D.PHARM • SECOND YEAR

Pharmacology

CHAPTER 4

Drugs Acting on the Central Nervous System



ENGLISH CHAPTER NOTES

DIPLOMA IN PHARMACY

GENERAL ANAESTHETICS: DEFINITION AND CLASSIFICATION

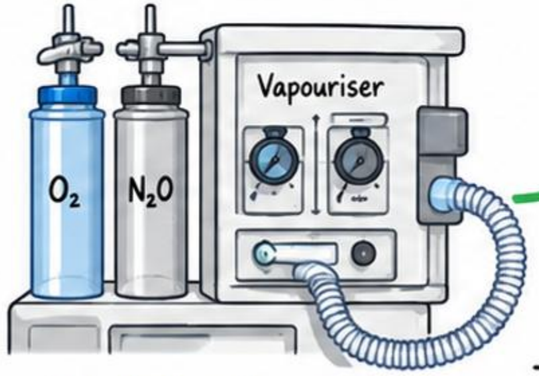
General anaesthesia is a controlled, reversible state used for painless surgery. Its aims include loss of consciousness, amnesia, analgesia, immobility or muscle relaxation and suppression of harmful reflexes. A combination of drugs is often used because one agent may not provide every component.

Main CNS sites:

Cortical networks and the reticular activating system are depressed.

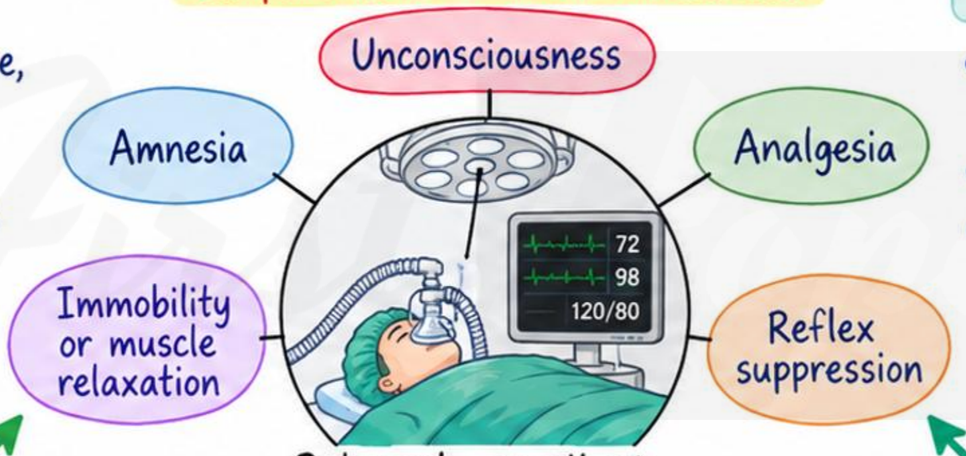
A. INHALATIONAL ANAESTHETICS

- Volatile liquids: halothane, isoflurane, sevoflurane, desflurane.
- Gases: nitrous oxide, xenon.
- Main role: maintenance; some agents can also induce anaesthesia.



Inhalational agents

Components of balanced anaesthesia



Balanced anaesthesia

B. INTRAVENOUS ANAESTHETICS

- Induction agents: propofol, thiopentone, etomidate, ketamine.
- Adjunct agents: midazolam, fentanyl.
- Main role: rapid induction, short procedures or balanced anaesthesia.



Intravenous agents

Based on onset and duration

Ultra-short acting	Short acting	Longer controllable administration
thiopentone, propofol — rapid induction	etomidate — short procedures or induction	inhalational agents — maintenance

Memory line: IV agents usually start anaesthesia; inhalational agents commonly maintain it.

GENERAL ANAESTHETICS: ACTIONS, DOSES AND MAC

PHARMACOLOGICAL ACTIONS

CNS

- loss of consciousness, sedation and amnesia
- suppression of protective reflexes
- dose-dependent CNS depression

CARDIOVASCULAR SYSTEM

Vasodilation and myocardial depression may cause hypotension. Effect varies with the agent and patient.

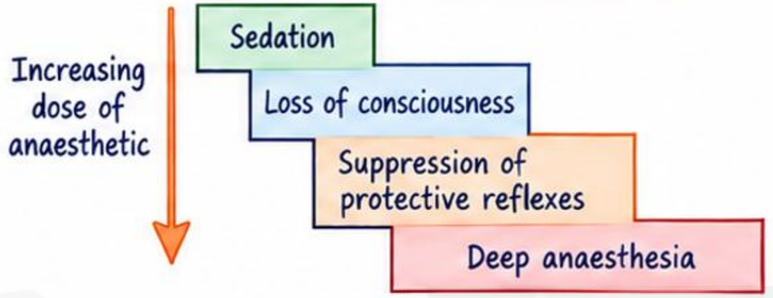
RESPIRATORY SYSTEM

Most agents can depress breathing; rapid IV dosee may cause apnoea. Ketamine usually preserves spontaneous respiration better, but airway complications can still occur.

OTHER EFFECTS

- muscle relaxation may be strengthened by neuromuscular blockers
- postoperative nausea and vomiting can occur

Dose-dependent CNS depression





Heart
(myocardial depression and hypotension)

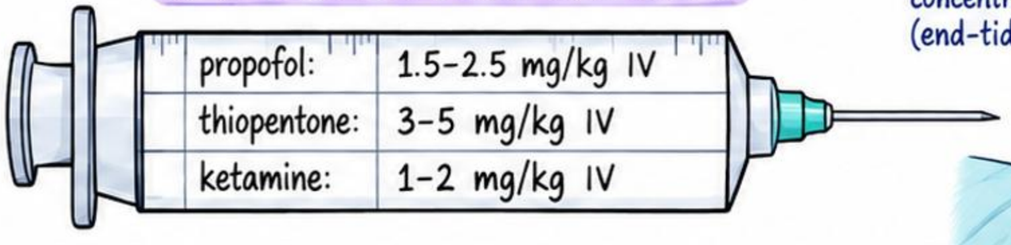


Lungs
(depressed breathing, possible apnoea)



Muscle
(relaxation, enhanced by neuromuscular blockers)

IV INDUCTION DOSE EXAMPLES



propofol:	1.5–2.5 mg/kg IV
thiopentone:	3–5 mg/kg IV
ketamine:	1–2 mg/kg IV

Doses are individualized and given by trained professionals with monitoring.

MAC: MINIMUM ALVEOLAR CONCENTRATION

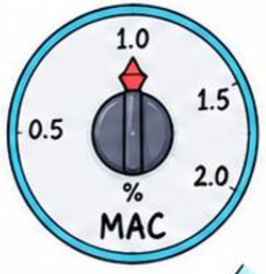
MAC is the end-tidal inhaled concentration that prevents movement in response to a surgical stimulus in 50% of patients.

Lower MAC means greater potency.

- sevoflurane: about 1.8%
- isoflurane: about 1.2%
- nitrous oxide: about 105%; therefore it cannot produce full surgical anaesthesia alone at normal atmospheric pressure and is used with other agents.

What does MAC mean?

Inhaled anaesthetic concentration (end-tidal) →



→ Prevents movement in 50% of patients in response to a surgical stimulus.



Movement prevented in 50% of patients (MAC).

GENERAL ANAESTHETICS: USES AND SAFETY

INDICATIONS

- induction and maintenance of general anaesthesia
- short surgical or dental procedures: propofol or ketamine
- electroconvulsive therapy, ECT: propofol or methohexital
- refractory status epilepticus: thiopentone in specialist care
- analgesia or procedural sedation: nitrous oxide or ketamine

PERI-OPERATIVE PATHWAY

INDUCTION

- start general anaesthesia
- e.g. propofol, ketamine, thiopentone

→

MAINTENANCE

- continue general anaesthesia
- volatile anaesthetics, nitrous oxide or intravenous agents

→

RECOVERY

- stop agents
- return of consciousness and spontaneous ventilation

MALIGNANT HYPERTHERMIA

Triggers: volatile anaesthetics plus or minus succinylcholine in a susceptible person.

Warning signs: rapidly rising carbon dioxide, tachycardia, muscle rigidity and later hyperthermia.

Emergency sequence:

stop trigger

↓

give 100% oxygen

↓

IV dantrolene

↓

active cooling and supportive correction of acidosis, potassium and organ complications.

IMPORTANT CAUTIONS



hepatic disease: avoid or carefully assess halothane



cardiovascular instability: propofol may worsen hypotension



raised intracranial pressure: needs specialist assessment and controlled ventilation; ketamine is not an automatic absolute contraindication



acute porphyria: avoid barbiturates such as thiopentone



pregnancy: individual risk-benefit assessment and obstetric-anaesthetic care



known malignant-hyperthermia susceptibility: avoid triggering volatile anaesthetics and succinylcholine

ADVERSE EFFECTS

- Postoperative nausea or vomiting, respiratory depression, hypotension, arrhythmias with some agents and delayed recovery.

Halothane can cause arrhythmia and rare severe hepatic injury.

SAFETY RULE

General anaesthesia requires airway equipment, oxygen, circulation support and continuous monitoring.

SEDATIVES AND HYPNOTICS: CLASSIFICATION

Definition: Sedatives reduce anxiety and produce calming at lower doses.
Hypnotics induce and maintain sleep at higher doses.
The same drug may have both effects depending on dose.

Based on duration:

short acting:
triazolam, zolpidem — sleep induction
hours

intermediate acting:
lorazepam, temazepam — sleep maintenance
6 – 24 hours

long acting:
diazepam, clonazepam — anxiety or seizures; more next-day effects
> 24 hours

Depth of effect:

Wakefulness | Mild sedation | Moderate sedation | Deep sedation | Hypnosis (sleep)

Increasing dose → increasing CNS depression → sleep

Based on drug class:

1. BENZODIAZEPINES, BZDs
Diazepam, lorazepam, triazolam.
Enhance GABA-A receptor action.

2. NON-BZD Z-DRUGS
Zolpidem, zaleplon, eszopiclone.
Preferential sleep-promoting GABA-A effects; usually short acting.

3. BARBITURATES
Phenobarbital, secobarbital.
Greater respiratory-depression and overdose risk; now limited uses.

4. MELATONIN RECEPTOR AGONIST
Ramelteon.
Helps regulate the sleep-wake cycle.

5. SEDATING ANTIHISTAMINES
Hydroxyzine, diphenhydramine.
H1 blockade causes drowsiness; anticholinergic effects may occur.

6. OLDER AGENT
Chloral hydrate is largely obsolete because safer options exist.

Key point: Choice depends on the reason for treatment, onset, duration, age, comorbidities and dependence risk.

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