

Please read this bit first

This CPD/ CEU exercise is designed to take approximately two hours as a small group exercise within your laboratory. The Thistle QA CPD No is: **MT00025**.

Please keep a register of those taking part in the exercise. When the exercise is completed, please ask using the above email address, and we will send you a sheet showing the correct responses to each question.

Each attendee should claim two CPD points for completing the questions correctly, by retaining a copy of the relevant Thistle QA Participation Certificate as proof of registration on a Thistle QA EQA.

March 2007

Gilbert's syndrome: an overview

Taken from; G M Hirschfield and G J Alexander & Ann Clin Biochem 2006' 43: 340-343

Gilbert's syndrome (GS) is a benign and inherited state characterized by mild, lifelong, unconjugated hyperbilirubinaemia in the absence of haemolysis or evidence of liver disease. This synopsis outlines the pathophysiology and investigation appropriate for this innocent anomaly.

Introduction:

Of the many causes of jaundice, Gilbert's syndrome (GS) is probably the most common and most innocuous. It was first described at the turn of the twentieth century by Augustine Gilbert and Pierre Lereboullet (*La cholémie simple familiale*). GS (also known as Gilbert-Lereboullet Syndrome, Icterus Intermittens Juvenalis, Meulengracht's Disease and Unconjugated Benign Bilirubinaemia) occurs in approximately 2-7% of the population. The condition is defined and characterised by intermittent unconjugated hyperbilirubinaemia with accompanying jaundice in the absence of haemolysis or underlying liver disease (liver histology is normal but biopsy is normal but biopsy is not needed for diagnosis). In most patients, the hyperbilirubinaemia of GS manifests itself during adolescence or early adulthood. The total serum bilirubin concentration usually rises and fluctuates between 20 and 50 $\mu\text{mol/L}$. The reported incidence depends on the value selected as the upper limit of normal for bilirubin, the analytical method used, and the thoroughness of exclusion of other causes of serum hyperbilirubinaemia. Although the syndrome is genetic, many people do not have a clear family history and both autosomal dominant and recessive patterns of inheritance have been suggested.

The molecular basis of GS

The hereditary hyperbilirubinaemias include those resulting in predominantly unconjugated hyperbilirubinaemia (GS and Crigler-Najjar syndrome Types I and II), and those resulting in predominantly conjugated hyperbilirubinaemia (Dubin-Johnson syndrome, Rotor syndrome and several forms of intrahepatic cholestasis).

Clinical definition, consequences and laboratory investigation

The characteristics of GS are normal liver function tests, normal liver histology, delayed clearance of bilirubin from the blood and mild jaundice that tends fluctuate in severity. The hyperbilirubinaemia is often exacerbated by prolonged fasting, surgery, infection, physical exertion and alcohol ingestion, and may exceed the upper limit of normal, sometimes by as much as three to four times. Standard liver enzyme tests remain within the normal reference range (Figure 1), unless of course there is co-existing, unrelated liver disease. In addition, where tested, there is no bilirubin and subnormal amounts of urobilinogen in the urine. It is most important to consider GS as a condition with no clinical consequences for adults, other than the potential anxiety generated for the patient.

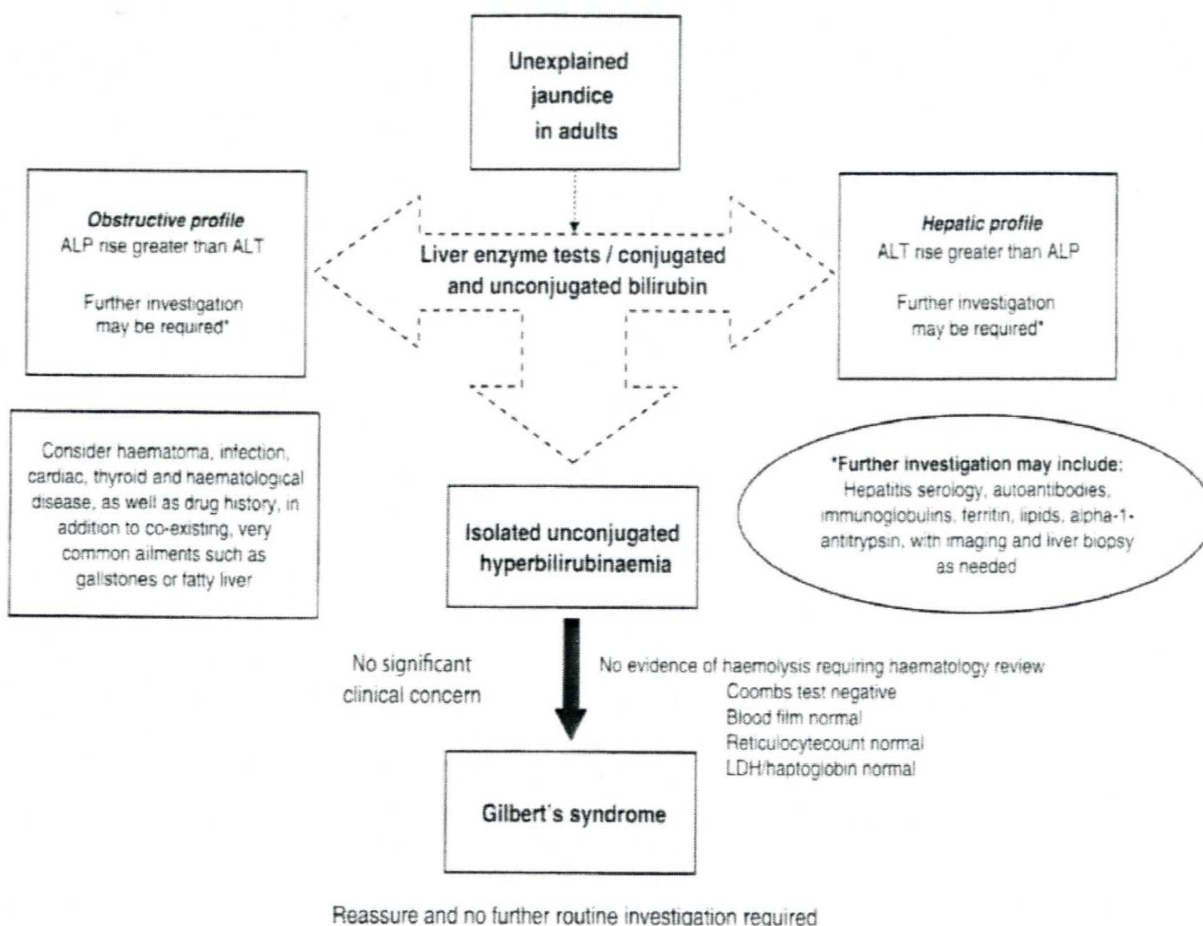


Figure 1. Outline pathway for investigating unexplained jaundice in adults

A diagnosis of GS is hence usually one of exclusion, when there is evidence of:

1. Unconjugated hyperbilirubinaemia, often noted on several occasions;
2. No evidence of haemolysis (normal full blood count, reticulocyte count, blood film, Combs' test, haptoglobin and lactate dehydrogenase levels);
3. Normal liver enzyme test results; and
4. An absence of other disease processes associated with unconjugated hyperbilirubinaemia.

Less frequent causes of unconjugated hyperbilirubinaemia, such as reabsorption of large haematomas, ineffective erythropoiesis, cardiac disease, rhabdomyolysis, drugs and thyrotoxicosis, do on occasion need to be considered.

Conclusion

GS is manifestly an extremely common cause of unconjugated hyperbilirubinaemia which is easily diagnosed, and for which no discernible morbidity or mortality exists in the overwhelming majority of individuals. Only very rarely is it clinically relevant (neonates and possibly those receiving irinotecan chemotherapy) and therefore for the majority reassurance is all that is needed with, in particular, avoidance of unnecessary investigations.

CPD Questions:

1. Review the mechanism For the breakdown of haemoglobin. Be sure you understand the mechanism for bilirubin protection.
2. Discuss the investigation of unexplained jaundice in adults?

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