

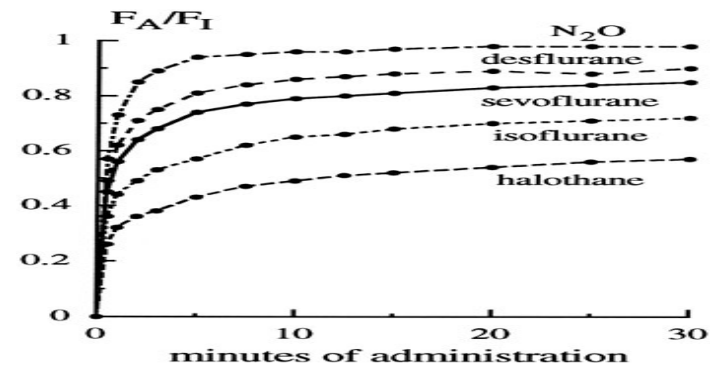
Inhalational Agents

Pharmacokinetics

- The pharmacokinetics of inhalational agents is divided into four phases
 - Absorption
 - Distribution (to the CNS)
 - Metabolism (minimal)
 - Excretion (minimal)
- The ultimate goal is to establish a particular partial pressure of an agent in the lungs
 - This partial pressure will equilibrate with the CNS tissue to produce an anesthetized state
- At equilibrium the following applies
$$P_{\text{CNS}}=P_{\text{blood}}=P_{\text{Alveoli}}$$

Uptake and Distribution

- Inhalational anesthetic uptake is commonly followed by the ratio of fractional concentration of alveolar anesthetic to inspired anesthetic (F_A/F_I)
- Uptake into the bloodstream is the primary determinant of F_A
- The greater the uptake (in blood), the slower the rate of rise of F_A/F_I
 - Uptake is proportional to tissue solubility
 - The gases with the lowest solubilities in blood (i.e. desflurane) will have the fastest rise in F_A/F_I
 - They also have the fastest elimination
 - Rate of rise of F_A/F_I is proportional to clinical effect (i.e. the faster the rate of rise, the faster the induction and also elimination)



The rise in alveolar (F_A) anesthetic concentration toward the inspired (F_I) concentration is most rapid with the least soluble anesthetics, nitrous oxide, desflurane, and sevoflurane. It rises most slowly with the more soluble anesthetics, for example, halothane. All data are from human studies. (Adapted from Yasuda N, Lockhart SH, Eger EI II *et al*: Comparison of kinetics of sevoflurane and isoflurane in humans. *Anesth Analg* 72:316, 1991; and Yasuda N, Lockhart SH, Eger EI II *et al*: Kinetics of desflurane, isoflurane, and halothane in humans. *Anesthesiology* 74:489, 1991.)

Factors That Increase or Decrease the Rate of Rise of F_A/F_I

•INCREASE	•DECREASE	
Low λ_B	High λ_B	The lower the blood:gas solubility, the faster the rise in F_A/F_I
Low Q	High Q	The lower the cardiac output, the faster the rise in F_A/F_I
High \dot{V}_A	Low \dot{V}_A	The higher the minute ventilation, the faster the rise in F_A/F_I
High $(P_A - P_v)$	Low $(P_A - P_v)$	At the beginning of induction, P_v is zero but rises rapidly (thus $[P_A - P_v]$ falls rapidly) and F_A/F_I increases rapidly. Later, during induction and maintenance, P_v rises more slowly so F_A/F_I rises more slowly.

Parameters as described in Equation 15-16: λ_B , blood solubility; Q , cardiac output; \dot{V}_A , minute ventilation; P_A , P_v , pulmonary arterial and venous blood partial pressure. (Clinical Anesthesia 5th Edition; Barash, P.; Lippincott Williams and Wilkins; 2006)

Pharmacodynamics

- All inhalational agents decrease CMO_2 and increase CBF (via direct vasodilatation)
 - Increases in CBF can in turn increase ICP
- All agents cause a dose-related decrease in blood pressure
- All agents produce muscle relaxation
- The older inhalational agents (halothane, enflurane) cause decreases in myocardial contractility
 - The newer agents have little to no effect
- All inhalational agents produce a dose-dependent depression of the ventilatory response to hypercarbia and hypoxia

Nitrous Oxide

- Low potency (MAC 104%)
- Insoluble in blood
 - Facilitates rapid uptake and elimination
- Commonly administered as an anesthetic adjuvant
- Does not produce skeletal muscle relaxation
- Can potentially contribute to PONV
- Can diffuse into air filled cavities and cause expansion of air filled structures (pneumothorax, bowel, middle ear, ET tube balloons, etc.)
 - Often contraindicated in these settings

Isoflurane

- Highly pungent
- Second most potent of the clinically used inhalational agents (MAC 1.2%)
- Preserves flow-metabolism coupling in the brain
 - Highly popular for neuroanesthesia
- Has been implicated for causing "coronary steal"
 - Dilation of "normal" coronary arteries causing blood to be diverted away from maximally dilated, stenotic vessels to vessels with more adequate perfusion
- Causes vasodilation
 - Decreases BP
 - Increases CBF (usually seen at 1.6 MAC)
 - Minimal compared to halothane
 - Increases ICP (usually at above 1 MAC; short lived)
 - Minimal compared to halothane

Sevoflurane

- Half as potent as isoflurane (MAC 1.8%)
- Quick uptake and elimination
- Sweet smelling, non-pungent
- Quick uptake and sweet smell make this agent very popular for inhalational induction
- Potent bronchodilator
- Can form CO in dessicated CO₂ absorbent
 - Can cause fires
- Forms Compound A in CO₂ absorbent
 - Recommended to keep fresh gas flows >2 L/min

Desflurane

- Blood:gas solubility coefficient equal to N₂O
- Very quick uptake and elimination
- Low potency (MAC 6.6%)
- High vapor pressure
 - Must be stored in a heated, pressurized vaporizer
- Very pungent
 - Can cause breath-holding, bronchospasm, laryngospasm when administered to an awake patient via face mask
- Can form CO in dessicated CO₂ absorbent
- Can cause an increased sympathetic response (tachycardia, hypertension) when inspired concentration is increased rapidly

References

1. Clinical Anesthesia 5th Edition; Barash P., Cullen B., Stoelting R.; Lippincott Williams and Wilkins, 2006
2. Miller's Anesthesia 6th edition; Miller R.; Churchill Livingstone, 2005
3. The Pharmacology of Inhalational Anesthetics 3rd edition; Eger E., Eisenkraft J., Weiskopf R.; Library of Congress, 2003
4. Yasuda N, Lockhart SH, Eger E *et al*: Comparison of kinetics of sevoflurane and isoflurane in humans. *Anesth Analg* 72:316, 1991
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