
بسم الله الرحمن الرحيم

Anticholinergic drugs;

Cholinergic antagonists,

Cholinergic blockers,

Cholinergic receptor blocking drugs,

By

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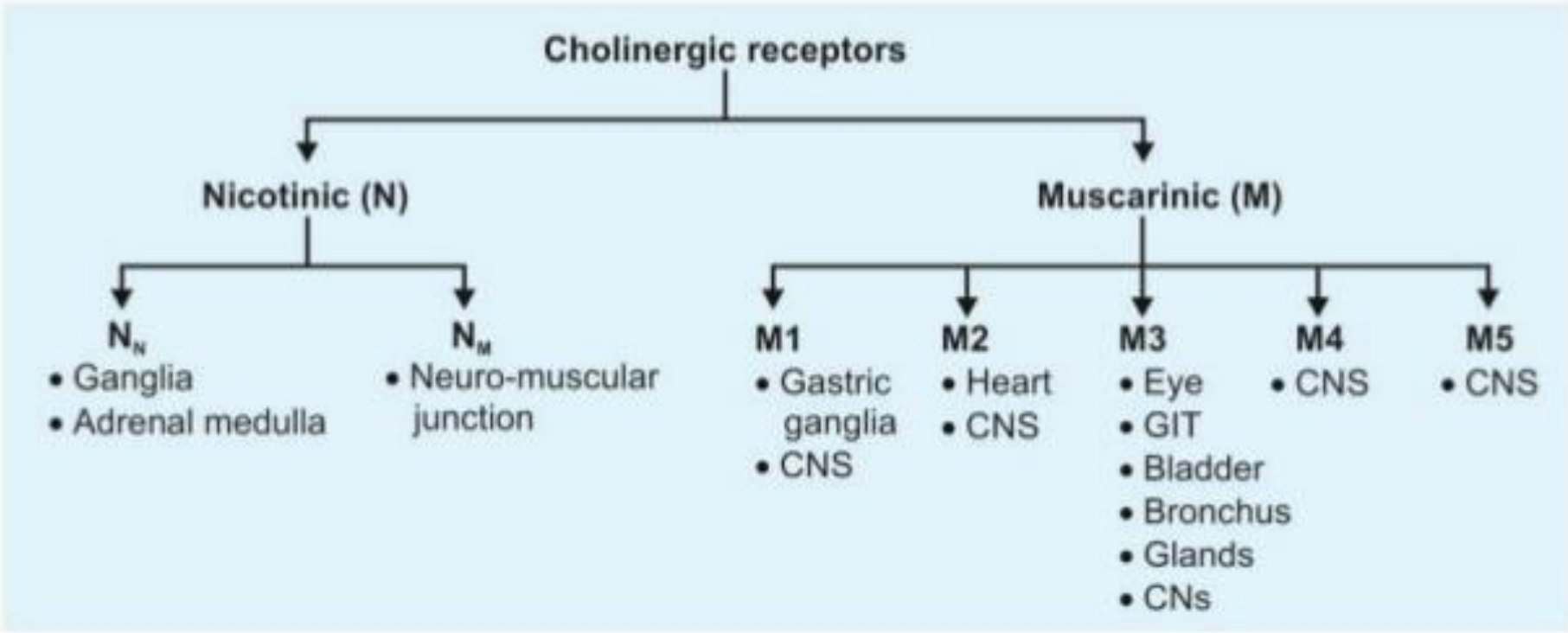
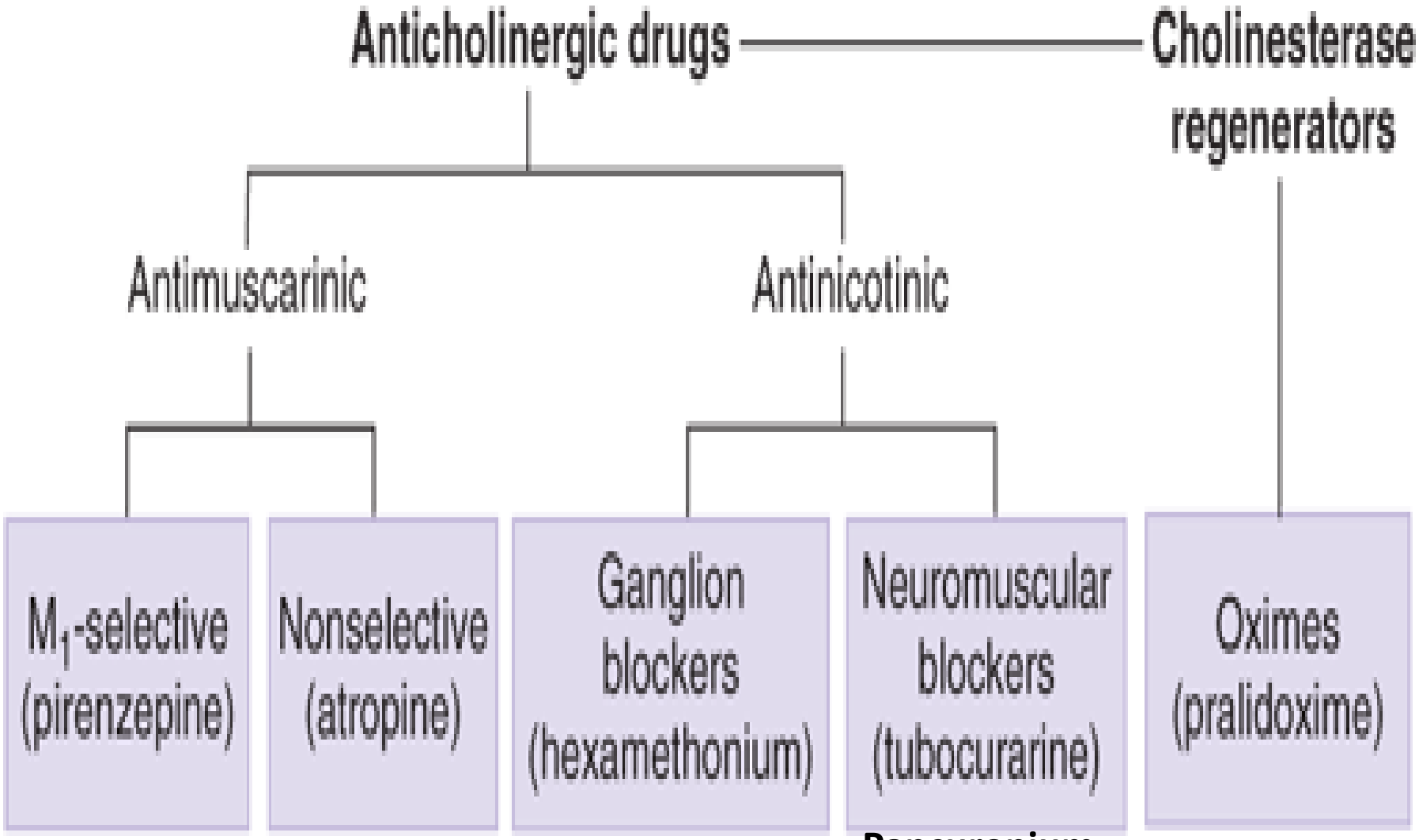
Classification of Cholinergic Receptors



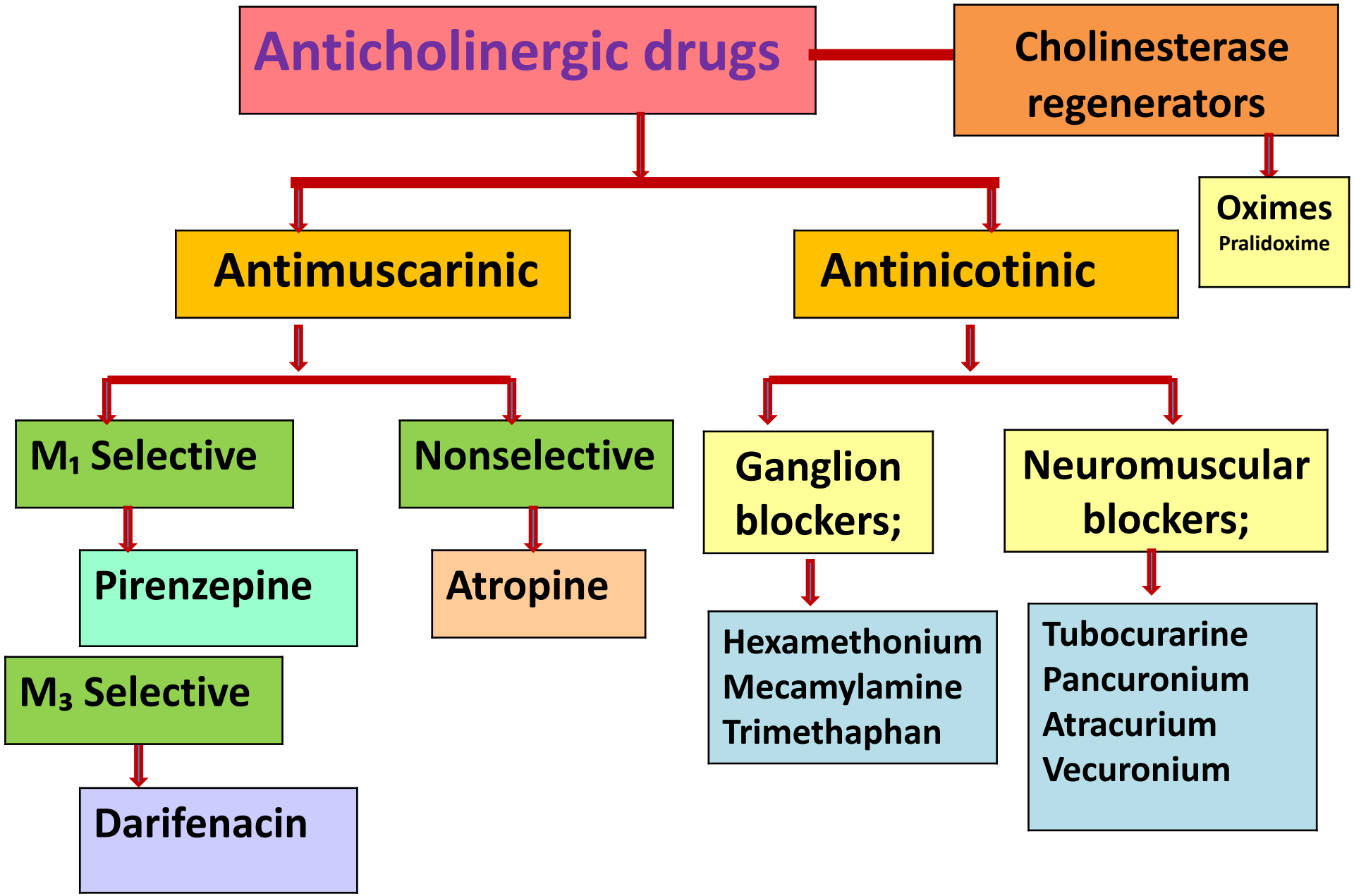


M1 -- Pirenzepine
M3 -- darifenacin

Mecamylamine
Trimethaphan

Pancuronium
Atracurium
Vecuronium

Diactylmonoxime


Anticholinergic drugs
Cholinesterase regenerators
Oximes
Pralidoxime
Antimuscarinic
Antinicotinic
M1 Selective
Nonselective
Ganglion blockers;
Neuromuscular blockers;
Pirenzepine
Atropine
Hexamethonium
Mecamylamine
Trimethaphan
Tubocurarine
Pancuronium
Atracurium
Vecuronium
M3 Selective
Darifenacin

Antimuscarinic drugs; (Parasympatholytics, Muscarinic receptor blocking drugs)

- **Naturally occurring alkaloids;**
  - **Atropine (Hyoscyamine).**
    - (*Atropa belladonna* & in *Datura stramonium*)
  - **Scopolamine (Hyoscine)**
    - (Hyoscyamus niger)
    - Levo-isomers are much more active (100 times) than the dextro-isomers.

➢ Semisynthetic or synthetic;

substitutes of belladonna alkaloids;

- **Tertiary amines;**
  - **Dicyclomine, Oxyphencyclamine, Oxybutynin.**
  - **Homatropine, Cyclopentolate, Tropicamide.**
- **Quaternary Amines;** (less lipid soluble)
  - **Ipratropium, Tiotropium, Glycopyrolate,**
  - **Isopropamine, Propantheline.**

➢ Other drugs with anti-muscarinic activity;

- **Antihistamines, TCA, Phenothiazines.**

Classify antimuscarinics according to their clinical uses;

- **Antispasmodics (Spasmolytics);**
  (Drugs used in GIT & genitourinary conditions)
  - **Tertiary Amines:**
    1). Atropine 2). Scopolamine 3). Dicyclomine
    4). Oxyphencyclamine 5). Oxybutynin
  - **Quaternary Amines:**
    1). Anisotropine 2). Clidinium 3). Glycopyrolate
    4). Isopropamine 5). Mepenzolate
    6). Methantheline 7). Propantheline.
- ***Anti-ulcer drugs*:**
  – Pirenzepine, Telenzepine, Dicyclomine.

➢ Anti-Parkinsonian;

1). Benzhexol
2). Benztropine
3). Bipridine
4). Procyclidine
5). Chlorphenoxamine
6). Tolterodine

➢ Mydriatics;

1). Atropine,
2). Homatropine
3). Cyclopentolate
4). Tropicamide
5). Eucatropine.

➢ Anti-asthmatic and to treat COPD;

– Ipratropium —Tiotropium.

➢ Pre-anesthetic agents;

– Atropine, — Glycopyrrolate.

➢ Drugs for Stress incontinence, irritable bladder;

– Oxybutynin, Tolterodine & Darifenacin.

Selectivity of Anti-Muscarinic drugs;

- **Non-Selective;**
  - **Atropine,**
  - **Hyoscine.**
  - highly selective for all muscarinic receptors.
- **M_1 – Antagonists:**

  1). Pirenzepine **2). Telenzepine**

  3). Dicyclomine.
- **M_2 – Antagonists;:**

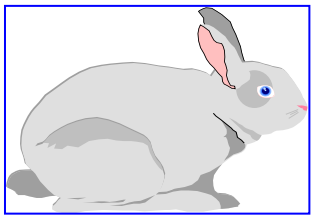
  1). Methoctramine **2). Gallamine(also at Nm)**
- **M_3 – Antagonists:**

  1). Darifenacin **2) Oxybutynin,**

  3). Tolterodine.

Pharmacokinetics;

- **Most are tertiary comp. & well *absorbed* from:**
  GIT & Conjunctiva or even Transdermal.
  So Atropine & Hyoscine are rapidly absorbed and widely *distributed* & significant levels to CNS are achieved within ½hr.
- ***Quaternary* comp. are less lipid soluble and are almost free of central effects.**
- **50%** of atropine is **metabolized in the liver** and **50% excreted unchanged** in urine.
- It has $\mathbf{t_{1/2}}$ **2–3 hrs**. All systemic effects rapidly decline but of eye persist for > 72 hrs.
- **Some rabbits** have a specific **atropine esterase** which degrades atropine very rapidly.



PHARMACODYNAMICS;

Mode of action;

- **Atropine** and other antimuscarinic drugs bind to **muscarinic receptors** and **competitively block** the **action of Acetylcholine** at these receptors.
- **Atropine** is a **inverse agonist** at the muscarinic receptors and binds them in the dynamic state.
- **Others** are **competitive muscarinic antagonists.**

PHARMACOLOGICAL EFFECTS;

CNS; (M_1, M_2, M_3, M_4, M_5 Receptors);

- **Atropine** has a ***stimulant action on the CNS*** *especially at high doses*.
- Atropine **stimulates medullary centers** – vagal, respiratory and vasomotor.
- **High doses** cause **cortical excitation**, restlessness, disorientation, hallucinations and delirium followed by respiratory depression and coma.
- By blocking the relative cholinergic over-activity in basal ganglia, it **suppresses tremors and rigidity in parkinsonism.**
- ***Hyoscine*** *produces* ***central depressant effects*** even at low doses. **Amnesic action**—block short term memory.

CVS; (M_2 Receptors);

- Atropine causes ***tachycardia*** due to blockade of M_2-receptors on SA node.
  - *The tachycardia is more **marked in young adults** than* in children and the elderly.
- Atropine ***shortens the refractory period of AV conduction***, especially if it has been depressed by high vagal tone.
- Atropine does **not influence BP.**
  - Normal dose has **no effect on blood vessels.**
- **Dilatation of cutaneous vessels** of the **face,** head, neck and trunk **----** **Atropine flush** **--- red as a beet** **---** diagnostic of overdose.

- **Atropine causes -- Transient initial bradycardia**, especially at low doses.
  - By **blocking Presynaptic M_1 receptors** (autoreceptors) on vagal postganglionic fibers that normally limit ACh release in the SA node and other tissues.
  - Transient **initial vagal stimulation (in CNS).**
  - **Clinical significance** – when used along with neostigmine for reversal **(Atropine + neostigmine** to antagonize curare like drugs) may cause bradycardia.
    - Atropine to be given a few minutes before neostigmine to avoid summation.


Thank You