Gastro-Intestinal tract module

Semester: 1
Session: 7
Lecture 1

Liver, Gallbladder and pancreas(L1)

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This Lecture was loaded in blackboard and you can find the material

Clinical chemistry and metabolic medicine. 7th Edition,Martin A. Crook [2006].

Gastrointestinal system – crash course. 3rd Edition, Mosby [2008]

For more detailed instructions, any question, or you have a case you need help in, please post to the group of session.

Learning objectives

1- Types of toxins that effect the GIT and the liver.

2- GIT defence mechanisms.

3- Failure of GIT defence mechanisms.

4- Role of the liver in handling of bile pigment,hormone,drug and toxin including alcohol.

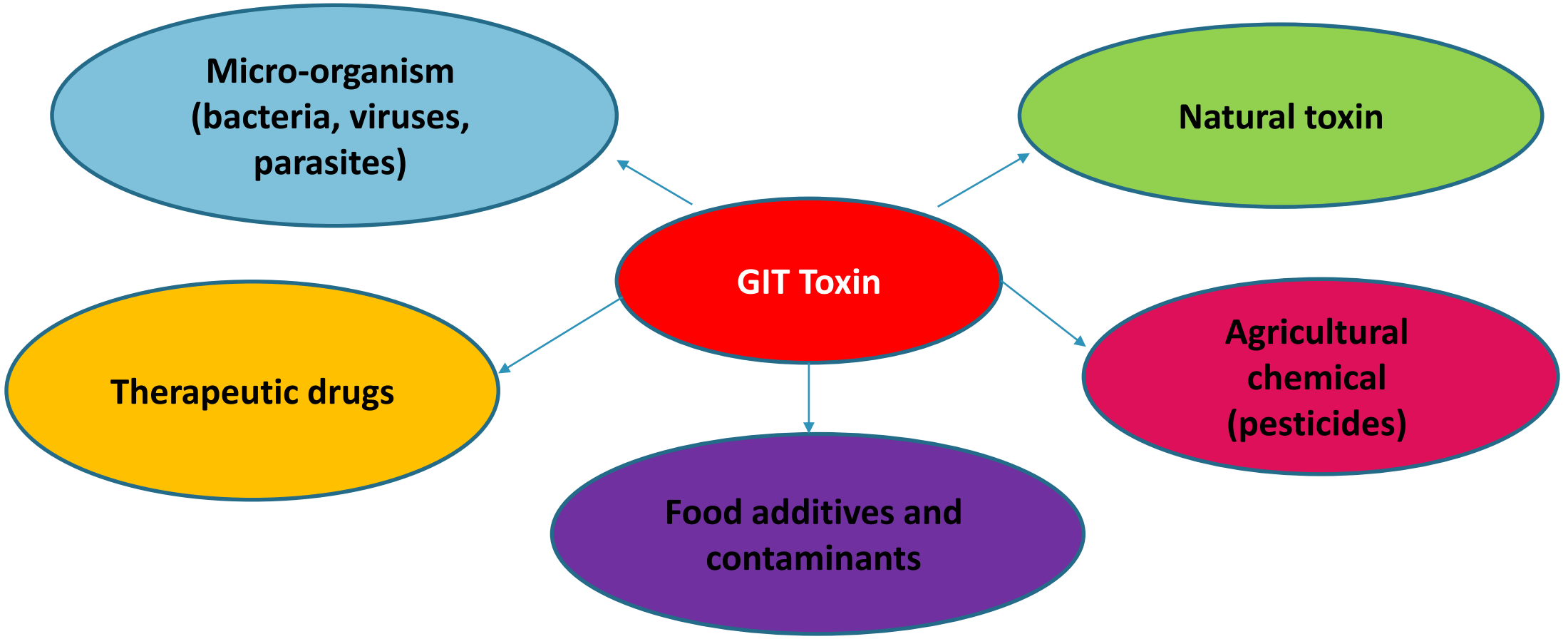
5- Liver and blood protein synthesis.

6- Liver function tests.

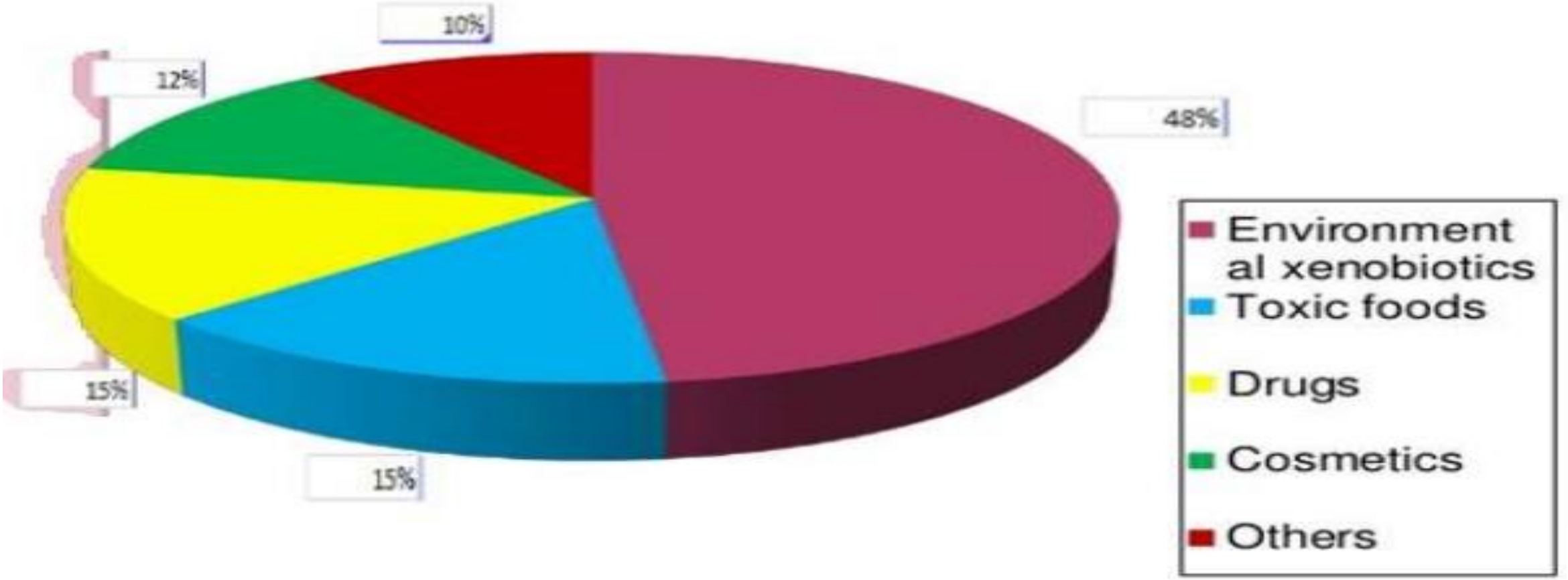
7- Causes and effect of jaundice

8-Distinguish pre- hepatic, hepatic and post- hepatic jaundice.

GIT toxins (xenobiotic) LO1



HUMAN EXPOSURE TO DIFFERENT XENOBIOTICS



GASTROINESTINAL DEFENCE MECHANISMS (LO2)

1-Saliva : Lysozymes, IgA , HCO_3^-

2- gastric acid secretion, low PH act as bactericidal agent.

3-Secretion of Digestive Enzymes : E.g. Pancreatic enzymes that able to cause damage to the cell wall of the bacteria.

4- Epithelial crypt cells secrete fluid in to the lumen, which combined with GI motility tend to wash out bact. And toxin.

5- Secretion of Mucous by epithelial villous cells(decrease the adherence of the microbes)

GASTROINESTINAL DEFENCE MECHANISMS (LO2)

6- The lymphoid tissue of the GIT (Peyers patches).

7- Hepatic and pancreatic secretions, bile acid have antimicrobial properties.

8- Release of cell protective molecules a- immunoglobulin A (Ig A).

b- antimicrobial peptides.

9- Rapid epithelial cell turnover , combined with peristalsis .

10-The Cytoskeleton of epithelial cells with intracellular tight junction that prevent the passage of toxins.

FAILURE OF DEFENSE MECHANISM (LO3)

1- Mouth :

A- Excessive salivation .

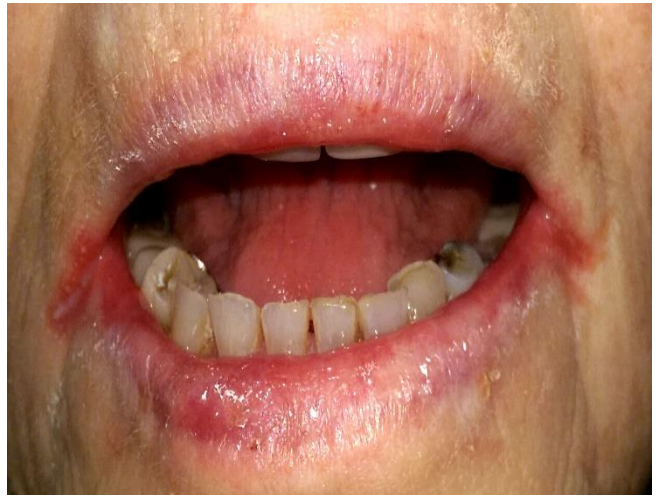
Cholinergic drugs.

B- Decreased salivation .

Anticholinergic drugs .

C- Stomatitis .

Anticancer drugs



FAILURE OF DEFENSE MECHANISM (LO3)

1- Mouth :

D-Gingivitis .

Calcium channel blockers(anti hypertensive drugs)

E-Oral mucosal ulceration.

Corrosive materials **and** Irritant chemicals.

F- Toxic parotitis .

Doxycycline.

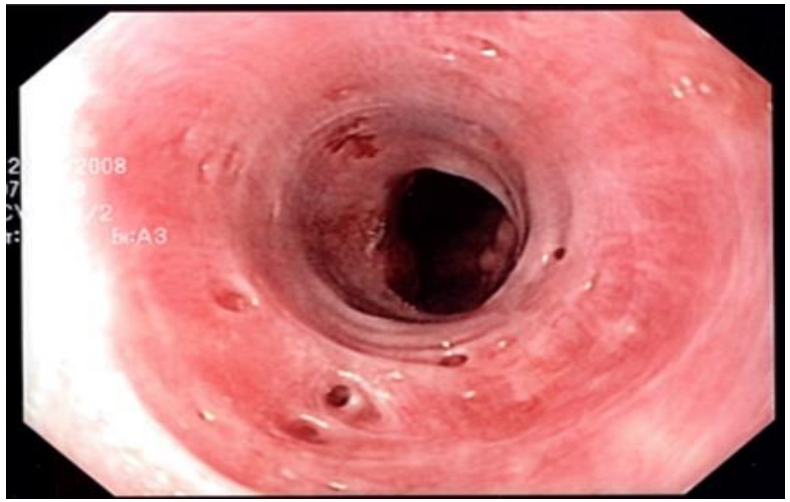
FAILURE OF DEFENSE MECHANISM (LO3)

2- Esophagus :

a. Esophagitis, which may vary from diffused inflammation to sever necrotizing ulceration with hemorrhage.

Which result in retro-sternal chest pain and dysphagia.

b- Gastro-Esophageal reflux .

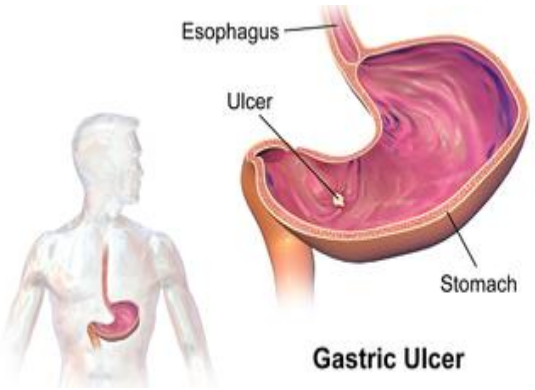


FAILURE OF DEFENSE MECHANISM (LO3)

3- Stomach :

a. Nausea and vomiting.

b. Diarrhea and abdominal cramp (pain).



Gastric Ulcer

c. Focal necrosis, erosions and ulcerations .

FAILURE OF DEFENSE MECHANISM (LO3)

4- Intestine :

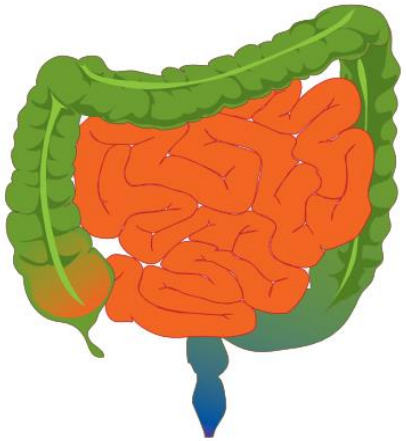
a- Alteration in intestinal motility (diarrhea, constipation)

b- Changes in mucosal absorptive or secretary function.

c- Ischemic changes.

d- Ulceration and hemorrhage .

e- Changes in the micro-flora ???



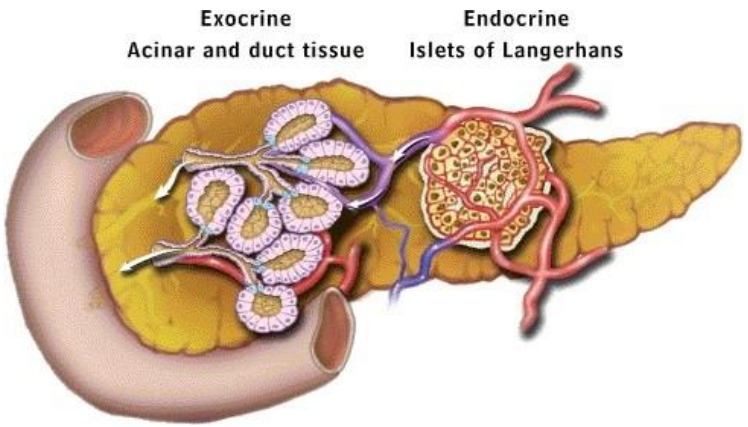
FAILURE OF DEFENSE MECHANISM (LO3)

5- Pancreas:

a- Pancreatitis

(Vomiting, Abdominal pain and Increased pancreatic enzymes(amylase).

b- Diabetes Mellitus through destruction of beta cells .



Liver (LO 4)

The excretory and detoxification function include

a- Metabolism and excretion of bilirubin.

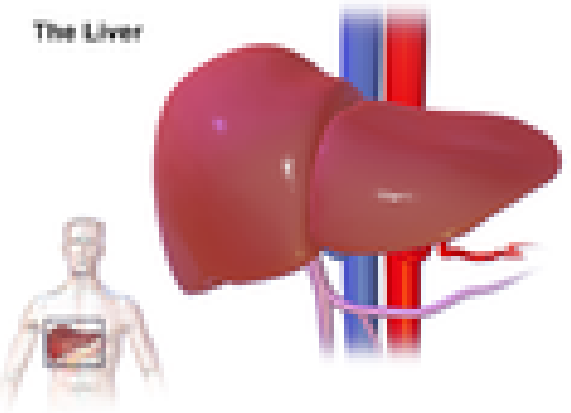
b- Removal of toxic ammonia by converting it to urea.

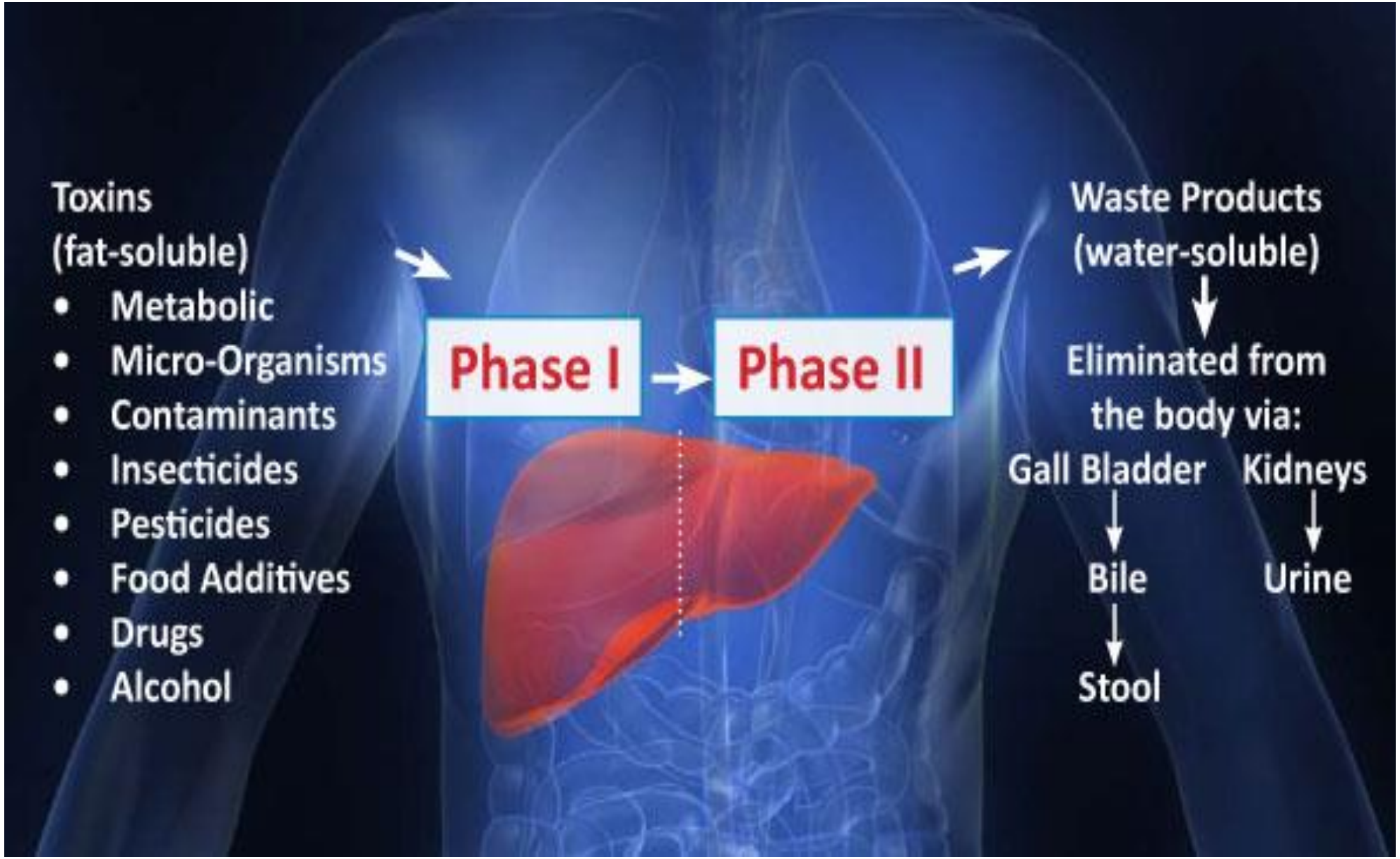
c- Drug metabolism by endoplasmic reticulum enzymes.

d- Toxin extracted by Kupffer cell.

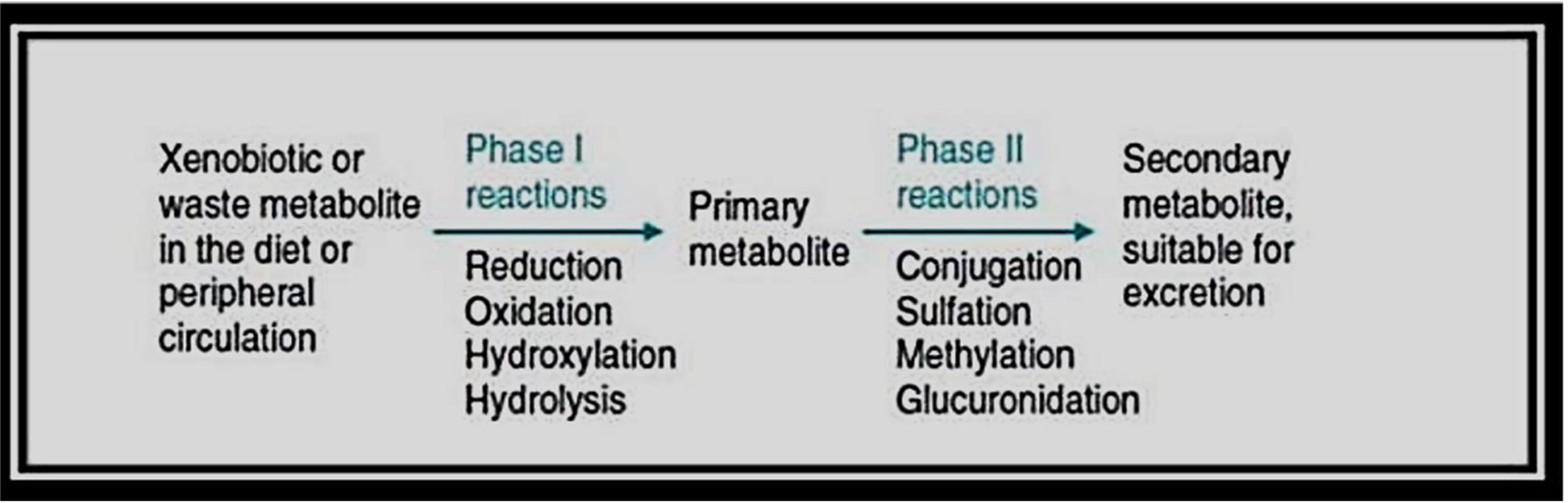
e- Steroid hormones , are inactivated by conjugation with

Glucuronate and Sulphate.




Toxins
(fat-soluble)
• Metabolic
• Micro-Organisms
• Contaminants
• Insecticides
• Pesticides
• Food Additives
• Drugs
• Alcohol
Phase I
Phase II
Waste Products
(water-soluble)
Eliminated from
the body via:
Gall Bladder
Kidneys
Bile
Urine
Stool

Metabolism of xenobiotic.LO4



Oxidation(LO4)

Oxidation of alcohol. Primary aliphatic and aromatic alcohols are oxidized to corresponding acids

1- Methanol → formaldehyde → formic acid

2- Ethanol → acetaldehyde → acetic acid

3- Benzoyl alcohol → benzaldehyde → benzoic acid

Why the liver is the target organ for toxin (xenobiotic) induced injuries ???

Synthetic function (L0 5)

1- Plasma proteins mainly a- albumin

b- complement

2- Coagulation factors, fibrinogen 1, factor 2 (prothrombin) and 10 9 7 2

3- Lipoproteins, such as VLDL , HDL.

blood-sample-liver-function-test-260nw-1082759915.wdp.jxr

Liver function tests (LO6)

❖ Excretory function:

1. TSB(Total serum bilirubin)
2. D.B (direct bilirubin)

❖ Synthetic Function:

1. Albumin
2. Prothrombin time

Liver function tests LO6

❖ Cell damage :

1- Transaminases ALT , AST

Inflammatory disease ALT > AST

Infiltrative disease AST > ALT

2- Alkaline phosphatase related to biliary tract (cholestasis)

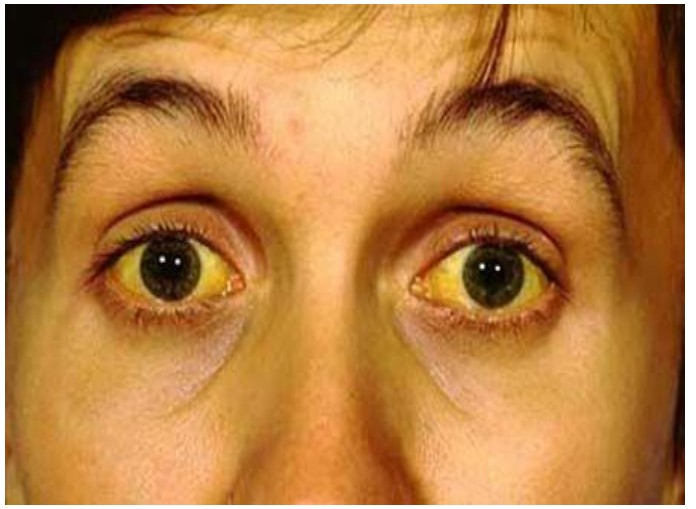
3- Gamma glutamyl transferase (GGT) 1. Enzyme induction

2. Hepatocellular damage

Test	Normal range
Total bilirubin	5-17 µmol/L 0.1-1.0 mg/dl
Alkaline phosphatase (ALP)	35–130 IU/L
Aspartate transaminase (AST)	5–40 IU/L
Alanine transaminase (ALT)	5–40 IU/L
Gamma-glutamyl transpeptidase (GGT)	10–48 IU/L
Albumin	35–50 g/L 3.5-5.0 g/dL
Prothrombin time (PT)	12–16 second

JAUNDICE (LO7)

Is yellowish discoloration of skin, sclera and mucus membrane become clinically apparent when the plasma bilirubin concentration reaches about 50 µmol /L (3 mg/dL).

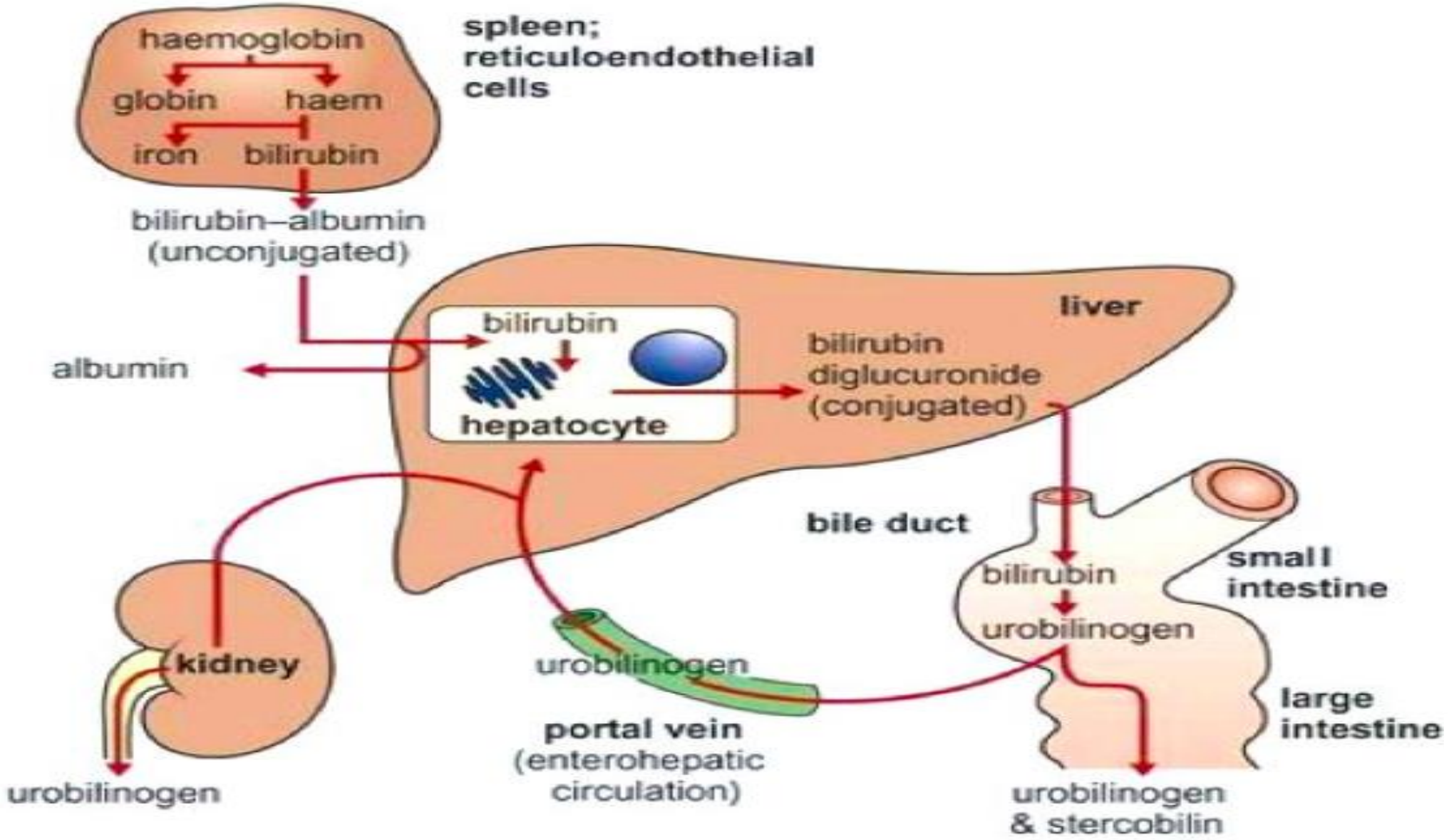


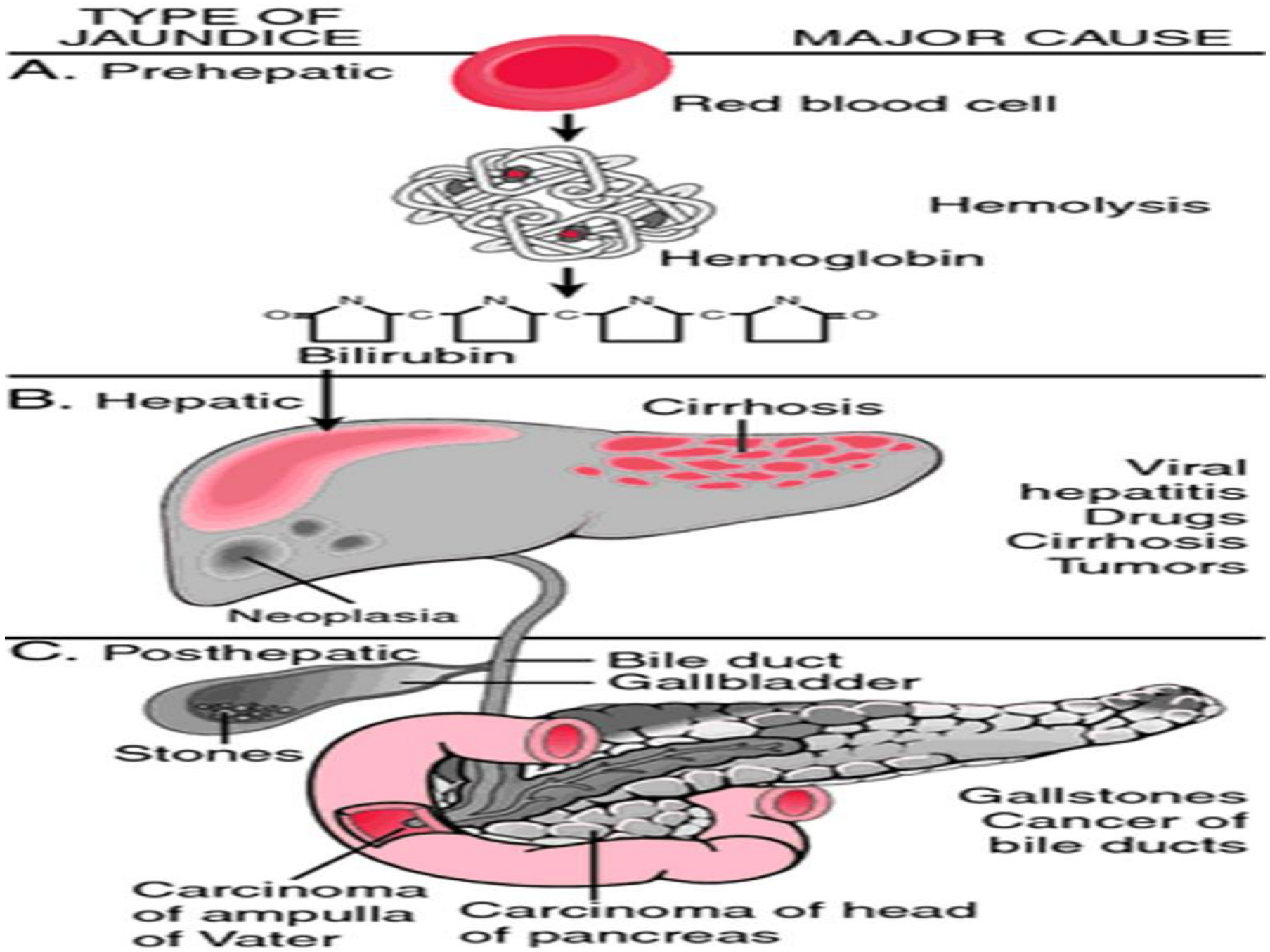
1. Prehepatic : bilirubin excretion exceeds the normal capacity.
2. Hepatic : normal bilirubin load cannot conjugate.
3. Post hepatic : biliary flow is obstructed.

Bilirubin Metabolism(LO7)

- Unconjugated bilirubin formed mainly in spleen by the breakdown of hemoglobin.
- It is insoluble and transported in the plasma bound to albumin.
- Taken up by the liver by active transport, where it is conjugated with Glucuronic acid by enzyme uridine diphosphate Glucuronyl transferase.
- converted in the hepatocytes into conjugated bilirubin (water-soluble).
- It is excreted into the bile canaliculi and via the main bile ducts into the duodenum.

- 10% of the unconjugated bilirubin is reduced to urobilinogen by small intestinal bacteria, reabsorbed in the terminal ileum, and then excreted in the urine (enterohepatic circulation).
- 90% is converted by colonic bacteria to stercobilinogen which is excreted in faeces.


haemoglobin
globin
haem
iron
bilirubin
spleen; reticuloendothelial cells
bilirubin–albumin (unconjugated)
albumin
bilirubin
hepatocyte
liver
bilirubin diglucuronide (conjugated)
bile duct
bilirubin
urobilinogen
small intestine
large intestine
kidney
urobilinogen
portal vein (enterohepatic circulation)
urobilinogen
urobilinogen & stercobilin


TYPE OF JAUNDICE
MAJOR CAUSE
A. Prehepatic
Red blood cell
Hemolysis
Hemoglobin
Bilirubin
B. Hepatic
Cirrhosis
Viral hepatitis
Drugs
Cirrhosis
Tumors
Neoplasia
C. Posthepatic
Bile duct
Gallbladder
Stones
Gallstones
Cancer of bile ducts
Carcinoma of ampulla of Vater
Carcinoma of head of pancreas

Causes and features

❖Pre-hepatic jaundice (haemolytic) (LO7,8)

i. Congenital abnormalities of red cell structure or content

(e.g. hereditary spherocytosis, sickle cell disease, thalassemia).

ii. Autoimmune haemolytic anaemia.

iii. Transfusion reactions.

iv. Drug toxicity

Causes and features

❖Hepatic jaundice (hepatocellular) (LO7,8)

A. Hepatic unconjugated hyperbilirubinaemia :

i. **Gilbert's syndrome. Deficiency or abnormalities of unconjugated bilirubin uptake system.**

ii. **Crigler– Najjar syndrome. Abnormality of conjugation process enzymes.(deficiency in bilirubin uridine diphosphate glucuronosyl transferase enzyme).**

Hepatic jaundice (hepatocellular)LO7,8

B. Hepatic conjugated hyperbilirubinaemia.

Infection

- Viral (e.g. hepatitis A, B, C, CMV)
- bacterial (e.g. liver abscess)
- parasitic (e.g. amoebic)

Drugs

- paracetamol overdose
- Antipsychotics
- Antibiotics

Non-infective

- chronic active hepatitis
- alcohol-related.

Post-hepatic jaundice (obstructive) LO7,8

conjugated hyperbilirubinaemia.

Intraluminal

- Common bile duct stones
- Blood clot
- Parasites :
  e.g. Hydatid daughter cyst

Mural abnormalities

- Cholangiocarcinoma
- Congenital atresia
- Sclerosing cholangitis
- Biliary cirrhosis
- Traumatic
  post-surgical stricture

Extrinsic compression

- Pancreatitis
- Tumors e.g.
  head of pancreas
- Lymphadenopathy
  of portal hepatic
  nodes

Types of jaundice	Urine		Blood				LO8
	Urobilinogen	Bilirubin	Indirect bilirubin	Direct bilirubin	AST & ALT	ALP & GGT	Prothrombin time
Hemolytic jaundice	Increased	Nil	Increased	Normal	Normal	Normal	Normal
Hepatocellular jaundice	present	Present	Increased	Increased	Marked increased	Normal or mild increased	Abnormal
Obstructive jaundice	Decreased or absent	Present	Normal	Increased	Normal or mild increased	Marked increased	Abnormal

LO7

In which conditions parenteral administration of vitamin k is recommended for correction of prolong PT ,and why?

A-Obstructive jaundice

B-Hepatocellular jaundice


Thank
You