

UNIT 1

COURSE NAME: PHARMACOLOGY

TOPIC: ADME

CASE STUDY PUZZLE 1: The Overdosed Coffee Addict

Topic: Absorption & First-Pass Effect

Scenario: A 19-year-old student takes **30 tablets of 200 mg caffeine** (total 6,000 mg) to stay awake. He usually drinks coffee (oral caffeine).

• Onset of tremors: 15 minutes

• Peak plasma [caffeine]: $80 \mu g/mL$ at 1 hour

• Normal coffee peak: $6 \mu g/mL$ after 200 mg

Puzzle Ouestions:

1. Why such a **rapid onset** despite oral route?

2. Estimate bioavailability (F) of oral caffeine.

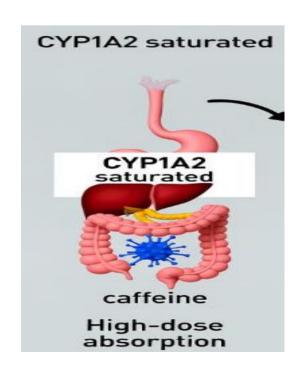
3. What organ is **saturated**?

Answer Key:

1. **High dose** \rightarrow **saturates first-pass metabolism** in liver $\rightarrow \uparrow$ systemic absorption.

2.
$$F = \frac{\text{AUC}_{\text{oral}}}{\text{AUC}_{\text{IV}}} \approx \frac{80 \times \text{dose}_{\text{coffee}}}{6 \times 6000} = 0.13 \text{ or } 13\%$$
(Typical F for caffeine = ~100%, but **saturated**).

3. **CYP1A2 enzyme in liver** \rightarrow nonlinear kinetics.



CASE STUDY PUZZLE 2: The Vanishing Antibiotic

Topic: Volume of Distribution (Vd)

Scenario: A 70 kg septic patient receives 1 g IV vancomycin.

- Plasma [vanco] at 1 hr: 20 μg/mL
- Expected peak: 30–40 μg/mL
- Patient is **edematous** (40 L total body water).

Puzzle Questions:

- 1. Calculate Vd.
- 2. Why is concentration **lower than expected**?
- 3. Adjust dose for next time?

Answer Key: 1.

$$V_d = \frac{\text{Dose}}{C_0} = \frac{1000 \text{ mg}}{20 \text{ mg/L}} = 50 \text{ L}$$

(Normal Vd = $0.7 \text{ L/kg} \times 70 = 49 \text{ L} \rightarrow \text{normal}$, but edema $\uparrow \text{ TBW} \rightarrow \text{dilutes}$). 2. Third-spacing in sepsis $\rightarrow \uparrow \text{Vd} \rightarrow \downarrow \text{ plasma}$ []. 3. Increase loading dose to 1.5-2 g.



CASE STUDY PUZZLE 3: The Prodrug That Wasn't

Topic: Metabolism (Prodrug Activation)

Scenario: A 55-year-old man with herpes is prescribed valacyclovir 1 g TID.

- Day 3: No improvement
- Plasma [acyclovir]: $<0.5 \mu g/mL$ (target $>3 \mu g/mL$)
- Genetic test: CYP2C19 poor metabolizer

Puzzle Questions:

- 1. What type of drug is valacyclovir?
- 2. Why is acyclovir level **low**?
- 3. Alternative drug?

Answer Key:

- 1. **Prodrug** (valacyclovir \rightarrow acyclovir via **hepatic esterase**, not CYP).
- 2. Poor absorption or esterase deficiency (not CYP2C19). Likely malabsorption.
- 3. Use **IV acyclovir** (active drug).



CASE STUDY PUZZLE 4: The Toddler's Tea Party

Topic: Clearance & Half-Life

Scenario: A 3-year-old (15 kg) accidentally drinks **50 mL of cough syrup** (dextromethorphan 15 mg/5 mL = 150 mg).

- t½ in adults: 4 hours
- Child is drowsy at 12 hours post-ingestion
- Plasma [DXM]: **80 ng/mL** (toxic >50 ng/mL)

Puzzle Ouestions:

- 1. Estimate t½ in child.
- 2. Calculate **clearance** (Cl) if Vd = 6 L/kg.
- 3. When will [DXM] < 25 ng/mL?

Answer Key: 1.

 $t_{1/2} \approx 12 \text{ hr (prolonged due to immature CYP2D6)}$

2.
$$Cl = \frac{\ln(2) \cdot V_d}{t_{1/2}} = \frac{0.693 \cdot (6 \cdot 15)}{12} = 5.2 \text{ L/hr}$$

3.
$$t = \frac{\ln(80/25)}{0.693/12} \approx 36 \text{ hr}$$



CASE STUDY PUZZLE 5: The Dialysis Surprise

Topic: Excretion & Dialyzability

Scenario: A 60-year-old on hemodialysis takes metoprolol 100 mg BID.

- Pre-dialysis [metoprolol]: 400 ng/mL
- Post-dialysis (4 hr): 380 ng/mL
- Dialyzer: high-flux, blood flow 350 mL/min

Puzzle Questions:

- 1. Is metoprolol dialyzable?
- 2. Estimate extraction ratio.
- 3. Better beta-blocker for dialysis patient?

Answer Key:

- 1. No highly protein-bound (95%), large Vd.
- 2. $ER = \frac{400-380}{400} = 5\%$ (negligible)
- 3. **Atenolol** or **carvedilol** (less protein binding).

