PARASYMPATHOMIMETICS (DIRECTLY ACTING)

DR. ATTIYA MUNIR
AP PHARMACOLOGY

SOURCES:
BERTRAM G. KATZUNG BASIC & CLINICAL PHARMACOLOGY 15TH EDITION
GOODMAN AND GILMAN'S THE PHARMACOLOGICAL BASIS OF THERAPEUTICS 13TH EDITION.

MOTTO AND VISION

- To impart evidence based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine

LEARNING OBJECTIVES

- At the end of this session, students will be able to:

✓ Recall the organization and physiology of parasympathetic system

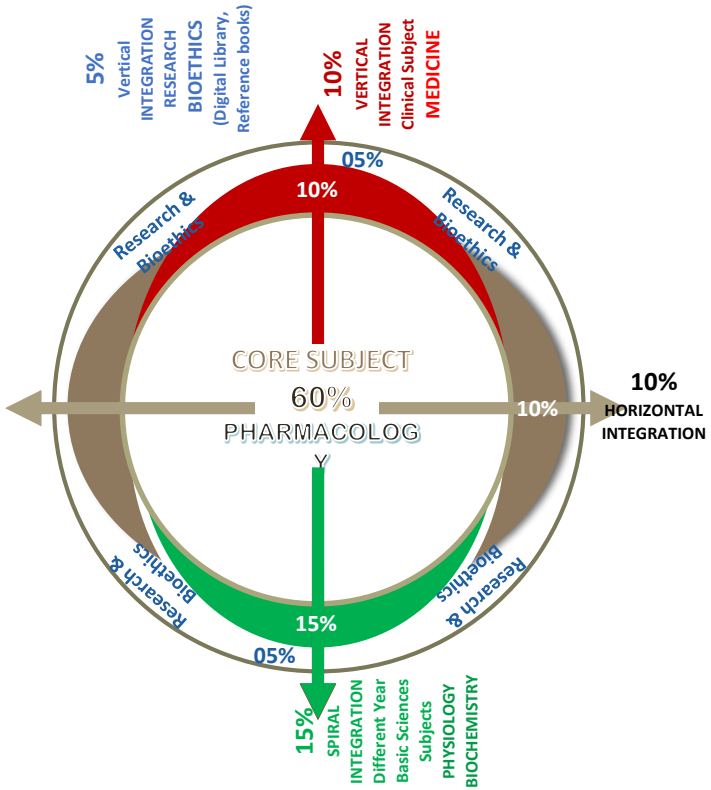
✓ Classify cholinomemitics

✓ Identify the location of cholinergic receptors and molecular mechanism of their activation

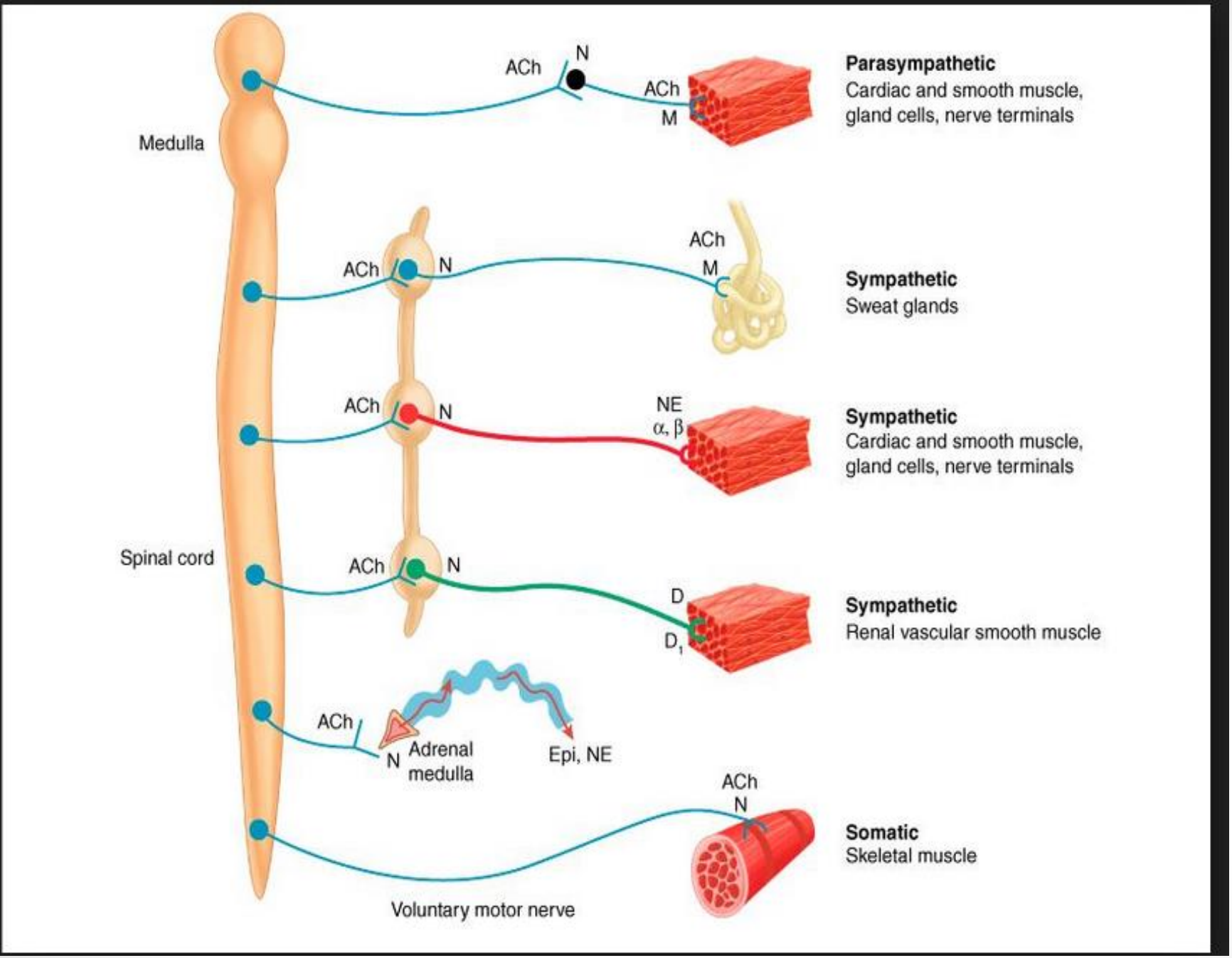
✓ Describe the pharmacological effects produced by activation of these receptors

✓ Describes uses and adverse effects of cholinomimetics

Prof. Umar's Clinically Oriented Integration Model
For Basic Sciences Interactive Lectures



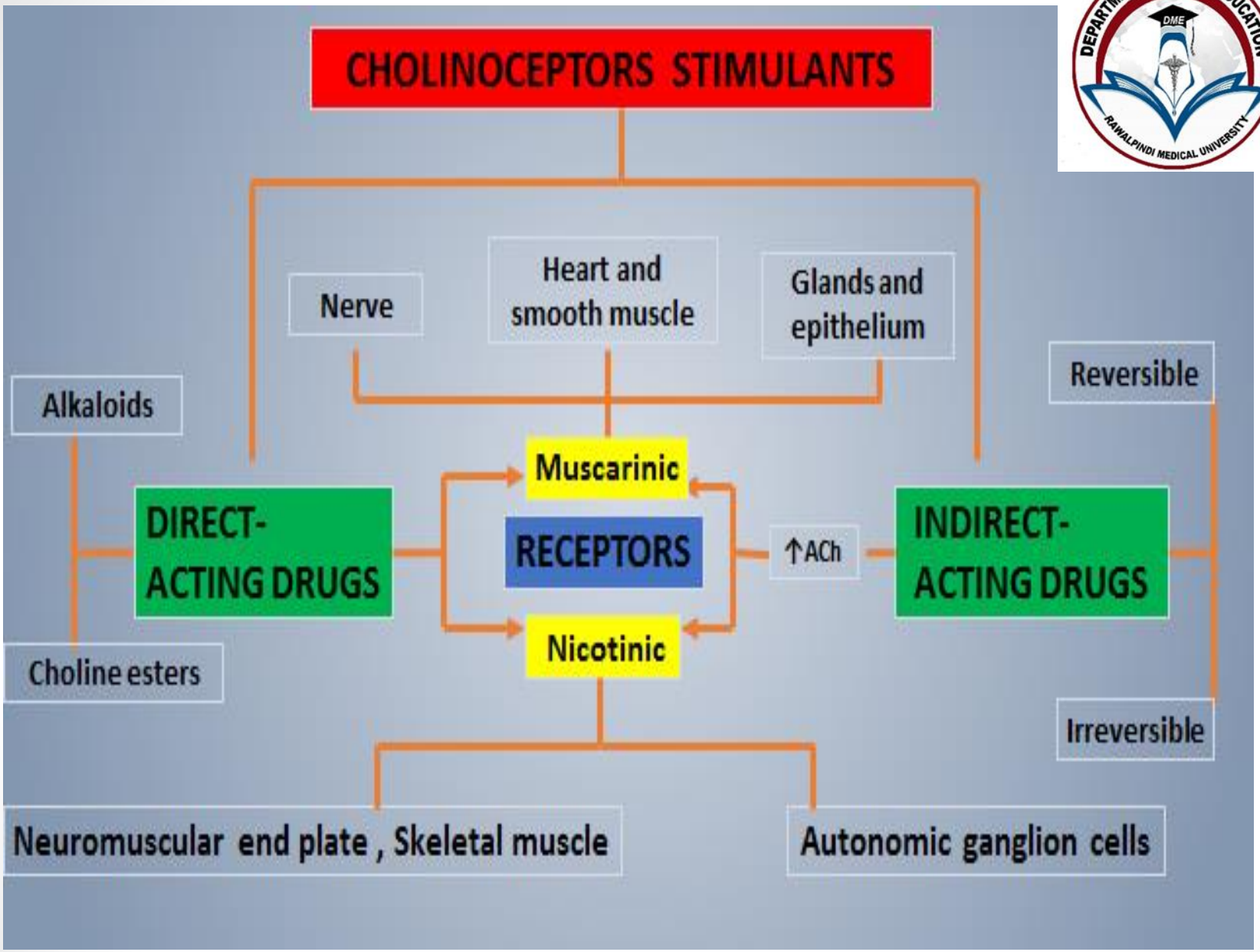
3rd Year Pharmacology LGIS	
Core Subject – 60%	
Pharmacology	
Horizontal Integration – 10%	
Same Year Subjects	• Pathology (10%)
Vertical Integration – 10%	
Clinical Subjects	• Medicine (10%)
Spiral Integration – 15%	
Different Year Basic Sciences Subjects	• Physiology (10%) • Biochemistry (5%)
Vertical Integration – 05%	
Research & Bioethics	



Spiral integration-Physiology

INTRODUCTION

- CHOLINERGICS/CHOLINOMIMETICS/PARASYMPATHOMIMETICS
- DRUGS THAT PRODUCE ACTIONS SIMILAR TO PARASYMPATHETIC NERVOUS SYSTEM
- DIRECTLY ACTING-ACTS DIRECT ON TO THE RECEPTORS


CHOLINOCEPTORS STIMULANTS
Nerve
Heart and smooth muscle
Glands and epithelium
Alkaloids
Reversible
Muscarinic
DIRECT-ACTING DRUGS
RECEPTORS
↑ACh
INDIRECT-ACTING DRUGS
Nicotinic
Choline esters
Irreversible
Neuromuscular end plate , Skeletal muscle
Autonomic ganglion cells

CLASSIFICATION
DIRECT ACTING CHOLINERGICS

CHOLINE ESTERS

- ACETYLCHOLINE
- BETHANECOL
- CARBACHOL
- METHACHOLINE

CHOLINOMIMETIC ALKALOIDS

- Mainly Muscarinic Agonists
- Mainly Nicotinic Agonists

MAINLY MUSCARINIC AGONISTS

- Natural Alkaloids
  - Muscarine
  - Pilocarpine
  - Arecholine
- Synthetic Alkaloids
  - Oxotremorine
  - Aceclidine
  - Cervimiline

MAINLY NICOTINIC AGONISTS

Natural Alkaloids

- Nicotine
- Lobeline

Synthetic Alkaloids

- Dimethylphenylpiperazinium(DMPP)

PHARMACOKINETICS

- Esters-Quaternary ammonium group
- Pilocarpine, Nicotine, Lobeline –Tertiary natural compounds ,well absorbed
- Muscarine, quarternary amine, toxic, present in some mushrooms
- Excretion –through kidneys and increased by?

PHARMACOKINETICS

Direct-acting, muscarinic agonists	
Bethanechol	Oral, IM activity Poor lipid solubility: does not enter CNS; not active in eye after topical application Duration: 0.3–2 h
Pilocarpine	Oral, IM activity Good lipid solubility, topical activity in eye
Muscarine	Low lipid solubility but readily absorbed from gut

Direct-acting, nicotinic agonists	
Nicotine	High lipid solubility, absorbed by all routes For smoking cessation: usually used as gum or transdermal patch Duration: 4–6 h
Varenicline	High lipid solubility, oral activity Duration: ~12 h
Succinylcholine	Highly polar, used IV Duration: 5–10 min

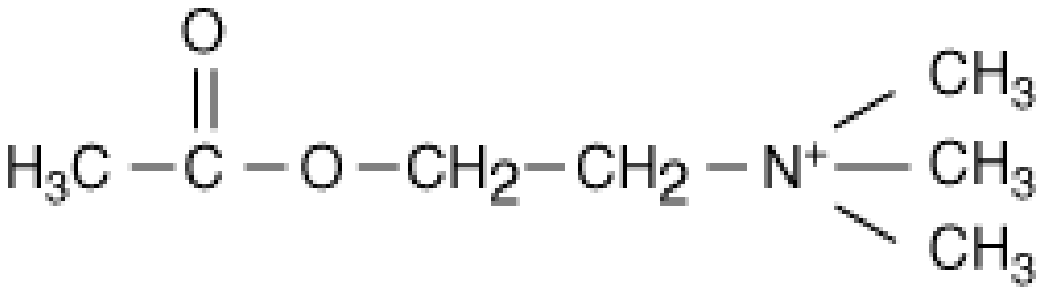
MAO

- Muscarinic receptors
- Auto receptors
- Nicotinic receptors

ACETYLCHOLINE

CHEMISTRY

An ester of acetic acid and choline



Acetylcholine

Core subject

Organ system effects

ORGAN	RECEPTOR	ACTIVITY
EYE		
Iris circular muscle	M_3	Contracts
Ciliary muscle	M_3	Contracts
HEART		
SA node	M_2	Decelerates
Contractility	M_2	Decelerates
Blood VESSELS	M_3, M_5	Relaxes

Organ system effects

ORGAN	RECEPTOR	ACTIVITY
Bronchiolar smooth muscle	M_3	Contracts
Gastrointestinal tract		
Walls	M_3	Contracts
Sphincters	M_3	Relaxes
Secretions	M_3	Increases
Genitourinary smooth muscles		
Bladder wall	M_3	Contracts
Sphincter	M_3	Relaxes
Uterus, Pregnant	M_3	Contracts

NICOTINIC ACTIONS OF ACETYLCHOLINE

- **NEUROMUSCULAR JUNCTION**: ACTIVATION OF NEUROMUSCULAR ENDPLATE
- DEPOLARIZATION OF MEMBREANE POTENTIAL
- CONTRACTION OF SKELETAL MUSCLES
- FLACCID PARALYSIS DUE TO PERSISTENT DEPOLARIZATION
-

- **AUTONOMIC GANGLIA**: STIMULATION FOLLOWED BY DEPRESSION

- THE EFFECTS ARE ACCORDING TO THE PREDOMINANT SYSTEM.

THERAPEUTIC USES OF DIRECTLY ACTING CHOLINERGICS

- EYES:
- SKIN
- GIT
- RESPIRATION

Vertical integration-

ADVERSE EFFECTS

- **EYES**:
- **CVS**:
- **RESPIRATORYSYSTEM**:
- **GENITOURINARY**

CONTRAINDICATIONS

- Bronchial asthma
- GI or urinary tract obstruction
- Peptic ulcer
- Recent myocardial infarction
- Coronary insufficiency
- Hyperthyroidism

ADVERSE EFFECTS OF NICOTINE

- **ACUTE EFFECTS**
- **CHRONIC EFFECT**

RESEARCH

- Patel, N.M. and Dewaswala, N., 2020. Parasympathomimetic medications.

- Padda IS, Derian A. Bethanechol. InStatPearls [Internet] 2022 Jul 19. StatPearls Publishing.

The principle of beneficence is the obligation of physician to act for the **benefit of the patient** and supports a number of moral rules to protect and defend the right of others, prevent harm, remove conditions that will cause harm, help persons with disabilities, and rescue persons.

It is worth emphasizing that, the language here is one of positive requirements. The principle calls for not just avoiding harm, but also to benefit patients and to promote their welfare.

EOLA

- Which of the following is the primary 2nd messenger process in the contraction of the ciliary muscles of the eye when focusing on near objects?

a. cAMP
b. cGMP
c. DAG AND IP3
d. NO
e. Na influx

- Important role in cognitive function especially memory involves agonist activity at which of the following receptors?

a. M1
b. M2
c. M3
d. M4
e. M5

- Which of the following smooth muscles is relaxed by cholinomimetics

a. Bronchial smooth muscles
b. Ciliary muscles of the eye
c. Detrusor
d. GIT
e. Trigone