Top Drawer Spotlight

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Overview

- Cellular Membrane Electrolyte Gradients
  - Electrolyte Gradients
  - Resting vs Threshold vs Action Potential
- Medications administered during
  - Pre-operative
  - Induction
  - Maintenance
  - Emergence

Electrolyte Gradients

- Positively-charged molecules
  - Sodium (mostly outside the cell)
  - Potassium (mostly inside the cell)
- Negatively-charged molecules
  - Chloride (mostly outside the cell)
  - Inorganic Phosphate (mostly inside the cell)
- Your reports are extracellular numbers!

Electrolyte Gradients

- Extracellular
  - + Sodium 140 mEq/L
  - + Potassium 4 mEq/L
  - ++ Calcium 2.4 mEq/L
  - ++ Magnesium 1.2 mEq/L
  - - Chloride 103 mEq/L
  - -- Inorg Phos 4 mEq/L
- Intracellular
  - + Sodium 14 mEq/L
  - + Potassium 140 mEq/L
  - ++ Calcium 0.0001 mEq/L
  - ++ Magnesium 58 mEq/L
  - - Chloride 4 mEq/L
  - -- Inorg Phos 75 mEq/L

Your reports are extracellular numbers!

Membrane Potential

- Resting Potential
  - Varies within a cell: typically anywhere from -60 to -90
  - The lower the resting membrane potential, the harder it is for the cell to reach threshold.
- Threshold Potential
  - Consistent within a cell, but varies between cell types.
  - Once threshold is hit, Action Potential cannot be stopped.

We can control a cell's action by controlling the cell's ability to reach threshold.

Pre-operative

- **Goals during the pre-operative period:**
  - Get to know the patient (history and physical exam)
    - We DO NOT sedate the patient before we interview them!
  - Pre-operative procedures (regional block)
  - Then…if needed….we can sedate/relax the patient.

Pre-operative Medications

- **Benzodiazepines**
  - Decrease anxiety
  - Typically given IV, but may be given IM or orally (kids)
  - Examples
    - midazolam (Versed)
    - diazapam (Valium)

Pre-operative Medications (Benzodiazepines)

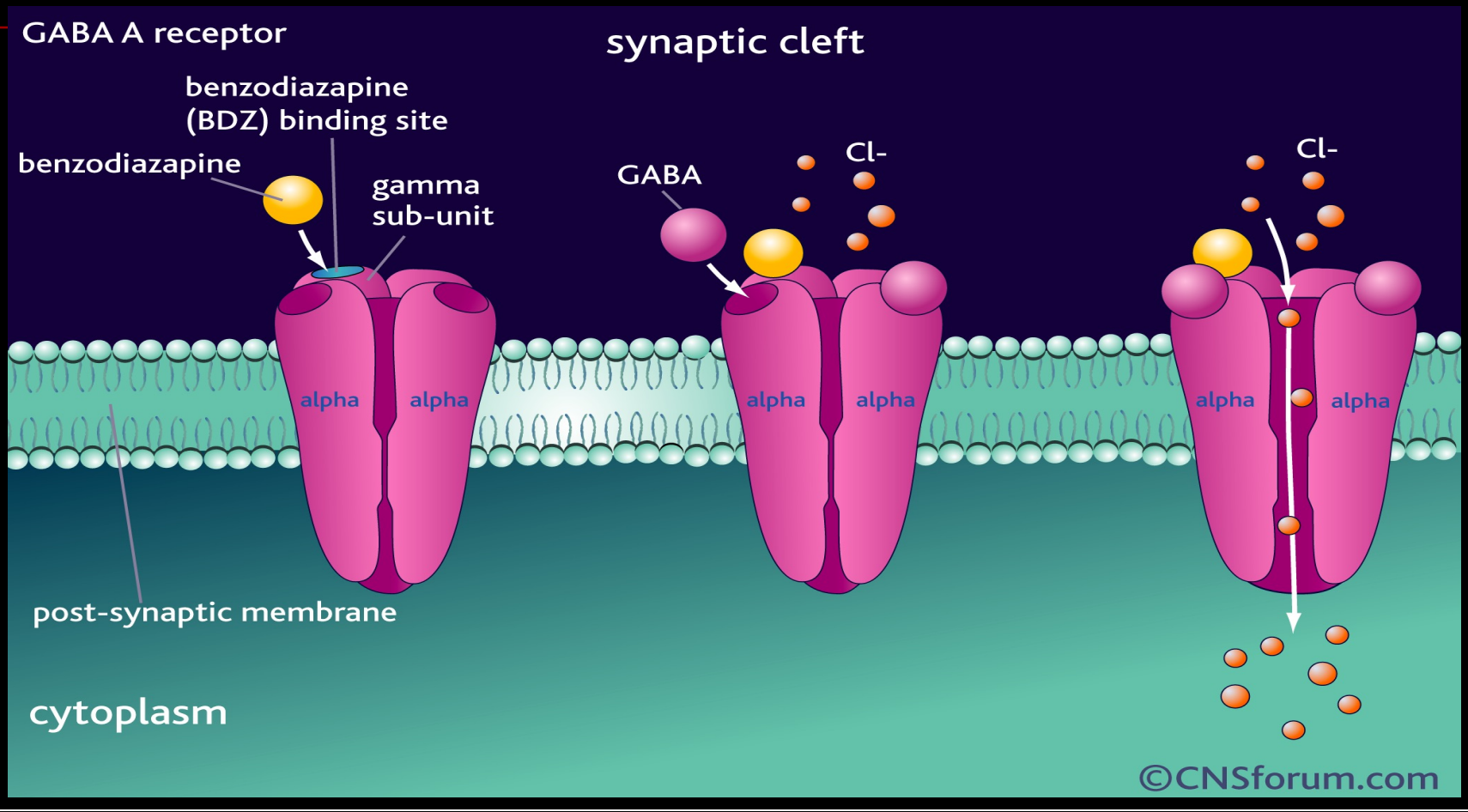
Before

After

Pre-operative Medications (Benzodiazepines)

- **Mechanism of Action**
  - Enter the bloodstream
  - Bind with GABA-A receptors on target cells
  - Once the GABA-A receptors are activated, opens up chloride (Cl^-) channels.
  - Chloride (Cl^-) moves from outside the cell to inside the cell.
  - Negative charges (such as Cl^-) entering a cell is INHIBITORY to that cell!

Pre-operative Medications (Benzodiazepines)



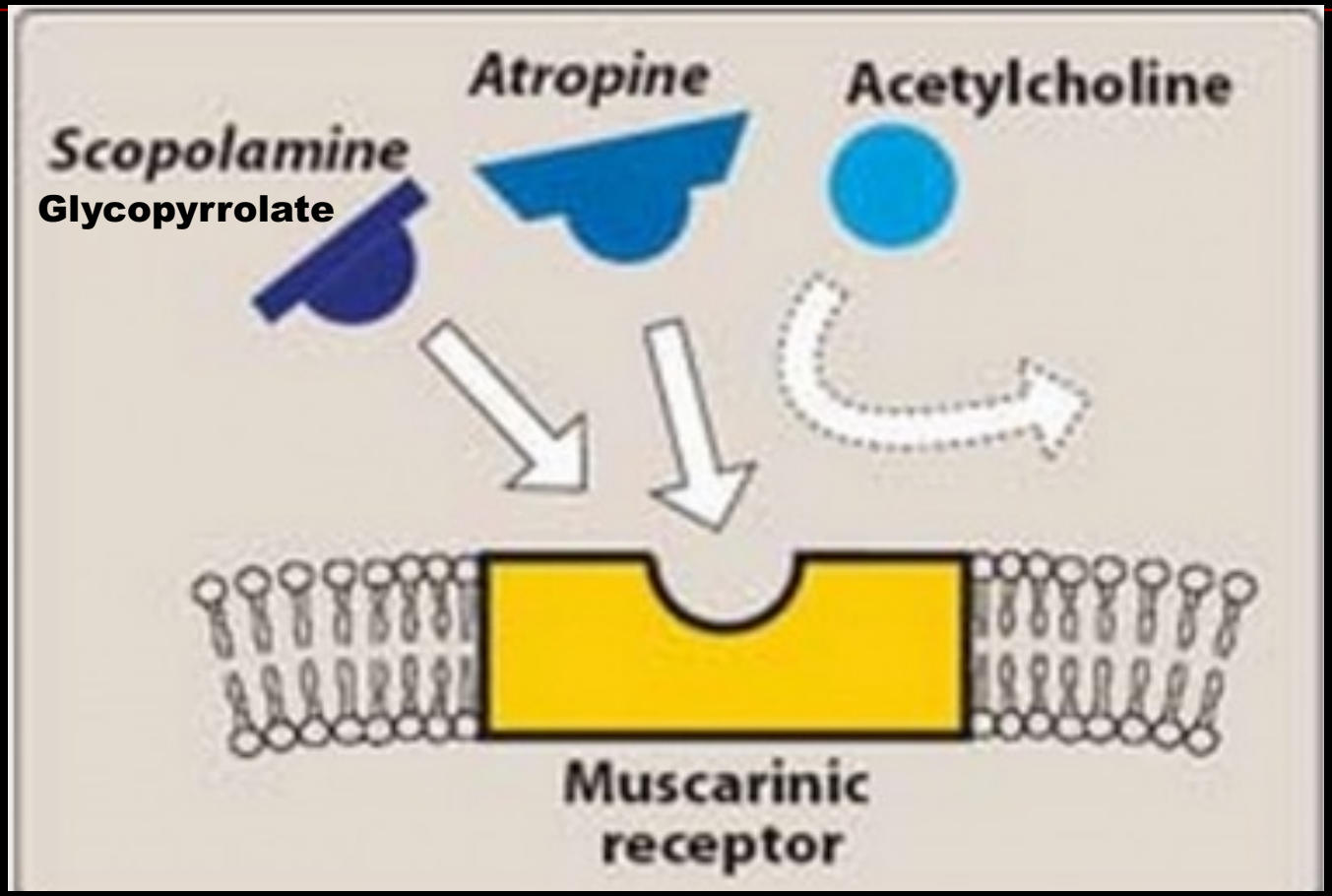
Pre-operative Medications

- **glycopyrrolate (Robinul)**
  - Decreases saliva
  - Increases heart rate
  - Given IV

Pre-operative Medication (glycopyrrolate)

- **Mechanism of Action**
  - Enters the bloodstream
  - Binds with muscarinic receptors on target cells
  - Acetylcholine (neurotransmitter) also binds with muscarinic receptors to bring about various responses (increased saliva, decreased heart rate, etc.)
  - Once bound with muscarinic receptors, glycopyrrolate prevents (blocks) acetylcholine from binding. Thus, blocks acetylcholine's target cell responses (increased saliva, decreased heart rate, etc.)

Pre-operative Medications (glycopyrrolate)



Induction of Anesthesia

- Predictable sequence of medications
  1. Medications for loss of consciousness
     - (Ex. propofol, etomidate, ketamine)
  2. Medications to provide pain relief from intubation/start of surgery
     - (Ex. fentanyl, sufentanil, remifentanil)
  3. Medications to provide skeletal muscle relaxation (AFTER the patient is asleep!)
     - (Ex. succinylcholine, rocuronium, vecuronium)

Induction (propofol)

- Induces a loss of consciousness
- Does NOT provide pain relief
- Causes pain on injection
- Has the potential to significantly decrease the blood pressure, thus we must administer cautiously, or not at all, in hemodynamically unstable patients.

Induction (propofol)

- **MECHANISM OF ACTION**
  - Enters the bloodstream
  - Binds with GABA receptors
  - GABA receptor activation is INHIBITORY in the central nervous system (CNS)
  - If the CNS is inhibited…

  the person loses consciousness

Induction (etomidate)

- Induces a loss of consciousness.
- Does NOT provide pain relief.
- Unlike propofol, etomidate does NOT decrease the blood pressure (may be a more appropriate induction drug for hemodynamically unstable patients).
- Suppresses corticosteroid synthesis by the adrenal glands.

Induction (etomidate)

- **MECHANISM OF ACTION**
  - Enters the bloodstream
  - Binds with GABA receptors
  - GABA receptor activation is INHIBITORY in the central nervous system (CNS)
  - If the CNS is inhibited…

  the person loses consciousness

Induction (ketamine)

- Dissociative anesthetic = Patient does not appear to be anesthetized (open eyes, swallowing), but they are not processing information.
- Can be used to induce anesthesia
- Very effective pain reliever
- Hallucinogenic
  (Special-K: used in recreational settings)

Induction (ketamine)

- Does NOT lower blood pressure – May be beneficial for patients who are critically ill.
- Can cause post-operative delirium

Induction (ketamine)

- **MECHANISM OF ACTION**
  - Blocks NMDA receptors
  - NMDA receptors are excitatory
  - Thus…if you BLOCK excitatory receptors, you get a loss of responsiveness
  - Additionally, ketamine induces a release of endogenous opioids (endorphins)
  - Other mechanisms that are not well understood.

Maintenance

- Definition: The time between placing the patient under anesthesia until the patient is awoken from anesthesia.
- Drugs given during the maintenance phase are used to keep the patient asleep, immobile, comfortable, and most importantly…alive!

OPIOIDS


Fentanyl
50 mcg per mL
(100 mcg per 2 mL)


Hydromorphone
HCl Injection, USP
40 mg/20 mL (2 mg/mL)
FOR SUBCUTANEOUS, INTRAMUSCULAR OR SLOW INTRAVENOUS USE
20 mL Multiple Dose Vial
Mfd. by: WEST-WARD

Opioids

- Opioid: Any drug that binds with and brings about a response in opioid receptors (mu, kappa, delta).
- Opioid receptors are found in both the CNS (brain & spinal cord) and throughout the body.
- Alters the perception of pain
  - Aware of presence of pain but don't care
- Can produce pain relief, euphoria, respiratory depression, nausea, itching, constipation.

Opioids (fentanyl)

- Synthetic opioid (not derived from poppy)
- Around 100x more potent than morphine
- Can be used for acute and chronic pain
- Additionally can be used in conjunction with midazolam for sedation procedures (endoscopy, port placements, etc.)

Opioids (fentanyl)

- **MECHANISM OF ACTION**
  - Strong affinity for the mu opioid receptors
  - Mu receptor activation leads to:
    - Pain relief
    - Sedation
    - Reduction in BP (slight)
    - Euphoria
    - RESPIRATORY DEPRESSION!
    - Itching
    - Nausea

Opioids (sufentanil)

- Most potent opioid we use!!!
  - around 500x more potent than morphine
- Typically used for long procedures (> 3 hours) and administered as an infusion.

Opioids (sufentanil)

- **MECHANISM OF ACTION**
  - Strong affinity for the mu opioid receptors
  - Mu receptor activation leads to:
    - Pain relief
    - Sedation
    - Reduction in BP (slight)
    - Euphoria
    - RESPIRATORY DEPRESSION!
    - Itching
    - Nausea

Opioids (remifentanil)

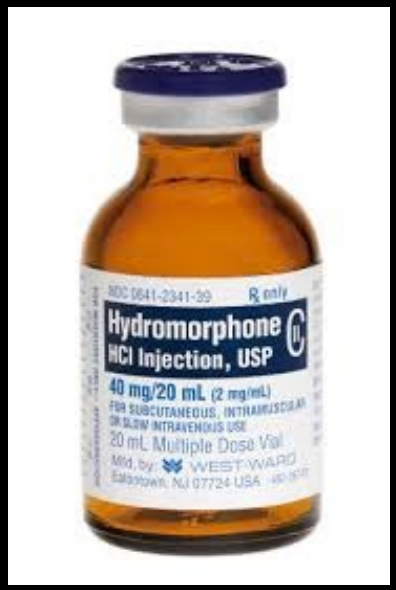
- Most rapidly acting opioid we use
- Given by bolus and infusion
- Primarily used for stimulating/painful procedures of short duration
- Expensive drug!!!

Opioids (remifentanil)

- **MECHANISM OF ACTION**
  - Strong affinity for the mu opioid receptors
  - Mu receptor activation leads to:
    - Pain relief
    - Sedation
    - Reduction in BP (slight)
    - Euphoria
    - RESPIRATORY DEPRESSION!
    - Itching
    - Nausea

Opioids (hydromorphone)

- Derivative of morphine
- Slightly longer duration of action when compared to fentanyl
- Mechanism of action is the same as the other opioids.

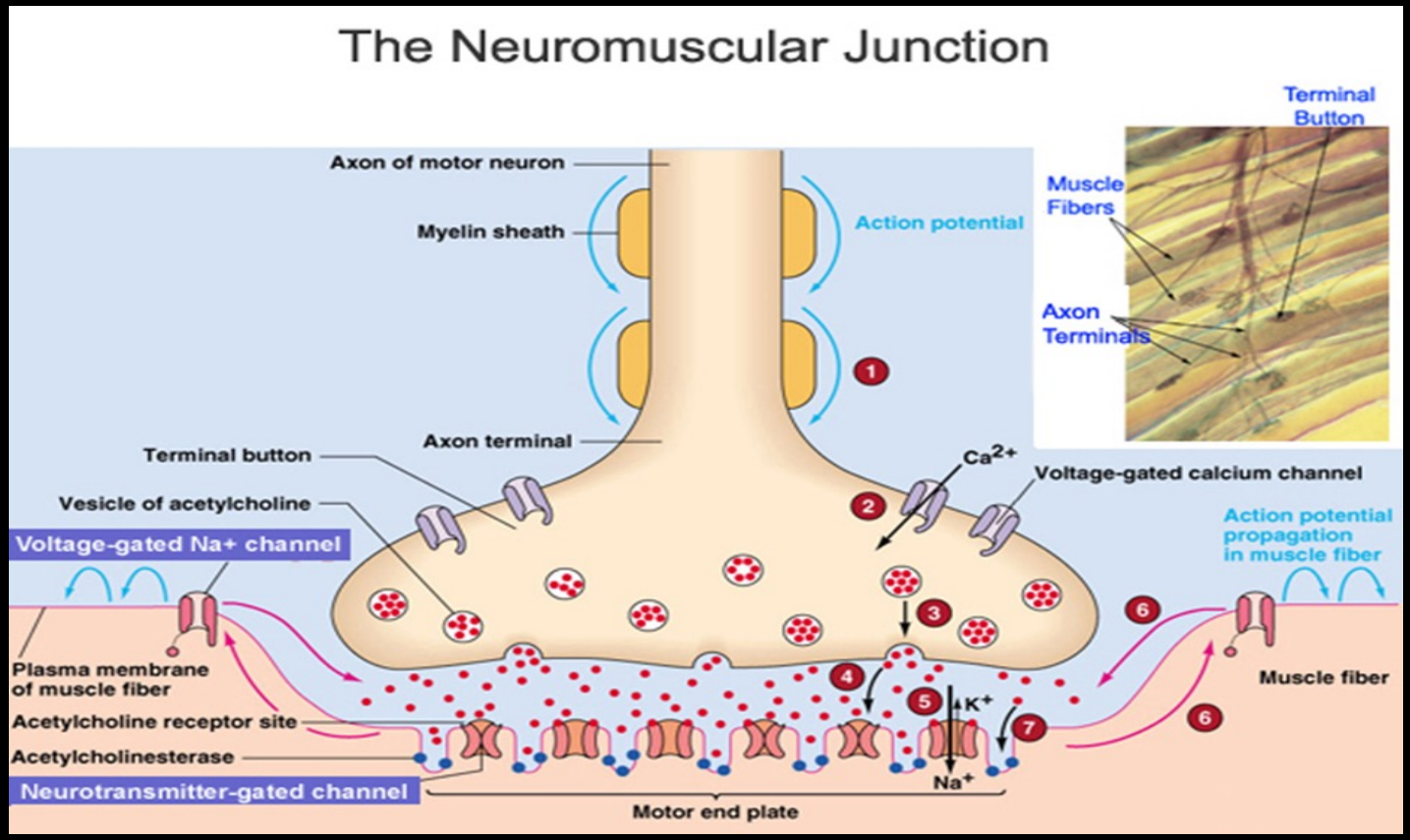


Muscle Relaxants (a.k.a. neuromuscular blocking drugs)

Muscle Relaxants (a.k.a. neuromuscular blocking drugs)

- **Muscle relaxation (paralysis) is necessary in certain situations**
  - Allow for better operating conditions
  - Prevent unwanted movement during delicate procedures
- **Divided into two basic categories**
  - Depolarizing (succinylcholine)
  - Non-depolarizing (rocuronium, vecuronium, cisatracurium)

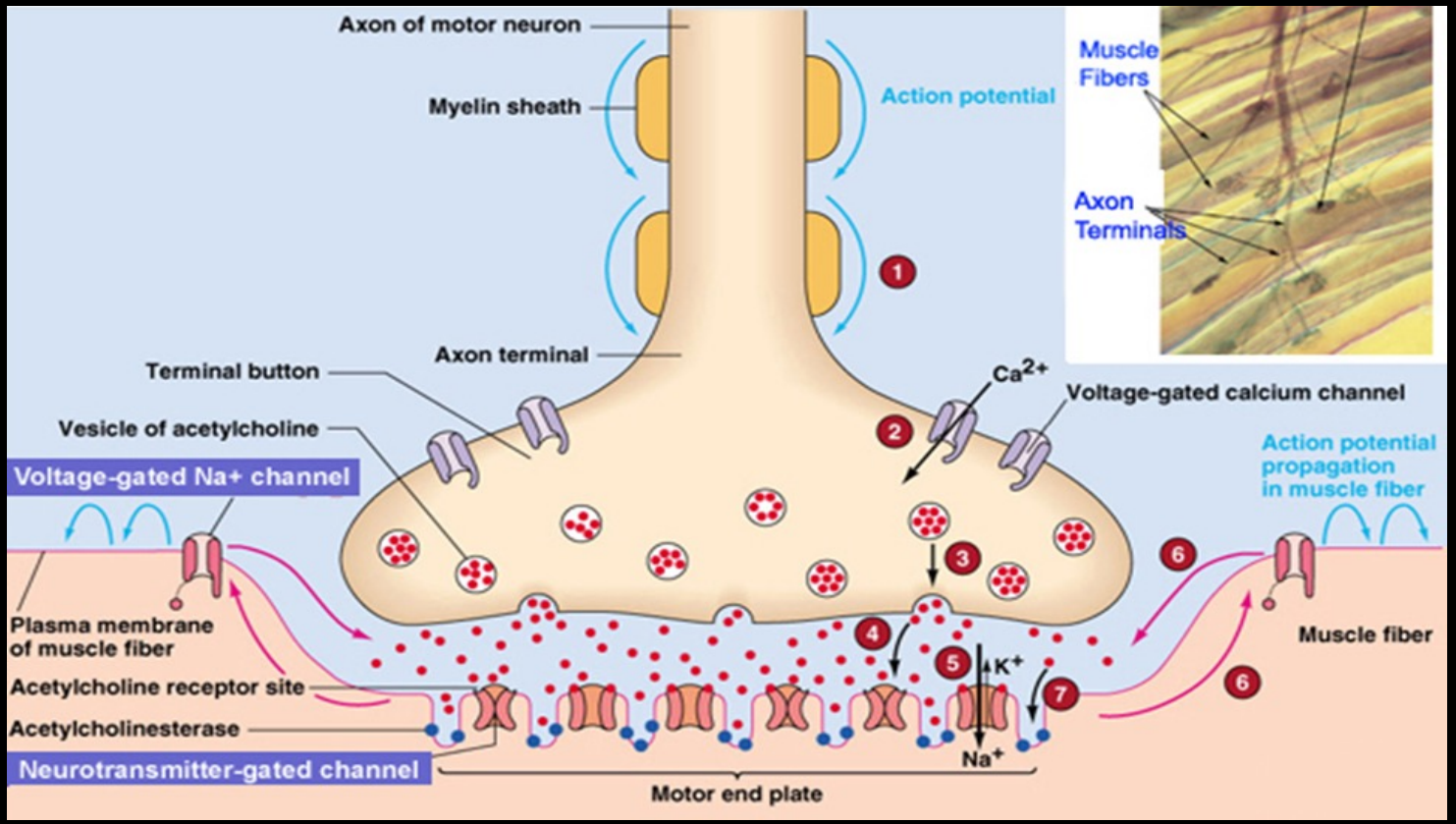
Muscle Relaxants (a.k.a. neuromuscular blocking drugs)



Depolarizing Muscle Relaxants (succinylcholine)

- **Useful for short-term paralysis (3 to 5 minutes)**
  - Rapid sequence induction
  - Laryngospasm
  - Person needs intubation but not paralysis for the surgery
- **Triggering agent for malignant hyperthermia!**

Depolarizing Muscle Relaxants (succinylcholine)



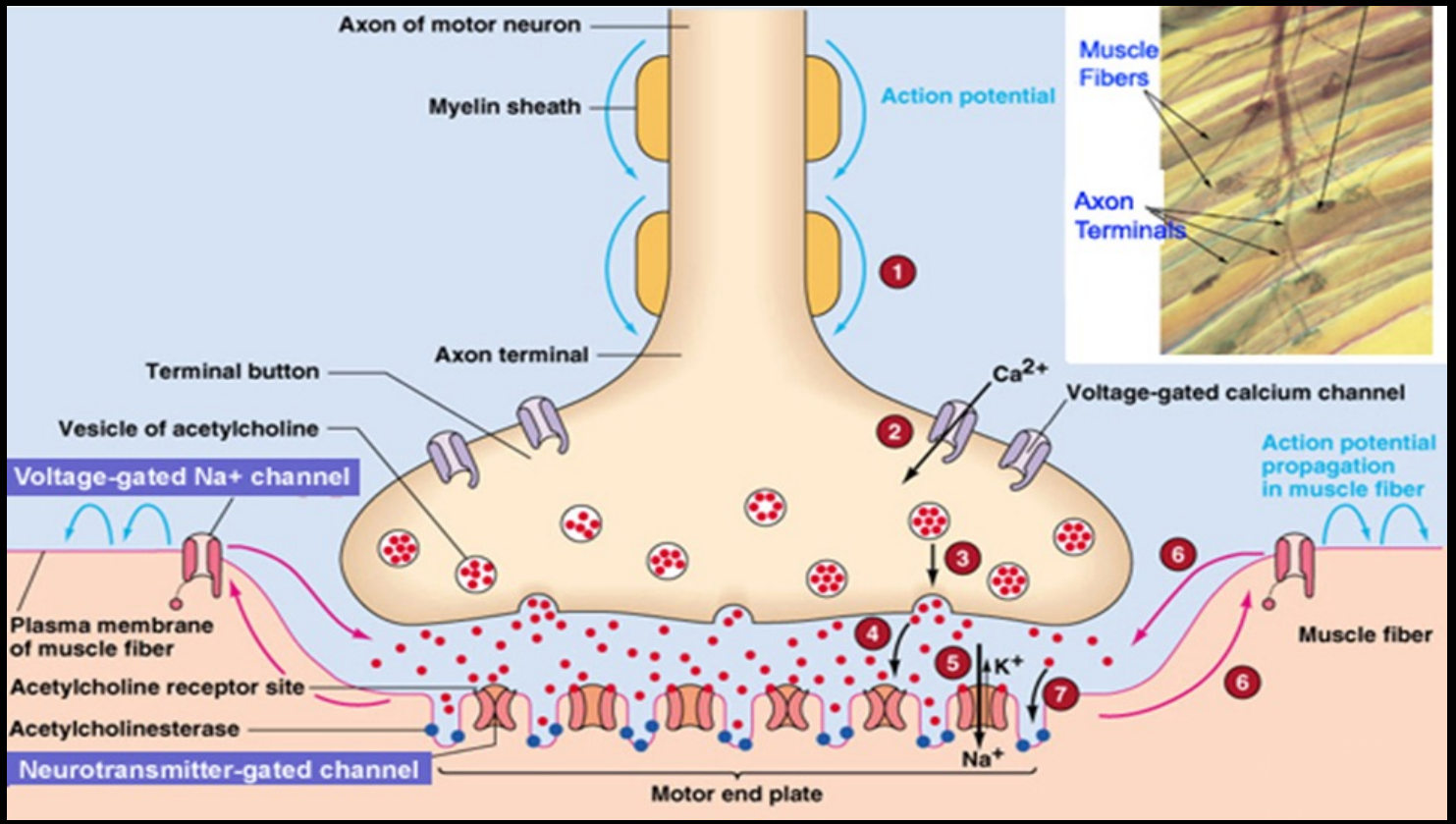
Depolarizing Muscle Relaxants (succinylcholine)

- **MECHANISM OF ACTION**
  - Succinylcholine binds with acetylcholine receptors on motor end plate.
  - Post-synaptic membrane depolarizes and the skeletal muscle contracts (fasciculates).
  - Succinylcholine is NOT metabolized by acetylcholinesterase, thus the muscles cannot contract again (until succinylcholine diffuses away from the receptors)

Non-depolarizing Muscle Relaxants

- Provide paralysis for an extended period of time (> 20 minutes)
- Examples
  - Rocuronium
  - Vecuronium
  - Cisatracurium
  - Others

Non-depolarizing Muscle Relaxants



Non-depolarizing Muscle Relaxants

- **MECHANISM OF ACTION**
  - Non-depolarizing muscle relaxants bind with acetylcholine receptors and BLOCK acetylcholine from binding.
  - If acetylcholine cannot bind with their receptors on the post-synaptic membrane, muscle contraction cannot occur.
  - If muscle contraction cannot occur, the patient cannot move.

Inhaled Anesthetics

- Used as a means to maintain a steady level of anesthesia throughout the procedure.
- Delivered via inhalation
  - Mask
  - LMA
  - Endotracheal tube

Inhaled Anesthetics

- **ISOFLURANE**
  - Cheap
  - Airway irritant
  - Least expensive
- **DESFLURANE**
  - Requires special vaporizer
  - Airway irritant
  - Very expensive and worst environmental offender of these three choices
    - Cost can be minimized by using lower fresh gas flows
- **SEVOFLURANE**
  - Smells acceptable
    - Inhalation induction
  - Expensive

Inhaled Anesthetics

- **MECHANISM OF ACTION**
  - Full mechanism is unknown
  - Multiple theories
  - Most plausible: Inhaled anesthetics enhance inhibitory channels and block excitatory channels.

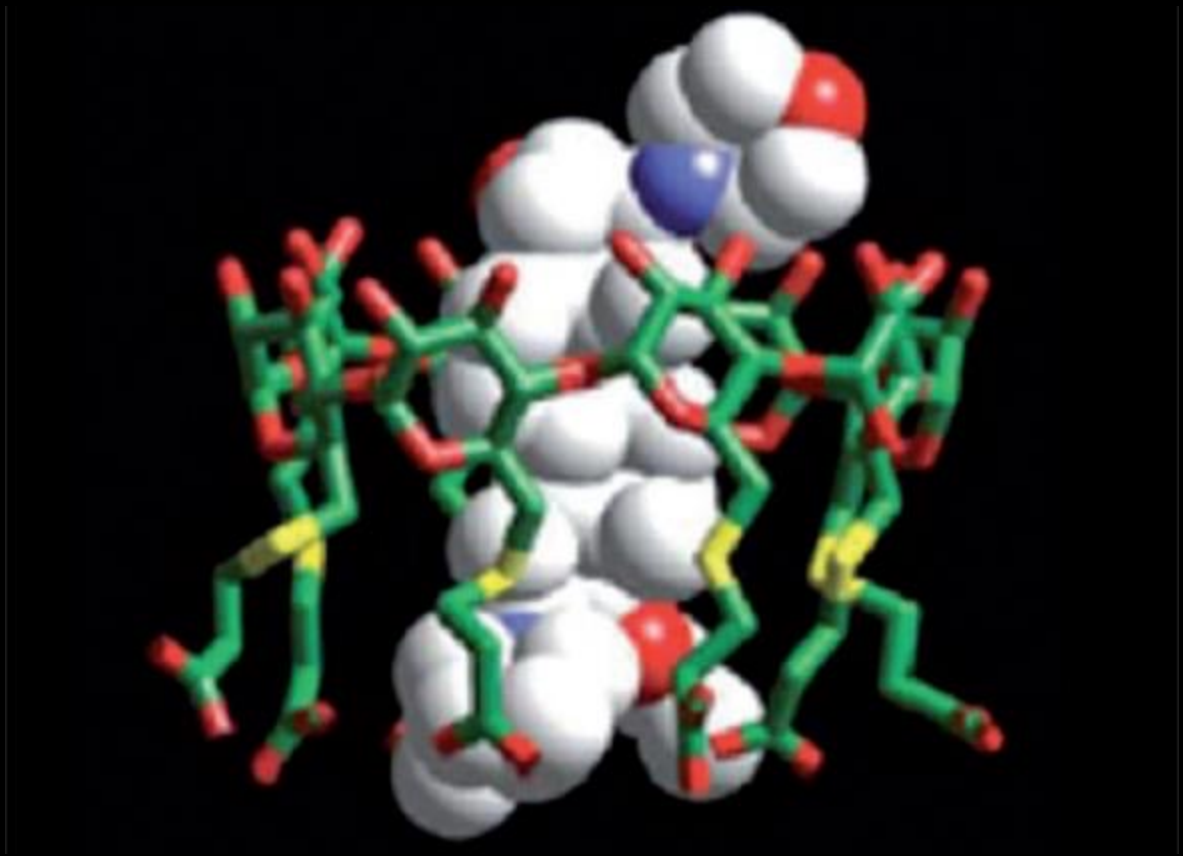
Emergence

- Definition: The period of time between the initiation of waking the patient up and the time at which the patient has regained consciousness.
- Drugs given during the emergence phase are used to reverse muscle paralysis, reduce the incidence of nausea, and keep the patient comfortable.

Emergence (sugammadex)

- Administered to patients to “reverse” muscle paralysis by encapsulating the neuromuscular blocking drug.
- Unlike the older drug, neostigmine, the patient does NOT need any neuromuscular function before reversal (monitored with TOF).
- Additionally, it doesn’t have to be administered along with an antimuscarinic drug (e.g. glycopyrrolate)

Emergence (sugammadex)



Emergence (sugammadex)

- **MECHANISM OF ACTION**
  - Sugammadex encapsulates the aminosteroid NMBDs.
  - Vecuronium and rocuronium are encapsulated with high affinity and pancuronium is encapsulated with low affinity.
  - When encapsulated, the NMBD cannot bind to its receptor and block neuromuscular function.
  - Inability to prevent neuromuscular function = patient not paralyzed anymore.

Emergence (neostigmine)

- **MECHANISM OF ACTION**
  - Acetylcholine (ACh) acts across the neuromuscular synapse to cause a muscular reaction.
  - If ACh molecules were not broken down, our muscles would continue to fire because the junction would continue to be stimulated.
  - A naturally occurring enzyme, acetylcholinesterase (AChE) breaks down ACh.
  - Neostigmine inhibits the enzyme AChE, allowing ACh to accumulate in the synaptic junctions.

Emergence (neostigmine vs sugammadex)

- **Neostigmine**
  - ▲ Neostigmine is fairly inexpensive.
  - ▼ It increases the quantity of ACh in the synaptic junction, so it works by causing an over-abundance of ACh (not by removing the offending party).
  - ▼ If Train of Four (TOF) is not at least two, then this medication can be detrimental by actually causing a muscular block!

Emergence (neostigmine vs sugammadex)

- **Sugammadex** (is awesome)
  - ▼Sugammadex is expensive (patent until January 2026 or later).
  - ▲ It binds with neuromuscular blockers which allows the normal amount of ACh to work as normal.
  - ▼ Can invalidate hormonal birth control for up to two months (mostly likely two weeks).
  - ▼ If given too quickly, it can cause temporary bradycardia (use with caution in hemodynamically unstable patients).

Emergence (glycopyrrolate)

- **MECHANISM OF ACTION**
  - Binds with muscarinic receptors to prevent too many muscarinic actions.
  - If neostigmine binds AChE, then we have an overabundance of ACh which can lead to too many muscarinic symptoms (too much saliva, bradycardia).
  - If we bind SOME of those ACh receptors with glycopyrrolate, then we prevent these excessive muscarinic symptoms (it's all about balance!)

Emergence (ondansetron)

- Administered to decrease the incidence of nausea and vomiting.
- More effective and safer than other antiemetics.
- Typically administered 15 – 30 minutes before the conclusion of the case.
- **MECHANISM OF ACTION:**
  - Ondansetron blocks 5-HT3 (serotonin) receptors.
  - Prevents serotonin release
  - Without serotonin, the vomiting reflex is less active.

THANK YOU!

- Everyday each member of our team (anesthesia techs, CRNAs, anesthesiologists, residents, SRNAs) plays a vital role in safely guiding the patients through the dangers of an anesthetic.
- Never forget how IMPORTANT you are to that process!