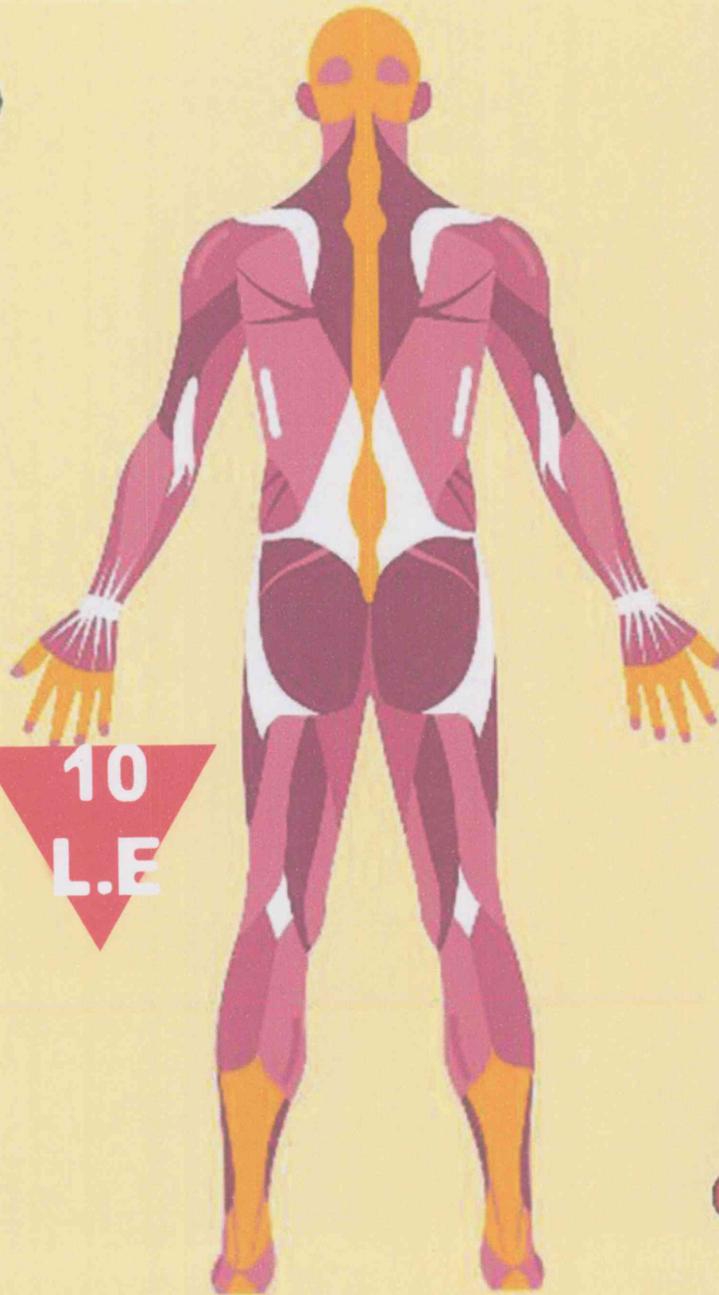
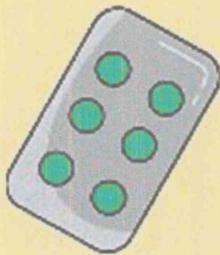


LEVEL 1 - SEMESTER 2

# PHARMACOLOGY

## MSK

### L5



10  
L.E



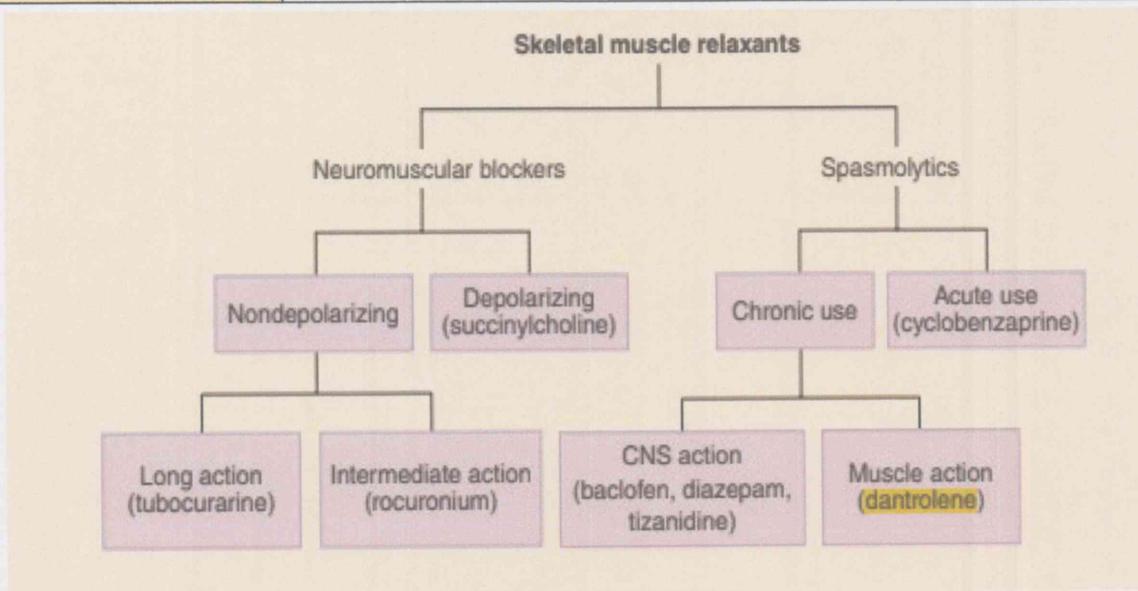
Dr. M. M.

# Skeletal Muscle Relaxants

▪ **Def:** Drugs that decrease muscle tone and or cause ms paralysis.

▪ **Classification:**

<b>I. Peripheral skeletal muscle relaxants</b>	• Act at the <b>neuromuscular junction</b> or within the <b>contractile process</b> .
<b>II. Centrally acting skeletal muscle relaxants</b>	• Drugs acting on <b>brain higher centers</b> or at the <b>spinal cord</b> .



## Peripherally Acting Skeletal Muscle Relaxants

▪ **Classification:**

A. Drugs act on neuromuscular junction	B. Drugs act on muscle contractile mechanism
1. Neuromuscular blockers 2. Botulinum toxin	1. Dantrolene

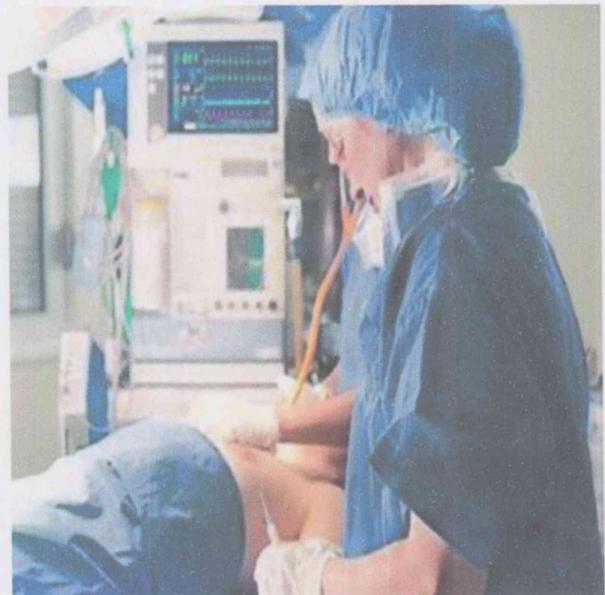
## Neuro-muscular blockers (NMB)

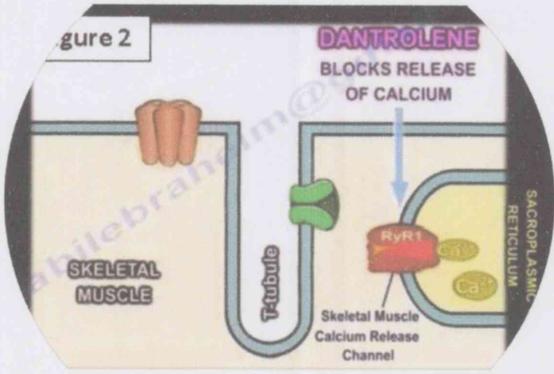
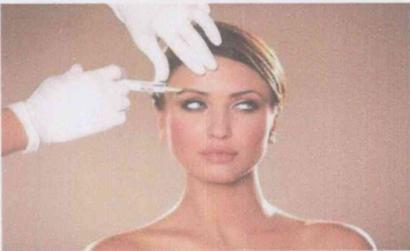
### ▪ Classification: MCQ

A. Non-depolarizing	B. Depolarizing
<ol style="list-style-type: none"><li>1. Long acting (Pancuronium)</li><li>2. Intermediate (Atracurium, Vecuronium)</li><li>3. Short acting (Mivacurium)</li></ol>	<ol style="list-style-type: none"><li>1. Succinylcholine</li></ol>

### ▪ Clinical indications:

- The most important use of NMB is as **adjuvants to general anesthesia** for induction of muscle relaxation during surgery.
- Facilitation of intubation (**endotracheal intubation**).
- Adjunct to **electroconvulsive therapy** for prevention of injury.

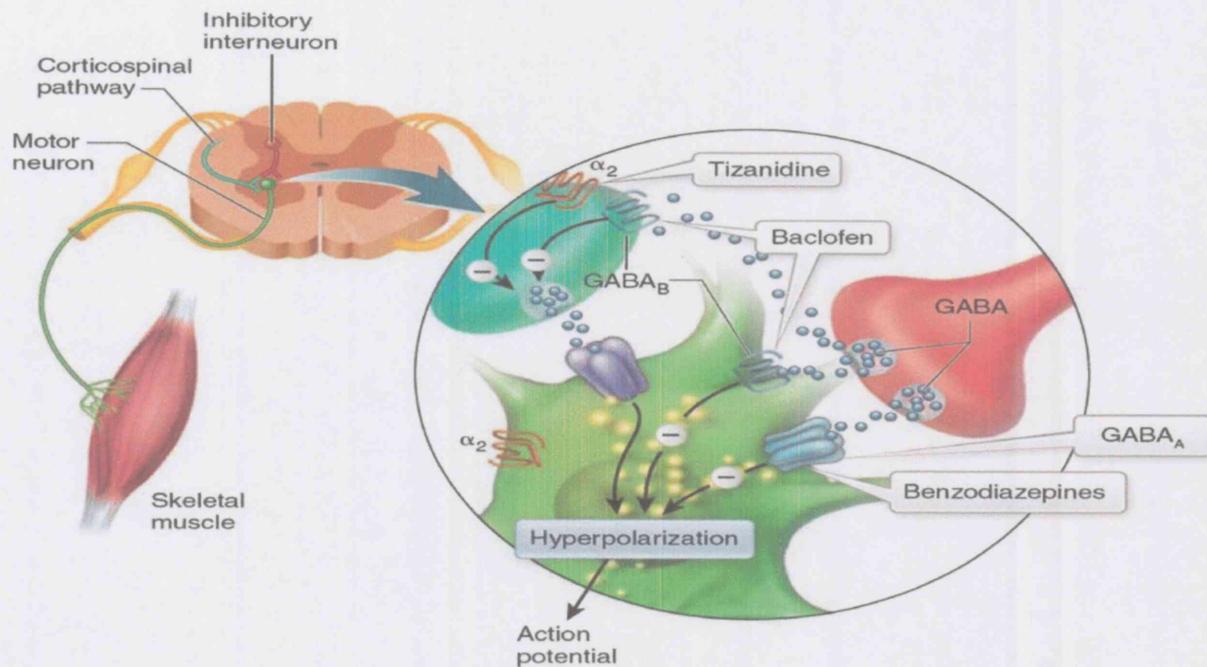


	<b>C. Botulinum toxin</b>	<b>D. Dantrolene</b>
<b>Overview</b>	<ul style="list-style-type: none"> <li>Neurotoxic protein produced by the <b>bacterium Clostridium botulinum</b>.</li> </ul>	<ul style="list-style-type: none"> <li><b>Direct-Acting</b> skeletal muscle relaxants.</li> </ul>
<b>MOA</b>	<ul style="list-style-type: none"> <li><b>Inhibits the release of ACh from motor nerve terminals</b> leading to skeletal muscle paralysis.</li> </ul>	<ul style="list-style-type: none"> <li><b>Inhibits Ca<sup>2+</sup> release from the sarcoplasmic reticulum</b> of skeletal muscle cells leading to <b>Inhibition</b> muscle contraction.</li> </ul>  <p>The diagram, labeled 'Figure 2', illustrates the mechanism of Dantrolene. It shows a cross-section of a skeletal muscle cell with a T-tubule and a sarcoplasmic reticulum. The sarcoplasmic reticulum contains RyR1 (Ryanodine Receptor 1) channels and Skeletal Muscle Calcium Release Channels. Dantrolene is shown as a green ring-shaped molecule that binds to the RyR1 channel, blocking the release of calcium ions (Ca<sup>2+</sup>) from the sarcoplasmic reticulum into the cytoplasm. This process is labeled 'DANTROLENE BLOCKS RELEASE OF CALCIUM'. The diagram also shows a hand holding a finger, representing muscle contraction, which is inhibited by the lack of calcium release.</p>
<b>Uses:</b>	<ul style="list-style-type: none"> <li>Injected <b>locally to treat local muscle spasm</b> e.g. in cervical dystonia blepharospasm &amp; Chronic migraine headache.</li> <li>Used for <b>cosmetic reduction of facial wrinkles</b></li> </ul>  <p>The image shows a person's face with a hand holding a syringe, illustrating the cosmetic use of Botox for wrinkle reduction.</p>	<ul style="list-style-type: none"> <li><b>Treatment of:</b> <ul style="list-style-type: none"> <li><b>Malignant hyperthermia</b> after halothane/succinylcholine exposure. <b>MCQ</b></li> <li><b>Neuroleptic malignant syndrome</b> caused by antipsychotics.</li> <li><b>Spastic conditions</b> (Cerebral palsy, Spinal cord injury).</li> </ul> </li> </ul>
<b>S/E:</b>		<ul style="list-style-type: none"> <li><b>Hepatotoxicity</b></li> </ul>

## Centrally Acting Skeletal Muscle Relaxants

### Classification:

A. Drugs act on higher centers	B. Drugs act on neuronal transmission in the spinal cord
1. Mephenesin congeners e.g.: Carisoprodol, chlorzoxazone 2. Benzodiazepines e.g.: Diazepam 3. Cyclobenzaprine	1. Baclofen 2. Tizanidine



### Drugs act on higher centers

#### General mechanism:

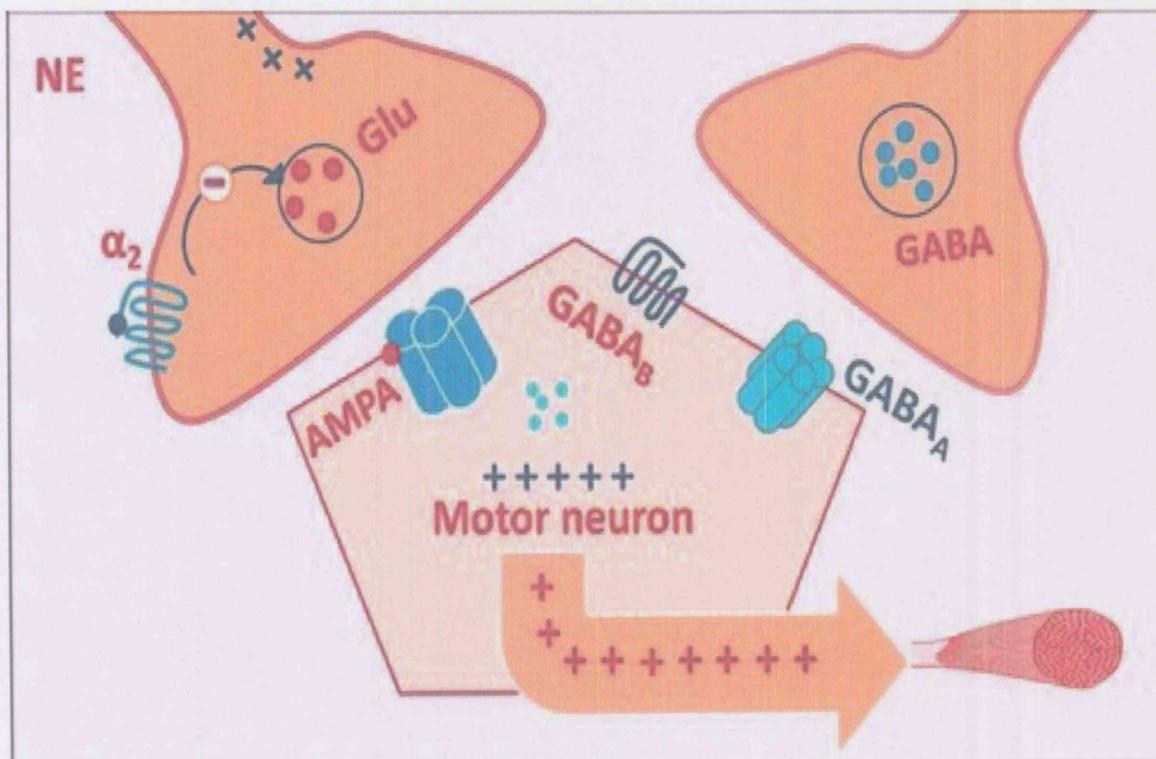
- They selectively **depress spinal and supraspinal polysynaptic reflexes** involved in the regulation of muscle tone. **MCQ**
- All centrally acting muscle relaxants do have some **sedative property** causing **drowsiness, dizziness, and sleepiness**.
- They have **NO effect on neuromuscular transmission or muscle fibers**.
- Prolonged use may lead to **dependency** (especially benzodiazepines).

➤ They include:

	<b>Carisoprodol, Chlorzoxazone:</b>	<b>Diazepam:</b>	<b>Cyclobenzaprine:</b>
<b>Nature</b>	<ul style="list-style-type: none"> <li>• Pharmacologically similar to <b>mephenesin</b>.</li> </ul>	<ul style="list-style-type: none"> <li>• Prototype of <b>benzodiazepines</b> (BZDs).</li> </ul>	<ul style="list-style-type: none"> <li>• Structurally related to <b>tri-cyclic antidepressants</b>.</li> </ul>
<b>Character</b>	<ul style="list-style-type: none"> <li>• Longer duration of action.</li> <li>• Better tolerated orally.</li> </ul>	<ul style="list-style-type: none"> <li>• Acts on <b>GABA-A receptors</b> → Facilitates GABA inhibitory effect.</li> </ul>	<ul style="list-style-type: none"> <li>• It reduced skeletal muscle hyperactivity within the central nervous system in the <b>brain stem</b>.</li> </ul>
<b>Use</b>			<ul style="list-style-type: none"> <li>• It is used for treatment of <b>acute spasm resulting from muscle injury</b>.</li> <li>• <b>but it is not effective in cases of cerebral palsy or diseases of the brain &amp; spinal cord.</b></li> <li>• <b>Used with caution in patients with myocardial infarction (MI), arrhythmias, or severe cardiovascular disease.</b></li> </ul>

## Drugs act on neuronal transmission in the spinal cord

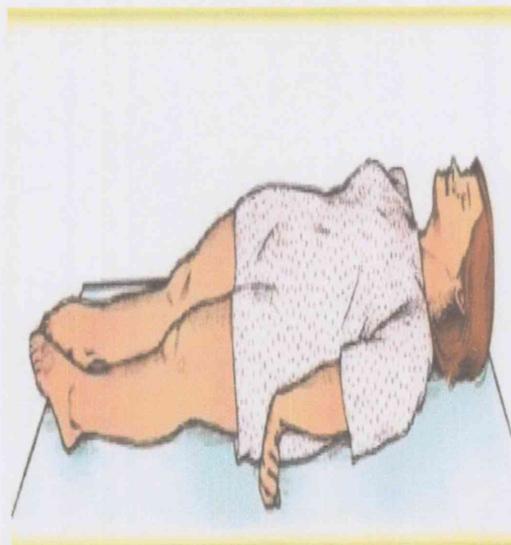
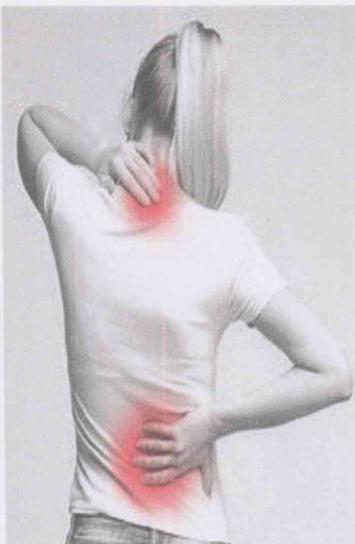
<b>Baclofen</b>	<ul style="list-style-type: none"><li>• It is a GABA derivative that <b>selectively stimulates GABAB receptors in the spinal cord</b> → ↓ release of excitatory transmitters. <b>MCQ</b></li></ul>
<b>Tizanidine</b>	<ul style="list-style-type: none"><li>• It is a centrally acting <math>\alpha_2</math> agonist with greater effect on <b>presynaptic <math>\alpha_2</math> in the spinal cord</b>, so it inhibits neurotransmission and inhibits spinal firing. <b>MCQ</b></li><li>• Tizanidine is similar to clonidine with <b>fewer peripheral effects</b>.</li></ul>



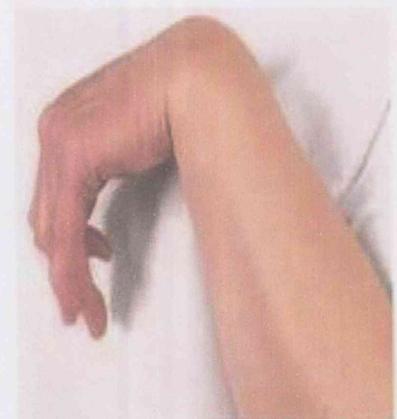
# Centrally Acting Skeletal Muscle Relaxants

## Spasmolytics

<b>Definition:</b>	<ul style="list-style-type: none"><li>• <b>Drugs reduce</b> excess muscle tone or spasm in injury or CNS dysfunction.</li><li>• <b><u>They may act in the</u></b> CNS, spinal cord, or directly on the muscle.</li></ul>
<b>Goals of therapy:</b>	<ul style="list-style-type: none"><li>• They reduce spasm, which reduces pain and improves mobility.</li></ul>
<b>Clinical indications:</b>	<ul style="list-style-type: none"><li>• <b>Spastic neurological conditions</b> (e.g. Hemiplegia, paraplegia, spinal injuries, multiple sclerosis....).</li><li>• <b>Anxiety and nervous tension.</b></li><li>• <b>Torticollis, backache</b></li><li>• <b>Acute muscle spasms</b> (Overstretching of a muscle, sprain, tearing of ligaments and tendons, dislocation, fibrositis, bursitis, rheumatic disorders)</li></ul>



Chronic Spasticity



## Centrally Vs Peripherally Acting Skeletal Muscle Relaxants

	Centrally acting	Peripherally acting (NMB)
<b>MOA</b>	<ul style="list-style-type: none"> <li>Decrease muscle tone <b>without</b> reducing voluntary power</li> <li>Selectively inhibit <b>polysynaptic reflexes</b> in CNS.</li> </ul>	<ul style="list-style-type: none"> <li>Cause muscle paralysis, voluntary movements lost</li> <li>Block <b>neuromuscular transmission</b>.</li> </ul>
<b>Effect on CNS</b>	<ul style="list-style-type: none"> <li>Cause some CNS depression</li> </ul>	<ul style="list-style-type: none"> <li>No effect</li> </ul>
<b>Route:</b>	<ul style="list-style-type: none"> <li>Given <b>orally</b></li> <li>Sometimes parenterally</li> </ul>	<ul style="list-style-type: none"> <li>Practically always given <b>IV</b></li> </ul>
<b>Use:</b>	<ul style="list-style-type: none"> <li><b>Used in</b> spastic neurological conditions, anxiety, tetanus....</li> </ul>	<ul style="list-style-type: none"> <li><b>Used for</b> short term purposes (surgical operations)</li> </ul>

# Classification

