Anesthetics

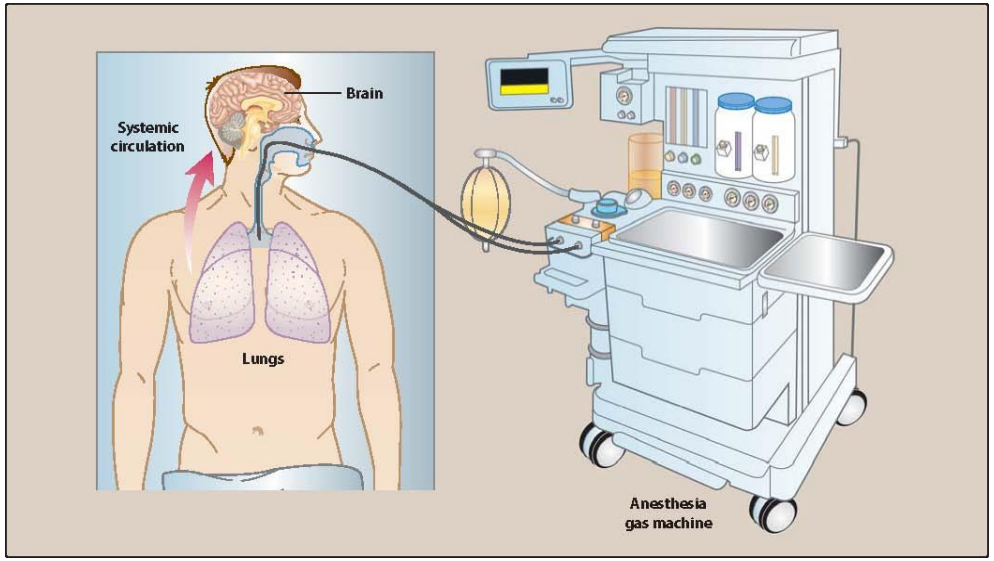
Lecture 12 part 2

Inhalational Anesthetics

Inhalational Anesthetics

- Primarily used for maintenance of anesthesia following induction by IV agents.
- Depth of anesthesia correlates with inhaled concentration.
- Less risk of cardiac/respiratory depression than IV agents.
- No antagonists.

usually termination the effect by redistribution

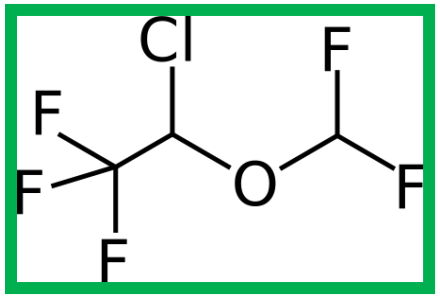


Inhaled anesthetics

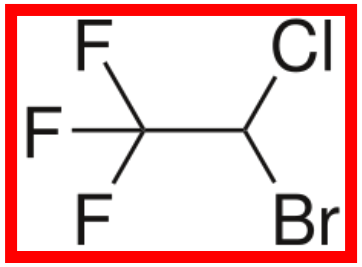
1- Halogenated(with Cl^-,F^-,I^-) Volatile liquids:

now is rarely used

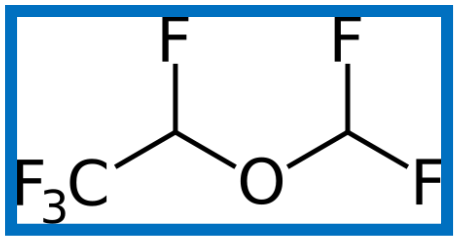
* Halothane



* Isoflurane



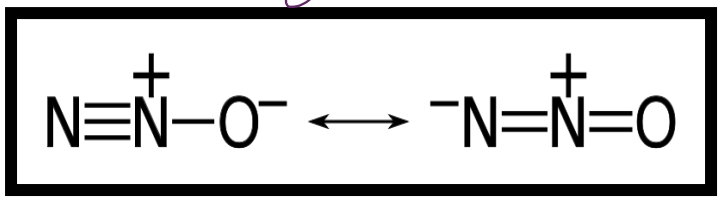
* Desflurane



* Sevoflurane

2- Gases: Nitrous oxide → used in dentist as analgesic

↳ inorganic gas



Mechanism of Action of Inhalational Anesthetics is UNKNOWN!

Possible mechanisms:

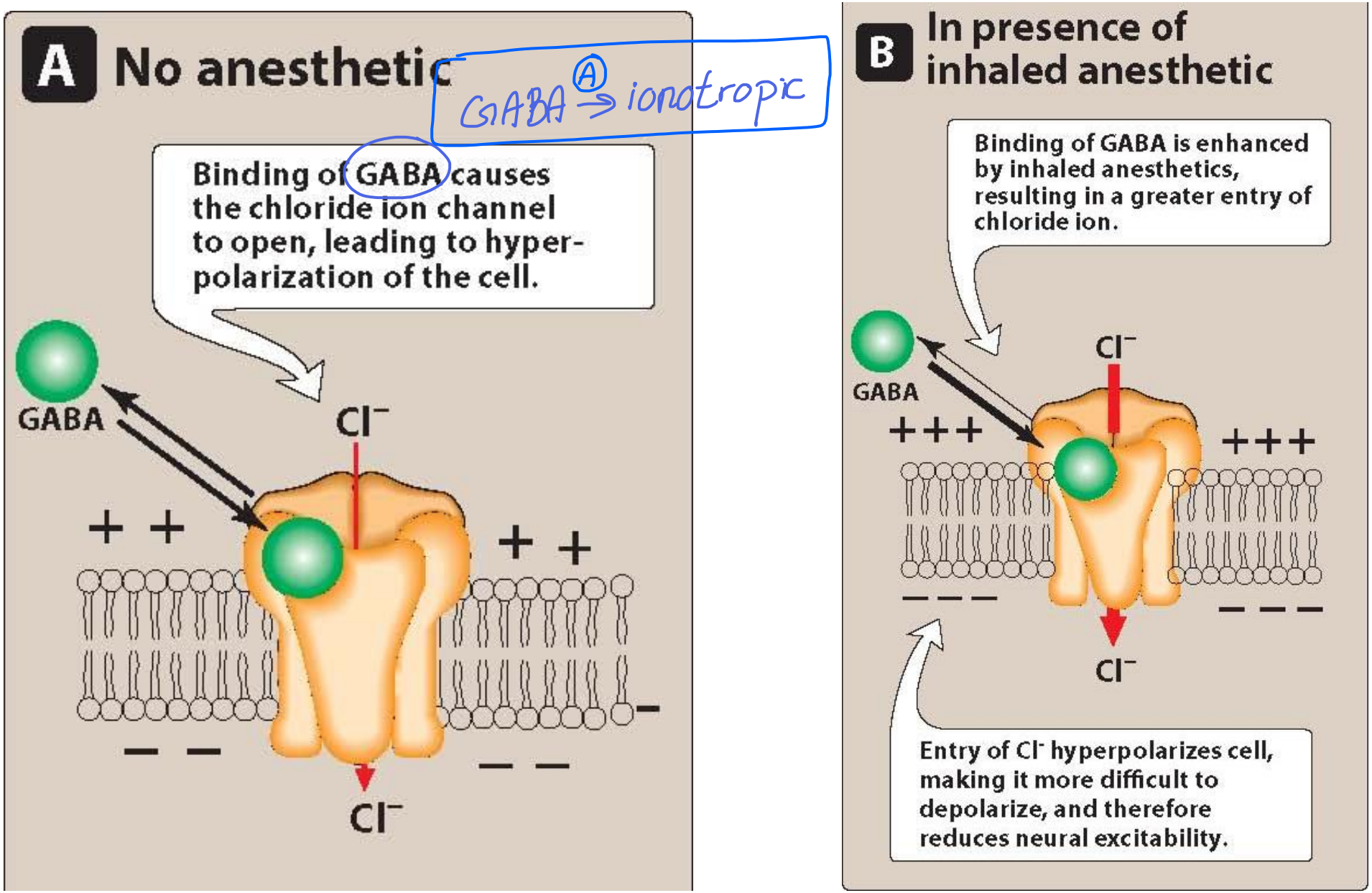
1. Increase the sensitivity of $GABA_A$ receptors to GABA

   (nitrous oxide, ketamine have no effect on GABA)

2. Inhibition of NMDA receptors

3. Increase the activity of glycine receptors in the spinal chord → inhibitory NT

4. Block excitatory postsynaptic currents of nicotinic receptors



GABA Ⓐ ⇒ ionotropic

like Bz and barbiturate

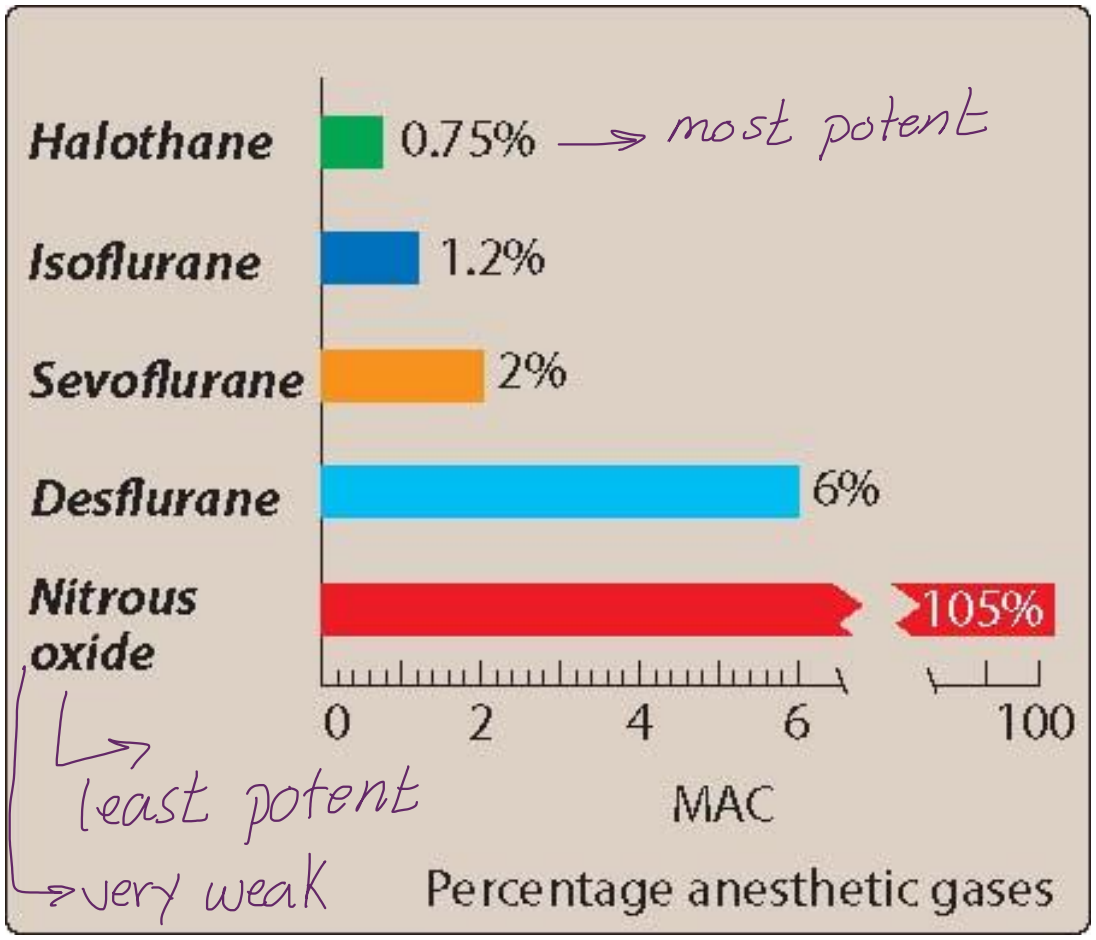
Potency: MAC

Minimum Alveolar Concentration (MAC)

- The end-tidal concentration of an inhalational anesthetic needed to eliminate movement in 50% of patients stimulated by a standardized incision.
- MAC = ED_{50} of an anesthetic
- MAC is expressed as percentage of alveolar gas mixture/ partial pressure as % of 760 mm of Hg.

Potency: MAC

* inverse relationship between MAC and the potency of the anesthetic



* Factors affect the MAC :-

1 ↑ MAC

- Hyperthermia
- Chronic alcohol abuse
- ↑CNS catecholamines

* كلو البدا ↓ less potent

* فلازم نزيد لـ dose

2 ↓ MAC

- Increased age
- Hypothermia
- Pregnancy
- Sepsis
- Concurrent use of an IV anesthetic
- α_2 agonists

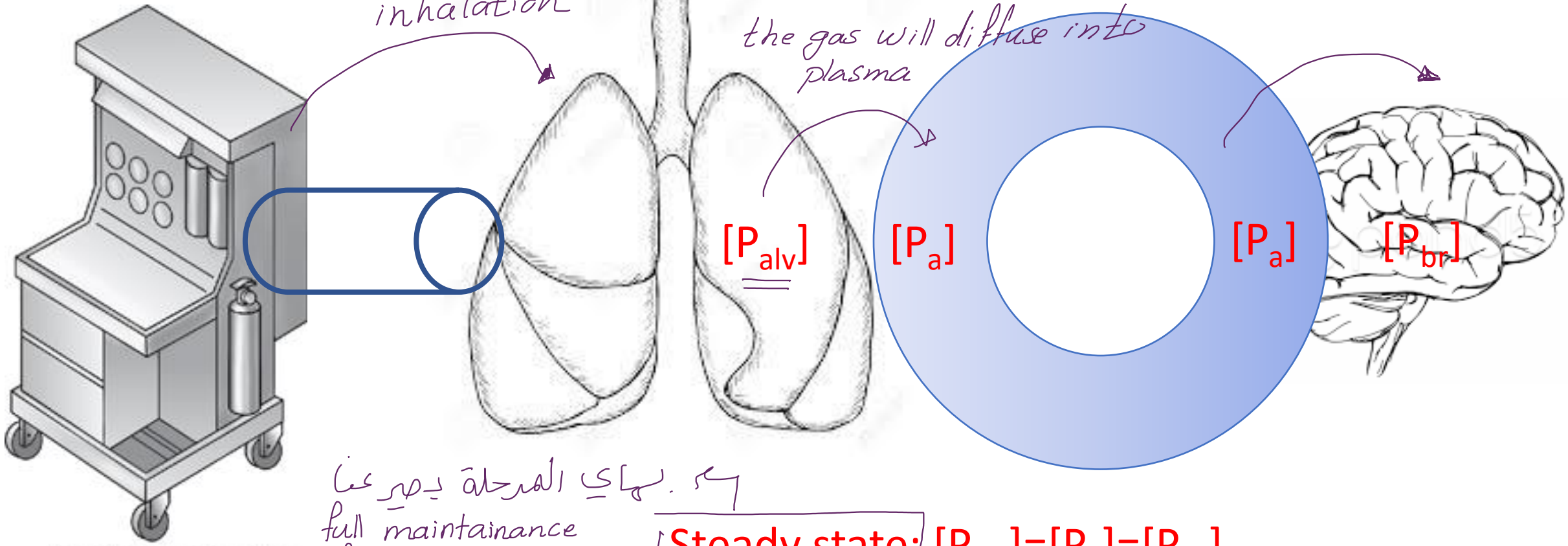
* كلو البدا ↑ more potent

* فلازم تقلل لـ dose

Distribution

The pharmacologic effect of an inhalation agent is determined by the partial pressure of the anesthetic in the brain [P_{br}]

[P_{br}] depends on alveolar partial pressure [P_{alv}] which is controlled by pressure at the origin of the respiratory pathway.



في نهاية المرحلة يصير عنا full maintainance of anesthesia.

Steady state: $[P_{alv}]=[P_a]=[P_{br}]$

نتحكم في الـ Palv عن طريق التحكم في الـ Pbr

anesethia ← حرية إ

Factors affecting equilibrium/steady state

I. Alveolar Wash-In

"Replacement of normal lung gases with inspired anesthetic mixture"

II. Anesthetic Uptake

"most important"

blood stream إ على تنتقل ما

a. Solubility in blood
b. Cardiac output
c. Tissue type
d. Alveolar:venous gradient

Solubility

[anesthetic] in blood / [anesthetic] in aleveoli = coefficient
طردي
عكسي
Soluble in the blood الدوا هاد بتعكس قديش

- Determined by **blood:gas partition coefficient** [the ratio of the concentration of the anesthetic in the blood to the concentration of the anesthetic in the gas phase=solubility of an anesthetic in blood]

(aleveoli)

if blood:gas coefficient is Low

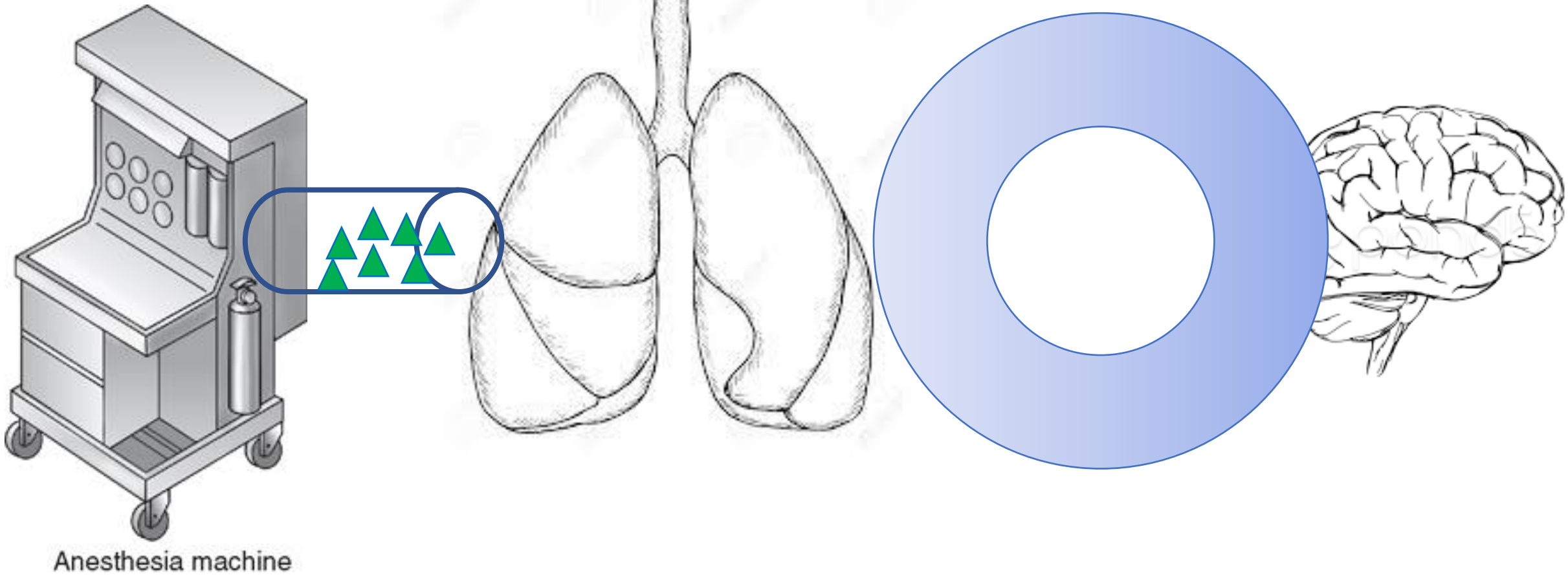
- **Low** blood solubility → **few** anesthetic molecules are required to raise [P_a] → **Less** time for induction and recovery

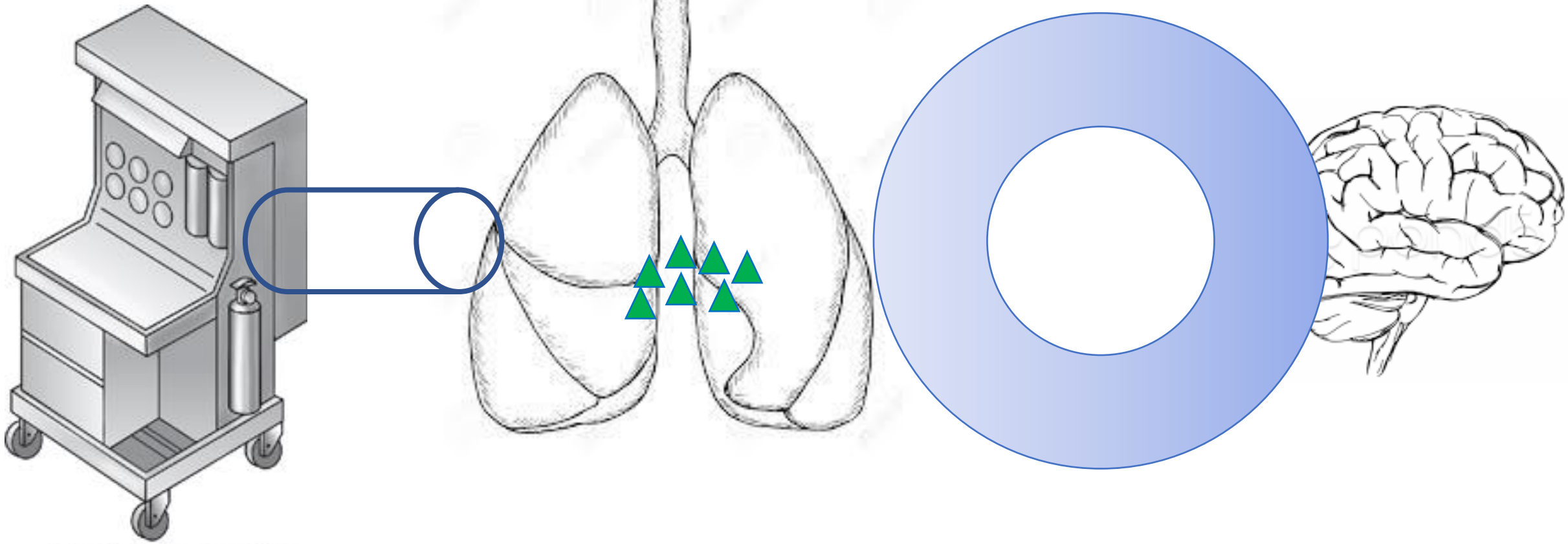
"rapid"

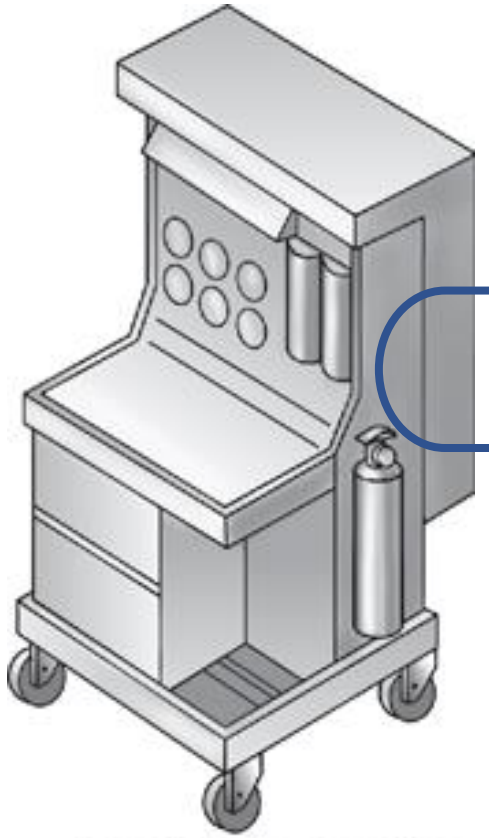
- **High** blood solubility → **more** anesthetic molecules are required to raise [P_a] → **more** time for induction and recovery

"slower"

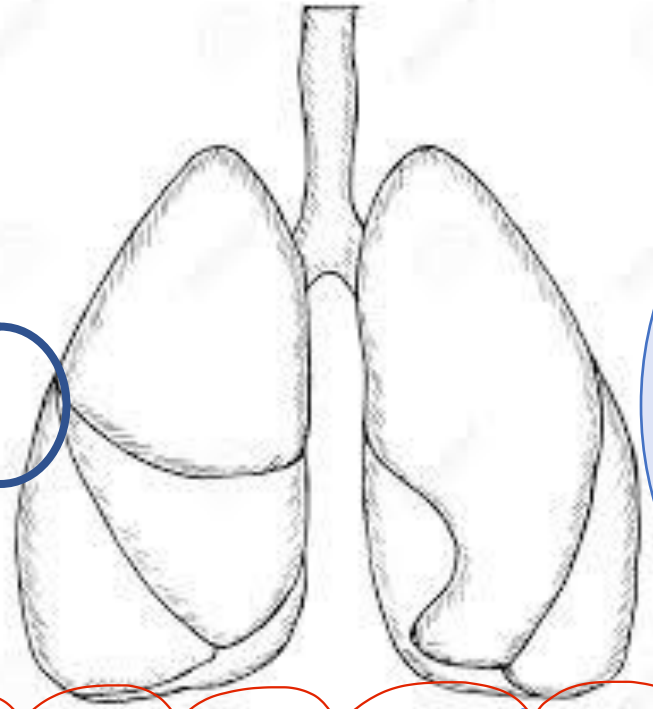
* العلاقة بين blood:gas coefficient و rate of induction of anesthia و recovery ← inverse

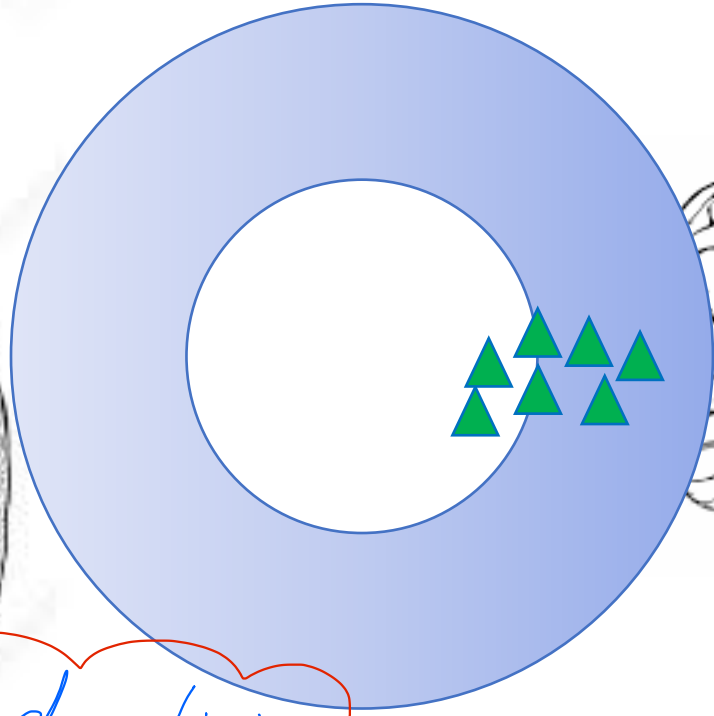


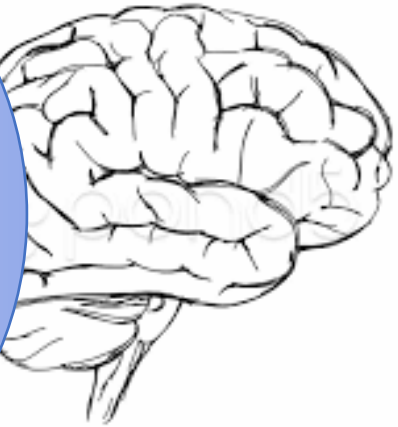




Anesthesia machine







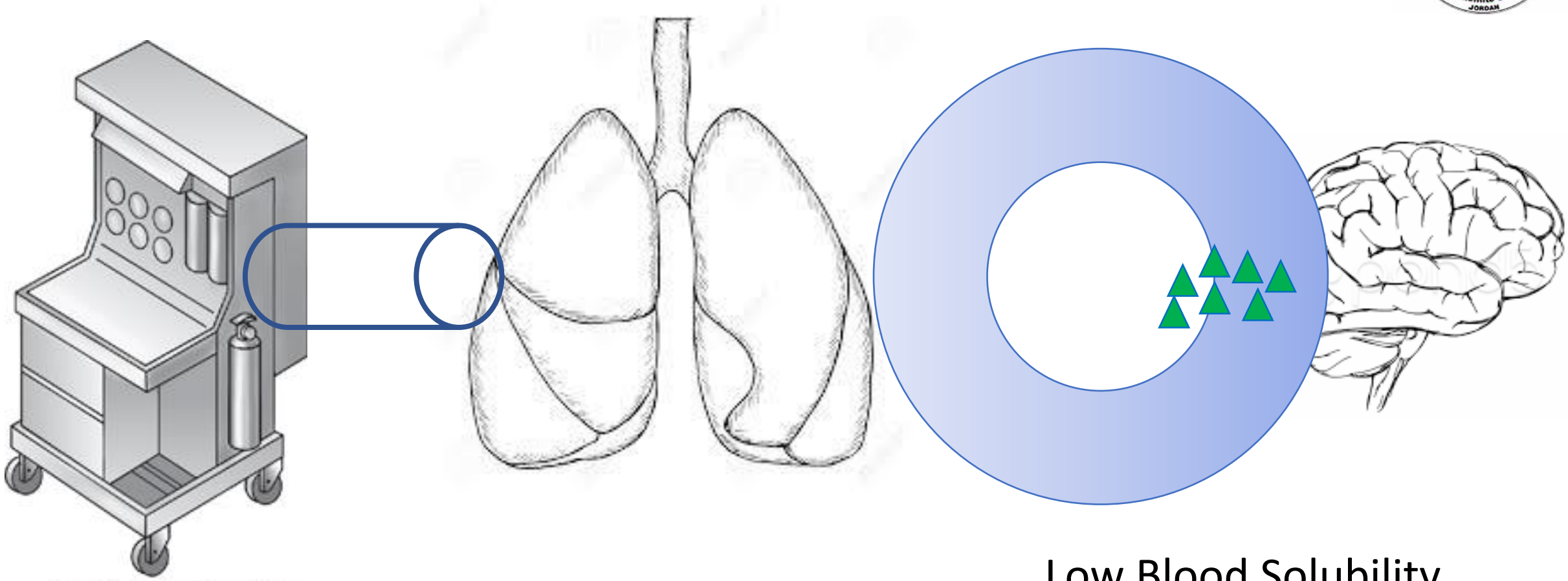
Slower rate of induction

بالتالي رح ياخد وقت اطول to induce anesthia and recovary.

more drug molecule وبالتالي بدنا to raise the Pa of (gas)

High Blood Solubility

it will stay in the circulation for prolonged period of time



Anesthesia machine

Low Blood Solubility

Larger percentage of drug molecule will diffuse from blood circulation to the brain

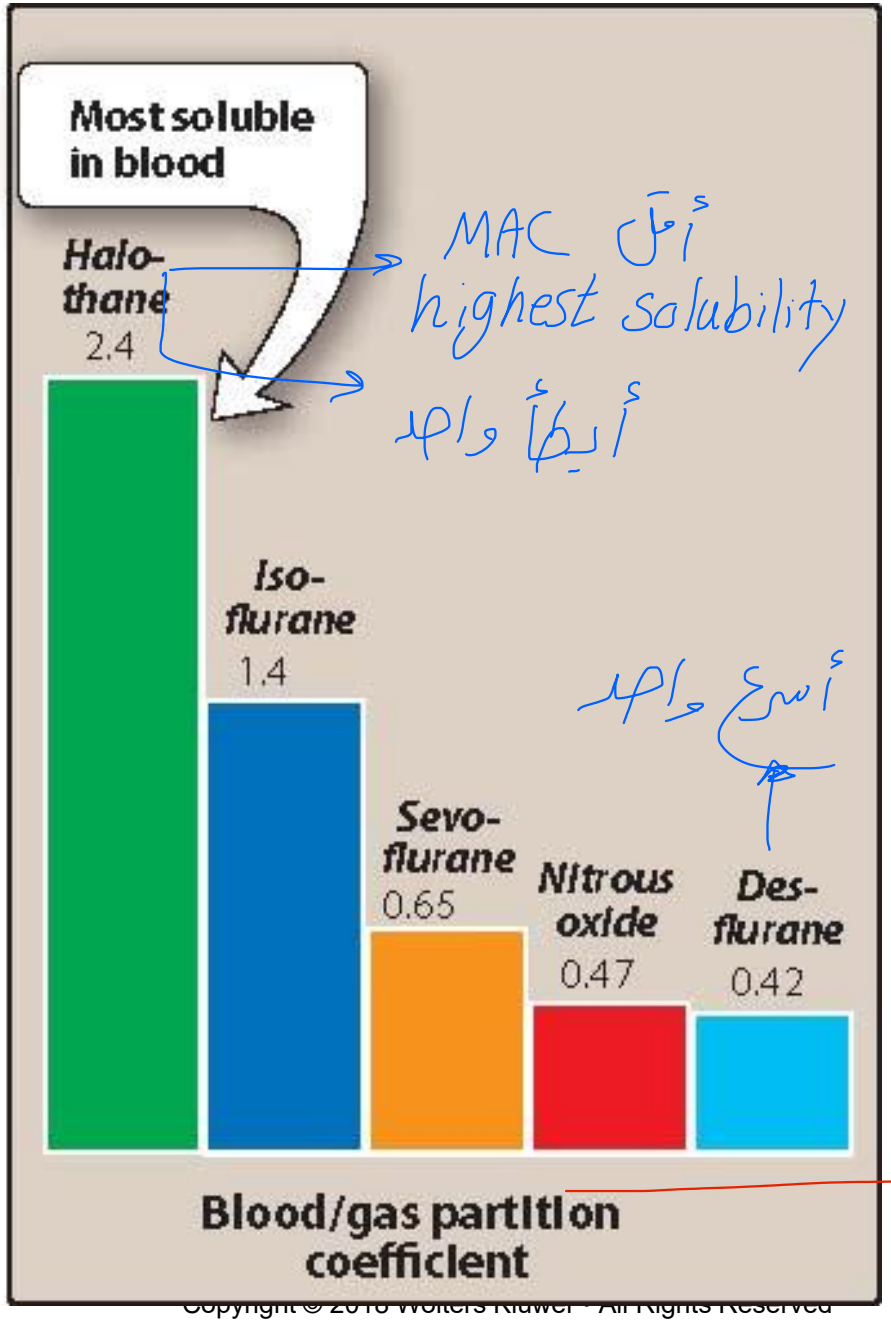
will rais the cerebral partial pressure of the anesthetic

Faster rate

inverse relationship

1. MAC
(↓MAC → the drug is more potent)

2. solubility
(↓blood:gas coefficient → the drug is faster in induction anesthsia)



MAC أقل highest solubility

أبطأ واطلع

أسرع واطلع

* واللي بوصل لـ Steady state أسرع

the Low solubility

تلات لو جاب الرسمة في سلايد 98 بتقدر تحدد حسب الـ MAC فقط مين الأقوى..

most potent one ?
dependon MAC only
* We can't detrmine in this figure.

* invers relation ship

Cardiac Output

- CO affects washing the anesthetic to peripheral tissue (NOT the site of action)

COMPARE TO IV ANESTHETICS?

High CO → Increase pulmonary blood flow (more removal to the periphery) → slow rise in [P_{alv}] → slow induction → slower recovery

brain. بعيدة عن الـ

Low CO → ↓ pulmonary blood flow (less removal to the periphery) → **fast** rise in [P_{alv}] → **faster** induction

Differences in Tissue Type on Uptake

$$\text{Steady State} \sim \frac{\text{Blood flow to the tissue}}{\text{Capacity of tissue to store the anesthetic (proportional to tissue volume)}}$$

Tissue Type	Perfusion (Blood Flow)	Capacity
Brain, heart, liver , kidney, endocrine glands	Good	Low
Skeletal muscles	Poor	Large
Adipose tissue	Poor	Large
Bone, cartilage	Poor	Low

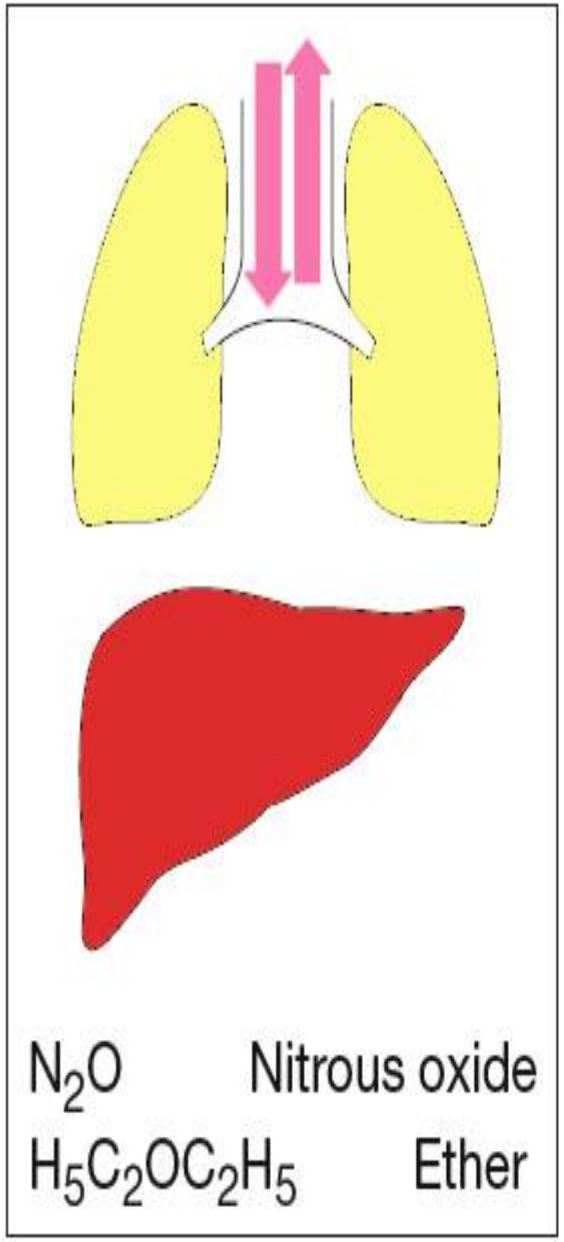
Elimination

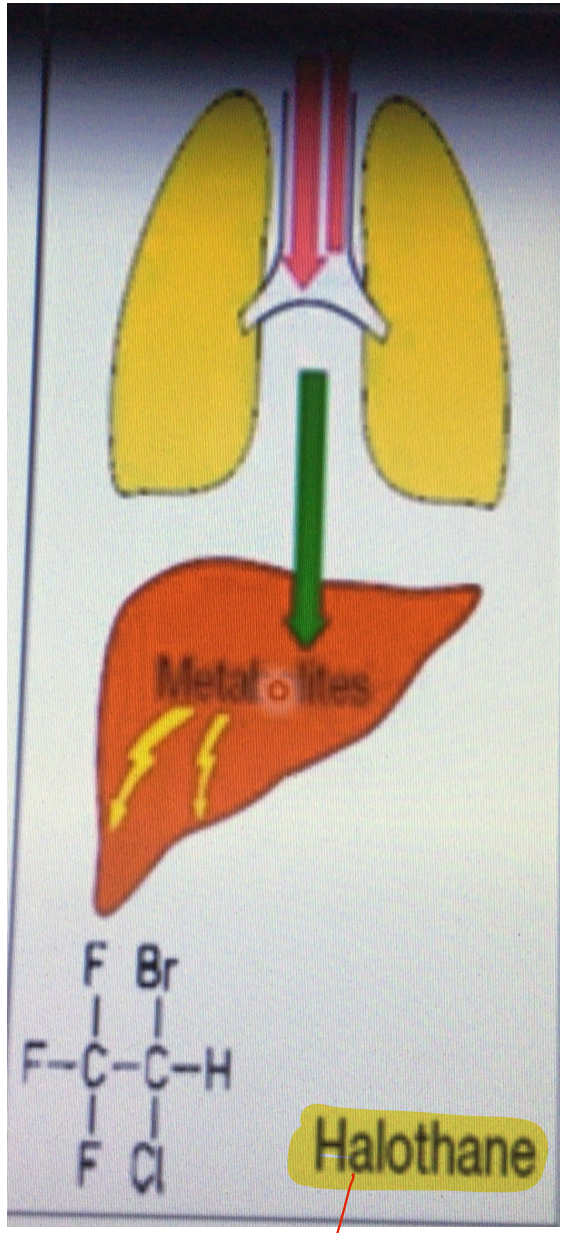
- The time to recovery from inhalation anesthesia depends on the rate of elimination of anesthetics from the brain after the inspired concentration of anesthetic has been decreased.

- Inhaled anesthetics that are relatively insoluble in blood (low blood: gas partition coefficient) and brain are eliminated at faster rates than more soluble anesthetics.

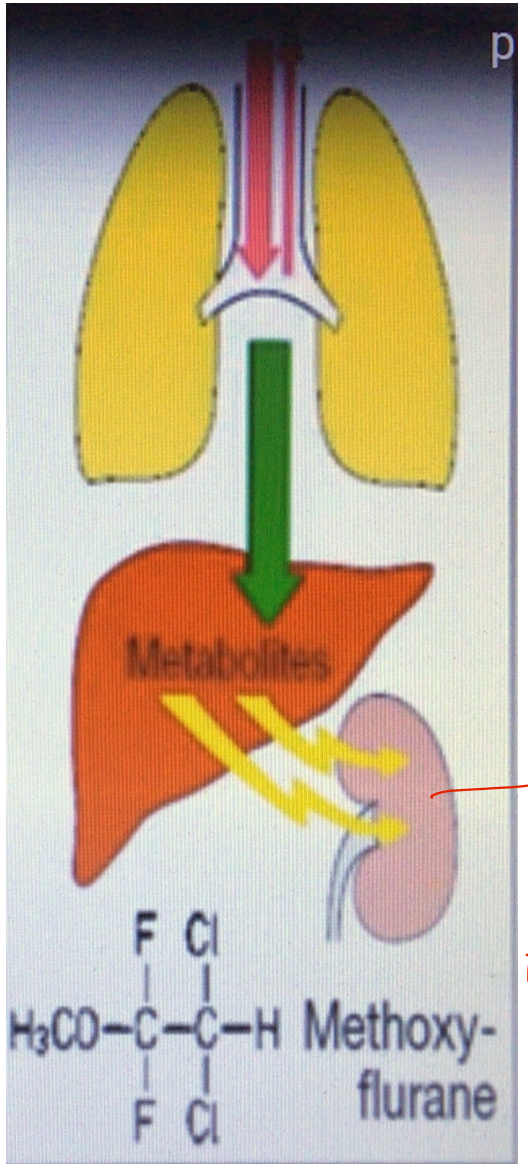
* majority of elemination of halothane happens through the lung

All inhaled anesthetics are eliminated mainly through lungs





heavily metabolised by the liver



its metabolite excreted through the kidney.

Elimination routes of different volatile anesthetics

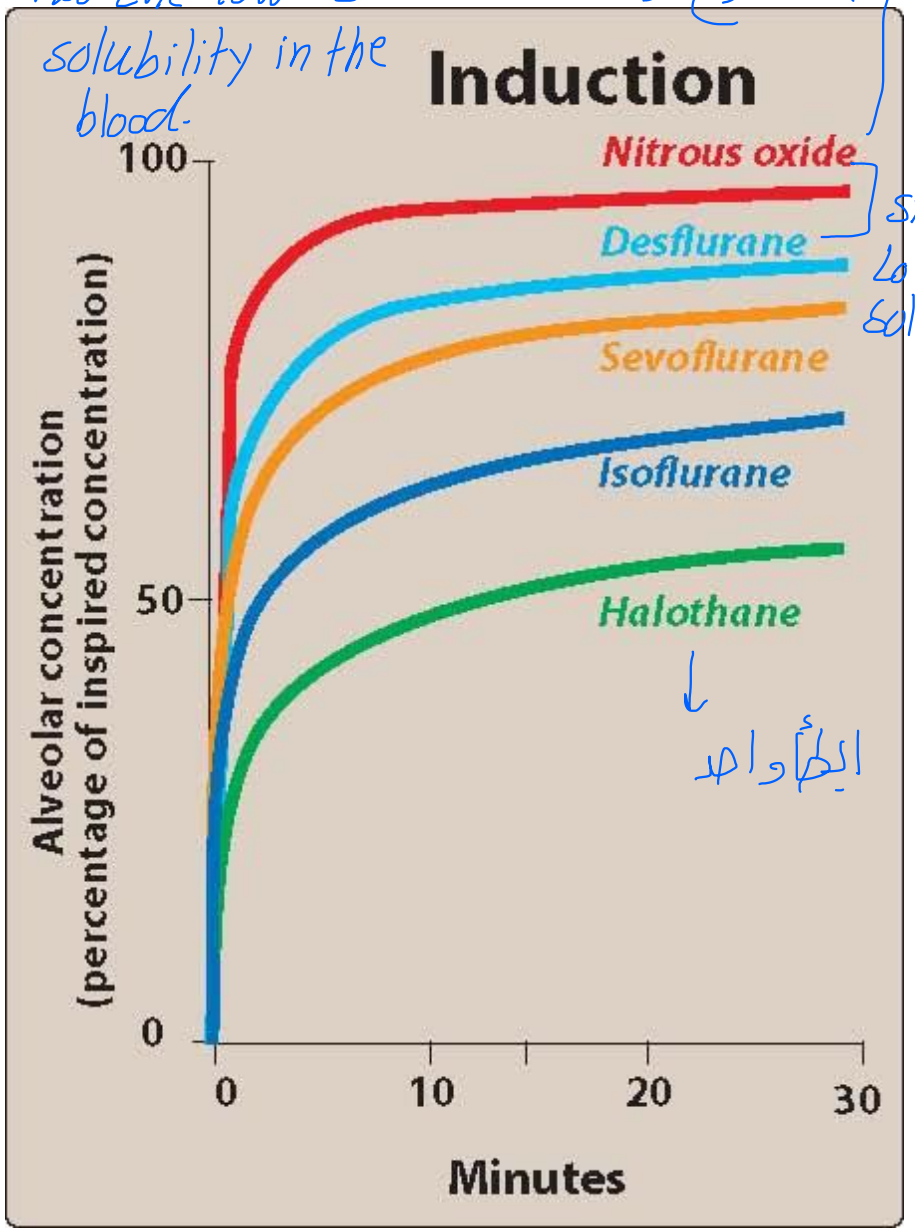
Recovery

- The duration of exposure to the anesthetic can have a marked effect on the time of recovery. If exposure to the anesthetic is short, recovery may be rapid.

- Clearance of inhaled anesthetics by the lungs into the expired air is the major route of their elimination from the body

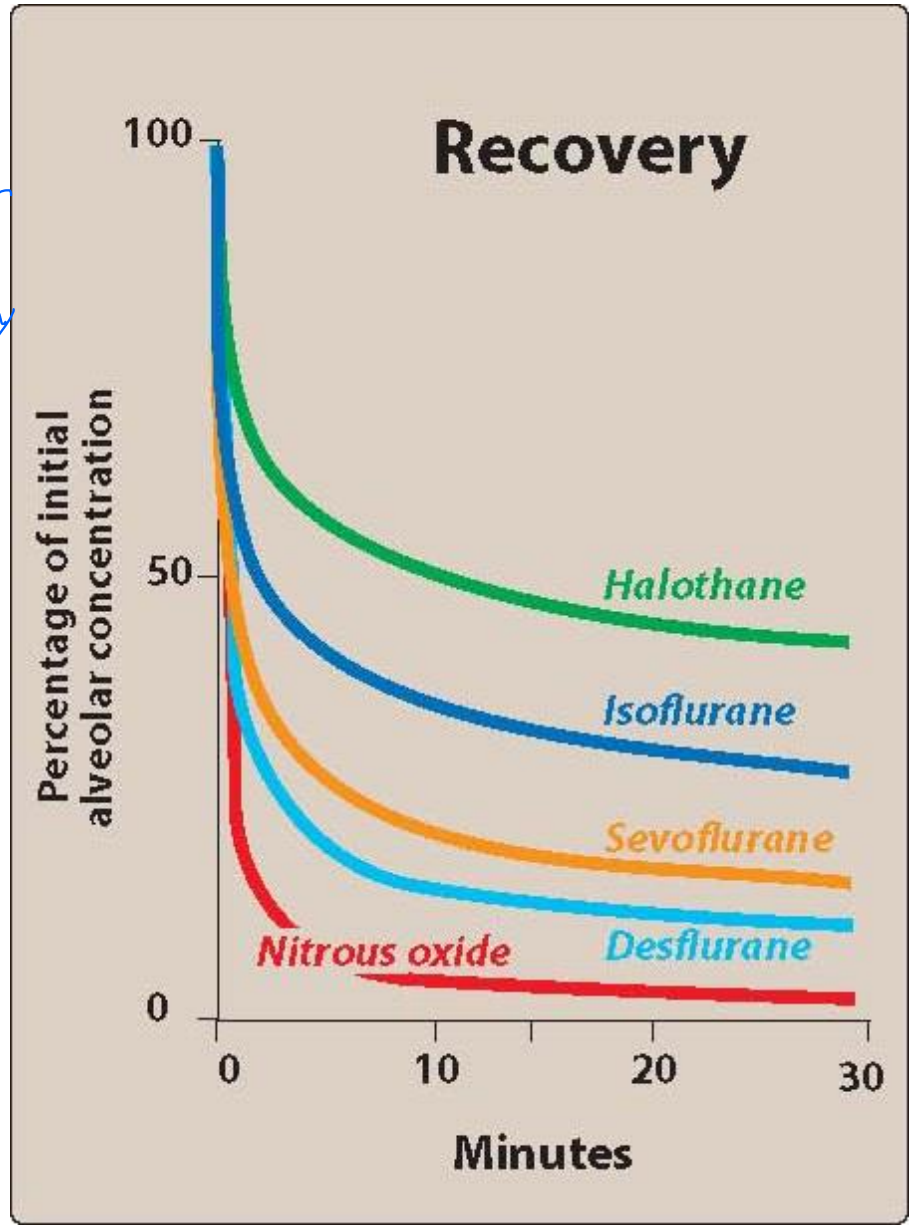
has the lowest solubility in the blood.

اسرع واحد



similar low solubility

ابطأ واحد



ابطأ

اسرع

Isoflurane

- Has a pungent smell → stimulates the respiratory reflexes → NOT used for inhalational induction ONLY for maintainance.
- Causes hypotension
- Solubility? Induction time?
- Low cost
- Longer surgeries

Desflurane

ONLY for maintainance as isoflurane.

- Respiratory irritant → NOT used for inhalational induction
- Causes hypotention
- Low blood solubility → very fast induction and recovery
- Higher cost
- Better for short surgeries

Sevoflurane → used to induce anesthesia in pediatric age population

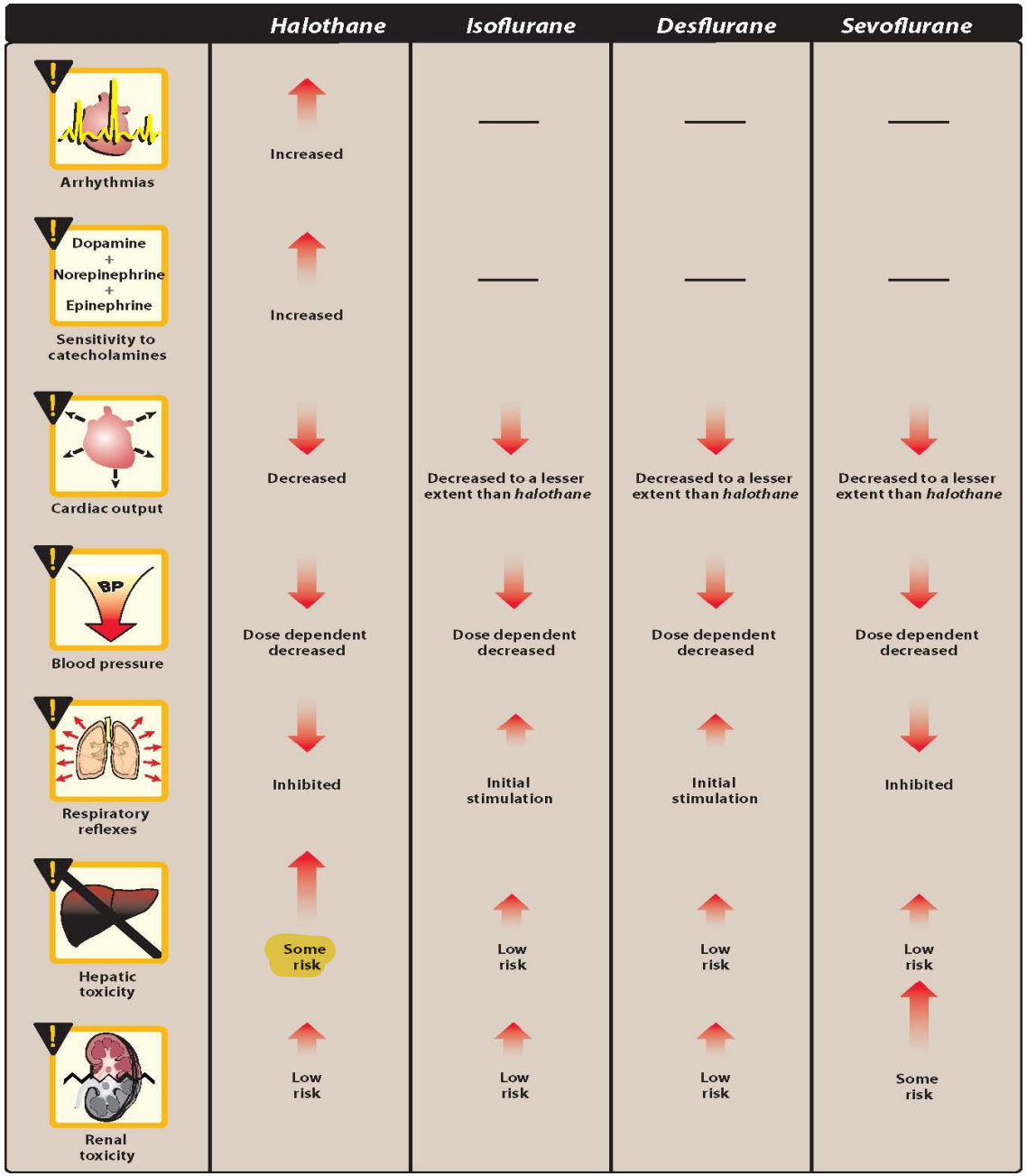
- Low pungency and respiratory irritation → can be used for inhalational induction
- Low solubility

Nitrous Oxide

Least potent one.

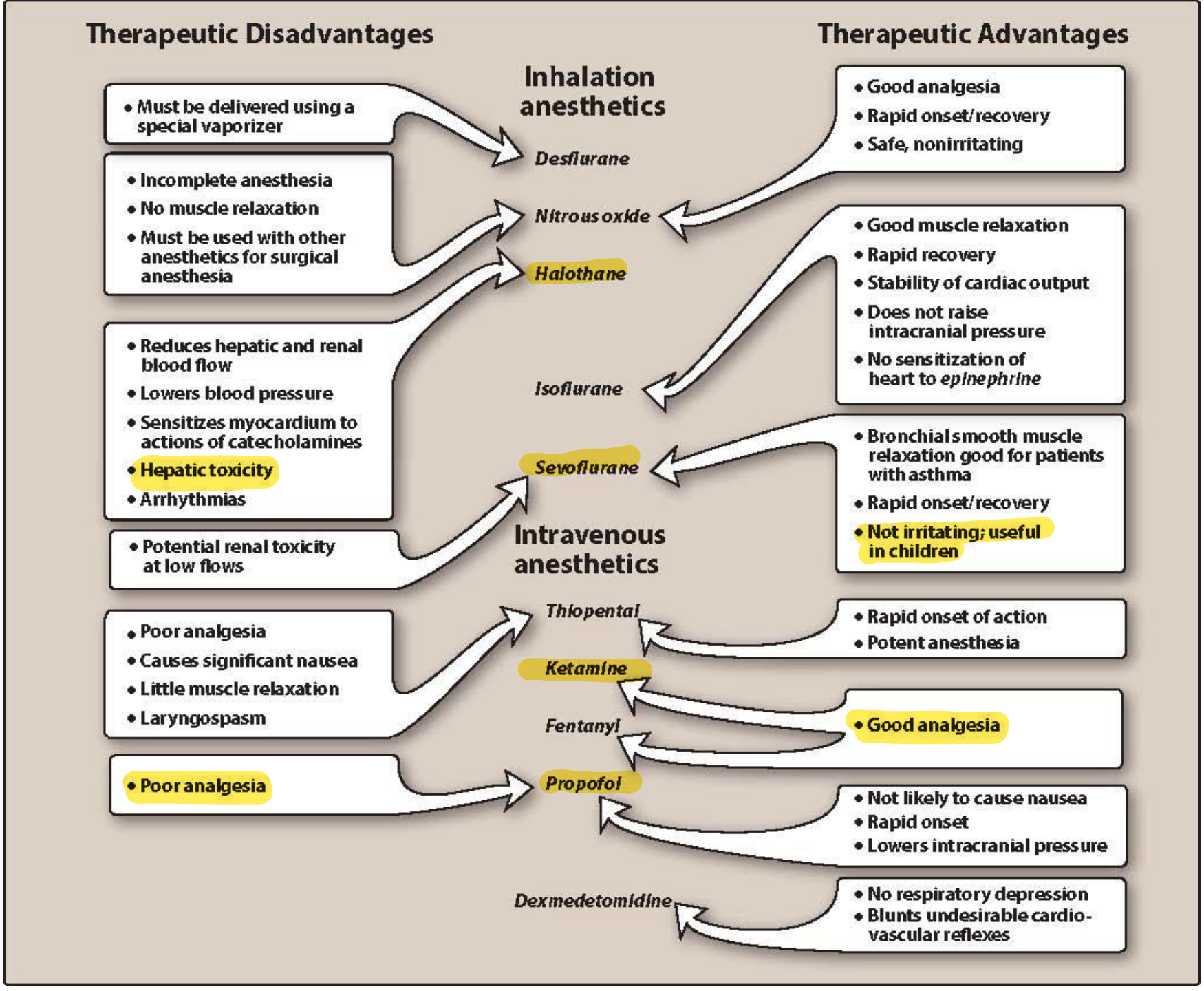
Nitrous Oxide

- Gas (inorganic).
- Very rapid induction and recovery.
  - Why? very low blood solubility.
- least potent, highest MAC value.
- Poor anesthetic, good analgesic
- Administered with O_2 to avoid diffusion hypoxia (to produce sedation - dentistry)
- Administered with other inhalational agents for general anesthesia



Malignant Hyperthermia

- Rare anesthesia complication (only in susceptible patients; autosomal dominant)
- Exposure to: halogenated anesthetics, succinylcholine
- Life threatening
- Due to uncontrolled, excessive increase in skeletal muscle oxidative metabolism
- Treatment: dantrolene



Anesthetic Adjuncts

Anesthetics Adjuncts

Anxiolytics
- Benzodiazepines
-midazolam

Facilitation of intubation
- Neuromuscular blocking agents

Anticholinergics
- WHY?

↓ Secretion in the airway tract (congestion)

↓ gastric acid secretion
- H_2 antagonists
-famotidine
-ranitidine

Analgesics
- NSAIDS
- Paracetamol
- Opioids (fentanyl)

Prevent allergic reactions
- antihistamines
-diphenhydramine

Antiemetics
- ondansetron → serotonine antagonist

except propofol

Stages of Anesthesia

INDUCTION

- Mostly using intravenous anesthetics
  - *propofol* → most commonly used
- Produce unconsciousness in 30-40 seconds very fast
- Could use an inhalational agent e.g., pediatric
  - → like sevoflurane

MAINTENANCE

- Mostly using inhalational agents
- Combined with fentanyl (opioid) to produce analgesia

RECOVERY

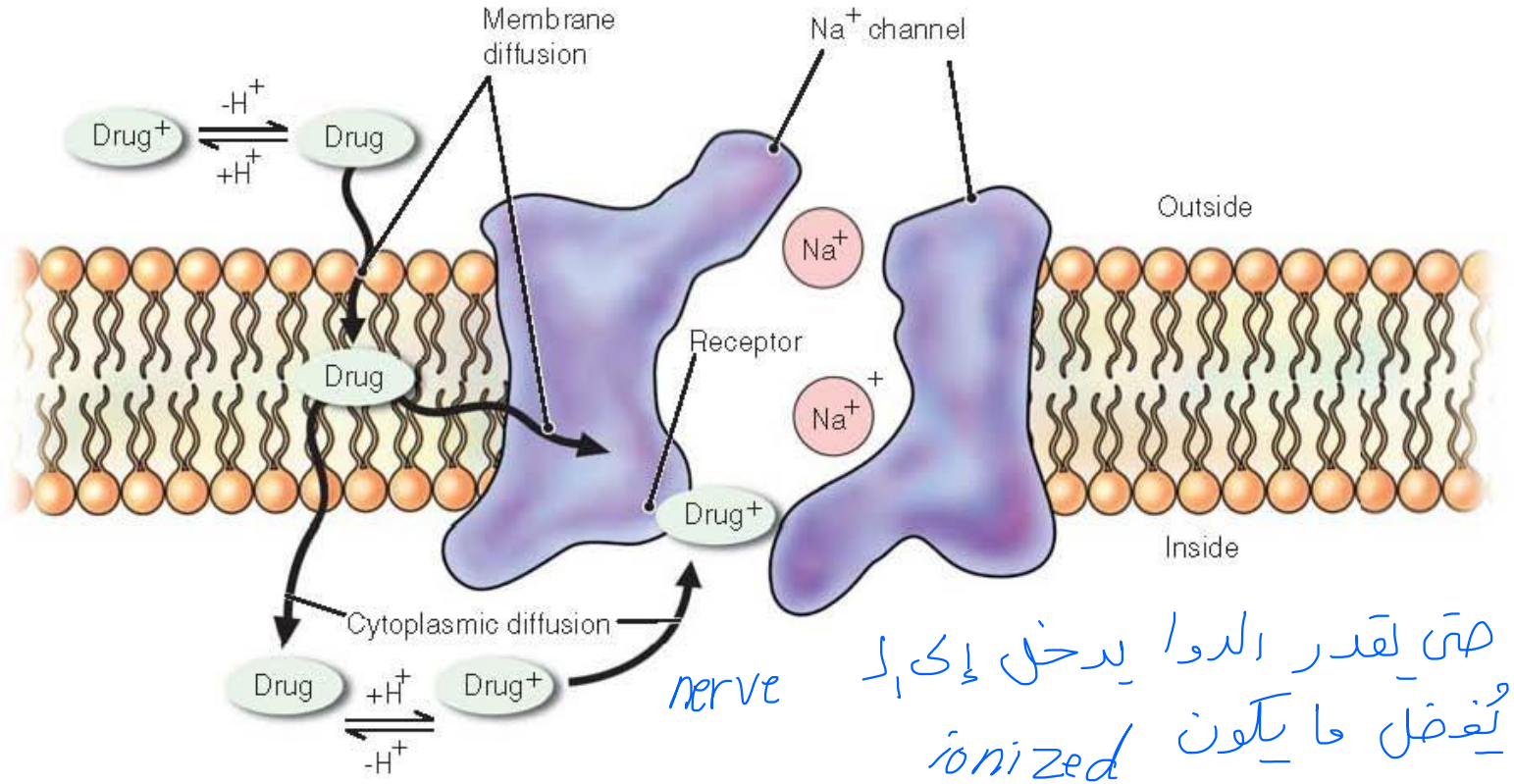
- Recovery happens due to the **redistribution** rather than metabolism

Local Anesthetics

Local Anesthetics

- Low doses: block sensory conduction
- High doses: block motor impulses (paralysis)

- **Mechanism of action:** "Sodium channels blockade"



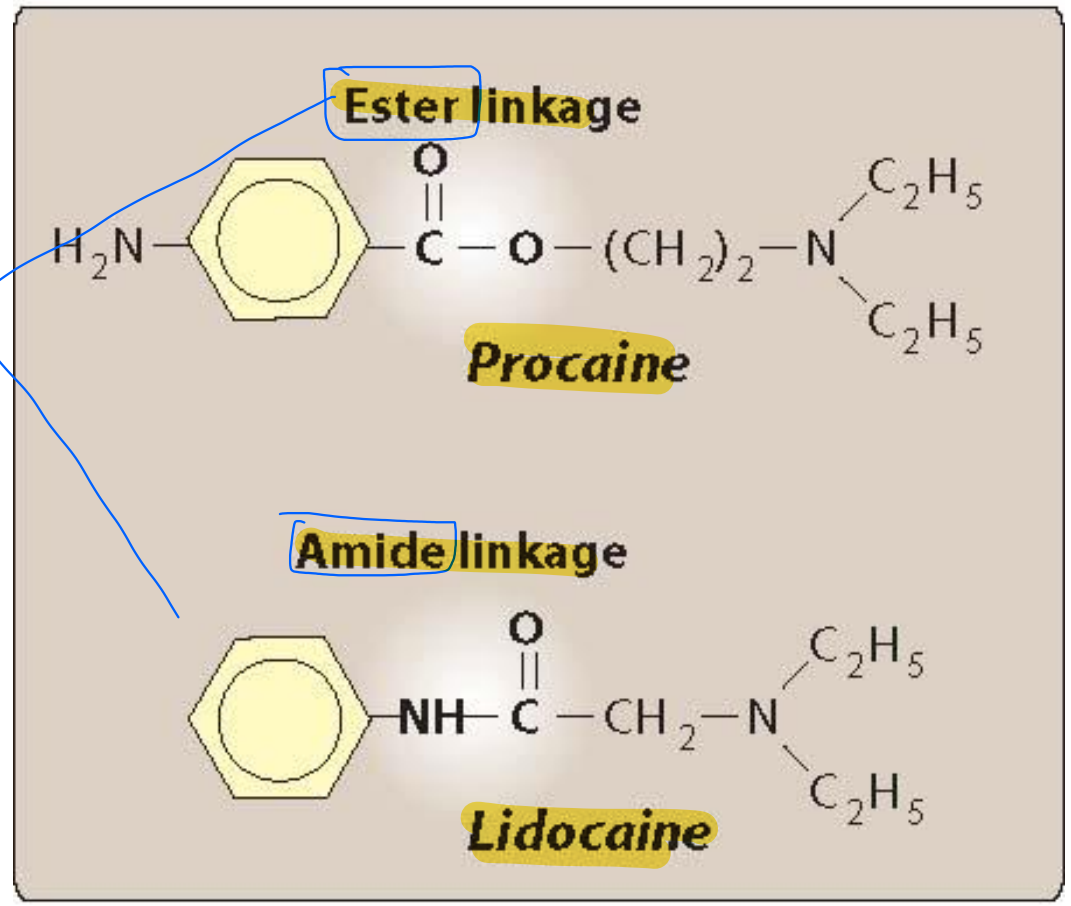
* حتى يقدر الدوا يدخل إلى الـ nerve يُفضل ما يكون ionized

* حتى يدخل على الـ Na+ channel ويسكرها يُفضل يكون (charged/ionized)

GAs appear to act by depressing synaptic transmission (unlike local anesthetics which act primarily by blocking axonal conduction)

Delivery Options

- Topical
- Infiltration (dentist)
- Perineural
- Neuraxial
  - Spinal
  - Epidural
  - Caudal



weak acids

LOCAL ANESTHETICS: AMIDES
Bupivacaine MARCAINE
Lidocaine XYLOCAINE
Mepivacaine CARBOCAINE
Ropivacaine NAROPIN

LOCAL ANESTHETICS: ESTERS
Chloroprocaine NESACAINE
Procaine NOVOCAINE
Tetracaine PONTOCAINE

Local Anesthetics

Actions:

- **Vasodilation** + sensory block
  - leads to rapid diffusion → short duration of action
  - overcome by adding a vasoconstrictor e.g., *epinephrine*

to increse the duration of action

- **Antiarrhythmic**
  - e.g., *lidocaine*

Local Anesthetics

Duration of actions:

- **Factors affecting the duration of action:**

1. Tissue pH
2. Nerve morphology
3. Concentration
4. Lipid solubility
5. pKa (most important)

myelinated
unmyelinated

تعتمد الدواء يدخل اسرع

"to block Na^+ channel"

- lower pKa → more ionized at physiologic pH → faster
- What happens if the tissue is infected?

↳ pH → more acidic → less drug available in ionized form.

Hepatic metabolism does NOT affect duration of action of local anesthetics

Systemic Toxicity

- What if a local anesthetic was administered frequently or inadvertently in the vein (IV)?

❑ Local Anesthetic Systemic Toxicity (LAST)

1. Altered mental status
2. Seizures
3. Cardiovascular instability

Treatment: Lipid Rescue Therapy (20% lipid emulsion infusion)

CHARACTERISTIC	ESTERS • *Procaine* • *Tetracaine* • *Chloroprocaine* • *Cocaine*	AMIDES • *Lidocaine* • *Mepivacaine* • *Bupivacaine* • *Prilocaine* • *Ropivacaine*
Metabolism	Rapid by plasma cholinesterase	Slow, hepatic
Systemic toxicity	Less likely	More likely
Allergic reaction	Possible- PABA derivatives form	Very rare
Stability in solution	Breaks down in ampules (heat, sun)	Very stable chemically
Onset of action	Slow as a general rule	Moderate to fast
pK_a's	Higher than physiologic pH (8.5–8.9)	Close to physiologic pH (7.6–8.1)

DRUG	POTENCY	ONSET	DURATION
Procaine	Low	Rapid	Short
Chloroprocaine	Low	Rapid	Short
Tetracaine	High	Slow	Long (spinal)
Lidocaine	Low	Rapid	Intermediate
Mepivacaine	Low	Moderate	Intermediate
Bupivacaine	High	Slow	Long
Ropivacaine	High	Moderate	Long

- Thank you
- Questions?