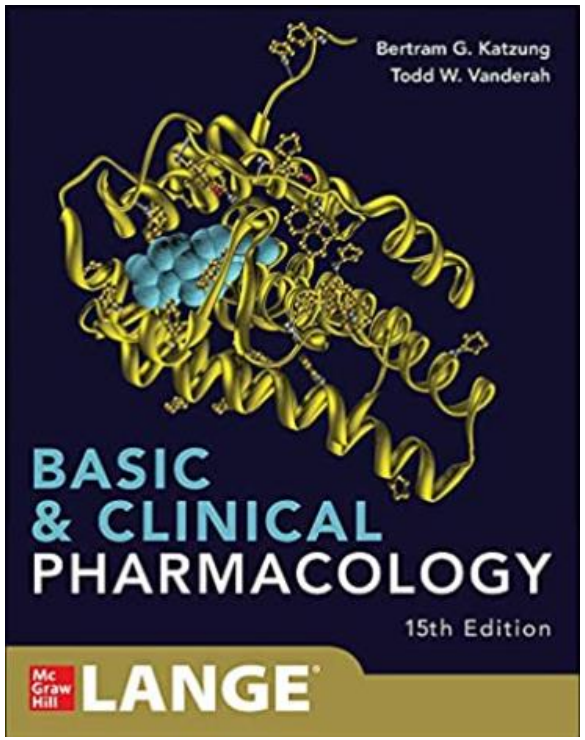
اصول فارماکولوژی
(داروشناسی)

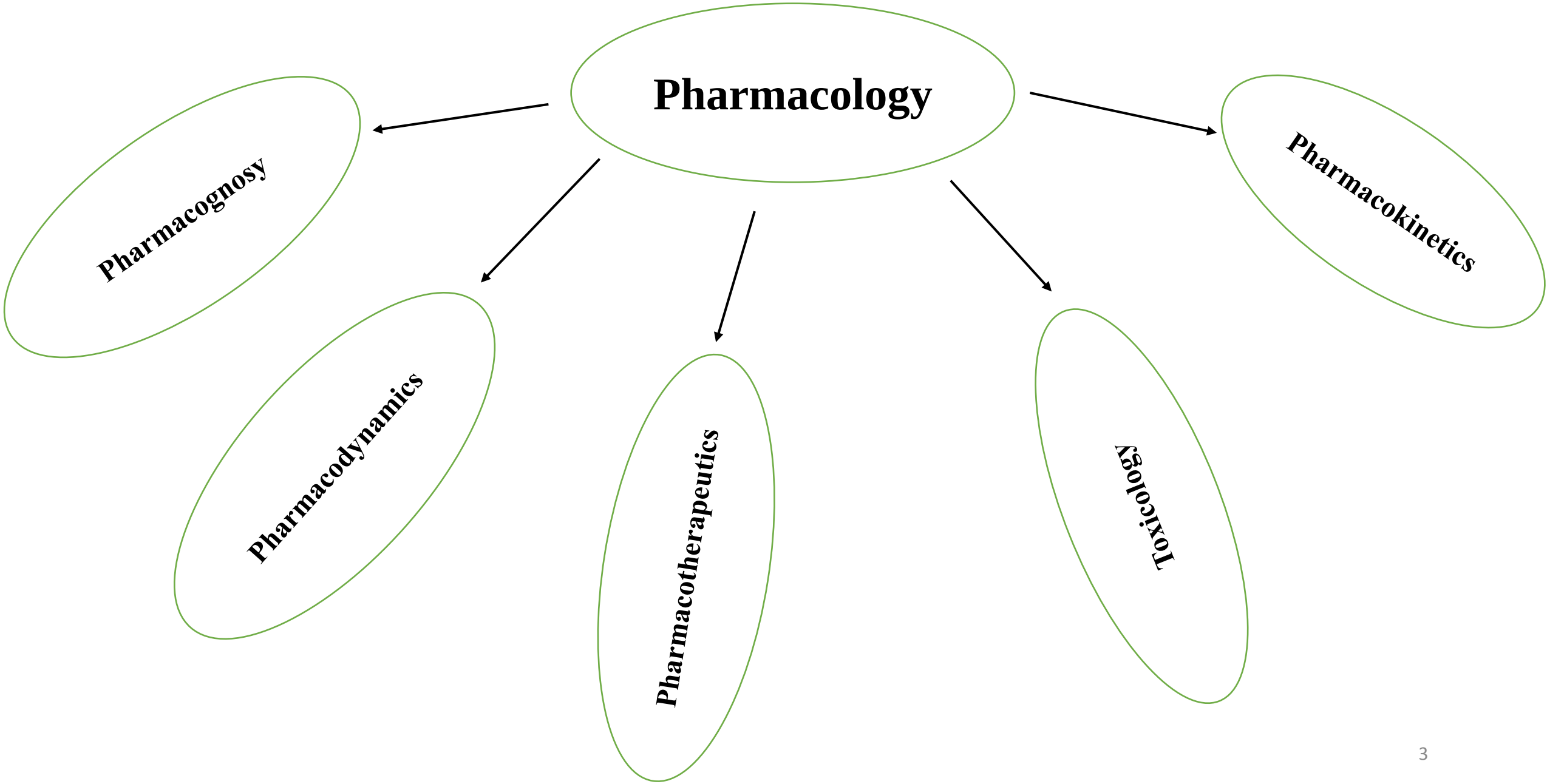


رشته پرستاری

Pharmacology

- Pharmacology (from *pharmakon,* the Greek word for drug) is the study of drugs (substances that produce changes in the body) and the characterization of their:
  - Structure, targets, and mechanisms of action
  - Distribution in and handling by the body
  - Effects on the body, including desirable responses (**efficacy**) and undesirable side-effects (***toxicity***)
  - Drugs include caffeine, nicotine, alcohol in addition to chemicals that are abused (e.g., cannabis, heroin, etc.), food constituents (vitamins, minerals, amino acids, etc.) and cosmetics.

- Pharmacology can be studied at multiple "levels": molecular, (sub)cellular, tissue, whole animal, or population
  - ***Clinical pharmacology*** is the study of drugs in human patients
  - ***Toxicology*** is the study of harmful rather than therapeutic effects
  - ***Pharmacy*** involves manufacture, preparation, and dispensing of drugs


Pharmacology
Pharmacognosy
Pharmacodynamics
Pharmacotherapeutics
Toxicology
Pharmacokinetics

What is drug?

A drug is any chemical substance that causes a change in an organism's physiology or psychology when consumed.

The origin of the drug
- Natural
  - Plant
  - Animal
  - Mineral
- Synthetic

Root of administration:
- Edible (pills and syrup)
- Rubbing (ointment and drops)
- Inhalation (inhalation)
- Injection (ampoule) or suppository

General definitions

- Drug dose
- Dose amount
- Consumption time
- Daily dose
- Root of administration
- The right dose: patient's age, height, weight, gender, liver and kidney function
- Drug interactions: Grapefruit

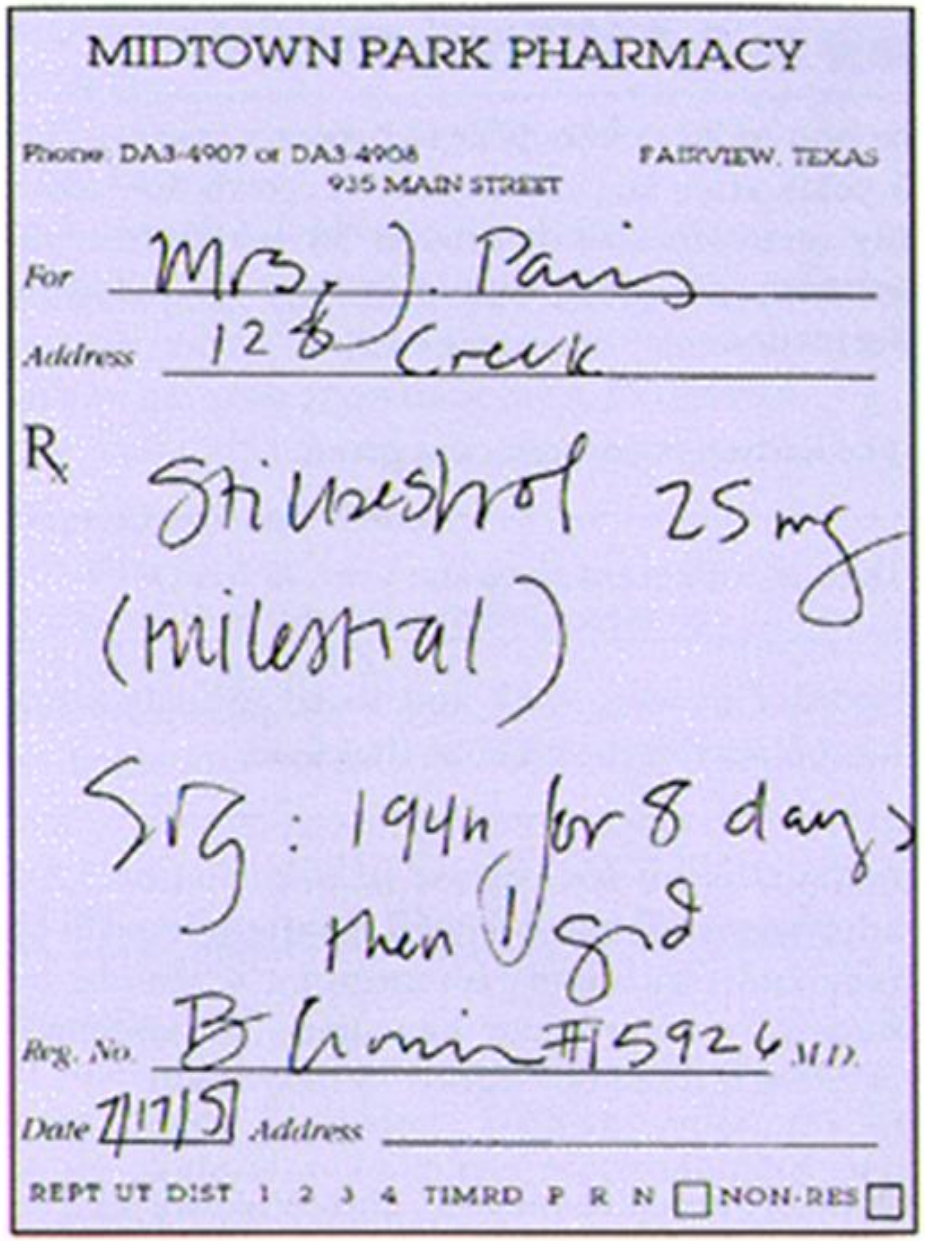
Terminology for Patients

- Drug (medication)
- Pharmacological agent
- Produces biological effect

- Non-Prescription (Over-the-Counter or OTC)
  - Safe if instructions followed
  - No prescription necessary

Terminology (con't)

- Prescription Drug
- Safe under supervision
- Prescribed by licensed practitioner


MIDTOWN PARK PHARMACY

Phone DA3-4907 or DA3-4908 FAIRVIEW, TEXAS
935 MAIN STREET

For Mrs. J. Paris

Address 128 Creek

℞ Stilnoctol 25 mg
(milestral)

Sig: 1 qhs for 8 days
then 1 qod

Reg. No. B Lamin #15926 M.D.

Date 7/17/15 Address

REPT UT DIST 1 2 3 4 TIMRD P R N ☐ NON-RES ☐

Terminology (con't)

- Non-Prescription (Over-the-Counter or OTC)
  - Safe if instructions followed
  - No prescription necessary

Terminology (con't)

- Recreational Drug
  - Use for pleasant psychological/physical effects
  - No therapeutic intent

Principles of drug administration

- The five rights:

- Right Drug
- Right Dose
- Right Time
- Right Route
- Right Patient

Drug Names/Classifications

- Drugs have many names: chemical, generic (scientific, officially approved), and commercial (trade, brand)
  - Brand names differ in different countries and with different products
  - Scientists (and physicians) should use generic and not trade names

- Generic names are those in national pharmacopeias
  - Pharmacopeias originally were books for medical materials (*materia medica*) with information about sources, extraction methods, assays but now usually contain info about pure drugs

- Increased harmonization in choosing generic names and in using common endings for certain drug classes
  - -olol for β-blockers, -caine for local anesthetics, -clovir for antiviral (herpes) drugs, -prils for ACE inhibitors, etc

Drug Nomenclature (Names)

- Chemical Name
  - Atomic/molecular structure
- Generic Name (OFFICIAL)
  - Derived from chemical name
  - Listed in US Pharmacopedia & Formulary
- Trade Name (Brand)
  - Selected by Manufacturer
  - Copyrighted

Chemical Name	*Generic Name*	*Trade Name*
7-chloro-1,3-dihydro-1-methyl-5 phenyl 2H-1, 4-benzodiazepin 2-one	*Diazepam*	*Valium®*
Ethyl 1-methyl 4-pheyli-sonipecotate hydrochloride	*Meperidine*	*Demerol®*
acetylsalicyclic	*Aspirin*	*Ecotrin®*

Drug Classifications

- Pharmacologic Classification
  - Similar Characteristics
  - Similar Chemical Make up
  - examples: Penicillins, Beta Blockers
- Therapeutic Classification
  - Used for similar effect
  - May not have similar chemical make up
  - Examples: Antihypertensives, Antibiotics

New Drug Development

- FDA monitors process
- Animal Trials
- Human Trials
  - first healthy clients
  - next small clients with the disease
  - next large of clients with disease
  - on going reporting of side effect

Resources for Drug Information

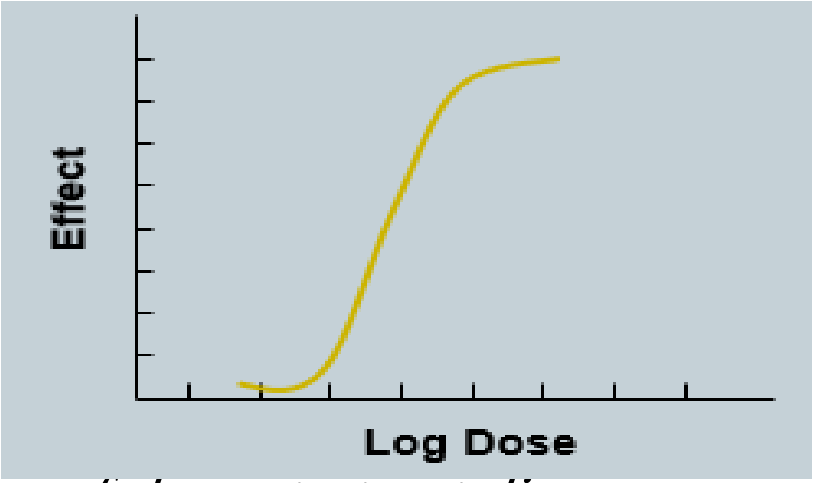
- Pharmacopeia
  - Official resource: US Pharmacopeia (USP), British Pharmacopeia (BP)
- Compendia
  - Non Official
  - American Formulary, Facts & Comparisons, USP Dispensing
- Pharmaceutical Firms
  - Physician's Desk Reference (PDR)
  - PDR for OTC

Drug Standards

- Purity -uncontaminated
- Bioavailability -absorbed and transported to target site
- Potency - strength, power, measurable effect
- Efficacy - effectiveness, measurement difficult
- Safety & Toxicity - adverse effects

Important “pharmaco” terminology

- Pharmacodynamics: *(“drug action”)* includes the measurement of responses to drugs and how such responses relate to *drug dose and concentration at a target site*



- Pharmacotherapy: *the use of drugs to treat disease*
  - *Requires knowledge of drugs, physiology, and pathology*

Important “pharmaco” terminology

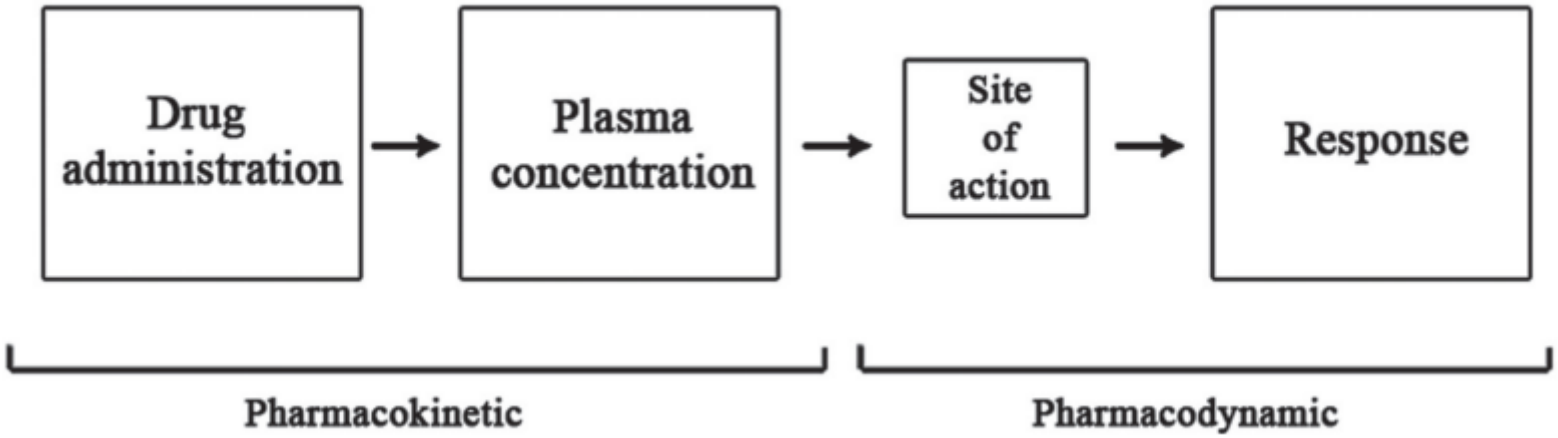
- Pharmacoepidemiology: investigates the effects of drugs on populations

- Pharmacoeconomics: examines the cost-effectiveness of drug treatments

- Pharmacogenetics and pharmacogenomics: study the influence of genetic variation on pharmacodynamic and pharmacokinetic properties of drugs

The Two Key Aspects of Pharmacology

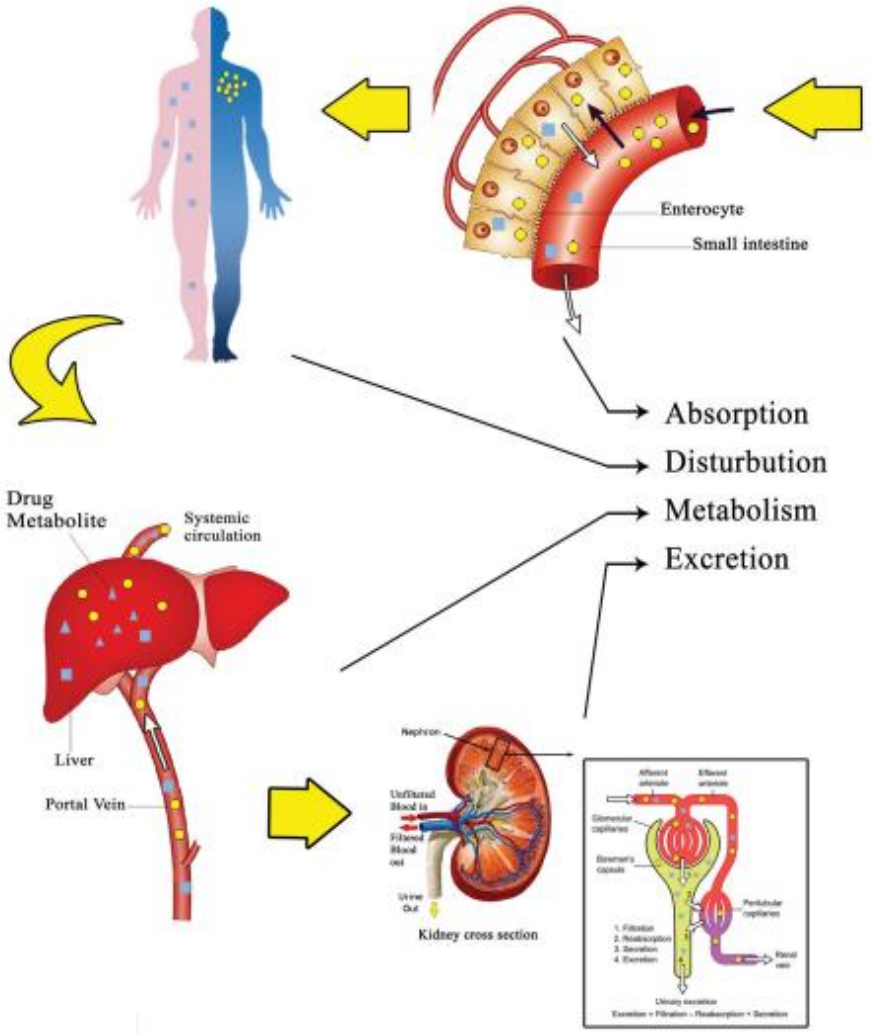
- Pharmacokinetics (PK)
- Pharmacodynamics (PD)



Pharmacokinetic–pharmacodynamic relationship

Pharmacokinetics (ADME)

- Absorption: drug gets into bloodstream
- Distribution: drug gets tissues
- Metabolism: is “changed” so that it can be excreted
- Excretion: irreversible loss of drug from the body



Pharmacokinetics (ADME) (con't)

- Dose
- Dosing interval
- Clearance
- Bioavailability
- C_{max}
- T_{max}
- Volume of distribution (V_d)
- Absorption half-life (t ½)
- First pass effect

Absorption Depends on:

Route of administration

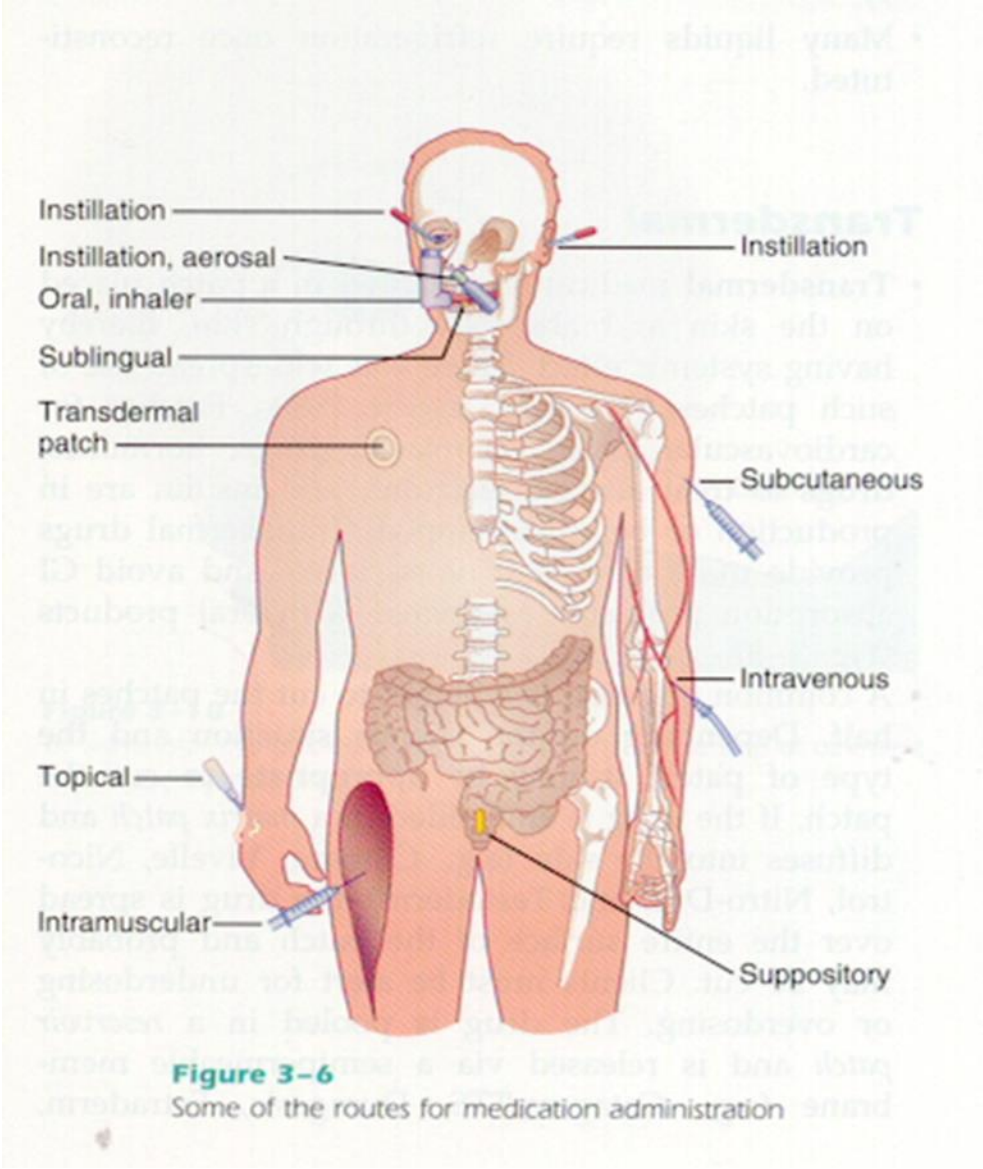


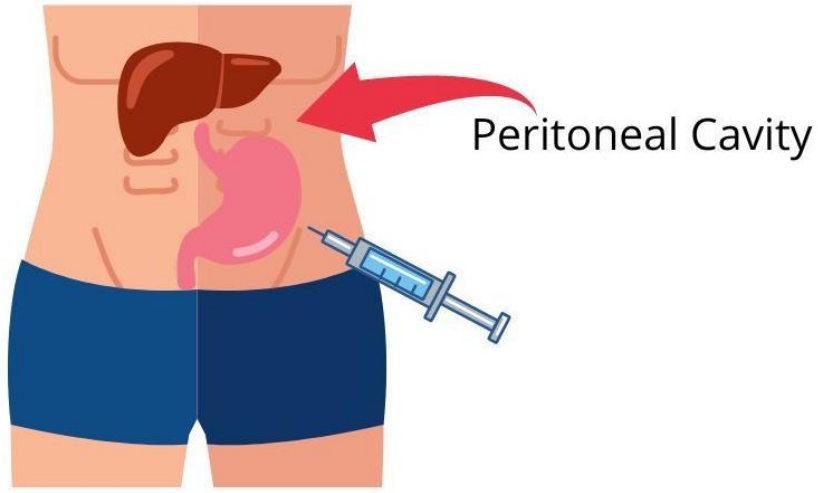
Figure 3–6
Some of the routes for medication administration

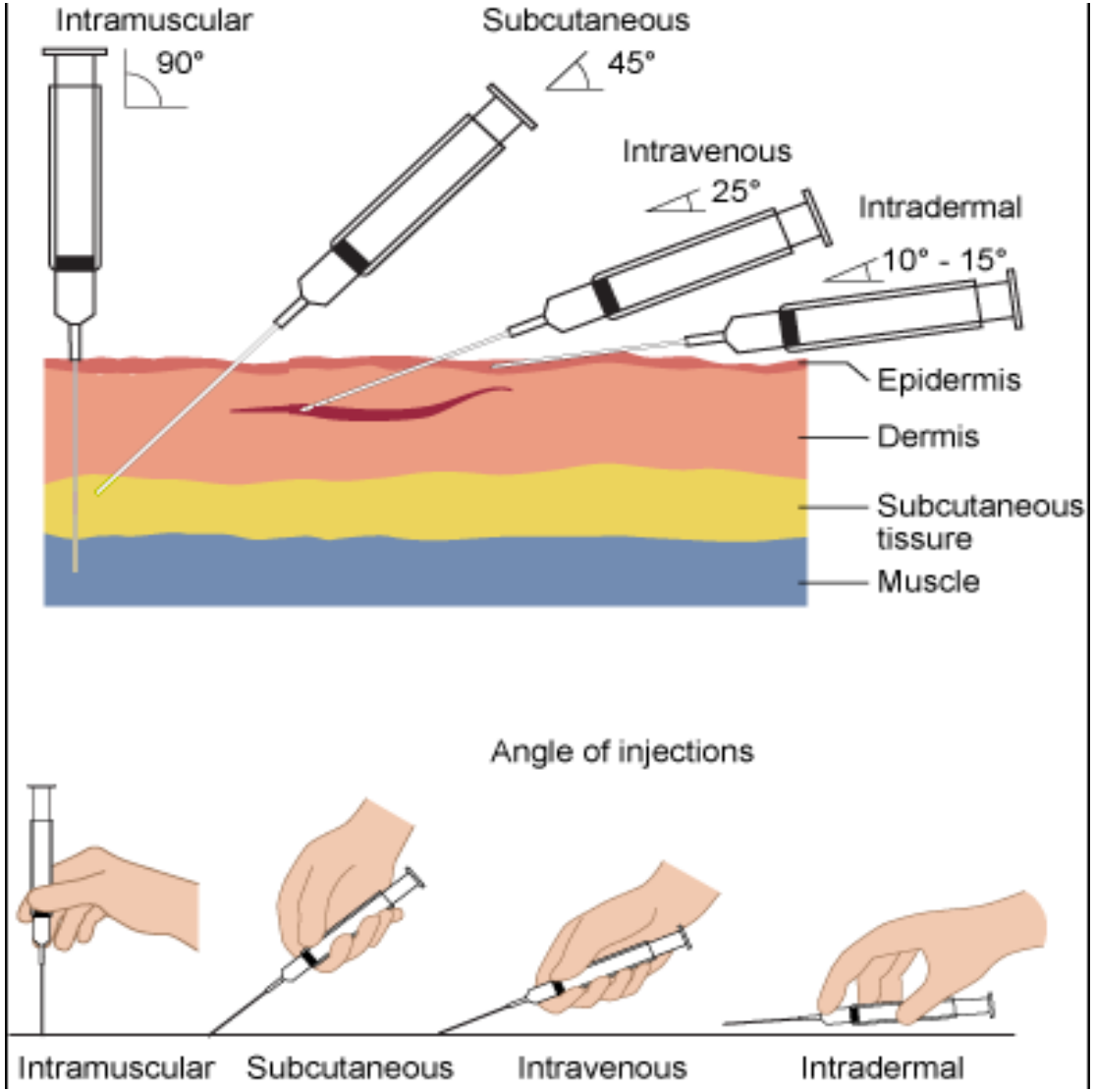
Route of administration

- Oral →
  - Pills
  - Syrups/Suspensions
  - Compressed tablet
  - Sustained Release Oral
  - Sublingual / Buccal →
    - Rapid absorption and response
    - Highly vascular areas
    - Avoids “First Liver Bypass”

Route of administration (con't)

- Intramuscular (IM)
- Subcutaneous (SC)
- Intravenous (IV)
- Intradermal (ID)
- Intraperitoneal (IP)





Route of administration (con't)

- Inhalation:

- Nebulizer-administrated medication (1 to 5 μm)
- Aerosolized medication (MDI)
- Dry-powder inhalers (DPI)
- Vaporizer-administered medication
  - **Hot**
  - **Cold**

Route of administration (con’t)

- Ophthalmic

- Eye drop
- Lothion
- Ointment
- Emultion

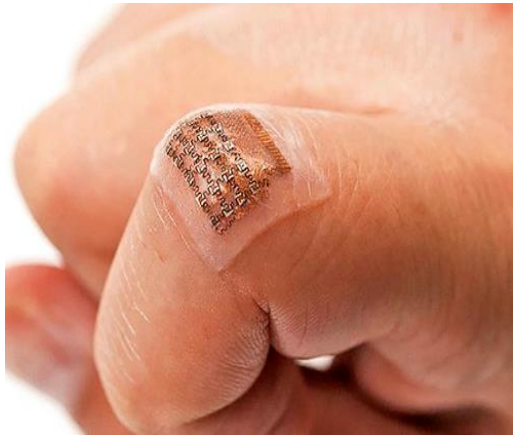
Route of administration (con’t)

- **Transdermal**

Patch:

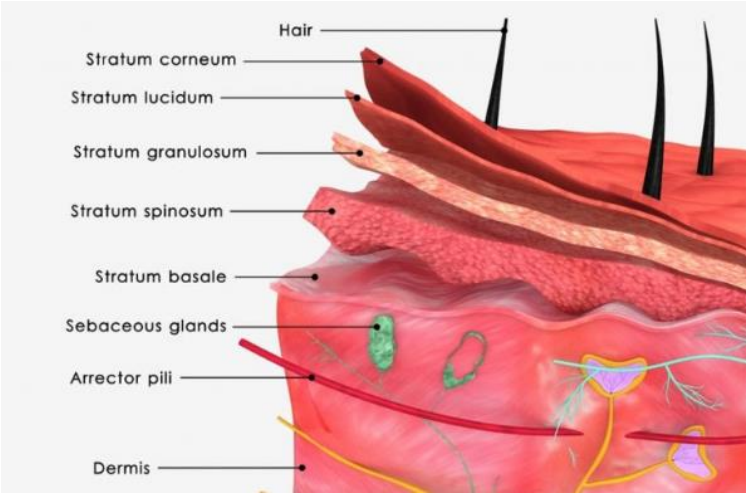
✓ Reservoir

✓ Matrix



- Quit Smoking
- Reducing pain
- Controlling nausea
- Treating hormonal disorders
- Contraception in women

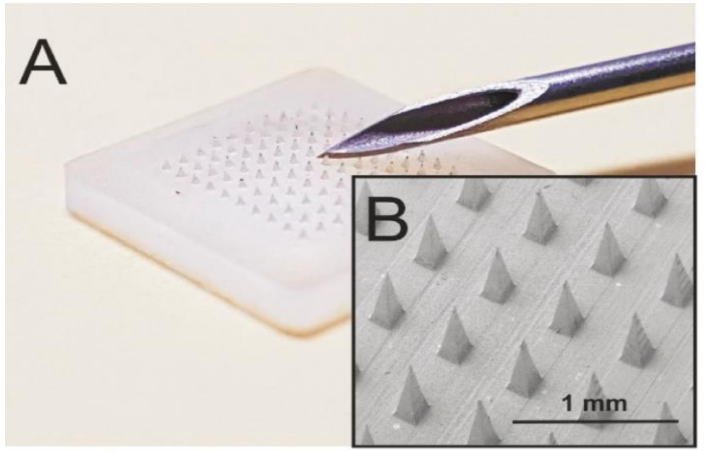
- Stratum corneum



Route of administration (con’t)

- **Transdermal**
- Transcellular pathway
- Intercellular pathway
- Microneedles

- Devices and formulations for transdermally administered substances include:
- Transdermal patch
- Transdermal gel
- Specially formula



Scopolamine ⟶ Motion sickness
Nitroglycerin ⟶ Angina
Rivastigmine ⟶ Alzheimer's

Route of administration (con't)

- **Rectal/vaginal**

- **Advantages**
  - Nausea, NPO, difficulty swallowing
  - Avoids first liver bypass (FPE)

- **Disadvantages**
  - Maybe erratic absorption
  - May cause irritation

Route of administration (con't)

- Topical

- Applied directly to a part of the body

Pharmacodynamic (PD)

- Pharmacodynamics is the study of a drug's molecular, biochemical, and physiologic effects or actions.
- Pharmacodynamics is the study of how a drug affects an organism.
- The effect of drug on the body.

Pharmacodynamic (con’t)

- There are four principle protein targets with which drugs can interact:

1. **Enzymes**:

- Inhibitors
- Inducers
- Activators
- (e.g. neostigmine and acetyl cholinesterase)

Pharmacodynamic (con’t)

2 . Membrane carriers:

- Enhancer (RE)
- Inhibitor (RI)
- Releaser (RA)

Pharmacodynamic (con’t)

3 . Ion channels:

- Blocker
- Opener

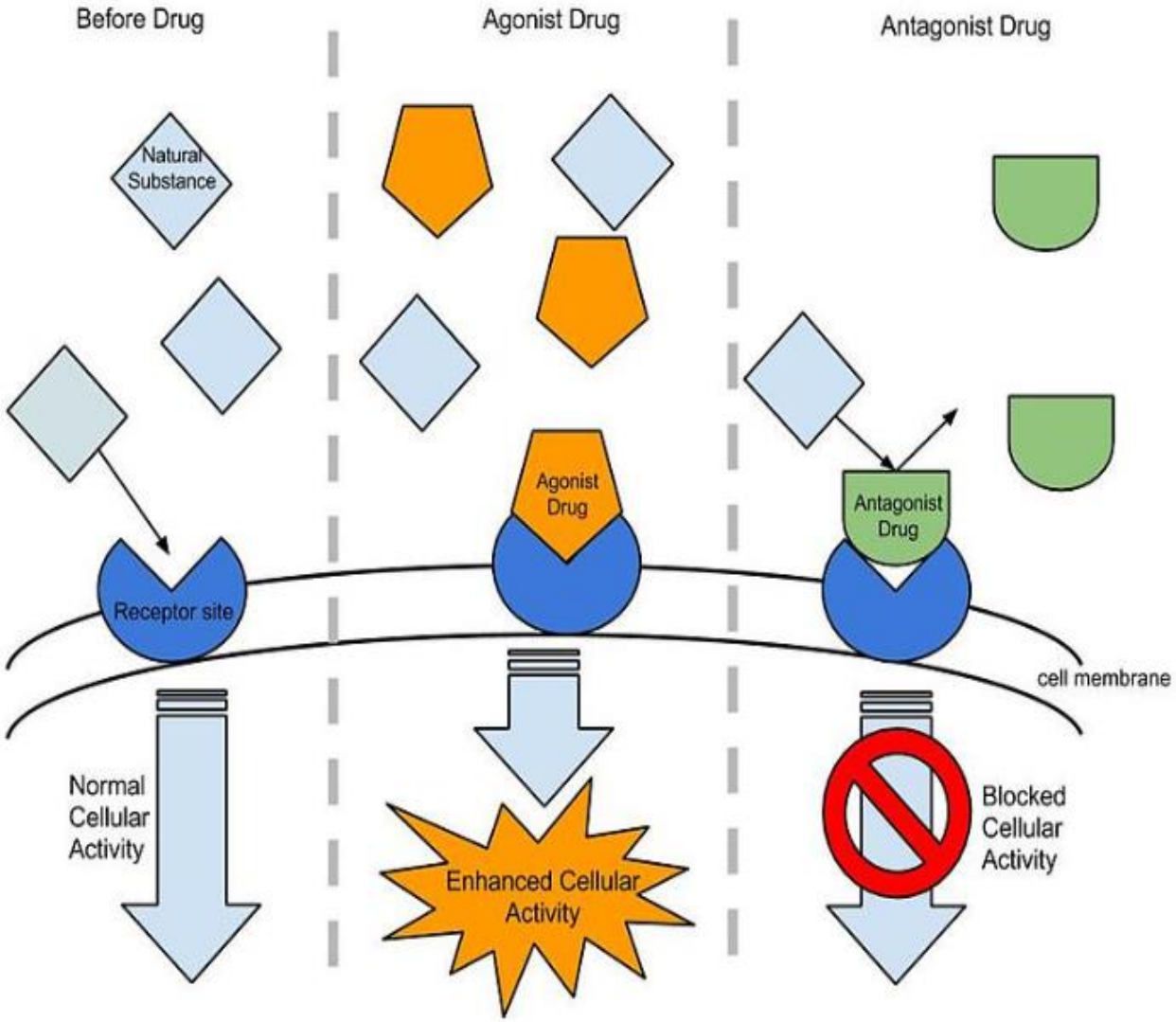
- (e.g. nimodipine and voltage-gated Ca^{2+} channels)

Pharmacodynamic (con’t)

4 . Receptor:

1. Agonists:

- ✓ Full ⟶ Isoprotereno , Morphine
- ✓ Partial ⟶ Buspirone, Aripiprazole
  Buprenorphine, Norclozapine
- ✓ Inverse ⟶ Cannabinoid

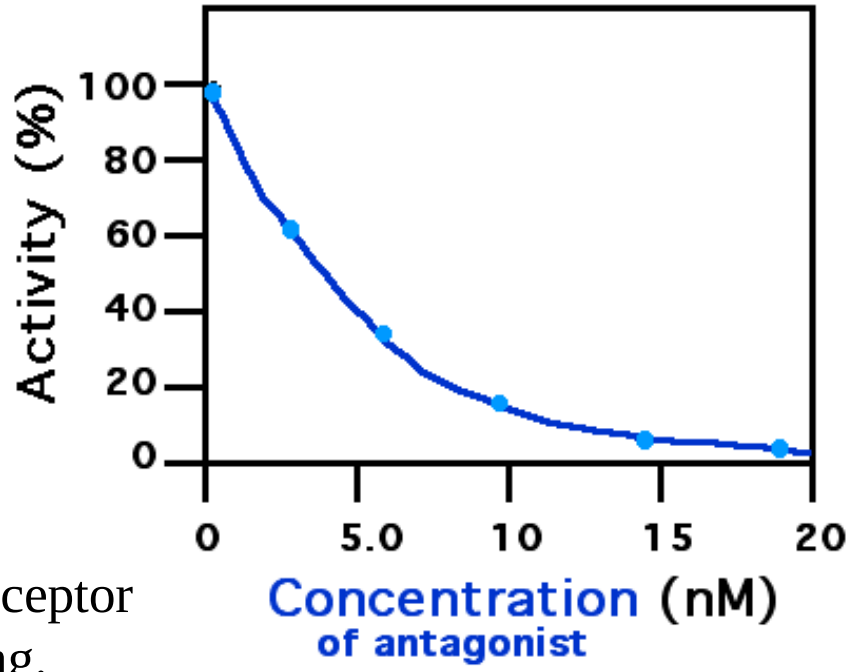


Pharmacodynamic (con't)

4 . **Receptor:**

2 . Antagonists: (blockers)

- **Alpha blockers**
- **Beta blockers**
- **Calcium channel blockers**



✓ Competitive

✓ Non-competitive

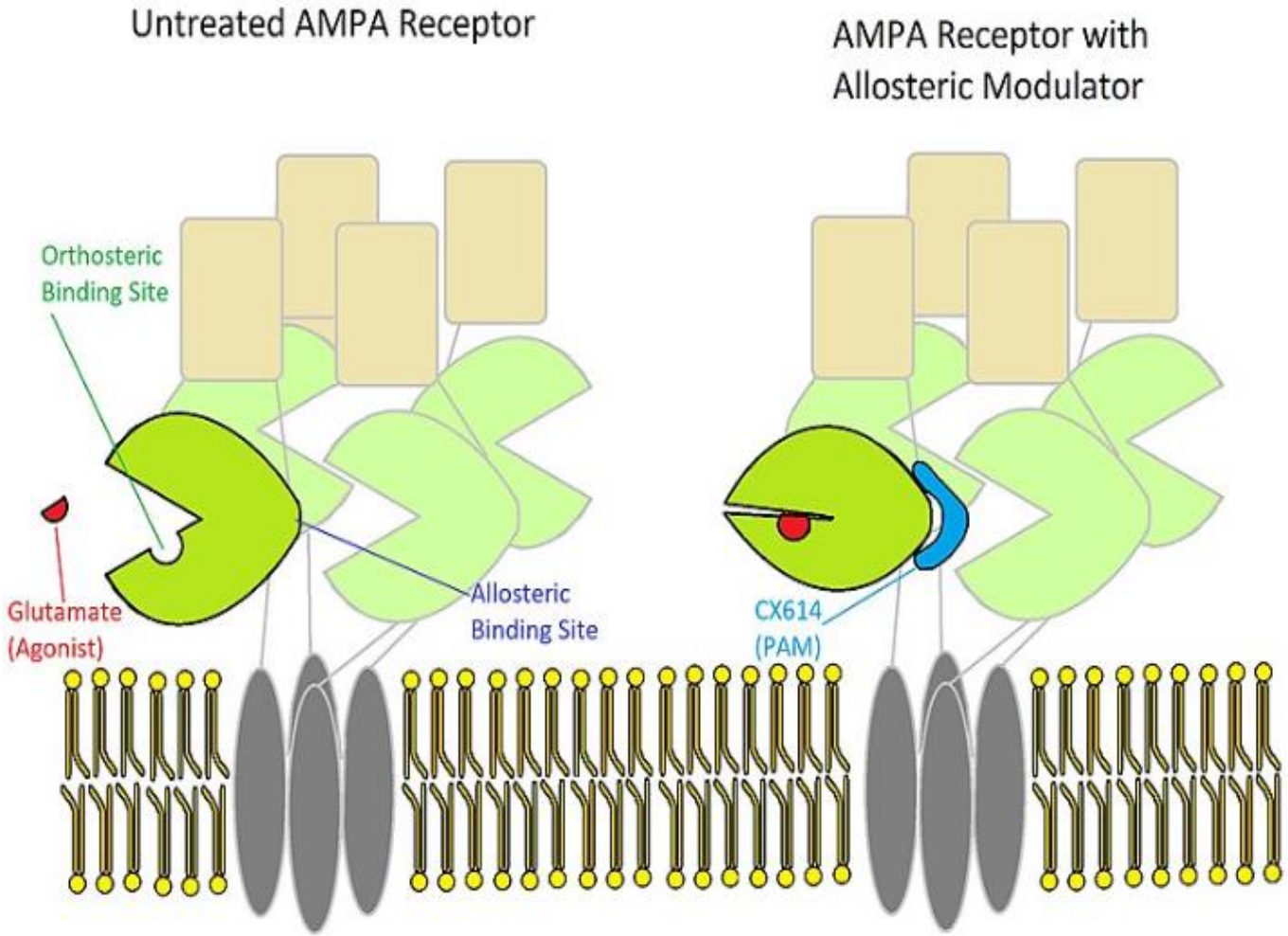
Note: Antagonists will block the binding of an agonist at a receptor molecule, inhibiting the signal produced by a receptor–agonist coupling.

Pharmacodynamic (con’t)

4 . Receptor:

3 . Allosteric modulator:

- ✓Positive allosteric modulators (PAM)
- ✓Negative allosteric modulators (NAM)
- ✓Neutral allosteric modulators



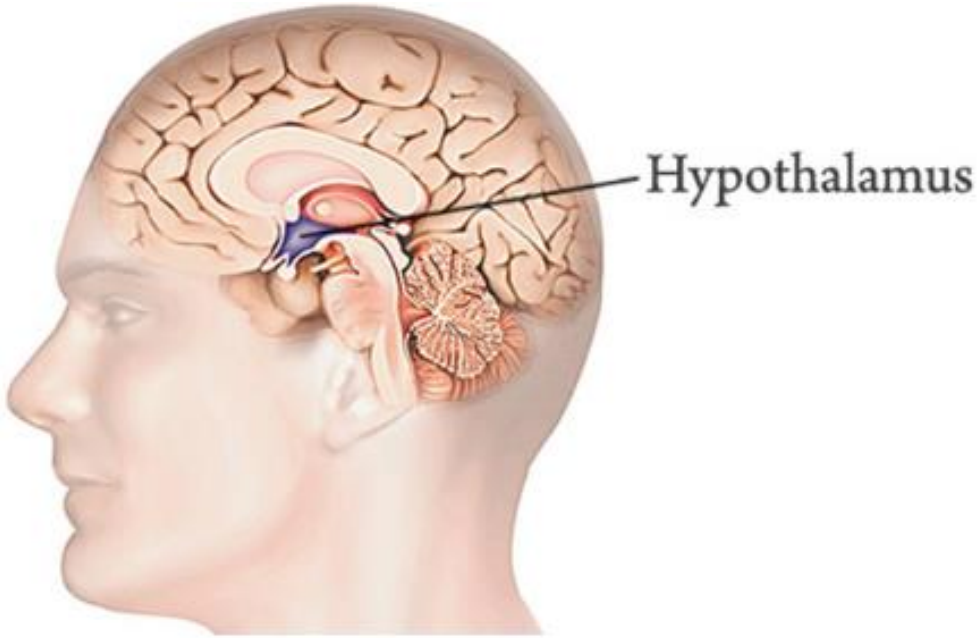
CX614, a PAM for an AMPA receptor binding to an allosteric site and stabilizing the closed conformation

Nervous system

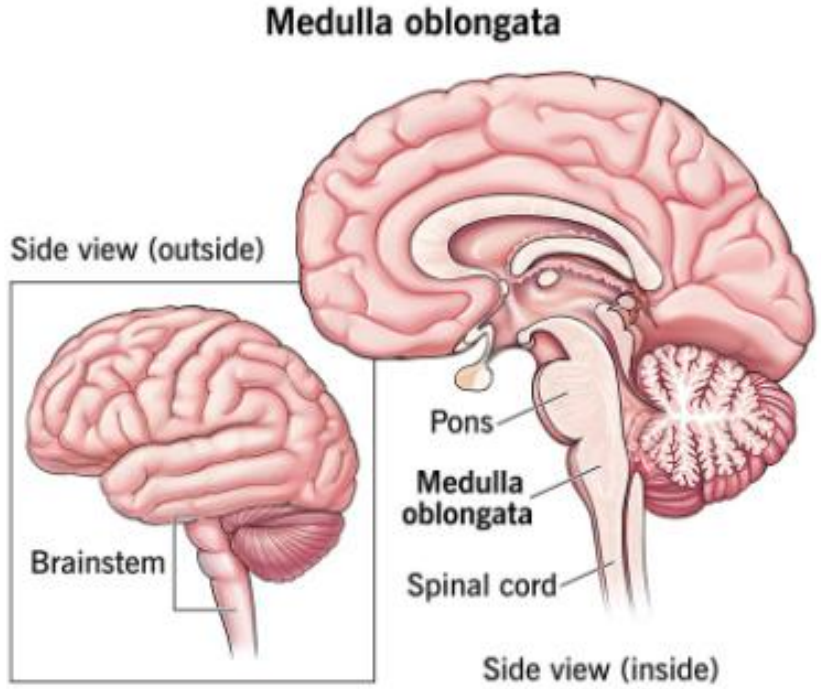
- Peripheral nervous system (PNS)
  - Somatic Nervous system
  - Autonomic Nervous System
    - Parasympathetic
    - Sympathetic
- Central nervous system (CNS)
  - Brain
  - Spinal cord

Nervous system (con't)

Hypothalamus



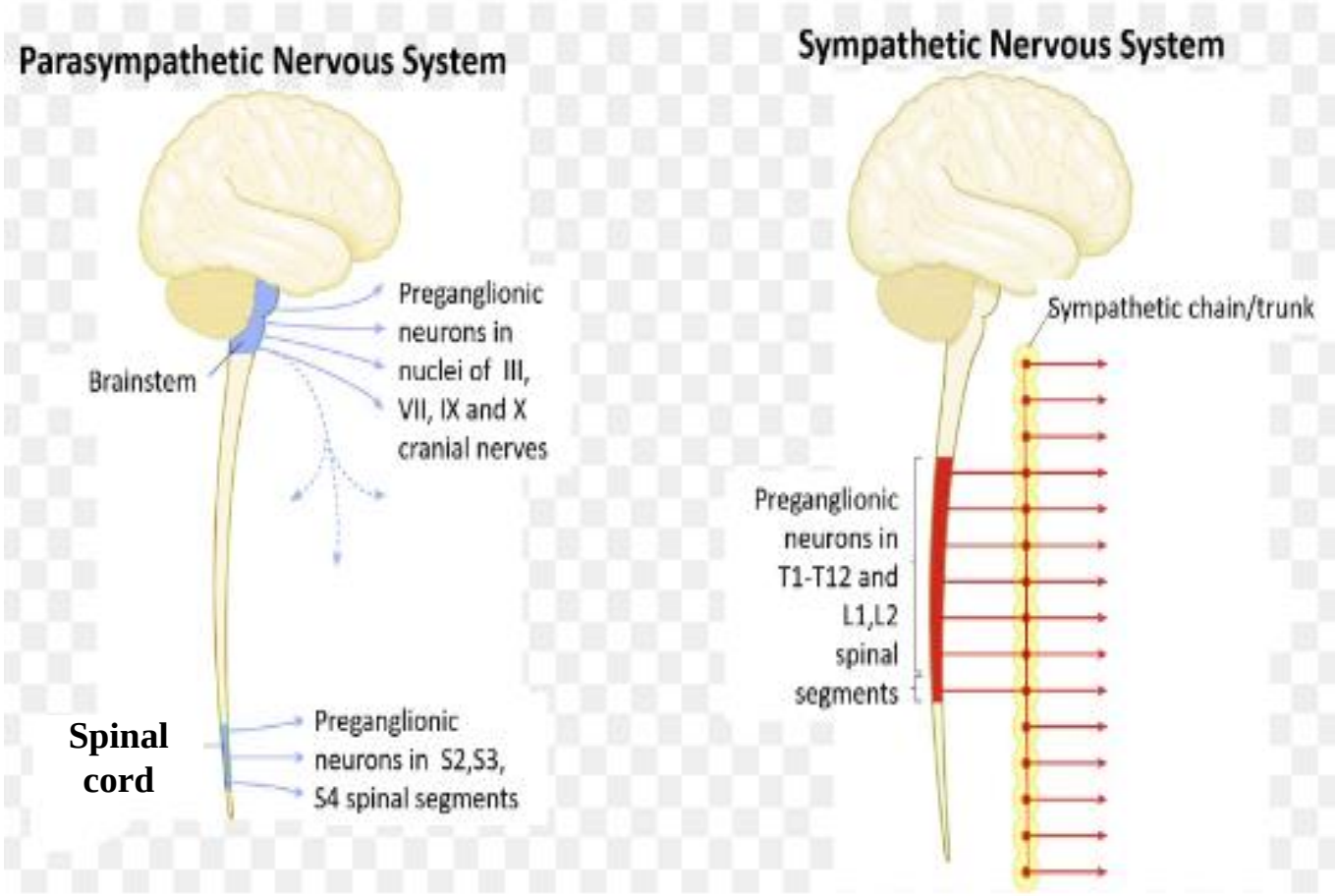
Medulla oblongata



Nervous system (con’t)

Autonomic Nervous System

- Sympathetic
- Parasympathetic (cholinergic)

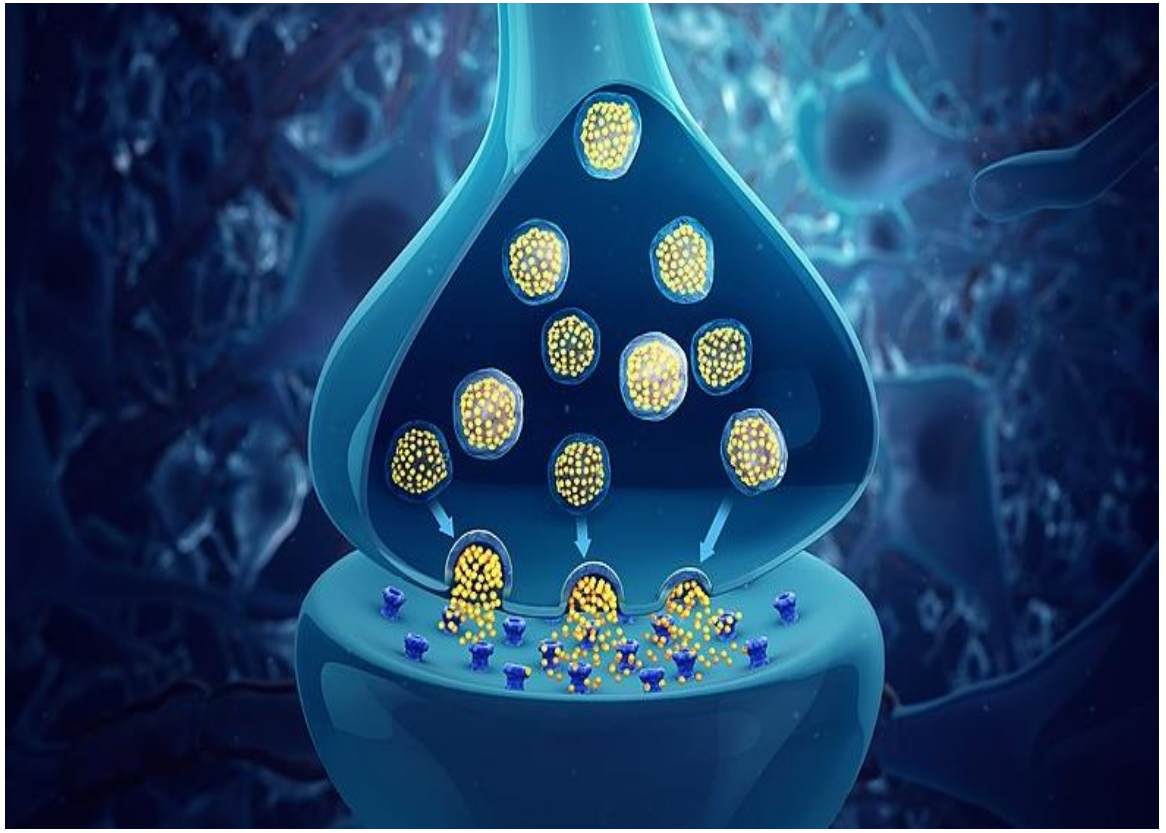


Nervous system (con’t)

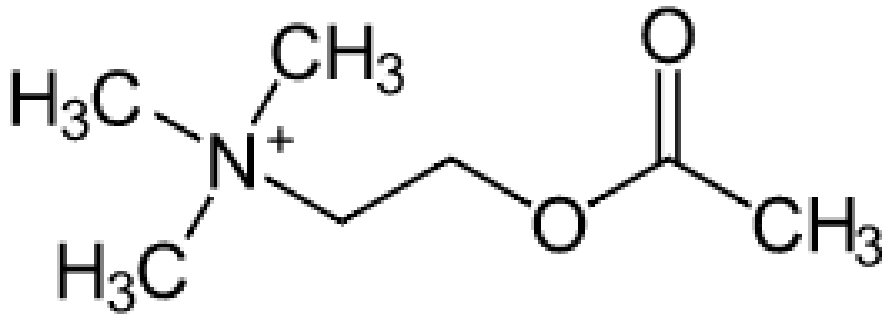
Chemical mediator of autonomic nervous system:

- Neurotransmitter
  1. Biological formation
  2. Storage
  3. Liberation
  4. Operation
  5. Inactivation

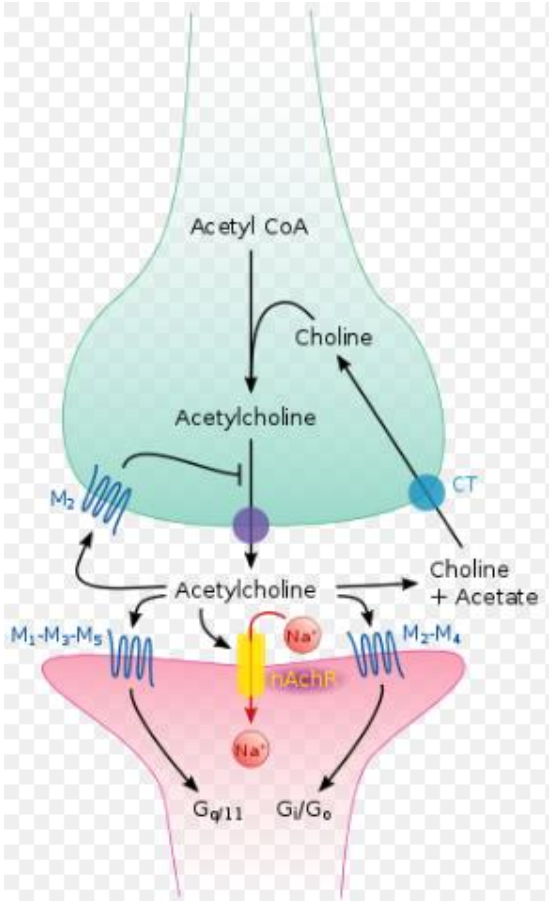
- Stimulating effect
- Inhibitory effect
- Depolarization
- Repolarization



Acetylcholine



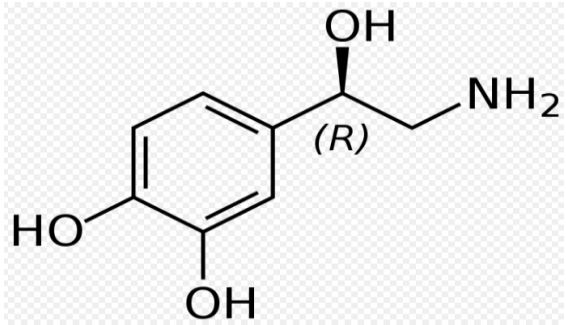
Formula: $C_7NH_{16}O_{2+}$
Receptors: nicotinic, muscarinic



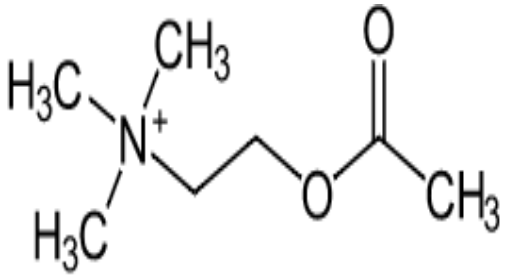
Nervous system (con't)

Neurotransmitter

- Norepinephrine → Sympathetic (Adrenergic :Receptor: α,β)
- Acetylcholine → Parasympathetic (Cholinergic: Receptor: N,M)
- Dopamine
- Histamine
- Glutamate
- Serotonin



Norepinephrine



Acetylcholine

FDA classification of drugs during pregnancy

- A: This group of drugs are called drugs allowed during pregnancy.
- Example: Ferrous sulfate (pills containing iron such as Ferfolik, Folikofer, Fefol, Folairon, and Ferroglobin) , Levothyroxine (thyroid hormone medicine)

- B: There are not enough studies on pregnant women to assess the risk to the fetus in the first trimester of pregnancy.
- Example: Amoxicillin, Amoxicillin with clavulanic acid , Erythromycin

- C: If the benefits of using the drug for pregnant women outweigh the harms of the drug, the drug may be prescribed.
- Example : Expectorant C, Codeine expectorant

FDA classification of drugs during pregnancy

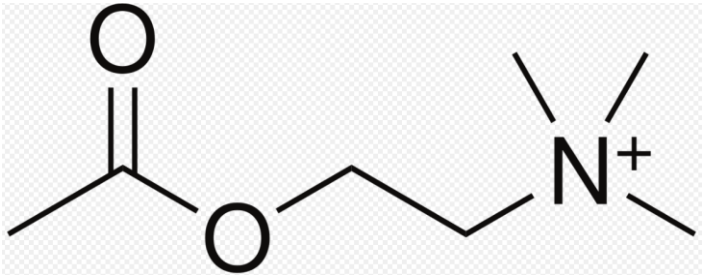
- D: In this group of drugs, studies and results show the existence of danger for the human fetus.
- Example: Bismuth , Belladonna

- X: The use of these drugs during pregnancy is prohibited and they are called prohibited drugs in pregnancy.
- Example: Isotretinoin, Leflunomide

Nervous system (con't) Receptors:

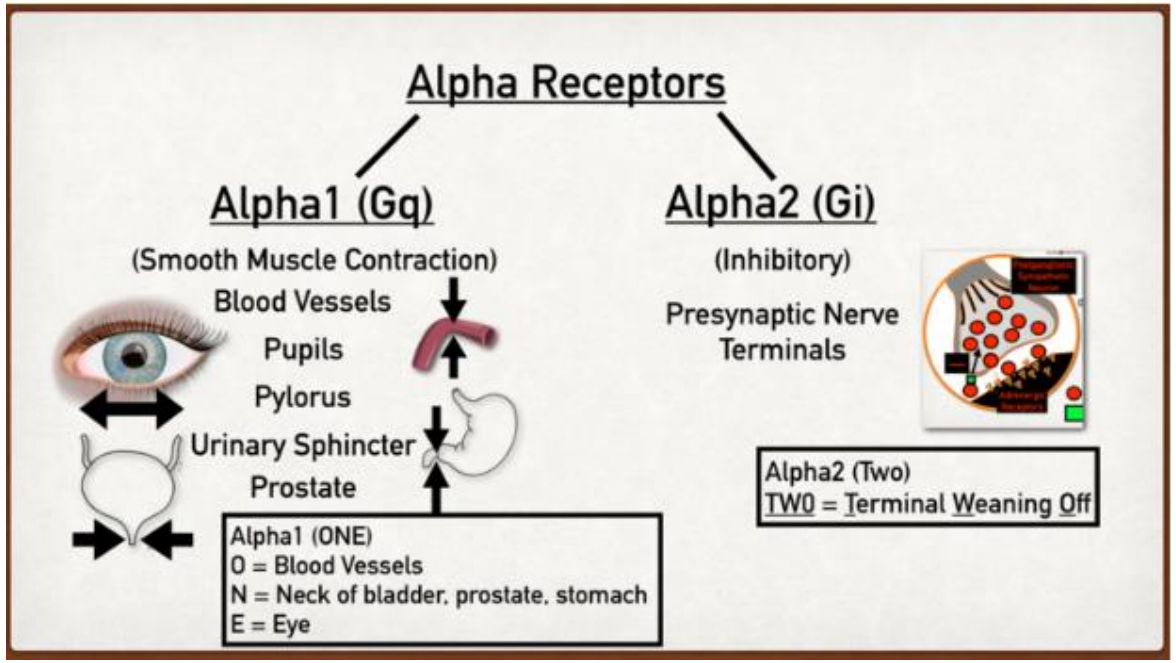
1. Cholinergic
   1. Muscarinic acetylcholine receptor (mAChR)
      - M1
      - M2
      - M3
   2. Nicotine acetylcholine receptor (nAChR)

2. Adrenergic
   - α
     - α١
     - α٢
   - β
     - β١
     - β٢
     - β٣

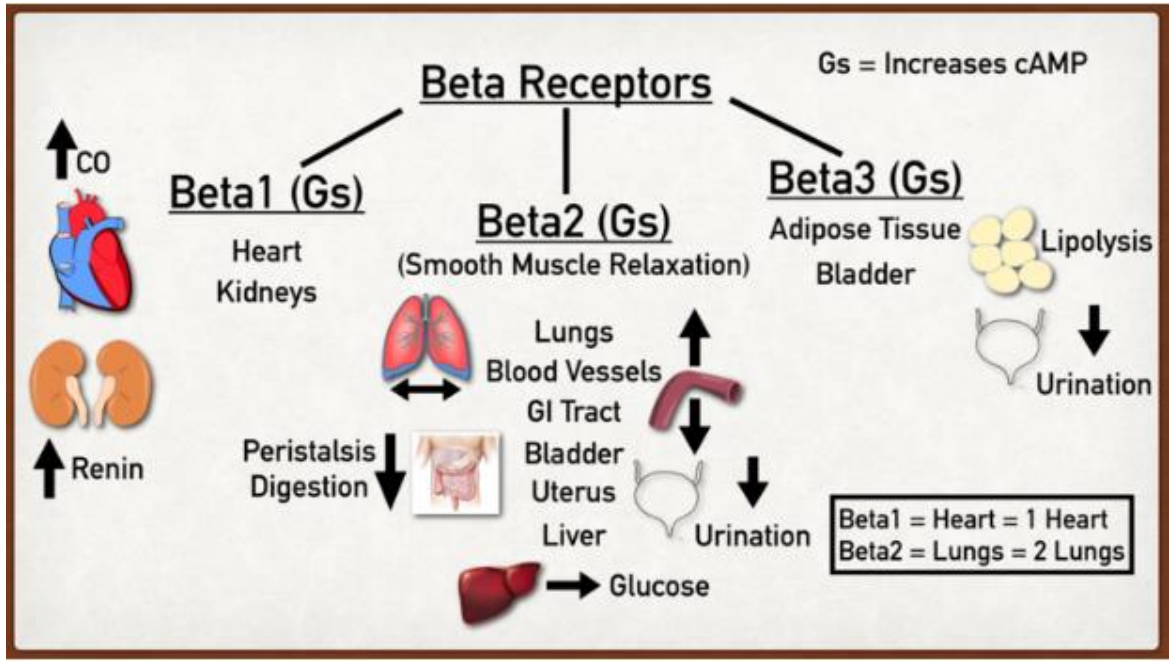


Acetylcholine

Nervous system (con't) Receptors:



Alpha Receptors



Beta Receptors

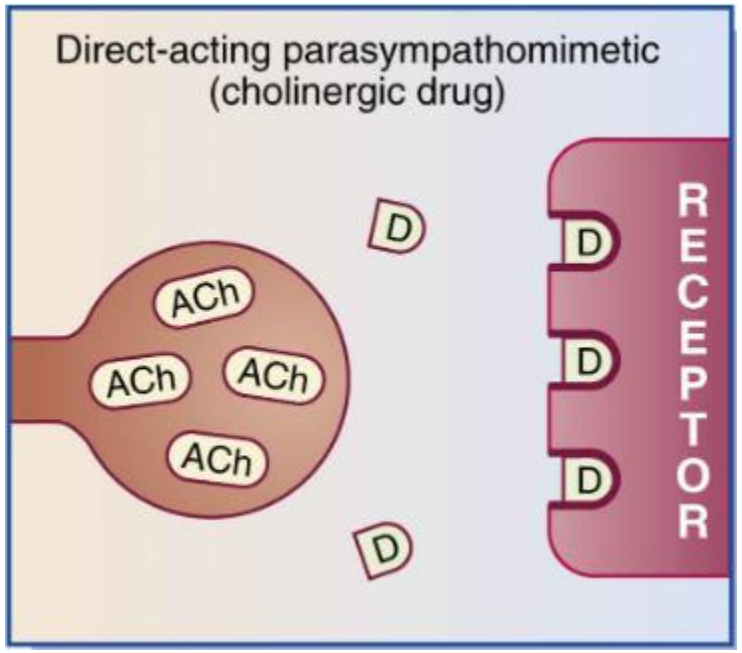
Nervous system (con't)

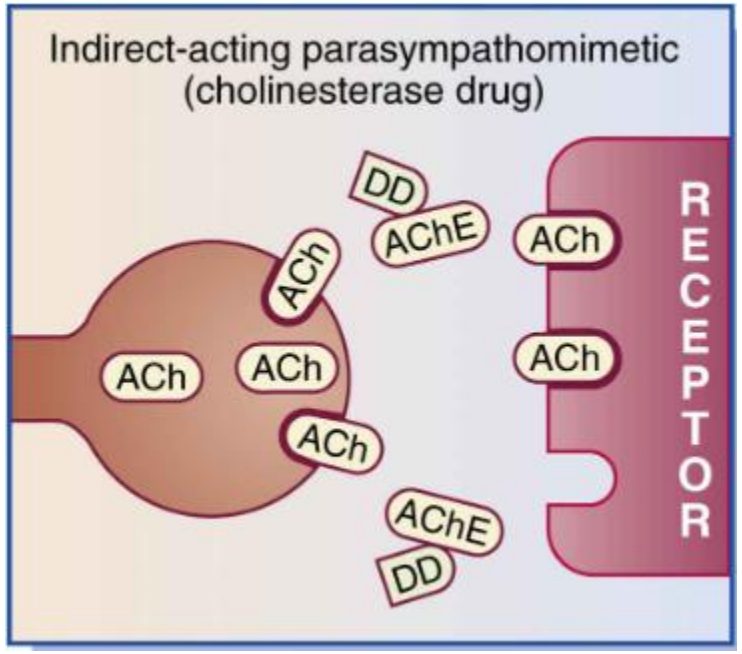
Cholinergic drugs

Cholinergic drugs

(Parasympathomimetic drugs)

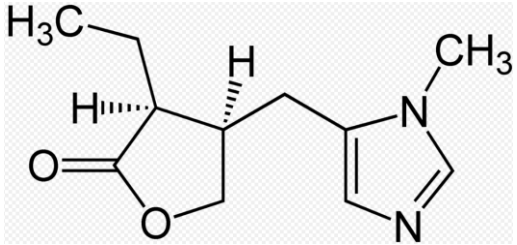
- Direct acting
  - Muscarinic
  - Nicotine
- Indirect acting
  - Reversible
  - Irreversible



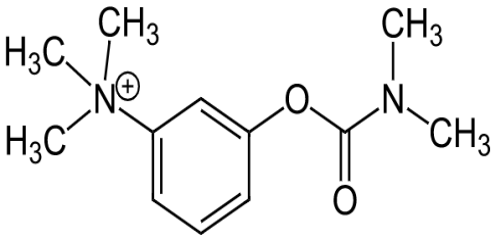


Nervous system (con’t)

- **Pilocarpine:**
- Direct-Acting Cholinergic Agonists
- Muscarinic receptor agonist
- Formula: $C_{11}H_{16}N_2O_2$
- Routes of administration: Topical eye drops, by mouth



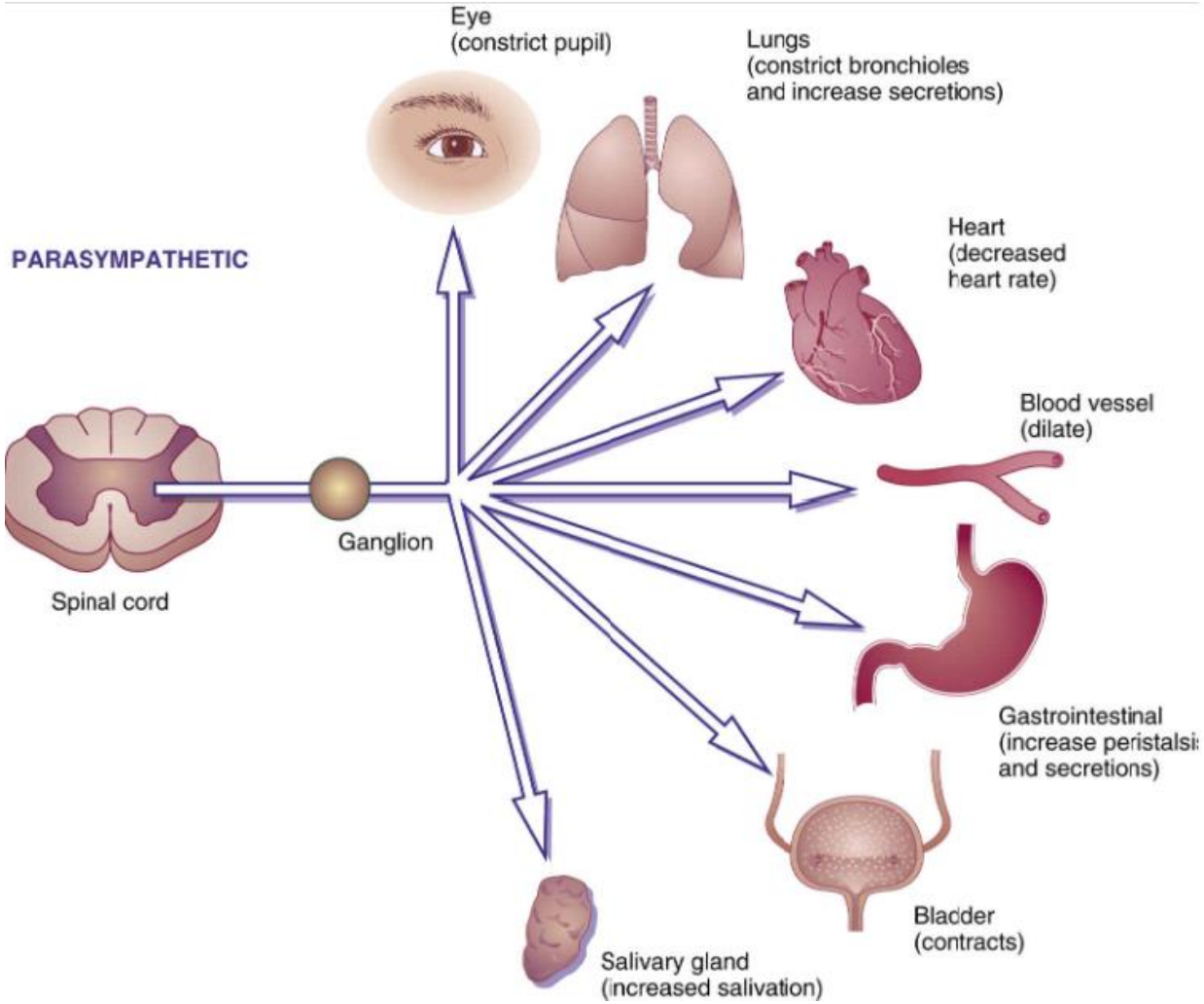
- **Neostigmine:**
- Indirect-Acting Cholinergic Agonists



Nervous system (con’t)

Cholinergic drugs
(Parasympathomimetic drugs)

Examples:
Cevimeline
Fampridine
Neostigmine
Bethanechol
Pyridostigmine



Nervous system (con't)

- Parasympatholytic (Anticholinergic drugs)

- Anticholinergics are substances or drugs that prevent the effect of acetylcholine by blocking the acetylcholine receptor (muscarinic or nicotinic) on the membrane of the target cell or postsynaptic cell.

- The most famous anticholinergic substances are anticholinergic drugs such as hyoscine, dicyclomine, atropine, trihexyphenidyl, benztropine, and bipyridine.

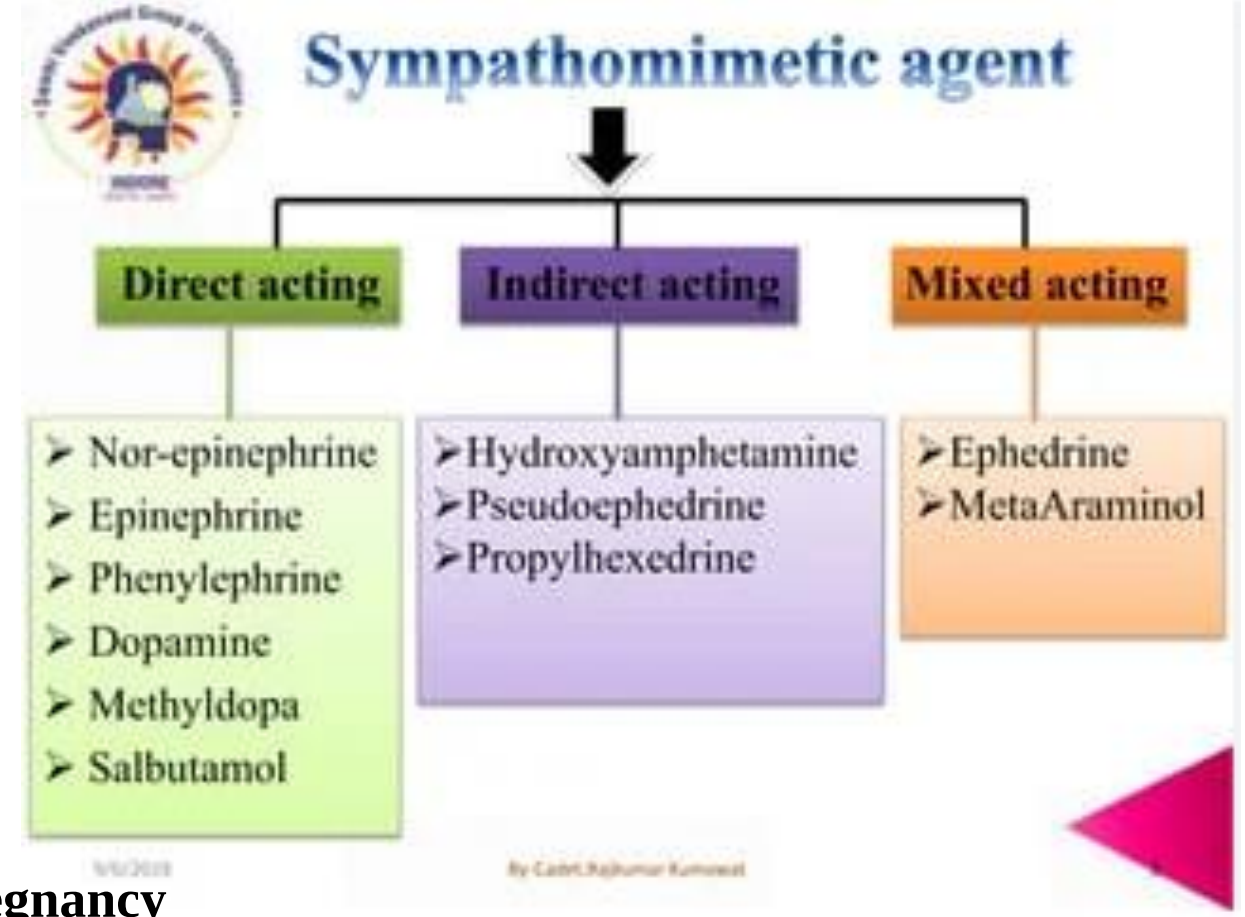
Nervous system (con't)

Adrenergic Drugs: (Sympathomimetic drugs)

Direct acting

β α

Indirect acting



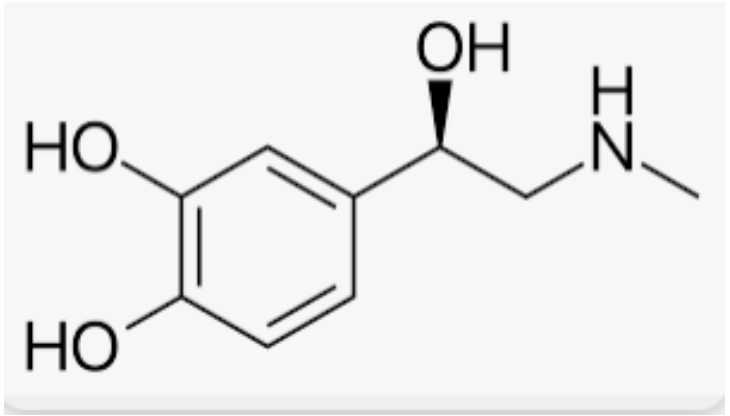
Note: They are placed in group C during pregnancy

Nervous system (con't)

Adrenergic Drugs: (Sympathomimetic drugs)

- **Heart** → β_1 receptors → ↑ Ca^{2+} ↑ heart beat ↑ O_2 consumption

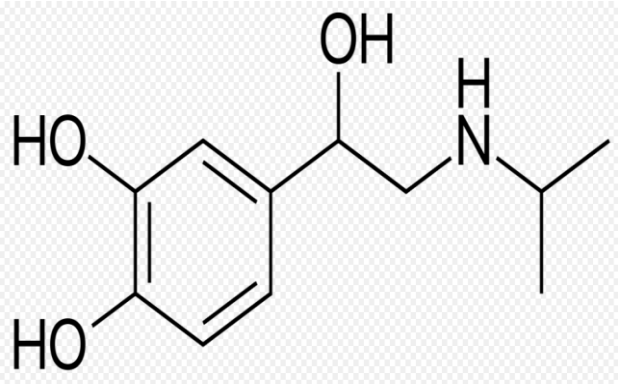
  Adrenaline (Epinephrine) : Group C in pregnancy



Nervous system (con't)
Adrenergic Drugs: (Sympathomimetic drugs)

- **CNS:** nervousness, headache, dizziness, nausea, visual blurring
- Adrenaline (Epinephrine) and Isoprenaline: In appropriate dose, improves blood flow

Note: Group X in pregnancy

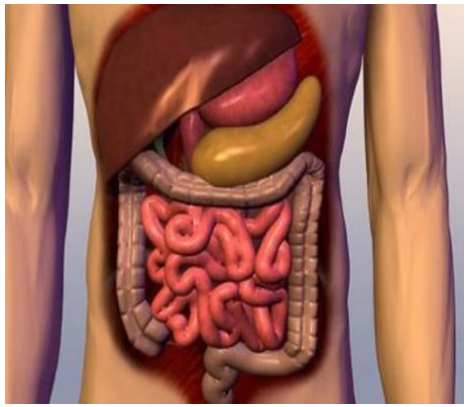


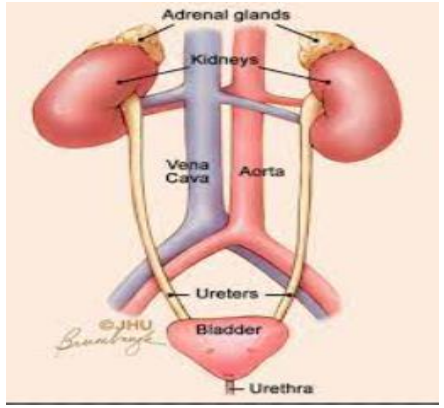
Nervous system (con't)

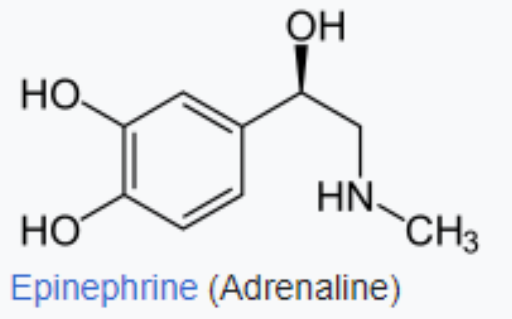
Adrenergic Drugs: (Sympathomimetic drugs)

- **Digestive and Urinary system:**

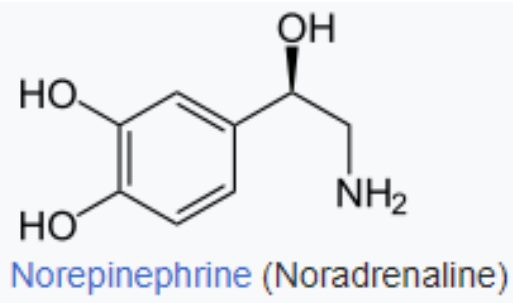
Catecholamines
- Epinephrine (Adrenaline)
- Norepinephrine (Noradrenaline)
- Dopamine: C



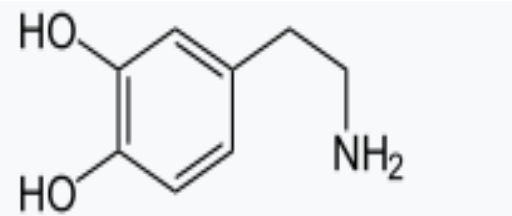




Epinephrine (Adrenaline)



Norepinephrine (Noradrenaline)



Dopamine

Nervous system (con't)

Adrenergic Drugs: (Sympathomimetic drugs)

- Eye ⟶ α Receptor ⟶ Mydriasis / Glaucoma

- Apraclonidine (C) ⟶ α_2 agonist
- Phenylephrine (C) ⟶ α agonist

Mydriasis

Nervous system (con't)

Adrenergic Drugs: (Sympathomimetic drugs)

- Respiratory System → β_2 Bronchial smooth muscles
  → Dilation of pulmonary vessels → Allergic asthma

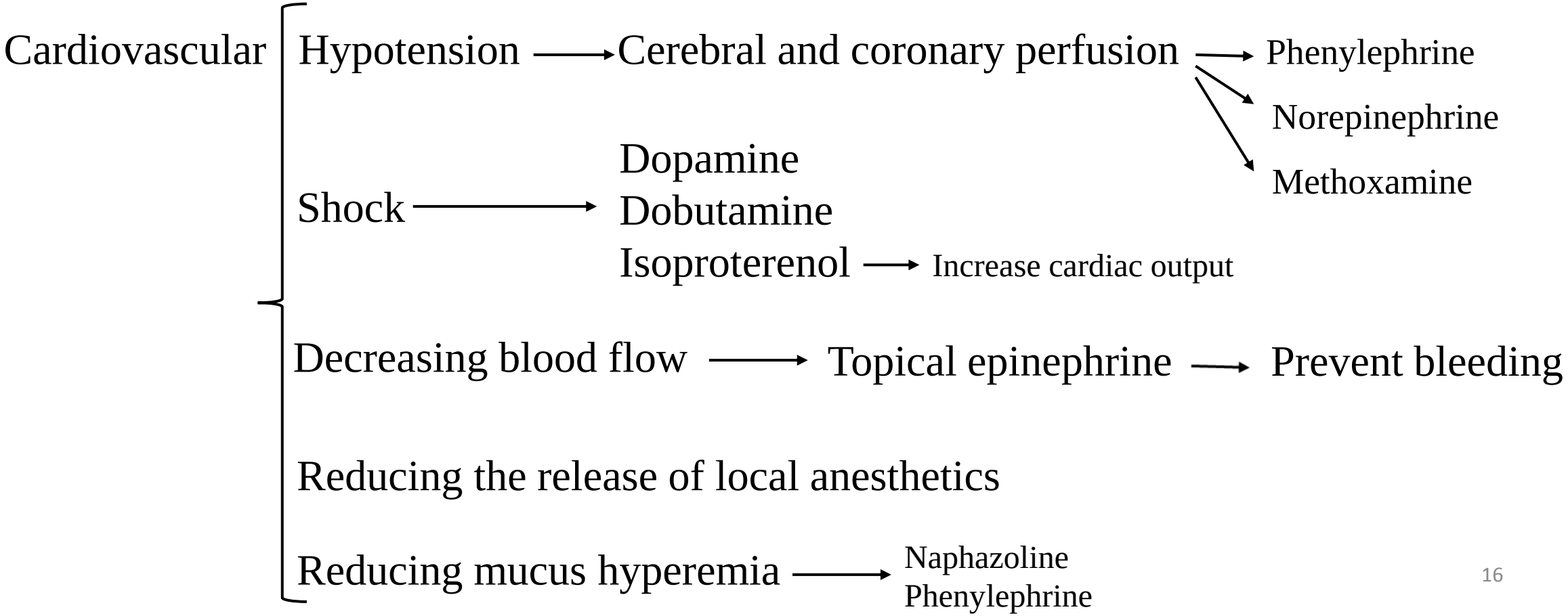
Nervous system (con't)

Adrenergic Drugs: (Sympathomimetic drugs)

- Indirect acting → Ephedrine (C) Dosage forms: Tablets: 20 mg
  Injection: 50 mg
  → Amphetamine (C) (Methylphenidate Brand Ritalin)
  → Cocaine (C)

Nervous system (con't)
Adrenergic Drugs: (Sympathomimetic drugs)

- Indirect acting: Clinical application



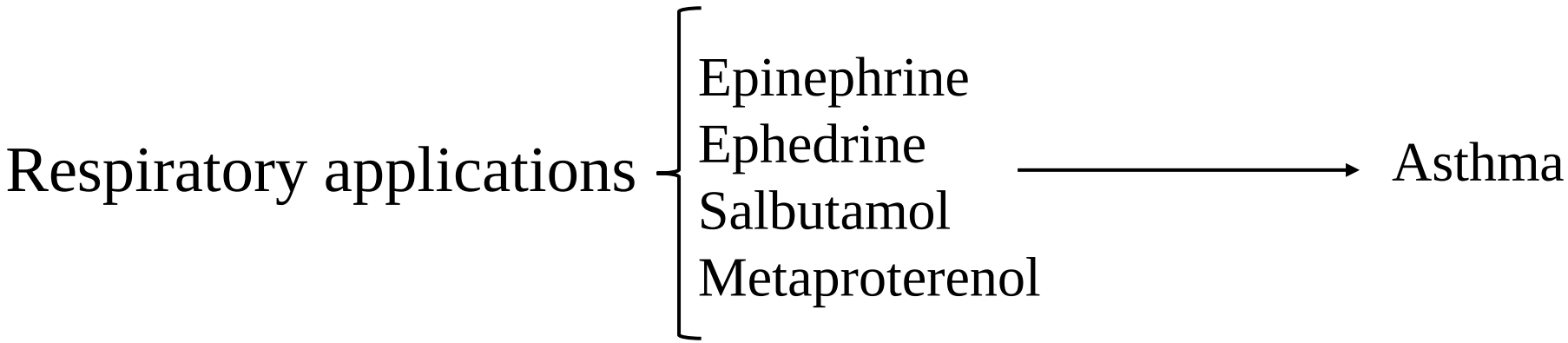
Nervous system (con’t)
Adrenergic Drugs: (Sympathomimetic drugs)

- Indirect acting: Clinical application

Respiratory applications { Epinephrine, Ephedrine, Salbutamol, Metaproterenol } → Asthma

Nervous system (con’t)
Adrenergic Drugs: (Sympathomimetic drugs)

- Indirect acting: Clinical application



Nervous system (con’t)
Adrenergic Drugs: (Sympathomimetic drugs)

Indirect acting: Clinical application

- Anaphylactic shock → Epinephrine
  - → Corticosteroid
  - → Antihistamine

Nervous system (con’t)

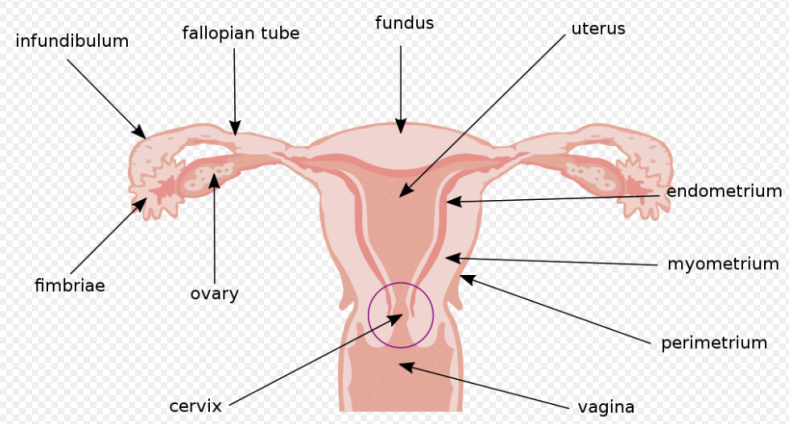
Adrenergic Drugs: (Sympathomimetic drugs)

Indirect acting: Clinical application

- Ophthalmic applications ⟶ Epinephrine ⟶ Glaucoma

Nervous system (con't)

Adrenergic Drugs: (Sympathomimetic drugs)



Indirect acting: Clinical application

Uterine applications

Terbutaline: (B)

Pharmaceutical forms: tablets, sprays and ampoules

Salbutamol: (A)

Pharmaceutical forms: spray, tablet and syrup

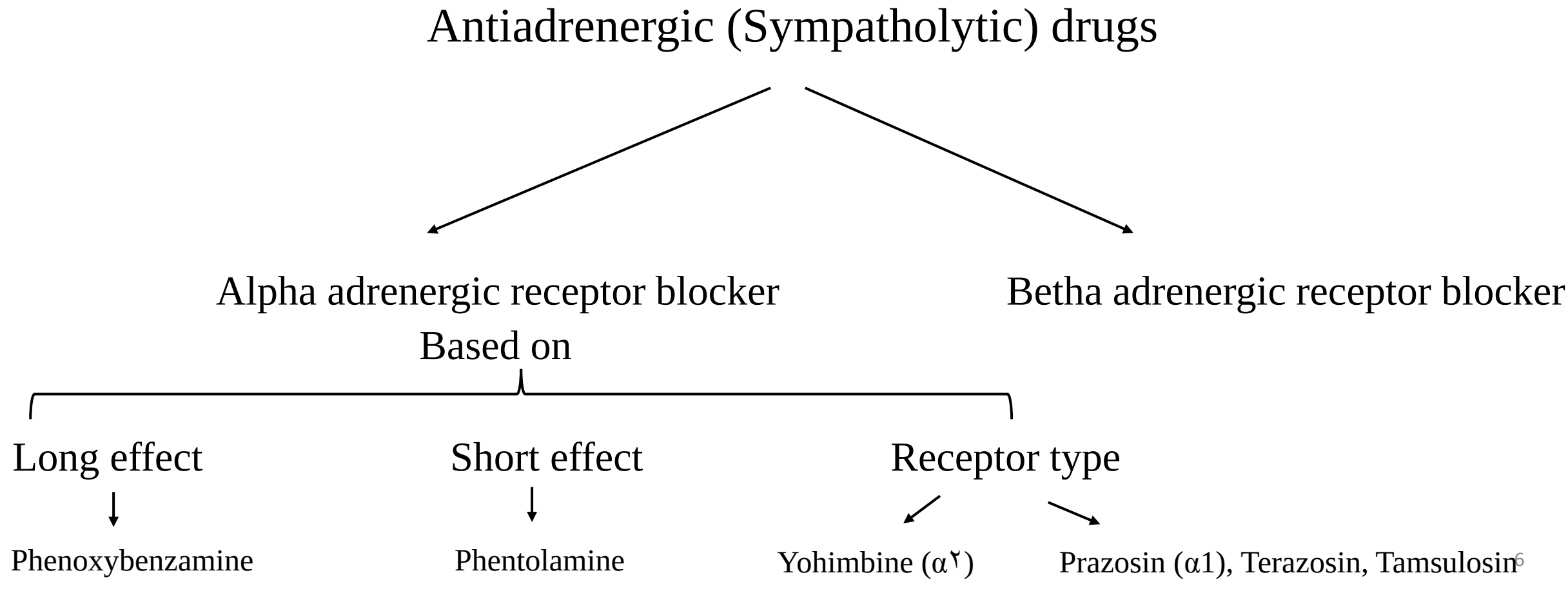
Nervous system (con’t)

Adrenergic Drugs: (Sympathomimetic drugs)

Indirect acting: Clinical application

Side effects and toxicity
- Brain complications
- Cardiovascular complications

Nervous system (con't)
Antiadrenergic Drugs: (Sympatholytic drugs)



Nervous system (con't)
Antiadrenergic Drugs: (Sympatholytic drugs)

Antiadrenergic (Sympatholytic) drugs:

Betha adrenergic receptor blocker

based on:

1. Binding to the receptor → Atenolol, esmolol, metoprolol, esbutolol
2. Relative agonist activity → Esbutolol and pindolol
3. Function of local anesthesia → Timolol
4. Fat solubility → Propranolol
5. Duration of effect → Nadolol

Nervous system (con't)
Antiadrenergic Drugs: (Sympatholytic drugs)

Antiadrenergic (Sympatholytic) drugs

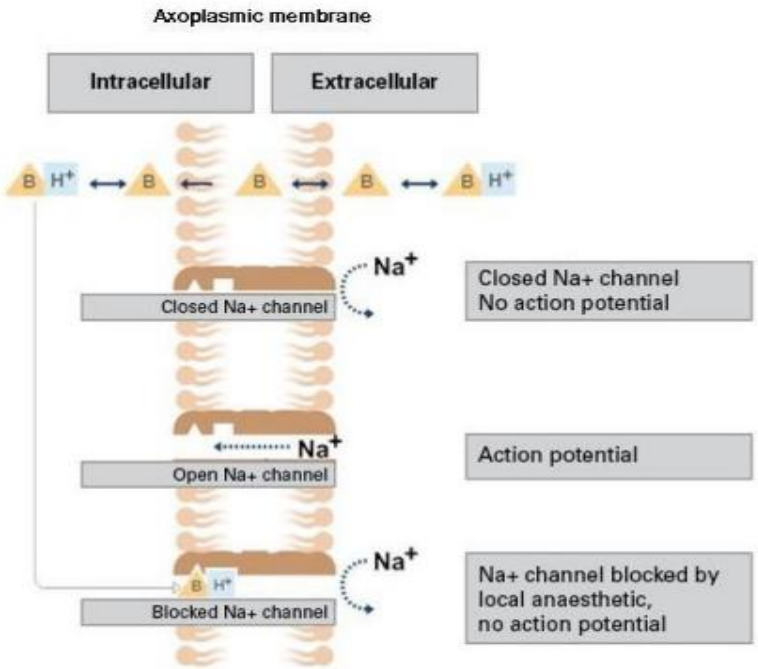
Betha adrenergic receptor blocker : Clinical applications

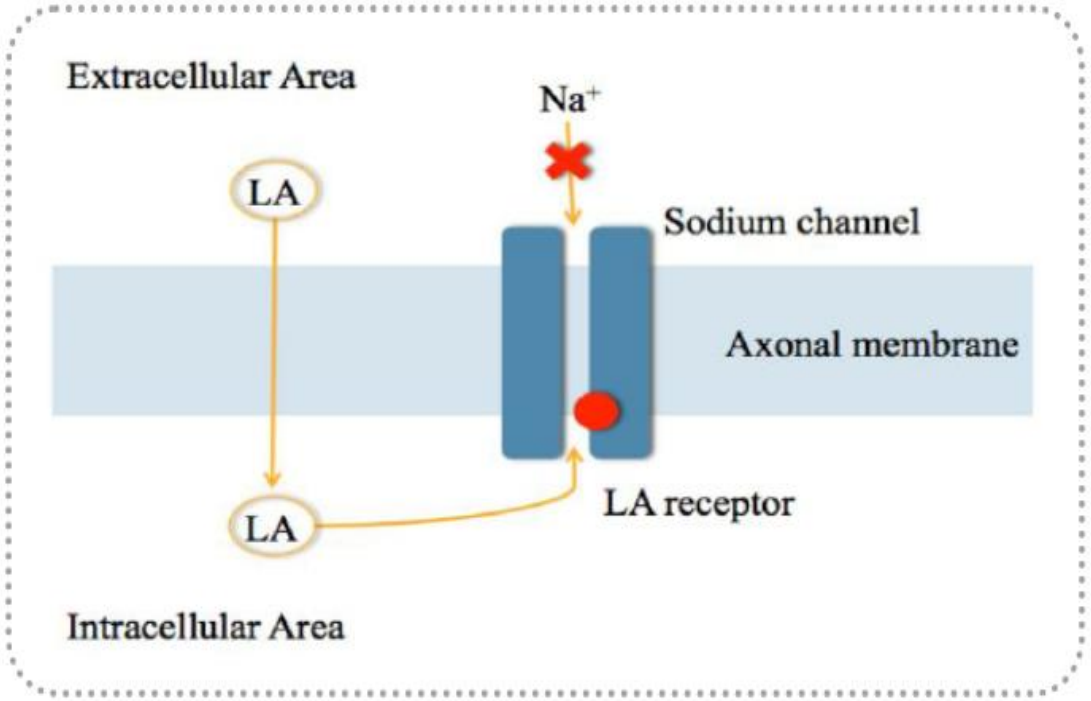
- Hypertension
- Cardiac arrhythmia ⟶ Propranolol (C)
- Glaucoma ⟶ Timolol (C)
- Neurological diseases ⟶ Propranolol (C)

Local anesthetics (LA) Muscle Relaxers

Local anesthetics (LA)

- Mechanism of action

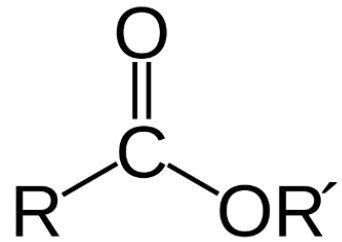




Local anesthetics (LA)

Esters

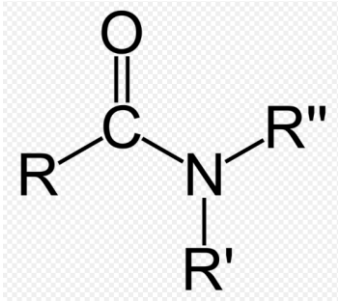
- long effect → Tetracaine → **C**
- short effect → Procaine → **B**
- Superficial anesthetic → Cocaine ، benzocaine → **C**



Ester functional group

Amides

- long effect → Bupivacaine → **C**
- Medium effect → Lidocaine → **B**



Amide functional group

Local anesthetics (LA)

Effective agents in nervous system block by local anesthetics:

- Amount of LA
- Addition of vasoconstrictor drug to LA
- Alkalization of LA
- Place of nerve block

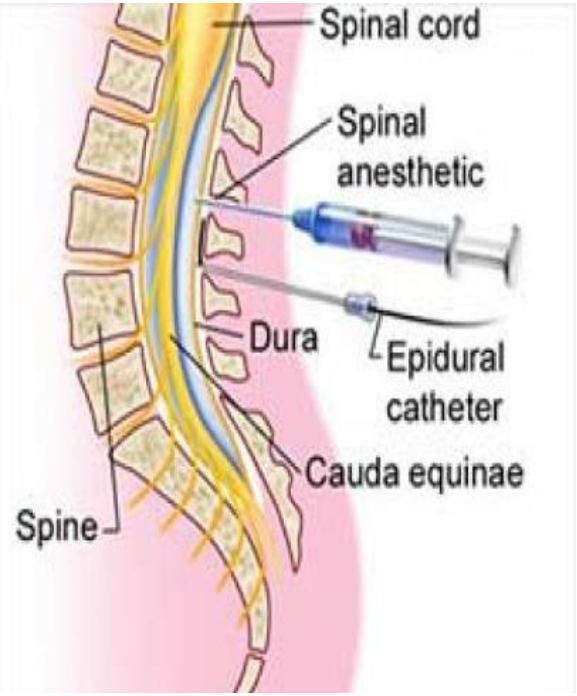
Local anesthetics (LA)

Types of anesthesia

1. Short-term anesthesia
2. Secretory anesthesia

} Local anesthesia

3. Peripheral nerve block
4. Nervous numbness (Network anesthesia)
5. Epidural anesthesia
6. Spinal anesthesia
7. Bier block anesthesia
8. Local anesthesia in body cavities



Local anesthetics (LA)

Root of administration

- Injectable → Lidocaine
- Ointment → Lidocaine
- Spray → Lidocaine
- eye drop → Tetracaine
- gel

Local anesthetics (LA)

- Pharmacokinetics
  - Absorption
  - Metabolism
    - Esters → Metabolized in plasma
    - Amides → Metabolized in the liver
- Pharmacodynamics → They block sodium channels

Local anesthetics (LA)

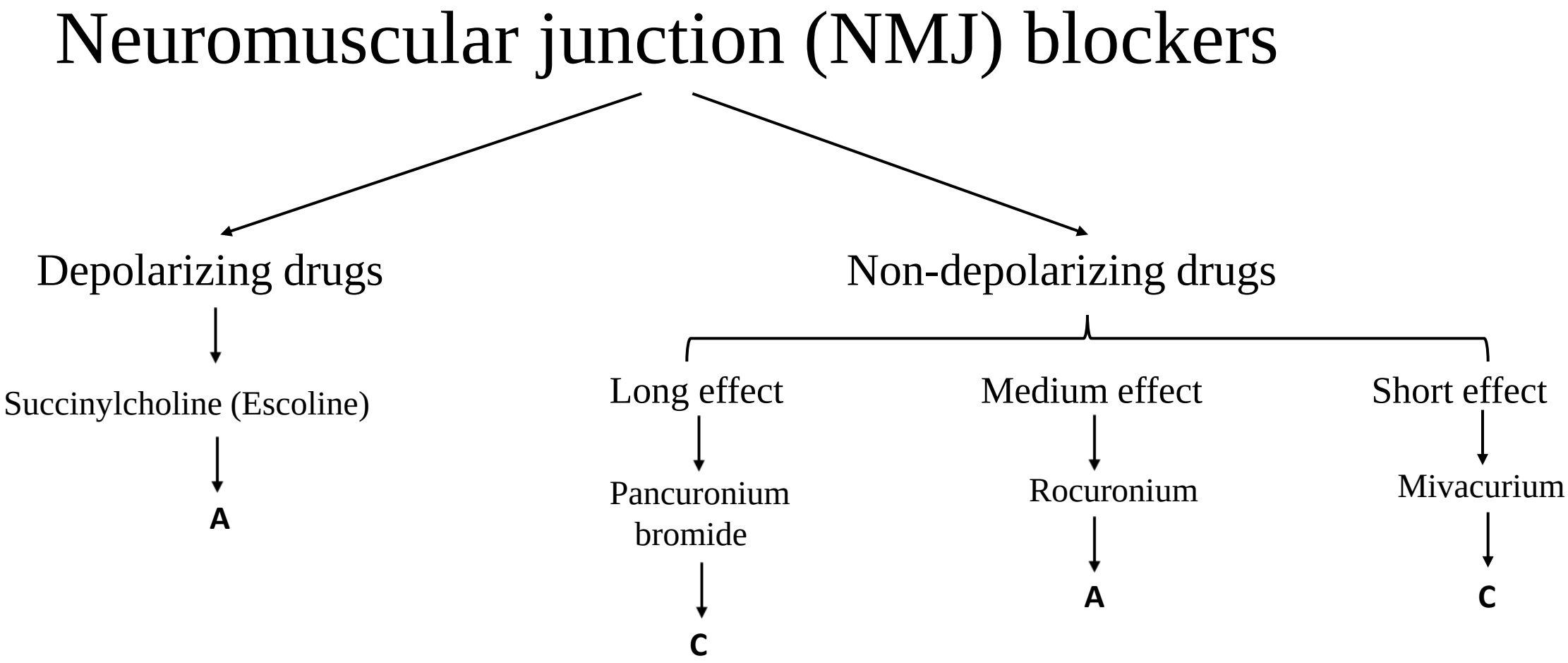
Side effects

- Neurological → Drowsiness and seizures
- Cardiovascular → Dilatation of blood vessels (except cocaine)
- Other complications → Esters can cause allergic reactions

Muscle relaxant

- Mechanism of muscle contractior
- Muscle relaxants

Muscle relaxant



Muscle relaxant

Side effects

Depolarizing drugs

- Muscle pain after surgery
- Hyperkalemia
- Increased intragastric pressure (puke)

Non-depolarizing drugs

- Respiratory paralysis
- Histamine release
- Cardiac m receptor inhibition
- Autonomic ganglion block

Antihypertensive drugs

Antihypertensive drugs

- Systolic blood pressure
- Diastolic blood pressure