Bilirubinuria

Bile (mainly conjugated bilirubin) is converted to urobilinogen by intestinal bacteria. Most of the urobilinogen is excreted in faeces or reabsorbed and transported back to the liver to be reconverted into bile. The remaining urobilinogen (about 1% of total) is excreted in the urine.

- The amount of conjugated bilirubin present in serum in healthy subjects is small (less than 10% of total bilirubin). An elevated level of conjugated serum bilirubin implies liver disease. Therefore, because only conjugated bilirubin appears in urine, bilirubinuria also implies liver disease.
- Unconjugated bilirubin is tightly bound to albumin, not filtered by the glomerulus and absent from urine even with raised serum levels of unconjugated bilirubin. A positive test for urine bilirubin confirms that any raised plasma levels are from conjugated hyperbilirubinaemia.
- Bilirubinuria can be an early feature of hepatobiliary disease but may be absent despite increased serum bilirubin.
- In the assessment of a patient with raised total bilirubin, urinalysis for bilirubin and urobilinogen, together with LFTs, may be helpful in identifying the underlying pathology.

Bilirubin fractions present in blood and urine

- **Unconjugated:**
  - Albumin-bound in serum.
  - Measured as indirect-reacting bilirubin.
  - Never present in urine.
- **Conjugated:**
  - Unbound in serum.
  - Measured as direct-reacting bilirubin.
  - Present in urine.

Method of testing

The bilirubin pad on the multi-reagent dipstick detects bilirubin using a diazo reagent. This is a very nonspecific test and will produce many false positive results. Further testing will be required.

The colour change indicating a positive reaction may be a subtle transition among shades of beige and is sometimes obscured by the colour of the urine itself (eg, in marked haemoglobinuria).

Common causes of raised bilirubin and urobilinogen

**Raised conjugated bilirubin (bilirubinuria)**

- Hepatocellular disease and posthepatic or cholestatic disease (intrahepatic and extrahepatic), including drug toxicity as well as pancreatic causes of obstructive jaundice.
- Inherited defects in excretion - eg, Dubin-Johnson syndrome, Rotor’s syndrome.

**Raised unconjugated bilirubin (no bilirubinuria)**

- Gilbert's syndrome
- Haemolysis
- Post viral hepatitis
- Mild chronic hepatitis
- Crigler-Najjar syndrome

Urinary urobilinogen

- Normally excreted in small amounts into the urine.
- A very sensitive but nonspecific test to determine liver damage, haemolytic disease and severe infections.
- Increases in early hepatitis, mild liver cell damage and mild toxic injury, even without an increase in serum bilirubin.
- Decreased or absent in obstructive jaundice.

False negative and false positive reactions on dipstick testing
False negative:
- Aged urine samples: conjugated bilirubin hydrolyses to unconjugated bilirubin if left at room temperature.
- Exposure to UV light: UV light converts bilirubin to biliverdin, resulting in false negative reactions.
- Patient taking rifampicin.
- Ascorbic acid: high concentrations of vitamin C inhibit the reaction.

False positive:
- Patient taking phenothiazines.

Further reading & references
- Bilirubin; Lab Tests Online, 2016
- Provan D; Oxford Handbook of Clinical and Laboratory Investigation, 3rd Ed, 2010, Oxford University Press.
- Worrell D et al; Oxford Textbook of Medicine, 2003

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