Inhalation anesthetics

is an agent that possess anaesthetic qualities that are administered by breathing through an anaesthesia mask or ET tube connected to an anaesthetic machine.

The substances that are brought into the body via the lungs and are distributed with the blood into the different tissues.
The main target of inhalation anesthetics is the brain.
Action of inhalation anesthetics

sedation, hypnosis, amnesia ~ supra spinal mechanism

immobilizing effect ~ spinal cord mechanism

inhalation agent action

enhance inhibitory synap transmission by modulation of GABA receptor

suppress excitatory synap transmission by reducing release and action of glutamate
Pharmacokinetics of Inhaled Anesthetics
FGF (fresh gas flow) is determined by the vaporizer and flowmeter settings.

$F_I$ (inspired gas concentration) is determined by (1) FGF rate; (2) breathing-circuit volume; and (3) circuit absorption.

$F_A$ (alveolar gas concentration) is determined by (1) uptake ($\text{uptake} = \lambda \cdot A \cdot V \times C(A-V) \times Q$); (2) ventilation; and (3) the concentration effect and second gas effect:
   a) concentrating effect
   b) augmented inflow effect

$F_a$ (arterial gas concentration) is affected by ventilation/perfusion mismatching.
Uptake and distribution

Inspired concentration (Fi)

concentration effect

second gas effect

alveolar ventilation ($V_A$)

Alveolar partial pressure of gas

solubility

cardiac output

gradient of tension in venous blood - alveolar ($P_V - P_A$)
Gas A is more soluble in fluid.
Gas B
Less soluble in fluid
Important characteristics of inhalation anes. which govern the anesthesia

- Solubility in the blood (blood : gas partition coefficient)
- Solubility in the fat (oil : gas partition coefficient)
blood : gas partition coefficient

- Is the measure of solubility in the blood
- Determine the rate of induction and recovery of inhalation anesthesia
- Lower the blood : gas partition coefficient – faster the induction and recovery: N2O
- Higher the blood : gas partition coefficient – slower the induction and recovery: halothane
BLOOD GAS PARTITION COEFFICIENT

- Alveolus
  - Nitrous oxide
  - Halothane
- Blood
  - Blood: gas partition coefficient
    - 0.47
- Brain
  - Rate of induction
    - Fast
    - Slow
Oil : gas partition coefficient

Is the measure of lipid solubility

Lipid solubility correlate strongly with the potency of the drug

Higher the lipid solubility – potent anesthetic e.g. halothane
Minimum alveolar concentration (MAC)

MAC value is a measure of inhalational anesthetic potency. It is defined as the minimum alveolar anesthetic concentration (% of the inspired air) at which 50% of patients not respond to a surgical stimulus.
Factors affecting the MAC

**INCREASE MAC**
- CHILDREN
- HYPERTHERMIA
- HYPERNATREMIA
- HYPERTHYROID
- CNS HYPO-OSMOLARITY
- ANXIETY
- DRUG: amphetamine
  - physostigmine

**DECREASE MAC**
- AGING
- HYPOTHERMIA
- HYPOTHYROID
- PREGNANCY
- ALCOHOLIC INTAKE
- CNS HYPER-OSMOLARITY
- DRUG: barbiturate
  - opioid
  - sedation
  - alpha-2-agonist
<table>
<thead>
<tr>
<th>Anesthetic</th>
<th>B:G PC</th>
<th>O:G PC</th>
<th>Features</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Halothane</td>
<td>2.3</td>
<td>220</td>
<td>PLEASANT</td>
<td>Arrhythmia, Hepatitis, Hyperthermia</td>
</tr>
<tr>
<td>Enflurane</td>
<td>1.9</td>
<td>98</td>
<td>PUNGENT</td>
<td>Seizures, Hyperthermia</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>1.4</td>
<td>91</td>
<td>PUNGENT</td>
<td>Widely used</td>
</tr>
<tr>
<td>Sevoflurane</td>
<td>0.62</td>
<td>53</td>
<td>PLEASANT</td>
<td>Ideal</td>
</tr>
<tr>
<td>Desfluran</td>
<td>0.42</td>
<td>23</td>
<td>IRRITANT</td>
<td>Cough</td>
</tr>
<tr>
<td>Inhalation Anesthetic</td>
<td>MAC value %</td>
<td>Oil: Gas partition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----------------------</td>
<td>-------------</td>
<td>--------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitrous oxide</td>
<td>&gt;100</td>
<td>1.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desflurane</td>
<td>7.2</td>
<td>23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sevoflurane</td>
<td>2.5</td>
<td>53</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoflurane</td>
<td>1.3</td>
<td>91</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Halothane</td>
<td>0.8</td>
<td>220</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Metabolism and elimination of inhaled anesthetics

Mostly of inhaled agents eliminated via exhalation

The rates of liver metabolism in the human body are approximately 10 to 20 percent for halothane, 2.5 percent for enflurane, about 0.2 percent for isoflurane, and zero percent for nitrous oxide.
Ideal Inhalation anesthetics

- provide a quick induction and emergence from anesthesia
- provide good analgesia, muscle relaxation
- quick changes and easy maintenance of anesthesia
- no side effects
- non-flammable, non-explosion
- not expensive
- free from pollution

Unfortunately, the real world of medicine doesn’t provide us with such an ideal agent
Inhalation anesthetic agents

Anesthetic gas:
- ethylene, nitrous oxide, xenon

Volatile agent
- ethers: Diethyl ether, Methoxypropane, Vinyl ether
- halogenated ether: Desflurane, Enflurane, Isoflurane, Methoxyflurane, Sevoflurane
- haloalkanes: Chloroform, Halothane, Trichloroethylene
Pharmacological Profile of Currently Used Inhaled Anesthetics

Isoflurane (Forane)

- produces a dose-dependent reduction in blood pressure due to peripheral vasodilatation.
- can cause coronary artery vasodilatation that might lead to coronary artery steal syndrome.
- Induction with isoflurane alone can lead to coughing and apneic periods.
- trigger malignant hyperthermia.
Sevoflurane (sevorane)

- undergoes temperature dependent degradation by baralyme and soda lime. Therefore, it cannot be used in low flow or closed systems anesthesia.

- Sevoflurane reacts with CO$_2$ absorbents to form Compound A that is metabolized to nephrotoxins and can lead to kidney damage.
Sevoflurane (sevorane) cont.

- produces a dose-dependent decrease in arterial blood pressure due to peripheral vasodilatation.
- rapid induction of anesthesia due to its low solubility in blood
- The low tissue solubility of sevoflurane results in rapid elimination and awakening.
- trigger malignant hyperthermia.
Pharmacological Profile of Currently Used Inhaled Anesthetics (cont)

Desflurane (Suprane)

- requires the use of electrically heated vaporizers.
- is a popular anesthetic for day case surgery
- induction and recovery is fast, cognitive and motor impairment are short lived
- produces a dose-dependent reduction in arterial blood pressure due to peripheral vasodilatation
- may cause coughing and excitation during induction
- trigger malignant hyperthermia.
Pharmacological Profile of Currently Used Inhaled Anesthetics (cont)

Nitrous oxide

- supports combustion
- is a potent analgesia but weak anesthetic
- Its low solubility results in rapid induction or awakening.
- does not cause hypotension and respiratory depression
Nitrous oxide (cont)

- long term use in excessive quantity associated with
  - vit B12 deficiency anemia due to reduced hemopoiesis
  - neuropathy, tinnitus, numbness in extremity
- chronic use in animal: teratogenic, fetotoxic
- irreversibly oxidize CO atom of vit B12 enzyme; methionine synthetase affect to myelin formation
Nitrous oxide diffuses into air containing cavities 34 times faster than nitrogen can leave that space. This can cause dangerous accumulation of volume and increase in pressure in closed spaces such as bowel, middle ear, pneumothorax, pneumocranium, pneumo-peritoneum, or cuffs of endotracheal tubes.

The main danger is the occurrence of hypoxemia so the maximum dose of nitrous oxide should not exceed 70 percent.
Nitrous oxide (cont)

Diffusion hypoxia

Outpouring of large volumes of nitrous oxide during the first 5 to 10 minutes of recovery from anesthesia may displace alveolar oxygen and produce diffusion hypoxia. This can be avoided by application of 100 percent oxygen during that time.