Porphyrias

They are due to defect of the enzymes in the pathway for heme biosynthesis , intermediates of the pathway accumulate and may have toxic effects on the nervous system that cause neuropsychiatric symptoms .

When porphyrinogens accumulates , they may be converted by light to porphyrins , which react with molecular oxygen to form oxygen radicales , these radicales may cause sever damage to the skin .

PORPHYRIAS

GLYCINE + SuccinylCoA

↓ — *ALA synthase(rate limiting step,this enzyme regulated by feed Back inhibition by the final product , heme)*

δ-aminolevulinic acid(ALA)

↓ — *ALA dehydratase* — **ALA-dehydratase porphyria**

Porphobilinogen(PBG)

↓ — *PBG deaminase* — **Acute intermittent porphyria**

hydroxymethylbilane

↓ — *Uroporphyrinogen III cosynthase* — **Congenital erythropoietic porphyria**

uroporphyrinogen III

↓ — *Uroporphyrinogen decarboxylase* — **Prophyria cutanea tarda**

coprophyrinogene III

↓ — *Coproporphyrinogen oxidase* — **Herediatary coproporphyria**

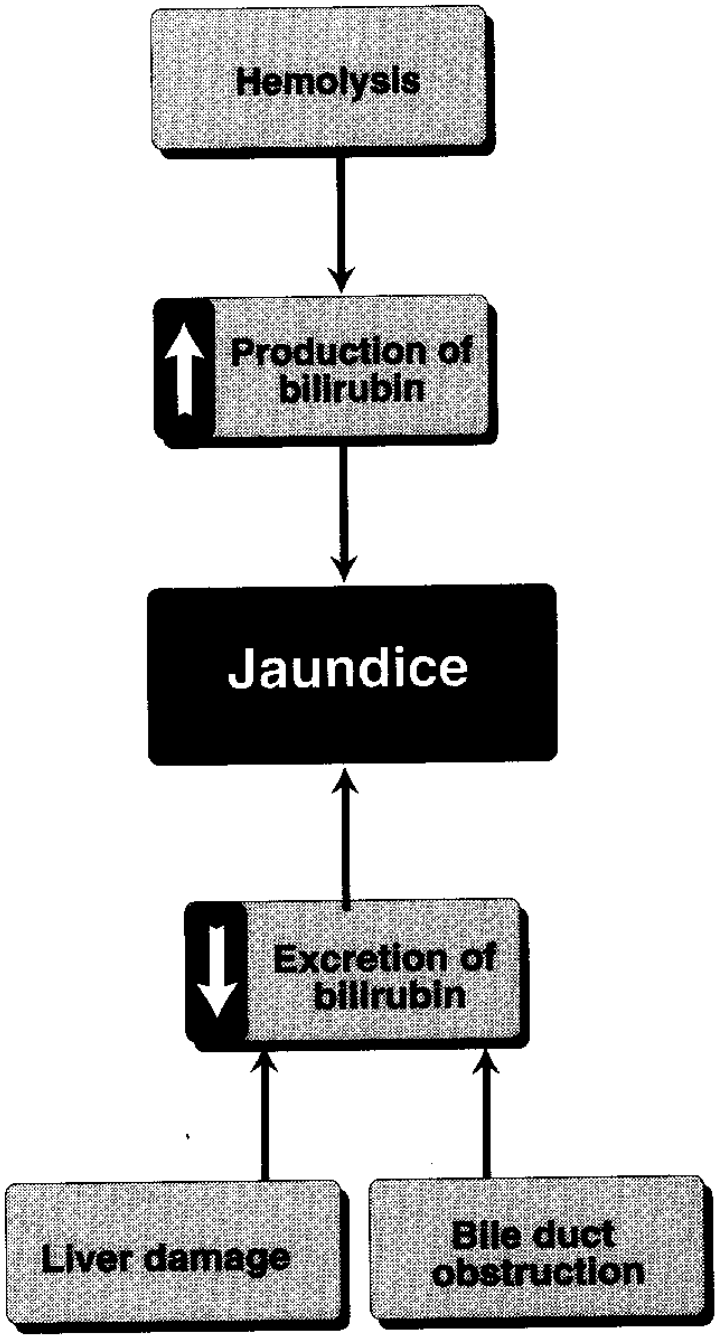
Protoporphyrinogene IX

↓ — *Protoporphyrinogen oxidase* — **Variegate porphyria**

protoporphyrin IX

↓ — *Ferrochelatase* — **Erythropoietic protoporphyria**

Heme



Jaundice

Hyperbilirubinemia:

(It is a yellowish discoloration of the tissues due to the deposition of

bilirubin) (The state indicated when the value of serum bilirubin is about 2.0 mg/ dl or more).

Two forms:

Direct bilirubin: Conjugated with glucoronic acid

Indirect bilirubin: unconjugated, insoluble in water.

Causes of hyperbilirubinaemia :

1- Increased production of **bilirubin** by hemolysis or blood disease .

2- Abnormal uptake or conjugation of bilirubin .

3 – Decreased exretion .

(Major causes of jaundice)

1 . Prehepatic A . Hemolysis

B . Ineffective erythro – poiesis

2 . Hepatic A . Pre-microsomal , drugs e.g. Rifampicin will interfer with the bilirubin uptake .

B . Microsomal , viral hepatitis .

C . Post-microsomal , impired excretion , hepatitis, lymphoma , cirrhosis , intrahepatic obstruction .

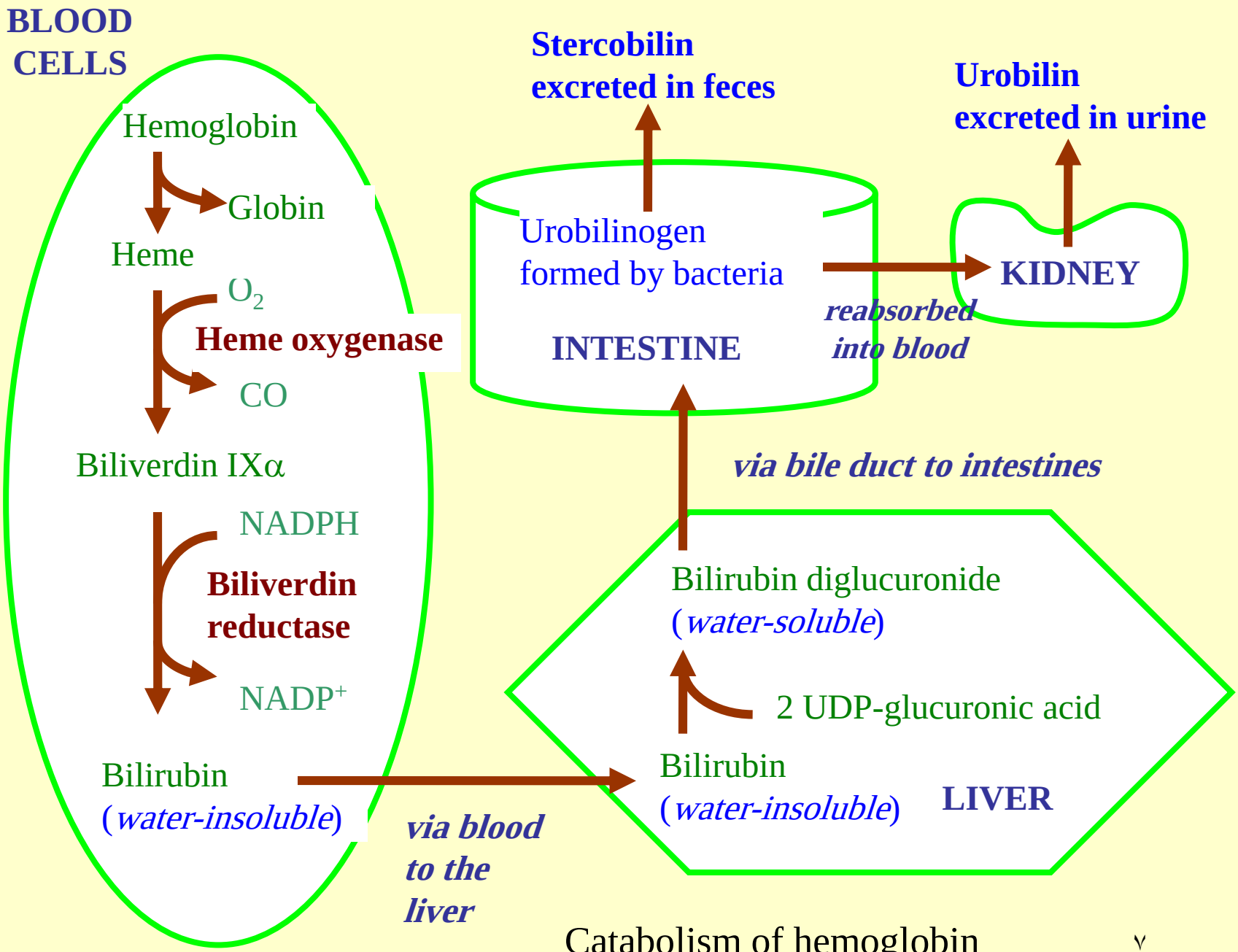
3 – post - hepatic Gallstones , Biliary stricture , Carcinoma of the pancreas or biliary tract or cholangitis .

(plasma enzymes)

1. The enzyme used in the assessment of the liver function are SGOT , SGPT together with Serum Alkaline phosphatase and δ - Glutamyl transferase .
2. SGPT and alkaline ph. are more specific for disease of the liver .
3. In hepatitis , Serum level of the GOT and GPT increase 20 times than the normal range .
4. In obstruction jaundice , Serum Alkaline phosphatase increase 10 times than the normal range .
5. δ - GT also increase in liver disease .

CLINICAL PREMISE

Newborns often have a yellowish tint to their skin. This condition is known as jaundice and results from the infant ridding itself of "fetal" hemoglobin which will be replaced by "adult" hemoglobin. As you will learn in this lecture, catabolic products from hemoglobin are removed by the liver. However, the infant's liver is often too immature to handle the excessive breakdown products. Instead they accumulate giving the yellowish tint. Exposure to mild UV light from the sun is usually sufficient to destroy these compounds , although in very severe cases blood dialysis may become necessary as these byproducts can be toxic.



Catabolism of hemoglobin

Most common diseases affecting the liver are :

1 . Hepatitis : damage to liver cell . It is usually caused by viral infection A , B, C , D and E or by toxins e.g. alcohol , paracetamol , CCl4 or fungal toxins . SGOT and SGPT increase then returns to normal range after recovery with in 20-30 days , while in cases with hepatitis B and C viruses , the enzymes remain elevated .

2. Cirrhosis : increased fibrous tissue formation which lead to shrinkage of the liver and decreased hepatocellular function . Causes of cirrhosis include chronic excessive alcohol intake and wilson's disease (wilson's disease is characterized by deceased biliary excretion of copper , copper is deposited in the liver) . Serum bilirubin level is elevated .

3 . Tumors : the liver is a common site for tumor metastasis . plasma alk. phosphatase activity is increased .

4 . Obstruction of bile flow : due to pathological diseases or presence of stones . SGOT , SGPT , TSB and Serum Alk. phosphatase are increased .