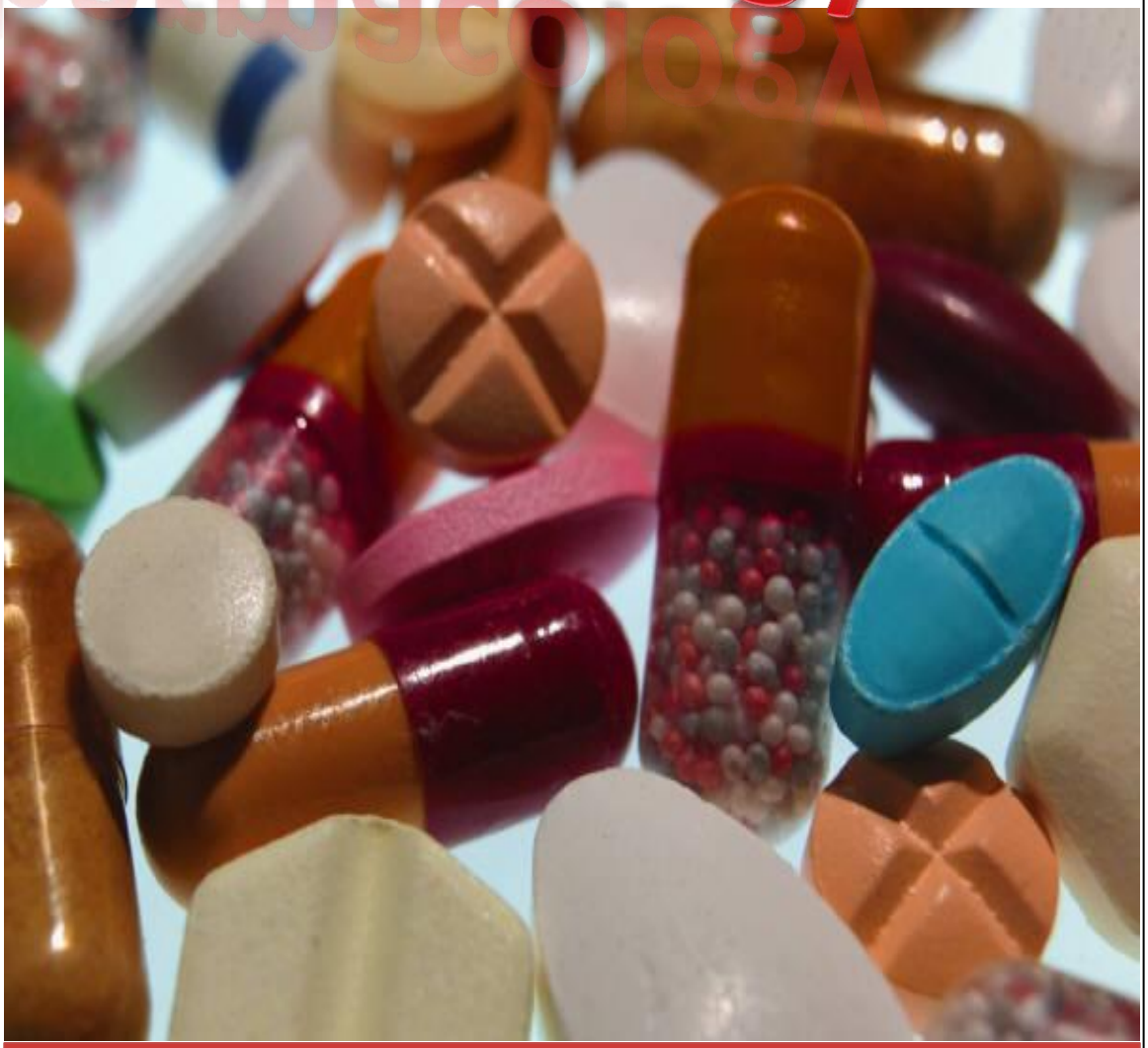
pharmacology



By:.

Team of pharmacology

2nd pharmacology lecture:

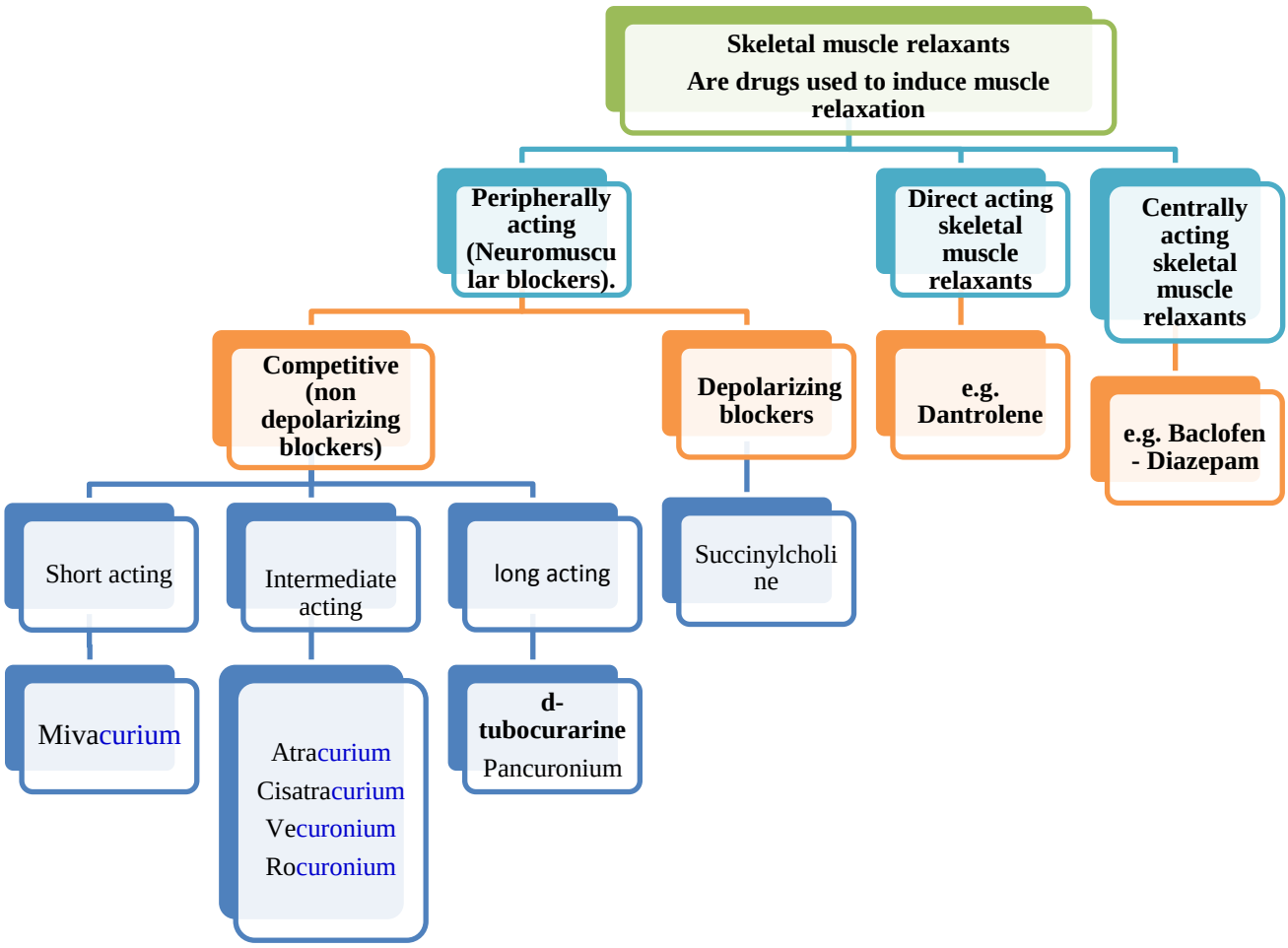
Skeletal Muscle Relaxants

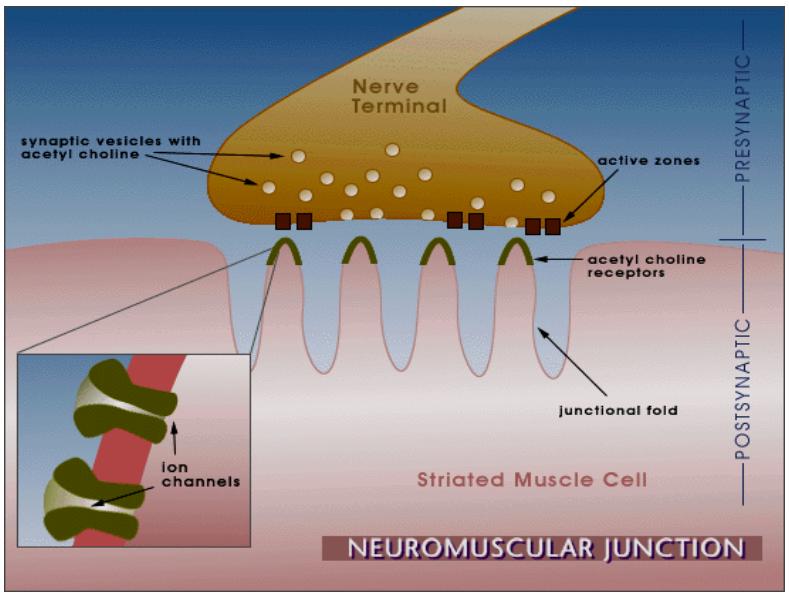
Lecture's objectives:

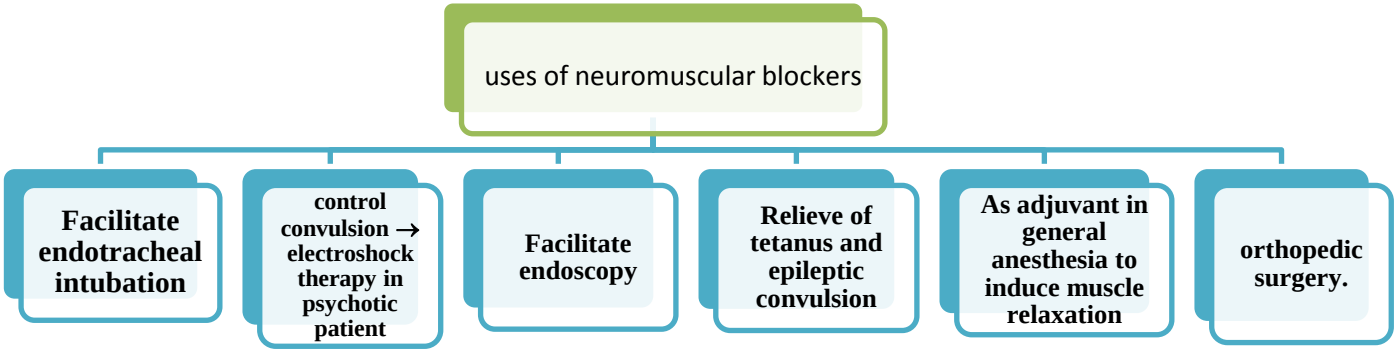
1. Be familiar to the classification of skeletal muscle relaxants.

2.The uses and classification **(Competitive and depolarizing)** of neuromuscular blockers.

3.Mechanism of action, pharmacokinetics, pharmacological action and examples of competitive and depolarizing neuromuscular blockers.


Skeletal muscle relaxants
Are drugs used to induce muscle relaxation
Peripherally acting (Neuromuscular blockers).
Direct acting skeletal muscle relaxants
Centrally acting skeletal muscle relaxants
Competitive (non depolarizing blockers)
Depolarizing blockers
e.g. Dantrolene
e.g. Baclofen - Diazepam
Short acting
Intermediate acting
long acting
Succinylcholine
Mivacurium
Atracurium
Cisatracurium
Vecuronium
Rocuronium
d-tubocurarine
Pancuronium


Nerve Terminal
synaptic vesicles with acetyl choline
active zones
PRESYNAPTIC
acetyl choline receptors
POSTSYNAPTIC
junctional fold
ion channels
Striated Muscle Cell
NEUROMUSCULAR JUNCTION



Competitive NM blockers:
mechanism of action

- Are competitive antagonists
- Compete with Ach for the nicotinic receptors present in post-junctional membrane of motor end plate.
- No depolarization of post-junctional membrane

لان اذا قل cholinesterase بيزيد الـ (ACH)لان
الـ cholinesterase يدمر الـ(ACH)
بالتالي اذا زاد ACHراح
competitive blocker لـ displacement يسوي

Pharmacokinetics

Pharmacokinetics

- **They are polar compounds (have low V.D.)**
  - **inactive orally & taken parenterally**
  - **Do not cross placenta & CNS**
- **Metabolism depend upon kidney or liver**

Except

Mivacurium *(degraded by pseudo cholinesterases)*

Atracurium *(spontaneous degradation in blood)*

Pharmacological actions:

- **Skeletal muscle relaxation.**
- **They produce different effects on CVS**
- **Some release histamine and produce hypotension**
  - **d.Tubocurarine**
  - **Atracurium**
  - **Mivacurium**
- **Others produce tachycardia (↑ H.R)**
  - **Pancuronium**

Depolarizing Neuromuscular Blockers

Mechanism of Action

- combine with nicotinic receptors in post-junctional membrane of neuromuscular junction → initial depolarization of motor end plate → muscle twitching → Persistent depolarization → paralysis

Drug	Duration	Side effects	Notes
Tubocurarine	Long 1-2 h	Hypotension	# Renal failure
Pancuronium	Long 1-2 h	Tachycardia	# Renal failure
Atracurium	Short 30 min.	Transient hypotension Histamine release	Spontaneous degradation Used in liver and kidney failure
Vecuronium	Short 40 min.	Few side effects	# Liver failure
Mivacurium	Short 15 min.	Transient hypotension Histamine release	Metabolized by pseudocholinesterase # Choline esterase deficiency
Succinyl choline	Short 10 min.	Hyperkalemia Arrhythmia Increase IOP	# CVS Diseases # Glaucoma # Liver disease

Malignant hyperthermia

- Is a rare inherited condition that occurs upon administration of drugs as:
  - general anesthesia e.g. halothane
  - neuromuscular blockers e.g. suxamethonium
- Inability to bind calcium by sarcoplasmic reticulum in some patients due to genetic defect
- ↑ Ca release, intense muscle spasm, hyperthermia

Spasmolytics : They reduce muscle spasm in spastic states

Baclofen:

- Centrally acting
- GABA agonist – acts on spinal cord.

Diazepam (Benzodiazepines):

- Centrally acting
- facilitate GABA action on CNS.

Dantrolene:

- direct action on skeletal muscles.
- Used in treatment of malignant hyperthermia

Uses of spasmolytics

They reduce muscle spasm in spastic states produced by :

- Spinal cord injury
- Cerebral stroke
- Cerebral palsy

Dantrolene

Mechanism of Action

- It interferes with the release of calcium from its stores in skeletal muscles (sarcoplasmic reticulum).
- It inhibits excitation-contraction coupling in the muscle fiber.

Uses

Malignant Hyperthermia.

Spastic states.

IV, orally t ½ = 8 - 9 hrs.