Inhalational anesthetic agents

Inhalational anesthetic Agents

- They are synthetic, colorless liquids at room temperature that are non flammable and administered as a vapor from a vaporizer on the anesthetic machine.

- A dose-related depression of cardiorespiratory function is common to each of these inhalational agents.

- Produce smooth muscle relaxation:
  - Decrease in cerebrovascular resistance.(↑ perfusion)
  - Bronchodilation.

Inhalational anesthetic Agents

Modern inhaled anesthetics are halogenated partly or entirely with fluorine. Fluorination provides greater stability and lesser toxicity.

The most commonly used inhaled anesthetics in modern anesthesia include volatile liquids (i.e., halothane, enflurane, isoflurane, desflurane, and sevoflurane) and a single gas (i.e., nitrous oxide). None of these inhaled anesthetics meets all the criteria of an “ideal” inhaled anesthetic.

Inhalational anesthetic Agents

Mechanism of action:

All inhalational anesthetic agents stimulate inhibitory receptors (GABA receptors) except Nitrous oxide which inhibit stimulatory receptors (NMDA receptors)

Inhalational agents are compared to one another according to their minimal alveolar concentration (or "**MAC"**) values.

The MAC value: minimum alveolar concentration of anesthetic required to suppress movement (motor response) to a surgical incision (pain stimulus) in 50% of patients.

Knowledge of the MAC value allows one to compare the potencies of different inhalational agents.

 MAC > Potency **&** MAC > Potency.

Agent	MAC%
Nitrous oxide	105
Halothane (Fluothane)	0.75
Isoflurane (Forane)	1.2
Desflurane (Suprane)	6.0
Sevoflurane (Ultane)	2.0

'able 13.1: Factors which alter anaesthetic requirements (MAC).

Increased MAC	No change in MAC	Decreased MAC
Hyperthermia Chronic drug abuse: Ethanol Acute use of amphetamines Hyperthyroidism	Gender Duration of anaesthesia Carbon dioxide tensions: $PaCO_2$ 21 - 95 mmHg Metabolic acid-base status Hypertension	Increasing age Hypothermia Severe hypotension Other anaesthetic agents: opioids, benzodiazepines Acute drug intoxication: Ethanol Pregnancy Hypothyroidism Other drugs: clonidine, reserpine

Onset of action:

The **rapidity** at which the anesthetic state is reached depends on how quickly the anesthetic inhalational agent reaches the brain to exert its effects.

A. Factors determining how quickly the inhalational agent reaches the alveoli :

1. The inspired **concentration** (dose) of anesthetic gas being delivered by the anesthetic machine (concentration effect).
2. The **carrier gas flow rate** through the anesthetic machine.
3. The amount of **alveolar ventilation** (Minute ventilation)

   V = Respiratory Rate x Tidal Volume
4. **Blood solubility** of anesthetic agent.

B. Factors determining how quickly the inhalational agent reaches the brain from the alveoli in order to establish anesthesia:

1. The **rate of blood flow** to the brain.
2. The **lipid solubility of the inhalational agent** (to cross blood brain barrier).
3. **Concentration gradient:** The **difference in the arterial and venous concentrations** of the inhalational agent.

Vaporizers are **color-coded** to prevent filling of vaporizers with the wrong anesthetic (prevent over dose or lower dose).

Halothane (red)

Enflurane (orange)

Isoflurane (purple)

Sevoflurane (yellow)

Desflurane (blue)

Nitrous Oxide

- Nitrous oxide ("laughing gas") is a nonirritating potent analgesic but a weak general anesthetic.

➢ Nitrous oxide undergoes **very little metabolism** and **excreted** by expiration**.**

➢ It has a **rapid onset and a quick recovery** of 3 to 10 minutes due to its low solubility in blood.

➢ Its **low potency (**high **MAC = 105%)** limits the amount that can be administered.

➢ Nitrous oxide is 34 times more soluble than nitrogen which mean that N20 diffusion between compartments is much faster than nitrogen. This property results in three special anesthetic phenomena. 1- Second gas effect
2- Diffusion hypoxia
3- Closed air spaces

Second gas effect

At the beginning of anaesthesia, N20 leaves the alveoli much faster than other gases can leave.

The result is an increase in the concentration of other gases in the alveoli (oxygen, and other inhalational agents) which leads to increase in their partial pressure.

This increase in partial pressure speeds the onset in inhalational anesthetic effect, and is referred to as **the second gas effect.**

Diffusion hypoxia

- Diffusion hypoxia may result **at the end of the anesthesia.**
- As nitrous oxide is discontinued, the body stores of nitrous oxide are released and flood the alveoli, **diluting the oxygen** present in the alveoli.
- When only room air is administered at the end of the anesthetic, the dilution of oxygen may be sufficient to create a hypoxic mixture, and result in hypoxemia.
- The administration of **high flow 100% oxygen** at the end of an aesthetic may avoid hypoxemia.

Closed air space

Closed air spaces will expand in the presence of nitrous oxide due to the differences in solubility of nitrogen and nitrous oxide.

With the administration of 66% N2O, a closed air space will expand 2 times in volume over a period of approximately 15 minutes.

=> For this reason N2O is contraindicated in patients with **a pneumothorax, eye bubble, tympanic membrane graft, closed loop bowel obstruction, air embolism,** or any other closed air space in the body

Halothane

- Most potent inhalational anaesthetic (MAC of 0.75%)

- Very soluble in blood and low soluble in adipose (prolonged emergence).

- Halothane's popularity in adult anaesthesia has declined because of its implication in causing **Arrhythmias**.

Halothane hepatitis: is believed to occur in approximately 1 in 10,000 halothane anaesthetics. (NOT hepatotoxic in children)

Risk Factor : Patients exposed to multiple anesthetics at short interval,middle-aged obese women, and person with a familial predisposition to halothane toxicity .

Presents as postoperative fever, jaundice, eosinophilia, and occasionally extensive hepatic necrosis and death.

Hepatitis following isoflurane and enflurane exposure is very rare.

The main route of excretion is through the lungs, but approximately 15-20% of halothane is metabolized by the liver.

Halothane Side Effects

1. **Trigger Malignant Hyperthermia.**
2. **Hypotension.**
3. ↑ **ICP.**
4. **Postoperative Hepatitis.**
5. **Arrhythmias**
6. **Bradycardia.**

Enflurane

- Stable, nonflammable liquid (at room temp.).
- MAC 1.68%.
- Enflurane lowers the threshold for **seizures**.

Desflurane

- Provides very rapid onset and recovery.
- Desflurane is unique in that it boils at room temperature (requiring administration via a special heated vaporizer).
- Desflurane has a MAC value of 6%.
- Causes **renal toxicity ?**
- Cardiovascular, respiratory, neurological and neuromuscular effects are similar to those of isoflurane.

Isoflurane

- MAC value of **1.2%**

- Not as well tolerated as halothane because of its pungent odour and tendency **to irritate the airways**. (coughing and breath-holding if administered too quickly)**.**

- The preferred agent for **neurosurgical procedures** as it causes the least increase in cerebral blood flow and intracranial pressure.

Sevoflurane

- Is metabolized in the liver. Approximately 3-5% of sevoflurane is broken down in this fashion.
- Has a MAC value of 2%.
- Is more **pleasant smelling** and is well suited for inhalational induction of anaesthesia.
- Production of a renal toxin called **"compound A"** at low fresh gas flows has lead to the recommendation that sevoflurane be administered with a minimum of two liters of fresh gas flow.

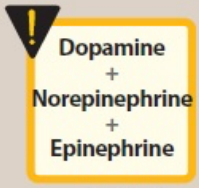
- Anaesthesia sufficient for laryngeal mask placement and intubation can be achieved after three to five minutes of breathing a high concentration of Sevoflurane.

Contraindications

- Trigger Malignant hyperthermia.
- Hypotension .
- Elevated ICP.
- Renal toxicity .

Desflurane & Sevoflurane

- While structurally **similar** to their parents Halothane and Isoflurane, the **substitution** of a couple of key chlorine atoms with fluorine atoms results in their lower observed solubility. (Low blood soluble agents => rapid actions)
- This translates clinically into a more rapid induction and recovery from anaesthesia.

	Halothane	*Isoflurane*	*Desflurane*	*Sevoflurane*
 Arrhythmias	↑ Increased	—	—	—
 Dopamine + Norepinephrine + Epinephrine Sensitivity to catecholamines	↑ Increased	—	—	—
 Cardiac output	↓ Decreased	↓ Decreased to a lesser extent than *halothane*	↓ Decreased to a lesser extent than *halothane*	↓ Decreased to a lesser extent than *halothane*
 Blood pressure	↓ Dose dependent decreased	↓ Dose dependent decreased	↓ Dose dependent decreased	↓ Dose dependent decreased

 Respiratory reflexes	Inhibited	Initial stimulation	Initial stimulation	Inhibited
 Hepatic toxicity	Some risk	Low risk	Low risk	Low risk
 Renal toxicity	Low risk	Low risk	Low risk	Some risk

Trigger Malignant Hyperthermia

- Is a life-threatening condition, which creates a hypermetabolic state in patients with a hereditary skeletal muscle defect. It is most commonly caused by administering **halogenated anaesthetic agents (not Nitrous oxide)** or depolarizing neuro-muscular agents such as **Succinylcholine**. There is no way to pre-identify patients who may develop MH, but if the signs and symptoms develop, you should interfere.

- Duchenne dystrophy, myotonia, osteogenesis imperfecta, and central-core disease, are **susceptible to malignant hyperthermia**.

- **Treatment**: IV **dantrolene** (2.5 mg/kg), stop anaesthesia adminesteration and supportive treatment for each manifestation.

- Mortality rate is 50% .

- Any Question

Thank You