

Pharmacokinetics-II

FCMS-Year 2

FOMB

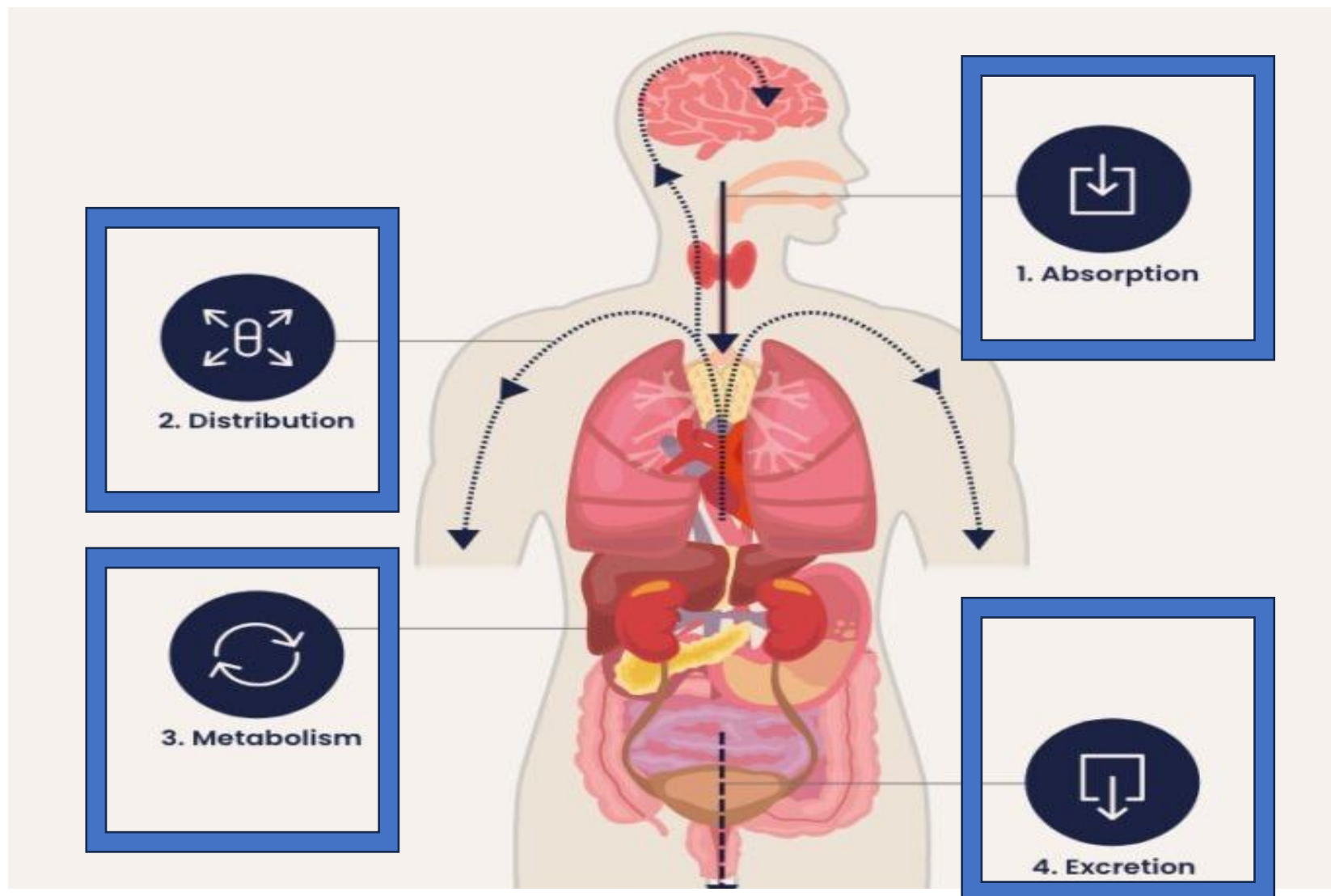
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By the end of this session students should be able to:

1. Explain the process of drug metabolism and the factors affecting it.
2. Identify routes of drug excretion and factors affecting it.

Pharmacokinetics:



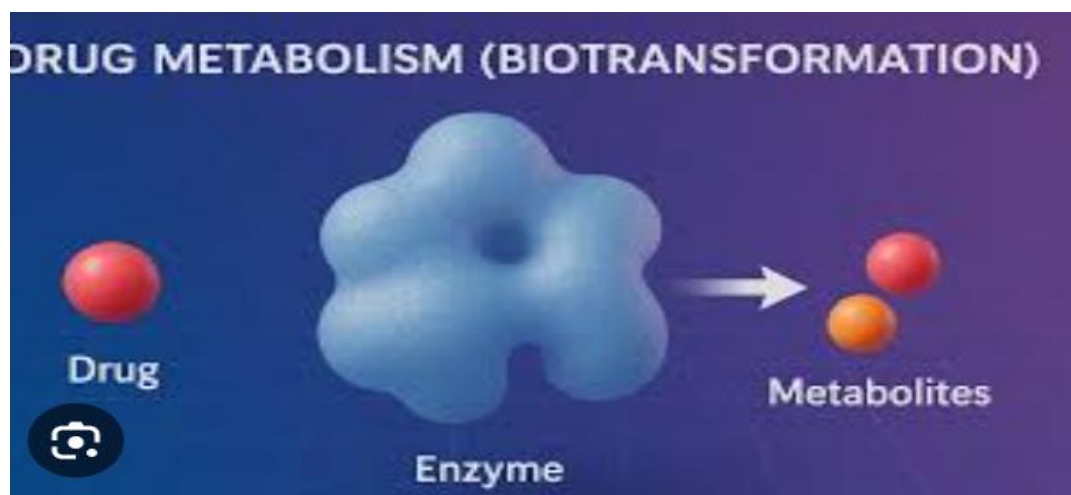
N.B.

- Most drugs are **lipid soluble** (to be able to penetrate the phospholipid cell membrane easily)
- These lipid soluble drugs can not be eliminated from the body in the urine (Because urine is a watery media)
- So, drugs must be **converted from lipid soluble form to water soluble form** (This is called **metabolism**)
- The **liver** is the main organ responsible for metabolism of most drugs

3- Metabolism (Biotransformation)

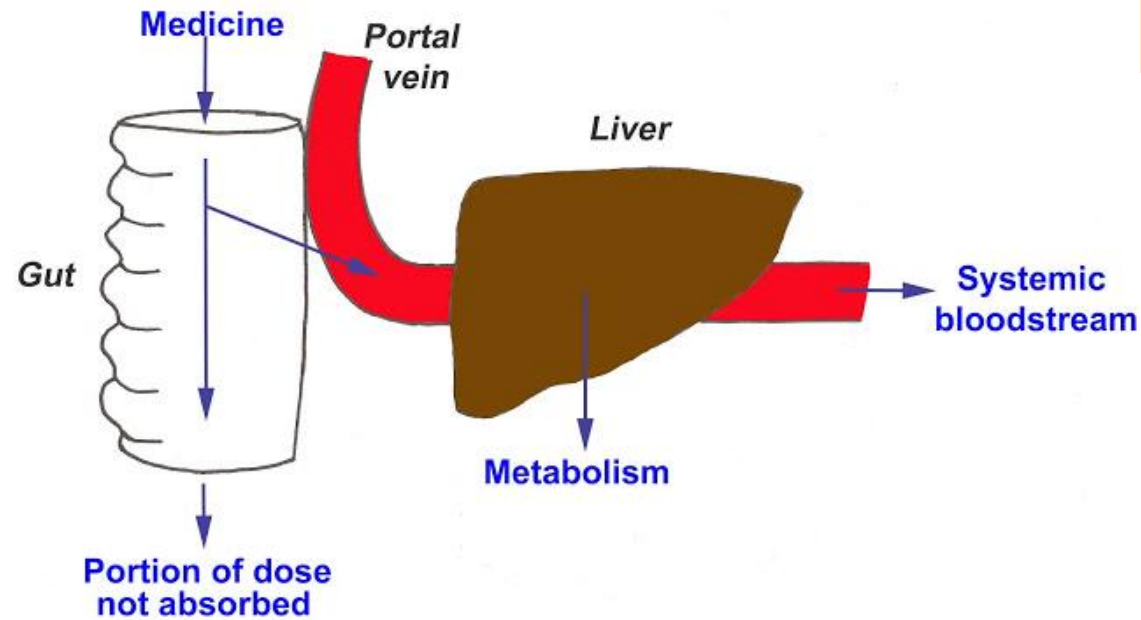
Definition:

The conversion of lipid-soluble drugs into water-soluble metabolites.



The main site of drug metabolism

Is the liver

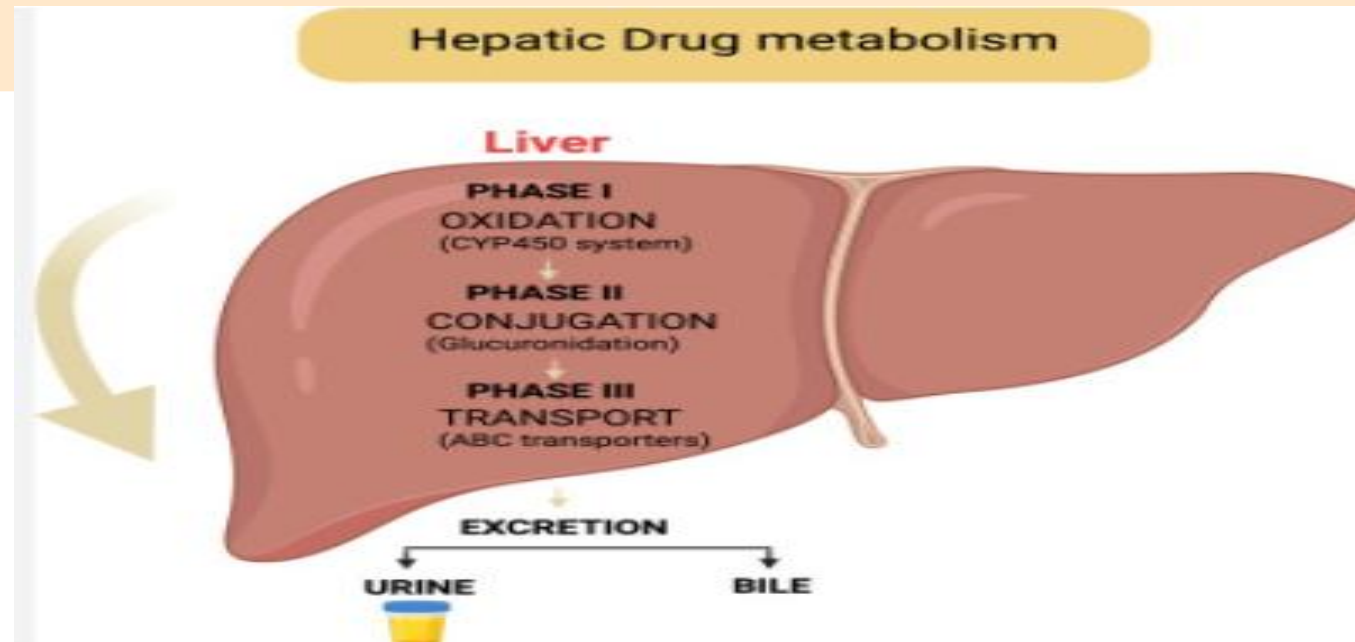


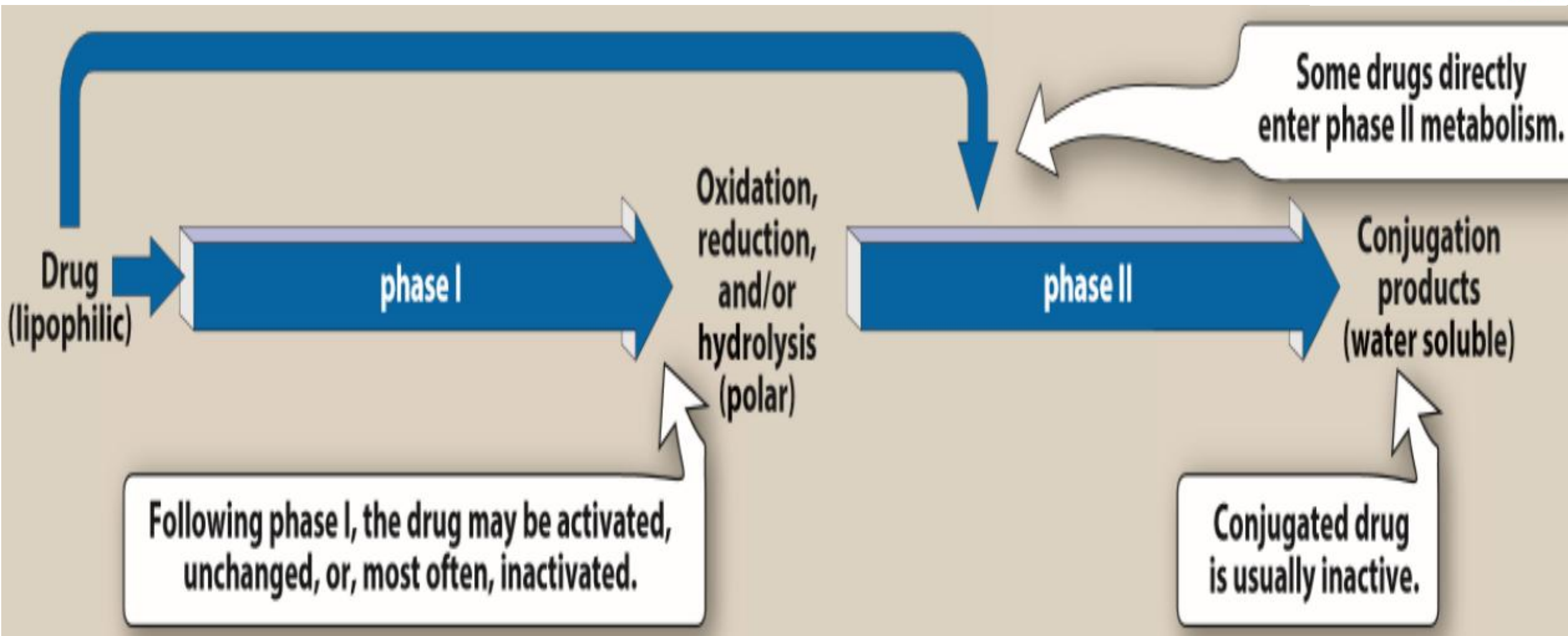
First-pass metabolism

The liver metabolizes drugs via two types of reactions

phase-I reactions

&/Or Phase-II reactions





Factors affecting hepatic drug metabolism:

I- Factors increasing the rate of metabolism

called (Hepatic
enzyme **enhancers**)

Effect

- Increase rate of drug metabolism into inactive form
- Resulting in decreasing the plasma concentration of the active form of the drug
- And decrease in its duration and intensity (Therapeutic failure)

e.g.:

- Pollution
- Some drugs (e.g. Rifampicin)

Effect

- Slow rate of drug metabolism into inactive form
- Resulting in Increasing the plasma concentration of the active form of the drug
- And Increase in its duration and intensity
(Adverse effects and toxicity)

e.g.:

- Starvation
- grapefruit
- Some drugs (e.g. Ketoconazole)

II- Factors Decreasing the rate of metabolism

called (Hepatic
enzyme **Inhibitors**)

<https://www.youtube.com/watch?v=Fzh8mOOYywo>

Activity 1

A 40-year-old female is receiving oral contraceptive pills. Recently she is diagnosed with tuberculosis and started rifampicin therapy. Two months later she discovered that she is pregnant however she is compliant to the oral contraceptive pills.

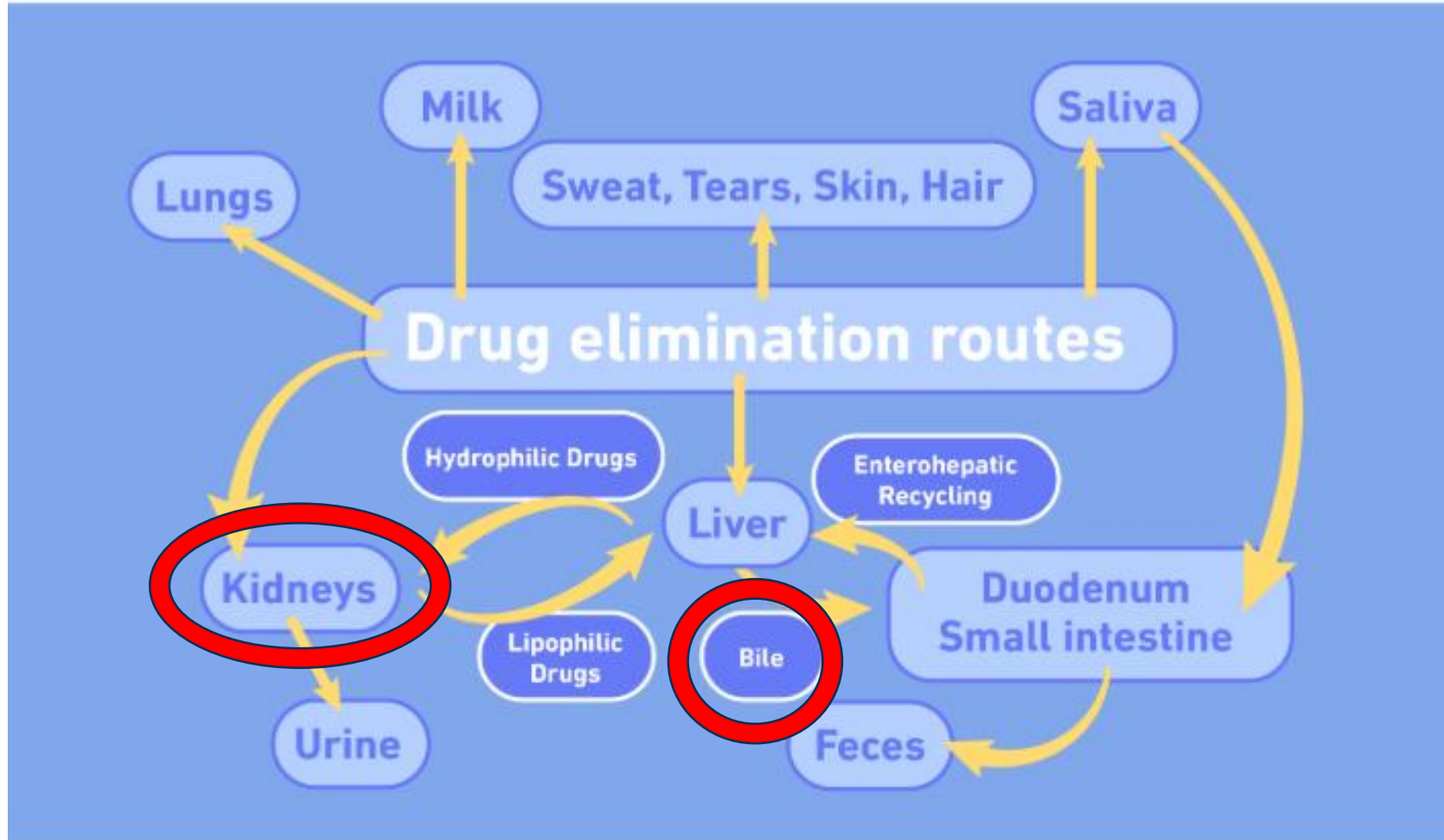
Explain the reason behind failure of contraception in her condition.



4- Elimination

- **Definition:**
the removal of an administered drug from the body.
- **It is accomplished in two ways**
 - 1- *excretion of an unmetabolized drug in its intact form*
 - 2- *or by metabolic biotransformation followed by excretion.*

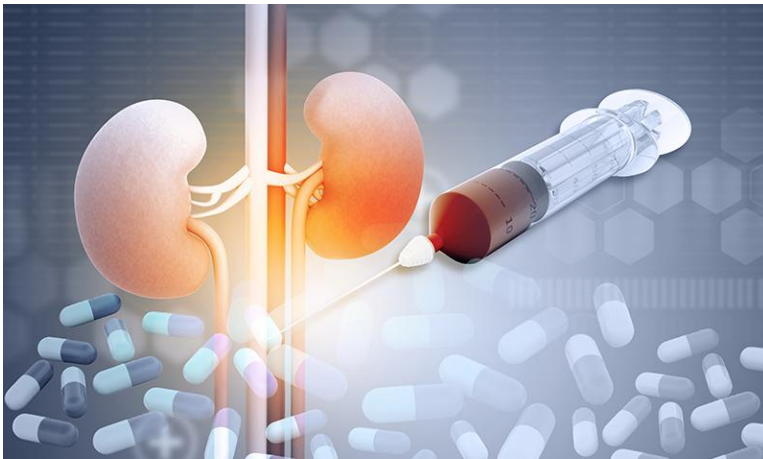
Routes of drug elimination



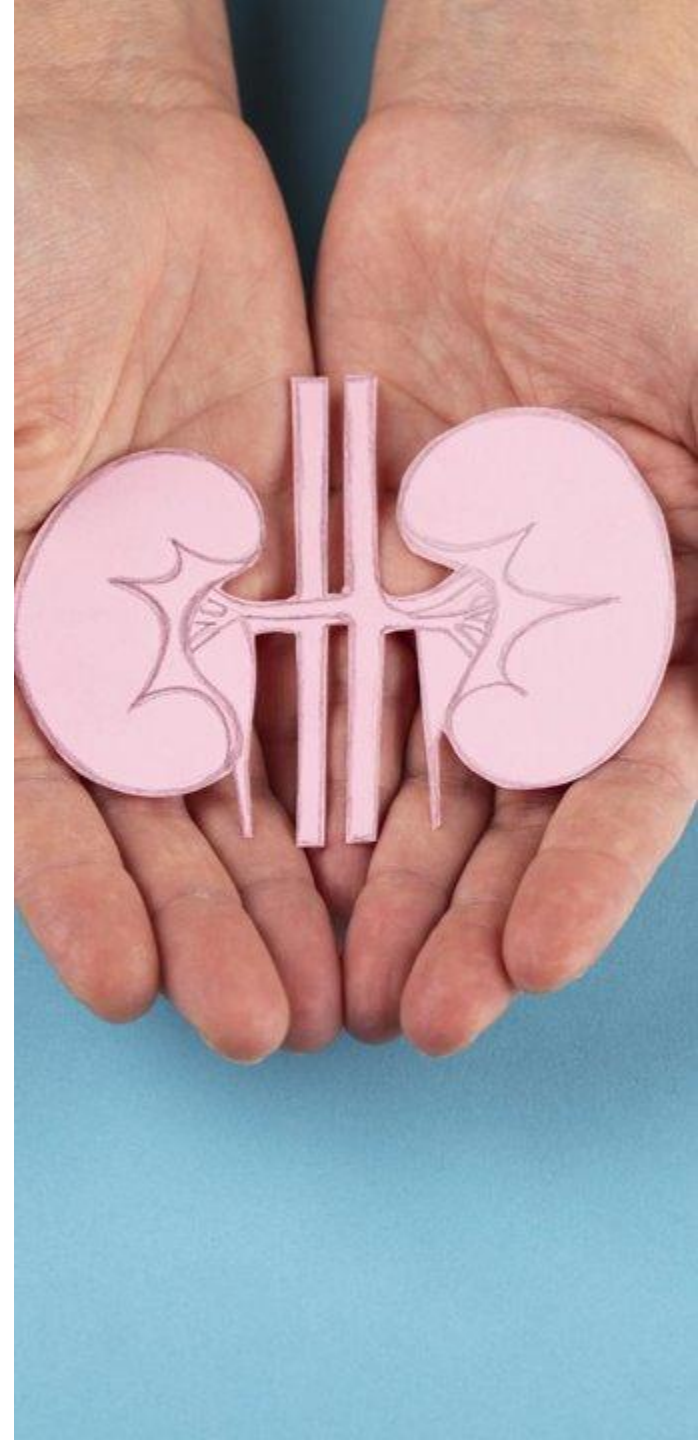
Routes of drug elimination:

A- Renal Drug Elimination

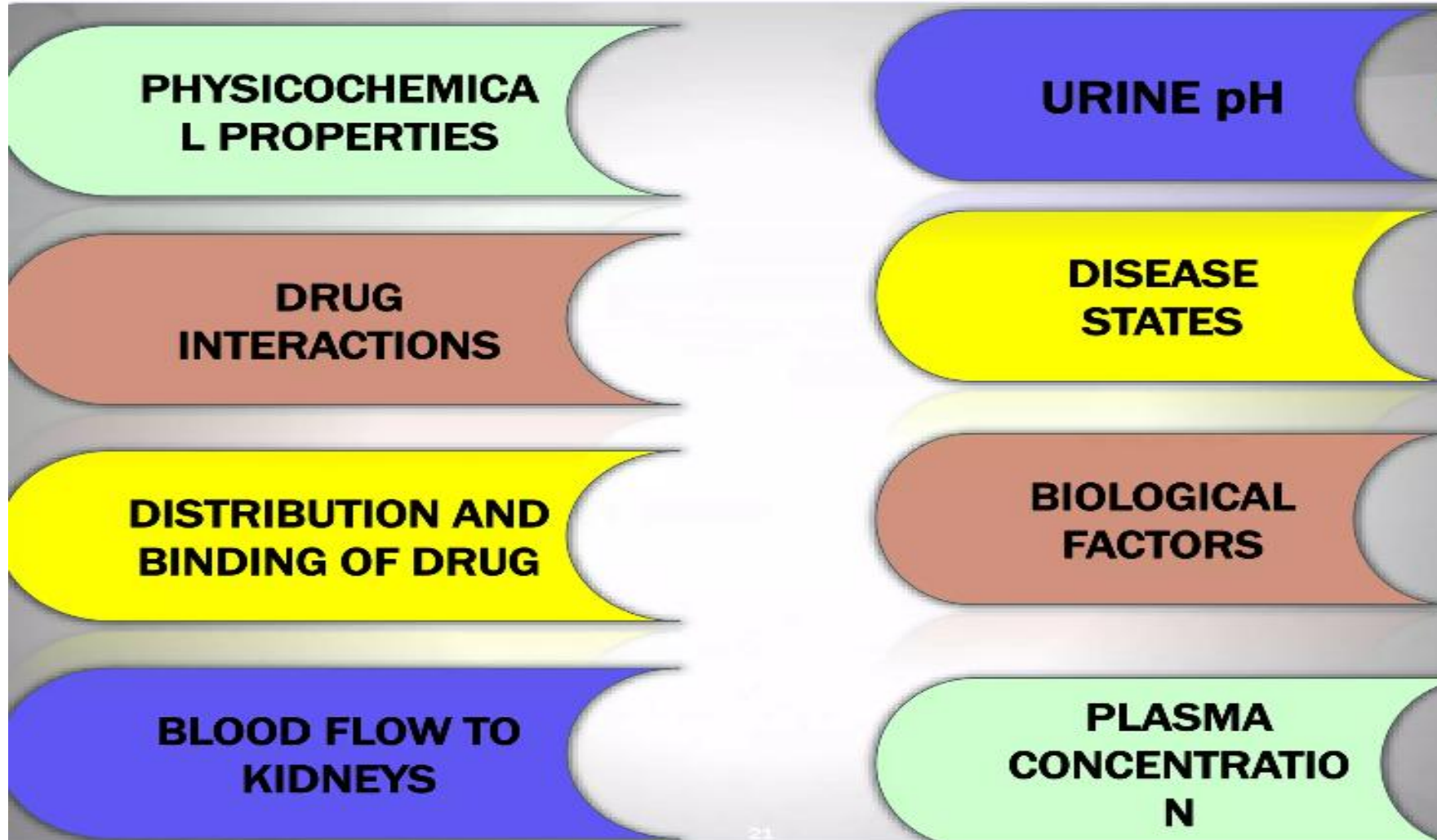
- The kidneys filter drugs through glomeruli and tubules
- E.g. Aminoglycosides (antibiotics)



<https://www.youtube.com/watch?v=795CmRHVRUs>



Factors affecting renal excretion of drugs



Activity

A 68-year-old patient treated with **gentamicin** for sepsis develops **hearing loss and decreased urine output** after 7 days of therapy. Lab results show **elevated creatinine (3.2 mg/dL)** indicating renal impairment.

Questions & Answers

Q1: Why did the patient develop hearing loss?

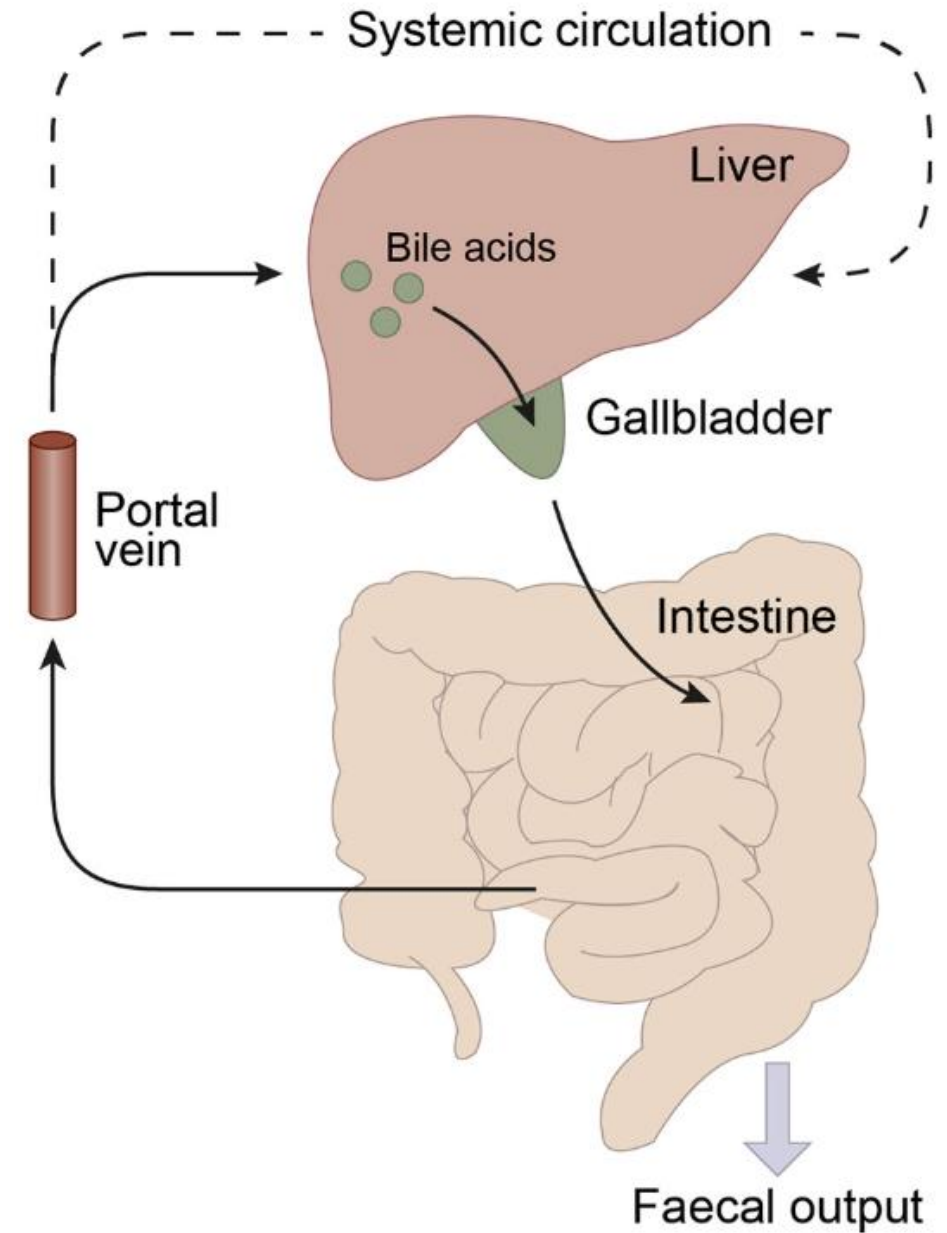
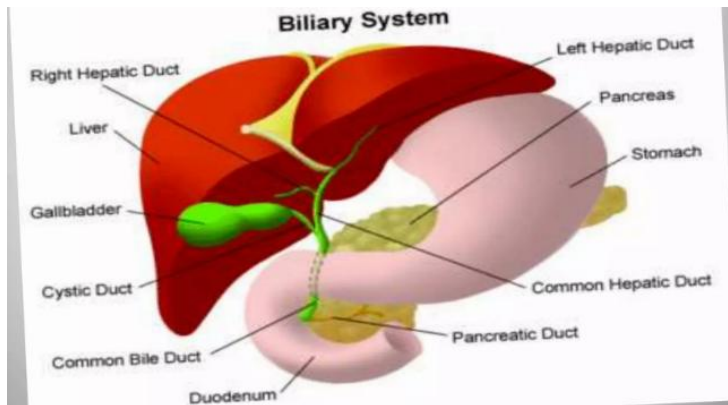
Q2: What should be done immediately?

Q3: How can this be prevented in future?



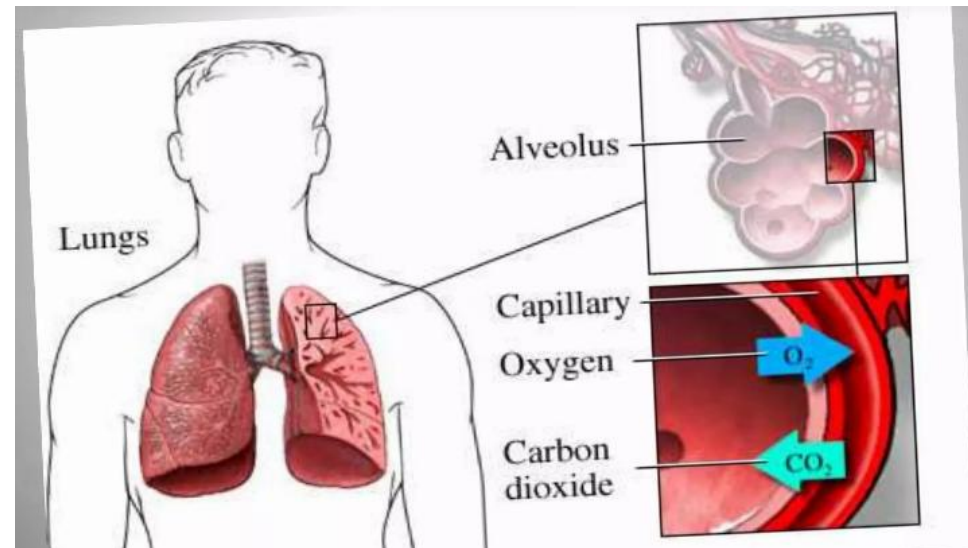
B- Biliary Drug Excretion

- Drugs secreted into **bile** and eliminated via **feces**
- some drugs are **reabsorbed** after being secreted into bile
- This is called **enterohepatic recycling**
- This results in **longer duration of drug action of drugs**



C- Pulmonary Drug Elimination

- Volatile drugs like anesthetic gases are eliminated primarily through pulmonary excretion.

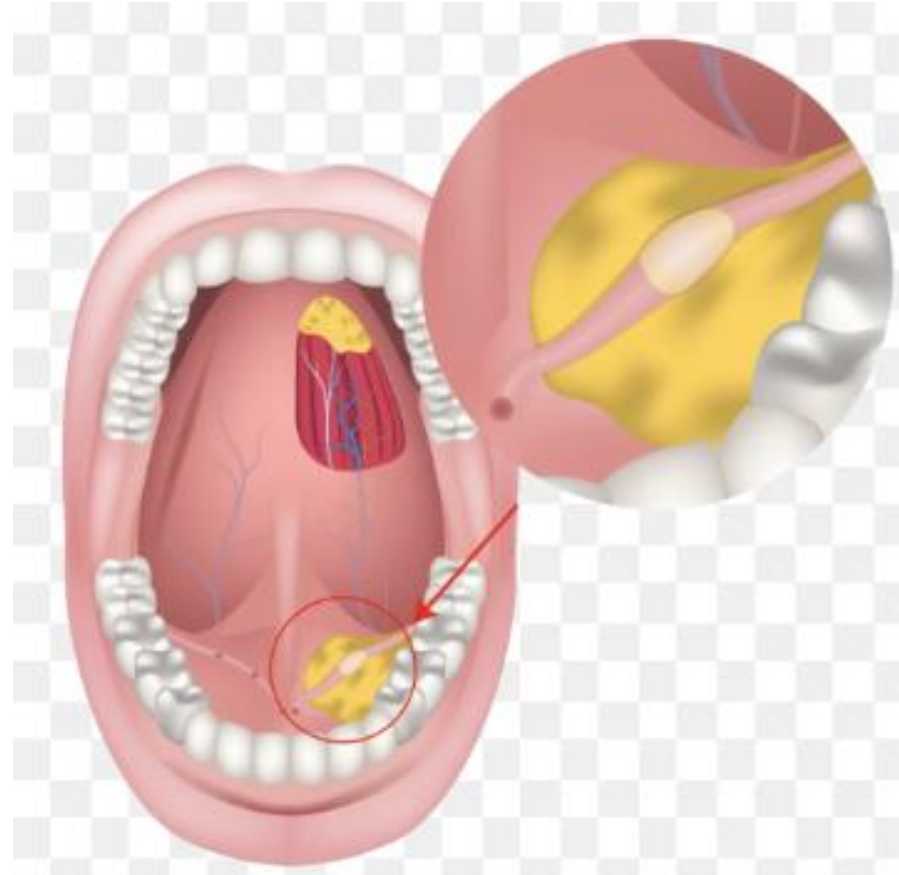


D- Breast milk

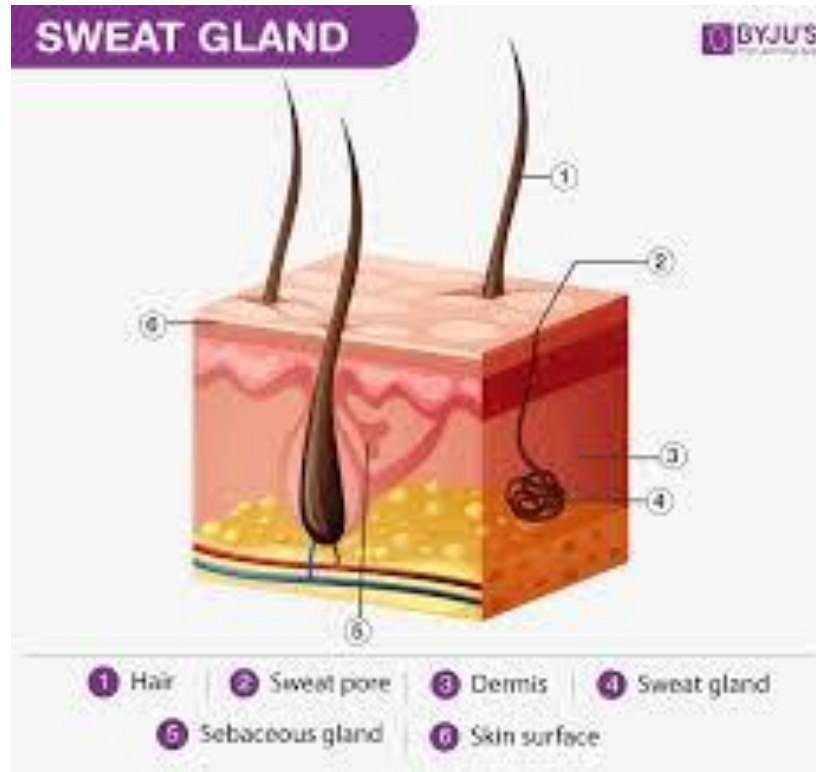
- Some drugs are excreted in breast milk in lactating females
- This can cause adverse effects to the baby



E- Salivary excretion



F- Skin excretion (Sweat)



g- Gastrointestinal (Fecal) excretion



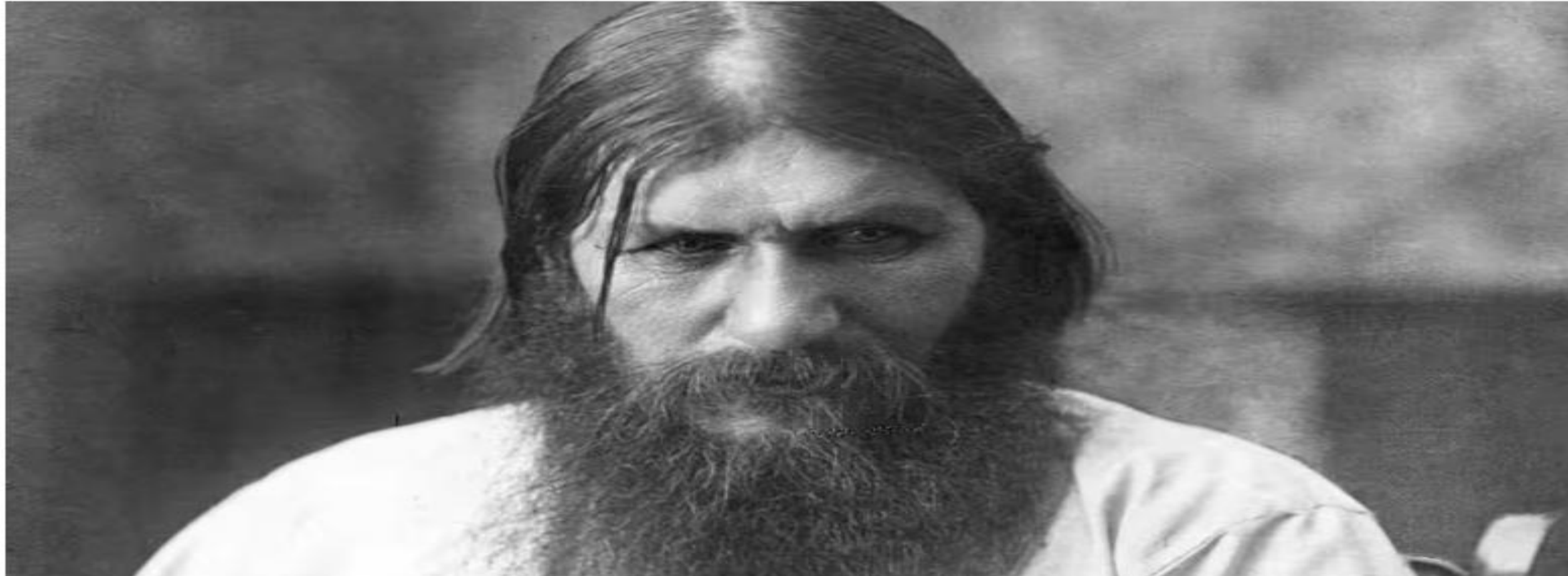
Activity

A 54-year-old female with history of hypertension treated with propranolol. She started a low carbohydrate low calorie diet in which she was receiving only 600 kcal/day with large number of grapefruits. Now she presents to the emergency department complaining of drowsiness, blurring vision and dizziness. Examination revealed tachycardia (HR 110 beats/minute) and hypotension (BP 90/55mmHg)

What is your explanation of her condition?

Poisoned, shot and beaten: why cyanide alone may have failed to kill Rasputin

Theories around the death of Grigori Rasputin still abound 100 years after the event. We examine the scientific credibility of some of the claims



Quiz

- <https://create.kahoot.it/share/pharmacokinetics-2/93cfc900-c498-45bb-aae7-55c7f8a2e87e>

Take home message

- Pharmacokinetics include Absorption, Distribution, metabolism, and elimination
- Metabolism is the conversion of lipid soluble drugs into water soluble form
- Metabolism occurs mainly in the liver via phase 1 and/or phase 2 reactions
- Factors affecting metabolism include hepatic enzyme enhancers and hepatic enzyme inducers

ENZYME INDUCERS AND INHIBITORS

FACTOR TYPE	EXAMPLES	CLINICAL IMPLICATION
Enzyme Inducers	Rifampicin, Carbamazepine, Smoking	Increase metabolism → reduced drug effect
Enzyme Inhibitors	Cimetidine, Grapefruit juice, Erythromycin	Decrease metabolism → toxicity risk

Essential Readings

- Karen Whalen, Richard Finkel, Thomas A Panavelil. Lippincott Illustrated Reviews Pharmacology. 7th ed. 2019. Philadelphia Wolter Kluwer Puplisher. (9-12)