

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ
(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)



الجاني

Pharmacology | FINAL 3

Skin Pharmacology Pt.3 & Muscle Relaxants Pt.1



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خَابَ وَخَسِرَ مَنْ أَذْرَكَ رَمَضَانَ وَلَمْ
يُغْفِرْ لَهُ

Drugs for Psoriasis

It is an inflammatory condition of the skin, characterized by some changes, such as erythematous scaling plaques (as in the Figure). It manifests with increased epidermal cell proliferation. Psoriasis appears to have both genetic factors and T-cell-mediated immune components.

- **Acitretin:**
 - **Related to isotretinoin.**
 - **Given orally.**
 - **Hepatotoxic and teratogenic** (Which is characterized in incomplete growth of the limbs, cleft lip & cleft palate).
 - **Patients should not become pregnant for 3 years after stopping treatment, and also should not donate blood** (Same thing with isotretinoin, since the drug will be in the circulation and may cause teratogenicity if donated to a pregnant woman).
 - Sometimes it is hard to treat psoriasis, because of the **plaques formed.**
 - For treatment, sometimes we start **with corticosteroids, which are anti inflammatory agents**

Categories of drugs in pregnancy

Extra table for more understanding

Pregnancy Category	Description
A	Appropriate human studies - no risk
B	Insufficient human studies, but animal research suggests safety <u>or</u> : Animal studies show issues but human studies show safety
C	Insufficient human studies, but animal studies show problems <u>or</u> : No animal studies, and insufficient human studies
D	Human studies, with/without animal research show fetal risks, but the drug is important to some women to treat their conditions
X	Fetal risks are evident; there are no situations where the risk/benefit justifies use

- Paracetamol and antibiotics are **categorized in A/B**.
- **X IS ABSOLUTELY CONTRAINDICATED** (notice that harm increases as we go down through the table).
- When prescribing category c or d for a pregnant woman, you should weigh the benefits against the risks and refer back to her OBGYN.
- This classification is not used anymore, new drugs have this information and descriptions on the leaflet, but some doctors still refer back to it.

Drugs for Psoriasis

- **Tazarotene:**
 - **Topical.**
 - **Anti-inflammatory and antiproliferative actions.**
 - **Teratogenic. Also, can cause burning, stinging, peeling, erythema, and localized edema of skin.**
- **Calcipotiene:**
 - **Synthetic vitamin D₃ derivative**

Patients who took this drug noticed improvements, especially in plaque psoriasis



Mechanism of action and side effects are **guaranteed** exam questions. 😊

New Drugs for Psoriasis

Apremilast (Otezla) **oral**

- psoriasis and psoriatic arthritis (**psoriasis associated with rheumatoid arthritis**).
- It may also be useful for other immune system-related inflammatory diseases .
- The drug acts as a **selective inhibitor of the enzyme phosphodiesterase 4 (PDE4)** and **inhibits spontaneous production of TNF-alpha** from human rheumatoid synovial cells.
- Apremilast is useful in psoriasis with psoriatic arthritis because TNF- α is involved in many immune-mediated inflammatory disorders.

Apremilast

Side Effects :

- diarrhea
- nausea.
- stomach pain.
- vomiting.
- headache.
- sore throat, cough, and fever.
- sneezing, runny nose, and nasal congestion.

Symptoms are very similar to upper respiratory infections, like sneezing , runny nose and nasal congestion.

New Drugs for Psoriasis

Deucravacitinib (Sotyktu)

Any drug that ends with (inib) is a monoclonal antibody, but this drug is NOT.

- A new oral treatment option for adults with plaque psoriasis.
- moderate-to-severe plaque psoriasis
- It is a once-daily oral medication with its clinical trials in moderate-to-severe psoriasis demonstrating superior efficacy to apremilast
- MOA: Allosteric inhibitor of TYK2 → Tyrosine kinase enzyme
- Side effects: runny nose, congestion, or sore throat, sore on mouth, lips, gums, tongue or roof of mouth, Ulcers in the oral cavity, acne.

This drug is an immune modulator, that's why some of the side effects are related to the respiratory system

New Drugs for Psoriasis

Roflumilast (Zorvye) cream Topical

Similar to Apremilast

- Selective, long-acting inhibitor of the enzyme phosphodiesterase-4 (PDE-4). It has anti-inflammatory effects :
 - chronic plaque psoriasis.
 - an effective topical therapy for use on all psoriasis- affected areas including body, face, and intertriginous areas. Areas with folds, and it happens due to friction.
- Intertriginous areas examples :
 - 1) armpits.
 - 2) areas with fat folds in overweight people.



The commercial names of drugs, found between brackets , are not for memorization unless stated otherwise

New Drugs for Psoriasis

Tapinarof (Vtama)

Very new drug

- **Tapinarof (Vtama)** is a topical (on the skin) medication used to treat plaque psoriasis in adults.
 - MOA: immune modulation, skin-barrier normalization, and antioxidant activity.
 - It's convenient to use because it's only applied once daily

Exact mechanism is unknown

Drugs for Psoriasis IV administration

- **Biologic Agents:**

- **Etanercept:**

- **Dimeric fusion protein of TNF receptor linked to the Fc portion of human IgG₁**

A monoclonal antibody with a humanized Fc portion is coupled to a component targeting the TNF receptor, which reduces TNF activity.

- **approved for the treatment of psoriasis, psoriatic arthritis and ankylosing spondylitis in adults**

Psoriasis is an autoimmune disease.

Anti-inflammatory Agents

- Topical Corticosteroids:
 - Hydrocortisone.
 - Prednisolone and Methylprednisolone.
 - Dexamethasone and Betamethasone.
 - Triamcinolone.
 - Fluocinonide.

“Don’t worry
about them ;)”

Dr,p.Alia said.

Back in the day, they used Tar القطران , some cultures still do.

Anti-inflammatory Agents

- **Topical Corticosteroids:**

- **Absorption:**

- **1% of hydrocortisone applied to the ventral forearm.**
- **0.14 times of hydrocortisone applied to the plantar foot.**
- **0.83 times of hydrocortisone applied to the palm.**
- **3.5 times of hydrocortisone applied to the scalp.**
- **6 times of hydrocortisone applied to the forehead.**
- **9 times of hydrocortisone applied to the vulvar skin.**

Just know that these are anti inflammatory drugs and could be used for various skin conditions, psoriasis and eczematous dermatitis being some of them.

Don't worry about this slide ;))

Anti-inflammatory Agents

- **Topical Corticosteroids:**
 - **Absorption:**
 - Absorption increased with inflammation.
 - Increasing the concentration does not proportionally increase the absorption.
 - Can be given by intralesional injection.

Anti-inflammatory Agents

- **Topical Cortcosteroids:**
 - **Dermatologic disorders very responsive to steroids:**
 - **Atopic dermatitis.**
 - **Seborrheic dermatitis.**
 - **Lichen simplex chronicus.**
 - **Pruritus ani.**
 - **Allergic contact dermatitis.**
 - **Eczematous dermatitis.**
 - **Psoriasis.**

Contact dermatitis can resemble eczema in appearance. However, atopic dermatitis is a chronic inflammatory skin disease that may flare without an obvious trigger, whereas allergic contact dermatitis occurs due to exposure to specific allergens or chemicals that trigger a delayed hypersensitivity reaction.

Anti-inflammatory Agents

- **Topical Cortcosteroids:** Will be given in the endocrine system inshAllah
 - **Adverse Effects:**
 - Suppression of pituitary-adrenal axis.
 - Systemic effects.
 - Skin atrophy. Decreased thickness of skin
 - Erythema.
 - Pustules.
 - Acne.
 - Infections.
 - Hypopigmentation.
 - Allergic contact dermatitis.

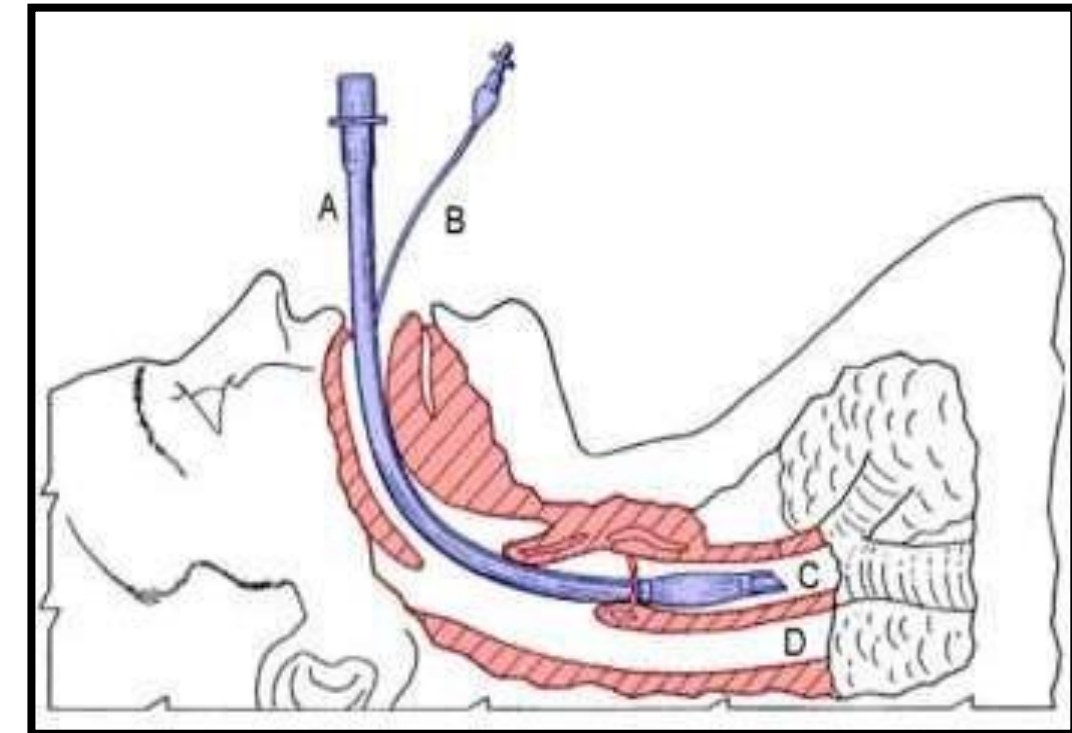
Anything that affects
the immune system
can lead to
inflammation

Peripherally Acting Skeletal Muscle Relaxants

Dr. Alia Shatanawi

Peripherally Skeletal Muscle Relaxation Uses:

- **In conjugation with General Anesthetics** (not to cause anaesthesia, they don't cause the patient unconscious):
 - **Facilitate intubation of the trachea.**
 - Before surgery, we have to intubate the patient by inserting a tube through their mouth then down their trachea. To make this process effective, we use those peripherally acting relaxants, also they will enable us to reach the surgical site. (it's easier to manipulate a relaxed muscle than to manipulate a constricted one).
 - **Facilitate mechanical ventilation.**
 - **Optimized surgical working conditions.** (When doing a surgery, it is easier to cut or move a relaxed muscle rather than a contracted one).



History of Skeletal Muscle Relaxants



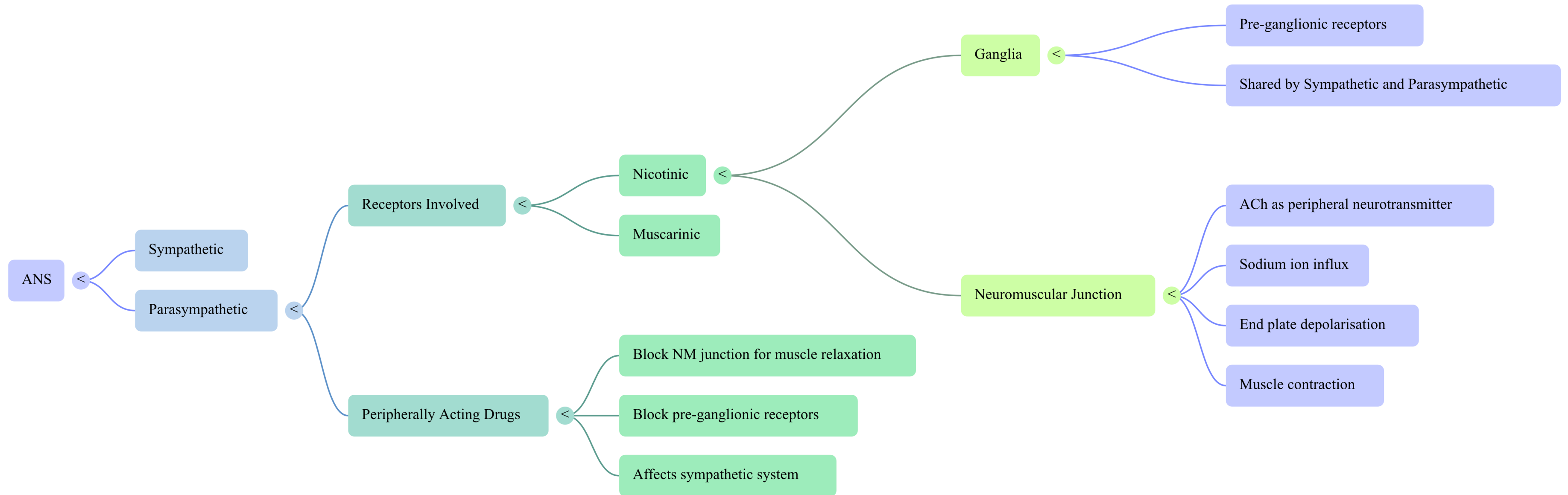
- Curare (antagonist of the nicotinic receptors at NM junction) is a common name for various plant extract **alkaloid arrow poisons** (it was used as a poison arrow for hunting by causing paralysis of the animal muscle) originating from **Central** and **South America**.
- Source:** *Chondrodendrone tomentosum* and *Strychnos toxifera*. (Don't worry about these).
- Tubocurarine** name because of packing in “hollow bamboo tubes”

History of Skeletal Muscle Relaxants



- That make us thinking : **Why this paralytic poison didn't affect the person who ate the animal that was injected with this poison?**
 - **It can't be absorbed** due to its structure (highly polar compound) and that's why those drugs are **given IV when being used as a muscle relaxant.**

Quick revision regarding ANS



Classification

Skeletal muscle relaxants

Centrally acting

- Diazepam and other benzodiazepines
- Methocarbamol
- Chlorzoxazone
- Tizanidine
- Baclofen
- Gabapentin

These are for CNS, 3rd year, 2nd Semester.

Peripherally acting

Acts on Neuromuscular junctions.

Drugs acting at NMJ

Drugs directly acting on skeletal muscle

- Dantrolene

Depolarizing blockers

- Succinylcholine
- Decamethonium

Only Clinically used Depolarizing Skeletal Muscle relaxant.

Used in studies (Very short lived to be used in humans).

Non-depolarizing blockers (Competitive blockers)

- d-TC
- Pancuronium
- Doxacurium
- Pipecuronium
- Vecuronium
- Atracurium
- Rocuronium
- Mivacurium

Long acting

Intermediate acting

Short acting

Tubocurarine, it is the prototype of this group, it is not used nowadays.

Others

- Botulinum toxin A

Depends on the procedure's length.

Can be used for short procedures.

Acetylcholine

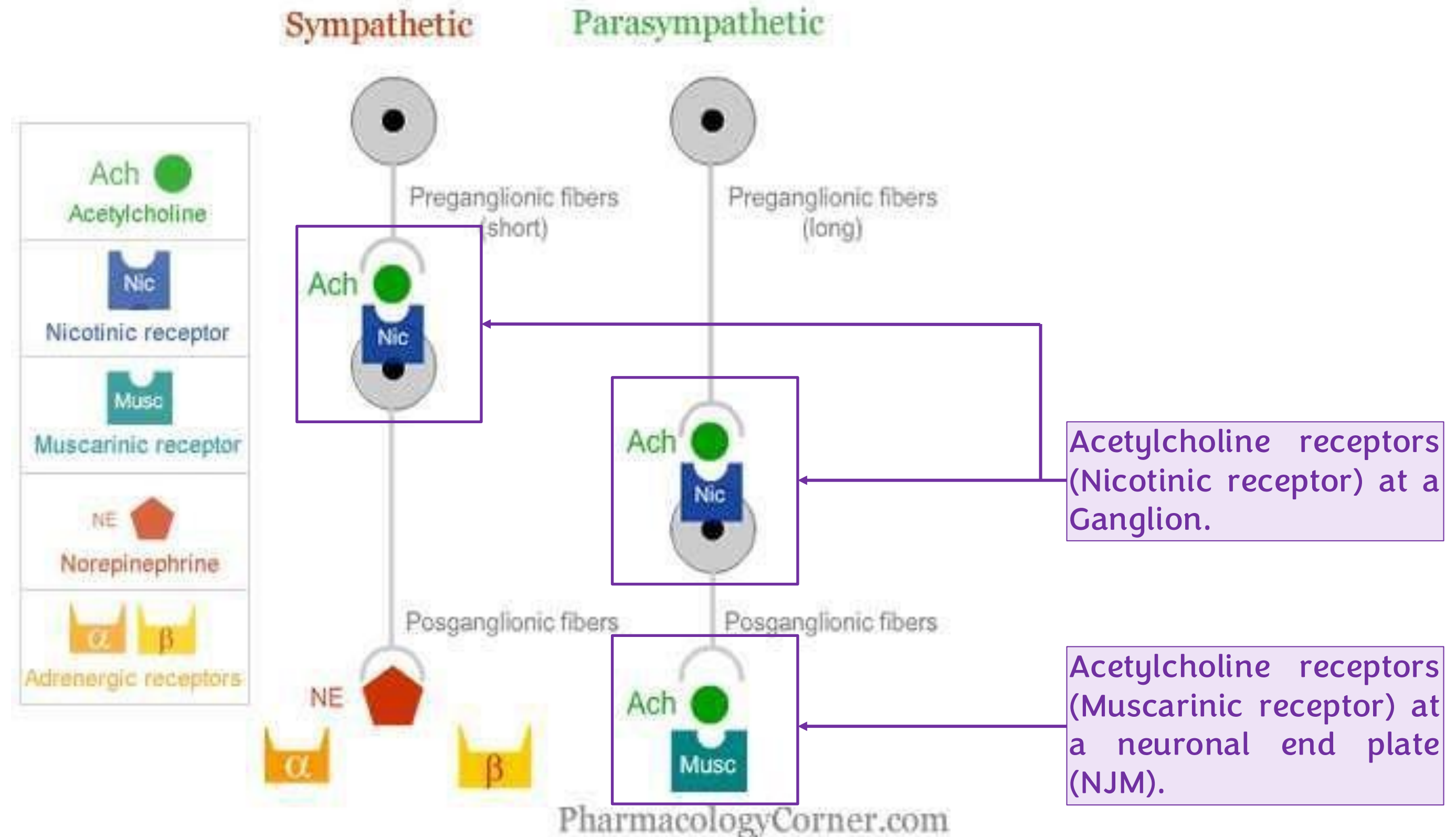
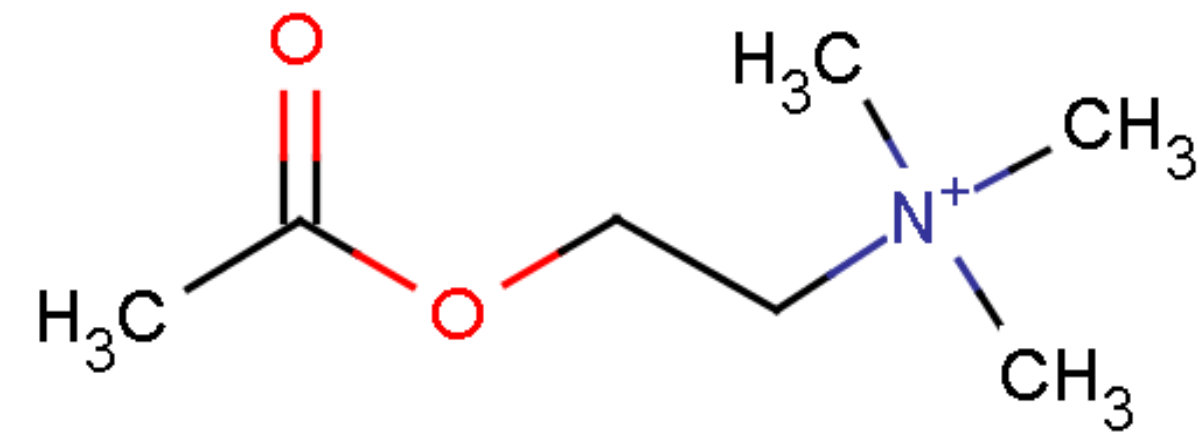
➤ Acetylcholine is a major neurohumoral transmitter at **autonomic, somatic and central nervous system**, it is secreted (present) at :

- 1) All preganglionic sites (Both Parasympathetic and sympathetic).
 - When we study drugs later and their side effects, we are going to find that their side effects is related to being **non-selective for Ach receptors** on both Sympathetic & Parasympathetic.
- 2) Skeletal Muscles. **(The effector cells of NMJ)**.
 - We have 2 types of Ach receptor, the M Type (Muscle type) and N type (Nerve Type) [remember that we have a specific selectivity toward one type, so if we are using a drug with high dose we may lose selectivity and it start affecting the other receptor type and we start to see adverse effect.
- 3) CNS: Cortex Basal ganglia, spinal cord and others **(Many drugs that are used for Alzheimers are related to Ach)**.

Acetylcholine

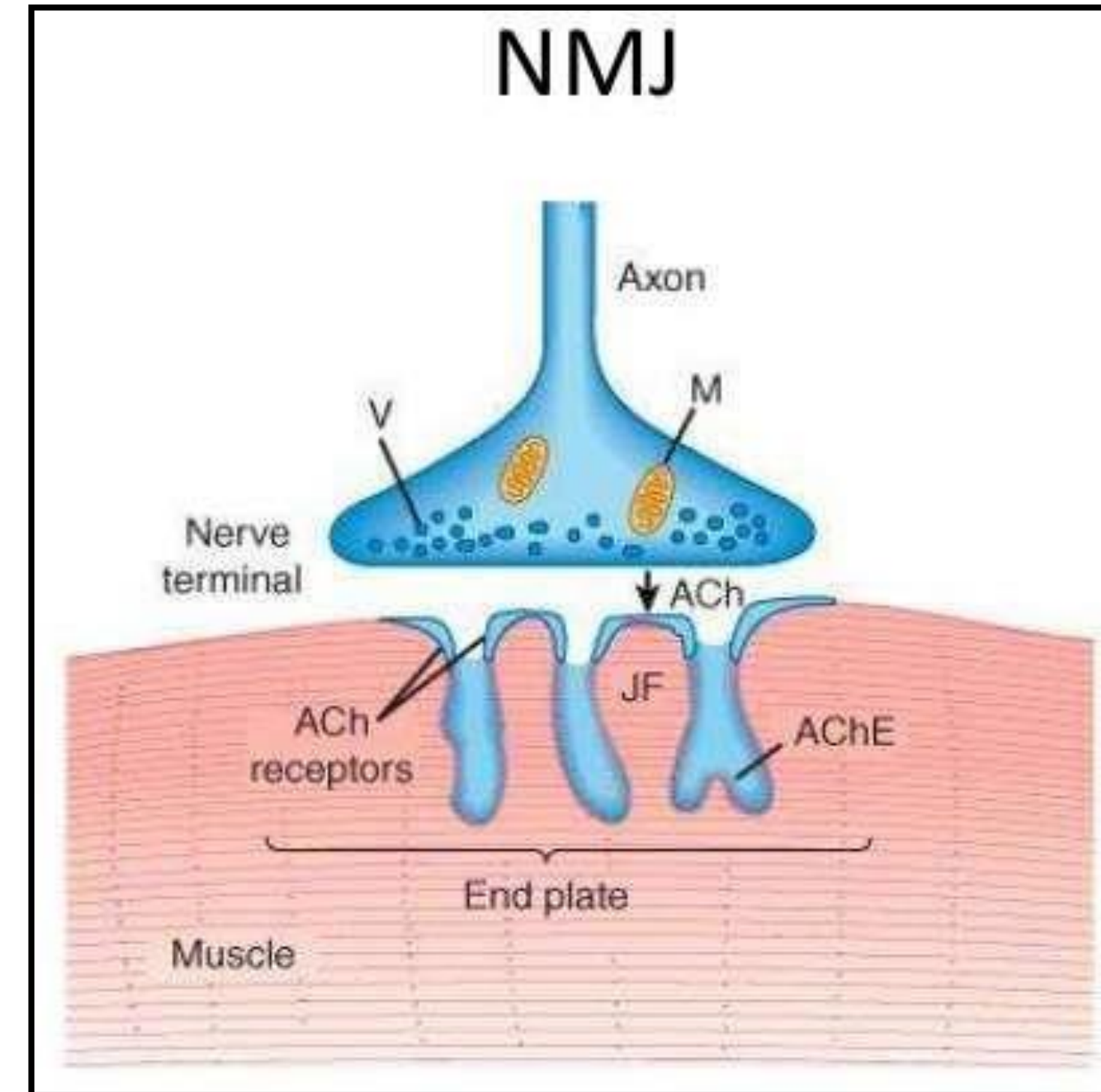
- Parasympathetic Stimulation → Acetylcholine (ACh) release at **neuroeffector** junction → biological effects Sympathetic stimulation → Noradrenaline (NA) at neuroeffector junction → biological effects.

Acetylcholine

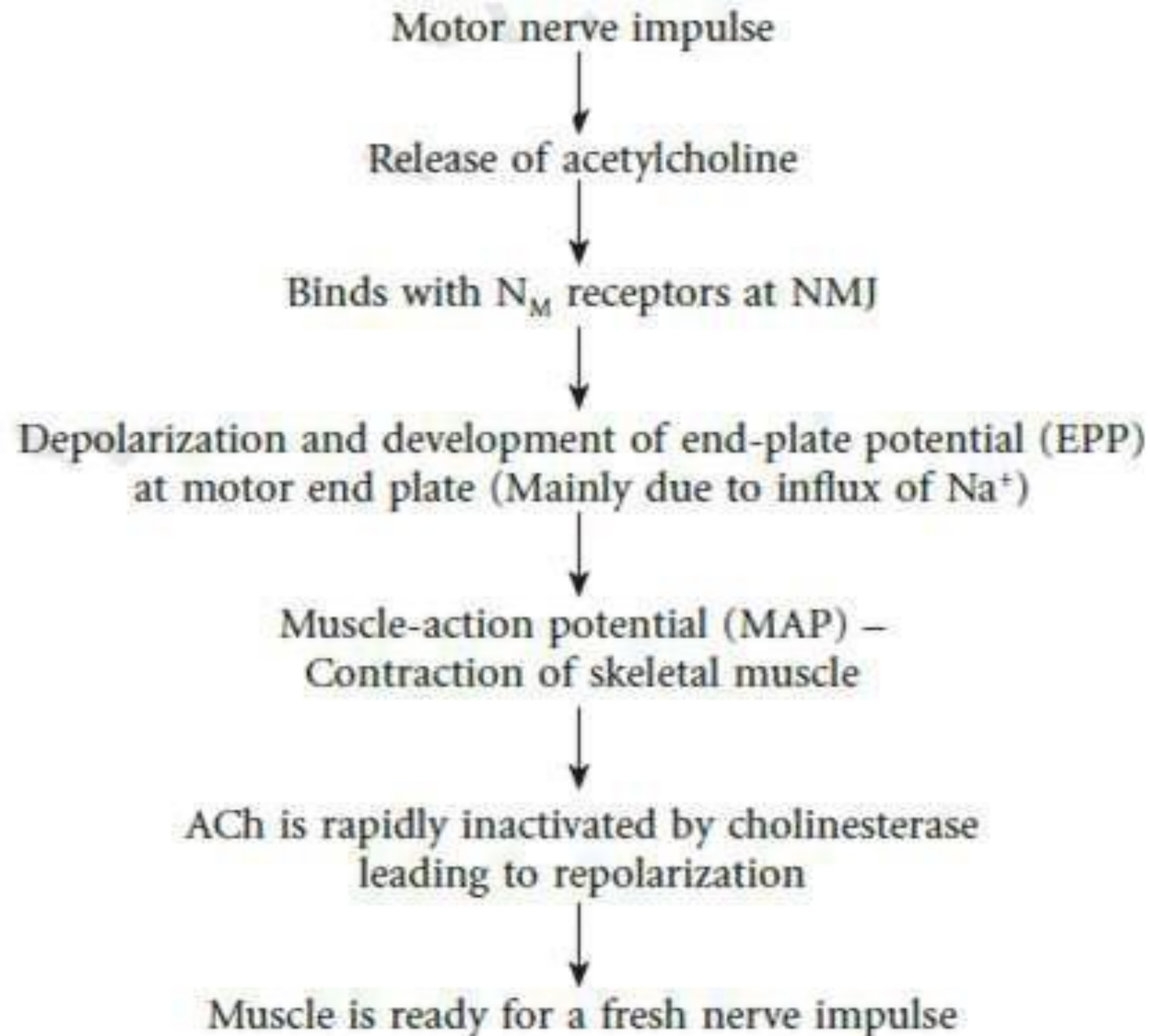


Neuromuscular Junction (NMJ)

- 1) Release of transmitters occurs when **voltage-sensitive calcium channels in the terminal membrane are opened**, allowing an influx of calcium.
 - 2) The resulting increase in intracellular calcium causes fusion of vesicles with the surface membrane and exocytotic expulsion of acetylcholine and co-transmitters into the junctional cleft.
 - 3) The released ACh will bind to **nicotinic receptors (Ligand gated sodium channels)** on End plate, resulting in opening of the channel → Sodium influx → depolarization → Calcium channels opening (on Sarcoplasmic reticulum and on Sarcolemma) → Muscle contraction (as we learned in Physio MID).
- The main ways of ACh intact is by Acetylcholinesterase enzyme.



Physiology of Skeletal Muscle Contraction



Peripherally acting Neuromuscular Blockers

- **Depolarizing Blockers** – mimic the action of **acetylcholine (Ach)** :
 - It is going to bind to Ach receptors and open ligand gated sodium channels
→ → **Muscle contraction! we are taking about muscle relaxant, how can a drug that causes muscle contraction to be on the list ?**
Ans : What happens actually that these drugs are going to cause excessive muscle contraction to a level that causes muscle paralysis.
 - Agonists.
 - Example : Succinylcholine (SCh) **which is the only drug used clinically.**

Peripherally acting Neuromuscular Blockers

- **Non-Depolarizing** – interferes with the action of Ach :
 - 1) **Competitive Blockers (Antagonist)** : They are going to bind to receptors, preventing the binding of ACh → Prevents Contraction.
 - Further divided into :
 - 1) Short non- depolarizing drugs.
 - 2) Intermediate non- depolarizing drugs.
 - 3) long acting non- depolarizing drugs.

رسالة من الفريق العلمي:



For any feedback, scan the code or click on it.



Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	Slide 23	Nonadrenaline	Noradrenaline
V1 → V2			