Peripherally Acting Skeletal Muscle Relaxants

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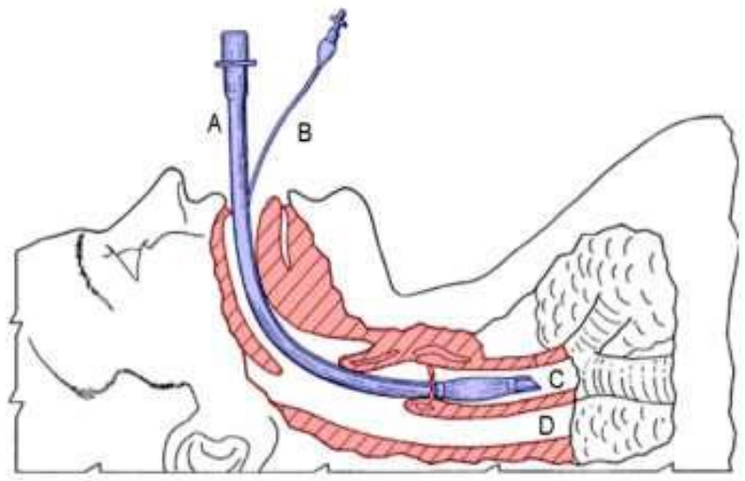
Peripherally Skeletal Muscle Relaxation Uses:

In conjugation with General Anesthetics:

- Facilitate intubation of the trachea because it is easier to enter tube in or cut Relaxed muscle than contracted one.
- Facilitate mechanical ventilation
- Optimized surgrical working conditions

→ because we paralised diaphragm.



* Ach is important transmitter in sympathatic & parasympathetic systems
  → target nicotinic and muscrinic receptor
  nicotinic → ganglia
neuromuscular Junction

History of Skeletal Muscle Relaxants

- Curare is a common name for various plant extract alkaloid arrow poisons originating from Central and South America.
- Source: *Chondrodendrone tomentosum* and *Strychnos toxifera*
- Tubocurarine name because of packing in "hollow bamboo tubes"

not for memorizing

father of these drugs.

* this drug does not absorped in G.I. system in human.

So we can use it intravenously.

Classification

in minor surgical procedure

- **Skeletal muscle relaxants**
  - **Centrally acting** ← only one that use clinically
    - Diazepam and other benzodiazepines
    - Methocarbamol
    - Chlorzoxazone
    - Tizanidine
    - Baclofen
    - Gabapentin
  - **Peripherally acting**
    - **Drugs acting at NMJ** ← nicotinic receptor.
      - **Depolarizing blockers**
        - Succinylcholine
        - Decamethonium
      - **Non-depolarizing blockers (Competitive blockers)**
        - Long acting
          - d-TC
          - Pancuronium
          - Doxacurium
          - Pipecuronium
        - Intermediate acting
          - Vecuronium
          - Atracurium
          - Rocuronium
        - Short acting
          - Mivacurium
    - **Drugs directly acting on skeletal muscle** → target calcium ion.
      - Dantrolene
    - **Others**
      - Botulinum toxin A

Botux → prevent Ach release.

Acetylcholine

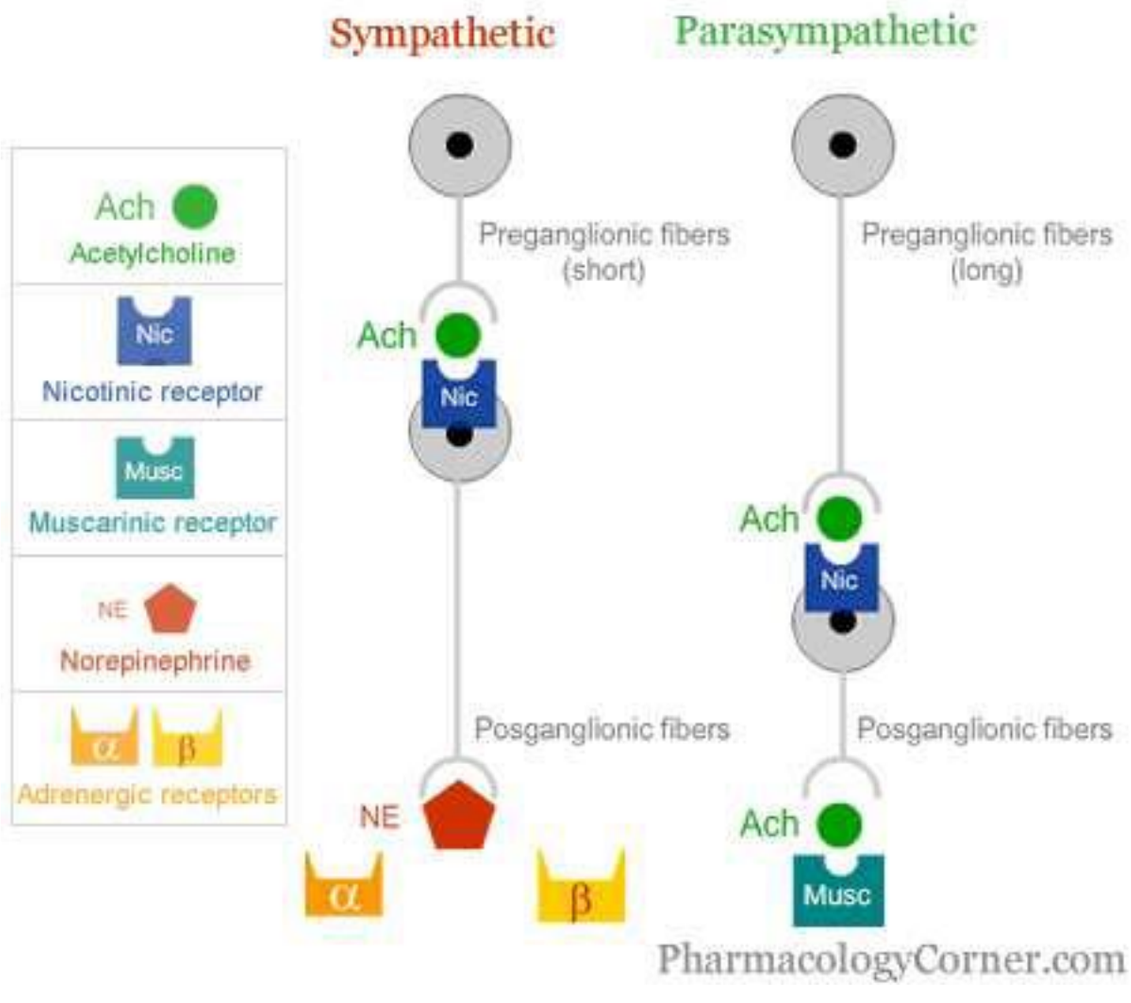
Acetylcholine is a major neurohumoral transmitter at autonomic, somatic and central nervous system:

.1All preganglionic sites (Both Parasympathetic and sympathetic(

.2Skeletal Muscles

.3CNS: Cortex Basal ganglia, spinal cord and others

Parasympathetic Stimulation – Acetylcholine (ACh) release at neuroeffector junction – biological effects Sympathetic stimulation – Nonadrenaline (NA) at neuroeffector junction – biological effects



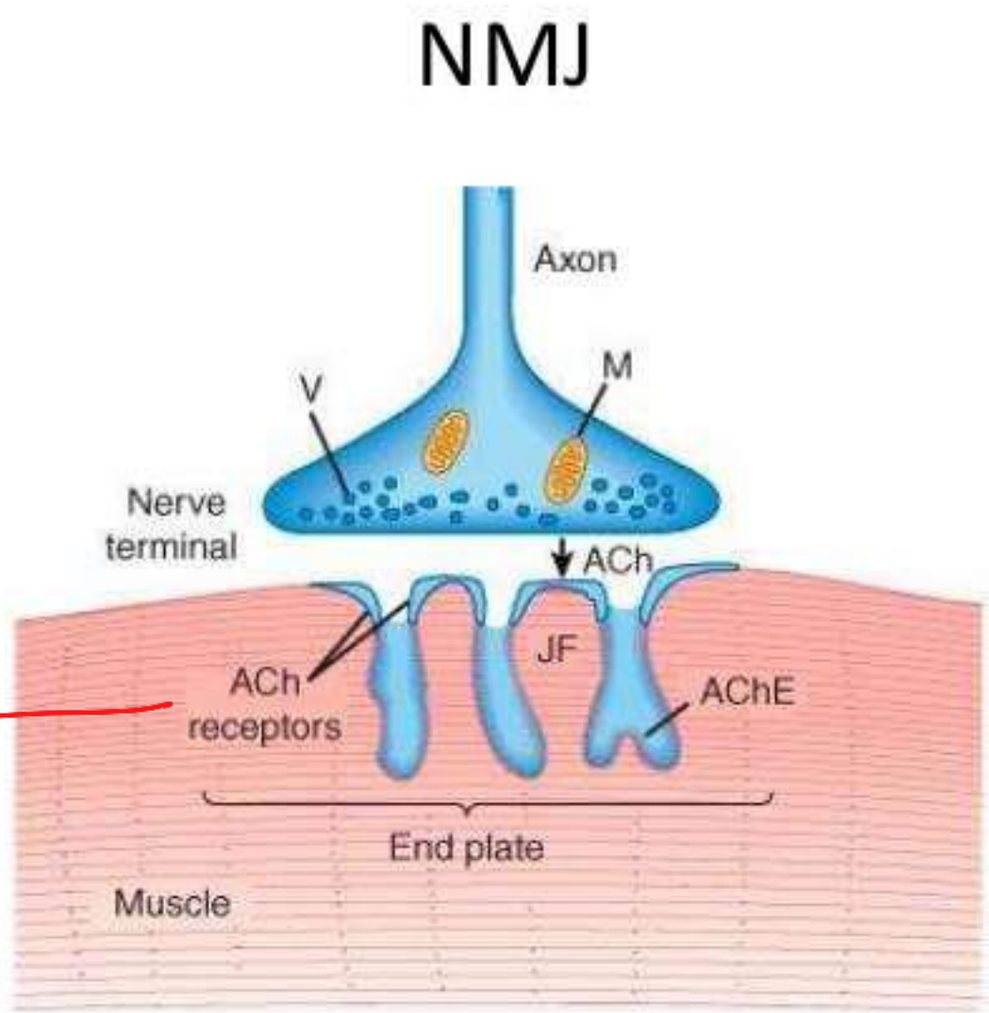
* most of our organs under effect of sympathatic and parasympathatic

* so the effect of nicotine will be on the high % of Autonomic branch on that organ

heart tissue → S. is more.

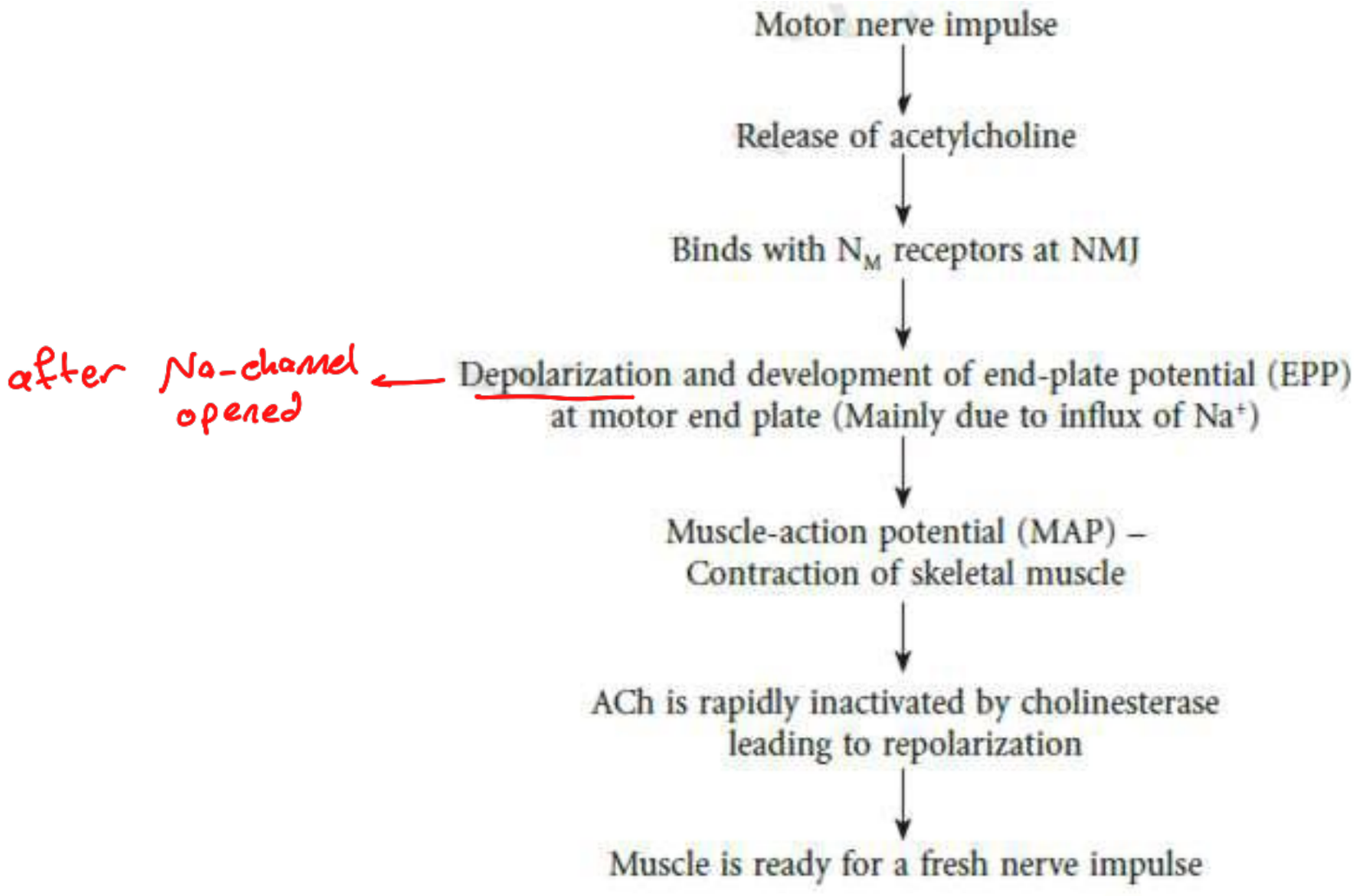
Vessels → only S.

Neuromuscular Junction (NMJ(



Na^+ ion-channel receptor

Physiology of Skeletal Muscle Contraction



Peripherally acting Neuromuscular Blockers

Depolarizing Blockers – mimic the action of **acetylcholine (ACh(**

↳ and in chemical structure also.

–Agonists

–Succinylcholine (SCh) is the only drug used clinically

- **Non-Depolarizing** – interferes with the action of ACh

–Competitive Blockers (Antagonist(

–Further divided into short, intermediate and long acting non- depolarizing drugs

Depolarizing Block - Succinylcholine

* Agonist.

→ Bind for the receptor.

•Succinylcholine have affinity and **sub-maximal/ intrinsic** activity at Nm receptor.

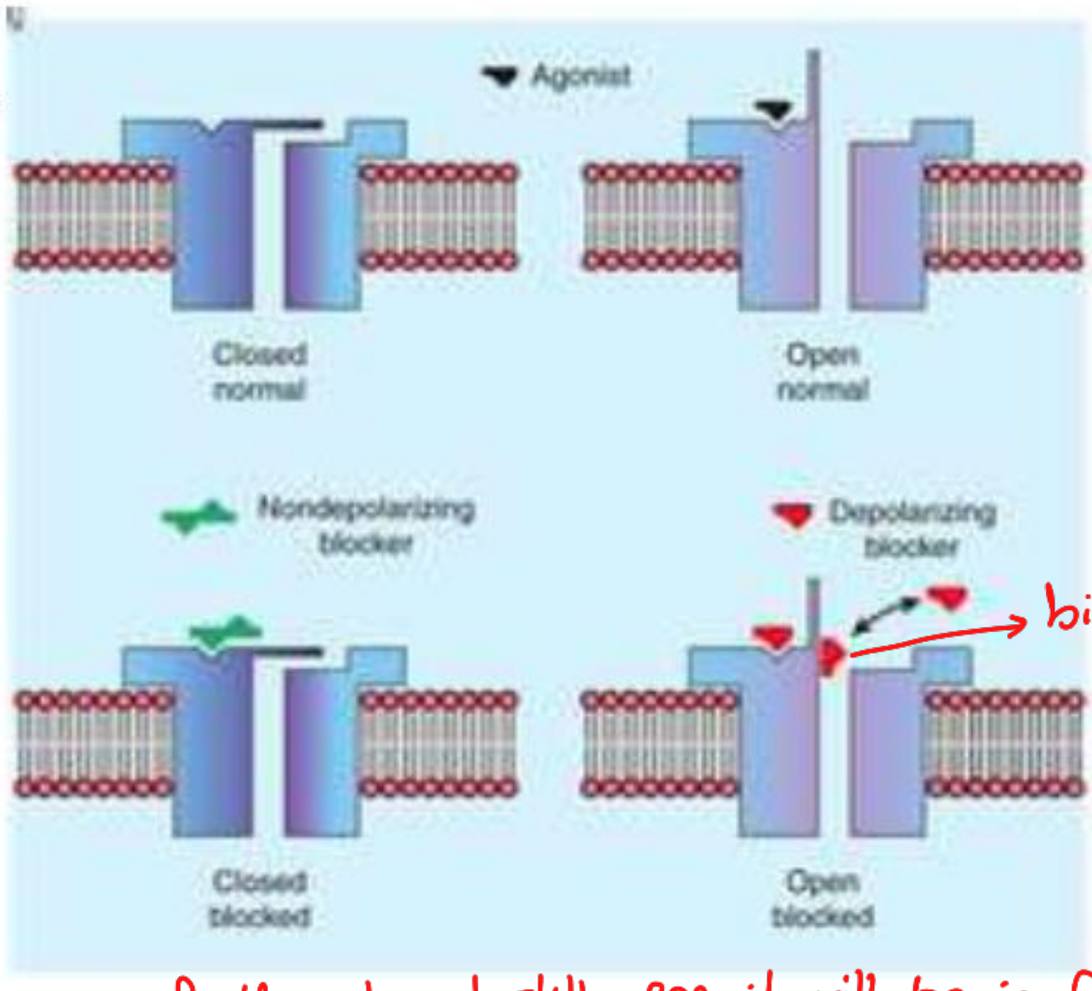
↓ able to activate the cascade to give the effect after Binding.

•It acts on sodium channels, open them and causes initial twitching and fasciculation. → very fast contraction, it is short in duration.

•It does not dissociate rapidly from the receptors resulting in prolonged depolarisation and inactivation of Na+ channels.

Mechanism of Action: Succinylcholine

Nicotinic ACh Receptor



bind inside the channel also.
so prolonging the opening of the channel.

∴ so if the channel still open it will be in Refractory period (paralysis)

Succinylcholine acts on the Nicotinic receptors of the muscles, stimulates them and ultimately cause their relaxation.

This process occur in two phases:

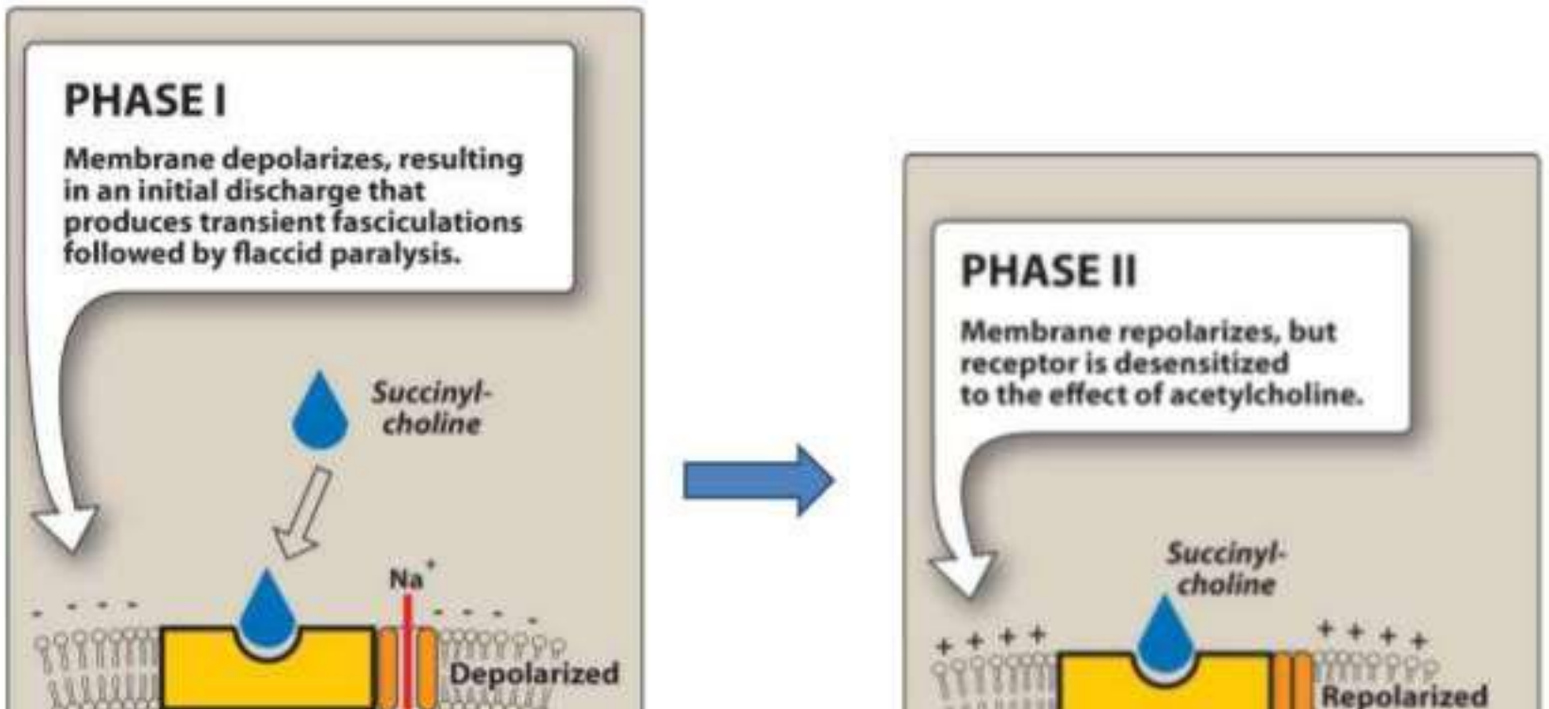
initially

↳ •Phase I: During Phase I (depolarizing phase), they cause muscular fasciculations while they are depolarizing the muscle fibers.

•Phase II: After sufficient depolarization has occurred, phase II (desensitized phase) sets and the muscle is no longer responsive to Ach released by the nerve endings.

the effect of Succinylcholine is 10 min (all phases)

so it use for trachial intubation



Succinylcholine

Advantages:

- Most commonly used for Tracheal intubation
- Rapid onset (1-2 min(→ How much time it need to start working.
- Good intubation conditions – relax jaw, separated vocal chords with immobility, no diaphargmatic movements

Because
- Short duration of action (5-10 minutes(→ for short proceduers
- Dose 1-1.5mg/kg
- Used as continous infusion occasionally

Disadvantages:

- Cardiovascular: unpredictable BP (→ Blood pressure), heart rate (↳ depends on dose) and arrhythmias (→ because efflux of k^+ lead to hypercalemia.)
- Fasciculation
- Muscle pain → give another drug that relax the muscle so I skip the fast twitch phase.
- Increased intraocular pressure
- Increased intracranial pressure
- Hyperkelemia: k+ efflux from muscles, life threatening in Cardiac Heart Failure, patient with diuretics etc

* this Category of drugs cause cardiovascular diseases because it affect sympathatic and parasympathatic systems.

Non-Depolarising Drugs

→ So the Antagonist conc. must be higher than agonist.

- Competitive Blockers having no intrinsic activity of nicotinic receptor.
  → Just prevent action of agonist.
- These are of 3 types based on their activity:

– *Long Acting :* d-TC, Pancuronium, Pipecuronium, Gallamine (Kidney Excretion(

– *Intermediate :* Vecuronium, Rocuronium, Atracuronium (eliminated by liver(

– *Short Acting :* Mivacuronium, Ropcacuronium)inactivated by plasma cholinesterase(

قال رسول الله صلى الله عليه وسلم:"**من يُرِدِ الله به خيرا يُفَقِّهْهُ في الدين**"

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