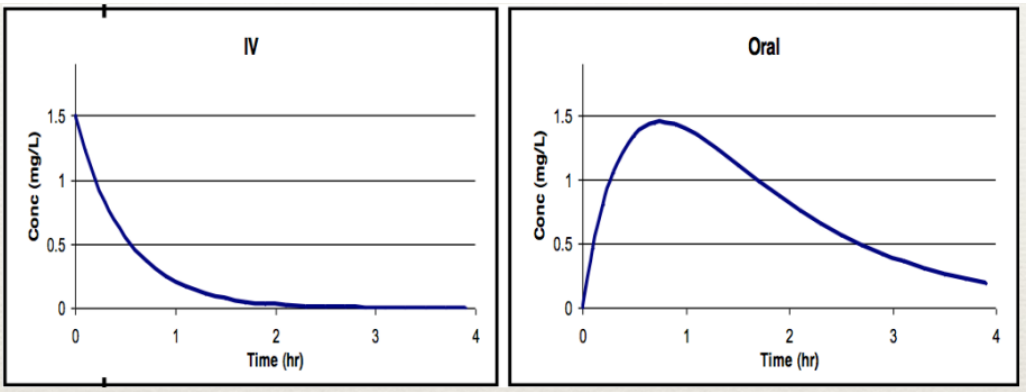
LADME – What body does to the drugs (PK)

Liberation (Disintegration + Dissolution)	**Release of drug from its dosage form after administration** • Some drugs are liberated slowly (e.g. controlled release [CR], sustained release [SR], extended release [XR]). If not specified, the drug is **immediate release** (IR). • Older people need lower dose than younger people (due to renal/liver impairment) • Children's weight and body surface area used to calculate safe dosing as their physiological systems are still developing (reduced stomach acid production, etc.)

Absorption	**Movement from site of administration to bloodstream (across lipid bilayer)**
	• For oral, most absorption occurs in small intestine. Drugs then undergoes first-pass through liver via portal circulation (vein) before travelling in systemic circulation to tissues
	• Measured by **bioavailability** (fraction of administered dose that reaches systemic circulation unchanged/not metabolized) - rate & extent (area under curve)
	  ○ Usually Drug **Bioavailability = AUC of [*Route of Administration*]/ AUC of IV**
	  ○ Depends on route of administration
	• **Generics** are required to be **bioequivalent** (produce similar plasma conc. of active ingredient – **similar T_{max}, C_{max}, AUC**)
	• **Different dosage forms** are **NOT bioequivalent** (e.g. XR and IR)
	• **Affected by food** (empty stomach means faster movement to small intestine)

Distribution	**Movement from bloodstream into tissues (sites of action)**
	• Measured by **apparent volume of distribution** (**V_d = Amount/Conc**.)
	  ○ Amount = mg; Conc. = mg/L in plasma
	  ○ **Small V_d = Higher conc. in plasma**
	  ○ Used to **calculate loading dose**

Metabolism (biotransformation)	**Chemical transformation to aid elimination from body (carried out by enzymes to create metabolites, which occurs in primarily in liver & also lungs, GIT)** • Makes drug less lipophilic/more polar. **Lipophilic = Hydrophobic = Non-Polar** • If drug has "high first-pass effect", higher dose required.
Excretion	**Removal of drugs/metabolites from body (through bloodstream into kidneys & bladder)** • More lipophilic drug = More likely to be Reabsorbed • Metabolites are more polar/less lipophilic & is less likely to be reabsorbed than parent drugs.



In Oral, rate of absorption > rate of elimination initially, until absorption comes to an end & drug conc. falls as rate of elimination > rate of absorption.	In IV, only elimination occurs.

Elimination = Removal via Metabolism + Excretion

- Measured by **clearance (CL) or elimination rate**
- At SS, rate of administration = rate of elimination (usually 4-5 half-lives to reach SS)