

## reviews

# The Nose and Sleep-Disordered Breathing\*

## What We Know and What We Do Not Know

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**The relationship between sleep-disordered breathing (SDB) and nasal obstruction is unclear. In order to better understand, we performed an extensive computer-assisted review and analysis of the medical literature on this topic. Data were grouped into reports of normal control subjects, patients with isolated nasal obstruction, and those with SDB. We conclude that SDB can both result from and be worsened by nasal obstruction. Nasal breathing increases ventilatory drive and nasal occlusion decreases pharyngeal patency in normal subjects. Nasal congestion from any cause predisposes to SDB. Although increased nasal resistance does not always correlate with symptoms of congestion, nasal congestion typically results in a switch to oronasal breathing that compromises the airway. Moreover, oral breathing in children may lead to the development of facial structural abnormalities associated with SDB. We postulate that the switch to oronasal breathing that occurs with chronic nasal conditions is a final common pathway for SDB.**

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**Key words:** nasal obstruction; nose; obstructive sleep apnea syndrome; rhinitis; sleep-disordered breathing

**Abbreviations:** AHI = apnea-hypopnea index; CPAP = continuous positive airway pressure; EDS = excessive daytime sleepiness; EMG = electromyography; NARES = nonallergic rhinitis with nasal eosinophilia syndrome; NR = nasal resistance; OSAS = obstructive sleep apnea syndrome; Pes = esophageal pressure; SDB = sleep-disordered breathing; UARS = upper airway resistance syndrome

Sleep-disordered breathing (SDB) is common, afflicting as much as 2 to 4% of the population.<sup>1</sup> The most studied form, obstructive sleep apnea syndrome (OSAS), occurs most often in middle-aged men and obese individuals. Thus, risk factors for OSAS were originally thought to be morbid obesity and male gender. As our understanding of OSAS and other forms of SDB improved, other risk factors

surfaced. These include central obesity, family history, smoking, alcohol consumption, menopause, ethnicity, and craniofacial abnormalities.<sup>2</sup> We have observed a number of patients in our pulmonary, allergy, and sleep medicine practices who have nasal disorders, including allergic rhinitis, in association with SDB. Since both nasal obstruction and SDB are common and occur together, we asked if there is a cause-and-effect relationship. In order to address this question, a brief review of the anatomy and physiology of the nose, nasal airway resistance, syndromes of rhinitis, as well as how they relate to disturbance of sleep seems appropriate.

### LITERATURE REVIEW

Computer-based literature searches were used to identify all reports and reviews concerned with nasal conditions and SDB. These reports were read by the authors, reanalyzed, and grouped into those evaluat-

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ing nasal-associated effects on SDB in normal control subjects, patients with nasal conditions or SDB, and children.

#### ANATOMY AND PHYSIOLOGY OF THE NOSE

The nose is lined by pseudostratified epithelium resting on a basement membrane, separating it from deeper submucosal layers. The submucosa contains mucous, seromucous, and serous glands.<sup>3</sup> The small arteries, arterioles, and arteriovenous anastomoses determine regional blood flow. Capacitance vessels, consisting of veins and cavernous sinusoids, determine nasal patency. Constriction and relaxation of these venous capacitance vessels is regulated by the sympathetic nervous system. The cavernous sinusoids lie beneath the capillaries and venules, are most dense in the inferior and middle turbinates, and contain smooth-muscle cells controlled by the sympathetic nervous system. Loss of sympathetic tone or, to a lesser degree, cholinergic stimulation causes this sinusoidal erectile tissue to become engorged. Cholinergic stimulation causes arterial dilation and promotes the passive diffusion of plasma proteins into glands and the active secretion by mucous glands in cells.

Novel neurotransmitters, including substance P, calcitonin gene-related peptide, and vasointestinal peptide, have been detected in nasal secretions after nasal allergen challenge of patients with allergic rhinitis.<sup>4</sup> Antidromic stimulation of sensory nerve fibers in the nose can release a variety of neurotransmitters including substance P, a mediator of increased vascular permeability. Because neurotransmitters also produce changes in regional blood flow and glandular secretion, their role in rhinitis may be important.

#### ORIGINS OF NASAL RESISTANCE

Nasal patency is predominantly controlled by changes in the capacitance vessels. Nasal airway resistance is responsible for approximately two thirds of the total airway resistance.<sup>5</sup> Primary sites of nasal obstruction to airflow include the nasal vestibule, the nasal valves, and the nasal turbinates (Fig 1).

The nasal valve, the location of minimal cross-sectional area of the nares, contributes most to total nasal resistance (NR). The entire nasal valve area resembles an inverted cone. It is bounded by the nasal septum medially, posterior end of the upper lateral cartilage, piriform aperture (lateral fibrofatty tissue, frontal process of the maxilla, floor of the nose), and the anterior head of the inferior turbinate

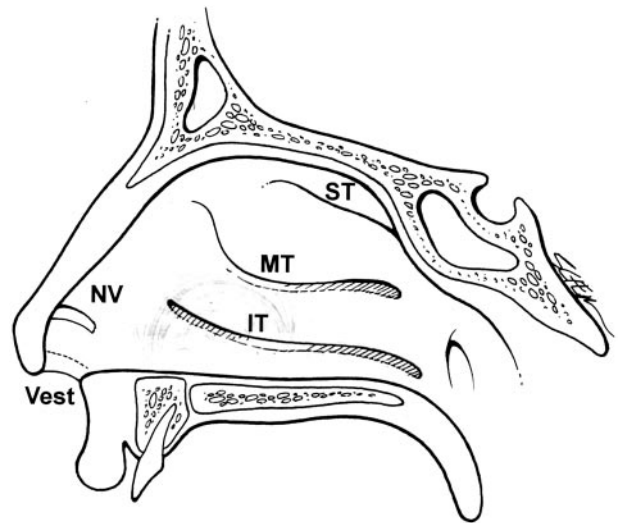


FIGURE 1. Cross-section of nasal cavity. Vest = nasal vestibule; NV = nasal valve; IT = inferior turbinate; MT = middle turbinate; ST = superior turbinate.

posteriorly.<sup>6</sup> This functional complex of compliant and dynamic tissues covers a distance of several millimeters. The valve lumen is regulated by lateral and medial erectile mucosa, modulated laterally by the tone of alar muscles, and stabilized by bone and cartilage. Septal erectile tissue, although not readily recognizable endoscopically, is clearly demonstrated by CT and histologically in cadaver studies.<sup>7,8</sup>

NR is greatest during infancy, decreases with age, and is primarily controlled by vascular engorgement in the middle and inferior turbinates.<sup>9</sup> Exercise increases sympathetic discharge, which vasoconstricts the nasal capacitance vessels thereby decreasing nasal airflow resistance.<sup>10,11</sup> Similarly, sympathomimetic medications, such as oxymetazoline, decrease nasal congestion via topical vasoconstriction.<sup>12</sup>

The physiologic variation in nasal patency, known as the *nasal cycle*, is mediated by changes in the engorgement of the submucosal capacitance vessels in the middle and lower turbinates. The magnitude of NR alternates between the two nasal cavities every 2 to 4 h in 60 to 70% of healthy individuals.<sup>11,13</sup> Posture also influences the degree of vascular congestion. Nasal obstruction increases bilaterally as a subject assumes the supine position, and increases in the dependent nasal passage in the lateral recumbent position.<sup>14</sup> This may have implications in the development of SDB in susceptible individuals.

#### CLINICAL SYNDROMES ASSOCIATED WITH SYMPTOMS OF NASAL OBSTRUCTION

Symptoms of nasal obstruction include stuffiness, congestion, pressure, or difficulty breathing through

one or both nasal passages. The nasal obstruction may result from a variety of anatomic abnormalities and rhinitis (Table 1).<sup>15</sup> In rhinitis, symptoms result from dilation of venous capacitance vessels in the nasal submucosa, mucosal edema, and excess secretions.

Syndromes of rhinitis may be divided into acute, allergic, infectious, perennial nonallergic, and miscellaneous categories (Table 2).<sup>16</sup> Allergic rhinitis is a symptom complex characterized by paroxysms of sneezing; itching of the eyes, nose, and palate; rhinorrhea; and nasal obstruction. Between 10% and 20% of the US population is affected, and the prevalence in urban areas is increasing. The prevalence is lowest in children < 5 years old, rises to a peak in early adulthood (as high as 24% in the United States), and declines thereafter.<sup>17</sup> It is often associated with postnasal drip, cough, irritability, and fatigue. The swollen nasal mucosa of patients with acute allergic rhinitis is pale and blue but becomes erythematous and indurated with chronic allergen exposure.<sup>18</sup> Symptoms develop when persons inhale airborne antigens (allergens) to which they have been previously exposed and have made IgE antibodies. These include cat salivary proteins, horse dander, murine urinary proteins, pollens, house dust mite feces, and mold spores. These IgE antibodies bind to IgE receptors on mast cells in the respiratory mucosa and to basophils in the peripheral blood. When IgE molecules on their surface are bridged by allergen, mast cells release preformed, granule-associated chemical mediators. They also generate other mediators and cytokines that lead to nasal inflammation and, with continued allergen exposure, chronic symptoms.

Two to 6 h after the initial allergen exposure, symptoms may recur with a second release of mast cell mediators coincident with maximum mast cell cytokine production. This late-phase nasal allergic reaction occurs in approximately 50% of patients with seasonal rhinitis undergoing nasal challenge

**Table 1—Anatomic Abnormalities Causing Nasal Obstruction**

Septal deviation
Nasal polyps
Concha bullosa
Choanal atresia
Neoplasms
Granulomatous disease (eg, sarcoidosis, Wegener granulomatosis)
Hypothyroid myxedema
Adenoid hypertrophy
Meningocele
Foreign body
Postoperative/posttraumatic synechiae

**Table 2—Syndromes of Rhinitis\***

Allergic
Acute
Seasonal
Perennial
Occupational
Infectious
Acute (viral, bacterial)
Chronic
Specific: bacterial, fungal
Nonspecific: associated with immune deficiency
Perennial nonallergic
Idiopathic (vasomotor rhinitis)
NARES
Miscellaneous forms
Hormonal: pregnancy, hypothyroidism, etc.
Drug induced: associated with aspirin sensitivity, rhinitis medicamentosa, antihypertensives, etc.
Food associated: gustatory, IgE mediated, preservative induced
Atrophic rhinitis ( <i>Klebsiella ozaenae</i> )
Mechanical: hypertrophied turbinates, deviated nasal septum, foreign body, nasal polyps
Granulomatous: Wegener granulomatosis, sarcoidosis, midline granuloma

\*Adapted from Dykewicz and Fineman.<sup>16</sup>

with allergen. This is associated with elevated levels of the same mediators noted in the immediate reaction except that prostaglandin D<sub>2</sub> is not detected. This inflammatory response is thought to cause the recurrence of symptoms and to induce chronic symptoms, especially chronic nasal obstruction.

Nonallergic rhinitis with nasal eosinophilia syndrome (NARES) occurs in as many as 15% of patients with rhinitis. It is characterized by perennial symptoms, an older average age than in patients with allergic rhinitis (39 years vs 25 years), and less nasal itching and sneezing.<sup>19</sup> Formation of IgE to inhalant allergens is unusual. The clear nasal secretions contain > 25% eosinophils. Fifty percent of patients with NARES have sinusitis, 33% have nasal polyps, and 14% have asthma.

Vasomotor rhinitis is a common form of perennial nonallergic rhinitis associated with chronic nasal congestion intensified by rapid changes in temperature and relative humidity, odors, or alcohol consumption. Several lines of evidence suggest that symptoms result from nasal autonomic nervous system dysfunction. Patients have little nasal itching or sneezing and often no family history of allergy, but headaches, anosmia, and sinusitis are common. Positive immediate hypersensitivity skin test responses to inhalant allergens and nasal eosinophilia are unusual.

Atrophic rhinitis is a syndrome of progressive atrophy of the nasal mucosa in elderly patients who

experience chronic nasal congestion and perceive a bad odor. Rhinitis medicamentosa develops after chronic use of vasoconstrictor nasal sprays or intranasal cocaine abuse; patients have chronic nasal obstruction and nasal inflammation manifest as beefy red nasal membranes on physical examination. Nasal obstruction may also be a side effect of antihypertensive drugs especially those with vasodilatory capacity. Rhinitis of pregnancy and rhinitis associated with birth control pills or hypothyroidism reflect nasal obstruction that occurs on a hormonal basis. The coexistence of nasal polyps with rhinitis suggests chronic sinusitis, aspirin hypersensitivity, coexistent allergic fungal sinusitis, or cystic fibrosis.

#### CORRELATION OF NASAL OBSTRUCTION WITH SYMPTOMS AND MEASUREMENT

There are several clinical paradoxes concerning nasal obstruction. Symptoms of nasal obstruction often correlate poorly with actual resistance to airflow. For example, patients who have atrophic rhinitis following extensive turbinate resection may perceive nasal obstruction despite objective evidence of excellent nasal patency. Some patients may have significant nasal mucosal edema or nasal polyps but report no symptoms of nasal obstruction.<sup>15</sup> The distribution of ventilation between mouth and nose in patients with allergic rhinitis may not correspond to the degree of nasal obstruction.<sup>20</sup> Mouth breathing, particularly in children, does not always signify severe nasal obstruction.<sup>21</sup> Nasal congestion measured subjectively by symptom score or by direct visualization is imprecise.

The “sniff test” observation of a single forced inhalation through the nose is unreliable as a clinical method of assessing nasal airflow because of nares alar collapse in some patients<sup>11</sup>; however, obstruction of nasal airflow is suggested on physical examination by audible nasal congestion as a patient inhales forcibly through the nose. The patency of each nasal passage may be assessed individually as the patient sniffs while the clinician compresses the contralateral nostril. Structural or dynamic assessment of nasal obstruction often clarifies the clinical impression or symptomatic report of nasal obstruction. A number of tests have been used to provide quantitative and qualitative data on nasal obstruction and nasal airflow. In order to interpret the literature of SDB, a review of these other tests is required.

#### ASSESSMENT OF NASAL AIRWAY STRUCTURE

Structural abnormalities of the nose may be evaluated objectively by clinical examination, fiberoptic

rhinoscopy, rhinostereoscopy, or radiologic studies (CT and MRI). Details of the radiographic evaluation of the nose will not be reviewed here.

Fiberoptic rhinoscopy, the insertion of a flexible telescope into the nasal cavity, allows the detailed visualization of the posterior two thirds of the nose not visible with a nasal speculum inserted into the anterior nares. The procedure is generally well tolerated, and has particular clinical value when nasal obstruction is persistent or unilateral and whenever direct visualization of the nasal passages and the pharynx might facilitate diagnosis.<sup>22,23</sup>

Rhinoscopy has limitations since it is unlikely to detect structural or mucosal displacement of the medial or lateral wall of the nasal valve < 1 mm, a distance that nonetheless may exponentially affect nasal resistance or patency. These changes in resistance and airflow are readily detectable by rhinomanometry<sup>24,25</sup> or acoustic rhinometry (see below). Rhinostereoscopy uses a precise surgical microscope to make direct and noninvasive topographic measurements of the nasal mucosa. This technique is reviewed elsewhere.<sup>9,26</sup>

#### ASSESSMENT OF NASAL AIR FLOW AND RESISTANCE

Dynamic measurements of nasal congestion include nasal peak flow, rhinomanometry, and acoustic rhinometry. Each procedure has its limitations, but most have diagnostic sensitivities between 80% and 95% for nasal obstruction<sup>9</sup> (Table 3).

##### *Nasal Peak Flow*

Nasal peak flow test is inexpensive, easy to perform, and may have potential use in outpatient clinical trials or for home assessment of daily variations in nasal obstruction<sup>27,28</sup>; however, it is highly effort dependent, and results may vary widely, especially between patients.<sup>29</sup> This technique involves measuring the peak inspiratory nasal airflow with a modified peak flow device (*eg*, In-check nasal inspiratory flowmeter; Clement Clarke; Harlow, UK). Although peak flows do not measure resistance, nasal

**Table 3—Assessment of Nasal Airway Flow**

Structural
Dynamic
Nasal peak flow
Rhinomanometry
Acoustic
Chilled mirrors
Oscillometry

peak flow measurements correlate well with measurements of resistance and have their greatest usefulness in the detection of large changes in nasal patency in individual subjects.<sup>30</sup>

### Rhinomanometry

Since air flows from an area of high pressure to an area of low pressure, pressure gradients and flow measurements may be used to calculate NR. Rhinomanometry, the measurement of nasal airway resistance, is probably the test most frequently performed because it measures both flow and resistance. It is classically divided into passive or active phases, and into anterior or posterior rhinomanometry. Active rhinomanometry requires the subject to generate airflow through the nose by their own effort. Passive rhinomanometry utilizes external generation of a constant flow of air at a given pressure and requires no respiratory effort. Active rhinomanometry is a quick test to perform, and the International Committee on Standardization of Rhinomanometry recommends it for most studies.<sup>9,31</sup> Anterior and posterior rhinomanometry primarily differ in the location of the transducer used to measure posterior pharyngeal pressure. Anterior rhinomanometry may be affected by deformation of the anterior nares and/or valves, nasal cycling, and by the instrument inserted to the nares for measurement.<sup>11</sup> Posterior rhinomanometry does not have these disadvantages, but is more expensive and requires more patient cooperation, with approximately 15% of subjects being unable to place the probe properly in the oral cavity.<sup>32</sup> Despite these drawbacks, it is an excellent tool for determining the degree of airflow obstruction before and after surgical procedures and medical interventions (Table 4). It may also help to distinguish functional causes of upper airway obstruction from structural causes. For example, decongestants or exercise will improve airflow due to inflammation and vascular engorgement, whereas fixed abnormalities such as concha bullosa do not change after exercise or decongestants.<sup>33</sup> Rhinomanometric measurements before and after treatment with a potent intranasal decongestant agent are recommended.<sup>16,31</sup>

### Acoustic Rhinometry

Acoustic rhinometry, a technique used widely in Europe, evaluates nasal obstruction by analyzing reflected sound waves introduced through the nares.<sup>34–36</sup> It is generally easy to perform, is non-invasive, and does not require patient cooperation like many of the other evaluation procedures. It produces an image that reflects variations in the cross-sectional dimensions of the nasal cavity and

**Table 4—Indications and Clinical Uses for Rhinomanometry**

Objective measurement of subjective symptoms of rhinitis
Allergic rhinitis
Nonallergic rhinitis
Distinguish functional causes of nasal obstruction from structural causes
Measure therapeutic response to specific therapy
Medical
Antihistamines
Decongestants
Anti-inflammatory therapy
Allergen-specific immunotherapy
Immunomodulation
Surgical
Adenoidectomy
Nasal polypectomy
Turbinectomy
Rhinoplasty
Septum repair
Assessment of anatomic variation
Determine response to nasal provocation
Evaluate upper airway resistance in obstructive sleep apnea
Medicolegal evaluation and documentation
Evaluate functional or suspected psychosomatic nasal complaints

closely approximates nasal cavity volume and minimal cross-sectional area. The short measurement period (10 s) makes this procedure easy to use in all patients, even children.<sup>37</sup> The results of parallel determinations by acoustic rhinometry and rhinomanometry are comparable<sup>38</sup>; however, nasal airway resistance cannot be easily computed from acoustic rhinometry data. Acoustic rhinometry has been reviewed in detail elsewhere.<sup>30</sup>

### Other Dynamic Methods To Measure Nasal Patency

Chilled mirrors or other polished surfaces have been used for more than a century to detect asymmetry in nasal expiratory airflow. The patient exhales through the nose against a polished surface held close to the nostrils, and dimensions of the two resulting areas of condensation are noted and compared. Camera recordings of thermographic surfaces or calibration by concentric markings on the condensing surface enhances this technique.<sup>29</sup>

Oscillometry measures impedance in order to calculate NR. A loudspeaker is applied first to the nostrils and then to the mouth to generate sinusoidal oscillations that are superimposed on normal breathing. The difference between the two impedance measurements provides data for resistance calculations.<sup>39</sup>

In summary, symptoms of nasal congestion often correlate poorly with actual resistance to airflow. Structural or dynamic assessment of nasal obstruc-

tion often clarifies the clinical impression or reported nasal symptoms. A number of diagnostic options are available. Fiberoptic rhinoscopy permits direct, three-dimensional visualization of the nasal passages, and is generally well tolerated. CT, MRI, and rhinostereoscopy (where available) provide greater structural detail.

Nasal congestion as evaluated by symptom score or by direct visualization is unreliable and highly variable. Measurement of nasal peak flow is inexpensive and has the potential advantage of permitting home assessment of nasal obstruction to airflow. It also may be more sensitive to mucosal changes than rhinomanometry.<sup>40</sup> An abnormal peak flow should prompt consideration of more detailed studies, such as rhinomanometry or acoustic rhinometry. Unlike nasal peak flow measurements, rhinomanometry is not effort dependent and measures nasal resistance as well as airflow. Rhinomanometry has been used previously to evaluate SDB (see below).

## SDB

SDB is a spectrum of breathing abnormalities related to increased airway resistance that includes snoring, the upper airway resistance syndrome (UARS), and the OSAS. Snoring and OSAS are common. Snoring affects 19 to 37% of the general population and > 50% of middle-aged men.<sup>41</sup> The estimated prevalences of OSAS in men and women are 9% and 4%, respectively.<sup>42</sup> The prevalence of UARS in the adult general population is unknown, but has been estimated to be as high as 10 to 15% as defined by adults with snoring and excessive daytime sleepiness (EDS).<sup>43</sup>

### Snoring

Snoring is sound generated from the upper airway due to vibration of the uvula and soft palate. It occurs during inspiration, and rarely in expiration.<sup>44</sup> Snoring is associated with changes in the caliber of the upper airway, which reduces flow and increases airway resistance. These changes may not be significant enough to produce clinical symptoms or create disruption in sleep.<sup>45</sup> Snoring under these circumstances is termed *primary snoring*. When it occurs in conjunction with disordered sleep, it may be associated with symptoms that range from daytime sleepiness to severe OSAS with nocturnal hypoxemia and multiple cardiovascular effects.

Snoring and OSAS are thought to represent opposite ends of a continuum of SDB; however, snoring may actually represent a distinct comorbidity. Support for this concept is found in the characterization of sleep-related breathing disorders with clinically

significant symptoms that occur in the absence of snoring.<sup>46</sup> To date, there has been no study that conclusively demonstrates an evolution from snoring to OSAS. Also, studies have shown improvement in snoring but not OSAS following upper airway surgery. These combined factors lend weight to the concept of snoring as a discrete condition, which may have additive or synergistic effects on SDB.

### UARS

The UARS is characterized by sleep-related flow limitation and increases in upper airway resistance that precipitates arousals resulting in fragmented sleep and EDS.<sup>47</sup> By definition, these alterations occur without apneas or desaturations. This term was first applied to patients who had EDS defined by a shortened mean sleep latency on a multiple sleep latency test, without clear cause documented by overnight polysomnography.<sup>48</sup> These patients were assumed to have idiopathic hypersomnia. Utilizing “invasive polysomnography” with an esophageal pressure (Pes) transducer and full-face pneumotachograph increased upper airway resistance as demonstrated by increasingly negative inspiratory Pes in conjunction with reduced oral/nasal airflow.

UARS events are typically short (one to three breaths), with EEG arousals and immediate reduction in upper airway resistance after arousal. Such events are termed *respiratory effort-related arousals*. Generation of negative intrathoracic pressure seems to be the physiologic change that causes arousal. The mechanoreceptors associated with arousals may be located in the upper airway, as topical anesthetic applied to this area has been shown to create more negative Pes and to delay arousal times.<sup>49,50</sup>

### OSAS

Like UARS, patients with OSAS also display sleep fragmentation and EDS. The clinical manifestations are typically more severe and include both “hypopneas” in which there is partial collapse of the upper airway with either an arousal or oxygen desaturation for 10 s, or “apneas” resulting in complete collapse of the upper airway for 10 s. Oxygen desaturation in OSAS can be quite severe.

The primary site of airway collapse is the posterior pharynx, an area of minimal bony support, which relies on musculature for patency. Patients with OSAS have been shown to have smaller airways, but no particular minimal airway predictive volume of OSAS has been determined. Increased muscle tone during waking hours prevents obstruction while the subject is awake. Collapse occurs with the onset of sleep and relaxation of this support.<sup>51</sup> The differences between gender, men having a higher preva-

lence than women particularly prior to female menopause, is thought to be related to less upper airway compliance (more rigidity) in women, perhaps an effect of female sex hormones.<sup>52</sup> As the apnea continues, desaturation occurs, inducing hypoxemia, vasoconstriction of the pulmonary vascular bed, and increase in pulmonary artery pressures. Upper airway obstruction prevents inhalation but exhalation continues, further reducing lung volumes and worsening desaturation. Attempted inspiration against the obstruction further decreases intrathoracic pressure, which eventually triggers a central arousal<sup>53</sup> and stimulates the sympathetic nervous system. Heart rate and BP both rise in response,<sup>54</sup> and oxygen saturation improves but may not return to baseline before the next apneic episode.

### Diagnosis of SDB

The diagnosis of SDB is usually based on overnight polysomnography, where a variety of physiologic parameters are monitored in an attended laboratory setting. These parameters typically include the following: EEG, electromyography (EMG) of chin and legs, electrooculography, nasal and oral airflow or pressure, chest and abdominal effort, ECG (lead II), and oxygen saturation. Some sleep laboratories also monitor snoring with a snore microphone, end-tidal carbon dioxide, EMG of the masseter muscle, and EMG of intercostal muscles. The patient will usually stay overnight in the sleep laboratory for a minimum of 6 to 7 h for data accumulation. The polysomnogram is then examined for sleep stages utilizing the EEG, electrooculography, and chin EMG channels; respiratory events utilizing the airflow or nasal pressure channel, effort channels, and oximetry; arrhythmias; and body movements. Arousals and awakenings from sleep are also quantitated. An arousal is scored when there is a shift in the EEG to an  $\alpha$  or  $\theta$  rhythm for 3 s.<sup>55</sup> An awakening is scored when these  $\alpha$  or  $\theta$  waves persist for > 15 s.

From these calculations, an assessment can be made as to the degree of sleep disruption that

occurred during the study and the severity of SDB. Sleep disruption can be assessed in a number of ways, including the following: the arousal index (the number of arousals per hour of sleep), the number and frequency of sleep stage changes, the percentage of time spent in stage 1 (light sleep) or stage 0 (awake), the sleep efficiency (amount of time asleep divided by amount of time recorded), and the time spent awake after sleep onset. Most sleep laboratories calculate an apnea-hypopnea index (AHI) to assess SDB severity. This index is the number of apneic episodes plus the number of hypopneic events divided by the total sleep time as measured in hours. An AHI > 5 is considered abnormal. Decisions about treatment revolve around the degree of SDB and the amount of sleep disruption.

### RELATIONSHIPS BETWEEN THE NOSE AND SDB

Only a few studies have examined the relationship of increased NR and SDB. Anecdotal evidence for a relationship between nasal obstruction, impaired sleep, memory loss, and excessive daytime somnolence were first noted in the 1800s (Table 5).<sup>56,57</sup> These observations triggered other studies evaluating the relationship of the nose and SDB. These studies will be reviewed here by the different patient populations studied: normal control subjects, patients with increased NR, patients with SDB including snorers, and children.

#### Normal Control Subjects

Several studies have been performed in normal volunteers to elucidate the effect of nasal obstruction, nasal dilation, and nasopharyngeal anesthesia on upper airway responsiveness and/or sleep. When humans sleep, the muscle tone in the oropharynx and muscle responsiveness to stimuli decrease. There is evidence to suggest that receptors in the nasopharynx may have an effect on muscle tone in

**Table 5—Studies Evaluating the Relationship Between Nasal Obstruction and SDB: Early Data**

Source/Year	Study Population	Source of Obstruction	Conclusions
Carpenter <sup>56</sup> /1892	Not described	Nose	Disturbed sleep, insomnia, nightmares, impaired intellect and memory were attributed to nasal obstruction
Wells <sup>57</sup> /1898	10 patients (8 with EDS)	Nose	Correction of nasal obstruction relieved EDS
Luke et al <sup>58</sup> /1966, Lubart <sup>59</sup> /1968, Levy et al <sup>60</sup> /1967	Pediatric	Nose and hypertrophied adenoids	Adenoidal obstruction may cause cor pulmonale; cor pulmonale was relieved after adenoidectomy
Cottle <sup>61</sup> /1978	Not described	Nose	"Nasal nocturnal syndrome": breathing difficulty when supine, restless sleep, sudden awakening, gasping respirations, and snoring

the oropharynx. White et al<sup>62</sup> examined the effects on sleep of blocking nasal receptors using 4% lidocaine local anesthesia, which was sprayed into the nose and the nasopharynx in a carefully controlled study of 10 male subjects. Administration of lidocaine increased nasal and pharyngeal obstruction and was associated with a fourfold increase in SDB events. This included an equal number of obstructive and central apneas. These results suggest that nasal receptors are sensitive to airflow and may be important in maintaining respiratory rate and upper airway patency.

These findings were supported in another study,<sup>63</sup> which measured minute ventilation during obligate nasal or mouth breathing in normal subjects during sleep. Ventilation was greater with the nasal breathing, supporting the notion that nasal airflow has a stimulant effect on breathing. Centrally controlled airway tone (phasic activity) of the upper airway is higher with nasal breathing than oral breathing.<sup>64</sup>

Another study<sup>65</sup> examined the effects of topical vasoconstrictors on sleep. Phenylephrine sprayed into the nasopharynx and oropharynx decreased both NR and pharyngeal resistance in normal subjects. The decrease in pharyngeal resistance was independent of the change in NR and upper airway muscle activity, suggesting that the de-

crease was a direct effect of phenylephrine on the pharyngeal mucosa; therefore, vasoconstriction of the tissues of the nasopharynx does not have a significant effect on the patency of the pharyngeal airway in normal subjects.

Several studies have investigated the effects of experimental nasal occlusion on sleep in normal subjects (Table 6). In four of five such studies,<sup>66-68,70</sup> nasal occlusion was induced immediately prior to sleep. In the other study,<sup>69</sup> nasal occlusion was induced during the entire day prior to, and during, the sleep study. The participants in all these studies had disturbed sleep as manifested by increased arousals and/or awakenings, frequent sleep stage changes, and less stage III and IV sleep. In those studies that monitored for SDB, participants also had increased SDB with apneas and/or hypopneas associated with EEG arousals.

Taken together, these studies on normal subjects support the notion that nasal breathing increases ventilation by stimulation of certain receptors in the nasal airway. Dilating the nasal airway does not necessarily change the patency of the oral airway; however, occluding the nasal airway may produce decreased patency of the oropharynx. Thus, nasal obstruction may trigger the induction of SDB even in normal individuals.

**Table 6—Studies Evaluating the Relationship of Artificially Induced Nasal Occlusion and SDB\***

Source/Year	Study Population	Technique of Nasal Occlusion	Observations	Effect of Nasal Occlusion
Zwillich et al <sup>66</sup> /1979	7 normal adults	Balloon-fitted nasal cannula	Full-night PSG (with or without nasal obstruction)	Disturbed sleep: increased awakenings; frequent stage changes; increase in apnea (tenfold in 3)
Zwillich et al <sup>67</sup> /1981	10 normal men (25 to 45 yr old)	2 hollow plastic cylinders	Full-night PSG (with or without nasal obstruction)	Decreased stages III and IV, two increase in apnea associated arousals/awakenings
Olsen et al <sup>68</sup> /1981	8 normal men	Petroleum jelly and cotton	Full-night PSG (with or without nasal obstruction, ENT examination, complete PFT)	Increased SDB events, awakenings, REM latency, stage I, sleep stage changes; 1 subject had frank obstructive sleep apnea
Lavie et al <sup>69</sup> /1983	10 normal adults (5 men)	Adhesive tape on nostrils	PSG: baseline, 2 nights with one nostril occluded, 2 nights with both nostrils occluded	Increased apneas and microarousals with nonapneic breathing
Wilhoit and Suratt <sup>75</sup> /1987	7 normal men	Petroleum jelly and gauze	Full-night PSG (with or without nasal obstruction)	Increased SDB in all, increased EMG activity in alae nose and genioglossus
Lavie and Rubin <sup>71</sup> /1984	10 healthy adults (6 sons of sleep apnea patients, 4 age-matched control subjects)	Adhesive tape on nostrils	PSG: adaptation night, baseline and nasal occlusion. Control subjects studied 4 nights (2 with nasal occlusion)	Increased apneas in sons of obstructive sleep apnea patients compared to control subjects

\*PSG = polysomnography; ENT = ear, nose, and throat; PFT = pulmonary function testing; REM = rapid eye movement.



## Patients With Abnormal NR

Several reports evaluated the effects of increased NR secondary to an anatomic obstruction or to nasal inflammation like that seen in allergic rhinitis. Increased NR (using a pediatric feeding tube to measure transmural pressure) in awake, upright subjects was not predictive of SDB in 683 patients referred for evaluation of SDB<sup>72</sup>; however, epidemiologic studies<sup>73</sup> of middle-aged adults have shown that complaints of nasal congestion, particularly nocturnal nasal congestion, are a strong independent risk factor for habitual snoring. Similarly, patients with complaints of nasal congestion due to allergy have been reported to be 1.8 times (odds ratio) more likely to have moderate-to-severe SDB compared to those without symptomatic nasal congestion.<sup>74</sup> This group of articles suggests that the presence of nasal congestion may predispose patients to OSAS even though actual measurements of NR are not abnormal.

Two studies<sup>70,76</sup> evaluated patients with anatomic nasal obstruction before and after surgery for nasal septal deviation. These patients consistently exhibited a worsening of sleep quality, increased SDB, and frequent oxygen desaturation postoperatively compared to preoperatively, in association with the attendant nasal packing. Short-term packing of the nose therefore can clearly result in SDB. It cannot be determined from this short-term trial whether this effect would continue over time if nasal obstruction persisted or if adaptive changes would occur.

The chronic eosinophilic mucosal inflammation associated with allergic rhinitis results in nasal obstruction and increased NR. Although clinicians are aware that allergic rhinitis results in sleep disruption and fatigue, there are few studies investigating its role in SDB (Table 7). Two studies<sup>77,78</sup> showed that exacerbations of allergic rhinitis cause an increase in SDB and sleep disruption. A third, placebo-controlled study<sup>79</sup> showed treatment of allergic rhinitis with nasal steroids resulted in significant subjective improvement in sleep quality.

These studies suggest that, although objective measures of NR cannot predict SDB, individuals with symptoms of nasal congestion have more snoring and SDB. Allergic rhinitis, when active, may result in poor sleep quality and SDB that improves with treatment. These findings may explain the symptoms of fatigue so common in patients with allergic rhinitis, and explain data showing an increased quality of life in patients treated for allergic rhinitis.<sup>80–82</sup>

## Patients With SDB

The studies in this section will deal with SDB in the form of snoring, UARS, and OSAS. Some of the studies chose to specifically differentiate these types of SDB and are noted with such designations herein.

In one study mentioned above,<sup>72</sup> there was no correlation between upright, awake NR and the degree of SDB in patients referred for SDB.<sup>72</sup> A second study<sup>83</sup> measured NR in 36 patients with

**Table 7—Studies Evaluating the Relationship Between Adult Allergic Rhinitis and SDB\***

Source/Year	Study Population	Diagnostic Method	Observation	Conclusion
Lavie et al <sup>77</sup> /1981	14 patients (9 males) 7 normal controls	Anamnesia about duration of disease, sneezing and nasal discharge, ENT examination; nasal smears for eosinophil count	PSG for 2 nights	During exacerbation of allergic rhinitis: periodic breathing and microarousals
McNicholas et al <sup>78</sup> /1982	10 patients	Hypersensitivity to ragweed pollen (history, skin testing), excluded asthma, medications held	PSG for 2 nights: first during peak ragweed season (with symptoms), and 6 to 8 weeks later with no symptoms	During symptomatic phase of allergic rhinitis: higher NR, and increased obstructive apneas
Young et al <sup>74</sup> /2001	911 patients	History of allergy, hay fever causing nasal congestion, on allergy medication	PSG, questionnaire: EDS, sleep history; rhinometry	Nighttime nasal obstruction associated with allergic rhinitis caused EDS, snoring, nonrestorative sleep. Those with nasal congestion associated with allergic rhinitis are 1.8 times more likely to have SDB
Craig et al <sup>79</sup> /1998	20 patients	Positive skin test responses to perennial allergen	Nasal symptoms, subjective sleep, EDS during double-blind, placebo-controlled trial of nasal steroid vs placebo	Nasal congestion and subjective sleep improved in those treated with nasal steroid and not with placebo

\*See Table 6 for expansion of abbreviations.

OSAS using basal anterior active rhinomanometry in both upright and supine positions, and found 7 of 36 patients with abnormal upright NR, 9 of 36 patients with a normal upright but abnormal supine NR, and 20 of 36 patients with normal NR in both positions. There was no correlation between NR and AHI; however, two other studies<sup>84,85</sup> compared patients with either snoring or OSAS to normal subjects and found higher levels of NR in the SDB group as measured by rhinomanometry. In one study, the patients with SDB (both snorers and OSAS) switched from nasal to oronasal breathing during sleep more frequently.<sup>84</sup> The change to oronasal breathing has been postulated to increase the work of breathing and peripheral pulmonary resistance by triggering the “nasal-pulmonary” reflexes, and the end result is alveolar hypoventilation.<sup>86</sup> A study<sup>87</sup> of nasal flow volume loops in a group of patients with OSAS showed that the area under the flow volume loop independently contributed to the prediction of AHI as compared to normal subjects. These studies suggest that although the degree of NR is not predictive of SDB, the presence of increased NR may result in a switch to oronasal breathing during sleep, which further compromises the airway and increases work of breathing.

Nasal inflammation has been shown to be present in patients with OSAS compared to control subjects, as measured by nasal lavage before and after sleep. Increased numbers of cells, specifically neutrophils, and increased concentration of bradykinin-like and vasoactive intestinal peptide-like immunoreactivity were found in the absence of symptoms of rhinitis<sup>88</sup>; therefore, patients with SDB but without obvious symptoms of rhinitis may have increased concentration of inflammatory mediators in the nose.

Perhaps the best way to examine the role of NR in patients with SDB is to reduce the resistance and examine the effect on sleep and breathing. This has been done in a variety of ways. Mechanical nasal dilators are marketed to relieve snoring, and have been shown to have a similar effect on NR as measured by active posterior rhinometry as a topical decongestant (fenoxazoline hydrochloride).<sup>89</sup> Their effect on snorers without significant nasal pathology is unclear, as some studies<sup>90</sup> failed to demonstrate changes in SDB events or arterial oxygen saturation levels, while others<sup>91</sup> showed improvement in sleep quality, ease of breathing, and a decreased intensity of snoring. In patients with OSAS, one study<sup>92</sup> showed that only 4 of 21 patients with moderate-to-severe OSAS had a significant reduction in SDB events, while another study<sup>93</sup> showed no significant change in SDB events in a group of patients with

UARS. It appears that the overall effect on SDB with mechanical nasal dilators is likely small and inconsistent.

Dental prostheses have been used to treat all forms of SDB. These devices keep the upper and lower jaws opposed during sleep and advance the mandible forward. This prevents posterior movement of the mandible during sleep and increases nasal breathing. When evaluated in a group of snoring patients without symptoms of OSAS, one type of prosthesis did not alter the frequency or intensity of snoring or sleep quality or oxygen saturation despite decreasing SDB events<sup>94</sup>; from this one small study, it does not appear dental prostheses improve SDB by any effect on the nasal airway.

Reducing NR by surgical correction of nasopharyngeal anatomic obstruction has been examined by a number of investigators (Table 8). Surgical approaches have included correction of the nasal valve area, septoplasty, and turbinate reduction. Only one small study<sup>95</sup> ( $n = 6$ , no control subjects) examined the effect of correction of nasal valve obstruction, showing both subjective and objective improvement in snoring and daytime somnolence. Two uncontrolled studies<sup>96,98</sup> in patients with nasal obstruction showed that septoplasty or turbinate reduction had some positive effects on SDB. In one study,<sup>96</sup> 77% (47 of 113 patients) who snored had improvement or elimination of snoring postoperatively. The second study<sup>98</sup> involved patients with mild OSAS where cephalometrics (measurements made from a standardized lateral head radiograph) were performed preoperatively; patients with abnormal cephalometrics (increase in mandibular plane to hyoid, decreased posterior airspace, retroposition of mandible, or length of soft palate), implying a skeletal anatomic defect, did not respond to improvement of their nasal airway. In a study<sup>99</sup> of a diverse group of adults ( $n = 94$ ) and children ( $n = 55$ ) with SDB, who had a variety of surgical procedures (including uvulopalatopharyngoplasty, midline laser glossectomy, and nasal surgery), significant improvement (defined as 75% reduction in AHI or a postoperative AHI < 10) occurred in only 48% of adults.

Nasal surgery has been shown to decrease continuous positive airway pressure (CPAP) requirements in a group of patients with OSAS; however, the degree of SDB was not significantly improved and snoring improved in only 34%.<sup>100</sup> Radiofrequency treatment of turbinate hypertrophy in CPAP users was shown to subjectively improve nasal obstruction and self-reported CPAP adherence.<sup>101</sup>

It appears from this group of surgical series that surgical improvement of the nasal airway may be most effective to improve SDB in those patients without skeletal anatomic abnormalities. Surgery

**Table 8—Effect of Surgical Correction of Nasopharyngeal Obstruction on SDB\***

Source/Year	Surgical Procedure	Observation	Conclusion
Dayal and Phillipson <sup>95</sup> /1985	Nasal surgery for correction of nasal valve area (n = 6)	6 of 6 improvement in snoring, EDS, AHI postoperatively	Role of nasal surgery in mild obstructive sleep apnea needs further assessment
Fairbanks <sup>96</sup> /1985	Correction of nasal septum and turbinate deformity for chronic nasal obstruction (n = 113)	42% had preoperative snoring, 77% of snorers had postoperative elimination of snoring	Nasal obstruction contributes to snoring and surgical correction may relieve/decrease snoring
Series et al <sup>97</sup> /1992	Septoplasty, turbinectomy, polypectomy; all with obstructive sleep apnea (n = 20)	Nasal resistance decreased postoperatively, no difference in baseline and postoperative apneas or oxygen desaturations, AHI normalized in those with normal cephalometrics (n = 4)	Nasal surgery has limited efficiency in treatment of adult obstructive sleep apnea, role of preoperative cephalometrics remains to be determined
Series et al <sup>98</sup> /1993	Septoplasty, turbinectomy, polypectomy, all with obstructive sleep apnea (n = 14), patients matched by body mass index and AHI comparing normal and abnormal cephalometrics	Nasal resistance decreased equally in both groups, AHI < 5 in all but one with normal cephalometrics, AHI unchanged in those with abnormal cephalometrics	Normal cephalometrics may identify patients with mild obstructive sleep apnea with nasal obstruction who will benefit from surgery; craniofacial abnormalities make it unlikely that nasal surgery will improve obstructive sleep apnea
Nishimura et al <sup>99</sup> /1996	Children, adenoidectomy with or without tonsillectomy (n = 55); adults, UPPP with or without nasal surgery, midline laser glossectomy (n = 94)	35 children had AHI > 5, 30 had 75% reduction in AHI, 40 adults had 75% decrease in AHI, 18 adults showed no improvement	Children showed dramatic improvement with surgery; adults also responded but to a lesser degree

\*UPPP = uvulopalatopharyngoplasty.

also often improves snoring and decreases CPAP levels in patients with an abnormal nasopharynx.

### Children

A number of common features of childhood predispose to SDB. Allergic rhinitis is common in children, as is adenoidal and tonsillar hypertrophy. The latter is the leading cause of SDB in children, and corrective surgery is usually curative.<sup>102</sup> Nasal obstruction secondary to adenoidal enlargement may result in changes of the craniofacial structures during growth and development. These latter effects may have long-lasting consequences on craniofacial structures, and we postulate that they may predispose to SDB.

Epidemiologic studies have shown that children with habitual snoring frequently have allergies. Allergic sensitization, as assessed by radioallergosorbent test, has also been associated with increased prevalence of OSAS.<sup>103</sup> At least one study<sup>104</sup> has shown that treatment of allergic rhinitis in children with nasal steroids decreases SDB events without any change in adenoidal or tonsillar size. The long-term effects of allergic rhinitis on adenoidal and tonsillar size are unknown.

Adenotonsillectomy results in marked improvement of SDB in > 80% of children.<sup>102</sup> One study<sup>105</sup> showed that children with SDB have larger adenoids and tonsils (as measured by cephalometrics) than age-matched control subjects; interestingly, skeletal abnormalities appeared to also play a role, particularly in older children ( $\geq 5$  years old). These children had more protrusion of the maxilla (as measured by the angle measured from the sella to the nasion to subspinale; Fig 2). This suggests that adenoidal hypertrophy is a major factor for SDB in younger children (aged 1 to 4 years), in contrast to older children, where adenoidal hypertrophy and bony changes combine to increase risk. Another controlled study<sup>106</sup> in which cephalometrics were performed on children showed that the angle measured from the sella to the nasion to the supramentale and hyoid position was significantly less in SDB children than control subjects, even at an early age, and did not improve with aging. The authors suggested that genetic factors governing facial bone development may play a role in retrognathia in children with SDB. These skeletal changes often give a child a characteristic facial appearance, sometimes called *adenoid faces*. These children have a long, narrow face, a short upper lip, prominent upper incisor teeth, a high arched palate, and lips-apart mouth breathing.

Whether large adenoids lead to development of adenoid faces skeletal structure or preexisting abnor-

## CONCLUSION

SDB appears to result from several common pathways, including anatomic and neuromuscular abnormalities of the upper airway. Our review provides convincing evidence that there is an association between SDB and nasal obstruction. Available data suggest that nasal obstruction resulting from allergic rhinitis may precipitate SDB, at least in the short term.<sup>77-79</sup> Unfortunately, to date, there are no compelling data to demonstrate specific causality between nasal obstruction and persistent SDB. Most of the studies reviewed herein are either short-term, used odds ratios, or only examined subjective measures to analyze the effect on SDB. Clearly, further studies are needed to prove specific causality.

### *Future Directions*

Several theories have tried to explain the relationship between SDB and nasal obstruction. Of these, the following theories are most credible: (1) the switch from nasal to oronasal breathing (due to nasal obstruction) causes loss of nasal airflow resulting in decreased nasal receptor-derived stimulation of ventilation and changes in phasic activity leading to decreased upper airway patency; and (2) the increased nasal airway resistance (due to nasal obstruction) generates an increased negative inspiratory force/pressure causing turbulence in the relaxed soft tissues and upper airway collapse (retropharyngeal) resulting in upper airway obstruction and SDB.

These hypotheses are based on a few studies that have used varying methods and small numbers of study subjects and therefore require further confirmation. If this is found to be true, technologies and treatments aimed at facilitation of nasal breathing should be explored further in the context of SDB. In the interim, use of topical nasal steroids in patients with SDB and preferential use of nasal CPAP in treatment may be reasonable.

Longitudinal studies in children with nasal obstruction are required to determine the risk factors for SDB, including the relationship of nasal obstruction to structural abnormalities of the face and upper airway. It is possible that certain congenital variations in facial structures are deleterious to nasal breathing and exacerbated by nasal obstruction from other causes. Knowledge of these factors could be useful in preventing the development of SDB.

The effect of CPAP on the nasal airway is relatively unexplored. Anecdotally, it appears that CPAP may increase nasal inflammation and, in some, promote vasomotor rhinitis. It is possible this may lead to decreased adherence to treatment. This is another area in need of further research.

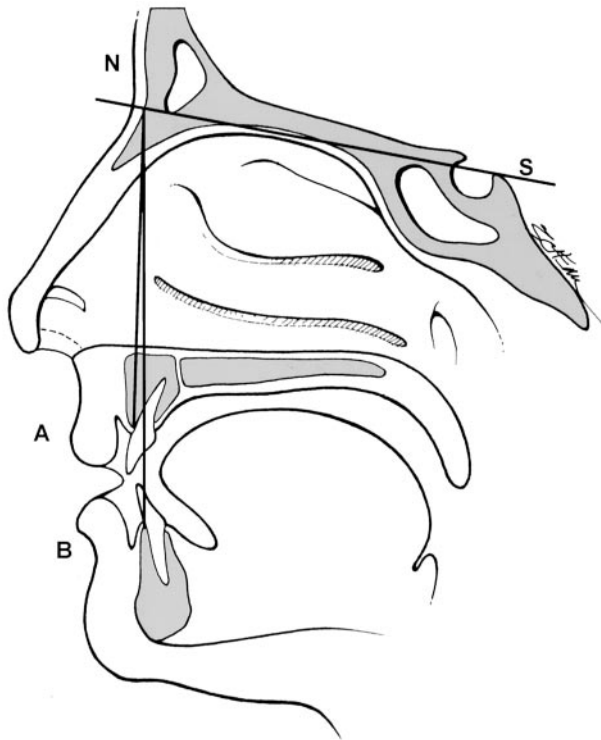


FIGURE 2. Cephalogram showing bony angles. S = sella; N = nasion; A = subspinale; B = supramentale.

malities of skeletal structure promote adenoidal hypertrophy has been investigated. Shintani et al<sup>105</sup> found that snoring in children with SDB started, on average, very early (22.7 months of age) and OSAS developed approximately 1 year later (34.7 months of age). The SDB group had maxillomandibular micro- or retrognathia, hyperdivergence, posterior rotation of the mandible, and adenotonsillar hypertrophy. Orthodontic examinations in the SDB group showed posterior cross bite, anterior open bite, and lip incompetence. These authors concluded that oral breathing causes the development of craniofacial abnormalities, and hypothesize that the continuous respiratory effort in the oral airway results in stretching of soft tissues that cause hyperextension of the head imposing a passive tension on the layers of soft tissue that cover the face and neck. The effect of this stretching unloads posterior and inferior forces on the facial skeleton that, over time, results in development of the “long-face morphology” (adenoid faces).

In children, obstruction of the upper airway by enlarged tonsils and adenoids clearly plays an important role in the pathophysiology of SDB, and may lead to growth characteristics of the bony structures that predispose to upper airway obstruction later in life. The association between SDB and allergic rhinitis appears strongest in children.

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