**Definition**

- **Substance abuse**
  - *A syndrome manifested by a behavioral pattern in which the use of a given psychoactive drug, or class of drugs, is given a much higher priority than other behaviors that once had higher value (DSM IV-TR)*
  - The essential feature of dependence is a cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues substance use despite significant substance-related problems.
Definition

• **Tolerance**
  – The needs of increasing dose to reach same effect

• **Drugs Craving**
  – Abnormal wanting to ingest drugs again

• **Drugs Withdrawal**
  – Syndrome that occurs after discontinuing drugs

• **Drugs Cues**
  – Any cues related to drugs that abused in the past, including: friends, the dealers, needles that remind the patient to the situation when he consumed the drugs, this cue can lead to drugs craving phenomenon

Mechanism of Tolerance
Mechanism of Tolerance

• Receptor desensititation
• Neuronal death
• Increased drugs metabolism
• Needs for further inhibition

Drugs or substance frequently abused

• Sedatives and hipnotics
• Alcohol
• Antidepresant
• Opioids
• Amphetamine
• Cocain
• Inhalant
• Phencyclidine
Patophysiology of Substance dependence

- Sedative-hipnotics, alcohol by GABA stimulation
- Opioids by opioid mu receptor stimulation
- Amphetamine and cocaine by inhibiting DA, 5HT reuptake channel
- Nicotin by stimulating muscarinic ach receptor
- Inhalant by stimulating muscarinic Ach

Addiction vicious cycle

- Drug Seeking
- Indirect Drug Effects
- Unpleasant Drug Effects
- Positive Direct Effects of Drug in Brain (Dopamine Reward Pathway)
- Drug Taking
Alcohol dependence

- DSM IV CRITERIA FOR ALCOHOL DEPENDENCE
  - A maladaptive pattern of alcohol use, leading to clinically significant impairment or distress, as manifested by 3 or more of the following, occurring at any time within the same 12-month period: Tolerance, as defined by either of the following:
    - A need for markedly increased amounts of alcohol to achieve intoxication or desired effect
    - A markedly diminished effect with continued use of the same amount of alcohol
  - Withdrawal, as manifested by either of the following:
    - The characteristic withdrawal syndrome for alcohol
    - Alcohol, or a closely related substance, is taken to relieve or avoid withdrawal symptoms
  - Alcohol is often taken in larger amounts or over a longer period than was intended.
  - There is a persistent desire or unsuccessful effort to cut down or control alcohol use.

- A great deal of time is spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects.
- Important social, occupational, or recreational activities are given up or reduced because of alcohol use.
- Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol (e.g., continued drinking despite recognition that an ulcer was worsened by alcohol consumption)
Alcohol Abuse

• Effect on CNS
  – GABA A agonist
  → General depressant
  → Anticonvulsant
  → Euphorant
  → Related to Thiamine deficiency
  → Wernicke-Korsakoff Syndrome

• Skin and Muscle
  – Erythropoietic protoporphyria. Psoriasis vulgaris and acne rosacea (red nose), Myopathy

• Cardiovascular
  – Arrhythmia, increased risk CV disease

• Blood
  – Anemia

• GI
  – GI malignancy
  – Gastritis, stomatitis
  – Diarrhea

• Endocrine
  – Hipoactivity of thyroid and pancreas

• Immune system
  – Develop autoantibodies to smooth muscle, mitochondria, and nuclei,
Alcohol intoxication

- Recent ingestion of alcohol
- Clinically significant maladaptive behavior or psychological changes (e.g., inappropriate sexual or aggressive behavior, mood lability, impaired judgment, impaired social or occupational functioning) that developed during, or shortly after, alcohol ingestion
- One (or more) of the following signs, developing during, or shortly after, alcohol use:
  - Slurred speech
  - Incoordination
  - Unsteady gait
  - Nystagmus
  - Impairment in attention or memory
  - Stupor or coma
- The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

Possible sequelae of various blood alcohol concentration (BAC)

- 0.03 mg% → Euphoria
- 0.05 mg% → Mild coordination problems
- 0.1 mg% → Ataxia (5-6 drinks in a 2-hour period)
- 0.2 mg% → Confusion
- 0.3 mg% → Coma and death
Management of Alcohol intoxication

- Supportive care
- Flumazenil IV if there is sign of respiratory depression (must be in ICU setting)
- Thiamine supplementation

Treatment of Alcohol dependence

- Behavioural treatment
- Total abstinence
- Benzodiazepin replacement and tapering off
- Thiamin
- Other psychoactive as indicated
Nicotin

• The most widely substance of abuse in the world

Why Nicotine is one of SOA

• it has centrally mediated, psychoactive effects that are reliably discriminated from placebo
• Nicotine produces pleasurable or euphoriant effects,
• nicotine functions as a positive reinforcer Both animals and human smokers will self-administer nicotine over placebo
• Fourth, tolerance to the effects of nicotine develops after repeated administration
• Finally, an abstinence syndrome is observed when regular nicotine administration is discontinued
Pharmacokinetic Profile of Nicotine

- A typical smoker will take 10 puffs on a cigarette over a period of 5 minutes that the cigarette is lit. The acute effects of nicotine dissipate in a few minutes, causing the smoker to continue dosing frequently throughout the day to maintain the drug's pleasurable effects and prevent withdrawal.

Effect of nicotine in CNS

- alleviate stress and anxiety,
- facilitate learning and memory performance, and can function
- to control appetite and weight.
Sign of Nicotine Withdrawal

- dysphoric or depressed mood;
- insomnia;
- irritability, frustration, or anger;
- anxiety;
- difficulty concentrating;
- restlessness;
- decreased heart rate; and (h) increased appetite or weight gain.

Treatment of Nicotine Abuse

- Behavioral intervention
- Pharmacological
  - Bupropion
  - Nicotine replacement:
    - Transdermal
    - Gum
    - Inhaler
  - Nicotine receptor antagonist (CHAMPIX)
Amphetamines

• Most commonly abused is:
  – MDMA (3,4-methylenedioxymethamphetamine) AKA Ectasy
  – Methamphetamine AKA SABU

Amphetamine mechanism of action

• By inhibiting serotonin reuptake channel ➔ increase serotonin and dopamine release in Mesolimbic area
Effect amphetamine in CNS

- heightened states of introspection and intimacy along with temporary freedom from anxiety and depression, yet without distracting alterations in perception, body image, and sense of self.
- losing defensive anxiety,
- feeling more emotionally open and accessing feelings and thoughts not ordinarily available to them
- self-esteem, ability to communicate with significant others,
- capacity for achieving empathic rapport, interest in and capacity for insight, strengthened capacity for trust and intimacy, and enhanced therapeutic alliance

Amphetamine intoxication

- Recent use of amphetamine or a related substance (e.g., methylphenidate). B. Clinically significant maladaptive behavioral or psychological changes (e.g., euphoria or affective blunting; changes in sociability; hypervigilance; interpersonal sensitivity; anxiety, tension, or anger; stereotyped behaviors; impaired judgment; or impaired social or occupational functioning) that developed during, or shortly after, use of amphetamine or a related substance. C. Two (or more) of the following, developing during, or shortly after, use of amphetamine or a related substance: (1) Tachycardia or bradycardia (2) Pupillary dilation (3) Elevated or lowered blood pressure (4) Perspiration or chills (5) Nausea or vomiting (6) Evidence of weight loss (7) Psychomotor agitation or retardation (8) Muscular weakness, respiratory depression, chest pain, or cardiac arrhythmias (9) Confusion, seizures, dyskinesias, dystonias, or coma D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder. Specify if: With perceptual disturbances From American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Text rev. Washington, DC: American Psychiatric Association; 2000, with permission.
Amphetamine unwanted effect

- induce paranoia, suspiciousness, and overt psychosis that can be difficult to distinguish from paranoid-type schizophrenia;

Amphetamine withdrawal state

- fatigue, insomnia or restless hypersomnia, unpleasant dreams, hyperphagia, psychomotor agitation or retardation, dysphoria, anhedonia, and fragmented attention span. These symptoms can be intense and may be protracted.
MDMA Mechanism of Action

- Serotonin is released from the presynaptic neuron.
- Ecstasy binds to serotonin receptors, increasing the release of serotonin.
- Increased serotonin levels in the synaptic cleft.
- Serotonin receptors are activated, leading to the effects of MDMA.

MDMA Mechanism of Action

- Normal: Serotonin is released, but not increased.
- During Ecstasy: Serotonin is released significantly, leading to elevated mood.
- After Ecstasy: Serotonin levels return to normal, but depression-like feelings persist due to reduced serotonin availability.
Long term effect of Ectasy

Treatment of abuse

- Behavioral treatment
- Antidepressant
Heroin AKA Putauw

- Heroin is a highly addictive drug, and its abuse has repercussions that extend far beyond the individual users.
- The health and social consequences of drug abuse—HIV/AIDS, violence, tuberculosis, fetal effects, crime, and disruptions in family, workplace, and educational environments—have a devastating impact on society and cost billions of dollars each year.

Pharmacology

- A diacetyl derivative of morphine, a white powder as harmless looking as powdered sugar
- Highly fat soluble $\rightarrow$ rapid acting in the CNS
- Act on opioid receptor, especially on mu opioid receptor
Heroin Effect Acute

- Within 30 to 60 seconds of injection, heroin produces a surge of pleasurable emotions (the rush) that lasts for about one minute.
- This is followed by a warm flushing of the skin, a contraction of the pupils (miosis), dry mouth, a heavy feeling in the arms and legs, and feeling of sleepiness (the nod). Stress, anxiety, and physical pain are reduced.
Heroin Withdrawal

- sneezing, runny nose, hot and cold flashes, nausea, stomach cramps and vomiting, diarrhea, and gooseflesh
- hyperventilation, hypothermia joint pain, tremors, and twitching
- movements, particularly of the feet and elevated pulse rate, blood pressure, and temperature.

Long term effect of heroin

- Addiction
- Death cause by overdose
Overdose Death of Heroin

- Tolerance Phenomena
- Uncontrolled quality of Street heroin
- Compulsive use of Heroin
- Co morbid Psychiatric Illness
- Cause mainly by respiratory depression

Other Problems Caused by Heroin

- Infection: HIV, Hepatitis
- Stroke and cardiovascular event
- Family and social problems
- Increased of Crime and prostitution
Treatment of opioid Addiction

• Total abstinence
  – Cold Turkey
  – Hawari Protocols
• Opioid substitution
  – Metadon programs
  – Buprenorphin

Cannabis
Pharmacology

- Active compound is: delta-9-tetrahydrocannabinol
- Act in the brain via Cannabinoid-1 receptor, that enhance dopamin release in mesolimbic circuiti
- Route: inhalation, oral

Effect on CNS

- mild euphoria, an alternation of sensory acuity, and a distortion of time perception.
- suppresses rapid eye movement (REM) nondream sleep.
- increases brain limbic stimulation and is thought to activate the pleasure/reward system in the brain.
Cannabis intoxication

- high”: mild euphoria; relaxation and perceptual alterations, including time distortion; and the intensification of ordinary experiences such as eating, watching films, listening to music, and engaging in sex. When used in a social setting, the “high” may be accompanied by infectious laughter, talkativeness, and increased sociability

Cannabis intoxication

- Motor skills, reaction time, motor coordination, and many forms of skilled psychomotor activity are impaired while the user is intoxicated
- Psychosis (rare)
Withdrawal and dependence

- Do occurs but usually mild

Cocain
Cocaine Pharmacology

• Cocaine is the most potent stimulant of natural origin.
• Cocaine occurs naturally in the leaves of Erythroxylon coca
• Route of administration: oral by chewing leaf, inhalation, injection
• Act by blocking dopamine-serotonin reuptake channel --. Dopamine surge in mesolimbic pathway

Cocaine Use
Effect of Cocaine in CNS

- euphoria, increased energy and libido, decreased appetite, hyperalertness, and increased self-confidence

Cocaine intoxication

- anxiety, agitation, irritability, confusion, paranoia, and hallucinations may also occur.
- Sympathomimetic effects
  - include dizziness, tremor, hyperreflexia, hyperpyrexia, mydriasis, diaphoresis,
  - tachypnea, tachycardia, and hypertension.
- Cardiac arrhythmia, seizure
Cocaine effect on Chronic use

- Frank depression
- Dysphoria

<table>
<thead>
<tr>
<th>Treatment of Cocaine addiction</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Behavioural treatment</td>
</tr>
<tr>
<td>• Abstinence</td>
</tr>
<tr>
<td>• Antidepressant</td>
</tr>
</tbody>
</table>