REVIEW ARTICLE

Pediatric Obstructive Sleep Apnea Syndrome

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Objective: To review evidence-based knowledge of pediatric obstructive sleep apnea syndrome (OSAS).

Data Sources and Extraction: We reviewed published articles regarding pediatric OSAS; extracted the clinical symptoms, syndromes, polysomnographic findings and variables, and treatment options, and reviewed the authors' recommendations.

Data Synthesis: Orthodontic and craniofacial abnormalities related to pediatric OSAS are commonly ignored, despite their impact on public health. One area of controversy involves the use of a respiratory disturbance index to define various abnormalities, but apneas and hypopneas are not the only abnormalities obtained on polysomnograms, which can be diagnostic for sleep-disordered breathing. Adenotonsillectomy is often considered the treatment of choice for pediatric OSAS. However, many clinicians may not discern which patient population is most appropriate for this type of intervention; the isolated finding of small tonsils is not sufficient to rule out the need for surgery. Nasal continuous positive airway pressure can be an effective treatment option, but it entails cooperation and training of the child and the family. A valid but often overlooked alternative, orthodontic treatment, may complement adenotonsillectomy.

Conclusions: Many complaints and syndromes are associated with pediatric OSAS. This diagnosis should be considered in patients who report the presence of such symptoms and syndromes.

Arch Pediatr Adolesc Med. 2005;159:775-785

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Understanding obstructive sleep apnea syndrome (OSAS) in children requires knowledge of the physiology of sleep and breathing. There is an immediate increase in upper airway resistance with sleep onset, with an initial "overshoot" in this resistance that decreases very quickly. Still, this resistance during established sleep is mildly higher than during wakefulness.[1] There is also a slight decrease in tidal volume with sleep. This decrease will be more pronounced with the occurrence of rapid eye movement (REM) sleep. These mild decreases will be compensated by a slight increase in breathing frequency to keep minute ventilation normal. Breathing frequency decreases during the first 2 years of life but stays the same thereafter; it has been calculated to range from a maximum of 16 to 18 breaths/min in non-REM sleep and 17 to 19 breaths/min during REM sleep.[2,3]

The obesity epidemic, evident in the United States and industrialized countries, has complicated the investigation of obstructive sleep apnea (OSA) and related syndromes. Fat distribution varies according to genetic, sex, and hormonal patterns and the inherent relationship among these 3 factors. It is common for fat to deposit in the abdominal region. Such abdominal obesity will lead to chest-bellows impairment, as seen in restrictive thoracic disorders. Although it may not lead to upper airway obstruction, abdominal obesity may worsen the poor gas exchange that may already exist because of OSAS. Sleep will always worsen the gas exchange in these subjects when they are in the supine position and when they achieve REM sleep. During REM sleep, the associated atonia eliminates contractions of the accessory respiratory muscles and the abdominal muscles, which engage in active expiration.[2,3] Also, REM sleep is associated with further flattening of the diaphragm's position.[2] These physiological changes worsen gas exchange in subjects with abdominal obesity and may even lead to REM sleep–related hypoventilation with some degree of carbon dioxide (CO_2) retention. Upper airway impairment, per se, is not directly related to this CO_2 retention. It has, however, been hypothesized that abnormal gas exchange during sleep may impair the coordination of time-related contractions of both upper airway dilator muscles and inspiratory muscles.

Table 1. Complaints Reported by Parents Regarding Their Children

Age Group and Age			
Infants, 3-12 mo	**Toddlers, 1-3 y**	**Preschool-aged Children**	**School-aged Children**
Disturbed nocturnal sleep with repetitive crying	Noisy breathing or snoring	Regular, heavy snoring	Regular, heavy snoring
Poorly established day/night cycle	Agitated sleep or disrupted nocturnal sleep	Mouth breathing	Agitated sleep
Noisy breathing or snoring	Crying spells or sleep terrors	Drooling during sleep	Abnormal sleeping positions
Nocturnal sweating	Grouchy and/or aggressive daytime behavior	Agitated sleep	Insomnia
Poor suck	Daytime fatigue	Nocturnal awakenings	Delayed sleep phase syndrome
Absence of normal growth pattern or failure to thrive	Nocturnal sweating	Confusional arousals	Confusional arousal
Observation of apneic events	Mouth breathing	Sleepwalking	Sleepwalking
Report of apparent life-threatening event	Poor eating or failure to thrive	Sleep terrors	Sleep talking
Presence of repetitrive earaches or URI	Repetitive URI	Nocturnal sweating	Persistence of bed-wetting
	Witnessed apneic episodes	Abnormal sleeping positions	Nocturnal sweating
		Persistence of bed-wetting	Hard to wake up in the morning
		Abnormal daytime behavior	Mouth breathing
		Aggressiveness	Drooling
		Hyperactivity	Morning headache
		Inattention	Daytime fatigue
		Daytime fatigue	Daytime sleepiness with regular napping
		Hard to wake up in the morning	Abnormal daytime behaviors
		Morning headache	Pattern of attention-deficit/hyperactivity disorder
		Increased need for napping compared with peers	Aggressiveness
		Poor eating	Abnormal shyness, withdrawn and depressive presentation
		Growth problems	Learning difficulties
		Frequent URI	Abnormal growth patterns
			Delayed puberty
			Repetitive URI
			Dental problems appreciated by dentist
			Crossbite
			Malocclusion (class II or III)
			Small jaw with overcrowding of teeth

Abbreviations: OSAS, obstructive sleep apnea syndrome; URI, upper respiratory tract infection.

Obstructive sleep apnea syndrome was described in children in 1976.[4] Although children may present with OSAS, the literature had established by 1982 that children had other abnormal respiratory effort patterns during sleep that were frequently associated with snoring and clinical symptoms.[5]

EPIDEMIOLOGY

No definitive population-based study has evaluated the presence of OSAS in children. Previous studies were performed in different settings and implemented a variety of tools. Some considered regular nocturnal snoring a marker of chronic obstructive breathing during sleep. The percentage of individuals younger than 18 years who have been reported with regular heavy snoring oscillated between 8% and 12%. Subjects in other studies underwent polygraphic monitoring, but these studies were limited in terms of sample size and testing difficulties; initial studies estimated OSAS prevalence to be between 1% and 3%.[6-15] More recently, many specialists have estimated OSAS prevalence to be between 5% and 6%. Although better monitoring techniques during polysomnography (PSG) have shown that more abnormal breathing events are present,[16] the definitive data are still lacking.

CLINICAL SYMPTOMS

Abnormal narrowing in the nose, nasopharynx, oropharynx, or hypopharynx causes abnormal air exchange during sleep, which in turn leads to clinical symptoms. These symptoms will vary with age. Recognition of the problem is often only noted in older children, who are able to articulate complaints. **Table 1** indicates the parental complaints of children seen at sleep clinics over time.[17-25]

Abnormal breathing during sleep has been associated with specific clinical problems and findings. The clinical interview of a child suspected of having sleep-disordered breathing (SDB) must lead to systematic questioning of the parents regarding their child's symptoms; the parents may not associate the occurrence of these symptoms with abnormal breathing during sleep. **Table 2** outlines syndromes that have been shown to be related to SDB and are subsequently controlled after the appropriate treatment of the breathing disorder has been initiated.[20,24,26-51] Some of the syndromes are related to maxillomandibular development[26] and are more connected to orthodontic practice. Pediatricians do not traditionally consider orthodontic problems to be part of a child's health issues, but in light of the

Table 2. Syndromes Related to Abnormal Breathing During Sleep

Chronic snoring
Daytime fatigue
Daytime sleepiness
Sleep maintenance insomnia
Sleep-phase delay
Confusional arousal
Sleep talking
Sleep terror
Sleepwalking
Enuresis (primary or secondary)
Morning headache
Nocturnal migraine
Periodic limb movement
Learning or memory problem
Attention-deficit/hyperactivity disorder
Abnormal social contact (psychologically withdrawn)
Depressive affect
Hypotension with orthostasis
Fainting (rare)
Hypertension (rare)
Cor pulmonale (rare)
Nocturnal asthma or nocturnal wheezing
Crossbite
Pathologic overjet
Overcrowding of teeth
Impacted wisdom teeth

related health care cost and syndromic association, they should.

CLINICAL EVALUATION AND DIAGNOSIS OF SDB

Sleep-disordered breathing in a child will be suspected on the basis of parental complaints. The presence of 1 of the syndromes listed in Table 2 should lead to a thorough interview of the behavior during sleep as well as sleep-related factors associated with SDB.[17-50]

The suspicion of SDB indicates the need not only for a general pediatric evaluation but also for a thorough evaluation of the upper airway anatomy. Clinically, it involves a comprehensive examination of its successive segments. Starting with the nose, one should look for asymmetry of the nares, a large septal base, collapse of the nasal valves during inspiration, a deviated septum, or enlargement of the inferior nasal turbinates (**Figure 1**). Next, the oropharynx should be examined for the position of the uvula in relation to the tongue. The scale developed by Mallampati et al[52] scale may help to evaluate this position. The size of the tonsils should be compared with the size of the airway; application of a standardized scale is useful.[53] The presence of a high and narrow hard palate, overlapping incisors, a crossbite, and an important (>2 mm) overjet (the horizontal distance between the upper and lower teeth) are indicative of a small jaw and/or abnormal maxillomandibular development. This clinical evaluation provides important details of the upper airway anatomy and identifies anatomical risk factors that can predispose one to development of abnormal breathing during sleep.

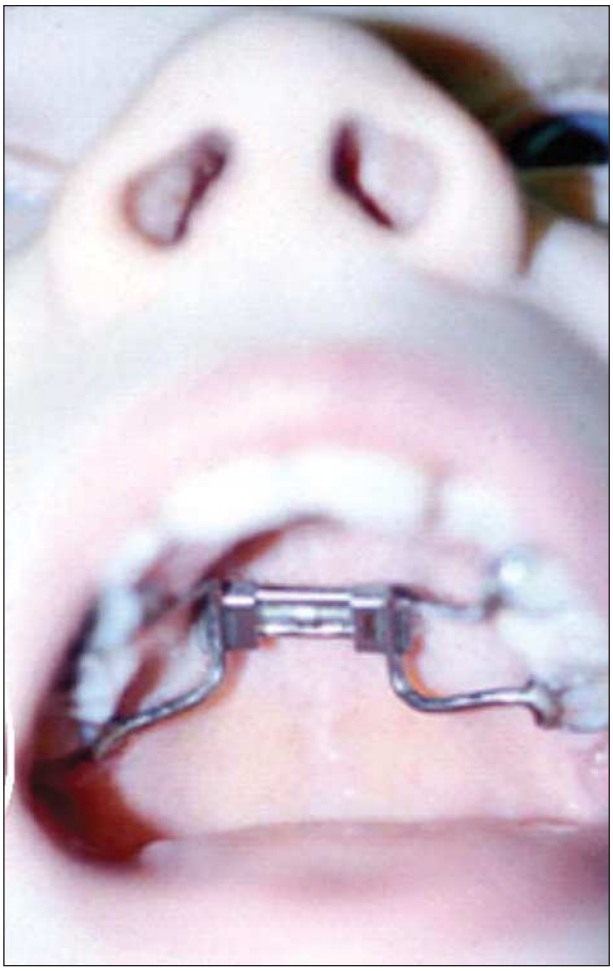


Figure 1. Illustration of many anatomical abnormalities in a 7-year-old child, including asymmetry of the nares, an enlarged septal base, large medial crus, deviation of the septum to the right, and a narrow and high-arched palate. A rapid maxillary distractor has been placed to widen the maxillary cavity, decrease the height of the soft palate, and enlarge the bony aspects of the nose.

The results of this examination must be summarized because the different anatomical narrowings have additive effects. The apparent sizes of tonsils and adenoids are not the only anatomical findings that determine whether or not SDB is present. A change in flow due to an abnormal nose, secondary development of turbulence, and the increased collapsibility at specific vulnerable points in the upper airway are elements to consider.

A complex interaction occurs between nasal breathing and maxillomandibular growth. Abnormal nose breathing in very young individuals leads to an increase in nasal resistance and mouth breathing with secondary impairment of maxillomandibular growth,[54-62] as shown experimentally in young rhesus monkeys.[63] The first 4 years of age are of particular importance because 60% of the adult face is built during that period.[64] Otolaryngological and orthodontic data have clearly demonstrated the impact of enlarged tonsils, adenoids, and nasal turbinates and upper airway allergies on orofacial growth in children.[21,55-70]

Other factors may be considered. Neck circumference and the presence of fatty infiltration should be noted,

but no scale correlates neck circumference with age or pathologic findings. The overall aspect of the face can be appreciated. The frontal aspect of the face can be subdivided into superior, middle, and inferior portions. These portions are approximately the same length in a normal child. The upper part of the bridge of the nose and the part just below the nares represent the middle third of the face. In individuals with a maxillomandibular risk factor for OSA, the lower third of the face may be longer than expected. The terms *long face* and *long-face syndrome* have been used.[21,26]

OBJECTIVE CONFIRMATION OF SDB

Testing during sleep is the only way to confirm the presence of SDB. Controversy exists concerning the need for and type of test to be performed. Some of the measures used for this testing include questionnaires and scales, home monitoring, and PSG.[71-74]

Questionnaires with specific emphasis on the common symptoms associated with SDB have been implemented. Although questionnaires may be helpful in directing the attention of parents to the diurnal and nocturnal symptoms of SDB, the sensitivity and specificity of the questionnaires are not sufficient for affirming the presence of SDB.[23,75-77]

Home monitoring with or without videotaping has also been used. Ambulatory monitoring with recording of cardiac and respiratory variables has been suggested as the first diagnostic step in testing for SDB. These devices can detect the presence of drops in oxygen saturation (Sa_{O_2}), apneas, and hypopneas; affirm the diagnosis of SDB; and lead to treatment. Associated videotaping may confirm abnormal breathing behavior. This approach may recognize severe SDB but fails to identify the presence of associated sleep disorders and partially obstructed breaths. A negative test result does not rule out the diagnosis of SDB and must be followed by PSG; however, a positive finding may lead to faster treatment.[78-80]

Polysomnography is the only test that may exclude the diagnosis of SDB. It must always include monitoring of sleep/wake states through electroencephalography (EEG), electro-oculography, chin and leg electromyography, electrocardiography, body position, and appropriate monitoring of breathing. A nasal cannula–pressure transducer, oral thermistor, chest and abdominal belts, a neck microphone, and pulse oximetry are recommended, but variable montages are used.

Respiratory efforts can be investigated by a variety of means during PSG. Although infrequently used, the best approach involves measuring esophageal pressure (Pes) movements. A less reliable approach is to monitor intercostal/diaphragmatic electromyography. A recently developed analysis of this signal appears promising but needs further testing in children.[81] Levels of CO_2 may be monitored using a nasal cannula with measurement of end-tidal CO_2 levels. However, the combination of 2 cannulas in the nose of a child may disturb sleep and have a negative impact on nasal breathing; thus, a transcutaneous CO_2 electrode will often be needed for this measurement.[16,82,83]

Sleep-disordered breathing has consequences related to the repetitive changes induced by a decrease in the size of the upper airway during sleep. As a compensatory first step, there will be an increase in breathing frequency (tachypnea) and in respiratory efforts.[5,84,85] The selected response is related to the decrease in size of the upper airway and the age of the subject. Following the classic equation of breathing frequency × tidal volume = minute ventilation, tachypnea is a more common finding in young children with small and relatively unstable chests, a population with mild to moderate breathing impairment during sleep.[5,84,85] Despite better chest stability, this response will also be seen in older children. Tachypnea and an increase in inspiratory efforts have been seen in the same children in association with airflow limitation. The mechanisms behind a specific response and the relationship with sleep state are unknown.

The repetitive challenges resulting from a reduction of upper airway size have negative consequences on a child's well-being. However, the normative data for many of the studied variables are still unclear. The polygraphic normative data on sleep duration and sleep stages are available in children 7 years and older.[86] The frequency of short arousals during sleep (ie, EEG arousals lasting ≥3 seconds that can be reliably scored by 3 years of age[87]) is unknown for different age groups, but abnormal breathing patterns during sleep have been identified (**Table 3**).[85]

INTERPRETATION OF THE PSG

There are controversies concerning PSG[71,84] because many existing criteria are based on information obtained from small studies. Other recommendations were taken by consensus, which means they were not necessarily based on data; still others were based on information collected with outdated technology. The specificity and sensitivity of many of the indices used have never been calculated. Only 1 study has looked at polygraphic respiratory patterns, their frequency of occurrence, their change in frequency with treatments, and their impact on the clinical outcome associated with polygraphic changes in prepubertal children.[84]

One of today's most debated issues is what type of respiratory event should be scored and tabulated. Another issue is determining when "pathology" is present.[23,76,84] Historically, the presence of OSA was easy to recognize with simple albeit relatively insensitive equipment (thermistors). Based on the variability of breathing frequency from birth to 2 years of age, an apnea was defined as "longer than 2 breaths." For many years, there was a consensus that OSA, a complete cessation of air exchange at the nose and mouth, was associated with clinical symptoms. It was shown that removal of the obstructive apnea led to improvement of the symptoms. The initial criterion for an abnormal PSG finding was at least 1 obstructive apnea per hour of sleep.[89]

However, pathologic findings also occurred without complete absence of air exchange. To improve the scoring system, clinicians used the term *hypopnea*, but there is no consensus as to what a hypopnea is. Following adult criteria and using thermistors with limited sensitivity, clinicians suggested that a hypopnea should last "longer than 2 breaths."[4] Also, the airflow signal from the combined

Table 3. Abnormal Breathing Patterns

Term	Definition
Apnea	Absence of airflow at nose and mouth for >2 breaths, independent of desaturation or change in EEG; subdivided into central, mixed, or obstructive apnea based on airflow and Pes recording
Hypopnea	Reduction by ≥50% in nasal flow signal amplitude for ≥2 breaths; scored independently from Sa_{O_2} drop or EEG arousal; often but not always associated with snoring.
Abnormal respiratory effort	Reduction in nasal flow of <50% with flattening of nasal cannula signal (flow limitation)[7] and decrease in the mouth signal (thermistor); often seen with snoring and increased effort shown on Pes signal defined as Pes crescendo or continuous sustained effort
Pes crescendo[8]	Sequence of ≥4 breaths that show increasingly negative peak end-inspiratory pressure; may be seen with flow limitation on nasal cannula
Continuous sustained effort[9]	Repetitive, abnormally negative peak end-inspiratory pressures, ending at same negative inspiratory pressure without a crescendo pattern; associated with discrete flow limitation on nasal cannula–pressure transducer signal, with "flattening" of the breath signal curve for ≥4 successive breaths
Pes reversal[8]	Termination of abnormal increase in respiratory effort with abrupt switch to a less negative peak end-inspiratory pressure.
Respiratory event–related arousals	As defined by the American Academy of Sleep Medicine, patterns of progressively negative pressure terminated by a sudden change in pressure to a less negative level and an arousal event lasting ≥10 s[88]
Tachypnea	Increase in respiratory rate, above that seen during quiet unobstructed breathing, by ≥3 breaths/min in non-REM sleep, or 4 breaths/min in REM sleep, for ≥30 s; no changes in Sa_{O_2}, Pes, or EEG were required[11]

Abbreviations: EEG, electroencephalography; Pes, esophageal pressure; REM, rapid eye movement; Sa_{O_2}, oxygen saturation.

nasal-oral thermistors should decrease by at least 50% of normal baseline breathing. Hypopneas should be terminated with an EEG arousal or a drop in Sa_{O_2} of at least 3%.[23,76] By these criteria, the finding was considered to be pathologic if the obstructive apnea index was at least 1 or if the apnea-hypopnea index was at least 5 events per hour.

Some children with very noisy breathing at night and enlarged tonsils and adenoids had a normal score at PSG but had clinical symptoms[90,91] that led to adenotonsillectomy. Also, other SDB syndromes without an associated abnormal apnea-hypopnea index but with an elevated respiratory disturbance index (RDI) were controlled with nasal continuous positive airway pressure (CPAP) or upper airway surgery.[85] Although an apnea-hypopnea index of at least 5 was considered pathologic, there was the recognition that apnea and hypopnea as defined did not encompass all pathologic breathing during sleep. Hence, an arousal index was calculated; thus, snoring sequences that were terminated with an EEG arousal were scored. The association of apnea-hypopnea and other measurements led to the use of the term *RDI*. This term acknowledges that the defined PSG patterns did not encompass all abnormal breathing events.

The introduction of the nasal cannula–pressure transducer system[16,92] allowed a more accurate recognition of abnormal breathing during sleep, as this technique based on nasal flow is semiquantitative. It allows better recognition of partially obstructed breaths. A hypopnea was defined when flow decreased by 30% of a normal breath. However, many still require an EEG arousal and/or an Sa_{O_2} drop, despite previous demonstration that clinical consequences can be obtained without a change in Sa_{O_2}. An RDI of more than 5 events was used on the basis of previous habits.

A minority of sleep clinics monitored respiratory efforts using Pes. These groups showed that snoring without hypopneas was associated with abnormal efforts and an induction of EEG arousals. Based on Pes recordings,[83,85] specific patterns were recognized and defined, such as "Pes crescendos," "sustained respiratory effort," and "Pes reversals." Some evidence suggests that these patterns were frequently, but not always, seen with abnormal nasal flow on the nasal cannula–pressure transducer recording. However, a flow limitation ranging from normal to a 30% decrease at the nasal cannula was usually seen with these patterns. The nasal flow limitation was described as a flattening of the nasal flow curve; several patterns of abnormal curves have been described. It may be easier to visually recognize a change of the Pes than a flattening of the nasal curve.[83,85]

The application of these Pes-related definitions showed that children who had no apneas or hypopneas, Sa_{O_2} drop of 3% or more, or EEG arousals presented with clinical complaints and clinical sleep-related syndromes, primarily parasomnias.[32,33] By applying these criteria, a clinical outcome study performed at the Stanford University Sleep Disorders Clinic, Stanford, Calif, focused on clinical complaints and the presence of clinical symptoms and signs. Complete treatment of the sleep-related upper airway problem with resolution of symptoms and signs was associated with fewer than 1 of the events included in the RDI.[84] Persistence of symptoms and signs was associated with the continued presence of an event that was not necessarily an apnea or a hypopnea. Instead, the breathing event was noted to be a "flow limitation with an increase in respiratory effort" or merely an increase in respiratory effort, and a cutoff point for the RDI of greater than or equal to 1.5 events per hour of sleep was found.[84] However, an RDI of greater than or equal to 1.5 events per hour is based on only 1 outcome study, even if several clinical studies have indicated the validity of such a cutoff point.[32,45,84]

ANS AND BREATHING PATTERNS DURING SLEEP

An increase in respiratory efforts is associated with changes in autonomic nervous system (ANS) settings. These changes will affect the cardiovascular system in an indi-

vidual with a normal ANS.[49] One may want to evaluate these changes to recognize an abnormal pattern and determine whether they may be detrimental. The following 2 types of responses can be seen when an increase in respiratory effort occurs during sleep: activation or arousal with cortical involvement.

Activation is a clinical neurophysiology term defined by Moruzzi and Magoun[93] during the course of their study of the ascending reticular formation; it is related to the recruitment of sensory inputs that will lead to a polysynaptic motor response after relay of sensory input in the brainstem and subcortical structures. The nucleus ambiguous receives information that simultaneously leads to efferent responses through the nucleus tractus solitarius. This relay leads to a simultaneous ANS stimulation, and an autonomic activation will lead to an increase in sympathetic tone.

An ANS response may be seen with brainstem reflexes leading to full reopening of the upper airway without EEG cortical arousal, or it may be seen as the consequence of an EEG cortical arousal. The presence of cortical arousals will be associated with clinical symptoms, such as complaints of excessive daytime somnolence, irritability, or unrefreshing sleep. The role of repetitive activation is unknown in children.

The determination of how much airway size changes and the duration of the change needed to lead to cortical arousal are unknown. Sleep stages may play a role in the type of response seen, but no definitive information is available in prepubertal children.

The pulse transit time, which measures the transit time of the pulse wave from approximately the aortic valve to the wrist, and the peripheral arterial tonometry are 2 variables that were added to PSG to help recognize an arousal.[94-97] None of these devices can distinguish between a brainstem reflex and a cortical arousal response. The importance of the sympathetic response could be a relatively accurate indicator of cortical involvement, but the studies to validate such distinction have not yet been published. Based on a commercially designed algorithm involving heart rate and finger plethysmography, the peripheral arterial tonometry does not really reflect the balance between the sympathetic and parasympathetic systems during sleep. The pulse transmit time also has limitations of interpretation. When used to identify cortical arousals related to SDB, both techniques have false-positive and false-negative findings, which limit the accuracy of interpretation.[97] The monitoring of these different variables has, however, shown that repetitive snoring can be associated with activation and/or EEG arousal.

CHANGES IN EEG SLEEP PATTERNS

Historically, an EEG alpha or an alpha and beta arousal lasting 3 seconds at the termination of an abnormal breathing event was required to score an event. However, several studies have shown that limited upper airway occlusion may end with a burst of delta waves or a K complex.[98] The use of a sleep scoring system, based on analysis of the cyclic alternating pattern (CAP), demonstrated the negative effect of these bursts.[99-101] The CAP scoring system is based on recurrent bursts of delta waves and K complexes with or without superimposed alpha waves within a period of 60 seconds intertwined with low EEG amplitude. The CAP is a normal phenomenon that occurs between wakefulness and slow-wave sleep or, at the end of night, between REM sleep and well-established, repetitive sleep-spindle sleep. It indicates a transition from one stable state to another and is not seen in REM sleep. CAP is typically a transient period during which a greater instability of sleep may occur with a greater chance to enter a light sleep or even to awaken. An abnormal CAP rate, defined in different age groups in children,[100,101] indicates an instability of non-REM sleep as well as a difficulty in reaching a new stable state.[99] CAP is associated with autonomic activation and may lead to awakening and large sympathetic discharge. Chervin et al[102,103] have also reported a novel approach to evaluate EEG findings with abnormal breathing during sleep, based on an algorithm investigating the EEG changes seen, with each abnormal inspiration associated with increased effort. The algorithm recognizes the changes in brain wave activity with increased inspiratory effort. When adenotonsillectomy is successful in relieving abnormal breathing during sleep, the abnormal EEG pattern disappears. Furthermore, the daytime symptoms, particularly sleepiness, abate. This analytic technique needs to be tested further.

GENETIC RISK FACTORS OF SDB

Genetic[64,104-112] and environmental risk factors have been identified in the development of SDB; they are associated to variable degrees. Oral mucosa thickness has been identified as an ethnic risk factor in African Americans, and skull base length has been noted to be an ethnic risk factor in Far East Asians.[108,109] African American and Far East Asian populations have been shown to have significantly higher risk than Caucasians when age, sex, and body mass index are considered.[64,104-112] The familial trait of dolichocephaly (or narrow face) has also been implicated as a risk factor, independent of ethnicity.[51,111] Familial cases of SDB are seen in all ethnic groups. Genetic investigations are performed, although there is currently no clear indication for a specific gene location responsible for increased risk. The strongest current indicators have been related to facial morphotype.[64] Clearly, there is an increased risk of SDB in a family in which a member is affected.[104-106,110-112] Pediatricians should, therefore, systematically question other family members about sleep-related problems when there is a positive history of SDB (**Figure 2**).

TREATMENT

There is an overall consensus that children with SDB should undergo evaluation by an otolaryngologist for surgical treatment. It is also clear that the well-described but extremely complex interaction between nasal breathing and facial growth is important, even if it is rarely investigated.[51]

Treatment for short-term outcomes indicates that adenotonsillectomy with or without radio frequency treatment of nasal inferior turbinates is the first approach to consider.[85,113,114] Independent of the size of tonsils or adenoids, adenotonsillectomy will provide more airway

space. Two points must be emphasized. First, outcome investigation has shown that isolated tonsillectomy or adenoidectomy is not as effective as adenotonsillecomy.[84,115] Also, if enlarged turbinates are present, radio frequency treatment of the nasal turbinates should be performed at the same time, while the child is under general anesthesia. Performance of adenotonsillectomy without performance of nasal turbinate treatment may have a negative impact on the outcome.[84] Outcomes of adenotonsillectomy have been reviewed,[113] but no review addresses the reasons for failure. A recent study examined the short-term outcomes to understand why results were incomplete.[115] Surgeons often use techniques that are not aimed at maximally opening the airway; they may fail to treat the nose simultaneously with the adenotonsillectomy; and others simply do not recognize the craniofacial changes that contributed to the SDB.

Only 2 studies[116,117] have looked at the long-term outcome of regular adenotonsillectomy performed in prepubertal children. After evaluating the outcomes to a minimum of 10 years later, both studies indicated that there was failure to control the problem because of the presence of hypopneas and apneas at the long-term follow-up recordings. Demonstration of the absence of apneas and hypopneas within 6 weeks to 3 months after surgery was requested in 1 of the 2 studies.[116] The long-term outcome in that study linked the recurrence of abnormal breathing during sleep to the absence of dealing with a narrow maxilla and/or mandible at the time of the initial surgery and the later occurrence of tongue/mucosal enlargement at the time of puberty, when 90% of orofacial adult growth had already occurred.

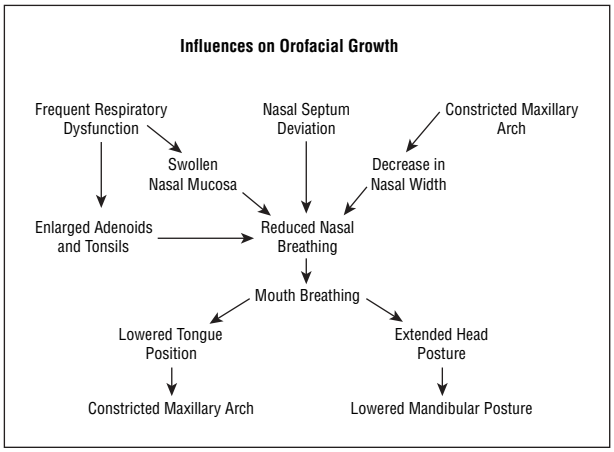


Figure 2. Influences of sleep-disordered breathing on orofacial growth.

Adenotonsillectomy has been performed in association with orthodontic treatment.[118] Rapid maxillary distraction (RMD) is an orthodontic technique that is based on the bone formation process. A distractor anchored to 2 molars on both sides applies daily pressure, pushing apart both halves of the maxilla; bone then grows from the borders of the cartilage.[118,119] This technique pushes the soft tissues laterally, decreases the height of the soft palate, and enlarges the nasal orifices.[118] Rapid maxillary distraction may be associated with distraction of the mandible, but because no midcartilage is present, there is very limited widening. This fact may limit the degree of maxillary widening with RMD (**Figures 1**, **3**, and **4**). Slow maxillary distraction is based on similar principles and optimizes the degree of widening at the different growth periods that occur in prepubertal children. Rapid and slow maxillary distractions are performed between 5 and 11 years of age. Distraction results in widening of the palate and the nose; thus, this procedure remedies nasal occlusion related to a deviated septum, for which little can be done before 14 to 16 years of age. Even when performed in association with adenotonsillectomy, however, orthodontics may not control all SDB. Abnormal mandibular or maxillomandibular anteroposterior development is a bigger challenge. Nasal CPAP will be the recommended treatment until further orthognathic surgery[120] can be performed.

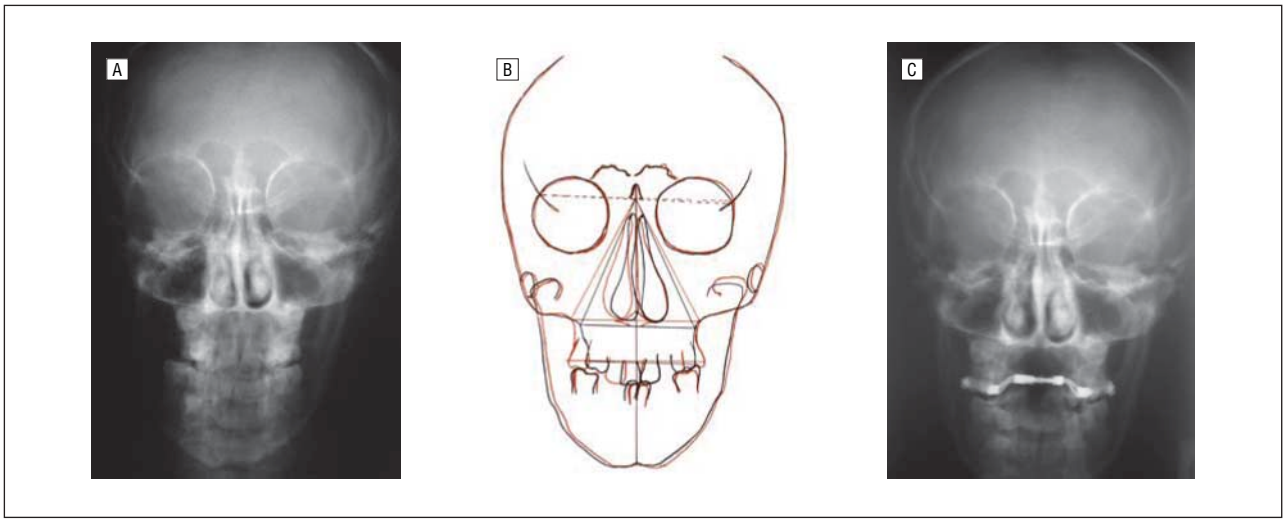
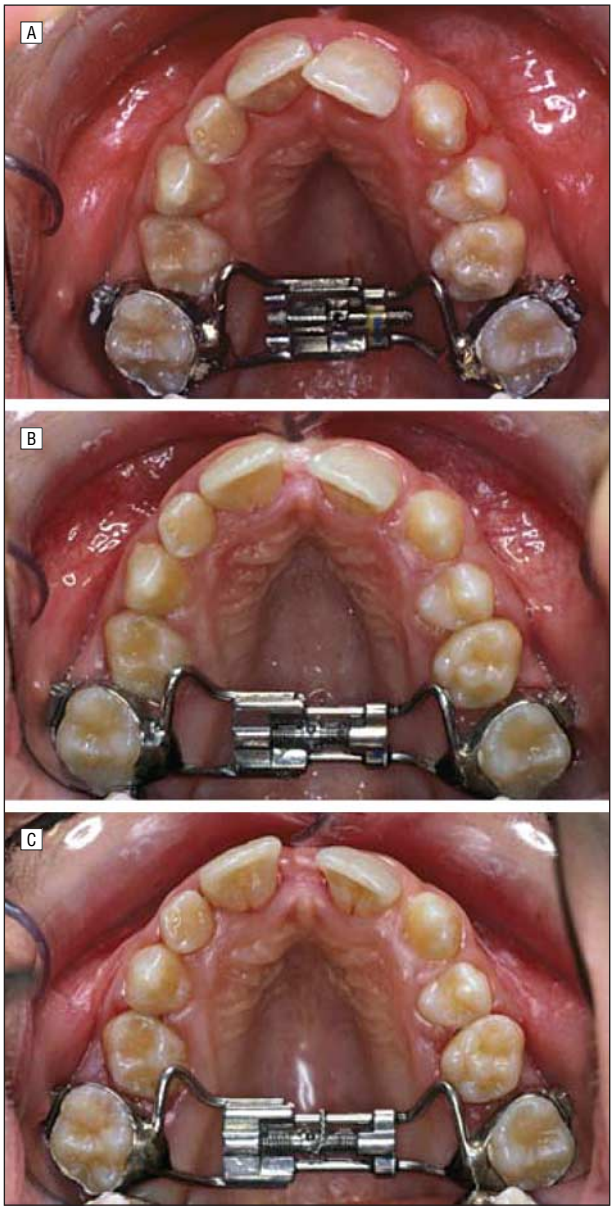


Figure 3. The significant impact of rapid maxillary distraction. A, Frontal cephalometric study demonstrates a narrow maxillary arch before distraction. B, Drawing superimposing the image in A and the postdistraction image (shown in C) to show the widening of the maxillary and nasal cavities.The patient's right inferior turbinate is closely approximated to the septum. C, The frontal cephalometric demonstrates that the maxillary arch has been opened since the distractor has been placed. The nasal cavity has also been altered because the patient's right inferior turbinate is now farther from the septum than it was before placement of the distractor.



Home nasal CPAP has been used in infants, prepubertal children, and pubertal children. The first report of its usefulness in children in 1986 was a prospective study that followed up 5 children, aged 3 to 11 years, for 10 months.[121] Similar findings were reported in several large retrospective studies (**Table 4**).[103,122-127] These studies primarily involved children older than 12 months. Infants aged 8 to 18 weeks were followed up from the onset of treatment through the first 12 months of age in a study in 1995[124]; that study was replicated in 1999.[126]

The difficulty in the application of nasal CPAP relates to training the family and child and finding the appropriate nasal interface. Children often need to be trained to tolerate the facial interface. (Behavioral modification techniques and daytime training may help with this training.) Continuous positive airway pressure is very useful when the SDB is related to major craniofacial deformities or other illnesses. If the upper airway problem is complicated by neuromuscular disease, nasal bilevel treatment may be used.

Regular follow-up should be performed within the first 3 months to evaluate mask fitting.[124] Because of rapid craniofacial growth of young children, CPAP should be evaluated every 6 months. An annual visit with a craniofacial specialist should occur to affirm that the headgear and mask do not worsen a maxillary growth deficiency.[128] Clinicians should encourage the use of humidification, aggressively treat allergies and/or rhinitis, and check nasal patency. In light of children's favorable response to surgery with or without orthodontic and antiallergic treatment, nasal CPAP should only be a second consideration.

Orthognathic surgery entails shifting bones and disrupting the bone growth structures.[120] Such an approach is normally postponed until 10 to 13 years of age. Two surgical techniques used in patients with SDB are mandibular distraction osteogenesis and maxillomandibular advancement.

Figure 4. Rapid maxillary distraction demonstrates progressive improvement in the crowding of a child's teeth, from immediately after insertion of the distractor (A) to 3 weeks later (C). Progressive widening is indicated by the space between the 2 frontal incisors.

Table 4. Nasal CPAP in Children

Source	Type of Study	PSG	Conclusions
Guilleminault et al,[121] 1986	Feasibility study of 5 children in hospital; prospective 10-mo home study of 5 children	Before, during titration, and during follow-up	Feasibility with parent training; 4 of 5 infants daily use of CPAP at 10-mo; follow-up
Waters et al,[122] 1995	Retrospective review of 80 children aged 12 d to 15½ y	For diagnosis and titration	86% of parents completed training; 12.5% dropped out
Marcus et al,[123] 1995	Retrospective study of 94 children aged 3-12 mo; applied after adenotonsillectomy in 76%; first treatment in 23 children	For diagnosis and titration	1 Dropout
Guilleminault et al,[124]1995	Prospective study of infants aged 8-18 wk at entry and systematic follow-up for 12 mo; family underwent screening at entry for understanding of treatment	For diagnosis, treatment, and each follow-up retitration	Need to readjust equipment and pressure on regular basis owing to fast craniofacial growth in infancy
Rains,[125] 1995	Prospective study of 4 children aged 3-12 y; training of parents	For diagnosis and titration	Follow-up for 3 mo; effective treatment; no dropout for 3 mo; 1 dropout thereafter
McNamara and Sullivan,[126] 1999	Prospective study of 24 infants aged 6-51 wk for 12 mo	For diagnosis, titration, and regular follow-up	Family training and support; continuous use in 18 children; effective treatment
Downey et al,[127] 2000	Retrospective study of 18 children aged <2 y		12 Children successfully treated

Abbreviations: CPAP, continuous positive airway pressure; PSG, polysomnography.

Mandibular distraction osteogenesis is very similar to RMD, but it is applied to the mandible when a maxillary and mandibular widening are needed and when the slow mandibular orthodontic distraction cannot achieve the needed result.[120] A vertical transection of the maxilla is performed between the 2 central incisors and a distractor is used as in RMD. Widening of 12 to 14 mm can be obtained easily in 3 weeks. Orthodontic treatment is similar to that described with RMD. By 12 to 13 years of age, both procedures can be performed simultaneously to provide an anterior displacement of the tongue and enlargement of the retrolingual airway space.[120]

Maxillomandibular advancement is a very successful procedure. Nevertheless, it is major surgery that should be performed after there has been appropriate orthodontic treatment. Surgeons who perform this procedure must have a good understanding of upper airway mechanics and dental problems. It may be performed at any time during childhood, but it is often postponed until 11 to 12 years of age.[129]

A controversial issue is how early to perform adenotonsillectomy. Most will agree that adenotonsillectomy is often performed by 24 months of age. However, OSA has been noted as early as 3 weeks of age, and cases of heavy snoring and clinical symptoms in children aged 6 to 24 months are actually common. Adenotonsillectomy has been performed as early as 6 months of age.[112]

Several advances have been made in sleep medicine. Apneas and hypopneas are not the only indicators of abnormal breathing during sleep. In this rapidly evolving field, it has been challenging to establish new scoring criteria, despite the availability of new technologies. However, the clinical findings and the PSG results should be used to determine the diagnosis and to guide treatment recommendations.

Accepted for Publication: March 9, 2005.
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REFERENCES

1. Worsnop C, Kay A, Kim Y, Trinder J, Pierce R. Effect of age on sleep onset-related changes in respiratory pump and upper airway muscle function. *J Appl Physiol*. 2000;88:1831-1839.
2. Orem J, Montplaisit J, Dement WC. Changes in the activity of respiratory neurons during sleep. *Brain Res*. 1974;82:309-315.
3. Orem J. Control of the upper airway during sleep and the hypersomnia sleep apnea syndrome. In: Orem J, Barnes CD, eds. *Physiology in Sleep*. Orlando, Fla: Academic Press Inc; 1980:273-313.
4. Guilleminault C, Eldridge FL, Simmons FB, Dement WC. Sleep apnea in eight children. *Pediatrics*. 1976;58:23-30.
5. Guilleminault C, Winkle R, Korobkin R, Simmons FB. Children and nocturnal snoring: evaluation of the effects of sleep related respiratory resistive load and daytime functioning. *Eur J Pediatr*. 1982;139:165-171.
6. Teculescu DB, Caillier I, Perrin P, Rebstock E, Rauch A. Snoring in French preschool children. *Pediatr Pulmonol*. 1992;13:239-244.
7. Owen GO, Canter RJ, Robinson A. Snoring, apnoea and ENT symptoms in the paediatric community. *Clin Otolaryngol*. 1996;21:130-134.
8. Lu LR, Peat JK, Sullivan CE. Snoring in preschool children: prevalence and association with nocturnal cough and asthma. *Chest*. 2003;124:587-593.
9. Shin C, Joo S, Kim J, Kim T. Prevalence and correlates of habitual snoring in high school students. *Chest*. 2003;124:1709-1715.
10. Urschitz MS, Guenther A, Eitner S, et al. Risk factors and natural history of habitual snoring. *Chest*. 2004;126:790-800.
11. Castronovo V, Zucconi M, Nosetti L, et al. Prevalence of habitual snoring and sleep-disordered breathing in preschool-aged children in an Italian community. *J Pediatr*. 2003;142:377-382.
12. Anuntaseree W, Rookkapan K, Kuasirikul S, Thongsuksay P. Snoring, and obstructive sleep apnea in Thai school-age children: prevalence and predictive factors. *Pediatr Pulmonol*. 2001;32:222-227.
13. Gislason T, Benediktsdottir B. Snoring, apneic episodes and nocturnal hypoxemia among children 6 months to 6 years old: an epidemiologic study of lower limit of prevalence. *Chest*. 1995;107:963-966.
14. Brunetti L, Rana S, Lospalluti ML, et al. Prevalence of obstructive sleep apnea in a cohort of 1207 children from the south of Italy. *Chest*. 2001;120:1930-1935.
15. Rosen C, Larkin E, Kirchner H, et al. Prevalence and risk factors for sleep-disordered breathing in 8- to 11-year-old children: association with race and prematurity. *J Pediatr*. 2003;142:383-389.
16. Trang H, Leske V, Gaultier C. Use of nasal cannula for detecting sleep apneas and hypopneas in infants and children. *Am J Respir Crit Care Med*. 2002; 166:464-468.
17. Guilleminault C, Korobkin R, Winkle R. A review of 50 children with obstructive sleep apnea syndrome. *Lung*. 1981;159:275-287.
18. Goodwin JL, Babar SI, Kaemingk KL, et al. Symptoms related to sleep-disordered breathing in white and Hispanic children: the Tucson Children's Assessment of Sleep Apnea Study. *Chest*. 2003;124:196-203.
19. Ali NJ, Pison D, Stradling JR. Snoring, sleep disturbances and behavior in 4-5 years old. *Arch Dis Child*. 1993;68:360-366.
20. Guilleminault C, Khramtsov A. Upper airway resistance syndrome in children: a clinical review. *Semin Pediatr Neurol*. 2001;8:207-215.
21. Contencin P, Guilleminault C, Manach Y. Long-term follow-up and mechanisms of obstructive sleep apnea (OSA) and related syndromes through infancy and childhood. *Int J Pediatr Otorhinolaryngol*. 2003;67(suppl 1):S119-S123.
22. Marcus CL. Sleep-disordered breathing in children. *Am J Respir Crit Care Med*. 2001;164:16-30.
23. American Academy of Pediatrics. Clinical practice guidelines: diagnosis and management of childhood obstructive sleep apnea syndrome. *Pediatrics*. 2002; 109:704-712.
24. Goldstein NA, Pugazhendhi V, Rao SM, et al. Clinical assessment of pediatric obstructive sleep apnea. *Pediatrics*. 2004;114:33-43.
25. Kaynak H, Kaynak D, Ostura I. Does frequency of nocturnal urination reflect the severity of sleep-disordered breathing? *J Sleep Res*. 2004;13:173-176.
26. Kolar JC, Salter EM. *Cranio-Facial Anthropometry: Practical Measurement of the Head and Face for Clinical, Surgical, and Research Use*. Springfield, Ill: Charles C Thomas Publisher; 1997:334.
27. Cinar U, Vural C, Cakir B, Topuz E, Karaman MI, Turgut S. Nocturnal enuresis and upper airway obstruction. *Int J Pediatr Otorhinolaryngol*. 2001;59:115-118.
28. Weider DJ, Sateia MJ, West RP. Nocturnal enuresis in children with upper airway obstruction. *Otolaryngol Head Neck Surg*. 1991;105:427-432.
29. Marcus CL, Carroll JL, Koerner CB, Hamer A, Lutz J, Loughlin GM. Determinants of growth in children with the obstructive sleep apnea syndrome. *J Pediatr*. 1994;125:556-562.
30. Nieminen P, Löppönen T, Tolonen U, Lanning P, Knip M, Löppönen H. Growth and biochemical markers of growth in children with snoring and obstructive sleep apnea. *Pediatrics*. 2002;109:e55.
31. Bar A, Tarasiuk A, Segev Y, Phillip M, Tal A. The effect of adenotonsillectomy on serum insulin-like growth factor–I and growth in children with obstructive sleep apnea syndrome. *J Pediatr*. 1999;135:76-80.
32. Guilleminault C, Palombini L, Pelayo R, Chervin RD. Sleepwalking and sleep terrors in prepubertal children: what triggers them? *Pediatrics*. 2003;111: e17-e25.
33. Goodwin JL, Kaemingk KL, Fregosi RF, et al. Parasomnias and sleep disordered breathing in Caucasian and Hispanic children: the Tucson Children's Assessment of Sleep Apnea Study. *BMC Med*. 2004;2:14.
34. Chervin RD, Dillon JE, Bassetti C, Ganoczy DA, Pituch KJ. Symptoms of sleep disorders, inattention, and hyperactivity in children. *Sleep*. 1997;20:1185-1192.
35. Owens J, Spirito A, Marcotte A, McGuinn M, Berkelhammer L. Neuropsychological and behavioral correlates of obstructive sleep apnea syndrome in children: a preliminary study. *Sleep Breath*. 2000;4:67-78.
36. Gozal D, Pope DW Jr. Snoring during early childhood and academic performance at ages thirteen to fourteen years. *Pediatrics*. 2001;107:1394-1399.
37. Chervin RD, Archbold KH, Dillon JE, et al. Inattention, hyperactivity, and symptoms of sleep-disordered breathing. *Pediatrics*. 2002;109:449-456.
38. Urschitz MS, Guenther A, Eggebrecht E, et al. Snoring, intermittent hypoxia and academic performance in primary school children. *Am J Respir Crit Care Med*. 2003;168:464-468.

39. Kaemingk KL, Pasvogel AE, Goodwin JL, et al. Learning in children and sleep disordered breathing: findings of the Tucson Children's Assessment of Sleep Apnea (TuCASA) prospective cohort study. *J Int Neuropsychol Soc*. 2003; 9:1016-1026.
40. Melendres MC, Lutz JM, Rubin ED, Marcus CL. Daytime sleepiness and hyperactivity in children with suspected sleep-disordered breathing. *Pediatrics*. 2004; 114:768-775.
41. O'Brien LM, Mervis CB, Holbrook CR, et al. Neurobehavioral implications of habitual snoring in children. *Pediatrics*. 2004;114:44-49.
42. Marcus CL, Greene MG, Carroll JL. Blood pressure in children with obstructive sleep apnea. *Am J Respir Crit Care Med*. 1998;157:1098-1103.
43. Enright PL, Goodwin JL, Sherrill DL, Quan JR, Quan SF. Blood pressure elevation associated with sleep-related breathing disorder in a community sample of white and Hispanic children: the Tucson Children's Assessment of Sleep Apnea study. *Arch Pediatr Adolesc Med*. 2003;157:901-904.
44. Kwok KL, Ng DK, Cheung YF. BP and arterial distensibility in children with primary snoring. *Chest*. 2003;123:1561-1566.
45. Guilleminault C, Khramsov A, Stoohs RA, et al. Abnormal blood pressure in prepubertal children with sleep-disordered breathing. *Pediatr Res*. 2004;55:76-84.
46. Amin RS, Carroll JL, Jeffries JL, et al. Twenty-four–hour ambulatory blood pressure in children with sleep-disordered breathing. *Am J Respir Crit Care Med*. 2004;169:950-956.
47. Shiomi T, Guilleminault C, Stoohs R, Schnittger I. Obstructed breathing in children during sleep monitored by echocardiography. *Acta Paediatr*. 1993; 82:863-871.
48. Cloward TV, Walker JM, Farney RJ, Anderson JL. Left ventricular hypertrophy is a common echocardiographic abnormality in severe obstructive sleep apnea and reverses with nasal continuous positive airway pressure. *Chest*. 2003; 124:594-601.
49. Ozdemir H, Altin R, Sogut A, et al. Craniofacial differences according to AHI scores of children with obstructive sleep apnoea syndrome: cephalometric study in 39 patients. *Pediatr Radiol*. 2004;34:393-399.
50. Redline S, Tishler PV, Schluchter M, Aylor J, Clark K, Graham G. Risk factors for sleep-disordered breathing in children. *Am J Respir Crit Care Med*. 1999; 159:1527-1532.
51. Guilleminault C, Quo SD. Sleep-disordered breathing: a view at the beginning of the new millennium. *Dent Clin North Am*. 2001;45:643-656.
52. Mallampati SR, Gatt SP, Gugino LD, Desai SP, Waraksa B, Liu PL. A clinical sign to predict difficult tracheal intubation: a prospective study. *Can Anaesth Soc J*. 1985;32:429-434.
53. Friedman M, Tanyeri H, La Rosa M, et al. Clinical predictors of obstructive sleep apnea. *Laryngoscope*. 1999;109:1901-1907.
54. O'Ryan FS, Gallagher DM, LaBanc JP, Epker BN. The relation between nasorespiratory function and dentofacial morphology: a review. *Am J Orthod*. 1982; 82:403-410.
55. Linder-Aronson S. Effects of adenoidectomy on the dentition and facial skeleton over a period of five years. In: Cook JT, ed. *Transactions of the Third International Orthodontic Congress*. London, England: Crosby Lockwood Staples; 1975:85-100.
56. McNamara JA. Influence of respiratory pattern on craniofacial growth. *Angle Orthod*. 1981;51:269-300.
57. Linder-Aronson S, Woodside DG, Lundstrom A. Mandibular growth direction following adenoidectomy. *Am J Orthod*. 1986;89:273-284.
58. Subtelny JD. Oral respiration: facial maldevelopment and corrective dentofacial orthopedics. *Angle Orthod*. 1980;50:147-164.
59. Cheng MC, Enlow DH, Papsidero M, Broadbent BH Jr, Oyen O, Sabat M. Developmental effects of impaired breathing in the face of the growing child. *Angle Orthod*. 1988;58:309-320.
60. Behlfelt K, Linder-Aronson S, McWilliam J, Neander P, Laage-Hellman J. Dentition in children with enlarged tonsils compared to control children. *Eur J Orthod*. 1989;11:416-429.
61. Woodside DG, Linder-Aronson S, Lundstrom A, McWilliam J. Mandibular and maxillary growth after changed mode of breathing. *Am J Orthod Dentofacial Orthop*. 1991;100:1-18.
62. Behlfelt K, Linder-Aronson S, Neander P. Posture of the head, the hyoid bone, and the tongue in children with and without enlarged tonsils. *Eur J Orthod*. 1990; 12:458-467.
63. Harvold EP, Tomer BS, Vargervik K, Chierici G. Primate experiments on oral respiration. *Am J Orthod*. 1981;79:359-372.
64. Gaultier C, Guilleminault C. Genetics, control of breathing, and sleep-disordered breathing: a review. *Sleep Med*. 2001;2:281-295.
65. Canova CR, Downs SH, Knoblauch A, Andersson M, Tamm M, Leuppi JD. Increased prevalence of perennial allergic rhinitis in patients with obstructive sleep apnea. *Respiration*. 2004;71:138-143.
66. Rappai M, Collop N, Kemp S, DeShazo R. The nose and sleep-disordered breathing: what we know and what we do not know. *Chest*. 2003;124:2309-2323.
67. Mansfield LE, Diaz G, Posey CR, Flores-Neder J. Sleep disordered breathing and daytime quality of life in children with allergic rhinitis during treatment with intranasal budesonide. *Ann Allergy Asthma Immunol*. 2004;92:240-244.
68. Chng SY, Goh DY, Wang XS, Tan TN, Ong NB. Snoring and atopic disease: a strong association. *Pediatr Pulmonol*. 2004;38:210-216.
69. Williams EF III, Woo P, Miller R, Kellman RM. The effects of adenotonsillectomy on growth in young children. *Otolaryngol Head Neck Surg*. 1991;104: 509-516.
70. Linder-Aronson S. Effects of adenoidectomy on dentition and nasopharynx. *Trans Eur Orthod Soc*. 1972:177-186.
71. Rosen CL. Obstructive sleep apnea syndrome in children: controversies in diagnosis and treatment. *Pediatr Clin North Am*. 2004;51:153-167.
72. Whiteford L, Fleming P, Henderson AJ. Who should have a sleep study for sleep related breathing disorders? *Arch Dis Child*. 2004;89:851-855.
73. Tarasiuk A, Simon T, Regev U, Reuveni H. Willingness to pay for polysomnography in children with obstructive sleep apnea syndrome: a cost-benefit analysis. *Sleep*. 2003;26:1016-1021.
74. Praud JP. Snoring in children: still many questions, only a few answers. *Pediatr Pulmonol Suppl*. 2004;26:169-171.
75. Carroll JL, McColley SA, Marcus CL, Curtis S, Loughlin GM. Inability of clinical history to distinguish primary snoring from obstructive sleep apnea syndrome in children. *Chest*. 1995;108:610-618.
76. American Thoracic Society. Standards and indications for cardiopulmonary sleep studies in children. *Am J Respir Crit Care Med*. 1996;153:866-878.
77. American Thoracic Society. Cardiorespiratory sleep studies in children: establishment of normative data and polysomnographic predictors of morbidity. *Am J Respir Crit Care Med*. 1999;160:1381-1387.
78. Flemons WW, Littner MR, Rowley JA, et al. Home diagnosis of sleep apnea: a systematic review of the literature: an evidence review cosponsored by the American Academy of Sleep Medicine, the American College of Chest Physicians, and the American Thoracic Society. *Chest*. 2003;124:1543-1579.
79. Brouillette RT, Morielli A, Leimanis A, Waters KA, Luciano R, Ducharme FM. Nocturnal pulse oximetry as an abbreviated testing modality for pediatric obstructive sleep apnea. *Pediatrics*. 2000;105:405-412.
80. Nixon GM, Kermack AS, Davis GM, Manoukian JJ, Brown KA, Brouillette RT. Planning adenotonsillectomy in children with obstructive sleep apnea: the role of overnight oximetry. *Pediatrics*. 2004;113:e19-e25.
81. Stoohs RA, Blum HC, Knaak I, Guilleminault C. Non-invasive estimation of esophageal pressure based on intercostal EMG monitoring. *IEEE IMB*. 2004:3867-3869.
82. D'Andrea LA. Diagnostic studies in the assessment of pediatric sleep-disordered-breathing: techniques and indications. *Pediatr Clin North Am*. 2004;51: 169-186.
83. Guilleminault C, Poyares D, Palombini L, Koester U, Pelin Z, Black J. Variability of respiratory effort in relationship with sleep stages in normal controls and upper airway resistance syndrome patients. *Sleep Med*. 2001;2:397-406.
84. Guilleminault C, Li KK, Khramtsov A, Pelayo R, Martinez S. Sleep disordered breathing: surgical outcome in prepubertal children. *Laryngoscope*. 2004; 114:132-137.
85. Guilleminault C, Li K, Khramtsov A, Palombini L, Pelayo R. Breathing patterns in prepubertal children with sleep-related breathing disorders. *Arch Pediatr Adolesc Med*. 2004;158:153-161.
86. Ohayon MM, Carskadon MA, Guilleminault C, Vitiello MV. Meta-analysis of quantitative sleep parameters from childhood to old age: developing normative values across the life span. *Sleep*. 2004;27:1255-1273.
87. Wong TK, Galster P, Lau TS, Lutz JM, Marcus CL. Reliability of scoring arousals in normal children and children with obstructive sleep apnea syndrome. *Sleep*. 2004;27:1139-1145.
88. American Academy of Sleep Medicine Task Force. Sleep-related breathing disorders in adults: recommendations for syndrome definitions and measurement techniques in clinical research: the report of the American Academy of Sleep Medicine Task Force. *Sleep*. 1999;22:667-689.
89. Marcus CL, Omlin KJ, Basinki D, et al. Normal polysomnographic values for children and adolescents. *Am Rev Respir Dis*. 1992;146:1235-1932.
90. Guilleminault C, Pelayo R. . . . And if the polysomnogram was faulty? *Pediatr Pulmonol*. 1998;26:1-3.
91. Goldstein NA, Pugazhendhi V, Rao SM, et al. Clinical assessment of pediatric obstructive sleep apnea. *Pediatrics*. 2004;114:33-43.
92. Serebrisky D, Cordero R, Mandeli J, Kattan M, Lamm C. Assessment of inspiratory flow limitation in children with sleep-disordered breathing by a nasal cannula pressure transducer system. *Pediatr Pulmonol*. 2002;33:380-387.
93. Moruzzi G, Magoun HW. Brainstem reticular formation and activation of EEG. *Electroencephalogr Clin Neurophysiol*. 1949;1:455-473.

94. Katz ES, Lutz J, Black C, Marcus CL. Pulse transit time as a measure of arousal and respiratory effort in children with sleep-disordered breathing. *Pediatr Res*. 2003;53:580-588.
95. Tauman R, O'Brien LM, Mast BT, Holbrook CR, Gozal D. Peripheral arterial tonometry events and electroencephalographic arousals in children. *Sleep*. 2004; 27:502-506.
96. Pillar G, Bar A, Betito M, et al. An autonomic ambulatory device for detection of AASM defined arousals from sleep: the WP100. *Sleep Med*. 2003;4: 207-212.
97. Poyares D, Guilleminault C, Rosa A, Ohayon M, Koester U. Arousal, EEG spectral power and pulse transit time in UARS and mild OSAS subjects. *Clin Neurophysiol*. 2002;113:1598-1606.
98. Black JE, Guilleminault C, Colrain IM, Carillo O. Upper airway resistance syndrome: central electroencephalographic power and changes in breathing effort. *Am J Respir Crit Care Med*. 2000;162:406-411.
99. Terzano MG, Parrino L, Chervin R, et al. Atlas, rules and recording techniques for the scoring of the cyclical alternating pattern (CAP) in human sleep. *Sleep Med*. 2001;2:537-554.
100. Bruni O, Ferri F, Miano S, et al. Sleep cyclic alternating pattern in normal preschool-aged children. *Sleep*. 2005;28:220-230.
101. Lopes MC, Rosa A, Roizenblatt S, Guilleminault C, Passarelli C, Tufik S. Cyclic alternating pattern in peripubertal children. *Sleep*. 2005;28:215-219.
102. Chervin RD, Burns JW, Subotic NS, Roussi C, Thelen B, Ruzicka DL. Method for detection of respiratory cycle–related EEG changes in sleep-disordered breathing *Sleep*. 2004;27:110-115.
103. Chervin RD, Burns JW, Subotic NS, Roussi C, Thelen B, Ruzicka DL. Correlates of respiratory cycle–related EEG changes in children with sleep-disordered breathing. *Sleep*. 2004;27:116-121.
104. Redline S, Tishler PV, Tosteson TD, et al. The familial aggregation of obstructive sleep apnea. *Am J Respir Crit Care Med*. 1995;151:682-687.
105. Guilleminault C, Partinen M, Hollman K, Powell NB, Stoohs R. Familial aggregates in obstructive sleep apnea syndrome. *Chest*. 1995;107:1545-1551.
106. Mathur R, Douglas NJ. Family studies in patients with the sleep apnea-hypopnea syndrome. *Ann Intern Med*. 1995;122:174-178.
107. Redline S, Tishler PV, Hans MG, Tosteson TD, Strohl KP, Spry K. Racial differences in sleep-disordered breathing in African-Americans and Caucasians. *Am J Respir Crit Care Med*. 1997;155:186-192.
108. Ng TP, Seow A, Tan WC. Prevalence of snoring and sleep breathing–related disorders in Chinese, Malay and Indian adults in Singapore. *Eur Respir J*. 1998; 12:198-203.
109. Li KK, Kushida C, Adornado B, et al. Obstructive sleep apnea syndrome in the Asian population. *Sleep*. 1999;22:S104-S105.
110. Ovchinsky A, Rao M, Lotwin I, Goldstein NA. The familial aggregation of pediatric obstructive sleep apnea syndrome. *Arch Otolaryngol Head Neck Surg*. 2002; 128:815-818.
111. Guilleminault C, Pelayo R, Leger D, Clerk A, Bocian RC. Recognition of sleep-disordered breathing in children. *Pediatrics*. 1996;98:871-882.
112. Pillar G, Lavie P. Assessment of the role of inheritance in sleep apnea syndrome. *Am J Respir Crit Care Med*. 1995;151:688-691.
113. Lipton AJ, Gozal D. Treatment of obstructive sleep apnea in children: do we really know how? *Sleep Med Rev*. 2003;7:61-80.
114. Zettergren-Wijk L, Linder-Aronson S, Nordlander B, Agren K, Svanborg E. Longitudinal effect on facial growth after tonsillectomy in children with obstructive sleep apnea. *World J Orthod*. 2002;3:67-72.
115. Guilleminault C, Li KK, Quo S, Inouye R. A prospective study of surgical outcomes of children with sleep-disordered breathing. *Sleep*. 2004;27:95-100.
116. Guilleminault C, Partinen M, Praud JP, Quera-Salva MA, Powell N, Riley R. Morphometric facial changes and obstructive sleep apnea in adolescents. *J Pediatr*. 1989;114:997-999.
117. Tasker C, Crosby JH, Stadling JR. Persistence of upper airway narrowing during sleep, 12 years after adenotonsillectomy. *Arch Dis Child*. 2002;86: 34-37.
118. Pirelli P, Saponara M, Guilleminault C. Rapid maxillary expansion in children with obstructive sleep apnea syndrome. *Sleep*. 2004;27:761-766.
119. Vercellino V, Griffa A, Bello L, et al. Maxillary expansion in pediatric patients with respiratory problems. *World J Orthod*. 2003;4:126-134.
120. Guilleminault C, Li KK. Maxillomandibular expansion for the treatment of sleep-disordered breathing: preliminary result. *Laryngoscope*. 2004;114:893-896.
121. Guilleminault C, Nino-Murcia G, Heldt G, Baldwin R, Hutchinson D. Alternative treatment to tracheostomy in obstructive sleep apnea syndrome: nasal continuous positive airway pressure in young children. *Pediatrics*. 1986;78: 797-802.
122. Waters KA, Everett FM, Bruderer JW, Sullivan CE. Obstructive sleep apnea: the use of nasal CPAP in 80 children. *Am J Respir Crit Care Med*. 1995;152: 780-785.
123. Marcus CL, Ward SL, Mallory GB, et al. Use of nasal continuous airway pressure as the treatment of childhood obstructive sleep apnea. *J Pediatr*. 1995; 127:88-94.
124. Guilleminault C, Pelayo R, Clerk A, Leger D, Bocian RC. Home nasal CPAP in infants with sleep-disordered breathing. *J Pediatr*. 1995;127:905-912.
125. Rains JC. Treatment of obstructive sleep apnea in pediatric patients: behavioral intervention for compliance with continuous nasal continuous positive airway pressure intervention. *Clin Pediatr (Phila)*. 1995;34:535-541.
126. McNamara F, Sullivan CE. Obstructive sleep apnea in infants and its management with nasal continuous positive airway pressure. *Chest*. 1999;116: 10-16.
127. Downey R III, Perkin RM, Mac Quarrie J. Nasal CPAP use in children younger than 2 years of age. *Chest*. 2000;117:1608-1612.
128. Li KK, Riley R, Guilleminault C. An unreported risk in the use of home nasal CPAP and home nasal ventilation in children: mid-face hypoplasia. *Chest*. 2000; 117:916-918.
129. Shatz A. Indications and outcomes of adenoidectomy in infancy. *Ann Otol Rhinol Laryngol*. 2004;113:835-838.