# CBN 0601: Pharmacology / Toxicology

# Pharmacology …

The interaction of chemical substances (drugs) with living organisms (humans)

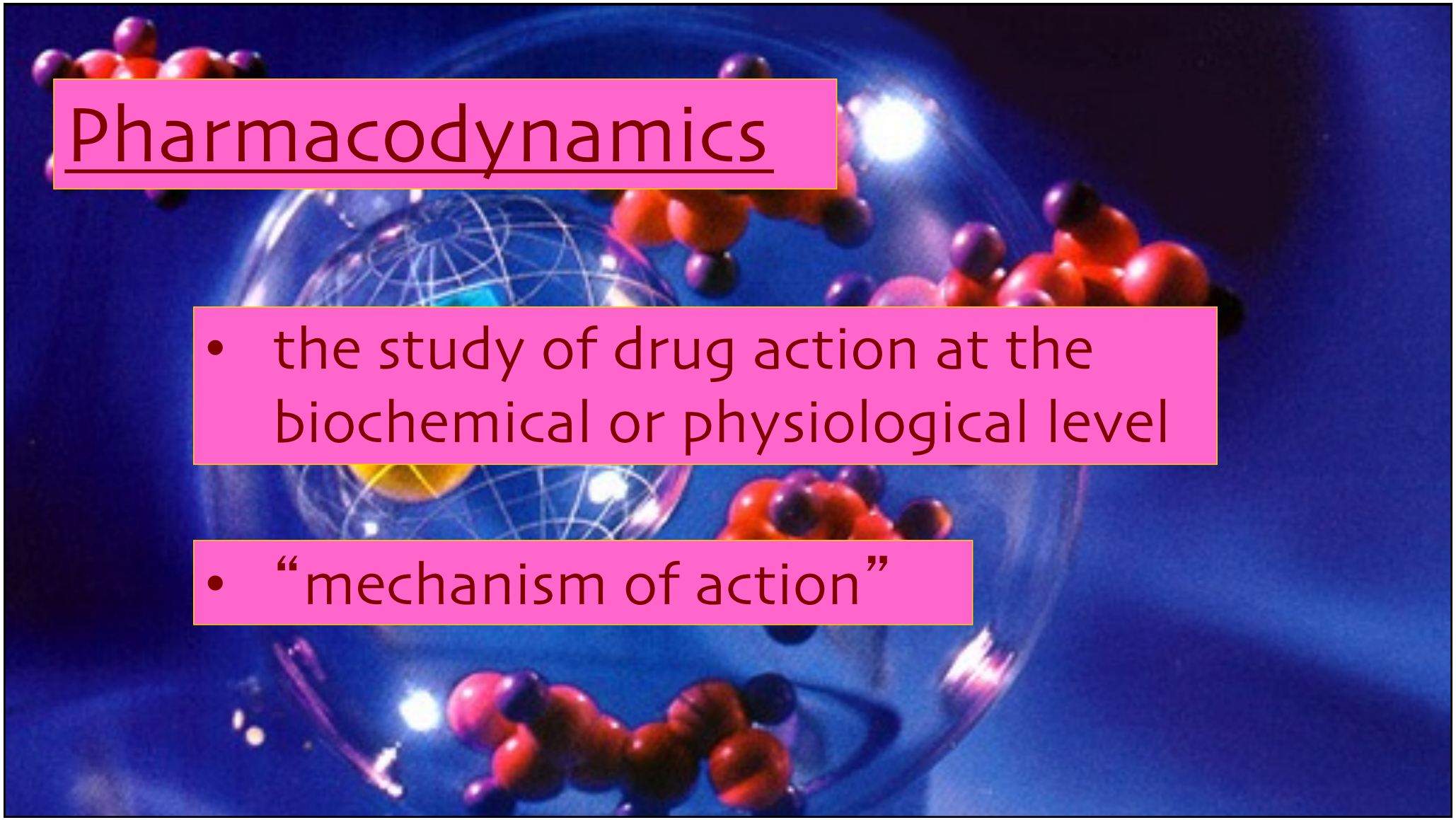
# Pharmacology …

- consists of (1) pharmacodynamics and (2) pharmacokinetics

  "pharmaco" = drugs

  "dynamics" = dynamics

  "kinetics" = movement



# Pharmacodynamics

- the study of drug action at the biochemical or physiological level
- "mechanism of action"

# Pharmacokinetics …

- study of how drugs:

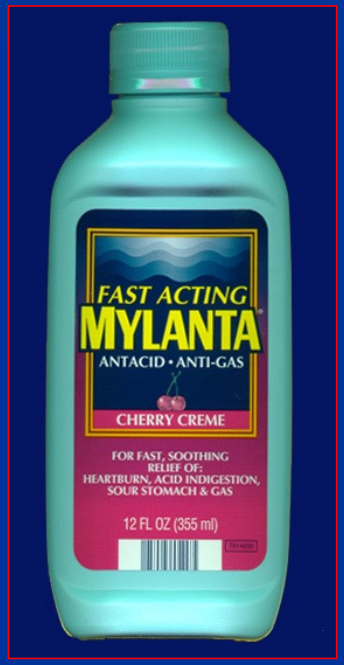
  (1) enter the body

  (2) reach site of action

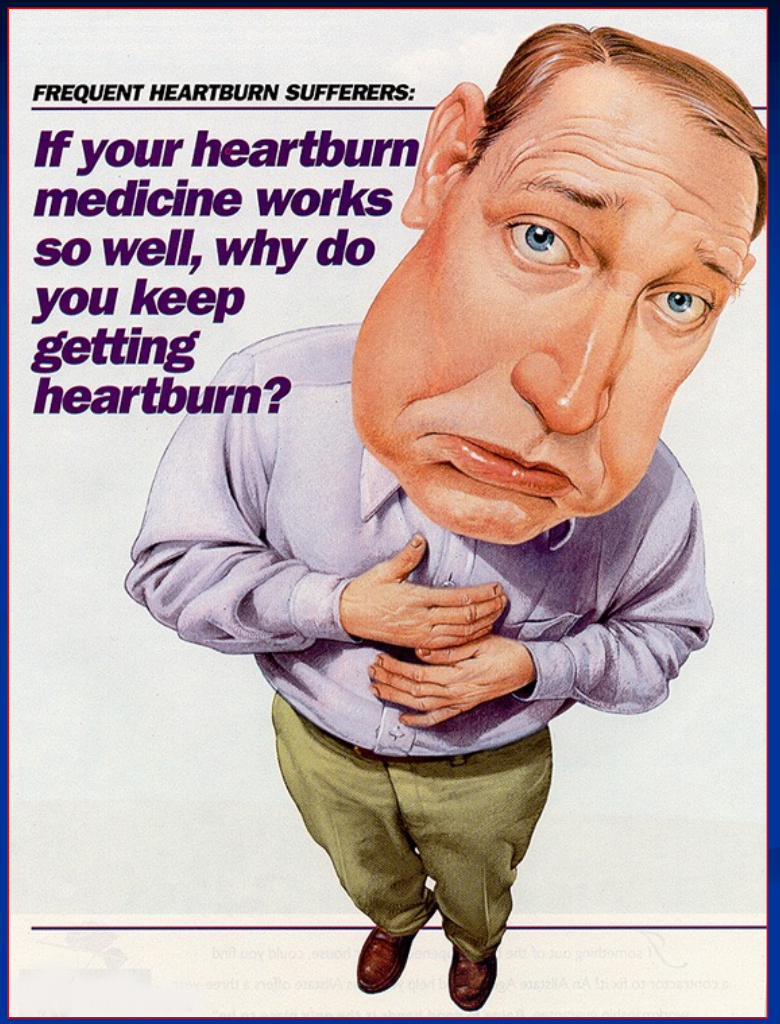
  (3) are eliminated
  from the body

# Pharmacodynamics

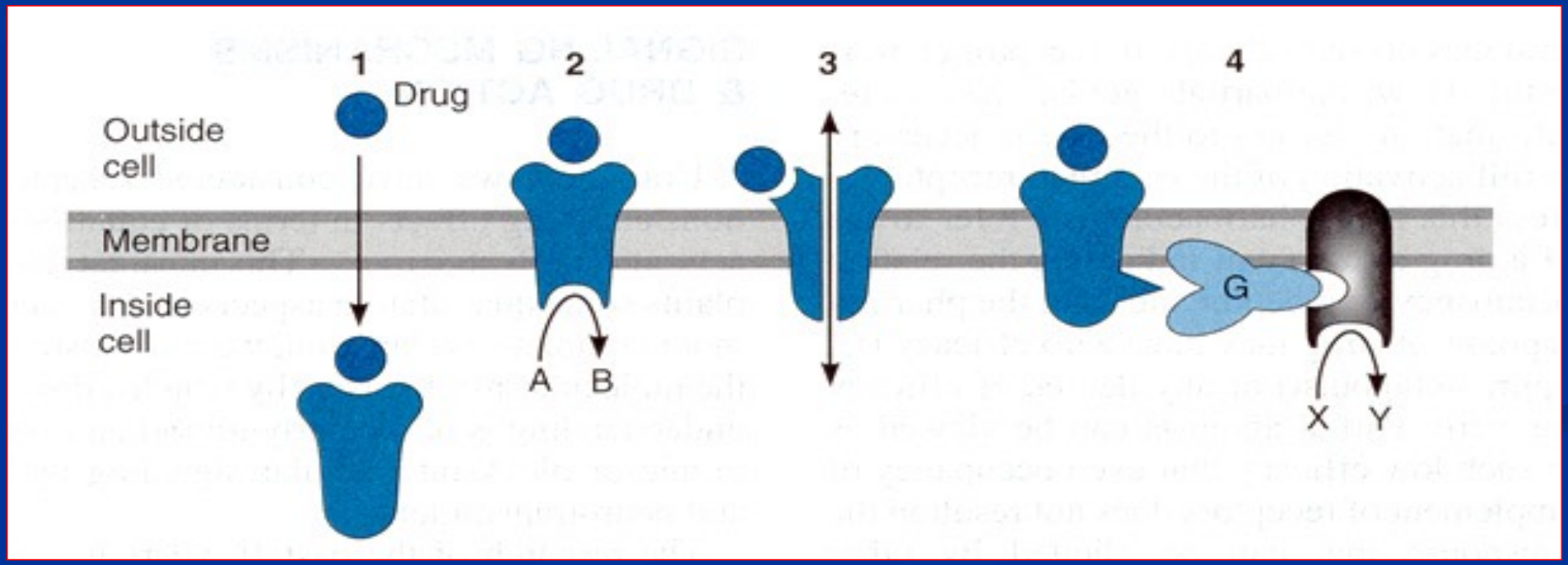
A. Drugs that change the environment of cells …





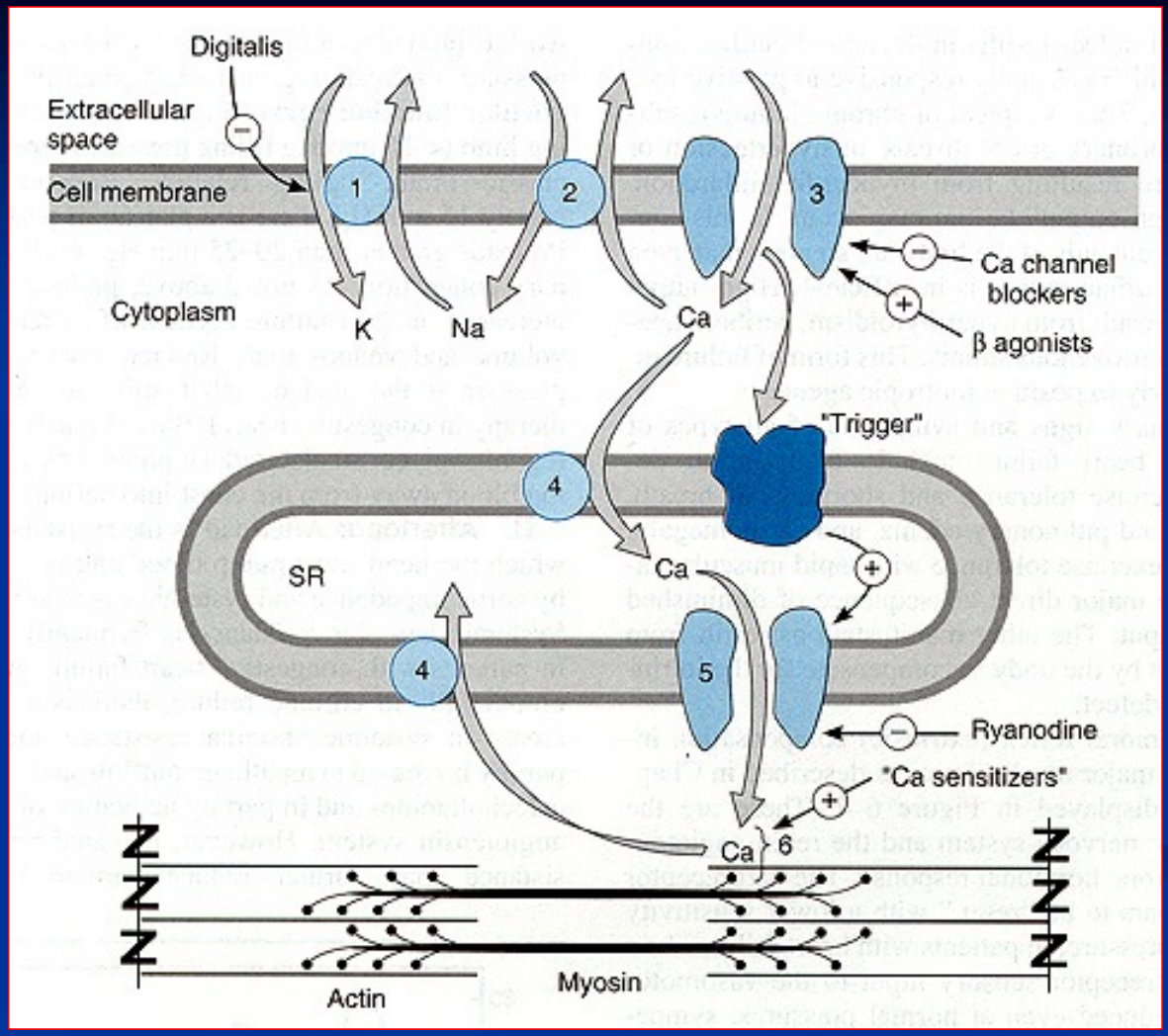


# B. Drugs which selectively bind to receptors on cell membranes → alter cellular physiology

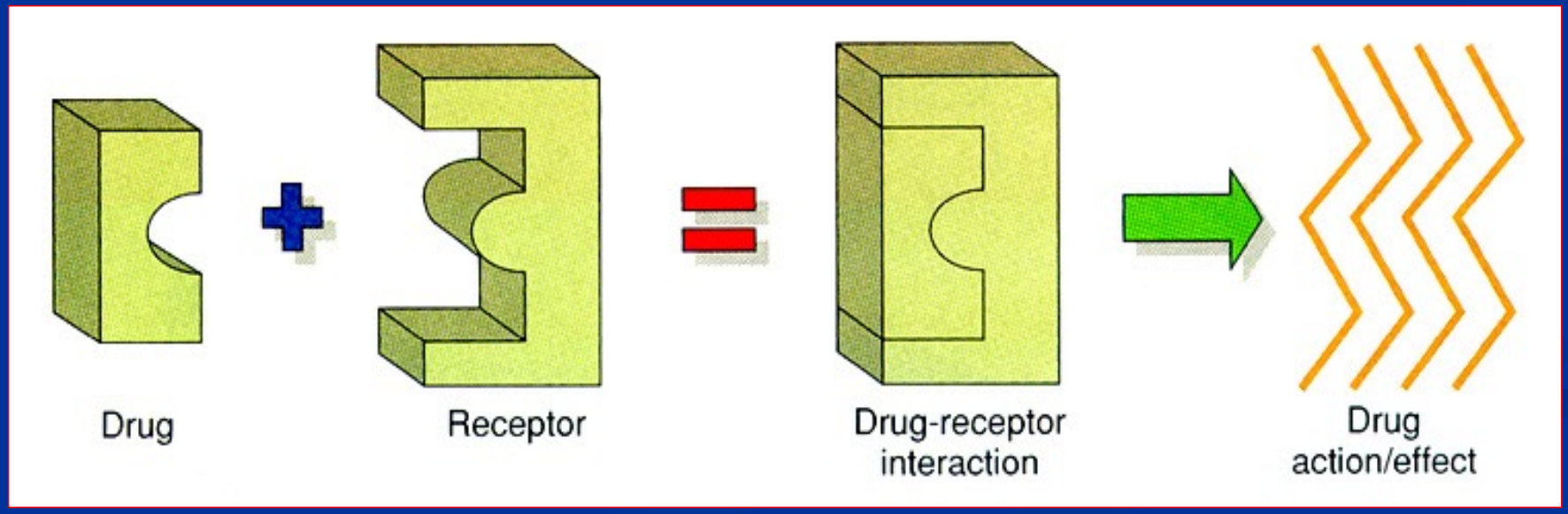


# Example of Drug-Receptor Interaction:

## Digoxin (Digitalis)



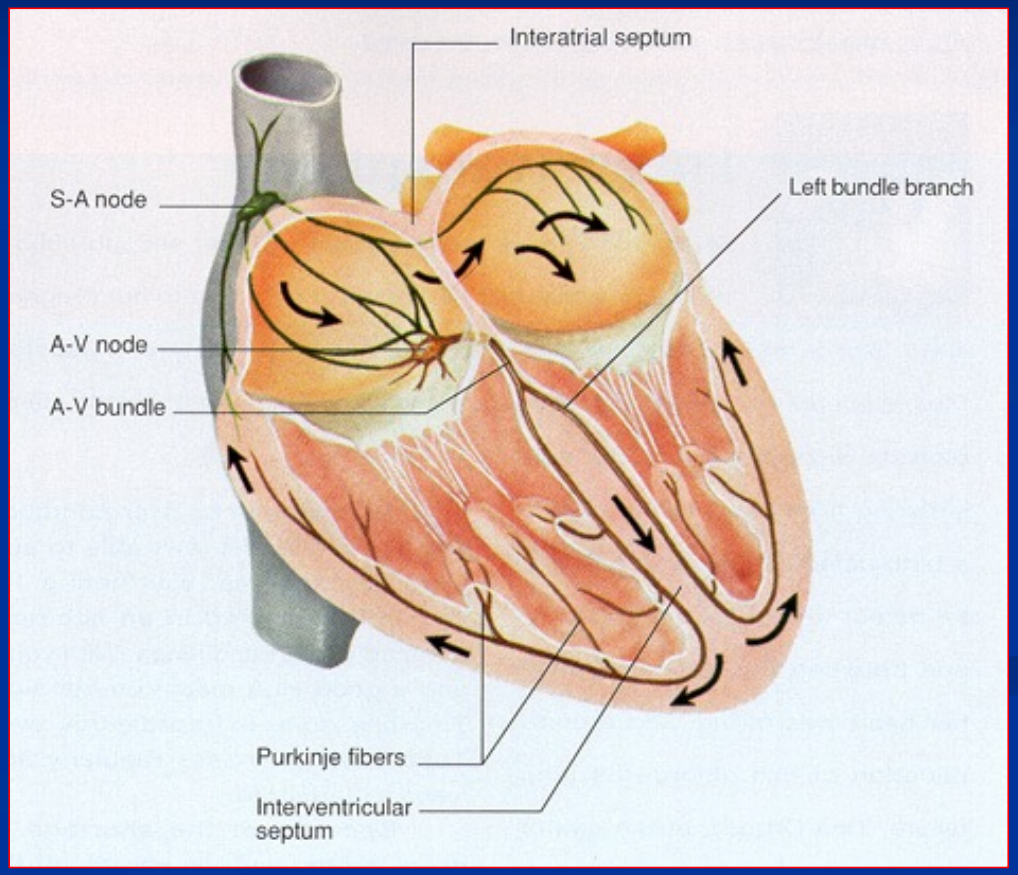
Definition: Agonist is a drug which binds to a specific receptor and produces a physiological effect by stimulating the receptor.



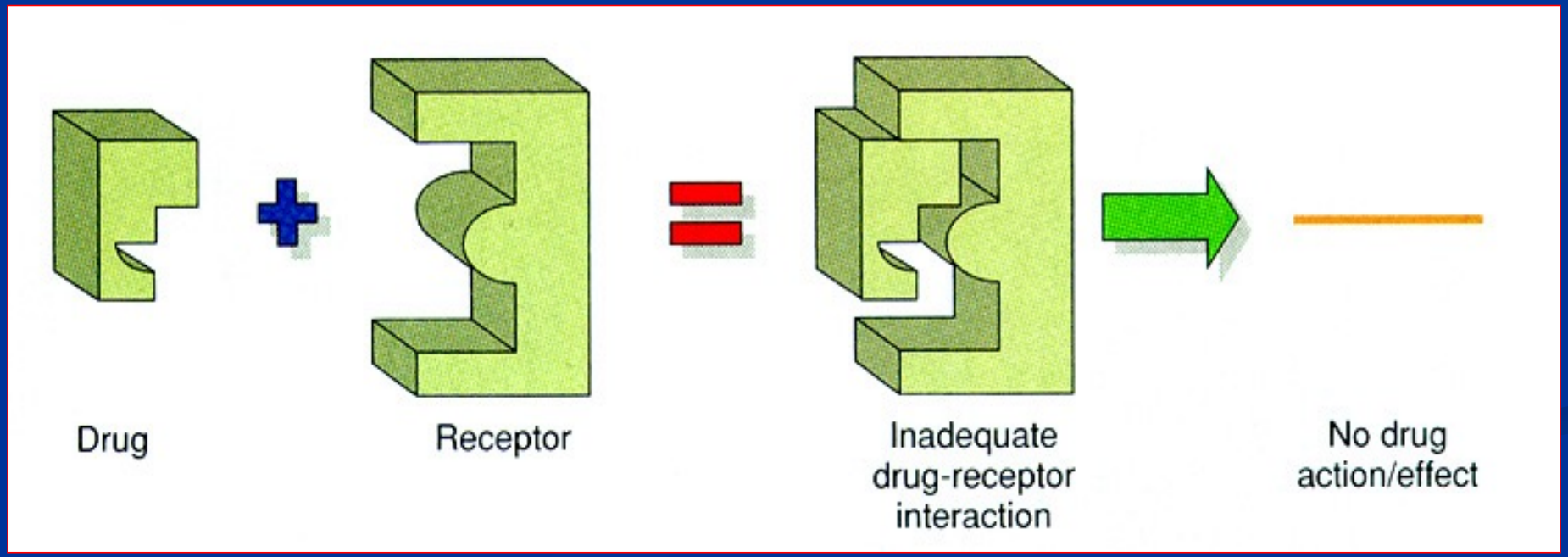
# Agonist (Example)

## Norepinephrine (NE)

NE: stimulates beta-1 receptors on the SA node
→ increases HR
→ increases BP



Definition: Antagonist is a drug which binds to a specific receptor and blocks other substances from stimulating the receptor.



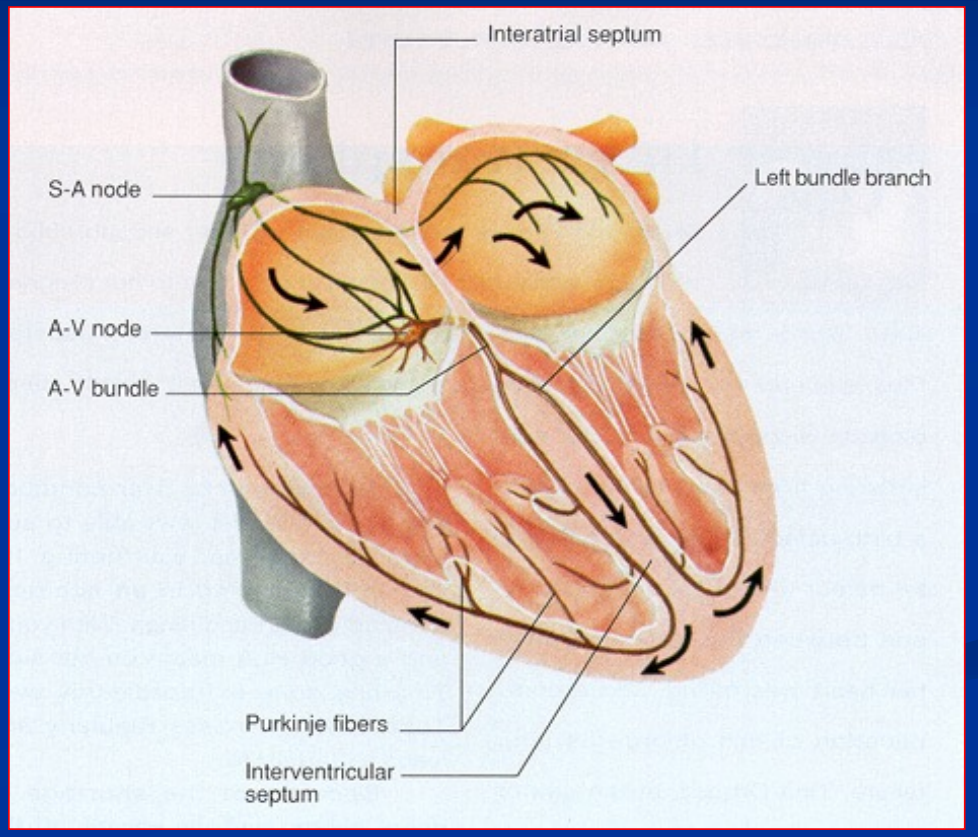
# Antagonist (Example)

Propranolol (Inderal)

Propranolol: blocks beta-1 receptors on the SA node

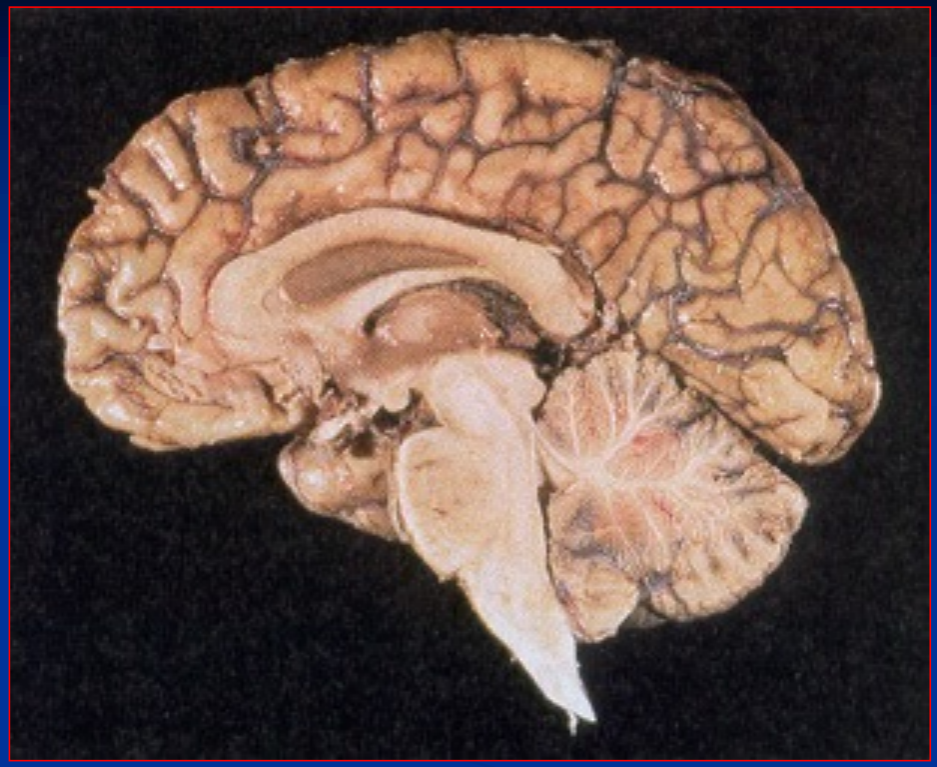
→ decreases HR

→ decreases BP



# Antagonist (Example)

## Naloxone (Narcan)



Naloxone blocks mu-opioid receptors in the respiratory center of the medulla oblongata

→ reverses respiratory depression in opioid overdose due to heroin, morphine, and other narcotics

# New Classification: Inverse Agonist

Diphenhydramine (Benadryl)

Diphenhydramine binds to histamine receptors and induces a conformational change in the receptor


→ prevents histamine from binding to its H-1 receptor
→ prevents allergic reactions and symptoms

# Receptor Binding Characteristics

a. affinity: drug ability to bind to its receptor

- agonist → affinity
- antagonist → affinity

b. efficacy: drug ability to stimulate its receptor

- agonist → efficacy
- antagonist → no efficacy

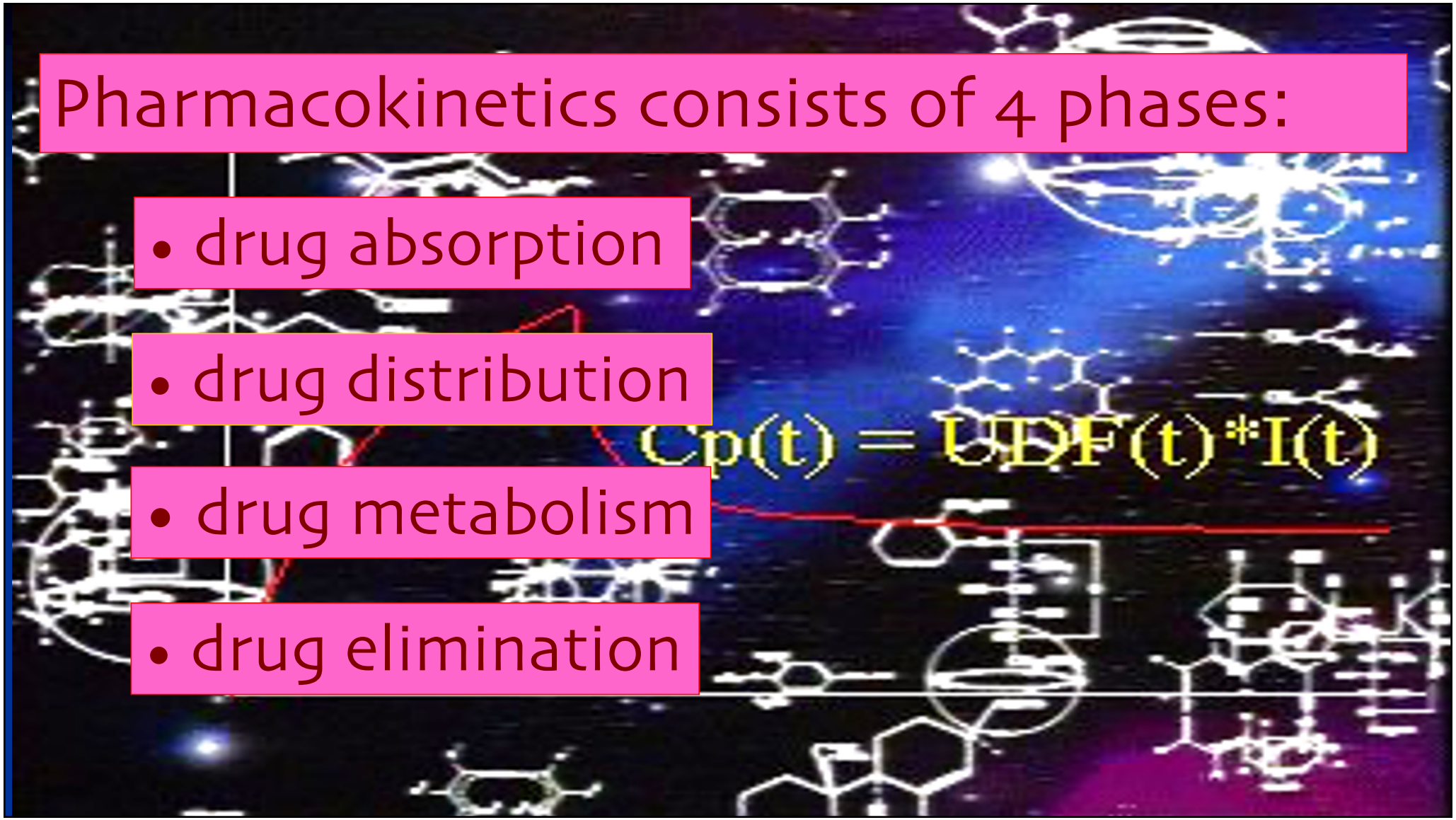
# Competitive Inhibition

morphine (agonist) ←→ naloxone (antagonist)

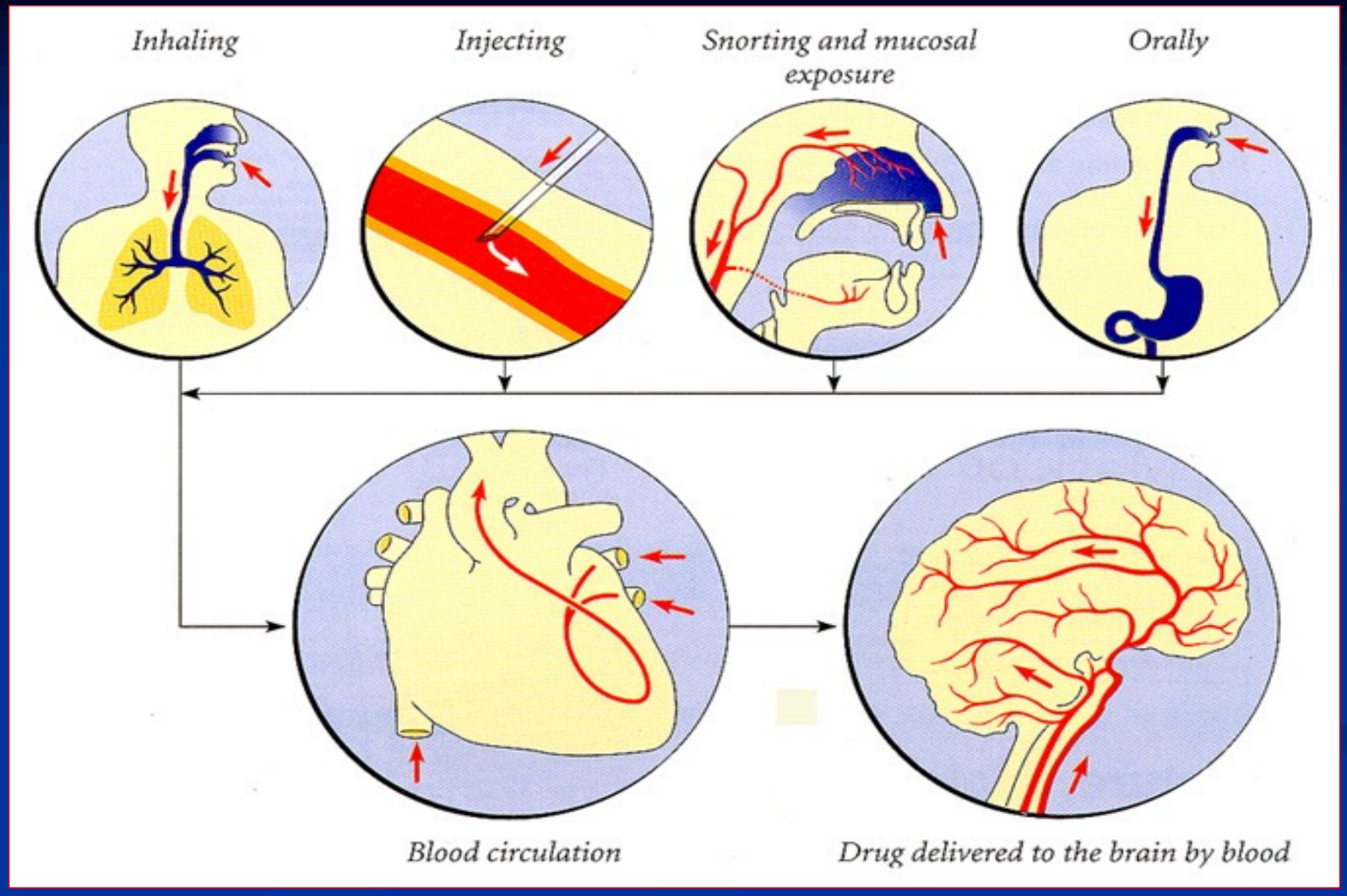
diazepam (agonist) ←→ flumazenil (antagonist)

acetylcholine (agonist) ←→ atropine (antagonist)

naloxone (Narcan): mu-opioid receptor antagonist
flumazenil (Romazicon): benzodiazepine (GABA) receptor antagonist
diazepam (Valium): benzodiazepine (GABA) receptor agonist
acetylcholine (ACh): cholinergic (muscarinic) receptor agonist


Pharmacokinetics consists of 4 phases:
• drug absorption
• drug distribution
• drug metabolism
• drug elimination
Cp(t) = UDF(t)*I(t)

# Absorption


Inhaling
Injecting
Snorting and mucosal exposure
Orally
Blood circulation
Drug delivered to the brain by blood

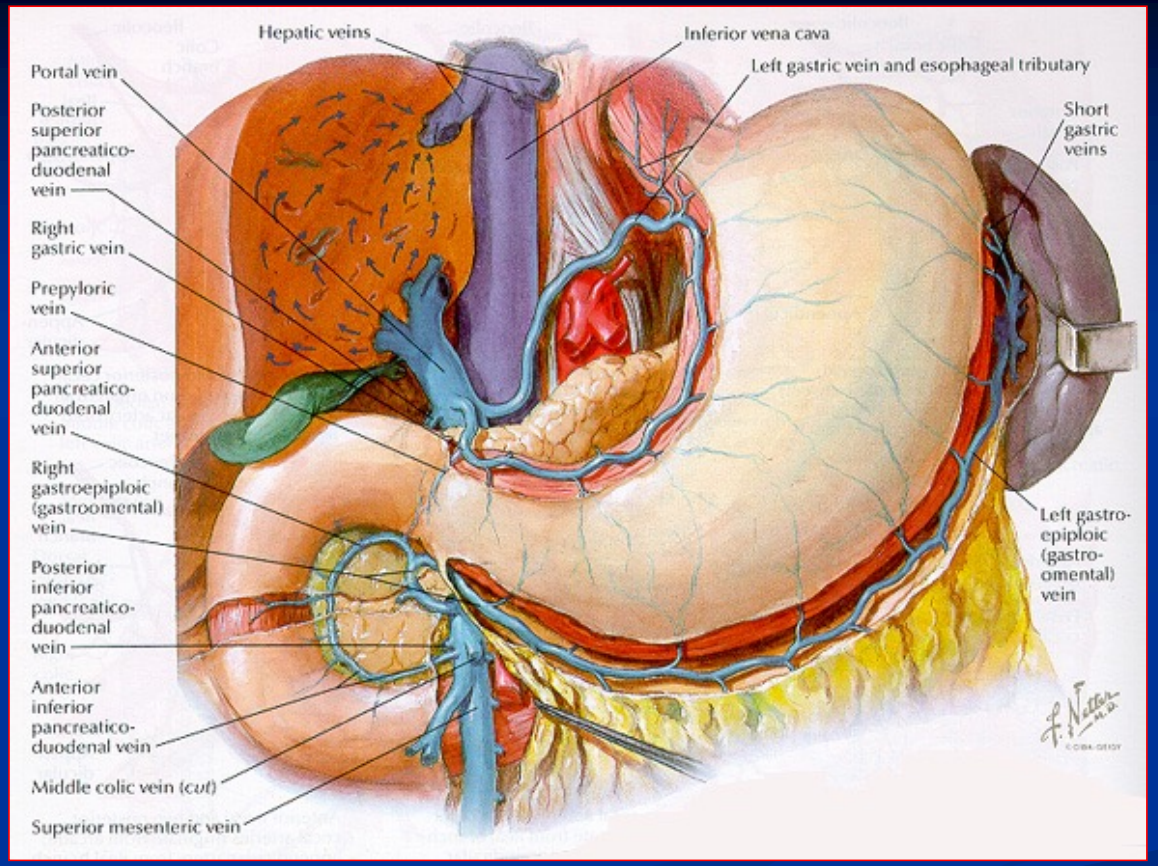
# Oral (PO)

drug is ingested

absorbed from stomach / intestine

enters hepatic portal system

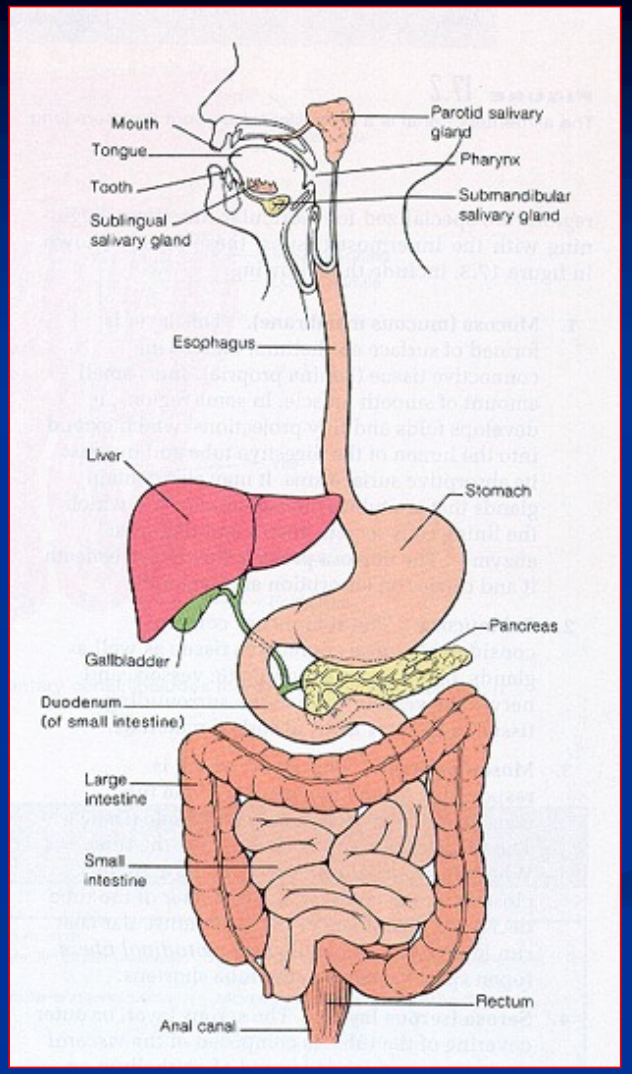
liver




drug enters general circulation

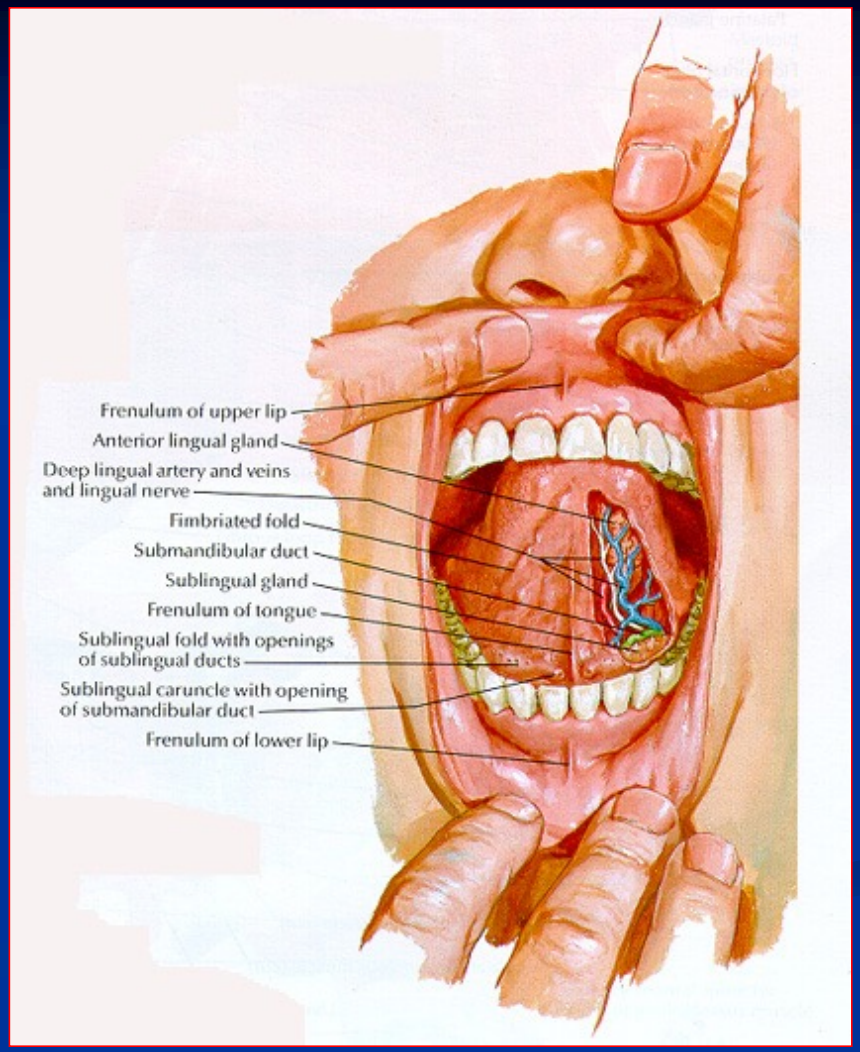
# Oral (cont.)

- oral route is convenient and economical
- once absorbed into the bloodstream, the drug enters the liver, where it may be metabolized ("first-pass effect")



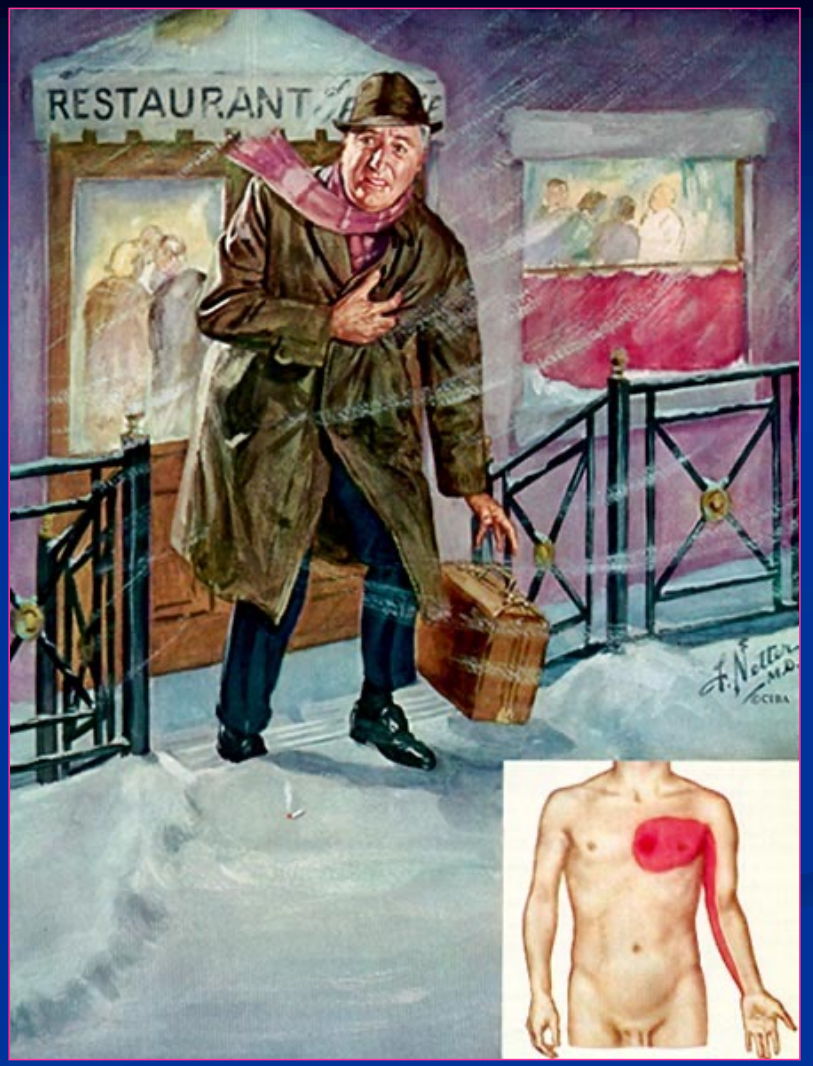
# Sublingual

- drug is dissolved and absorbed under the tongue

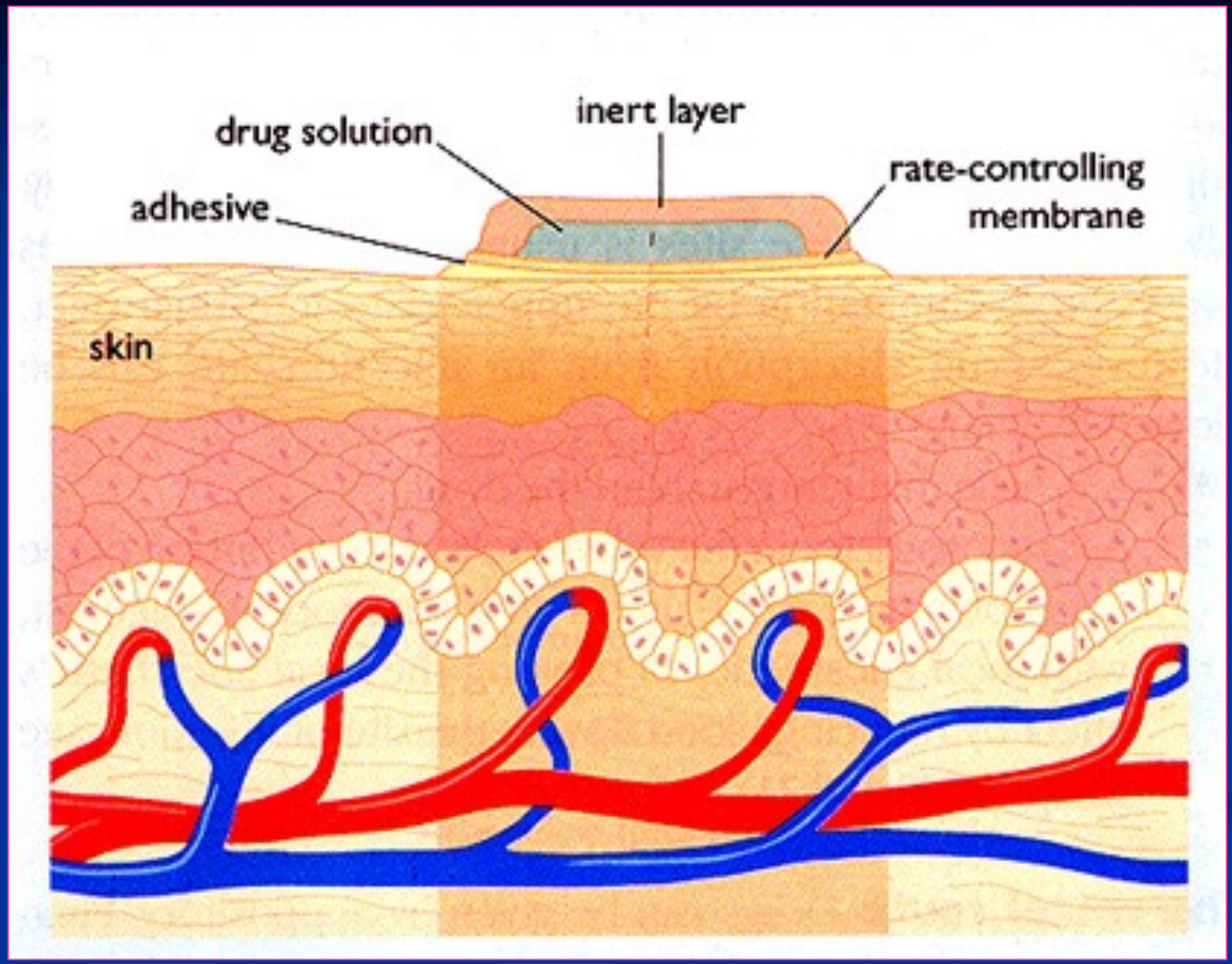


# Sublingual

## Example: Nitroglycerin SL

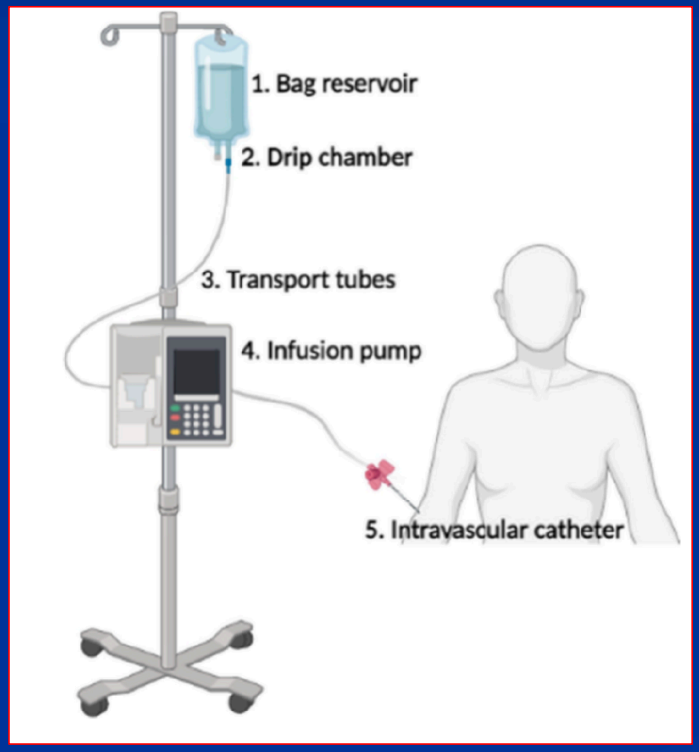



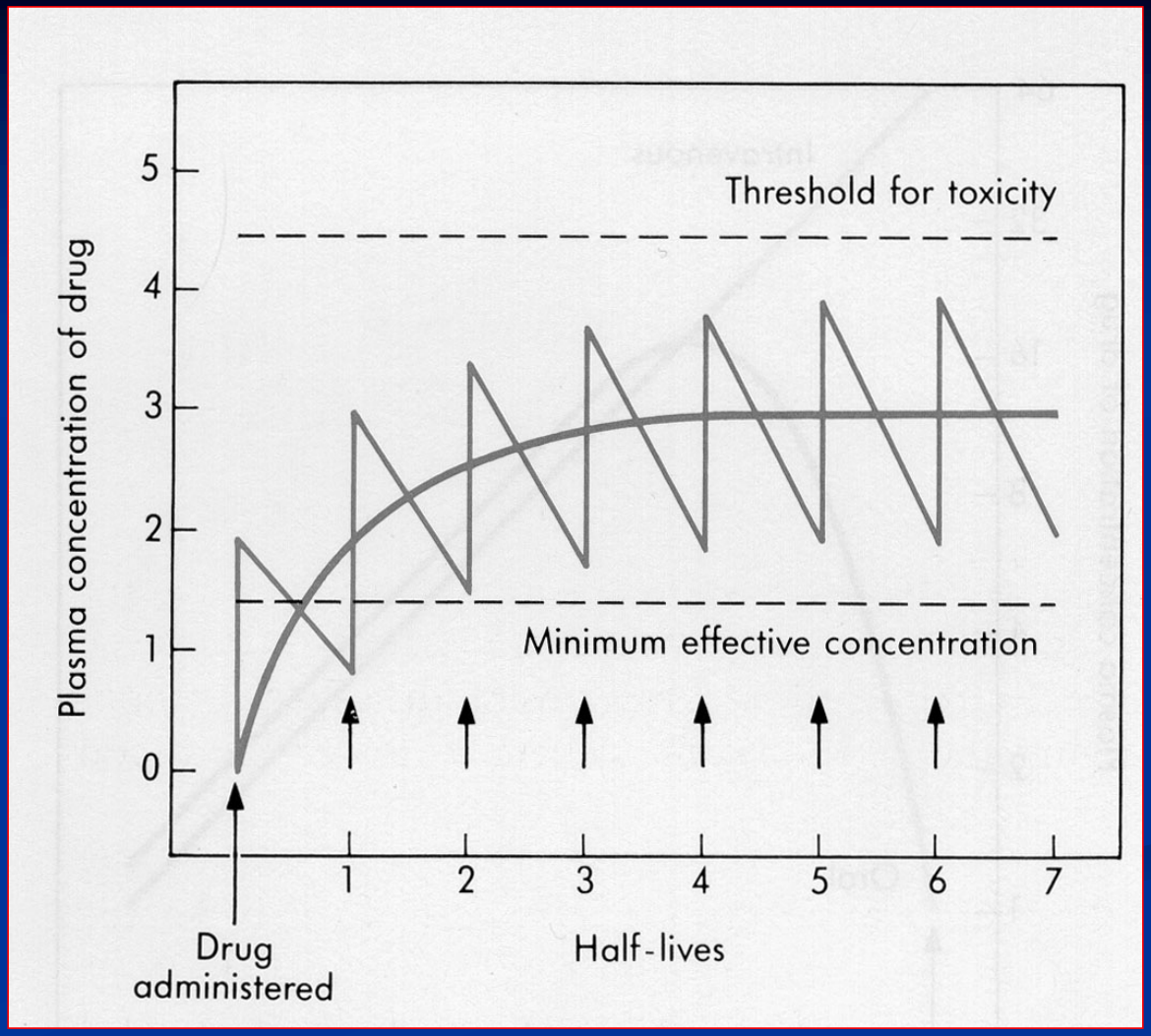
Transdermal



# Transdermal

## Continuous vs Intermittent Drug Dosing Regimens

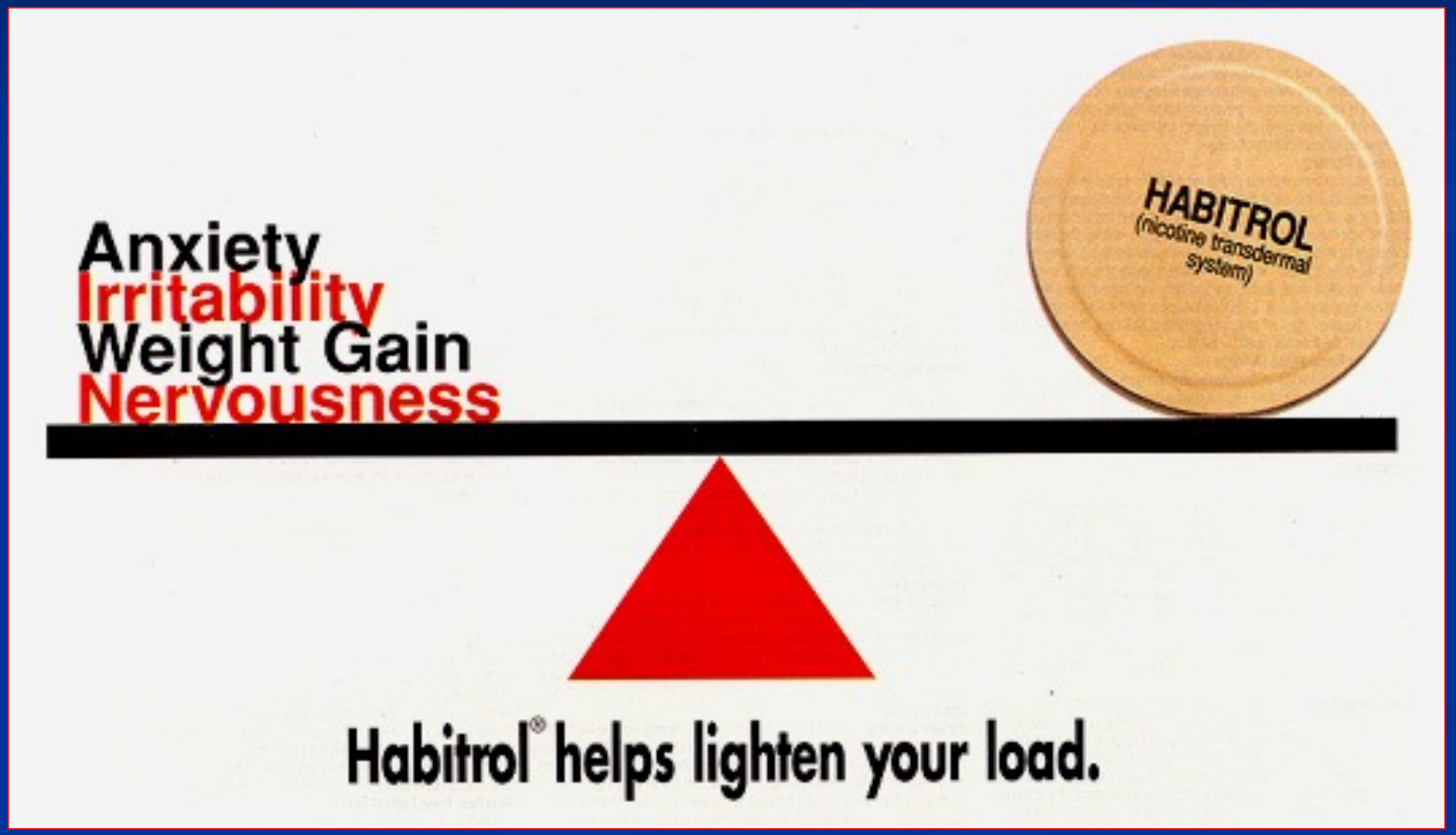


# Transdermal (cont.)

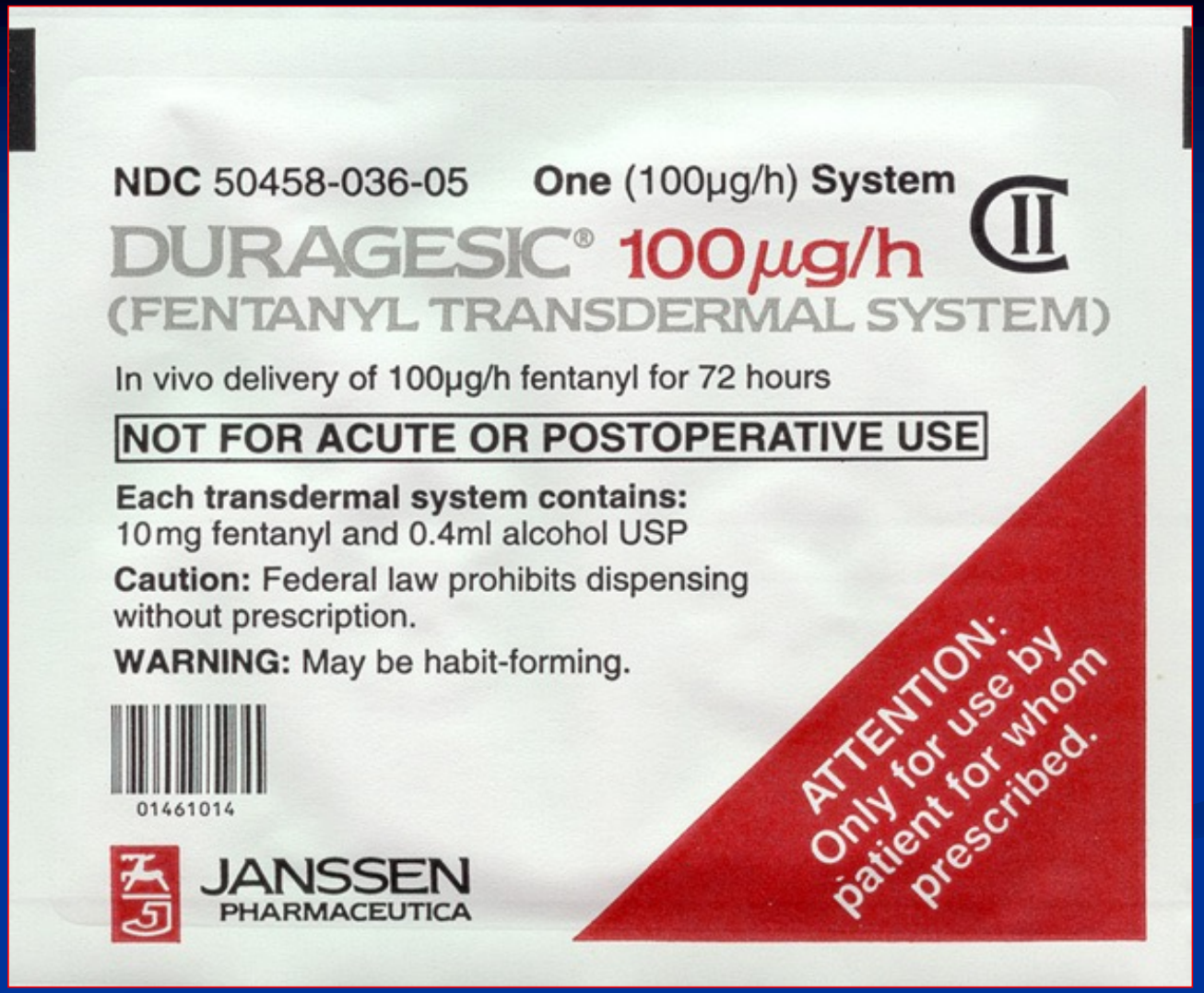
- drug patch provides continuous drug dosing
- local skin irritation may occur
- drug enters the general circulation before passing through the liver

# Example: Transdermal Nicotine Patch



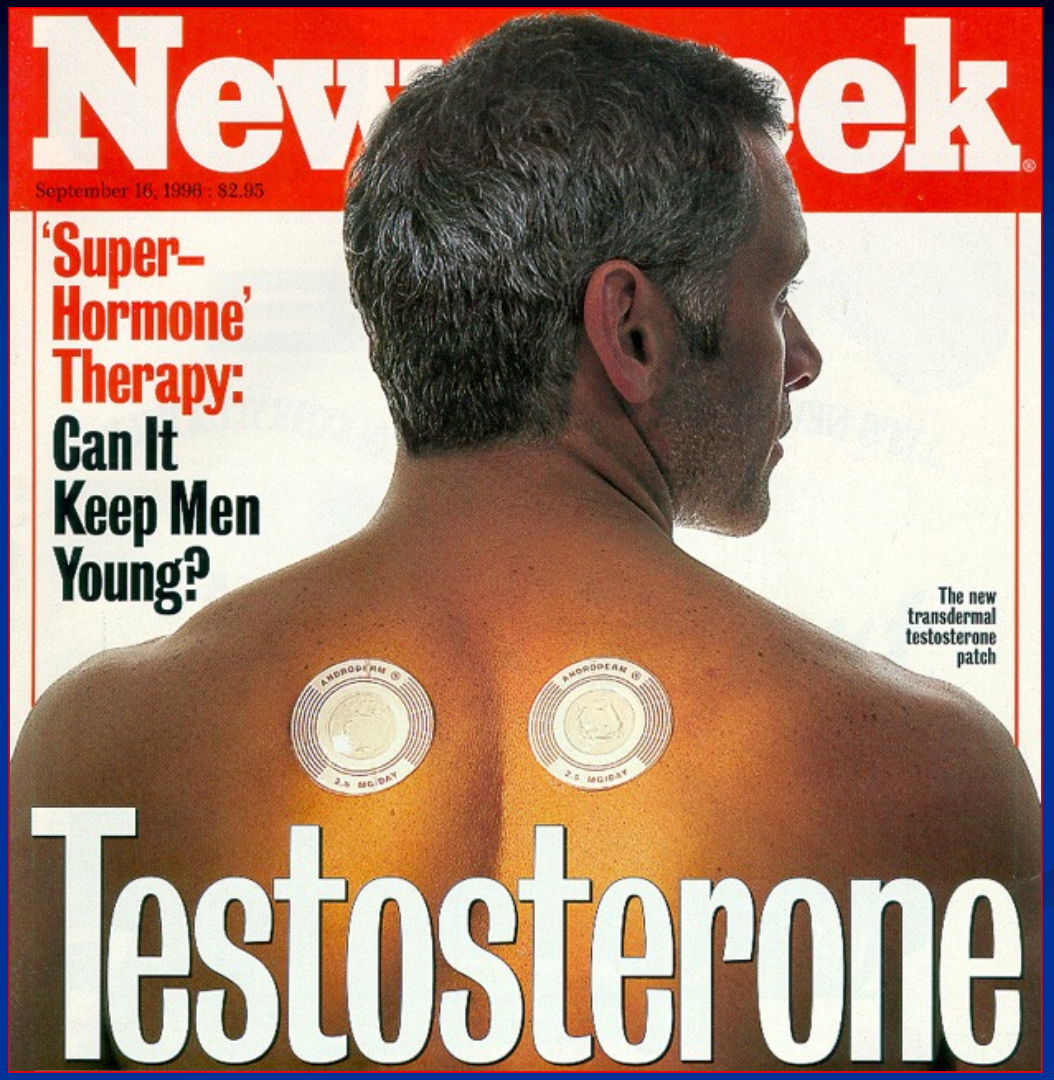
# Transdermal (cont.)

Example: Duragesic (Fentanyl) Patch



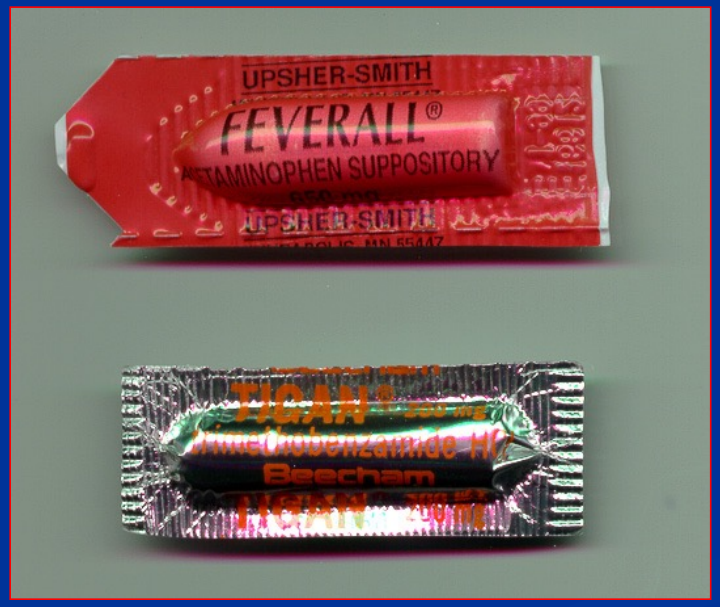
Transdermal (cont.)

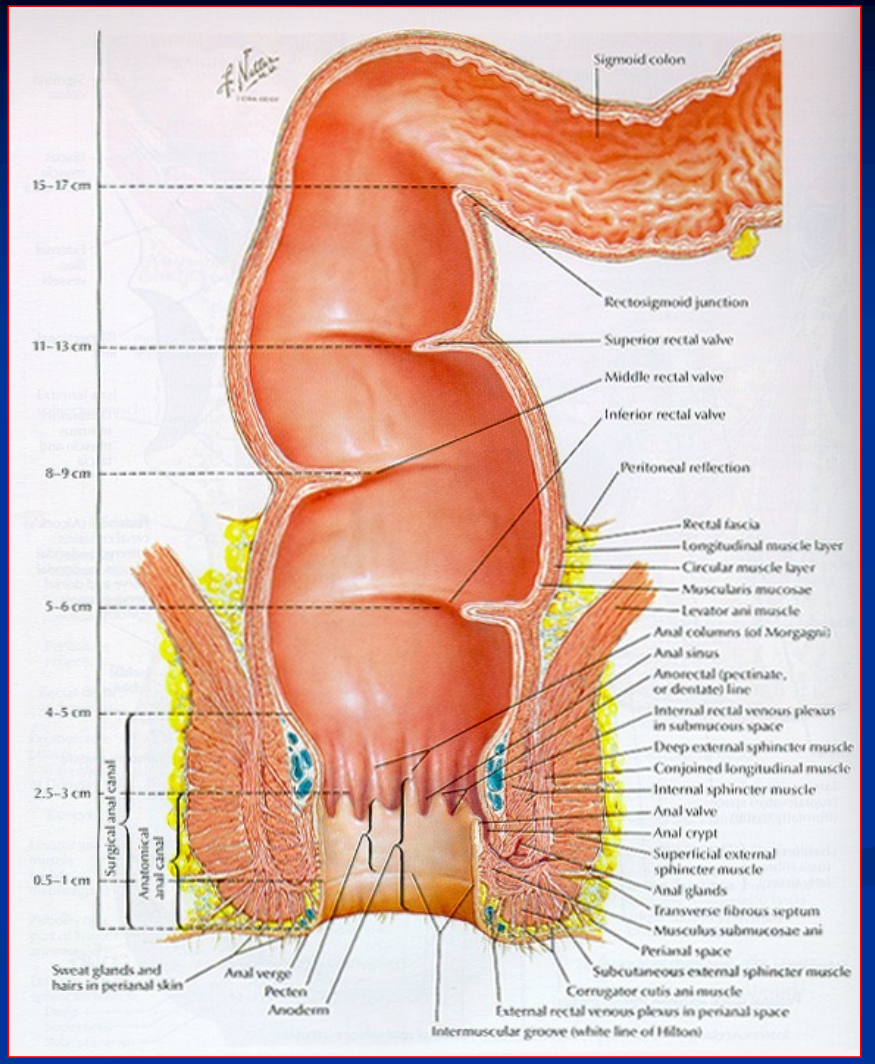
Example: Androderm (testosterone) Patch



# Rectal

Example: Acetaminophen (Tylenol) suppository



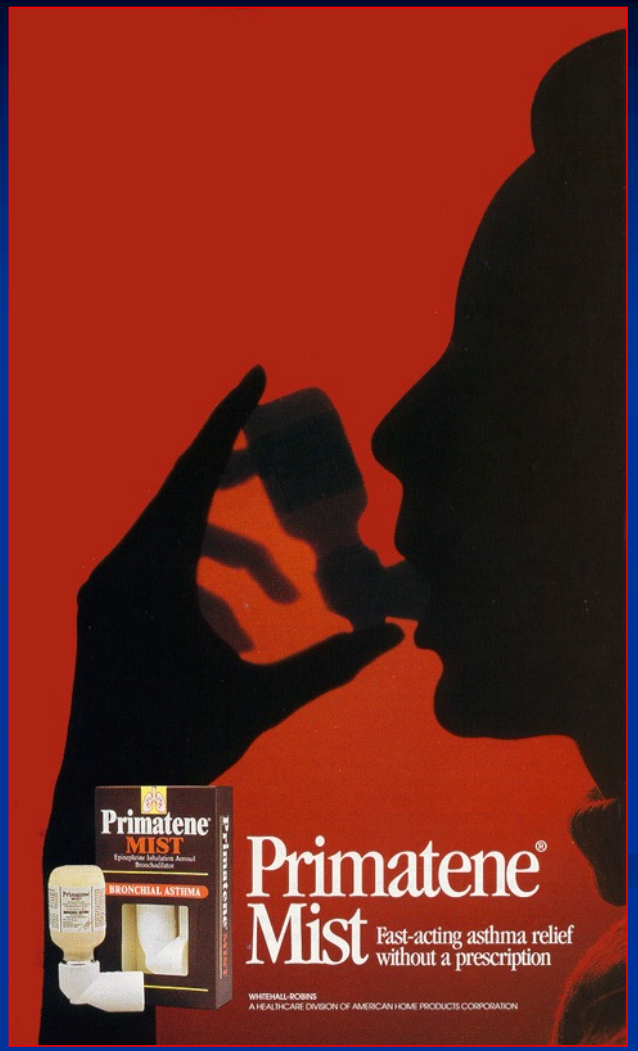



## Rectal (cont.)

- rectal route is convenient in unconscious or vomiting patients
- disadvantage: drug may be incompletely or erratically absorbed

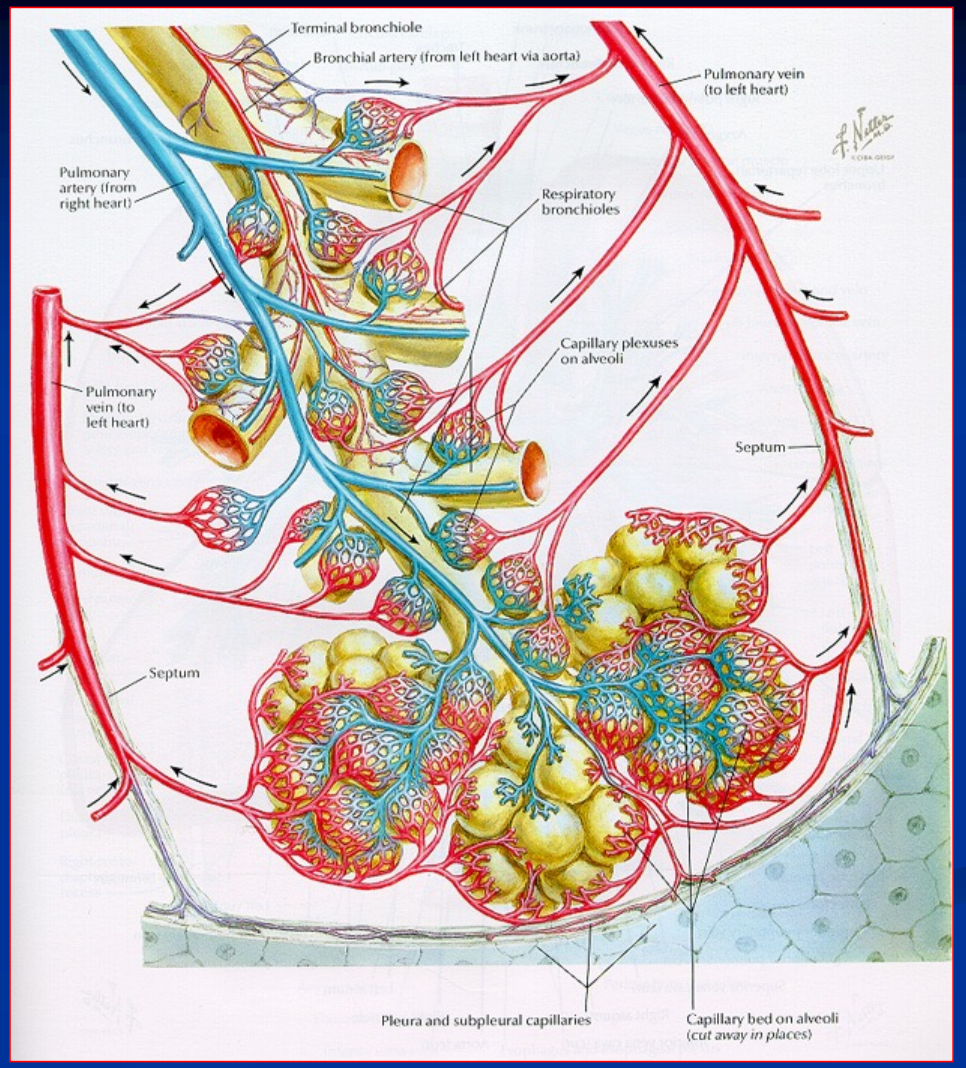
# Inhalational

- drug is inhaled as a gas or aerosol into the lungs where it either exert a localized effect on lungs (e.g., bronchodilation) or ....



... the drug enters the bloodstream through the lungs

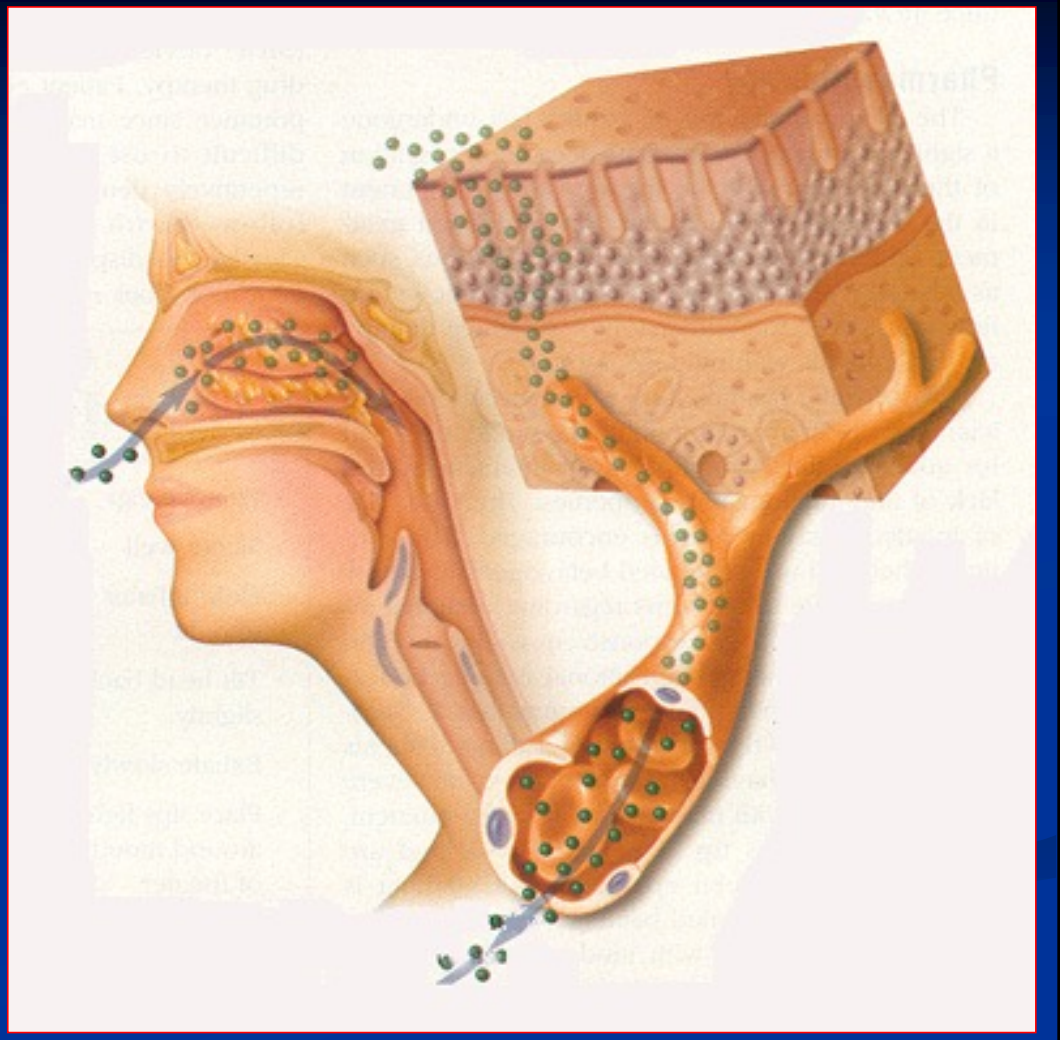
- inhaled drug produces a rapid onset since it enters the general circulation shortly after being inhaled



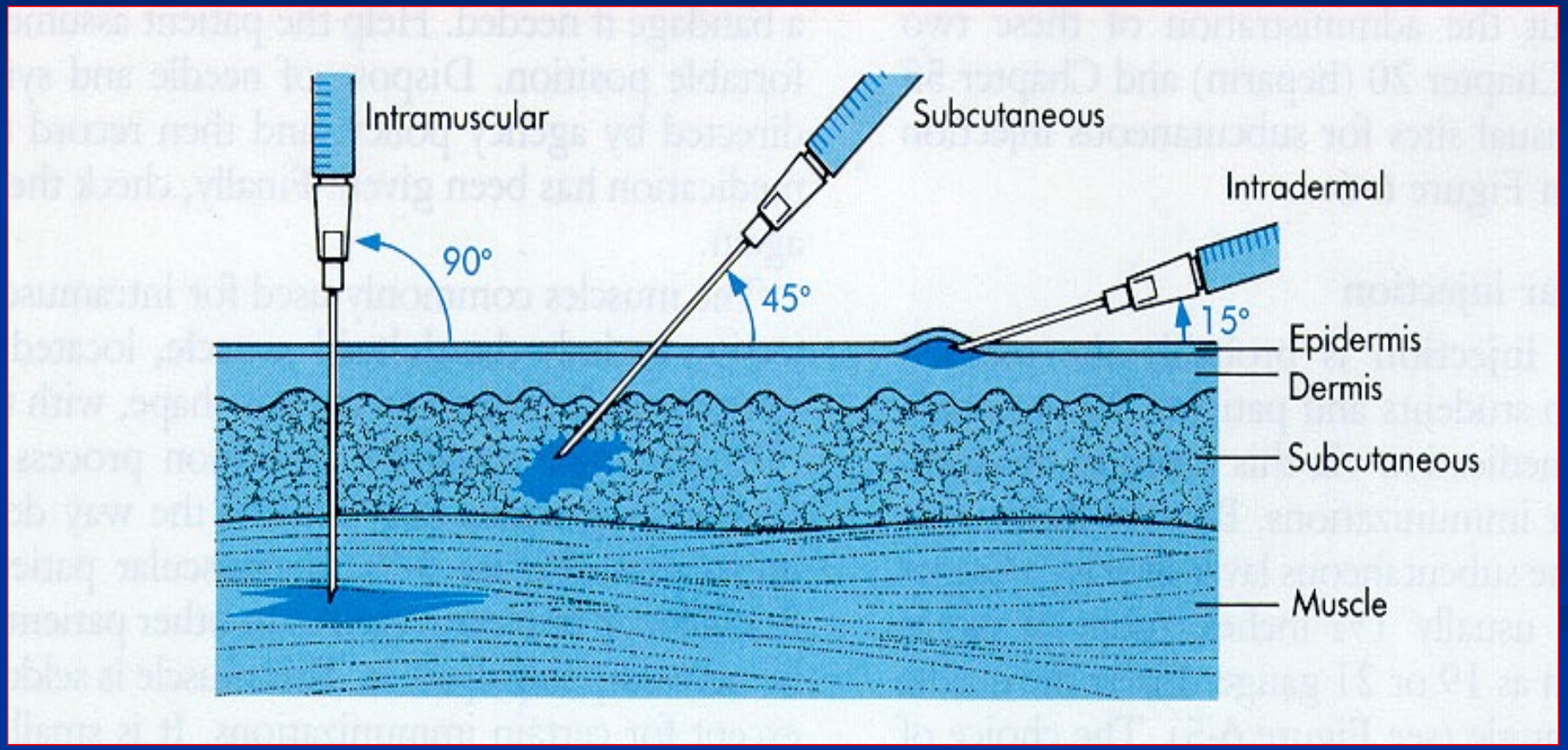
# Intranasal


NDC 0078-0311-90
2 VIALS & APPLICATORS
SANDOZ
Miacalcin®
Nasal Spray
(calcitonin-salmon)
Nasal Solution
200 IU calcitonin-salmon
per actuation, 2200 IU/mL
FOR INTRANASAL USE ONLY
REFRIGERATE UNTIL OPENED
Caution: Federal law prohibits
dispensing without prescription.
200 IU/dose 2 mL size


Neo-Synephrine®
PHENYLEPHRINE HCl 0.5%
FAST RELIEF
GOES RIGHT
TO THE CORE
OF YOUR
CONGESTION
NASAL
DECONGESTANT
REGULAR
STRENGTH
SPRAY
1/2 FL OZ
(15 ml)



# Parenteral route (IV, IM, & SC)



# Parenteral route (cont.)

- advantages:
  - drug response: IV >IM> SC
  - avoids unpredictable absorption processes of GI tract
  - useful in unconscious or uncooperative patients

# Parenteral (cont.)

- disadvantages:
  - requires sterile conditions to prevent infections
  - more costly than other routes of administration
  - once injected, a drug cannot be retrieved
  - pain at injection site

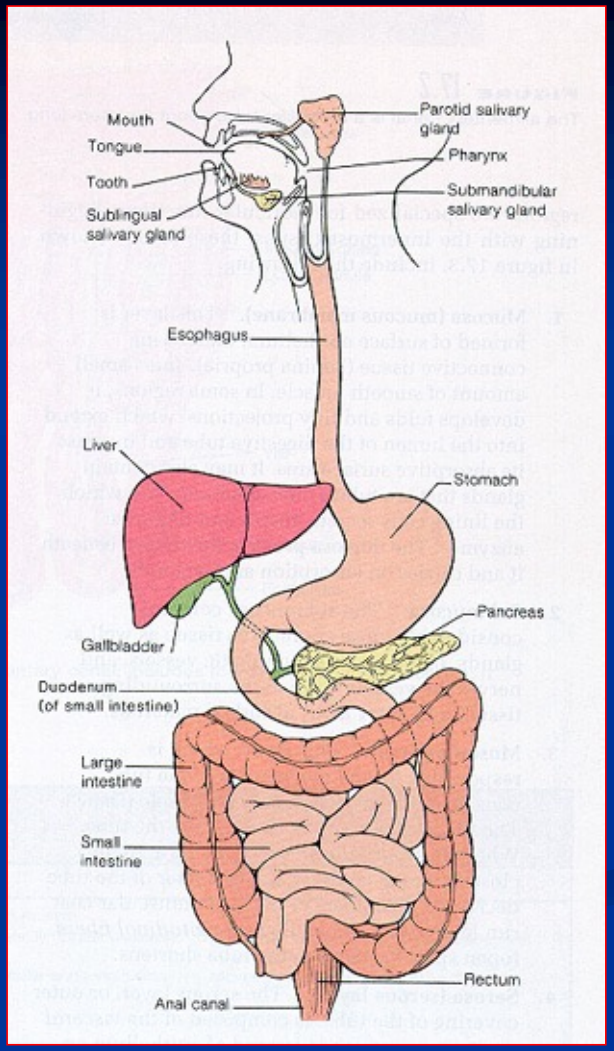
# Drug Distribution

- general rule: small and highly lipophilic drug molecules penetrate cell membranes, capillaries, and physiological barriers (i.e., placenta, blood-brain-barrier, etc...) more readily than larger, polar (non-lipophilic) drug molecules

# Characteristics of Drug Absorption (GI tract)

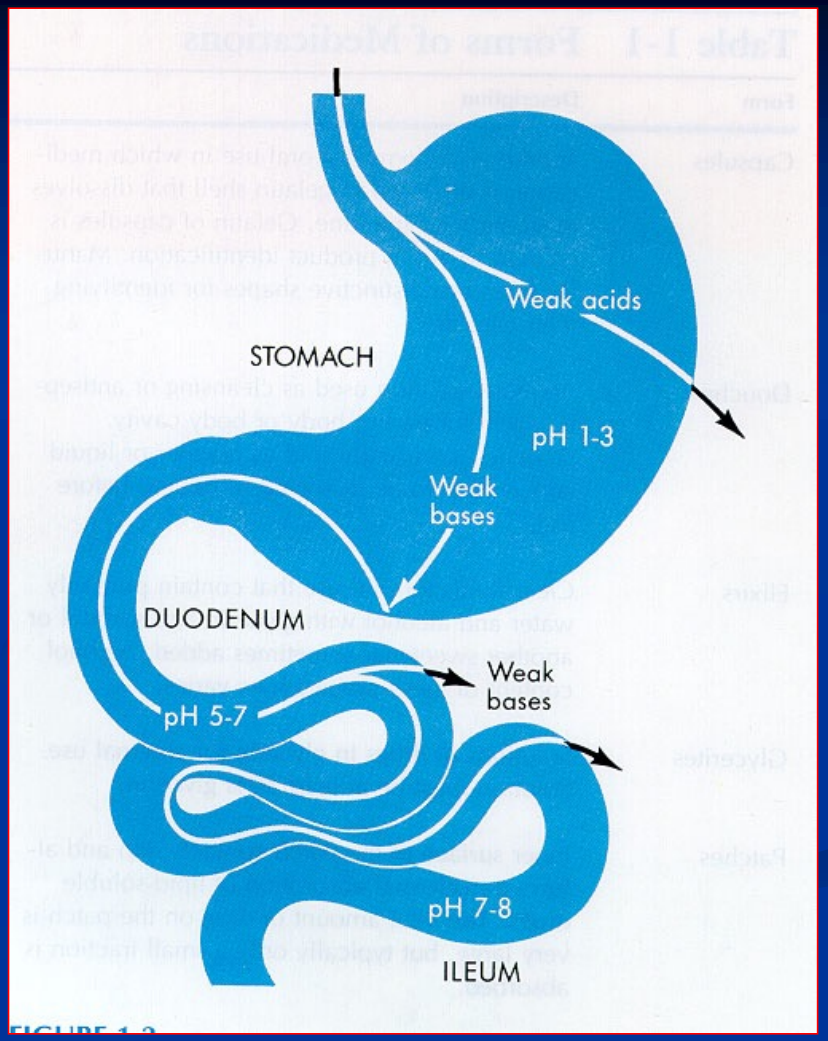
a. drugs must be relatively lipid-soluble to pass through the membranes of the GI tract

b. drugs either exist in lipid-soluble form or non-lipid soluble form depending on their pH environment



# Characteristics of Drug Absorption (GI tract)

- pH environment changes along the GI tract:
  - stomach (highly acidic)
  - small intestine (slightly alkaline)



# Bioavailability

- describes what proportion of the administered drug is available to produce a pharmacologic response
- factors influencing bioavailability:
  - drug dissolution
  - inert ingredients (binders, disintegraters, lubricants, buffers, etc...)

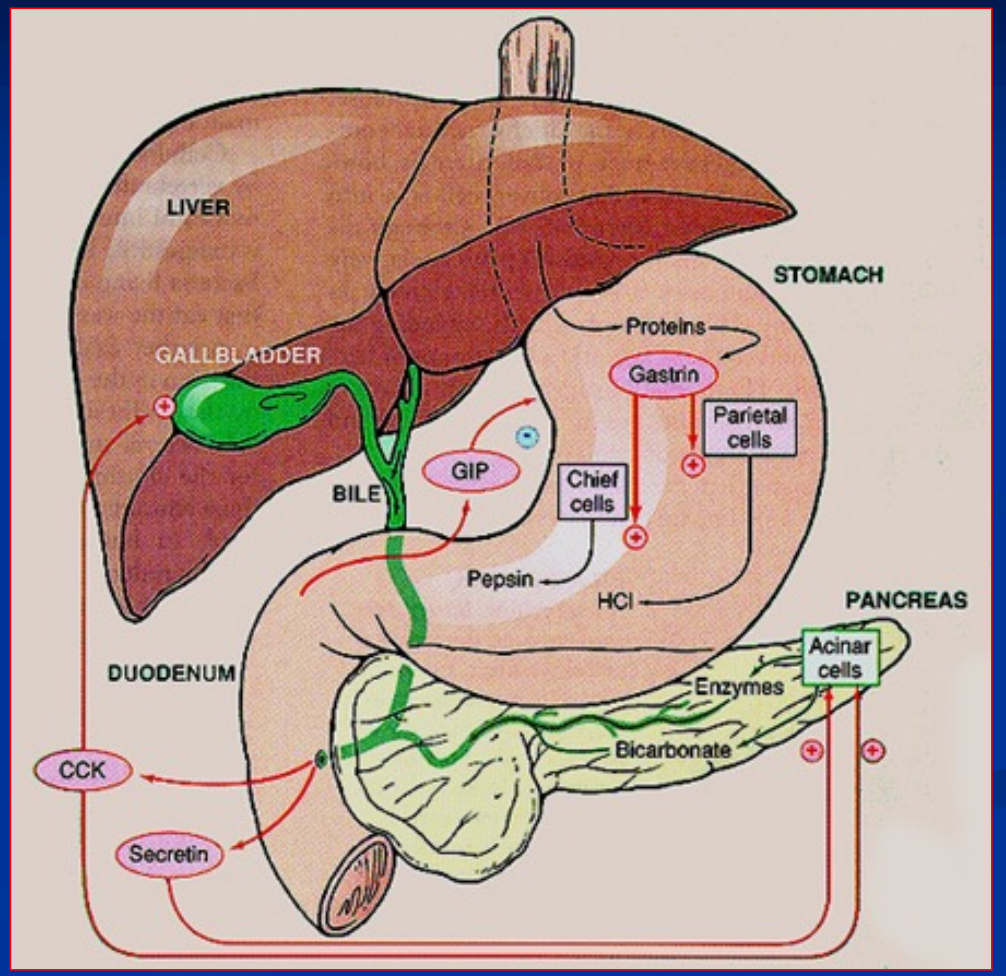
# Factors influencing bioavailability: GI Tract

- presence of food may affect dissolution and absorption of drugs
  - Tetracycline (TCN) + dairy products
    - → TCN binds to calcium
    - → unabsorbed TCN excreted in feces

## ii. GI tract (cont.)

- achlorohydria
- deficiency in pancreatic and intestinal secretions

  → prevents dissolution of enteric-coated tablets

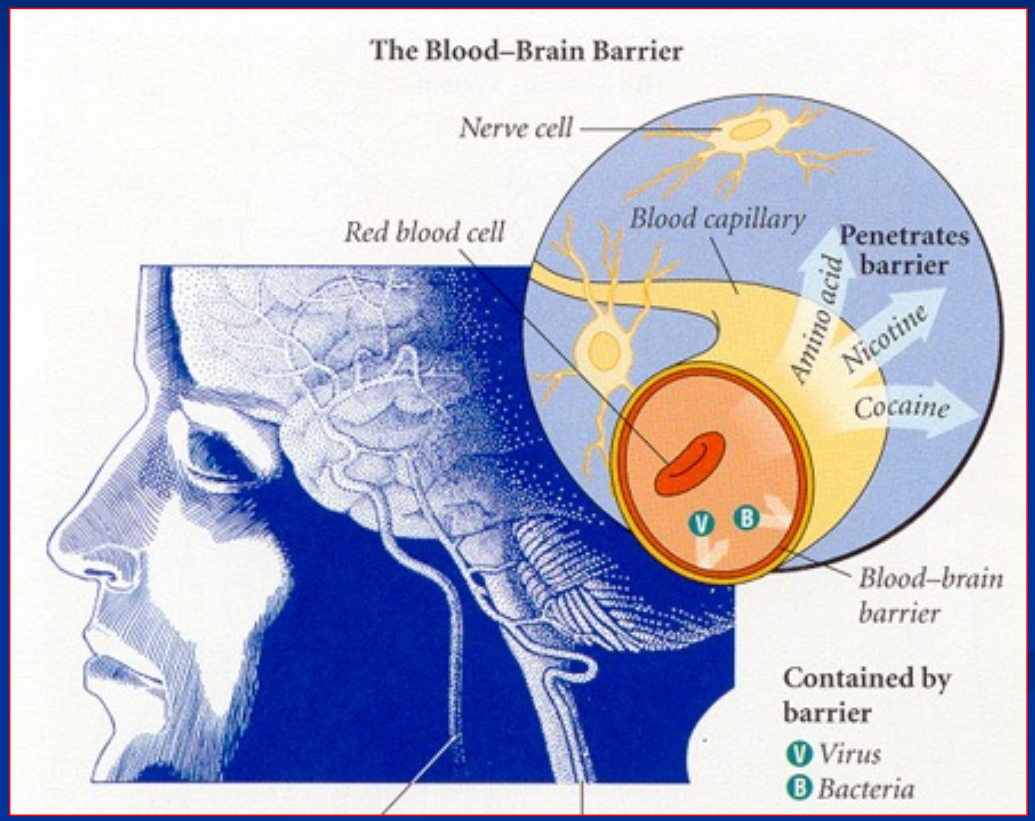


# Drug Distribution (cont.)

- the degree to drug distribution depends on the physical and chemical properties of a drug and its ability to penetrate cell membranes, capillaries, blood-brain barrier, placenta, etc....

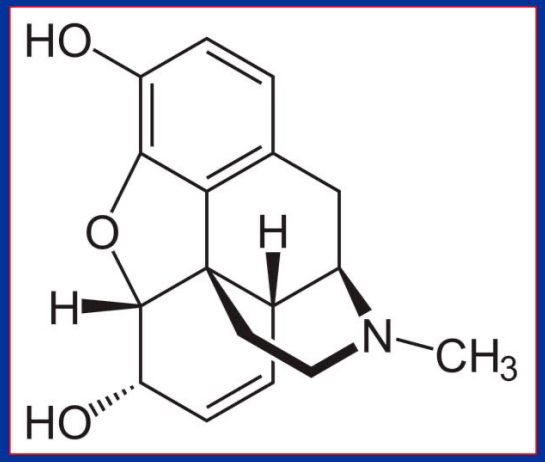
# Blood-Brain-Barrier (BBB)

- only lipid-soluble drugs and very small molecules are capable of crossing the BBB to exert an effect on the brain

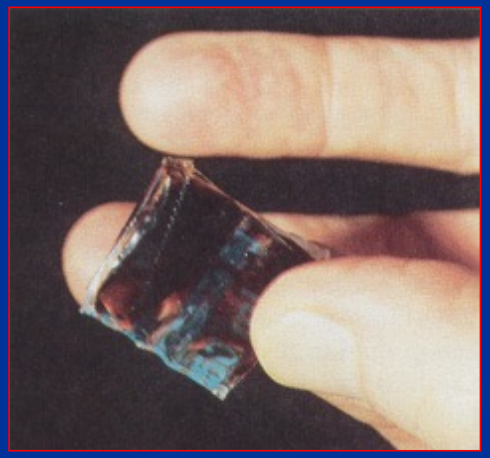


# Blood-Brain-Barrier (cont.)

- heroin crosses the BBB more readily than morphine because of its greater lipid solubility factor




Morphine



Mexican “tar” Heroin

# Drug Distribution: Plasma Protein Binding

- many drugs bind to plasma reversibly with plasma proteins (e.g., albumin)
  - only unbound or "free" drug may:
    - diffuse through capillary walls
    - produce a pharmacological effect
    - be metabolized
    - be excreted

# Plasma Protein Binding (cont.)

"free" drug ←→ protein-bound drug

circulating drug reservoir

prolongs the action of drugs

# Plasma Protein Binding and Drug-Drug Interactions

Aspirin (ASA)

↓

ASA displaces warfarin from albumin binding site

↓

increase in "free" warfarin drug levels

↓

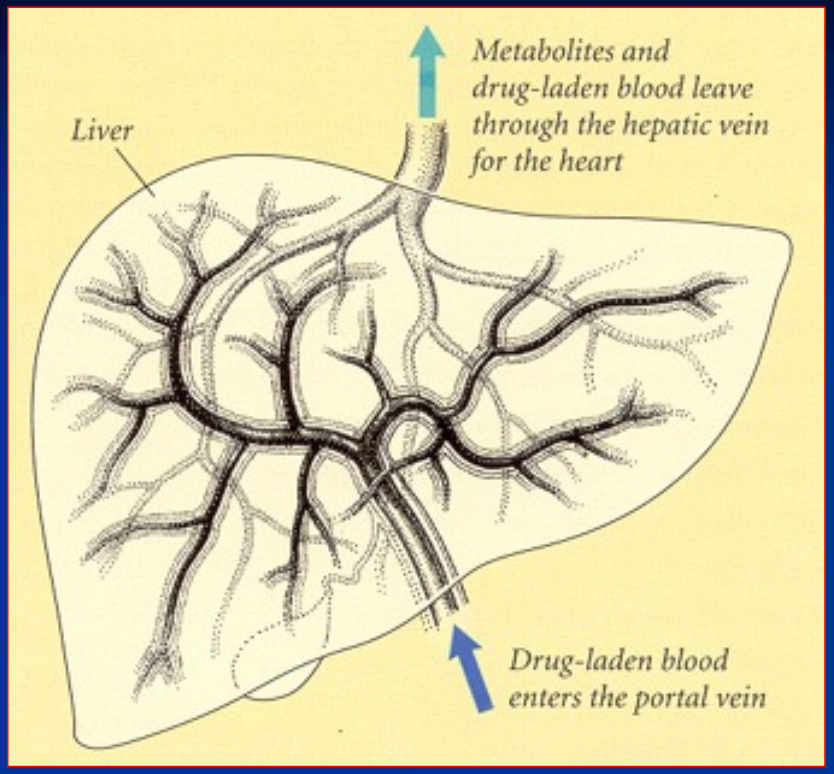
increases risk of bleeding

- Warfarin (Coumadin) is an anticoagulant.
- Aspirin (ASA) is an antiplatelet drug.

# Tissue Trapping

- certain tissues (e.g., adipose tissue) are capable of trapping or storing drugs temporarily or permanently, converting them into “inactive” form
- when drugs leave the tissue-binding site, they become active again

# Drug Biotransformation (Drug Metabolism)




- the liver is the major organ responsible for metabolizing drugs

- the liver converts lipid-soluble drugs to water-soluble drug → excreted by kidneys

# "First-Pass Effect" of the Liver

- the "first-pass effect" of the liver inactivates potentially harmful chemicals and drugs before being distributed in the general circulation throughout the body

# Induction / Inhibition of Drug Metabolism (Liver)

i. induction of enzymes (metabolism)

(nicotine)

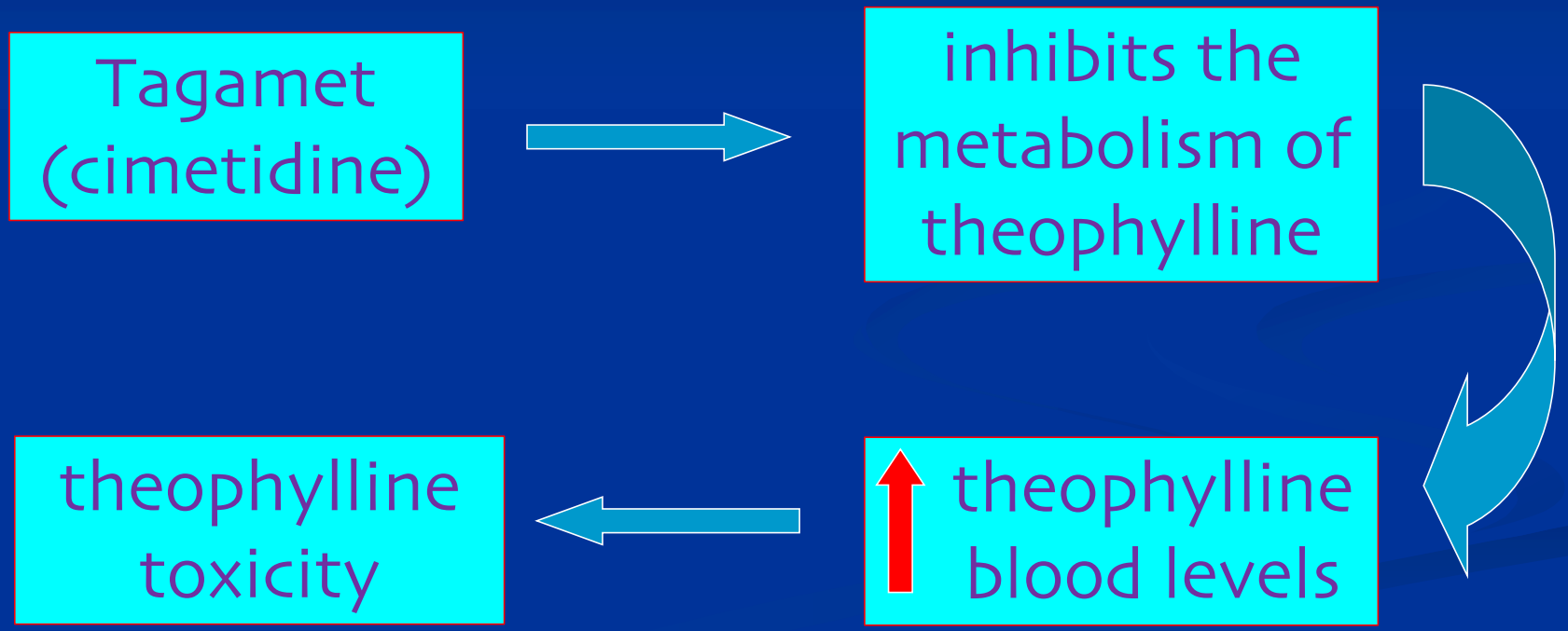
induces metabolism of theophylline

theophylline blood levels

wheezing

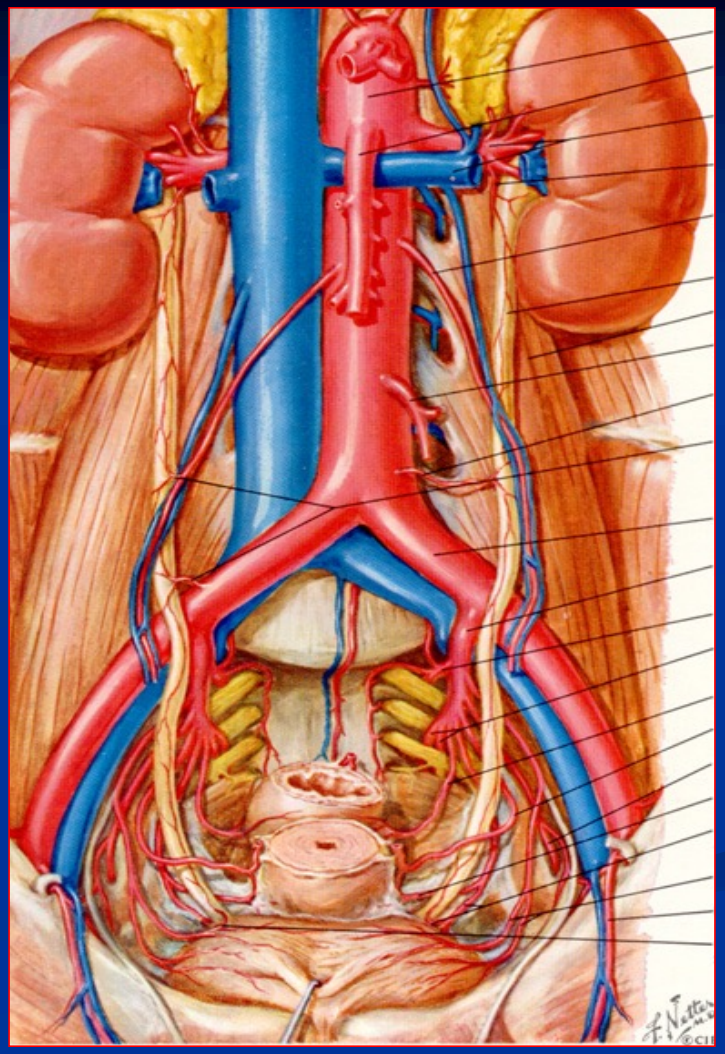
# Induction / Inhibition of Drug Metabolism (Liver)

## ii. inhibition of enzymes (metabolism)



# Drug Elimination (Kidneys)

- it is estimated that kidney function decreases by 10% per decade of life after 20 years of age



# Elimination of Drugs in the Feces

(a) metabolized drug → bile → feces

(b) enterohepatic recirculation

- metabolized drug is secreted in bile

  → enters small intestine

  → reabsorbed and returns to liver

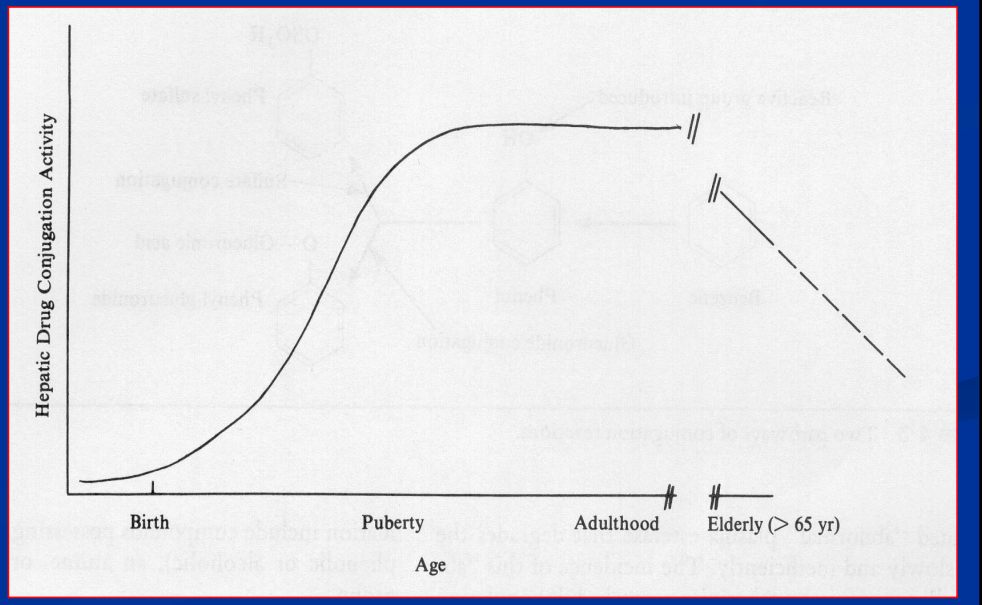
  → secreted in bile

# Drug Elimination & Age Considerations

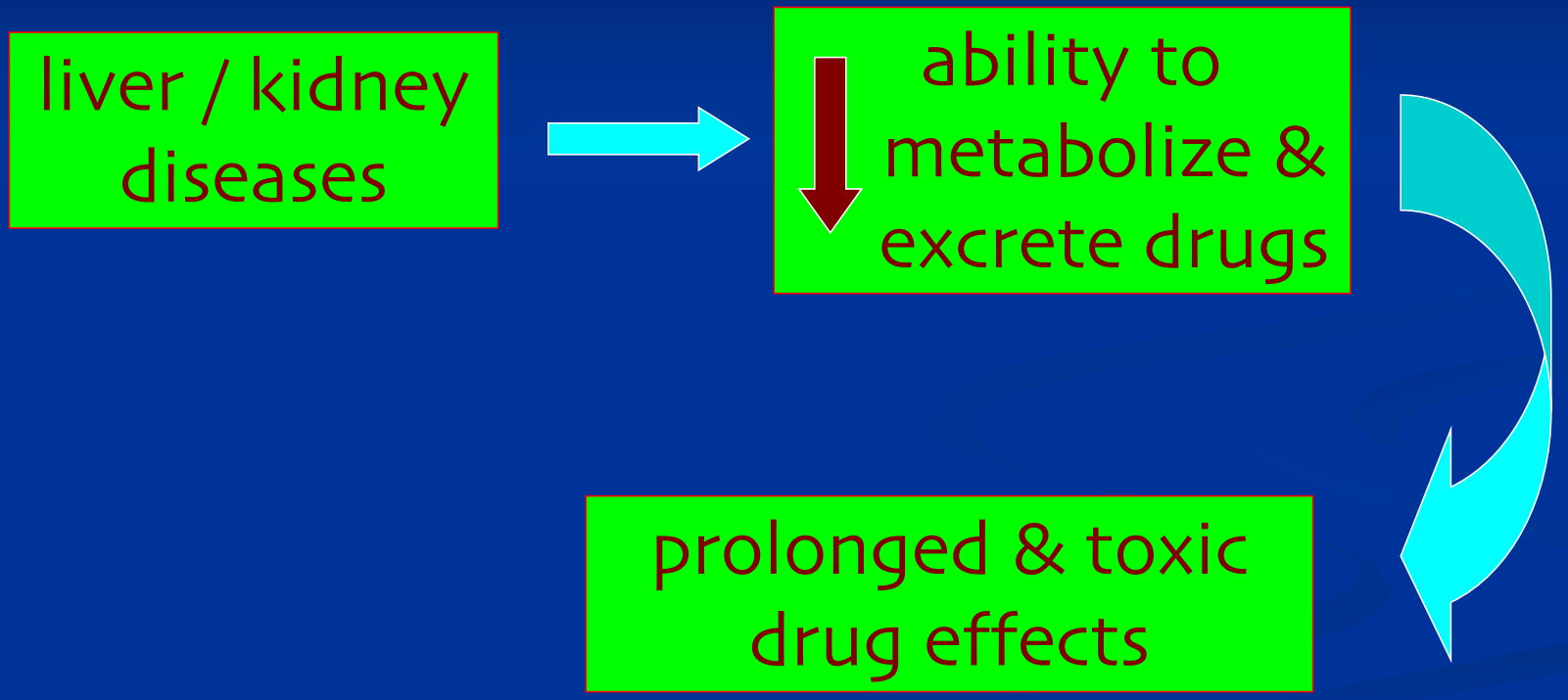
- infants → underdeveloped ability to metabolize and excrete drugs

- elderly → impaired ability to metabolize and excrete drugs

Drug Metabolism (Liver) and Age Considerations

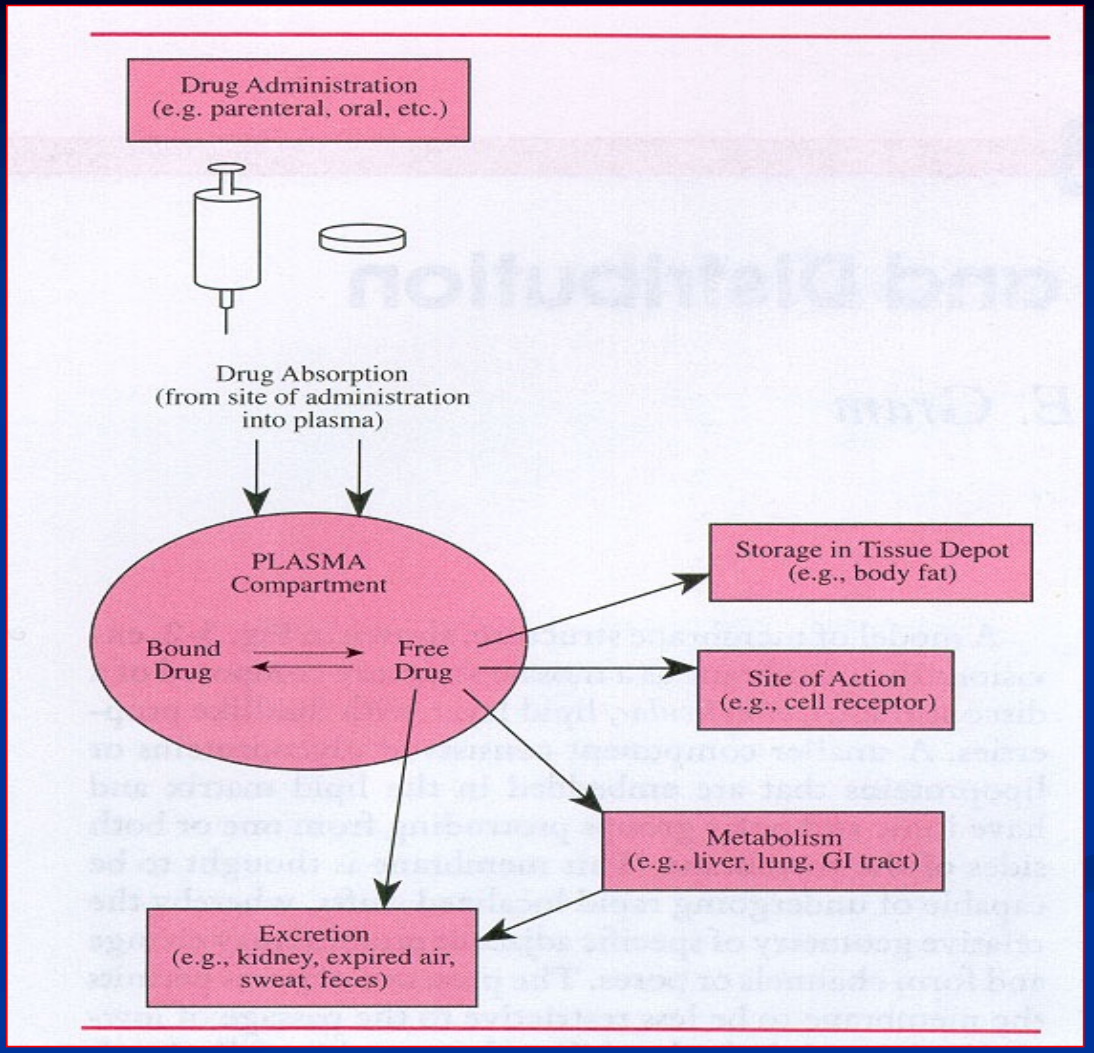


# Disease & Drug Elimination Rates



# Summary:

## Pharmacodynamics
## &
## Pharmacokinetics




PHARMACY
CLOSED