• Q1. The rate of increase in the alveolar concentration of a volatile anesthetic relative to the inspired concentration \( (F_A/F_I) \) plotted against time is steep during the first moments of inhalation with all volatile anesthetics. The reason for this observation is that…

• Q2. Cardiogenic shock has the greatest impact on the rate of increase in \( F_A/F_I \) for which volatile anesthetic?

• Q3. Which of the following maneuvers would NOT increase the rate of an inhalation induction?

A. Increasing alveolar ventilation
B. Substitution of desflurane for isoflurane
C. Overpressurizing
D. Carrying out the induction in Dallas vs. Denver
E. Placement of patient on an inotrope infusion
Inhalation Pharmacokinetics

FGF: (Fresh gas flow) determined by vaporizer and flow meters

$F_I$: (Inspired gas concentration) determined by FGF, circuit volume, circuit absorption

$F_A$: (Alveolar gas concentration) determined by uptake, ventilation, concentration and 2nd gas effect

$F_a$: (Arterial gas concentration) effected by V/Q mismatching
Machine to the CNS

- Fresh gas + agent from vaporizers leave machine and enters circuit
- Concentration decreases as it mixes with gas and is absorbed
- Slowly rises as the circuit compartment equilibrates with FGF
- Concentration of anesthetic gas leaving the circuit (not machine) is $F_i$
Machine to the CNS

- In the lungs, dead space + alveoli gas further dilutes circuit gas
- Fractional concentration of gas in the alveoli is $F_A$
- Anesthetic then passed across alveolar-capillary membrane
- Depends on anesthetic concentration and solubility
- Further diluted in the blood and is diffused to various tissues
- Dependent on various gas/tissue solubility constants (brain:blood, etc)
Machine to the CNS

- Three physiological tissue groups
  - Vessel rich (brain, heart, liver, kidneys, endocrine organs)
  - Muscle
  - Fat
- Anesthetic delivered to VRG rapidly due to high blood flow
- Muscle and fat also receiving anesthetics but has little influence on emergence in cases < 4 hours

<table>
<thead>
<tr>
<th>Group</th>
<th>% Body Mass</th>
<th>% Cardiac Output</th>
<th>Perfusion cc/min/100gm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vessel Rich</td>
<td>10</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Muscle</td>
<td>50</td>
<td>19</td>
<td>3</td>
</tr>
<tr>
<td>Fat</td>
<td>20</td>
<td>6</td>
<td>3</td>
</tr>
</tbody>
</table>
\[ \text{F}_a / \text{F}_i \text{ Ratio} \]

- Initial rise is similar in all gases due to lack of uptake into the blood
- There is also dilution with existing gas in the lungs, thus low FRC and increasing \( V_A \) (Alveolar ventilation) speeds induction
- Highly soluble gases experience much more uptake, thus the much slower rise in \( \text{F}_A / \text{F}_I \)
Factors affecting $F_I$

- Fresh gas flow rate
- Volume of breathing system
- Absorption by the machine and circuit
- This is why your monitor never reads the same as your vaporizer dial
- Higher rates, smaller breathing system volumes and lower absorption results in $F_I$ being closer to fresh gas concentration.
Factors affecting $F_A$

- Uptake
- Ventilation
- Concentration
Uptake

- \( V_B = \delta_{b/g} \times Q \times \frac{(P_A - P_v)}{P_B} \)
- \( V_B = \) Blood uptake
- \( \delta_{b/g} = \) blood:gas coefficient
- \( Q = \) cardiac output
- \( P_A = \) alveolar partial pressure
- \( P_v = \) mixed venous partial pressure
- \( P_B = \) barometric pressure

Increasing uptake DECREASES the rate in which \( F_A \) increases
Cardiac Effects

- Increasing cardiac output increases the amount of blood flowing through the lungs
- This increases the uptake
- Results in slowing the rise in $F_A/F_I$
- This is why gas inductions are FASTER in patients with heart failure.
- This overall effect is bigger on agents that are MORE soluble
- The rate of rise for insoluble agents is almost independent of cardiac output
Ventilation

- Uptake lowers the alveolar partial pressure
- Can be countered by increasing alveolar ventilation
- This effect is more obvious with the more soluble anesthetics since they experience more uptake
Concentration

- Effects of uptake also countered by increasing concentration
- Increasing concentration also increases the rate of rise of $\frac{F_A}{F_I}$
- Concentration Effect
- Augmented inflow effect
- Effect greatest with nitrous because we can give high concentrations of it
- Explains why nitrous is higher on the curve than des even though it is less soluble
**Concentration Effect**

- Assume 50% uptake
- 20% gas concentration = 20 parts gas + 80 parts air
- After uptake, there will be 10 parts gas + 80 parts air leftover
- 11% concentration
- 80% gas concentration = 80 parts gas + 20 parts air
- After uptake, there will be 40 parts gas + 20 parts air
- 67% concentration
- So 4x more gas leads to 6.1x increase in concentration
Augmented Gas Inflow

• Taking previous example, after uptake the gas volume is replaced by gas from the circuit

• **Example 1**: After uptake there are 10 parts gas and 80 parts air. The 10 parts that were absorbed are replaced by the 20% circuit concentration. After replacement there are 12 parts gas and 88 parts air. Results in 12% concentration vs. 11% (without augmentation)

• **Example 2**: After uptake there are 40 parts gas and 20 parts air. The 40 parts absorbed are replaced with 80% circuit gas. Results in 72 parts gas and 28 parts air.
2nd Gas Effect

- Applies to situations where two gases are given simultaneously (inducing with sevo + nitrous)
- The uptake of the 2nd gas (nitrous) will increase the concentration of the first gas (sevo)
- **Example:** 2 parts sevo + 70 parts nitrous + 28 parts oxygen. Assume uptake of nitrous is 50%. After uptake, 2 parts sevo, 35 parts nitrous, 28 parts oxygen. Sevo concentration now 3.1% (2/65)

*This effect is theoretical only and has little clinical significance*
Question 1

The rate of increase in the alveolar concentration of a volatile anesthetic relative to the inspired concentration ($F_A/F_I$) plotted against time is steep during the first moments of inhalation with all volatile anesthetics. The reason for this observation is that…

A. Volatile anesthetics decrease blood flow to the liver
B. There is minimal anesthetic uptake from the alveoli into pulmonary venous blood
C. Volatile anesthetics initially increase cardiac output
D. The volume of the breathing circuit is small
E. Volatile anesthetics reduce alveolar ventilation
Question 1

**ANSWER B**

Remember that $\text{Uptake} = \delta_{b/g} \times Q \times [(P_A - P_v) / P_B]$

Initially there is no volatile anesthetic in the alveoli to create the pressure gradient necessary for uptake. This is why all volatiles rise similarly at the start.

The liver has nothing to do with rate of induction

Increasing cardiac output increases uptake. This slows the rate in which alveolar gas concentration rises.

Reduction in alveolar ventilation also slows the rate in which gas concentration rises.
Question 2

Cardiogenic shock has the greatest impact on the rate of increase in $F_A/F_I$ for which volatile anesthetic?

A. Isoflurane
B. Desflurane
C. Sevoflurane
D. Nitrous oxide
E. The impact is the same for all agents
Question 2

**ANSWER A**

Changes in cardiac output have little impact on insoluble agents but profound effects on highly soluble ones. Remember that uptake is dependent on cardiac output so lowering cardiac output will decrease uptake, and thus speed induction.
Question 3

Which of the following maneuvers will decrease the rate of an inhalation induction?

A. Increasing alveolar ventilation
B. Substitution of sevoflurane for isoflurane
C. Over pressurizing
D. Carrying out the induction in Dallas vs. Denver
E. Placement of patient on an inotrope infusion
Question 3

**ANSWER E**

Remember that Uptake = $\delta_{b/g} \times Q \times [(P_A - P_v) / P_B]$

Increasing alveolar ventilation speeds induction because it increases the amount of anesthetic coming from the machine to replace absorbed gas.

Over pressurizing speeds induction via the concentration effect.

Inductions are quicker with less soluble agents.

Lower altitudes (high barometric pressure) decrease uptake of gas, thereby increasing speed of gas inductions.

Inotropes increase cardiac output, which increases uptake, which decreases speed of gas inductions.
Various Properties

<table>
<thead>
<tr>
<th>Agent</th>
<th>Mac %</th>
<th>Mac &amp; in &gt; 65 year old</th>
<th>Blood/Gas Coefficient</th>
<th>Vapor Pressure @ 20°C</th>
<th>Boiling Point °C</th>
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<tbody>
<tr>
<td>Nitrous</td>
<td>104</td>
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(From Barash 5th edition, pg 386)