Pharmacology / Toxicology

Diphenhydramine (Benadryl) is _____.

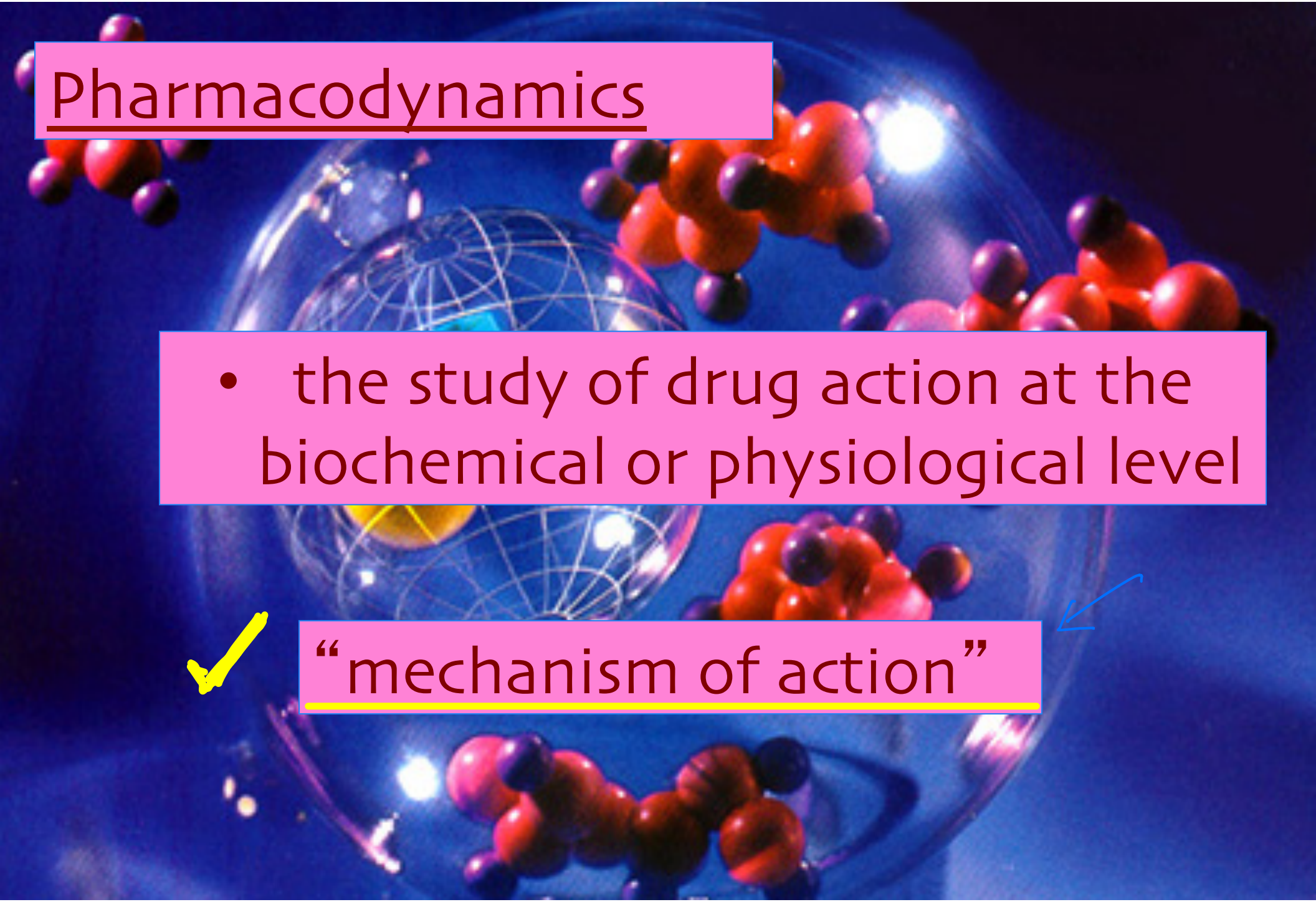
- ○ (A) an "inverse agonist"
- ○ (B) an antihistamine which prevents allergic reactions.
- ○ (C) an "inverse antagonist."
- ● (D) A & B
- ○ (E) A, B, & C

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:

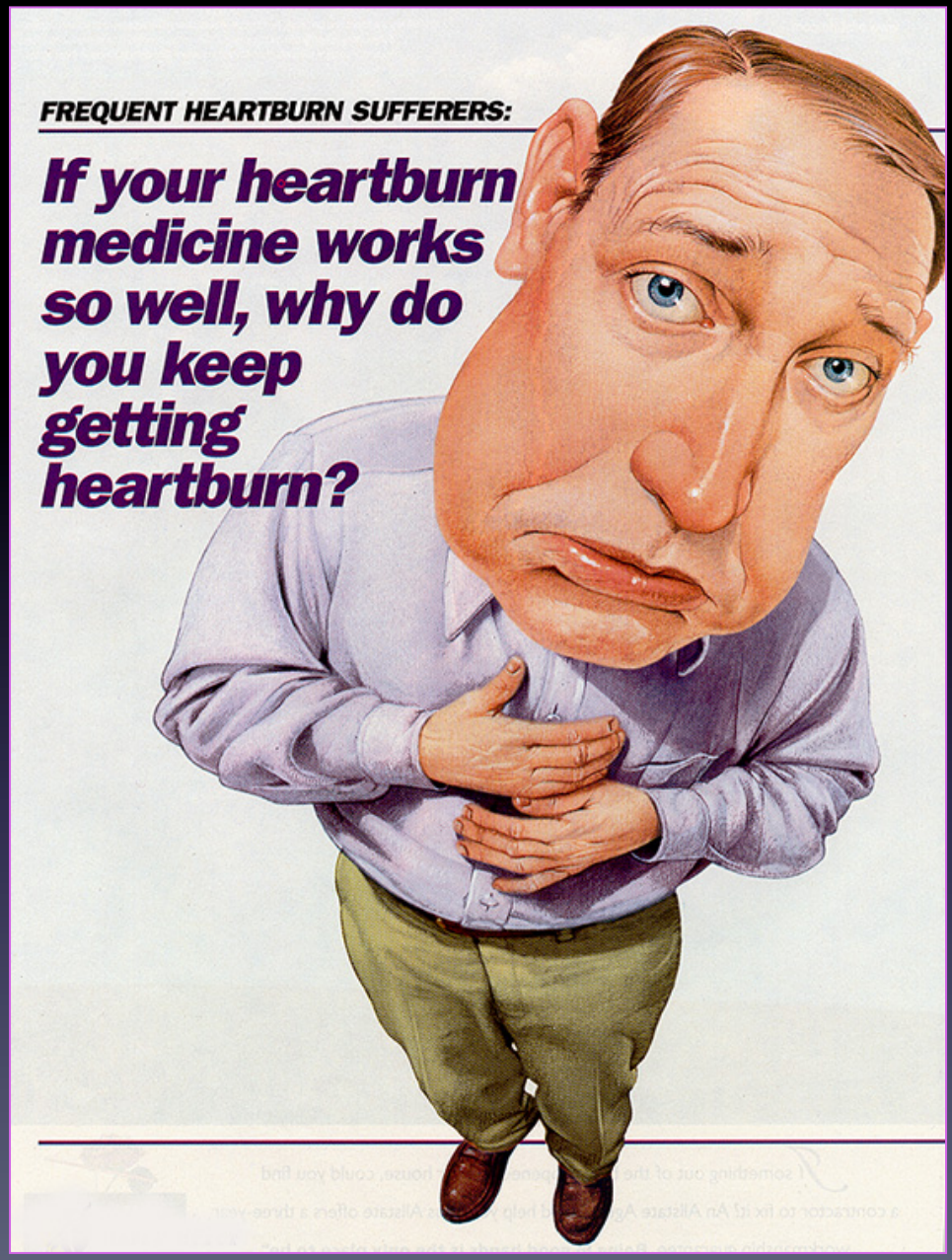
(1) enter the body

(2) reach site of action

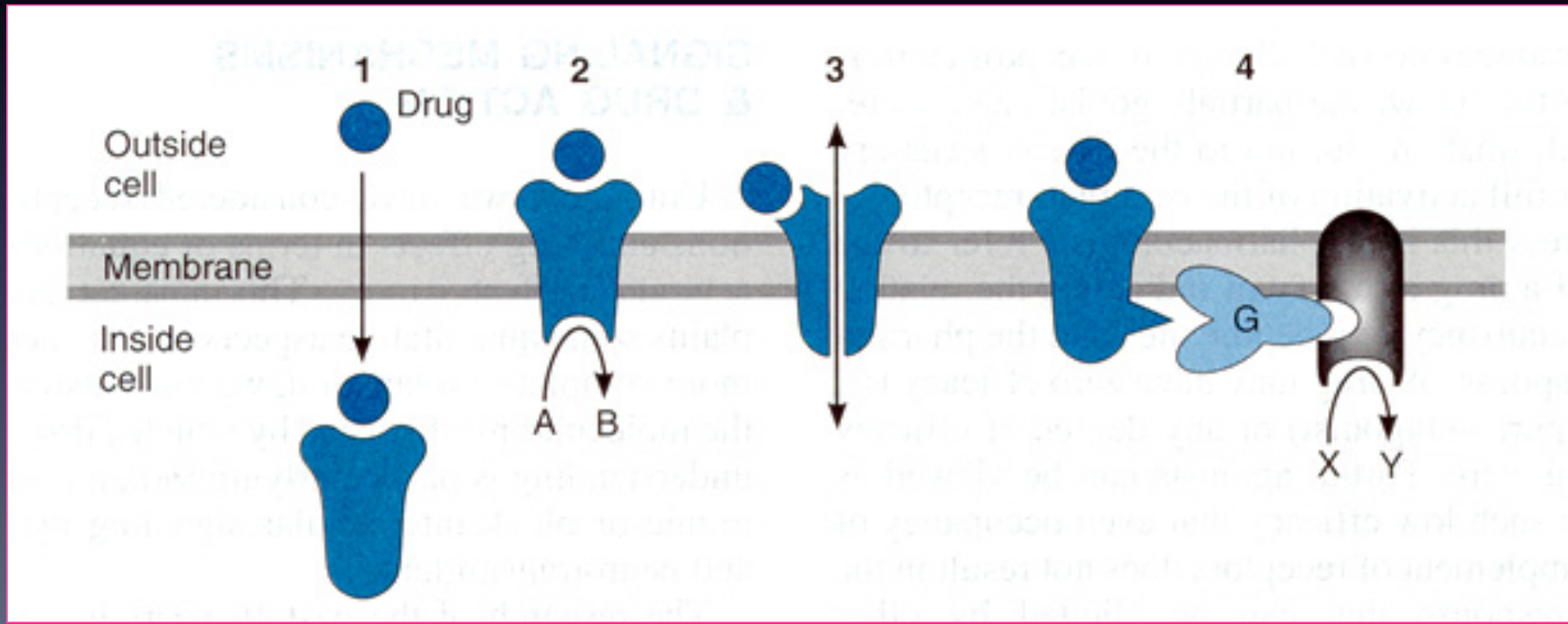
(3) are eliminated from the body

PHARMACODYNAMICS

A. Drugs that change the environment of cells

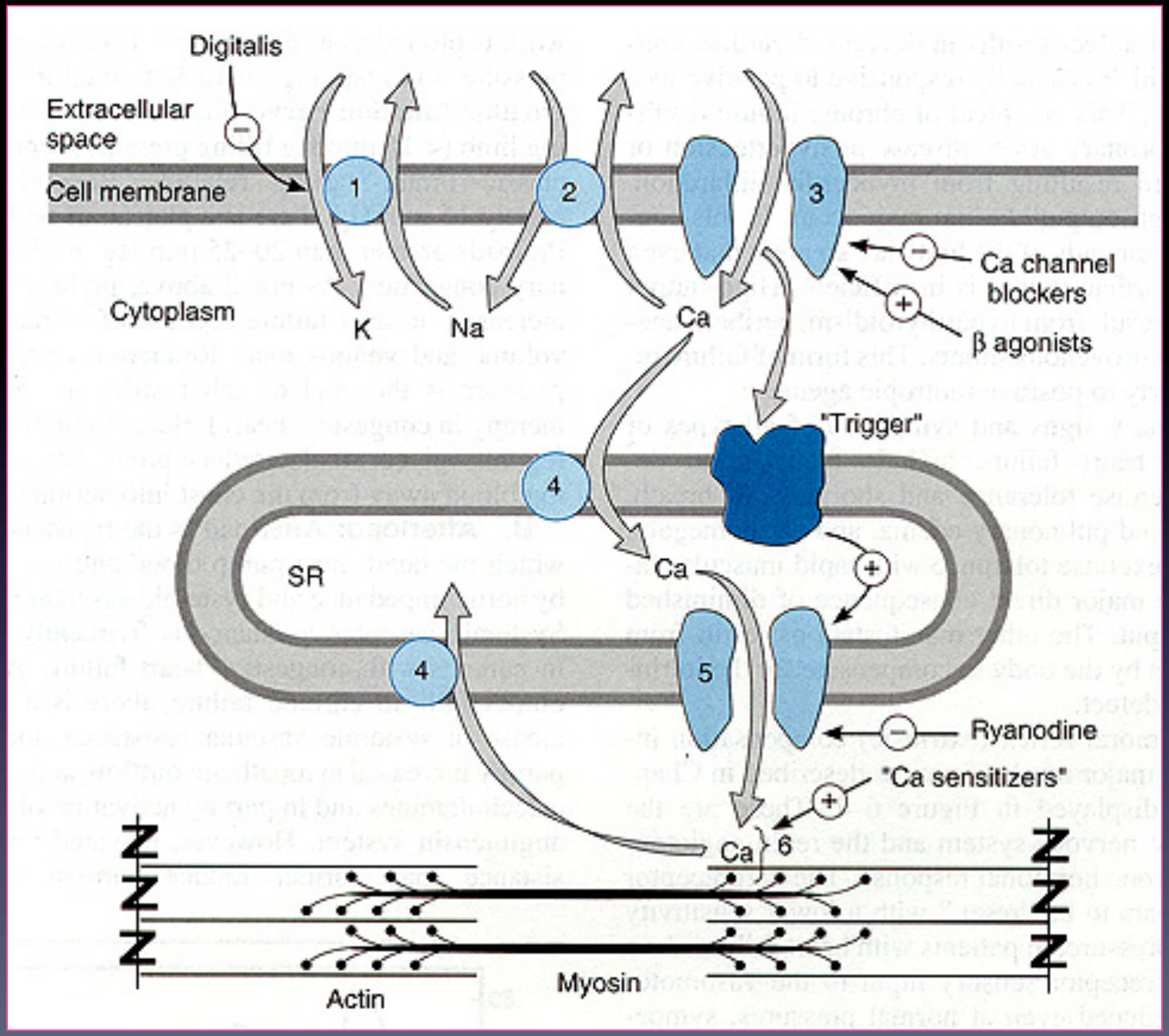


B. Drugs which bind to receptors on cell membranes and alter cellular physiology --> drug receptor interaction ("lock-and-key" mechanism)

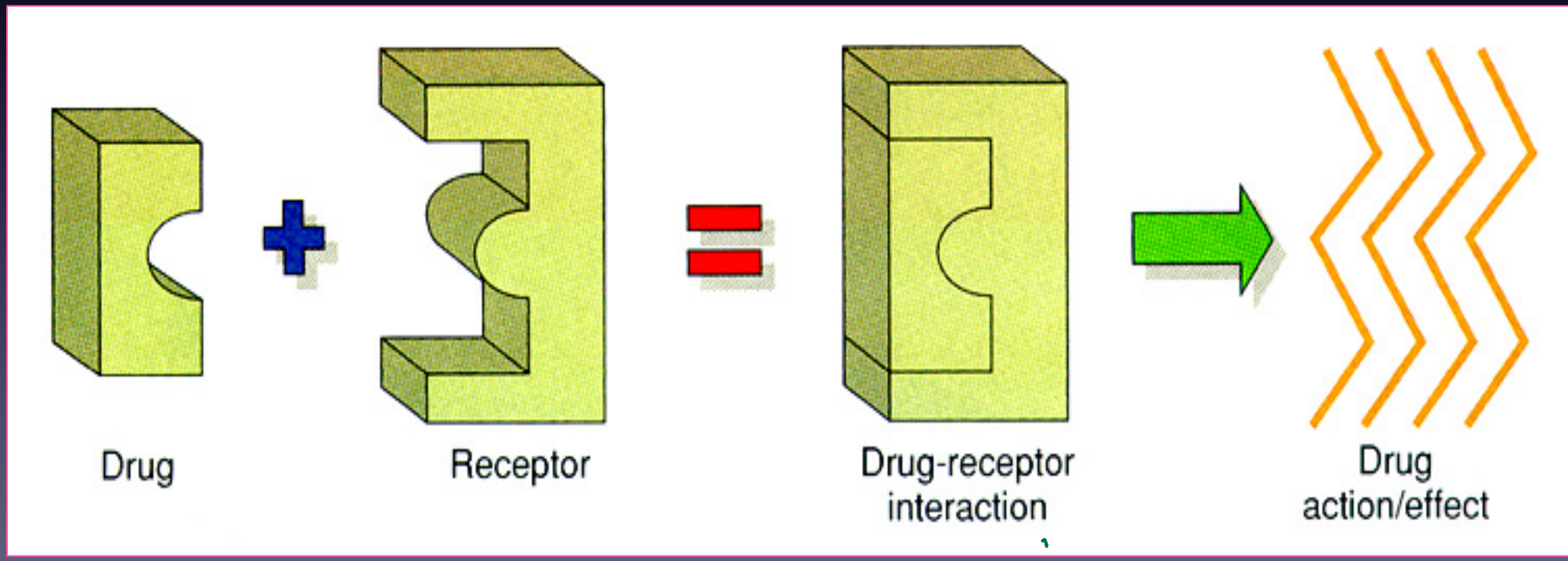


example:

digoxin
(Lanoxin)



agonist - drug which binds to a specific receptor and produces a physiological effect by stimulating the receptor

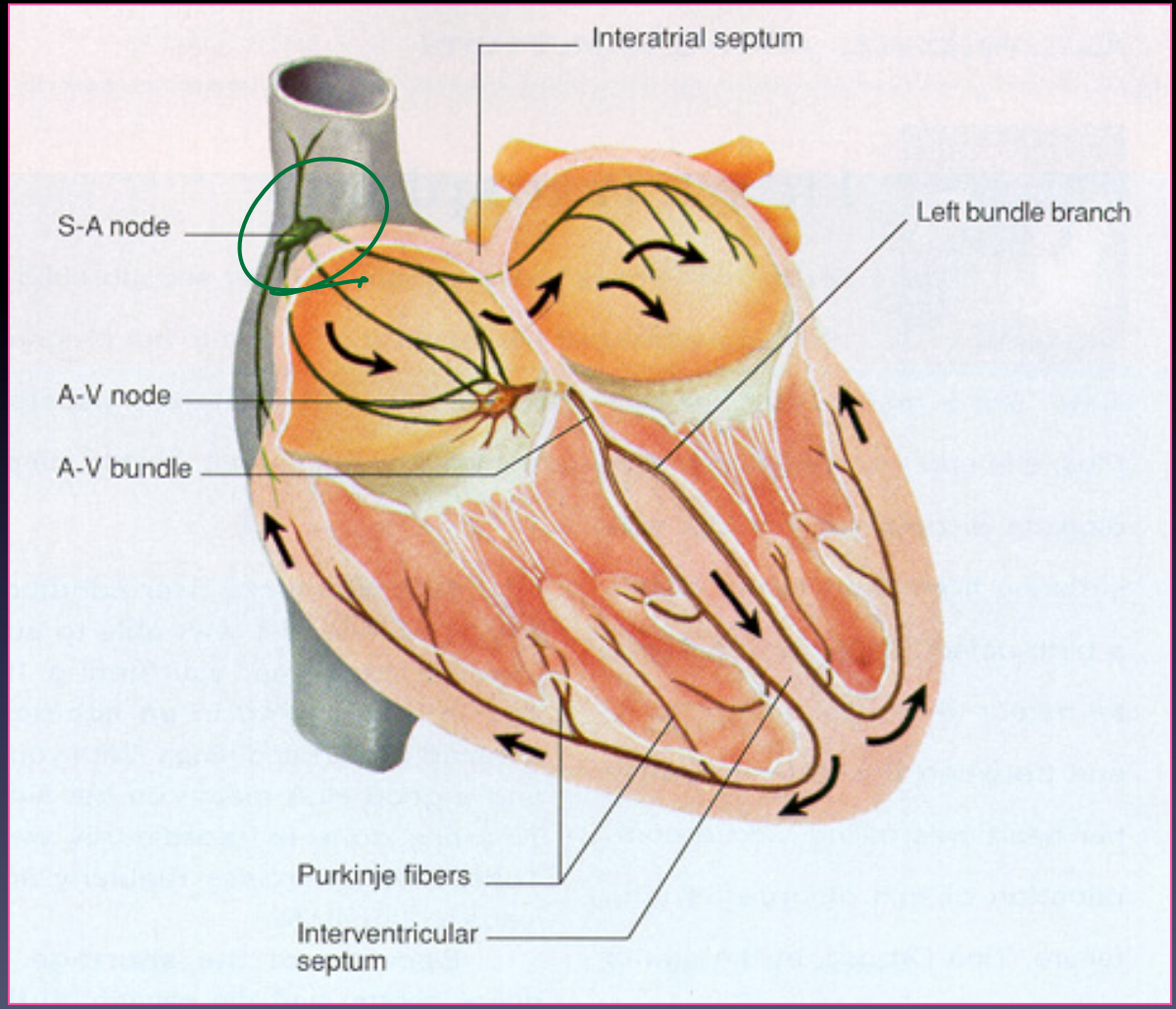


✓ whereas propranolol (Inderal) blocks β_1 receptors → ↓ HR → ↓ BP

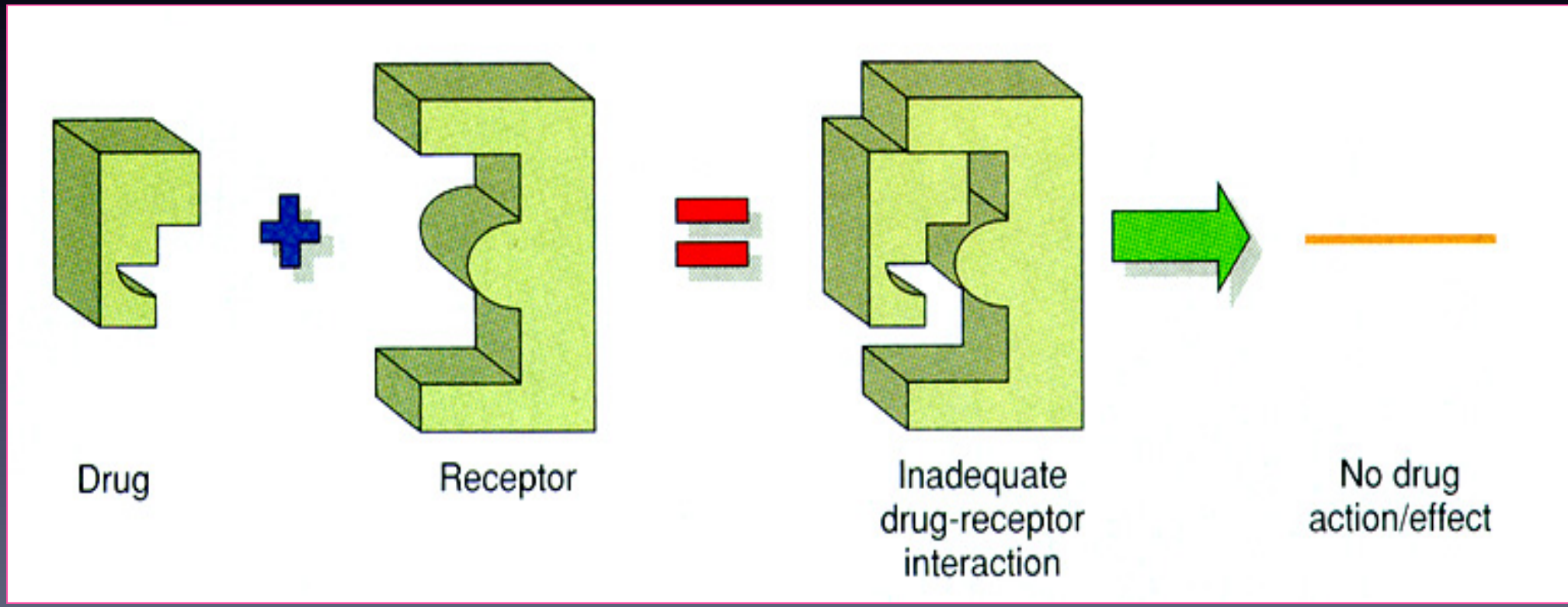
✓ Norepinephrine (NE)

--> stimulates beta-1 receptors (SA node)

--> increases heart rate



antagonist - drug which binds to a specific receptor and blocks other substances from stimulating the receptor



antagonist (cont.)

"inverse agonist"

Benadryl (diphenhydramine)

~~blocks~~ alters histamine receptors --> ~~blocks~~ prevents allergic reactions

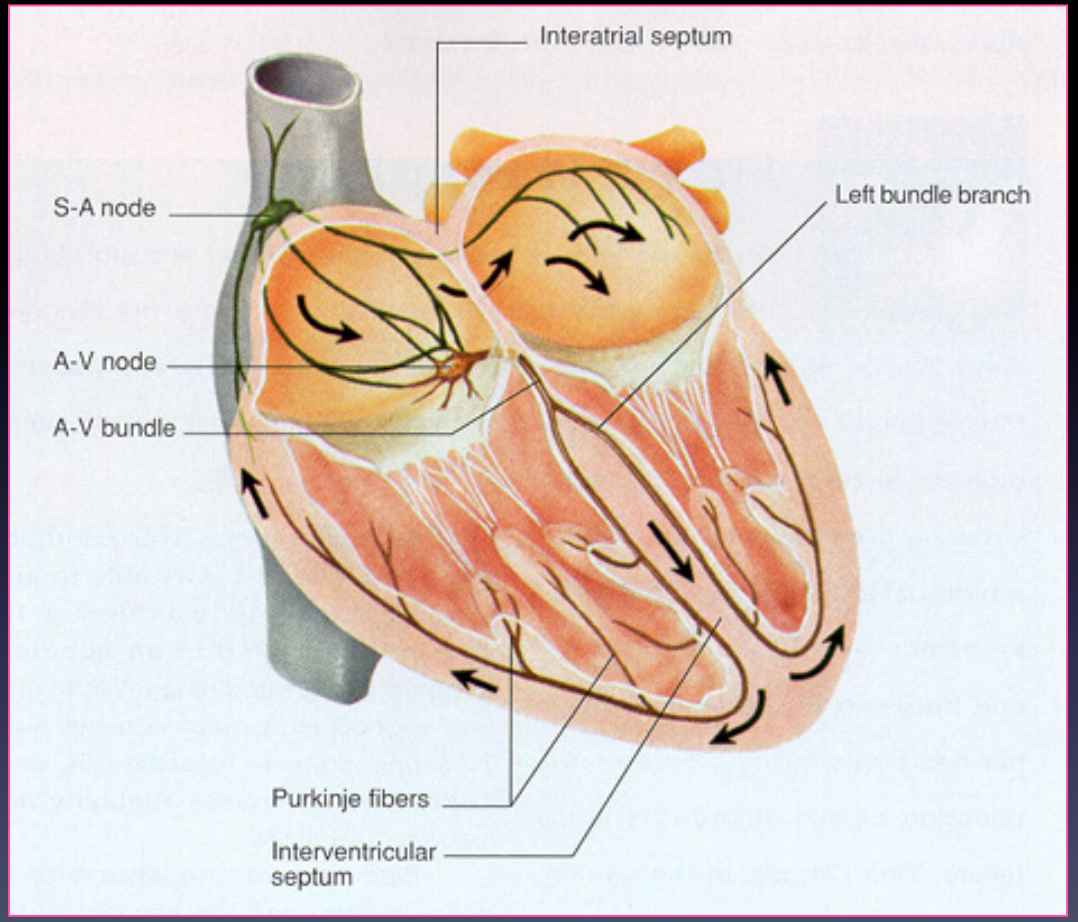
antagonist (cont.)

✓

Inderal (propranolol)

--> blocks beta-1 receptors on SA node

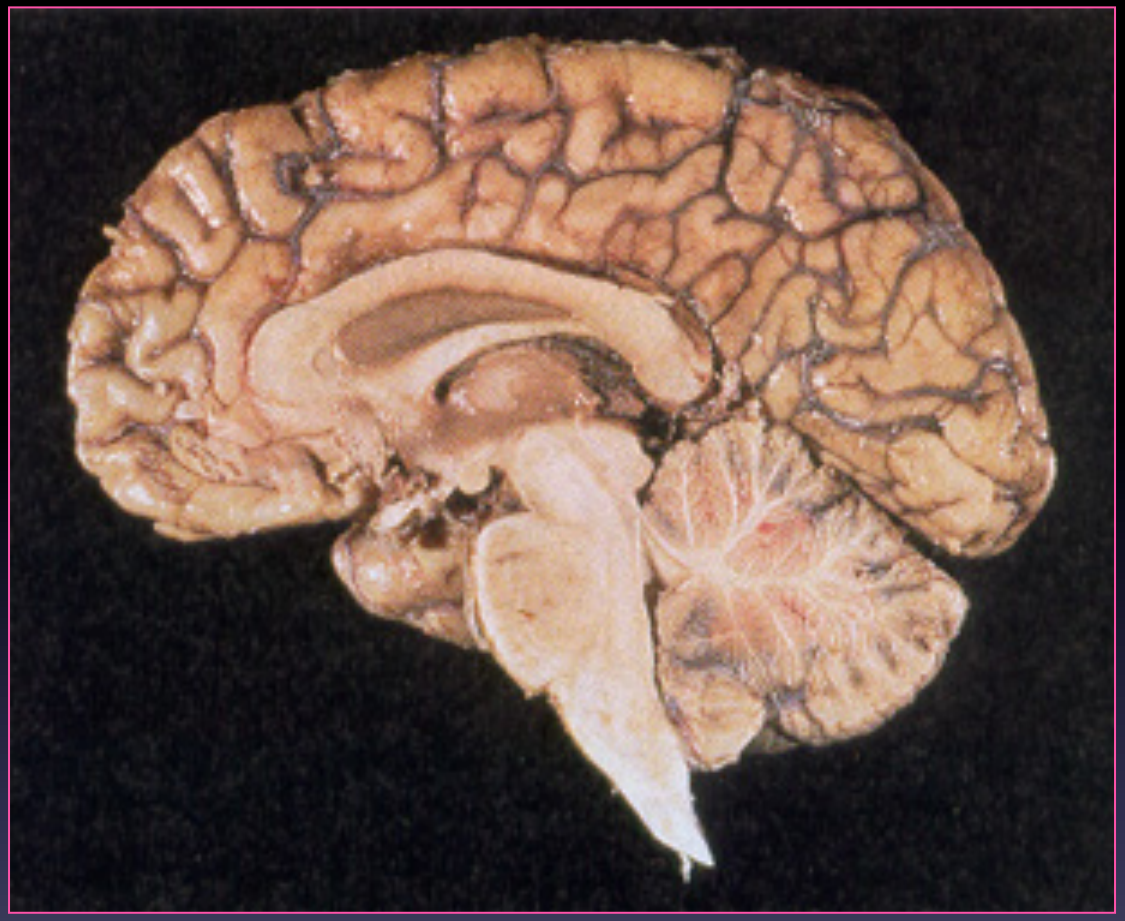
--> decreases heart rate



antagonist (cont.)

Narcan (naloxone)

--> blocks narcotic receptors in respiratory center (medulla oblongata)



--> reverses respiratory depression due to heroin (narcotic overdose)

Receptor Binding Characteristics

a. affinity - drug's ability to bind to a receptor

- agonist --> affinity
- antagonist --> affinity

b. efficacy - drug's ability to stimulate its receptor

- agonist --> efficacy
- antagonist --> no efficacy

Competitive Inhibition

morphine (agonist)<--> Narcan (antagonist)
(naloxone)

Valium (agonist) <--> Romazicon (antagonist)
(diazepam) (flumazenil)

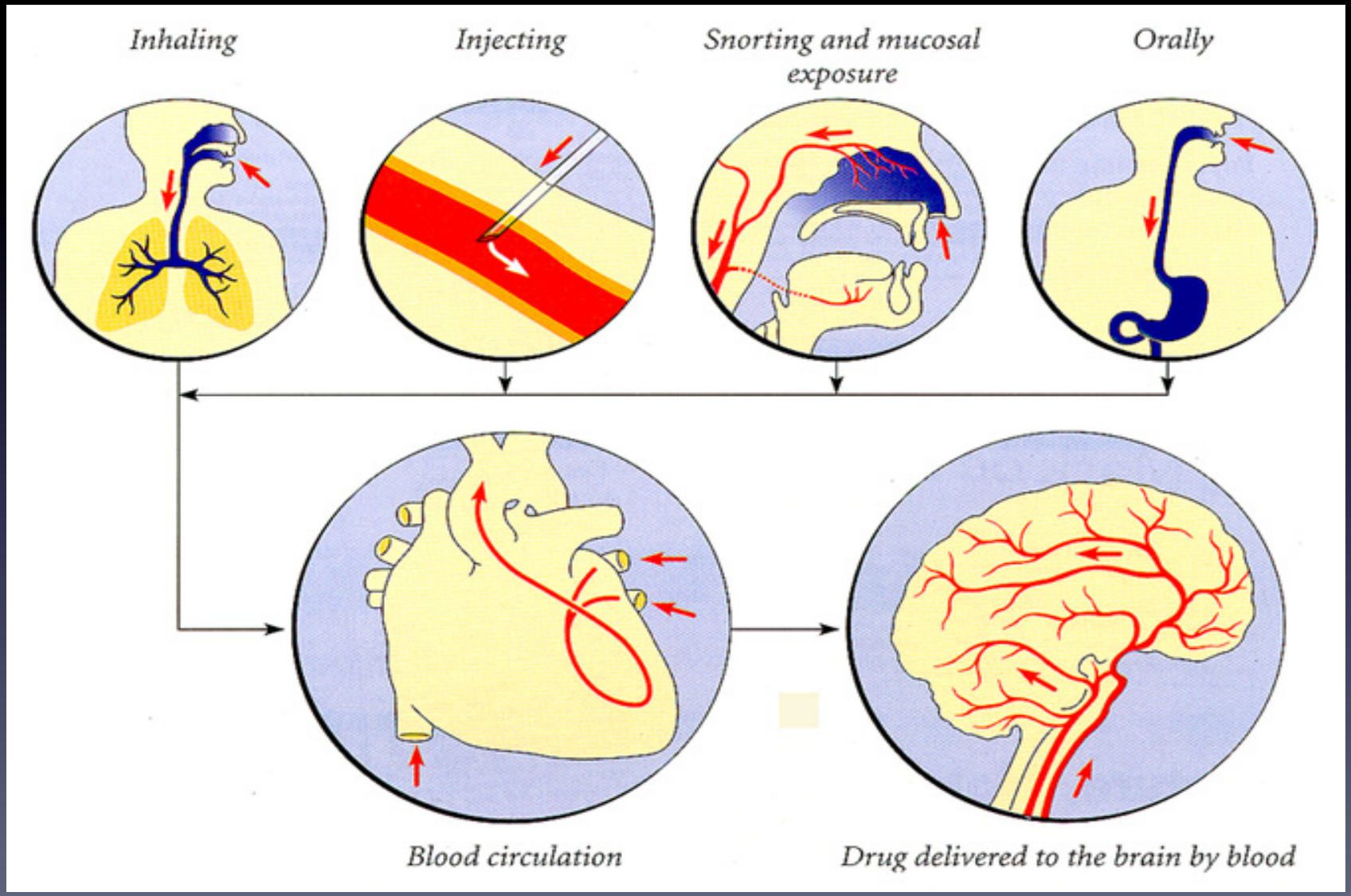
ACh (agonist) <--> atropine (antagonist)
(acetylcholine)

Pharmacokinetics

- drug absorption
- drug distribution
- drug metabolism
- drug elimination

$$Cp(t) = \frac{UDF(t) * I(t)}{CL}$$

Drug Absorption



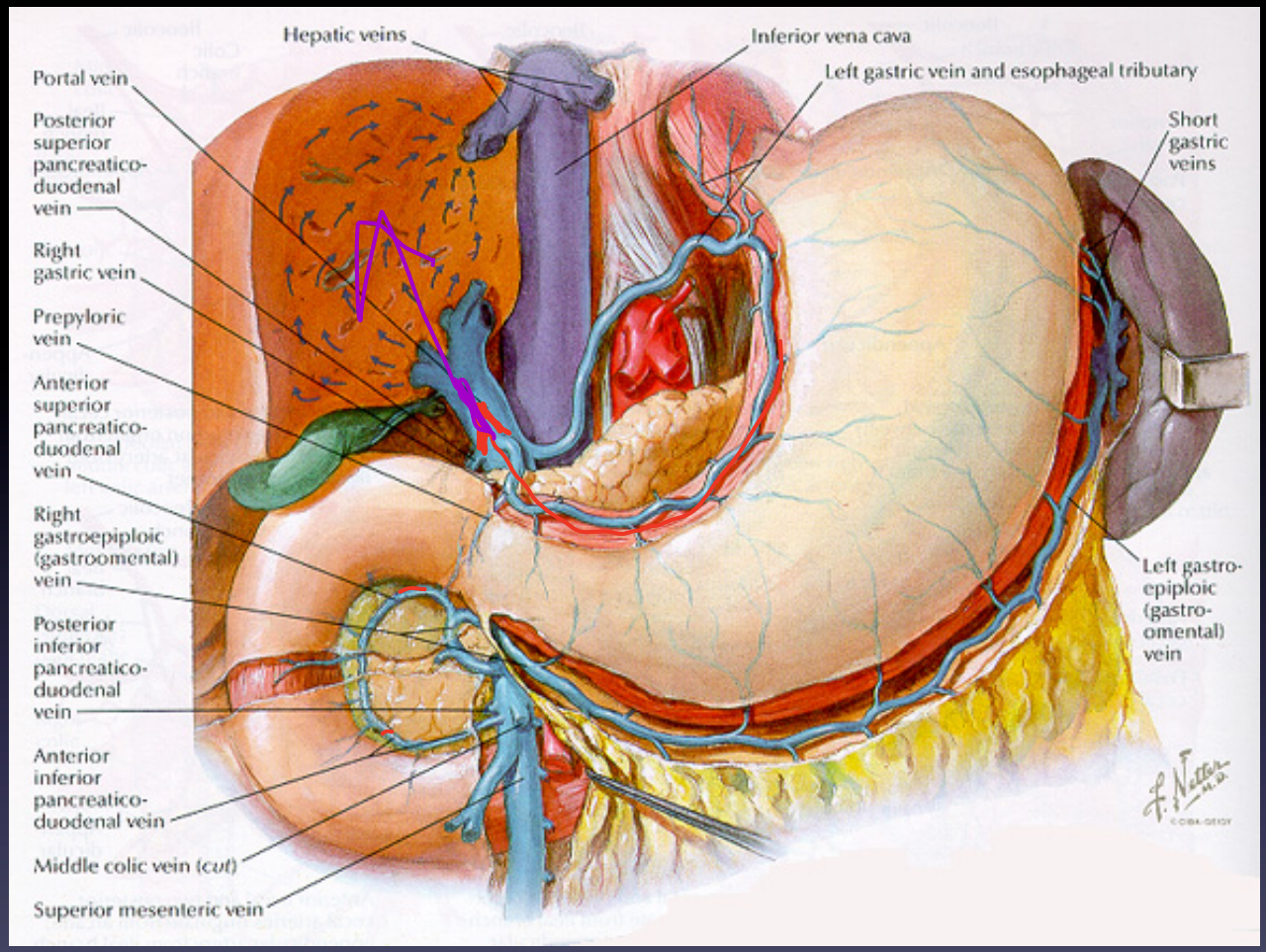
Oral (PO)

drug is ingested

absorbed from stomach/intestine

enters hepatic portal system

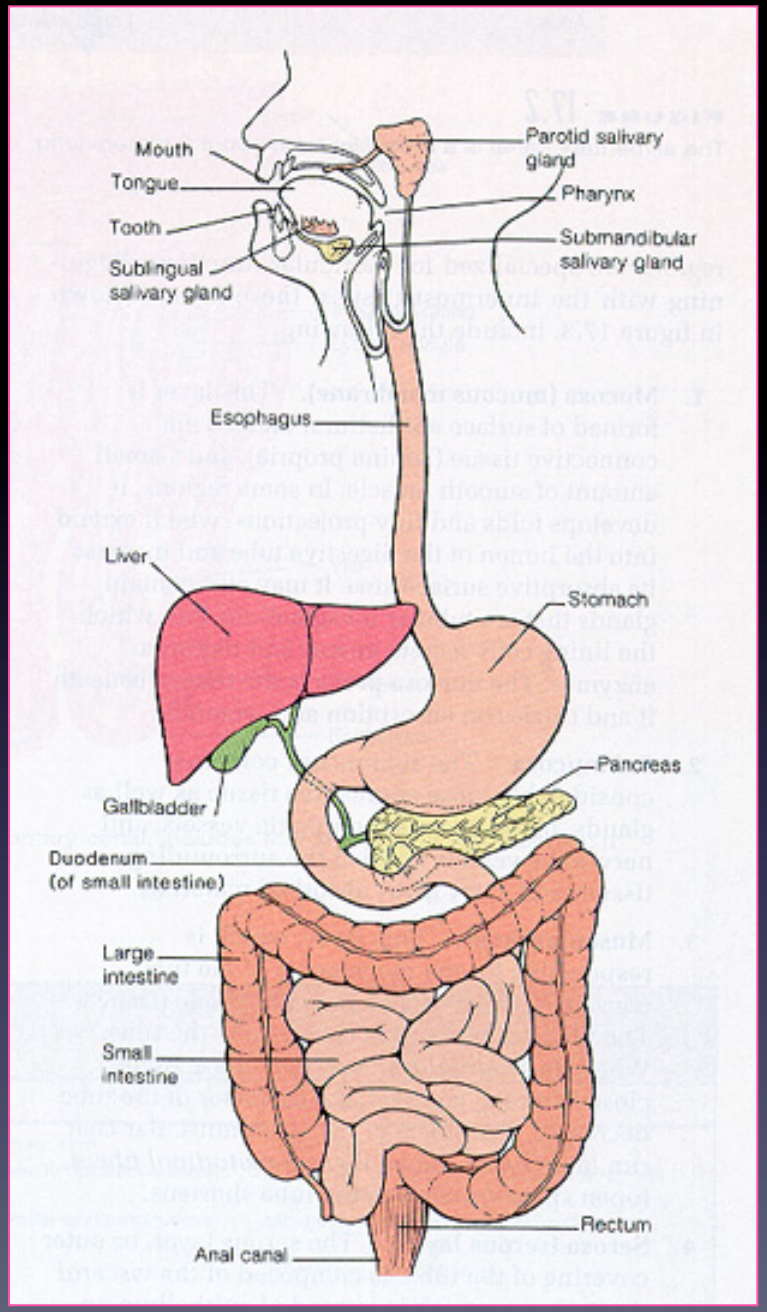
liver → enters general circulation



Oral (cont.)

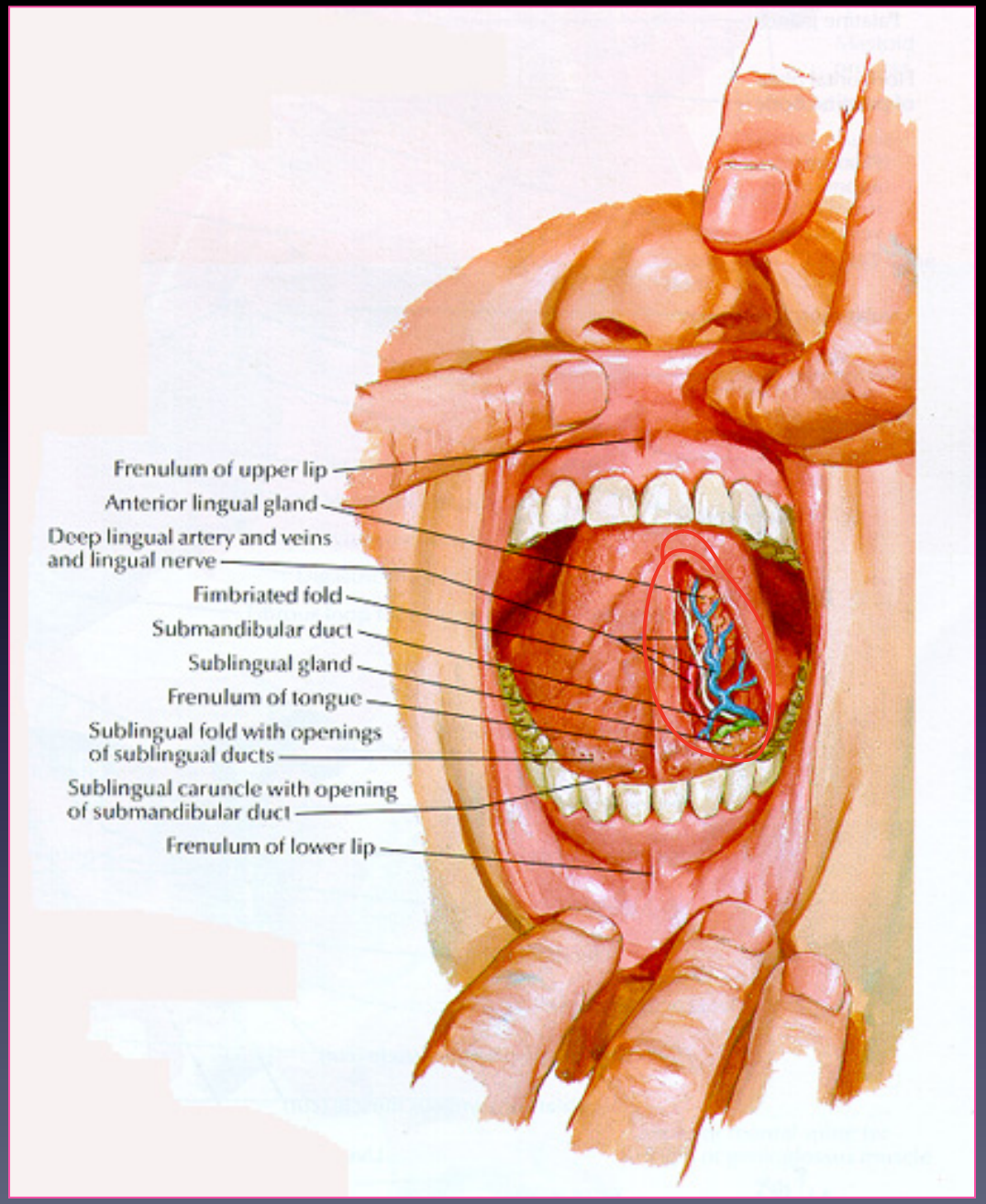
- oral route is convenient and economical
- once absorbed into the bloodstream, the drug enters the liver, where it may be metabolized ("first-pass effect")

oral route of administration undergoes the 1st-pass effect

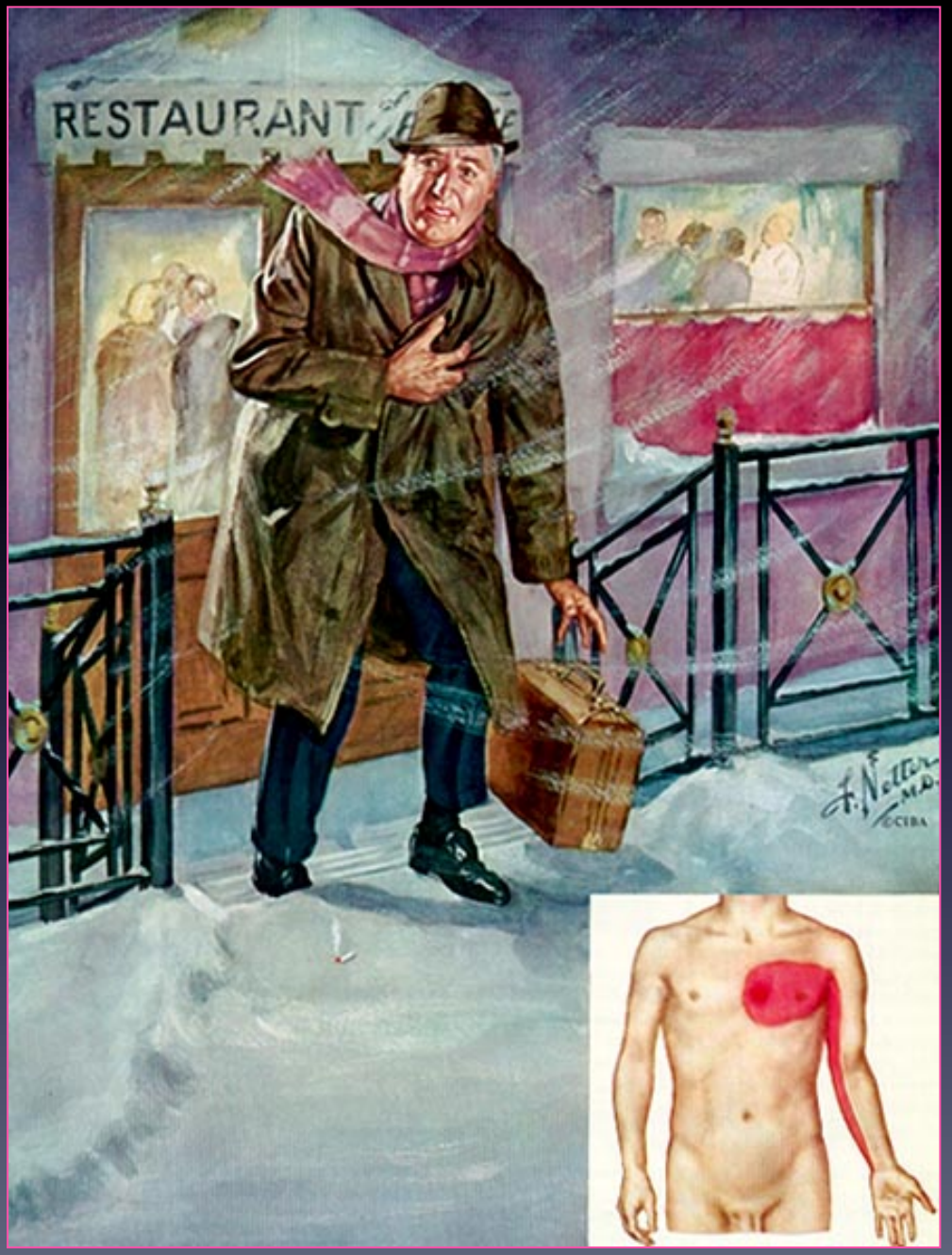


Sublingual

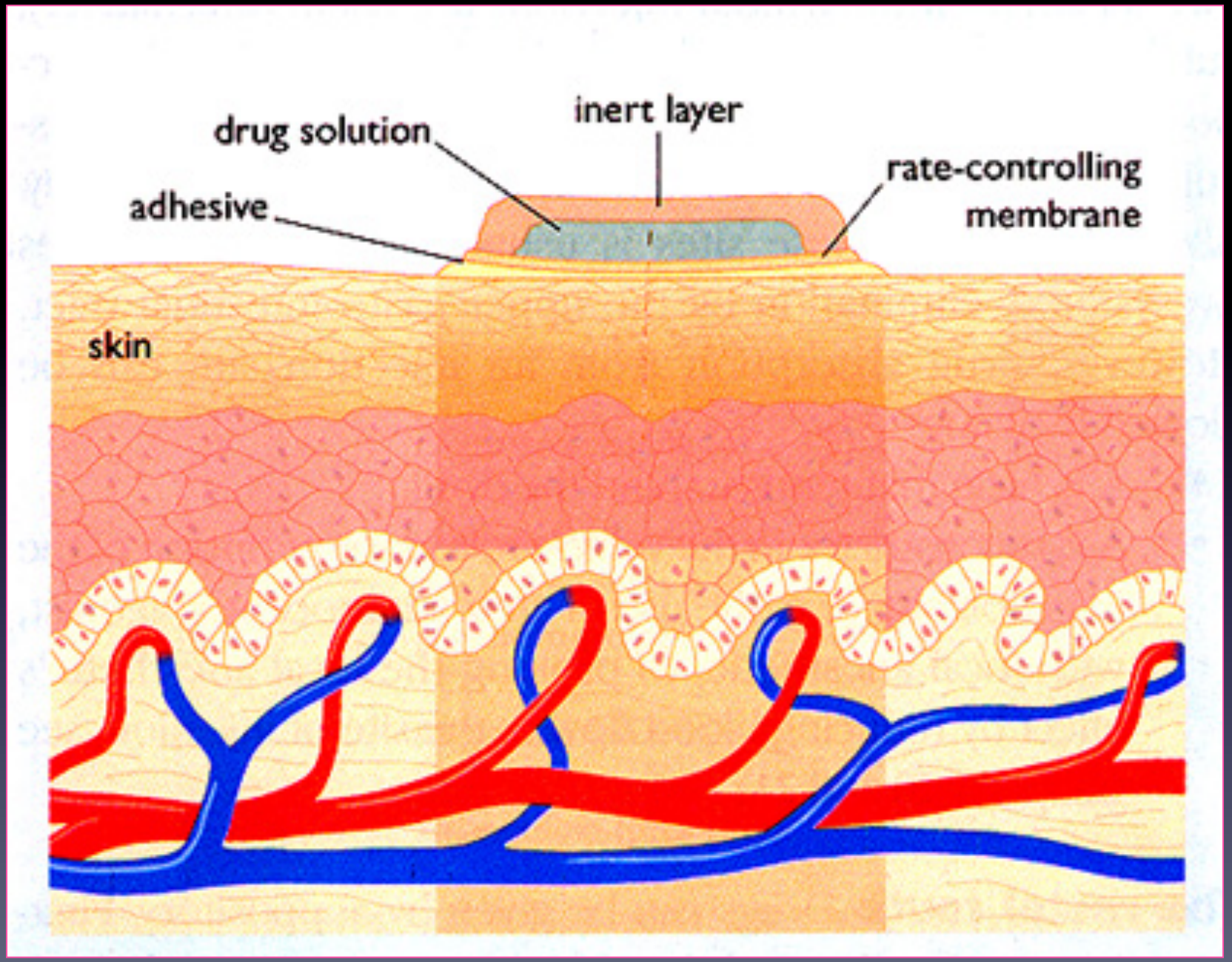
- drug is dissoloved and absorbed under the tongue



Nitroglycerin (NTG) sublingual tablets



Transdermal



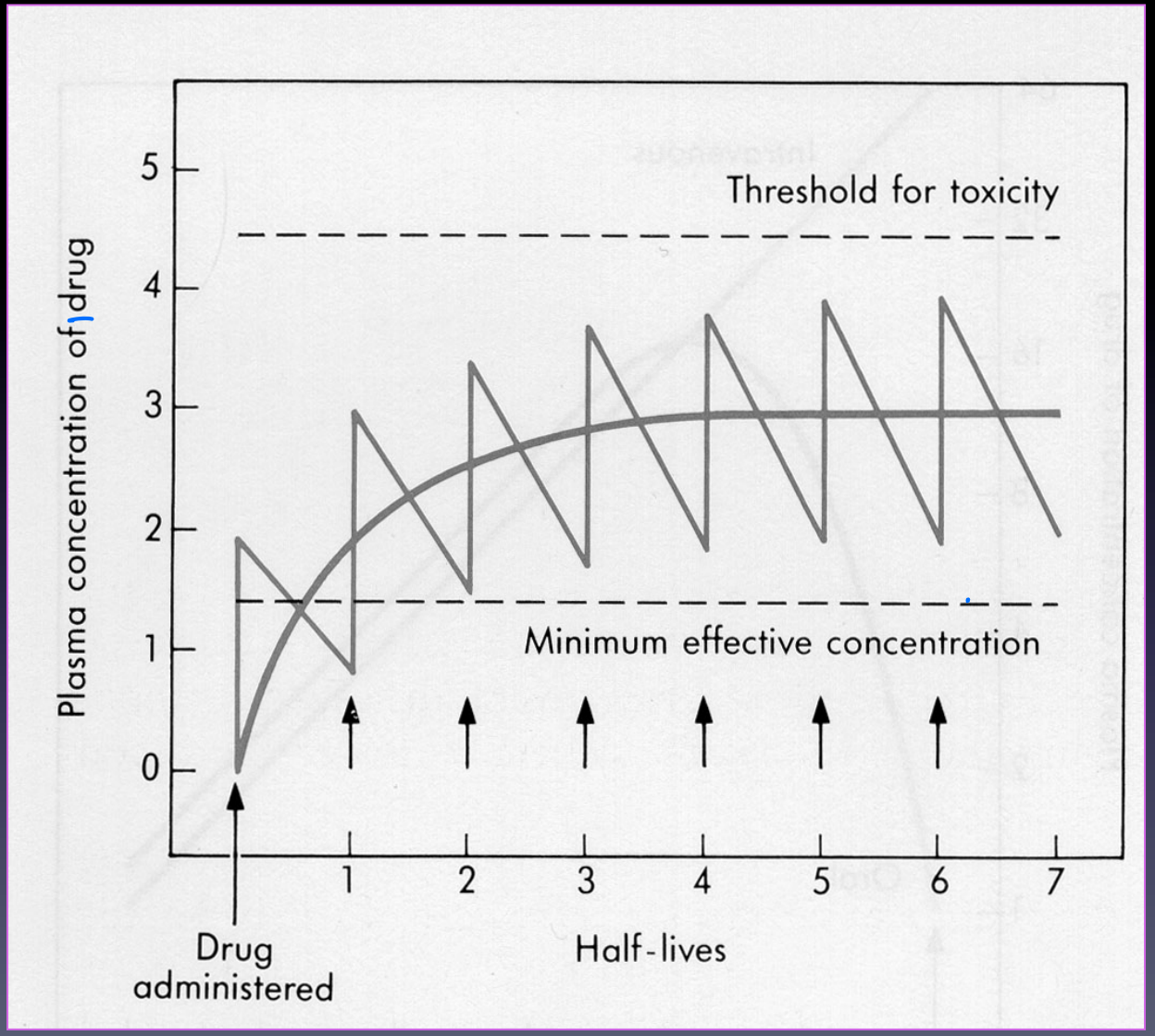
Transdermal (cont.)

Duragesic (Fentanyl) Patch

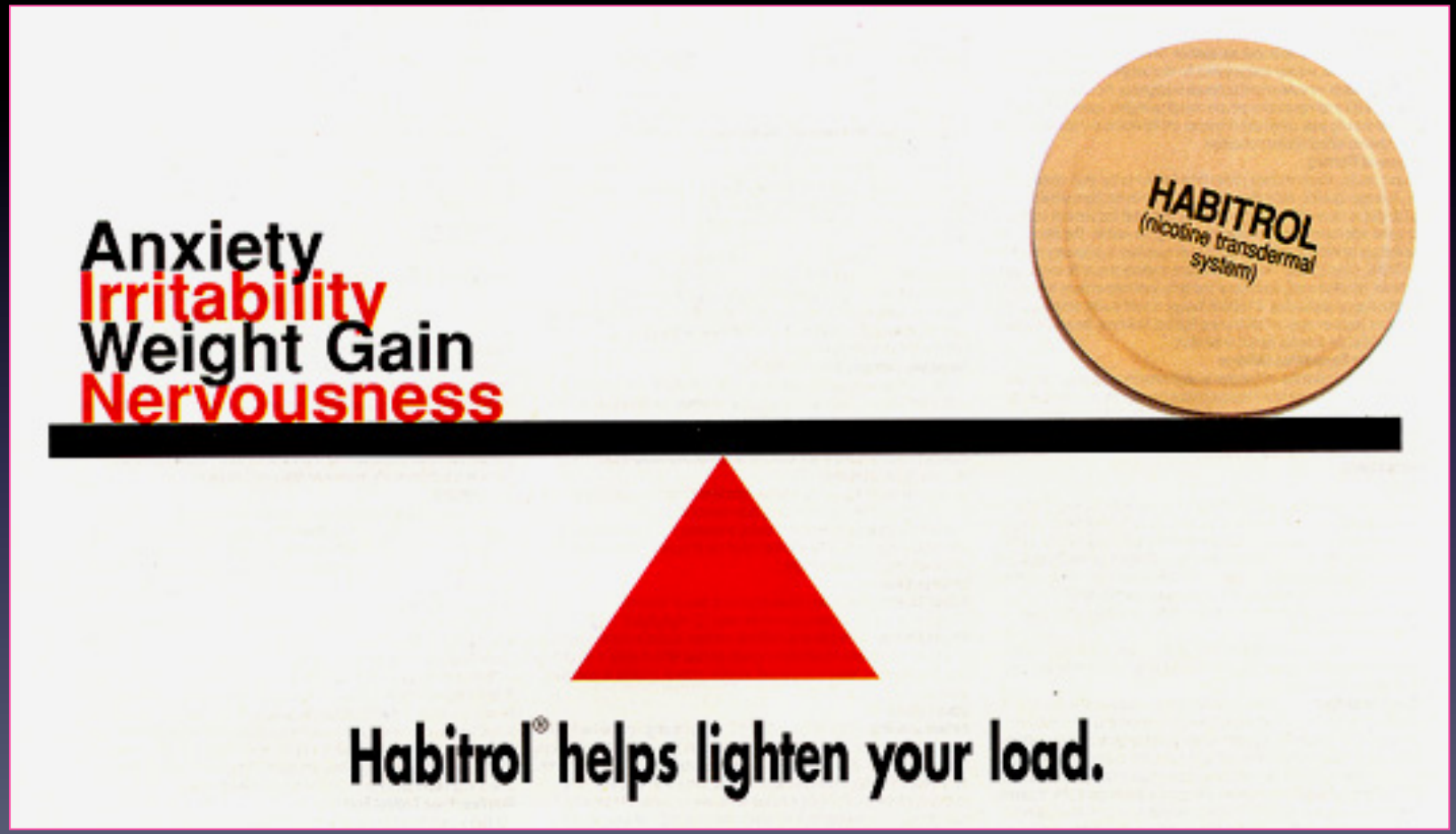
- drug patch provides continuous drug dosing
- local skin irritation may occur
- drug enters the general circulation before passing through the liver

CONCEPTS

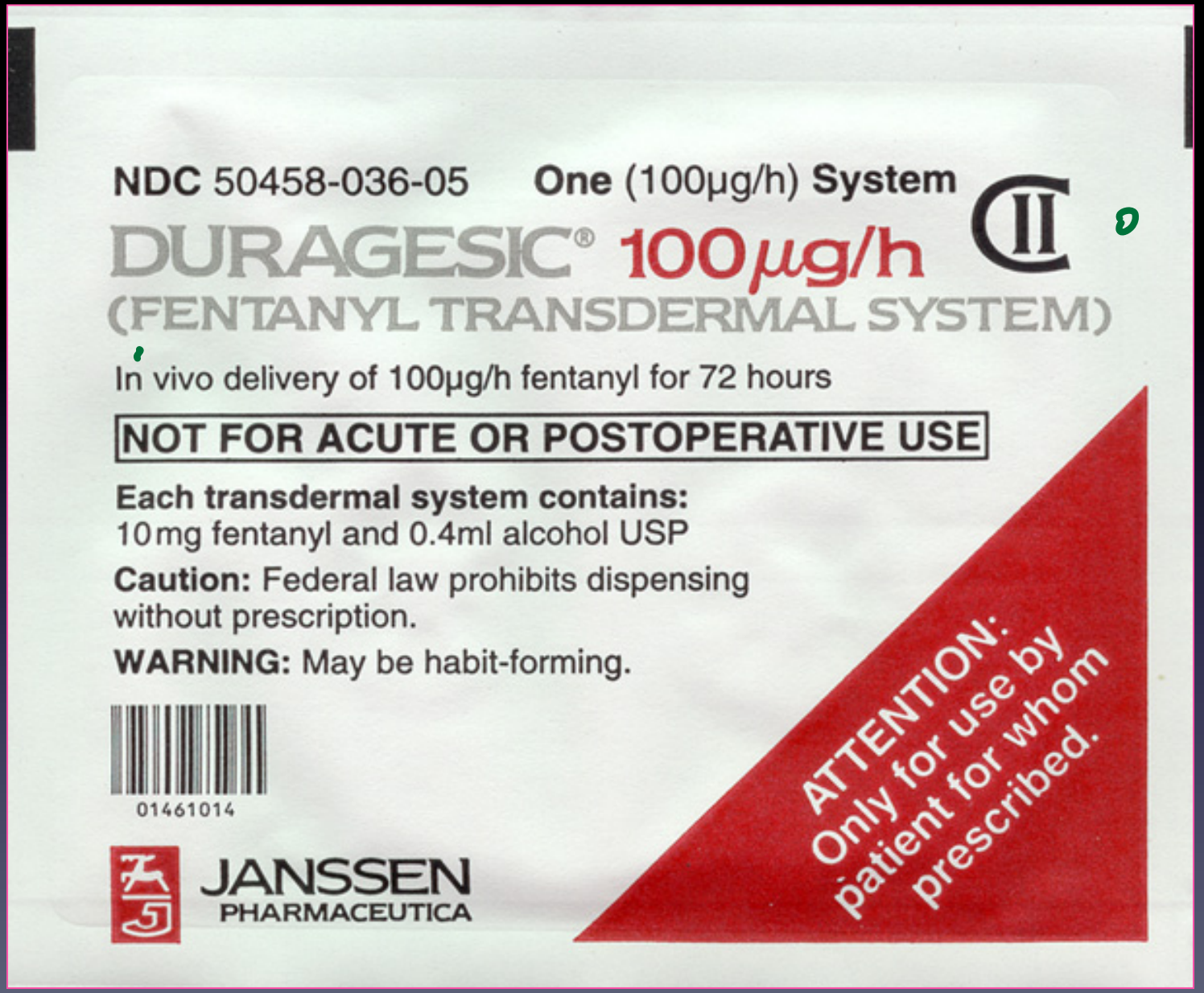
- continuous vs intermittent dosing regimens
- peaks & troughs
- drug half-life
- drug steady-state concentrations



Habitrol (nicotine transdermal system)

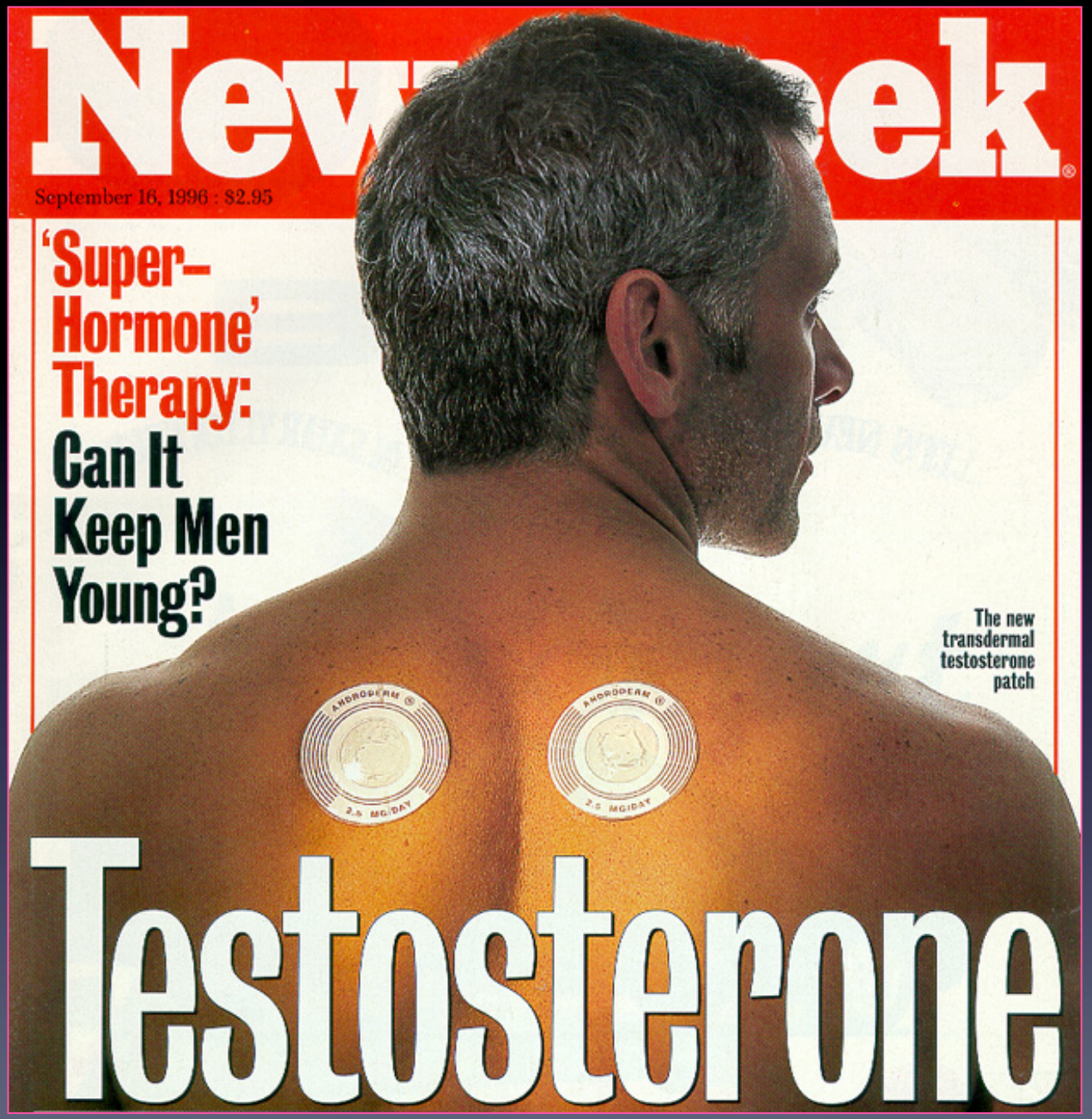


Duragesic Patch



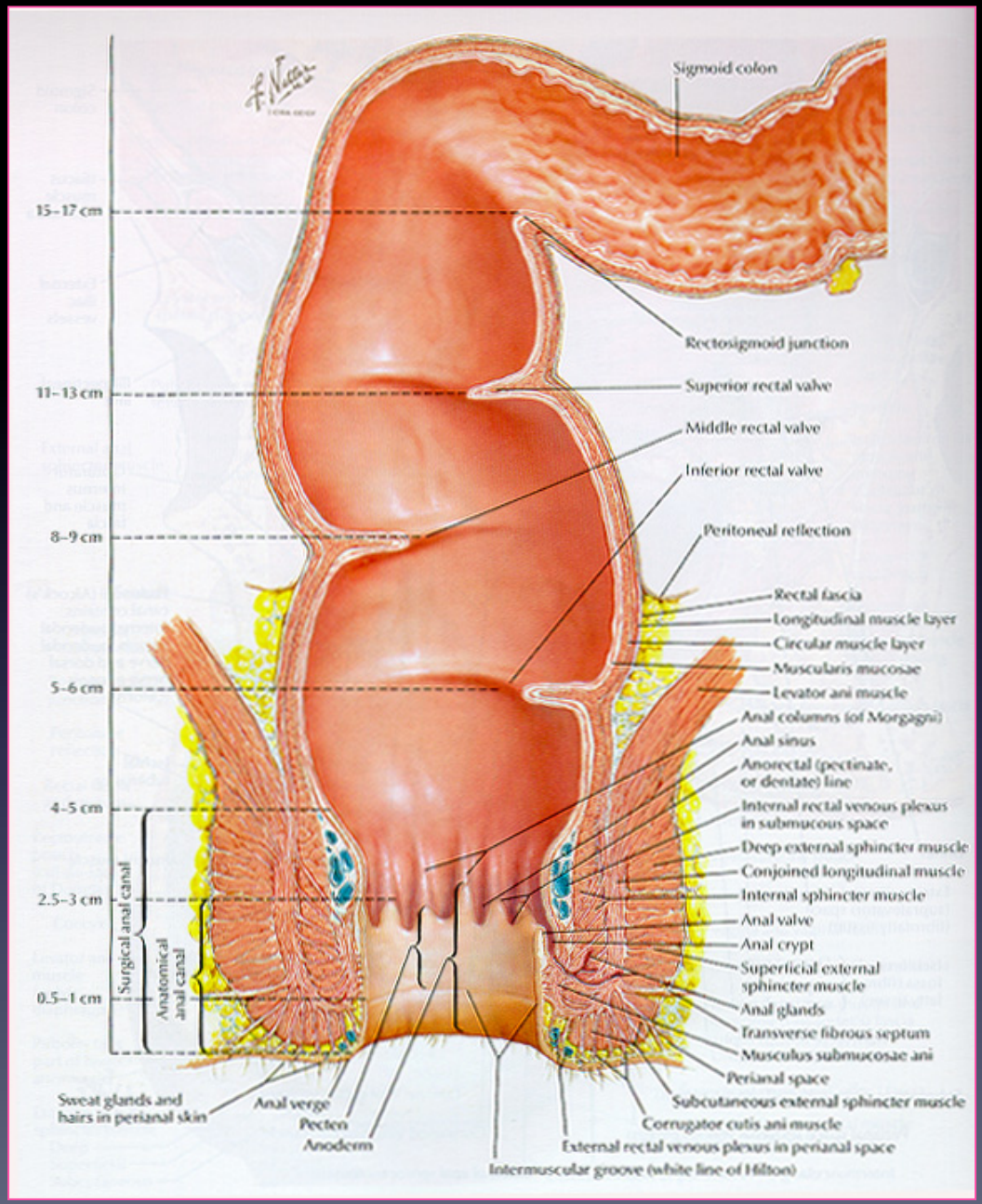
Androderm

(testosterone)



Rectal (PR)


UPSHER-SMITH
FEVERALL®
ACETAMINOPHEN SUPPOSITORY
UPSHER-SMITH
TIGAN®
Trimethobenzamide HCl
Beecham

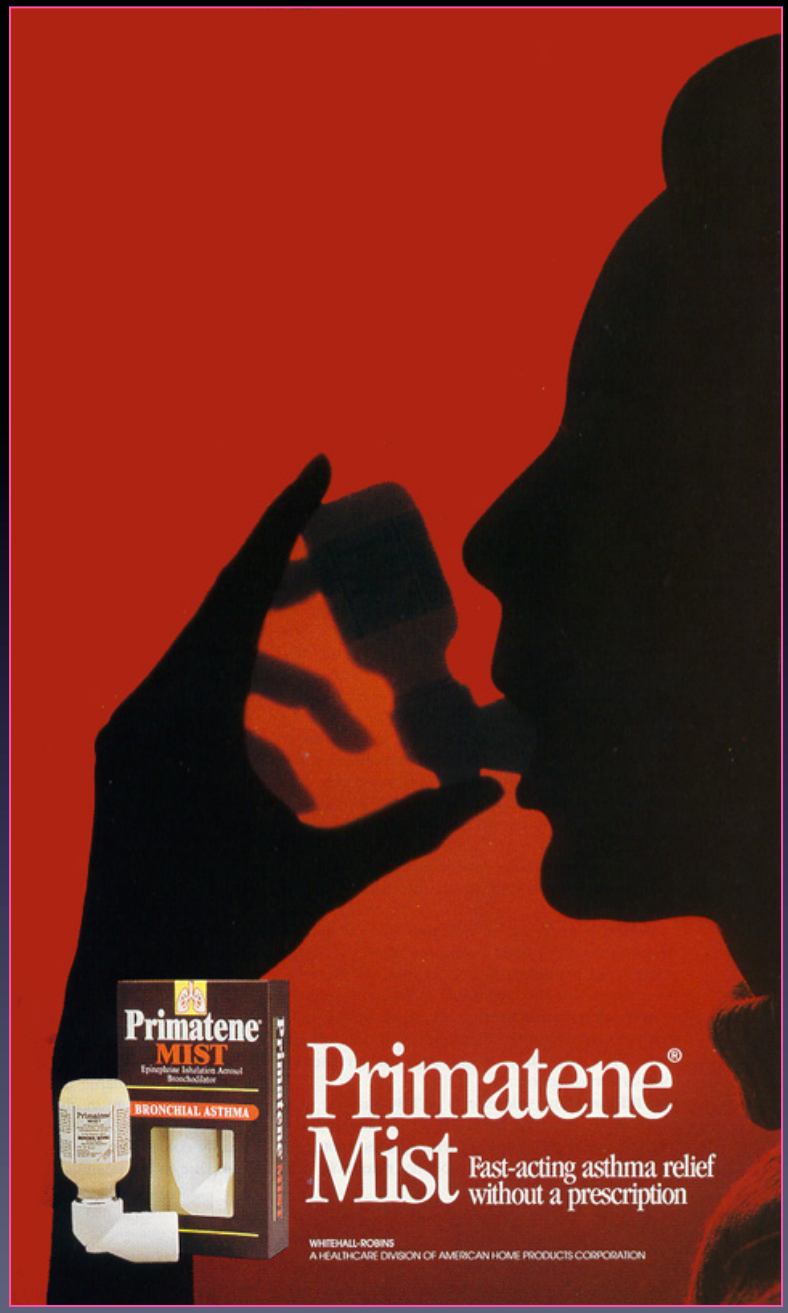

Sigmoid colon
15–17 cm
Rectosigmoid junction
11–13 cm
Superior rectal valve
Middle rectal valve
Inferior rectal valve
8–9 cm
Peritoneal reflection
Rectal fascia
Longitudinal muscle layer
Circular muscle layer
Muscularis mucosae
5–6 cm
Levator ani muscle
Anal columns (of Morgagni)
Anal sinus
Anorectal (pectinate, or dentate) line
4–5 cm
Internal rectal venous plexus in submucous space
Deep external sphincter muscle
Conjoined longitudinal muscle
2.5–3 cm
Internal sphincter muscle
Anal valve
Anal crypt
Superficial external sphincter muscle
0.5–1 cm
Anal glands
Transverse fibrous septum
Musculus submucosae ani
Perianal space
Subcutaneous external sphincter muscle
Corrugator cutis ani muscle
External rectal venous plexus in perianal space
Intermuscular groove (white line of Hilton)
Surgical anal canal
Anatomical anal canal
Sweat glands and hairs in perianal skin
Anal verge
Pecten
Anoderm

Rectal (cont.)

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

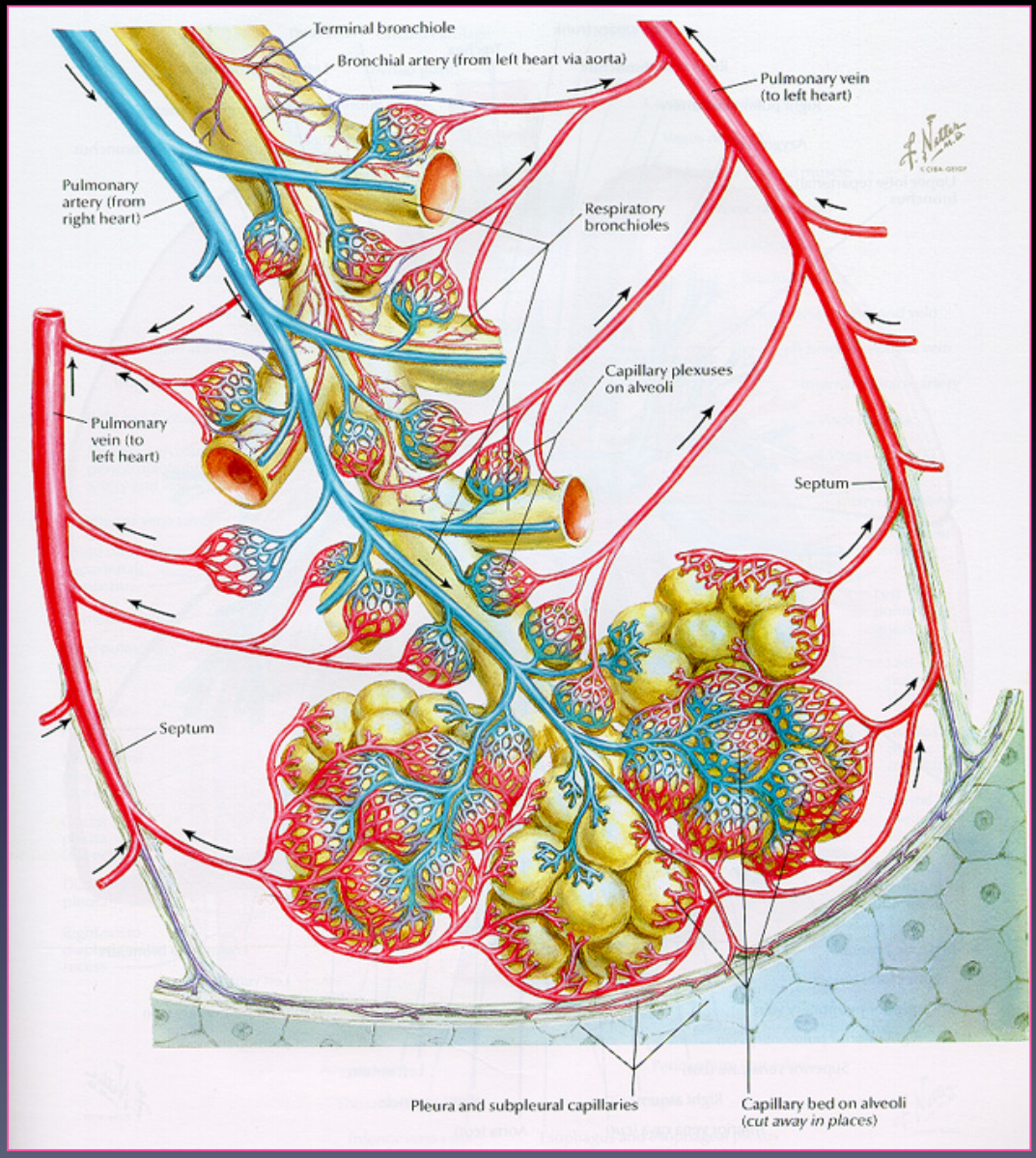
Inhalational

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

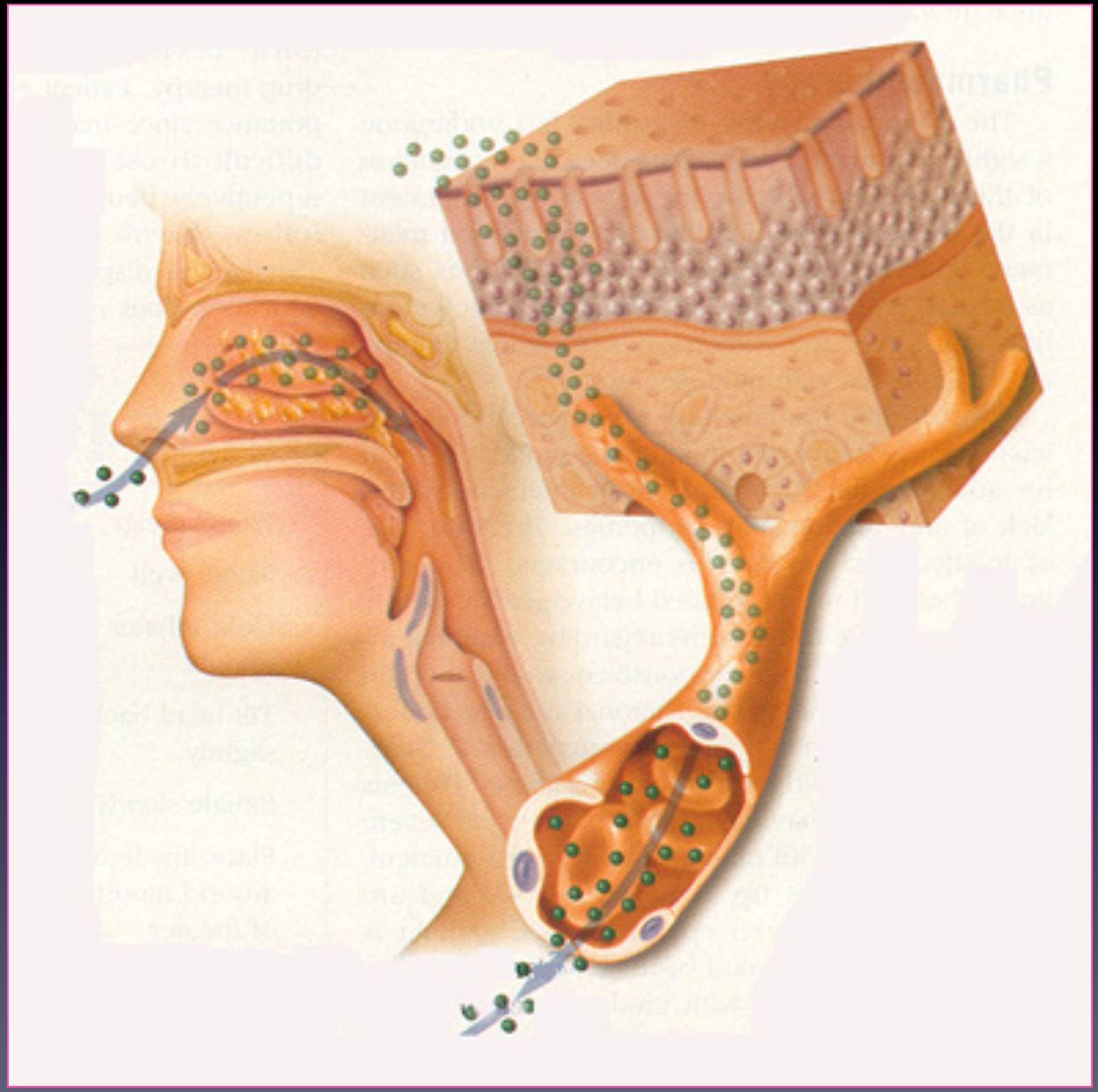


... the drug enters the bloodstream through the lungs

- inhaled drug produces a rapid onset since it circulates to the brain shortly after being inhaled

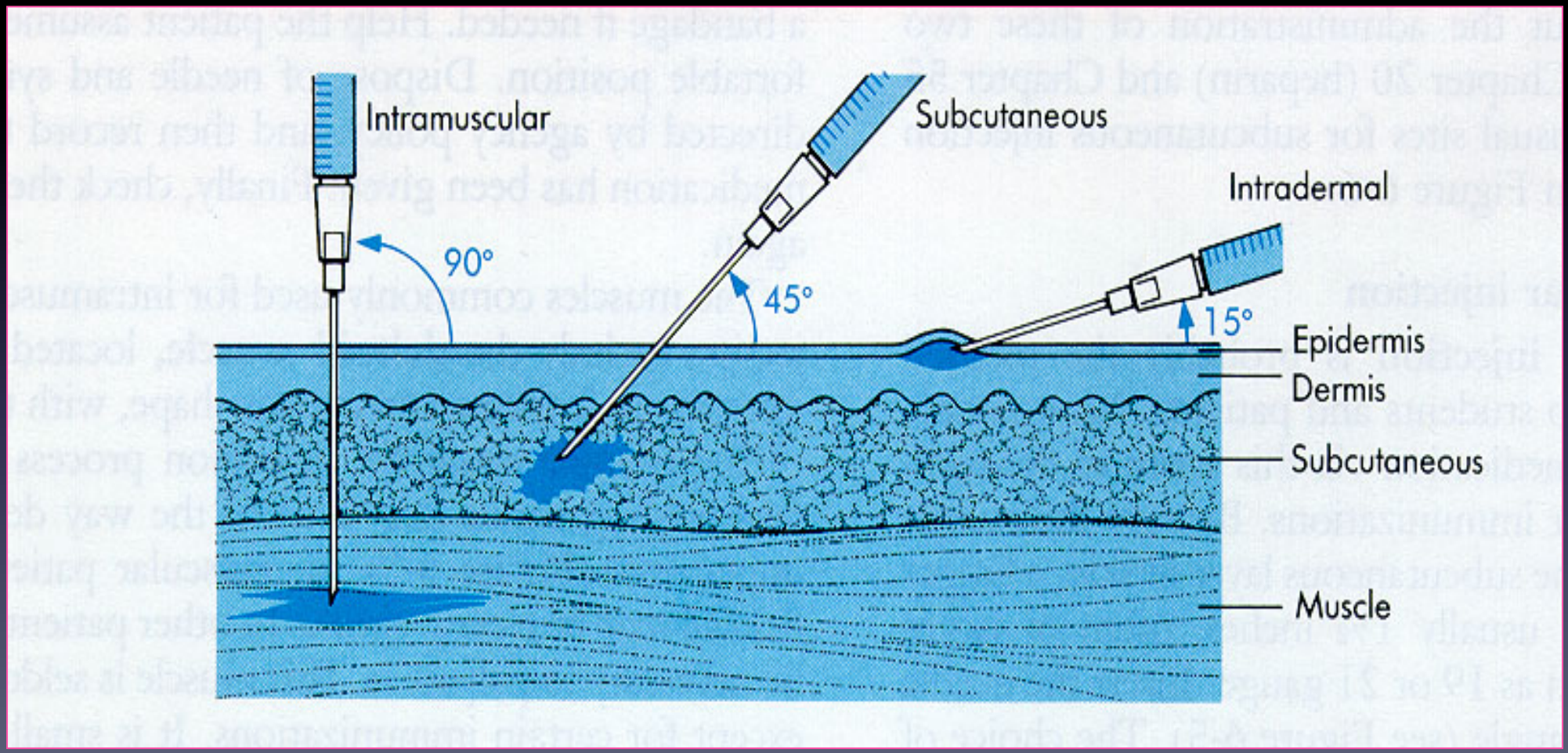


Intranasal



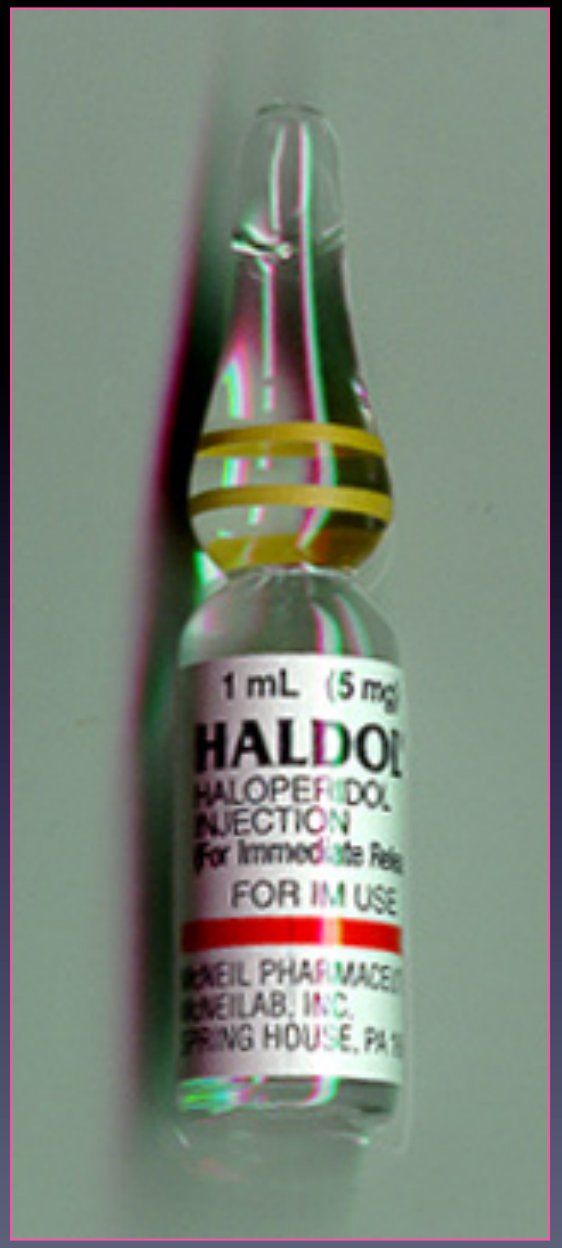
Intranasal route (cont.)

Parenteral route (IV, IM, & SQ)



Parenteral route (cont.)

- advantages:
  - drug response: IV >IM> SQ
  - 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

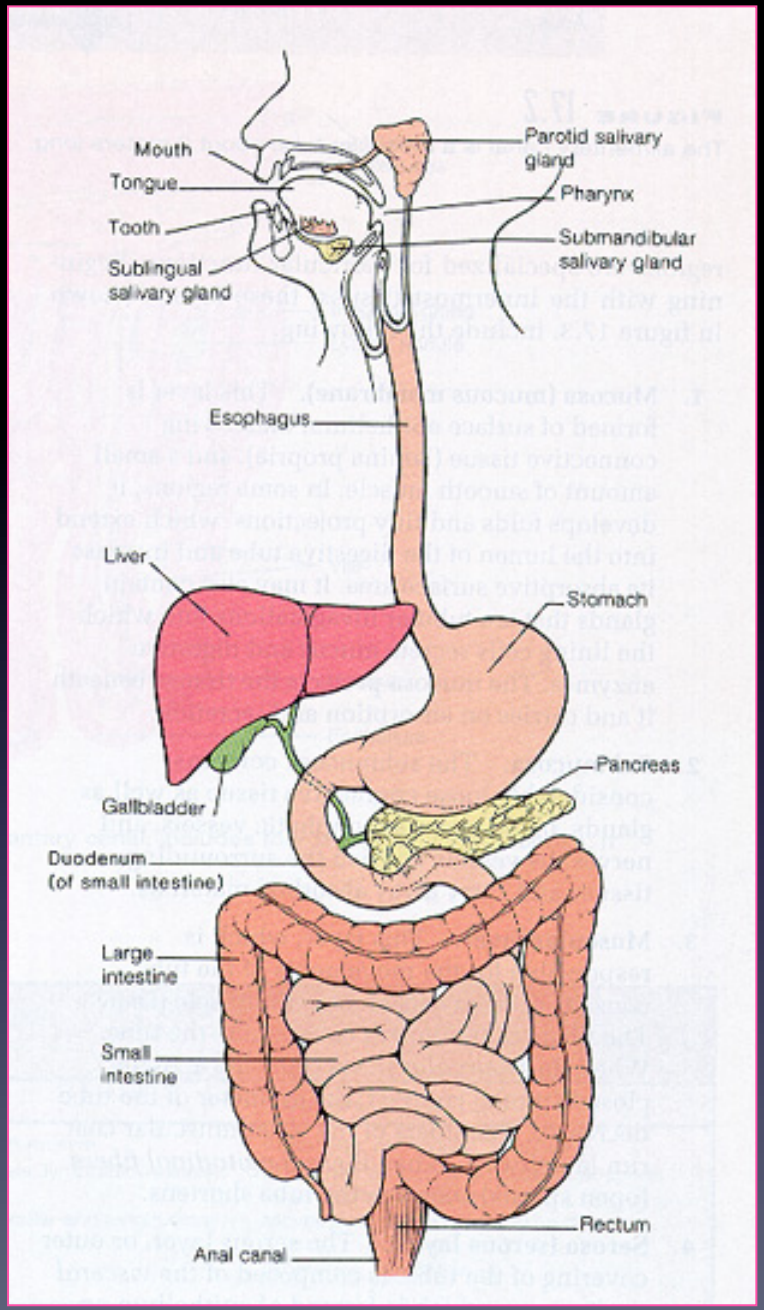
Drug Distribution

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

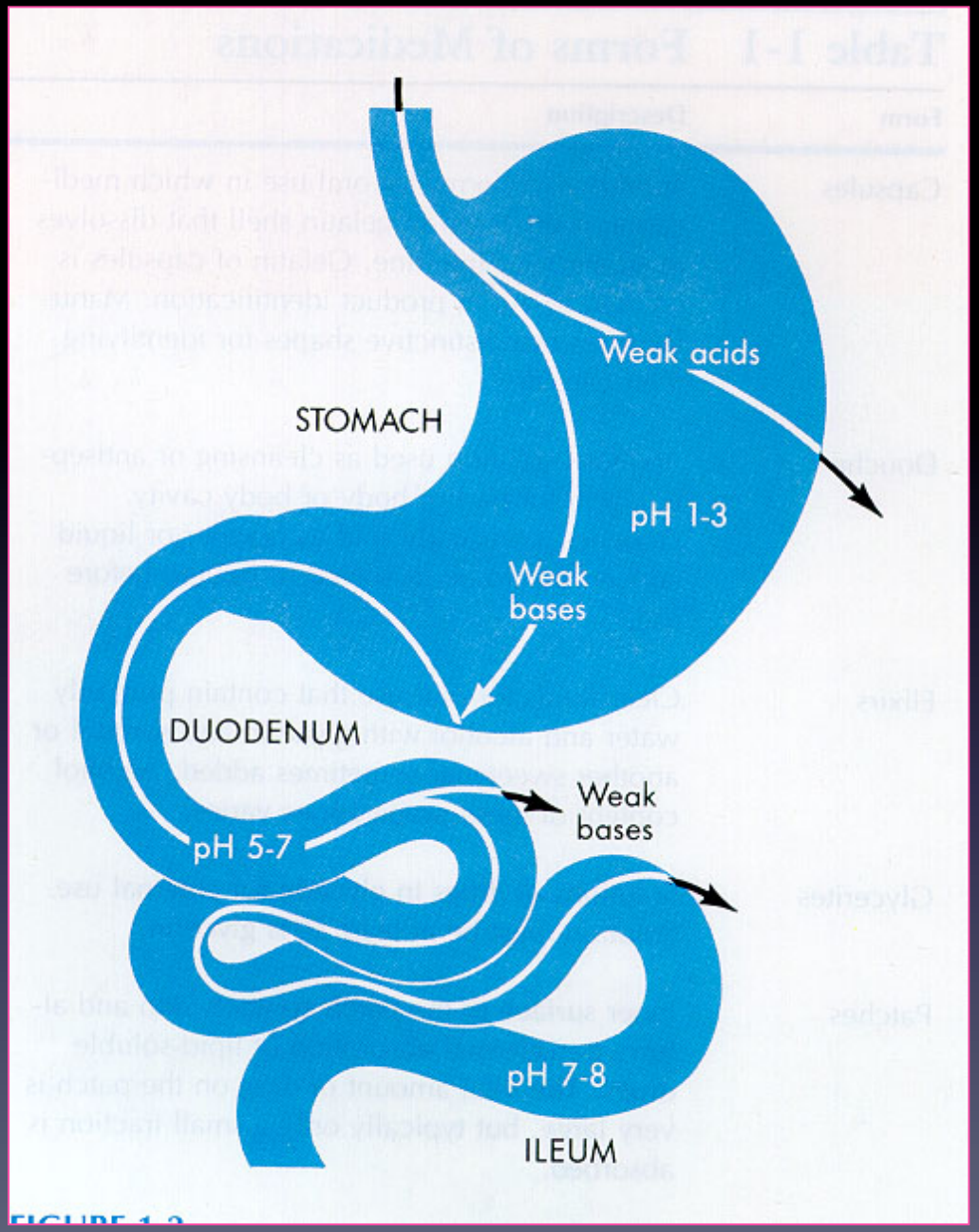
b. drugs either exist in lipid-soluble form or non-lipid soluble form depending on their pH environment



pH environment changes along the GI tract:

i. stomach (highly acidic)

ii. small intestine (slightly alkaline)



Bioavailability

- describes what proportion of the administered drug is available to produce a pharmacologic response
- factors influencing bioavailability:

  i. drug dissolution

  - inert ingredients (binders, disintegraters, lubricants, buffers, ect...)

- factors influencing bioavailability (cont.):

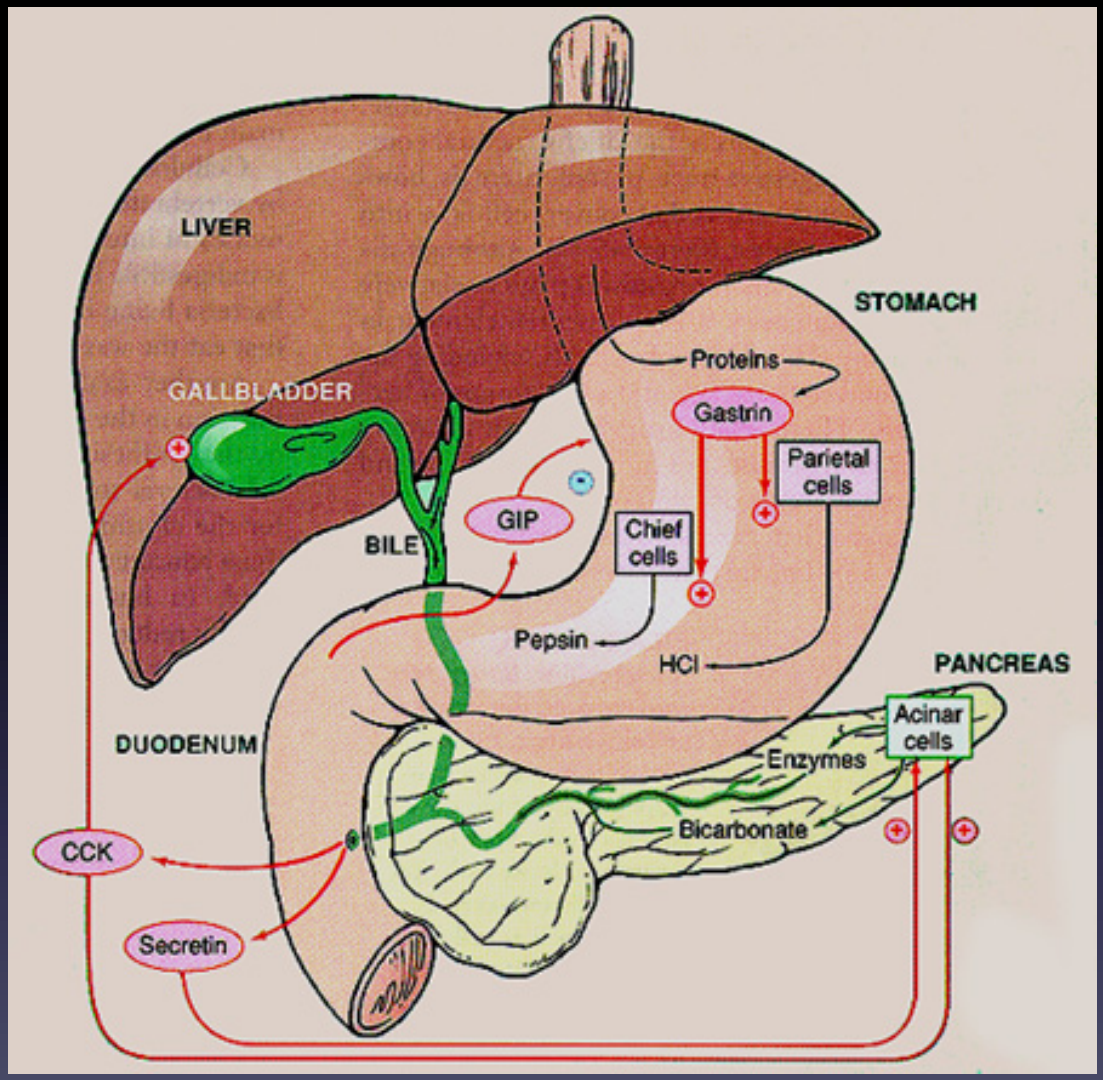
ii. GI tract

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

ii. GI tract (cont.)

- achlorohydria
- deficiency in pancreatic and intestinal secretions

  --> prevents dissolution of enteric-coated tablets

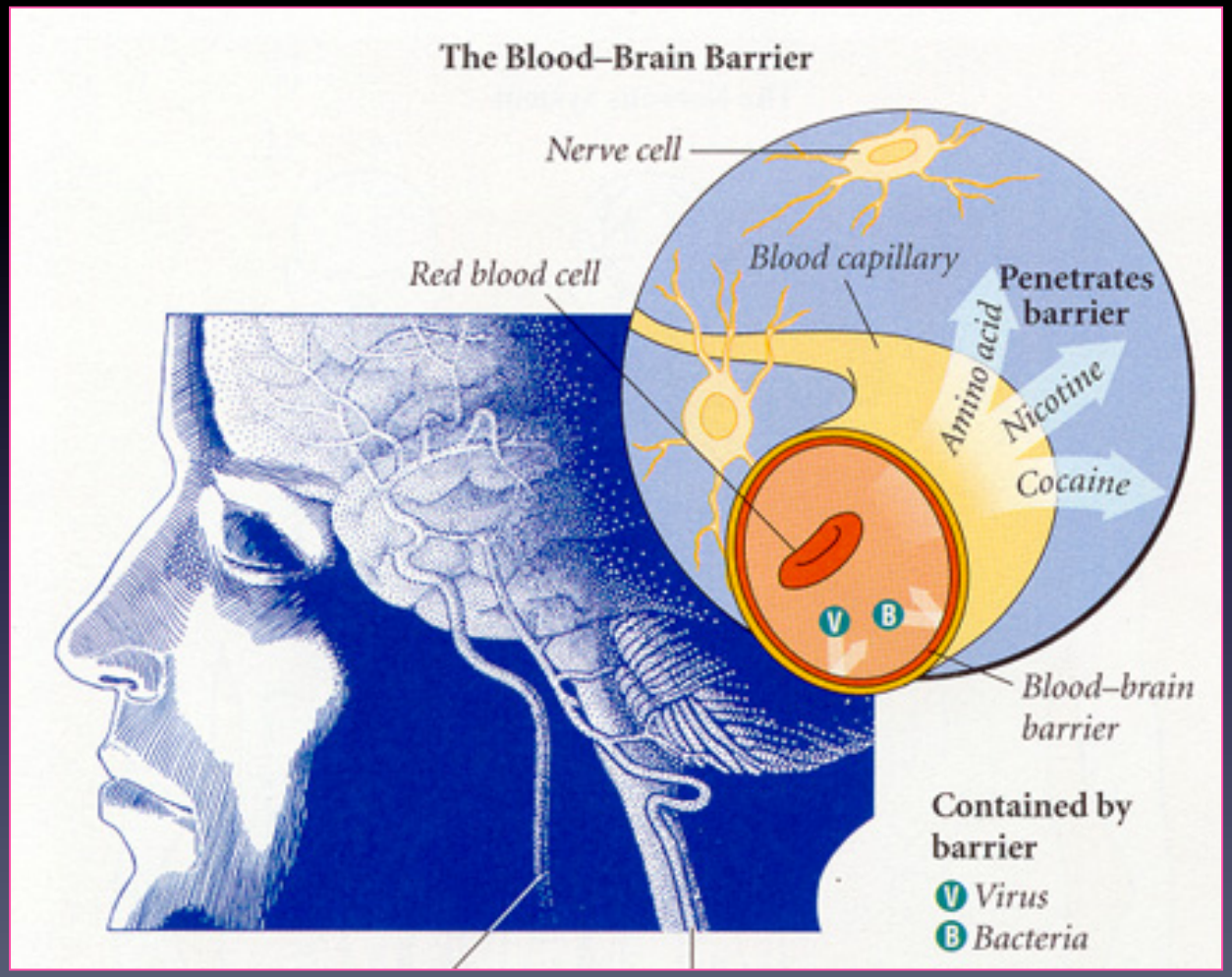


Drug Distribution (cont.)

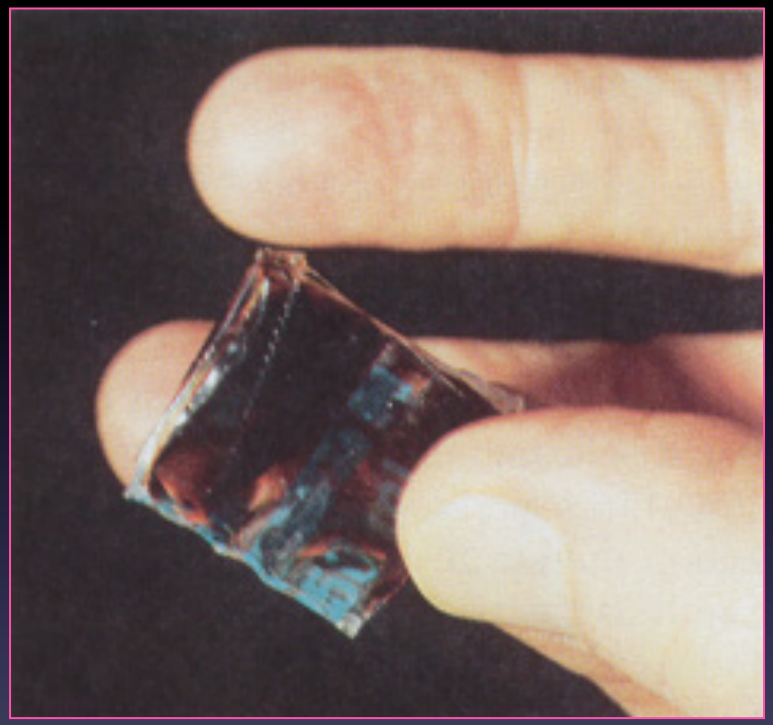
- the degree to drug distribution depends on the physical and chemical properties of a drug and its ability to penetrate cell membranes, capillaries, blood-brain barrier, placenta, etc....

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.)



Mexican “tar” Heroin

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

Plasma Protein Binding

- many drugs bind to plasma reversibly with plasma proteins (e.g., albumin)

a. 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 (cont.)

Drug-Drug Interactions

✓

Aspirin

↓

displaces Coumadin from albumin binding site

↓

increase in “free” warfarin drug levels

↓

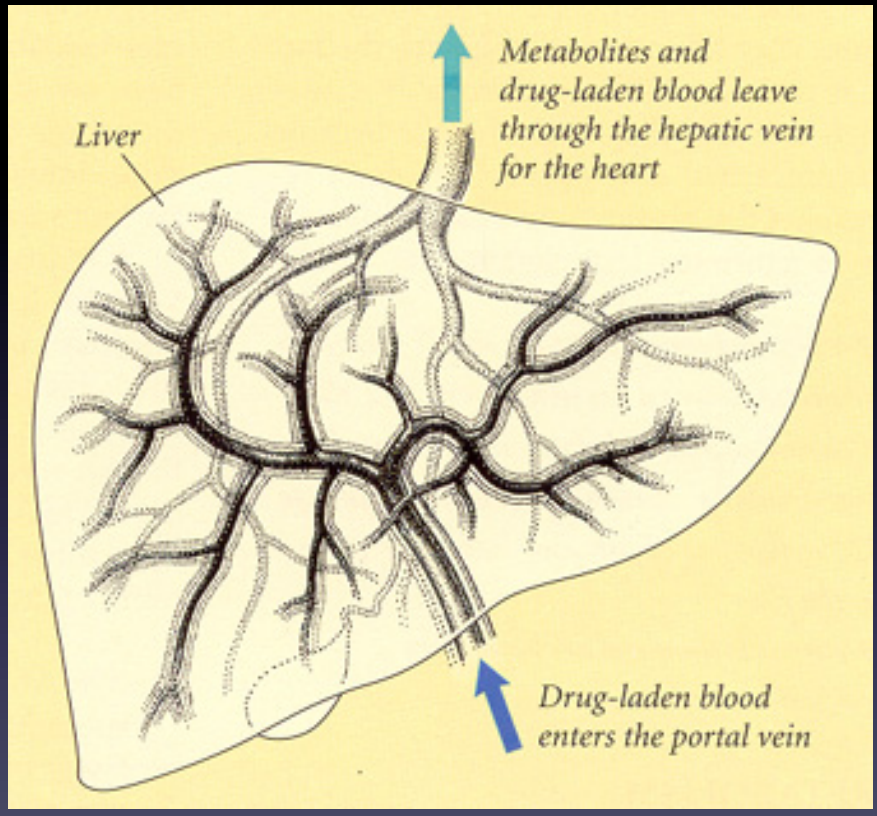
increases bleeding potential

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



- lipid-soluble drug --> water-soluble drug --> 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 throughout the body

Induction / Inhibition of Drug Metabolism

i. induction of enzymes (metabolism)

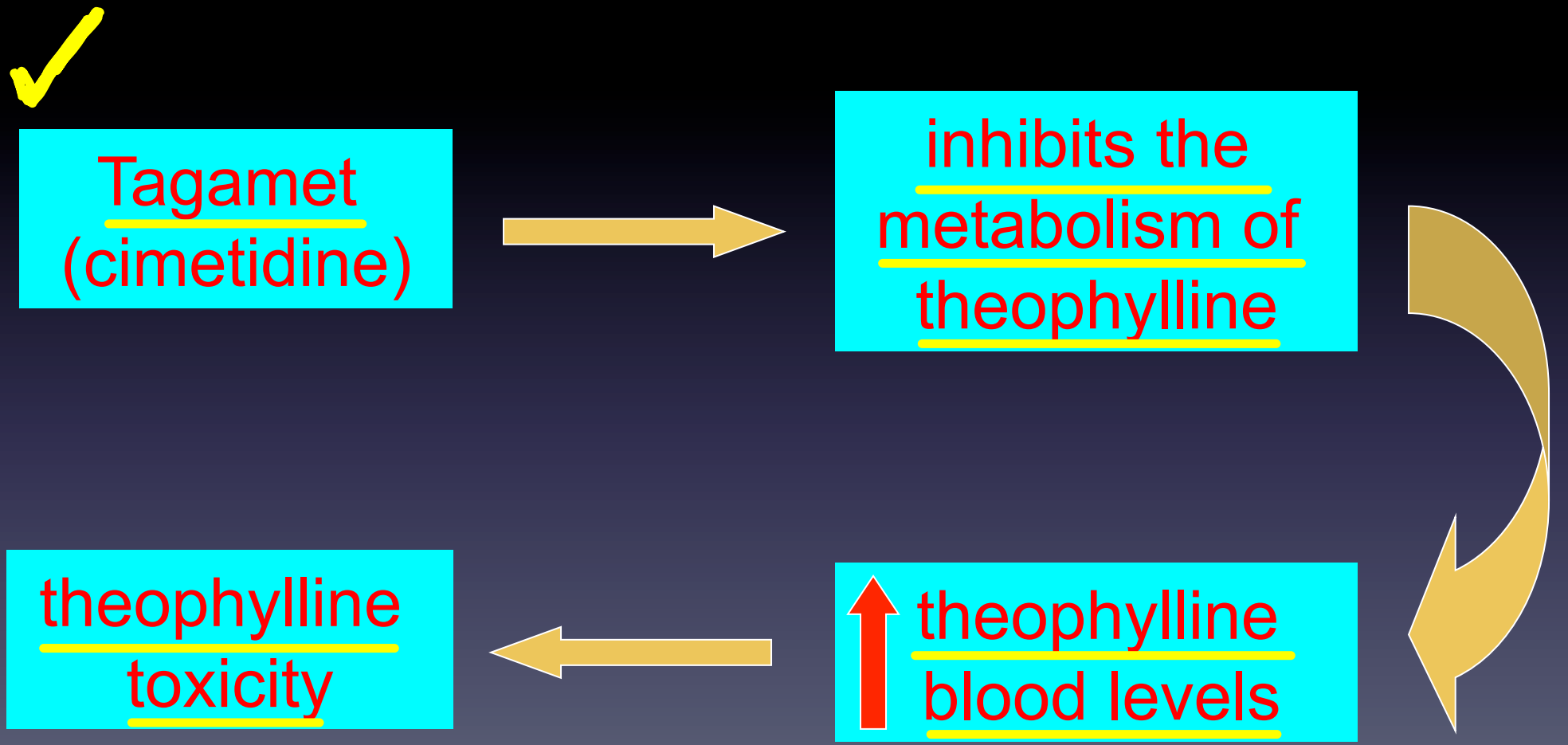
(nicotine)

induces metabolism of theophylline

theophylline blood levels

wheezing

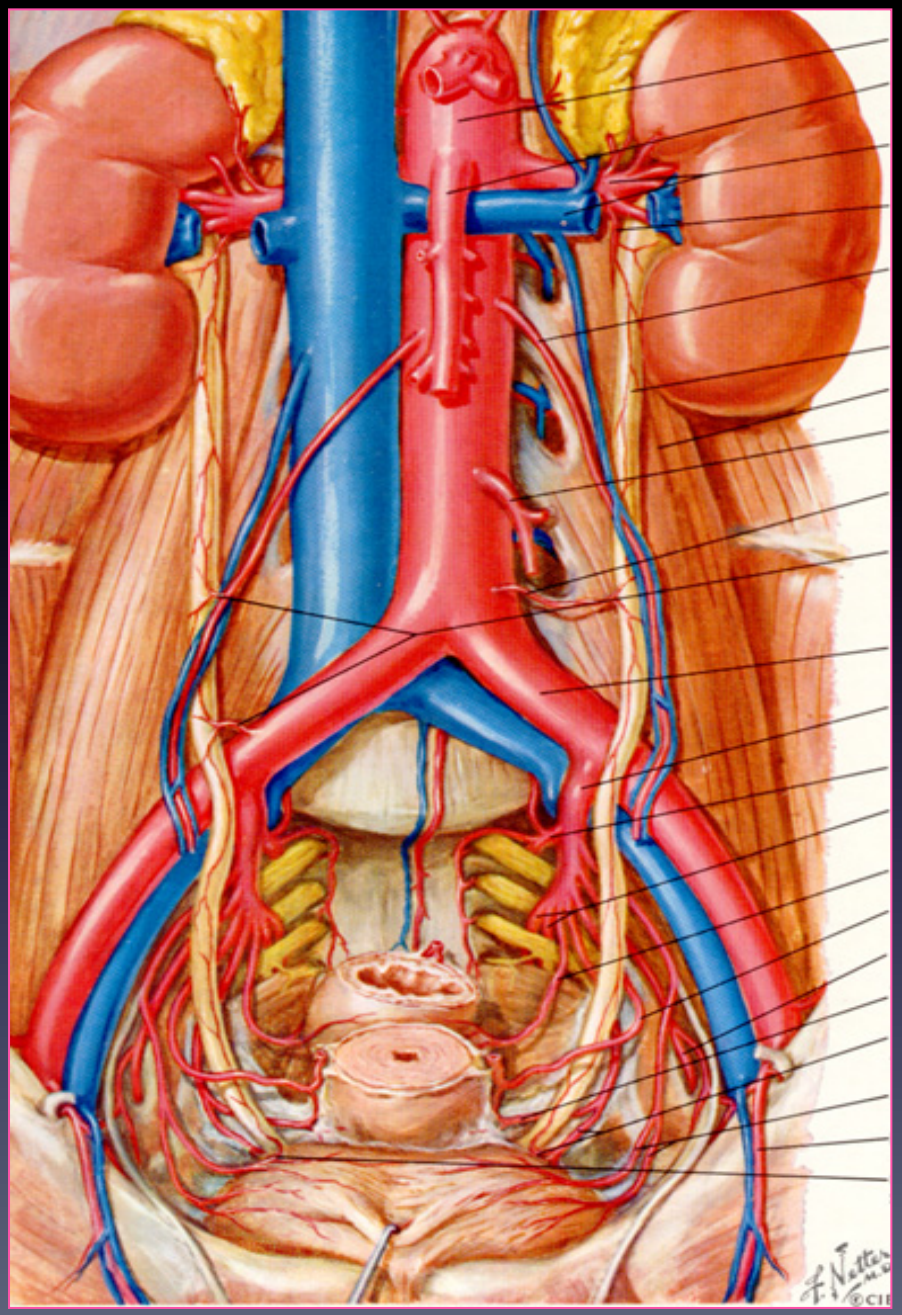
ii. inhibition of enzymes (metabolism)



Drug Elimination (Kidneys)

- drug elimination → kidneys
- drug metabolism → liver

- it has been 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 --> secreted in bile

  --> small intestine

  --> return to liver

  --> secreted in bile

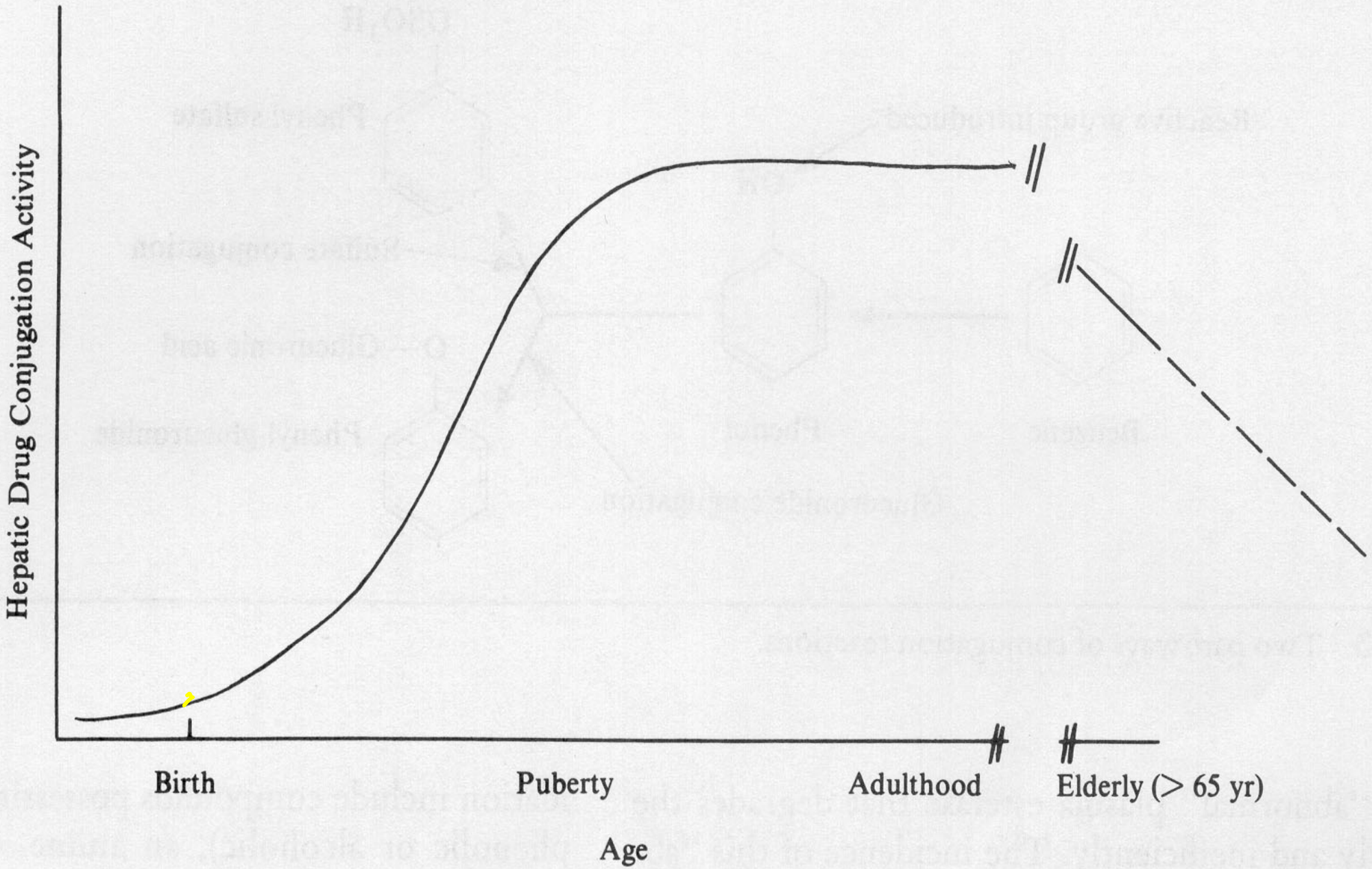
Elimination by Kidneys after Drug Metabolism

Elimination by Kidneys Directly into Urine

Drug Elimination & Age Considerations

i. infants --> underdeveloped abilities to metabolize and excrete drugs

ii. elderly --> impaired abilities to metabolize and excrete drugs


Hepatic Drug Conjugation Activity
Birth
Puberty
Adulthood
Elderly (> 65 yr)
Age

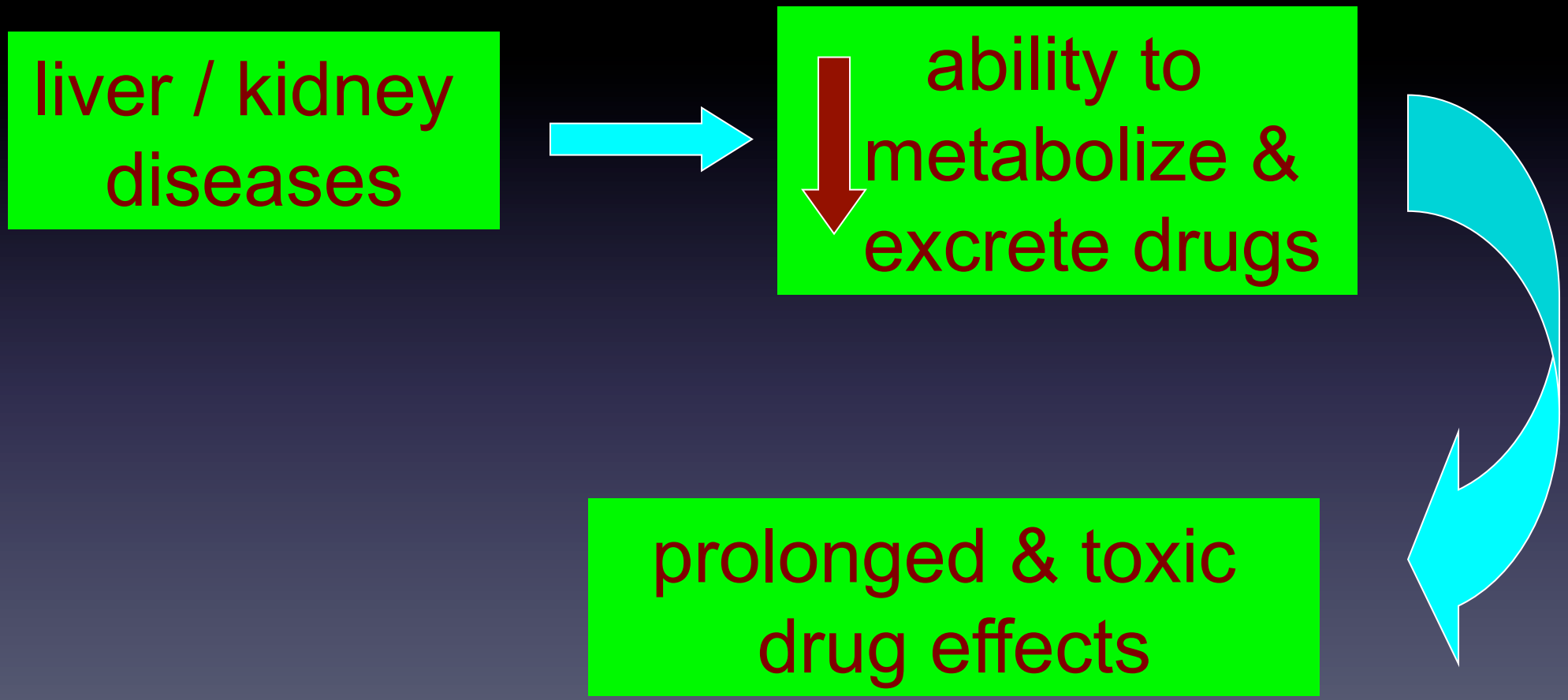
Geriatric Considerations

i. Absorption (cardiac output)

ii. Distribution (plasma proteins)

iii. Metabolism

Disease & Drug Elimination Rates

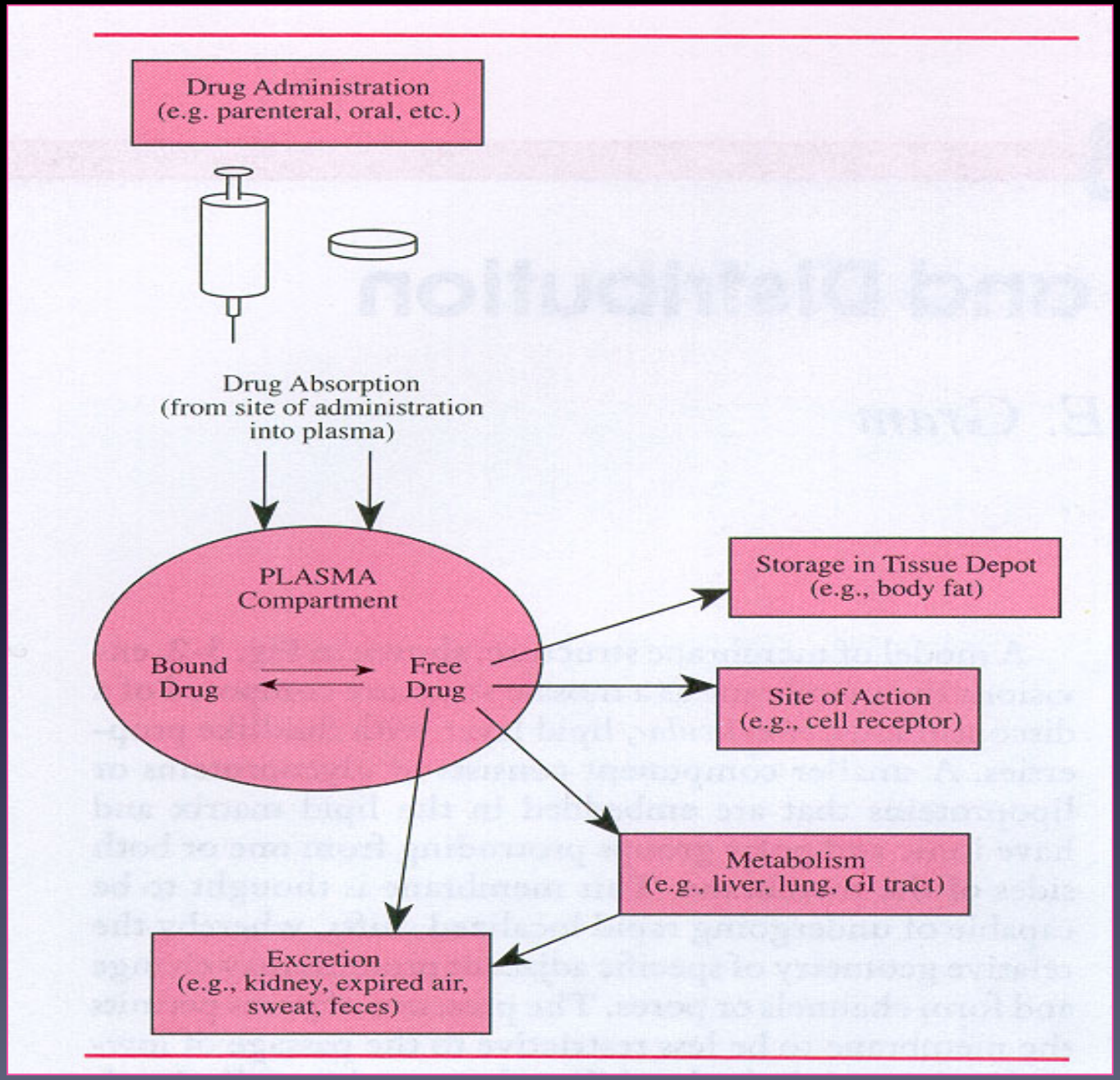


Summary

Pharmaco-dynamics

&

Pharmaco-kinetics




PHARMACY
CLOSED