

## HEADACHE AND SLEEP DISORDERS IN CHILDREN

by Regina Patrick RPSGT



Children who have headaches have a higher than normal prevalence of sleep disorders. This link may be more important than scientists have previously realized. Studies are beginning to show that headache disorder subtypes are associated with specific sleep disorders. For example, children who have migraines without aura are more likely to suffer from insomnia while children who have tension headaches are more likely to suffer from sleep-disordered breathing. Such findings are helping scientists to develop new ways to improve treatment in children who suffer from headache and sleep disorders.

The prevalence of headache disorders in children 7 years or older is estimated to be between 37 and 51 percent<sup>1</sup>. The prevalence of headache disorders increases by the teen years to about 57 to 82 percent in adolescents 15 years or older. Headache disorders that commonly occur in children are: migraines, tension headache, and cluster headache.

Migraine headache is the most common type of headache in children. It is experienced as a one-sided head pain and may be accompanied by irritability, nausea, vomiting, constipation or diarrhea, or light sensitivity. Visual symptoms (called an aura) may herald an attack. Examples of auras are seeing flashing lights or luminous zigzags around objects.

Tension headache is experienced in the occipital region as a dull, continuous, generalized pain. The pain can last for weeks or months at a time. Tension headaches are classed as episodic if the

pain ceases in six months or less and classified as chronic if the pain continues for more than six months. Tension headaches tend to occur after prolonged periods of overwork, emotional strain, or other stress.

Cluster headache usually manifests about 2 to 3 hours after sleep onset. It is experienced as a sudden, one-sided, excruciating pain felt over the eye or in the forehead. The attack may be associated with tearing, runny nose, or elevated body temperature. Attacks last from 15 minutes to an hour and occur in clusters. That is, attacks may occur a few times per day for several weeks then suddenly stop. Cluster headaches usually begin in adulthood. However, there are reports in the medical literature of cluster headache disorder appearing as early as toddler age.

One link between headache disorders and sleep may lie in the neurotransmitter serotonin. Serotonin plays a role in sleep. For example, serotonergic neurons in the brainstem rapidly fire during wake when serotonin levels are at their highest then increasingly slow their activity (as serotonin levels fall) as a person goes through each deepening stage of non-rapid eye movement (non-REM) sleep. The neurons nearly cease their activity during REM sleep when serotonin levels are at their lowest. Interestingly, studies show that serotonin levels suddenly decrease at the onset of migraine headaches, tension headaches, and cluster headaches. When these headaches occur during sleep, they tend to occur in association with rapid eye movement sleep or slow wave sleep – the sleep stages at which serotonin levels are low<sup>5</sup>. Scientists do not know why the sudden drop in serotonin occurs in these headache disorders. One possibility may be due to a faster breakdown of serotonin. During the onset of the headache, urinary levels of the serotonin metabolite, 5-hydroxyindoleacetic acid (5-HIAA) increase dramatically. The connection between low serotonin levels and headache has led to the development of triptan drugs. These drugs are serotonin agonists. They bind to serotonin receptors and mimic the actions of serotonin. With serotonin receptors stimulated, triptan drugs (e.g., sumatriptan) can quickly abolish a headache once it begins.


The histaminergic system and the beta-adrenergic system are two other neurological systems that may link sleep and headache disorders. Neurons of the histaminergic system are activated by histamine; neurons of the beta-adrenergic system are activated by epinephrine.

Histamine is a substance synthesized from the amino acid histidine. It acts as a neurotransmitter in the central nervous system. In the brain, histamine receptors are found primarily in the hypothalamus, a brain structure which plays a role in sleep as well as in the modulation of pain. Stimulation of one type of receptor – the histamine<sub>1</sub> (H<sub>1</sub>) receptor – can result in vasodilation and wakefulness. Antihistamine drugs block the vasodilation actions of histamine<sub>1</sub> receptors. This blocking action may be why antihistamines can thwart headache pain in some people.

Antihistamine drugs now undergoing development interact at the histamine<sub>3</sub> (H<sub>3</sub>) receptor. Drugs that selectively block the effects of the H<sub>3</sub> receptor (i.e., they block the actions of H<sub>3</sub> but not other histamine receptors) can promote wakefulness while drugs that selectively stimulate the H<sub>3</sub> receptors can result in sedation.


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## BILIRUBIN: TOTAL, INDIRECT, AND DIRECT

Don Steinert MA, RRT, MT



**B**ilirubin 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'Cruz<sup>2</sup> 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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