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GILBERT SYNDROME INFORMATION SHEET

INTRODUCTION

Gilbert syndrome is usefully defined by its full name "familial benign unconjugated hyperbilirubinemia", as this covers the important aspects of the condition. Gilbert's syndrome is an inherited condition, with no significant clinical consequences, which is manifested by increased concentration of bilirubin in the blood, most of which is unconjugated.

PATHOGENESIS

Gilbert syndrome is caused by decreased hepatic levels of the enzyme glucuronosyltransferase. As this enzyme is responsible for the glucuronidation (conjugation) of bilirubin in the liver, reduced activity of this enzyme leads to an accumulation of unconjugated bilirubin in the circulation. The genetic defect has been identified as the presence of two additional nucleotides in the promoter region of the gene leading to reduced gene expression and therefore reduced enzyme activity. In affected individuals the enzyme is usually functioning at about 25% of normal levels. Of interest the syndrome may be passed to recipients of liver transplantation if the donor was affected.

In people with Gilbert syndrome the level of bilirubin is commonly slightly always elevated, but may be further increased by starvation, surgery, fever, infection, excessive exertion, or alcohol ingestion. The bilirubin concentration is reduced by barbiturates, and this has been proposed as a diagnostic test. Unfortunately, this test lacks specificity as barbiturates lowers serum bilirubin in most people, whatever the cause.
The syndrome is common in the Australian population with a frequency of between 2 and 5%.

PRESENTATION AND CLINICAL FINDINGS

Typically Gilbert syndrome presents by the finding of a mild elevation of bilirubin in a set of liver function tests ordered for another purpose. The bilirubin typically fluctuates in the range of 20 – 40 µmol/L although normal values may occur, and results as high as 80 µmol/L may be seen in patients who have not consumed food for several days. Occasionally individuals with this condition may be noticed to have a fluctuating pale jaundice although it remains unnoticed in most cases. The condition does not usually present until after the second decade of life.

Of note patients with Gilbert syndrome do not have pruritus and have no abnormalities in colouring of their stool or urine. Neonates with Gilbert syndrome may develop jaundice earlier and maintain jaundice longer than unaffected babies.

Recent evidence suggests that people with Gilbert syndrome may show increased toxicity compared to unaffected individuals following use of medications which are metabolised by

glucuronidation in the liver. This has been reported with some anti-cancer agents and with paracetamol, where they may be more prone to toxicity after paracetamol overdose. In persons with an increased bilirubin load, eg chronic haemolysis from hereditary spherocytosis, an increased tendency to form gallstones has been described in those who also have Gilbert syndrome. These patients may also have higher serum bilirubin concentrations than those without Gilbert, as has been described for G6PD deficiency crises and beta-thalassaemia.

DIAGNOSIS

The diagnosis of Gilbert Syndrome is generally made by the finding of an isolated elevation of bilirubin in an adult with no other liver function test abnormalities. In this setting no further testing is generally required. If there is any need for further confirmation a conjugated bilirubin should be measured, which in Gilbert syndrome will make up less than 20% of the total bilirubin. Gilbert syndrome does not lead to abnormalities in other liver function tests.

The main differential diagnosis for an elevated unconjugated bilirubin is haemolysis so it may be useful to exclude this with a full blood count and reticulocyte count. A liver biopsy is never indicated for the diagnosis of Gilbert in an uncomplicated setting, but if performed will show no abnormalities by light microscopy.

MANAGEMENT

As there is no increased morbidity or mortality associated with this condition, no treatment is required. The major effect of the condition may be over-investigation or interference with other diagnoses.