Physicians encourage pregnant women who smoke to stop the habit to reduce the harmful effects of nicotine on an unborn child (e.g., low birth weight; reduced uterine, umbilical, and cerebral blood flow). Because the amount of nicotine that an infant ingests through breastmilk is considered small and harmless, a physician may not think to caution a breastfeeding mother to continue refraining from smoking once a child is born. As a result, lactating mothers typically resume smoking soon after delivery. However, some studies indicate that small amounts of nicotine ingested through breastmilk can disrupt an infant’s sleep/wake cycles and increase the risk of sudden infant death syndrome (SIDS).

Nicotine & Sleep

Nicotine is a poisonous alkaloid with a bitter, burning taste that is found in tobacco leaves. The most common source of nicotine is cigarette smoke. Other sources of nicotine are snuff, chewing tobacco, and nicotine patches. At low doses nicotine gives one a sense of alertness and calmness and has a stimulatory effect on various organs (e.g., it increases heart rhythm, respiration rate, and gastrointestinal tract motility). At higher levels, it slows the heart rhythm, respiration rate, and decreases gastrointestinal tract motility. At toxic levels (60 milligrams or greater), nicotine can cause respiratory failure.

Nicotine interacts with adrenergic and cholinergic receptors in the central nervous system (CNS). Its interaction with adrenergic neurons alters the release of neurotransmitters that play a role in sleep/wake cycles. For example, nicotine stimulates the release of dopamine and serotonin in the brain. Increased levels of these neurotransmitters in brain regions that control sleep (e.g., reticular formation) may explain some of nicotine’s effect on sleep architecture. Adult smokers have a longer latency to sleep, more difficulty in initiating and maintaining sleep, longer latency to the first period of rapid eye movement sleep (REM sleep, now called “stage R sleep” in the AASM Manual for the Scoring of Sleep and Associated Events), less total sleep time, lower sleep efficiency, higher percentages of stages N1 sleep (formerly “stage 1 sleep”) and N2 sleep (formerly “stage 2 sleep”), and a lower percentage of slow-wave sleep.

Nicotine has a comparable effect on the sleep architecture of infants.

Infant Sleep

An infant’s sleep architecture consists of “quiet” sleep and “active” sleep. Active sleep corresponds to adult stage R sleep and quiet sleep is the infant’s “stage N sleep” (formerly “non-REM” or “NREM” sleep). At times, features of both stages can be present making it difficult to determine an infant’s sleep stage. This is called indeterminant sleep. Indeterminant sleep typically occurs during the transition from active stage R sleep to quiet stage N sleep.

Active sleep is characterized by conjunctive rapid eye movements, low muscle tone, low amplitude theta waves, and an irregular breathing pattern consisting of short central apneas intermixed with periods of rapid breathing. Unlike stage R sleep in adults, body movements may occur during active sleep in infants. Quiet sleep is characterized by lack of rapid eye movements, increased muscle tone, a regular breathing pattern, and no body movements - except for phasic movements associated with sucking or startles.

Newborn infants first enter active sleep, which is then followed by quiet sleep. Total sleep time in a newborn consists of 50 percent active sleep and 50 percent quiet sleep. At approximately 4 to 6 weeks of age, sleep spindles (a feature of stage N2 sleep) begin to appear. By approximately 8 to 12 weeks of age, the low-frequency, high-amplitude waves of slow wave sleep develop. After about three months, an infant - like an adult - first enters stage N sleep (which now consists of stages N1 to N3) followed by stage R sleep.

Nicotine & Breastfeeding Infants

A recent study at the Monell Chemical Senses Center in Philadelphia demonstrated the short-term effect of nicotine on sleep in breastfed infants. The study was headed by Julie Mennella and used 15 mother-infant pairs as subjects. All of the infants’ mothers smoked.

Each mother-infant pair was tested on two days. On the first test day, the mothers smoked 1 to 3 cigarettes, but not in the presence of their child. They then breastfed their infants ad lib during a 3.5-hour period. At the end of this period, the infants took a nap. For the second test day (one week later), the mothers refrained from smoking for 12 hours before breastfeeding their infant ad lib for the 3.5-hour period, after which the infants took a nap. On both test days, Mennella and coworkers measured the amount of nicotine in each of the mother’s milk before breastfeeding. They also monitored the infants during their nap for sleep latency, time spent in active and quiet sleep, number of sleep periods during the nap, longest sleep period, and total sleep time.

The researchers found that on the day the mothers smoked, their breastmilk contained about 12.4 nanograms of nicotine per milliliter of breastmilk and the researchers estimated that the infants were ingesting 548.9 nanograms of nicotine per kilogram of the infant’s body weight. On the day that the mothers did not smoke, their breastmilk contained about 10.2 nanograms of nicotine per milliliter of breastmilk; the researchers
estimated that the infants ingested 127.1 nanograms of nicotine per kilogram of the infant’s body weight. They noted that infants had a 37-percent reduction in total sleep time when their mothers smoked soon before breastfeeding. Total sleep time reduction resulted from two factors: the first being decreased amounts of both active and quiet sleep and the second, a shortening of the longest sleep period during the nap. Since refraining from smoking allowed the infants to have a more normal sleep architecture, Monnella and coworkers concluded that nicotine ingested through breastfeeding can have a short-term, disruptive effect on an infant’s sleep.

**Nicotine, CNS & SIDS**

Scientists have long noted a higher incidence of SIDS in infants of mothers who smoke.7 SIDS is the inexplicable, unexpected death of an apparently healthy infant aged one year or younger. Some scientists believe SIDS occurs when hypoxia resulting from apneic episodes during sleep does not trigger an infant to arouse and start breathing. This impaired arousability may be the result of the action of nicotine on CNS structures involved in respiration, on peripheral chemoreceptors involved in respiration, or both.

Some studies point to nicotinic receptors in the pre-Botzinger complex as one CNS site where nicotine may impact respiration. The pre-Botzinger complex is a small group of neurons located in the respiratory center in the lower medulla. The pre-Botzinger complex contains neurons that are activated only during inspirations (i.e., inspiratory neurons) and neurons that set one’s respiratory rhythm (i.e., pacemaker neurons). University of California, Los Angeles (UCLA) researchers Xuesi Shao and Jack Feldman found that perfusing nicotine onto the pre-Botzinger complex can increase the respiration rate.2 From this they concluded that nicotine may modulate the function of other neurotransmitters (e.g., glutamate) that activate the pre-Botzinger complex neurons. Other researchers have found that prolonged overstimulation of nicotinic receptors in brainstem structures controlling respiration may in turn enhance the inhibitory actions of peripheral dopaminergic neurons (e.g., carotid bodies) that modulate the inspiratory drive.3 The reduction in inspiratory drive slows the respiration rate and decreases the normal response (rapid, deep breathing) to hypoxia.

Life-threatening central apneas can occur when the pre-Botzinger complex is damaged. For example, Feldman in a 2005 study was surprised to find that animals in which half the neurons in the pre-Botzinger complex had been destroyed initially had central apneas but only during stage R sleep.4 As time progressed over a 4 to 5 day period, the central apneas began to occur in stage N sleep and then ultimately when the animals were awake. He hypothesized that neuronal loss in the pre-Botzinger complex may play a role in the sudden death of adults during sleep. Supporting Feldman’s conclusion, Italian researchers Anna Lavezzi and Luigi Matturri – the first scientists to identify the pre-Botzinger complex in humans – noted structural alterations such as decreased neuronal number and underdevelopment of the pre-Botzinger complex’s connections to the reticular formation in infants that have died of SIDS and in fetuses that die late in gestation.9

**Nicotine, Dopamine & SIDS**

Nicotine may modulate the actions of dopamine in the carotid bodies and thereby contribute to SIDS.10 A carotid body is a small neurovascular structure located on the left and right carotid arteries that trigger increased respiration rate when stimulated by hypercapnia (i.e., high blood carbon dioxide level), hypoxia (i.e., low blood oxygen level), or increased blood acidity. A carotid body contains type I cells which are surrounded by type II cells. Swedish researcher Hans Holgert and coworkers propose that nicotine may impact dopamine activity in the following way.10 First, nicotine induces type I cells to release dopamine. The dopamine may either bind to dopaminergic receptors on type I cells or bind to dopaminergic receptors on afferent neurons (i.e., neurons that relay signals to the brain) that synapse with type I cells. Once bound, dopaminergic transmission of signals from the carotid body to the brain is inhibited. This in turn decreases the respiratory response to hypoxia, which may lead to apnea and to SIDS.

**Conclusions**

Nicotine withdrawal can impair an infant’s sleep. If a mother has smoked throughout her pregnancy, her infant

*Continued on page 24...*
Continued from page 23...

may be born addicted to nicotine and begin to suffer withdrawal symptoms as soon as 12 hours after birth.11 Nicotine withdrawal symptoms in infants can manifest as crying, irritability, intestinal distress, tremors, muscular rigidity, and insomnia.6,11,12

Sleep-medicine professionals often fail to ask parents about an infant’s exposure to nicotine. Staff members at sleep centers that do infant studies may need to consider asking parents questions about their infant’s exposure to nicotine. These questions include:

Does the mother smoke soon before breastfeeding?
Does the mother use nicotine patches or other forms of nicotine products?

Is the mother a mild, moderate or heavy smoker?
Note that the greater the degree of maternal addiction, the more disrupted is the infant’s sleep.6 Eliminating passive nicotine exposure can improve an infant’s sleep, thwart the miseries of nicotine withdrawal, and reduce the risk of SIDS.

References


