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Course Name	**: D. Pharm**
Year	**: Second Year**
Subject Name	**: Pharmacology**
Topic Name	**: General Anaesthetics**

Ch – 4.5

GENERAL ANAESTHETICS

General anaesthetics (GAs) are drugs which causes reversible loss of all sensation and consciousness. The main features of general anesthesia involves loss of sensation (pain), Sleep and amnesia, immobility and muscle relaxation and also involves abolition of somatic and autonomic reflexes.

Pharmacological actions:

* Loss of all sensation, especially pain

*Sleep (consciousness) and amnesia

* Immobility and muscle relaxation

Classification of General Anaesthetics:

A. Inhalational

1. **Inhalation Gas: E.g.:** Nitrous Oxide (N_2O), Xenon
2. **Volatile Liquid: E.g.:** Halothane, Enflurane, Isoflurane, Desflurane, Sevoflurane

B. Intravenous

1. **Intravenous – Inducing Agent: E.g.:** Thiopentone Sod., Sod Propofol, Etomidate
2. **Slow acting:**

a. Phencyclidine derivative (Dissociative Anesthesia): E.g.: Ketamine

b. Benzodiazepam: E.g.: Diazepam, Lorazepam

c. Opioid Analgesics: E.g.: Fentanyl

STAGES OF ANAESTHESIA

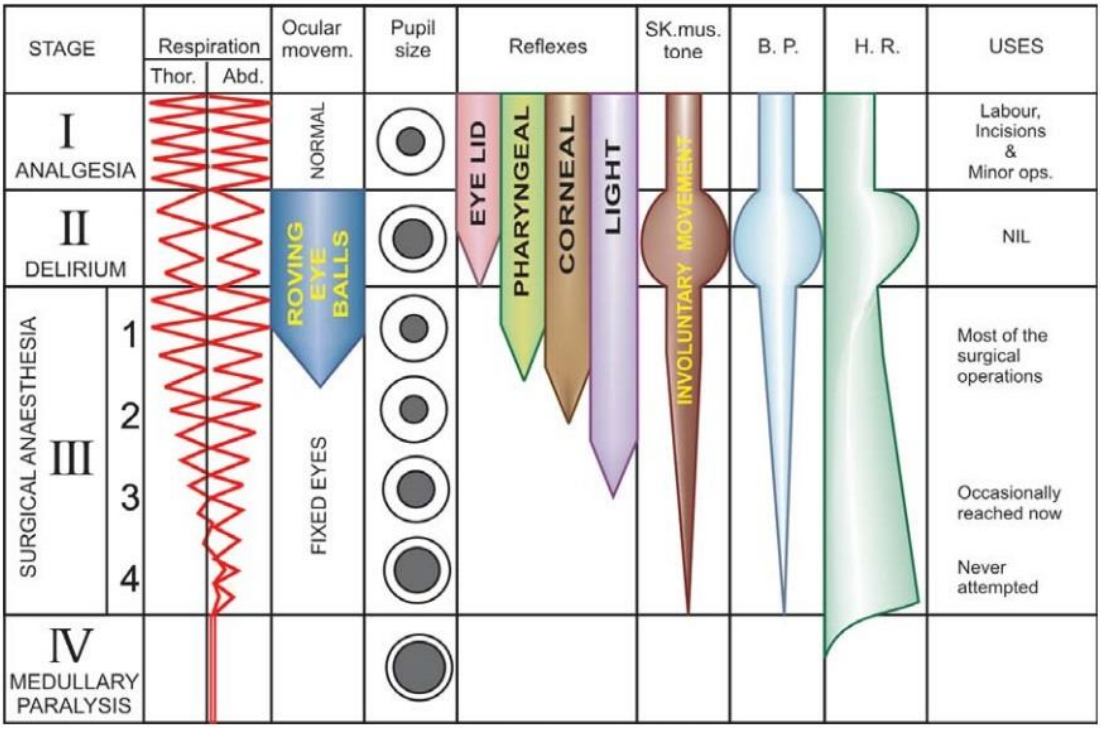
The main four stages if anesthesia are:

1.Stage of analgesia: Starts from anesthetic inhalation and lasts upto the loss of consciousness. Pain is slowly decreased but patient remains conscious and amnesia appear at the end. Respiration
is normal during this stage.

2.Stage of delirium: Consciousness during this stage is fully lost but patient may appear excited (muscle tone increases). Heart rate and BP may rise and pupils may dilate due to sympathetic stimulation.

3.Surgical Anaesthesia: Starts from regular respiration to cessation of breathing. It basically involves Roving eyeballs and fixed at end, loss of corneal reflexes, and pupil starts dilating (light reflex lost).

4.Medullary Paralysis: Breathing stops and failure of circulation and this leads to death.



Mechanism of General Anaesthetics:

S. No.	Drug Name	Mode of action
1.	Nitrous Oxide	Nitrous oxide acts as an N-methyl-d-aspartate (NMDA) receptor antagonist.
2.	Halothane	Halothane is a cerebral vasodilator that enhances CBF and decreases cerebrovascular resistance in a dose-dependent manner.
3.	Enflurane	rapidly induces anesthesia via the stimulation of inhibitory neural channels and the inhibition of excitatory neural channels.
4.	Isoflurane	inhibition of neurotransmitter-gated ion channels such as GABA, glycine, and N-methyl-d-aspartate (NMDA) receptors in the central nervous system (CNS)
5.	Thiopentone Sod.	binds at a distinct binding site associated with a Cl- ionopore at the GABAA receptor, increasing the duration of time for which the Cl-ionopore is open.
6.	Sod Propofol	believed to be due to a direct depressant effect on the chemoreceptor trigger zone and vagal nuclei.
7.	Ketamine	Ketamine interacts with N-methyl-D-aspartate (NMDA) receptors, opioid receptors, monoaminergic receptors, muscarinic receptors and voltage sensitive Ca ion channels.

INHALATIONAL ANAESTHETICS

These anesthetics diffuse across pulmonary and tissue barriers. The potency and partial pressure in brain decide the depth of anesthesia. The speed of induction of anesthetic effects depends upon:

1. Solubility: Large amount of anesthetics that are highly soluble in blood must be dissolved before PP is raised. The change in PP in blood leads to consequent induction and slow recovery. Drugs with low blood : gas partition coefficient (Nitrous oxide) induce quickly

2. Inspired Gas Partial Pressure: A higher partial pressure of the gas in lungs will result in more rapid achievement of anesthetic levels in blood. Thus, a quick induction can be made by administering the GA at high concentration at start

3. Ventilation rate: The greater the ventilation than there will be more rapid increase in alveolar and blood partial pressure of the anesthetic agent and more rapid will be onset of anesthesia.

4. Pulmonary blood flow: Higher the pulmonary blood flows, slower will be the rise in partial pressure of gas and thus onset of anesthesia is reduced. In contrast lower the blood flow rate, inset will be faster.

5. Cerebral Blood Flow: Gas is rapidly delivered to highly perfused organ (Brain). This can be hastened by inhalation of CO_2 which causes vasodilation which further leads to acceleration of induction and recovery.

PHARMACOLOGICAL ACTIONS OF INHALED ANAESTHETICS

1. CNS:

- Inhaled anesthetics decrease brain metabolic rate.
- They generally reduce vascular resistance and increase cerebral blood flow and may increase intracranial pressure.
- High concentration of Enflurane may cause spike and wave activity and muscle twitching, but this effect is limited to this drug only

2. Cardiovascular effects:

- Inhalational anesthetics decrease arterial blood pressure moderately.
- Enflurane and Halothane are myocardial depressants by reducing Ca^{2+} concentration while Isoflurane causes peripheral vasodilation.
- Nitrous oxide is less likely to lower blood pressure than are other inhalational anesthetics.

3. Respiratory effects:

- Rate of respiration may be increased but the tidal volume is decreased which may cause increase in arterial CO2 tension.
- Nitrous oxide may or may not effect respiration while Halothane and Isoflurane causes greater depression of respiration.

ADVERSE EFFECTS

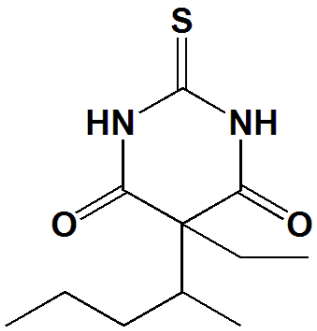
a) Prolonged exposure to nitrous oxide decreases methionine synthase activity and may lead to megaloblastic anaemia.
b) Some Patients may develop malignant hyperthermia when exposed to halogenated anesthetics.
c) Renal insufficiency may be one of the problems after using prolonged anesthesia.

INTRAVENOUS ANAESTHETICS

Several chemical classes of drugs are used as intravenous agents in anesthesia: for eg:

1. BARBITURATES:

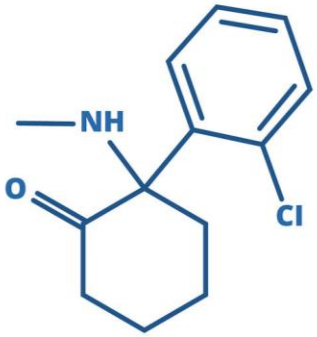
- Thiopental and methohexital have high lipid solubility which promotes rapid entry into the brain, results in anesthesia less than one minute.
- It is used for short surgical procedures.



Thiopental

2. KETAMINE:

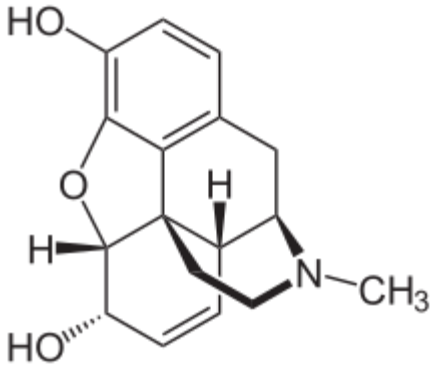
- It produces dissociative anesthesia, patient remains conscious but has marked catatonia and amnesia.
- The drug is a cardiovascular stimulant and this action may lead to increase in intracranial pressure.



ketamine

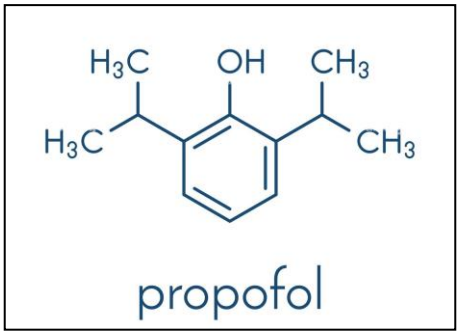
3. OPIOIDS:

- Morphine and fentanyl are used with other CNS depressants in anesthesia regimens and are valuable in high risk patients who might not survive a full general anesthetic.
- If administered iv may cause chest wall rigidity and can impair ventilation.



4. PROPOFOL:

- Produces anesthesia at a rate similar to intravenous barbiturates but recovery is rapid.
- It may show antiemetic action.
- Propofol can cause marked hypotension during induction of anesthesia.
- Total body clearance of Propofol is greater than hepatic blood flow.



5. BENZODIAZEPINES:

- Midazolam is widely used with inhaled anesthetics and iv opioids.
- The onset of its CNS effects is slower than that of Thiopental and has longer duration of action.