Jaundice
differential diagnostics

Definition

- Icterus (jaundice) is a yellowish coloring of sclerae and skin caused by elevation of plasmatic bilirubin
- Icterus is a most apparent clinical feature of liver disorders
- Up to 300 mg of bilirubin is produced daily, especially in the RES cells (liver, spleen), in the bone marrow from immature RBCs which never left the marrow (shunt bilirubin), and from hepatic heme and myoglobin

Bilirubin

- Bilirubin produced this way does not exceed 20 µmol/L, is not soluble in water. In serum, it is stored in solution binding to albumin.
- In this manner, bilirubin is transported to the hepatocyte.
- Upon entering the hepatocyte, it is released from the bond and binds to ligandin inside the hepatocyte
- In the endoplasmic reticulum, it is conjugated with glucuronic acid in the presence of glucuronyl-transferase, creating mono- and di-glucuronide.

Bilirubin

- Conjugated bilirubin is easily water-soluble, we call it direct bilirubin
- Conjugated bilirubin is excreted to small intestine and is metabolised by colonic bacteria to urobilinogen, then stercobilinogen and finally stercobilin
- A portion of stercobilinogen is reabsorbed from the intestine back to the circulation and brought again to the hepatocyte, which allows its excretion via bile. This is called enterohepatal circulation of bile colors

Bilirubin

- Conjugated bilirubin – DIRECT
- Unconjugated bilirubin - INDIRECT

Icterus types

- 1. pre-hepatal - hemolytic
- 2. hepatocellular - parenchymatous
- 3. cholestatic - obstructive
- 4. icterus in familial non-hemolytic hyperbilirubinaemia

1. Pre-hepatal icterus

- **Hemolytic**
- **Increased amount of bilirubin enters the hepatocyte (e.g. in hemolysis)**
- **The capacity of liver's bilirubin metabolism is exceeded. Elevated levels of unconjugated bilirubin are found in circulation. As it is not water-soluble, it cannot be proven in urine. It crosses the hematoencephalic barrier and causes kernicterus in neonates – a brain-damaging condition**

1. Pre-hepatal icterus

- Higher offer of bilirubine also means higher conjugation and higher transport to the intestine
- Stool is hypercholic, there is positive urobilinogen in urine as part of it is excreted via kidneys
- Lab: blood count – anemia
- Reticulocytosis
- Liver tests may be normal, bilirubin is elevated

2. Hepatal - parenchymatous

- **This type of icterus is caused by a damage to the hepatocyte (virus hepatitis, liver cancer)**
- **The hepatocyte is unable to sufficiently conjugate the offered bilirubin**
- **Plasmatic levels of both conjugated and unconjugated bilirubins are elevated. Both bilirubin and urobilinogen can be found in urine**
- **The damaged hepatocyte is unable of entero-hepatal circulation**
- **Stool is hypocholic**

2. Hepatal - parenchymatous

- **Liver tests are usually elevated, but can also be normal. Cholesterol level is normal or slightly lowered**

3. Cholestatic - obstructive

- **Cholestasis is an interruption of drainage of bile to the intestine. It is located on various levels of the biliary tract**
- **A- intrahepatal**
- **B- extrahepatal (dilation of bile ducts is present)**

3. Cholestatic - obstructive

Localization of obstruction:

- **1/ bile pole of the hepatocyte – secretion blockade (drug-induced jaundice)**
- **2/ intrahepatal bile ducts / PBC/**
- **3/extrahepatic bile ducts- gallstones in bile ducts, choledochlithiasis, stenoses**
- **Stool is acholic, urine is dark, skin is itching, due to retention of cholic acids**

3. Cholestatic - obstructive

- **Lab: elevation of obstruction enzymes – ALP, GMT**
  AST and ALT may be elevated
  cholesterol is elevated
- **There is manifestation of fat and fat-soluble vitamin resorption disorder, steatorhea**

4.Gilbert’s syndrome

- **Familial nonhemolytic hyperbilirubinaemia**
- **Occurrence: 2-5%**
- **Jaundice intensity varies, usually not exceeding 70 µmol/L**
- **It is always the unconjugated bilirubin, which elevates under stress situations**

Differential diagnostics guidelines

- **1/ case history - Ask about circumstances under which jaundice has manifested**
- **Painless? After dietary excesses? Joint pain? Signs of virosis?**

Differential diagnostics guidelines

- **2/ Lab tests:**
- **Blood count (WBC, anemia?)**
- **Biochemistry, AST, ALT, GMT, ALP, conjug.+unconjug. bilirubin, CRP**
- **Hepatitis markers, immunology**

Differential diagnostics guidelines

- **3/ ultrasound – focus especially on:**
- **Liver parenchyma**
- **Cholecystolithiasis**
- **Dilation of bile ducts**

Differential diagnostics guidelines

- If bile duct dilation is present, perform
- 4/ ERCP
- PTC

ERCP

- Endoscopic Regrograde Cholangiopancreaticography
- Diagnoses of the cause of obstruction of bile duct or pancreatic duct systém
- Therapy
- Specific endoscope (duodenoscope)
- X-ray

Extrahepatic bile duct obstruction

- l/ choledocholithiasis , hepatikolithiasis
- 2/ stenoses of biliary ducts
- stenoses have two ethiologies – benign and malignant

a/ benign

- may occur after laparoscopic cholecystectomy as a complication arising from thermical damage in the region of Calot's triangle (cystohepatic triangle)
- chronic pancreatitis – enlargement and fibrous change of the head of pancreas
- oppression by an enlarged hydropic gall bladder, so called Mirizzi syndrome

b/malignant etiology

- stenoses of bile ducts of malignant etiology occur in
- pancreatic tumors
- gall bladder tumors
- hepatic tumors
- metastases
- generalized tumors of intestinal origin
- enlarged lymph nodes in vicinity of bile ducts

Differential diagnostics guidelines

- **If bile duct dilation is not present, evaluate**

- **5/ Hepatitis markers**

  and refer patients to the Infectious ward

Differential diagnostics guidelines

- **6/ in hepatopathies of unclear etiology, perform liver biopsy**