General Anesthesia

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General Anesthesia

- **Definition:**

  Loss of memory, awareness and pain sensation during a surgical procedure, together with loss of reflexes, and skeletal muscle relaxation.

Features of an Ideal General Anesthetic

- Rapid loss of awareness and memory.
- Analgesia to limit reflexes.
- Minimal and reversible influence on vital signs.
- Skeletal muscle relaxation.
- Operating room safety.
- Rapid emergence or recovery.

Balanced Anesthesia:

- Multi drug approach to managing the patient's anesthetic needs.

Phases of Anesthesia

- Induction
- Maintenance
- Emergence = Recovery

Stages of Anesthesia

Classically Described for Ether Anesthesia:

. **Stage I: " Analgesia"**

Amnesia and euphoria.

. **Stage II: "Excitement"**

Delirium and combative behavior.

. **Stage III: "Surgical Anesthesia"**

Anesthesia, regular respiration and decreasing eye movements.

. **Stage IV: "Medullary Depression"**

Respiratory and cardiac depression and arrest and no eye movements.

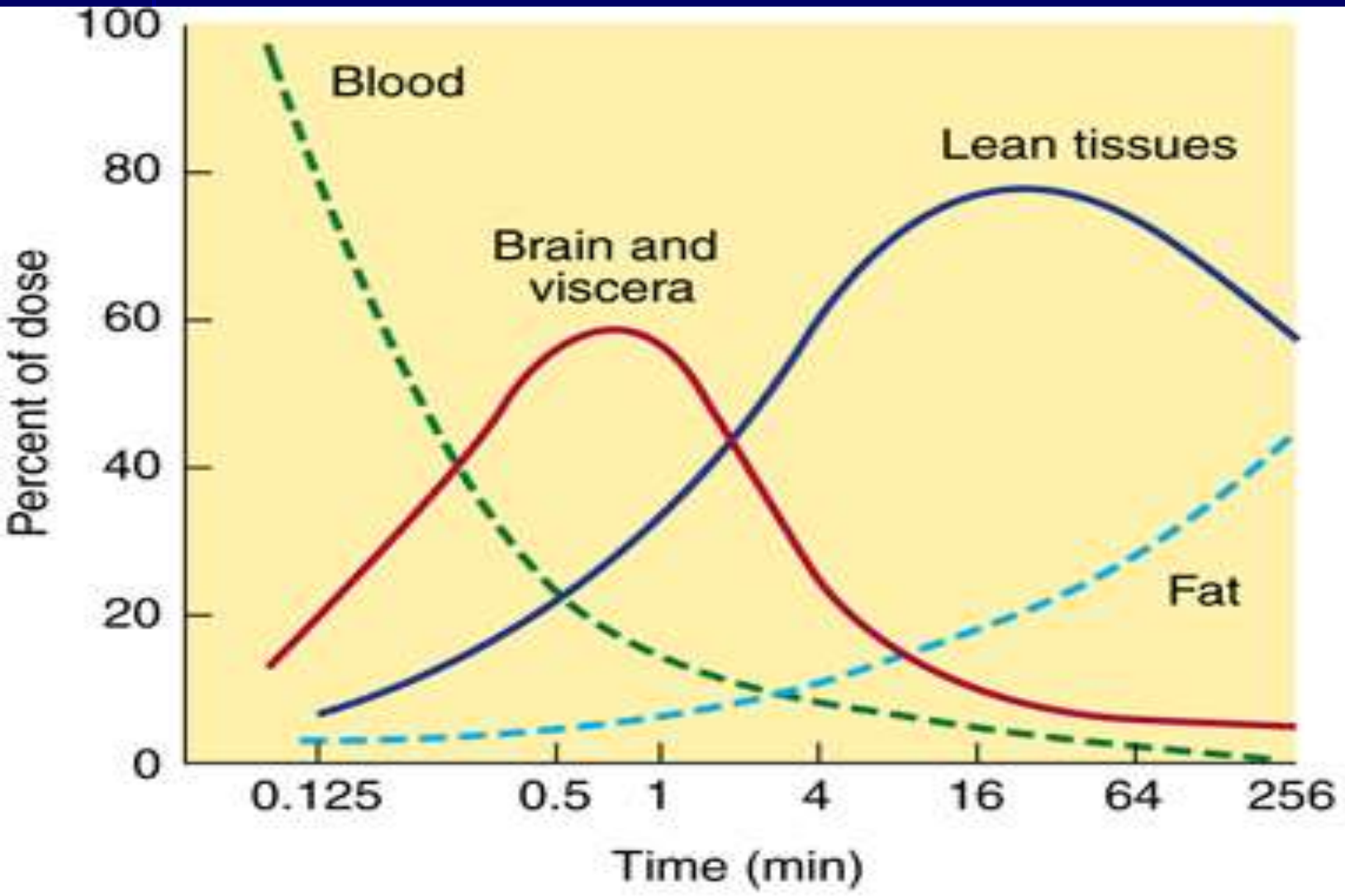
Preanesthetic Medications " Premedication"

- Opioids
- Benzodiazepines
- Antimuscarinics
- Antihistamines
- Antiemetics

Intravenous Anesthesia

- **Highly lipid soluble.**
- **Very short $t_{1/2\alpha}$.**
- **Slowly metabolized & excreted so termination of action depends on: Redistribution** (recovery times are similar despite remarkable differences in metabolism)
- **Repeated administration leads to delayed awakening.**
- **Computer assisted i.v. administration (*Total Intravenous Anesthesia TIVA*).**

Redistribution of thiopental after IV bolus administration.



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Intravenous Anesthesia

General Uses:

- **Ideally suitable for Induction.**
- **Maintenance of short procedures.**
- **In combination to produce balanced anesthesia.**
- **Supplement inhalational anesthesia.**

Ultra Short Acting Barbiturates

- **Thiopental** ------- most popular i.v. agent for induction
- **Methohexital** -------- very short acting, less ppt.
- Weak acids, can precipitate .
  - If given in an artery?
- Patients may react to painful stimuli but:
  - Unaware, Do not remember.
- Cardiorespiratory depressants

Benzodiazepines

- **Diazepam** --- viscous formulation, so can precipitate.
- **Midazolam** --- aqueous , t½ 2hrs.
- **Lorazepam** --- long t½, viscous.
- All do not depress cardiorespiratory function.

- ***Flumazenil,*** ***is the antidote for overdose.***

Ketamine

- ***Dissociative Anesthesia:***
  - Profound analgesia, amnesia and superficial sleep.
  - Patient appears awake and reactive but does not respond to sensory stimuli.
- Blocks glutamic acid at NMDA receptor
- Children , IM
- Ambulatory conditions ---used in military.

Ketamine

- ***Catatonia(جامود)*: a state of apparent unresponsiveness to external stimuli in a person who is apparently awake, with mild increase in muscle tone, eyes opened and nystagmus(رأرأة العين).**
- **Pharyngeal and laryngeal reflexes are maintained resulting in laryngospasm, cough, salivation and vomiting.**
- **Maintains cardiovascular function.**

Ketamine

- May evoke excitatory and hallucinatory phenomena during emergence, so needs a quiet recovery room.
- Might also cause shivering, tachycardia, increased intracranial and intraocular pressures.

Propofol

- Most popular IV anesthetic, replaced thiopental.
- Available as an emulsion, which is rapidly metabolized.
- Not analgesic but lowers dose of opioid needed.
- ICU patients: prolonged sedation in ventilated patients.
- Also used in balanced anesthesia and TIVA.
- Produces euphoria--- good for induction.
- Anti-emetic, better postoperative period.
- Pain at site of injection, muscle tremors.

Narcotics

Suitable for cardiac surgery.

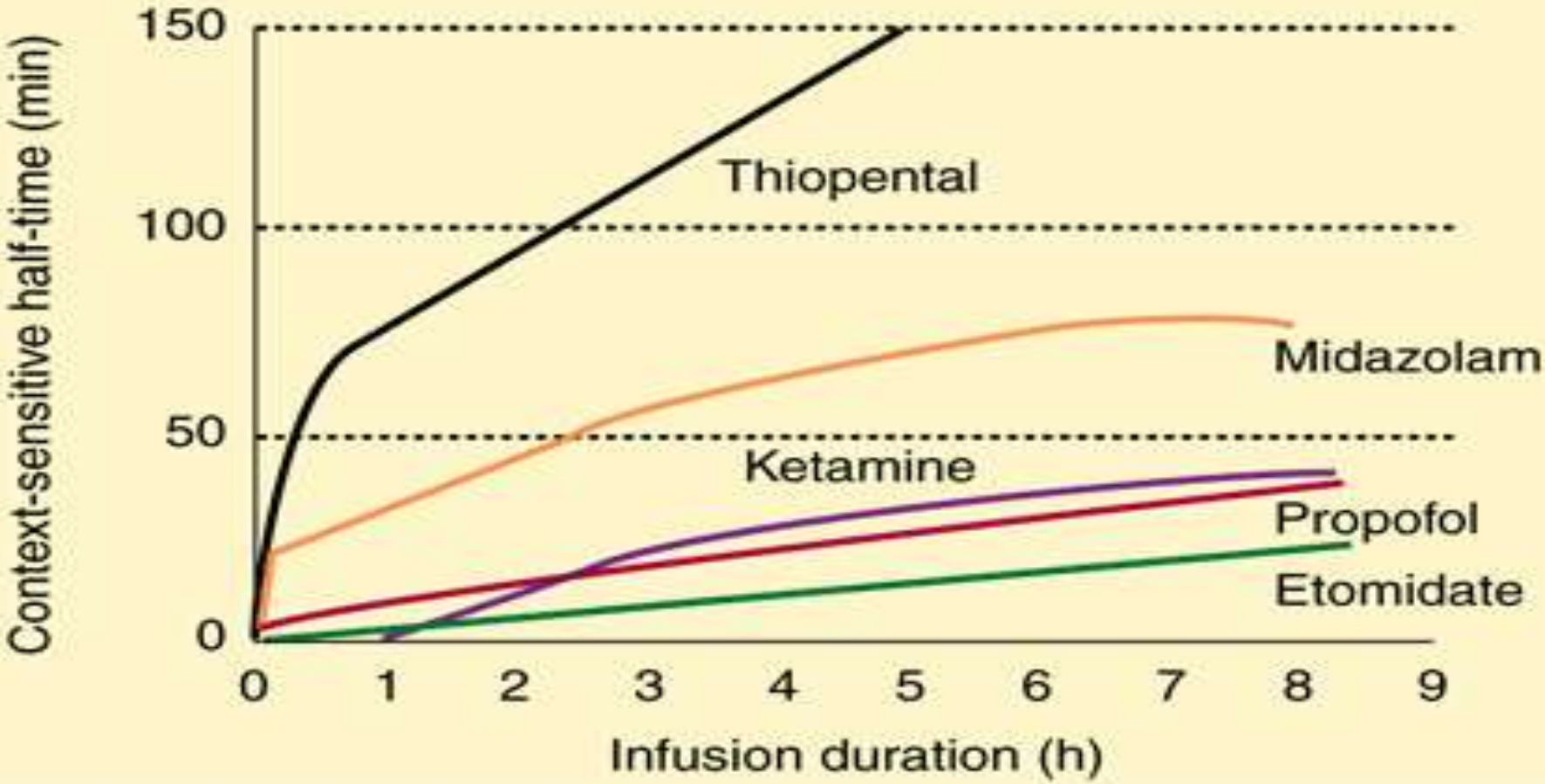
- **Not good amnesic.**
- **Supplement others.**
- **Continuous infusion will depress ventilation.**

Narcotics

- Morphine ----- lowers BP , Bronchospasm
- Meperidine ----- Increases HR
- Fentanyl
- Sufentanil
- Alfentanil
- Remifentanil.

- **Dexmedetomidine**
- Alpha 2 receptor agonist, which are present in the autonomic nervous system as well as centrally.
- Don’t produce adequate surgical anesthesia when used alone.
- Produces hypnosis by working in locus ceruleus and analgesia by working in the spinal cord, hypnosis resembles physiological sleep.
- Can cause cardiovascular side effect.
- Used as supplement to reduce the use of opioids and others.
- Useful in many other conditions such as hypertension and drug withdrawal.

Half-life time of common intravenous anesthetics



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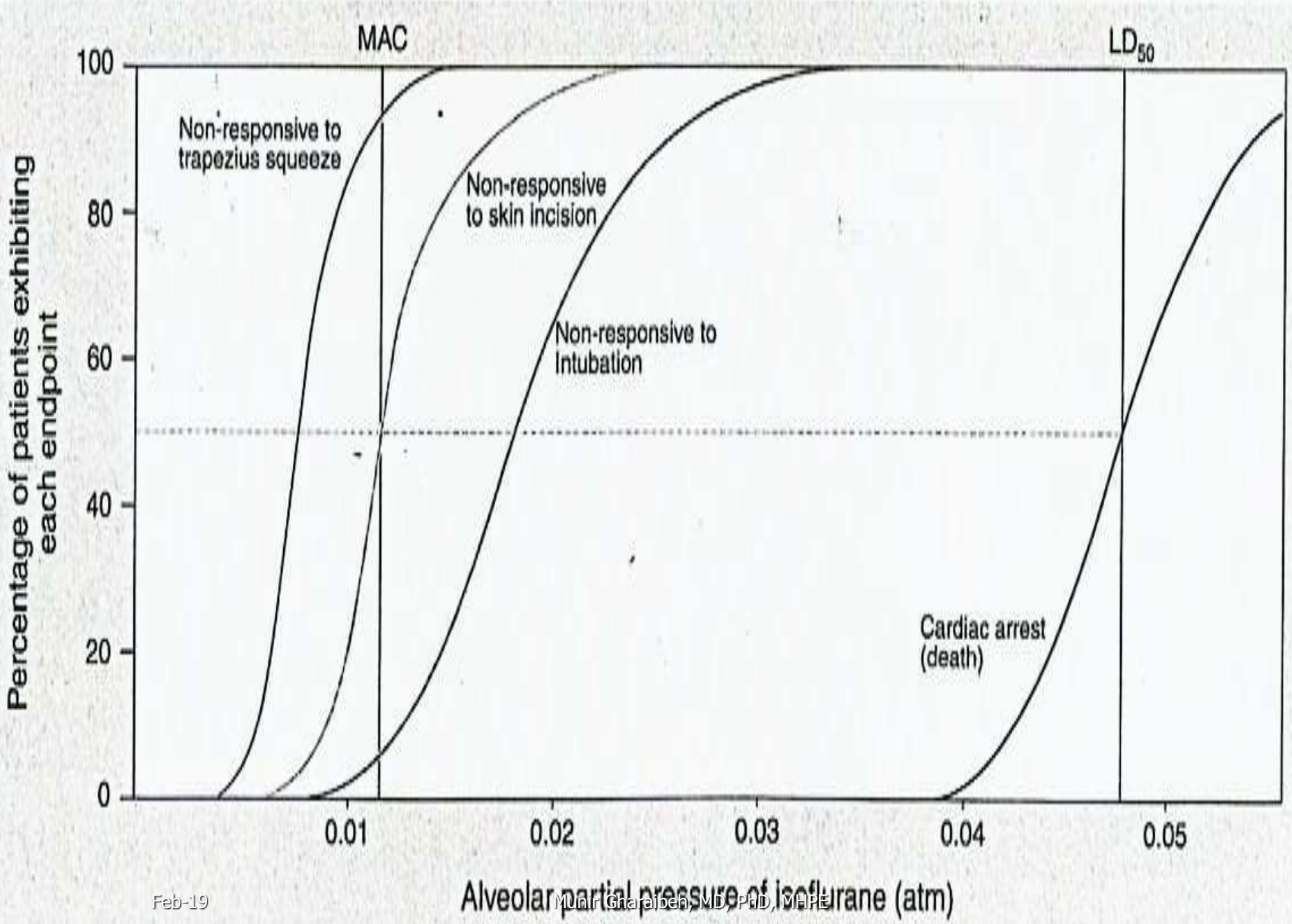
Inhalational Anesthesia

- Gases or Volatile Liquids
- Elimination is by the lungs
- Equilibrate with tissues.
- Metabolism is slow
- Interaction with tissues and liquids is physical.

Inhalational Anesthesia

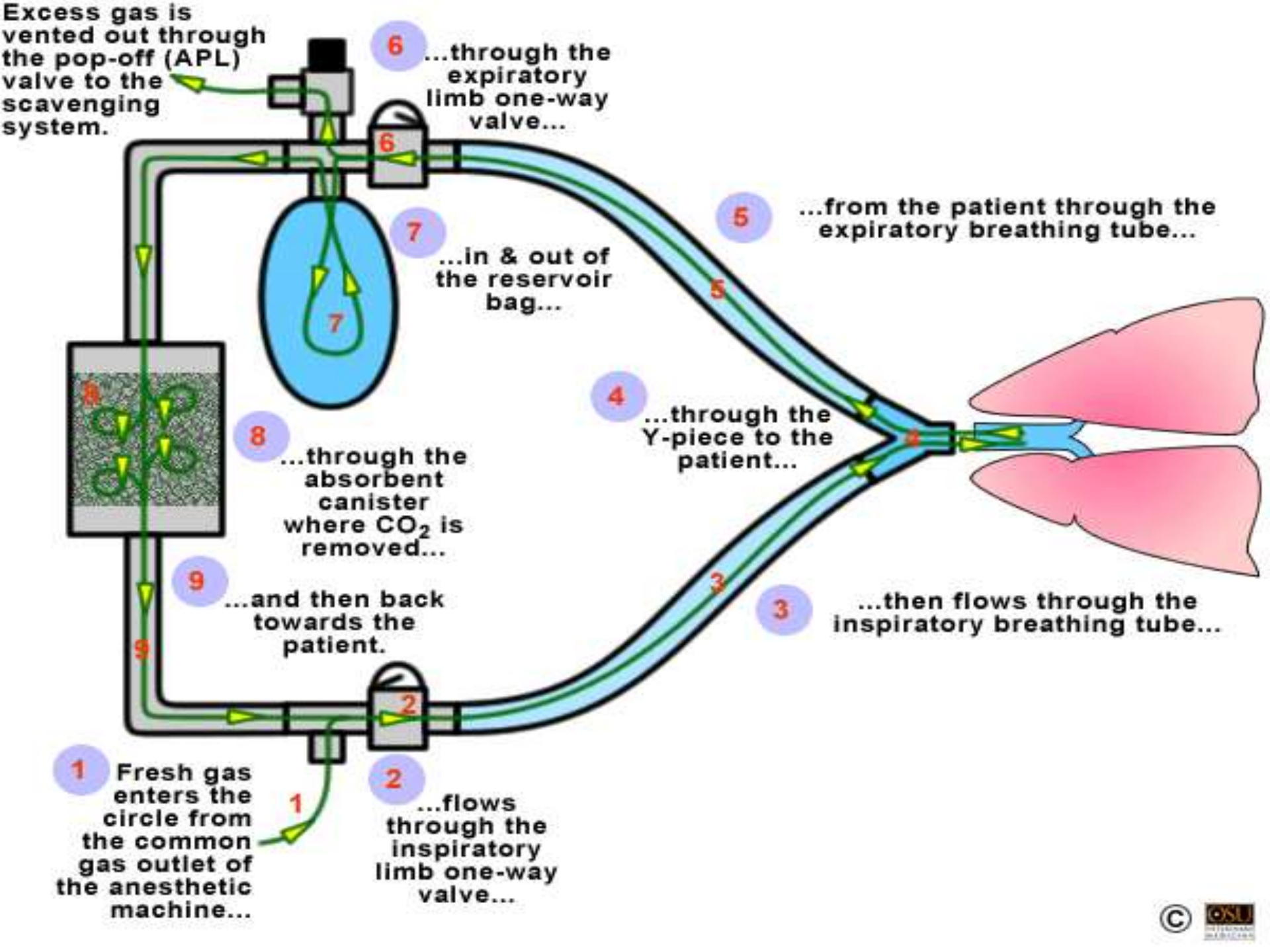
- MAC = Minimum Alveolar Concentration
  - Measure of general anesthetic potency.
  - Alveorlar tension required to produce surgical anesthesia in 50% of patients (immobility after exposure to a noxious stimulus like a knife incision).


MAC
LD50
100
80
60
40
20
0
Non-responsive to trapezius squeeze
Non-responsive to skin incision
Non-responsive to intubation
Cardiac arrest (death)
Percentage of patients exhibiting each endpoint
0.01
0.02
0.03
0.04
0.05
Alveolar partial pressure of isoflurane (atm)

Inhalational Anesthesia

- Delivering System
- Alveoli
- Blood -------- CNS
- Tissues

Anesthesia Machine


Excess gas is vented out through the pop-off (APL) valve to the scavenging system.
6
...through the expiratory limb one-way valve...
6
7
...in & out of the reservoir bag...
7
5
...from the patient through the expiratory breathing tube...
5
4
...through the Y-piece to the patient...
4
8
...through the absorbent canister where CO_2 is removed...
8
9
...and then back towards the patient.
9
3
...then flows through the inspiratory breathing tube...
3
2
...flows through the inspiratory limb one-way valve...
2
1
Fresh gas enters the circle from the common gas outlet of the anesthetic machine...
1

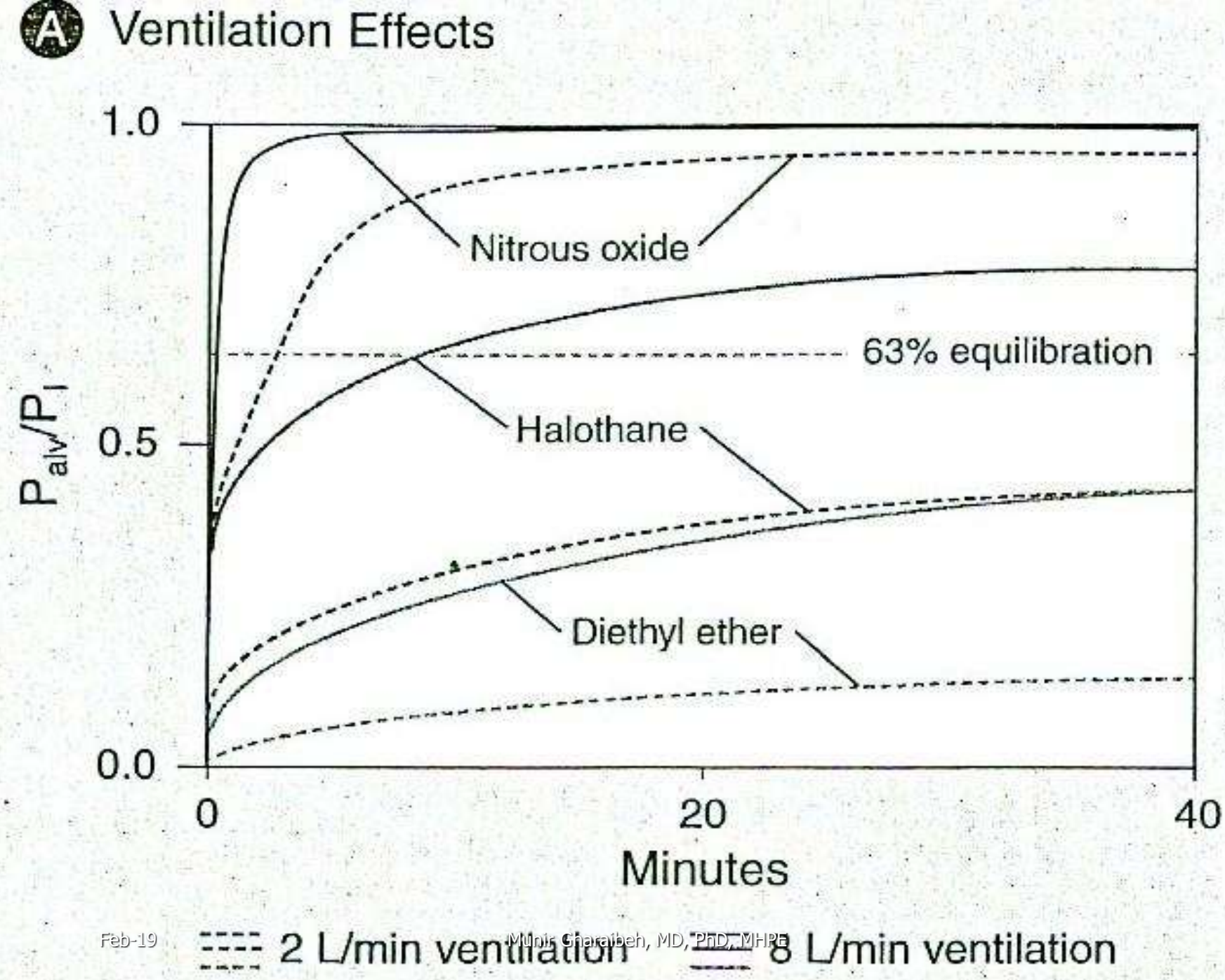
Inhalational Anesthesia

Alveolar Tension ..... Brain Tension

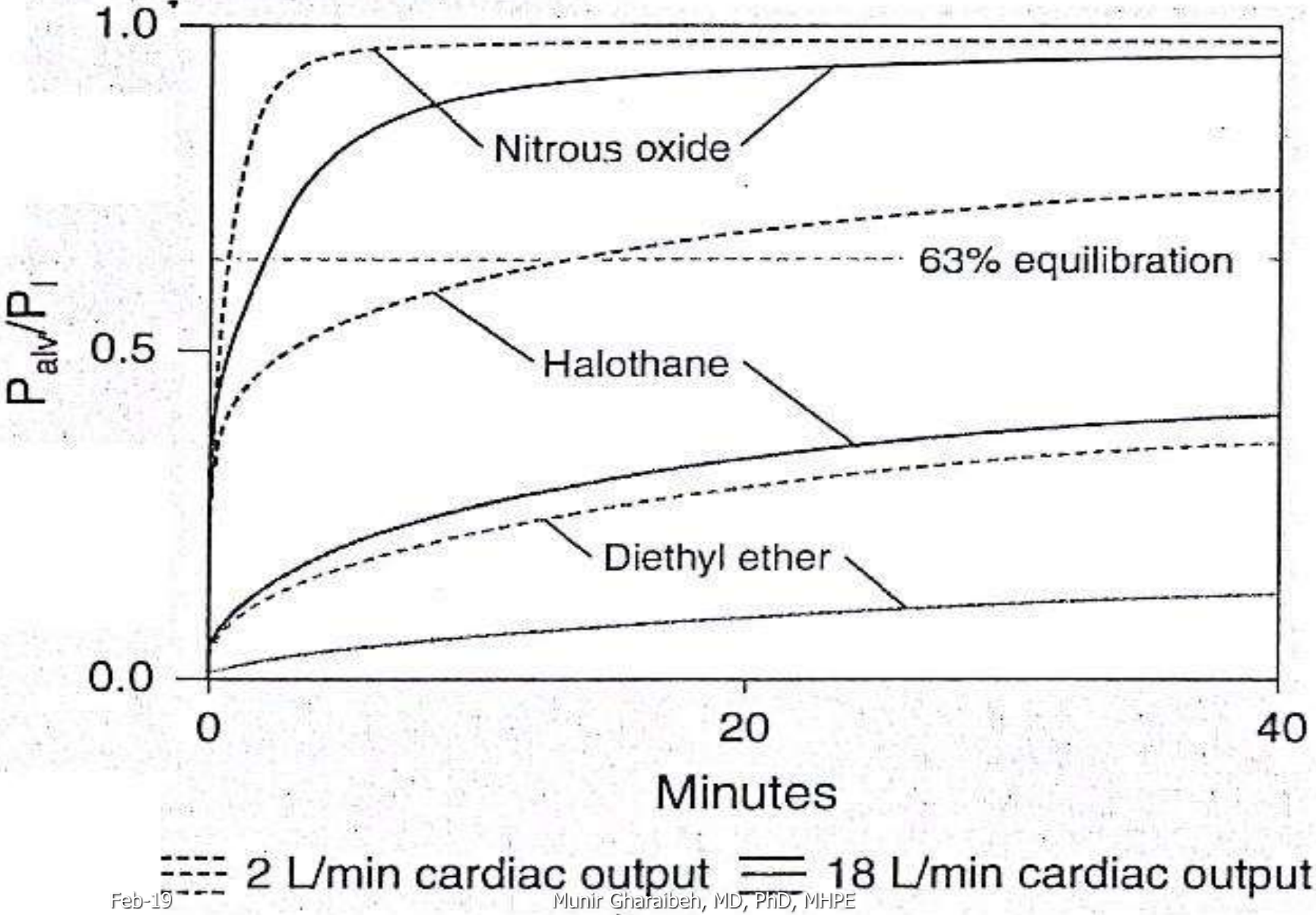
Rate of Rise in Alveolar Tension Depends on:

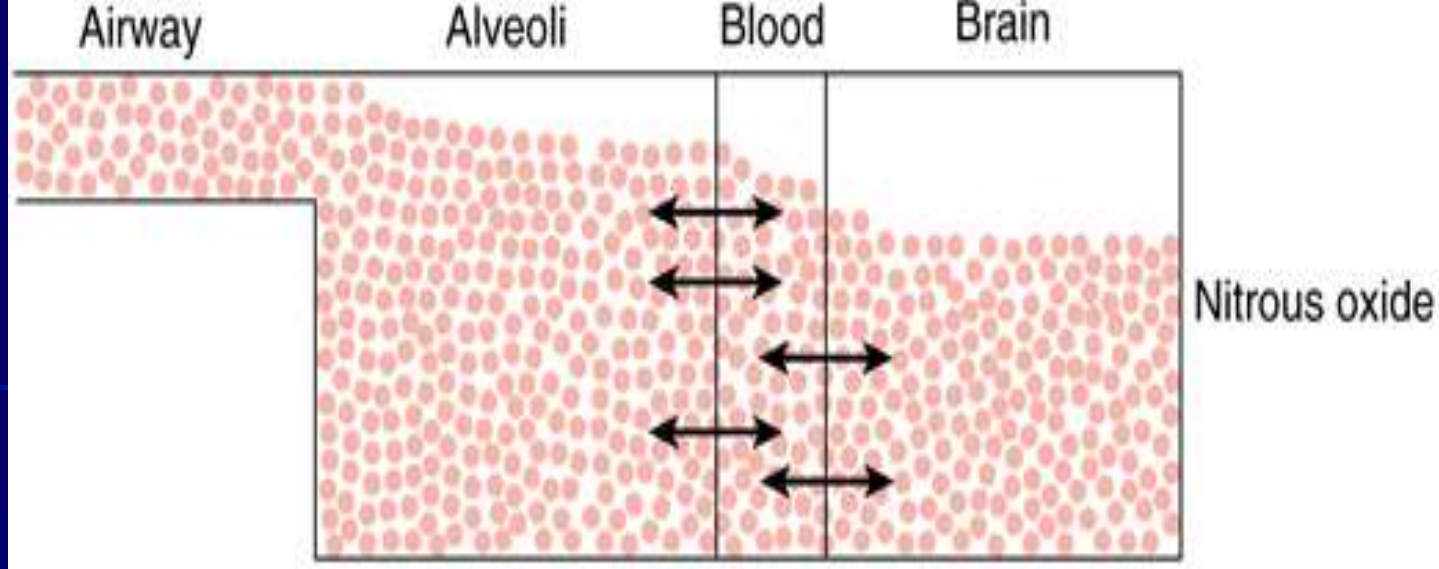
- **Inspired tension.**
- **Pulmonary ventilation**

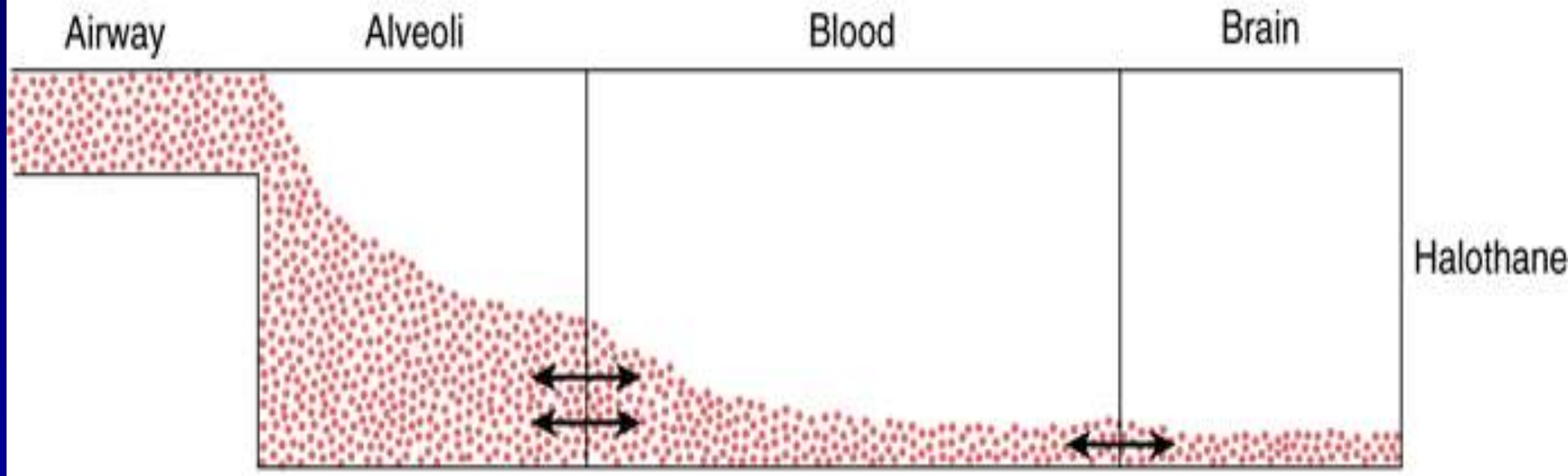
- **Transfer from alveoli to Blood:**
  - **a. Pulmonary BF(or Cardiac Output)**
  - **b. Solubility in blood.**
- **Loss from blood to tissues**


A Ventilation Effects
1.0
0.5
0.0
P_{alv}/P_I
Nitrous oxide
63% equilibration
Halothane
Diethyl ether
0
20
40
Minutes
2 L/min ventilation
8 L/min ventilation

B Cardiac Output Effects







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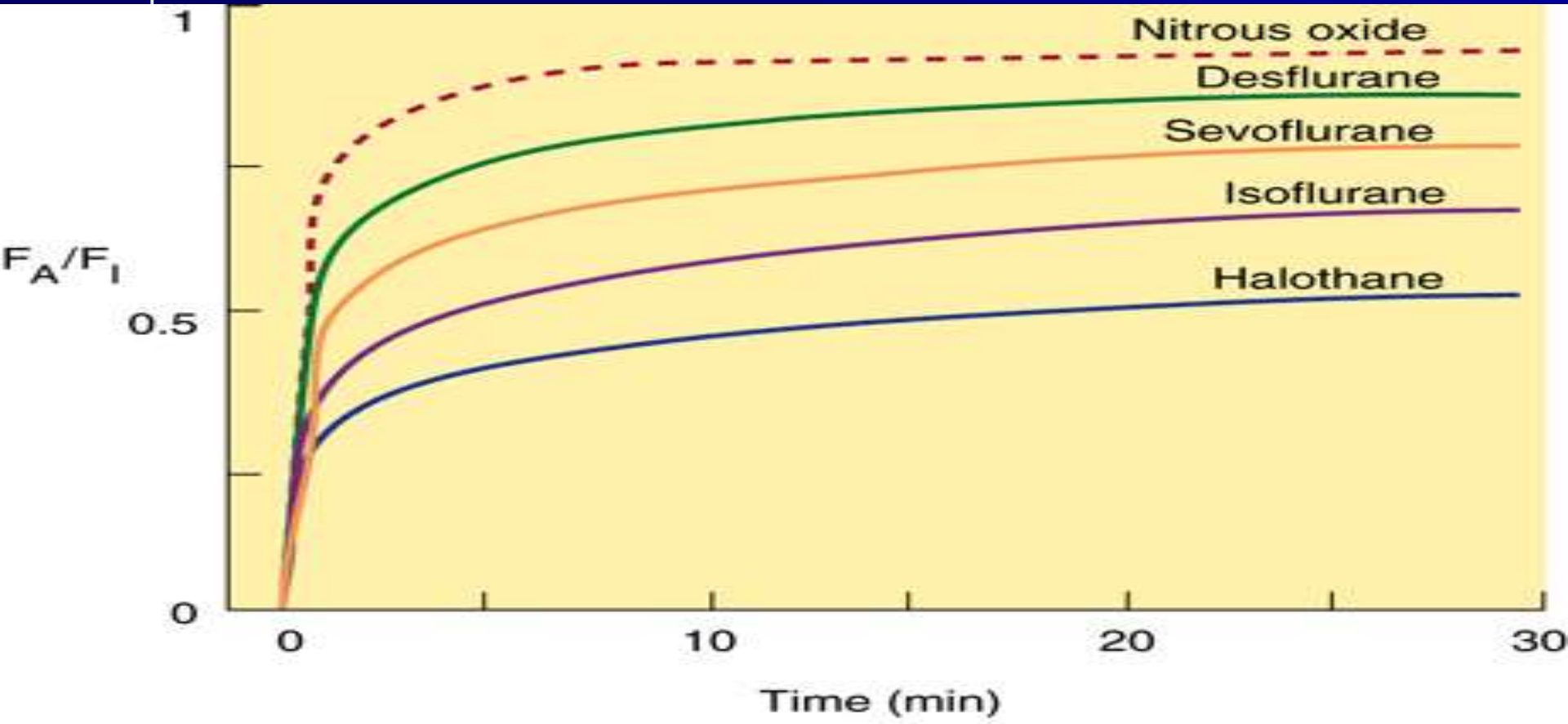
Induction of anesthesia is slower with more soluble anesthetic gases

- Solubility in blood is represented by the relative size of the blood compartment (the more soluble, the larger the compartment).
- Relative partial pressures of the agents in the compartments are indicated by the degree of filling of each compartment.
- For a given concentration or partial pressure of the two anesthetic gases in the inspired air, it will take much longer for the blood partial pressure of the more soluble gas (halothane) to rise to the same partial pressure as in the alveoli.
- Since the concentration of the anesthetic agent in the brain can rise no faster than the concentration in the blood, the onset of anesthesia will be slower with halothane than with nitrous oxide.

The alveolar anesthetic concentration approaches the inspired anesthetic concentration faster for the least soluble agents



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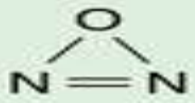


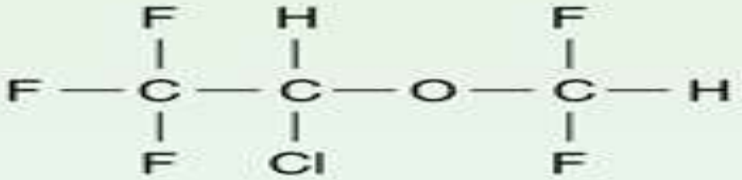
Nitrous oxide

Halothane

Enflurane

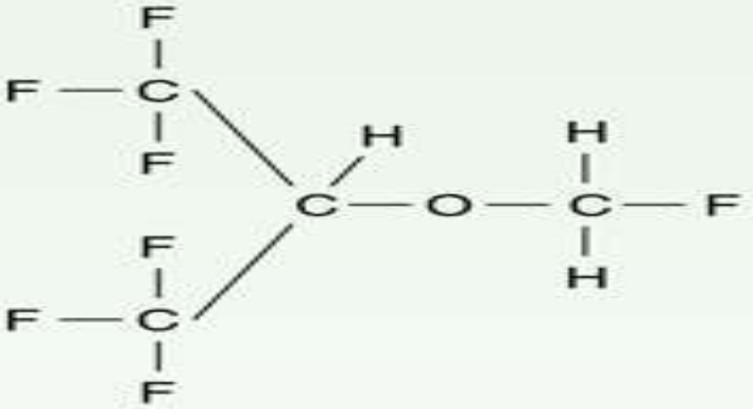
Xe

Xenon



Isoflurane

Desflurane



Sevoflurane

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Table 25–1 Pharmacologic Properties of Inhaled Anesthetics.

Anesthetic	Blood:Gas Partition Coefficient[1]	Brain:Blood Partition Coefficient[1]	Minimal Alveolar Concentration (MAC) (%)[2]	Metabolism	Comments
Nitrous oxide	0.47	1.1	> 100	None	Incomplete anesthetic; rapid onset and recovery
Desflurane	0.42	1.3	6–7	< 0.05%	Low volatility; poor induction agent (pungent); rapid recovery
Sevoflurane	0.69	1.7	2.0	2–5% (fluoride)	Rapid onset and recovery; unstable in soda-lime
Isoflurane	1.40	2.6	1.40	< 2%	Medium rate of onset and recovery
Enflurane	1.80	1.4	1.7	8%	Medium rate of onset and recovery
Halothane	2.30	2.9	0.75	> 40%	Medium rate of onset and recovery

[1] Partition coefficients (at 37°C) are from multiple literature sources.

[2] MAC is the anesthetic concentration that produces immobility in 50% of patients exposed to a noxious stimulus.

Table 31-2. Summary of Major Characteristics of Important Anesthetics

	Analgesia	Blood pressure	Respiration	Muscle relaxation	Prominent adverse effects	MAC	Blood-gas partition coefficient at 37°C	Vapor pressure at 20°C (torr)
Ether	4+	↑	↑	3+	Flammable; slow action	1.9	12	425
Halothane	2+	↓	↓↓	+	Myocardial depression; hepatotoxicity?	0.77	2.3	243
Methoxyflurane	3+	↓	↓↓	+	Renal toxicity	0.16	12	23
Enflurane	2+	↓	↓↓	2+	Respiratory and cardiovascular depression	1.68	1.8	175
Isoflurane	2+	↓	↓↓	2+	Respiratory and cardiovascular depression	1.15	1.4	239
Chloroform	2+	↓	↓↓	+	Hepatotoxicity; narrow margin of safety	0.77 In dogs		160
Nitrous oxide	4+	Little change	Little change	None	Weak anesthetic—need other agents as well	105%	0.47	Gas
Cyclopropane	2+	↑	↓	2+	Flammable; expensive	9.2%	0.4	Gas

Halogenated Anesthetics
Halothane:

First practical anesthetist, Widely used

- Non flammable , Non toxic , Sweet odor .
- Complete anesthetist only in high doses .
- Cardiorespiratory depressant , Sensitizes the heart to NE.

Halothane

Hepatic Necrosis(1/35.000).

Hypersensitivity: Abs detected.

Abortion : In animals.

Enflurane

- More N.M. Blockade
- Rapid Induction & emergence
- Sensitizes heart to catecholamines.
- EEG Changes------ seizures.
- Releases fluoride ions.

Isoflurane

- Similar but: maintains C.O
- Less metabolized i.e. less hepatotoxicity
- Less nephrotoxicity
- Most popular

Desflurane

- Low solubility
- Rapid Induction & Emergence
- Outpatient procedures.
- Irritating

Methoxyflurane

- Sweet smelling
- Slow induction & emergence due to high solubility.
- Profound analgesia.
- BP is maintained.
- Renal toxicity.

Sevoflurane

Nonhalogenated Anesthetics Nitrous Oxide:

- Cardiac depressant but stimulates the sympathetic system.
- Lowers tidal volume but increases respiratory rate.

Very weak, MAC = 105%.

- Almost insoluble in blood so very rapid induction.
- Analgesic= 25% of Morphine
- Used in dentistry and was used in labor.
- Used in combination and for induction.

Ether

- Historical.
- Irritant , Flammable , Explosive.
- Complete anesthetic.
- Safe except for postoperative nausea, vomiting and bad odor.

Cyclopropane.

Chloroform.

Mechanisms of Anesthetic Actions

- Non specific Physical Interactions with membrane components.
- Many simple, unreactive compounds like xenon, produce general anesthesia.
- Anesthetic potency is closely related with lipid solubility(Overton-Meyer Correlation), not with chemical structure.

Theories of Anesthetic Actions

- Earlier theories of anesthesia postulated interaction with the lipid membrane bilayer.
- Interaction with membrane ion channels.
- Enhancing the activity of inhibitory GABAA receptors and other ligand-gated ion channels.
- Activation of a subfamily of potassium channels(the two-pore domain K+ channels).
- Inhibition of the excitatory NMDA receptors.