Inhalational Anesthetics

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• Pharmacokinetics

• Pharmacodynamics
Pharmacokinetics

= the study of the relationship between:
- a drug’s dose
- tissue concentration
- elapsed time

i.e. what the body does to a drug.
Pharmacodynamics

= the study of drug action, including toxic responses.

i.e. *what a drug does to the body.*
Overview

[Diagram showing a circuit involving heart, lungs, and brain with annotations F_I and F_A]
Factors affecting inspiratory concentration ($F_I$)

1. Fresh gas flow rate (mainly)
2. Volume of breathing circuit
3. Absorption by machine / circuit
Factors affecting alveolar concentration ($F_A$)

1. Uptake
2. Ventilation
3. Concentration
Factors affecting alveolar concentration ($F_A$)

**Uptake**

- Partial pressure difference
- Alveolar blood flow
- Solubility in blood
- Tissue uptake
Factors affecting alveolar concentration ($F_A$)

Tissue Uptake

- **Vessel-rich groups**
  brain / heart / liver / kidney / endocrine organs
  1st to take up & 1st to fill (limited capacity)

- **Muscle group**
  slower uptake (less well perfused)
  greater capacity (larger vol) - so uptake lasts hrs

- **Fat group**
  perfusion similar to muscle group
  much higher gas sol in fat, so huge total capacity

- **Vessel-poor group**
  insignificant uptake
  bone / ligaments / teeth / hair / cartilage
Factors affecting alveolar concentration ($F_A$)

**Ventilation**

- The lowering of alveolar partial pressure can be countered by $\uparrow$ alveolar ventilation.

- The effect of $\uparrow$ ventilation will be most obvious for soluble anesthetics, since they are more subject to uptake.
Factors affecting elimination.

1. Biotransformation - *minimal*
2. Transcutaneous loss - *insignificant*
3. **Exhalation** – *factors that speed induction also speed recovery*
Pharmacodynamics - Theories of Action

- No predominant structure-activity relationship.
- No single macroscopic site of action.

- Unitary hypothesis = all inhalational agents share a common mechanism action at molecular level – supported by Meyer-Overton rule.

- Meyer-Overton rule = anesthetic potency of inhalational anesthetics correlates directly with lipid solubility.
Pharmacodynamics -

Minimum Alveolar Concentration

$= F_A$ that prevents movement in 50% of patients in response to surgical incision

- MAC values roughly additive

- $\approx 1.3$ MAC prevents movement in 95%.

- 0.3-0.4 MAC associated with wakening.
## Factors affecting MAC

<table>
<thead>
<tr>
<th>↑ MAC</th>
<th>↓ MAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperthermia (if &gt; 42°C)</td>
<td>hypothermia (5-7% per degree)</td>
</tr>
<tr>
<td>HyperNa</td>
<td>hypoNa</td>
</tr>
<tr>
<td>chronic ETOH</td>
<td>hyperCa</td>
</tr>
<tr>
<td>↑ neurotransmitters</td>
<td>hypo-osmolality</td>
</tr>
<tr>
<td>acute amphetamine</td>
<td>metabolic acidosis</td>
</tr>
<tr>
<td>cocaine</td>
<td>P&lt;sub&gt;aO&lt;/sub&gt;&lt;sub&gt;2&lt;/sub&gt; &lt; 40 mmHg</td>
</tr>
<tr>
<td>MAOI / TCA</td>
<td>P&lt;sub&gt;aCO&lt;/sub&gt;&lt;sub&gt;2&lt;/sub&gt; &gt; 95 mmHg</td>
</tr>
<tr>
<td>levodopa</td>
<td>acute ETOH</td>
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<tr>
<td>ephedrine</td>
<td>chronic amphetamine</td>
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<tr>
<td></td>
<td>cannabinol</td>
</tr>
<tr>
<td>youth (highest @ 6mo)</td>
<td>LAs (except cocaine)</td>
</tr>
<tr>
<td>multiple GA's</td>
<td>Li / chlorpromazine / hydroxyzine</td>
</tr>
<tr>
<td></td>
<td>α&lt;sub&gt;2&lt;/sub&gt;-agonists</td>
</tr>
<tr>
<td></td>
<td>verapamil / Ca-channel blockers</td>
</tr>
<tr>
<td></td>
<td>α-methyldopa / reserpine / clonidine</td>
</tr>
<tr>
<td></td>
<td>opioids / barbs / benzo / ketamine</td>
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<tr>
<td></td>
<td>pancuronium</td>
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<tr>
<td></td>
<td>increasing age</td>
</tr>
<tr>
<td></td>
<td>pregnancy</td>
</tr>
<tr>
<td></td>
<td>anemia (HCT&lt;10%)</td>
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<tr>
<td></td>
<td>MAP &lt; 40 mmHg</td>
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</tbody>
</table>
Clinical Pharmacology - CNS

- Dose-dependent CNS depression

- Uncouple CMRO$_2$ & CBF
  - i.e. ↓ CMRO$_2$ / ↑ CBF (except N$_2$O)
Clinical Pharmacology - CV

- Hemodynamic depression:
  - halothane / desflurane ➔ ➔ contractility
  - isoflurane / sevoflurane ➔ vasodilation
Clinical Pharmacology - Pulm

- Respiratory depression:
  - $\downarrow \downarrow V_t$
  - $\downarrow$ respiratory rate
- Blunt CO$_2$ response - $\uparrow$ apneic threshold
- Abolish hypoxic ventilatory response
- Good bronchodilation (esp sevo / iso)
## Clinical Pharmacology

<table>
<thead>
<tr>
<th></th>
<th>Halothane</th>
<th>Isoflurane</th>
<th>Desflurane</th>
<th>Sevoflurane</th>
<th>N₂O</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓CMRO₂ most</td>
<td>↓CMRO₂</td>
<td>↑HR most</td>
<td></td>
<td>↑CMRO₂</td>
<td></td>
</tr>
<tr>
<td>Cerebrovasodilation – prevent with hyperventilation</td>
<td>Theoretical coronary steal – avoid hypoten / brady</td>
<td>CO with dessicated baralyme</td>
<td>Nephrotoxicity: metabolized $\rightarrow$ Fl Avoid in renal failure.</td>
<td>Compound A: $\triangleright$ dry baralyme $\downarrow$ lowflow $\uparrow$ T $\uparrow$ hi concentration</td>
<td></td>
</tr>
<tr>
<td>Sensitizes heart to catechol.s</td>
<td>Maintains hepatic $O₂$ supply best</td>
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<tr>
<td>Hyperthermia w/ MAOIs (like MH)</td>
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- Potentiate non-depolarizing nmb
- MH triggers
- “Halothane” hepatitis - multiple exposures / family hx - autoimmune
- Avoid in pregnancy
- Depresses myocardial activity, but sympathomimetic (beware CAD)
- Maintains hepatic $O₂$ supply best!
- Compound A: $\triangleright$ dry baralyme $\downarrow$ lowflow $\uparrow$ T $\uparrow$ hi concentration
- $\nabla$ muscle relaxation
- PONV ?