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- [Reports Manager](#)
- [PLAB1-PLAB2 NOTES](#)
- [Administration](#)
- [Sign Out](#)

Resource view

Resource name Toxicology PLAB 1 Notes

Resource description Toxicology

Resource content

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TOXICOLOGY AND PHARMACOLOGY LECTURE

COMMON FEATURES OF DRUG POISONING

Tachycardia or irregular pulse (AF)	Salbutamol, tricyclic, quinine
Respiratory depression	Opiates, Benzodiazepine
Hypothermia	Phenothiazine, barbiturates
Hyperthermia	Amphetamine, cocaine, ecstasy
Coma	Benzodiazepines, alcohol, tricyclic antidepressant, barbiturates, opioids
Seizure	Hypoglycaemia, tricyclic, phenothiazine, theophylline
Dilated pupils	Amphetamines, cocaine, quinine, Tricyclic antidepressant.
Hypoglycaemia	Insulin, oral hypoglycaemia agents, alcohol, salicylates
Metabolic acidosis	Alcohol, methanol, paracetamol, carbon monoxide poisoning, salicylates
Renal failure	Salicylates, paracetamol, NSAIDs
Constricted pupils (pin point pupil)	Opiates, organophosphates

GENERAL MANAGEMENT OF DRUG POISONING

1. Maintain airway if it is compromised
1. Give oxygen to maintain oxygen saturation above 92%
1. Generally take care of the airway, breathing and circulation. If hypotensive give intravenous fluids.
1. Torsades de pointe treat with magnesium sulphate
1. Arrhythmia from tricyclic anti-depressant should be treated with 50ml of 8.4% sodium bicarbonates via a central line or large vein
1. Metabolic acidosis increases the risk of seizure it should be treated with correction of hypoxia and intravenous fluids and not settling still then 250ml of 1.26% sodium bicarbonate.
1. Treat seizures with intravenous lorazepam 2-4mg or diazepam 10-20mg in adults.
1. If patient is agitated treat with oral or IV diazepam
1. Use antidotes if required
1. Induced vomiting is not of any use and potentially dangerous
1. Give activated charcoal (50g) orally within 1 hour of ingestion
1. Medication like lithium, iron, methanol and ethylene glycol are not bound to charcoal
1. Gastric lavage is rarely needed. It should only be done if life threatening. And it should not be used in patients with reduced consciousness due to risk of aspiration.
1. Haemodialysis can improve outcome in severe cases of overdose e. g digoxin, ethylene glycol, lithium, methanol and salicylates

SPECIFIC OVERDOSE

1. PARACETAMOL POISONING

1 tablet of paracetamol is 500mg

150mg/kg or > 12g of paracetamol is considered as a dangerous dose

Key Points:

- 1 tablet = 500 mg
- **Dangerous dose** is >12 g (24 tablets) or >150mg/kg
- **Time since ingestion** is crucial to determine management.
- Drug levels are checked **4 hours after ingestion**
- Treatment with N-acetylcysteine is determined by the paracetamol treatment **graph**
- N-acetylcysteine is most effective when given **within 8 hours after ingestion**
- Other blood tests are INR, plasma creatinine, U&E, LFT, ABG

Management:

- **Management if time since ingestion is unknown:** Start treatment with NAC immediately.
- **Management within 1 hour of ingestion:** Give activated charcoal if >12g or 150 mg/kg. Take bloods 4 hours post ingestion and use graph to determine if NAC needed.
- **Management within 4 hours of ingestion:** Take drug levels 4 hours post ingestion and use graph.
- **Management at 4-8 hours from ingestion:** Take drug levels immediately and use graph. Wait for paracetamol levels.
- **Management 8-15 hours from ingestion:** If >12 g or 150 mg/kg start treatment immediately. If drug levels are below treatment line and patient asymptomatic, stop treatment.

- **Management 15-24 hours from ingestion:** If >12g or 150 mg/kg start treatment immediately. If drug levels and bloods at 24 hours post ingestion are normal and patient asymptomatic, stop treatment.
- **Management >24 hours since ingestion:** If >12g or 150 mg/kg or bloods abnormal or patient symptomatic, start treatment immediately. Seek expert opinion.

Staggered Overdose: overdose in a prolonged period of time.

The normogram cannot be used

If dangerous level i.e. 150mg/kg or 12g use N-acetylcysteine

Check INR or PT, U&E, LFT and FBC.

1. **BENZODIAZEPINE:**

Example of benzodiazepine: chlordiazepoxide, diazepam are long acting benzodiazepine, lorazepam is a short acting.

Causes drowsiness, hypotension, coma, respiratory depression, CNS depression, coma.

Toxicity is worse alcohol or other CNS depressant medication.

Treatment: Antidote is Flumazenil.

1. **SALICYLATE: e.g. aspirin**

Symptoms:

1. Vomiting
2. Tinnitus
3. Deafness.

In severe cases confusion, seizures, initially respiratory alkalosis then metabolic acidosis, pulmonary oedema

Toxicity >500mg/kg can cause death

Give activated charcoal if ingestion less than 1 hour ago and took more than >120mg/kg

Check 2 hours post ingestion if patient symptomatic.

If asymptomatic check at 4 hours after ingestion.

Investigation: U&E, PT or INR, Blood glucose causes hypoglycaemia), ABG can cause hypokalaemia

Treatment:

If salicylate >500mg/kg then IV 8.4% sodium bicarbonate 225ml over 1 hour

Alkalinization of urine

4. **ANTIDEPRESSANT**

Tricyclic antidepressant (amitriptyline, dosulepin)

Symptoms:

1. Tachycardia
2. Dilated pupils
3. Urinary retention
4. Hyperreflexia
5. Divergent squint
6. Hypotension
7. Seizures
8. Coma
9. Arrhythmias
10. Prolonged QRS complex

5. **Selective serotonin reuptake inhibitors (SSRIs)**

e.g. paroxetine, sertraline, fluoxetine, citalopram

Symptoms: nausea, vomiting, tremor, serotonic syndrome

6. **Selective norepinephrine reuptake inhibitors**

e.g. venflaxine cause same symptoms as TCA

7. **Mirtazepine:** vomiting, nausea and drowsiness

Management:

Activated charcoal if taken within 1 hour

If QRS >120ms after overdose give 8.4% sodium bicarbonates 50ml serotonin syndrome may occur after taking 2 or more antidepressant e.g. TCA, SSRI or MAOI

8. OPIOIDS

EXAMPLES: codeine, morphine, dihydrocodeine, fentanyl, tramadol, methadone, pethidine.

Features:

1. Reduced consciousness
2. Respiratory depression
3. Pin point pupils
4. Hypotension
5. Vomiting and nausea
6. Respiratory rate < 12
7. Patient may have puncture marks on the arms.

Management:

Naloxone IV 0.4 - 2mg.

Can also be given IM for which its effect can be more prolonged.

N.B: The plasma half life of naloxone is shorter than that of most opioid, so the repeated doses are often required. This is especially true with long acting opiates e.g. Morphine sulphate tablets or methadone where naloxone infusion might be needed.

N.B: Opiates accumulate in the body in people with renal impairment. Therefore opiate toxicity should be suspected in all patients with unexplained type 2 respiratory failure.

1. RECREATIONAL DRUGS**FEATURES:**

Stimulant drugs such as NMDA (ecstasy), amphetamines, cocaine. lysergic acid diethylamide (LSD) may cause severe agitation, tachycardia, sweating, pyrexia, dilated pupils, hypertension, arrhythmia and seizures.

Severe cases result in coma, rhabdomyolysis, renal failure and subarachnoid haemorrhage, myocardial infarction, repeated seizures and death.

SPECIFIC FEATURES

1. **COCAINE:** Coronary artery aneurysm, myocardial ischaemia and infarction and aortic dissection. Also subarachnoid aneurysm.
2. **Ecstasy:** causes severe hyponatremia and water intoxication
3. **Gamma hydroxybutyrate (GHB)** may cause bradycardia, hypotension, reduced consciousness and coma associated with severe withdrawal symptoms;

Management:

1. Measure U&E, LFTs, Creatinine phosphokinase (CK)
2. Perform ECG and monitor cardiac rhythm
3. Hypertension settles with diazepam if still persistent then use glycerine tri-nitrate
4. Treat cocaine induced chest pain and ECG changes with diazepam, aspirin and nitrates
5. Amphetamine tachycardia can be treated with beta blockers

1. IRON OVERDOSE

1. Common in children of pregnant mothers, after left unsupervised and ingested mother's iron tablets. The iron tablets are red in colour and child may vomit reddish-brown materials.
2. Iron tablets=iron sulphate
3. Features: nausea and vomiting metabolic acidosis, stomach ulcers, liver failure, Brain damage. Brain damage and coma.

NB: stomach ulcers may cause stricture.

Investigation: serum iron levels

Treatment : Desferoxamine, if not improving then dialysis.

11. DIGOXIN

Reduced cognition, yellow-green visual haloes, nausea, vomiting, cardiac arrhythmia.

Treatment: digoxin specific anti-body fragment.

12.CYANIDE

Dizziness, headache, breathlessness, shock, odour of bitter almonds. No Cyanosis

Treatment: oxygen, sodium nitrite and sodium thiosulphate, dicobalt edetate.

12. METHANOL

Headache, breathlessness, photophobia, papilloedema, optic atrophy, blindness.

Treatment: Gastric lavage, bicarbonate infusion, ethanol plus IV calcium.

13. CARBON MONOXIDE

Pink skin, headache, vomiting, tachycardia, tachypnoea, fits, coma and cardiac arrest

Investigation: serum carbon monoxide levels, oxygen levels might be high.

Management: 100% hyperbaric oxygen, mannitol for cerebral oedema.

14. ETHYLENE GLYCOL (anti-freeze)

GI upset, neurological involvement, cardiorespiratory collapse, acute renal failure,

Treatment: gastric lavage, bicarbonate infusion, ethanol, IV calcium.

15. ORGANOPHOSPHATE:

Salivation, lacrimation, urination, diarrhea, sweating, small pupils, bradycardia, respiratory depression, muscle fasciculation

Treatment: Atropine and pralidoxime

16. PARAQUAT

Nausea, vomiting, diarrhea, painful oral ulcers, alveolitis, renal failure

Treatment: activated charcoal.

17. LITHIUM TOXICITY

Vomiting, diarrhea, coarse tremor, decreased consciousness, ataxia, increased tone, hypokalaemia

Treatment: IV fluid and haemodialysis

18. PHENYTOIN TOXICITY

Gum hypertrophy and cerebellar signs e.g. nystagmus, ataxia, diplopia, dizziness etc.

Investigation: serum drug levels

Phenytoin toxicity: renal failure and liver failure:

Check U&E, INR and drug levels

19. BETA BLOCKERS AND CALCIUM CHANNEL BLOCKERS

Bradycardia, hypotension and arrhythmia

Treatment: Atropine

20. ANTI-PSYCHOTICS:

Low blood pressure, ECG changes, extrapyramidal side effects: tremor and hyperprolactinaemia.

21. NSAIDs:

Renal failure and heart failure.

Investigation: check U&E

22. LSD:

Visual hallucinations, agitation, excitement, tachycardia and dilated pupils. Hypertension and pyrexia may occur.

Massive overdose may lead to coma, respiratory arrest and coagulation disturbances.

Treatment is supportive.

23. ECSTASY:

Euphoria, agitation, sweating, dilated pupils, ataxia, teeth grinding, headache, tachycardia, hypertension.

Can lead to renal failure, liver failure, cerebral haemorrhage and coma.

Treatment:

1. Consider activated charcoal if less than 1 hour since ingestion.
2. Observe for at least 4 hours
3. Monitor ECG, pulse, blood pressure and temperature

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[Back](#)



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