GENERAL ANAESTHETICS

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CLASSIFICATION OF GENERAL ANAESTHETICS

- **Inhalational anaesthetics**
  - **Gas**

    Eg: Nitrous oxide
  - **Volatile Liquids**

    Eg: Ether

    Halothane

    Isoflurane

    Desflurane

- **Intravenous Anaesthetics:**
- **Fast acting drugs:**

  Eg: Thiopentone sodium

  Propofol

  Etomidate
- **Slow acting drugs:**
- Benzodiazepines:
  - Diazepam, Lorazepam, Midazolam
- Dissociative anaesthetics:
  - Ketamine
- Opioid analgesia:
  - Fentanyl

NITROUS OXIDE

- It is a colourless, odourless, heavier than air, non-inflammable gas supplied under pressure in steel cylinders. It is cheap and commonly used.
- It is non-irritating, but low potency anaesthetic.
- Unconsciousness cannot be produced in all individuals without concomitant hypoxia.
- Patients maintained on 70% N_2O + 30% O_2 along with muscle relaxants often recall the events during anaesthesia, but some lose awareness completely.
- Nitrous oxide is a good analgesic; even 20% produces analgesia.
- Muscle relaxation is minimal.
- Onset of N_2O action is quick and smooth, recovery is rapid, because of its low blood solubility. Post-anaesthetic nausea is not marked.
- It tends to increase sympathetic tone.

NITROUS OXIDE

- Nitrous oxide is generally used as a carrier and adjuvant to other anaesthetics.
- A mixture of 70% N_2O + 25–30% O_2 + 0.2–2% another potent anaesthetic is employed for most surgical procedures.
- N_2O has little effect on respiration, heart and BP.
- It increases cerebral blood flow and tends to elevate intracranial pressure.
- As the sole agent, N_2O (50%) has been used with O_2 for dental and obstetric analgesia.
- It is nontoxic to liver, kidney and brain.
- However, prolonged N_2O anaesthesia has the potential to depress bone marrow and cause peripheral neuropathy.
- Metabolism of N_2O does not occur; it is quickly removed from the body by lungs.

ETHER (DIETHYL ETHER) $C_2H_5 — O — C_2H_5$

- Highly volatile liquid, produces irritating vapours which are inflammable and explosive.
- Ether is a potent anaesthetic, produces good analgesia.
- It is highly soluble in blood. It is not hepatotoxic.
- **MOA:** It produces marked muscle relaxation by reducing ACETYLCHOLINE output from motor nerve endings.
- **DISADVANTAGES:**
- Induction is prolonged and unpleasant with struggling, breath holding, salivation and marked respiratory secretions.
- Recovery is slow; post-anaesthetic nausea, vomiting and retching are marked.
- Respiration and BP are generally well maintained.
- Ether is not used now in developed countries because of its unpleasant and inflammable properties.
- **USAGE:**
- However, it is still used in developing countries, particularly in peripheral areas because it is—cheap, can be given by open drop method (though congestion of eye, soreness of trachea and ether burns on face can occur) without the need for any equipment, and is relatively safe even in inexperienced hands.

HALOTHANE (Fluothane)

- It is a volatile liquid with sweet odour, non-irritant and non-inflammable.
- Solubility in blood is intermediate—induction is reasonably quick and pleasant.
- It is a potent anaesthetic— control of administered concentration is essential.
- For induction 2–4% and for maintenance 0.5–1% is delivered by the use of a special vaporizer.
- It is not a good analgesic or muscle relaxant, but it potentiates competitive neuromuscular blockers.
- **ADR:**
- Halothane causes direct depression of myocardial contractility by reducing intracellular CALCIUM concentration.
- Cardiac output is reduced with deepening anaesthesia. BP starts falling early and parallels the dept Heart rate is reduced.
- Halothane causes relatively greater depression of respiration; breathing is shallow and rapid.
- Cerebral blood flow increases.
- Ventilatory support with added oxygen is frequently required.
- Pharyngeal and laryngeal reflexes are abolished early and coughing is suppressed

HALOTHANE (Fluothane)

- It inhibits intestinal and uterine contractions.
- It can prolong delivery and increase post-partal blood loss.
- Urine formation is decreased. Hepatitis occurs rarely.
- A genetically determined reaction *malignant hyperthermia occurs rarely.*
- Rapid external cooling, bicarbonate infusion and 100% O_2 inhalation can be done.
- **Pharmacokinetics:**
- About 20% of halothane that enters blood is metabolized in the liver, the rest is exhaled out.
- Elimination may continue for 24–48 hours after prolonged administration due to accumulation in fatty and other tissues.
- Recovery from halothane anaesthesia is smooth and reasonably quick.
- **ADR:** Shivering may occur but nausea and vomiting are rare.
- Psychomotor performance and mental ability remain depressed for several hours after regaining consciousness. Halothane toxicity is less frequent in children.
- **USE:** Halothane is a popular anaesthetic in developing countries, because it is relatively cheap and non-irritant, non-inflammable, pleasant with relatively rapid action. It is particularly suitable for use in children. In adults, it is mainly used as a maintenance anaesthetic after i.v. induction.

ISOFLURANE (Sofane)

- This fluorinated anaesthetic is currently the routinely used anaesthetic all over.
- It has totally replaced its earlier introduced isomer enflurane.
- Isoflurane is somewhat less potent and less soluble in blood as well as in fat than halothane, but equally volatile. It is mildly pungent.
- Compared to halothane, it produces relatively rapid induction and recovery.
- **Dose:** 1.5–3% induces anaesthesia in 7–10 min; 1–2% is used for maintenance.
- **ADR:**
- Magnitude of fall in BP is similar to halothane. Heart rate is increased.
- Respiratory depression is prominent and assistance is usually needed.
- Secretions are slightly increased.
- Uterine and skeletal muscle relaxation is similar to halothane.
- Metabolism of isoflurane is negligible.
- Renal and hepatic toxicity has not been encountered.
- Post-anaesthetic nausea and vomiting is low.
- Pupils do not dilate and light reflex is not lost even at deeper levels.
- **Advantages:** Better adjustment of depth of anaesthesia. Low toxicity.
- It does not provoke seizures and is particularly suitable for neurosurgery.

INTRAVENOUS ANAESTHETICS

- **FAST ACTING DRUGS**
- These are drugs which on i.v. injection produce loss of consciousness in one arm-brain circulation time (~11 sec).
- They are generally used for induction because of rapid onset of action.
- Anaesthesia is then usually maintained by an inhalational agent.
- They also serve to reduce the amount of maintenance anaesthetic.
- **THIOPENTONE SODIUM:**
- It is an ultrashort acting thiobarbiturate, highly soluble in water yielding a very alkaline solution, which must be prepared freshly before injection.
- **DOSE:** Injected i.v. (3–5 mg/kg) as a 2.5% solution, it produces unconsciousness in 15–20 sec.
- Its undissociated form has high lipid solubility— enters brain almost instantaneously.
- Initial distribution depends on organ blood flow—brain gets large amounts.
- Consciousness is regained in 6–10 min.
- Hepatic metabolism occurs (elimination t½ is 8–12 hr).
- Thiopentone is a poor analgesic.

- **THIOPENTONE SODIUM:**
- **ADR:**
- It is a weak muscle relaxant; does not irritate air passages.
- BP falls immediately after injection mainly due to vasodilatation, but recovers rapidly.
- Cerebral blood flow is reduced.
- Laryngospasm occurs generally.
- Shivering and delirium may occur during recovery.
- Pain in the postoperative period likely to induce restlessness.
- **USE:** It can be used solely for short operations that are not painful.
- Occasionally used for rapid control of convulsions.
- Facilitates verbal communication with psychiatric patients and for 'narcoanalysis' of criminals.
- **PROPOFOL:**
- Currently, propofol has superseded thiopentone as an i.v. anaesthetic, both for induction as well as maintenance.
- It is an oily liquid employed as a 1% emulsion.
- Unconsciousness occurs in 15–45 sec and lasts 5–10 min.

- **PROPOFOL:**
- **Pharmacokinetics:**
- Propofol distributes rapidly (distribution t½ 2–4 min).
- Elimination t½ (100 min) is much shorter due to rapid metabolism.
- **Advantages:**
- It lacks airway irritancy and is not likely to induce bronchospasm: preferred in asthmatics.
- It is particularly suited for outpatient surgery.
- Incidence of postoperative nausea and vomiting is low; patient acceptability is very good.
- ADR:
- Excitatory effects and involuntary movements are noted in few patients.
- Fall in BP occurs, but short lasting.
- Produces dose-dependent respiratory depression.
- Pain during injection is frequent.
- ***Dose:*** *2 mg/kg bolus i.v. for induction; 100–200 µg/kg/min for* maintenance.

SLOWER ACTING DRUGS

Benzodiazepines (BZDs):

- In addition to preanaesthetic medication, BZDs are now frequently used for inducing, maintaining and supplementing anaesthesia as well as for 'conscious sedation'.
- Relatively large doses (diazepam 0.2–0.3 mg/kg or equivalent) injected i.v. produce sedation, amnesia and then unconsciousness in 5–10 min.
- But amnesia persists for 2–3 hr and sedation for 6 hr or more.
- Recovery is further delayed if larger doses are given.
- BZDs are poor analgesics : an opioid or N_2O is usually added if the procedure is painful.
- By themselves, BZDs do not markedly depress respiration, cardiac contractility or BP, but when opioids are also given these are seen.
- BZDs decrease muscle tone.
- They do not provoke postoperative nausea or vomiting.
- **USE:**
- These are preferred for endoscopies, cardiac catheterization, angiographies, conscious sedation during local/regional anaesthesia and fracture setting.

- ***Diazepam:***
- ***Dose:*** *0.2–0.5 mg/kg by slow undiluted* injection in a running i.v. Drip.
- This technique reduces the burning sensation in the vein and incidence of thrombophlebitis.
- ***Lorazepam:***
- *Three times more potent, slower* acting and less irritating than diazepam.
- It distributes more gradually—awakening may be delayed.
- ***Dose:*** *2–4 mg (0.04 mg/kg).*
- ***KETAMINE:***
- It induces a so called '***dissociative anaesthesia***' *characterized by* profound analgesia, immobility, amnesia with light sleep.
- The patient appears to be conscious, i.e. opens his eyes, makes swallowing movements and his muscles are stiff, but he is unable to process sensory stimuli and does not react to them.
- Thus, the patient appears to be dissociated from his body and surroundings.
- The primary site of action is in the cortex and sub-cortical areas.
- Respiration is not depressed, bronchi dilate, airway reflexes are maintained, muscle tone increases.

- ***KETAMINE:***
- Non-purposive limb movements occur.
- Heart rate, cardiac output and BP are elevated due to sympathetic stimulation.
- Emergence delirium, hallucinations and involuntary movements occur in upto 50% patients during recovery;
- **DOSE:**
- A dose of 1–2 mg/kg i.v. or 3–5 mg/kg i.m. produces effects within a minute, and recovery starts after 10–15 min, but patient remains amnesic for 1–2 hr.
- Children tolerate the drug better.
- Ketamine is rapidly metabolized in the liver and has an elimination t½ of 2–4 hr.
- **USES:**
- Ketamine has been used for operations on the head and neck
- In patients who have bled
- In asthmatics.
- In those who do not want to lose consciousness and for short operations.
- It is good for repeated use; particularly suitable for burn dressing.

- ***FENTANYL:***
- This highly lipophilic, short acting (30–50 min) potent opioid analgesic related to pethidine *is generally given i.v. at* beginning of painful surgical procedures.
- It is frequently used to supplement anaesthetics in balanced anaesthesia.
- **ADR:**
- After i.v. fentanyl (2–4 µg/kg) the patient remains drowsy but conscious and his cooperation can be commanded.
- Respiratory depression is marked.
- Heart rate decreases.
- Cerebral blood flow and O_2 consumption are slightly decreased.
- Nausea, vomiting and itching often occurs during recovery.
- **USES:**
- Combined with BZDs, it can reduce the need for inhaled anaesthetics for diagnostic, endoscopic, angiographic and other minor procedures in poor risk patients, as well as for burn dressing.
- Relieves postoperative pain.

COMPLICATIONS OF GENERAL ANAESTHESIA

During Anaesthesia

- Respiratory depression
- Salivation, respiratory secretions.
- Cardiac arrhythmias
- Fall in BP
- Aspiration of gastric contents
- Laryngospasm
- Awareness: dreadful perception and recall of events during surgery.
- Delirium and convulsions.
- Fire and explosion.

After Anaesthesia

- Nausea and vomiting.
- Persisting sedation
- Impaired psychomotor function.
- Pneumonia
- Organ toxicities: liver, kidney damage.
- Nerve palsies
- Emergence delirium
- Cognitive defects