Kinetics of Inhaled Anesthetic Agents

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Dr. James Philip has performed funded research on Isoflurane, Sevoflurane, and Desflurane. He is often supported by the manufacturers of these drugs to teach about these drugs. Gas Man® and Med Man Simulations is a nonprofit charitable organization. The original Kety (Anesthesiology 1950) approach is used first, followed by a repeat using Gas Man®
Kinetics of Inhaled Anesthetic Agents

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that distributes Gas Man®, worldwide
Gas Man® Picture shows the anesthesia path
Gas Man® Picture shows path of anesthetic tension forward,
and back to lungs (alveoli)
and back to breathing circuit
I will use this picture for clarity
Focus on the Alveolar Tension Curve
Alveolar Tension Curve

Alveolar response to an Inspired Step

The time course of alveolar tension = $P_A$
in response to a step change in
inspired tension = $P_I$

$P_I \rightarrow P_A$
Alveolar response to a step change in inspired agent
Inspired Step

A / I

1.0

0.0

0 1 2 3 minutes (time)
Pure Lung wash-in
Without Uptake into Blood

is the same as
Cardiac Output = zero ( CO = 0) or
Drug solubility in blood = zero (λ = 0)
Call this Zerothane
Alveolar response to a step change in inspired Zerothane is an exponential curve.
Time constant, $\tau$ (tau), is the time required to achieve 63% of the final value.*

$\tau = 0.5 \text{ min}$

* Derive in long course
Universal Truth for linear fully-mixed systems

$$\tau = \frac{V}{F}$$

$\tau$ = time constant, time for exponential curve to reach 63% of completion

$V$ = effective volume of the compartment

$F$ = effective flow into the compartment

Effective = actual x solubility
Now, add uptake into blood

Uptake into blood produces an Alveolar Tension Plateau
Inspired Tension

Pure Lung wash-in Without Uptake into Blood
Alveolar Tension Plateau

Plateau is produced by Removal by Blood

Inspired

0 1 2 3 minutes (time)
Alveolar Tension Plateau

A / I

Inspired

Delivery

Removal

Alveolar Plateau

0.0

0 1 2 3

minutes (time)
Alveolar Tension Plateau

Inspired

Delivery = $V_A$

Removal = $CO \cdot \lambda$

0 1 2 3 minutes (time)
The graph shows the alveolar plateau times for various anesthetics:

- **Hal**
- **Enf**
- **Sevo**
- **Iso**
- **N₂O**
- **Des**

The y-axis represents the A/I ratio, while the x-axis shows time in minutes. The graph illustrates the time it takes for each anesthetic to reach its alveolar plateau.
Alveolar Plateau Heights

- Zerothane
- Infinithane

A / I

0.0

1.0

0

3 minutes (time)

Ht

1

1.24

1.00

0.54

0.66

0.38

0.24

0.00
Alveolar Plateau Heights and solubilities

<table>
<thead>
<tr>
<th></th>
<th>Ht</th>
<th>λ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zerothane</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Infinthane</td>
<td>.00</td>
<td>Inf.</td>
</tr>
</tbody>
</table>

- Hal: 1.3
- Enf: 2.4
- Iso: .38
- Sevo: .54
- N₂O: .67
- Des: .66
Alveolar Plateau Height Equation

\[ \text{Plateau Ratio} = \frac{A}{l} = \frac{1}{1 + \frac{CO \lambda}{V_A}} \]

Zerothane

<table>
<thead>
<tr>
<th>Drug</th>
<th>Ht</th>
<th>( \lambda )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Des</td>
<td>.66</td>
<td>.42</td>
</tr>
<tr>
<td>N(_2)O</td>
<td>.54</td>
<td>.67</td>
</tr>
<tr>
<td>Sevo</td>
<td>.38</td>
<td>1.3</td>
</tr>
<tr>
<td>Iso</td>
<td>.24</td>
<td>2.4</td>
</tr>
<tr>
<td>Enf</td>
<td>.24</td>
<td>2.4</td>
</tr>
<tr>
<td>Hal</td>
<td>.24</td>
<td>2.4</td>
</tr>
</tbody>
</table>

A / I

0.0

1.0

0.0

1.0

3 minutes (time)

Inf.
Venous Return brings anesthetic back to alveoli
Venous Return converts Plateau

Plateau produced by Removal by Blood

Inspired

Alveolar

Plateau

0.0

1.0

A / I

0

1

2

3 minutes (time)
Venous Return converts Plateau into Tail
Venous Return converts Plateau into Tail

VRG = Brain, etc.
Alveolar Tension Curve sections named

- Inspired
- Initial Rise
- Knee
- Plateau
- Tail

3 minutes (time)
Next, Real drugs and real curves
Real drugs and real curves

Yasuda & Eger, 1991

Des
Sev
Iso
Hal

\[ \frac{P_A}{P_I} \]

Minutes of administration

30

1.0

A / I
What is the similarity among these curves?

Des
Sev
Iso
Hal

\[ \frac{P_A}{P_l} \]

Minutes of administration

30
Initial rise follows the same Zerothane curve

Des
Sev
Iso
Hal

$\frac{P_A}{P_I}$

Minutes of administration

30
What is the difference between these curves?
Plateau Height is the only kinetic difference!
And, plateau height is determined by $\lambda$.
Blood / Gas Solubility

Dominates Inhalation Kinetics

Determines

how closely

Expired Tension

approaches

Inspired Tension

in the first few minutes

of anesthesia
This was
The Alveolar Tension Curve
in its first few minutes
A structure-behavior model shows this

Flows link locations
A structure-behavior model shows this
Gas Man® model and math appear to be correct for induction and emergence.

(A) **Wash-in**
360 minutes = 6 hr
15 minutes

(B) **Wash-out**
after breathing 1 MAC for 1 hr.

(C) Wash-out
after breathing 1 MAC for 2 hr.

(D) Wash-out
after breathing 1 MAC for 4 hr.

(E) Wash-out
after breathing 1 MAC for 12 hr.

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**Bouillon T, Shafer S. Editorial**
– Hot air or full steam ahead?
An empirical pharmacokinetic model of potent inhaled agents.
*Brit J. Anaes.*
Eger & Shafer used Gas Man® to explore Context-sensitive Decrement Times.

Emergence from shorter anesthetics (0.5 - 4 hrs)

Gas Man® simulations

High flow vs low flow for control of depth and control of cost
Bolus up and bolus down with Vaporizer, FGF; Insp, Exp
to achieve rapid change in brain level
Vital Capacity Induction
Important Gas Man® teaching

Brain Delay after an End-Tidal change

~ 3 minutes, for all agents

(Brain/Blood Solubility ~ 1.5, all agents)

Use Trend Graph of ET Agent to see this in OR
8/15/2011 6 hour case

2%
Gas Man® and Agent Monitor

Gas Man® does the hard part
Predict how long it will take ET to get to MAC_{awake}
Your Gas Monitor shows you the easy part
Once ET = 0.33 MAC, brain will get there in 3 minutes
Learn Kinetics

In OR: Observe Vaporizer Setting, Inspired, Expired, Depth
In Simulation: Experiment with many possibilities
Download Gas Man® via Department Intranet Site
www.bwhanesthesia.org / Education /Gas Man download
Thank you