# 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.