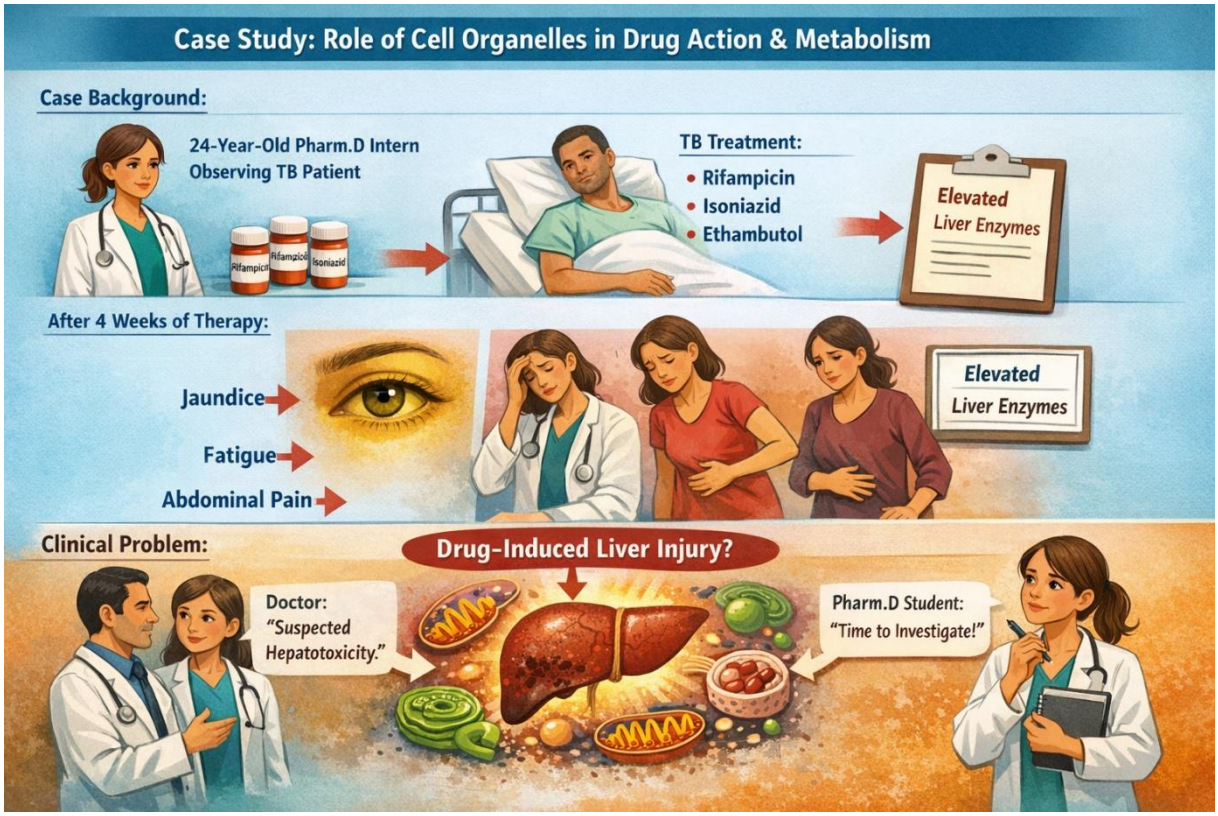
Case Study: Role of Cell Organelles in Drug Action & Metabolism



Case Background:

A 24-year-old female Pharm.D intern is observing a patient undergoing treatment for tuberculosis (TB).

The patient is prescribed Rifampicin, Isoniazid, and Ethambutol. After 4 weeks of therapy, she reports yellowing of eyes, fatigue, and abdominal discomfort. Laboratory investigations reveal elevated liver enzymes.

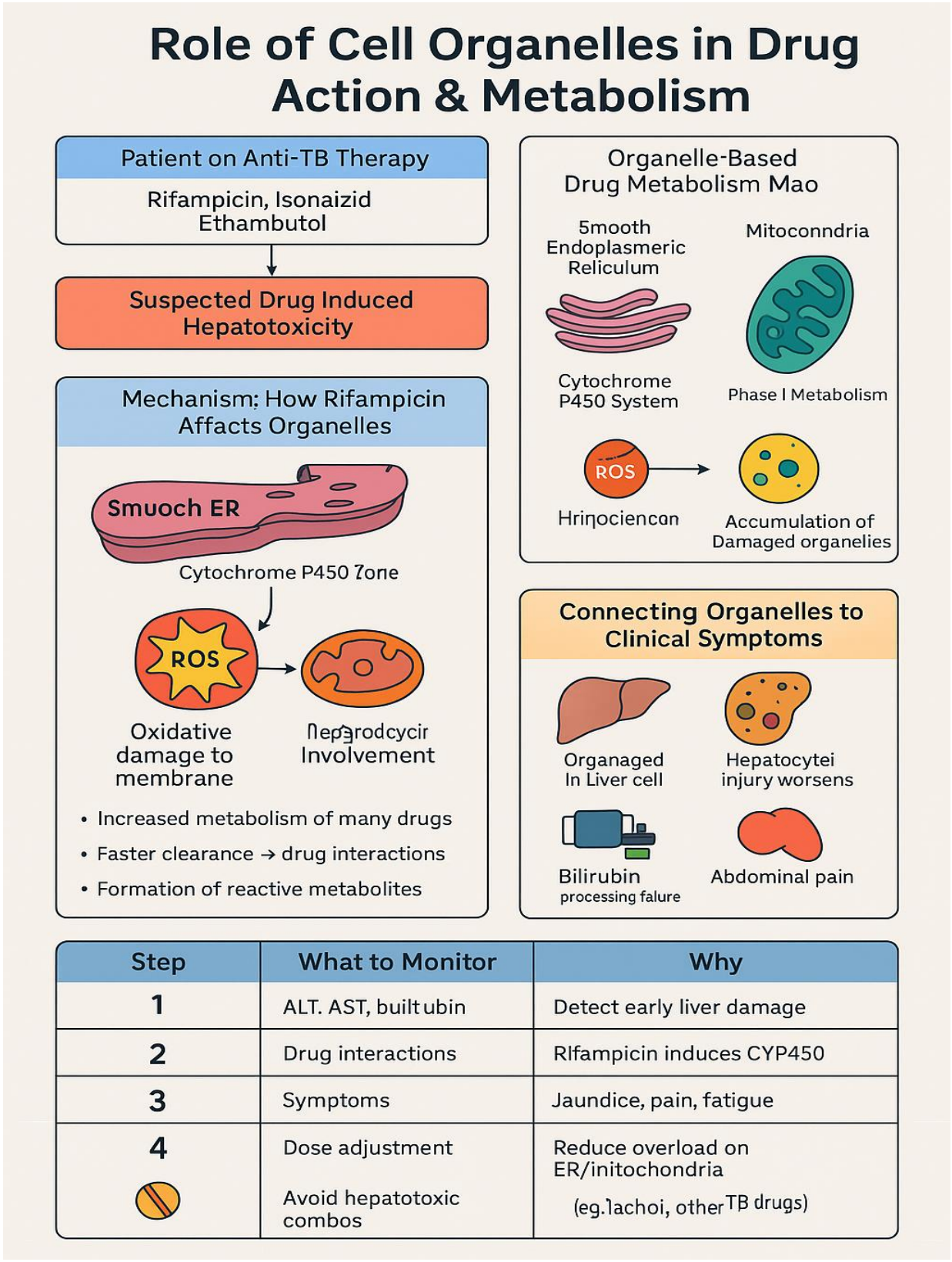
Clinical Problem:

- The treating physician suspects drug-induced hepatotoxicity.
- The Pharm.D student is asked to explore the cellular basis of this adverse reaction.

Learning Objectives:

1. To link drug metabolism to specific cell organelles (ER, mitochondria, lysosomes).
2. To understand how drug-induced organelle dysfunction leads to clinical symptoms.
3. To evaluate pharmacological strategies to minimize organelle-mediated toxicity.

Case Questions



Step	What to Monitor	Why
1	ALT. AST, built ubin	Detect early liver damage
2	Drug interactions	RIfampicin induces CYP450
3	Symptoms	Jaundice, pain, fatigue
4	Dose adjustment Avoid hepatotoxic combos	Reduce overload on ER/initochondria (eg.lachoi, other TB drugs)

Q1. Which organelle is primarily responsible for Phase I metabolism of Rifampicin?

Q2. Explain the role of cytochrome P450 enzymes in drug metabolism within this organelle. Q3. How does induction of smooth ER enzymes by Rifampicin contribute to drug interactions? Q4. Why might mitochondrial dysfunction also occur during anti-TB therapy?

Q5. Suggest monitoring and preventive strategies to reduce hepatotoxicity in this case.

Facilitator Notes / Teaching Guide

- Rifampicin induces cytochrome P450 enzymes located in the smooth endoplasmic reticulum (ER).
- Enhanced enzyme activity increases metabolism of co-administered drugs (drug-drug interactions).
- Overproduction of reactive oxygen species may spill over, leading to mitochondrial damage and hepatotoxicity.
- Lysosomes may be secondarily involved due to accumulation of damaged organelles (autophagy dysfunction).
- Clinical connection: Pharm.D students should understand how drug action extends to cellular organelles, impacting both efficacy and safety of pharmacotherapy.

Standard Reference Inspiration:

- "The Inner Life of the Cell" (Harvard/XVIVO educational animation).
- "Little Girl Lost - A Case Study on Defective Cellular Organelles" (Tracie Y. Hudson, NSTA).
- HarvardX: Cell Biology - Mitochondria (Harvard University Online).