

BILIRUBIN: TOTAL, INDIRECT, AND DIRECT

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Bilirubin is derived mainly from the heme moiety of hemoglobin molecules and is liberated when senescent red blood cells are removed from the circulation by the reticuloendothelial system. The bilirubin thus found in the plasma is bound to albumin and is known as unconjugated or indirect bilirubin. In this state the indirect bilirubin is not water soluble; and, in the newborn, potentially dangerous. In the liver, the bilirubin is taken up by hepatocytes and bound to specific carrier proteins. It is then transported to the smooth endoplasmic reticulum, where it undergoes conjugation, principally with glucuronic acid, to form a diglucuronide; this process is catalyzed by the enzyme bilirubin-uridyl diphosphate glucuronyl transferase. The newly formed conjugated (direct-bilirubin) is now water soluble.

The conjugated bilirubin can now be transported to the small and large intestine. In the large intestine the bilirubin is converted by bacterial action into urobilinogen, a colorless compound. Some urobilinogen is absorbed from the gut into the portal blood; but the hepatic uptake of this is incomplete. A very small quantity reaches the systemic circulation and is excreted in the urine. Most of the urobilinogen in the gut is oxidized in the colon to a brown pigment, stercobilin, which is excreted in the stool.

Indirect Bilirubin

Reference Values:

Adult: 0.1-1.0 mg/dl, 1.7-17.1 micromol/l (SI units)

Child: same as adult

Elevated indirect bilirubin can occur in autoimmune- or transfusion-induced hemolysis, in hemolytic processes caused by sickle cell anemia, in pernicious anemia, and with malaria and septicemia. Internal hemorrhage into soft tissues and the body cavity can cause the bilirubin to rise in five to six hours. In congestive heart failure and severe liver damage such as cirrhosis and hepatitis, both indirect and direct bilirubin levels will increase. Indirect bilirubin frequently increases because the damaged live cells cannot conjugate normal amounts, which leads to increased, unconjugated bilirubin.

Levels of indirect serum bilirubin may increase in hemolytic disease, such as erythroblastosis fetalis, in newborns. The newborn's liver is immature, and when extremely high levels of bilirubin occur, irreversible neurologic damage, referred to as kernicterus (destructive changes in gray matter in the brain), can result. There is no laboratory test for indirect bilirubin. Indirect bilirubin is calculated by subtracting direct bilirubin from the total bilirubin:

$$\text{Total bilirubin} - \text{Direct bilirubin} = \text{Indirect bilirubin}$$

In newborn infants, only the total is determined, and this represents the indirect bilirubin only.

Total and Direct Bilirubin

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Headaches and Sleep Disorders... Continued from page 61

Polysomnography can be instrumental in determining if a child's headaches are caused by a hidden sleep disorder. Physicians Ugur Isik and O'Neill F. d'Cruz² reported several cases of cluster headache manifesting as a parasomnia in toddlers. In one case, the subject, a 2 year old boy, would awaken about 2 – 3 hours after going to sleep, cry inconsolably, and would push his head against the corner or headbang or attempt to stand on his head; the episode could last up to 30 minutes. In the second case, a 2 1/2 year old girl, would awaken screaming inconsolably within 3 hours of going to sleep and would attempt to bury the left side of her face in her mother's shoulders; the episode would resolve in 5 – 15 minutes.



**"My phone plan lets me call five friends free.
Now I just gotta find five friends."**

Isik et al. were able to diagnose the children based on videography of nocturnal events and careful questioning of parents. (Both children were successfully treated with drug therapy.) Although they did not use polysomnography, Isik et al. advocate its use to help determine if a sleep disorder could be contributing to a headache disorder or vice versa. They point out that several polysomnographic studies by other researchers show that the majority of people with cluster headaches have undiagnosed OSA and that treating the OSA (e.g., positive airway pressure therapy) can resolve the headaches.

A headache disorder impacts many aspects of a child's life. A child may miss school causing poor school performance; or he may suffer the consequences of insufficient sleep (daytime sleepiness, falling asleep in class, etc.); or he may have impaired cognitive functioning; or he may suffer behavior problems such as hyperactivity. Effectively treating a headache disorder can prevent this. However, an untreated sleep disorder can negatively impact treatment a child may be undergoing for his headache disorder. With poor sleep quality contributing to symptoms of a headache disorder, controlling headache symptoms may be difficult (e.g., requiring higher and doses of medication, poor pain control, etc.). Therefore, sleep workers may need to question parents about symptoms of sleep disorders in a child who is diagnosed with headache disorder. This can lead improved treatment not only for the sleep disorder but also for the headache disorder.

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Reference Values:

Adult: Total: 0.1-1.2 mg/dl, 1.7-20.5 micromol/l (SI units).
Direct (conjugated): 0.1-0.3 mg/dl, 1.7-5.1 micromol/l (SI units).
Child: Newborn: Total: 1-12 mg/dl, panic level is > 15 mg/dl, 17.1-205 micro-moles/l (SI units). Child: 0.2-0.8 mg/dl.

Direct or conjugated bilirubin is frequently the result of obstructive jaundice, either extrahepatic (from stones or tumor) or intrahepatic in origin. Conjugated bilirubin cannot escape in the bile into the intestine and thus backs up and is absorbed into the blood stream. Damaged liver cells cause a blockage of the bile sinusoid, increasing the serum level of direct bilirubin. With hepatitis and decompensated cirrhosis, both direct and indirect bilirubin may be elevated.

How do you know if your patient may have a bilirubin problem? The most obvious is jaundice, which appears as yellowing of the skin and sclera (white part of the eye). Other conditions may cause yellowing or darkening of the skin (e.g., carotinemia, Addison's disease, quinacrine ingestion), but in these conditions scleral and mucosal discoloration are absent. The most important initial step is to define whether the jaundice is predominately due to an elevation of unconjugated or of conjugated bilirubin. If jaundice is primarily due to unconjugated bilirubin, evaluation for hemolysis is appropriate. In patients with elevated conjugated bilirubin, the clinical challenge lies in distinguishing whether biliary obstruction, impaired hepatic excretion, or hepatocellular injury is the cause. Many drugs, from antibiotics to vitamins, may also have an effect on bilirubin values.

Finally, some interesting factors that can affect laboratory results. A high-fat dinner prior to testing may affect bilirubin levels. Carrots and yams may increase the serum bilirubin level (with even a jaundice-type appearance in the patient)! Hemolysis of the blood sample can give inaccurate results. The tube should not be shaken! Most of all, if your patient is jaundiced-check the chart-again!

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Student Paper: Botulism... Continued from page 64

by physicians and respiratory therapists. When wound botulism the source of the infection, the site must be cleared to prevent continuing production of the toxin.

Discussion and conclusion

While researching this disease I have once again come to respect even more the physicians who have to diagnose patients with one or more of the thousands upon thousands of possible diseases. I understand how difficult it must be to get a definitive diagnosis for a disease when tests are deemed inconclusive, symptoms are very general or end up not being characteristic of the disease at all. That is why it is even more important for respiratory therapists to maintain communication with physicians and other medical staff so that we can share our knowledge of respiratory diseases, respiratory therapy and ventilator management.