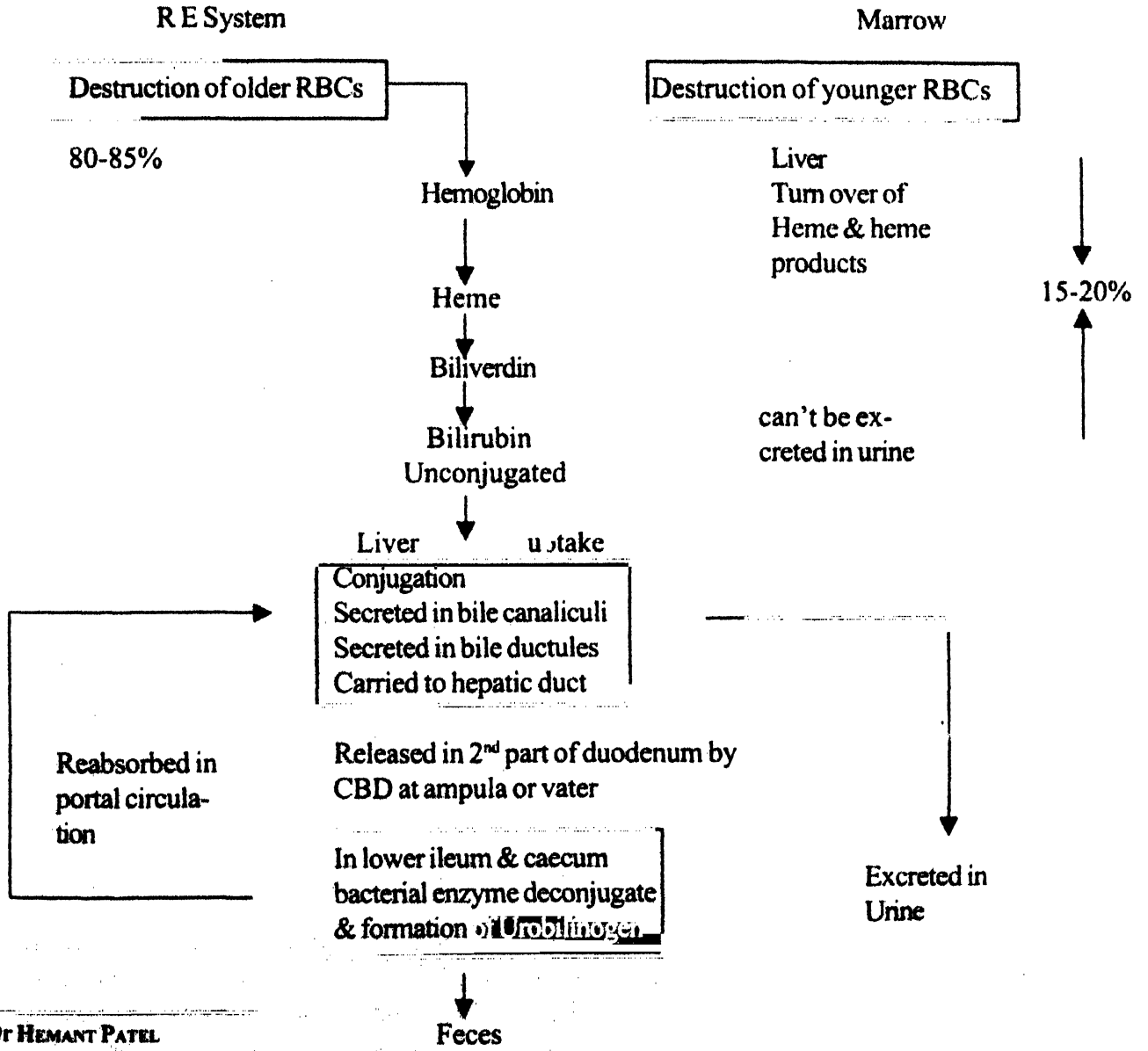
Approach to Jaundice

Jaundice is yellow discoloration of skin, mucous membrane and sclera due to yellow pigmentaion of plasma is caused by accumulation of bilirubin. Jaundice is clinically evident when serum bilirubin level exceeds 2-2.5mg %. Unconjugated (indirect) bilirubin cant be excreted in urine and so rise in unconjugated bilirubin though gives rise to yellow discoloration of skin and sclera urine remains free of bile salts and bile pigments. Such type of jaundice is called Acoluric Jaundice.

The Source And Precursors Of Bilirubin & Steps In Its Subsequent Metabolism And Excretion:



Dr Hemant Patel
9, Kamal Kunj, Bhaudaji Road
Mumbai 400 019
Tel: 4145865

Disorders in Metabolism of bilirubin upto hepatic conjugation give rise to isolated rise in unconjugated bilirubin.

Disorders in steps beyond conjugation, gives rise to increased conjugated bilirubin with raised ALT, AST (suggestive of Hepatocellular insult) Alkaline Phosphatase and GGTP (indicating cholestasis)

It is important to ask for complete LFT with prothrombin time and CBC & Platelet count with urine routine in a of suspected case of Jaundice, ideally at the first visit.

I. LFT should be analyzed carefully. In patients with isolated raised levels of unconjugated bilirubin, with other parameters of LFT if normal, consider following conditions.

1. **Over production of bilirubin:**
   a. Increased RBC breakdown–Hemolytic Anemia
      - Ineffective erythropoiesis
      - Mismatched blood transfusion
      - Massive blood transfusion
   b. Resorption of hematoma
2. **Decreased hepatic uptake:**
   a. Prolonged Fasting
   b. Sepsis
3. **Reduced Transferase activity, decreased bilirubin conjugation**
   a. Transient - Neonatal jaundice
   b. Hereditary - Gilberts syndrome
      - Crigler Najjar type II (I)
   c. Drugs-Chloramphenicol, Pregnandiol
   d. Hepatocellular disease
   e. Breast milk Jaundice: Pregnandiol & Fatty acids in breast milk.
   f. Sepsis

ISOLATED CONJUGATED HYBERBILIRUBINAEMIA SHOULD PROMPT YOU TO THINK OF:

1. Dubin–Johnson syndrome
2. Rotor Syndrome.

II. Raised direct bilirubin with predominantly raised SGPT & SGOT but AlK PO_4 < 3 X N is suggestive of Hepatocellular insult, as in

1. Viral Hepatitis: Acute A, E - h/o travel, eating outside
Raised IgM antibodies
Acute B (C) blood transfusion, surgery, and sexual exposure & infected individual IgM antibodies to HBc +ve
Chronic hepatitis & fluctuating SGPT & almost normal S bilirubin
Super infection with additional virus
2. Drugs-INH, Rifampicin, Statins, NSAIDS, Carbamezapin, Phenytoin, Methotrexate.
3. Alcoholic hepatitis: usually associated & leukocytosis (Fever), hepatomegaly, parotid swelling, spider naevi, palmar erythema, testicular atrophy
This may progress to irreversible alcoholic cirrhosis suggested by SGOT >SGPT, low albumin and raised globulins, e/o Portal hypertension.
4. Ischemic Liver injury: sudden & profound hypotension due to any cause eg. Myocardial infarction.
5. Liver Congestion: Rt ventricular failure
Hepatic venous obstruction
6. Metabolic or inherited disorders
Wilson's disease: family h/o Liver problem, young pt extra pyramidal symptoms, kFring convulsion, SGOT>SGPT
Low Sceruloplasmin ?vp
Increased 24 hrs Urinary Copper
Hemochromatosis: Increased intestinal absorption of Iron
Antitrypsin deficiency: (May be cholestatic)
7. Autoimmune Hepatitis: Female, young-middle aged associated other autoimmune disorders. ANA/ASMA +ve
8. Cirrhosis: Active cirrhosis

III. Raised direct bilirubinemia with predominantly raised Alk PO_4 > 3XN, raised GGTP but SGPT/ SGOT < 200 IU is suggestive of block to bile out flow, which could be intrahepatic where bile duct is patent or extrahepatic where bile duct is blocked / deformed.

1) Intrahepatic Cholestasis:

a) Diffuse Infiltrative disorders
   i) Granulomatous disease – Tuberculosis, sarcoidosis
   Granulomatous picture - drugs like allopurinol, Quinidine, NSAIDS, INH
   ii) Infiltrative Malignancy-Lymphoma
   iii) Amyloidosis

b) Inflammation of intra Hepatic Biliary Radicles (IHBR) or / and portal tracts
   i) Primary Biliary Cirrhosis (PBC) Middle aged female, prolonged h/o pruritus, darkening of skin, Anti mitochondrial Antibody (AMA) +ve
   ii) Secondary Biliary Cirrhosis
   iii) Primary sclerosing cholangitis (20%) intra hepatic small bile ductules affected

c) Drugs: Chlorpromazine, chlorpropamide, methimazole, captopril, NSAIDs, Sulbactum + Amoxycilin H/o Rash, Fever, Urticaria, Arthralgia, Jaundice
   Estrogen, anabolic steroids, OC pills: only Pruritus jaundice may follow, but no rash, fever, Arthralgia

d) Prolonged Cholestasis in Viral A (E): Pt looks OK with SGPT/SGOT declining but has persistently raised S Bilirubin
   Alcoholic hepatitis can also give rise to similar picture

e) Benign Recurrent Intrahepatic Cholestasis (BRIC) Familial, young, repeated episodes of Nausea, vomiting, malaise, precipitated by infection, Alk PO_4 raised but without relative rise in GGTP

f) Recurrent Cholestasis of pregnancy:
   H/o pruritus with or without jaundice, jaundice may follow 2-3 wks later. H/o similar complaints in previous pregnancy may be present, or may occur in subsequent pregnancy.

Other liver abnormality during pregnancy could be:

i) Acute fatty liver of pregnancy in 3rd trimester. Presence of jaundice indicates poor prognosis and only treatment to save mother is to terminate the pregnancy.

ii) Emesis gravidarum is common in the early part of pregnancy but when persists and associated with dehydration and jaundice, it is called Hyperemesis gravidarum. SGPT raised but less than 250 and S Bilirubin mildly raised.

iii) Pre-eclampsia and eclampsia may be associated with abnormal LFT & Jaundice. HELLP, is Hemolysis, elevated liver enzyme low platelets, may be seen as a severe form eclampsia and treatment is termination of pregnancy.

iv) Jaundice in pregnancy may not always be related to pregnancy and could be like any other jaundice in non-pregnant patient.

v) Sepsis : Multifactorial

vi) Post-operative period: Multifunctional.

Raised S Bilirubin (direct) with raised AlkPo4 > 3xN and e/o bile duct obstruction, consider Extrahepatic biliary obstruction.

a) Intraductal obstruction
   - Gall stones
   - Biliary malformation (atresia, choledochal cyst)
   - Infection (Ascariasis, Clonorchis)
   - Malignancy (Cholangiocarcinoma)
   - Sclerosing cholangitis (Ass & Ulcerative colitis)
   - Trauma (Hemobilia)

b) Compression of biliary ducts
Malignancy (Pancreatic Carcinoma, lymphoma, metastatic portal lymph nodes)
Inflammation (pancreatitis)

How to investigate Cholestasis?

Always confirm origin of raised Alk Po4 in hepatobiliary pathology usually it will be accompanied with raised GGTP.
Ask for Abdominal sonography.
Look for IHBR Dilatation or CBD stone / dilated
No IHBR dilated ask for MRCP/EUS to locate the obstruction
CBD pathology needs further evaluation and either EUS/MRCP or therapeutic ERCP.

How to Differentiate Medical from Surgical Jaundice

Medical	Surgical
History: Prodrome, Travel, blood Transfusion, alcohol abuse H/o Drugs	Episodic abd-pain vomiting, fever & chills h/o previous surgery
Stools: Transiently clay coloured	progressively pale stools
Itching: Transient	Progressive
Stigmata of liver disease and its complications present	Abdominal scar may be present s/o previous surgery, RHC mass tenderness
S. bilirubin Raised with SGPT > 10 x N Alkpo4 < 3 x N	Raised with SGPT < 10 x N Alk po4 > 1 x N
Response to Inj Vit K - Poor	Good

Approach to pt with Fever and Jaundice

a) Fever follows jaundice: think of cholangitis eg. Infection in blocked bile; CBD stone, CBD structure, malignancy

b) If jaundice follows fever: consider

Signs/symptoms	Malaria	Leptospirosis	Dengue	Typhoid	Amoebic Liver
Bodyache	-	+	+	-	-
Conjunctival suffusion	-	+	-	-	-
RHC tenderness	-	-	-	-	+
WBC count	L/N	High	L/N	L with Cosinopenia	High
Platelet count	L/N	L/N	L	N	N
CPK	-	High	-	-	-
LDH	High	-	-	-	-
Stic test	Peripherla Smeal MF Antigen	Dark field microscopy Ism Ab	ISM Ab	Blood culture	IHA for E.H. USG

Boy: Did you hear about the crazy scientist who crossed a lion with a parrot?

Girl: What did he get?

Boy: Nobody knows, but when it talks-you listen!