

Lecture :Chapter 20: Licit and Illicit Drugs

Harm reduction:

- Harm reduction (or harm minimization) refers to a range of public health policies designed to reduce the harmful consequences associated with drug use and other high-risk activities.
- Skin infections from unsafe injection practices are the most common, even when free needle exchanges are available.
- Stigmata of intravenous drug use are commonly seen in association with injection site ulcer, abscess, deep vein thrombosis, venous ulcer and post-phlebotic limb.
- Injectors may be very adept at gaining vascular access for the administration of drugs, and any clinician should be aware of the wide variety of sites that may be used for injection.
- Infections like: HIV, hepatitis C.

Commonly misused drugs:

Drug group	Examples
Stimulants	Amphetamines, Captagon, cocaine, ephedra, khat
Opiates and opioids	Naturally occurring opiates, synthetic opioids
Sedative hypnotics	Zolpidem
Hallucinogens	LSD (lysergic acid diethylamide), mescaline
Dissociative anaesthetics	GHB (γ -hydroxybutyrate), PCP (phencyclidine), <i>Salvia divinorum</i>
Cannabinoids	'Spice', THC (tetrahydrocannabinol)
Solvents	Toluene, glue, lighter fuel
New synthetic agents	Piperazines

Stimulants

- **Cocaine** prevents the reuptake of dopamine, serotonin (causing serotonin syndrome) and all catecholamines, especially norepinephrine.
- It is this last action that explains most of the vascular disease (scarring, microcalcification and irregular heart beat).
- Heavy cocaine users may occasionally manifest paranoid symptoms but this is an uncommon event.
- When frank psychosis does occur, it is often in the form of **Magnun syndrome**, where users believe that 'bugs' are crawling out of their skin (called formication).
- The unique feature of **methamphetamine psychosis** is that it may reoccur years after drug usage has been discontinued.
- Its occurrence seems to be related to methamphetamine-induced **damage to cortical white matter**.
- These pathological changes are quite easily visualized with magnetic resonance imaging (MRI) scanning.
- This ability is not shared by cocaine or other stimulants.
- The most feared consequence of any type of stimulant abuse is the syndrome referred to as **'excited delirium'**.
- The syndrome, often lethal, is notable for the acute onset of hyperthermia and agitated violent behaviour that often culminates in a sudden unexplained death.

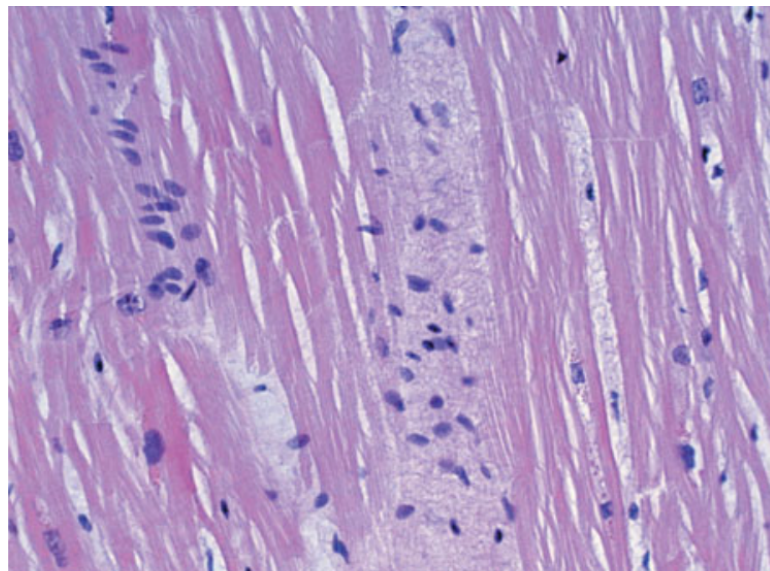


Figure 20.7 Fibrosis of the heart secondary to stimulant abuse.

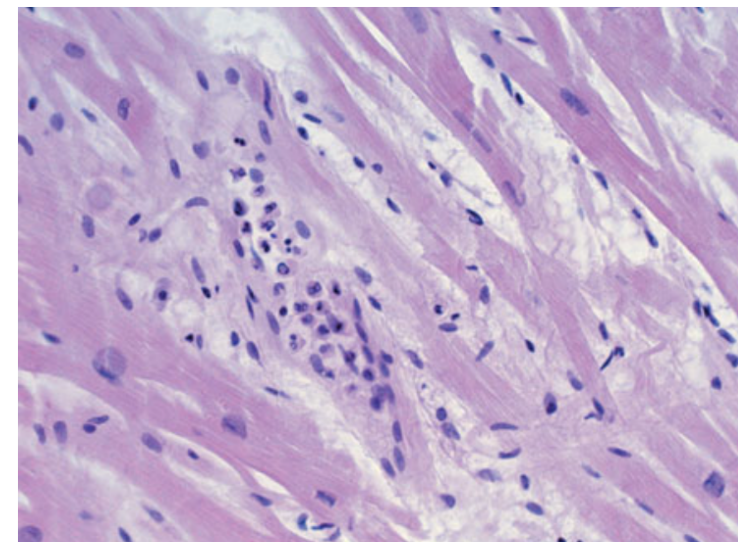


Figure 20.8 Zone of micro-infarction in the heart secondary to stimulant abuse.

Opiates and opioids

- both exert their effects by binding to the μ 1 opiate receptor located on neurons throughout the brain.
- Similar receptors are also found in the intestine, explaining why opiate users are almost always constipated.
- Stimulation of the μ 1 receptor relieves pain, depresses respiration and reduces gut motility.
- The only important difference between heroin, morphine and all the other synthetic opioids is their relative affinity for the μ 1 receptor.
- best-known sign of acute use of opiates is the presence of **pinpoint pupils** .
- **Withdrawal from opiates** ('clucking', 'rattling') leads to a number of different symptoms: gooseflesh, rhinorrhoea, lacrimation, yawning, abdominal pain, muscle pain and diarrhoea and vomiting.
- Heroin smokers, for example, can develop a specific type of brain degeneration that is not very different from 'mad cow' disease; however, these cases remain very uncommon.



Figure 20.12 Pinpoint pupils following opiate intake.

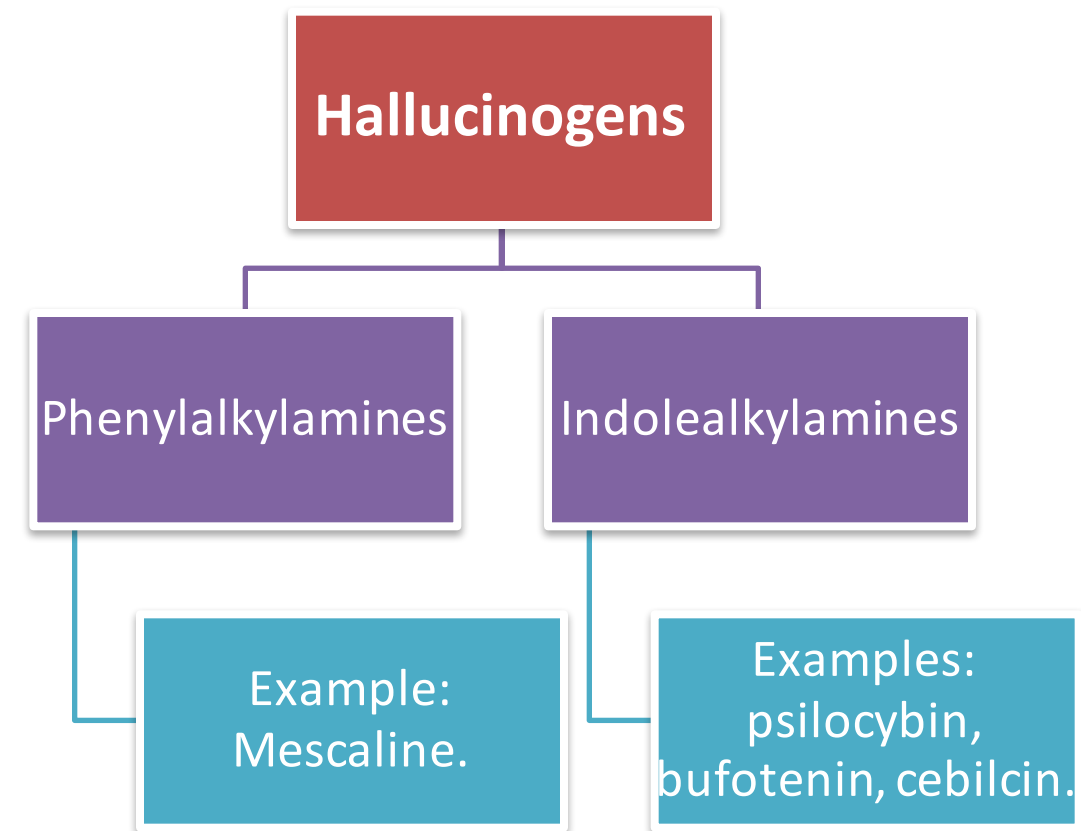
Sedative hypnotics

- A very long list of prescription medications is available for the treatment of insomnia.
- The drugs most frequently prescribed for insomnia (which may also have an anxiolytic action) include **benzodiazepines (BZs), non-benzodiazepines (nonBZs) and antidepressants**.
- The BZs have long been the drug of choice for the treatment of insomnia, but long-term use leads to dependence and abrupt discontinuation can even lead to the occurrence of seizures.
- The nonBZ hypnotics are more effective at speeding the onset of sleep than BZs and are thought to have fewer side effects and drug interactions.
- Antidepressants are considered third-line drugs for the treatment of insomnia and, in most countries, have not been approved for the treatment of insomnia.

Hallucinogens

Hallucinogens share five common properties:

1. changes in mood and perception
2. Minimal impairment of intellect or memory
3. Use is not associated with agitation
4. There are minimal side effects
5. Craving and addiction do not occur



Hallucinogens vs. Amphetamines

- The most important distinction appears to be that, at worst, use of hallucinogens leads only to **behavioural toxicity**.
- However, the hallucinatory ‘designer’ amphetamines have been responsible for many **deaths**, often a result of hyperthermia and multisystem failure.

Dissociative anaesthetics

❖ Five drugs fall into this category:

- phencyclidine (PCP)
- Ketamine
- γ -hydroxybutyrate (GHB)
- dextromethorphan
- *Salvia divinorum*.

Mechanism of Action:

- Phencyclidine (PCP), ketamine, γ -hydroxybutyrate (GHB), dextro- methorphan share the same mechanism of action.
- They block the NMDA receptor, the predominant molecular mechanism involved in memory function and learning.
- The fifth one; Salvia has no effect on the NMDA channel, Instead, it specifically blocks the κ receptor which will result in intense feelings of unhappiness and depression but it also has hallucinogenic (psychotomi-metic) effects.

Marijuana

- Street names: (Weed, hash, skunk)
- It is a drug that interacts with many different receptors.
- The active ingredient in Marijuana is **tetrahydrocannabinol (THC)**
- The body produces compounds similar to THC, they're called **"endocannabinoids"**
- **Endocannabinoids bind with specific endocannabinoid receptors known as C1 and C2.**
- THC also interacts with with the benzodiazepine receptor and opioid receptors.
- **It increases pulse rate, decreases the cardiac output, leading to syncope.**
- THC remains in the body fat stores for a very long time (> 1 month).
- It is then slowly released back into the circulation in response to dieting and stress.
- Both conditions lead to increased secretion of ACTH and cortisol that, in turn, can also cause THC stored in fat to be released.
- **As marijuana is stored in fat tissue, the interpretation of post-mortem blood levels is almost impossible.**
- **After death, as individuals cells die, they release their drug content and there is no way to differentiate between THC that was ingested just before death from drug that was ingested 1 month earlier.**

Solvents

Solvents such as toluene volatilize at room temperature, allowing users to inhale the fumes, a practice referred to as 'huffing'.

Clinical examination:

- Traces of the inhalant (glue) around an individual's mouth and face, with the persistent odor of the relevant inhalant.
- Singeing of beard or hair, or evidence of old burn injury to the face.

Toluene, as opposed to the solvents is found in:

- hair spray
- dry-cleaning fluid
- gasoline

Most often responsible for:

- fatal intoxication.
- disruption of normal cardiac electrical activity.

Inhalation of any solvent will result in:

- Transient euphoria
- Headache
- Ataxia
- Damage to the brain white matter
- Distinctive pattern can be identified in the MRI scans of chronic abusers.

New Synthetic Agents and Legal Highs ..

These drugs are commonly known as legal highs:

- 1. Piperazines** (derived from piperazine): Medicinal use of piperazines is banned in many countries.
- 2. Benzyl chloride**

Piperazines Derivatives

1-Benzylpiperazine (BZP) is a stimulant. It is sold as a legal alternative to amphetamine, methamphetamine and MDMA. It interacts with numerous different receptors.

Adverse effects :

- Confusion & agitation
- vomiting
- Anxiety & Palpitations
- higher plasma levels of BZP are associated with an increased incidence of seizures.
- Co-ingestion of ethanol increases the likelihood of adverse BZP-induced symptoms, but reduces the incidence of BZP seizures.

Small doses: piperazine TFMPP (trifluoromethylphenylpiperazine) is said to produce effects like those of MDMA.

Large doses: when combined with BZP, or alcohol or both, it may be toxic. (TFMPP + BZP side effects are agitation, anxiety, hallucinations, vomiting, insomnia and migraine).

2-Meta-chlorophenylpiperazine (MCPP) is also a piperazine and a non-selective serotonin receptor agonist.

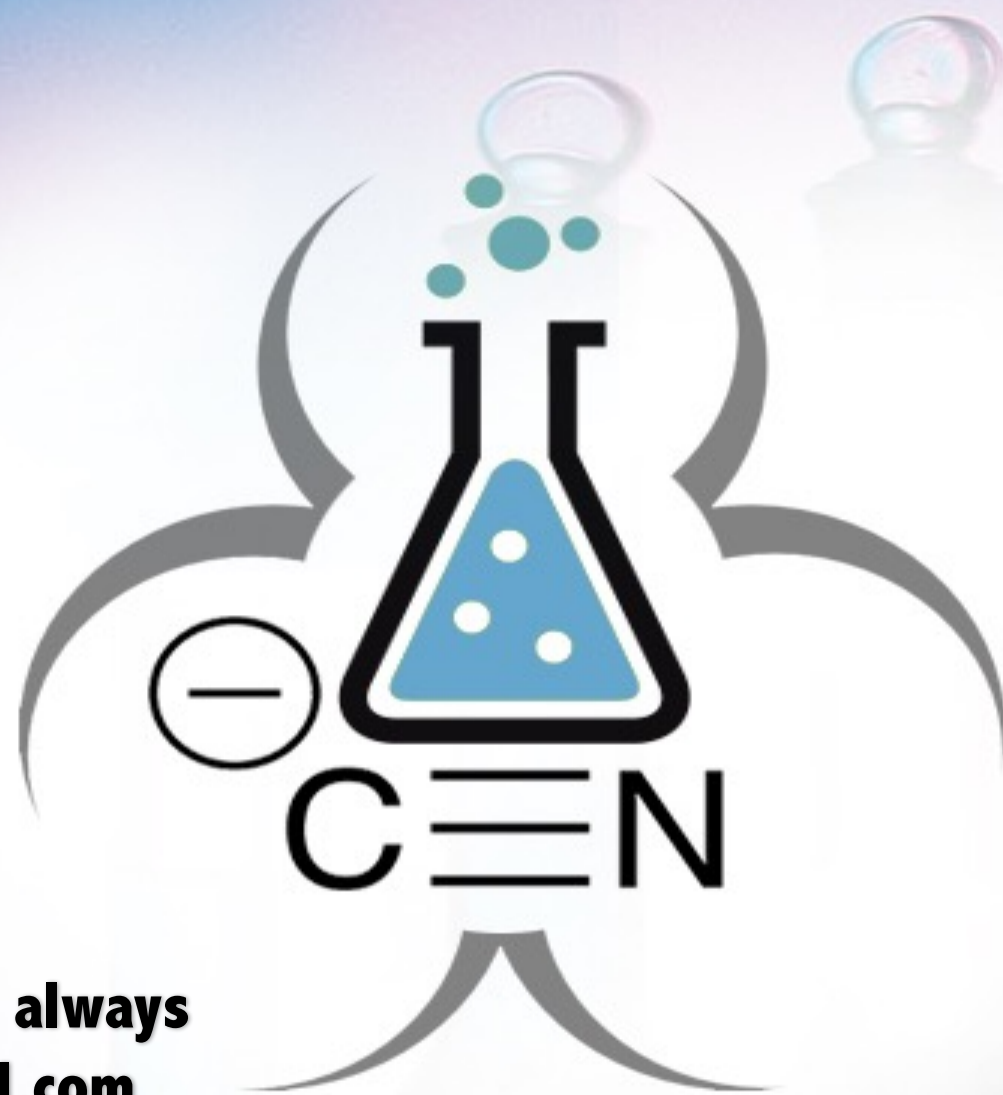
- MCPP causes headaches in humans.
- 10% of those who take MCPP will develop a migraine headache.
- 90% of individuals who commonly suffer from migraines will have an attack if challenged with MCPP.

Some of amphetamine analogues containing paramethoxy group are known to cause:

- severe hyperthermia
- death

Drug facilitated sexual assault...

- **Alcohol** is the most important drug that facilitates sexual assault.
- ❖ Certain drugs have been identified as having particular potential for use in Drug facilitated sexual assault and these include:
 - Ethanol, chloral hydrate, BZs, nonBZ sedative-hypnotics, GHB, Ketamine, Opioids, dextromethorphan, barbiturates, anticholinergics, antihistamines.
- ❖ Determining the possible drug group involved, and the time at which it was involved:
 - Clinical examination
 - Sampling of (blood, urine and hair).



**If you have any questions You can always
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