DRUG EXCRETION

- Drugs & their metabolites are irreversibly transferred from internal to external environment.

Rate of Excretion = Rate of filtration + Rate of Secretion − Rate of Reabsorption

① Glomelar filtration:-

- 1st step in formⁿ of urine
- Unidirectional process
- High degree of filtrⁿ for water soluble compounds & restricts high M.W drugs / matter.

  filtrate contains LMW (< 500 D) & are water soluble
- Driving force is obt 4m hydrostatic pressure of blood flowing in capillaries.
- Proteins bound drugs are not filtered ∴ of HMW

  GFR value = 125 ml/min or per day.

  ↑ GFR ↑ urine prodⁿ.

② Tubular Reabsorption:

- In renal tubule, for glucose & amino acids.
- Drug reabs indicates excretion rate values are less than GFR
- Moves solutes & water out of filtrate and back into bloodstream.

③ Tubular Secretion:

- In Proximal tubule.
- Drug diffuses against the conc gradient 4m the blood capillaries across the renal tubular memb
- H⁺, creatinine & drugs will be removed 4m the blood through the peritubular capillary network into the collecting duct.
- End product is urine.

Factors affecting Excretion of drugs.

- Urine excretion $\propto \frac{1}{\text{lipophilicity}}$

Higher lipid solubility, ↑ in VoD of drugs & reduces renal excretion.

- Protein bound drugs has long $t_{1/2}$.
- $Cl \propto \frac{1}{V_d}$
- Basic drugs are more excreted.
- pH change causes passive tubular re-abs of drugs.
- R.E is 10% lower in ♀ than ♂
- In newborns is 30-40% less than adults & attains maturity betn 2.5-5 mnths
- Furosemide ↑ the excretion of gentamicin by displacing gentamicin from its protein binding sites.
- Excretion of digoxin is decresed by diazepam.

NON-RENAL ROUTES

Other than kidneys.

① Biliary Exc;

- Enterohepatic excretion.
- By hepatic cells of liver, Active Secretion.
- Unchanged drugs which passes through liver are excreted in bile.

Other drugs get metabolized in liver befor excreted in bile

- Secreted drug is reabs in S.I & undergoes enterohepatic cycling. rest is feaces.

Drug abs - Secreted in bile - Reabs in S.I - Enterohepatic cycling

- Bile secretion in liver & stored in gall bladder.

> 300 D

Biliary $Cl = \frac{\text{Biliary excretion rate}}{\text{plasma drug conc.}}$

Based on Bile / plasma conc. ration., comps are!

Group A: Ration = 1

eg: Na, k, Cl^- ions, glucose.

Group B: >1

10 - 1000

eg:- Bile salt, bilirubin, glucuronide, Creatinine, Sulfobromophthalein conjugates.

Group C: <1

eg:- Sucrose, insuline, PO_4^-, P.L, mucoproteins

② Pulmonary Exc:

- For Exc^n of gaseous & volatile subs.

eg:- Gaseous anaesthetics, Nitrous oxide.

@ Alcohol (slowly)

③ Salivary Exc:

- Saliva p^H 5.8 - 8.4 (p^H 6.4)
- Passive diffusion.
- Drugs blood conc can be det by detecting the amount of drug excreted in saliva

eg:- Caffeine, theophylline, phenytoin.

④ Mammary Exc:

- Into milk. (p^H 6.4 - 7.6)
- Passive
- Agents that cross BBB.
- Drug exc in milk = $\frac{\text{milk}}{\text{Plasma D.C}}$

>1 for basic drugs.

⑤ Skin / Dermal Exc:

- Via sweat & follow p^H partition hypothesis.
- Passive

eg:- Benzoic acid, Salicylic acid, Alcohol, Antipyrine, Pb, Hg, As.

⑥ GIT Excretion:- Nicotine

CLEARANCE

- Hypothetical vol of body fluids containing drug from which the drug is removed / cleared in sp time.

$$Cl = \frac{\text{Elimination rate}}{\text{plasma D.c}} \quad ml/min$$

- Renal clearance (RCl_R)

$$Cl_R = \frac{\text{Rate of Elimination by kidney}}{\text{plasma drug conc.}}$$

Vol of blood / plasma that is completely cleared of the unchanged drug by the kidney per unit time.

$$Cl_R = \frac{(d\,D_u/dt)}{C_p}$$

$$Cl_R = \frac{\text{Rate of (filt}^n + \text{Sec}^n - \text{Reabs)}}{\text{plasma drug conc.}}$$

$Cl_R \propto GFR$

- Renal cl. of drug is compared to the Std Ref - inulin which is cleared completely by GF only.

$$\text{clearance ratio} = \frac{\text{Ratio of drug Cl}}{\text{inulin Cl}}$$

$$\text{Renal Cl ratio} = \frac{\text{Renal Cl of drug}}{\text{renal Cl of creatinine}}$$

(1) Excretion ratio

For Glucose –	RCiR	& RCl_R (ml/min)
lipophilic drug –	0-1	< 130
Creatinine, insuline –	1	130
Ionic drugs –	>1	>130
Isodopyracet, PAH –	5	650

Det of Cl_R:

① Graphical Methods:

- Slope of curve

$\left(\frac{dDu}{dt}\right)$ / C_p

$> (dDu/dt)$ – steeper slope, Cl is greater.

$< (dDu/dt)$ – slope is smaller.

Cl_R = Urinary drug exc rate / Plasma drug conc.

② Model Independent Methods:

Total amt of drug excreted in urine (Du^∞),

$$Cl_R = \frac{Du^\infty}{(AUC)_0^\infty}$$

$(AUC)_0^\infty$ → Total Area under curve of drug abs.