Sleep and Respiratory Physiology in Children

Kristie R. Ross, MD, MS*, Carol L. Rosen, MD

KEYWORDS

• Respiration • Reference values • Oxygen saturation • Carbon dioxide • Sleep/physiology • Child • Infant • Adolescent

KEY POINTS

- The maturation of respiratory physiology during sleep contributes to the unique features of childhood sleep disorders.
- Ventilation decreases during sleep in children as it does in adults, with variability related to sleep state.
- Knowledge of the range of normal values of respiratory parameters during sleep, including respiratory rates, oxygen saturation, measures of carbon dioxide, and number and patterns of apneas, is crucial for the physician to evaluate common sleep disorders in children.

INTRODUCTION

Sleep is a critical determinant of health. As a child develops from infancy through adolescence, important changes in respiratory physiology occur. Maturational changes of breathing during sleep contribute to the unique features of childhood sleep disorders. The clinician's ability to evaluate common disorders related to sleep in children, including apnea of prematurity, sudden infant death syndrome (SIDS), apparent life threatening events (ALTE), obstructive sleep apnea syndrome, and other forms of sleep-disordered breathing relies on an understanding of normal patterns of breathing during sleep across the ages. The purpose of this article is to review respiratory physiology during sleep throughout childhood.

OVERVIEW OF NORMAL RESPIRATION DURING SLEEP

Breathing during sleep is controlled by voluntary and behavioral factors in addition to metabolic and mechanical factors.[1] Chemical information is relayed through peripheral chemoreceptors in the carotid and aortic bodies. The carotid chemoreceptors, although small, have a uniquely high blood supply, and sense the arterial concentration of O_2 and relay the information to the medulla. The carotid body chemoreceptors are responsible for about 90% of the ventilatory response to hypoxemia. Chemosensory function in the carotid bodies is immature at birth and increases with age. Carbon dioxide (CO_2) is also sensed in the carotid body, accounting for 20% to 50% of the response to arterial hypercapnia. The remaining response to hypercapnia comes from central brainstem receptors in the medulla. The central chemoreceptors respond primarily to changes in pH, mediated by CO_2 tension, in the cerebrospinal fluid. Laryngeal chemoreflexes (LCR) located in the epithelium that surrounds the airway respond to acidic solutions with reflexes that include startle, swallowing, laryngeal constriction, apnea, and bradycardia. Mechanical information sensed through receptors in the lung and chest wall are also relayed to the

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Division of Pediatric Pulmonology and Sleep Medicine, Department of Pediatrics, Rainbow Babies and Children's Hospital, Case Western Reserve University School of Medicine, 11100 Euclid Avenue, RBC 3001, Cleveland, OH 44106, USA
* Corresponding author.
E-mail address: Kristie.ross@uhhospitals.org

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medulla via the vagal nerve. Higher central nervous system centers can override the respiratory centers to control nonbreathing functions such as speaking and laughing. These voluntary and behavioral controls are affected by sleep state. Clinical problems associated with disorders of respiratory control are listed in **Box 1**.

In general, ventilation decreases during sleep compared with wakefulness, but varies with sleep state. During non–rapid eye movement (NREM) sleep, breathing is regulated primarily by carbon dioxide and is characterized by the absence of behavioral controls. Breathing is regular with reduced tidal volume and respiratory rate compared with wakefulness, resulting in decreased minute ventilation. This decline, in combination with the supine position and decrease in intercostal muscle tone, results in a decrease in functional residual capacity. Upper airway tone and lung volume also decrease during sleep, resulting in increased upper airway resistance. Compared with the regular breathing seen during NREM sleep, breathing during rapid eye movement (REM) sleep is irregular in terms of both respiratory rate and tidal volume. Short central respiratory pauses are common during REM sleep in children. Inhibition of tonic activity of the intercostal muscles during REM results in a further decline in functional residual capacity. At the same time, activity of the diaphragm remains stable, and this incoordination between the intercostal muscles and diaphragm results in paradoxic chest and abdominal movement during REM sleep that usually resolves by the age of 3 years. A relative decrease in upper airway muscle tone when diaphragmatic contractions remain unchanged can predispose to obstructive apnea, especially when the airway is already small or narrow. Finally, hypoxic and hypercapnic ventilatory drives decrease during sleep. Therefore, normal children experience a small increase in the partial pressure of CO_2 and a small decrease in arterial oxyhemoglobin saturation (Spo_2) during sleep. The magnitude of these changes has not been systematically studied in large pediatric samples of healthy children, but is believed to average 2% for Spo_2 and 4 to 6 mm Hg for CO_2.[2] These sleep-related changes in ventilation, upper airway stability, and gas exchange can be exaggerated in children with underlying pulmonary, upper airway, and neuromuscular problems, resulting in increased vulnerability to sleep-disordered breathing. Differences between newborn and adult respiratory systems that make the infant more vulnerable to ventilatory failure are summarized in **Box 2**.

DEVELOPMENTAL CHANGES IN RESPIRATORY CONTROLLERS

Postnatally there is an increase in the hypoxic sensitivity (resetting) of both carotid and aortic chemoreceptors, and a diminishing influence of descending inhibitory effects on breathing in hypoxia.[3] Compared with the adult, peripheral chemoreceptors assume a greater role in the newborn. Although not essential for initiation of fetal respiratory movements, animal studies show that peripheral chemoreceptor denervation in the newborn period results in severe respiratory impairment and a high probability of sudden death. In the newborn, steady-state hypoxia produces a transient increase in ventilation followed by a decrease back to or below baseline level. With maturation, this biphasic response to hypoxia changes to a sustained ventilatory response. By contrast, a steady-state response to CO_2 is present at all ages from birth and increases with advancing postnatal age. There are only limited data on ventilatory responses in different sleep states in infants, but the directionality is similar to the findings in adults, with responses to hypoxia and hypercapnia that are reduced in REM compared with NREM sleep. In the newborn, hypercapnia and hypoxic ventilatory responses interact to augment respiratory responses. With increasing age, peripheral chemoreceptors undergo progressive decrement in their relative sensitivity.[4] LCR responses are significantly more active in the immediate postnatal period compared with later in life, and the pattern of the response also changes with maturation. The predominant LCR response in the newborn includes swallowing and apnea, and differs from the LCR responses seen in the older infant or adult (cough and the expiration reflex).[5,6]

VENTILATION, RESPIRATORY PATTERNS, AND APNEAS

Normative data on tidal volume and minute ventilation in children are not readily available, as most studies have focused on describing respiratory rates and patterns, gas exchange, and the frequency and type of apneas seen in healthy children of various ages. More data are available for preterm and full-term infants in the first months of life than for children and adolescents, but several new reports of normative sleep and breathing data in these age groups have been published.[7–9]

Respiratory Frequency

As would be predicted from knowledge about the inverse relationship between respiratory rate and body size in other mammals,[10] respiratory rates