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**QUESTION NO 1:** Enumerate various routes of drug administration, explain parenteral routes in detail ?

**ANSWER:**

**Various routes of drug administration:**

- 1)** Enteral
- 2)** Parenteral
- 3)** Others

**Parenteral:**

Parenteral routes of the administration include the subcutaneous intramuscular, and intravenous routes.

The parenteral route introduce drug directly across the body's barrier defenses into the systemic circulation or other vascular tissue.

**Used for:** it is used poorly absorbed drug from the GI tract ( heparin ) ,agents that are unstable in the GI tract ( insulin ). It is also used for treatment of unconscious patients require a rapid onset of action. In addition these routes have the highest bioavailability and are not subject to first-pass metabolism or harsh GI environment.

**intravenous:**

**iv** Administering drug directly into vein.

Most common route drug not absorbed orally e.g. etracerium

**Advantage:** Avoid GI tract and so the first pass metabolism rapid effect and maximum control over circulating drugs.

**Limitation:** can not be recalled by emesis or activated charcoal high chance infection

**Interamascular: (IM)** administering drug deep into muscles

Aq sol of drug is suspended in non aqueous vehicle PEG release drug slowly over time. Providing sustained effect.

e.g. haloperidol decanoate ( neuroleptic effect )

**Subcutaneous ( SC)** administering drug into the skin.

It is like I'M injection and slower than iv

Lower the risks associated with IV

## **QUESTION NO 2:**

What does water compartment means, explain it's types in detail ?

### **Means of water compartment:**

The two main fluid compartments are the intracellular and extracellular compartments. The intracellular compartment is the space within the organism's cells; it is separated from the extracellular compartment by cell membranes.

### **it's types:**

#### **plasma compartment:**

it separate the human body in four different compartments. The four compartments consist of two intracellular and two extracellular compartments. The two intracellular compartments, the blood plasma and interstitial fluid are separated by the capillary walls. If a drug has very large molecule weight or bind extensively to plasma proteins, it is too large to move out through the endothelial slit junction of the capillaries and thus, is effectively stuck within the plasma vascular compartment. As a conclusion, the drug distributes in a volume (the plasma) that is about six percent of the body weight or in a 70kg individual about 4 liter of body fluid Heparin.

#### **Extracellular fluid:**

it is the term for the many fluids that exist in an organism outside of cells of the organism, but sealed within the body cavities and vessels. Extracellular fluid that travels in the circulatory system is blood plasma, the liquid component of blood. If a drug has a low molecular weight but is hydrophilic it can move through the endothelial slit junctions of the capillaries into the interstitial fluid. However hydrophilic drugs cannot move across the lipid membranes of cells to enter the water phase inside the cell. Therefore these drugs distribute into a volume that is the sum of the plasma water and the interstitial fluid, which together constitute the extracellular fluid. This is about twenty (20) percent of the body weight or about 14 liter in a 70-kg individual Aminoglycoside antibiotics.

#### **Total body water:**

The ICF makes up about 60 percent of the total water in the human body, and in an average-size adult male, the ICF accounts for about 25 liters (seven gallons) of fluid. This fluid volume tends to be very

stable, because the amount of water in living cells is closely regulated. If a drug had a low molecular weight and is hydrophobic, not only can it move into the interstitium through the slit junctions but it can also move through the cell membranes into the intracellular fluid. The drug, therefore distributes into a volume of about sixty percent of body weight or about 42 L in a 70-kg individual. Ethanol exhibits this apparent volume of distribution.

### **Other sites:**

In pregnancy the fetus may take up drugs and thus increase the volume of distribution. Drugs that extremely lipid soluble such as thiopental may also have unusually high volumes of distribution.

**QUESTION NO 3:** What are the drug elimination stages explain briefly ?

What does total body clearance means ?

### **ANSWER: Drug elimination:**

Removal of a drug from the body occurs via a number of routes, the most important being through the kidney into the urine. Other routes include the bile, intestine, lung, or milk in nursing mothers.

### **Renal elimination of drug:**

Glomerular filtration.

Proximal tubular secretion.

Distal tubular reabsorption.

### **Glomerular filtration:**

is the first step in urine formation and constitutes the basic physiologic function of the kidneys. It describes the process of blood filtration in the kidney, in which fluid, ions, glucose, and waste products are removed from the glomerular capillaries.

Drugs enter the kidney through renal arteries which divide to form a glomerular capillary plexus. Free drug ( not bound to albumin ) flows through the capillary slits into Bowman's space as part of the glomerular filtrate. The glomerular filtration rate ( 125 ml/min is normally about twenty percent of the renal plasma flow (600 ml/min)

### **Proximal tubular secretion:**

It represents the primary kidney mechanism for eliminating hundreds of commonly prescribed medications, including cephalosporins, quinolone antibiotics, diuretics, antidiabetic medications, antiviral agents, and chemotherapies.

Drugs that were not transfer into the glomerular filtrate leave the glomeruli through efferent arterioles, which divide to form a capillary plexus surrounding the nephric lumen in the proximal tubules by two energy requiring active transport ( carrier requiring ) system one for anions ( for example, deprotonated form of weak bases )

### **Distal tubular reabsorption:**

Uncharged drugs may diffuse out of the kidney and escape elimination. Manipulating the pH of the urine may alter this process by changing the ionization of the weak acids and bases. This process was described in Chapter 3 in the context of passive diffusion of drugs across membranes.

As a drug move toward the distal convoluted tubule it's concentration increases and exceeds that of the perivascular space , the drug if uncharged, may diffuse out of the nephric lumen back into the systemic circulation. Manipulating the PH of the urine to increase the ionized form of the drug in the lumen may be used to minimize the amount of back-Diffusion, and hence increase the clearance of an undesirable drug. As a general rule, weak acid can be eliminated by alkalization of the urine, whereas elimination of weak bases may be increased by acidification of the urine.

### **Quantitative aspects of renal drug elimination:**

#### **Extraction ratio:**

This ratio is the decline of drug concentration in the plasma from the arterial to the venous side of the kidney. The drugs enter the kidneys at concentration C1 and exit the kidneys at concentration C2 the extraction ratio= $C1/C2$ .

#### **Excretion rate:**

The excretion ratio is determine equation:

The elimination of a drug usually follows first order kinetics.

$$\text{Excretion rate} = (\text{clearance}) (\text{plasma concentration})$$

$$\text{mg/min} \quad \text{ml/min} \quad \text{mg/min}$$

#### **Total body clearance:**

The total body ( systemic) clearance CLt is the sum of the clearance from the various drug – metabolizing and drug- eliminating organs.

Major organ is kidney .

Sometime liver also contribute to drug loss through metabolism and /or excretion in the bile

A patient with renal failure may sometimes benefit from a drug that is excreted by this pathway into the intestine and feces rather than through the kidney. Some drug may also be reabsorbed by through the enterohepatic circulation, thus prolonging their half-life.

Total clearance can be calculated by using of the following equation .

$$CL_{total} = CL_{hepatic} + CL_{renal} + CL_{pulmonary} + CL_{other}$$

$$CL_{total} = Ke Vd$$