General Anesthesia

Munir Gharaibeh, MD, PhD, MHPE
School of Medicine,
The University of Jordan,
February, 2019

Lecture Notes
Done by: Nadia Sweis
Corrected by: Jaleel Sweis

General Anesthesia

- **Definition:**

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

Extra Note: Anesthesia is a relatively new practice with the first successful attempt being in 1846. It is a Latin word that means "without feeling of pain". General anesthesia differs from local anesthesia in that the latter is intended for a certain area only.

This picture represents "butchering medicine", in which amputation surgery was done without anesthesia. Complications and post-surgical infections were especially a concern, since infections were only recently discovered in the 1880's by Koch, making surgery all the more distressing.

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.** *(Note: Recall that prolonged rest can cause undesirable effects such as Deep Vein Thrombosis, aspiration pneumonia and bed sores).*

Balanced Anesthesia:

- **Multi drug approach to managing the patient's anesthetic needs.** *(Since no single agent has all of the features).*

Phases of Anesthesia

- **Induction**
- **Maintenance**
- **Emergence = Recovery**

Stages of Anesthesia

Classically Described for Ether Anesthesia:

. Stage I: " Analgesia"

Amnesia(loss of memory) **and euphoria.**

Ether was the first successful anesthetic agent in 1846.

. Stage II: "Excitement"

Delirium and combative behavior. *(Note: This excitement also occurs with most CNS depressants such as alcohol. It happens due to the disinhibition of inhibitory mechanisms).*

. 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. *(Toxicity)*

Preanesthetic Medications
" Premedication"

- **Opioids** *(Analgesics)*
- **Benzodiazepines** *(Sedatives to reduce apprehension)*
- **Antimuscarinics** *(Atropine-like drugs to reduce secretions)*
- **Antihistamines** *(For allergy)*
- **Antiemetics** *(Because anesthetics cause vomiting)*

- *Note: General anesthesia is divided into intravenous anesthesia and inhalational anesthesia. We usually start with Intravenous anesthesia due to its rapid onset of action.*

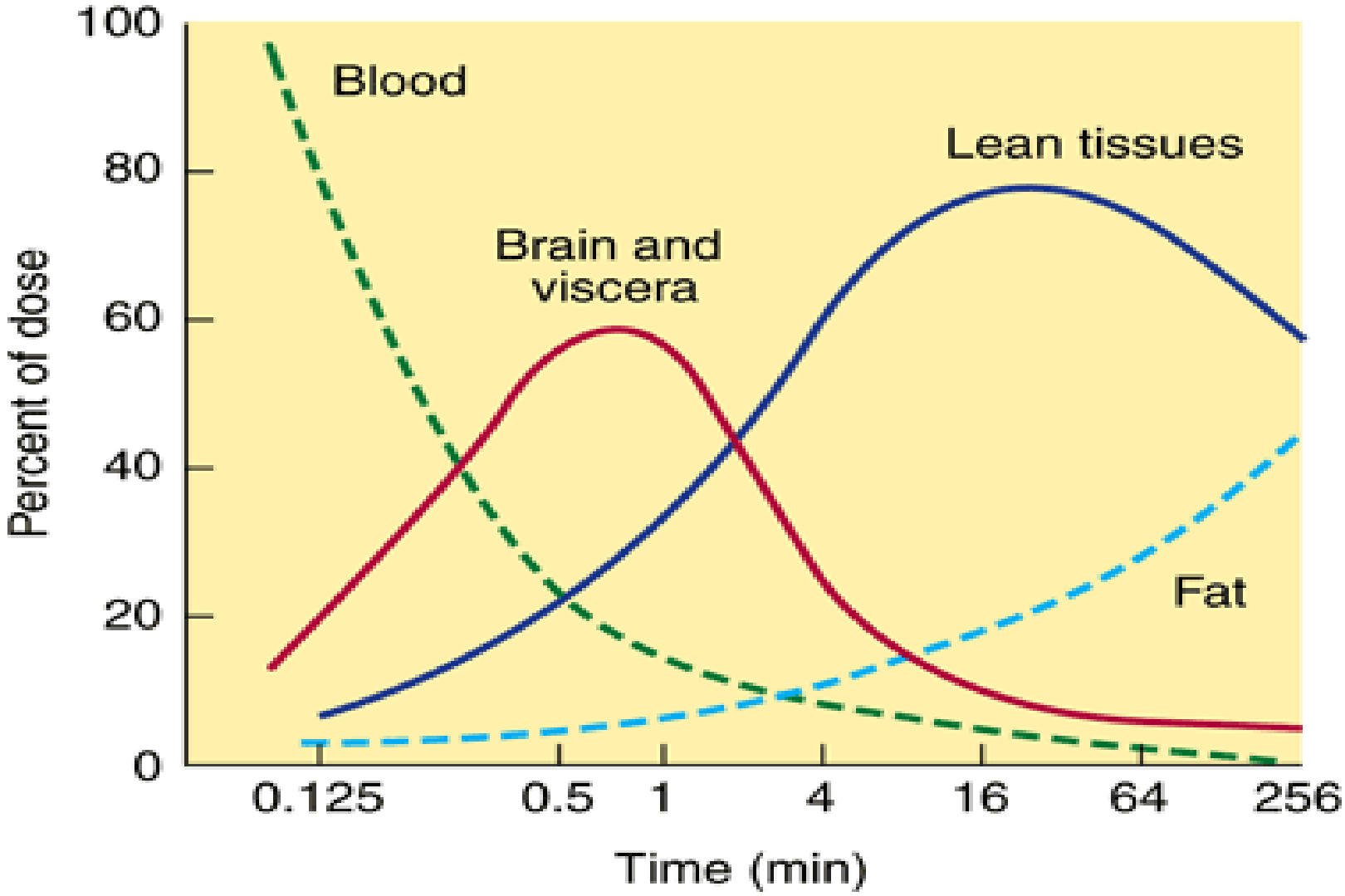
Intravenous Anesthesia

- **Highly lipid soluble.**
- **Very short t½α.**
- **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 IV administration (*Total Intravenous Anesthesia TIVA).*** *(Used to control the drug's level).*

Extra Lecture Note

- After being distributed throughout the blood, intravenous anesthetics then pass to the highly perfused viscera, mainly the brain. This happens very rapidly since they are highly lipid-soluble. They accumulate there initially and produce their effects. This action is terminated by the excretion of the drug from the circulation. When the level of the drug in the blood goes down, the accumulated drug in the brain will diffuse back to the circulation, and by that the level of the drug in the brain decreases.
- Generally, the drug will be excreted from the blood to the lean tissues such as the muscles, so it ends up accumulating there. Keep in mind that at first, the drug accumulates in the brain, but after its excretion, it will have accumulated in the lean tissues. To better understand this, take a look at the graph in next slide, and notice how the concentration of the drug in the blood decays after 64-256 minutes of administration. The lean tissues and fat are not as heavily perfused, which explains their initial low concentration of the drug.

Redistribution of thiopental after IV bolus administration.



Source: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology, 12th edition*: www.accessmedicine.com

Intravenous Anesthesia

General Uses:

- **Ideally suitable for Induction.**
- **Maintenance of short procedures.**
- **In combination to produce balanced anesthesia.**
- **Supplement inhalational anesthesia.***(During surgery if the patient seems weakly anesthetized, we give him intravenous anesthesia to supplement inhalational anesthesia).*

Ultra Short Acting Barbiturates

- **Thiopental: most popular IV agent for induction**
- **Methohexital: very short acting, less ppt.**

(Extra note: barbiturates work on GABA receptors. They can either be short, ultra-short, intermediate, or long-acting. They were widely used for the treatment of epilepsy. These ultra-short acting barbiturates are hypnotics or CNS depressants, but they are not analegesics. The patient is put to sleep in a few seconds after a bolus dose of these drugs).

- **Weak acids, can precipitate.**
  - **If given in an artery?** *(The doctor skipped this).*

- **Patients may react to painful stimuli but:**
  - **They will be unaware, and they 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, and are generally better than the barbiturates.**
- ***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**
- **Useful in children since it can be given intramuscularly (IM).**
- *Used in* **Ambulatory conditions --- used in military.** *(Usually not used in general surgery; it does not cause muscle relaxation).*

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.**
- *Extra note:*

  They are good analgesics.

Narcotics

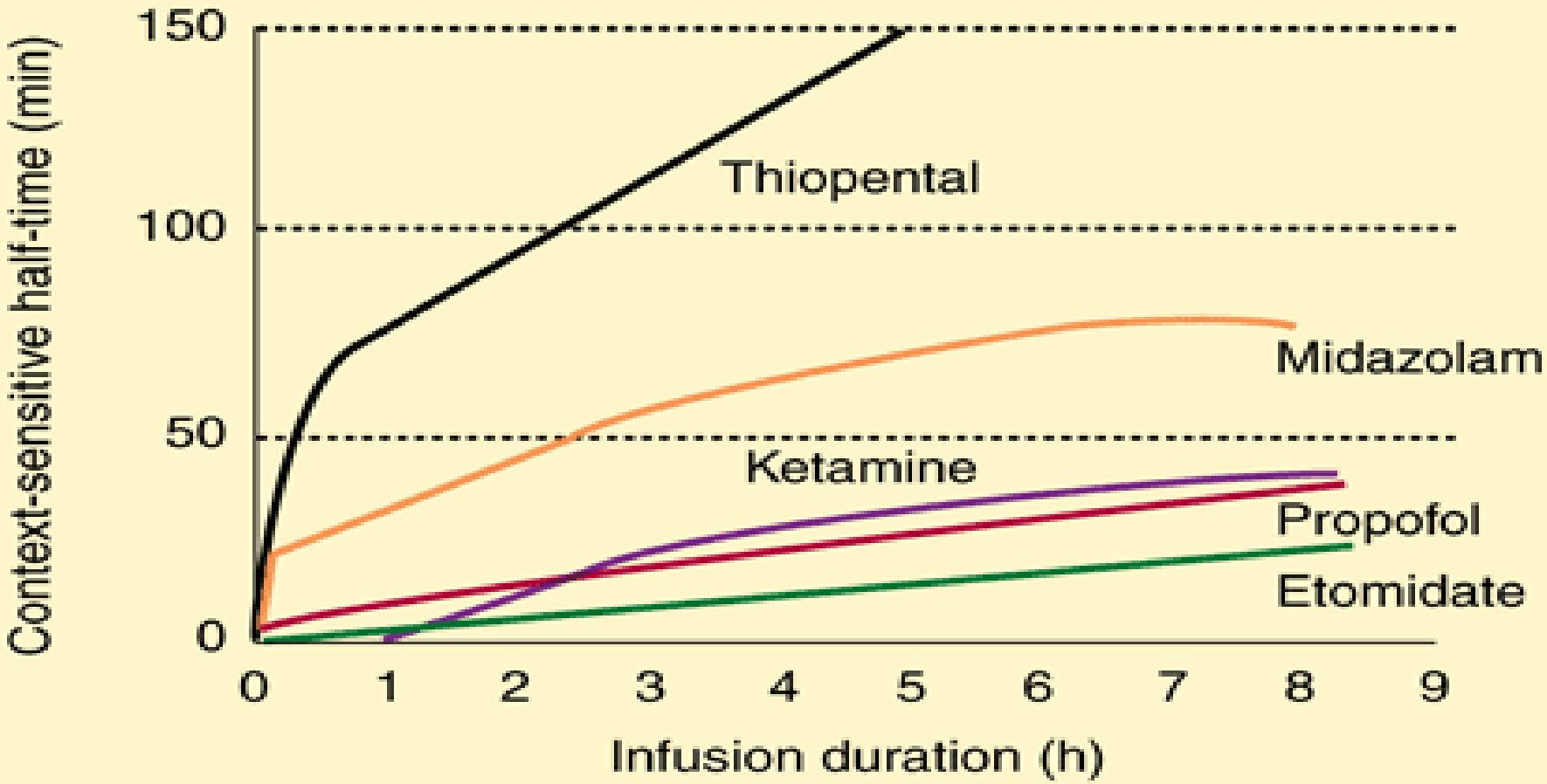
- **Morphine: lowers BP, Bronchospasm**
- **Meperidine: Increases HR**
- **Fentanyl**
- **Sufentanil**
- **Alfentanil**
- **Remifentanil.**

- **Dexmedetomidine**
- Alpha 2 receptor agonist, which are present in the autonomic nervous system as well as centrally. *(Note: They are inhibitory receptors in the brain).*
- 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. *(Unlike benzodiazepines and thiopental)*
- 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.

- **Regarding the graph in the next slide:**

- Context-sensitive half-time describes the elimination half-life after discontinuation of a continuous infusion as a function of the duration of the infusion.
- In other words, this graph represents the half-lives of the various intravenous anesthetic agents *after discontinuation of continuous infusion. (Remember, though, that the half life is usually determined after a single-dose administration, regardless of the route).*
- For thiopental, increasing the infusion duration to 5hrs greatly increases the half-life, while the half-life of midazolam is moderately increased, and that of propofol is very slightly increased within acceptable limits, making propofol the best in that regard.

Half-life time of common intravenous anesthetics



Source: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology, 12th edition*: www.accessmedicine.com

Inhalational Anesthesia

- **Gases or Volatile Liquids**
- **Elimination is by the lungs** *(and so is administration; which is through a mask for gases, or an endotracheal tube).*
- **Equilibrate with tissues.**
- **Metabolism is slow**
- **Interaction with tissues and liquids is physical** *(and not with receptors).*

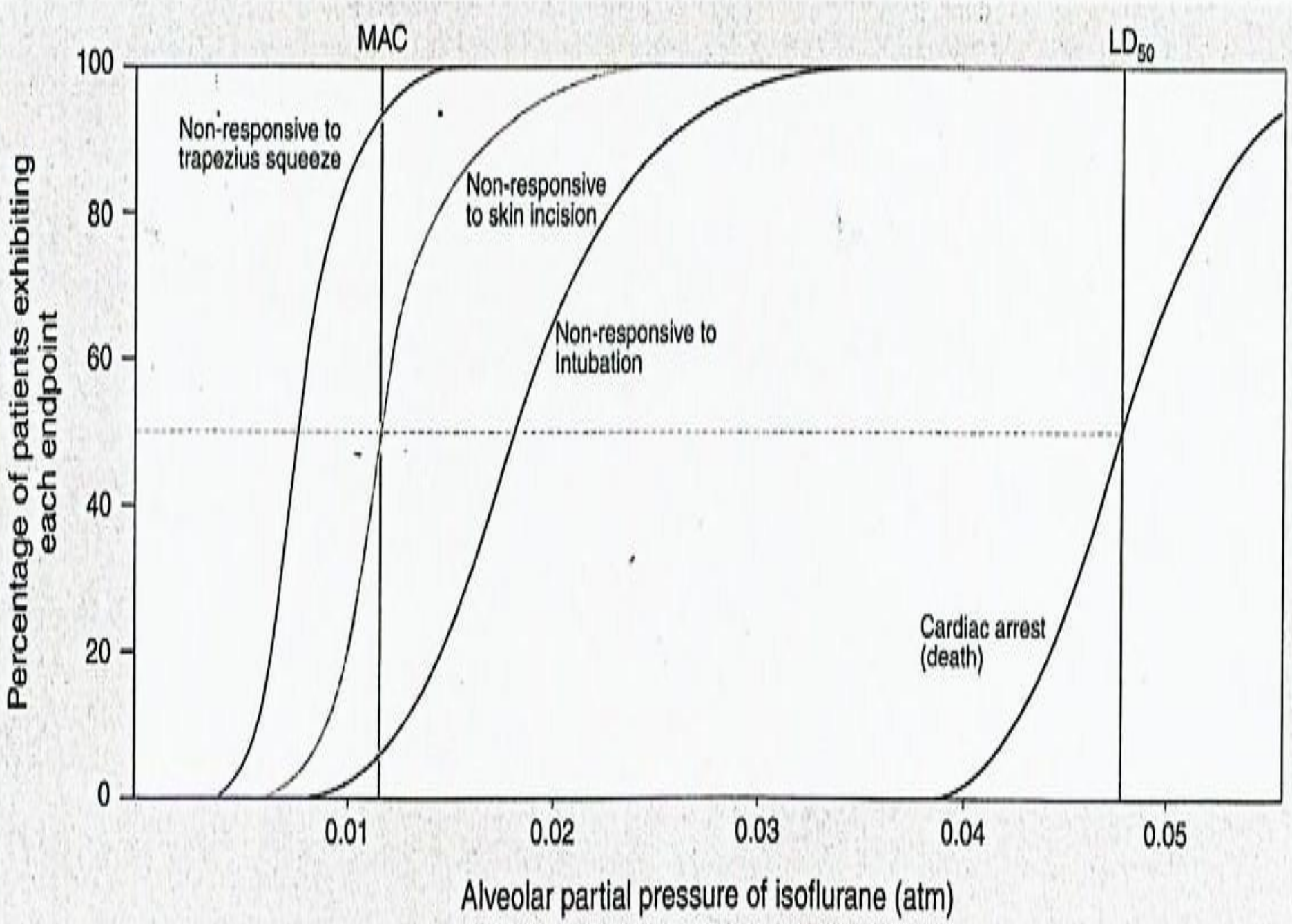
- *Extra note: The practice of general anesthesia started with inhalational rather than intravenous anesthetics. The use of intravenous anesthetics started much later.*
- *Volatile liquids take the fluid form when under pressure and evaporate when this pressure is relieved.*

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).**
  - *Remember that potency is the minimal dose capable of producing an action and is usually measured by the ED50; which is the Effective Dose that produces 50% of the maximal effect.*

Extra Notes Regarding The Next Curve

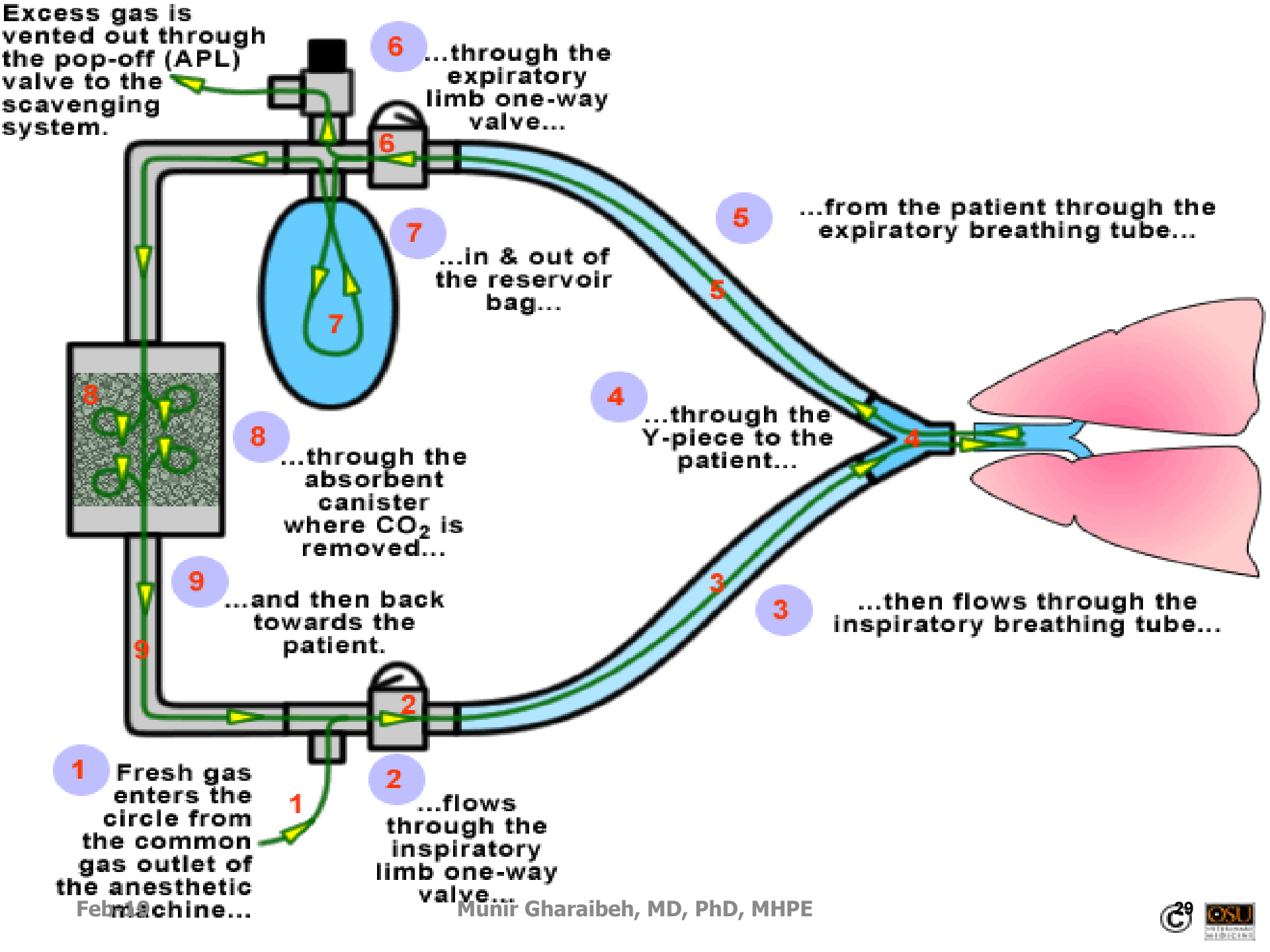
- Our goal is to achieve a concentration higher than the MAC, since we would want to produce surgical anesthesia in 100% of patients.
- This graph contains various dose-response curves. Notice that the ED50 (or the MAC) required to produce non-responsiveness to skin incisions is higher than that of the trapezius squeeze. This means that you need a higher concentration of the drug to produce non-responsiveness to skin incisions, while a lower concentration is sufficient to produce non-responsiveness to trapezius squeeze.
- To introduce gases and vapor directly to the alveoli by endotracheal intubation, the patient should have first reached the stage of non-responsiveness to intubation (It's impossible to intubate a patient if their gag reflex is still intact. We need a sufficient concentration of anesthesia to eliminate that reflex).
- Increasing the dose to a certain level will cause toxicity, and that is evident in the last lethal curve. Notice that the MAC for cardiac arrest is less than 0.05. The more the lethal curve is shifted to the right, the safer the agent.


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

- *We need a* **Delivering System**
- *The substance should be delivered to the* **Alveoli**
- *It should then diffuse to the* **Blood** *then the* **CNS**
- *And finally to other* **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
8
8
...through the absorbent canister where CO_2 is removed...
4
...through the Y-piece to the patient...
4
9
...and then back towards the patient.
9
3
3
...then flows through the inspiratory breathing tube...
2
1
Fresh gas enters the circle from the common gas outlet of the anesthetic machine...
1
2
...flows through the inspiratory limb one-way valve...