Gilbert's Syndrome

Gilbert's syndrome is a hereditary hyperbilirubinemia, which is caused by decreased activity of UDP-glucuronosyltransferase. This enzyme works to conjugate lipophilic bilirubin into a water-soluble, excretable form. Thus patients who are symptomatic with Gilbert's syndrome show elevated unconjugated bilirubin levels in their lab results. Often, patients are asymptomatic, but can develop mild jaundice in instances where they are fasting, under stress, or have been ingesting alcohol.



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Pathophysiology

Decreased UDP-Glucuronosyltransferase Activity

Down-arrow Upside-Down-Pineapple-cake with Glue-transformer

Patients with this hereditary disorder have decreased UDP-glucuronosyltransferase activity. Keep in mind that Gilbert's syndrome differs from Crigler-Najjar syndrome, where patients have absent enzyme activity. This is an enzyme of the glucuronidation pathway that transforms lipophilic, unconjugated bilirubin into a conjugated form, which is water-soluble and excretable.

Decreased Bilirubin Conjugation

Down-arrow Belly-ribbon-dancer with Congas

The symptoms that arise from Gilbert's syndrome come from an enzyme defect leading to decreased bilirubin conjugation. This mechanism of disease differentiates Gilbert's syndrome from Dubin-Johnson syndrome and Rotor's syndrome, in which patients can conjugate bilirubin but are unable to excrete it out of hepatocytes.

Signs and Symptoms

Often Asymptomatic

Thumbs-up

Gilbert's syndrome is a very common disorder, and often patients are asymptomatic. This lack of symptoms is because patients still have some UDP-glucuronosyltransferase activity.

Jaundice (Mild)

Jaundice-janitor

There are several instances in which patients with Gilbert's syndrome can show symptoms of hyperbilirubinemia. They can become jaundiced from fasting, periods of stress, or if they are ingesting alcohol. There are a handful of medications that also inhibit UDP-glucuronosyltransferase, which could also lead to jaundice in these patients. Severe cases are seen by yellowing of the skin tone and yellowing of the sclera in the eye.

Fasting

Starving

Fasting can lead to jaundice in patients with Gilbert's syndrome. This is because fasting may also increase the bilirubin load, and the resulting hyperbilirubinemia may be exaggerated because of the reduced expression of the UDP-glucuronosyltransferase enzyme.

Stress

Stressed-out

Stress, psychological or physiological (through illness), may unmask unconjugated hyperbilirubinemia in older persons, leading to jaundice. Gilbert syndrome is usually diagnosed around puberty, possibly because of the inhibition of bilirubin glucuronidation by endogenous steroid hormones, a period of hormonal stress.

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Alcohol Intake

Alcoholic-martini

Alcohol ingestion may lead to jaundice in patients as it may adversely affect UDP-glucuronosyltransferase activity, which is already impaired. It should be noted that patients with Gilbert's syndrome may report a lower-than-normal alcohol tolerance and can complain of hangover-like symptoms from very little drinking.

Labs

Increased Unconjugated Bilirubin

Up-arrow Un-conga Belly-ribbon-dancer

Due to defective UDP-glucuronosyltransferase activity, patients show increased unconjugated bilirubin levels upon blood testing. This is an important distinction that differentiates Gilbert's syndrome from Dubin-Johnson or Rotor syndrome, both of which are contrastingly associated with increased levels of conjugated bilirubin.

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