



SKELETAL MUSCLE RELAXANTS

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Classification Of Skeletal Muscle Relaxants:

**Neuromuscular blockers
(NMBs)**

Spasmolytic drugs

Skeletal muscle relaxants

1- **NMB**: are drugs used to produce muscle paralysis or reduce muscle tone and alleviate muscle spasms or spasticity.

2- **Spasmolytics**: They act on the central nervous system (CNS) or directly on the skeletal muscles to relieve conditions such as muscle spasms, spasticity, and associated pain.

1-Neuromuscular blockers (NMBs)

Competitive (non-depolarizing) NMBs

منافس
Non-competitive
depolarizing
مكافئ
مكافئ

Non-competitive (depolarizing) NMBs:

competes with Ach for
nicotinic (N_m) receptors at
the motor end plate,
causing muscle paralysis

(small and large doses) ?

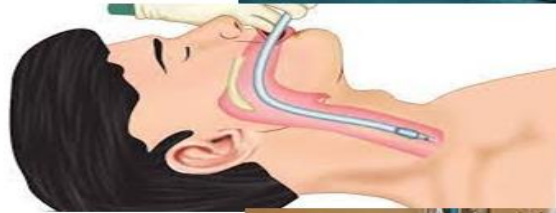
❖ They cause sustained depolarization of the motor end plate, leading to muscle paralysis.

❖ They produce initial stimulation of muscle (fasciculations) followed by paralysis.

contraction followed by block.

Therapeutic uses:

- 1) Skeletal muscle relaxation during surgery.
- 2) Facilitation of endotracheal intubation.
- 3) To facilitate mechanical ventilation.
- 4) To control severe convulsions during electroconvulsive therapy (ECT).

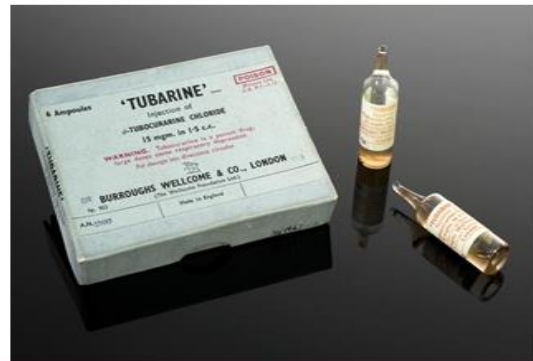
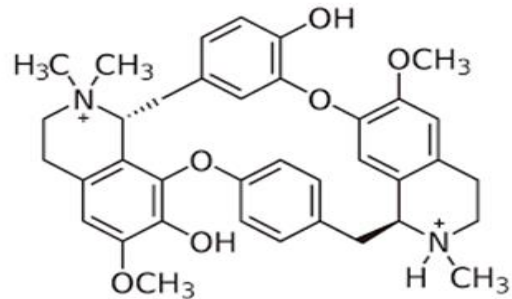


Competitive (Non-depolarizing) NMBs

(1) D-Tubocurarine (Curare)

PK

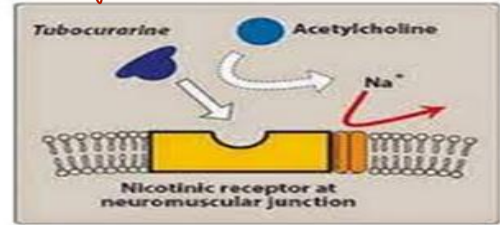
- It is a quaternary ammonium compound → given parentally & not absorbed orally.
- It has a rapid onset.
- Recovery occurs within 30-60 min.
- It does not cross BBB → No CNS actions.
- Excreted mainly in urine.



Mechanism of action:

Non-depolarizing.

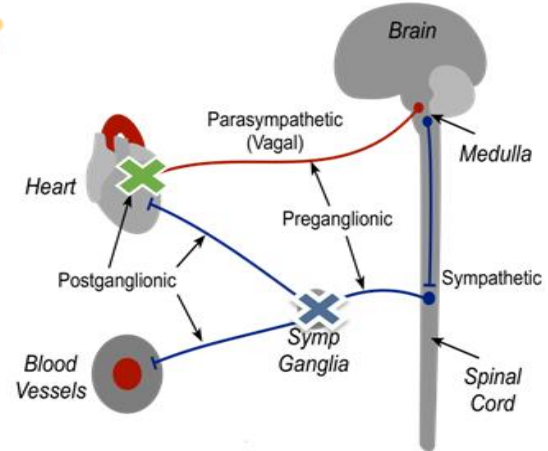
1) Competes with acetylcholine for nicotinic receptors in the motor plate (paralysis) (SD).



2) Close ion channel of receptor (LD)

3) Curare is a weak ganglion blocker. *Autonomic*

4) Histamine release (moderate).



Pharmacological actions:

1) Skeletal muscle

- skeletal muscle paralysis in the following order: Small rapidly contracting muscles of the eye, face, fingers & neck, then the muscles of limbs & trunk are affected & the last muscles to be paralyzed are the intercostal muscles, then the diaphragm.
- Recovery occurs in the reverse order.

لین لما یبنا نظوه
منا شوی وقتے ضعف
الریغی تیل و ریا

2) CVS

Hypotension due to:

- Weak ganglion blocking effect.
- Histamine release $\rightarrow \uparrow VD, BC$
 $\downarrow \downarrow BP$
- Decreased venous return as a result of muscle paralysis $\rightarrow \downarrow \downarrow COP$.



Adverse effects

i. Hypotension.

ii. Bronchospasm.

iii. Allergy. (Histamine release).

iv. Curare apnea: Death from overdose occurs due to paralysis of respiratory muscles.

• Treatment of toxicity:

1) Artificial respiration with O₂ under pressure.

2) Neostigmine; preceded few minutes by atropine (to avoid marked bradycardia).

Contraindications:

1) Bronchial asthma.

2) Renal diseases.

3) Allergy.

الخلاصة المبسطة جدًا











النوع	المثال	ماذا يفعل
Depolarizing	Succinylcholine	ينشط receptor ثم paralysis
Non-depolarizing	Pancuronium	يمنع receptor مباشرة

كلاهما يستهدف nicotinic Nm أساسًا.

لكن بعض الـ non-depolarizing قد يؤثر عرضيًا على muscarinic receptors.

نقطة صغيرة يحبها دكاترة الفارما في الامتحان:
ليس كل non-depolarizing يسبب tachydia؛ هذا مشهور أكثر مع Pancuronium.

ملاحظة
لاحقًا.

	Duration/ min	Potency	Ganglion blocker	Histamine release	Special
Curare	30-60min/2 min	1			<u>Non-Selective.</u> ←
Gallamine (Flaxidil)	15-35 min	(1/5 of curare).			tachycardia (M ₂ blocker)
Pancuronium	60-90 min	6			tachycardia (↑NE release) ↘
Atracurium Cisatracurium → Contraindicated in epilepsy.	15-35 min 90/3 min			less	(Hofmann elimination by ester hydrolysis) Seizure less with Cisatracurium
Mivacurium	10-20 min/2 min			mild	(pseudochole esterase enzyme).
Rocuronium amiosteroids	20-30 min/1 min	Used instead of succinylcholine for endotracheal intubation			Hepatic elimination
Vecuronium amiosteroids	30-40 min				Hepatic elimination

Drug- drug interactions

1- **Cholinesterase inhibitors** increase acetylcholine levels at the neuromuscular junction by preventing its breakdown, directly counteracting d-tubocurarine's competitive blockade of nicotinic receptors, thereby reversing neuromuscular blockade. ✓

2- **Botulinum toxin type A** potentiates d-tubocurarine's neuromuscular blocking effects through additive inhibition of acetylcholine release, leading to major synergy and risks.

3- **Aminoglycoside antibiotics** enhance the effect of curare by inhibition of acetylcholine release.

4- **Halogenated hydrocarbon anesthetics (halothane)** enhance the effects of NMB.

This synergy increases the risks of prolonged paralysis, especially during recovery.

5- **Calcium channel blockers (e.g., verapamil, nifedipine, diltiazem)** involve significant potentiation of neuromuscular blockade. they reduce calcium influx at the neuromuscular junction, impairing acetylcholine release.

Depolarizing (Non-competitive) NMBs

Succinylcholine (suxamethonium)

Successive choline $\xrightarrow{2 \times 1-120}$ succinylcholine

- It is composed of two molecules of acetylcholine connected by an ether linkage.

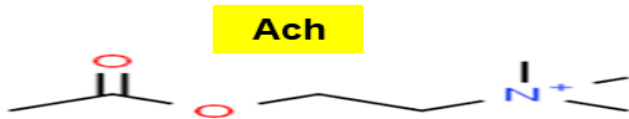
- Not absorbed orally, not pass BBB.

لا يمتص عن طريق الفم
لا يمتص في الدم المحيطي
نفاذ

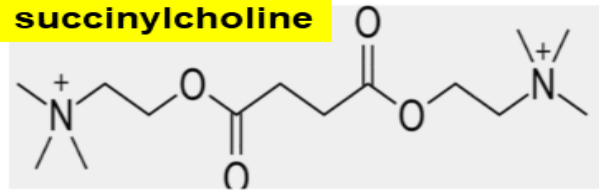
- Short acting (5-10 min).

- Metabolized by pseudocholine esterase (PLASMA) in two steps: a rapid step into succinyl monocholeline, then a slow step into succinic acid + choline.

عناصير كيناز
2 molecules
من أكل Ach



succinylcholine



• Mechanism of action

• It has two phases of block:

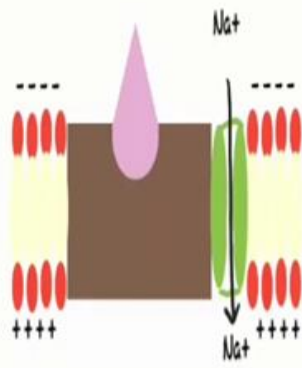
Phase I: *Non-selective* *يعني ما يميز بين عصب الـ ganglia و عصب الأخرى*

❖ It binds to nicotinic receptors on the neuromuscular junctions & acts as an agonist (depolarization of the motor end plate & initially causing fasciculation).

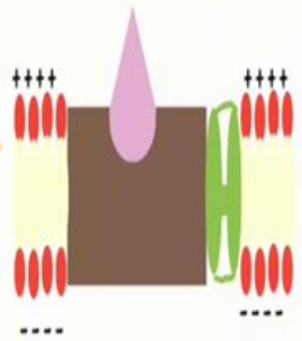
Phase II (desensitization):

❖ Prolonged depolarization of receptors produces spontaneous closure of Na^+ channels, which become partially reversible.

❖ The slow dissociation and metabolism of succinylcholine at receptors lead to persistent depolarization, transmission failure & muscle paralysis.



Phase I
Depolarising phase



Phase II
Desensitising phase

Pharmacological actions:

- 1) Skeletal muscle paralysis is preceded by fasciculations, and this produces postoperative pain.
- 2) It stimulates both sympathetic and parasympathetic ganglia (LD).
- 3) It is a mild histamine releaser.

Therapeutic uses

- 1) It is very useful in endotracheal intubation because of its rapid onset and short duration of action.

Adverse effects

1- Succinylcholine apnea

Treatment of succinylcholine toxicity (apnea) 🚑

① Artificial respiration.

-After diagnosis of the phase block:

In phase I: give fresh frozen plasma or a fresh blood transfusion to restore the cholinesterase enzyme. → لأنه موجود في البلازما

In phase II: I.V. neostigmine or Edrophonium preceded by atropine. (X)

2) Post-operative muscle pain.

3) Malignant hyperthermia (pharmacogenetic defect): treated by I.V. dantrolene.

4) Hyperkalemia which can cause arrhythmias. → cardiac arrest!

5) Increased intra-abdominal & intra-gastric pressures.

6) Increased IOP.

relaxation لا يزيد ارتخاؤ العين + يعمل to the extra-ocular muscles to the risk

muscarinic المبرقحزاق المحبودة غ البقرة.

Contraindications

1. Deficiency of pseudocholinesterase.
2. Glaucoma or eye injury.
3. Hypersensitivity to the drug.
4. Severe tissue damage.
5. History of malignant hyperthermia.

Malignant hyperthermia

معلومات عن المخدرات الاربعة رافلو succinylcholine او inhalational anesthetic

التهمة يحدث

Calcium storm inside the muscle
والتهمة بسبب زيادة الكالسيوم

Muscle lysis → Metabolism explodes → CO₂ rise → Heat rises → Muscle breaks

MH = Calcium overload

تم التاج

Muscle rigidity	1
CO ₂ (early sign)	2
Hyperkalemia	3
Bradycardia	4
Acidosis	5

أهم ثلاث كلمات في الامتحانات
Malignant Hyperthermia أو سوء حال سريع من Succinylcholine

Succinylcholine - ↑CO₂ - Dantrolene

سببها

- Trigger: Succinylcholine / volatile anesthetics
- Early sign: ↑ End-tidal CO₂
- Treatment: Dantrolene

Spasmolytic Drugs

They are used to decrease skeletal muscle spasm

1- Centrally acting (on CNS):
mephenesin & baclofen

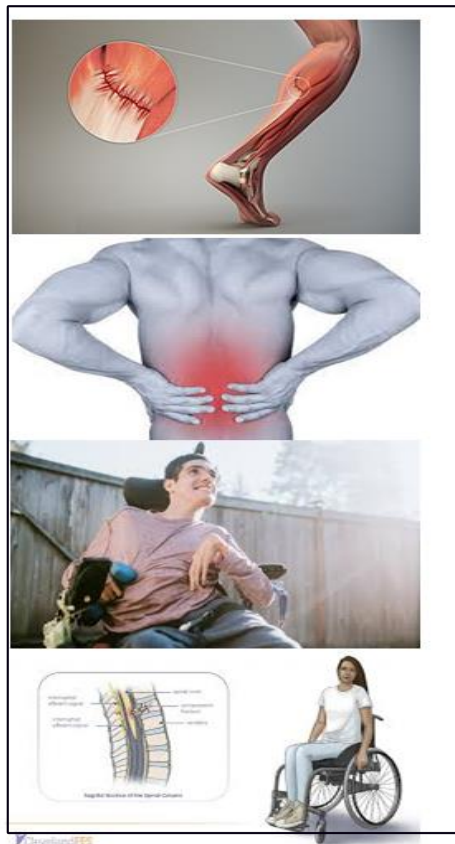
2- Direct or peripherally acting (on skeletal muscles): dantrolene

3. Botulinum Toxin (Botox): Blocks acetylcholine release at the neuromuscular junction, leading to muscle paralysis



Therapeutic Uses

- 1) Spasticity of skeletal muscles due to local causes e.g. trauma, inflammation & rheumatism.
- 2) Low back pain syndrome.
- 3) Cerebral causes of spasticity e.g. cerebral palsy & strokes.
- 4) Spinal causes of spasticity e.g. spinal cord injury or degenerative diseases.



Mephenesin

CNS

- ❖ Taken orally.
- ❖ Acts on the subcortical (spinal) polysynaptic pathway → muscle relaxation without hypnosis or anesthesia.
- ❖ It is used in:
 1. Strychnine poisoning (specific antidote).
 2. Painful muscle spasm and stiffness.

التغيم العضلي

Baclofen

CNS

Mechanism of action.

- A selective GABA_B agonist, which produces inhibition of the release of excitatory transmitters in the brain and spinal cord.
- It also decreases pain transmission in the spinal cord by decrease release of substance P from the nerve ending of primary afferent sensory neurons.

• Indications of Baclofen:

❖ Used in muscle spasticity due to spinal cord lesions (e.g. spinal cord injury).

❖ Baclofen is not an appropriate treatment for muscle spasm associated with an acute injury.

ليس مستحسن في الحادة
الحركية

Diazepam

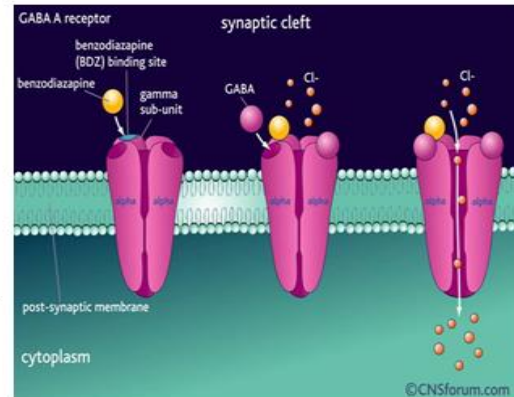
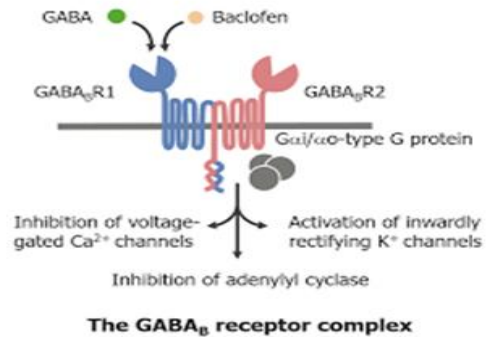
1- GABA A agonist

2- Enhancing polysynaptic and presynaptic inhibition on the spinal motor neurons.

uses:

A. Spasticity

B. Skeletal muscle spasm due to local trauma or disc prolapse



Tizanidine

❖ It is a new α_2 -adrenoceptor agonist.

❖ Mechanism of action: Stimulates α_2 -adrenoceptors in the CNS muscle relaxation.

❖ Taken orally.

❖ It has fewer CVS effects.





Dantrolene

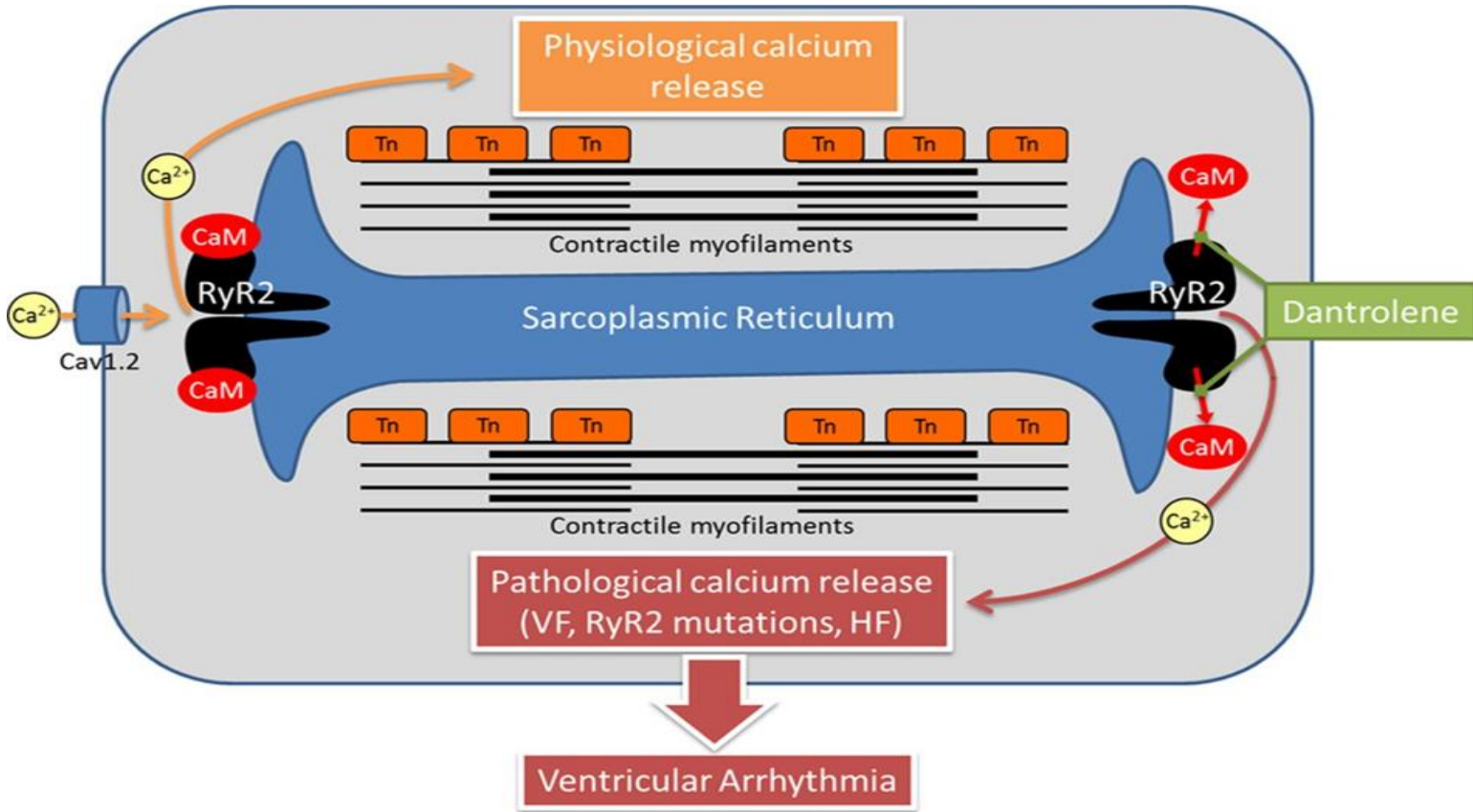
❖ Mechanism of action:

- Acts directly on skeletal muscle and so has minimal CNS effects.
- It relaxes skeletal muscles directly by interfering with the release of Ca^{+2} from the sarcoplasmic reticulum.
- Indications: (oral or IV)
 1. Treatment of chronic muscle spasm caused by spinal cord (e.g. spinal cord injury) or cerebral (e.g. Cerebral palsy) causes.
 2. Treatment of malignant hyperpyrexia.
 3. Treatment of the neuroleptic malignant syndrome.

Adverse effects

1. Hypotension.
2. Muscle weakness.
3. Diarrhea.
4. Damage to the liver (with long-term use).
5. Drowsiness, vertigo, and dizziness (with long-term use).

العلاج الأساسي:
الدواء المنقذ هو Dantrolene
وهو يعمل على منع خروج Ca^{2+} من الـ sarcoplasmic reticulum.
خلاصة قصيرة للحفظ (مهمة للطب):
= Malignant hyperthermia
genetic disorder → triggered by anesthetics → uncontrolled Ca^{2+} release in skeletal muscle → rigidity + hyperthermia → treated with Dantrolene.



Malignant hyperthermia VS NMS

Feature	NMS	Malignant Hyperthermia
Trigger	Antipsychotics	Anesthetics + succinylcholine
Onset	Days	Minutes
Cause	Dopamine blockade	Ca ²⁺ release from SR
Treatment	Dantrolene, Bromocriptine	Dantrolene

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Thank you!