DRUGS OF ABUSE

AMPHETAMINES:

PRODUCE CENTRAL AND PERIPHERAL SYMPATHOMIMETIC EFFECTS

LETHAL COMPLICATIONS INCLUDE SEVRE HYPERTHERMIA, ACUTE CORONARY SYNDROME, DYSRHYTHMIA, AORTIC DISSECTION AND ICH

LONG-TERM USE LEADS TO NEURO-PSYCHIATRIC SEQUELAE

SUPPORTIVE CARE AND BENZODIAZEPINE USE ARE CENTRAL TO MANAGEMENT

RISK ASSESSMENT:

- Small doses, especially in non-tolerant individuals, can produce significant toxicity
- Hyperthermia, headache, focal neurological signs or chest pain herald potentially life-threatening complications
- Seizures occur in ~4%

TOXIC MECHANISM:

- Amphetamine is structurally related to ephredine → enhance catecholamine release and block their reuptake → CNS and peripheral noradrenergic, dopaminergic and serotonergic stimulation results
- Long-term CNS effects occur as a result of receptor adaptation as well as permanent destruction of dopaminergic pathways
- MDMA (ecstasy) at standard recreational doses sometimes causes SIADH → profound hyponatraemia, coma and convulsion

CLINICAL FEATURES:

- Most frequent presentation is agitation, sweating with ↑HR and BP
- CNS effects:
    - Euphoria
    - Anxiety, dysphoria, agitation/aggression
    - Paranoid psychosis with visual/tactile hallucination
    - Hyperthermia, rigidity/myoclonic movements
    - Seizures
- CARDIOVASCULAR:
    - ↑HR/BP
    - ACS/dysrhythmia
    - APO/acute cardiomyopathy
- PERIPHERAL SYMPATHOMIMETIC:
    - Mydriasis, sweating, tremor
- MEDICAL COMPLICATIONS:
    - RHABDOMYOLYSIS → renal failure, dehydration

    - HYPONATRAEMIA → due to SIADH and↑ water intake
    - AORTIC/CAROTID DISSECTION
    - SUBARACHNOID AND INTRACRANIAL HAEMORRHAGE
    - ISCHAEMIC COLITIS
- In those with altered mentation → CT brain for ICH, BSL and sodium level
- Serum.urine amphetamines do not assist management

MANAGEMENT:

- Immediate intervention required if → ↑BP, seizures, agitated, ↑temp, ↓Na
- Treat ↑HR/BP with titrated benzodiazepines
- BETA-BLOCKERS ARE CONTRAINDICATED (unopposed alpha blockade)
- Seizures managed along standard lines
- Benzodiazepines for agitation → second line use droperidol or olanzapine
- Immediate correction of hyponatraemia indicated if Na<120 with altered mentation → GIVE 4ML/KG OF 3% HYPERTONIC SALINE
    - Resolution of SIADH manifests within 24 hours with diuresis and correction of sodium
- No role for decontamination or antidotes
- ACS is managed along standard lines, but DO NOT FORGET TO CT THE HEAD PRIOR TO ANTICOAGULATION IF HEADACHE IS A FEATURE OF THE PRESENTATION

BENZODIAZEPINES:

INVOLVED IN UP TO ONE-THIRD OF DELIBERATE SELF POISONINGS

EXCELLENT PROGNOSIS WITH SUPPORTIVE CARE OF CNS DEPRESSION

RISK ASSESSMENT:

- Isolated benzo overdose usually causes only mild sedation irrespective of dose
- ALPRAZOLAM overdose associated with greater degree of CNS depression
- Zolpidem/zopiclone rarely cause severe CNS ↓ when taken alone
- CO-INGESTION with other CNS depressants raises the risk

TOXIC MECHANISM:

- Act by enhancing GABA mediated neurotransmission → they do this by binding to GABA-a receptor and ↑ the frequency of chloride channel opending
- Zolpidem and zopiclone are not benzos but act at the same receptor complex

TOXICOKINETICS:

- Rapidly absorbed orally
- Most highly protein bound
- Hepatic metabolism
    - Diazepam → desmethyldiazepam, oxazepam, temazepam
- Duration of effect depends on CNS tolerance and redistribution, rather than elimination time

CLINICAL FEATURES:

- Onset of symptoms within 1-2 hours
- Profound coma rare → more common in the elderly
- In very large ingestions → beware hypothermia, ↓HR ↓BP

MANAGEMENT:

- Basic resuscitative measures are normally sufficient to ensure survival
- No role for decontamination or enhanced elimination
- ANTIDOTE:
    - FLUMAZENIL → limited role in overdose:
        - Competitive benzodiazepine antagonist, structurally similar to midazolam
        - Indications are limited:
            - Accidental paediatric ingestion with compromised airway
            - Deliberate OD with compromised airway with no airway skills available
            - DIAGNOSTIC → useful if avoids further test
            - REVERSAL OF BENZODIAZEPINE CONSCIOUS SEDATION
        - CONTRAINDICATIONS:

        - KNOWN SEIZURE DISORDER
        - Co-ingestion with pro-convulsant
        - Known BENZO DEPENDENCE
        - QRS prolongation → raises suspicion of TCA OD
    - Give 0.1-0.2mg IV and repeat every minute titrating to level of consciousness
    - Re-sedation is expected at ~90 minutes
    - ADVERSE REACTIONS:
        - Benzo withdrawal, seizures
- Profound coma, tachycardia or 12-lead ECG changes suggest a co-ingested agent

CANNABINOIDS:

MARIJUANA IS THE MOST WIDELY USED RECREATIONAL ILLICT DRUG IN AUSTRALASIA

CAN CAUSE UNPLEASANT BUT BENIGN SYMPTOMS IN ADULTS, BUT IN KIDS CAN CAUSE SIGNIFICANT CNS DEPRESSION

RISK ASSESSMENT:

- **THERE ARE NO REPORTS OF DEATH DIRECTLY RELATED TO T.H.C. USE**
- Dose-related effects:
  - Low-dose → mild sedation, disinhbition, disorientation, euphoria
  - HIGH-DOSE → tachycardia, ↓BP (postural), CNS depression, perceptual disturbance (even psychosis)
  - Chronic use can lead to long-term neuropsychiatric sequelae

TOXIC MECHANISM:

- Central sympathomimetic and anti-emetic properties
- Acts on cannabinoid receptors (CB-1 centrally, CB-2 on immune cells)
- Augments dopamine release
- Delta-9 THC is the most potent component

TOXICOKINETICS:

- Rapidly and completely absorbed by inhalation
- Elimination half life is SEVERAL DAYS

CLINICAL FEATURES:

- Acute symptoms may last up to four hours (inhalation), 8 hours (ingestion)
- CNS:
  - Ataxia, incoordination
  - CNS depression
  - Coma in children (lasting up to 36 hours)
- CARDIOVASCULAR:
  - ↑HR
  - Orthostatic hypotension
- PSYCHIATRIC:
  - Euphoria
  - Anxiety, agitation
  - Hallucination/delusion → can lead to acute psychosis
- RESPIRATORY (RARE)
  - Pneumothorax, pneumomediastinum
- CANNABINOID HYPEREMESIS SYNDROME:
  - Occurs in chronic users

- Episodes of vomiting that are very difficult to control → high incidence of repeated therapeutic showering in hot water!!
- DIAGNOSIS OF EXCLUSION
- Resolves with abstinence

MANAGEMENT:

- No role for urine cannabinoids (positive for up to 3 days after acute use and 4 weeks after chronic usage)
- Cannabis intoxication is benign and self-limiting → supportive care and benzos for agitation
- Children who have ingested marijuana should be observed for 4 hours → prolonged coma can occur

COCAINE:

POWERFUL SYMPATHOMIMETIC AND LOCAL ANAESTHETIC PROPERTIES → POTENTIALLY LETHAL IN OVERDOSE → SEVERE HYPERTHERMIA, HYPERTENSION, MYOCARDIAL ISCHAEMIA

RISK ASSESSMENT:

- Ingestions over 1g are potentially lethal → 20-30mg is usual "line"
- Toxic dose is highly variable and small doses in non-tolerant individuals may lead to significant intoxication
- In pregnancy, cocaine is teratogenic and ↑s miscarriage and foetal demise
- Presence of the following heralds life-threatening complications:
    - Hyperthermia
    - Headache
    - Cardiac conduction abnormalities or chest pain
    - Focal neurological signs

TOXIC MECHANISM:

- Toxicity results from sympathomimetic, vasospastic and sodium channel blocking effects
- Sympathomimetic effects are due to blockade of presynaptic catecholamine reuptake → dissection, acute cardiomyopathy, ICH
- Vasospasm and endotherlial fissuring → ACS
- Sodium channel blockade (fast myocardial channels) → ventricular dysrhythmias similar to TCA
- CNS excitation → hyperthermia, psychomotor acceleration, seizures

TOXICOKINETICS:

- Peak concentrations are reached fastest with IV/inhalation administration
- Rapidly metabolised by liver and plasma cholinesterases → only 1% excreted in urine unchanged

CLINICAL FEATURES:

- Major manifestations usually occur within one hour and last several hours
- CNS:
    - Euphoria
    - Anxiety, dysphoria, agitation/aggression
    - Paranoid psychosis with visual/tactile hallucinations
    - Hyperthermia, rigidity, myoclonus
    - Seizures
- CARDIOVASCULAR:
    - Severe tachycardia and hypertension
    - Arrhythmia
    - ACS (either vasospastic or thrombotic)
    - QT prolongation
    - APO

- PERIPHERAL SYMPATHOMIMETIC:
    - Hyperthermia
    - Muscle fasciculations
    - Mydriasis, sweating and tremor
- CLINICAL FEATURES ASSOCIATED WITH MEDICAL COMPLICATIONS:
    - Hyperthermia induced rhabdomyolysis, renal failure and cerebral oedema
    - Aortic and carotid dissection
    - SAH/ICH
    - Ischaemic colitis
    - Pneumothorax
    - Pneumomediastinum

MANAGEMENT:

- ECG → detects ischaemia but may also show a BRUGADA-type pattern of changes. Beware that the sensitivity for detecting ischaemia in cocaine-users is lower!
- Immediate management priorities → dysrhythmia (inc VT), hypertension, hyperthermia, seizures, severe agitation
- VT → SODIUM BICARBONATE (50-100MMOL) → if refractory LIGNOCAINE 1.5MG/KG BOLUS FOLLOWED BY 2MG/MIN INFUSION
- ACS → manage along standard lines EXCEPT WITHOLD BETA-BLOCKERS (risk of unopposed alpha stimulation)
- Sinus tachy and hypertension → titrated benzodiazepines
    - If hypertension refractory to benzos → PHENTOLAMINE 1mg IV, VASODILATOR INFUSION (nitroprusside, GTN)
- No role for decontamination, enhanced elimination or antidotes
- Treat agitated delirium early with benzodiazepines

GAMMA-HYDROXYBUTYRATE (GHB)

IN EXCESS → RAPID ONSET OF CNS AND RESPIRATORY DEPRESSION, MYOCLONIC JERKING AND BRADYCARDIA

MANAGEMENT IS SUPPORTIVE

COMPLETE RECOVERY WITHIN 4-6 HOURS

RISK ASSESSMENT:

- Twice standard recreational dose (30-40mg) is capable of causing coma, and variable dose preparations are ubiquitous
- Co-ingestion with other CNS depressants raises risk

TOXIC MECHANISM:

- GHB is a breakdown product of GABA, but its mechanism of action is unclear

TOXICOKINETICS:

- Rapidly absorbed, presence of food ↓s bioavailability
- GHB rapidly oxidised to carbon dioxide and water with zero order kinetics (elimination complete in 4-6 hours)

CLINICAL FEATURES:

- Standard doses produce rapid onset of euphoria, enhanced sexual desire/performance/orgasm
- In overdose, brief euphoria followed by rapid onset of coma → sudden recovery of consciousness occurs within 2-3 hours. Resolution of coma MAY BE ABRUPT and some even forcefully extubate themselves
- Deaths are reported from airway obstruction, aspiration or respiratory arrest
- Tolerance develops with regular use

MANAGEMENT:

- Specific investigations are rarely required
- Potential early threats include coma, respiratory depression, loss of airway protection
- Bradycardia is common, but no specific management is required
- Those who are clinically well at two hours can be discharged
- Short-term intubation and ventilation may be required

OPIOIDS:

INTOXICATION CAUSES CNS AND RESPIRATORY DEPRESSION → DEATH IS DUE TO RESPIRATORY FAILURE

GOOD SUPPORTIVE CARE ENSURES SURVIVAL

THE SPECIFIC ANTIDOTE (NALOXONE) ASSISTS IN AIRWAY AND BREATHING MANAGEMENT

DEXTROPROPOXPHENE CAN CAUSE SEIZURES AND ARRHYTHMIA DUE TO SODIUM CHANNEL BLOCKING EFFECTS

PETHIDINE IS IMPLICATED IN THE SEROTONIN SYNDROME AND REPEATED THERAPEUTIC DOSES ARE ASSOCIATED WITH SEIZURES

RISK ASSESSMENT:

- Life-threatening CNS and respiratory depression frequently occur JUST ABOVE THE ANALGESIC DOSE
- Opioid use by naïve patients or in the setting of co-ingestion ↑s severity of CNS depression
- Opioid intoxication is THE LEADING CUASE OF DEATH BY POISONING IN CHILDREN
    - Ingestion of a single tablet or mouthful of methadone syrup can cause respiratory arrest
    - More than 5mg/kg of codeine can cause respiratory arrest

TOXIC MECHANISM:

- Agonist activity at mu-receptor responsible for euphoria, analgesia, dependence and sedation/respiratory depression
- Multiple other opioid actions are responsible for the side effects (nausea/vomiting → dopamine, constipation → peripheral gut mu-receptor, pruritus → histamine release

CLINICAL FEATURES:

- Classic opioid toxidrome consists of:
    - CNS depression
    - Respiratory depression (rate and depth)
    - Miosis
- Duration depends on pharmacokinetics → heroin short, methadone 24 hours
- Death caused by apnoea, loss of airway protection
- Aspiration may result from vomiting
- Tachycardia in response to hypercarbia, hypoxia
- Complications→ hypothermia, skin necrosis, compartment syndrome, rhabdomyolysis and hypoxic brain injury

MANAGEMENT:

- Blood or urine levels do not assist management
- Attention to airway and breathing are paramount
- In rare event of ventricular arrhythmia with dextropropoxyphene → SODIUM BICARBONATE
- Activated charcoal may play a role in overdose of controlled-release preparation
- ANTIDOTE = NALOXONE:
    - Opioid antagonist used as an adjunct in opioid intoxication
    - INDICATIONS:
        - Reversal of CNS and respiratory depression → often used empirically
        - Avoid in dependent individuals unless CNS/respiratory depression is significant
    - PHARMACOKINETICS:
        - POOR ORAL BIOAVAILABILITY
        - Elimination half life ~60-90minutes
    - 100microg IV initially, or 400 IM/SC if no access
    - Doses >400microg are rarely required with heroin overdose, but larger doses may be required in overdose from partial opioid agonists
    - RE-SEDATION is very unusual with heroin but can occur following overdose on controlled release tablets or methadone → CONSIDER NALOXONE INFUSION at 2/3 initial dose per hour
    - In opioid tolerant patients, a dose-dependent production of a withdrawal syndrome can occur