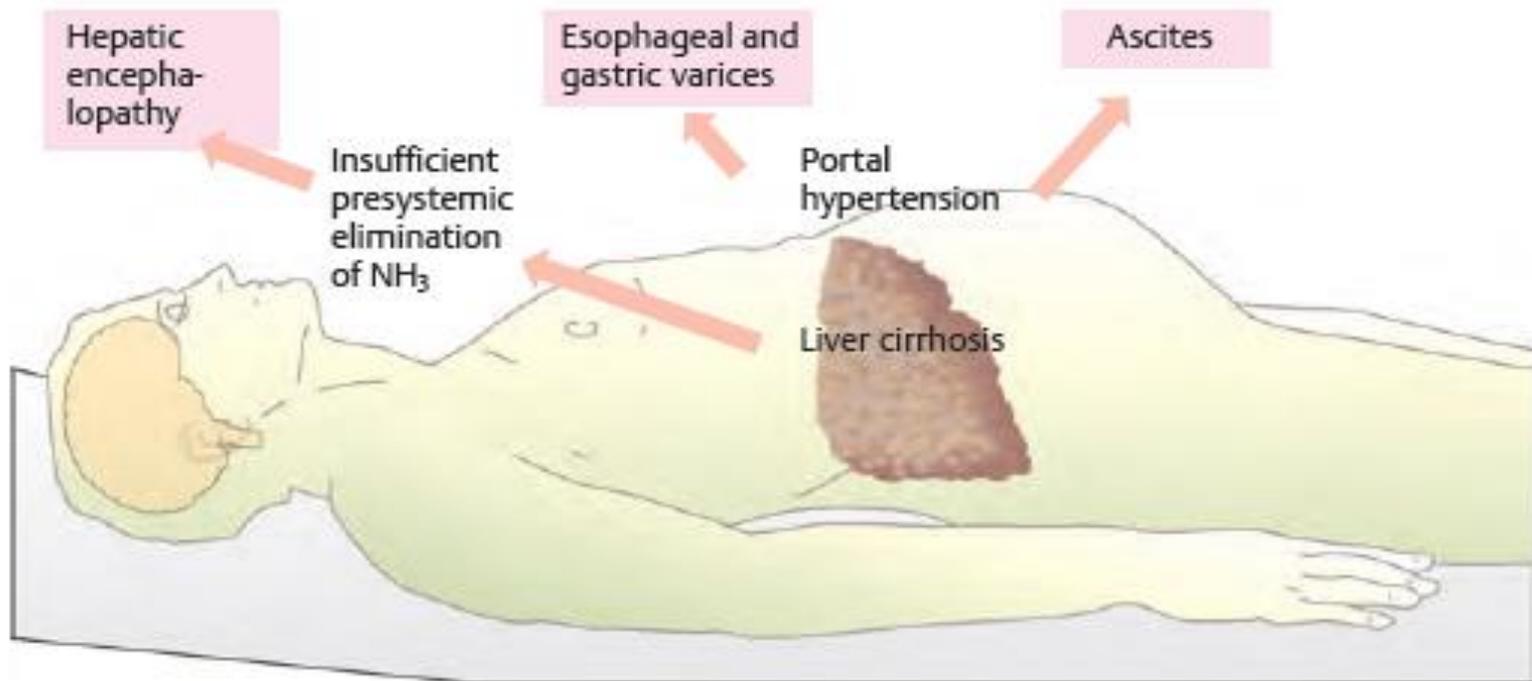
Chronic Intoxication

CNS	Wernicke syndrome, Korsakoff psychosis, cerebral atrophy, cerebellar atrophy, and alcoholic polyneuropathy
GI system	Peptic ulcers, esophagitis, gastritis, pancreatitis, and malnutrition
Liver	Steatosis, hepatitis, and cirrhosis (Figs. 15.1 and 15.2)
Muscle	Cardiomyopathy and skeletal muscle myopathy
Fetus	Fetal alcohol syndrome
Other	Face puffy, cheeks and nose flushed, eyes bloodshot, palmar erythema, rhinophyma, acne rosacea, and spider nevi



Liver cirrhosis

- Liver cirrhosis occurs when hepatocytes die and are replaced by connective tissue. Hepatic blood flow is impaired, causing portal hypertension, which in turn causes ascites and the formation of varices. The normal functioning of the liver is reduced, including the elimination of toxins, which can then build up and affect the functioning of the brain.



Fetal alcohol syndrome

- *Fetal alcohol syndrome* is the term used to describe a spectrum of disorders that can occur in a fetus if a woman drinks alcohol when pregnant. It includes the following: abnormal facial features, growth deficiencies, vision or hearing deficits, and mental disabilities, such as difficulty in learning, memory problems, poor attention span, and poor communication skills.



Alcohol/Ethanol

- **Tolerance, dependence, and withdrawal.**
- Withdrawal symptoms in chronic users of alcohol include tremor, sweating, anxiety, irritability, nausea, vomiting, and insomnia. These symptoms will be mild to moderate in 80 to 85% of patients and more severe in 15 to 20%.
- Severe withdrawal, known as delirium tremens, is seen in ~1%.
- — Benzodiazepines are cross tolerant with alcohol and will alleviate withdrawal symptoms, but they do not have the same stimulating effects on the central nervous system (CNS) as alcohol.
- — For serious complications or delirium tremens, replace fluids and electrolytes and treat symptoms.
- Treat arrhythmias with lidocaine or procainamide, severe tremor with propranolol, and hallucinations and paranoia with a phenothiazine or haloperidol.



Delirium tremens

- Delirium tremens is a disorder that occurs as a result of alcohol withdrawal (onset ~72 h after the last drink).
- Signs include increased pulse, reduced blood pressure, tremors, fits and visual or tactile hallucinations.
- Treatment is with diazepam.



Drugs to Manage Alcoholism

- Acute intoxication rarely requires treatment. Management includes supporting ventilation, maintaining temperature, and correcting dehydration, acidosis, or electrolyte imbalance. Gastric lavage (stomach pumping) is rarely necessary. Chronic intoxication may be treated with the agents listed below.
- **Naltrexone**
- Mechanism of action. Naltrexone is an opioid antagonist similar to naloxone but with greater bioavailability and longer duration of action. It apparently blocks the ability of alcohol to activate dopaminergic reward pathways.
- **Pharmacokinetics**
- — Orally active, but also available in once-monthly injectable, extended-release form
- **Side effects**
- — Nausea and liver damage (in high dosages)
- **Contraindications**
- — Liver failure or acute hepatitis



Drugs to Manage Alcoholism

- **Disulfiram (Antabuse)**
- Mechanism of action. Disulfiram is an inhibitor of aldehyde dehydrogenase. If alcohol is taken in the presence of disulfiram, blood acetaldehyde levels increase, producing flushing, dyspnea (shortness of breath), nausea, thirst, chest pain, and palpitations.
- The effects are intended to be unpleasant so as to discourage alcohol ingestion; however, they can be serious and even life-threatening.
- *Note:* Patients must be informed to avoid alcohol, or their life may be in danger. This includes avoiding sauces, cough syrups, and liquid cold medicines that contain alcohol.



Toxicology of Other Alcohols

Methanol

- Metabolism. Methanol is metabolized to formaldehyde by alcohol dehydrogenase. This occurs
- at about one fifth of the rate of ethanol. It is then further metabolized to formic acid.
- Effects
 - — Metabolic acidosis and organ damage
 - — Methanol can cause blindness by damaging the optic nerve.



Benzodiazepines

- Diazepam, Midazolam, Temazepam, Triazolam, Flurazepam, Clonazepam, Oxazepam, Lorazepam, and Alprazolam
- **Intoxication** with benzodiazepines produces progressive CNS depression with increasing dose. They may be fatal at high doses due to respiratory depression and cerebral hypoxia.
- **Tolerance, dependence, and withdrawal**
 - — Tolerance develops to the effects of benzodiazepines.
 - — Physical dependence can occur.
 - — Withdrawal symptoms are generally opposite the effects of the drugs: anxiety, insomnia, and convulsions (in severe withdrawal). They can be minimized by slowly decreasing the dose to wean the patient from the drug.



Barbiturates

- Thiopental, Phenobarbital, Thiomytal, Methohexital, Amobarbital, Pentobarbital,
- and Secobarbital
- **Intoxication**
- — Same as for benzodiazepines
- **Tolerance, dependence, and withdrawal**
- — Tolerance develops to their sedative and hypnotic effects. No tolerance develops to the anticonvulsant actions of barbiturates.
- — True physical dependence occurs.
- — Moderate withdrawal consists of rebound increases in rapid eye movement (REM) sleep, insomnia, and anxiety. Seizures and delirium can occur in patients taking high doses for long periods. These patients should be withdrawn slowly to avoid these serious complications



Stimulants

Amphetamines and Cocaine

- **Effects**

- — CNS actions include euphoria, decreased fatigue, alleviation of sleepiness, and decreased appetite.
- Amphetamines and cocaine may also increase libido and talkativeness. Restlessness may occur, and the heart rate may increase.
- — After prolonged self-administration (a “run”) with amphetamines, prolonged sleep, apathy, and depression are common.
- — Sympathetic effects may be absent in chronic users.
- — Chronic toxicity produces anxiety and confusion, leading to paranoia and psychosis, which is indistinguishable from schizophrenia.

- **Uses**

- — Cocaine is sometimes used as a local anesthetic agent.
- — Amphetamines are used for attention deficit/hyperactivity disorder (ADHD) and narcolepsy.



Intoxication

Amphetamines and Cocaine

- — Acute intoxication causes hyperpyrexia, convulsions, and shock. It may result in death.
- Treatment involves chlorpromazine which will block many of the acute effects of amphetamines, and diazepam to control convulsions. Acidification of the urine will enhance excretion.
- Death can occur following acute cocaine use by convulsions or cardiac arrhythmias.
- Chlorpromazine can be used.
- — Chronic intoxication may cause toxic syndrome. Signs and symptoms of toxic syndrome include visual, auditory hallucinations, and tactile hallucinations; paranoia and changes in affect. Treatment for paranoid delusions and excitement involves dopamine antagonists (haloperidol).
- Acidification of the urine will facilitate excretion



Tolerance, dependence, and withdrawal Amphetamines and Cocaine

- — Marked tolerance develops to amphetamines but not to cocaine.
- — Dependence is common and produces an extremely intense drug craving. Physical dependence is minor.
- — Withdrawal may include prolonged sleep, laziness, fatigue, overeating, and, occasionally, depression. Craving may persist for years.



Hallucinogens

Psychedelic Hallucinogens

- d-Lysergic Acid Diethylamide (LSD), Psilocybin, and Mescaline
- These agents differ primarily in potency. LSD is extremely potent.
- Mechanism of action. Their mechanism is unclear, but they are serotonin agonists
- Intoxication. Psychedelic hallucinogens may produce vivid visual hallucinations and profound
- changes in thought processes, with confusion alternating with seemingly vivid perceptions and foresight, but these depend greatly on the situation and the individual.
- Side effects
 - — Paranoia, panic reaction, and overt psychosis.
 - — Synesthesias and “flashbacks” are unique features (seen in up to 15% of users).
- *Note:* No deaths due to direct drug effects have been reported.



Hallucinogens

Psychedelic Hallucinogens

- Treatment
 - — Involves emotional support and antianxiety agents, phenothiazines, or barbiturates in doses to produce sleep
- Tolerance, dependence, and withdrawal
 - — Tolerance and cross-tolerance will occur.
 - — No dependence or withdrawal



Cannabis

Marijuana and Hashish

- Marijuana is the dried mix of flowers and leaves from the female Cannabis Sativa plant.
- Hashish is the resin, or sap, harvested from the plant.
- Hashish oil is the essential oil of the female Cannabis Sativa plant
- The main psychoactive ingredient is tetrahydrocannabinol (THC). Endogenous cannabinoid receptors have been discovered along with an endogenous ligand, anandamide.



Cannabis

Marijuana and Hashish

- **Effects**

- — CNS effects: relaxation, sense of well-being, euphoria, and spontaneous laughter. Shortterm
- memory and capacity to carry out goal-directed behavior are impaired, and there is also motor impairment. THC has variable effects on mood, emotion, and social feelings.
- — Heart: tachycardia (paroxysmal atrial tachycardia) may occur.
- — Respiratory system: the lungs are adversely affected by smoke.
- — Reproductive system: changes in the menstrual cycle, decreased sperm count and motility, and increased number of abnormal sperm



Withdrawal Symptoms

Marijuana addiction is also linked to a withdrawal syndrome that can make it hard to quit. Symptoms include:

- irritability,
- sleeping difficulties,
- craving,
- anxiety, and
- increased aggression.



Cannabis

Marijuana and Hashish

- .
- **Uses**
- — Antiemetic in cancer chemotherapy patients
- **Tolerance, dependence, and withdrawal**
- — Tolerance develops to the effects of THC.
- — Physical dependence does not occur.
- — A withdrawal syndrome has not been defined. Many individuals stop using marijuana with no craving.

