Differential diagnosis of jaundice

Normal bilirubin values are 2.0-17.0 µmol/l. If serum bilirubin rises above about 20 µmol/l, we speak of hyperbilirubinemia. At higher levels, it begins to build up in the tissues, leading to **subicterus** (yellowing of the sclera-covered parts of the eyelids, soft palate; serum bilirubin around **30-80 µmol/l**), and then eventually when high enough jaundice (icterus). Pathologies of low bilirubin are not described. Total bilirubin in the blood is mainly represented by unconjugated bilirubin. The terms "direct" and "indirect" bilirubin come from Van den Bergh, according to the method of determination. Direct = conjugated, indirect = unconjugated. In the urine, the bilirubin is always conjugated. In the CNS (in newborns: kernicterus), in areas of immature or damaged blood-brain barrier, there is always unconjugated bilirubin. According to the etiology, we distinguish hyperbilirubinemia and jaundice:

- **unconjugated** - large amount of bilirubin and the liver cannot keep up and is not able to metabolize (conjugate) it sufficiently
- **conjugated** - blocked bile secretion
- **mixed**

Hyperbilirubinemia with unconjugated bilirubin predominating

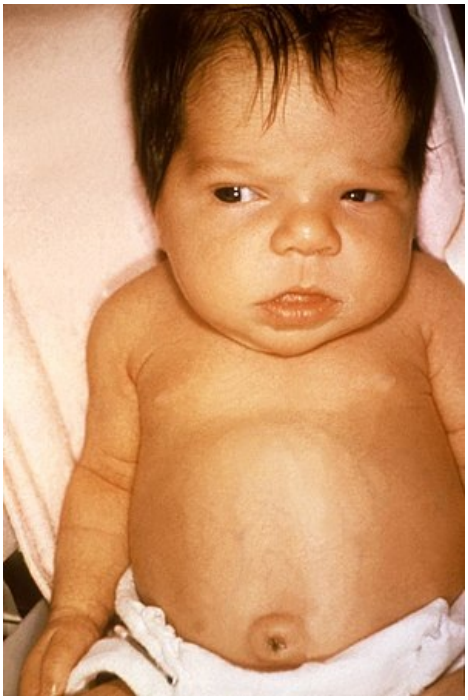
Jaundice: scleral discoloration

Hyperbilirubinemia with increased bilirubin production

- Most often due to hemolysis, less often: rhabdomyolysis, crush syndrome, etc...
- the capacity of the liver to conjugate and excrete bilirubin is large, so hemolytic jaundice occurs only during massive and/or prolonged hemolysis, which occurs in autoimmune hemolysis, in sickle cell anemia,hereditary spherocytosis, toxic or allergic reaction, in disorders of erythropoiesis (thalassemia...), hypersplenism.

Icterus neonatorum

- In addition to hemolysis, the immaturity of the liver also plays a role
- occurs in almost half of newborns (70-80 µmol/l) in the first five days
- breastfed infants have higher values (UGTA1 enzyme inhibitor in milk) - this is not usually associated with neurological damage
- other problems are e.g., fetal erythroblastosis, ABO incompatibility...
- pathological jaundice - within 24 hours after delivery, over 220 µmol/l
- phototherapy - decomposition of bilirubin in the skin by light in the range of 425–475 nm - photoisomers (they are no longer dangerous for the CNS).



Icterus neonatorum

Hyperbilirubinemia with reduced conjugation

Gilbert's syndrome

- Chronic, small elevation in bilirubin, usually no more than 50–70 µmol/l, subicterus only, decreased hepatic activity of UGTA1 (TATA box mutation, decreased expression, AD, 10–12% of population)
- is often diagnosed on accident
- bilirubin acts as free radical scavenger, hyperbilirubinemia protects against oxidative stress

Crigler-Najjar syndrome

- AR, complete (type I) or partial (type II) UGTA defect
- type I completely lacks conjugated bilirubin, unconjugated bilirubin levels are around 300–800 µmol/l
- jaundice occurs shortly after birth. Without phototherapy, individuals soon die of CNS involvement.
- for type II - concentration approx. 350 µmol/l

Hyperbilirubinemia with conjugated bilirubin predominating

Hyperbilirubinemia in excretion disorders

Dubin-Johnson syndrome

- Benign, AR, symptoms: jaundice only
- coproporphyrin I is elevated in the urine for unknown reasons

- a defect in the canalicular system by which bilirubin is secreted from hepatocytes

Rotor syndrome

- Also rare, similar to the previous one.

Hyperbilirubinemia in biliary outflow disorders

- Obstruction or inflammation, obstructive jaundice - cholecystitis, cholangiitis, cholelithiasis, primary biliary cirrhosis, and tumors of the head of the pancreas or bile ducts.

Intrahepatic cholestasis

- A number of drugs can cause this: estrogens, steroids, some ATB…
- characterized by increasing levels of bile acids and liver enzymes in the blood as well.

References

Related articles

- Icterus • Hyperbilirubinemia in newborns and infants • Juvenile hyperbilirubinemia
- Biliary obstruction parameters

Source

- BENEŠ, Jiří. *Studijní materiály* [online]. [cit. 2009]. <http://jirben.wz.cz>.

Literature

- HAVLÍK, Jiří. *Infektologie.* 2. edition. Praha : Avicenum, 1990. pp. 393. ISBN 80-201-0062-8.

- LOBOVSKÁ, Alena. *Infekční nemoci.* 1. edition. Praha : Karolinum, 2001. pp. 263. ISBN 80-246-0116-8.