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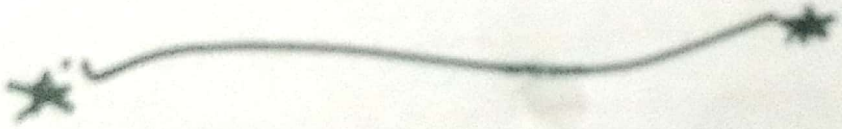
PAPER Pharmacology.



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Q3)..... DRUG ELIMINATION & BODY CLEARANCE

DRUG ELIMINATION:

Drug elimination is defined as to put an end, pharmacologically active drug into an inactive form and its removal from body (or)

Removal of drug from the body either by metabolism (inactive metabolites) or excretion (drug with active metabolites) is called drug elimination.

MAJOR ROOTES OF ELIMINATION:

Kidney (most-common), liver, lung, intestine, saliva, milk, tears, sputum, vaginal-secretions.

KIDNEY DRUGS ELIMINATION

most of drugs are excreted through kidney so stages involved in renal-drug excretion are:

(i) Glomerular filtration
(ii) Tubular-secretion
(iii) Tubular re-absorption

(i) Glomerular Filtration:

Under high hydrostatic pressure most of drugs (except macromolecules), not bound to plasma proteins are freely filtered from glomerulus → bowmans capsule →

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Proximal tubules → loop of Henle's → distal-convoluted tubules → collecting ducts → goes out as urine form.

FACTORS AFFECTING GFR:

1. Drug molecular size
2. Drug molecule-shape
3. plasma-protein-binding
4. Glomerulonephritis → ↑GFR, ↑filtration-pressure → ↑Drug excretion.

(ii) ACTIVE-TUBULAR-SECRETION:

- process of active transport-mediated excretion of charged-drugs (polar) by proximal renal-tubules.

⇒ polar-drugs cannot filter through bowman's capsule therefore need carrier-mediated-energy dependent transport system for weak acid and weak bases.

⇒ carrier-mediated transport can achieve maximal-drug clearance even when most of drug is bound to plasma-protein.

Anion-drugs removal (weak-acid)
furosemide, penicillin, bile-salt, aspirin etc.

Cations-drug-removal (weak-bases): Epinephrine,

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adrenaline, neostigmine, cimetidine etc.

DISTAL-TUBULAR-REABSORPTION:

•Drugs moving towards distal tubules, concentration increases and exceeds that of perivascular space and if uncharged, diffuses out of nephric lumen → systemic circulation. Maintaining urine PH to increase ionized form of drug in lumen may be used to minimize amount of back-diffusion hence increase clearance of an undesirable drug.

NOTE:

• => Weak acid elimination by alkalinization of urine
=> Weak-base elimination by acidification of urine.

(b) TOTAL-BODY-CLEARANCE

DEFINITION:

•Sum of clearances from various drug metabolizing and drug eliminating organs. While clearance is defined as "Ratio of rate of elimination of a drug to its concentration in plasma"

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DENOTION:

Total body clearance denoted by C_L, C_{LT}.

EXPLANATION:

=) Pharmacokinetic - parameter
=) of elimination

=) C_{LT} basically measures ability of a body to eliminate - drug in given unit of time.

=) Clearance basically quantify drug elimination from plasma without reference to mechanism involved.

=) Elimination is a process while clearance is a parameter.

SITE OF CLEARANCE:

=) Kidney (main - organ)
=) Sometimes liver

FORMULA:

Total - body clearance can be calculated by following equation

$$C_{LT} = Cl_{liver} + Cl_{renal} + Cl_{pulmonary} + Cl_{others}$$

$$C_{LT} = K_e V_d \longrightarrow (A)$$

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FACTORS AFFECTING CLEARANCE:

1. Blood flow to clearance organ
2. Extraction capacity of clearance organ
3. Condition of clearance organ (normal or diseased)
4. plasma-protein-binding

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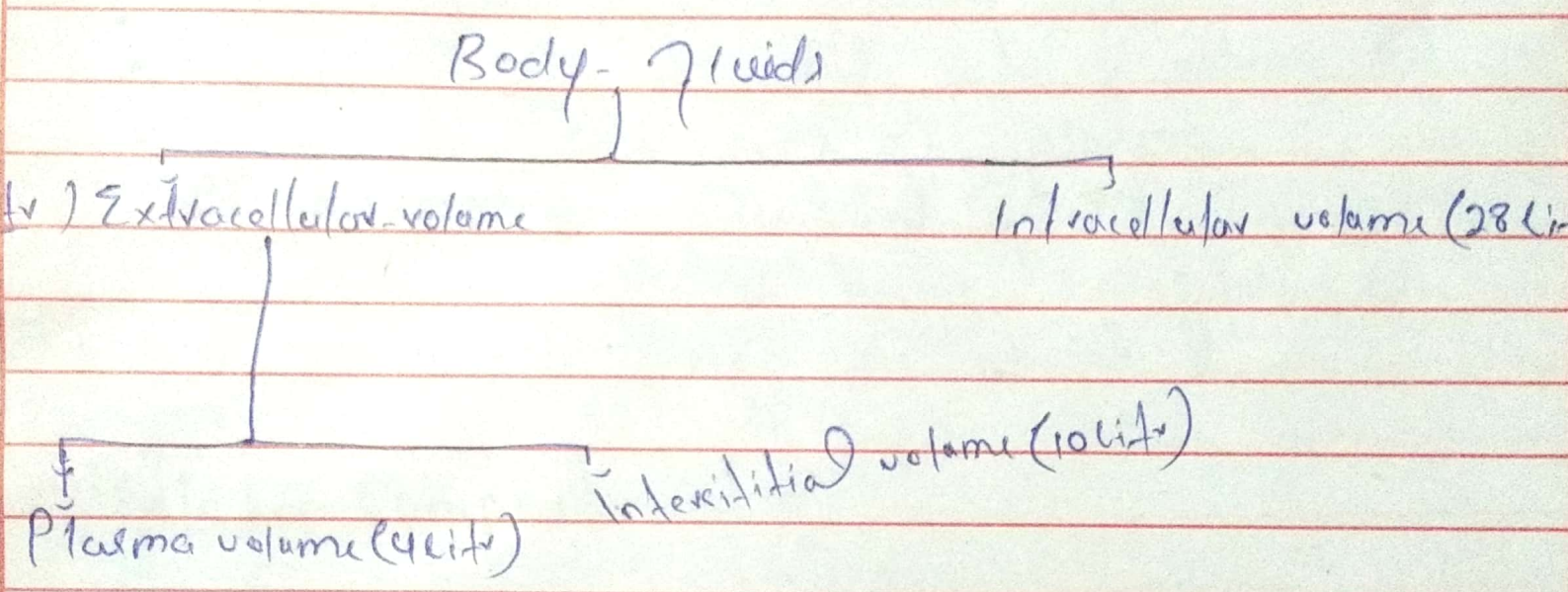
Q2)---- WATER- COMPARTMENT

INTRODUCTION:

- means how body fluids are distributed throughout body within cells, vessels, intercellular spaces etc.

WATER-COMPARTMENTS:



While total body fluid (42 Litre)
- ⇒ Plasma
- ⇒ Interstitial
- ⇒ Intracellular

→ 42 Litre.

Plasma-component:

- If drug having large molecular weight or bind to plasma proteins, too large to move out through slit junctions of capillaries, trapped within plasma-compartment.

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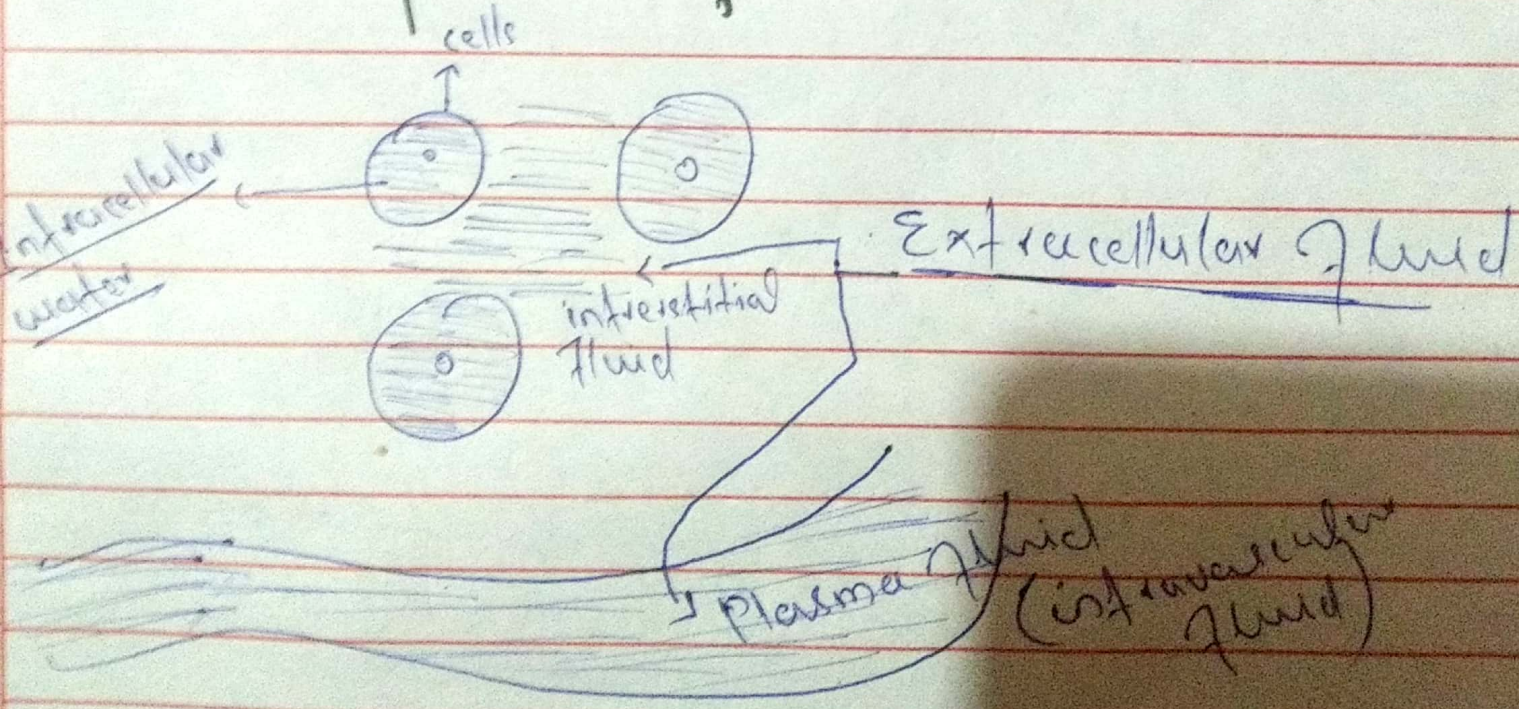
as a consequence drug distributes in plasma about 6% of body weight in 70 kg individual.

Extracellular fluid:

Low molecular weight drug but is hydrophilic can move through endothelial slit junctions into interstitial fluid.

⇒ ① drug distribute into a volume of that is the sum of plasma water and interstitial fluid. This is about 20% of body weight or 14 Lt of 70 kg individual.

Water Compartments:



Q1)----?

ROUTES OF DRUGS ADMINISTRATION

INTRODUCTION:

As we know that whenever we give some drugs to a patient, pharmacist/doctor also tell him how to take drug. So some of the routes by which a patient can take drugs are:

ROUTES:

① ⇒ Enteral route
- oral
- sublingual
- rectal

② ⇒ Topical route

③ Inhalational route
- oral
- Nasal

④ Parenteral route/Injection
- Intramuscular
- Intravenous
- Subcutaneous
- Intrathecal
- Intradermal

⑤ Intra-cavity route
- intraperitoneal
- intra-pericardial
- intra-articular
- intra-pleural.

These are the routes of drugs-administration.

PAREENTERAL-ROUTE / INJECTION:

=> Drug administration directly across the body's defense into systemic circulation or other vascular tissue.

MERITS:

① indicated incase of poorly absorbed drug from GI → circulation or agents which is unstable in GI tract.

② For treatment of unconscious patient means incase of emergency, rapid onset of action is required so parenteral route is used.

③ Having no first-pass-metabolism.

④ Highest bioavailability.

DE-MERITS:

=> Irreversible route of drug administration, once entred into body cannot be throw out.

=> Administration may cause pain, few, allergic reactions, infection

① INTRAVENOUS: Direct administration into vein
=> most common route
=> rapid onset of action
=> avoid 1st-pass-metabolism

⇒ high chances of infection (limitation)

INTRAMUSCULAR = Drugs deep into muscle

SUBCUTANEOUS = Drugs administration in under the skin.

⇒ It is like IM injection but slower than IV.