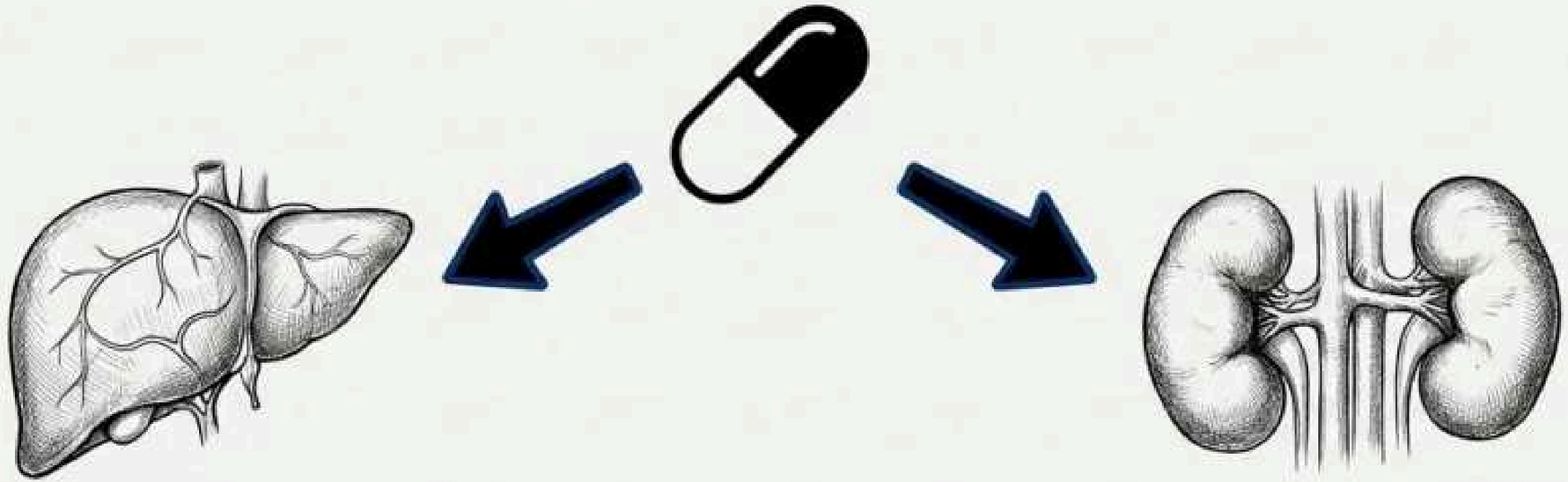
The Body Defends Itself by Altering and Expelling Foreign Chemicals

¶ 3.1



Metabolism: Chemical Change

Chemically alters foreign substances

Excretion: Physical Removal

Physically filters and removes products

Duration in Body = Dosing Frequency

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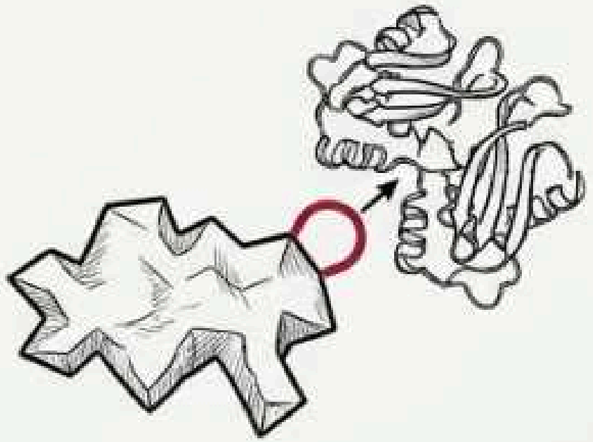
Transforming Fat-Soluble Drugs for Physical Excretion

Step 1



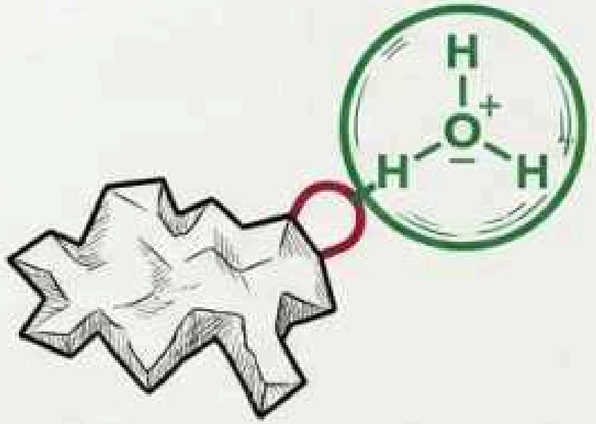
Kidneys simply reabsorb fat-soluble drugs

Phase One



Oxidation adds a reactive chemical hook

Phase Two



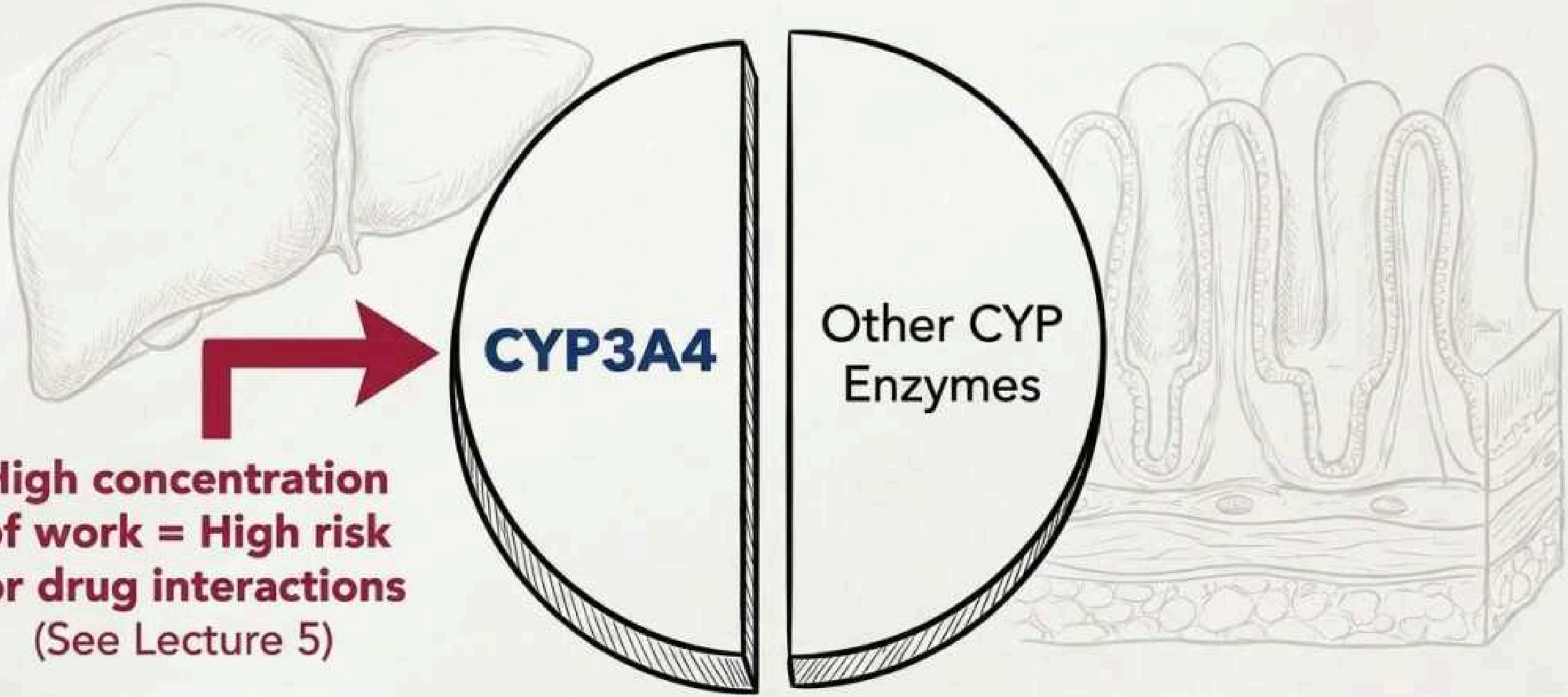
Conjugation attaches a large water-loving molecule

Fat-Soluble → Water-Soluble

Passable in urine or bile

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The Cytochrome P450 Bottleneck in the Liver and Gut

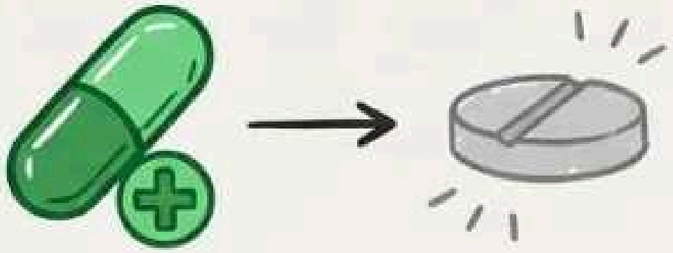
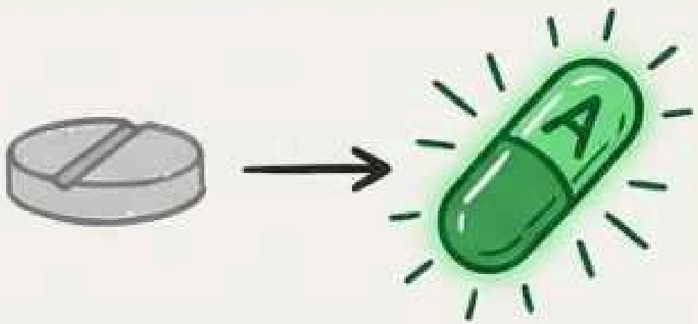
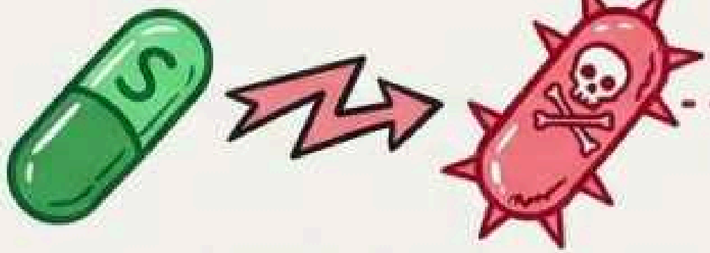
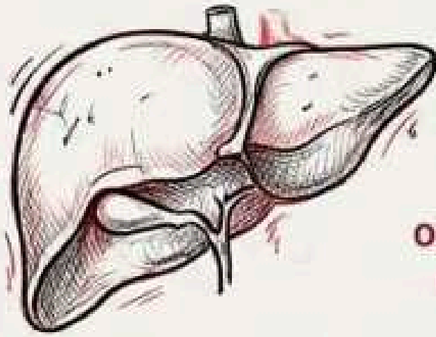


High concentration of work = High risk for drug interactions

(See Lecture 5)

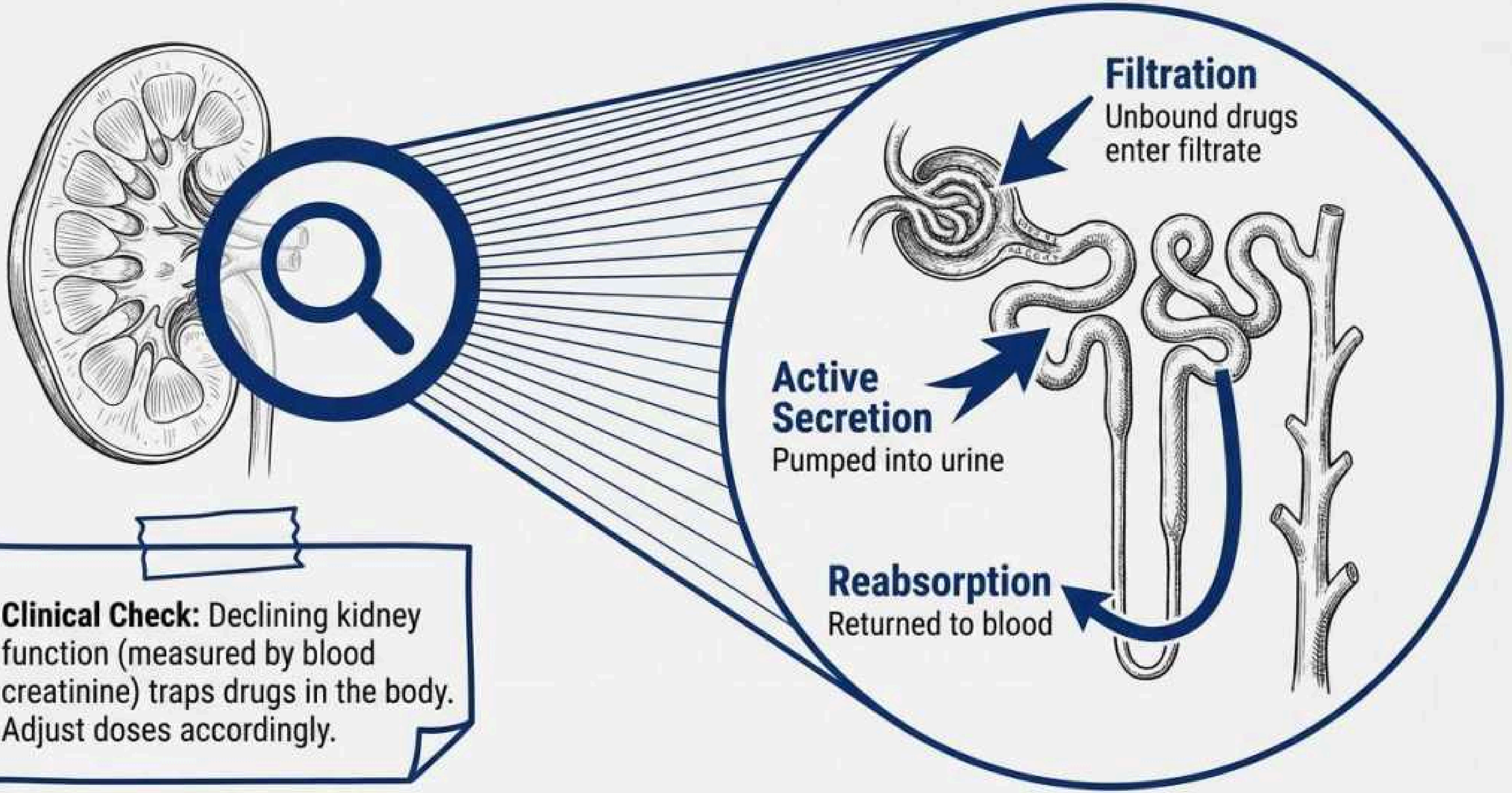
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Metabolism Can Inactivate, Activate, or Weaponize Drugs

Inactivation		Handles the vast majority of drugs
Activation		Prodrug conversion (e.g., Codeine → Morphine via CYP)
Harmful Product	 	Paracetamol (Acetaminophen) is safe at recommended doses, but overdose overwhelms liver defenses causing severe damage.

Gemini Notebook

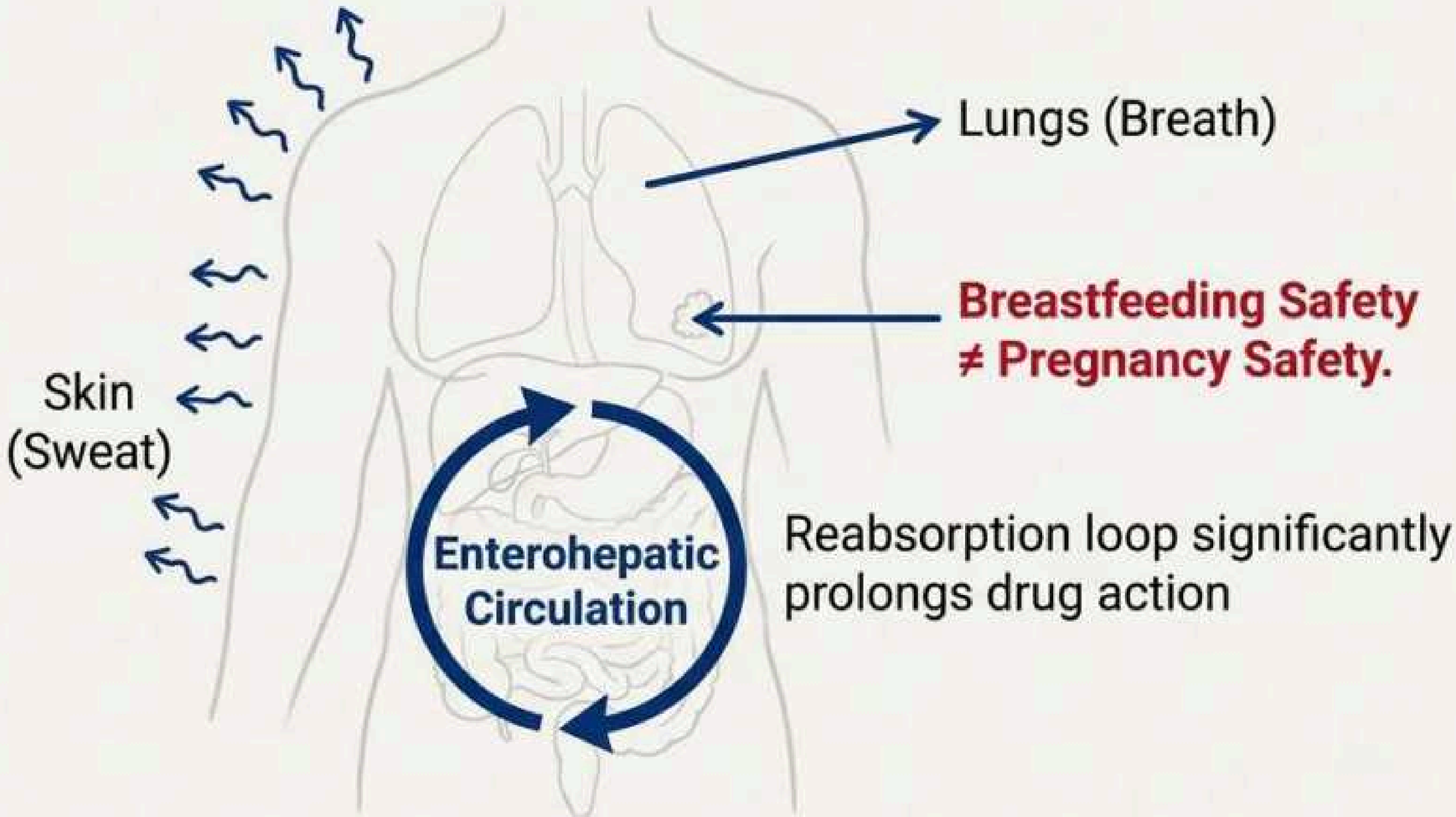
Renal Excretion Mechanics Within the Nephron



Clinical Check: Declining kidney function (measured by blood creatinine) traps drugs in the body. Adjust doses accordingly.

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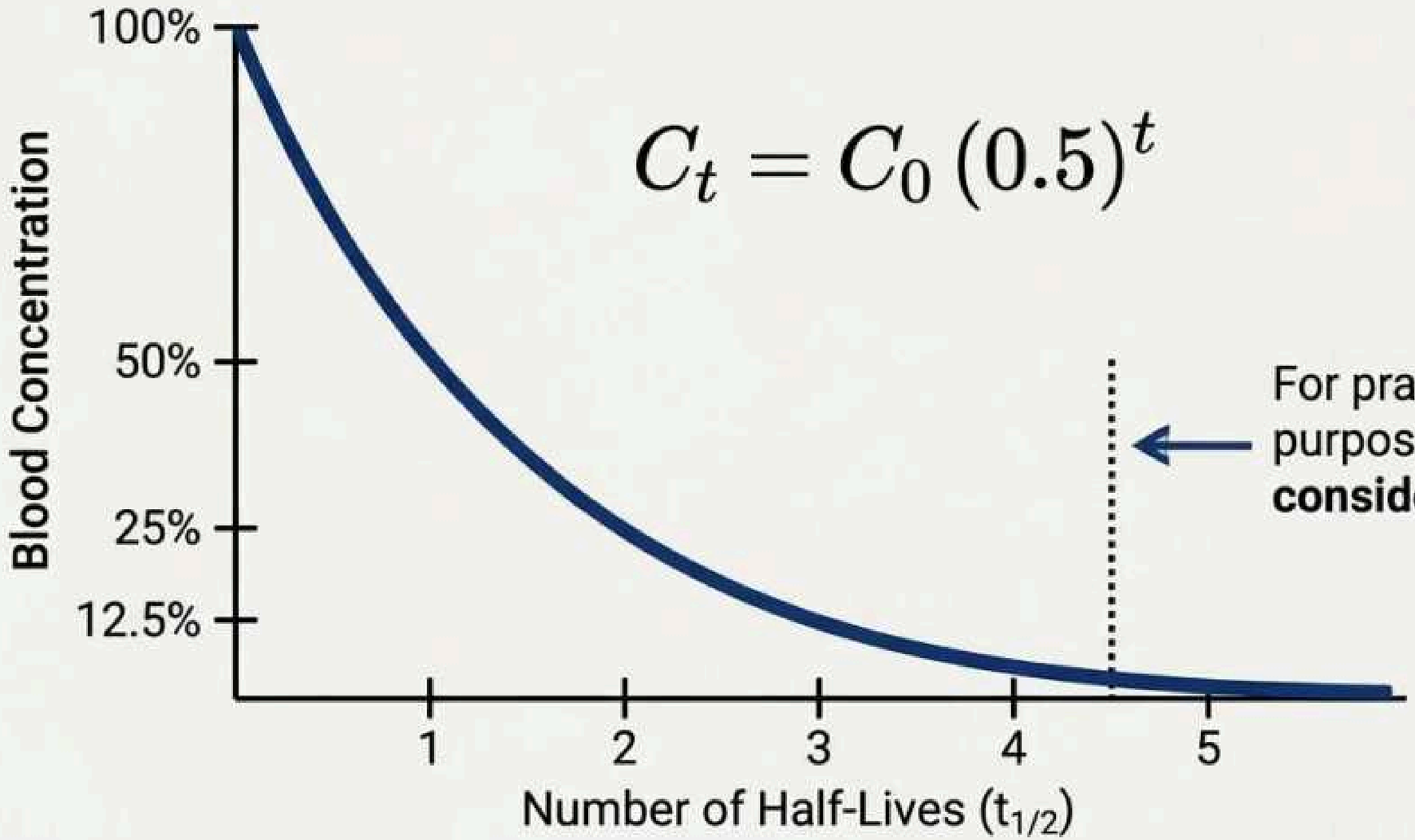
Alternative Excretion Routes and the Enterohepatic Loop



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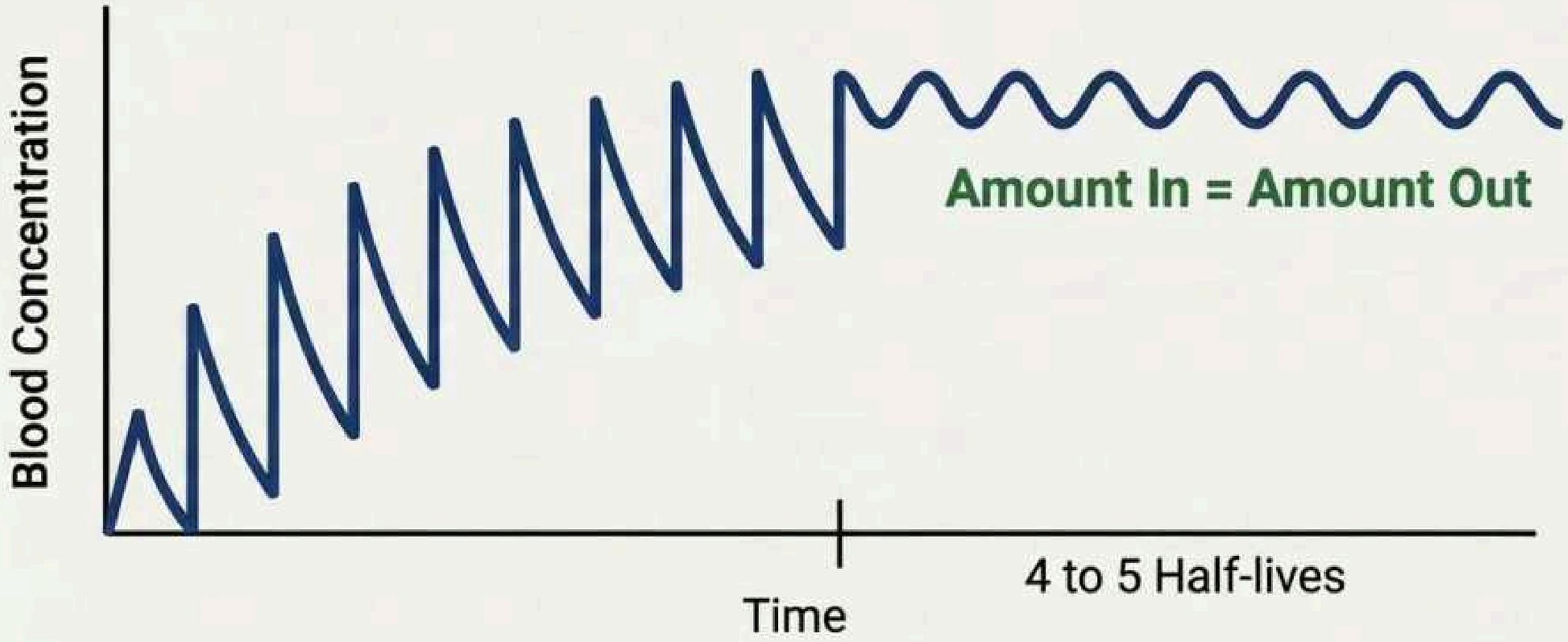
The Mathematics of Drug Clearance over Time

$$C_t = C_0\,(0.5)^t$$



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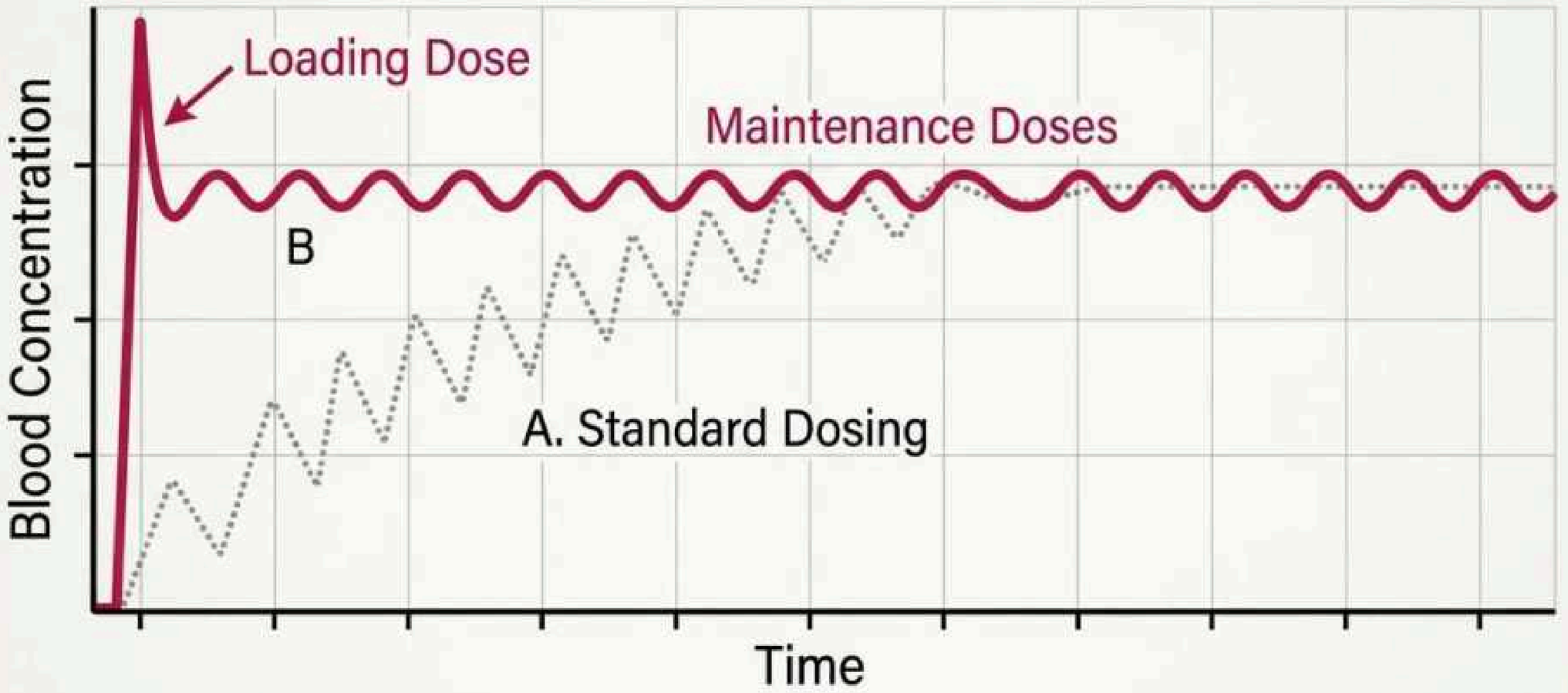
Reaching Steady State Through Repeated Dosing



This is why patients must wait days or weeks for full effect, and must continue taking medication even if it doesn't seem to work at first.

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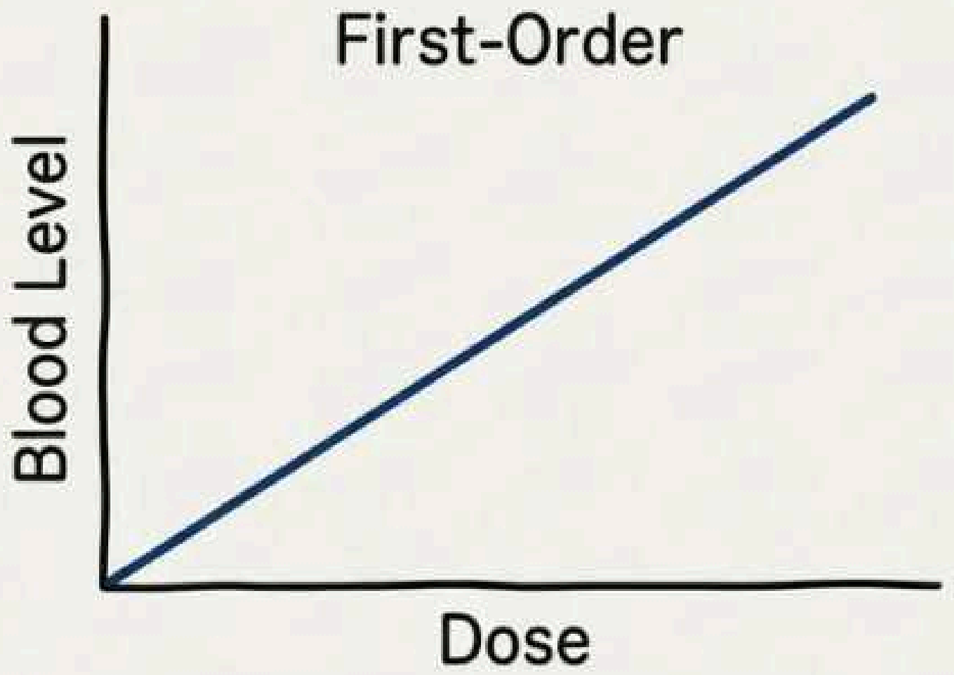
Bypassing the Wait with Loading Doses



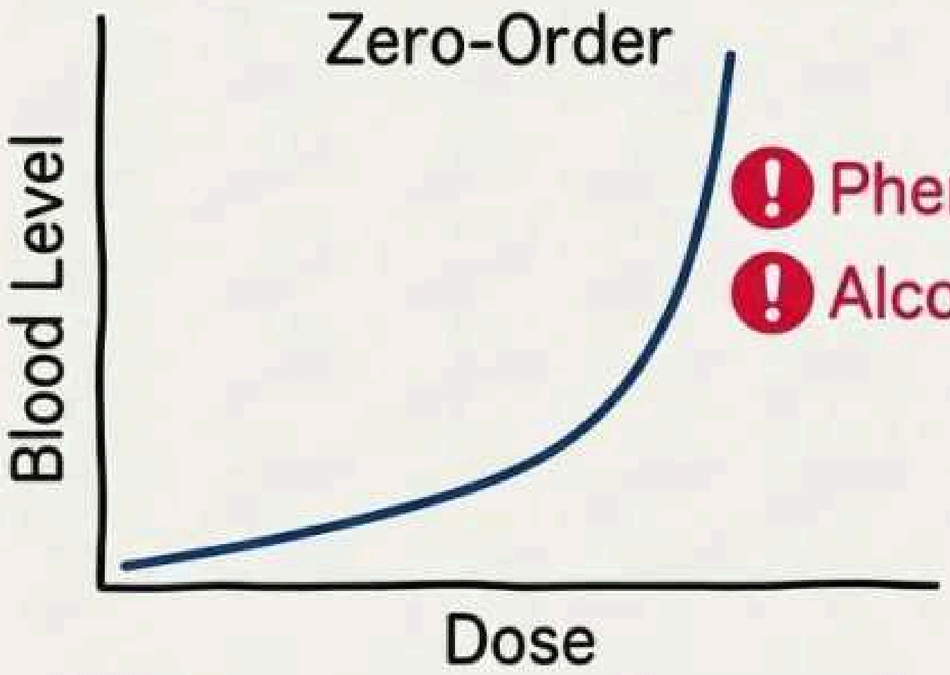
- Maintenance doses are strictly set by how fast the body clears the drug.
- Calculations require prescriber training and are not for self-medication.

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When Enzymes Saturate: Zero-Order Kinetics



Constant Fraction Removed



Fixed Amount Removed
(Enzymes Saturated)

Small dose changes cause massive, unexpected blood level spikes, requiring strict monitoring.

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Knowledge Check: Applying the Half-Life Rule

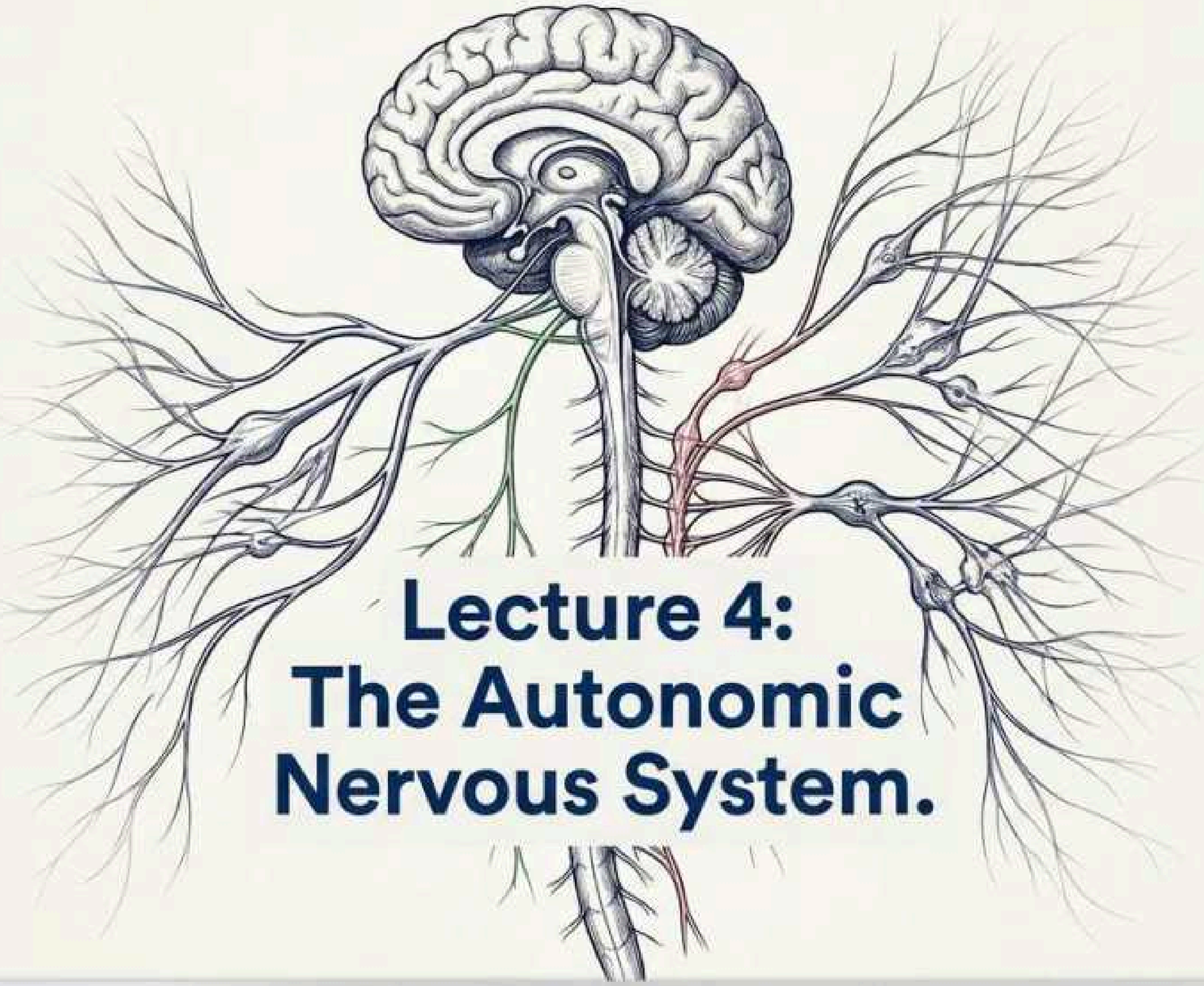
A drug has a half-life of about one day. Taken daily, how long to reach steady state? How long to leave the body after the last dose?

1 day x 4 to 5 half-lives = 4 to 5 days	1 day x 4 to 5 half-lives = 4 to 5 days

The math works identically for accumulation and elimination.

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Next: Applying Pharmacokinetics to the Nervous System



Lecture 4: The Autonomic Nervous System.

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