Skeletal Muscle Relaxants Pharmacology

Skeletal muscle relaxants are pharmacologic agents that induce relaxation or paralysis of skeletal muscle by interrupting neuromuscular transmission. These drugs are mainly used:

- As **adjuncts in general anesthesia** to facilitate **endotracheal intubation** and optimize surgical conditions by preventing muscle contractions.
- In **ICU settings** for mechanical ventilation.
- To manage **spasticity** from neurological disorders (central acting agents).

Mechanism of Action

Most skeletal muscle relaxants exert their effect by interfering with the **transmission of acetylcholine (ACh)** at **nicotinic receptors** on the **motor end plate** of skeletal muscles.

They can either:

- **Block ACh receptor activation** (**non-depolarizing agents**),
- Or **mimic ACh**, causing sustained depolarization (**depolarizing agents**),
- Or act **centrally** to reduce muscle tone via CNS pathways (**centrally acting agents**).

Classification

A. Centrally Acting Skeletal Muscle Relaxants

Used to relieve **muscle spasms** and **spasticity** due to neurological conditions (e.g., MS, cerebral palsy).

Drug	Key Characteristics
Baclofen	GABAB agonist; reduces spinal reflexes. Used in spasticity (e.g., MS).
Tizanidine	?2-adrenergic agonist; reduces excitatory input to motor neurons.
Carisoprodol	Sedative muscle relaxant; abuse potential.
Methocarbamol, Chlorzoxazone, Metaxalone	General CNS depressants.
Diazepam	A benzodiazepine; enhances GABAA inhibition at spinal cord level.

> Baclofen is preferred in **spasticity** due to **multiple sclerosis**, while tizanidine is useful in **muscle spasm-related pain**.

B. Direct-Acting Skeletal Muscle Relaxants

Drug	Mechanism	Use

Drug	Mechanism	Use
Dantrolene Sodium	Blocks ryanodine receptor (RyR1) in sarcoplasmic reticulum, inhibiting Ca2+ release.	Treats **malignant hyperthermia** and **neuroleptic malignant syndrome**.

> Dantrolene is **life-saving** in cases of **malignant hyperthermia** (a rare but fatal reaction to succinylcholine or volatile anesthetics).

C. Neuromuscular Blocking Agents (NMBAs)

Used in surgery, ICU sedation, and rapid-sequence intubation.

1. **Non-depolarizing Agents** (Competitive antagonists)

These agents **block ACh** from binding nicotinic receptors without depolarizing the membrane.

Agent	Duration	Notes
d-Tubocurarine	~30 min	Obsolete; histamine release, ganglion blockade.
Pancuronium	Long	May cause **tachycardia** (M2 receptor blockade).
Vecuronium, Rocuronium	Intermediate	Fewer cardiac effects; **rocuronium** used for rapid intubation.
Atracurium	Intermediate	**Organ-independent metabolism** (Hofmann elimination); useful in renal/hepatic failure.
Mivacurium	Short	Rapidly hydrolyzed by plasma cholinesterases.

> The effects of **non-depolarizing agents can be reversed** using **acetylcholinesterase inhibitors** like **neostigmine** or **pyridostigmine**, often given with atropine or glycopyrrolate to block muscarinic side effects.

2. **Depolarizing Agent**

Agent	Mechanism	Duration	Notes
Succinylcholine (Suxamethonium)	Persistent depolarization of the motor end plate ? inactivation of Na? channels ? flaccid paralysis	Rapid onset (~60 sec), short duration (~5–10 min)	Used in **rapid-sequence intubation**

- Not degraded by **acetylcholinesterase**, but by **pseudocholinesterase** in plasma.

- Initial **fasciculations** followed by flaccid paralysis.

  Succinylcholine is contraindicated in:

  - Patients with **pseudocholinesterase deficiency** (prolonged apnea),
  - Risk of **hyperkalemia** (burns, crush injuries, neuromuscular diseases),
  - **Increased intraocular/intracranial pressure**.

Adverse Effects of Neuromuscular Blockers

Drug	Side Effects
d-Tubocurarine	Histamine release ? **bronchospasm**, **hypotension**, **urticaria**; ganglionic blockade
Pancuronium	**Tachycardia**, **hypertension** due to M2 blockade
Succinylcholine	**Hyperkalemia**, **malignant hyperthermia**, **bradycardia**, **increased IOP/ICP**, **fasciculations**, **myalgia**
Atracurium	Can cause **seizures** (laudanosine metabolite)

Reversal of Neuromuscular Blockade

- **Non-depolarizing agents**: Reversible with **anticholinesterases** (e.g., neostigmine + atropine/glycopyrrolate).
- **Depolarizing agents (succinylcholine)**: Not reversed pharmacologically; effects wear off spontaneously. **Prolonged effects** in pseudocholinesterase deficiency.