QUESTION 36

A 24-year-old man develops acute severe tonsillitis with high fever (39.8°C). He is treated with erythromycin. The next day he is noticed to be icteric. Abdominal examination is unremarkable.

Blood investigations show:

- white cell count 18.5 x 10^9/L [4.0-11.0]
- normal differential
  - haemoglobin 145 g/L [120-160]
  - platelet count 395 x 10^9/L [150-400]
- sodium 140 mmol/L [135-150]
- potassium 4.5 mmol/L [3.5-5.0]
- urea 8.5 mmol/L [3.6-9.3]
- creatinine 0.09 mmol/L [0.06-0.12]
- bilirubin 78 μmol/L [3-23]
- alkaline phosphatase (ALP) 46 U/L [30-115]
- gamma glutamyltranspeptidase (GGT) 55 U/L [<65]
- aspartate transaminase (AST) 35 U/L [5-40]
- alanine transaminase (ALT) 32 U/L [5-40]
- albumin 40 g/L [40-52]

The most likely explanation for his jaundice is:

A. haemolysis
B. Epstein-Barr virus.
C. Gilbert’s syndrome.
D. Wilson’s disease.
E. erythromycin.

This question is a combination of gastro and ID I guess

Most disorders associated with increased bilirubin production are due to **A. haemolysis**. In this scenario haemolysis could result from

- Mis- diagnosed Epstein barr virus
- Secondary to severe acute illness

Probably expect to see other blood changes ie anemia so his normal hb rules this out as a diagnosis

**B. Epstein-Barr virus.** Can result in Haematologic abnormalities including haemolytic anaemia and can also have a mild hepatitis – so jaundice only is not the most common presentation could have abnormal LFT’s also. The answer is therefore not B

**C. Gilbert’s syndrome.** Is the most common inherited disorder of bilirubin glucuronidation LFTs generally normal and can present following febrile illness / stressful situation

It is not **D. Wilson’s disease.** – would have other LFT changes

**E. erythromycin.** The most frequent side effects of oral erythromycin preparations are gastrointestinal and are dose related. They include nausea, vomiting, abdominal pain, diarrhoea and anorexia. There have been rare reports of pancreatitis. There have been reports of hepatic dysfunction, with or without jaundice, occurring in patients receiving erythromycin products. Hepatic dysfunction would suggest abnormal LFTs

Jaundice / hyperbilirubinemia

Two Major Categories of hyperbilirubinemia

1. plasma elevation of predominantly unconjugated bilirubin due to
   a. overproduction of bilirubin
   b. impaired bilirubin uptake by the liver
   c. abnormalities of bilirubin conjugation
2. plasma elevation of both unconjugated and conjugated bilirubin due to
   a. hepatocellular diseases
   b. impaired canalicular excretion
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iii. biliary obstruction

**plasma elevation of predominantly unconjugated bilirubin due to overproduction of bilirubin**
- Haemolysis – **Most disorders associated with increased bilirubin production are due to haemolysis**
- extravasation
- shunt hyperbilirubineamia

**impaired bilirubin uptake by the liver**
- heart failure, liver disease – portosystemic shunts
- gilbert’s syndrome – **The most common inherited disorder of bilirubin glucuronidation**
  - autosomal recessive inheritance 9% general population – UGT1A1*28 allele
  - usually diagnosed in young adults who present with mild, predominantly unconjugated hyperbilirubinemia. Rarely diagnosed prior to puberty when alterations in sex steroid concentrations affect bilirubin metabolism leading to increased plasma bilirubin concentrations. More commonly diagnosed in males
  - diagnosis usually in clinical setting associated stress: fasting, febrile illness, menses in women, otherwise normal LFTs apart from elevated predominantly unconjugated hyperbilirubinemia. Diagnosis definite in patients who continue to have normal lab studies (other than the elevation in plasma bilirubin) during the next 12 to 18 months
  - no specific therapy required – apart from recognition of disease and avoidance of some drugs

**drugs**
- rifamycin antibiotics
- probenecid
- flavaspadic acid
- bunamidyl (cholerectographic agent)

**abnormalities of bilirubin conjugation**

**Acquired**
- neonatal
- maternal milk
- lucy-Driscoll
- Wilson’s disease
  - Autosomal recessive defect in cellular copper transport, with a prevalence of approximately 1 case in 30,000 live births in most populations. An impairment in biliary excretion leads to the accumulation of copper in the liver. Over time the liver is progressively damaged and eventually becomes cirrhotic.
  - Multiple mutations in gene ATP7B
  - Clinical presentation
    - Rare before age 6 and almost always before age 30
    - Adolescents tend to present with liver disease while young adults are more likely to present with neuropsychiatric disease
    - Several different syndromes of hepatic disease
      - Chronic hepatitis – approx 40% wilson’s disease patients
      - Asymptomatic liver function abnormalities increases ALT, AST or bilirubin concentrations
      - Portal hypertension
      - Fulminant hepatic failure
    - Neuropsychiatric disease
      - Range of presentations, personality, deterioration in performance, depression paranoia and catatonia
      - 35% of patients with wilsons disease
      - CSF – raised copper concentrations

**Inherited**
- Hyperthyroidism
- Chronic persistent hepatitis

**Crigler-Najjar I**
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- Crigler-Najjar II
- Gilbert’s Syndrome