

General Anesthesia

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General Anesthesia

2 parts

①

GENERAL ANESTHESIA I

Phases of anesthesia

②

General Anesthesia II

Pharmacology (Drugs used in anesthesia)

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labelled



GENERAL ANESTHESIA II PHARMACOLOGY (DRUGS USED IN ANESTHESIA)

I have no disclosure

Objectives:

- * **Classes of drugs used in different types of anesthesia: GA and LA**
- * **Indications, contraindications and side effects of commonly used anesthetic drugs**
- * **Common reversal agents used in anesthesia practice**

① local ②
② topical

reversal agent
GA →
LA →
opioid

Types of Anesthesia:

- **General Anesthesia**

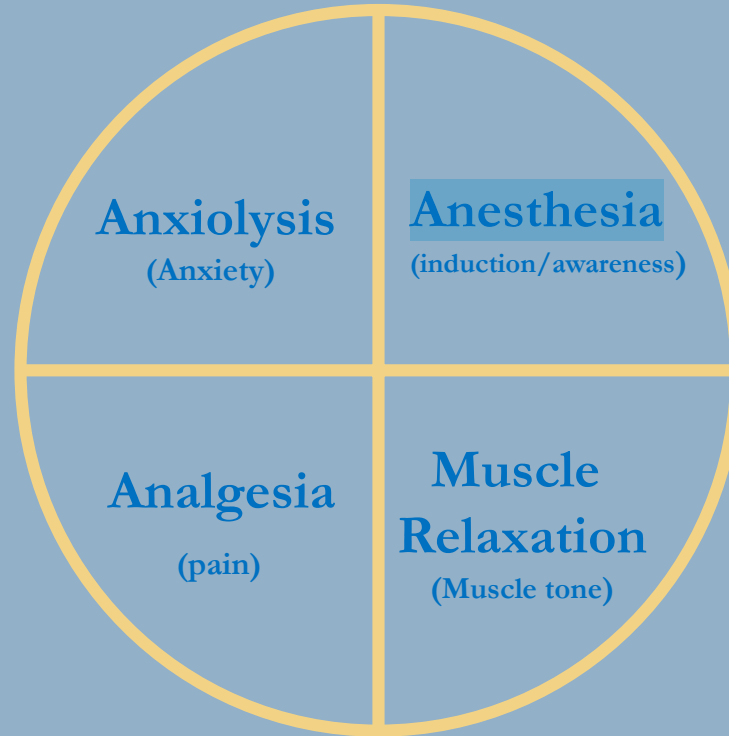
- Local & Regional Anesthesia

Pharmacology used in

General Anesthesia

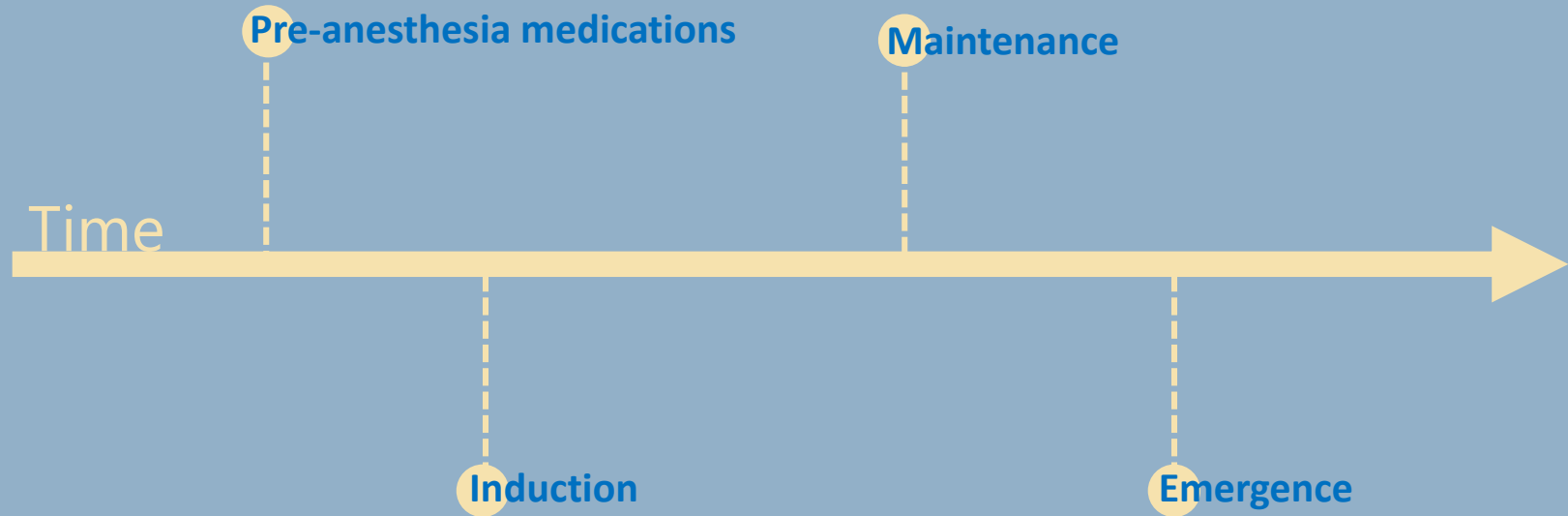
Goals for optimal state of ..

Balanced Anesthesia



Pharmacology used in

General Anesthesia



Pharmacology used in

General Anesthesia

GA pharmacology

Inhalational agents

Intravenous agents

Gas

Volatile liquids

Hypnotic agents

block for word memory
Benzodiazepines

met for Pain
Analgesic agents

complaint for everything
Dissociative agents

met for muscles Relaxing
NeuroMuscular blockers

Nitrous oxide
Zenon

Ether
Halothane
Isoflurane
Desflurane
Sevoflurane

Propofol
Etomidate
Thiopental
Methohexitone

Midazolam
Lorazepam
Diazepam

Opioids
Non-opioid

Ketamine

m

Pharmacology used in

General Anesthesia

Inhalational agents: **Nitrous oxide**



Advantages

- Analgesic properties
- Rapid onset/offset
- Minimal CVS depressant \ effect

Disadvantages

- Weak anesthetic agent (used combined in 30 -70 %)
- Trigger nausea/ vomiting
- Rapidly diffuse and expand air containing cavities → avoid in PNTx or bowel obst.
- Inactivation of B12-dependent enzymes → Megaloblastic anemia
- Teratogenic (animal)
- ? Abuse

Pharmacology used in

General Anesthesia

Inhalational agents: **Isoflurane**



Advantages

- Low biotransformation (less fluoride) → no nephrotoxicity, no hepatotoxicity
- * Inexpensive

Disadvantages

- **Coronary vasodilator** → Potential for **coronary steal Effect.**
- **Pungent**
- **Slow onset/offset**
- **Tachycardia**

Pharmacology used in

General Anesthesia

Inhalational agents: **Sevoflurane**



Advantages

* Least pungent. Fast onset-
Offset. Less tachycardia
→ **best inhaled induct agent**

Disadvantages

• ? Nephrotoxic (**fluoride** and **Degradation to Compound A**),
Nephrotoxic in animals ↷

Pharmacology used in

General Anesthesia

Inhalational agents: **Desflurane**



Advantages

* Most rapid onset/offset

Disadvantages

- Very pungent → can lead To bronchospasm



Pharmacology used in

General Anesthesia

Inhalational agents: **MAC = potency**

What is MAC ?

It's the minimum alveolar concentration

It's unitless value comparing **potency** of inhaled anesthesia

Reference point (**1 MAC**) = alveolar concentration of inhaled anesthesia at which **50% of patients** will not move in response to a standard surgical stimulus

At 1.3 MAC → 95% of patients will not move in response to surgical stimulus

At 0.15 to 0.5 MAC → 50% of patient will open eyes on command

MAC is an **additive value** (i.e; 0.5 MAC of N₂O, + 0.5 MAC of sevoflurane = 1 MAC)

Pharmacology used in

General Anesthesia

Inhalational agents: **MAC = potency**

Name	MAC
Isoflurane	1 %
Sevoflurane	2 %
Desflurane “d”	6 %



Pharmacology used in

General Anesthesia

Intravenous agents: **Propofol**



- It's insoluble alkyphenol formulated in lipid emulsion
- It augments **GABA receptors**
- Lipid emulsion support **bacterial growth** (use within 12hrs)
- Contains egg yolk (avoid w/ clear hx of **egg anaphylaxis**)
- Prolonged infusion of propofol can lead to **(PRIS): Propofol Related Infusion Syndrome**

Pharmacology used in

General Anesthesia

Intravenous agents: **Propofol**

	Physiological changes
HR	↔ ↓
MAP	↓ ↓ ↓
contractility	↓
CBF	↓ ↓ ↓
ICP	↓ ↓ ↓
Ventilatory drive	↓ ↓ ↓



Pharmacology used in

General Anesthesia

Intravenous agents: **Etomidate**



- Favored to **used** in hemodynamically unstable patient (gentle on hemodynamics)
- Can cause adrenal suppression

Pharmacology used in

General Anesthesia

	Physiological changes
HR	↔
MAP	↔ ↓
contractility	↔
CBF	↓ ↓
ICP	↓ ↓
Ventilatory drive	↓

Intravenous agents: **Etomidate**



Pharmacology used in

General Anesthesia

Intravenous agents: **Dexmedetomidine**



- It's a selective $\alpha 2$ -adrenergic agonist
- Has sedative, amnestic and analgesic effects
- Desirable for **sedation** with minimal respiratory depression
- Lead to less use of opioids if combined with them
- High cost
- Dose dependent **hypotension and bradycardia**

Pharmacology used in



General Anesthesia

	Physiological changes
HR	↓
MAP	↑ bolus ↓ infusion
contractility	↔
CBF	↓
ICP	↔
Ventilatory drive	↔ ↓

Intravenous agents: **Dexmedetomidine**

DEXMEDETOMIDINE

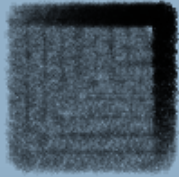
4 mcg/mL

Dt. _____ Tm. ____:____ Init. ____



Pharmacology used in

General Anesthesia



Intravenous agents: **Ketamine**



- It's NMDA receptor antagonist
- Produce **dissociative hypnosis** and analgesia
- Potent **bronchodilator** but increases oral secretion
- Less opioids used when combined with them
- **Preserve** respiratory and CVS function
- Dose dependent psychomimetic effect (**hallucinations**) → decreased with co-administration of Benzodiazepines
- Can be used for uncooperative patients (oral/ IM routes)

Pharmacology used in

General Anesthesia

Intravenous agents: **Ketamine**

	Physiological changes
HR	↑ ↑
MAP	↑ ↑
contractility	↓
CBF	↑
ICP	↔ ↑
Ventilatory drive	↔

sympathomimetic



Pharmacology used in

General Anesthesia

Intravenous agents: **benzodiazepines** (e.g; midazolam)



- It augments GABA receptors
- It's a potent anxiolytic
- It produces amnesia
- It's potent **anticonvulsant**
- Can be antagonized by Flumazenil

Pharmacology used in

General Anesthesia

	Physiological changes
HR	↔
MAP	↔ ↓
contractility	↔
CBF	↓
ICP	↔
Ventilatory drive	↓

Intravenous agents: **benzodiazepines** (e.g; midazolam)



Pharmacology used in

General Anesthesia

	Physiological changes
HR	↔ ↓
MAP	↓ ↓
contractility	↔
CBF	↓ N ₂ O
ICP	↓
Ventilatory drive	↓

Intravenous agents: **Opioid**

* **Suppress pain through action on Mu, Kappa, Delta opioid receptors**

All of these are Receptors

- **Directly inhibit ascending nociceptive transmission and activate descending pain control**
- **Trigger chemoreceptors → nausea/vomiting**
- **Can cause respiratory depression and chest wall rigidity**
- **Can lead to urinary retention**

Pharmacology used in

General Anesthesia

Intravenous agents: **Opioid: (Fentanyl)**

- 1- **Quick** onset and quick redistribution
- 2- Peak respiratory depression after **5-15 min**
- 3- **Less** emetic effect than Morphine
- 4 - Cleared by **liver**



Pharmacology used in

General Anesthesia

Intravenous agents: Opioid: (**Morphine**)

- 1- Cross blood-brain barrier **slowly**
- 2- Peak effect may be delayed **10-40 min**
- 3- Cleared by **kidneys** → adjust dose in renal failure
- 4- Higher **histamine** release



Pharmacology used in

General Anesthesia

Intravenous agents: **Opioid: (Remifentanyl)**

- 1- Cleared by **rapid** metabolism **by esterase enzyme**
- 2- known for causing more **bradycardia**



Pharmacology used in

General Anesthesia

Intravenous agents: Opioid: (**Meperidine**)

- 1- used for analgesia and for **post operative shivering**
- 2- its metabolized by liver to active metabolites (nor-meperidine) that get excreted by kidneys
- 3- Nor-meperidine **can cause seizure** → caution with Elderly, renal impairment or chronic dosing
- 4- Structural similarity to atropine → cause **high HR**



Pharmacology used in

General Anesthesia

Intravenous agents: **Opioid reversal (Naloxone)**

Indication: opioid overdose or
its S.Es of opioid related respiratory depression or opioid related purities

Onset : 1-2 min

Mechanism: competitive inhibitor of opioid receptors

How to use: use smallest dose then titrate to desired clinical effect or RR or level of alertness

S.Es: can cause hypertension an dysrhythmias, pulmonary edema, or delirium

Pharmacology used in

General Anesthesia

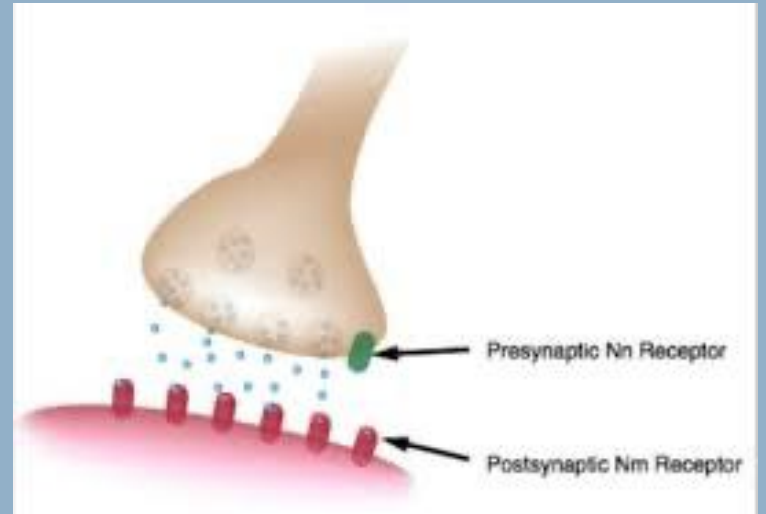
Intravenous agents: **Neuromuscular blockade (NMB) agents**

- * Works at **postsynaptic** nicotinic acetylcholine receptors
- * Stop conduction of nerve impulse → **skeletal muscle**

Paralysis

* **Used to:**

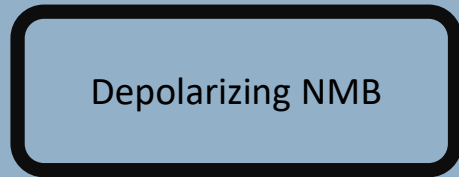
- improve intubating conditions
- facilitate mechanical ventilation
- Provide muscle relaxation for surgical manipulation



Pharmacology used in

General Anesthesia

Intravenous agents: **Neuromuscular blockade (NMB) agents**



1- **Mimic Ach** → bind cholinergic receptors keeping the ion channel open
→ Cause **prolong depolarization** (seen as diffuse muscle contraction)

2- activated occupied receptors can't react to further Ach (overwhelmed) → muscle paralysis arisen



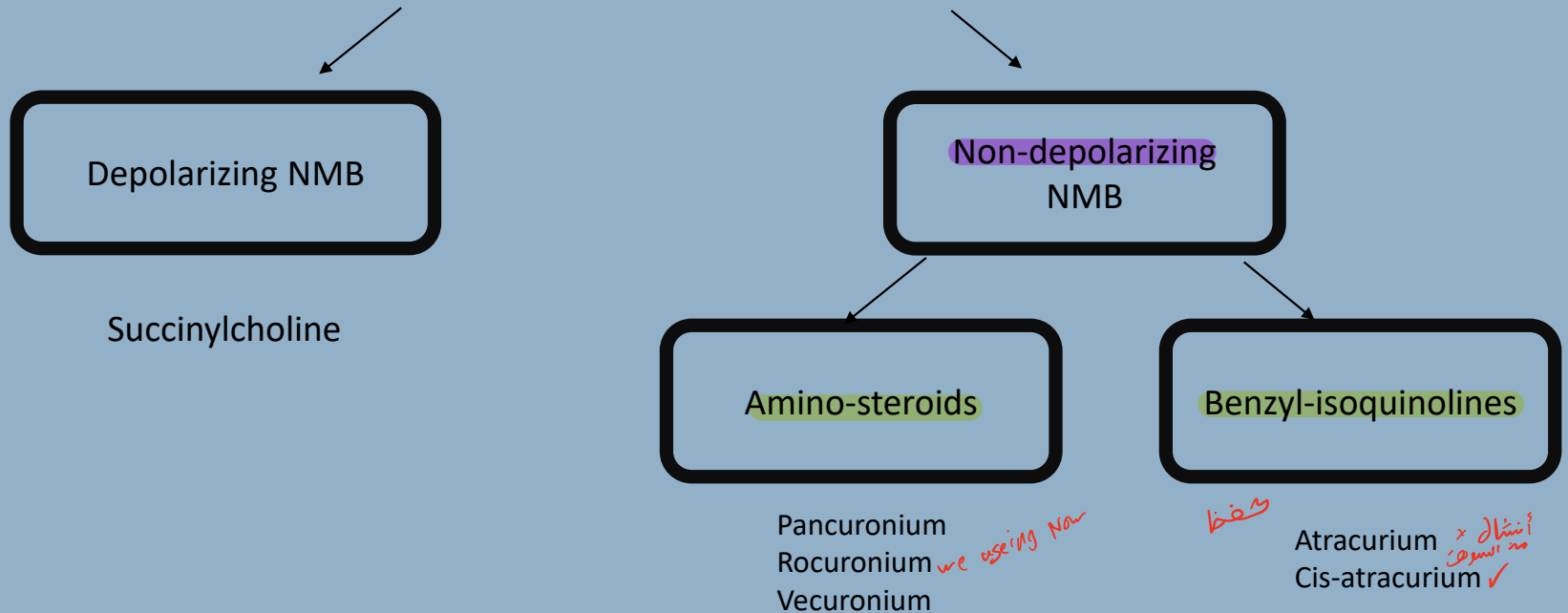
1- **Competitive Ach receptors antagonist** → no space for Ach to bind its R → muscle paralysis arisen

2- action of non-depolarizing NMB can be removed
By increasing Ach in the synaptic cleft

Pharmacology used in

General Anesthesia

Intravenous agents: Neuromuscular blockade (NMB) agents



Pharmacology used in

General Anesthesia

Intravenous agents: **Neuromuscular blockade (NMB) agents**

Class	Name	Advantage	Clearance	S.Es
Depolarizing NMB	Succinylcholine	Rapid onset/ultra short	Rapid hydrolysis in the plasma by plasma cholinesterase enzyme	Can trigger MH
Non-depolarizing NMB	Atracurium		Cleared by Hofmann Elimination	Dose-dependent histamine release
	Cis-atracurium	Doesn't cause histamine release	Cleared by Hofmann Elimination	
	Pancuronium		Mainly kidney	Long acting/ slow onset Vagolytic → high HR, BP
	Rocuronium	Short onset / can be used in RSI Doesn't cause histamine release	Hepatic and renal	
	Vecuronium	Doesn't cause histamine release	Mainly liver	Has active metabolites (avoid infusion)

Pharmacology used in

General Anesthesia

Intravenous agents: **Neuromuscular blockade (NMB) agents**

NMB – Reversal:

1- Cholinesterase inhibitors: allowing Ach to build up at the synaptic cleft, and overcome non-depolarizing NMB agents

- e.g; Neostigmine/Glycopyrrolate
- adding anti-muscarinic agent with Neostigmine can decrease its S.E, such as: bradycardia, bronchospasm, high secretions and miosis ...etc

2- Suggammadex: encapsulates **amino-steroid** class of nondepolarizing NMB only. High affinity to Rocuronium. Has S.Es of bradycardia & hypersensitivity reaction

Types of Anesthesia:

- General Anesthesia

- **Local & Regional Anesthesia**

Pharmacology used in

Local & Regional Anesthesia

Local anesthesia:

Definition:

Local anesthetics produce a transient and reversible loss of sensation (analgesia) in a circumscribed region of the body without loss of consciousness

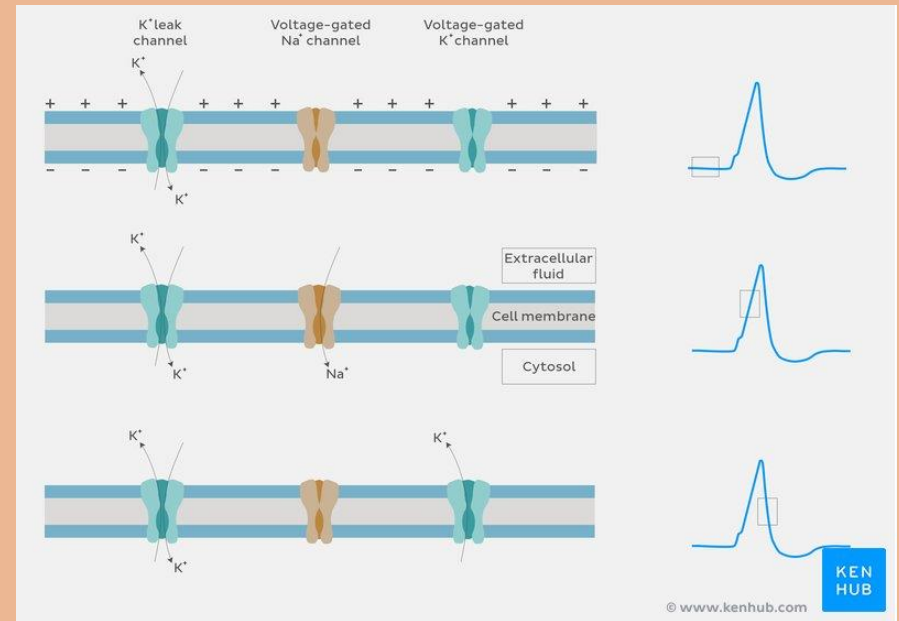
- Topical
- Local infiltration

Pharmacology used in

Local & Regional Anesthesia

Mechanism of action:

- Na channel blocker
- Preventing generation and conduction of nerve impulse



Pharmacology used in

Local & Regional Anesthesia

Classification of LA



Esters

- Benzocaine
- Procaine
- Proparacaine

Amide

- Bupivacaine (Marcaine)
- Lidocaine
- Mepivacaine (Carbocaine)

Pharmacology used in

Local & Regional Anesthesia

Esters

- Benzocaine
- Procaine
- Proparacaine

Amide

- Bupivacaine (Marcaine)
- Lidocaine
- Mepivacaine (Carbocaine)

Max doses:

- Lidocaine: 5 mg/kg
- Lidocaine + Epinephrine: 7 mg/kg • Ropivacaine: 2-3 mg/kg
- Mepivacaine: 5 mg/kg
- Bupivacaine: 2-3 mg/kg
- Levobupivacaine: 2 mg/kg

Pharmacology used in

Local & Regional Anesthesia

LA toxicity:

CNS, usually affected first → followed by CVS

Progressive signs:

1- light headedness → circumoral numbness/metallic taste → facial tingling →
Tinnitus → slurred speech → seizure → unconsciousness → Respiratory arrest

2- → CV arrest . Can have dose dependent myocardial depression → hypotension, dysrhythmia

Pharmacology used in

Local & Regional Anesthesia

LA toxicity:

What to do ?

- 1- stop injecting Local anesthetics
- 2- call for help
- 3- protect airway / 100 % FiO₂
- 4- if seizure arisen → Rx with Benzodiazepines/ propofol
- 5- if cardiac arrest → Rx with CPR and rx of arrhythmia
- 6- consider **20% lipid emulsion** (no role for propofol)



Thank you