Jaundice (icterus)

Icterus or **jaundice** (latin *icterus*) is a yellow discolouration of tissues that is visible on the skin, mucous membranes and whites of the affected person. The yellow discolouration of the tissues in jaundice is caused by the accumulation of bilirubin , which diffuses into the tissues after depletion of the binding capacity of albumin (with bilirubinemia above 35 µmol / l). Jaundice is only a **symptom** 'accompanying a number of disease states and not the disease itself.

Metabolism of bilirubin

náhled|400px|Metabolismus hemu. The breakdown of erythrocytes releases hemoglobin, which further breaks down into hem and globin. Hem is then transformed into biliverdin and it is transformed into **unconjugated bilirubin**. Unconjugated bilirubin is then transported to blood proteins (albumin) to the liver, where it is conjugated to glucuronic acid. **Conjugated bilirubin** it is soluble in water (during accumulation it can therefore be excreted in the urine) and is excreted from the liver into the bile ducts, which gradually merge and open into the main bile duct. Through the bile duct, bilirubin as part of bile also enters the intestine, where it is converted to stercobilinogen under the influence of intestinal bacteria and causes a brown discoloration of the stool. Part of bilirubin is degraded by the bacteria urobilinogen, which is reabsorbed into the circulation and is excreted in the urine (so-called enterohepatic circulation). Subsequent oxidation of urobilinogen to urobilin gives the concentrated urine a dark yellow color.[1]

In short, the metabolic process described above can be described as follows: **heme → biliverdin → unconjuagted bilirubin → conjugated in liver → conjugated bilirubin → bile → stool → excretion / absorption (enterohepatic circulation) and conversion to urobilinogen**.

If for any reason **bilirubin** (whether conjugated or unconjugated) **begins to accumulate in the body**,**jaundice** occurs. The disorder can be at any level of its metabolism.

Signs and symptoms

1. **macroscopic** – colouring of sclera, skin, mucous membranes and body fluids:

- *flavin* jaundice – yellow/green, in hemolytic icterus,
- *verdin* jaundice – greenish, in obstructive icterus,
- icterus *melas* – olive gray-green, with severe obstructive jaundice,
- *rubin* jaundice – orange-yellow, in hepatocellular jaundice.

In addition, in newborns (immature blood-brain barrier) a yellow-green discoloration of the nuclei of the thalamus, cerebellum, basal ganglia and olive nuclei of the oblongate can be observed. **nuclear icterus** (kernicterus).

2. **microscopic** – well detectable in the kidneys, where bilirubin forms granules in the proximal tubules, pigmented cylinders in the distal tubules.

Classification

náhled|300px|vpravo|Icterus: yellow colouring of the sclera in patients with hepatitis A **1. according to the type of elevated bilirubin:**

- **unconjugated icterus** – hemolytic icterus,
- **mixed icterus** – hepatic icterus,
- **conjugated icterus** – obstructive icterus.

2. according to the cause:

- **prehepatic** (hemolytic, dynamic, flavin) – increased production of bilirubin,
- **hepatic** (hepatocellular, hepatotoxic, rubin) – failure of bilirubin transport to hepatocytes, failure of intracellular transport and conjugation, failure of excretion into bile,
- **posthepatic** (obstructive, cholestatic, mechanic, verdin) – failure of bilirubin transport bile duct.

Type of icterus	Bilirubin in blood		Urine		Stool
	Indirect	Direct	Bilirubin	Urobilinogen	
Prehepatic	+	normal	−	+	hypercholic
Hepatic	+	+	+	+	hypocholic
Posthepatic	*slight* +	+	+	−	acholic

Prehepatic

The dominant proportion is increased red blood cell breakdown (intravascular or extravascular hemolysis). As the red blood cells break down more, a lot of hemoglobin is released and a large amount of bilirubin is made in the body. This amount exceeds the liver's capacity to conjugate and eliminate bile from the body. The accumulating bilirubin then turns the tissues yellow. Serum concentrations of unconjugated bilirubin increase (which is insoluble and does not pass into the urine - acholuria), bile flows into the intestine and contains an increased amount of bilirubin - more urobilinogen is formed (is absorbed into the blood and excreted by the kidneys - urobilinogen in urine) and stercobilinogen (which darkens in air to form stercobilin - hypercholic stool). Flavic jaundice appears on the skin, bile acids do not enter the circulation and there is no itching (pruritus) of the skin.

Examples are jaundice in hemolytic anemias (hereditary spherocytosis, immune destruction of erythrocytes, malaria), in pernicious anemia, administration of incompatible transfusion and [[Hyperbacteria] neonates and infants |], where it occurs as icterus neonatorum simplex or icterus neonatorum gravis.

Hepatic

Damage to the liver tissue for any reason will cause it ***makes conjugation and excretion of bilirubin in the bile difficult***. Bilirubin begins to accumulate in the body again and jaundice develops. Conjugated bilirubin (soluble in water, excreted in the urine and given a dark color) and unconjugated bilirubin accumulate in the body. The intestinal contents are hypocholic, the skin color is orange-yellow (ruby jaundice). This group of causes includes a number of diseases:

- **Liver damage from alcohol**: Alcohol abuse damages the liver and leads to alcoholic steatosis to cirrhosis. Jaundice is a rather late and very serious symptom of liver damage in alcoholic-cirrhotic patients.
- **Wilson disease**: Hereditary disease characterized by the accumulation of copper in the liver, damages it and the whole process can again end in cirrhosis.
- **Infectious hepatitis**: It is an infectious disease of the liver caused by many types of viruses - they are called the letters A-F. Infectious hepatitis A, B, C, D are especially known. Yellowing as a manifestation of liver damage in infections may or may not occur, jaundice is most typical of infectious hepatitis A
- **Liver Tumours**: Advanced malignant liver tumor, for whatever cause, may be accompanied by jaundice. The tumor tissue of a malignant tumor destroys the surrounding healthy liver tissue.
- **Autoimmune hepatitis**: Inflammation of liver tissue that is non-infectious. It is more common in women. The consequences are serious and the whole process can end in cirrhosis again.
- **Liver damage from toxic substances (excluding alcohol)**: There are a number of toxic substances that damage liver cells. These are, for example, high doses of paracetamol or poisoning by poisons of some fungi (amanitin and phalloidin in green toadstool), chloroform, amphetamines, carbon tetrachloride. Jaundice can accompany acute poisoning with all these substances.
- **Genetic disorders**: There are genetic disorders that cause impaired bilirubin uptake, conjugation, or excretion:
  1. increase in indirect (unconjugated) bilirubin,
     - Gilbert syndrome – defect of bilirubin glucuronidation, possibly also disorder of bilirubin uptake by hepatocytes,
     - Crigler-Najjar syndrome – reduced UDP-glucuronate transferase activity (completely absent - type I or only partially - type II), manifests itself after delivery (kernikterus),
  2. increase in direct (conjugated) bilirubin,
     - Dubin-Johnson syndrome – hepatic bilirubin secretion into the bile, UDP-glucuronate transferase activity is normal, microscopically visible hepatocyte pigmentation,
     - Rotor syndrome – similar to Dubin-Johnson syndrome, but without pigmentation.

Posthepatic

Posthepatic or obstructive jaundice is a disorder of bile drainage. Conjugated bilirubin cannot be excreted in the gut and begins to accumulate in the body similar to previous types of jaundice. Because bile does not enter the intestine at all in this type of jaundice, the stool is not stained with bile pigments and is *light to whitish.* The absence of bile in the intestine causes malabsorption of fats - steatorrhea, which can result in a deficiency of fat-soluble vitamins (hypovitaminosis A, D, E, K). In addition, accumulating bile acids often cause **persistent itching of the skin**. Again, conjugated bilirubin accumulates and may be excreted in the urine, causing a dark discolouration of the urine, but no urobilinogen is found in the urine.

Bile duct obstruction leads to bile congestion (cholestasis) - first it is compensated by the accumulation of bile in the gallbladder (water and salt resorption - its content is dark and dense). Bile from small bile ducts enters the interstitium of the liver, later up to the Disse space (initially in the center of the lobes and spreads to the periphery), where it forms the so-called **bile thrombi**. Ascending infection from the intestine is often associated (*Escherichia coli*) – purulent cholangitis is formed with sepsis, inflammation leads to fibroproduction to the so-called. **cholestatic liver cirrhosis** (secondary billiary cirrhosis)
Causes:

- **Tumours of pancreas**: A tumor growing out of the pancreas can very often compress the bile duct and thus prevent the outflow of bile. Painless sudden jaundice in an elderly person is a classic symptom.
- **Gallbladder tumors**: A gallbladder tumor can suppress the bile duct in a similar way to a pancreatic tumor, and the symptoms will be exactly the same. Again, sudden painless jaundice develops.
- **Effects of alcohol**: Alcohol has a double effect on the liver. First, it damages liver tissue and its ability to conjugate bilirubin. Second, alcohol prevents liver cells from releasing bile into the bile duct and thus causes a condition similar to classical bile duct obstruction.
- **Cholelithiasis**: If the gallbladder clogs the bile duct, in addition to painful colic, jaundice can also occur during prolonged obstruction.
- **Autoimmune cholangiohepatitis**: It is a condition similar to autoimmune hepatitis. In this case, the patient's immune system attacks the small bile ducts in the liver and damages them. It causes a disorder of bile flow into the bile ducts and the accumulation of bilirubin in the body.
- **Congenital atresia of the bile ducts**
- **Biliary tract injury during surgery (cholecystectomy)**

Diagnostics

- An important history is whether the jaundice occurred suddenly or if the patient has any other symptoms (anorexia, nausea, pain, fever, whitish stools, itchy skin, dark urine), (ab) alcohol use, etc. It is important to examine the abdomen by palpation.
- Of the others, level detection is used liver enzymes from blood (ALT, AST, GGT, ALP), which are increased in hepatocyte damage (rather increased in**ALT, AST**) and in **obstructed bile ducts** (rather increased **GGT, ALP**).
- From blood samples we can also detect the presence of viral infection in individual types of infectious hepatitis.
- Naturally, the level of bilirubin itself can also be determined from the blood, the high concentration of which is decisive for the diagnosis of jaundice. In addition to the level, we are interested in whether it is unconjugated or conjugated bilirubin.**Unconjugated** bilirubin informs us about **incraesed breakdown of red blood cells** and **conjugated by liver damage or impaired bile flow**.
- The examination is then supplemented by imaging methods:
  - ultrasound,
  - endoscopy: ERCP,
  - MRCP.
- Other examination methods according to the specific suspicion of a certain disease.

Prevention and treatment

For prevention and treatment, see individual diseases. Jaundice is a very serious symptom and suspicion must be reported to a doctor immediately. Jaundice can indicate **infections, dangerous tumors, poisoning and liver damage in general**.

Summary video

náhled|center|upright=1.6|Video v angličtině, definice, patogeneze, příznaky, komplikace, léčba.

Links

Related articles

- Differential diagnosis of jaundice
- Hyperbilirubinemia of newborns and infants ■ Juvenile hyperbilirubinemia
- Hepatitis ■ Liver tumours

Sources

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References

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