Opiates overdose

Substance	Opiates example: Morphine, Codeine, heroin, tramadol, methadone.
Introduction	Opioid overdose occurs due to excessive consumption of opioids. It occurs due to prescription drug abuse, altered pharmacokinetics and memory related issues associated with old age.
Usual fatal dose	Morphine 200 mg Codeine 800 mg (7 to 14 mg/kg) Heroin 50 mg
Mechanism of toxicity	Opioids act on • μ (mu) receptor: opioid analgesic • k (kappa) receptor • δ (delta) receptor: spinal and supraspinal analgesia • σ (sigma) receptor. Mu and delta receptors appear to be involved in systems that influence mood, reinforcing effects, respiration, pain, blood pressure, and endocrine and gastrointestinal functions. Kappa receptors are able to produce endocrine changes and analgesia.
Clinical Symptoms	• Triad of coma, pinpoint pupils, and respiratory depression due to pathognomonic for opiate poisoning during therapeutic overdose, accidental overdose (in addicts), or deliberate overdose (suicidal). • Pupil dilates in the presence of severe acidosis, hypoxia, or respiratory depression. • Hypotension may be due to opiate-induced arteriolar and venous dilation. Bradycardia is also reported. • Bradypnoea is common in opiate poisoning. Respiratory rates of less than 8/minute. Snoring due to

	a failure to maintain the patency of the upper airway, Gurgling may occur due to accumulation of pulmonary oedema fluid. • Non-cardiogenic pulmonary oedema ("heroin-lung") manifested as rales, • pink frothy sputum, significant hypoxia, and bilateral fluffy infiltrates. • Morphine-induced seizures are primarily seen in neonates. • Cramping and constipation as well as sphincter of Oddi spasm may occur. • Hyperkalaemia in the presence of rhabdomyolysis and acute renal failure.
Diagnosis	• Needle marks, dermal scars (suggestive of addiction). • Evidence of hypoglycaemia, hypoxia, and hypothermia. • Most opiates can be detected in urine or blood by RIA, GC, GC-MS, or HPLC. • Empirical administration of naloxone, (can precipitate reaction in addicts).
Treatment	• Supportive care - Maintain ABC - Endotracheal intubation assisted ventilation. - Ipecac-induced emesis is contraindicated due to CNS depression and seizures. - activated charcoal can be used in patients, who are conscious, and airway is normal. • Naloxone is the antidote of choice for opiate poisoning. • Physostigmine salicylate (0.04 mg/kg IV) can be used, if the

	regular opiate antidotes are not available, for reversing respiratory depression. It increases acetylcholine levels reticular formation of the brainstem which is suppressed by opiates. • Convulsions: Benzodiazepines • Hypoglycaemia (or treat with intravenous dextrose 50 ml IV in an adult, or 2 ml/ kg in 25% dextrose for a child). • Hypotension: Infuse 10 to 20 ml/kg of isotonic fluid and place in Trendelenburg position or administer dopamine. • Prevention of rhabdomyolysis: Early aggressive fluid replacement is the mainstay of therapy and may help prevent renal insufficiency.

Antidepressants

Depression is a disorder characterised by feelings of intense sadness and despair, slowing of thought process, impaired concentration, constant worry, agitation, and self-deprecation. Depression is treated by antidepressants.

Antidepressants are classified as

1. **Norepinephrine (or noradrenaline) reuptake inhibitors**

a. Tertiary amine tricyclics: amitryptiline, clomipramine, doxepin, imipramine, trimipramine.

b. Secondary amine tricyclics: amoxapine, desipramine, maprotiline, nortriptyline, protriptyline.

2. **Selective serotonin reuptake inhibitors:** Citalopram, duloxetine, fluoxetine, fluvoxamine, milnacipran, oxaflozane, paroxetine, pizotifen, sertraline, venlafaxine.

3. **Monoamine oxidase inhibitors:** Isocarboxacid, iproniazid, moclobemide, pargyline, phenelzine, pimozide, selegiline, toloxatone, tranylcypromine.

4. **Atypical antidepressants:** Bupropion, mirtazepine, nefazodone, trazodone.

Class of antidepressants	MOA	Fatal dose	Clinical Manifestations
Tricyclic antidepressants	They act by inhibiting voltage-gated sodium channels in myocardial cells, blocking of H1, H2, and D2 receptors, as well as muscarinic receptors, inhibiting alpha-adrenergic receptors, interacting with GABA receptors, and inhibiting the transport and reuptake of biogenic amines at nerve terminals. The toxicity of cyclic antidepressants is mainly due to effects on myocardium, CNS, and peripheral vasculature.	• Serum drug level of more than 1000 ng/ml (10 to 20 mg/kg PO) is usually fatal. The therapeutic range for most tricyclic antidepressants is 100 to 260 ng/ml. • Children following the ingestion of as little as 250 ng of imipramine or amoxapine	• Short term seizures (especially common with maprotiline and amoxapine), tachycardia, hypotension, agitation, hallucinations, confusion including anticholinergic delirium, hyperthermia, ataxia, urinary retention, and coma. • Anticholinergic effects (mydriasis, tachycardia, urinary retention, decreased gastrointestinal motility) are common, but may be masked in severe overdose. • Miosis may be present in deeply comatose patients. Nystagmus may occur. Rhabdomyolysis and renal failure may result from prolonged seizures or coma. • metabolic acidosis may develop in patients with prolonged seizures or hypotension.

	They exhibit anticholinergic, adrenergic, and alpha-blocking properties		• Neuroleptic malignant syndrome (NMS) has been reported. • Amitryptiline overdose may be associated with peripheral neuropathy, polyradiculoneuropathy, and extrapyramidal manifestations. • **Symptoms associated with tricyclic antidepressant withdrawal** may include nausea, diarrhoea, malaise, myalgias, headache, anxiety, agitation, mania, insomnia, nightmares, arrhythmias and ventricular ectopy.

Treatment:

- Supportive measures:
  a. Maintain airway, breathing and circulation.
  b. Airway: intubate if indicated; Monitor arterial blood gases. Administer oxygen if necessary.
  c. Circulation: Treat hypotension with IV crystalloids, inotropes(dopamine), vasopressors (noradrenaline), etc
- Gut decontamination:
  a. Stomach wash (within the first 6 hours).
  b. Activated charcoal (1 gm/kg).
- Enhance drug elimination:
  a. Multiple-dose activated charcoal.
  b. Diuresis, Haemoperfusion and haemodialysis are not effective.
- Treat convulsions:

a. Diazepam 0.1 mg/kg IV (or) Phenytoin 15 mg/kg IV infusion. If untreated, then barbiturates (phenobarbitone) is indicated.

- Treat arrhythmias:
  a. Serum alkalinisation to a pH of 7.45 to 7.55 using intravenous boluses of sodium bicarbonate
  b. Intubation and hyperventilation may be used as an adjunct to sodium bicarbonate to achieve serum alkalinisation, with careful monitoring of blood gases to avoid profound alkalaemia.
  c. Conventional antiarrhythmics may be given but quinidine, disopyramide, and procainamide are contraindicated, as their effects on myocardial conduction are like that of the tricyclic antidepressants.
  d. Bradycardia or heart block—alkalinise to 7.40 to 7.45 pH; isoprenaline; pacemaker.

NSAIDS

Non-Steroidal Anti-Inflammatory Drugs (NSAID) are classified as follows

■ Pyrazolones—oxyphenbutazone, phenylbutazone.
■ Propionic acids—benoxaprofen, carprofen, fenbufen, fenoprofen, flurbiprofen, ibuprofen, ketoprofen, naproxen, oxaprozin, pirprofen, suprofen, tiaprofenic acid.
■ Fenamic acids—flufenamic acid, meclofenamic acid, mefenamic acid.
■ Heterocyclic acetic acids—etodolac, indomethacin, ketorolac, sulindac, tolmetin, zomepirac.
■ Aryl acetic acids—diclofenac, alclofenac.
■ Oxicams—isoxicam, piroxicam, tenoxicam.
■ Sulfonanilide—nimesulide.

Mechanism of Action:
NSAIDs inhibits cyclo-oxygenase enzyme and prevents the synthesis of prostaglandins, prostacyclins, and thromboxane.

NSAIDs also inhibit kreb's cycle, which leads to anaerobic metabolism causing raise in lactate and ketone bodies. Metabolic acidosis occurs consequently.

Clinical Manifestations:

GI: GI irritation, nausea, vomiting, abdominal pain, diarrhoea and rarely GI bleed.
Metabolic: metabolic acidosis, respiratory alkalosis, hyponatremia, hypokalemia, hyperkalemia and hypoglycaemia may occur.
CNS: tinnitus, confusion and headache are commonly reported, rarely seizures are also reported.
Hematologic: increase in bleeding time due to reversible inhibition of thromboxane production, resulting in decreased platelet aggregation.
Renal dysfunction: fluid and electrolyte imbalance.

Treatment:

- Supportive care: by giving isotonic IV fluids such normal saline, which corrects both fluid and electrolyte imbalance, thereby addressing metabolic acidosis and renal dysfunction.
- Gut decontamination methods: not indicated due to GI problems and in case of mefenamic acid poisoning, it can cause seizures. Hence these methods are contraindicated.
- Antidotes: There is no specific antidote, however, proton pump inhibitors (PPIs) can be given to address GI problems.
- Seizures can be treated either with IV dextrose/glucose or benzodiazepines.
- Elimination enhancement methods are not effective, since these drugs have shorter half-life.

Radiation Poisoning

Radiation is a form of energy, whose sources are synthetic and naturally occurring.

• Small quantities of radioactive materials occur naturally in the environment (atmosphere, water, and food) and are referred to as internal exposure.

• External exposure results from sunlight radiation and from synthetic and naturally occurring radioactive materials.

• Radiation poisoning is also known as radiation sickness, where symptoms occur from excessive exposure to ionizing radiation.

Radiation is of two types: ionizing and non-ionizing radiation.

Ionizing Radiation • Ionizing radiation induces somatic changes in cells and tissues by displacing electrons from their atomic nuclei, resulting in the intracellular ionization of molecules. • Depending on the dose and length of exposure, the effects can be immediate, chronic, or delayed. The most important targets are the DNA-molecules, where direct or indirect actions of radiation could result in lesions, such as base damage, single- strand breaks and double-strand breaks.

Double-strand breaks are considered the most serious DNA- lesions, since they can result in the cleavage of chromatin and might not be successfully repaired by the cell. The occurrence of DNA-lesions and, especially, of double-strand breaks will increase with increasing radiation exposure and will lead to a higher risk of cell death • Thus, reversible or irreversible DNA changes are induced, initiating a series of events that culminate in the production of a mutagenic response, a carcinogenic response, the inhibition of cell replication, or cell death.

SOURCE OF IONIZING RADIATION

Medical Sources: diagnostic x-rays; cobalt irradiation for the treatment of cancers; the injection of radioactive iodine which concentrates in the thyroid for treatment of Graves' disease.

Occupational exposure: nuclear reactors, linear accelerators, and sealed cesium, americium, and cobalt sources used in therapeutic instruments and detectors.

Symptoms of Radiation Poisoning: the severity of damage depends on duration of exposure, strength of exposure.

SKIN CHANGES: Cutaneous radiation syndrome (CRS) refers to the skin symptoms of radiation exposure; a transient and inconsistent redness(associated with itching); a latent phase may occur and last from a few days up to several weeks, when intense reddening, blistering, and ulceration of the irradiated site are visible.

- nausea and vomiting, Diarrhea, Headache, Fever, Dizziness and disorientation, Weakness and fatigue, Hair loss, Bloody vomit and stools from internal bleeding, Infections, Low blood pressure.

Treatment:

Prophylactic drugs such as corticosteroids can be given to sooth the damage.

Decontamination by removing the cloths and washing the body using soap and water.

Wound exposure: treat with normal saline.