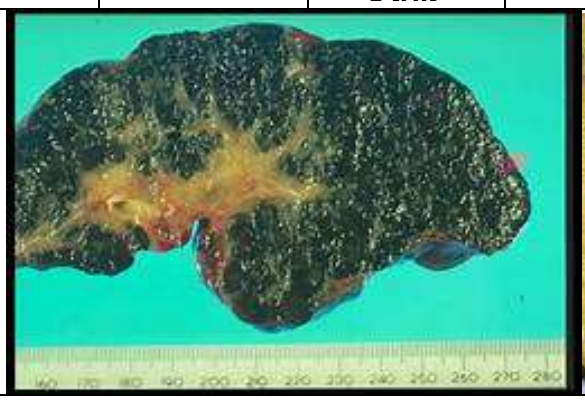
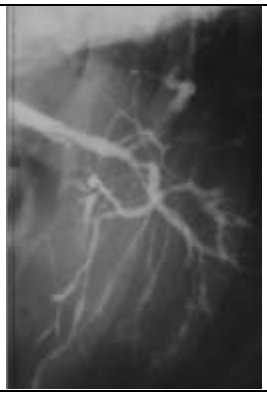
Liver

Pigmentary Changes (jaundice)

Liver:	• ***Is enlarged***
External surface:	• ***Very finely-granular*** • ***Smooth in some parts*** • ***Dark green in colour***
Cut surface:	• ***Dilated intrahepatic bile-ducts***
Consistence:	• ***Firm***

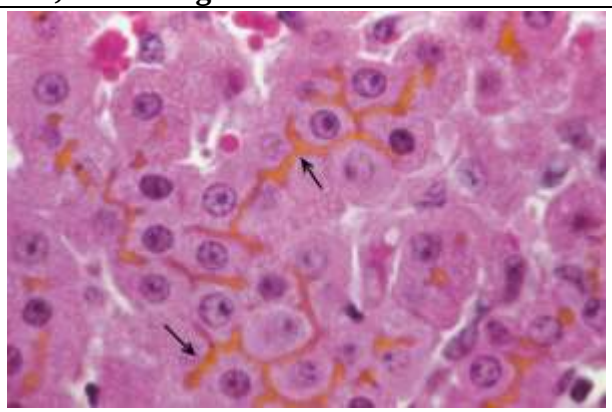




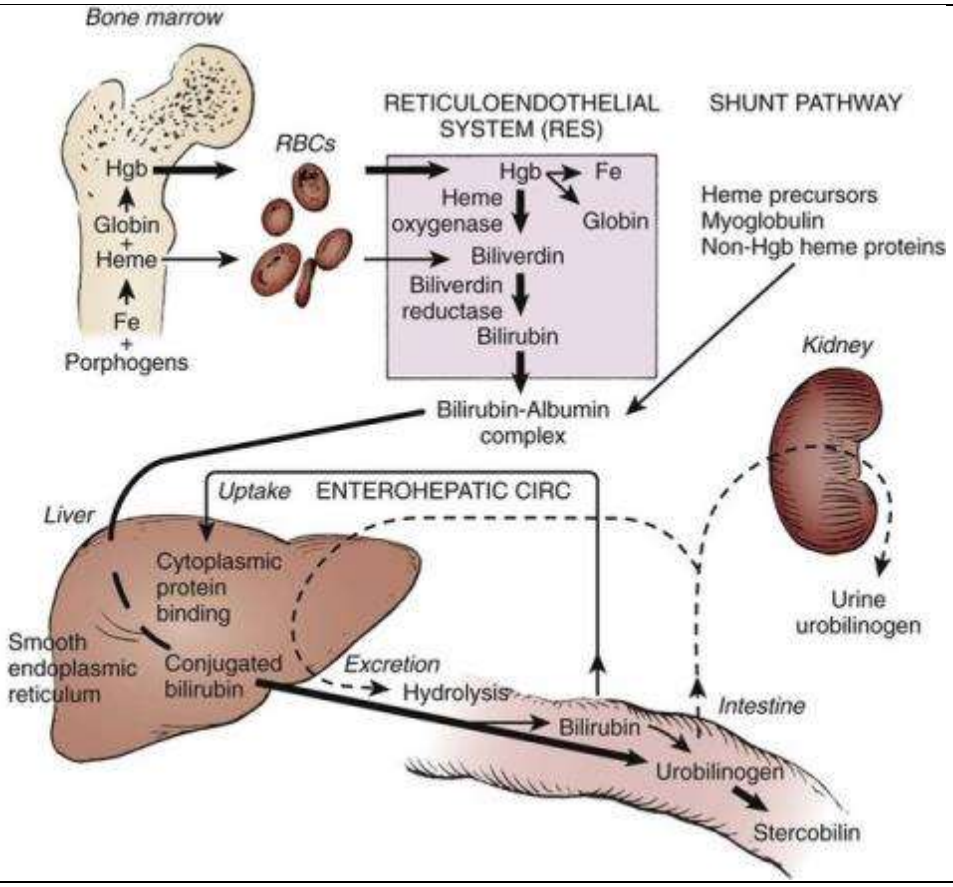
N.B.I:
This liver was removed at autopsy from a case ***of obstructive jaundice.***

N.B.2:

- **Jaundice (icterus) is coloration** (pale yellow to deep orange) by ***bile-pigment*** in the blood.
  - of the ***Skin, Mucous membranes tissues & Sclera***
- The internal organs are also pigmented with the exception of the C.N.S. (except in infants where the nuclear grey matter of the brain may be coloured ***(kerni-icterus).***
- **The *sweat may be coloured* but not the tears, saliva or gastric secretion.**

The liver was deep yellow and green after formalin fixation.
The surface was nodular, and cut surfaces were firm.

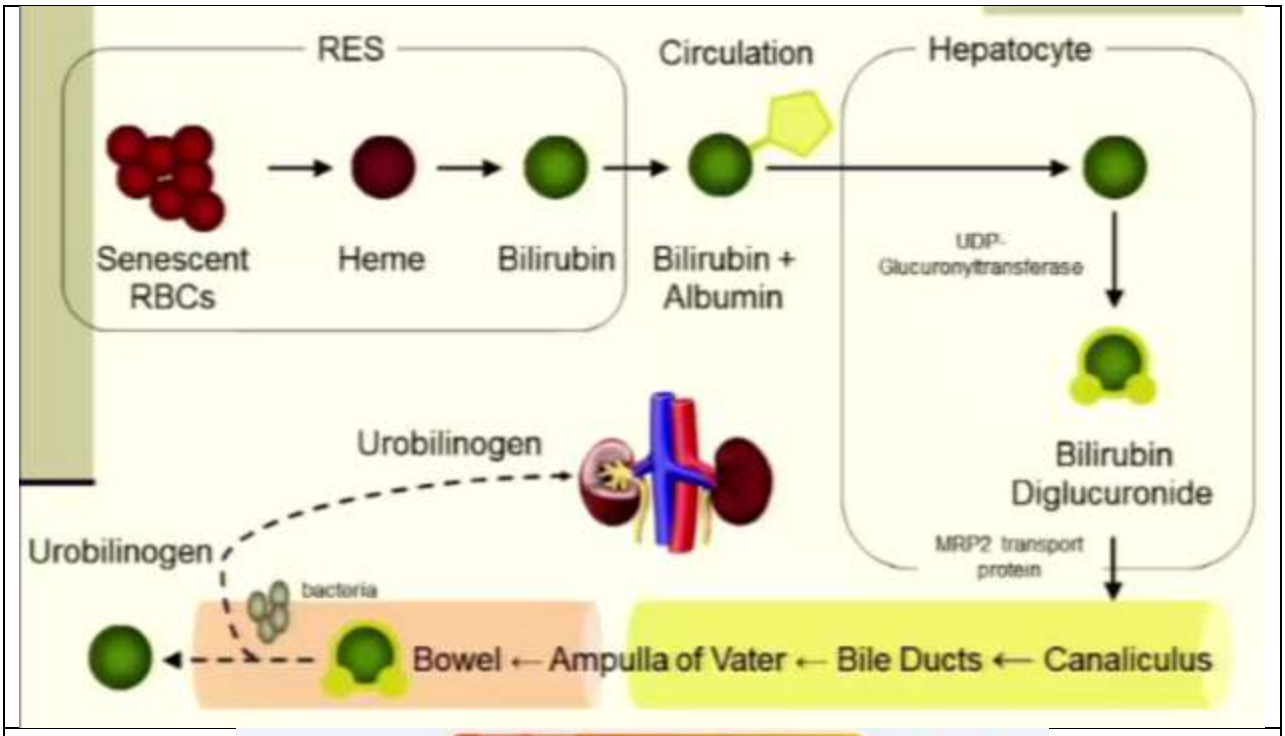


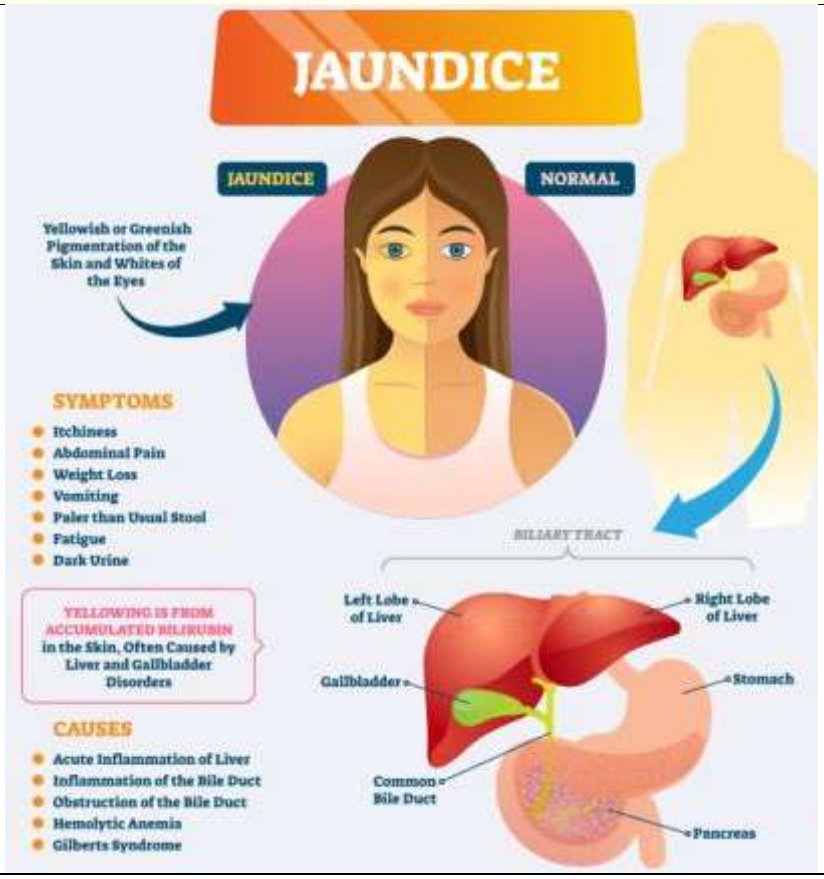
- ***Physiology of bilirubin formation***
- **Bilirubin is formed** by the breaking down of haemoglobin by the Reticulo-endothelial cells ***mainly in the bone marrow and to a lesser extent in the liver and spleen.***
- Under normal conditions bilirubin ***is present in a small limited quantity in the circulating blood and it gives no yellow coloration and is called "haemobilirubin".***
- **Haemobilirubin *(is conjugated with protein and does not filter in the kidney)* reaches the liver, passes through the liver cells *(where it dissociate from the protein and is conjugated with glucuronic acid and become water soluble and can pass in urine)* to reach the bile canaliculi and is excreted in the bile.**
- **Before its arrival to liver, it is called pre-hepatic bilirubin** *Into Hepatic bilirubin.*
- *In its passage through the liver cells, it is changed **to post-hepatic bilirubin (or cholibilirubin)** i.e., then changed to post-hepatic bilirubin (or **"cholibilirubin")** i.e., the liver cells contain an enzyme which helps the **conjugation of glucuronic acid with haemobilirubin**.*
- *This cholibilirubin, which is excreted by liver-cells to the bile canaliculi to the hepatic ducts, **is stored in the gall bladder** and, from time to time, it passes in the common bile duct (C.B.D.) to reach the duodenum; sometimes, for simplicity, it is called **"bilirubin".***
- **In the intestine, it is acted upon by bacteria and is changed to *"stercobilinogen".***

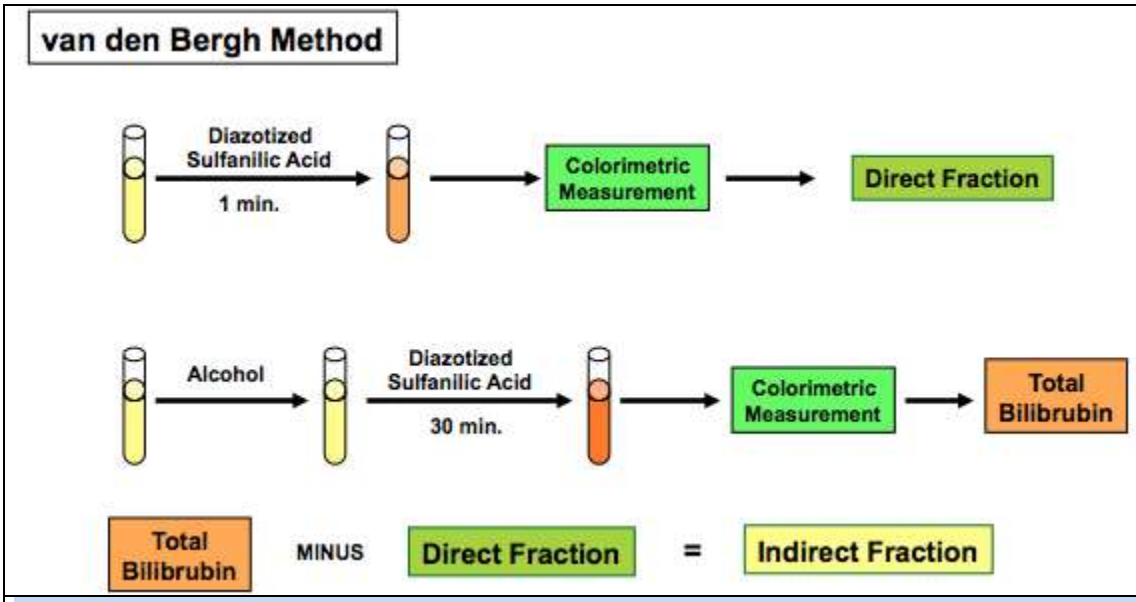
The main portion of stercobilinogen passes in faeces (and gives it its colour) and as such is called *stercobilin (when voided out).*

The other small portion is absorbed, passes in blood and reaches back the liver; part of this is re-excreted as such into the bile and, another part escapes into the general circulation (systemic) and thus reaches the kidney.

*This last part can be excreted by the kidney as **"urobilinogen"** and is oxidized into **urobilin** (when voided out in urine which it colours).*


RES
Circulation
Hepatocyte
Senescent RBCs
Heme
Bilirubin
Bilirubin + Albumin
UDP-Glucuronyltransferase
Bilirubin Diglucuronide
Urobilinogen
Urobilinogen
bacteria
MRP2 transport protein
Bowel ← Ampulla of Vater ← Bile Ducts ← Canaliculus


JAUNDICE
JAUNDICE
NORMAL
Yellowish or Greenish Pigmentation of the Skin and Whites of the Eyes
SYMPTOMS
Itchiness
Abdominal Pain
Weight Loss
Vomiting
Paler than Usual Stool
Fatigue
Dark Urine
YELLOWING IS FROM ACCUMULATED BILIRUBIN in the Skin, Often Caused by Liver and Gallbladder Disorders
CAUSES
Acute Inflammation of Liver
Inflammation of the Bile Duct
Obstruction of the Bile Duct
Hemolytic Anemia
Gilberts Syndrome
BILIARY TRACT
Left Lobe of Liver
Right Lobe of Liver
Gallbladder
Stomach
Common Bile Duct
Pancreas



The presence of cholibilirubin in an Albuminous fluid could be detected by a simple test called **van den Bergh test**; the reaction may be:

1. Indirect (a positive reaction in an alcoholic solution): This is so with:

(1) Haemolytic bilirubin produced by the R.E.S.

2. Delayed direct: Is a reaction given by the haemolytic type of bilirubin.

3. Direct (a positive reaction even without the presence of alcohol).

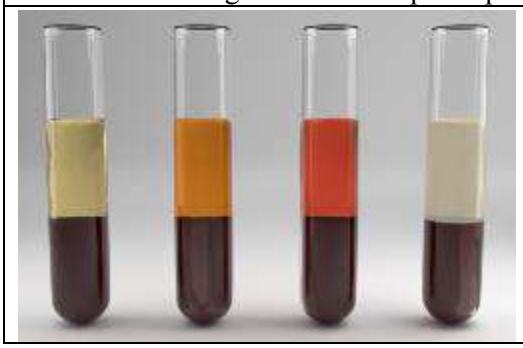
This is so with

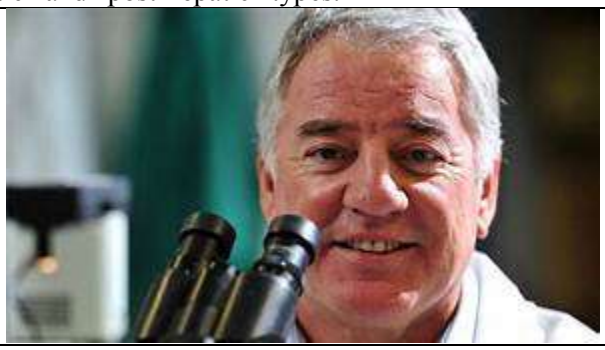
(1) The bile in the gall bladder 'cholibilirubin" and

(2) The "obstructive bilirubin of obstructive jaundice".

4. Mixed or biphasic: Indicates the presence of both types of bilirubin (Haemo-bilirubin and cholibilirubin).

- It is present in the toxic form of jaundice. i.e., the parenchymatous type (hepatocellular) where bilirubin production is usually normal, but the liver is functionally incapable of excreting all the pigment → retention jaundice; and hence, some Haemo-bilirubin passes through the liver uncharged and accumulates in the circulation (if alone → delayed direct reaction).
- Secondary cholangitis of small ducts may cause some obstruction to bile-capillaries → intralobular obstruction and disorganization → regurgitation jaundice; and hence, some hepato-bilirubin is reabsorbed into the blood (if alone → direct reaction).
- The sum of the two reactions to ether (delayed direct + immediate direct) → the biphasic reaction; the bilirubin being a mixture of "pre-hepatic" and "post-hepatic" types.





Formation of Bilirubin from Heme

Heme is degraded **in RE system (esp. liver & spleen)**
85% from RBCs
15% from turnover of immature RBCs & cytochromes

Heme

⇩ heme oxygenase

biliverdin (green)

⇩

bilirubin (red-orange)
bile pigments

⇩

In Blood with albumin
UNCONJUGATED BILIRUBIN
(or INDIRECT BILITUBIN)

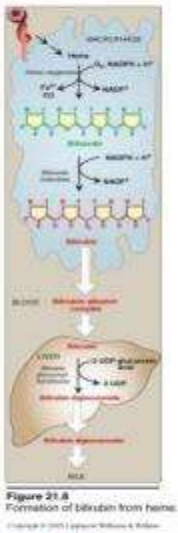


Figure 21.8
Formation of bilirubin from heme.

Salicylates & sulfonamides can displace bilirubin from albumin & so bilirubin enters CNS causing **neural damage**

Jaundice may be:				
I. Hepatic:	**1. Congenital**			
	2. Hepatocellular:	(a) Hepatitis and (b)Cirrhosis.		
	3. Hepatocanalicular:	(a) Intrahepatic obstruction. (b) Toxicity with chlorpromazine		
II. Pre-hepatic	**Disorders of haemolysis.**			
III. Post-hepatic	**Extrahepatic obstruction:**	(a) Intermittent (by a stone). (b) Complete (by carcinoma of pancreas).		

N.B.3:
(A) Retention jaundice (non-obstructive)

I. Lowered excretory power of liver due to sickness of liver-cells → accumulation of bile pigment in the blood

Hepatic jaundice (toxic jaundice)

(a) Mild (in catarrhal jaundice).
(b) Severe (in acute yellow atrophy; eclampsia; yellow fever).
(c) In severe bacterial infections; spirochetal jaundice; relapsing fever; malaria.

II. Increased production of bilirubin by undue haemolysis; the parenchyma, if affected, is only late.

1) Haemolytic jaundice

(a) ***Haemolytic anaemias*** (pernicious; sickle-cell; splenomegaly).

(b) Haemolytic poisons.

(c) ***Pneumonia*** (destruction of blood in lung and toxic degenerative changes in liver-cells).

(d) ***Cardiac decompensation*** (chronic venous congestion with ischaemia of liver-cells and excessive blood destruction).

(e) ***Marked haemolysis*** (in

- ***Septicemia with haemolytic streptococci;***
- ***Reaction after incompatible blood-transfusion;***
- ***Intraperitoneal haemorrhage;***
- ***Ruptured tubal pregnancy;***
- ***Snake-bite;***
- ***Certain drugs.***

2) Acholuric jaundice due to increased fragility of red cells → haemolytic icterus, anaemia and splenomegaly,

(a) ***Physiological jaundice of the newborn (congenital and hereditary)*** *due to ina***bility of the relatively immature liver to deal with the increased load of blood pigment from the rapid haemolysis of excess red cells produced by** the bone marrow and destroyed by the R.E.S.

(b) ***Pathological jaundice of the newborn (acquired acholuric jaundice):***

- It is not of familial nature & is recognized at adult life; less severe jaundice and more severe anaemia.
- ***It is due to:***
  - ***a. Erythroblastosis foetalis (Rh or ABO incompatibility);***
  - ***b. sepsis;***
  - ***c. syphilis;***
  - ***d. congenital hepatitis;***
  - ***e. Hemoglobinopathies.***