Clinical and Economic Advantage of Low Blood/Gas Solubility

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Objectives - Attendees will learn the following:

1. Blood/Gas Solubility is the key to understanding uptake of volatile anesthetics.

2. Low blood/gas solubility makes alveolar tension follow inspired tension closely and facilitates clinical control including fast wake up.

3. Low blood/gas solubility facilitates low fresh gas flow and thereby reduces cost.
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Low blood/gas solubility (solubility) is an important property of the new inhalation anesthetics. Indeed, the pharmacokinetics of inhalants is pivotally dependent upon this physical property. And, understanding and using pharmacokinetics is crucial to clinical practice, helping or hurting our control of anesthesia depth. Pharmacokinetics explains what goes on as an inhaled agent progresses from the vaporizer to the patient's brain.

The quantitative effect of solubility on E/I plateau height, overpressure ratio, wake up time, and lung wash depends on the path the agent traverses as it moves from vaporizer to brain. The path of anesthetic agent is shown in Figure 1, the Gas Man Picture

Figure 1. Gas Man Picture represents the structure and behavior of the pharmacokinetic model for volatile anesthetics.
The Alveolar Tension Curve in Response to a Step Inspired Change

In Figure 1, anesthetic travels the path from vaporizer (DEL) to breathing circuit (CKT), to lungs (ALV), to arterial blood (ART), and to tissues (VRG [e.g., brain, heart], MUS, FAT). Anesthetic tension or partial pressure moves along this path and tensions equalize in locations or compartments, eventually. Concentration varies inversely with solubility, leads to confusion, so the term concentration is avoided here.

Each compartment along the anesthetic path imparts a predictable delay and/or a loss in anesthetic tension. The end result is a system that behaves in a predictable and measurable manner. Some choices of agent, fresh gas flow, and ventilation support control while others impede it. Because computer simulation data is similar to that collected in patients we will rely here on simulation to convey the important points.

The alveolar tension curve (ATC) describes the alveolar tension response to a step change in inspired anesthetic tension. The ATC has several components - Initial rise, plateau, knee, and tail.

The initial rise of the ATC is an exponential curve with asymptote = inspired tension and time constant tau (τ). Tau = ratio of lung volume (functional residual capacity or FRC) to lung flow (alveolar ventilation or VA). Thus, \( \tau = \frac{\text{Volume}}{\text{Flow}} = \frac{\text{FRC}}{\text{VA}} = 2 \text{ L} / (4 \text{ L/min}) = 0.5 \text{ minutes} \). The relationship is \( \frac{\text{Alveolar}}{\text{Inspired}} = 1 - e^{-t/\tau} \). Variations in FRC or VA lead to variations in tau.

The plateau of the ATC is formed by the effect of cardiac output removing drug from the alveoli. Alveolar Knee height is determined by the ratio of removal to delivery; the product of cardiac output and solubility removes while alveolar ventilation delivers. If we call the removal ratio \( R = \frac{\text{CO}}{\lambda} / \text{VA} \), then the alveolar plateau height is \( \frac{\text{A}}{\text{I}} = 1/(1 + R) \). When lung performance is perfect, arterial tension equals alveolar tension. Abnormalities of lung performance are dead space and shunt; these will not be considered here. The difference in plateau height is exclusively determined by the difference in blood/gas solubility. Solubility is the key to the kinetics of volatile anesthetics.

The knee of the ATC is formed as tissues tensions rise and anesthetic returned in mixed venous blood adds to that already in the alveoli, transforming the plateau into the knee of the ATC.

The tail of the ATC is formed from what would have been the knee as tissue tensions rise in successive compartments. Tissue tensions rise successively in VRG, Muscle, and Fat. VRG is the term used for fast tissues which have high perfusion compared with their volume. They are called the vessel-rich group (VRG) and include Brain, Heart, Kidneys, and Liver. Muscle is large and perfused less and comprises the next tissue group to equalize with the arterial blood. Fat appears large because of its high solubility and therefore has a slow rise in anesthetic tension. Fat tension never reaches significant levels during anesthesia of less than 12 hours duration.
Figure 2. ATCS (Alveolar Tension Curves) for desflurane (Des), sevoflurane (Sev), isoflurane (Iso), and halothane (Hal). Curves are from patients\textsuperscript{3} and numeric values are from computer simulation\textsuperscript{1}.

Low solubility causes alveolar tension to approach inspired tension closely. **Low blood/gas solubility makes alveolar tension follow inspired tension closely and facilitates clinical control.** When deepening anesthesia this averts the need for inspired overpressure to produce a high alveolar level or allows an achievable inspired level to produce high alveolar level and soon brain level. **The single breath induction with sevoflurane exemplifies the effect of low solubility on anesthesia induction; time required is < 1 minute\textsuperscript{3}.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Solubility</th>
<th>Plateau</th>
<th>Overpressure\textsuperscript{4}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hal</td>
<td>2.47</td>
<td>0.24</td>
<td>4.1</td>
</tr>
<tr>
<td>Iso</td>
<td>1.30</td>
<td>0.39</td>
<td>2.6</td>
</tr>
<tr>
<td>Sev</td>
<td>0.67</td>
<td>0.55</td>
<td>1.8</td>
</tr>
<tr>
<td>Des</td>
<td>0.42</td>
<td>0.66</td>
<td>1.5</td>
</tr>
</tbody>
</table>

**Low solubility facilitates wake up** because alveolar tension follows inspired tension closely and arterial blood with low anesthetic tension perfuses the brain which quickly achieves the same low tension. Wake up then occurs.

**Low solubility facilitates low fresh gas flow and thereby reduces cost.** In a standard partial-rebreathing circuit, when fresh gas flow is less than minute ventilation, expired gas forms a part of inspired gas. The closer expired tension is to inspired tension, the further fresh gas flow can be reduced to achieve the required inspired tension. Low solubility thus reduces cost in two ways. Fresh gas flow can be lower and still produce the required inspired tension. Required inspired tension is lower because alveolar tension is close to inspired tension. **Low flow and closed circuit desflurane anesthesia exemplify the cost savings**
achieved by low solubility. Closed circuit desflurane costs $1.80 (US) per hour\textsuperscript{1}. 
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Objectives - Readers and Lecture Attendees will learn the following:

1. Blood/Gas Solubility is the key property that determines the kinetics of volatile anesthetics.

2. Low blood/gas solubility makes alveolar tension follow inspired tension closely and facilitates clinical control including fast wake up.

3. Low blood/gas solubility facilitates low fresh gas flow and thereby reduces cost.