# Gilbert´s syndrome

**Gilbert-Meulengracht syndrome** (*Gilbert's disease*, juvenile jaundice, intermittent hyperbilirubinemia) is benign AR inherited unconjugated hyperbilirubinemia with intermittent jaundice. It is characterized by a chronic small increase in unconjugated serum bilirubin in the absence of bilirubin in the urine, no hyperhemolysis, and no other signs of liver disease. It is usually diagnosed in adolescents but manifests for life. It is more common in men than in women.

A typical manifestation is an **increase in bilirubin levels** during starvation, mental stress, physical exertion, intercurrent infection, operations, injuries, excess alcohol, in women in the premenstrual period. In contrast, bilirubin levels are reduced by excessive energy intake and by enzyme inducers.

Clinical manifestations are defined as **mild isolated unconjugated hyperbilirubinemia**, usually up to 80 µmol/l, rarely up to 100 µmol/l, without overt hemolysis and evidence of other hepatic impairment (except glucuronidation). The liver parenchyma is free of macroscopic or microscopic changes.

**Incidence**: 3 % of the population (some sources report 5–10 %)

## Etiology

This is a genetic **defect in bilirubin glucuronidation**, due to decreased hepatic glucuronyltransferase activity UGTA1 (a disorder of the TATAA box promoter region of the uridine diphosphoglucuronosyltransferase gene, decreased expression, AR, 10–12 % of the population).

## Clinical picture

Most of the sufferers have no problems at all, some patients suffer from **non-specific symptoms** – indigestion, weakness, increased fatigue, poor ability to concentrate - the difficulties do not correlate with the level of hyperbilirubinemia.

## Diagnosis

The diagnosis is based on a careful history, physical examination, and the fact that individuals are practically asymptomatic. In the laboratory, we demonstrate repeatedly fluctuating, isolated, unconjugated hyperbilirubinemia. Bilirubin values are usually between 30–50 µmol/l

- Hyperbilirubinemia should be detected repeatedly – at least 3×.
- Onlybilirubin levels and **no other laboratory findings** change during follow-up.
- About a third of patients have periods when bilirubin is perfectly normal.
- Ascension is often associated with infections, a fatty diet, starvation, alcohol consumption, physical exertion, or premenstrual tension.

During diagnosis, we must rule out hemolysis, ie there must be a normal blood count, including reticulocytes. In addition, liver tests are normal, negative HBsAg and anti HCV. A biopsy is not usually a benefit.

The fasting and phenobarbital test is no longer used today due to its non-specificity.

- **starvation test**:
  - after 2 days we reduce the energy supply to 400 kcal / day = 1680 J / day

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- **phenobarbital test**:
  - administration of 200 mg phenobarbital/day
  - serum bilirubin levels are reduced (enzyme induction principle)

## Differential diagnosis

### Diff. dg between Gilbert's syndrome and other hepatocyte involvement

- anamnesis – past infectious mononucleosis, contact with hepatitis
- serology, liver tests
- presence of hepatosplenomegaly
- **post-infection conditions** have intermittently elevated conjugated bilirubin

genetic testing

- it is necessary to distinguish Wilson's disease, which also has neurological symptoms, copper in the urine, when thinking about this diagnosis, we immediately do a liver biopsy - we find steatosis, a lot of copper in the

liver dry matter, molecular diagnostics – affects about 90 %)
- $\alpha_1$-antitrypsindefect , which does not manifest itself in children with typical emphysema, but rather with repeated respiratory infections, there is a very useful molecular diagnosis)

### Algorithm testing

1. blood count + reticulocytes
2. serum biochemistry
3. liver function – it is mainly reflected in the level of proteosynthesis - Quick, INR, aPTT, cholinesterase, which rises even in toxic liver disease, and prealbumin are mainly sensitive → but they are also acute phase proteins
4. immunology – can be chronic jaundice, Ig, CIK, ANAb
5. ceruloplasmin, $\alpha_1$-antitrypsin, haptoglobin (a marker of hemolysis)
6. serology – VHA, VHB, VHC, EBV, CMV, HSV, toxoplasma
7. stools for parasites
8. sono liver, spleen, gallbladder

### Diff. dg isolated unconjugated hyperbilirubinemia type hepatocyte

- ow-grade chronic hepatitis - difficult to distinguish without histology, often an increase in aminotransferases
- Crigler-Najjar syndrome – AR hereditary
  - type I – severe hyperbilirubinemia with danger of nuclear jaundice
  - type II – mild hyperbilirubinemia
- posthepatic bilirubinemia

## Therapy

No treatment is necessary. We must warn the patient that this is a benign condition with an excellent prognosis. In addition, the patient must follow a light liver diet.

## References

### Related articles

- Jaundice

### References


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