SNORING: CAUSES, DIAGNOSIS
AND TREATMENT
OTOLARYNGOLOGY RESEARCH ADVANCES SERIES

Handbook of Pulmonary Diseases: Etiology, Diagnosis and Treatment
Krisztián Fodor and Antal Tóth

Snoring: Causes, Diagnosis and Treatment
Eugene Lefebvre and Renaud Moreau
# CONTENTS

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Authors</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preface</td>
<td></td>
<td></td>
<td>vii</td>
</tr>
<tr>
<td>Chapter 1</td>
<td>Diagnostic Imaging Studies in Sleep-Disordered Breathing</td>
<td>Murat Songu and Zehra Hilal Adibelli</td>
<td>1</td>
</tr>
<tr>
<td>Chapter 2</td>
<td>Surgical Management of Sleep-Disordered Breathing</td>
<td>Murat Songu</td>
<td>31</td>
</tr>
<tr>
<td>Chapter 3</td>
<td>Snoring in Children: Controversies in Diagnosis and Treatment</td>
<td>Ioannis M. Vlastos and John K. Hajiioannou</td>
<td>63</td>
</tr>
<tr>
<td>Chapter 4</td>
<td>Staging of OSAHS: A Guide to Single Level or Multilevel Treatment</td>
<td>Michael Friedman and Meghan N. Wilson</td>
<td>87</td>
</tr>
<tr>
<td>Chapter 5</td>
<td>Breath of Life: Complexity and Heterogeneity in the Integration of Etiologic Components Associated with Sleep Disordered Breathing</td>
<td>G. Dave Singh and R. Chandrasekhar</td>
<td>109</td>
</tr>
<tr>
<td>Chapter 6</td>
<td>Snoring in Pediatric Patients</td>
<td>Marco Berlucchi and Piero Nicolai</td>
<td>127</td>
</tr>
<tr>
<td>Chapter 7</td>
<td>The Snoring Child: Questions are Many Answers are Few</td>
<td>Dawn Bolyard, Gayle Cavins, Michael Neeb and Ramalinga Reddy</td>
<td>141</td>
</tr>
<tr>
<td>Chapter 8</td>
<td>Intraoral Devices for the Management of Obstructive Sleep Apnea-Hypopnea</td>
<td>Daniele Manfredini and Luca Guarda-Nardini</td>
<td>151</td>
</tr>
<tr>
<td>Chapter 9</td>
<td>Snoring as a Symptom of Narrowing the Posterior Airway Space in Cleft Lip and Palate Patients with Velopharyngoplasty</td>
<td>Jan Rustemeyer</td>
<td>165</td>
</tr>
<tr>
<td>Chapter</td>
<td>Title</td>
<td>Authors</td>
<td>Page</td>
</tr>
<tr>
<td>---------</td>
<td>-------</td>
<td>---------</td>
<td>------</td>
</tr>
<tr>
<td>Chapter 10</td>
<td>Prevalence of Obesity in a Clinic Population with Obstructive Sleep Apnea Syndrome</td>
<td>Hrayr Attarian, Michelle Guignon, Rebecca White and Catherine Schuman</td>
<td>171</td>
</tr>
<tr>
<td>Chapter 11</td>
<td>Correlation of Neck Circumference with Severity of Obstructive Sleep Apnea in Women</td>
<td>Hrayr Attarian, Michelle Guignon, Rebecca White and Catherine Schuman</td>
<td>175</td>
</tr>
<tr>
<td>Chapter 12</td>
<td>Urological Aspects of Obstructive Sleep Apnea Syndrome</td>
<td>David Margel and Giora Pillar</td>
<td>179</td>
</tr>
<tr>
<td>Index</td>
<td></td>
<td></td>
<td>191</td>
</tr>
</tbody>
</table>
Snoring is a common symptom of airway obstruction, which is included in the spectrum of sleep-related breathing disorders. The manifestation may occur alone (primary snoring) or in association with other signs and symptoms such as rhinorrhea, hyponasal speech, cough, hypopnea, and sleep apnea. Furthermore, snoring in the pediatric population is increasing and has been identified as a primary health concern by the American Academy of Pediatrics. This increase has been associated with a rise in co-morbid disease processes such as asthma and allergies, lifestyle changes and increasing obesity in the pediatric population. This book examines the clinical picture, etiology, diagnosis and treatment of snoring in pediatric patients. A thorough review of the literature data on the efficacy of the different types of intraoral devices used in obstructive sleep apnea-hypopnea (OSAH) is also assessed, as well as the two common urological consequences in OSA patients, namely Erectile Dysfunction (ED) and nocturia. Other topics discussed in this book include the underlying etiologic factors associated with sleep disordered breathing (SDB), a review of diagnostic studies that have been used to assess upper airway anatomy in patients with sleep-disordered breathing and a discussion of a multi-disciplinary approach taken to address the interaction of etiological components associated with SDB, to identify the causative agent(s) in specific individuals seeking definitive resolution.

Chapter 1 - Sleep-disordered breathing (SDB) is a collective clinical term encompassing primary snoring, upper airway resistance syndrome (UARS), and obstructive sleep apnea (OSA). These syndromes currently are regarded to fall along a spectrum of severity concerning the same patophysiological condition. Primary snoring which is not accompanied by breathing impairment leads neither to sleep disturbances nor to increase in daytime sleepiness. Despite being a social problem, primary snoring does not necessarily affect a person’s physical health. In OSA there is, however, an imbalance between the forces dilating and occluding the pharynx during sleep. The muscle tone supporting the pharyngeal lumen is too low, and the inspiratory suction force, as well as the pressure of the surrounding tissue, which both narrow the pharynx, are too high. This results in termination of breathing (apneas) or reduced breathing phases (hypopneas). In UARS, an increase in respiratory arousals occurs in the absence of detectable apneas. On the contrary of primary snoring, OSA and UARS have an adverse effect on the daytime life quality. Major symptoms of OSA include intermittent snoring, daytime sleepiness and reduction in intellectual performance. Further symptoms are personality changes, impotence in men, morning headaches, and enuresis nocturna. The gold standard for the diagnosis of SDB is polysomnography (PSG). Though
helpful in identifying the individuals, PSG does not detect the site of obstruction. Currently, positive airway pressure (PAP) is considered the primary treatment of OSA [1]. Although highly effective, it is associated with low compliance rates. For this considerable group of patients in whom medical management alone has been of limited value, surgery becomes essential in the management algorithm.

Diagnostic studies have been used to assess upper airway anatomy in patients with this relatively frequent disorder. The aim is to reveal potential differences in upper airway anatomy and also to improve patient management and surgical treatment success. A diagnostic study, in order to be regarded as ideal, should identify individuals with sleep-disordered breathing, be cost-effective and readily available, and also should guide therapeutic as well as site-specific intervention with results that are predictable.

In this chapter, static radiologic imaging methods (lateral cephalometry, computed tomography scanning and magnetic resonance imaging) and dynamic scanning protocols (ultrafast CT or cine MRI) are discussed in detail.

Chapter 2 - Sleep-disordered breathing (SDB) is a spectrum of diseases, which includes snoring, upper airway resistance syndrome (UARS), obstructive sleep apnea-hypopnea syndrome (OSAHS), and obstructive sleep apnea (OSA). Contributing factors for SDB may involve physiologic, neurogenic, muscular, anatomic and developmental findings that demand a comprehensive evaluation before choosing the appropriate treatment.

The goals of the treatment of SDB should be aimed to reduce collapsibility and optimize the stability of the airway while decreasing morbidity and mortality. The nonsurgical management of SDB includes exercise, weight loss, decreased alcohol consumption, smoking cessation, altered sleeping position, and dental or nasal appliances [1]. It has been shown that weight loss improves and in some cases cures sleep-disordered breathing disorders and is clearly a low-morbidity treatment modality [2,3]. However, patient compliance has persistently been the drawback in these types of management. Studies reveal that over half the patients will not follow the conservative treatment or do not obtain sufficient relief from their snoring and look for surgical modalities to correct their problem [4]. Currently, positive airway pressure (PAP) is considered the gold standard treatment of OSA [5]. Although highly effective, it is associated with low compliance rates. Noncompliance has been categorized by Zozula as tolerance problems, psychological problems and lack of instruction, support, or follow-up [6]. Tolerance problems may be due to mask leaks, difficult exhaling, aerophagia, chest discomfort, bed partner intolerance or other side effects such as dry mouth, conjunctivitis, rhinorrhea, skin irritation, pressure sores, nasal congestion and epistaxis. Psychological problems include lack of motivation, claustrophobia, and anxiety. Certain interventions may promote compliance to PAP, such as correction of nasal obstruction, attention to mask-fit, desensitization for claustrophobia, heated humidification, patient education, regular follow-ups, compliance software, and support groups [7]. Despite these measures, PAP therapy remains a considerable challenge for many individuals with low compliance of 50% to 80% [8,9,10]; besides, 15% of patients refuse PAP after a single night’s use in the laboratory [11]. For this considerable group of patients in whom medical management alone has been of limited value, surgery becomes essential in the management algorithm. The rationale for surgical management of the upper airway is to alleviate or minimize the pathophysiologic derangements associated with upper airway obstruction. Surgery for SDB first became an area of study when Fujita [12] introduced the uvulopalatopharyngoplasty (UPPP) in 1981. Surgical management of snoring in adults
without evidence of obstruction has vast success but there is still no ideal surgical procedure for OSA. During the past decade, a variety of methods have been advocated for the surgical treatment of OSA but no single procedure has been proven to have the ideals that rationalize its singular use over other procedures.

In this chapter, current state of art in SDB, including preoperative assessment, surgical planning and postoperative management are discussed in detail.

Chapter 3 - Obstructive sleep disordered breathing in children is a relatively common problem, presenting in various ways, from primary snoring, without an observed decrease in quality of life, to obstructive sleep apnea with cognitive, cardiac and growth abnormalities. History, clinical examination, radiologic evaluations, sleep studies and other diagnostic modalities are reviewed. Since application and interpretation of these methods are not consistent in studies of snoring, a consensus on optimal treatment options has not been established.

Traditionally, adenotonsillectomy has long been the treatment of choice. Treatment failures or recurrences as well as the existence of causes and contributing factors other than adenotonsillar hypertrophy, like obesity, facial malformations, Down syndrome etc, have changed the concept of adenotonsillectomy as the ultimate cure. Several other treatment options have been proposed on their own or in combination. Continuous positive airway pressure, anti-inflammatory medications, maxillofacial and orthodontic treatments are reviewed suggesting the need of a multidisciplinary approach in some cases.

Finally, a diagnostic and treatment work up based on current evidence is proposed at the end of the chapter for otherwise normal children or children with specific conditions.

Chapter 4 - Obstructive sleep apnea/hypopnea syndrome (OSAHS) is often the result of obstruction at multiple anatomic sites. Nasal, palatal and hypopharyngeal obstruction, acting alone or in concert, are frequently identified as the cause of snoring and OSAHS. Even in cases where a single site is primarily involved, the increase in negative pressure may induce further obstruction in other areas. When surgical management of OSAHS is considered, a clear understanding of the complex relationship between the sites of obstruction is essential to surgical success. This article will review the concept of multilevel treatment based on clinical assessment. In addition to serving as a guide for clinical staging, it will review the published literature on the incidence of multilevel obstruction and the results of multilevel treatment.

Chapter 5 - Sleep disorders represent a spectrum of conditions including: upper airway resistance syndrome; snoring; and obstructive, central and complex sleep apnea *inter alia*. In the etiology of sleep disordered breathing (SDB), systemic and regional anatomical characteristics comply with physical laws, such as those pertaining to (non-laminar) fluid dynamics, as predicted by: Poiseuille’s law; the Reynold’s number; Bernoulli’s principle, and Newton’s second law of gravity. In addition, however, tissue properties adhere to physiologic laws such as Davis’ law and Wolff’s law. In this way, the upper airway can be regarded as the net functional space available for respiration during wakefulness and sleep, once these physical and physiologic laws have been complied with. Thus, an integration of the complexity and heterogeneity of the etiologic components associated with SDB is warranted. Therefore, the aim of this review is to delineate some of the underlying etiologic factors associated with SDB. These etiologic components can be simply classified as (1) Structural factors: such as cranial base morphology; nasal obstruction; maxillo-mandibular morphology (including malocclusion); hyoid bone position; and soft tissue hypertrophy (including craniofacial obesity), and (2) Systemic factors: such as genetic predisposition/defects
(including Ehlers-Danlos, Marfan and Floppy eyelid syndromes etc); central nervous systems anomalies (affecting the medulla oblongata, thalamus etc through infections, such as poliomyelitis, encephalitis etc); and specific neurodegenerative diseases, such as dementia or Parkinson's disease. Therefore, in the clinical management of sleep disorders a multi-disciplinary approach must be taken to address the interaction of etiologic components associated with SDB, to identify the causative agent(s) in specific individuals seeking definitive resolution.

Chapter 6 - Snoring is a common symptom of airway obstruction, which is included in the spectrum of sleep-related breathing disorders. The manifestation may occur alone (primary snoring) or in association with other signs and symptoms such as rhinorrhea, hyponasal speech, cough, hypopnea, and sleep apnea. In the latter condition, which is better known as obstructive sleep apnea syndrome (OSAS), patients present nighttime and daily behavioral signs and symptoms that can result, in extreme cases, in serious cardiovascular impairment (i.e., cor pulmonale). In a pediatric age, the most frequent cause of snoring is adenoid hypertrophy. This disorder is probably the most frequent disease occurring in children and, when associated with palatine tonsil hypertrophy, leads to OSAS. In the past, adenoid size was evaluated by lateral soft-tissue X-ray of the nasopharynx, although, at present, nasal endoscopy is considered the gold standard to assess adenoid hypertrophy. To date, adenoidectomy, which is the most frequent surgical indication in childhood, is considered the treatment of choice to resolve nasal obstruction and snoring due to adenoid pads. In the last decade, clinical researches on the utility of topical intranasal steroids for chronic nasal obstructive symptoms due to adenoid hypertrophy have been reported with encouraging results. This chapter is focused on the clinical picture, etiology, diagnosis, and treatment of snoring in pediatric patients. In particular, non-surgical treatments of adenoid hypertrophy are analyzed and the author’s personal experience on the efficacy of topical nasal steroid for treatment of adenoid hypertrophy is presented.

Chapter 7 - Snoring in the pediatric population is increasing and has been identified as a primary health concern by the American Academy of Pediatrics. The increase has been associated with a rise in co morbid disease processes such as asthma, allergies, lifestyle changes and increasing obesity in the pediatric population. It is estimated that 3 to 14% of children snore.

In the pediatric patient, snoring can present as a mild annoyance to family members trying to sleep at night, and a source of teasing and embarrassment for the child. But snoring may be a symptom that represents very serious health concerns for the child. Unlike adults, snoring in children is not always synonymous with obstructive sleep apnea. There are varying degrees of snoring in the pediatric population ranging from mild to severe. The outcomes may differ and may not be consistent with the severity of snoring.

The diagnosis, evaluation and treatment of snoring are often different processes in children than they are in their adult counterparts. Symptom presentation may differ as well. Differential diagnosis varies as the physical and developmental stages of the child unfold.

Evaluation of the snoring child demands a physical examination along with a thorough family, school, behavior and health history. Diagnostic testing typically includes overnight polysomnography as the “gold standard” for determining the extent to which snoring is associated with sleep disordered breathing. Without such a comprehensive evaluation, the final diagnoses often remain ambiguous, with a treatment plan lacking in direction and efficacy.
The question of snoring is frequently overlooked by healthcare providers. Time constraints may not allow for an open discussion regarding the child’s sleep habits, and healthcare providers may be prone to dismiss the symptom as insignificant and meaningless. However, the snoring child in the absence of objective evidence of obstructive sleep apnea needs to be followed closely. Even primary snoring has been shown to be associated with decreased cognitive function and behavioral problems. The best venue for evaluation, treatment and follow up of the snoring child is found in a multidisciplinary pediatric sleep clinic, where adequate time and attention can be paid to the importance of sleep and snoring. Given the profound impact of sleep on a child’s physical, developmental, emotional, and psychosocial well being, such a clinic ensures the delivery of care that maximizes the probability of returning the child to optimal health.

Chapter 8 - Obstructive sleep apnea-hypopnea (OSAH) is a breathing disorder that is characterized by apneic and hypoapneic episodes occurring during sleep. OSAH is included within the primary sleep disorders and much research has been carried out over the past decades to achieve standardization of diagnostic criteria. The American Academy of Sleep Medicine provides that, along with symptoms such as hypersomnolence, snoring and morning headache, an Apnea Hypoapnea Index (AHI) greater or equal to 5, where AHI is given by the number of episodes/per hour of sleep, is needed to make diagnosis of OSAH.

Apneic events are due to the obstruction of the upper airways during sleep. Such obstruction is caused by the collapse of pharynx and may also be partial, thus causing snoring sounds and hypoapnea.

The treatment of these disorders has not been standardized yet, being mainly based on empirical observations and suggestions, and intraoral devices are gaining attention as potentially useful tools in the management of OSAH symptoms.

This chapter will provide a thorough review of the literature data on the efficacy of the different types of intraoral devices used in OSAH patients.

Chapter 9 - Some patients with cleft lip/palate or isolated cleft palate seem to develop snoring as one possible symptom of an obstructive sleep apnoea syndrome (OSAS) after velopharyngoplasty (VPP).

The aim of this paper was to determine whether there was a difference in the posterior airway space (PAS) between patients with a VPP who snored and those who did not. Four standard parameters were measured in lateral cephalograms of 20 patients with cleft lip/palate and isolated cleft palate without diagnosis of further syndromes, e.g. Robin- sequence, having had VPP, in order to look for the dimension of PAS. Data were set in correlation to the symptom of snoring, and compared with those of 40 patients undergoing orthodontic treatment without clefting and with 20 patients with cleft lip/palate or isolated cleft palate but without VPP.

Metric parameters were significantly (p < 0.05) different in patients with clefting and snoring after VPP when compared with the group of cleft patients without snoring following VPP.

All patients with clefts exhibited at least in one dimension a constriction when compared with patients without clefting. In conclusion, cleft lip/palate and isolated cleft palate patients tend to have constrictions of the PAS. VPP may induce snoring and further narrowing. This makes a recall and analysis for OSAS mandatory.

Chapter 10 - Study Objectives: To identify the prevalence of obesity in a group of untreated obstructive sleep apnea syndrome (OSAS) patients.
Methods: Retrospective chart review of 398 adults with OSAS at Vermont Regional Sleep Center at Fletcher Allen Health Care and the University of Vermont College of Medicine; apnea hypopnea index (AHI), body mass index (BMI), Epworth sleepiness scale (ESS), age, and gender recorded.

Results: Participants were divided into 3 groups based on BMI, a group of 56 lean subjects with a BMI of <27 (14.1%), a group of 72 overweight, but not obese subjects with a 27 ≤ BMI ≤ 30 (18.1%) and a group of 270 obese subjects with a BMI of >30 (67.8%)

Conclusions: 32.2% of subjects with OSAS in our practice were not obese.

Chapter 11 - Objective: Correlate increasing NC with severity of OSA in women as compared to men.

Methods: The authors retrospectively reviewed the charts of 287 consecutive OSAS patients who were diagnosed at our center over a period of 1 year.

Results: High correlation NC and AHI in both genders, r=0.383, p <0.01 in males, r=0.256 p<0.05 in females

Conclusion: Individuals with greater NC have more severe OSAS.

Chapter 12 - Obstructive sleep apnea (OSA) is a common disorder, affecting about 5% of the adult population over the age of 40. Little attention has been spent on the Urological aspects of OSA. This chapter focuses on two common Urological consequences in OSA patients, namely Erectile Dysfunction (ED) and nocturia. This chapter describes the incidence, the pathophysiological mechanism and possible treatment of ED and nocturia in OSA patients.

Erectile dysfunction is strongly correlated to severe OSA, however conflicting results exist associating mild or moderate OSA to ED. There are several theories regarding the mechanism of ED in OSAS patients. Organic causes may result from nerve involvement caused by hypoxia, blood vessels abnormalities caused by the increased nocturnal blood pressure and sympathetic activation in OSAS, and potentially hormonal causes like the low level of androgens in OSAS. Psychological causes on the other hand may result from apnea-induced daytime somnolence or depressed mood commonly seen in apnea patients. Both short and long-term treatment with continuous positive airway pressure (CPAP) has been shown to improve erectile function in OSA patients.

Nocturia has been defined by the International Continence Society as “the complaint that the individual has to wake up at night one or more times to void”. In the past, older men with nocturia were often assumed to have benign prostatic hypertrophy and women were thought to have an unstable bladder or reduced bladder capacity. However, it is now recognized that nocturia can also be caused by nocturnal overproduction of urine (nocturnal polyuria). Data has been accumulating that nocturia may be induced by OSA. Recent studies have shown that nighttime urine production and atrial natriuretic peptide (ANP) excretion are elevated in patients with OSA, thereby. Thus, establishing the pathophysiologic mechanism of nocturnal polyuria associated with OSA. CPAP treatment in patients with OSA has been shown to significantly improve nocturia.

Both nocturia and erectile function considerably affect patients’ quality of life. The linkage between these disorders and OSA is therefore essential to all physicians treating OSA patients. Furthermore, non-compliance with CPAP is a major obstacle in treating OSAS and a possible benefit of CPAP on ED or nocturia may aid CPAP acceptance by the patients.
Chapter 1

DIAGNOSTIC IMAGING STUDIES IN SLEEP-DISORDERED BREATHING

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Sleep-disordered breathing (SDB) is a collective clinical term encompassing primary snoring, upper airway resistance syndrome (UARS), and obstructive sleep apnea (OSA). These syndromes currently are regarded to fall along a spectrum of severity concerning the same pathophysiological condition. Primary snoring which is not accompanied by breathing impairment leads neither to sleep disturbances nor to increase in daytime sleepiness. Despite being a social problem, primary snoring does not necessarily affect a person’s physical health. In OSA there is, however, an imbalance between the forces dilating and occluding the pharynx during sleep. The muscle tone supporting the pharyngeal lumen is too low, and the inspiratory suction force, as well as the pressure of the surrounding tissue, which both narrow the pharynx, are too high. This results in termination of breathing (apneas) or reduced breathing phases (hypopneas). In UARS, an increase in respiratory arousals occurs in the absence of detectable apneas. On the contrary of primary snoring, OSA and UARS have an adverse effect on the daytime life quality. Major symptoms of OSA include intermittent snoring, daytime sleepiness and reduction in intellectual performance. Further symptoms are personality changes, impotence in men, morning headaches, and enuresis nocturna. The gold standard for the diagnosis of SDB is polysomnography (PSG). Though helpful in identifying the individuals, PSG does not detect the site of obstruction. Currently, positive airway pressure (PAP) is considered the primary treatment of OSA [1]. Although highly effective, it is associated with low compliance rates. For this considerable group of patients in whom medical management alone has been of limited value, surgery becomes essential in the management algorithm.
Diagnostic studies have been used to assess upper airway anatomy in patients with this relatively frequent disorder. The aim is to reveal potential differences in upper airway anatomy and also to improve patient management and surgical treatment success. A diagnostic study, in order to be regarded as ideal, should identify individuals with sleep-disordered breathing, be cost-effective and readily available, and also should guide therapeutic as well as site-specific intervention with results that are predictable.

In this chapter, static radiologic imaging methods (lateral cephalometry, computed tomography scanning and magnetic resonance imaging) and dynamic scanning protocols (ultrafast CT or cine MRI) are discussed in detail.

1. LATERAL CEPHALEMOMETRY

Lateral cephalometry is a simple, well-standardized, inexpensive and readily accessible method of screening associated with low radiation exposure [2]. This method has commonly been used from early fifties in order to assess the growth of dentofacial skeleton, nevertheless it has been used in patients with SDB since 1983 [3]. Over the years, lateral cephalometric radiography has become one of the standard diagnostic tools to evaluate skeletal and soft tissue abnormalities contributing to obstruction, and have been the most common imaging method in evaluating the patients with SDB. Radiograms of the head and neck with special focus on several bony and soft tissue landmarks are involved in this traditional method. The parameters that are aimed to be measured include the distance between these set points and the angles between the lines connecting the landmarks (Figure 1; Table 1,2).

Lateral cephalometry provides substantial insights into the pathophysiology of OSA and demonstrates significant craniofacial characteristics associated with this disease. Even though it’s not easy to compare the results, some risk factors for OSA have been associated with certain cephalometric features. Mentioned risk factors are as follows: a thick and long soft palate, retroposition of the maxilla or mandible and particularly a more inferiorly positioned hyoid bone.

Figure 1. Lateral cephalometric landmarks (A) and variables (B) (These figures are copyrighted by the authors and may not be reposted, reprinted or otherwise used in any manner without the written permission of the authors).
Table 1. Lateral cephalometric landmarks

<table>
<thead>
<tr>
<th>Landmark</th>
<th>Name</th>
<th>Definition</th>
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<tr>
<td>PNS</td>
<td>Posterior Nasal Spine</td>
<td>Tip of the posterior spine of the palatine bone, at the junction of the</td>
</tr>
<tr>
<td></td>
<td></td>
<td>hard and soft palate</td>
</tr>
<tr>
<td>U</td>
<td>Tip of the Uvula</td>
<td>The most postero-inferior point of the uvula</td>
</tr>
<tr>
<td>TT</td>
<td>Tongue Tip</td>
<td>The tip of the tongue</td>
</tr>
<tr>
<td>V</td>
<td>Vallecule</td>
<td>Intersection of epiglottis and the base of the tongue</td>
</tr>
<tr>
<td>UPW</td>
<td>Upper Pharyngeal Wall</td>
<td>A point on the posterior pharyngeal wall identified by the extension of</td>
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<tr>
<td></td>
<td></td>
<td>the palatal (ANS-PNS) plane</td>
</tr>
<tr>
<td>MPW</td>
<td>Middle Pharyngeal Wall</td>
<td>A point on the posterior pharyngeal wall intersecting with a perpendicular</td>
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<tr>
<td></td>
<td></td>
<td>line from U (Tip of the uvula)</td>
</tr>
<tr>
<td>Go</td>
<td>Gonion</td>
<td>Most postero-inferior point on the mandible</td>
</tr>
<tr>
<td>LPW</td>
<td>Lower Pharyngeal Wall</td>
<td>A point on the posterior pharyngeal wall intersecting with a perpendicular</td>
</tr>
<tr>
<td></td>
<td></td>
<td>line from V (Vallecule)</td>
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<tr>
<td>H</td>
<td>Anterior Hyoid</td>
<td>The most anterior and superior point on the body of the hyoid bone</td>
</tr>
<tr>
<td>C3</td>
<td>Cervical Vertebra 3</td>
<td>The most antero-inferior point on the cervical vertebral body</td>
</tr>
<tr>
<td>Me</td>
<td>Menton</td>
<td>Lowermost point on the mandibular symphysis in the midline</td>
</tr>
<tr>
<td>S</td>
<td>Sella</td>
<td>Centre of sella turcica</td>
</tr>
<tr>
<td>N</td>
<td>Nasion</td>
<td>Anterior point of the intersection between the nasal and frontal bones</td>
</tr>
<tr>
<td>ANS</td>
<td>Anterior Nasal Spine</td>
<td>Tip of the anterior nasal spine</td>
</tr>
<tr>
<td>A</td>
<td>Subspinale</td>
<td>The most posterior point on the profile of the maxilla between</td>
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<td></td>
<td></td>
<td>the anterior nasal spine and the alveolar crest</td>
</tr>
<tr>
<td>B</td>
<td>Supramentale</td>
<td>The most posterior point on the profile of the mandible between</td>
</tr>
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<td>the chin point and the alveolar crest</td>
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Table 2. Lateral cephalometric variables

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<thead>
<tr>
<th>Variable</th>
<th>Name</th>
<th>Definition</th>
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<tbody>
<tr>
<td>1</td>
<td>SPL</td>
<td>Soft Palate Length</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Distance from PNS (Posterior Nasal Spine) to U (Tip of the uvula)</td>
</tr>
<tr>
<td>2</td>
<td>SPT</td>
<td>Soft Palate Thickness</td>
</tr>
<tr>
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<td></td>
<td>The maximal thickness of the soft palate measured perpendicular to PNS (Posterior Nasal Spine) to U (Tip of the uvula)</td>
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<tr>
<td>3</td>
<td>TGL</td>
<td>Tongue Length</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Distance between V (Vallecule) and TT (Tongue Tip)</td>
</tr>
<tr>
<td>4</td>
<td>TGH</td>
<td>Tongue Height</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Distance along the perpendicular bisector of the V (Vallecule) – TT (Tongue Tip) line</td>
</tr>
<tr>
<td>5</td>
<td>PNS-UPW</td>
<td>Nasopharyngeal Airway Space</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Distance from PNS (Posterior Nasal Spine) to UPW (Upper Pharyngeal Wall) along an extension of the nasal plane</td>
</tr>
<tr>
<td>6</td>
<td>U-MPW</td>
<td>Velopharyngeal Airway Space</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Distance from U (Tip of the uvula) to MPW (Middle Pharyngeal Wall)</td>
</tr>
<tr>
<td>7</td>
<td>PAS</td>
<td>Oropharyngeal Airway Space; Posterior Airway Space</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Distance between a point on the base of the tongue and another point on the posterior pharyngeal wall both determined by an extension of</td>
</tr>
<tr>
<td></td>
<td></td>
<td>a line from point B (Supramentale) through Go (Gonion)</td>
</tr>
<tr>
<td>8</td>
<td>V-LPW</td>
<td>Hypopharyngeal Airway Space</td>
</tr>
<tr>
<td></td>
<td></td>
<td>The distance from V (Vallecule) to LPW (Lower Pharyngeal Wall)</td>
</tr>
<tr>
<td>9</td>
<td>H-MP</td>
<td>Hyoid To Mandibular Plane</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vertical position of hyoid. Distance along a perpendicular line from anterior hyoid</td>
</tr>
<tr>
<td>10</td>
<td>H-C3</td>
<td>Hyoid to 3rd Cervical Vertebra</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anteroposterior position of hyoid. Distance between C3 and H (Anterior Hyoid)</td>
</tr>
</tbody>
</table>
The relationships of the cranium to the maxilla and the mandible are assessed by measuring angles between the sella, nasion, and anterior nasal spine (SNA angle) for the maxilla; and the sella, nasion, and supramentale (SNB angle) for the mandible (Figure 2). Normative data from various studies are summarized in Table 3.

Lateral cephalometry is non-invasive, easily available and relatively inexpensive. However, there are some problems with the technique in terms of the position of the patient, phase of respiration and roentgengraphic methodology as far as soft tissue landmarks are concerned. Lateral cephalometry provides a 2-dimensional, static image of a 3-dimensional, dynamic structure and is unable to provide volumetric data or evaluate important soft tissue structures including the uvulopalatal complex and tongue base. The method also does not provide any information related to tonsillar hypertrophy or other lateral soft tissue structures in the upper way.

**Figure 2.** Lateral cephalometric analysis, normal subject. SNA angle represents the relative position of the maxilla while SNB angle represents the relative position of the mandible to the skull base. (These figures are copyrighted by the authors and may not be reposted, reprinted or otherwise used in any manner without the written permission of the authors).

**Table 3.** Normative data for commonly used cephalometric measurements in men and women (Data from Acebo C, Millman RP, Rosenberg C, et al. Sleep, breathing, and cephalometrics in older children and young adults. Part Id Normative values. Chest 1996;109:664)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Men–mean</th>
<th>Women–mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft palate length</td>
<td>41.0 mm</td>
<td>37.3 mm</td>
</tr>
<tr>
<td>Distance from hyoid to mandibular plane</td>
<td>19.5 mm</td>
<td>15.8 mm</td>
</tr>
<tr>
<td>Oropharyngeal airway space</td>
<td>14.5 mm</td>
<td>13.7 mm</td>
</tr>
<tr>
<td>SNA angle</td>
<td>81.7 degrees</td>
<td>80.7 degrees</td>
</tr>
<tr>
<td>SNB angle</td>
<td>79.1 degrees</td>
<td>79.2 degrees</td>
</tr>
</tbody>
</table>

The findings obtained in the studies which used lateral cephalometry –when compared to the studies conducted with more complex imaging methods- reveal that cephalometry is capable of accurately evaluating the craniofacial soft and hard tissue structures [4,5].
Moreover, the American Academy of Sleep Medicine report in 2005 recommended that cephalometric evaluation should be performed when they are deemed necessary [6]. Attempts have been made to use lateral cephalometric analyses in order to distinguish both healthy controls and snorers from OSA patients, to determine the severity of the underlying SDB, to choose more successful candidates for surgery, to determine the appropriate type of surgery, and to evaluate the outcome of surgery.

1.1. Comparison between Obstructive Sleep Apnea Patients and the Healthy Controls

Many studies, based on lateral cephalometric analyses, reveal that there are differences in craniofacial and upper airway anatomy between OSA patients and the healthy controls (Figure 3).

The differences reported include a reduction in the size of nasopharyngeal and velopharyngeal airway space [7], a narrower oropharyngeal airway space [8-11], a longer soft palate [7,12], an increase in the thickness of the soft palate [13-17], a larger tongue [8], retroposition of the mandible [15] or the maxilla [18], elongated faces due to an inferior displacement of the mandibular body [8], micrognathia [19], an increased midfacial height [18], and differences in hyoid bone position [13,18,20], mainly the inferior displacement of the hyoid bone [8-11] (Figure 4). Comparing OSA patients with their siblings who did not have OSA, the distance from the hyoid bone to the mandibular plane was determined longer in individuals with OSA [21]. 150 of 155 OSA patients were revealed by Jamieson et al. to have at least two abnormalities on lateral cephalometric landmarks that differ from normative data in the literature [22].

![Figure 3. The lateral cephalogram of a healthy control (A) and a patient with severe obstructive sleep apnea patient (B).](image)

Ingman et al. did not report any differences in nasopharyngeal and hypopharyngeal soft tissues; however they reported a significant narrowing on the velopharyngeal level [23].
Bacon et al. determined that there were significant differences between the anterior cranial base length, lower facial height, and maxillary length of normal and OSA individuals [24].

They classified 80% of individuals correctly into sleep apnea and normal groups according to anatomic differences. The soft palate was described through several studies to be longer in OSA patients (AHI>10) (AHI: apnea-hypopnea index) [16,17,25-27] and in snorers (AHI≤10) [26] when compared to the control subjects. Battagel and L'Estrange revealed that the soft palate was not longer though its area was increased in OSA patients in contrast to the controls [14]. They also calculated a four-variable model, including soft palate area and the width of the pharynx where the soft palate was at its thickest. Using two velopharyngeal parameters, this model provided 100% discrimination between OSA and control groups. In contrast to other studies, Zucconi et al. did not find a significant difference in PAS, SNA, and SNB between the OSA patients and normal subjects [28].

1.2. Comparison between Obstructive Sleep Apnea Patients and the Snorers

Attempts have been made to use lateral cephalometric analyses to distinguish simple snorers from OSA patients. Patients with OSA have been shown to have a longer soft palate in addition to an inferiorly positioned hyoid bone and posteriorly displaced mandible when compared to snorers [27-29]. However the upper airway measurements studied in obese or elderly OSA patients were revealed by Meyer et. al not to be different from obese or elderly snorers.

1.3. Predicting the Severity of Sleep-Disordered Breathing

In many studies, cephalometric measurements have been correlated with PSG data to identify skeletal abnormalities correlating with the severity of the underlying SDB. Measurements through lateral cephalometric radiograms were gathered in the initial studies and the degree of SDB was tried to be calculated.
Patients with OSA have been demonstrated to have a small mandible that is located posteriorly, a narrow airway space and enlarged tongue and soft palate and a hyoid which is located inferiorly. All five variables mentioned above have also been shown to be significant determinants of the severity of apnea. Hou et al. reported that the mandibular body length, craniofacial extension and sella–hyoid distance were predictive variables for the AHI in patients with severe OSA [30]. Yucel et al. demonstrated that subgroup of patients with severe OSA more frequently showed differences in hyoid bone position and a soft palate thickness [31]. Dempsey et al. found that, patients who had maxillary deficiency, based on measurement from maxillary spine to porion (uppermost and outermost portion of bony external auditory canal), were five to seven times more likely to have moderate or severe sleep apnea if they were non-obese, and three times more likely if they were obese patients [32]. A study conducted with the participation of Japanese males shows that non-obese individuals have smaller SNA and SNB angles, correlating with severity of OSA [33]. Both Naganuma et al. and Young et al. have confirmed that certain anatomic variables, such as vertical hyoid bone position, velopharyngeal airway space, hyoid to mandibular plane distance and the degree of redundancy of mucosa in the arytenoid/aryepiglottic fold were predictive for the severity of OSA [34,35]. Rose et al. questioned the diagnostic relevance of lateral cephalometry for OSA, as they found no direct correlation between skeletal cephalometric findings and OSA severity; nevertheless, they also reported a correlation with hyoid bone position [36]. The retrospective analyses mentioned above help to identify the affinity for the patients who have and do not have OSA; however, prospective studies are needed in order to evaluate these regression formulas for their efficiency as diagnostic studies. Unfortunately, the prospective studies evaluating cephalometric measurements did not display a strong correlation with PSG data. Bates and McDonald evaluated 121 radiograms in a prospective study and found no factors that correlated significantly with the severity of OSA [37]. In a study by DeBerry-Borowiecki et al., deviations of anatomic measurements from those of normal subjects were also confirmed not to help predicting the severity of OSA [8]. Based on these data, we know that there is a mild difference in lateral cephalometric radiography measurements between normal individuals and OSA patients, and the differences noted are not significant enough to allow the use of lateral cephalometric radiographs alone as diagnostic procedure.

1.4. Predicting the Patients with a High Likelihood of Surgical Success and the Effect of Therapeutic Intervention

1.4.1. Nasal Surgery

Lateral cephalometry has been used to predict the effectiveness of nasal surgery on OSA patients. A study including 14 patients with OSA who underwent nasal surgery, suggested that the respiratory disturbance index (RDI) values of the patients with normal cephalometric radiograms were significantly decreased postoperatively, whereas the RDI values increased in those who have abnormalities on lateral cephalometric radiograms including an increase in the distance from hyoid to mandibular plane or a narrowed oropharyngeal airway space [38]. This study provides evidence that a narrowed hypopharyngeal airway space observed on
lateral cephalometric radiograms predicts a poor outcome for OSA patients who will have a nasal operation.

1.4.2. Soft Palate Surgery

The long-term follow-up of these patients has shown that surgical success rate for uvulopalatopharyngoplasty (UPPP) alone is less than 50%. Lateral cephalometry has been evaluated with regard to potential parameters to predict the postoperative results of UPPP in an attempt to improve surgical success.

In a retrospective analysis of 46 patients, Millman et al. concluded that the distance from hyoid to mandibular plane greater than 20 mm is statistically significant for predicting UPPP to be unsuccessful [39]. Riley et al. reported a significantly narrower oropharyngeal airway space and an increased distance from hyoid to mandibular plane in a review of cephalometric data pertaining to patients who have undergone an unsuccessful UPPP [40]. In a large retrospective review of nine papers including 168 patients, the rate of response to UPPP for OSA patients who had a reduction in size merely of the retropalatal region was 52.3%, whereas the rate of response was 5.3% for those who also had retrolingual narrowing to an extent [41].

Doghrami et al. suggested that preoperative cephalometry is not a reliable method with regard to predicting or improving the success of the surgical procedure [42]. Boot et al. could not find any cephalometric parameter predicting the success of UPPP [43]. In their retrospective study of 43 patients with OSA, Woodson and Conley also could not find a skeletal measurement predicting the outcome of UPPP in the entire study group [44]. Liu et al. investigated UPPP in conjunction with genioglossus advancement in a series of 44 cases and concluded that the unique predictive parameter was the apnea-hypopnea index (AHI) [45].

As for the prospective studies in literature, Gislason et al. evaluated 34 consecutive OSA patients, [46] responder and nonresponder groups did not significantly differ in terms of posterior airway space and hyoid to mandibular plane distance. Ryan et al. evaluated 60 consecutive OSA patients and noted that the oropharyngeal airway space was significantly narrower in responders when compared to nonresponders [47]. In another prospective study, Petri et al. evaluated 30 consecutive OSA patients and no significant difference in the size of oropharyngeal airway space between two groups was noted; however, a lowered hyoid position, an increased cranio-cervical angle, and the shortening of the maxilla were significantly associated with poor UPPP outcome [48].

The data concerning the predictive value of lateral cephalometric radiograms with regard to the success of UPPP is contradictory. The bulk of the data predicts that the patients who have narrowing in the retrolingual region will have a poor outcome following UPPP [40,41]; however, all of the prospective studies that are statistically more sound indicate that this has no effect on success [46-48]. Overall, the predictive value of lateral cephalometry for UPPP remains at least questionable.

1.4.3. Multilevel Pharyngeal Surgery

Since UPPP alone has a low rate of success in the management of OSA, many surgeons have adopted techniques to treat the area of the tongue base as well as the palate. Lateral cephalometric radiograms have been used in various studies to assess the outcome of
multilevel pharyngeal surgery and a couple of parameters on lateral cephalometric radiograms have been identified to predict the outcome. However, none of the studies revealed a correlation between the cephalometric parameters and the PSG data.

Ramirez et al. reviewed 12 postoperative patients with OSA who had undergone sliding mandibular osteotomy and hyoid bone suspension, and noted a significant increase in the size of oropharyngeal airway space and a statistically insignificant decrease in the distance from hyoid to mandibular plane [49]. No preoperative or postoperative cephalometric measurement or change in these measurements was correlated with the amount of reduction in the RDI, or the change in the lowest nocturnal oxygen saturation. In a review of 55 OSA patients treated with inferior sagittal mandibular osteotomy with hyoid myotomy and suspension, responders had a significantly less retruded mandible than nonresponders [50]. Riley et al. reviewed 40 OSA patients who had failed treatment with limited mandibular osteotomy with hyoid advancement, and were subsequently treated with advancement of the maxilla and mandible. Significant changes were observed in various measurements, but no direct relationship was noted between the changes in the size of oropharyngeal airway space and the changes in PSG data [51]. Yao et al. reviewed 19 postoperative patients with OSA who had undergone UPPP, mandibular osteotomy with genioglossus advancement, and hyoid myotomy with advancement [52]. Changes in the lateral cephalometric variables were almost statistically significant, but did not correlate with changes in PSG data. Eggensperger et al. performed a long-term evaluation of 15 patients after mandible advancement that had enlargement of the airway postoperatively and concluded that changes are noted following multilevel pharyngeal surgery; however, the changes on lateral cephalometric radiograms do not accurately reflect the impact of surgery on the severity of sleep apnea [53]. Liu et al. performed a prospective study concerning UPPP and genioglossus advancement in 44 patients but were unable to show any changes that predicted cure of OSA [45]. Similarly, Kuhnel et al. used the reposition system for tongue advancement in 28 males, and noted no correlation between improvement of airway dimensions and RDI [54].

Overall, it is possible to identify the patients who have severe mandibular deficiencies and to improve OSA through correction of skeletal abnormalities; on the other hand, the majority of OSA patients do not suffer severe skeletal abnormalities, thereby lateral cephalometry is not helpful in determining the patients who can be treated with multilevel pharyngeal surgery.

1.4.4. Maxillofacial Surgery and Oral Appliances

Lateral cephalometry is a standard tool in the preoperative evaluation of the craniofacial skeletal anatomy prior to maxillomandibular surgery. It can be regarded as a mandatory procedure and its value is beyond question [55,56]. Lateral cephalometry has been the standard diagnostic tool with regard to the evaluation of potential predictive parameters related to treatment success as well as the identification of dental adverse effects of oral appliances. Mayer and Meier-Ewert, have looked for cephalometric predictors of treatment success and reported that specific variables such as a narrow oropharyngeal airway space, a narrow SNB angle, a wider SNA angle and a short uvula were actually predictive for the therapeutic effect [57]. The existences of predictive cephalometric parameters were also confirmed by many other authors particularly in relation to hyoid bone position and oropharyngeal airway dimension [57-61]. Only Battagel et al. reported no identifiable cephalometric features to predict favorable response to the treatment [62].
The main restriction of lateral cephalometry is studying a three-dimensional object over a two-dimensional picture. This diagnostic tool provides two-dimensional static images in the sagittal plane and therefore does not provide information pertaining to transverse dimensions, cross-sectional shape or volume, or dynamic changes of the airway during sleep. In addition, lateral cephalometric radiograms are taken awake, and the examination during wakefulness provides only limited characterization of obstruction during sleep. This may explain why lateral cephalometry has not become a routine procedure in the diagnostic work-up of OSA as long as maxillomandibular surgery and oral appliances are not planned.

2. COMPUTED TOMOGRAPHY SCANNING

Computed tomography (CT) is a noninvasive technique that allows a detailed assessment of the entire upper airway. When compared to lateral cephalometry, CT scanning significantly improves soft tissue contrast, leads surgical interventions toward the abnormal anatomic sites and allows for precise measurements of cross-sectional areas at different levels. Although CT scan exquisitely displays bony details, it has a limited soft-tissue contrast resolution when compared to MRI scanning. This is particularly relevant to evaluating upper airway adipose tissue. Other restrictions of CT scan include expense and the radiation exposure every time a CT scan is taken.

The anatomy of the upper airway mainly represents the static dimensions of the airway during wakefulness, and does not have a high predictive value for diagnosing OSA. Efforts have been made to perform CT scans while asleep to assess the sleep anatomy. Several authors have used scanning protocols under hypnotic relaxation, sleep, sleep during apneas, and also compared wakefulness and sleep directly [63,64].

In order to examine the upper airway, various techniques of CT imaging can be applied which include standard axial CT with the option of three-dimensional reconstruction the upper airway structures, spiral CT that have the ability to provide volumetric images, dynamic CT with high imaging speed, and electron beam CT that allows for a dynamic evaluation. **Spiral (helical) CT** allows for a rapid acquisition of volumetric data of the part of the body under examination. The advantage of spiral CT includes the elimination of respiratory misregistration, decreased motion artifact, a shorter duration of examination, and high quality of reformatted images [65]. This modern technology allows for reconstruction of the data from CT scan in forms of 3-dimensional images (Figure 5). It is easier to assess the upper respiratory tract via three-dimensional reconstructed CT scan than it is by unreconstructed CT scans. It enables an accurate measurement of the airway dimensions and calculates airway volume. Static imaging may show areas of narrowing that predispose individuals to obstruction, but dynamic imaging can actually display episodes of obstruction. **Dynamic (cine or ultrafast) CT** scans allow for acquisition of eight contiguous slices in every 0.7 seconds. This high imaging speed allows for dynamic assessment of the upper airway. This technology allows for observation of dynamic obstructions of the upper airway during a respiratory cycle as well as measurements during natural sleep through a high scanning speed and relatively quiet scanning conditions [31,66-69]. Armstrong et al. utilized **optical coherence CT** that generates quantitative, real-time images of the upper airway that enables accurate determination of shape and size [70].
The authors described their validation of this technique with CT in five healthy subjects. In addition to the capability of continuously measuring the changes in the airway dimensions under a variety of conditions, the technique seems to have an upper hand with regard to patient comfort, minimal effect on sleep quality or architecture, and lack of radiation. Early shortcomings appear to include the restricted capacity to view the full circumference of the airway at all sites/levels and in all of the subjects, and the inability to track changes in airway caliber during rapid breathing.

Despite the low sensitivity of CT scans for the diagnosis of OSA, studies utilizing CT scanning have been able to show correlations between anatomic changes and improvement of OSA parameters. Another advantage of CT scanning in the supine position is the accurate measurement of upper airway cross-sectional area. However, CT scanning does have limitations: it is relatively expensive, there are patient weight limitations, excessive radiation exposure limits repeat studies, and there is poor contrast resolution of upper airway adipose tissue. Attempts have been made to use CT analyses in order to distinguish healthy controls from OSA patients, to determine the severity of the underlying SDB, to choose more successful candidates for surgery, to determine the appropriate type of surgery, and to evaluate the outcome of surgery.

2.1. Comparison between Obstructive Sleep Apnea Patients and the Healthy Controls

It has been confirmed via multiple studies that there are differences between OSA patients and healthy control subjects in terms of craniofacial and upper airway anatomy. OSA
patients were reported to differ from healthy controls by significant narrowing of the nasopharyngeal, oropharyngeal and hypopharyngeal cross-sectional areas; larger tongue and soft palate dimensions [4,71-75]. Caballero et al. demonstrated that the patients with OSA had a narrowing in the oropharynx while they had a significant widening in the hypopharynx during expiration when compared to the control subjects [76]. Shepard et al. determined that there are significant differences between OSA patients and healthy controls in terms of minimal upper airway cross sectional areas [77]. Based on a minimal upper airway cross sectional area of 1 cm² or less for OSA patients, 70% of individuals were classified correctly as sleep apnea and normal groups (Figure 6,7).

**Figure 6.** Axial bone window CT scan of a normal subject (A) and a patient with severe sleep apnea (B) at the level of C2 vertebra. The upper airway is smaller in the patient with sleep apnea. The amount of subcutaneous fat (white area at the back of the neck) is greater in the apneic.

**Figure 7.** Axial bone window CT scan of a normal subject (A) and a patient with severe sleep apnea (B) at the level of C3 vertebra during Muller Maneuver. Healthy volunteer during Muller maneuver shows no narrowing of the pharynx while the sleep apneic shows significant narrowing.
To define more accurately the site of obstruction during sleep, Horner et al. performed CT scans in OSA patients while they are both awake and asleep [78]. The scans revealed that the narrowest segment of the upper airway was the one posterior to the soft palate in majority of the patients, and that the minimal upper airway cross sectional area was narrowed significantly in OSA patients when compared to the control subjects.

The three-dimensional CT reconstruction studies revealed no statistically significant difference in airway dimensions between OSA patients and the control subjects. Using dynamic CT imaging, Galvin et al., found smaller oropharyngeal airways and nasopharyngeal airways in OSA patients versus normal controls [67]. Schwab et al. studied the effects of respiration on upper airway caliber using dynamic CT scanning in 15 normal subjects, 14 snorer/mildly apneic subjects, and 13 patients with OSA. They revealed that the upper airway was significantly smaller in apneic than in normal subjects, particularly at the retropalatal-low and retroglossal anatomic levels [69].

2.2. Predicting the Severity of Sleep-Disordered Breathing

In various studies cephalometric measurements have been correlated with PSG data to identify skeletal abnormalities that correlate with the severity of the underlying SDB. Initial studies gathered measurements from CT scans in order to calculate the degree of SDB.

Using reconstructed three-dimensional CT imaging, Lowe et al. demonstrated that there was a significant correlation between AHI and the ratio of tongue volume to airway volume in OSA patients [4]. Li et al. demonstrated a significant correlation of the retropalatal space and its lateral diameter with the RDI using three-dimensional CT scanning in a large group of 194 patients with SDB [79]. Yucel et al. described a narrower cross-sectional area and a thicker soft palate in patients with severe OSA compared to those with only mild-to-moderate OSA determined on dynamic CT imaging studies [31]. Vos et al. used the smallest cross-sectional area, the upper airway resistance and the BMI to predict the severity of OSA [80]. Unlike other studies, a prospective study with three-dimensional reconstructed CT scanning by Ryan et al. showed no correlation between polysomnographic data and upper airway volume measurements [81].

2.3. Predicting the Patients with a High Likelihood of Surgical Success and the Effect of Therapeutic Intervention

Attempts have been made to use CT scanning for the purpose to choose the candidates who are more likely to receive a successful surgery, and to determine the appropriate type of surgery. CT scanning is also used to assess the effect of therapeutic intervention with regard to the treatment with oral appliances.

2.3.1. Soft Palate Surgery

CT studies have been employed in an attempt to identify favorable surgical candidates for UPPP and to examine dynamic changes of the upper airway following surgery. Studies show
that CT imaging can distinguish responders from nonresponders to UPPP, and allow the selection of more appropriate surgical intervention for those deemed as nonresponders.

For the purpose of choosing the individuals that are more likely to undergo a successful surgery, Ryan et al. utilized three-dimensional constructed CT imaging and demonstrated that UPPP responders among OSA patients have smaller upper airway volumes, smaller upper airway to tongue volume ratios, and smaller oropharynx to soft palate volumes when compared with non-responders [81]. Larsson et al. showed significantly poorer success with patients who had widened tongue and genioglossus muscles [75].

CT scanning has also been used to evaluate the surgical results of UPPP. CT scans can correctly identify the OSA patients who were cured following UPPP or reveal inadequately performed UPPP procedures and also other causes of retropalatal narrowing which require further intervention. Changes in airway dimensions following UPPP correlate well with the cure of sleep apnea. Langin et al. concluded that a postoperative oropharyngeal enlargement seen in pharyngeal CT measures is associated with a good outcome in UPPP [82]. Shepard et al. showed that UPPP surgery more than doubled the size of upper airway cross-sectional area in his 23 patients with OSA [83]. Li et al. demonstrated that an extended uvulopalatal flap led to a significant increase in the size of retropalatal space in their 15 patients with OSA [84].

2.3.2. Multilevel Surgery and Oral Appliances

The upper airway was shown to enlarge following mandibular distraction osteogenesis in children and following maxillomandibular advancement in adults [85,86]. Gale et al. investigated the airway enlargement achieved with an oral appliance in 32 OSA patients and described a statistically significant increase in the minimal pharyngeal cross-sectional area [87]. Kyung et al. confirmed these results 5 years later by using cine CT imaging [88]. A non-adjustable oral appliance was demonstrated by Sam et al. to be able to enlarge the cross-sectional areas at the retropalatal and retroglossal levels and provide an increase in overall/total airway volume [89].

CT scanning has been and will continue to provide knowledge necessary to understand the impact of soft tissue and bony structures of the upper airway in the pathogenesis of OSA.

3. MAGNETIC RESONANCE IMAGING

The ideal upper airway imaging modality for patients with OSA should be inexpensive and noninvasive and be performed in the supine position without radiation. In addition, such an imaging technique should provide high-resolution anatomic representation of the airway and surrounding soft tissue structures with the capability of performing dynamic images during wakefulness and sleep. Such an imaging technique does not exist, although magnetic resonance imaging (MRI) is an excellent method to access the upper airway.

MRI achieves excellent soft tissue resolution; provides precise and accurate measurements of the upper airway and the surrounding tissue; obtains multiplanar images in the axial, sagittal, and coronal planes; allows three-dimensional assessments of tissue structures; permits volumetric data analysis including three-dimensional reconstruction images of the upper airway; and finally avoids ionized radiation exposure allowing for repetitive measurements. The advantages with regard to the lack of ionized radiation have
rendered MRI the imaging technique of choice for the assessment of children with SDB. Our understanding of the pathophysiology of OSA as well as the mechanisms underlying effective treatments such as weight loss, CPAP, oral appliances, and upper airway surgery has also been improved by MRI studies.

This diagnostic method, on the other hand, has some shortcomings. It is costly to perform and not commonly available; cannot be employed in patients with metallic implants such as pacemakers; difficult to perform in patients with claustrophobia and morbid obesity. MRI is difficult to implement in evaluating OSA because of its nature. Difficulties arise regarding concurrent sleep evaluation and possible requirement of sedation due to the noise produced by scanners. Most of the studies have relied on verbal response to determine wakefulness, while others have instituted EEG monitoring during MRI scanning. It has been difficult to monitor the level of sleep in the MRI scanner during the study due to the bulk of the machine. Some investigators have tried to deprive their patients of sleep prior to scanning, while others have resorted to the use of sedatives. Use of sedatives results in selective reduction in the upper airway muscle activity leading to alterations in sedated patients in terms of the pattern of obstruction when compared to the patients who are not sedated. These factors have limited the number of studies assessing MRI during documented sleep.

Advances in technology have decreased the number of limitations of MRI application for evaluating OSA patients. Volumetric MRI appears to be a powerful tool to assess and measure anatomic risk factors for OSA while dynamic (ultrafast) MRI provides multiple images at multiple sites with sufficient image quality allowing dynamic assessment of the pharyngeal musculature [12,90] (Figure 8,9).

![Figure 8. Dynamic single-slice images in the medial sagittal plane of a normal subject.](https://via.placeholder.com/150)

Attempts have been made to use MRI analyses in order to distinguish healthy controls from OSA patients, to determine the severity of the underlying SDB and to choose more successful candidates for surgery.
3.1. Comparison between Obstructive Sleep Apnea Patients and the Healthy Controls

Based on the analysis of MRI data acquired during awakeness, multiple studies have confirmed that there are differences between OSA patients and healthy controls in terms of craniofacial and upper airway anatomy (Figure 10, 11, 12). Reported differences can be both in children and adults. Fricke et al. compared children with or without persistent OSA after tonsillectomy and adenoidectomy and demonstrated that enlarged lingual tonsils were present in those with persistent disease [91].

Arens et al. found significant differences between children with and without OSA in terms of upper airway structures. An airway restriction was detected both in the adenoids and the tonsils and an enlarged soft palate was found in the affected group [92].

Fregosi et al. demonstrated a close dependency between the respiratory events and the size of the tonsils and the soft palate [93]. Shott et al. investigated children with Down syndrome with persistent airway obstruction following tonsillectomy and adenoidectomy and confirmed that recurrent adenoid tissue, glossoptosis, soft palate collapse, hypopharyngeal collapse and enlarged lingual tonsils were described as the source of airway obstruction [94]. Through static and dynamic imaging, potential differences in upper airway anatomy and structure have been also described in adults. Horner et al. concluded that in OSA patients, higher amount of fat was present in the soft tissue surrounding the collapsible segment of the pharynx [95]. Other anatomical conditions associated with SDB were the large volumes of the lateral pharyngeal walls and total soft tissue surrounding the upper airway [96]. Schotland et al. found that OSA patients had a higher amount of fat in genioglossus and geniohyoid muscles when compared to control subjects [97]. In a group involving a total of 48 OSA patients and healthy controls, Schwab et al. demonstrated through multivariable regression analysis that an increase in volume of tongue and lateral pharyngeal walls independently and significantly
increased the risk of having OSA [12]. Iida-Kondo et al. demonstrated a higher tongue volume in patients with OSA compared to healthy controls [98]. Okubo et al. compared the anatomic appearance of the mandible and soft tissue structures of the upper airway in patients with OSA to healthy controls [99]. Contrarily, some of the studies carried out with awaken subjects have not been able to distinguish OSA patients from control subjects. Ciscar et al. investigated 25 patients with dynamic MRI while awake and in spontaneous sleep, and found that velopharynx narrowing was similar in OSA and healthy controls during awakening [100]. Green et al. did not note any significant difference in between seven snoring and seven non-snoring subjects in terms of awake pharyngeal volumes [101]. Similar to Rodenstein et al. who could not find any correlation between pharyngeal volumes and RDI in awake OSA patients, Abbey et al. also concluded that there was no significant difference between nine snoring, six OSA, and eight normal patients regarding pharyngeal cross-sectional area [102,103].

**Figure 10.** Patient with severe OSA. (A) Sagittal projection shows narrowing at the uvulopalatal level. (B) Axial MR at the level of C2 vertebra. (C) Muller maneuver, sagittal projection, shows increased mobility of the soft palate. (D) Axial MR during Muller Maneuver at the same level.
Figure 11. Axial magnetic resonance imaging of a normal subject (A) and a patient with severe sleep apnea (B). The upper airway is smaller in the patient with sleep apnea. The apneic patient has more subcutaneous fat than the normal subject.

Figure 12. Mid-sagittal magnetic resonance imaging of a normal subject (A) and a patient with severe sleep apnea (B). The upper airway is smaller in the retropalatal region and the soft palate is longer in the apneic patient. The amount of subcutaneous fat (white area at the back of the neck) is greater in the apneic.

Advances in technology allow for some scanning during sleep; however, examination expenses and lack of a comfortable sleep environment continue to restrict the ability to use this modality during sleep. Schoenberg et al. performed an asleep, EEG-confirmed evaluation of eight OSA patients by using dynamic MRI without sedatives administration for sleep induction [104]. Ikeda et al. compared patients with OSA and healthy controls during wakefulness and spontaneous sleep [105]. While no pharyngeal airway narrowing was observed in the healthy subjects, the narrowing seen in the OSA patients was significant during wakefulness and even more significant during sleep.
The majority of these studies confirm the differences in upper airway anatomy between OSA patients and healthy controls however they do not have enough patients or data to distinguish between OSA, snoring, and normal patients.

3.2 Predicting the Severity of Sleep-Disordered Breathing

Multivariate analysis of 25 patients conducted by Ciscar et al., demonstrated that airway dimensions are of no use for in predicting the severity of OSA [100]. Jager et al. studied 16 OSA patients during awake periods, and could not find a correlation between airway measurements and the RDI [106].

3.3. Predicting the Patients with a High Likelihood of Surgical Success and the Effect of Therapeutic Intervention

With regard to surgical treatment, MRI has been used to detect the site of airway obstruction for the surgical intervention and to assess potential effects of surgery on upper airway anatomy [107,108]. In radiofrequency surgery, MRI has been used to visualize postoperative effects on the soft tissue of the soft palate and the tongue base [109-111]. These studies revealed no change in the upper airway anatomy during wakefulness which indicates that these interventions work rather through functional changes in the collapsibility of upper airway than an enlargement of it. Eight patients were evaluated by Terris et al. before and 2–3 days after laser assisted uvulopalatopharyngoplasty (LAUP) and it was observed that cross-sectional area at the palate was not significantly changed, while RDI was almost doubled, and AHI was significantly increased [112]. These results provide further evidence that MRI is not sensitive to changes which effect sleep parameters on PSG. In a study of 12 OSA patients who has undergone hyoid myotomy alone as the initial treatment, awake MRI imaging revealed that there was a more pronounced increase in the size of retrolingual space in responders when compared to nonresponders [113].

In concern with conservative treatment, Sanner et al. evaluated 13 OSA patients by ultrafast MRI regarding the effects of mandibular advancement devices and concluded that the use of such a device can prevent pharyngeal obstruction in a subgroup of patients, at least during wakefulness [114]. Gao et al. reported potential anatomic criteria as assessed with MRI for successful treatment with mandibular advancement devices [115]. MRI has been also used to assess the effects of continuous positive airway pressure (CPAP) on the upper airway of OSA patients. However, the results were contradictory. Abbey et al. and Ryan et al. showed an increase in pharyngeal size with the use of nasal CPAP while Collop et al. showed no change in pharyngeal volumes [102,116,117].

Overall, MRI has neither become a standard procedure in the diagnostic work-up for patients with SDB nor a common method for decision making in the management of the disease regarding surgical versus non-surgical treatment. A number of issues remain unresolved: First, MRI during sleep is possible but not easy to perform and measurements during wakefulness. Also, the results of MRI, even when performed during sleep, can only provide information concerning a short period of time. Finally, the restricted availability and associated costs are additional limiting factors. Although MRI has substantially improved our
understanding of SDB, it has not yet become a part of routine clinical evaluation of patients suffering this condition. Further advances in technology as well as future prospective studies that will demonstrate the usefulness of MRI in surgical planning and improved outcomes are needed to determine the role of MRI in evaluating OSA patients.

4. FLUOROSCOPY

Fluoroscopy provides a widely available modality to assess dynamic airway anatomy and sites of obstruction, and can be performed asleep in order to observe obstructive episodes in OSA patients. Somnofluoroscopy combines fluoroscopy with PSG to evaluate the sites of obstruction radiologically during episodes of apnea and hypopnea while the subject is asleep. Advantages of fluoroscopy include direct observation of obstructive sites during episodes of apnea, and availability of fluoroscopy in most hospitals. Drawbacks include high amount of radiation exposure, superimposition of structures in patients who have thick and short necks, and the possible need for sedation to attain sleep during the procedure. Newer digital fluoroscopy systems cause less radiation exposure and provide shorter examination times.

Somnofluoroscopy has been used to make observations concerning the site of obstruction and to guide surgical planning. One of the earlier studies accomplished in 1983 utilized fluoroscopy in order to examine the site of collapse in OSA patients during wakefulness [73]. In all of the OSA patients, obstruction was initiated at the junction between the soft palate, base of tongue, and posterior pharyngeal wall. In 1985 Walsh and his colleagues, used asleep fluoroscopy (somnofluoroscopy), to make observations on 40 OSA patients, and showed that the site of obstruction and site of initiation of obstruction were variable in this group of OSA patients [118]. Somnofluoroscopy has been used in the pediatric population in order to demonstrate site of obstruction in medically complex patients. In a group of 70 patients with single-site treatment of obstruction or normal examination with persistent symptoms, there was demonstration of glossoptosis in 24% of patients as the cause of airway obstruction [119].

Fluoroscopy also allows evaluation of the entire airway in addition to upper airway evaluation. The selection of patients with the narrowest level of airway and initial level of obstruction in the oropharynx led to an increase in the success rate of UPPP outcome from 42% to 67% [120]. Two subsequent studies utilizing digital fluoroscopy to examine awake supine OSA patients examined the collapsibility of the upper airway and the use of fluoroscopy to predict the outcome of OSA surgery. In the first, no difference in velopharyngeal area and velopharyngeal collapsibility was observed between controls and patients with complete obstruction [121]. In the second study, no predictors for successful outcome of LAUP were found [122].

Fluoroscopy provides a dynamic evaluation of the airway, especially to recognize a collapse of airway during sleep. Although asleep studies are clearly superior to awake imaging studies, asleep fluoroscopy will probably not be commonly used to assess OSA patients, because of the time that obtaining the scan requires, the exposure to radiation, and availability of the facilities proper for asleep studies.
SUMMARY

As the interest in SDB has increased, various attempts have been made to assess upper airway anatomy in patients suffering this relatively frequent disorder [123,124]. The techniques of airway evaluation presented in this chapter have significantly increased our understanding of SDB. Lateral cephalometry has demonstrated significant craniofacial characteristics associated with SDB. Specific cephalometric characteristics have been repeatedly mentioned as a risk factor for OSA; particularly the more inferiorly positioned hyoid bone. However, this diagnostic tool provides two-dimensional static images in the sagittal plane and therefore does not provide information pertaining to transverse dimensions, cross-sectional shape or volume, or dynamic changes of the airway during sleep. This may explain why lateral cephalometry has not become a routine procedure in the diagnostic work-up of OSA as long as maxillomandibular surgery and oral appliances are not planned. Many studies have attempted to detect the site of collapse with the help of CT, MRI and fluoroscopy in patients with SDB. Beneficial effects on treatment and patient selection for surgical intervention have repeatedly been postulated but have not been demonstrated to date. Several considerations have to be made concerning the assessment of the patient. One should realize that the findings obtained during wakefulness cannot always predict the site of collapse, partly because the additional effect of muscle relaxation during sleep can result in an increased collapsibility. Moreover, the results of these techniques, even when performed during sleep, can only provide information concerning a short period of time and are limited to the supine position. In general clinical practice, the restricted availability, the associated costs and the associated ionized radiation at least for CT scanning are additional limiting factors.

Although all these additional techniques for upper airway assessment which are superior to simple clinical assessment have substantially improved our understanding of SDB, their significance in daily practice is limited. There is not enough convincing data supporting the use of these methods for the outcome of treatment and indicating that these techniques are superior to the routine clinical assessment.

CONFLICT OF INTEREST STATEMENT

The authors have no financial relationship with a commercial entity that has an interest in the subject of this manuscript.

REFERENCES


Sleep-disordered breathing (SDB) is a spectrum of diseases, which includes snoring, upper airway resistance syndrome (UARS), obstructive sleep apnea-hypopnea syndrome (OSAHS), and obstructive sleep apnea (OSA). Contributing factors for SDB may involve physiologic, neurogenic, muscular, anatomic and developmental findings that demand a comprehensive evaluation before choosing the appropriate treatment.

The goals of the treatment of SDB should be aimed to reduce collapsibility and optimize the stability of the airway while decreasing morbidity and mortality. The nonsurgical management of SDB includes exercise, weight loss, decreased alcohol consumption, smoking cessation, altered sleeping position, and dental or nasal appliances [1]. It has been shown that weight loss improves and in some cases cures sleep-disordered breathing disorders and is clearly a low-morbidity treatment modality [2,3]. However, patient compliance has persistently been the drawback in these types of management. Studies reveal that over half the patients will not follow the conservative treatment or do not obtain sufficient relief from their snoring and look for surgical modalities to correct their problem [4]. Currently, positive airway pressure (PAP) is considered the gold standard treatment of OSA [5]. Although highly effective, it is associated with low compliance rates. Noncompliance has been categorized by Zozula as tolerance problems, psychological problems and lack of instruction, support, or follow-up [6]. Tolerance problems may be due to mask leaks, difficult exhaling, aerophagia, chest discomfort, bed partner intolerance or other side effects such as dry mouth, conjunctivitis, rhinorrhea, skin irritation, pressure sores, nasal congestion and epistaxis. Psychological problems include lack of motivation, claustrophobia, and anxiety. Certain interventions may promote compliance to PAP, such as correction of nasal obstruction, attention to mask-fit, desensitization for claustrophobia, heated humidification, patient education, regular follow-ups, compliance software, and support groups [7]. Despite these
measures, PAP therapy remains a considerable challenge for many individuals with low compliance of 50% to 80% [8,9,10]; besides, 15% of patients refuse PAP after a single night’s use in the laboratory [11]. For this considerable group of patients in whom medical management alone has been of limited value, surgery becomes essential in the management algorithm. The rationale for surgical management of the upper airway is to alleviate or minimize the pathophysiologic derangements associated with upper airway obstruction. Surgery for SDB first became an area of study when Fujita [12] introduced the uvulopalatopharyngoplasty (UPPP) in 1981. Surgical management of snoring in adults without evidence of obstruction has vast success but there is still no ideal surgical procedure for OSA. During the past decade, a variety of methods have been advocated for the surgical treatment of OSA but no single procedure has been proven to have the ideals that rationalize its singular use over other procedures.

In this chapter, current state of art in SDB, including preoperative assessment, surgical planning and postoperative management are discussed in detail.

1. PREOPERATIVE ASSESSMENT

It is well-accepted that successful surgical outcome depends on proper patient selection and the type of surgical procedure performed, and the experience of the surgeon. Hence, a systematic approach is necessary to maximize safety and improve outcomes [13].

1.1. Patient Selection

One of the most important aspects of surgical treatment is to identify appropriate candidates who will benefit from the surgery. SDB can originate from different segments of the upper airway; therefore, the entire upper airway must be examined during evaluation. This must be performed before polysomnography and before any therapeutic decision. Each patient will have a very specific problem, and some may need a combination of procedures, whereas others may not be candidates for surgery at all. The clinical examination, endoscopic pharyngoscopy and imaging of the upper airway serve as a guide to determine the site(s) of obstruction and the surgical procedure(s) adequately. The ultimate goal is to predict success in the selection of the appropriate surgical procedure.

Anamnesis

A detailed history is crucial in identifying behavioral factors contributing to poor sleep architecture and excessive daytime somnolence. History of snoring, daytime sleepiness, gasping for air, and period of witnessed apnea, as reported by the patient and the patients’ bed partner, are important indications for treatment. Using a sleepiness scale is worthwhile for assessing excessive daytime sleepiness. The Epworth sleepiness scale is the most commonly used self-administered questionnaire designed to measure the general level of daytime somnolence and the probability of falling asleep in different situations (Table 1). The score is calculated on the basis of a total of 24 and excessive daytime sleepiness is considered to occur if the score is above 10.
Table 1. Epworth sleepiness scale

Patients are asked to grade from 0 to 3 their likelihood of falling asleep in contrast to just feeling tired in certain situations (The total score will be between 0 and 24).

Level of sleepiness
0 = would never doze
1 = slight chance of dozing
2 = moderate chance of dozing
3 = high chance of dozing

Situations:
- Sitting and reading
- Watching TV
- Sitting inactive in a public place (theater, meeting)
- As a passenger in a car for 1 h without a break
- Lying down to rest in the afternoon
- Sitting and talking someone
- Sitting quickly after lunch (without alcohol)
- In a car while stopped in traffic

Surgical history, particularly concerning the ENT field (tonsillectomy, adenoidectomy, septoplasty, etc.), is collected. The medical status of the patient is also assessed during the initial consultation and determines if the patient is a surgical candidate. Craniofacial characteristics (retrognathia, micrognathia), cardiopulmonary dysfunction, irritants like tobacco and alcohol, sedative medications reducing neuromuscular control of the upper airway during sleep and genetic factors are considered as major factors in the management of SDB patients and should be questioned. The surgeon should also listen to the patients about their concerns and expectations which may differ than those of the physician. Thus, educating a patient about SDB and expected outcomes of surgery should be guaranteed before any intervention.

**Physical Examination**

Physical examination includes a general inspection and a thorough examination of the upper respiratory tract. Most patients with sleep apnea are overweight with short, thick necks. The body mass index (BMI) and neck circumference should be evaluated because it has been shown that the surgical outcomes can be influenced by these factors [14]. BMI is calculated by the formula: weight(kg)/height(m²). The relationship of BMI and the presence and severity of OSA has been previously established [15,16]. Most surgeons performing procedures for OSA agree that patients who have a BMI 40 or greater have a poor prognosis for cure after UPPP [17,18]. Neck circumference, which is also an indicator of obesity, should be also measured. Flemmons has noted that neck circumference increases are associated with the presence of hypertension, and increased witnessed gasping, therefore, the percentage incidence of OSA increases [19].

In the head and neck region, the upper airway should be examined for a number of abnormalities. A detailed physical examination, including the nose, soft palate, lateral pharyngeal walls, and tongue base, is designed to identify the potential anatomic sites that are susceptible to collapse and to identify characteristics that directly contribute to the
pathophysiology of OSA. The nasal airway is the beginning of the airway conduit, and resistance in nasal airflow can play a major role in snoring. A patent nasal airway with minimal resistance is important to the overall stability of the upper airway. The external examination of the nose can identify compromises in nasal airflow such as a deviated dorsum, constricted nasal width, tip ptosis, and soft tissue asymmetries (Figure 1). Most nasal pathology can be treated pharmacologically; therefore, medication should be the first line of treatment. The position of the maxilla and mandible relative to the cranial base is manifested by the categorization of the dental occlusion (Figure 2). The skeletal position of the maxilla and mandible is best determined by cephalometric imaging. The oral examination of the palate is significant in determining the overall stability the oropharyngeal airway. The overall length of the soft palate, thickness of the soft palate, and anatomic findings associated with the lateral tonsillar pillars and size of the tonsils if present are important in surgical treatment planning.

Figure 1. A patient with a deviated nasal septum (Medical photography consent form is obtained from the patient).

Figure 2. Emergency tracheotomy performed by the author due to difficult intubation in a patient with severe micrognathia (Medical photography consent form is obtained from the patient).
The position of the posterior third of the tongue base relative to the posterior pharyngeal wall and epiglottis should be noted. Again, cephalometric analysis of the posterior airway space is helpful in evaluating the base of tongue relative to the soft palate and posterior pharynx.

Assessing the position of the tongue in relationship to the palate is based on observations defined by Mallampati and modified by Friedman [20,21]. Friedman tongue position (FTP) I, allows the observer to visualize the entire uvula, tonsils, and tonsillar pillars. FTP II allows visualization of the uvula, but not the tonsils. FTP III allows visualization of the soft palate, but not the entire uvula, and FTP IV allows visualization of the hard palate only (Figure 3).

The size of the tonsils also plays an important role in the staging and management of OSA patients. Tonsil size (TS) is graded from 0 to 4. TS 0 represent post-tonsillectomy patients. TS 1 implies tonsils hidden within the pillars. TS 2 represents tonsils that extend to the pillars. TS 3 refers to tonsils that extend beyond the pillars, but not all the way to the midline, whereas TS 4 tonsils (also known as “kissing tonsils”) reach the midline (Figure 4).

![Figure 3](image1.png)

**Figure 3.** Friedman tongue position (This figure is copyrighted by the author and may not be reposted, reprinted or otherwise used in any manner without the written permission of the author) (Modified from Friedman M, Ibrahim H, Bass L. Clinical staging for sleep disordered breathing. Otolaryngol Head Neck Surg 2002;127:15).

![Figure 4](image2.png)

**Figure 4.** Tonsil size (This figure is copyrighted by the author and may not be reposted, reprinted or otherwise used in any manner without the written permission of the author) (Modified from Friedman M, Ibrahim H, Bass L. Clinical staging for sleep disordered breathing. Otolaryngol Head Neck Surg 2002;127:15).

The exact location of pharyngeal collapse is often difficult to predict with certainty. More confounding is the fact that the area is often not a single area at all but involves a combination of retropalatal and retroglossal collapse [22]. Accurate identification of the exact sites of
collapse should aid the surgeon in procedure selection, thereby improving success rates. This challenge in identifying the areas of anatomic abnormality has led to the development of diagnostic techniques, including fiberoptic airway endoscopy with the Muller maneuver and imaging techniques, among others.

*Fiberoptic nasopharyngoscopy:* Direct visualization of the upper airway from the nose to the larynx aids in the identification of potential areas of airway collapse and is well recommended in patients with SDB. First, the nasal airway is evaluated for nasal pathology. The nasopharynx is then examined to rule out obstruction from adenoids, polyps, masses, or cysts (Figure 5). The patient is then asked to perform a Muller’s maneuver, which is forced inspiratory effort with the mouth and nose closed, to determine if there is obstruction at the level of the soft palate. The fiberoptic examination proceeds to the level of the oropharynx, and the base of the tongue is evaluated along with the tonsillar tissues. Since most obstruction during sleep occurs at the retropalatal and retroglossal areas, this portion of the examination is important. The patient is asked to perform another Muller’s maneuver as the endoscope is passed into the hypopharynx. The position of the base of tongue to the epiglottis and posterior pharyngeal wall is observed to assess the retropositioning of the base of tongue. The larynx and vocal cords are also evaluated to rule out any supraglottic, glottic, or subglottic pathology.

*Sleep Endoscopy:* The use of artificial sleep using intravenous medications, while the investigators observe the potential areas of obstruction with a fiberoptic endoscope, has been controversial and not universally accepted [23].

*Imaging Techniques:* The diagnostic imaging techniques in SDB are covered in Chapter 1.

![Figure 5](image.jpg)

**Figure 5.** Fiberoptic nasopharyngoscopy demonstrating the adenoid pad in the nasopharynx.

**Polysomnography**

Preoperative evaluation must include a thorough review of a polysomnography (PSG) which is a vital part of the preoperative evaluation. These data will guide appropriate surgical
treatment, as well as preoperative and postoperative management. The apnea hypopnea index (AHI), or the number of apneas and hypopneas per hour of sleep, indexes the severity of the condition. This categorization alone with oxygen desaturations classifies the patient as having mild, moderate, or severe OSA. There is a significant increase in morbidity associated with an AHI greater than 20 per hour, and those patients with higher AHI values have been linked to a greater incidence of perioperative airway complications [24]. It also has been shown that with more severe OSA (by both AHI and apnea index), UPPP tends to be less successful [18,25]. The SaO₂ data as stated previously should be examined to determine the awake baseline and mean SaO₂ sleep desaturations because lower values are indicative of potential perioperative respiratory compromise [21]. The best but not routinely performed objective test to determine the site of obstruction is multilevel pressure measurements during sleep [26]. Multilevel pressure sensors would provide us with a measurement of obstruction at the palate and tongue base.

1.2. Surgical Planning

Selection of the appropriate surgical procedures for reconstruction of the upper airway remains the most difficult task for the surgeon in the treatment of SDB. Due to the difficulty in predicting a single site of obstruction, most surgeons currently advocate a multiphase approach. In fact, information gathered from the preoperative assessment, including anamnesis, physical examination, fiberoptic nasopharyngoscopy, imaging techniques and polysomnography can provide useful information regarding the exact sites of obstruction [27]. Surgical procedures are also selected dependent upon the experience and knowledge of the surgeon performing them. Besides, patient’s desire and preference can clearly influence outcomes and must be considered. Informed consent must be obtained, and patients should be educated regarding the rationale of surgery, associated risks, and benefits. The most logical surgical approach should be minimizing surgical intervention to avoid unnecessary surgery.

Definition of Successful Treatment

Today, surgical success is defined as meeting the criteria used by Sher et al. [25]: 50% improvement in respiratory disturbance index (RDI) to a final absolute value below 20, or the apnea index (AI) to below 10. These objective criteria of success are less than ideal, because the normal RDI is 5 or less.

2. SURGICAL MANAGEMENT OF SNORING

2.1. Nasal Surgery

It is universally accepted that the nasal airway must be functional before addressing the collapse of the airway. In patients with nasal obstruction, opening the nose is appropriate, independent of any effect on snoring. Most nasal airway pathology may be treated pharmacologically; however, septoplasty, turbinate reduction, or both may be necessary to achieve airway stability. Submucosal RF cautery to the turbinates to open the nose can be
performed at the time the soft palate is treated in the office, and is regularly effective [28]. Correction of symptomatic nasal septal deflections is usually performed in combination with turbinate reduction.

The relationship between nasal obstruction and SDB has been demonstrated by numerous investigations [29,30,31]. Therefore, the treatment of nasal obstruction plays an important role in the management of SDB. It must be emphasized that opening an obstructed nose is not regularly effective in improving snoring or OSA, although it should improve nasal breathing, nasal PAP tolerance and compliance [32,33].

2.2. Soft Palate Radiofrequency Ablation

Radiofrequency ablation (RF) of tissue has many applications in the medical and surgical fields. Powell and Riley first adapted this modality to treat redundant tissue of the upper airway in patients with SDB. RF has several advantages as compared to traditional techniques when treating SDB. This procedure is minimally invasive and can be performed on an outpatient basis. The advantages of RF over electrocautery and laser energy surgery exist in its precision and safety. The targeted tissue temperatures stay within 60 to 90°C, thus limiting heat damage to the tissue. Electrocautery and laser temperatures are significantly greater (750–900°C) and in excess of the desired therapeutic need. This difference allows for a more accurate, minimally invasive, and less morbid procedure without compromising treatment efficacy. The cost of RF treatment is high, and may require purchase of a disposable RF needle electrode, an additional expense. In addition, an RF generator is needed, and this cost must be amortized, adding to the expense. Eventually, the effectiveness of the RF treatment decreases, and it may need to be repeated. UPPP has a reported success rate of approximately 40–50% for improving mild to moderate OSA, although surgical efficacy appears to decrease over time [34,35].

![Figure 6](Image)

**Figure 6.** The radiofrequency electrode is entered high in the soft palate so that the end point of the electrodes is just above the uvula but not in the uvula itself (A). Radiofrequency treatment pattern with two paramedian (B) and with one midline - two lateral (C) locations (This figure is copyrighted by the author and may not be reposted, reprinted or otherwise used in any manner without the written permission of the author).
**Procedure**: The main goal, in RF treatment plan is to deliver sufficient energy for appropriate tissue removal to produce the necessary fibrosis of the musculature without damaging the overlying oral or nasal surface mucosa. However, there is no clear formula for achieving this balance. The radiofrequency electrode is entered high in the soft palate so that the end point of the electrodes is just above the free end of the palate in midline, paramedian, or lateral locations (Figure 6A). The midline and paramedian locations are within the thicker portion of the soft-palate musculature owing to the presence of the musculus uvulae; they can therefore tolerate larger amounts of energy than the lateral locations that include the levator veli palatini and tensor veli palatini muscles. Typically, two paramedian lesions or one midline and two lateral lesions are created during each treatment session (Figure 6B,C). RF is well-tolerated. The incidence of postoperative complications is exceedingly low. Mucosal ulceration or sloughing was defined as a minor complication. Airway obstruction, hemorrhage, palatal fistula, and severe dysphagia are potential serious negative outcomes. We experienced a rare case of uvulopalatal necrosis associated with radiofrequency ablation in a patient with snoring (Figure 7A,B,C).

![Figure 7. Uvulopalatal necrosis associated with radiofrequency on the postoperative day 5 (A), day 7 (B) and day 90 (C) (With permission from Prof. Cemil Mutlu).]

### 2.3. Injection Snoreplasty

Palatal injection snoreplasty was introduced as an inexpensive, minimally invasive office procedure that treats palatal snoring. Basically, a sclerotherapy agent is injected into the submucosal layer to support fibrosis and scarring to stiffen the soft palate [36]. Most commonly used agent is sodium tetradecyl sulfate [37]. It has a longstanding excellent safety record for the treatment of varicose veins, and it has very low cost. Exclusion criteria for this procedure include comorbid diseases that interfere with wound healing, marked tonsillar hypertrophy, previous surgical procedures for snoring, and significant OSA. Complete cessation or a significant reduction in snoring was reported by 92%. However, the rate of snoring relapse was 18% at long-term follow-up [36,38].
Procedure: The primary injection site is in the midline just above the uvula (Figure 8A). Two ml of the sclerotic agent is injected into the soft palate within the submucosal plane. A translucent bubble of fluid which turns to a hemorrhagic color within 2–3 min as the sclerosing agent takes effect is observed. The final result is a fibrotic palate that is retracted superiorly, with the oropharyngeal airway widened. For the patient undergoing a repeat injection, the injection sites differ. Reinjection into the midline is usually difficult because of the already stiffened midline soft palate; therefore, the soft palate is injected lateral to the primary injection site, with 1 ml of the sclerosing agent on each side (Figure 8B). Injection snoreplasty offers the advantage of mild pain without a significant recovery period. The most common reported complications are palatal swelling. Rare but serious complications include mucosal ulceration, palatal fistulae, and anaphylaxis to the agent.

2.4. Laser-Assisted Uvulopalatoplasty

Laser assisted uvulopalatoplasty (LAUP) is an office-based procedure that was introduced in 1990 for the management of snoring. LAUP progressively shortens and tightens the uvula and palate through a series of carbon dioxide laser incisions and vaporizations. Walker demonstrated a 48% success rate; however, 21% of patients had worsening of their SDB following LAUP [39].

Procedure: Most of the uvula is amputated, and the soft palate is incised by vertical trenches up to the muscular sling 1–2 cm lateral to the uvula. Surrounding mucosal or tonsillar pillar tissue may also be vaporized. This technique requires a CO2 or equivalent laser, but does not need a new hand-piece for each treatment. Because the cost of the laser must be considered, the expense of the procedure is necessarily higher than non-laser procedures. The associated pain is greater than with RF submucosal tightening, and the need for multiple
procedures is a deterrent. There are some concerns, however, regarding the safety of performing this surgery on an ambulatory basis, because of possible early postoperative edema of the upper airway [40,41]. As a result of these concerns, as well as significant postoperative pain, LAUP has become less popular for the treatment of OSA.

2.5. Cautery-Assisted Palatal Stiffening Operation

Cautery-assisted palatal stiffening operation (CAPSO) is a recently developed single office-based procedure performed with local anesthesia for the treatment of palatal snoring. CAPSO seem to have some effectiveness in the treatment of snoring and mild OSA especially caused by obstruction at the palate level.

Procedure: A midline strip of soft palate mucosa is removed, and the wound is allowed to heal by secondary intention. The flaccid palate is stiffened, and palatal snoring ceases.

The procedure avoids the need for multiple-stage operations and does not rely on expensive laser systems or radiofrequency generators and hand pieces [42,43].

2.6. Pillar® Palatal Implant System

The stiffening of the soft palate by insertion of three or more small barbed implants has been found to decrease snoring [44]. The Pillar® Palatal Implant System (Restore Medical, Inc., St. Paul, Minnesota, U.S.) is an innovative technique introduced in clinical practice in 2003 for the treatment of snoring by means of biocompatible and inert polyethylene terephthalate implants. The procedure can be performed quickly in the office under local anesthesia with minimal morbidity. The rationale for this therapy is to stiffen the soft palate, and thus reduce snoring. Implantation imparts a degree of rigidity to the palate. Additional stiffening of the palate is achieved by fibrosis and formation of capsule in response to the inflammatory reaction [45]. The Pillar Implant received FDA clearance for the treatment of snoring and mild-to-moderate OSA.

Procedure: The Pillar® Palatal Implant System consists of an applicator with a curved needle at the tip, in which the implant is pre-loaded. The implant is deployed through the needle when the slider in the delivery tool is advanced. Each delivery tool contains one implant. The curved needle has three markings: a full insertion marking, a halfway depth marking, and a needle tip marking. Preoperatively, the oral cavity should be prepped with chlorhexidine gluconate (0.12% to 0.2%) rinse to decrease the chance of implant infection. The first step consists of injecting the soft palate with 1% lidocaine (1:100000 epinephrine) solution. The exact location of the insertion site is determined by palpating the junction of the soft and hard palate with the index finger. The implants should be adjacent to the hard palate, and should effectively “extend” the hard palate, as well as shorten the soft palate. The injections are performed close to the insertion sites, which are located at the junction between the hard and soft palate, right at the midline and 2 to 3 mm laterally on each side. The midline implant is inserted first. The needle is advanced to the full insertion depth marker (which should remain visible), thus creating a tunnel in the soft palate muscles into which the implant is then deployed (Figure 9A,B).
At this point, the device is unlocked and the slider is pushed half-way. The needle is then withdrawn until the halfway depth marker, and the slider is pushed all the way in, thus deploying the implant into the soft palate. The needle is then withdrawn following the curvature of the needle, by moving the delivery tool in an arching fashion. The two lateral implants are inserted in the same fashion, as close as possible to the midline implant, about 2 mm apart (Figure 9C). A good way of estimating this distance is by using the diameter of the needle (~2 mm). Pain and mild palatal swelling can occur postoperatively, yet they are transient. The most common complication is post-insertion extrusion. Different rates of extrusion have been noted from 2.7% to 8.8% [46,47]. One disadvantage is the relatively high cost of the implants.

2.7. Uvulectomy

Uvulectomy has been attempted for snoring management, but short-term results were poorer than those of other procedures [48].

3. SURGICAL MANAGEMENT OF OBSTRUCTIVE SLEEP APNEA

Obstructive sleep apnea, defined as an apnea–hypopnea index (AHI) of at least five events per hour, is a major public health problem in the United States that affects 24% of adult males and 9% of adult females [49]. Since uvulopalatopharyngoplasty was first introduced for the treatment of SDB in 1981, many other surgical procedures have been developed to enlarge the compromised upper airway. The surgical concept for the treatment of OSA is to enlarge the upper airway, thereby restoring its patency during sleep.
3.1. Uvulopalatopharyngoplasty

Ikematsu is credited with developing the uvulopalatopharyngoplasty (UPPP) for the treatment of habitual snoring [50]. This procedure was later adapted to treat SDB and snoring by Fujita in 1981 [12]. During the past 28 years, multiple variations have been developed to treat the obstructing tissues of the soft palate, lateral pharyngeal walls, and tonsils. Since its introduction, there has been considerable effort spent in studying the efficacy of this procedure in the management of SDB. Unfortunately, the results of these studies have shown that UPPP, as an isolated procedure for the treatment of OSA, has met with average results. The overall result yields a success rate of nearly 40% with UPPP surgery alone, using the criteria described by Sher et al [25]. By eliminating patients with retrolingual obstruction as the primary cause, postsurgical success rate increases to 52.3% [25]. On the other hand, it should be noted that, as an isolated procedure for snoring, success rate peaks up to 72.9% [27]. Patients who have isolated retropalatal obstruction would be appropriate candidates for UPPP. Friedman et al. stated that the success rate of UPPP is not related to the severity of the disease but is related to the site of obstruction [51]. Also, disease severity is not a prognostic factor in determining success after the procedure but it’s a secondary factor, which plays a role in determining the need for treatment.

Procedure: The original procedure described by Fujita recommends excision of redundant mucosa, with a single-layer closure under tension. Submucosal UPPP focuses on the importance of epithelial preservation and tension-free closure of the epithelium, and on the preservation of the majority of the mucosa of the soft palate and the anterior and posterior pillars. The tonsils are excised using any technique. If done properly, the tonsillar fossa is dry and the muscle fibers are still covered by fascia with minimal trauma to the anterior and posterior pillars at the end of tonsillectomy. After removal of both tonsils, the uvula is grasped and retracted anteriorly. A curvilinear horizontal incision is made on the mucosa at the base of the uvula posteriorly, preserving almost the entire posterior soft palate mucosa (Figure 10A). The incision is carried bilaterally and horizontally across the soft palate. The uvula and the submucosal tissue of the lower edge of the soft palate are excised (Figure 10B). Using a cold knife, the mucosa is separated from the muscle, releasing the posterior soft palatal mucosa (Figure 10C).

Figure 10. Submucosal uvulopalatopharyngoplasty (This figure is copyrighted by the author and may not be reposted, reprinted or otherwise used in any manner without the written permission of the author) (Modified from Friedman M, Landsberg R, Tanyeri H. Submucosal uvulopalatopharyngoplasty. Otolaryngol Head Neck Surg 2000;11:26–9).
The posterior pillar is then advanced anterolaterally. Elimination of pharyngeal redundant folds is achieved by approximation of the submucosa and muscular tissue of the tonsillar fossa and the soft palate, using interrupted sutures through the exposed pharyngeal musculature (Figure 10D). The mucosal flap edges are then loosely approximated, taking care not to undermine, using 3-0 chromic sutures [52]. It is recommended that the procedure be performed by experienced surgeons, as it may be associated with significant complications, including velopharyngeal insufficiency, dysphagia, persistent dryness, and nasopharyngeal stenosis [53,54,55].

3.2. Uvulopalatal Flap

Uvulopalatal flap (UPF) procedure is a modification of UPPP introduced by Powell in 1996 [56]. Indications for this procedure are similar to UPPP, except that it is contraindicated in the case of an excessively long or bulky palate or uvula in which such a flap could create an abnormal thickness to the palate [57]. UPF is preferred over UPPP in most cases because it provides the same anatomical results as UPPP, but reduces the risk of nasopharyngeal incompetence by using a potentially reversible flap that could be taken down in the early postoperative period. The UPF also provides less postoperative pain and fewer complaints of foreign-body sensation [56]. The UPF results for OSA were comparable to the UPPP results.

The success of UPF in conjunction with hypopharyngeal surgery for the treatment of OSA was 70–78%, and long term success was 65% [58,59].

Procedure: Instead of removing the uvula and soft palate, the uvula is pulled away from the pharyngeal wall and reflected back toward the soft palate, expanding the oropharyngeal space. The flap is designed on the soft palate, one angle of which is on the uvula and the opposite angle is on the soft palate near the hard-palate and soft-palate junction.

Figure 11. Uvulopalatal flap (This figure is copyrighted by the author and may not be reposted, reprinted or otherwise used in any manner without the written permission of the author).
The outline is not brought onto the edge of the palate. It can be carried out laterally to achieve the lateral advancement. The mucosa, submucosa with glands, and fat on the lingual surface of the uvula and soft palate are stripped away from the muscular layers (Figure 11A).

The uvula is reflected back toward the soft palate and fixed into its new position with a 3-0 polyglactin suture (Figure 11B). Tonsillectomy is performed avoiding damage to the underlying musculature. The palatopharyngeal muscle is pulled anterolaterally and sutured to the palatoglossal muscle. Several interrupted sutures are placed through the muscles between the two palatal arches. This reversible procedure can be performed as a one-stage surgery on an outpatient basis.

### 3.3. Z-Palatoplasty

The goal of Z-palatoplasty (ZPP) technique is to widen the space between the palate and the posterior pharyngeal wall, between the palate and the tongue base, and to widen the lateral dimensions of the pharynx. This is accomplished by changing the scar contracture tension line to an anterolateral vector, and by widening the anteroposterior and lateral oropharyngeal air spaces at the level of the palate. This technique includes all patients who have had previous tonsillectomy, as well as patients who have small tonsils and those who have unfavorable tongue positions. None of the palatal musculature is resected, thereby minimizing the risk for permanent velopharyngeal insufficiency.

**Procedure:** Two adjacent flaps are outlined in the palate (Figure 12A). The anterior midline margin of the flap is halfway between the hard palate and the free edge of the soft palate, and the distal margin corresponds to the free edge of the palate and uvula.

![Figure 12. Z-palatoplasty](This figure is copyrighted by the author and may not be reposted, reprinted or otherwise used in any manner without the written permission of the author) (Modified from Friedman M, Ibrahim H, Vidyasagar R. Z-palatoplasty (ZPP): a technique for patients without tonsils. Otolaryngol Head Neck Surg 2004;131:89–100).
The mucosa from only the anterior aspect of the two flaps is subsequently removed (Figure 12B). The two flaps are then separated from each other by splitting the palatal segment down the midline (Figure 12C), extending them laterally, and dividing the palatoglossus muscle (Figure 12D). A two-layer closure is then done, which brings the midline all the way to the anterolateral margin of the palate (Figure 12E,F). The primary closure is done at the submucosal level, which then enables a tension-free closure of the mucosa [60]. Complications of the procedure are comparable to those of classic UPPP and include bleeding, postnasal drip, dysphagia, foreign body sensation, and temporary or permanent velopharyngeal insufficiency.

3.4. Lateral Pharyngoplasty

The role of the lateral pharyngeal muscular walls in the pathogenesis of OSA is crucial. Lateral pharyngoplasty produces better clinical and polysomnographic outcomes in the treatment of OSA than does UPPP, without resultant differences in the cross-sectional measurements of the pharyngeal airway between these treatments [61].

**Procedure:** The procedure is routinely performed under general anesthesia. The lateral pharyngoplasty initiates with a bilateral tonsillectomy if had not been previously performed. After removing the tonsils, palatoglossus and palatopharyngeus muscles are identified (Figure 13A). Then, superior pharyngeal constrictor (SPC) muscle is undermined and elevated within the tonsillar fossa as far as its glossopharyngeal part.

Once detached from the lateropharyngeal space, SPC muscle is sectioned in a cranial to caudal direction, resulting in two muscle flaps: one medially based flap that was not further manipulated and one laterally based flap that was sutured anteriorly to the same-side palatoglossus muscle with three separate stitches. Then, a half thickness incision over the oral face of the soft palate is performed, straight from the lateral base of the uvula extending laterally and superiorly to a point approximately 0.5 cm proximal to the soft palate lateral margin and within a height corresponding to that reached by the lateral superior traction of the upper part of the palatopharyngeus muscle, creating, then, a palatine laterally based flap (Figure 13B).

A transverse subtotal section of the palatopharyngeus muscle in its superior part is performed, creating a superior and an inferior flap (Figure 13B). This superior flap and the palatine flap is sutured in a Z-plasty fashion, and they covered the superior part of the tonsillar fossa (Figure 13C).

The inferior part of the tonsillar fossa was then closed by suturing the inferior palatopharyngeus muscle flap to the anterior pillar. Every step was then repeated on the opposite side and, the distal one third of the uvula was removed and sutured for hemostasis (Figure 13D) [62].

As the mylopharyngeal and glossopharyngeal parts of the SPC muscle are cut, swallowing difficulties, as expected, were the most troublesome effects of this procedure. Patients also complained that foods got stuck in their throats, causing cough and discomfort. Permanent velopharyngeal incompetence, a possible complication in palatal surgeries, is very rare with this procedure.
3.5. Transpalatal Advancement Pharyngoplasty

In 1993, Woodson described a technique of removing midline bone of the palate and advancing the soft palate into the defect. This procedure advanced the palate medially and was combined with mucosal advancement flaps along the lateral border of the soft palate to improve the lateral airway [63]. Transpalatal advancement pharyngoplasty alters the hard palate and the soft tissue attachments of the posterior maxilla. The indications for this procedure are persistent retropalatal obstruction after UPPP, and OSA in patients who have small tonsils and without excessively thick and long soft palate.

Procedure: A palatal incision begins at the centre of the hard palate and continues bilaterally to the posterior direction, medial to the greater palatine foramen (Figure 14A). The incision is then flared laterally to the buccal mucosa. A mucoperiosteal flap is elevated, exposing the hard palate and the proximal soft palate (Figure 14B). Only enough tensor is exposed to provide a grasp for subsequent sutures, usually 5 to 8 mm. Electrocautery is used...
so that the soft palate is separated from the hard portion of the palate and the nasopharynx is exposed (Figure 14C). A posterior portion of 1 cm of the hard palate is removed by means of a Kerrison rongeur or a drill, exposing the posterior nasal septum (Figure 14D). Palatal burr holes are placed (Figure 14E). A tapered free needle passes a doubled suture through the drill holes into the nasopharynx. The suture, in a figure-of-eight is grasped in the nasopharynx, withdrawn from the mouth and then secured medially and laterally in the tensor aponeurosis. While an assistant retracts the palate anteriorly, the sutures are tied. A tension-free closure is performed with fine absorbable sutures [64]. Postoperatively, velopharyngeal insufficiency has been rare. Dysphagia may occur for several weeks postoperatively. Sensation of globus, mucocilliary dysfunction, dry throat, excessive salivation, and increased aspiration may occur but seem to be rare and less common than with traditional UPPP techniques. Rarely, palatal flap necrosis and a subsequent oronasal fistula may occur.

Figure 14. Transpalatal advancement pharyngoplasty (This figure is copyrighted by the author and may not be reposted, reprinted or otherwise used in any manner without the written permission of the author) (Modified from Woodson BT. Transpalatal advancement pharyngoplasty for obstructive sleep apnea. Op Tech Otolaryngol Head Neck Surg 2000;11:36–40).

### 3.6. Tongue Base Temperature-Controlled Radiofrequency

The frictional heat generated by radiofrequency (RF) results in tissue injury, and leads to tissue volume reduction [65]. The first prospective study of RF tongue reduction demonstrated a marked improvement of RDI from 40 to 18 with no changes in speech or
swallowing [66]. The success of multiple RF treatments to the tongue base, in a review of 11 series, ranges from 20% to 83%, using the surgical success criteria previously mentioned [67]. Multiple other reports have shown RF tongue reduction to be efficacious in improving OSA [68,69]. Currently, RF airway treatment is often performed as an adjunctive procedure, along with other hypopharyngeal airway surgical procedures. Complications included a superficial tongue ulceration that resolved spontaneously, persistent pain on swallowing that resolved after several weeks, and a tongue abscess that required drainage.

3.7. Tongue Base Suture Suspension

Tongue-base suture suspension procedure is a minimally invasive, safe and effective procedure addressing obstruction in the hypopharynx and tongue base. This technique utilizes a submucosal suture that is anchored to the genial tubercle to prevent the tongue from occluding the pharynx when muscle activity is reduced during sleep. The reported success rates of isolated tongue-base suture suspension procedure have been variable [67,70,71]. However, the procedure is routinely performed with UPPP to maximize outcomes. In combination with UPPP, suture suspension of the tongue has a success range of 20 to 57% [72,73].

![Figure 15. Tongue base suture suspension procedure](This figure is copyrighted by the author and may not be reposted, reprinted or otherwise used in any manner without the written permission of the author).

Procedure: The surgery is performed under general anesthesia. The suspension suture is looped from the anchor screw on the inner surface of the mandible to the base of the tongue (Figure 15A). The suture is tightened down with some tension to create a hammock effect for the tongue (Figure 15B). Associate risks of the procedure are low and are limited to infection, injury to tooth roots, and detachment of the anchor screw. Mild complications can be
associated with this surgery. Sialadenitis (salivary gland inflammation), wound infection, trauma to the neurovascular bundle of the tongue, and dysphagia can occur.

3.8. Tongue Base Resection (Midline Glossectomy)

The removal of the center part of the tongue base using a laser evaporation technique or lingualplasty was described by Fujita and Woodson [74]. They reported a 77% success rate in their series [75]. The success rates of tongue base resection procedures in the literature can be variable, ranging from 25% to 83% [67]. Currently, tongue reduction surgery is undertaken due to significant morbidities. Protective tracheotomy, particularly pain, postoperative dysphagia and an extended hospital stay were occasionally required due to postoperative edema as well as excessive bleeding.

3.9. Genioglossus Advancement

The genioglossus advancement (GA) procedure is limited to moving the geniotubercle with the genioglossus insertion forward without moving the mandible. The genioglossus muscle is attached to the lingual surface of the mandible at the geniotubercle and also to the hyoid complex just above the larynx. Movement forward of either or both of these anatomic structures will stabilize the tongue base along with the associated pharyngeal dilators. In 1986, Riley developed the rectangular osteotomy technique to advance the genial tubercle for patients with hypopharyngeal obstruction [76]. This advancement places tension on the tongue musculature, and thus limits the posterior displacement during sleep. In general, GA is performed with other sleep apnea surgical procedures such as UPPP and hyoid advancement to maximize the improvement. The overall success rates of GA procedure have been variable, ranging from 23% to 77% [67,77,78]. Genioplasty is technically simple; surgical outcome is not consistent, but can be improved with appropriate patient selection.

Figure 16. The genioglossus advancement procedure (This figure is copyrighted by the author and may not be reposted, reprinted or otherwise used in any manner without the written permission of the author).
**Procedure:** A lateral cephalometric radiograph and a panoramic dental radiograph are critical in the preoperative planning to identify the genial tubercle and to assess the root length of the mandibular canine and central incisor teeth. Sclerotic bone in the symphyseal region of the mandible aids in locating the genial tubercle. Surgery can be performed under intravenous sedation or general anesthesia. A rectangular osteotomy on the symphysis of the mandible is performed. The rectangular window of symphyseal bone consisting of the geniotubercle is advanced anteriorly, partially rotated to prevent retraction back into the floor of the mouth, and immobilized with a titanium screw (Figure 16A,B) [79].

The potential risks associated with GA are quite limited, but include infection, hematoma, injury to the genioglossus muscle, and paresthesia of the lower teeth. The most serious complication of this procedure is mandibular fracture, which occurs when the osteotomy violates the inferior border of the mandible or induces lesions at the roots of the teeth.

### 3.10. Hyoid Advancement

The hyoid bone is in intimate relationship with the tongue base and pharyngeal musculatures, and thus is an integral aspect of the upper airway anatomy. The genioglossus and geniohyoid muscles as well as the middle pharyngeal constrictors insert on the hyoid bone. Consequently, the position of the hyoid complex is important in maintaining the patency of the hypopharyngeal airway. The hyoid bone may be repositioned anteriorly, by attaching it to the thyroid cartilage to expand the airway. Van de Graaff reported that anterior hyoid advancement improved the posterior airway space in a canine model [80]. In 1984, Kaya was the first to demonstrate this concept in human subjects [81]. In 1986, Riley popularized the inferior sagittal osteotomy of the mandible with hyoid myotomy suspension, which attempts to move the hyoid bone cranial and anterior for the treatment of the hypopharyngeal constriction [76].

Riley’s method was later modified by Hörmann, who avoided cutting the stylohyoid ligaments and did not perform a myotomy of the suprathyroidal and infrahyoidal musculature in order to be less invasive and more effective [82]. As with other sleep apnea surgical procedures, the success rates of hyoid advancement can be variable, ranging from 17% to 65% [61,78,83]. Hyoid advancement (or suspension) (HA) is usually performed in conjunction with GA to improve OSA [61,78]; however, some surgeons elect to combine it with UPPP alone [83]. HA may be combined instead with radiofrequency to the ventral surface and base of tongue [84].

**Procedure:** The hyoid bone and thyroid cartilage are exposed. The inferior hyoid body dissected remaining the majority of the suprathyroidal musculature intact. The hyoid is advanced over the thyroid lamina and immobilized with three or four permanent sutures placed through the superior aspect of the thyroid cartilage (Figure 17A,B). The main problem with HA is the requirement for an external incision on the neck, which may not be readily accepted by all patients. The associated surgical risks are low, but include infection, seroma formation, transient aspiration and dysphagia [85].
3.11. Maxillomandibular Advancement

Maxillomandibular advancement (MMA), the current gold standard for OSA, is the most effective sleep apnea surgical procedure currently available. MMA is advocate as an initial intervention by some surgeons, especially for the patients with severe OSA or significant maxillomandibular deficiency. The first reports of mandibular skeletal surgery for OSA were done by Kuo in 1979 and Bear in 1980. This surgery specifically addresses hypopharyngeal or base-of-tongue obstruction [86,87]. The success rate is usually between 75% to 100% [88,89], with a long-term success approaching 90% [90,91].
Procedure: The procedure consists of mobilizing the maxilla and mandible to achieve anterior displacement of the maxillomandibular complex. Lefort I maxillary osteotomy with rigid plate fixation and a bilateral sagittal split mandibular osteotomy with bicortical screw fixation of titanium plates in the advanced position is performed (Figure 18A,B).

To maximize the airway expansion, an advancement of at least 10 mm is usually recommended; however, it is important to achieve maximal advancement while maintaining a stable dental occlusion and a balanced aesthetic appearance. MMA is technically demanding and has substantial expense. Patient perception of the surgical outcome has been favorable. Although many patients may be left with “prominent jaws,” very few patients are dissatisfied with their appearance [92]. Loss of the airway is rare but the most feared complication following surgery. Although MMA is considered a fairly invasive procedure, associated surgical risks are low including bleeding, infection, and partial numbness of the cheek, lower lip, chin and palate. Skeletal relapse resulting in malocclusion can also occur in up to 15% of patients, and therefore, coordinated treatment with an orthodontist may be necessary when indicated [93].

3.12. Tracheotomy

While tracheotomy bypasses the entire upper airway obstructions, the associated psychosocial problems, social implications and morbidity preclude its widespread use. The current use of tracheotomy primarily serves as a temporary measure for airway protection in patients with severe sleep apnea with either morbid obesity or significant craniofacial anomalies that pose a high risk for airway compromise in the perioperative period. Permanent tracheotomy as a long-term treatment of OSA remains an option in morbidly obese patients with obesity hypoventilation syndrome, or in patients with significant craniofacial anomaly for whom all other forms of nonsurgical and surgical treatments have failed [94,95].

4. Pediatric Specific Procedures

In children, tonsillectomy and adenoidectomy represent the major surgical intervention and, if needed, radiofrequency treatment of the nasal turbinates combined with aggressive treatment of allergies. Adjunctive treatment in children includes maxillary and mandibular distraction via orthodontics.

4.1. Tonsillectomy and Adenoidectomy

Childhood OSA is typically recognized at age 2–8 years when the tonsils and adenoids are the largest in relation to the airway size (Figure 19) [96]. In children, tonsillectomy and adenoidectomy (TNA) have provided successful treatment of OSA in the majority of patients, because the obstruction is usually caused by enlarged tonsils or adenoids. The goal is to maximize the size of the upper airway by removing tonsillar and adenoid tissue. TNA is considered highly effective for treating OSA with success rates of 75–100% [97,98,99]. The
The majority of children experience improvement in growth [100], quality of life [98], behavior [101], right ventricular function (102), neurocognitive function [103], and school grades [104]. Children experiencing other sleep-related disturbances, such as night terrors, sleepwalking, or nocturnal enuresis, also improve after TNA [105,106]. The most common perioperative complication of TNA is bleeding [107]. Morbidly obese children undergoing TNA may be considered at a higher risk of postoperative respiratory compromise [108].

![Figure 19](image1.png)  
**Figure 19.** The lateral cephalogram of a healthy control (A) and a patient with adenoid hypertrophy and severe obstructive sleep apnea patient (B).

### 4.2. Maxillary and Mandibular Distraction

![Figure 20](image2.png)  
**Figure 20.** Maxillary and mandibular distraction procedure (This figure is copyrighted by the author and may not be reposted, reprinted or otherwise used in any manner without the written permission of the author).
Distraction osteogenesis is a safe surgical technique in the management of children or young adults with mild or moderate OSA. The incremental skeletal movement allows accommodation of the soft tissue, thus enabling large skeletal movement that usually cannot be achieved by conventional techniques. Maxillary distraction osteogenesis requires an orthodontic device anchored to two upper molars on each side of the jaw, which applies daily pressure causing each half of the maxilla to grow apart (Figure 20A,B).

This technique aims to expand the hard palate laterally, raise the soft palate, and widen the nasal passage. This provides more space for the tongue and prevents it from falling posterior and occluding the oropharynx during sleep. Rapid maxillary distraction needs to occur before the cartilage becomes bone, between the ages of 5 and 16 years. Mandibular distraction osteogenesis, may be required if noninvasive orthodontic procedures is not able to achieve sufficient mandibular widening. Widening of 12 to 14 mm can be obtained easily in 3 weeks (Figure 20C,D) [109]. This approach is normally postponed until 10 to 13 years of age, and by 12 to 13 years of age both rapid maxillary distraction and mandibular distraction osteogenesis can be performed simultaneously. The distractors are usually left in place for 3 months to provide stability of the maxilla and mandible until the newly formed bone is completely ossified.

5. POSTOPERATIVE MANAGEMENT

Although fortunately rare, life-threatening complications have been associated with sleep apnea surgery [110,111]. Fatalities in the early postoperative period have been related to airway obstruction due to pharmacological sedation and surgical edema especially in patients who have hypopharyngeal obstruction [112]. Nasal PAP use during the perioperative period has shown to protect patients from airway obstruction and hypoxemia, and is highly encouraged, especially in cases of severe OSA [113,114]. As with any intervention that involves resection of the soft palate and oropharyngeal structures, significant pain and dysphagia can be expected during the first 24 to 72 hours postoperatively. Another well-known complication is bleeding and can occur at any time until the healing process is completed. Velopharyngeal insufficiency, globus sensation over the following months, nasopharyngeal stenosis and abscess formation, are rare but possible complications.

SUMMARY

Developments in the area of SDB management appear to concentrate on combining previously known methods and on optimizing methods of patient selection. Currently, no single procedure is effective in treating all SDB patients. Treatment should be tailored to the anatomy of each patient. Combined surgical procedures can achieve success rates of about 70% to 99%. Even taking all these developments into account, however, nasal PAP continues to be the gold standard treatment for OSA. Nevertheless, the disappointing long-term compliance rates of 40 to 60% among PAP users have to be regarded as a major challenge warranting more aggressive exploration of both surgical and nonsurgical alternatives for OSA therapy.
CONFLICT OF INTEREST STATEMENT

The author has no financial relationship with a commercial entity that has an interest in the subject of this manuscript.

REFERENCES


Surgical Management of Sleep-Disordered Breathing


Chapter 3

SNORING IN CHILDREN: CONTROVERSIES IN DIAGNOSIS AND TREATMENT

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ABSTRACT

Obstructive sleep disordered breathing in children is a relatively common problem, presenting in various ways, from primary snoring, without an observed decrease in quality of life, to obstructive sleep apnea with cognitive, cardiac and growth abnormalities.

History, clinical examination, radiologic evaluations, sleep studies and other diagnostic modalities are reviewed. Since application and interpretation of these methods are not consistent in studies of snoring, a consensus on optimal treatment options has not been established.

Traditionally, adenotonsillectomy has long been the treatment of choice. Treatment failures or recurrences as well as the existence of causes and contributing factors other than adenotonsillar hypertrophy, like obesity, facial malformations, Down syndrome etc, have changed the concept of adenotonsillectomy as the ultimate cure. Several other treatment options have been proposed on their own or in combination. Continuous positive airway pressure, anti-inflammatory medications, maxillofacial and orthodontic treatments are reviewed suggesting the need of a multidisciplinary approach in some cases.

Finally, a diagnostic and treatment work up based on current evidence is proposed at the end of the chapter for otherwise normal children or children with specific conditions.

Keywords: snoring, sleep apnea, polysomnography, adenotonsillectomy.

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Snoring is a common finding in childhood. Overall prevalence of parent-reported snoring by any definition in a recent meta-analysis was 7.45% (95% confidence interval, 5.75-9.61)[1] Snoring is the most common manifestation of obstructive sleep apnea and primary or habitual snoring represents one end of the spectrum of sleep-related breathing disorders.[2] Terms like central, obstructive or mixed sleep apnea, upper airway resistance syndrome and obstructive alveolar hypoventilation that are used in adults, applied also in children although definitions and specific characteristics of each condition may vary in relation to age.

The stereotype of “Joe the fat boy, who goes on errands fast asleep and snores as he waits on the table” from Dickens’ Posthumous Papers of the Pickwick Club, is difficult to erase [3] although children who snore rarely have this kind of phenotype. On the contrary, daytime sleepiness in children with sleep apnea is the exception, not the rule [4]. Instead of being sleepy, the child may have non-specific behavioral difficulties such as abnormal shyness, hyperactivity, developmental delay, and aggressive behaviour [5].

Pathogenesis and risk factors, clinical consequences (adverse effects), presentation (symptoms and signs), diagnosis and treatment options are reviewed. A practise pathway at the end of the chapter summarises clinical evaluation and treatment of children with snoring.

**PATHOGENESIS AND RISK FACTORS**

Many of the same conditions that predispose to snoring in adults are also causative in infants and children. However, not all predisposing factors cited in adults have the same impact in children. Adenotonsillar hypertrophy, albeit rare in adults, is probably the most commonly recognised pathogenic factor. This explains why sleep disordered breathing is most common in young children (pre-school and early school years), with a peak prevalence around 2–8 years, and subsequent declines in frequency [6] The highest incidence of obstructive sleep apnea coincides with the time of greatest hyperthrophy of tonsils and adenoids, typically during the 4th and 6th year of life [7]. However, symptoms may appear even earlier; in one study 14 patients with OSA aged under 18 months were reported to have symptoms that first appeared at 2 to 6 months of age [8].

Lymphadenoid tissue will especially proliferate in children exposed to environmental irritants, such as cigarette smoke[9, 10]. More recently, a potential link between viral respiratory infections during infancy and the proliferative properties of upper airway lymphadenoid tissues has emerged, whereby early viral infections may predispose for increased risk of adenotonsillar hypertrophy[6]. Laboratory data suggests that respiratory syncytial virus and other viruses, like Ebstein-Barr, may induce neuroimmunomodulatory changes within adenotonsillar tissues, predisposing them to increased proliferation [11]. This theory remains to be corroborated by epidemiologic studies.[12]

Whereas neither the size of the adenoid pad nor the size of the airway is predictive for the degree of airway obstruction, the size of the tonsils is weakly associated with the amount of obstruction [8]. Interestingly, several studies have failed to show a strong correlation between upper airway adenotonsillar size and OSA[13-17]. It has been proposed that such discrepant findings may be explained by the varying proportion of obese children included in each of these studies [6].
Interactions between BMI and tonsil/adenoid size have been independently implicated in the risk for OSA [16]. It has also been shown that the severity of OSA is proportional to the degree of obesity [18-21]. Moreover, it is likely that the ratio between habitual snorers and those with clinically relevant OSA among obese children may differ from the ratios reported for non-obese children [22]. Another finding that suggests the existence of physiological differences between obese and nonobese airways is that obese children with OSA had more obstructive events in the supine position, whereas obstructive events in nonobese children with OSA were more severe in the prone or side positions [23]. As it is analysed further in this chapter childhood obesity, which became an epidemic all over the world the latest years, is a significant factor that need to be considered in the diagnosis and treatment of the snoring child.

Abnormal craniofacial morphology is another important consideration in children with snoring. A variety of craniofacial disorders are associated with obstructed breathing, especially those with midface hypoplasia, such as Crouzon, Apert, Treacher Collins and Klippel Feil. Robin sequence (micro-retrognathia, glossoptosis and palatal cleft) is commonly related with severe upper airway obstruction in which symptoms other than snoring predominate. Snoring in children with Down syndrome is probably multifactorial. Small nasopharynx and oropharynx, macroglossia and other craniofacial abnormalities constitute snoring a challenging problem in these children [24].

Craniofacial dysmorfies like retrognathia can be seen in syndromic patients and in isolation from other abnormalities. Later cases are more commonly encountered in outpatient clinics. Unsatisfactory dental arch relationships, retrognathia and hypognathia, should be looked for in every child presented with snoring since they may contribute by themselves or in combination with tonsillar and/or adenoidal hypertrophy in increased airway resistance and sleep disordered breathing (SDB) [25]. Craniofacial anatomy is the result of both genetic and “environmental” determinants [26]. Black ethnicity, Far East origin and a family member with sleep disordered breathing were found to be predictors of SDB [27]. Regarding “environmental” determinants of craniofacial morphology, narrower maxilla, mandibular retrognathia and longer lower facial height are the typical findings of the “long face syndrome” reported in children with chronic upper airway obstruction, which can be at least partially reversible after treatment [25]. Although it is difficult to quantify the presence of craniofacial anomalies in children with snoring, the recognition that snoring persist or recurs after adenotonsillectomy in some children, highlights the importance of looking systematically for craniofacial and dental anomalies in children referred for treatment of snoring [26].

Neuromuscular disorders, like muscular dystrophy, can also contribute significantly to pharyngeal obstruction. Snoring (and possible sleep apnea) is a common referral symptom to otolaryngologist for these children. Genioglossus and stylopharyngeus are probably the two most important muscles that span the pharynx and reduce pharyngeal obstruction. A family trait in decreased genioglossus muscle activity has been shown [28].

In addition to pharyngeal obstruction, other causes of airway narrowing include allergic rhinitis, vasomotor rhinitis, chronic rhinosinusitis, upper respiratory tract viral infections, polyps, turbinate hypertrophy and deviated septum. These can be responsible for the acceleration of airflow (Venturi effect) and the increase of negative pressure (Bernoulli principle) that cause a partial or total collapse of the pharyngeal walls during sleep. Moreover,
the switch to the oral route for breathing changes the dynamics of the upper airway, predisposing to its collapse.

Children with allergic rhinitis often become mouth breathers and snore at night as a result of nasal obstruction and adenoidal hypertrophy, with congestion of the inferior turbinate[29]. A recent study in young children by McCoolley et al[30] has shown an increase in frequency of OSAHS in habitual snorers with allergic sensitization. In addition, increased nasal resistance, as measured by anterior rhinometry, has been found to correlate with severity of sleep apnea in children with adenotonsillar hypertrophy [31].

Deviated septum is an unusual finding in young children and only rarely encountered as the main causative factor of snoring in these ages. On the other hand, chronic rhinosinusitis is more often implicated. A history of sinus problems (adjusted odds ratio, 5.21; 95% confidence interval, 1.66–16.12] was found to be an independent predictor of sleep-disordered breathing in children and adolescents as part of a genetic-epidemiology study of sleep-disordered breathing [20].

Polyps, antrochoanal, those associated with cystic fibrosis etc, can also be found in cases of nasal congestion. Thus they should be incorporated in the differential diagnosis as well as other rare cases of nasal obstruction like hormonal changes during puberty and hypothyroidism [29].

Risk factors assessment and epidemiology data on snoring from infants are scarce. Most studies have focused on apnea and the exact incidence of snoring in these cases is unknown since snoring is not the cardinal symptom most of the times. It seems that prematurity is an important factor predisposing to infant apnea among others like anatomic and electrolyte abnormalities, errors of metabolism, drugs and poor thermoregulation. Nevertheless, sleep disturbance can be quite often manifested by symptoms other than snoring like cyanotic spells, change in muscle tone and stridor.

Coexistence of various pathologies or risk factors can be quite confusing when estimating a snoring child. For example, one can speculate that both obesity and tonsillar hypertrophy contribute in the developing of snoring and possible sleep apnea in an obese child with enlarged tonsils but it usually impossible to estimate the significance of each contributing factor or to predict the result of specific treatment. The problem becomes even more confusing when risk factors seem to have a cause and effect relationship. For example, adenoid hypertrophy, allergic rhinitis or chronic rhinosinusitis can coexist with retrognathia. In such cases one can consider the possibility of “long middle face” or “adenoid face” syndrome due to chronic upper airway obstruction or the possibility of treatment failure after relief of obstruction due to coexistence of two different pathogenetic factors.

Clinical judgment as well as estimation of possible adverse effects and results of the diagnostic work up should be implicating for choosing appropriate treatment options

ADVERSE EFFECTS

Pediatric snoring is increasingly being recognized as no longer harmless. Recent research in children indicates that primary snoring, the mildest form of the sleep-disordered breathing spectrum, may also be associated with morbidity. Parentally-reported daytime sleepiness, hyperactivity, and aggressive behaviours have all been documented in children who snore,
even in the absence of OSA [32-35] Increasing concern surrounds the presence of pediatric snoring in the absence of OSAHS as potentially harmful to the delicate, developing pediatric central nervous system. The mechanism for this process is not completely known but is suspected to be via either from arousals that stem from snoring and partial airway obstruction and/or gas exchange abnormalities that may occur from snoring/partial airway obstruction in the snoring child [36].

Neurocognitive and behavioral dysfunction have been better studied in children with OSA and are well-characterized consequences of this disease. Schooling problems have been repeatedly reported in case series of children with OSA, and in fact may underlie more extensive behavioral disturbances such as restlessness, inattention, aggressive behaviour, excessive daytime sleepiness and poor schooling [58–63 In a British Medical Journal paper published in 1889 entitled “On some causes of backwardness and stupidity in children,”[37] it was reported that the child “who frequently suffers from headaches at school, breathes through his mouth instead of his nose, snores and is restless at night, and wakes up with a dry mouth in the morning, is well worthy of the solicitous attention of the school medical officer.’[29] Notwithstanding, improved learning and behaviour will occur after treatment in some children [38-42], thereby suggesting that the neurocognitive and behavioral deficits are at least partially reversible [6, 43].

Clinical evident events of OSA on the cardiovascular system are rare [8]. However, altered blood pressure regulation, systemic hypertension, cor pulmonale and changes in left ventricular geometry, have all now been reported in children with OSA [6] The most frequent cardiac arrhythmia associated with OSA in children is bradycardia.

Inflammatory processes are under investigation in children with OSA or habitual snoring. High sensitivity CRP, leukotrienes, IL-6, fibrinogen and other inflammatory mediators were found in the circulation, upper airway tissues and sputum, or exhaled condensates of children with OSA [12] Both habitual snoring and OSA syndrome are associated with increased airway inflammation in overweight children as assessed by higher eNO levels. Furthermore, it was demonstrated that childhood obesity in the absence of sleep-disordered breathing is not associated with increased airway inflammation [44].

Chronic nasal obstruction may result in an “adenoid face”. Mouth-breathing children habitually lower their mandible, which may influence dentoalveolar morphology, resulting in a high-arched palate, narrow maxilla, retrognathia, and increased lower facial height. This constellation of findings is similar to the reported cephalometric findings in children with OSA[32, 36, 37]. Thus, not only does upper airway obstruction predispose to snoring and OSA, but it may also has an adverse effect on craniofacial development, posing an increased future risk of OSA [25].

The development of this craniofacial anomaly is controversial and not shared universally [45]. However studies in monkeys and children have shown that upper airway obstruction with mouth breathing can induce craniofacial anomalies, that can improve or normalize after cure of sleep disordered breathing [46-48]. This normalization of some cephalometric measures after treatment of upper airway obstruction is not always the case. Long-term follow-up studies of children with OSA after adenotonsillar removal indicate an increased incidence of snoring, increased respiratory effort, and OSA, suggesting residual craniofacial narrowing [25].

Finally, other problems that can be found in children who snore, and especially those who are chronic mouth breathers, are poor dental hygiene and casts, possibly due to reduced
protective effect of saliva, decrease in quality of life[49-52] and failure to thrive. Although
the latest is not seen in every child who snores, on the contrary some are obese, several
theories on decreased body weight and growth retardation have been proposed. Reduced
secretion of growth hormone and insulin-like growth factor-I due to a reduction of REM
sleep[53-55], low energy intake as a result of difficulty swallowing and possible anosmia and
increased energy expenditure during sleep [56, 57] are the most important of them.

PRESENTATION

Pickwickian constellation of symptoms than includes OSA in association with obesity,
although frequently encountered in adults, is not common in children. Daytime sleepiness in
children with snoring and OSAS is the exception, not the rule. Instead of being sleepy, the
child may have non-specific behavioral difficulties such as hyperactivity, developmental
delay, and aggressive behavior. The possibility of a sleep disorder should be considered in
any child being evaluated for an attention-deficit disorder [5].

Quite commonly daytime symptoms of sleep disordered breathing are nonexistent or are
not reported by parents. A decrease in appetite, dislike for foods that require chewing like
meat, and a preference on soft foods may not be related by the parents to enlarged tonsils or
adenoids. In contrast night-time symptoms frequently frighten parents, especially loud
snoring and episodes of apneas that may be seem exceedingly long when in fact they last
mere seconds[8]. Frequent arousals from sleep, sleep walking, night terrors, excessive
sweating, and enuresis have also been reported [5].

Non obese children who are referred for snoring usually have audible mouth-breathing,
changes in the quality of speech like the “hot-potato” voice of the enlarged tonsils or the
hyponasal speech of adenoid hyperthrophy and midface elongation. The latest is believed to
be both an effect and a causative factor of obstructive apnea. Chronic rhinorrhea, allergic
symptoms or poor school performance can also be mentioned during consultation and should
be carefully evaluated.

DIAGNOSIS

A careful sleep history and questions regarding daytime symptoms is the first step in the
evaluation of the snoring child. Frequency of snoring, whether it is on every day basis, it is
seasonal or related or exaggerated by any specific factor like upper airway infection are of
interest. Quite often parents overestimate the severity of apneas and the doctor should clarify
their duration or provide instructions to caregivers for an appropriate estimation whenever it
is possible. Questioning about symptoms that parents may not attribute to sleep disorder or to
a common cause of snoring, like tonsillar and adenoid enlargement, chronic rhinosinusitis and
allergic rhinitis, is also important. More specifically poor school performance, hyperactivity,
poor appetite and frequent episodes of rhinorrhea are of interest.

On physical examination, adenoid face, mouth breathing, allergic signs like allergic
salute, supratip crease, sneezing, and long, silky eyelashes, are also of interest. Tonsillar
enlargement is usually numbered from 0 or 1 (in cases of small tonsils that are within tonsillar
fauces) to 4 (indicating enlarged tonsils obstructing the oropharyngeal aperture or at least 75% of the lateral airway dimension). Unfortunately, position of the tongue, cooperation of the child, interexaminers’ variations and other factors make this measurement unreliable for estimation of the exact degree of obstruction, especially during sleep.

Although clinical examination as well as endoscopy with the flexible endoscope can be very informative, there are cases like soft tissue masses, small midface craniosynostosis, lytic lesions, micrognathia or macroglossia (eg Beckwith-Wiedermann syndrome) where lateral radiographs are of value for the estimation of the size of the adenoid pad.

Adenoid pad is visible in lateral views in full term infants older than 6 months of age. Posterior nasopharyngeal masses in children younger than one month are abnormal. In addition, absence of posterior nasopharyngeal adenoidal tissue in a child older than 6 months of age may indicate prior adenoidectomy or an immunodeficient state. During the radiological examination, mouth should be closed, if possible, and head and neck should be extended otherwise may be misleading due to anterior buckling of the airway that creates a retropharyngeal “pseudomass”. A high kV, collimated, filtered, magnification technique results in a reduction of the dose of ionizing radiation and provides a more detailed view of the airway. A low kV technique is more appropriate when foreign bodies are suspected [8]. As it is shown in figure 1 apart from the adenoid pad, tonsillar size can also be estimated.

Figure 1. Lateral x-ray of the rhinopharynx. Enlarged adenoid pad (arrows) can be seen obstructing the rhinopharynx, although its exact size is difficult to be estimated. Quite often, as in this case, mouth is not closed during neck extension, especially in uncooperative children, contributing to further “narrowing” of the airway at the level of the tonsils.
Although published standards and precise methods of adenoidal measurements do exist, vague estimates of adenoidal enlargement are usually performed. Other radiological examinations reported in the literature are lateral fluoroscopy, which can be used to document the inspiration nasopharyngeal and oropharyngeal collapse in the sleep apnea lab and three-dimensional reconstructions that can be obtained easily with helical scanners and are used for preoperative planning of facial deformities [8].

Neither clinical examination nor lateral neck radiographs can predict obstructive apnea in all cases. A systematic review of 12 studies including 1058 children under age 18 compared evaluation by polysomnography with clinical evaluation by history and physical examination alone. Clinical evaluation had a positive predictive value (PPV) of 55.8% (95% CI, 42.1%–69.6%); no single component demonstrated sensitivity and specificity more than 65% [59]. Symptom questionnaires or scales have also a low specificity and sensitivity when compared to polysomnography results [60]. Brouilette et al [61] described the use of an OSA score that weighted the severity of three factors: difficulty breathing, snoring and apnea. This score was useful in predicting those with severe obstruction on formal polysomnography. Yet, milder forms that are most commonly encountered in children with snoring can not be evaluated sufficiently with this score.

X-ray cephalometrics can add in diagnosis, mostly by estimating adenoid pad size and avoiding flexible nasendoscopy, but they are not always useful. The role of cephalometrics in predicting the site of anatomic obstruction has led to contradictory data, which is not surprising given the fact that these static measurements of bony and soft tissue anatomy most likely do not reflect the dynamic changes in pressure that result in airway collapsibility [62]. In a prospective cohort study of 35 children comparing the tonsillar-pharyngeal ratio measured from lateral neck x-rays to overnight polysomnography, X-ray measurements predicted moderate or severe obstructive sleep apnea on polysomnography but did not accurately differentiate normal children from those with mild obstructive sleep apnea [17].

In conclusion, snoring as estimated by history, and adenotonsillar size as estimated by physical and radiological examination, have a high false positive rate (reflected by a low specificity) and a relative low positive predictive value when evaluating children with possible apneas. In a recent meta-analysis only 55% of patients with a “positive” clinical evaluation for OSAHS were subsequently found to have OSAHS by the specified polysomnographic criteria [59]. To the contrary, their negative predictive value (the importance of their absence, in simple words) is probably much higher. However, the clinician should have in mind that both extensive clinical history and thorough physical examination are unreliable predictors of disease [63] and supplementary examinations are required. In April of 2002, the Section on Pediatric Pulmonology, Subcommittee on Obstructive Sleep Apnea Syndrome of the American Academy of Pediatrics published a clinical practice guideline that addressed the diagnosis and management of childhood OSAS [64]. The guideline concludes that history and physical examination are poor at differentiating primary snoring from OSAS and polysomnography (PSG) was considered the gold standard for the differential diagnosis [5].

A pediatric PSG uses the same technology to record the same information as is recorded in adults. The recording includes electroencephalography, chin electromylogram, right and left electro-oculogram, electrocardiogram, limb movements, and breathing measurements, although not all of them are always employed in children. The breathing measurements usually monitored are airflow, respiratory effort, and pulse oximetry. End-tidal carbon
dioxide and esophageal pressure measurements are used in some but not all laboratories[5]. The terms central, obstructive and mixed apnea that are used in adults are also valid for children and infants but adult criteria cannot applied to this population. Apneic periods up to 10 seconds may be normal in neonates. “Significant apnea in neonates and infants includes episodes of greater than 20 sec of duration or episodes of less than 20 sec if accompanied by bradycardia to 20% below baseline heart rate or oxygen desaturation below 80% of baseline” [65].

In children and adolescents apneas are more frequent than in adults but shorter in duration. Obstructive apnea is usually defined as the absence of airflow with continued chest-wall and abdominal movement for at least 2 breaths [66, 67] or greater than 10 sec duration [8]. Hypopneas are defined as a decrease in nasal flow of ≥50% with a corresponding decrease in SpO2 ≥4% and/or with associated arousal [8]. Reduction in respiratory effort has also been used to determine hypopneas [8]. The Apnea Hypopnea Index (AHI) is defined as the number of apneas and hypopneas per hour of total sleep time (TST) whereas Sleep Disturbance Index (SDI) is defined in several different ways either synonymous or different by AHI. Average obstructive apnea indices were 0.03 per hour of total sleep time (TST) for 3- to 5-year-old children and 0.05 per hour of TST for ≥6-year-old children in a study of 542 healthy children [68].

End tidal carbon dioxide (ETCO2) and O2 saturation is believed by some researchers [69] to be better indicators of upper airway obstruction. Abnormal ETCO2 values are described by Marcus et al [67] as ETCO2 greater than 45mmHg for more than 60% of total sleep time (TST). Likewise, an O2 saturation less than 92% should be considered abnormal in the pediatric age group [67]. In the aforementioned normative study of 3.2-8.6 years old children [68], twenty percent of all subjects had end tidal carbon dioxide values of ≥45 mm Hg, and 2.2% had recorded values ≥50 mm Hg during ≥50% TST.

Sleep architecture and sleep-state proportions are also being calculated in a PSG study. Since there are no good EEG guideline to evaluate sleep quality, one must look for normal proportions of REM and delta sleep and review the overall sleep architecture. Non-REM sleep is the phase of sleep when airway resistance typically reaches the maximum [70]. However, it is during REM sleep that most of the respiratory events occur [68]. Paroxysmal reductions in pharyngeal dilator activity related to central REM sleep processes likely account for the disproportionate severity of OSA observed during REM sleep [25]. Sleep cyclicity is distinct between ≥6 and 3-5 years olds, with both age groups showing an initial brief rapid-eye-movement period, which is lengthening across the night, but only the older group shows a decrease in cycle length across the night.

Arousals are also of consideration since the final pathway for arousal from sleep seems to be the level of ventilatory effort. Specific criteria have not yet been developed for children and arousals are usually defined as recommended by the American Sleep Disorders Association Task Force report [71]. Finally body position during sleep that is the time percentage spent supine, side or prone can be calculated and is seems to affect AHI especially in older children, as it does in adults [68].

Some have questioned the reliability of a single-night PSG study. The possibility of a “first-night” effect, that is, a change in a patient’s sleep architecture due to unfamiliar surroundings, has been postulated. It seems that the first-night effect is rarely significant [72]. Sequential overnight polysomnography did not dramatically improve sensitivity or specificity over a single test in 2 prospective studies of children with suspected obstructive sleep apnea.
The larger study recruited 70 consecutive children (ages 2 to 17 years) from a sleep lab and performed polysomnography on 2 consecutive nights. The first test correctly identified obstructive sleep apnea in 64 children; the second identified 6 additional cases, all of which were “mild” [73].

On the other hand, abbreviated polysomnographies have inadequate sensitivity. A retrospective chart review included 143 children between 1 and 18 years of age with adenotonsillar hypertrophy referred for overnight polysomnography after normal or mildly abnormal “nap polysomnography.” Mildly abnormal nap polysomnography predicted abnormal overnight polysomnography, but normal nap polysomnography were not predictive of normal overnight polysomnography [74].

Currently, the relationships among various parameters of the PSG (apnea-hypopnea index, number of respiratory-related arousals per hour of sleep, oxygen saturation, number of oxygen desaturations < 90% per hour of sleep, and the end-tidal carbon dioxide value) and neuropsychologic parameters (intelligence, memory, attention and impulsivity, and academic performance) are being studied. Preliminary evidence suggests that memory impairment is correlated strongly with the degree of hypoxemia as indicated by the minimum arterial oxygen saturation value, whereas impairment in adaptive behaviour is correlated with the degree of sleep disruption as indicated by the respiratory arousal index. Intelligence and academic achievement are not related to any specific PSG parameter, but instead are best correlated with a composite of the parameters described [5].

However, in generally, outcomes data are severely lacking in pediatric SDB. No specific threshold of disease has been linked to neurobehavioral dysfunction. Combined data are unavailable because apneas and hypopneas are not reported in a uniform way. Although efforts to standardize definitions of these occurrences have been made [65], considerable variability in definition, evaluation, and reporting continues to cloud comparisons [75]. Different methods of recording AHI yield dramatically different diagnosis and assignment of severity [76]. For example, thermistors have the potential to be less sensitive to hypopneas than other methods of recording [77].

In addition, recommended use of PSG is based on the assumption that only the more severe forms of SDB, including OSAHS and upper airway resistance syndrome (UARS), require aggressive (surgical) treatment. A growing body of evidence suggests that snoring alone, even without OSAHS or hypoxemia, may be associated with neurocognitive impairment, particularly attention deficit hyperactivity disorder (ADHD) and learning disorders [10, 78, 79]. Children with habitual snoring lack apnea, hypopnea, respiratory effort–related arousals, and gas exchange abnormalities. This suggests that neuromuscular compensation was successful at attaining stable breathing during sleep, and that any increased respiratory effort remained below the threshold level for arousal. Nevertheless, children with habitual snoring may still have recognizable breathing abnormalities during sleep including inspiratory flow limitation, increased respiratory effort and tachypnea [80, 81], and evidence of subtle alterations in sleep homeostasis [81]. A related polysomnographic pattern, termed obstructive hypoventilation, features snoring, stable increased respiratory effort, and hypercapnia, but not frank apnea, hypopnea, or respiratory arousal [69]. Thus, a snoring child may undergo the best diagnostic test available (PSG) and be found to have no apnea, hypopnea, or hypoxemia, yet may still be at risk for a poor outcome [59].

In conclusion, obtaining a PSG on every child who is evaluated for snoring is not always useful and is obviously not feasible or practical. Yet, the current practice of using the clinical
evaluation alone is also not sufficient. A simple, inexpensive screening test that can be linked to SDB outcomes would be an ideal solution to this dilemma [59]. Several screening techniques have been proposed with variable results. For example, nocturnal pulse oximetry is believed to be highly predictive. A retrospective, cross-sectional study of 349 children between the ages of 6 months and 18 years determined that abnormal home pulse oximetry studies were highly predictive of obstructive sleep apnea on polysomnography (positive likelihood ratio 19.4), but that inconclusive or normal pulse oximetry studies were not predictive of negative polysomnographies [82]. In addition, video recordings have low specificity. In three prospective trials, home sleep video recordings were compared to overnight polysomnography showing an about 90% sensitivity and 52–68% specificity [73, 83]. Moreover, they require strong parental motivation as does audiotaping or sonography [64].

Sleep sonography is usually accomplished by using a tape recorder connected to a precordial stethoscope that overlies the trachea. Studies that evaluate the accuracy of sonography versus polysomnography in children have been reported and show a satisfactory correlation [84]. Sonography is considered a reasonable home test equivalent since there is an objective trend of increasing snoring index and loudness associated with increasing risk of OSAHS. However, the relationship is not pure; some patients who snore loudly and frequently did not have OSAHS and others who snore lightly do have OSAHS [36].

It is generally believed that techniques like sonography, videotaping, nocturnal pulse oximetry, and daytime nap polysomnography are helpful if results are positive, but have a poor predictive value if results are negative [74]. Multichannel home sleep testing has been proposed as a cost-effective, patient-friendly, scientifically valid technique of evaluating patients who present with symptoms of sleep-disordered breathing, typically snoring or daytime sleepiness [85]. It can be dispensed from the physician's office and has a 95% successful recording rate, but little available data exists on snoring children. The same applies for more sophisticated screening tests such as pulse transit time (PTT), arterial tonography, and dynamic CT scan that are under intense investigation but are not yet available or have not been studied extensively in children [59].

Finally, inflammatory markers have been proposed for the evaluation of children with snoring due to altered concentrations of some inflammatory mediators in children with obstructive hypoventilation or sleep apnea. High sensitivity CRP, leukotrienes, IL-6, fibrinogen and other inflammatory mediators were found in the circulation, upper airway tissues and sputum, or exhaled condensates of children with OSA. However, routine use of these inflammatory markers to evaluate disease severity is unjustified [12].

As a conclusion, the use of the clinical evaluation alone in the snoring child is expected to “overdiagnose” OSAHS [59]. Lateral neck radiographs and endoscopy can be useful mostly for the estimation of adenoid size. Sonography, video recordings, and other less labor-intensive methods than polysomnography have been developed for the assessment of the snoring child. Their diagnostic value is still under investigation and their use is not recommended for the evaluation of cases like children with Down syndrome or craniofacial malformations in which PSG should be a routine study [86] prior to their treatment. Nevertheless, one should have in mind that a snoring child may undergo the best diagnostic test available (PSG) and be found to have no apnea, hypopnea, or hypoxemia, yet may still be at risk for a poor outcome [59].
TREATMENT

Traditionally, adenotonsillectomy has been the treatment of choice for children with sleep disordered breathing and adenotonsillar hypertrophy. Adenotonsillectomy have been shown to improve PSG results [87], to relieve symptoms in the majority of these children and to improve their quality of life [88]. Moreover, it is generally accepted as the first line treatment in associated medical conditions like abnormal control of upper airway muscles, eg cerebral palsy [89], Down syndrome [90], and obesity [91] even in the absence of clear adenotonsillar hypertrophy [26] However, persistence or recurrence of snoring and sleep disordered breathing after adenotonsillectomy in these conditions is common.

Various methods have been used since the last century for tonsils’ excision. Cold knife, monopolar or bipolar, ligasure, coblation are among the most commonly utilized [92, 93]. In the UK tonsillectomy audit [94], with more than 40,000 patients studied, a “‘hot’ surgical technique for both dissection and haemostasis (diathermy or coblation) had a risk of haemorrhage that was around three times larger than cold steel tonsillectomy without the use of any ‘hot’ technique. There was, however, no strong statistical evidence for variations in the risk of return to theatre among most techniques”. Moreover, several methodological flaws have been reported that do not permit a strong recommendation on the use of a specific technique over the others.

Morbidity of tonsillectomy is an important consideration. Bleeding, pain, laryngospasm, vomiting and dehydration are some of the most common post operative problems that led to the proposal of several alternatives. Tonsillotomy or partial tonsillectomy or intracapsular tonsillectomy has been utilized with success in children with tonsillar hypertrophy. It is less painful but it may have a greater recurrence rate than tonsillectomy [95, 96]. It should also be avoided in children with recurrent tonsillitis. Pre- or interoperative corticosteroids’ administration and post-operative antibiotics’ prescription is believed by some to reduce morbidity [97-99].

Day case or outpatient tonsillectomy has been shown to be safe, to reduce direct and indirect, in terms of productivity, costs of care and to offer some psychological benefits in small patients and their parents [100]. Several guidelines concerning the outpatient management of children undergoing tonsillectomy have been released [101]. It is generally advised against outpatient tonsillectomy in those with an increased ASA score, in children younger than 2 years old of age or in children living far away from the hospital.

Adenoidectomy alone is generally safer than tonsillectomy with less morbidity and mortality. Curette, diathermy or shaver adenoidectomy are the most common utilized methods with comparable results [102]. However, it is indicated in cases of snoring when rhinopharyngeal obstruction is severe without tonsillar enlargement and complications like haemorrhage, post operative pain, even death in one in 40,000 adenoidectomies do occur [103].

In general, despite technological advancements in anaesthesiology and in surgery, mortality of tonsillectomy can be as one in 10,000 in certain cases, like obese children with sleep apnea [26]. This, as well treatment failures or recurrences and uncertainties of tonsillectomy’s benefit in some cases, has led in evaluation and application of several other surgical and nonsurgical treatments.
OTHER THAN ADENOTONSILLECTOMY, SURGICAL TREATMENT OPTIONS

Septal surgery is exceptional in children not only because nasal septum is usually straight but also due to concerns about violating cartilage growth centers in the septum. Syndromic children, children with cleft lip and palate or those who have experienced a nose trauma may benefit from septoplasty in case of a serious deviated septum. Septoplasty has been accused to adversely affect midface growth and anatomy although this is disputed lately [104]. Inferior turbinate reduction, nasal polypectomy or functional endoscopic sinus surgery are other viable options that can be employed in specific cases, for example in allergic children with turbinate hypertrophy or in cystic fibrosis cases where recurrences of nasal polyposis are common.

Craniofacial surgery is necessary in some children with syndromes like Apert’s or Crouzon’s [105] in case sleep apnea coexists. There is a randomized trial on maxillary destruction and adenotonsillectomy reported by Guilleminault et al. in children with OSA and narrow maxilla. Polysonomography after 3 months showed residual events severe enough to warrant the complementary intervention in all children [32]. In general, operations like mandibular or maxillomandibular advancement and other craniofacial operations are usually delayed until the teenage years or adulthood due to their potential complications. Snoring is not an indication unless there is documented sleep apnea by PSG.

There is also little experience in children with operations like uvulopalatopharyngoplasty, radiofrequency volume reduction of soft palate, hypopharyngeal and tongue base surgery, hyoid suspension or hypoglossal nerve stimulation. Concurrent adenoidectomy or tonsillectomy may be of benefit for these children [106]. Revision of a posterior pharyngeal flap may be necessary in cleft palate patients who had been operated because of velopharyngeal insufficiency if upper airway obstruction occurs at night [101]. Finally, tracheostomy is reserved for these children with OSA who can not be treated with other methods.

NON SURGICAL TREATMENT OPTIONS

Anti-inflammatory medications are probably the most common non surgical treatment applied in children who snore. As already mentioned upper airway inflammation has been proposed as an important component in children who snore either allergic, obese or otherwise healthy. The clinical benefit from anti-inflammatory therapy has been evaluated so far most often in open nonrandomized studies or studies of short duration. Both a short course of systematic prednisone [107] and a 6 weeks duration course of intranasal fluticasone [108] were ineffective in reducing symptoms. The latter trial on intranasal steroid was a randomized control trial that showed a statistically significant improvement in apnea hypopnea index as well as a decreased need for an adenotonsillectomy. However the trial was of short duration, symptoms, reported by parents did not improve and the children continued to have sleep related hypoxia of the same magnitude as before. On the contrary two other recent studies on the use of intranasal steroids in children with sleep disordered breathing due to
adenotonsillary hypertrophy, an open [109] and a double blind randomized trial [110] have shown an improvement both in symptoms and PSG results.

Montelukast, an antagonist of leukotriene receptors, was also examined as a potential beneficial medication after the discovery of increased expression of these receptors in adenoids and tonsils of children with SDB due to adenotonsillar hypertrophy [111, 112]. Once daily oral dose of montelukast may improve radiological and PSG findings as well symptoms in these children [112]. This medication in combination with nasal steroids may also be beneficial in children with mild but persistent SDB after adenotonsillectomy [113]. Although anti-inflammatory medications like nasal glucocorticoids and leukotriene receptors antagonists appear promising in children with obstructed sleep disordered breathing, several more preferably randomized control trials are required before general recommendations can be made on which patients can actually benefit from such treatment.

Nasal corticosteroids as well as decongestants and immunotherapy are of value in allergic children with or without adenotonsillar hypertrophy who snore by reducing nasal congestion. Choice of the appropriate medication will be dependent on several factors like classification of allergic rhinitis (intermittent, persistent, mild moderate and severe), parents preferences, type of allergies and other.

Continuous positive airway pressure (CPAP) delivered through the nose by way of a mask has been shown to be effective in both adults and children with sleep apnea [114-119]. Bi-level positive pressure ventilation (BiPAP) is also used with increased frequency and is believed to be highly effective in SDB children. As with nasal CPAP, BiPAP is plagued by problems with compliance and mask fit [8]. Lack of optimal equipment for young children, difficulties with compliance and increased cost deter their use in children with habitual snoring.

Oral appliances such as tongue retaining or mandibular repositioning devices are widely used in adults with SDB to increase the oropharyngeal space but most are cumbersome and poorly tolerated by children[8]. Moreover although they seem to be effective and are considered by many as first line treatment for snoring in adults, a few studies have related the use of mandibular repositioning appliances in children with SDB [26, 120] and it is not yet know how long the children need to wear the appliance for.

Apart from the use of oral mandibular advancement appliances, orthodontists today play an important role in the management of snoring with the increasing use of rapid maxillary expansion. The procedure consists of an active increase of the palatal transverse diameters by progressive opening of the midpalatal suture during 10-20 days, followed by a fixed retention time of 6-12 months [26]. This orthodontic treatment has been shown to reduce symptoms of SDB, to improve polysomnographic variables and to attain excellent tolerability [121, 122].

In the majority of the aforementioned studies, obese children were excluded or body weight was not calculated as a possible confounding factor. This is of importance since obesity is a major determinant for surgical outcome [123] and can be by itself an important cause of snoring. Researches have suggested dividing children with apnea in two categories: those with marked lymphadenoid hypertrophy in the absence of obesity and obese children with mild lymphadenoid hyperplasia [6]. A high failure rate of adenotonsillectomy in the second group has been reported [123]. Thus a reduction in body weight or in the weight-age percentile, possibly with the aid of a dietician, may be considered primarily for these children. This approach is strengthened by studies showing a weight gain after tonsillectomy [124] parents should be also informed for this possibility.
Current treatment interventions are mostly empirically driven and will remain as such unless more convenient and validated diagnostic tools are developed. Suggestions on the two most common questions that are of concern for clinicians who deal with snoring children can be seen in boxes 1 and 2. A treatment pathway for the majority of cases is proposed in Figure 2.

**Box 1. Is polysomnography (PSG) always necessary?**

- **Yes:** Normative values for children have been recently reported. PSG is generally considered as the gold standard for the diagnosis of OSAS and many scientific organizations recommend its use in children who snore.

- **No:** It is neither practical nor firmly related to a specific outcome. This means that its use is inconvenient, has great cost implications and more importantly we are unsure that a negative result (habitual snoring) does not entail any adverse consequences.

- **What is needed to be done?** Further studies that they will allow a better association of PSG and other related results (eg sonography) with specific physiologic and biologic outcomes are needed. Current treatment protocols should be considered experimental until explicit criteria are being developed. PSG is better reserved for children with specific problems, like Down syndrome or muscular dystrophy, whom surgical management is more hazardous. Data on combined PSG and other more convenient tests, like sleep sonography and pulse oximetry, are welcomed. Proposed treatment pathway can be seen in Figure 2.
Box 2. Is adenotonsillectomy (A/T) effective? Is actually needed?

Yes. A/T is both effective, in terms of improvement of quality of life and PSG results and compulsory for the treatment of sleep apnea in case of enlarged tonsils and adenoids.

No: Apart from the possibility of complications, neurocognitive impairments of SDB may not be completely reversible with A/T and there is also an important percentage of treatment failures. Current use of A/T as first-line treatment for sleep disordered breathing is not supported by robust, high-quality evidence.

What is needed to be done? Although a randomized control trial comparing A/T with a sham intervention is probably unethical in children with enlarged lymphadenoid tissue and sleep apnea, an analysis of multiple treatment options and their combinations in relation to parents' preferences in specifically defined groups of patients is feasible and necessary.

REFERENCES


INTRODUCTION

Obstructive sleep apnea/hypopnea syndrome (OSAHS) is often the result of obstruction at multiple anatomic sites. Nasal, palatal and hypopharyngeal obstruction, acting alone or in concert, are frequently identified as the cause of snoring and OSAHS. Even in cases where a single site is primarily involved, the increase in negative pressure may induce further obstruction in other areas. When surgical management of OSAHS is considered, a clear understanding of the complex relationship between the sites of obstruction is essential to surgical success. This article will review the concept of multilevel treatment based on clinical assessment. In addition to serving as a guide for clinical staging, it will review the published literature on the incidence of multilevel obstruction and the results of multilevel treatment.

FRIEDMAN TONGUE POSITION

The importance of determining the sites of obstruction has led to the development of numerous methods that attempt to predict the location of upper airway obstruction. These include snoring sound analysis, physical examination, computed tomography, magnetic resonance imaging, cephalometric studies, and fluoroscopy, among others. Although these methods have demonstrated value, the number of methods described is evidence of the lack of agreement that any single method is perfect. The most commonly used method is the Mueller maneuver (MM). Borowiecki and Sassin first described this maneuver for preoperative assessment of sleep-disordered breathing (SDB). [1] The MM consists of having the patient...
perform a forced inspiratory effort against an obstructed airway with fiberoptic endoscopic visualization of the upper airway. The test is simple to perform and widely used. Despite this, its use is controversial and no studies thus far have been able to validate the maneuver as a tool for patient selection. It is within this context that the Friedman tongue position (FTP) classification emerged.

Initially presented by Friedman et al. in 1999, [2] FTP (previously identified as the modified Mallampati palate position and subsequently as the Friedman palate position) has been found to be a simple method to approximate obstruction at the hypopharyngeal level. This classification is based on observations by Mallampati, who published a paper on palate position as an indicator of the ease or difficulty of endotracheal intubation by standard anesthesiologist techniques. [3] The Mallampati stages had only been studied in the context of difficult intubations; therefore two major modifications were incorporated into FTP for its use in sleep medicine. First, the anesthesiologist’s assessment is based on the patient protruding his or her tongue and the observer then noting the relationship of the soft palate to the tongue. FTP is based on evaluating the tongue in a neutral, natural position inside the mouth. Second, the Mallampati system had only three grades. Initially, FTP included four distinct positions, but we now believe that five positions are necessary to best describe the anatomy (Table 1). Due to these modifications and because this system describes the position of the tongue relative to the tonsils/pillars, uvula, soft palate, and hard palate, we have identified it as the Friedman tongue position (FTP). FTP has been studied extensively as it relates to OSAHS. As there are no studies that have been done on the modified Mallampati position in sleep medicine, the use of the term is inaccurate in the context of OSAHS.

The procedure for identifying FTP involves asking the patient to open his or her mouth widely without protruding the tongue. The procedure is repeated five times so that the observer can assign the most consistent position as the FTP. FTP I allows the observer to visualize the entire uvula and tonsils or pillars (Figure 1).

Table 1. Comparison of the original and the new FTP

<table>
<thead>
<tr>
<th>Original FTP system</th>
<th>New FTP system</th>
</tr>
</thead>
<tbody>
<tr>
<td>FTP</td>
<td>Anatomical structures visualized</td>
</tr>
<tr>
<td>I Tonsils and pillars</td>
<td>Entire uvula</td>
</tr>
<tr>
<td>II Uvula</td>
<td>Tonsils and pillars</td>
</tr>
<tr>
<td>III Soft palate</td>
<td>Base of the uvula</td>
</tr>
<tr>
<td>IV Hard palate</td>
<td>Tonsils and pillars</td>
</tr>
</tbody>
</table>

Soft palate
Figure 1. A, FTP I allows visualization of the entire uvula and tonsils/pillars. B, FTP IIa allows visualization of most of the uvula, but the tonsils/pillars are absent. C, FTP IIb allows visualization of the entire soft palate to the base of the uvula. D, In FTP III some of the soft palate is visualized but the distal structures are absent. E, FTP IV allows visualization of the hard palate only. This figure was originally published in Sleep Apnea and Snoring: surgical and non surgical therapy, Friedman M, ed., Chapter 16, Figure 16.1, Copyright Elsevier (2009).
FTP IIa allows visualization of the uvula but only parts of the tonsils are seen. FTP IIb allows visualization of the complete soft palate down to the base of the uvula, but the uvula and the tonsils are not seen. FTP III allows visualization of some of the soft palate but the distal soft palate is eclipsed. FTP IV allows visualization of the hard palate only (Figure 1).

Earlier publications have described only four FTPs. In our experience with the system over the years, we have found that in the previous staging system a majority of patients were classified as FTP III. With such a large number of subjects categorized into this one position we believe that it is clinically relevant to further stratify this group in terms of characteristics and response to surgical outcomes. We have found that expanding FTP II into two groups, FTP IIa and FTP IIb, provides the means for achieving this stratification. Although patients with FTP IIb may have been formerly classified as FTP III in the earlier staging system, they share surgical response rates more characteristic of FTP II.

Once FTP is determined, the information can be incorporated into two distinct algorithms which can provide insights regarding the diagnosis and management of OSAHS. First, the use of FTP enables the clinician to predict the presence of OSAHS. A thorough history is most often the only screening tool for OSAHS. Unfortunately, many patients who are in denial about their symptoms cannot be identified by history alone, and therefore go undiagnosed. Routine use of FTP can serve as a cost effective, non-invasive screening tool that will allow ready identification of patients who may suffer from OSAHS. Second, since FTP estimates the presence hypopharyngeal obstruction, determining FTP prior to surgical intervention can be instrumental in guiding the surgical management of OSAHS. Previous studies have demonstrated its ability to separate patients that will likely benefit from uvulopharyngopalatoplasty (UPPP) as a single modality treatment from those that will require multilevel surgical intervention [4,5].

**THE OSAHS SCORE**

The estimated prevalence of OSAHS is 2% in women and 4% in men. [6] There is also clear evidence that associates OSAHS with hypertension, insulin resistance, coronary heart disease, myocardial infarction and stroke, as well as compromised quality of life and significant social and emotional problems; [7] yet it is estimated that approximately 80% of cases remain undiagnosed [8]. Primary screening for OSAHS is by a thorough history. Patients who complain of snoring, excessive daytime sleepiness or observed apnea are usually the only ones who are further tested for OSAHS. The major drawback of such a screening system is that history, in the context of OSAHS, has a low sensitivity. The obstacles in elicitting history in sleep apnea patients are two-fold. First, because the patient is asleep when the pathology occurs, they are largely unaware of the problem and often deny symptoms. In such cases, only a history elicited from a bedpartner can offer sufficient insight into symptomology. Second, symptoms of OSAHS often overlap with other pathologies. For example, a patient complaining of excessive sleepiness and fatigue may very likely receive a full work-up for depression and not OSAHS.
Figure 2. A, Tonsils, size 0, s/p tonsillectomy. B, Tonsils, size 1, within the pillars. C, Tonsils, size 2, extend to the pillars. D, Tonsils, size 3, extend past the pillars. E, Tonsils, size 4, extend to the midline. This figure was originally published in Sleep Apnea and Snoring: surgical and non surgical therapy, Friedman M, ed., Chapter 16, Figure 16.2, Copyright Elsevier (2009).
History is always the starting point for the screening and diagnosis of any medical condition. This is generally followed by a physical examination that can confirm the history or can bring to attention new concerns not identified in the history. The known physical findings that are associated with OSAHS including BMI, neck circumference, and tonsil size, are routinely assessed and are well-defined. Descriptions of hypopharyngeal obstruction, however, have not been standardized. Oftentimes physical findings reflective of this condition are reported with arbitrary terms such as ‘crowded oropharynx,’ ‘macroglossia,’ ‘retrognathia,’ etc. This causes much confusion in both patient care and in reporting data. The routine use of FTP in the context of OSAHS can help standardize the description of hypopharyngeal obstruction.

FTP can be employed in an algorithm that can help identify patients with OSAHS. This system is based on three readily identifiable and reproducible physical exam findings and can provide a simple means for screening patients. The system relies on calculating the patient’s Body Mass Index (BMI), along with the assessment of the patient’s tonsil size and FTP. Tonsil size and BMI are assessed as follows. Tonsil size 1 implies tonsils hidden within the pillars. Tonsil size 2 implies the tonsil extending to the pillars. Size 3 tonsils are beyond the pillars but not to the midline. Tonsil size 4 implies tonsils that extend to the midline (Figure 2).

BMI is derived from the height and weight of the patient and is calculated using the formula BMI = weight (kg)/height (m)^2. The BMI is graded as grade 0 (< 20 kg/m^2), grade 1 (20–24.99 kg/m^2), grade 2 (25–29.99 kg/m^2), grade 3 (30–40 kg/m^2), and grade 4 (> 40 kg/m^2) according to previously published standards for obesity. Neck circumference has been shown to correlate well as a clinical predictor, but BMI is an alternative measure that was used. Once known, these three findings can be combined to calculate an OSAHS score. The OSAHS score can help identify patients that may have OSAHS via physical exam alone and does not rely on history. To calculate the OSAHS score the numerical values of these findings are summed:

\[
\text{OSAHS score} = \text{FTP (0 – IV)} + \text{tonsil size (0-4)} + \text{BMI value}
\]

Any value above an 8 is considered as a positive OSAHS score, whereas any value below 4 is considered a negative OSAHS score. A positive score has a positive predictive value of moderate OSAHS, defined as an Apnea/Hypopnea Index (AHI) > 20, of 90%, and is 74% effective in predicting severe OSAHS (defined as an AHI > 45). A negative score is 67% effective in predicting an AHI of < 20.

With the use of FTP and the OSAHS score, the number of undiagnosed cases may decrease. In cases where history is unclear, this algorithm may help identify patients that would have otherwise gone unnoticed. In other cases, this algorithm may provide the impetus for eliciting a more detailed history and performing further tests to confirm suspicion of OSAHS.
Uvulopalatopharyngoplasty (UPPP) is the most common surgical procedure performed by otolaryngologists for the treatment of OSAHS. Unfortunately, a meta-analysis of unselected patients treated with UPPP revealed that only 40.79% of patients had a ‘successful’ surgery defined by an AHI reduction of 50% and a postoperative AHI < 20 or an Apnea Index (AI) reduced by 50% and a postoperative AI < 10. Surgery with a 40% success rate is certainly less than ideal, and our ultimate goal, of course, is to develop a treatment with a much higher success rate. But in the absence of such a treatment, our goal would be to identify those patients who are likely to achieve cure with UPPP.

Currently, the most common method used to identify patients for surgery is based on the misconception that patients with mild/moderate disease are better candidates for UPPP than those patients with severe disease. Therefore, the procedure is often recommended for patients with mild/moderate OSAHS. Severity of disease, as determined by clinical symptoms, polysomnography results, or tools such as the Epworth Sleepiness Scale, has been shown not to correlate with surgical success. Studies have shown that patients with mild sleep disordered breathing based on clinical and polysomnographic data have no better chance of successful treatment with UPPP than patients with severe disease. [5] In fact, one study demonstrated that UPPP performed on patients with mild OSAHS (AHI < 15) not only fails to cure disease in 60% of cases but often makes it worse. [10] Using severity of disease for the identification of UPPP candidates is dubious at best, and at times results in negative outcomes.

The failure of UPPP to cure OSAHS has been clearly associated with sites of obstruction in the upper airway not corrected by the procedure. It is well known that OSAHS involves obstruction of the airway at multiple levels. Although palatal obstruction accounts for a large portion of the obstruction, hypopharyngeal obstruction can also play a significant role. UPPP alleviates obstruction at the level of the soft palate and tonsils, but does not address obstruction at the level of the hypopharynx. Therefore when devising a system that is intended to predict UPPP outcomes, anatomical considerations must be incorporated.

FTP, used as an estimation of hypopharyngeal obstruction, can be integrated into an anatomical staging system that can reliably predict surgical outcomes. This system relies on BMI, tonsil size, and FTP and can separate patients who will benefit from UPPP alone from those that will require multilevel surgical intervention. In this system stage I disease is defined as those patients with FTP I, IIa or IIb, tonsil size 3 or 4, and BMI < 40. Stage II disease is defined as FTP I, IIa or IIb and tonsil size 0, 1, or 2, or FTP III and IV with tonsil size 3 or 4, and BMI < 40. Stage III disease is defined as FTP III or IV and tonsil size 0, 1, or 2. Although somewhat controversial, most surgeons have found that patients with BMI > 40 have a poor prognosis for corrective UPPP and therefore these patients are automatically assigned to stage IV (Table 2). In addition, all patients with skeletal deformities such as micrognathia or mid-face hypoplasia are considered stage IV.

The rationale for such a staging system is that the success of UPPP is highly dependent on the anatomical relationship between palatal and hypopharyngeal obstruction. Stage I patients are those with large tonsils and favorable tongue position (I, IIa, IIb) indicating minimal hypoglossal obstruction. They are most likely to benefit from UPPP with tonsillectomy, as hypopharyngeal obstruction does not represent a significant component of
their disease. Stage III patients are on the opposite extreme of the spectrum with small or no tonsils and unfavorable tongue position (III or IV) indicating significant hypopharyngeal obstruction.

Table 2. Anatomic Staging system

<table>
<thead>
<tr>
<th>Stage</th>
<th>FTP</th>
<th>Tonsil size</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>I, IIa, IIb</td>
<td>3 or 4</td>
<td>&lt;40</td>
</tr>
<tr>
<td>II</td>
<td>I, IIa, IIb</td>
<td>0,1 or 2</td>
<td>&lt;40</td>
</tr>
<tr>
<td></td>
<td>III or IV</td>
<td>3 or 4</td>
<td>&lt;40</td>
</tr>
<tr>
<td>III</td>
<td>III or IV</td>
<td>0,1 or 2</td>
<td>&lt;40</td>
</tr>
<tr>
<td>IV</td>
<td>any</td>
<td>any</td>
<td>&gt;40</td>
</tr>
</tbody>
</table>

Table 3. Success rate of UPPP in the treatment of OSAHS based on anatomic staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Unsuccessful</th>
<th>Successful</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>6 (19.4%)</td>
<td>25 (80.6%)</td>
<td>31 (100%)</td>
</tr>
<tr>
<td>II</td>
<td>18 (62.1%)</td>
<td>11 (37.9%)</td>
<td>29 (100%)</td>
</tr>
<tr>
<td>III</td>
<td>68 (91.9%)</td>
<td>6 (8.1%)</td>
<td>74 (100%)</td>
</tr>
</tbody>
</table>

They are least likely to benefit from UPPP as UPPP will not address their hypopharyngeal obstruction. Stage II patients are those with either large tonsils and unfavorable tongue position or small tonsils and a favorable tongue position.

Table 3 demonstrates the evidence of success and failure rates of UPPP for the treatment of OSAHS according to aforementioned stages. Chi-square analysis demonstrates a highly significant relationship between stage and success of surgery. The Pearson chi-square = 54.2, with two degrees of freedom, and a two-sided \( p < 0.0001 \). Successful treatment of SDB with UPPP was most likely to be achieved in stage I patients (80.6%) and least likely in stage III patients (8.1%).

To further explore the relationship between the stages of disease and the efficacy of surgical treatment with UPPP, a stepwise multivariate discriminant analysis was performed. The preoperative criteria used to stratify patients into stages (BMI, tonsil size and FTP) were the only indices introduced into the stepwise analysis. The success or failure of treatment with UPPP was used as the categorical end point. Using \( F \) values of 3.84 for entry and 2.71 for removal, stepwise analysis eliminated BMI, keeping tonsil size and FTP as the best combination of indices for differentiating between success and failure. The classification coefficients calculated for tonsil size and FTP were used to construct Fisher’s linear classification functional equations. Fisher’s linear classification equation for each group takes the form:

\[
CF = \text{tonsils (Coef tonsils)} + \text{FTP (Coef FTP)} + \text{Constant}
\]

where \( CF \) is group classification function; tonsils is tonsil size; Coef tonsils is group classification coefficient for tonsil size; FTP is FTP classification; Coef FTP is group
classification coefficient for FTP; Constant is group constant.

A separate equation is constructed for each result, unsuccessful and successful.

In the present case:

Unsuccessful result = \((\text{tonsils})^{0.870} + (\text{FTP})^{5.319} + (-10.563)\)

Successful result = \((\text{tonsils})^{2.284} + (\text{FTP})^{2.333} + (-6.001)\)

To predict the success of UPPP in patients with OSAHS, enter the patient’s tonsil size and FTP into each of the above formulas and calculate. The equation totaling the numerical highest value is the predicted result. In the validation study, the above formulas were applied casewise to the 134 patients and correctly predicted 95% of the cases by result.

While results of surgical treatment are never completely predictable for any disorder, clinical staging of the disorder offers several important benefits. Staging systems are created to identify those clinical features of the disease process that can predict whether any particular treatment option will be valuable. The anatomic staging system in OSAHS offers a cost-effective, non-invasive, reproducible method to stratify patients based on anatomic variations. The use of this system in addition to detailed clinical examination, cephalometrics and Mueller maneuver can help improve surgical outcomes in OSAHS. Patients with stage I disease have better than an 80% chance of success with UPPP and should therefore undergo the procedure when non-surgical treatment has failed. Even patients with severe SDB had an 80% success rate if they had stage I disease based on this staging system. Patients with stage III disease should never undergo UPPP alone as a surgical cure for SDB. With an 8.1% success rate, the surgery is destined to fail. They should be treated with a combination of procedures that address both the palate and the hypopharynx. In our study, 78.3% of patients can be stratified into stage I or III. Patients with stage II disease do not fall into either extreme but probably can be treated similar to stage III patients.

**INCIDENCE OF MULTILEVEL OBSTRUCTION IN OSAHS PATIENTS**

The true incidence of multilevel obstruction is a subject of much debate. Fujita [11] first described different anatomic levels of obstruction in OSAHS. He recognized that half of the patients who underwent UPPP were non-responders. Most of the non-responders were identified as having multilevel obstruction. Combined oropharyngeal and hypopharyngeal obstruction was noted in 54.5% (36/66) of patients in his study. Thus, it is clear that Fujita himself never intended to suggest that UPPP will cure most patients with OSAHS. In 1993, Riley et al. reported their surgical experience, outlining a multilevel concept [45]. Each patient was classified as having single level obstruction involving oropharynx only (type 1) or the hypopharynx only (type 3). Multilevel obstruction was identified as type 2 and implied a combination of oropharyngeal and hypopharyngeal obstruction. Of the 239 patients, 93.3% (223 patients) were identified as having multilevel obstruction, type 2. Only 16 patients (6.7%) had single level obstruction. Of these, 10 patients had type 1 obstruction and six patients had type 3 obstruction.
This early classification by Fujita and Riley was based on physical examination of the patients with vague guidelines. Specific criteria for identifying unilevel versus multilevel obstruction were not reported. Subsequent development of the FTP allowed for a simplified method of staging the levels of obstruction. [3,4] The early data based on FTP indicated that approximately 25% of patients presenting with OSAHS had unilevel obstruction, while 75% had multilevel obstruction.

Many techniques have been reported to identify levels of obstruction. The most popular are the MM and cephalometry. Sleep endoscopy was proposed as a preferred method by den Herder et al. [5] who reported an unusually high number of single level obstructions. In their study of 127 patients, 63% had single level obstruction while only 37% had multilevel disease. The study, however, may have misidentified the level of obstruction. Tongue base obstruction pushing the palate backward causing secondary palatal obstruction may have been classified as primary palatal obstruction [6]. Another study by Abdullah van Hasselt confirmed the high incidence of multilevel disease, with 87% of their 893 patient population having multilevel obstruction [7].

**Multilevel Surgery Is Not Limited to Severe Disease**

Many otolaryngologists presume that although UPPP may not cure the patients with severe OSAHS, it is likely to be effective for patients with mild disease. There are, however, many studies indicating that the severity of disease is not a predictor of success with single level surgery [3,4,10]. Senior et al. studied a group of patients with mild OSAHS (AHI less than 15) [11]. These patients underwent UPPP and the success rate was only 40%. Friedman studied a series of patients with mild disease and showed an overall success rate of approximately 40% as well [3,4]. If most patients indeed have multilevel disease, the success for the surgical treatment of mild OSAHS is not better than that for treating severe disease. In fact, the basis of the Friedman staging system is that anatomic findings are the most significant factors, rather than severity of disease. Multilevel surgery should not be reserved exclusively for the treatment of severe disease. It is therefore reasonable that multilevel treatment should be considered for most patients with mild disease as well as most patients with severe disease. Since the majority of patients suffering from OSAHS do have multilevel disease and directing the therapy to a single anatomic level has a high potential for failure, the need for multilevel therapy is evident.

**History of Multilevel Treatment**

Historically, surgical treatment for OSAHS was often based on trial and error. Patients would invariably undergo UPPP as a first stage. If the disease was not eliminated, they would go on to have hypopharyngeal surgery. Planned multilevel surgery at a single stage however has now become standard in many centers.

Published data on multilevel treatment can be divided into four groups.
1. The most commonly performed multilevel approach includes a UPPP as a basic technique with a second procedure designed to improve the hypopharyngeal airway. Most commonly this includes genioglossus advancement, thyrohyoid advancement, radiofrequency tissue volume reduction of the tongue base, and in some cases tongue base suspension. [12–15] The success rate for these procedures has been reported to be between 20% and 100% and was based on retrospective studies on small groups of patients. The largest series reported by a single group was by Riley et al. [2] who studied 239 patients who underwent what they describe as phase I surgery. In their study, 223 patients (93.3%) underwent multilevel surgery (UPPP + GAHM) in the initial phase. Their success rate based on single stage multilevel treatment for patients with mild, moderate and severe OSAHS was 60%.

2. The second group of patients studied who have undergone multilevel treatment include those who have had more invasive and more radical hypopharyngeal surgery such as open tongue base resection. Because of the aggressive nature of these procedures, most of these patients had a temporary tracheotomy and required significant hospitalization. There was significant postoperative morbidity as well. The success rate in this group varied between 44% and 100% [2,15–18].

3. The third group of multilevel surgery for OSAHS included those patients undergoing bimaxillary advancement as part of the multilevel treatment program. Most of these patients had undergone a staged surgery often, with UPPP and genioglossus advancement as their primary procedure. This group was not included in the overall discussion and recommendation for treatment in this article.

4. ‘Multilevel minimally invasive treatment for mild/moderate OSAHS ’ will be discussed in the next section. This section also lists minimally invasive as well as invasive procedures to address obstruction at the level of the nose, oropharynx and hypopharynx.

MULTILEVEL MINIMALLY INVASIVE TREATMENT FOR MILD/MODERATE OSAHS

The ideal procedure for OSAHS patients would have low morbidity, allow reasonable success, have low risk of functional alteration of the original upper aerodigestive tract, and could be performed in a single stage. In our experience, patients with severe disease and obvious daytime sleepiness often have strong motivation for multilevel surgery with invasive procedures to address all obstructed sites. However, patients with mild or moderate obstructive sleep apnea are less likely to be willing to undergo aggressive surgical procedures.

Many options are available for minimally invasive treatment of palatal obstruction. Minimally invasive treatment options for retrolingual obstruction are limited, but have been in clinical use. There have been a few studies that looked at multilevel minimally invasive treatment. Steward studied 22 patients who underwent combined radio frequency reduction of the palate and the base of tongue and reported a success rate of 59%. [19] None of the patients had concomitant nasal surgery. Fischer et al. presented a similar study about multilevel minimally invasive surgery with radiofrequency on the palate, tonsil and tongue base for 15 OSAHS patients. [20] The results showed that the AHI changed from 32.6 ± 17.4
preoperatively to 22 ± 15 for a success rate of 33%. Whereas the majority of Fischer’s patients had moderate disease, Steward’s patients had mild-to-moderate disease.

In 2004, Stuck et al. published their surgical results with radiofrequency on the palate and base of the tongue for 18 OSAHS patients with mild/moderate disease. [21] They reported their success rate as 33.3% (by their definition of success, a postoperative AHI reduction of at least 50% and below a value of 15).

In 2007, we presented our experience on minimally invasive single-stage multilevel surgery (MISSMLS) for patients with mild/moderate OSAHS. [22] Our patients underwent three-level treatment that included nasal surgery, palatal stiffening by pillar implant technique and radiofrequency volume reduction of the tongue base with a minimum follow-up of 6 months. The results in a retrospective review showed that both subjective and objective outcomes improved significantly, and treatment morbidity was minimal and only temporary. Mean bedpartner’s snoring visual analog scale (VAS) decreased from 9.4 ± 0.9 preoperatively to 3.2 ± 2.4 postoperatively.

Epworth Sleepiness Scale (ESS) decreased from 9.7 ± 3.9 preoperatively to 6.9 ± 3.3 postoperatively. Mean AHI was reduced from 23.2 ± 7.6 to 14.5 ± 10.2. Classic success was achieved in 54 of 122 patients (47.5%).

Although there was a significant failure rate, patients that failed were candidates for additional procedures. The first stage procedures that were performed including pillar palatal implantation and radiofrequency tongue base tissue volume reduction in no way negatively affected their ability to undergo secondary UPPP or additional tongue base procedures. Thus, many of the patients in our study who failed went on to undergo classic UPPP combined with additional hypopharyngeal procedures. Presence of pillar implants in the palate did not affect the UPPP in any way that could be determined by the surgeons. Patients who underwent previous radiofrequency tongue base reduction were still candidates for additional radiofrequency treatment or other hypopharyngeal procedures. This MISSMLS approach resulted in a fairly high patient satisfaction rate even though many patients required secondary procedures.

MISSMLS offers reasonable improvement of both subjective symptoms and objective PSG findings in patients with mild/moderate OSAHS. Polysomnographic respiratory parameters, ESS and snoring VAS show statistically significant improvement in patients with mild/moderate OSAHS treated with MISSMLS.

The success rate of any protocol has to be weighed against associated morbidity and risks. The relatively low morbidity combined with reasonable success makes multilevel minimally invasive surgery for OSAHS worthwhile. It should be offered to patients when multilevel obstruction is identified in the context of mild/moderate disease and other non-surgical options have been excluded.

**SYSTEMATIC REVIEW OF THE LITERATURE ON MULTILEVEL TREATMENT FOR OSAHS PATIENTS**

There has been a significant increase in publications on the multilevel approach for OSAHS patients within the last 5 years. The procedures include modification of previously
invasive procedures, combination of minimally invasive techniques and classic surgery, and even minimally invasive single-stage multilevel surgery.

We recently reported on a systematic review of all English language literature on multilevel surgery for OSAHS patients as of March 31, 2007. [23] Article titles and abstracts were reviewed to determine article eligibility. We also identified relevant publications from the lists of references in this subset of articles. The study design and its corresponding level of evidence were clarified as follows: (1) Level 1 – randomized controlled trials or a systematic review; (2) Level 2 – prospective cohort study; (3) Level 3 – case–control study; (4) Level 4 – case series; and (5) Level 5 – expert opinion.

There were 49 papers (58 groups) selected for final inclusion after detailed review (Table 4). There were 1978 subjects included in the study with a pooled mean age of 46.2 years. The mean minimal time period from multilevel surgery to postoperative PSG was 7.3 months (range, 1–100 months).

The originally reported success rate in the included literature was 64.5%. However, the definition of success used by the authors of the various papers reviewed was not consistent. Therefore, a meta-analysis was performed to redefine the success rate to be consistent with the commonly agreed upon criteria – namely ‘a reduction in AHI of 50% or more and an AHI of less than 20.’ The recalculated success rate was 66.4%.

An improvement in lowest saturation of oxygen (LSAT) was reported in 18 out of 33 groups (54.5%) and the weighted average percentage change showed a 10.8% improvement after multilevel surgery. Bedpartner’s snoring VAS revealed an improvement in eight out of nine groups (88.9%) and the weighted average percentage change demonstrated a 65.1% decrease postoperatively. ESS showed an improvement in 23 of 26 groups (88.4%) and the weighted average percentage change improved by 43.0% postoperatively.

Multilevel surgery for OSAHS is obviously associated with improved outcomes, although this benefit is supported largely by level 4 evidence. Future research should conduct larger, higher level and longer-term studies to further validate the results.

**Table 4. Surgical techniques for OSAHS patients with multilevel treatment at the nasal level**

<table>
<thead>
<tr>
<th>Anatomical deformity</th>
<th>N0</th>
<th>N1</th>
<th>N2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Intervention</td>
<td>Minimally invasive technique</td>
<td>Invasive technique</td>
</tr>
<tr>
<td>Nasal Septum</td>
<td></td>
<td>Endoscopic septoplasty (no packing)</td>
<td>Septoplasty (+/- packing)</td>
</tr>
<tr>
<td>Nasal Valve Inferior Turbinate</td>
<td></td>
<td>Valve suspension</td>
<td>RF, laser or microdebrider inferior turbinoplasty</td>
</tr>
</tbody>
</table>
SHORT TERM VERSUS LONG TERM RESULTS OF MULTILEVEL TREATMENT

Most of the literature on multilevel treatment of OSAHS has reported short-term surgical results at 6 months or less after surgery. The success rate varied from 0% to 100%. Vicente studied the long-term efficacy of UPPP and tongue base suspension with the Repose system for severe OSASHS and reported a 78% success rate at 3 years after surgery. [14] Neruntarat performed uvulopalatal flap in conjunction with genioglossus advancement and hyoid myotomy (GAHM) in 46 patients and followed the short-term (6 months after surgery) and long-term (at least 37 months postoperatively) outcome. [48] The short-term and long-term success rates were 78.3% and 65.2%, respectively. Six (16.7%) patients with short-term success failed over the long term and these patients had significant increase in BMI.

The longest follow-up result in multilevel treatment was reported by Andsberg et al. using a 50% reduction in the Apnea Index as the definition for success. [34] They reported on 16 patients at 1 year and 8.4 years after surgery. Their success rates were 56% and 56%, respectively. The weights of the patients remained stable during the follow-up period. Although there is a perception that the long-term results are poorer than the short-term results for surgical treatment of OSAHS, these studies show the reduction in surgical success is only moderate and that the majority of maintain long-term successful outcomes.

SINGLE STAGE OR MULTI-STAGED SURGERY IN MULTILEVEL TREATMENT

Multilevel treatment can be performed in a single stage or in multiple stages. The major concern about single stage multilevel surgery for OSAHS involves its safety. Staging multiple procedures may be inconvenient for patients, but by doing so one can reduce the surgical morbidity per session. Single stage versus multi-stage treatment remains an area of controversy. Proponents of each approach have valid evidence that either approach is reasonable and safe. If the procedures are staged, the order in which sites are corrected is also controversial.

Olsen stated that when nasal obstruction is identified, it is usually addressed with a multi-staged procedure after the palate and hypopharyngeal areas are treated. [62] Hsu also stated that the timing of nasal surgery in patients undergoing other procedures for OSAHS remains controversial. [40] He feels that performing multi-staged procedures is a safer option in the surgical management of patients with moderate to severe OSAHS. The presence of blood, secretion or edema may add to the severity of obstruction in an already narrow and obstructed upper airway in patients with moderate to severe OSAHS. The addition of nasal packing may further compromise the airway.

However, most studies revealed that single stage surgery at multiple levels did not increase postoperative complications. [52,53,63] Single stage multilevel surgery can lower total hospitalization expenses when compared to multi-staged surgery. [53] Kieff and Busaba [64] studied the safety of same-day or overnight discharge and concluded that same-day discharge for patients who have undergone combined nasal and palatal surgery for OSAHS is relatively safe in selected cases when significant comorbid diseases are not present.
Most of the above literature preferred single stage surgery primarily focusing on nasal and palatal surgery without hypopharyngeal procedures. Experience with multilevel surgery including a hypopharyngeal procedure has shown the postoperative morbidity (the highest complication rate) of single stage and multi-staged surgeries to be 40.9% and 39.1%, respectively. [19,48] All of the complications were temporary.

Thus, on the issue of single or multiple stage surgery, our opinion is that it is safe and efficacious to perform multilevel surgery in one surgical session using minimally invasive techniques and with adequate postoperative monitoring for patients with mild/moderate OSAHS. When multilevel invasive procedures are necessary, the authors prefer to limit the number of levels to one or two per stage. Three-level invasive surgery is never performed in a single stage.

**ROLE OF NASAL SURGERY IN MULTILEVEL TREATMENT**

Multilevel treatment generally includes the palate and tonsil, as well as the hypopharynx. Often, a nasal corrective procedure is included as well. The importance of nasal breathing during sleep has been documented. [65] Nasal obstruction also plays a role in the pathogenesis of OSAHS. [66] According to the Bernouilli principle (Venturi effect), intraluminal pressure in the compromised airspace suddenly drops if the inspired airway accelerates to keep ventilatory volume constant. The effect further narrows the airspace (hypnogenic stenosis). When inspiratory negative pressure reaches a certain critical point in the effort to overcome increased upper airway resistance, a combination of redundant soft tissues and loss of pharyngeal muscle tone and decreased tongue muscle tone causes complete upper airway collapse on inspiration.

It is well known that nasal cross-sectional area reduced by septal deviation or other pathology causes increased nasal resistance and predisposes the OSAHS patients to downstream inspiratory collapse of the oropharynx, hypopharynx or both. [67,68] Correction of the nasal airway, however, does not always improve OSAHS. In fact it may result in an unexpectedly worse AHI postoperatively. Friedman et al conducted a prospective study of 50 consecutive patients with nasal airway obstruction and OSAHS to compare the effect of an improved nasal airway on OSAHS by use of subjective and objective measures [42]. The results demonstrated that although 98% of patients had subjective improvement in nasal breathing, 66% of patients did not notice any significant change in their snoring. Review of the polysomnographic data demonstrated that the group overall did not have significant changes in AHI or LSAT. The subgroup of patients with mild OSAHS showed the most significant worsening in their AHI. CPAP levels, however, required to correct OSAHS decreased significantly after nasal surgery. Verse et al. also reported a similar study with 26 adult patients who underwent nasal surgery as single level treatment of their sleep-related breathing disorders. [70] They concluded that nasal surgery alone had limited efficacy in the treatment of adult patients with OSAHS. Nevertheless, nasal surgery significantly improves sleep quality and daytime sleepiness independent of the severity of OSAHS.

Thus, nasal surgery alone does not consistently improve OSAHS when measured objectively. Depending on the severity of OSA, nasal airway reconstruction as an isolated procedure may contribute to decrease in CPAP pressures and improve CPAP compliance. The
most important value, however, of nasal surgery is as one stage in the multilevel treatment plan for OSAHS.

**SUGGESTED TECHNIQUES FOR MULTILEVEL TREATMENT**

When making a decision to select a treatment plan for the OSAHS patient, the balance between morbidity of treatment and severity of disease needs to be considered. We present an algorithm (Tables 4 to 7) used in our practice to plan treatment on the nose, palate, tonsil and hypopharynx. The entire surgical plan should be outlined prior to onset of treatment rather than embarking on a series of trial and error procedures.

It is also important to emphasize that the severity of disease and ease or difficulty of correction in OSAHS do not always correlate with the severity of anatomical obstruction. Thus, an algorithm for successful surgical treatment of OSAHS should be based on the combination of the anatomic abnormality and severity of disease (the symptoms of snoring alone vs. snoring and excessive daytime sleepiness and PSG data). The anatomic sites, nose, palate, tonsil and hypopharynx, are identified by N, P, T and H. The level of treatment is described by a number between 0 and 2 (0: no abnormality and therefore no intervention; 1: mild abnormality requiring minimally invasive intervention; 2: severe abnormality/disease requiring invasive correction). Each patient is identified as NxPxTxHx for treatment plan, where x represents a number from 0–2.

OSAHS patients with a BMI greater than 40 are automatically assigned to Friedman’s anatomic stage IV and are not candidates for upper airway surgery. Treatment with CPAP, bariatric surgery, or tracheostomy need to be considered in these patients. If BMI is less than 40 and the Friedman’s stage is I, II or III, the patient will be offered surgical modalities on nose, palate, tonsil and hypopharynx from minimally invasive techniques to invasive correction.

**Table 5. Surgical techniques for OSAHS patients with multilevel treatment at the palatal level**

<table>
<thead>
<tr>
<th>Anatomical deformity</th>
<th>P0</th>
<th>P1</th>
<th>P2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Intervention</td>
<td>Minimally invasive technique</td>
<td>Invasive technique</td>
</tr>
<tr>
<td>Palate and uvula</td>
<td>RF soft palate, pillar implants, CAPSO, laser-assisted uvuloplasty, uvulectomy, uvulopalatal flap</td>
<td>UPPP, Z-PP, lateral pharyngopalatoplasty, transpalatal advancement</td>
<td>pharyngoplasty</td>
</tr>
</tbody>
</table>
Table 6. Surgical techniques for OSAHS patients with multilevel treatment at the tonsils

<table>
<thead>
<tr>
<th>Anatomical deformity</th>
<th>T0</th>
<th>T1</th>
<th>T2</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Intervention</td>
<td>Minimally invasive technique</td>
<td>Invasive technique</td>
<td></td>
</tr>
<tr>
<td>Tonsil</td>
<td>_</td>
<td>RF tonsillar reduction, coblation tonsillectomy</td>
<td>Tonsillectomy</td>
</tr>
</tbody>
</table>

Table 7. Techniques for OSAHS patients with multilevel treatment at the hypopharyngeal level

<table>
<thead>
<tr>
<th>Anatomical deformity</th>
<th>H0</th>
<th>H1</th>
<th>H2</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Intervention</td>
<td>Minimally invasive technique</td>
<td>Invasive technique</td>
<td></td>
</tr>
<tr>
<td>Tongue base</td>
<td>_</td>
<td>RFBOT, BOT coblation, tongue base suspension (soft tissue-to-bone anchor system), oral appliance</td>
<td>Midline glossectomy, genioglossal advancement, thyrohyoid suspension, maxillomandibular advancement</td>
</tr>
</tbody>
</table>

**RISK MANAGEMENT AND COMPLICATIONS OF MULTILEVEL TREATMENT**

The complication rate for multilevel treatment is the sum of the complications for each of the individual procedures. In our systematic review 23 of multilevel surgery for OSAHS patients, the overall complication rate is 14.6%. The complication rates which developed in mild/moderate disease and severe disease were 16% and 14.2%, respectively.

Preoperative assessment for OSAHS patients should be performed by the anesthesiologist and discussed with the sleep surgeon. Eschmann catheter, rigid bronchoscopy and flexible intubation equipment should be available. Extubation is preferably carried out in the operating room once the patient is able to understand and follow commands and should not be done when the patient is combative. Airway compromise usually occurs in the immediate postextubation phase. In the perioperative period, use of a nasopharyngeal airway may help stent the compromised upper airway and can often be life-saving.

**CONCLUSIONS**

Friedman tongue position (FTP) is a physical finding that can help with the diagnosis and surgical management of OSAHS. FTP describes the position of the tongue relative to the
tonsils/pillars, uvula, soft palate, and hard palate and is easily assessed by physical examination of the oropharynx. When combined with tonsil size and BMI, FTP can be used to calculate an OSAHS score, which can help screen patients for OSAHS. FTP can also be integrated into an anatomical staging system that can help predict the likelihood of surgical success with UPPP. Stage I patients would most likely benefit from UPPP alone whereas stage II and stage III patients will likely need additional treatment to the hypopharynx.

For patients who either fail or are unwilling to pursue CPAP therapy, surgery offers a viable alternative chance to control OSAHS. The subjective and objective severity of OSAHS integrated with the degree of anatomic abnormality dictates the choice of surgical procedure(s). These vary from single to multilevel therapy using either minimally invasive or classic invasive techniques in various combinations. Multilevel treatment should be dictated by the presence of multilevel obstruction. Most patients with OSAHS have multilevel obstruction and should be considered for MISSMLS. It should not be reserved only for patients with severe OSAHS.

Although surgery for the treatment of OSAHS remains a relatively young medical discipline, more evidence-based data could help direct optimal surgical intervention for each patient and ultimately reverse or at least halt the multi-system damage caused by OSAHS.

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Staging of OSAHS


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Chapter 5

BREATH OF LIFE: COMPLEXITY AND HETEROGENEITY IN THE INTEGRATION OF ETIOLOGIC COMPONENTS ASSOCIATED WITH SLEEP DISORDERED BREATHING

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ABSTRACT

Sleep disorders represent a spectrum of conditions including: upper airway resistance syndrome; snoring; and obstructive, central and complex sleep apnea inter alia. In the etiology of sleep disordered breathing (SDB), systemic and regional anatomical characteristics comply with physical laws, such as those pertaining to (non-laminar) fluid dynamics, as predicted by: Poiseuille’s law; the Reynold’s number; Bernoulli’s principle, and Newton’s second law of gravity. In addition, however, tissue properties adhere to physiologic laws such as Davis’ law and Wolff’s law. In this way, the upper airway can be regarded as the net functional space available for respiration during wakefulness and sleep, once these physical and physiologic laws have been complied with. Thus, an integration of the complexity and heterogeneity of the etiologic components associated with SDB is warranted. Therefore, the aim of this review is to delineate some of the underlying etiologic factors associated with SDB. These etiologic components can be simply classified as (1) Structural factors: such as cranial base morphology; nasal obstruction; maxillo-mandibular morphology (including malocclusion); hyoid bone position; and soft tissue hypertrophy (including craniofacial obesity), and (2) Systemic factors: such as genetic predisposition/defects (including Ehlers-Danlos, Marfan and Floppy eyelid syndromes etc); central nervous systems anomalies (affecting the medulla oblongata, thalamus etc through infections, such as poliomyelitis, encephalitis etc); and specific neurodegenerative diseases, such as dementia or Parkinson's disease. Therefore, in the clinical management of sleep disorders a multi-disciplinary approach must be taken to address the interaction of etiologic components associated with SDB, to identify the causative agent(s) in specific individuals seeking definitive resolution.
INTRODUCTION

The pathogenesis of obstructive sleep apnea (OSA) is clearly heterogeneous. Factors that predispose a subject to OSA include: upper airway configuration or shape; skeletal structures; soft tissue characteristics; pharyngeal collapsibility (compliance and critical closing pressure); sensory changes; respiratory influences on the upper airway; effects of sleep on upper airway function; surface tension; neurotransmitters; gender, obesity and ethnicity [1]. Thus, the genesis of upper airway obstruction is multi-factorial and heterogeneous, and structural and anatomical factors in conjunction with tissue physiology, whether it is normal or abnormal, may predispose a patient to OSA. Therefore, dysfunction of the upper airway might be precipitated by anatomical/structural abnormalities in combination with the laws of nature. But, pathogenic factors that contribute to a given patient’s repeated upper airway collapsibility may vary from individual to individual [1].

In order to understand the pathophysiology of airway collapse one must first understand the sites of potential obstruction. The upper airway or the pharynx may be divided into its four constituent regions, which include the:

- Nasopharynx which is the uppermost part of the pharynx, extending from the posterior nasal apertures (choanae) to the superior part of the soft palate. The roof and posterior surface of the nasopharynx is formed by the cranial base. The nasopharynx is predominantly rigid, contributing to the patency of the upper airway.
- Retropalatal pharynx that extends from the hard palate to the caudal margin of the soft palate
- Retroglossal pharynx that extends from the caudal margin of the soft palate to the tip of the epiglottis
- Hypopharynx that extends from the glottis to the larynx

Figure 1. Current techniques used to directly visualize the upper airway include nasendoscopy where an endoscope is introduced through the nostril (inset). The pharyngeal isthmus appears as an elliptical lumen (outlined in orange).
The upper airway shape or the pharyngeal lumen of normal subjects is usually elliptical in outline when viewed on a transverse section (Figure 1), with the major axis in the medio-lateral plane and the minor axis in the antero-posterior plane.

However, the pharyngeal lumen of snorers and patients with OSA during wakefulness and sleep is more circular or elliptical, but in this case the major axis is in the antero-posterior plane [1].

1. PHYSICS OF AIRFLOW

Fluid dynamics deals with the topic of liquid and gaseous flow, and fluid flow can be classified as either laminar or turbulent. Air is technically considered to be a fluid. Under ideal conditions, airflow should be laminar or streamlined, where all the fluid particles flow in parallel lines. To determine whether fluid flow is laminar or turbulent, one calculates the Reynold’s number, which is the ratio of the product of fluid density times velocity times the distance traveled, yielding a dimensionless Reynold’s number (R) as shown by the equation

\[ R = \frac{\rho V D}{\mu} \]

where \( \rho \) = fluid density, \( V \) = Velocity, \( D \) = Distance and \( \mu \) = (dynamic) viscosity. Generally, fluid flow with a Reynold’s number < 2000 is considered to be laminar flow; R = 2000-4000 is considered transitional, and R > 4000 is considered to be turbulent flow. Thus, for nasal airflow, any increase in the numerator (fluid density, velocity or distance) or decrease in the denominator (viscosity) increases Reynold’s number.

Newton’s second law of motion also explains that if a force is placed on an object, it will change its acceleration in the direction of the force. This law of gravity applies to the tongue during sleep.

Thus, when a person lies in a supine position, the forces acting on the center of mass of the tongue result in vectors that essentially push the tongue inferiorly. Other factors or forces that may also be acting to pull the tongue inferiorly include; decreased muscle tonicity or relaxation (especially during REM sleep), and possibly a relative negative pressure effect, which further sucks the tongue inferiorly [2].

To counteract this gravitational descent of the tongue during sleep, Singh et al. [3] investigated the effect of a removable maxillary appliance with a posterior tongue restrainer (or tail).

That study found that the mean apnea-hypopnea index (AHI) fell by 73% (p < 0.001), and the mean SaO2 improved from 84% to 89% (p < 0.05) when using the tongue restraining appliance. It was concluded that the appliance is an effective approach in the management of OSA, assuming that the tongue is the source of the obstruction. However, the nasopharyngeal airway needs to be assessed also in patients suspected of having undiagnosed OSA.
2. Physiologic and Anatomical Structural Considerations

Generally, while the fluid density of air has a fixed value, the nasal cavity diameter varies in various parts of the nose. Therefore, a change in flow velocity ($V$) during nasal breathing will affect the Reynold’s number. One must keep in mind that the purpose of the turbinates in the nose is to warm and humidify inhaled air. Therefore, the turbinates can make relatively minor fluctuations in the fluid density or velocity. According to Simmen et al. [4], turbulence tends to occur in the nasal valve region of the nose. The nasal valve area is a complex three-dimensional structure consisting of several morphological structures that play a key role in nasal airflow [5]. The nasal valve area, from a physiologic standpoint, is the place of maximum nasal resistance or the flow-limiting segment of the nasal airway and passage. Therefore, minor fluctuations or constrictions in nasal cross-sectional area will drastically affect the airflow across the nasal route due to Poiseuille’s law (see below). The narrow passage, called the ostium internum nasi or internal nasal valve, is formed by the mobile lateral nasal wall, the anterior part of the nasal septum, the head of the inferior turbinate and the osseous piriform aperture [5]. The cross-sectional area of the internal nasal valve is determined by the angle formed by the connection of the upper lateral cartilage with the septal cartridge [6]. The inferior turbinate and the lateral nasal soft tissue constitute a minor portion of the internal nasal valve. An internal nasal valve is considered to have collapsed when the angle of the valve is $<10-15^\circ$[6]. Collapse of the nasal valve can be secondary to congenital, traumatic or iatrogenic causes. For example, collapse of the nasal valves often occurs from over-resection of the nasal dorsum and upper lateral cartilage during a septo-rhinoplasty [6]. Therefore, small changes in nasal morphology or nasal architecture may be associated with changes in function, including the precipitation of OSA.

Thus, the resistance to airflow in the upper airway is described by Poiseuille’s law. As airflow is directly proportional to the pressure difference that exists between the nose and the alveoli in the lung, the flow ($Q$) is directly proportional to the pressure difference ($\Delta P$) divided by the resistance ($\frac{1}{\pi r^4}$). In standard fluid dynamics notation:

$$\Delta P = \frac{8\mu L Q}{\pi r^4}$$

where $\Delta P$ is the pressure difference
$L$ is the length of the tube
$\mu$ is the dynamic viscosity
$Q$ is the volumetric flow rate
$r$ is the radius
$\pi$ is a mathematical constant

This powerful equation states that the resistance to flow is inversely proportional to the fourth power of the radius of the airway. It should be appreciated that a small change in radius will change the resistance of the airway to the fourth power. Singh et al. [7] found that the adult male nasopharyngeal airway is narrower in the anterior nasal valve region closer to the nostril, and wider in the distal regions of the nasopharyngeal airway. This finding could explain why snoring tends to be more commonly found in adult males. However, it should
also be noted that viscosity is temperature dependent. Thus, the viscosity of a gas increases with increasing temperature. Therefore, if a given individual has nasal obstruction in the form of septum deviation, turbinate hypertrophy, nasal polyps, nasopharyngeal tumor, etc. the airflow will be decreased by the decreased radius to the fourth power. Furthermore, if a patient is on Continuous Positive Airway Pressure (CPAP) therapy for the treatment of sleep disordered breathing (SDB) an improvement in the nasal passages will significantly improve airflow in the nose. Recently, Singh and Abramson [8] quantified and localized nasal changes after the placement of an intra-oral nasal dilation appliance. In that study, the nasopharyngeal airway was found to be 13% wider in the anterior nasal valve region while wearing the appliance. Thus, the use of an intra-oral nasal dilation appliance may be useful in the initial management of nasopharyngeal conditions, such as snoring, upper airway resistance syndrome and OSA, especially in cases where nasal obstruction is demonstrable.

Snoring is a common breathing disorder [2]. Breathing occurs due to the relative negative intra-thoracic pressure that is created by the diaphragm contracting. During laminar flow through the upper airway there is no snoring. However, when an obstacle or constriction is seen in the upper respiratory system, snoring may be heard. Any object that constricts or decreases airflow may create snoring. Also, any obstruction in the upper airway may require an increased inhalation pressure, which then generates a higher driving force by the diaphragm. Essentially, the “obstacle” theory of snoring [2] assumes that increased negative pressure that continues to increase to overcome the upper airway obstruction causes the pharyngeal structures to vibrate as air flows across various pharyngeal structures. This effect produces typical snoring. The uvula is cone-shaped muscular tissue that hangs down from the middle of the soft palate. In patients with OSA, the uvula is sometimes elongated and floppy, may obstruct the airway, and may give rise to snoring by vibrating as explained by Bernoulli’s principle. Essentially, Bernoulli’s Law states that as air flows through a pipe or cylinder, its velocity increases with a decrease in pressure at points of constriction. Thus, as air flows through narrow parts of the airway, its velocity increases and this sucks the pharyngeal structures inwards, generating snoring by their vibrations [2]. Thus, adipose deposition in the pharyngeal walls tends to reduce the total pharyngeal space and enhance its Venturi tube shape [2]. This constriction, in turn, increases the suction on the soft palate. Therefore, it has been found that an elongated uvula may contribute to SDB when a patient lies in a supine position.

Davis’ law is used in anatomy to describe how soft tissue changes or remodels due to the demands placed on it. Behind the nasal cavity are the nasal apertures or choanae. The floor of these openings is the hard palate, specifically the palatine bone posterior to the maxilla. If the maxilla is maldeveloped with a high-vaulted palate, the posterior nasal apertures may become elongated in the vertical plane. Attached to the pterygoid hamulus behind and below the palatine bone are the muscles of the soft palate, such as tensor palatini and levator palatini etc. Essentially, Davis’ law describes how a muscle will stretch when the bone that it is attached to is repositioned. In other words, if the bony framework of the hard palate is deformed, the muscles attached to it will be stretched, and Davis’ law, can be used to describe how muscle will lengthen in response to stretching. In fact, elongation of the soft palate is a common finding in patients with OSA, which may correlate with elongation of the posterior nasal apertures in the vertical plane. In addition, Wolff’s Law states that bone will remodel to accommodate muscle [9]. Thus, the bone will change shape or remodel to relieve muscle stress. Therefore, Davis’ law can be used to describe how muscle will lengthen in response to
stretching; and Wolff’s law predicts that bone adapts to the loads it is placed under, as shown using fractal analysis. However, it is posited here that the upper airway has primacy over both skeletal and muscular requirements, as the breath of life is essential for survival. Consequently, the patient may assume a characteristic forward head posture (cervical hyperlordosis) to maintain an adequate upper airway.

There are three sets of bony projections inside the nose called the conchae [10]. Clinically, the combination of these bones plus the respiratory mucosa overlying them is referred to as the nasal turbinates. There is a superior, middle and inferior turbinate. The superior and middle conchae are parts of the ethmoid bone, whereas the inferior concha is a separate bone, embryologically derived from cranial base cartilages. The inferior turbinate is predominately involved in nasal breathing. The function of the turbinates is to warm and humidify inhaled air [11]. If a person has turbinate hypertrophy, the amount of space in the nasal cavity that the air can flow through will be decreased. Therefore turbinate hypertrophy can lead to nasal congestion and difficulty in nasal breathing. Furthermore, patients on pressure therapy may have difficulty tolerating the CPAP due to increased nasal resistance subsequent to hypertrophic turbinates. Nasal steroids may be used to decrease the degree of turbinate hypertrophy. The causes of turbinate-related nasal congestion include: allergic rhinitis; acute rhinosinusitis; vasomotor rhinitis, and nasal polyps. Septal deviation can also contribute to difficulty in nasal breathing, as well as SDB. In these cases, tolerating CPAP may become more difficult through a complex mechanism. Septal deviation may cause nasal obstruction of one nasal airway with contralateral turbinate hypertrophy [11]. Furthermore, ipsilateral internal nasal valve stenosis may occur secondary to septal deviation [11]. Reddy et al. [11] in an histologic study on septal deviation, showed that the most commonly enlarged component was the contralateral inferior turbinate. In addition, nasal polyps are benign growths that develop from the lining of the nose or sinuses. Initial symptoms may be: difficulty breathing; nasal dripping; altered sense of smell, and snoring. Usually, nasal polyps present in adults over the age of 40 years. The main causes of nasal polyps include: allergies; chronic sinusitis, and chronic inflammation of indeterminate etiology [12]. Individuals that are sensitive to aspirin or non-steroidal anti-inflammatory drugs have a higher probability of developing nasal polyps. Therefore, mucosal swelling is not entirely responsible for inferior turbinate hypertrophy, and at times surgical bony turbinate reduction may be required to improve the nasal airway. Alternatively, nasal cavity volume increase may be considered to accommodate enlarged conchae.

Rhinitis is defined as inflammation of the nasal membranes. Allergic rhinitis is the most common cause of rhinitis [13]. Allergic rhinitis is a common condition, and is a constellation of symptoms that include nasal congestion and irritation of the eyes, generally caused by dust particles, dander or pollen. Allergic rhinitis may present in a seasonal or perennial manner with the above symptoms. Physical examination often reveals a pale, edematous mucosa, and eosinophilia on the nasal smear [11]. Other names for allergic rhinitis include hay fever and nasal allergy. Inflammation of the mucous membranes of the nose, eyes, Eustachian tubes, middle ear, sinuses and pharynx may also be present in allergic rhinitis. Essentially, the pathophysiology of allergic rhinitis involves exposure to an allergen, which causes a hypersensitivity immune response that would normally not occur in the general population. Antibodies are made against the allergen and mast cells release histamine. The histamine and other mediators cause nasal secretions. Certain individuals have a predominant genetic predisposition to develop allergic or IgE-mediated reactions to extrinsic proteins or allergens.
Thus, if a given individual has a compromised upper airway, for whatever reason, that condition may predispose them to SDB. Therefore, when evaluating a patient for possible SDB, a careful history for allergies should be taken. Referral to an allergist and/or medical treatment should be initiated along with their treatment for possible SDB. Worsening of SDB and/or CPAP compliance may be affected if allergic rhinitis is not co-treated along with the SDB.

In addition to nasal conditions, it is suspected that cranial base morphology might affect upper airway morphology. When craniofacial developmental patterns were compared in children with a prognathic facial appearance (following repaired cleft lip/palate) to their non-cleft counterparts, Singh et al. [14] found that patients with a cleft lip/palate exhibited deficient craniomaxillary growth. Earlier, Singh et al. [15] investigated how sphenoethmoidal allometry could be associated with a prognathic midfacial profile in a given ethnicity. Finite-element analysis (FEA) revealed that the anterior cranial base was shorter in Asian subjects when compared to their Caucasian counterparts, producing a prognathic facial appearance. Furthermore, when Banabilh et al. [16] compared differences in cranial base and airway morphology in non-obese, Asian adults with and without OSA, they found that the cranial base saddle angle was more acute in the OSA group and, in addition, using FEA a relative 58 per cent decrease in nasopharyngeal airway area was found above and behind the soft palate. In contrast, a 96 per cent increase in area associated with downward displacement of the hyoid bone was detected. Therefore, it was concluded that airway impairments associated with OSA can be associated with the morphology of the cranial base.

Any subtle maxillary or mandibular deficiency may predispose an individual to SDB. A smaller mandible or a posteriorly-displaced mandible is correlated with OSA [1]. Indeed, it is long been suspected that mandibular insufficiency/retrognathia or mandibular micrognathia may be associated with OSA. Banabilh et al. [17] studied dental arch morphology in the etiology of OSA. They reported that the mean upper and lower dental arch morphologies in patients with OSA were statistically different from respective control morphologies. Furthermore, FEA of the upper and lower arches indicated that the mean OSA configurations were narrower in the transverse plane compared with the control configuration, supporting the notion that size and shape differences in dental arch morphology are found in patients with OSA. Earlier, Singh et al. [18], investigated how orthodontic treatment of malocclusions might affect the upper airway. Using pre- and post-treatment lateral cephalometric radiographs of 53 children (mean age 12.9 years) a relative 31% increase in nasopharyngeal airway area was found above and behind the soft palate. Additionally, a 23% increase in oropharyngeal airway area was located behind the base of the tongue with a 9% increase in hypopharyngeal area in the hyoid region. Thus, upper airway improvements are associated with functional orthodontic treatments in actively growing children. On the other hand, in a similar study on 100 adult patients Singh and Krumholtz [19] found that following an orthodontic protocol that included midfacial development, a relative 22% increase in nasopharyngeal airway area was found above and behind the soft palate. As well, a 16% increase in oropharyngeal airway area was identified behind the base of the tongue, with a 13% increase in hypopharyngeal area at the level of the hyoid bone. Thus, it was concluded that upper airway changes in ‘non-growing’ adults are similar to those of actively-growing children undergoing functional orthodontic corrections. These findings suggest that genetically-encoded developmental mechanisms can be modulated by orthodontic appliances to enhance the upper airway in adults; the so-called ‘pneumopedic’ effect or non-surgical
airway remodeling. Therefore, these findings may help in the management of adults diagnosed with OSA.

Skeletal abnormalities also have a major role in the pathology of tissue collapse or SDB. Essentially, the bony structures of the face may predispose a patient to “compartment syndrome” if the soft tissue structures are bounded by a smaller, size-limited bony framework. If the mandible is small in size in the antero-posterior (AP) plane, then the space between the base of the tongue and the pharyngeal wall, termed the AP diameter, may also be reduced. Essentially, this retroglossal insufficiency may lead to airway obstruction. The hyoid bone in patients with OSA is also displaced [1]. The hyoid bone is a horseshoe-shaped bone located in the neck between the mandible and thyroid cartilage. The unique feature of the hyoid is that it is the only bone in the human body that is not attached to another bone. Instead, it is suspended in position by muscles and ligaments. Studies have shown that in individuals with SDB, the hyoid bone rests lower in the neck compared to normal individuals [20]. Indeed, Banabilh et al. [16] reported a 96 per cent increase in submandibular area associated with downward displacement of the hyoid bone in patients with OSA.

Obesity/neck size are also risk factors associated with OSA. Generally, a neck girth of 17in (43cm) or greater for men and 16in (40cm) or greater for women may predispose an individual to SDB. In one study, Banabilh et al. [21] studied craniofacial soft tissue hypertrophy associated with OSA. Using 3-D stereophotogrammetry, mean OSA and control facial configurations were computed. It was found that the body mass index and neck circumference were greater for the OSA group. As well, significant differences were found in facial shape between the two groups. Using FEA, these differences were localized in the bucco-submandibular regions of the face predominantly, indicating an increase in volume of 7-22% for patients with OSA. Thus, craniofacial obesity in the bucco-submandibular regions is associated with OSA, and may provide valuable screening information for the identification of patients with undiagnosed OSA.

In addition, macroglossia is a condition in which the tongue is larger than expected. There is a plethora of causes of macroglossia, which include congenital origins as well as acquired causes. Another condition that commonly causes macroglossia is acromegaly. Thus, acquired etiologies of macroglossia can be categorized as: metabolic; inflammatory/infectious; systemic; traumatic; neoplastic or infiltrative (amyloidosis) [22]. Another cause of a congenital macroglossia is Down syndrome. However, a recent study by Guimaraes et al. [23] showed that children with Down syndrome may not have true macroglossia, but may have relatively large tongues compared to the bony confines of the oral cavity. In the supine position, a patient with macroglossia is predisposed to OSA as a large tongue can cause airway obstruction. Thus, soft tissue structures such as the tongue, uvula, tonsils and pharyngeal fat pads etc. play a role in the patency of the upper airway [2]. Waldeyer’s tonsillar ring is a ring of lymphoid tissue in the oropharynx. Commonly, this lymphoid tissue becomes inflamed, and the tonsils and adenoids have to be surgically removed. Children with enlarged or infected tonsils present with snoring, OSA, mouth breathing and sometimes a failure to thrive or educational sub-performance. Interestingly, thickening of the lateral pharyngeal walls also appears to be a predominant factor in patients with OSA [1]. Other features associated with macroglossia include open bite deformity, mandibular prognathism and mandibular malalignment [22]. These features may, in turn, be precipitated by cranial base morphology, as alluded to above.
3. SYSTEMIC CONSIDERATIONS

There are many factors that contribute to the pathogenesis of OSA in the elderly or as a function of age. Essentially, apart from neurologic problems, the pathogenesis of OSA is a function of factors that affect pharyngeal patency. Thus, over a period of time any condition or situation that decreases pharyngeal patency could predispose an individual to OSA or SDB. With age, the upper airway becomes smaller and more collapsible. Therefore, this collapse approximates or encroaches on the airway of the patient with OSA. The upper airway collapses at a critical pressure, termed Perit [1]. Normal individuals have a negative Perit value. Thus, the more positive the Perit value is, the more collapsible the upper airway is. As individuals age, a combination of obesity, craniofacial changes and increased pharyngeal compliance have an additive or synergistic effect to increase Perit. Other factors involved in pharyngeal collapsibility include; muscle tone, impaired mechanoreceptor sensitivity, and function of the genioglossus and tensor palatini muscles. By stimulating the hypoglossal nerve, the genioglossus muscle contracts - thus increasing the retroglossal space [1]. Other factors that may contribute to SDB as an individual ages is possibly collapse of the nasal valve [7, 8]. In addition, low testosterone/estrogen or high testosterone has been implicated in the pathogenesis of OSA [1]. Therefore, postmenopausal women have an increased risk for OSA. Progesterone is a respiratory stimulant and may stabilize respiratory control, and it may also have a protective effect against the development of SDB [1]. On the other hand, testosterone may increase fat deposition in the neck, which leads to reduced airway size and may contribute to OSA [1, 21]. Still, the role of sex hormones and their mechanisms is still unclear in regard to SDB.

The control of breathing is a complicated mechanism that involves various parts of the brain and the brainstem, as well as the carotid body and the aortic bodies. A lesion or disruption anywhere in the circuit could predispose an individual to Central sleep apnea. Central respiratory neurons controlling respiration during sleep and wakefulness (metabolic or automatic) are located in the medulla, in the region of the nucleus tractus solitarius, nucleus ambiguous and nucleus retroambigualis [24]. Another area that may contribute to the pathogenesis of airway collapse from a control systems standpoint is respiratory instability. A control system essentially regulates or controls other systems or devices. The topic of respiratory instability or stability is controversial. Younes et al. [25] described respiratory control system instability by quantifying loop gain, which is the ratio of corrective response (ventilation) to a disturbance. A loop gain >1 signifies an unstable respiratory system [1]. Thus, Central sleep apnea syndromes are divided by the International Classification of Sleep Disorders into six categories [26], which include:

1. Primary Central sleep apnea
2. Central sleep apnea due to:
   a) Cheyne-Stokes breathing pattern
   b) High-altitude periodic breathing
   c) Medical conditions, not Cheyne-Stokes breathing
   d) Central sleep apnea due to drugs or substance
3. Primary Central sleep apnea of infancy
Central sleep apnea occurs when respiratory effort is diminished or absent in an intermittent or cyclic fashion due to central nervous system or cardiac dysfunction [26]. Patients with primary Central sleep apnea generally present with excessive daytime sleepiness, frequent arousals during the night, as well as complaints of insomnia. They also have shortness of breath upon awakening. Polysomnography data show > 5 Central apnea events/hour of sleep. The Cheyne-Stokes breathing pattern is associated with > 10 Central apnea events/hour, with a crescendo-decrescendo pattern of the tidal volume, as well as derangement of the sleep architecture. The condition is associated with heart failure, stroke and renal failure. Central sleep apnea due to high-altitude periodic breathing presents at altitudes usually above 4000m. Patients may complain of poor quality of sleep, frequent awakenings, and a sense of suffocation.

Endocrine functions and sleep are intimately tied together, and a lack of slow wave (Stage N3) sleep during development is associated with OSA. Furthermore, differences within children and adults, and gender differences also exist. In men, the onset of sleep, in concert with the first phase of slow wave sleep, results in the largest amount of growth hormone release in its circadian rhythm [27]. Growth hormone is closely associated with the onset of slow wave sleep, and typically peaks approximately 90 mins. after the onset of sleep [28]. In a pediatric or adolescent population, SDB may cause repeated arousals or disruption of sleep architecture. If a given individual is not able to have the proper amount of Stage N3 or slow wave sleep, the secretion of growth hormone will be disrupted. This disturbance will lead to growth delays or growth abnormalities. Children with SDB tend to present with a failure to thrive. Interestingly, with increasing age, there is a decrease of slow wave sleep, which corresponds to a decrease in growth hormone as well as IGF-1 levels [27].

There exists a higher prevalence of OSA in patients with a history of stroke or cardiovascular accidents. Thus, OSA is a strong risk factor for strokes. Furthermore, MRI of patients with OSA shows structural abnormalities in the gray and white matter in the brain [27]. The damage to the brain parenchyma may be secondary to repetitive cerebral ischemia. Generally speaking, a stroke leads to Central sleep apnea. However, a stroke that involves the brainstem or cranial nerves affecting the muscle tone of the upper airway may worsen OSA [27]. Other co-morbidities that may be involved in the cardiopulmonary pathophysiology of OSA along with stroke include: sympathetic activation; vascular endothelial dysfunction; oxidative stress and inflammation; metabolic effects; hypercoagulability, and hypertension [27, 29]. Cardiac complications of OSA include: cardiac ischemia; heart failure; pulmonary hypertension, and arrhythmias. The arrhythmias include; bradyarrhythmia, atrial fibrillation, premature ventricular complexes, and ventricular tachycardia [27]. All of these factors may directly and or indirectly play a role in the development of stroke associated with Central sleep apnea.

Poliomyelitis caused significant morbidity and mortality during the first half of the last century. Infected individuals can exhibit a range of symptoms as the virus enters the bloodstream [30]. While introduction of the polio vaccine in 1954 curtailed the incidence of new cases [30], a survey conducted in 1987 estimated that there were about 640,000 Americans living with the sequelae of paralytic polio [30]. In approximately 1% of infections, polio virus may spread into nerve fiber pathways, which includes the spinal cord, brainstem and motor cortex [30]. Here, the virus destroys the motor neurons. This is the development of paralytic poliomyelitis. The three major forms of paralytic poliomyelitis include spinal, bulbar and bulbospinal [30]. Bulbar polio makes up about 2% of the paralytic polio cases.
This variant affects the bulbar region of the brainstem, which is involved in respiration. Thus, any areas of the central nervous system involved in respiratory pathways, as well as the phrenic nerve, may result in respiratory failure and or a sleep disorder. Some of the symptoms include; increased muscle weakness, focal or generalized muscle atrophy, fatigue, pain and decreased ambulatory abilities [30]. This constellation of symptoms is commonly referred to as post-polio syndrome (PPS) [30]. It is believed that there may be progressively deinnervation of re-innervated motor units, persistence of polio virus, or induction of autoimmunity with consequence destruction of neural structures [30]. Muscle atrophy, breathing and swallowing difficulties, and sleep disorders are less common sequelae.

Central sleep apnea has been noted in a case report of a patient suffering from Japanese encephalitis (JE). This encephalitis is caused by the JE virus transmitted by the Culex mosquito. Only a small minority of patients develop clinically overt symptoms. The mortality rate is about 30%, but about half of the survivors have severe neurological sequelae [31]. There is no specific treatment available for JE. Necropsy studies have shown the thalamus, basal ganglia and midbrain as the common sites of pathology. Other conditions known to cause Central sleep apnea include: bulbar poliomyelitis; Western equine encephalitis; Listeria monocytogenes, brainstem encephalitis, and paraneoplastic brainstem encephalitis [31].

Essentially, neuro-degenerative diseases are defined as conditions where cells in the brain or spinal cord are damaged or lost over a period of time. Approximately 33-53% of patients with Alzheimer's disease have coexisting SDB [32]. The exact etiology of the coexistence is debatable but, SDB including laryngeal stridor, may have a higher prevalence in patients with Parkinson's disease than age-matched controls [32]. Patients with Parkinson's disease tend to have autonomic dysfunction, and the muscles of respiration are impaired secondary to the neurologic condition. There may be rigidity of muscles, as well as impairment of the central control of breathing. Stridor and laryngeal spasms may be seen in patients with Parkinson’s disease during the dystonic phase related to levodopa medication. After several years of levodopa treatment, patients with Parkinson’s disease may show an “on-off phenomenon” with rapid fluctuations in clinical features, such as choreiform dyskinesias during on-stage and dystonia and rigidity during off-stage dystonia [32]. Laryngeal spasms are also associated with off-stage diaphragmatic dyskinesia, and upper airway dysfunction [32]. Some of the nocturnal characteristics seen in patients with Parkinson's disease include decreased slow wave sleep and decreased REM sleep. Common sleep complaints include sleep maintenance insomnia, hypersomnia and parasomnias. More particularly, REM behavior disorders are reported in patients with Parkinson's disease [24].

Studies have demonstrated SDB and symptoms compatible with autonomic nervous system dysregulation in children with idiopathic congenital central hypoventilation syndrome (CCHS), Rett syndrome (Xq28, MECP2), and familial dysautonomia (9q31, IKBKAP) [33]. But, there is a lack of sleep studies in children with craniofacial malformations, chromosomal/genetic abnormalities, and in children with neuromuscular diseases [33]. For example, achondroplasia is an autosomal dominant skeletal dysplasia (4p16.3, FGFR3) in which respiratory compromise is due to an abnormal rib cage, small foramen magnum, cranial base dysmorphology, and midfacial hypoplasia [33]. In contrast, disorders with a protuberant tongue include the mucopolysaccharidoses e.g. Hunter syndrome, Hurler syndrome and Down Syndrome (Trisomy 21), all with identified genetic mutations, and often with severe SDB requiring early intervention. Genetic and familial craniofacial syndromes are often subdivided into those with micrognathia, midfacial hypoplasia, and protuberant tongue
disorders [33]. The micrognathia syndromes include Treacher Collins Syndrome, an autosomal dominant syndrome (5q32-33.1, TCOF1), and Pierre Robin sequence [33]. Infants with these syndromes can experience profound SDB, requiring aggressive intervention to prevent physiologic compromise [33]. The midfacial hypoplasia syndromes include Apert Syndrome (10q26, FGFR2), Crouzon Syndrome (10q26, FGFR2), and Pfeiffer Syndrome (8p11.2-p11.1 or 10q26, FGFR1 or 2) [33]. These are all autosomal dominant conditions, and typically represent a fresh mutation.

Children with midfacial hypoplasia often have increasingly severe SDB with advancing age due to craniofacial maldevelopment and surgical intervention. At the Center for Craniofacial Disorders, a preliminary study was undertaken on children with midfacial hypoplasia to test the hypothesis that morphologic airway improvements occur after midfacial distraction osteogenesis. In order to localize and quantify morphologic changes, homologous landmarks were digitized on the mid-sagittal slice of the MRI images prior to and after midfacial distraction osteogenesis (Figure 2). The landmark configurations were scaled to an equivalent size, using Procrustes superimposition, and subjected to pseudo-colored finite element scaling analysis. Figure 2 shows the results of that study.

Therefore, it was concluded that morphologic enhancement of the upper airway is demonstrable in patients undergoing midfacial distraction osteogenesis for the treatment of midfacial hypoplasia associated with congenital craniofacial syndromes such as Binder syndrome, frontonasal dysplasia as well as craniosynostoses affecting the midface.

Ehlers-Danlos syndrome (EDS) is a group of genetic disorders affecting humans with a defect in collagen biosynthesis. Depending on the individual mutation, the severity of the syndrome may vary. There are multiple sub-types in the classification of this disorder. Thus, EDS may present with: stretchy, soft and velvety skin, with a susceptibility to damage and scarring; flat feet; hypermobility; joint dislocation; joint pain, and visual problems. In addition, EDS is also associated with mitral valve prolapse. Verbraecken et al. [34] reported OSA coexisted in patients with Marfan's syndrome, while periodic limb movements were much more frequently reported in patients with EDS than in Marfan syndrome compared to unaffected controls.

Figure 2. The MRI image on the left shows the homologous landmarks that were digitized prior to and after midfacial distraction osteogenesis. The image on the right shows the pre- and post-treatment midfacial configurations superimposed and pseudocolored. The color scale indicates an increase in the upper airway (arrowed).
Furthermore, patients with EDS have a high-arched palate, and this feature may further predispose them to SDB. Marfan's Syndrome is a genetic autosomal dominant disorder with three basic connective tissue systems that are affected: the musculoskeletal system; the eyes (ectopia lentis - lens dislocation), and the cardiovascular system (mitral valve prolapse, aortic root dilation and aortic dissection) [35].

The defective gene is FBN1, which encodes a connective tissue protein, fibrillin-1. Abnormal production of fibrillin-1 monomers from a mutated gene disrupts the multimerization of fibrillin-1 and prevents microfibril formation [35]. Interestingly, the pathogenetic mechanism has been termed dominant-negative, because the mutant fibrillin-1 disrupts microform microfibril formation [35]. Thus, other fibrillin genes encode for normal fibrillin.

The general characteristics of patients with Marfan's syndrome are that they are generally tall, have long limbs and thin fingers. They may have cardiac complications, which include defects of the heart valves and aorta that could potentially lead to sudden death from a ruptured aortic aneurysm. In mitral valve prolapse, the leaflets of the valve do not tightly seal the left ventricle, and this causes prolapse or bulging of the mitral valve. Therefore, some of the blood leaks back into the left atrium causing a murmur. Other problems include; scoliosis, joint laxity, costochondritis and dural ectasia. The lungs are also affected. Restrictive lung disease secondary to pectus abnormalities and/or scoliosis is associated with Marfan's syndrome. Apart from spontaneous pneumothorax, patients with Marfan's syndrome are also predisposed to snoring and OSA.

Floppy eyelid syndrome (FES) is a relatively uncommon eye condition associated with flaccid and easily everted upper eyelids. Generally, it presents in obese, male patients over the age of 40 years. However, it can also present in women and non-obese patients. There is a strong association of FES with OSA. Generally, a patient presents with chronic papillary conjunctivitis of the upper palpebral conjunctiva [36]. Floppy eyelids evert spontaneously during sleep, resulting in chronic conjunctivitis of the upper eyelid [37]. Other eye conditions associated with FES include corneal abnormalities, eyelid abnormalities and glaucoma [37]. As well, FES is associated with other systemic conditions, which include obesity, hypertension, ischemic heart disease, diabetes and skin pathology [37]. The tarsal collagen appears to be normal in patients with FES [36].

However, several histologic studies have demonstrated a significant decrease in tarsal elastin using special stains, immunohistochemistry, and electron microscopy [36]. Other studies have described patients that were obese and had excessive craniofacial fat [37]. It was postulated that the facial configuration of these patients possibly increased the contact of the eyelids with a sheet or pillow, resulting in enhanced traction of the eyelids. Leibovitch and Selva [37] found that patients with FES and OSA were generally younger and had more severe degrees of OSA than patients with OSA alone. In addition, OSA may be associated with other ocular eye conditions, such as glaucoma, ischemic and non-ischemic optic neuropathy, and papilledema as a consequence of raised intracranial pressure [37]. Therefore, ontogenetic complexity and clinical heterogeneity are integrated in the precipitation of a spectrum of conditions associated with OSA and SDB.
CONCLUSION

The practice of sleep medicine requires a multidisciplinary approach. From pulmonary medicine to neurology to psychiatry to ophthalmology, the systemic problems in sleep medicine are multi-factorial. While the field is relatively young compared to other areas, sleep medicine-related technology is changing quickly as well as the knowledge base. However, ideal treatment protocols or a definitive cure are difficult to achieve, indicated by the wide range of procedures currently utilized. For example, Somers et al. [29] reported cardiovascular disease associated with SDB includes hypertension, heart failure, arrhythmias, renal disease, stroke and myocardial infarction inter alia. Clearly, these co-morbidities have a large economic impact in terms of healthcare management. Unfortunately, the standard of care, CPAP, does not help decrease the prevalence of the disorder as it does not treat the underlying problem, which is the upper airway. In any case, CPAP therapy in the latter half of life may not practical solution [38]. Furthermore, while surgical maxillo-mandibular advancement for the resolution of OSA may not be a first line procedure, generally it is thought to be one of the most effective. Thus, an optimal solution for SDB that not only decreases the incidence, but also decreases the prevalence of the disorder is required. First, research needs to be done on developing the optimal pediatric upper airway. If the child’s upper airway is slightly compromised it may become the nidus for the later development of SDB. Second, research is also required for optimization of the adult’s upper airway. Ultimately, delivery of an optimal solution or treatment for OSA may lay in the hands of the dental professional. Therefore, in addition to the systemic management noted above, a review of the common techniques used by dental professionals to treat patients with OSA need also to be reviewed.

The primary method used by dentists to manage mild, moderate and severe forms of OSA is a plethora of mandibular advancement devices (MADs). The basis of these devices emanated from the premise that in cardio-pulmonary resuscitation (CPR) the mandible is pulled forward to open the upper airway. While there is no doubt that this method opens an obstructed airway, it should be recalled that in CPR mandibular advancement is a short-term maneuver to rescue a patient in an emergency situation until the airway can be maintained through some other means. Thus, the long-term use of MADs needs to be addressed. Indeed, Chen et al. [39] found: increases in mandibular arch width; flattening of the curve of Spee; forward movement of mandibular segments in relation to the maxilla; opening of the bite; and concluded that a variety of occlusal changes occur with long-term MAD use for the treatment of OSA. Thus, long-term MAD therapy results in dramatic changes in the occlusion [40]. In addition, some patients diagnosed with OSA present with Class III malocclusion where the mandible is already in a protruded position, possibly secondary to cranial base morphology. Nevertheless, a large majority of patients fail CPAP therapy and resort to the use of MADs. The raison d’être for this substitution needs to be further examined.

Notwithstanding other issues, such as general discomfort, claustrophobia etc., one of the main proposals for the lack of compliance with CPAP is nasal resistance. Patients with reduced airflow through the nose resort to mouth-breathing during wakefulness. The application of air to a restricted nasal passage requires greater pressurization and hence patient discomfort. To bypass this scenario, patients and their dentists often resort to a MAD. However, these devices, ostensibly, convert a mouth-breathing patient during wakefulness to
a patient that is essentially mouth-breathing during the entire circadian rhythm. Given the fact that all humans are born as obligate nasal breathers, this conversion to exclusive mouth-breathing must be questioned. It is known that children that mouth-breathe tend to develop tonsillar hypertrophy, as the oral passage is unable to filter inhaled air as it lacks a respiratory mucosa. In addition, MADs, by definition, posture the mandible anteriorly in attempt to drag the tongue forwards, which is putatively the main culprit of the airway obstruction. In huskies, race-horses and other mammals subject to exertion, the tongue is reflexly protruded to unobstruct the upper airway. Therefore, there may be some merit is using devices that target the tongue instead of the mandible, especially those that do not rely on significant amounts of mandibular advancement [3]. On the other hand, there may be merit in addressing the underlying nasal resistance. In a preliminary study, Singh and Abramson [8] (2007) were able to demonstrate widening at the nasal isthmus while using an intra-oral nasal dilation device. Moreover, there are many studies investigating the effects of maxillary expansion on skeletal structures in actively-growing children.

By evaluating antero-posterior (AP) cephalometric radiographs, increases in maxillary, nasal and zygomatic widths have been demonstrated [41]. For example, analyses of short- and long-term effects of rapid maxillary expansion (RPE) followed with standard edgewise appliances were performed by Franchi et al. [42]. The greatest deformations were a widening of the maxilla and the base of the nose, so the nasal cavities were larger at the end of treatment. In investigations of the long- and short-term effects of RPE in 11 years old children treated with a Haas appliance, the greatest change was seen in widening of the maxilla and the base of the nose [43]. Similarly, when other maxillary expansion appliances are compared, increases in nasal width with significant effects on the palate, lacrimal and zygomatic bones have been noted [44]. However, RPE produces a force at the intermaxillary suture and in other structures of the craniofacial complex. Thus, the greatest widening is usually observed in the dento-alveolar areas, gradually decreasing through the upper structures, but the width of the floor of the nasal cavity can increase markedly as well [45]. Therefore, it is thought that RPE induces morphological changes in the naso-maxillary complex, and Singh et al. [18] were able to document these in children. Despite these reports, the upper airway changes that occur in passively-growing adults have not been fully related to the underlying skeletal changes. Nonetheless, it is likely that an osteogenetic-orthodontic protocol described by Singh and Krumholz [19] induces a phenomenon that is more in line with the Spatial Matrix hypothesis [46], inducing changes that invoke a biomolecular response, which can be best described as a ‘pneumopedic’ effect or non-surgical airway remodeling. Therefore, in the clinical management of sleep disorders a multi-disciplinary approach must be taken to address the interaction of etiologic components associated with SDB, to identify the causative agent(s) in specific individuals seeking definitive resolution.

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Snoring is a common symptom of airway obstruction, which is included in the spectrum of sleep-related breathing disorders. The manifestation may occur alone (primary snoring) or in association with other signs and symptoms such as rhinorrhea, hyponasal speech, cough, hypopnea, and sleep apnea. In the latter condition, which is better known as obstructive sleep apnea syndrome (OSAS), patients present nighttime and daily behavioral signs and symptoms that can result, in extreme cases, in serious cardiovascular impairment (i.e., cor pulmonale). In a pediatric age, the most frequent cause of snoring is adenoid hypertrophy. This disorder is probably the most frequent disease occurring in children and, when associated with palatine tonsil hypertrophy, leads to OSAS. In the past, adenoid size was evaluated by lateral soft-tissue X-ray of the nasopharynx, although, at present, nasal endoscopy is considered the gold standard to assess adenoid hypertrophy. To date, adenoidecтомy, which is the most frequent surgical indication in childhood, is considered the treatment of choice to resolve nasal obstruction and snoring due to adenoid pads. In the last decade, clinical researches on the utility of topical intranasal steroids for chronic nasal obstructive symptoms due to adenoid hypertrophy have been reported with encouraging results. This chapter is focused on the clinical picture, etiology, diagnosis, and treatment of snoring in pediatric patients. In particular, non-surgical treatments of adenoid hypertrophy are analyzed and the author’s personal experience on the efficacy of topical nasal steroid for treatment of adenoid hypertrophy is presented.
INTRODUCTION

Snoring is a low-frequency inspiratory sound due to vibration of soft tissues of oropharyngeal walls during sleep. The pathology is frequent not only in an adult population, but also in children. It may occur at any age in childhood with a higher incidence in prepuberal boys, and represents the most common symptom of sleep-breathing disorder (SBD). This latter disorder, which occurs in 1.5% to 12% of children [1], corresponds to a spectrum of illnesses with different degrees of severity ranging from primary snoring (PS) to obstructive sleep apnea syndrome (OSAS). In relation to the severity of the disorder, children may suffer from only snoring to other signs and symptoms (i.e., rhinorhea, hyponasal speech, cough, hypopnea, and sleep apnea). Correct diagnosis of the type of illness is mandatory to perform adequate and prompt treatment.

CLASSIFICATION OF SDB

SBD includes PS, obstructive hypoventilation (OH), upper airway resistance syndrome (UARS), and OSAS. PS is characterized by snoring without other signs and symptoms such as intermittent hypoxia, hypoventilation, apnea, hypercarbia, and sleep troubles [2]. OH is associated with prolonged periods of partial airflow obstruction throughout sleep, often with no arousal and/or oxygen saturation abnormalities, but with a repeated increase in carbon dioxide levels [3]. Described by Guilleminault et al. in 1993 [4], UARS identifies patients affected by snoring associated with labored breathing due to upper airway obstruction and transient arousals without gas exchange irregularities. Transient arousals may have an impact on nocturnal sleep leading to sleep fragmentation, consecutive isolated daytime sleepiness, and increased respiratory effort. Finally, OSAS, as defined first by the American Thoracic Society [5] and, subsequently, by the American Academy of Pediatrics [6], is “a disorder of breathing during sleep characterized by prolonged partial upper airway obstruction and/or intermittent complete obstruction (obstructive apnea) that disrupts normal ventilation during sleep and normal sleep patterns.” PS, OH, UARS, and OSAS probably correspond to different severe events of the same disease where PS and OSAS represent the lower and upper states, respectively.

RISK FACTORS

The upper respiratory tract is a collapsible muscular tube whose patency depends on muscular activity. Pathological situations that reduce airway size and/or neural function of dilator muscle may predispose to SBD.

Several risk factors can favor SBD. Allergic rhinitis, septal deviation, and hypertrophy of inferior turbinate may decrease nasal patency leading to mouth breathing. Clinical conditions narrowing the naso- and/or oro-pharyngeal space such as adenoidal and/or tonsil enlargement predispose to SBD. They are considered the most frequent risks factors for SBD in a pediatric age [1,7].
Obesity is another well-known predisposing factor for this disease in children since it narrows the upper airway and causes alteration of ventilatory control [8]. Moreover, nocturnal mouth respiration increases in obese patients when adenoidal and/or tonsillar hypertrophy is also present [9]. Exposure to parental smoking favors SBD in children, since smoking may cause edema and inflammation of respiratory mucosa, thereby reducing the size of the airway [10]. Children with Down’s syndrome are more prone to exhibit OSAS because of anatomical and functional anomalies (i.e., adenotonsillar hypertrophy, macroGLOSSia, midfacial hypoplasia, micrognathia, and muscular hypotonia) that favor a decrease of the respiratory tract and obesity [11]. Other genetic syndromes such as Pierre-Robin and Klippel-Feil sequences, Crouzon syndrome, achondroplasia, Apert syndrome, and Rubinstein-Taybi syndrome in which cranio-facial anomalies are present can also favor development of OSAS [12,13,14]. Because of predisposition to airway collapse throughout respiratory acts, connective tissue disorders (i.e., Marfan syndrome) are another risk factor. Finally, several neurological illnesses like Duchenne muscular dystrophy and cerebral palsy may predispose to SBD [15].

**PATHOPHYSIOLOGY**

SBD results from an intricate pathophysiological mechanism related to the size of pediatric ventilatory tract, predisposition of the airway to collapse, and neuromuscular compensation. Children affected by the disease show increased resistance along the respiratory tract during sleep [16] and/or a collapsible upper airway [17]. Reduction of the upper airway may be due to soft tissue hypertrophy (i.e., large adenoids, tonsils, and a soft palate) [18] or craniofacial abnormalities such as hypoplasia or retropositioning of the mandible or maxilla [19]. Finally, obesity is another anatomic anomaly that increases the risk for OSAS [20]. In fact, obese children have usually adenotonsillar hypertrophy [9] and, in addition, deposition of fat in the parapharyngeal space further reduces airway patency. Augmented airway collapse, which has been demonstrated in OSAS patients [21,22], may be related to a decreasing neuromotor response throughout sleep [23]. During wakefulness, pharyngeal dilator muscles such as the genioglossus and tensor palatini muscles maintain an open oropharynx, obtaining a stable ventilatory pattern. At sleep onset, a decrease of their activity with a propensity to pharyngeal collapse initiates. This condition leads to increased ventilatory variability that is especially observed during REM sleep and to an apneic threshold close to eupneic levels in non-REM sleep. For this reason, it is mandatory that neural inputs preserving an open airway are adequate, and otherwise OSAS can result [1,19].

**CLINICAL PICTURE**

As children are unconscious while sleeping, clinical history is best acquired by parents, brother, sister, or other people who sleep nearby or in the same room. For this reason, it is fundamental to interview family members.

Beyond snoring, children affected by PS usually suffer from dry mouth without any ventilation difficulty. In 1984, Guilleminault et al. [24] classified PS into 3 forms: 1) mild
when snoring is sporadically present and is not worrying for other persons; 2) moderate when it occurs every night and infrequently disturbs others; and 3) severe when snoring is always present and causes significant problems for other people.

UARS-patients present snoring associated with frequent awakenings that produce daytime symptoms such as poor attention, sleepiness, and hyperactivity.

OSAS, which has been recognized as a distinct clinical entity in children since 1976 [25], is characterized by several signs and symptoms. In fact, in addition to snoring, these patients can present difficulty in breathing during sleep, sleep-related pauses in breathing, and various episodes of arousals during sleep. Excessive sweating, nasal flaring, supra-sternal or intercostal retractions, and particular posture to attempt to decrease respiratory work to improve the diameter of the upper respiratory tract may also be observed. Parents sometimes describe choking, gasping, and/or apnea and, since the clinical picture is frequently worse in a supine position throughout sleep, they are obliged to move their children many times. This situation causes sleep disturbance for both parents and children. OSAS children have a higher risk for enuresis [26], but this is a useful clinical sign only if the child previously has been dry at night [27,28,29,30].

Night-time symptoms can also be associated with day-time symptoms. OSAS children can fall asleep in the classroom or during a trip in the car, have problems in maintaining attention at school, show “micro-sleeps” that may be confused with absence seizures, and hyperactivity. Other signs and symptoms that may be observed are restless sleep, chronic rhinorrhea, mouth breathing when awake, complicated swallowing, hearing problems (i.e., hearing loss due to effusive media otitis), frequent vomiting/nausea, and poor appetite [29].

Moreover, the presence of some symptoms in relation to the age of the patient may induce the suspicion of OSAS. In fact, one should consider OSAS in babies whenever difficulties in thriving, agitation, and recurrent upper airway infections, are seen, in young patients when atypical sleeping position, increased predisposition to infectious illnesses, non-normal speech, and absurd respiration are noted, or in school-aged children when abnormal activity school, poor attention, and awful behavior are observed.

**DIAGNOSIS**

A careful clinical history represents the first diagnostic step. During the day, snoring children may appear normal except for the presence of mouth breathing, although the occurrence of day-time symptoms, changes in behavior, and/or school activities can support the suspect of SBD. Sleep must be analyzed with particular attention and described with several details. It is fundamental to inquire about snoring, mouth breathing, episodes of apnea, specific sleep position, and to investigate about typical signs and symptoms of SBD.

Meticulous physical evaluation is the next step. It is mandatory to assess the size of tonsils and adenoids in relation to oro- and rhinopharyngeal space, respectively, as well as other disorders that could be responsible for upper respiratory tract obstruction such as a deviated nasal septum, hypertrophy of inferior turbinate, rhinosinusitis, nasal polyps, paranasal mucoceles, micrognatia, malocclusion, large tongue, high arched, and long palate. Upper airway examination is performed using endoscopes. To date, there are available several endoscopes with different size and types of optic fibers (i.e., rigid and flexible one). In
relation to age and compliance of child, the clinician will choose the most adequate endoscope. Moreover, cardiovascular and pulmonary examination can show alterations (i.e., cor pulmonale, systemic diastolic hypertension, pectus excavatum) suggesting increased work in breathing [1,31,32].

Unfortunately, clinical history and physical examination are not sufficient to distinguish PS from OSAS in children. In 1995, Carroll et al. [33] reported a retrospective study on 83 children with snoring and/or SBD undergoing polysomnography (PSG). All these patients were also assessed with a clinical obstructive sleep apnea score and other questions related to sleep, daytime symptoms, and breathing to differentiate PS from OSAS in a pediatric age. It was concluded that the obstructive sleep apnea score cannot distinguish children affected by PS from OSAS patients, whereas based on PSG, 48 children were classified as PS and 35 as OSAS. In 2004, Brietzke et al. [34] carried out a systematic review of the literature, and concluded that pediatric clinical history and physical evaluation are insufficient to reach a definitive diagnosis of the type SBD. Recently, Li et al. [35] evaluated a questionnaire instrument on 229 Chinese children. The survey showed a positive and negative predictive value of 81% and 57%, respectively. For this reason, overnight PSG is the diagnostic method of choice that can distinguish SBD between OSAS and other sleep-related respiratory disorders and quantify sleep-breathing abnormalities [1,2,31,36,37].

Because of the high costs and effort needed for PSG, and the increased demand of this diagnostic instrument particularly in a pediatric age [38,39], alternative methods have been proposed that are simpler than PSG, less expensive, and may be performed at home in some cases. Home procedures have the advantage of leaving the child in her/his natural sleeping environment thus improving the comfort and compliance of the patient. The lack of adequate personnel to resolve technical issues represents a disadvantage. In 1996, an Israeli study group [40] tested the efficacy of home video-recording of children during sleep for screening OSAS. Fifty-eight patients with suspected OSAS undertook PSG and their results were compared with the analyses of 30 min videotape of each child sleeping at home, obtaining a sensitivity and specificity of 94% and 68%, respectively. In this way, this technique can only favor selection of patients to undergo PSG. After 3 years, Lamm et al. [41] evaluated home audiotapes of breath sounds in 36 children throughout sleep. The parents of these patients were instructed to make a 15-min home audiotape that showed the characteristics of their child’s breathing. These findings were compared with their overnight PSG, but the results were not sufficiently specific to reliably distinguish PS from OSAS. In 2000, Brouillette et al. [42] estimated nocturnal pulse oximetry as an abbreviated testing modality for OSAS in a pediatric age. In this trial on 349 children, nocturnal oximetry was performed during PSG. Oximetry trend graphs were classified as positive for OSAS in 93 patients and negative or inconclusive in the remaining 256, with a positive and negative predictive value of 97% and 53%, respectively. Although motion or loose leads may cause artifacts leading to difficulty in interpretation, overnight pulse oximetry can predict an abnormal PSG, but a negative test cannot exclude OSAS. Finally, an American study [43] compared 1-hour daytime nap PSG to overnight PSG in 40 children affected by SBD. Sedation with chloral hydrate was used for nap PSG in about 75% of patients, whereas no sedation was necessary for overnight PSG. Notwithstanding the sedation, SBDs were underestimated by nap PSG. The diagnostic method had a positive predictive value of 100% and negative predictive value of 17% in predicting SBD. The authors concluded that nap PSG can be a helpful instrument for screening SBD-children and, whenever inconclusive, an overnight PSG is mandatory.
While all these procedures are useful, none can effectively diagnose OSAS. Thus, overnight PSG remains the gold standard to identify OSAS, to differentiate it from other types of SDB, and to estimate its severity [2,36,37]. This diagnostic procedure includes concurrent recording of several parameters. Electroencephalogram, electro-oculogram, and electromyogram to assess sleep stages; airflow monitoring, and end-tidal pCO2 measurements, while inductance plethysmography evaluates ventilation and respiratory activity; pulse oximetry reveals oxygen saturation; and electrocardiogram assesses cardiac rhythm and rate. Esophageal pH and pressure monitoring are considered two optional evaluations. During overnight PSG, an expert technologist constantly observes the patient under video and can act whenever there is a technical need such as replacement of sensors. Furthermore, it is helpful to record the sleep on digital video for eventual re-assessment.

The technical equipment used to perform PSG in a pediatric age is the same utilized in adults. However, some differences in methodology and normative values of PSG are used in the two groups of patients.

In a pediatric age, an overnight PSG should be performed in a child-friendly environment with the presence of a parent who should sleep in another bed or cot as her/his movements could cause interference with the diagnostic procedure and/or be confused as originating from the patient, whereas outpatient-screening studies should be only reserved for older children and/or adolescents. Sleep examination must be performed with no sedation since it alters respiratory activity, favoring an overestimate of the severity of SBD.

Although different results in overnight-PSG have been reported on two consecutive nightly recordings in an adult population, a single PSG is considered sufficient to diagnose SBD in pediatric patients.

In 2002, Katz et al. [44] assessed the night-to-night variability of respiratory and sleep parameters in 30 children affected by SBD using 2 different nocturnal PSG. No statistical differences were observed among respiratory variables (i.e., apnea index, apnea/hypopnea index, arterial oxygen saturation, and end-tidal partial pressure of carbon dioxide) or sleep parameters such as sleep efficiency, arousal index, percent rapid eye movement, and percent of slow wave sleep. Based on these results, the authors suggested that a single PSG is sufficient for children with a clinical picture suspicious for SBD.

Moreover, the use of age-adequate normative values for PSG is fundamental to diagnose SBD. In 1992, Marcus et al. [45] reported normal polysomnographic values for children and adolescents analyzing an overnight PSG of 50 normal pediatric patients. They concluded that the polysomnographic results in the pediatric population are different from those in adults and gave normal polysomnographic criteria (Table 1).

Overnight PSG does not need however to be performed in every child who snores. The American Academy of Pediatrics recommends carrying out the objective diagnostic procedure before surgical treatment [i.e., adenotonsillectomy (AT)] for SBD in a pediatric age.

Notwithstanding, a recent survey among members of American Society of Pediatric Otolaryngology demonstrated that the majority of pediatric ENT surgeons perform AT in children with SBD without preoperative PSG. In fact, they rely on clinical diagnosis rather than PSG to carry out an AT, whereas they use PSG when diagnosis is difficult [46].
Snoring in Pediatric Patients

Table 1. Normal values for overnight PSG in a pediatric age [45]

<table>
<thead>
<tr>
<th>NORMATIVE VALUES</th>
<th>NORMAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apnea hypopnea index (AHI; events/hour)</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Maximal end-tidal pCO2</td>
<td>≤ 53</td>
</tr>
<tr>
<td>Duration of hypoventilation</td>
<td>≤ 45%</td>
</tr>
<tr>
<td>Minimal Sp O2 (%)</td>
<td>92%</td>
</tr>
<tr>
<td>Fall in Sp O2 (%)</td>
<td>≤ 8%</td>
</tr>
</tbody>
</table>

**THERAPY**

Treatment of snoring is in relation to etiology and ranges from conservative management to surgery. When snoring is due to disorders such as allergic rhinosinusitis, non-invasive treatment with antihistamines, nasal or systemic steroids, and positional therapy (i.e., lying on the side during sleep) is the therapy of choice. In obese children, first-line treatment is weight reduction. Since this is not easy to achieve in a pediatric age, it is mandatory to perform a careful scheduling (i.e., meticulous planned calorie-reduced diet and a regular exercise program) under close follow-up by physician and an involvement of both patients and families [47].

If adenoidal hypertrophy (AH) (Figure 1) is the cause of SBD, adenoidectomy is considered definitive treatment. A negative effect on the systemic immunological system, the risk of the postoperative bleeding, and the possibility of recurrence are the main points of criticism of adenoidectomy [48,49,50].

![Figure 1. Endoscopic view of adenoidal hypertrophy (asterisk) totally obstructing the nasopharynx.](image)
To avoid these negative factors, in last decade, the efficacy of intranasal steroid in decreasing adenoid size and, successively, in improving chronic obstructive nasal symptoms has been assessed.

In the 1990s, Demain and Goetz [51] first described the utility of beclomethasone nasal spray in 17 patients with AH. After 6 months, significant decrease in adenoid pad size and improvement of symptomatology was observed in all children. Later, other authors tested the efficacy of different intranasal steroid molecules and reported interesting outcomes [52,53,54].

Based on these encouraging results, we evaluated the efficacy of mometasone furoate (MF) aqueous nasal spray in reducing adenoidal size and severity of obstructive nasal symptoms such as nasal obstruction, rhinorrhea, cough, snoring, and sleep apnea [55]. No adverse effects on nasal mucosa, no alteration on growth in children, no changes on the hypothalamic-pituitary-adrenal axis, and poor mucosal absorption of the drug compared to other nasal steroids were the main reasons that led us to study MF. Sixty children with AH scheduled for exclusive adenoidectomy were enrolled in a two-stage, prospective, randomized, placebo-controlled trial. Adenoidal size was evaluated by nasal endoscopy in all cases. In the first stage lasting 40 days, patients were randomly divided in 2 arms: 1) group A (30 children) undergoing intranasal mometasone therapy (50 μg/nostril/day) and 2) group B (the remaining 30 patients) receiving placebo saline nasal solution. Baseline demographics, symptoms, and choanal obstruction data were similar in both groups. At the end of this period, no changes were identified in the placebo group, whereas a significant reduction in the severity of symptomatology and adenoidal size was observed in 77.7% of the study group (Table 2). In the second stage, children defined as “responders” were divided randomly in 2 subgroups and underwent maintenance therapy for 3 months. Group A1 (11 cases) received nasal MF treatment on alternate days for the first 2 weeks per month, whereas group A2 (10 cases) continued daily steroid therapy for 2 weeks per month. After 3 months of maintenance-therapy, all patients were reassessed. At this evaluation, only choanal obstruction in group A2 was less than in group A1, whereas other parameters were similar between the 2 subgroups. Therefore, the successful results observed in the first period study were confirmed. It is worthwhile noting that these encouraging outcomes were obtained for patients affected only by AH.

Since no data about long-term intranasal maintenance therapy with MF for AH are available, in 2007 we reassessed the aforementioned “responder” patients after a long-term follow-up [56]. The most important feature observed in this study was that children continuing maintenance treatment showed a significant improvement in their clinical picture after a mean period treatment of about 2 years, thus allowing their definitive removal from surgical planning, whereas all patients voluntarily suspending maintenance therapy underwent adenoidectomy. Another important point is that maintenance therapy was well tolerated by children and that no local and/or systemic adverse effects were observed, notwithstanding the long-term intranasal steroid therapy.

At present, the mechanism by which a topical nasal steroid acts favorably on adenoids, reducing their size and improving chronic nasal obstructive symptoms, is not known. A lympholytic action, a decrease in adenoidal and nasopharyngeal inflammation, and modification of the adenoidal bacterial flora are the main hypotheses.
Table 2. Chronic nasal symptoms and choanal obstruction after the first 40 days of intranasal mometasone treatment

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal obstruction</td>
<td>1.000 (0.000 - 2.000)*</td>
<td>0.000 (0.000 - 0.000)*</td>
<td>p = 0.00005</td>
</tr>
<tr>
<td>Rhinorrhea</td>
<td>1.00 (0.00 - 1.50)*</td>
<td>0.00 (0.00 - 1.00)*</td>
<td>p = 0.041</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>0.000 (0.000 - 1.000)*</td>
<td>0.000 (0.000 - 0.000)*</td>
<td>p = 0.00034</td>
</tr>
<tr>
<td>Cough</td>
<td>1.00 (0.00 - 2.50)*</td>
<td>0.00 (0.00 - 1.0)*</td>
<td>p = 0.0033</td>
</tr>
<tr>
<td>Snoring</td>
<td>2.00 (0.00 - 2.00)*</td>
<td>0.00 (0.00 - 0.00)*</td>
<td>p = 0.00000005</td>
</tr>
<tr>
<td>Choanal obstruction</td>
<td>20.0 (12.5 - 32.5)*</td>
<td>0.0 (0.0 - 0.0)*</td>
<td>p = 0.007</td>
</tr>
</tbody>
</table>

*A (B - C) = Median (interquartile range) for continuous variables.

When AH is associated with tonsil hypertrophy, a clinical picture of OSAS may be present. Thus, AT is considered the therapeutic gold standard for children affected by this disorder [2,8,31,57], and the procedure allows successful results in 75% to 100% of cases. In 1993, Zucconi et al. [58] reported a 100% cure rate in 29 children with OSAS undergoing adenotonsillectomy. Five year later, Shintani et al. [59] described 134 patients affected by snoring and clinical sleep apnea. AT was performed in 114 children, obtaining a resolution of disease in 75.4% of cases. In another independent study published in 2000, AT was carried out in 21 children with OSAS. Symptoms and PSG results improved in all patients. Only 1 child showed a pathologic obstructive apnea/hypopnea index with mild postoperative obstructive symptoms [60].

Since surgery is usually curative, continuous positive airway pressure (CPAP) is considered as second-line treatment for OSAS in a pediatric age. The American Academy of Pediatrics recommends using CPAP for children with unsuccessful surgical results and/or contraindications to surgery [2]. This procedure is performed via nasal mask and allows the collapsed airway to remain open. Although CPAP is considered effective for the treatment of OSAS [61], its application should be always evaluated for the possibility of midfacial hypoplasia [62]. Finally, the use of CPAP should be reassessed yearly since OSAS may improve with the growth of child.

Other surgical procedures such as decongestion of inferior turbinates, septoplasty, removal of nasal polyps, tongue reduction, genioglossal advancement, hyoid myotomy and suspension, uvulopalatopharyngoplasty, maxillo-mandibular advancement, and tracheotomy are rarely performed in pediatric patients [8,36,57].

CONCLUSION

Snoring is a common symptom in a pediatric age and represents a manifestation of sleep-related breathing disorders. It can occur alone or in association with other signs and symptoms corresponding to illnesses with different severity. Snoring may due to various causes, although adenotonsillar hypertrophy is the more frequent risk factor. Even though several diagnostic procedures are available, overnight PSG remains the diagnostic technique of choice to diagnose, estimate, and definitively differentiate SBD. Conservative medical treatment is indicated whenever organic diseases have been excluded. Based on the results of our study, it may be helpful to treat children with intranasal steroid therapy who are affected
with AH before planning surgical treatment. Adenotonsillectomy is considered the gold standard to resolve OSAS, whereas CPAP should be utilized only as second-line management in selected cases.

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Chapter 7

THE SNORING CHILD:
QUESTIONS ARE MANY ANSWERS ARE FEW

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Ramalinga Reddy
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ABSTRACT

Snoring in the pediatric population is increasing and has been identified as a primary health concern by the American Academy of Pediatrics. The increase has been associated with a rise in co morbid disease processes such as asthma, allergies, lifestyle changes and increasing obesity in the pediatric population. It is estimated that 3 to 14% of children snore.

In the pediatric patient, snoring can present as a mild annoyance to family members trying to sleep at night, and a source of teasing and embarrassment for the child. But snoring may be a symptom that represents very serious health concerns for the child. Unlike adults, snoring in children is not always synonymous with obstructive sleep apnea. There are varying degrees of snoring in the pediatric population ranging from mild to severe. The outcomes may differ and may not be consistent with the severity of snoring.

The diagnosis, evaluation and treatment of snoring are often different processes in children than they are in their adult counterparts. Symptom presentation may differ as well. Differential diagnosis varies as the physical and developmental stages of the child unfold.

Evaluation of the snoring child demands a physical examination along with a thorough family, school, behavior and health history. Diagnostic testing typically includes overnight polysomnography as the “gold standard” for determining the extent to which snoring is associated with sleep disordered breathing. Without such a comprehensive evaluation, the final diagnoses often remain ambiguous, with a treatment plan lacking in direction and efficacy.

The question of snoring is frequently overlooked by healthcare providers. Time constraints may not allow for an open discussion regarding the child’s sleep habits, and healthcare providers may be prone to dismiss the symptom as insignificant and meaningless. However, the snoring child in the absence of objective evidence of
obstructive sleep apnea needs to be followed closely. Even primary snoring has been shown to be associated with decreased cognitive function and behavioral problems. The best venue for evaluation, treatment and follow up of the snoring child is found in a multidisciplinary pediatric sleep clinic, where adequate time and attention can be paid to the importance of sleep and snoring. Given the profound impact of sleep on a child’s physical, developmental, emotional, and psychosocial well being, such a clinic ensures the delivery of care that maximizes the probability of returning the child to optimal health.

**INTRODUCTION**

Snoring is a very common complaint heard from parents about their child. The conundrum for the health care provider becomes one of deciphering what the noise is and what to do about it. Unfortunately current literature about snoring in childhood is very limited. Frequently the literature links snoring with obstructive sleep apnea (OSA); however only 1 to 4% of children have OSA. In contrast, snoring is reported to be at a rate of 2 to 27% of the pediatric population (Perez, I.A., Ward, S.L. 2008; Marcus, C., Chapman, D. and Ward S. et al 2002 and Dayyat, E., Gozal, L., and Gozal, D. 2007). This clearly illustrates that the causes of snoring are not all explained by OSA, and that more research is needed to elucidate the cause and effect of habitual snoring on the child.

Snoring occurs at all ages from infancy to adolescence. It is observed more prevalently in the Black and Hispanic populations and in prepubertal boys (Perez, I.A., Ward, S.L. 2008). Risk factors for snoring include: a history of asthma, eczema, rhinitis, exposure to inhaled irritants such as tobacco smoke and car exhaust, and a parental history of snoring (Perez, I.A., Ward, S.L. 2008). Co-morbidities linked with snoring are inflammatory changes of the upper airway such as adenotonsillar hypertrophy and otitis media. Snoring, in the absence of obstructive sleep apnea has been associated with oxygen desaturation and with changes in sympathetic vascular tone which is predictive of cardiac risk in adulthood.

Snoring in infancy and childhood, once thought to be innocent, has recently gained new attention as studies now correlate snoring with poor cognitive function as well as somatic and behavioral effects when associated with arousals from sleep. (Fauroux, B 2007 and Karpinski, A., Scullin, M, and Montgomery-Downs, H. 2008) Several studies have documented the negative effects snoring has on attention span, hyperactivity, aggression, irritability, emotional peer relationships and somatic complaints. The studies also documented lower memory and intelligence scores in patients who snored when compared to peers who did not (Mitchell, K. 2006; Kennedy, J., Bluden, S., Hirte, C., et al. 2004 and Blunden, S., Lushington, K., Kennedy, D., et al. 2000). These along with the other associated morbidities of snoring in childhood set a mandate for evaluation and treatment of primary snoring even in the absence of associated sleep apnea.

**WHAT ARE THE ETIOLOGIES OF SNORING?**

The causes of snoring in children are many and can be classified into three main categories: congenital, acquired and miscellaneous. The commonality among the three
categories is that they in some way impair the flow of air through the nasal and oral cavities to the lungs. Their differences lie in the origin of the airflow impairment.

Congenital causes of snoring include conditions like craniofacial abnormalities, midfacial hypoplasias, retrognathia, Pierre-Robin Sequence, Down’s syndrome (hypotonia; macroglossia), Treacher Collin Syndrome, Golden Har Syndrome, mucopolysaccharidoses (Hunters, Hurlers), achondroplasia and Prader–Willi Syndrome. Each of these syndromes restructure the airway to cause turbulent airflow through the airway in different ways. Craniofacial and midfacial hypoplasia etiologies are skeletal in nature. They exhibit relatively smaller airways and in some cases macroglossia. Other etiologies such as Down’s syndrome and achondroplasia have more complex presentations with a small pharynx, altered muscle tone and macroglossia. Mucopolysaccharidoses are a group of metabolic disorders (Hunter’s, Hurler’s) that have complex obstructive characteristics such as macroglossia, deformed pharynx, short thick necks and instability of the cervical spine. Mucopolysaccharide formations deposit in the tracheal, epiglottic, tonsillar and adenoidal tissue further decreasing the pharyngeal space (Kuppersmith, R. 1996; Loughlin, G., Carroll, J., Marchls,C., 2000).

Acquired causes of snoring include infection, allergies, neoplasm and neurological origins. In these conditions the pharyngeal space is limited again but by different mechanisms. Infectious causes of snoring include Rhinosinusitis, Adenoiditis and Mononucleosis. In these instances there is inflammation and edema of the tissues compromising the patency of the airway. Mucous production increases at the same time occupying the pharyngeal space and causing obstruction. In allergic conditions such as allergic rhinitis and nasal polyps, inflammation and mucous production again play a role in narrowing the pharyngeal space.

Neoplasms such as adenoma and nasopharyngeal carcinoma distort the shape of the airway and cause airflow obstruction. The tumors may cause nerve dysfunction, impacting muscle function that keeps the airway patent. Alterations in vascular flow that supply the tissues of the airway may also be impeded upon causing decreased flow and diminished function of the airway tissue. Snoring may be a first sign of a neoplasm presence in the airway.

Neurologic conditions can also cause snoring. Cerebral Palsy exhibits variations in muscle tone, both hypotonic and hypertonic, which result in a multitude of complications that contribute to snoring. Hypotonia relaxes muscles of the upper airway during sleep to the point of pharyngeal collapse. Approximately 69% of patients with severe spasticity have silent aspiration and reflux (Odding, E., Roebroeck, M., and Hendrik, S. 2006). Cerebral Palsy patients are also prone to malocclusion and over-jetting of dentations, altering the structure and function of the oral cavity.

Miscellaneous conditions that also can cause snoring in children include foreign bodies in the nose, deviation of the nasal septum, and the effects of drugs or alcohol. Conditions which increase the amount of tissue in the pharyngeal area such as pharyngeal flap surgery for cleft palate can lead to post operative snoring. Obesity is increasingly being identified as a factor in pediatric snoring due to fatty infiltrates in the upper airway structures and fatty deposits in the subcutaneous tissue of the neck narrowing the airway and promoting pharyngeal collapse (Dayyat, E., Gozal, L., and Gozal, D. 2007; and Verhulst, S., Aerts, L., Jacobs, S., Schrauwen, N., et al. 2008). In addition there is evidence to suggest that obese children may have increased inflammation in the airway itself (Verhulst, S., Aerts, L., Jacobs, S.,
Exposure to environmental tobacco smoke has also been linked to children who snore. Smoke as an irritant can promote mucosal edema and inflammation resulting in proliferation of lymphoid tissue and narrowing of the pharyngeal area. (Dayyat, E., Gozal, L., and Gozal, D. 2007; Gozal, D., and Pope, D., 2001; and Corbo, G., Forastiere, F., Agabiti, N., et al. 2001).

**WHAT IS THE PATHOPHYSIOLOGY OF SNORING?**

Snoring is caused by vibration of upper airway structures during sleep. These structures include soft palate, uvula and lateral walls of the pharynx. The character and timbre of the sound produced depends on the site or sites of vibration. Although snoring is often heard during inspiration, it can be heard in expiration as well.

The upper airway from the nares to the larynx is a flexible and collapsible tube that performs various functions in respiration, swallowing, and phonation. In susceptible individuals snoring is produced when the intraluminal negative pressure during inspiration exceeds distending activity of the upper airway muscles, especially the genioglossus. Collapsibility is increased especially in REM sleep due to a decrease in upper airway muscle tone.

Data from the Wisconsin sleep cohort study revealed that habitual snorers tend to have a higher prevalence of apnea-hypopnea indices of 15 or higher (Young, T., Palta, M., and Dempsey J., et al. 1993). However snoring by itself lacked specificity for obstructive sleep apnea. Individuals with snoring share many of the upper airway features of patients with OSA and upper airway resistance syndrome.

Snoring should be differentiated from stridor, which results from narrowing of the airway at the level of the larynx, and from catathrenia, which is expiratory groaning during REM or Stage 2 sleep.

**WHAT NIGHTTIME SIGNS ARE ASSOCIATED WITH SNORING?**

The starting point for detecting snoring in children lies in the direct report of parents, or siblings who might share a bedroom with the patient. Not unlike adults, children often deny their snoring and are typically made aware of the problem by those within hearing distance at night.

Beyond the obvious sound effects of snoring, parents should make careful observations about the restfulness of their child’s sleep, and the presence of atypical behaviors during sleep. Snoring in children is frequently associated with agitated sleep, unusual sleep positions, and the characteristic bed coverings torn apart by night’s end. Parasomniac behaviors, such as sleepwalking, sleeptalking, night terrors, and enuresis, are frequently triggered by disturbed nocturnal breathing, which causes ‘partial arousals’ from deep sleep (Broughton R. and Chokroverty S., editor 1999). During such episodes, distinct portions of the brain are essentially awake and activated, while the majority of the frontal cortex remains asleep.
WHAT DAYTIME SYMPTOMS ARE ASSOCIATED WITH SNORING?

Sleep apnea in an adult patient is typically associated with significant daytime sleepiness and/or fatigue. However, this correlation is much weaker in children. Some do exhibit the hallmark symptoms of daytime sleepiness, fatigue, and tiredness throughout the daytime hours. This is frequently brought to the attention of parents by the child’s teacher, who may notice the child dozing off in class, or lying his or her head on the desk for some quick shut-eye when the opportunity presents. Physical fatigue and lethargy are best observed during gym class or outside recess, when physical activity levels are often noticeably diminished. While many children can hold their sleepiness at bay during the school hours, many succumb to the pressure with regular after-school napping. This then leads to a vicious cycle of poor sleep hygiene. After-school napping decreases the homeostatic drive to sleep, creating complaints of “insomnia” at an age-appropriate bedtime. Sleep onset is then pushed later and later into the evening, thereby shortening the total time available for nighttime sleep. The reduced sleep quantity, combined with poor sleep quality from SDB, then increase the pressure (and probability) for more daytime napping.

Perhaps more characteristic of pediatric patients with SDB is the seemingly contradictory symptom of daytime hyperactivity. Combined with the additional symptoms of rebellious and aggressive behavior, the symptom complex of the childhood snorer is best encapsulated as a failure of impulse control. This same dynamic is seen in the primary symptoms of inattention and lack of concentration – i.e., the failure to suppress the impulse to attend to competing stimuli vying for a child’s attention (Sterni, L. and Tunkel, D. 2003). Again teachers may be the best position to observe such impairments to a child’s academic performance, although the consequences can be readily seen by parents at report card time.

As a result of the above, children with SDB often present to the pediatrician’s office with significant behavioral and academic problems. Not surprisingly, a good number have already been diagnosed with ADD/ADHD, learning disabilities, or psychological disorders before anyone has even opened an inquiry into the quality or quantity of their nighttime sleep. Even when true versions of these disorders exist, SDB may exacerbate the offending symptoms. If left unaddressed, behavioral and pharmacological treatments may “bark up the wrong tree” for months or years on end (Gruber, R., Xi, T., Frenette, S. et al. 2009).

As the chapter title suggests, the correlation between sleep-related breathing disorders and daytime symptoms remains weak. Children with significant OSA frequently present with no apparent daytime symptoms, while children with primary snoring or only a mild degree of SDB often suffer from considerable daytime symptoms. Despite this somewhat confusing relationship, approximately two-thirds of children with SDB do have some measureable degree of cognitive impairment (Khadra, M., McConnell, K., VanDyke, R. et al. 2008).

One of the more frequently overlooked sequelae of sleep-disordered breathing is impaired growth or “failure to thrive.” The secretion of human growth hormone is highly correlated with delta sleep, which predominates the sleep patterns of a normal young child. The repetitive awakenings caused by SDB, however, continually interrupt the flow of delta sleep, or prohibit a child from entering delta sleep. This results in increased Stage 1 and 2 of NonREM sleep, and the depletion of growth hormone at critical points in pediatric development. Improved growth has been reported after treatment of SDB with adenotonsillectomy (Bonuck K., Freeman K., and Henderson J. 2009).
**EVALUATION OF SNORING**

**The Pediatric Sleep Study: Strengths and Weaknesses**

Perhaps the first and most basic question to be answered is whether or not the snoring is a sign of nocturnal sleep disordered breathing (SDB). Despite certain limitations, overnight polysomnography remains the “gold standard” for diagnosing SDB in children. Monitoring nocturnal respiration alone tells us nothing about the quality of the child’s sleep, while monitoring nocturnal EEG (Electroencephalogram) activity alone may indicate a sleep disturbance but tells us little about the cause. Overnight sleep studies combine EEG recordings with respiratory monitoring to help elucidate their complicated interaction. Added to this are EMG (Electromyogram), EOG (Electro-oculogram), and ECG (Electrocardiogram) recordings to further characterize sleep stages, and identify other consequences of SDB or other sources of sleep disruption.

Like adult polysomnograms, pediatric sleep studies yield results along a continuum of pathology from primary snoring to Upper Airway Resistance Syndrome to Obstructive Hypopnea to Obstructive Apnea. At the mild end of the continuum is primary snoring, defined as snoring that occurs in the absence of sleep apnea, without abnormal gas exchange, and without associated arousals from sleep and resultant disruption in sleep architecture. At the other end of the continuum lie children with true obstructive sleep apnea: complete or near complete occlusion of the upper airway that results in the entire spectrum of pathological sequelae, including oxyhemoglobin desaturations, EEG arousals and awakenings, and disturbed sleep architecture (Sterni, L. and Tunkel, D. 2003).

Somewhere in between these poles lies the child with Upper Airway Resistance Syndrome. This disorder is characterized by mild or partial upper airway obstruction that creates repetitive episodes of increased respiratory effort, but without abnormal gas exchange. However, these respiratory-related arousals (RERAs) do fragment sleep, often to the same degree as true apneas or hypopneas.

This last finding serves to highlight a crucial shift in our understanding of pediatric snoring over the past decade. No longer is the loudness of the child’s snoring or the number or type of apneic events of primary importance. Rather, the more salient question becomes to what extent snoring and disturbed breathing cause arousals, awakenings, sleep fragmentation, and disturbed sleep architecture. More current research suggests that these are the variables more closely tied to the behavioral and neurocognitive consequences of SDB. Again it is only through polysomnography that these questions can be adequately addressed (Leong, A. 2006).

Unfortunately, a sleep study has limitations, and may fall short of telling us everything we need to know about the impact and meaning of snoring. Consider the child who snores, has daytime symptoms suggestive of SDB, and yet exhibits normal sleep architecture and well-preserved sleep during the polysomnogram. Nocturnal oximetry may only skim the surface of more complex gas exchange abnormalities associated with snoring. Surface EEG recordings may fail to detect more subtle arousals and disruptions to sleep architecture caused by snoring alone. Perhaps polysomnographic studies remain as the “gold standard” simply because of their relative ease, availability, and cost. However, their sensitivity to underlying pathology may, at times, leave something to be desired.
A negative sleep study, therefore, should not automatically close the door to further evaluation and treatment of snoring. Measuring a new variable known as “regional cerebral oxygen concentration,” a recent study evaluated three groups of children: those with SDB, those with snoring but no measurable SDB, and healthy controls. Surprisingly, the lowest level of regional cerebral oxygen concentration was found in the snoring group, with the SDB group falling in the middle between snorers and controls. The authors explain this paradoxical finding by suggesting that the rise in blood pressure that typically accompanies sleep apnea may raise cerebral oxygen levels, – a process which does not take place in snorers alone (Khadra, M., McConnell, K., VanDyke, R. et al. 2008). This explanation finds further support in a recent study that conducted an acoustical analysis of pediatric snoring. In the absence of SDB, pediatric patients with snoring alone showed an increased frequency and severity of pulse oxygen desaturations (Brietzke, S., and Mair, E. 2007).

The evaluation of a child’s PSG must be differentiated from the results of a PSG done on an adult, as the normative values are quite different. An Apnea-Hypopnea Index of 5 may well be in the normal range for an adult, but signify significant pathology in a child. Several authors suggest that anything greater than an AHI of 1 is abnormal in a pediatric patient (Sterni, L. and Tunkel, D. 2003). Furthermore, it is important to evaluate and discriminate central sleep apnea in a pediatric polysomnogram, as these events can be the result of serious comorbidities requiring immediate treatment.

**Treatment**

When should a parent or clinician treat pediatric snoring as a clinically significant finding requiring further evaluation, as opposed to a simple nuisance to others? Perhaps the best answer is when the snoring impacts *either* the child’s nocturnal sleep in some observable way, *or* when the snoring is associated with any of the daytime symptoms described above. Even when a child’s nocturnal sleep seems normal, snoring should not be ignored in the presence of significant daytime symptoms. Snoring may impact the quality of sleep in subtle ways that are unnoticeable to the observing parent or co-sleeper, or unable to be ascertained through clinical history. The examination of pediatric snoring is a relatively new endeavor, but the prevailing evidence suggests it may be premature to consider any snoring in a child as “benign.”

Treatment for the snoring child depends on the findings of the objective evaluation. The most common source of snoring in children is obstruction which is most commonly caused by the tonsils and adenoids. Treatment may be surgical, pharmacologic or medical in nature. However the cause of snoring may not be unifocal and therefore treatment may, and often does, require more than one form of therapy for complete resolution.

Initial treatment should be aimed at treating life threatening issues such as apnea. The most frequent cause of apnea in children is adenotonsillar hypertrophy and the most immediate and common form of treatment is tonsil and/or adenoidectomy (Sorensen, P. 2001). Research has suggested that Adenotonsillectomy is associated with increased risk of respiratory compromise in children who snore and in children with sleep apnea, which warrants careful observation following the procedure (Sargi, Z., and Younis, R.T. 2007; Gerber M., O’Conner, D., Adler, E., et al. 1996 and Rosen, C., Andreas, L., Mahowald, M. et al. 1994). Other at risk groups are children less than 3 years of age, those with neuromuscular
Disorders and chromosomal abnormalities, and children with restless sleep and SDB. Removal of tonsils and adenoids may result in resolution of sleep apnea but repeat polysomnography is recommended to assure that sleep disorder breathing has been resolved. Continued snoring must be further evaluated for cause and treatment.

Other causes of snoring that may require surgery include cranial facial abnormalities and neurological compromise. These conditions may require the placement of a tracheostomy until corrective surgery can be performed which will relieve the obstruction but may not solve the problem and medical management of the cause may be needed. Some conditions may require uvulopalatoplasty which removes or shrinks the palate and throat tissue allowing for easier passage of air.

Medical management of snoring can include the use of airway appliances such as nasal airways but these may not be very well tolerated or effective. CPAP (continuous positive airway pressure) may help those who are not surgical candidates or who continue to obstruct post surgery but this does require appropriate equipment, selected specifically for the pediatric patient. Compliance is often an issue for the pediatric patient due to the annoyance of the equipment.

Pharmacological management includes treatment of the underlying causes of inflammation with medications. Nasal decongestants and antihistamines are used to help in controlling allergic conditions. Inflammatory issues may be treated with intranasal steroids and leukotrien modifier agents.

Sleep positioning may be used for the snoring child who does not have OSA to alleviate their symptoms. Sleeping on the side or with the head of the bed elevated have some benefit. Additionally good sleep hygiene with regular bedtimes and wake times contribute to the treatment of the pediatric snorer.

Other considerations include the management of asthma, gastroesophageal reflux and sinusitis as well as dietary management. This would include weight reduction for obesity and avoidance of foods that may increase mucous production associated with a food allergy.

Treatment for the snoring child is best found in a multidisciplinary clinic that specializes in the needs of the pediatric patient and can address the multiple domains of physical, psychosocial and emotional impact that a sleep diagnosis can involve. The pediatric sleep clinic should include pulmonologist, psychologist, nurse, polysomnographer, respiratory therapist; dietician and social worker to ensure comprehensive care that will return the child to an optimum state of health.

**CONCLUSION**

Children represent unique challenges in identifying, evaluating and treating the cause of their snoring. They differ significantly from adults in multiple areas including presentation, pathophysiology, evaluation and treatment and require specialized knowledge to achieve optimal outcomes. Snoring in children should not be taken for granted as a normal occurrence and should be treated as an ongoing pathology until proven to be resolved. It is imperative that practitioners listen to the parent when they complain of a child’s snoring and recognize it as a symptom of pathology and not just the family nuisance.
REFERENCES


Chapter 8

INTRAORAL DEVICES FOR THE MANAGEMENT OF OBSTRUCTIVE SLEEP APNEA-HYPOPNEA

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ABSTRACT

Obstructive sleep apnea-hypopnea (OSAH) is a breathing disorder that is characterized by apneic and hypoapneic episodes occurring during sleep. OSAH is included within the primary sleep disorders and much research has been carried out over the past decades to achieve standardization of diagnostic criteria. The American Academy of Sleep Medicine provides that, along with symptoms such as hypersomnolence, snoring and morning headache, an Apnea Hypoapnea Index (AHI) greater or equal to 5, where AHI is given by the number of episodes/per hour of sleep, is needed to make diagnosis of OSAH.

Apneic events are due to the obstruction of the upper airways during sleep. Such obstruction is caused by the collapse of pharynx and may also be partial, thus causing snoring sounds and hypoapnea.

The treatment of these disorders has not been standardized yet, being mainly based on empirical observations and suggestions, and intraoral devices are gaining attention as potentially useful tools in the management of OSAH symptoms.

This chapter will provide a thorough review of the literature data on the efficacy of the different types of intraoral devices used in OSAH patients.

INTRODUCTION

Obstructive Sleep Apnea-Hypopnea (OSAH) is a breathing disorder that is characterized by apneic and hypoapneic episodes occurring during sleep. The first studies on breathing disorders dated back to the XIX century, with the description of behavioral disturbances, daytime sleepiness and developmental abnormalities in some children who experienced severe breathing dysfunction during sleep.
Over the years, several terms and definitions have been used to indicate this disorder, which is now included within the American Academy of Sleep Medicine (AASM) classification of sleep disorders (AASM, 2001).

OSAH syndrome is considered a primary sleep disorder due to repetitive partial or total upper-airways obstructions which may even lead to oxygen desaturation and arousal, viz. awakening from sleep.

The OSAH severity is rated in accordance to the Apnea-Hypopnea Index (AHI), which is given by the number of obstruction episodes per hour of sleep and which has been also called Respiratory Disturbance Index (RDI). An apneic event is described as a complete cessation in oronasal airflow of at least 10 sec, while a substantial reduction (>50%) or even a moderate reduction (<50%) associated with oxygen desaturation (>3%) or arousals are defined hypopnea (AASM, 1999).

The literature is plenty of proposals for diagnostic approaches to these disorders, and the most widely adopted diagnostic criteria are those of the AASM, which provide that an AHI ≥ 5, along with symptoms such as daytime sleepiness, snoring and morning headache are requested to make diagnosis of OSAH.

Figure 1. Collapse of pharynx and reduction of the upper airways patency.
The pathophysiology of such disorders is not yet fully understood, but it has been proposed that a combination of both neuromuscular and anatomical factors may play some role in the pathogenesis of upper airways obstruction (Gleadhill et al., 1991). Obesity, male sex, menopausal state in women, individual variability in lung volume and ventilatory control have been identified as risk factors for OSAH. In particular, obesity is the most important risk factor, probably due to its influence on breathing characteristics during sleep and on upper airways structure and function (Malhotra and White, 2002).

Apneic-hypopneic events are due to the collapse of pharynx over the upper airways, which may cause their total or partial obstruction (Figure 1). A total obstruction provokes apnea, while a partial one is associated with hypopneic events and snoring.

The consequence of OSAH in terms of physical impairment and psychosocial distress are well described in the literature (He et al., 1988; Bondemark and Lindman, 2000; Walker-Engstrom et al., 2000). For instance, OSAH patients may sometimes manifest medical complications related to the presence of some concurrent cardiological diseases (i.e. arterious hypertension, cardiac insufficiency, angina pectoris). Psychosocial problems are due to the poor sleep quality that characterizes nighttime rest of these patients; indeed, apneic events interrupt sleep, and the higher the frequency of arousal episodes the more severe their consequences in diurnal activities (i.e. excessive daytime sleepiness, irritability, morning headache). Such consequences are important also in terms of their influence on one patient’s social activities, with a decreased energy to carry on habitual daily tasks, a reduced efficiency at work, and even an increased risk to have work or car accidents (Teran-Santos et al., 1999; Lindberg et al., 2001).

In the therapeutic phases, OSAH patients have been historically approached with a number of treatment modalities, ranging from cognitive-behavioral techniques to surgical interventions, all of which based on the attempt to restore a normal patency of the upper airways (Figure 2) (Eveloff, 2002).

Figure 2. Restoration of normal patency of the upper airways is the target of treatment.

In recent years, a growing attention has been put also on the use of intraoral devices in the treatment of OSAH symptoms, and several types of occlusal splints with different designs have been proposed (Hoekema et al., 2004). As a consequence of the introduction of such a therapeutic option, there is a need for a thorough multidisciplinary assessment of OSAH patients which includes also an accurate appraisal by the dental and maxillofacial professionals.
In this chapter, a review of the different intraoral devices will be provided, with focus on their design, proposed mechanism of action and efficacy.

**GENERAL CONSIDERATIONS ON INTRAORAL DEVICES**

The current first choice therapy for OASH is continuous positive airway pressure (CPAP), which keeps the upper airway patent during sleep; alternatively, several surgical procedures have been proposed and described in the literature. (Riley et al., 1997; Engleman et al., 2002). Unfortunately, both approaches may be associated with some undesired side effects, low compliance by some patients and uncertain positive effects; thus, intraoral appliances are becoming a popular alternative option.

On January 6th, 2009, a search in the National Library of Medicine’s PubMed Database was performed to identify all peer-review papers in the English literature dealing with the use of intraoral devices in the management of OSAH over the last 15 years. The search strategy provided the combination of the text terms “obstructive sleep apnea” with the words “intraoral devices”. To extend the search results, the words “intraoral” and “devices” were also changed with the words “occlusal” and “appliances” respectively.

A total of 95 papers, of which 24 were reviews, were identified by the search strategy. Their distribution by year revealed that the strong majority of papers have been published over the last decade (Figure 3).

The use of such devices is based on the assumption that they may produce positive changes in the position and morphology of upper airways, in order to avoid their collapse (Figure 4) (Schmidt-Nowara et al., 1995).

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![Figure 3](image.png)

**Figure 3.** Number of publications on the use of occlusal appliances/intraoral devices in the management of OSAH per year.
Intraoral Devices for the Management of Obstructive Sleep Apnea-Hypopnea

Figure 4. Mandibular advancement achieved by means of a dental appliance allows patency of the upper airways.

Oral appliances have been introduced in the OSAH field in 1980 and, at present, more than fifty types of devices are available on the market (Lowe, 2000).

On the basis of their supposed mechanism of action, intraoral devices for OSAH can be divided into three groups (Box 1).

Tongue Retaining Devices (TRD) and Mandibular Repositioning Appliances (MRA) have emerged as the most effective and widely used types of devices, while serious doubts have been put on the efficacy of the other appliances, viz. palatal lifting devices, labial shields, tongue posture trainers.

Thus, the following sections will provide description and literature data on the first two types of appliances.

**Box 1. Main types of intraoral devices for OSAH treatment**

1. Tongue Retaining Devices (TRD)
2. Mandibular Repositioning Appliances (MRA)
3. Others (Palatal lifting, Labial shields, Tongue posture trainers)
TONGUE RETAINING DEVICES

TRD are one-piece plastic or acrylic appliances that are anchored to the maxillary teeth and aim at repositioning the tongue in a more anterior position thanks to an incorporated cavity into which the patient is forced to keep the tongue.

Several versions of devices acting as tongue retainers or stabilizers have been designed, and even some pre-fabricated off-the-shelf products are currently available.

Unfortunately, data on the efficacy of those devices are scarce, despite an early positive report that demonstrated tongue retaining device to effectively reduce the number of OSAH episodes (Cartwright and Samelson, 1982).

Moreover, these appliances do not allow oral breathing and it has been suggested that patients’ compliance may be low in cases of subjects with imperfect nasal air passage.

Thus, the most consistent amount of literature has been produced on the following group of devices, those providing an advancement of mandibular body, which are the most used among the intraoral devices for the treatment of OSAH.

MANDIBULAR REPOSITIONING APPLIANCES

Mandibular advancement allows forward repositioning of the tongue, thanks to its insertion on the apophysis geni, and of the soft palate, due to the presence of palatoglossal muscle. Such advancements are likely to allow enlarging the upper airways.

Several hypothesis have been suggested to explain the effectiveness of mandibular repositioning appliances. The most widely diffused belief is that such devices simply allow increasing the diameter of the upper airways, thus preventing them from collapsing during the inspiratory phase of the breathing cycle. Nonetheless, it has also been hypothesized a more complex action on the pharynx motor system, which should be activated by an appliance-induced muscle stretching (Clark et al., 2000).

MAD may be manufactured either as a single-block appliance or a two-piece device, and may be custom-made or pre-fabricated (Eckhart, 1998). Mandibular advancement is the result of different action mechanisms: monobloc devices allow it due to the presence of flanges that force the jaw in an anteriorized position, while bibloc ones allow mandibular advancement by the presence of interarch rubber bands, pipes or poles. Pre-fabricated devices are obviously cheaper and easier to apply, while custom-made devices, which are supposedly more effective than the others, require the intervention of a dental professional and a dental laboratory by taking dental impressions, preparing casts, registering occlusal contacts and manufacturing the device (Figures 5-7).

The manufacturing characteristics of the devices, viz. single-piece vs. two-piece, are responsible for giving different freedom of movement to the patient’s mandible, and determine different potential positive effects and side effects.

For instance, monobloc devices force the mandible rigidly in a fixed anterior position, while bibloc ones allows the jaw to maintain its usual degrees of freedom. The long-term use of those devices forcing the mandible in a fixed position may potentially represent a risk factor for the onset of temporomandibular joint degenerative changes due to the static load exerted on the same fixed joint surface during nighttime parafunctions (Peretta and
Manfredini, 2009), even though evidence of this risk is still lacking due to the absence of literature studies assessing this issue. Moreover, it has been suggested that bibloc devices are more comfortable for the patient (Henke et al., 2000).

By contrast, monobloc appliances have been suggested to be more effective to avoid collapse of the upper airways due its prevention of any suppressing action on the tongue muscles (George, 2001).

Figure 5. Dental casts and bite registration to plan the desired mandibular advancement.

Figure 6. Appliance on dental casts.
Besides, taken singularly, the different devices have many minor manufacturing features and biomechanical characteristics that are responsible for the presence of many types of appliances on the market, more than ten of which are widely diffused among practitioners without any apparent evidence of superiority or specificity of indications over the others (Loube and Strauss, 1997).

**LITERATURE REVIEW ON EFFECTIVENESS AND COST-TO-BENEFIT RATIO**

The first review on the efficacy of oral appliances in the management of OSAH dated back to more than a decade ago, and was published on behalf of the American Sleep Disorders Association (Schmidt-Nowara et al., 1995).

The authors examined 21 studies, accounting for a total of 304 patients. About 70% of patients achieved a marked, viz. > 50%, AHI reduction, but only half of the patients reached physiological AHI values while wearing an occlusal appliance. The most frequent side effects were excessive salivation, unpleasant feeling at awakening, temporomandibular joint pain and sensation of occlusal instability, accounting for up 37% of patients needing to interrupt the treatment.

Moreover, as also pointed out by another study trying to differentiate literature findings on the basis of the type of occlusal appliance (Loube and Strauss, 1997), it seems that the methodological quality of the literature on OSAH and intraoral devices is far from reaching excellence.

The totality of literature studies is based on the use of mandibular repositioning appliances, among which, in sparse order, the Snore Guard, the Silent Night, the Mandibular Repositioning Device, the SNOAR Positioner, the Herbst Appliance, the Nocturnal Airway
Intraoral Devices for the Management of Obstructive Sleep Apnea-Hypopnea

Patency Appliance. All of them, like all the other devices on the market, are protected by a trademark and copyright laws.

In general, patients with an improvement in AHI index during a treatment with a MRA device also reported subjective improvement in their OSAH-related impairment, such as a reduced daytime sleepiness, an increased productivity at work and an improved sleep quality (Arai et al., 1998; Gotsopulos et al., 2002). All subjective improvement seem to find their plausible explanation in the related objective changes in sleep quality parameters, as measured by polysomnography (PSG) (Metha et al., 2001; Johnston et al., 2002).

Since the time of the first review, at least three other systematic analysis of the literature on OSAH and intraoral devices have been published (Mohsenin et al., 2003; Hoekema et al., 2004; lim et al., 2008), on which the following suggestions are based.

As above mentioned, the methodological quality of the literature on this issue is not sufficient, since only 13 studies met inclusion criteria for the meta-analytic review by Hoekema et al. to test the efficacy of oral appliances for OSAH and 17 were included in that by Lim et al. for the Cochrane Group. This means that, as unfortunately happens also in other fields of medicine, that the majority of studies provided useless data due to the presence of methodological shortcomings (i.e. unvalidated diagnosis, absence of follow up, unclear outcome parameters, lack of specifications for the drop-outs, and so on) that prevent from a pairwise comparison of results between different studies.

The most interesting findings came from studies comparing the effectiveness of occlusal appliances with that of other treatment approaches.

For example, a study comparing the quality of life of OSAH patients treated with intraoral devices or with uvulopalatopharyngoplasty (UPPP) showed that, even though the latter had a stronger positive impact on the patients’ subjective perception of their quality of life, objective PSG indexes of sleep quality decreased more markedly in patients wearing occlusal appliances. These positive effects were evident at one-year and were decreased at a four-year follow up (Walker-Engstrom et al., 2002).

Another study comparing the effectiveness of occlusal appliances with that of UPPP showed a significantly higher reduction in AHI in patients wearing appliances, but no differences were detected in any other PSG parameter (Wilhelmsson et al., 1999).

As for the comparison with continuous positive airway pressure, which is considered the treatment of choice for OSAH patients who have a good compliance, intraoral devices showed to be less effective to improve AHI, even though improvement in sleep efficiency was similar (Ferguson et al., 1996; Randerath et al., 2002).

In general, few studies are available on the relative effectiveness of different appliances (Hoekema et al., 1994).

Mandibular repositioning appliances seem to be superior to tongue retaining and palatal lifting devices on the basis of a single study on eight patients with severe OSAH (Barthlen et al., 2000).

Among MRA devices, monobloc ones seem to be better tolerated and give a slightly superior improvement in apnea indexes and sleep efficiency parameters with respect to bibloc devices (Rose et al., 2002).

Thus, despite the presence of several enthusiastic reports on the use of different types of intraoral devices for OSAH, it seems that much progress has to be made in terms of defining the indications and predicting the effectiveness of such appliances. Interestingly, it has been suggested that the predictability of a patient’s response to the use of a MRA is not reliable,
and that the study of some cephalometric parameters may be of usefulness to select those patients who may improve with treatment (Eveloff et al., 1994).

Indeed, while contrasting opinions emerged among researchers as for the superiority of one appliance over the others, it seems that consensus might be reached on the fact that patients with certain skeletal features may receive more benefit. In particular, patients with a long anterior cranial basis, a narrow mandibular angle and an increased upper face-to-lower face ratio were more positive responders (Liu et al., 2001). By contrast, patients with an open mandibular angle (>40°) were poorer responders.

From a biomechanical viewpoint, such findings may be due to a clock-wise mandibular rotation related to the use of an anterior repositioning appliance, which in turn provokes a stretching of genioglossal and suprathyroid muscles and a consequent collapse of pharynx.

A thorough list of anatomical feature to achieve a baseline differentiation between poor and good responders to a treatment with occlusal appliance includes the maxillary position, the size of oropharynx, the status of maxillary molars, the incisor overjet, the size of pharynx and soft palate, the body mass index and the patient’s age (Mohsenin et al., 2003).

Moreover, diagnostic deepening by means of sleep endoscopy, viz., exploration of the upper airways under induced physiological sleep, or cone beam computerized tomography may be useful to identify the collapsing tract of pharynx, which is another predictor for treatment efficacy.

In general, side-effects, and complications related with the use of oral appliances for OSAH are frequent, but in the majority of cases they are mild and well tolerated by the patient, and tend to cease with treatment (Fritsch et al., 2001). Compliance is usually good, and interruption of treatment is mainly related with the occurrence of pain within the temporomandibular joint are and/or the jaw muscles due to the forcedly anteriorized position. Nonetheless, studies with longer follow up periods are strongly needed to assess the frequency of late-onset TMJ disorders, the presence of which is worthy to be investigated even years after treatment.

Moreover, at present, little or no information is available on which treatment protocol is the most recommendable in terms of cost-to-benefit ratio.

**CONCLUSIONS**

Obstructive sleep apnea-hypopnea is a complex disease that has important implications for the patient’s general health. The pathophysiology of OSAH is yet to be fully understood, and a number of risk factors have been described so far, to the point that a multidisciplinary approach to the disease is strongly needed.

Many therapeutic approaches have been proposed over the years, and continuous positive airway pressure is the treatment of choice for severe OSAH. The low compliance associated with such treatment has led to search for alternative options, and patients with mild to moderate symptoms have been showed to benefit from the use of intraoral appliances that provide an advancement of the mandibular body.

Such appliances vary in their design in dependance of the underlying idea at the basis of their action, and share a common feature, which is to provoke a mandibular advancement and a consequent teeth disclusion.
Despite the promising data on their usefulness and their good compliance, the cost effectiveness of oral appliances has to be further investigated by means of longitudinal studies with long follow up periods to assess the late onset of temporomandibular joint disorders related to the use of such devices.

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Daniele Manfredini and Luca Guarda-Nardini


SNORING AS A SYMPTOM OF NARROWING THE POSTERIOR AIRWAY SPACE IN CLEFT LIP AND PALATE PATIENTS WITH VELOPHARYNGOPLASTY

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ABSTRACT

Some patients with cleft lip/palate or isolated cleft palate seem to develop snoring as one possible symptom of an obstructive sleep apnoea syndrome (OSAS) after velopharyngoplasty (VPP).

The aim of this paper was to determine whether there was a difference in the posterior airway space (PAS) between patients with a VPP who snored and those who did not. Four standard parameters were measured in lateral cephalograms of 20 patients with cleft lip/palate and isolated cleft palate without diagnosis of further syndromes, e.g. Robin- sequence, having had VPP, in order to look for the dimension of PAS. Data were set in correlation to the symptom of snoring, and compared with those of 40 patients undergoing orthodontic treatment without clefting and with 20 patients with cleft lip/palate or isolated cleft palate but without VPP.

Metric parameters were significantly (p < 0.05) different in patients with clefting and snoring after VPP when compared with the group of cleft patients without snoring following VPP.

All patients with clefts exhibited at least in one dimension a constriction when compared with patients without clefting. In conclusion, cleft lip/palate and isolated cleft palate patients tend to have constrictions of the PAS. VPP may induce snoring and further narrowing. This makes a recall and analysis for OSAS mandatory.

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INTRODUCTION

Snoring and sleep apnea are different sleep related breathing disorders. Nevertheless, there is only a quantitative difference between snoring and the obstructive form of sleep apnea. Snoring occurs in at least 20% of the population; 50% of the 50 years old male snore. Although in most of the cases only harmless snoring is assessed, it becomes serious if it leads to a continuous oxygen desaturation and a sleep disturbance or, if in cases of sleep apnea a postapnoic snoring is concerned [18]. Accordingly, the clinical symptom of “snoring” may lead to the diagnosis of an obstructive sleep apnoea syndrome (OSAS). Tiredness, depression, exhaustion, lack of concentration and impaired vigilance during daily activity are subjective symptoms felt by these patients [1]. Especially in children, this leads to deficits in executive functions and motor skills [17, 22]. It may even lead to the sudden infant death syndrome [5]. In large scaled polysomnographic examinations the number of minutes of apnoea and the drop of blood oxygenation can be determined and may confirm the diagnosis [4].

One reason for snoring with or without confirmation of OSAS could be a restriction of the posterior airway space (PAS), that can be measured by lateral cephalography [8]. Common factors for restriction are extreme skeletal dysgnathia, enlarged adenoids and/or tonsils and chronic infections of the upper airways and in some patients with clefts lip/palate or cleft palate, it develops following velopharyngoplasty (VPP) for speech improvement. It was the aim of this paper to find out whether snoring after VPP indicates a further narrowing of the PAS compared to patients without VPP.

METHODS

80 patients were studied (age: 11.8 ± 2.7 y, female / male : 35 / 45). No overweight (body mass index < 75 percentile), no persisting infections of the upper airways (naso-, oro- and hypopharynx), no enlarged tonsils, adenoids or other recognizable obstructions of the PAS were seen. Standardized lateral cephalograms of 20 patients after VPP according to Sanvenero-Rosselli’s method [21], embedding a superiorly based pharyngeal flap in the soft palate, were analysed postoperatively (6.1 y ± 1.9 y). In 11 subjects with cleft lip/palate and in 9 subjects with isolated cleft palate but without further syndromes, e.g. Robin- sequence, four standard linear measures were used calibered by Hochban and Brandenburg [8]: The posterior pharyngeal wall to the spina nasalis posterior along the maxillary plane (PAS – NL, a), to the soft palate along the occlusion plane (PAS – Occl, b), of the oropharynx up to the uvula point or the soft palate margin (shortest distance; PAS – UT, c) and of the hypopharynx along to the mandibular plane up to the dorsum of the tongue (PAS – ML, d) (Figure 1). The measurements were performed by two investigators in a double-blind arrangement. Mean data were correlated with the existence (+S) or the absence (-S) of snoring for more than one month reported by patients or parents (CLP + VPP + S, n = 11; CLP + VPP - S, n = 9), and compared with data from 40 patients of the same age without a cleft receiving orthodontic treatment (control group) and with 20 patients of the same age with clefting but without VPP and without snoring (CLP). The average dimensions of the planes measured in the control group were regarded as physiological, significant differences to these dimensions as pathological.
Figure 1. Lateral cephalogram of a twelve years old child with cleft lip and palate. Black lines: landmarks and planes for cephalometric analysis of craniofacial skeleton; blue contour: posterior airway space; red lines: four standard planes for measurement: a - posterior airway space – spina nasalis posterior (PAS – NL), b - posterior airway space – occlusion plane (PAS – Occl), c - posterior airway space – uvula point / soft palate margin (PAS – UT), d - posterior airway space – mandibular plane (PAS – ML).

Statistical significance between parameters of each group was checked by using Students’ t-test. Differences above the 95 % - confidence interval were regarded as statistically significant.

RESULTS

In all study groups, there was no correlation between restriction of PAS and age, sex or the type of clefting. The average dimension of PAS were not significantly different (p>0.05) among the groups regarding measure a. The measures b and d did also not differ among groups There was only a minor tendency for restriction in measure d found in patients with clefting and following VPP when compared with patients without clefting undergoing orthodontic treatment (control group). But there was a significant difference regarding measurement c (p<0.05) between patients after VPP without or with snoring when compared with the other two groups.

When summing up all significant pathological data per group, 60 % of all patients with clefts and 40 % of the patients with clefting plus VPP were found to have a narrow in at least one dimension. However, this holds true for only 6.7 % of the control group. In children with
clefts, VPP and with snoring, there were 35% with pathological data, this being significantly more than in all the other groups (p < 0.05).

**DISCUSSION**

Many patients with pharyngeal obstruction showed cephalometrically certain craniofacial characteristics, in particular maxillary and mandibular deficiencies, nasal obstruction [16], Pierre-Robin sequence and Goldenhar’s syndrome [2, 7, 9, 10]. Patients with cleft lip and palate but without consisting syndromes, sequences or associated anomalies are also known to suffer of dysgnathia and nasal obstructions caused by disturbed growth of the maxilla, partly due to operative procedures. When closing a cleft palate and when performing VPP, lengthening of the soft palate is aimed at and this may cause a narrowing of PAS - UT. A short PAS - UT dimension due to a longer soft palate was also described in OSAS patients [13].

It was realized that this is a typical abnormality in OSAS. Due to these results, scars, leading to a decrease of the pharyngeal wall resilience in the uvula region, could be a major aetiological factor for snoring with or without pharyngeal obstruction, too [14]. So Liao et al. [15] actually found a high incidence of snoring and polysomnographically diagnosed OSAS of 90% in children 6 months after VPP. Hochban et al. [11] did not find lasting sleep related breathing disturbances as a result of VPP in 25 cleft patients. However, according to the findings in our study reinforcement of PAS restriction by VPP was noted in a significant narrowing in the PAS – UT dimension. This in turn could lead to snoring in patients with cleft lip/palate or isolated cleft palate who underwent VPP, since it is well known that “snoring” indicates a restriction of the cranial PAS [18]. Accordingly, there were no significant differences in the frequency of pathologic data between the control group and patients with clefts and VPP who did not snore.

Resta et al. [19] reported that more than 46% of non-apneic obese patients had loud snoring, the percentage of this alteration was progressively higher with the increase of the Respiratory Distress Index (RDI), with almost 100% of the patients affected by severe sleep apnea having the symptom of snoring. Reports of the prevalence of habitual snoring in children ranged from 3.2% to 12.1%, and estimates of OSAS ranged from 0.7% to 10.3% [3, 22].

So especially in patients with clefts who have had VPP and who have a history of snoring for more than one month, polysomnographic investigations should be considered to rule out or to confirm OSAS. Hence, the decision for or against VPP must carefully consider both insufficient speech and the danger for obstructive snoring by further narrowing the PAS.

It is still not known whether operative procedures, such as maxillary advancement [2] with or without distraction osteogenesis [9], uvulopalatopharyngoplasty with CO₂ laser [6, 23] or simple severing of the pharyngeal flap, have a positive effect in patients with pharyngeal obstructions following VPP. Further clinical studies have to follow answering these questions. A new method for imaging velopharyngeal movement and function using gated magnetic resonance imaging [12] might be helpful by making a decision for therapy in future.
In conclusion, clefts of lip/palate or isolated cleft palate may lead to constriction of the PAS. VPP could induce permanent snoring and further narrowing of the PAS in patients with clefting. Polysomnographic analysis is recommended in this group of patients to diagnose OSAS.

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Chapter 10

PREVALENCE OF OBESITY IN A CLINIC POPULATION WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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ABSTRACT

Study Objectives: To identify the prevalence of obesity in a group of untreated obstructive sleep apnea syndrome (OSAS) patients.

Methods: Retrospective chart review of 398 adults with OSAS at Vermont Regional Sleep Center at Fletcher Allen Health Care and the University of Vermont College of Medicine; apnea hypopnea index (AHI), body mass index (BMI), Epworth sleepiness scale (ESS), age, and gender recorded.

Results: Participants were divided into 3 groups based on BMI, a group of 56 lean subjects with a BMI of<27 (14.1%), a group of 72 overweight, but not obese subjects with a 27 \textless BMI \textless 30 (18.1%) and a group of 270 obese subjects with a BMI of >30 (67.8%)

Conclusions: 32.2% of subjects with OSAS in our practice were not obese.

Keywords: Obstructive Sleep Apnea Syndrome, Body Mass Index, Gender, Age, Apnea Hypopnea Index, Epworth Sleepiness Scale.

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INTRODUCTION

Obesity is a well-known risk factor for obstructive sleep apnea syndrome (OSAS) especially in men and postmenopausal women. The relationship between OSAS and obesity and the different physical features associated with OSAS has been well documented, however, the prevalence of obesity in OSAS patients is not. OSAS occurs in non-obese individuals and looking for it exclusively among obese individuals may lead to missing this serious syndrome in a large number of subjects. The prevailing belief among sleep clinicians is that about 30% of patients with OSAS are not obese. A Medline search revealed only one study that addressed the prevalence of obesity in OSA that was conducted in France. They divided 140 OSA patients into lean body mass index (BMI) of <27 kg/m², overweight BMI 27-30 kg/m² and obese >30 kg/m² [1]. The French study found that their participants were comprised of 25.5% lean, 22.8% overweight and 51.4% obese individuals [2]. No such data is available using a US population. This research will evaluate the distribution of normal, overweight and obese individuals with OSA.

METHODS

Data was collected from charts during a retrospective review of 398 consecutive patients who had been diagnosed with OSAS at the Vermont Regional Sleep Center between January 2005 and August 2006. All subjects were 18 years or older and had an Apnea Hypopnea Index (AHI) of 5/hour or more and had either complaints of disturbed sleep or excessive daytime sleepiness or both. All demographic and medical data including age, gender, AHI, BMI, and Epworth Sleepiness Score (ESS) were coded and entered into the Statistical Package for the Social Sciences version 13.0 for analysis. All BMI and ESS recorded were the pretreatment values.

Obesity was defined as a body mass index (BMI) of >30 kg/m². Subjects with a BMI of <27 kg/m² were considered of normal weight and subjects with a BMI of 27-30 kg/m² and >30 kg/m² were considered overweight but not obese.

RESULTS

The sample consisted of 127 women and 271 men with a mean age of 49.39 years and a standard deviation of 12.57 years. The average BMI was 34.98 kg/m² with a range from 20.12 to 67.24 kg/m². The sample consisted of 14.1% normal weight, 18.1% overweight and 67.8% obese participants diagnosed with OSA. Of note, is that 32.2% of subjects were not obese. Women in our cohort had an average BMI of 37.15 kg/m² (range = 20.12-59.34) and 74.4% had a BMI of 30 or more so therefore were obese. Men in our cohort had an average BMI of 33.96 kg/m² (range = 20.12-67.24) and 64.9% had a BMI of 30 or more so therefore were obese.

Using the Pearson Correlation there was a significant correlation (p=0.292) found between increasing BMI and increasing AHI indicating worsening OSAS with increasing weight. The correlation was stronger in men than women (p=0.413 vs 0.243). There was no
correlation between degree of sleepiness (ESS values) and severity of OSA (AHI) but there was a weak correlation between ESS and BMI with a p value of 0.207 (p value in women was 0.281 and 0.185 in men).

**DISCUSSION**

It is widely accepted that non-obese individuals can also develop OSAS. An increase in BMI is more of a risk factor than a stable but high one. Previous studies have reported the importance of other physical features in developing OSAS such as upper airway soft tissue enlargement, including enlargement of the tongue, soft palate and soft tissues surrounding the upper airway. In non-obese OSA patients several cephalometric defects and soft tissue abnormalities have been described compared to their BMI-matched healthy controls [3]. Alcohol intake, age and waist circumference have been shown to be also independent risk factors for OSAS [4]. There is also a complex hormonal relationship between OSAS and obesity as demonstrated in changes in leptin levels and degree of improvement in nocturnal respiration [5].

In our population the percentage of lean OSAS sufferers was 14.1% vs 25.7% in the European study and the proportion of non-obese OSAS sufferers was 32.2% vs 48.6% in the European study. This discrepancy is most likely due to the overall higher prevalence of obesity in the USA vs. Western Europe (27.9% vs 17.2%) [6]. We did not find any correlation between the ESS scores and severity of OSAS as measured by the AHI. This was not a new finding as has been shown before by other researchers [7,8,9], even when bed partners filled out the ESS [9]. There were however a few papers reporting a correlation between ESS scores and severity of OSAS but for the most part those were smaller studies [10, 11, 12]. We also found a weak correlation between obesity and ESS despite the absence of one between the severity of OSAS and ESS. This was also a finding previously reported in the medical literature [13].

Our study has several limitations in addition to the small size of our group. We used BMI of 27kg/m² rather than the traditionally used 25kg/m² because we wanted to facilitate comparison with the European study cited above. Finally this was a retrospective chart review so the results may be skewed in addition all of our subjects had OSAS therefore we cannot assign odds ratios to any of the variables since we did not have a healthy control group. We will use this data as a launching pad and do a larger, controlled, prospective study to look at OSAS in the non-obese population.

**CONCLUSION**

This study establishes a prevalence of obesity in a US OSAS population. We hope our study further increases awareness to the presence of OSAS in lean individuals regardless of gender and age.
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Chapter 11

CORRELATION OF NECK CIRCUMFERENCE WITH SEVERITY OF OBSTRUCTIVE SLEEP APNEA IN WOMEN

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ABSTRACT

Objective: Correlate increasing NC with severity of OSA in women as compared to men.
Methods: We retrospectively reviewed the charts of 287 consecutive OSAS patients who were diagnosed at our center over a period of 1 year.
Results: High correlation NC and AHI in both genders, r=0.383, p <0.01 in males, r=0.256 p<0.05 in females
Conclusion: Individuals with greater NC have more severe OSAS.

Keywords: OSAS, Neck Circumference, Body Mass Index, Respiratory Disturbance Index, Female.

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INTRODUCTION

It is well established that having a neck circumference (NC) of 40 cm or more is one of the most significant risk factors for the development of Obstructive Sleep Apnea Syndrome (OSAS)[1-3], especially in adult males. The initial study that established the 40 cm neck circumference cutoff point as a risk factor for OSAS included only nine women [4]. Further studies involving a greater or equal number of women have produced data that is not as clear. In the landmark study, Guilleminault et al., demonstrated that the relationship of neck circumference to presence or absence of OSAS was less clear in women although still present men [5]. A subsequent study by Erdamar et al., did not show any correlation between the two measures regardless of gender [6].

Ferini-Strambi et al reported in 1999 that BMI and neck diameter significantly related to OSAS and snoring in middle aged Italian women but no correlation between severity of OSAS and size of the NC was made [7].

The goal of this study is to determine if there is a correlation between increasing neck circumference and severity of OSAS in women.

METHOD

We retrospectively reviewed the charts of 287 consecutive OSAS patients who were diagnosed at our center over a period of 1 year. All subjects were eighteen years or older and had an Apnea Hypopnea Index (AHI) of 5/hour or more. AHI, Body Mass Index (BMI), age, gender, NC, and Epworth Sleepiness Score (ESS) information was extracted from charts, and analyzed using the Statistical Package for the Social Sciences 13.0 for Windows (SPSS).

In our laboratory we consider a hypopnea a 30% or more reduction in airflow of 10 seconds duration or more with 4% oxyhemoglobin desaturation and or an arousal. Neck circumferences in our clinic are measured over the laryngeal prominence with the patient sitting upright.

RESULTS

The sample consisted of 286 subjects included eighty-one female subjects and two hundred and six male subjects. The samples mean age was 48.9 years with a range of 18 to 87. In the female group the mean NC was 38.9cm with a ranged of 30.5-53.3cm. In the male group the mean NC was 44.2 cm with a ranged of 35.6-58.4 cm. Using Pearson Correlations we found significant relationship between NC and AHI in both genders, r=0.383, p <0.01 in males, r=0.256 p<0.05 in females, indicating that individuals with greater NC had more severe OSAS. This correlation was stronger in men than women.
DISCUSSION

We expected to find a correlation between mean external neck circumference in female OSAS patients and the severity of OSAS. Although we did find a correlation this was not as strong as we had suspected. Comparing our results with previously published data revealed some interesting differences. The mean neck circumference in our female subjects, their mean BMI and their mean RDI were different than those reported in past studies.

The mean external neck circumference in female subjects with OSAS was reported as 35.1±3.8 cm by Guilleminault et al (5), 42.4 ± 4.3 cm by Resta et al (8), and 36.5 ± 4.2 cm by Dancey et al (9). Among our subjects the mean was 38.7 ± 4.6 cm.

Our subjects were overall heavier but had similar disease severity.

Guilleminault reported the mean RDI among the female subjects with OSAS as 26 event/hour and BMI in the same group as 26.2 kg/m² (5), Dancey as 12.4/hour (9) (AHI) and 31 kg/m² (BMI) and Resta 44·9 kg/m² (8)(BMI) and 33·8/hour (RDI). Our data showed a mean BMI of 36.9 kg/m² and a mean RDI of 27.5/hour.

This study is one of the first to look at the correlation between NC and RDI in both men and women. Two of the studies, Resta et al (8) and Dancey et al (9), discuss the association of NC and severity of OSA but did not look at the statistical analysis.

Guilleminault looked at predictive value and not at correlation of severity of OSAS with increasing neck size [5].

Erdamar’s study did not find any correlation between NC and RDI but they did not look at women vs. men and looked at the population as whole. Also their subjects were less overweight (mean BMI 28 kg/m² vs. 36.9 kg/m²) than ours and overall had smaller necks (mean NC 28 cm vs. 38.7 cm) but OSAS of similar severity (32 events/hr vs. 27.5 events/hr)(6). In that group female subjects had moderate OSAS without being on average as overweight as our subjects or having as large a neck as ours.

Based on our data and the comparison with previously published literature on the subject we conclude that for women with higher BMI and larger neck circumferences the relationship between NC and RDI (severity of OSAS) is more significant.

The mean NC in our group was 38.7 cm which is consistent with previous reports of NC > 38 cm being a risk factor for OSAS in women.

Our study suggests a weaker relationship between severity of OSAS in female subjects and NC, than the one in men. We recommend larger prospective controlled study looking at these relationships because our study was limited due to the nature of a retrospective study using information obtained during chart review, small number of subjects and the absence of a control group.

In conclusion: larger neck circumference is associated with more severe OSAS in women. This correlation is stronger for more overweight subjects and in men. Further studies are needed to elucidate the relationship between pharyngeal tissue anatomy and NC and its impact on the severity of OSAS and to establish a clear NC size above which women are at higher risk of developing OSAS. If we continue to apply male characteristics to women when trying to identify high risk groups we may be missing a significant number of people who may have a potentially fatal illness.
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UROLOGICAL ASPECTS OF OBSTRUCTIVE SLEEP APNEA SYNDROME

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ABSTRACT

Obstructive sleep apnea (OSA) is a common disorder, affecting about 5% of the adult population over the age of 40. Little attention has been spent on the Urological aspects of OSA. This chapter focuses on two common Urological consequences in OSA patients, namely Erectile Dysfunction (ED) and nocturia. This chapter describes the incidence, the pathophysiological mechanism and possible treatment of ED and nocturia in OSA patients.

Erectile dysfunction is strongly correlated to severe OSA, however conflicting results exist associating mild or moderate OSA to ED. There are several theories regarding the mechanism of ED in OSAS patients. Organic causes may result from nerve involvement caused by hypoxia, blood vessels abnormalities caused by the increased nocturnal blood pressure and sympathetic activation in OSAS, and potentially hormonal causes like the low level of androgens in OSAS. Psychological causes on the other hand may result from apnea-induced daytime somnolence or depressed mood commonly seen in apnea patients. Both short and long-term treatment with continuous positive airway pressure (CPAP) has been shown to improve erectile function in OSA patients.

Nocturia has been defined by the International Continence Society as “the complaint that the individual has to wake up at night one or more times to void”. In the past, older men with nocturia were often assumed to have benign prostatic hypertrophy and women were thought to have an unstable bladder or reduced bladder capacity. However, it is now recognized that nocturia can also be caused by nocturnal overproduction of urine (nocturnal polyuria). Data has been accumulating that nocturia may be induced by OSA. Recent studies have shown that nighttime urine production and atrial natriuretic peptide (ANP) excretion are elevated in patients with OSA, thereby. Thus, establishing the
Both nocturia and erectile function considerably affect patients’ quality of life. The linkage between these disorders and OSA is therefore essential to all physicians treating OSA patients. Furthermore, non-compliance with CPAP is a major obstacle in treating OSAS and a possible benefit of CPAP on ED or nocturia may aid CPAP acceptance by the patients.

1. **ERECTILE DYSFUNCTION (ED) AND OBSTRUCTIVE SLEEP APNEA (OSA)**

1.1. **Definition and Incidence**

1.1.1. **ED**

The NIH characterizes erectile dysfunction (ED) as the constant inability to attain or maintain a penile erection sufficient for satisfactory sexual intercourse [1]. According to the 1995 estimates, over 152 million men worldwide had ED. The projected prevalence for 2025 is 322 million men with the largest increase expected in developing countries [2]. It has been demonstrated that ED has a negative impact on patients' self-esteem, quality of life, and interpersonal relationship [3].

1.1.2. **OSA**

Obstructive sleep apnea (OSA) is defined by repetitive upper-airway occlusion (complete or partial), leading to a reduction in tidal breathing or cessation of breathing during sleep. It is a common medical problem. While early studies estimated that the prevalence is about 1% [4], more recent studies showed it is much more common. Severity is assessed by two parameters: the respiratory disturbance index (RDI), i.e. the number of sleep apnea episodes during an hour; and the minimal oxygen saturation (OxiMin), measured by pulse oximetry, during the apnea episodes. OSAS is associated with clinical complications such as: daytime somnolence, hypertension, ischemic heart disease, and increased risk of stroke [5-8]. Their underlying pathological mechanisms include recurrent intermittent hypoxemia and increased sympathetic activity, primarily at the termination of the apneic events [9,10].

1.2. **Association between OSA and ED**

Conflicting data exists regarding the relationship between OSAS and ED. Several studies have found a high prevalence of ED in patients with OSAS [11,12]. Fanfulla et al suggested that the mechanism for this association may be mediated by hypoxia induced occult nerve dysfunction [13]. Furthermore, a 40% improvement in ED after treating OSAS patients with CPAP (continuous positive airway pressure) has been reported [14]. A recent study [15] led by Mulhall from Cornel university has demonstrated a good correlation between the severity of sleepiness, as measured with the Epworth Sleepiness Score, and the severity of ED.

However, there are a few studies contesting this association. Schiavi et al tested 70 men [16], all of whom underwent four full night polysomnographic (PSG) studies with assessment
of nocturnal penile tumescence (NPT). They reported no correlation between sleep apnea and ED. In addition, Seftal and colleagues have recently studied 285 men suffering from ED. Subjects were given a short self-report questionnaire assessing risk factors for OSAS [17]. They concluded that although patients with ED report a variety of sleep problems, neither snoring nor suspected OSAS is related to ED.

Our group [18] evaluated 209 patients referred to a sleep clinic because of suspected OSA. All patients were given a sleep questionnaire, a revised IIEF questionnaire (comprised of three main questions: Sexual satisfaction, Erection during intercourse and Morning erection), and then underwent a full night in-lab polysomnography (PSG). There was a decrease in erectile function among all OSAS groups as compared to those without OSAS. However the only group that this reduction was statistically significant (p<0.05) in all ED dimensions was the severe OSAS (Respiratory Disturbance Index, RDI>40). Furthermore, the patients complaining of severe ED had the highest RDI. Stepwise multiple logistic regression analyses revealed that the predicting factors for ED in OSAS patients were age, morning tiredness and RDI.

The most important finding of this study is that severe OSAS is strongly related to ED. Mild or moderate OSAS, on the other hand, are only partially associated with ED. This fact might explain the contradicting data in previous studies.

Another substantial finding we reported, is the predictive value of various risk factors for ED in OSAS. We found that morning tiredness, age and RDI are the most important factors predicting ED in OSAS.

1.3. Pathophysiology

Penile erection is a neurovascular event modulated by psychological and hormonal factors [19]. On sexual stimulation, an increase in parasympathetic activity leads to a release of neurotransmitters from the cavernous nerve terminals and of relaxing factors from the endothelial cells of the penile vasculature. This results in smooth muscle relaxation in the arteries and arterioles supplying the erectile tissue and a several-fold increase in blood flow to the penis. Penile venous outflow is simultaneously occluded by a venous compression mechanism, maintained by the penile tunica albuginea. Smooth muscle relaxation is brought about by the release of nitric oxide (NO) from both the endothelial cells and neural tissue supplying the corpora cavernosa. Thus, disturbances in the basic neurovascular event or the modulating factors that control this event (psychological or hormonal) may be responsible for ED.

There are several theories regarding the mechanism of ED in OSAS. The causes may be organic such as: hypoxia induced neural dysfunction [13], blood vessel abnormalities caused by an increase in nocturnal blood pressure and sympathetic activation [20], or hormonal, such as low level of androgens [21]. Hypoxia is probably the most important factor causing ED in OSA. It has been shown to have a substantial effect on the endothelium, inducing production of various factors such as: platelet derived growth factor β, endothelin 1, and vascular endothelial growth factor [22]. It may also cause cavernosal fibrosis via transforming growth factor β (TGF-β) [23]. Studies in rabbit and human cavernosal tissue found that hypoxia inhibited endothelial-mediated relaxation [24]. Therefore, the number of apneic spells may be less important than the degree of hypoxia during these spells.
Psychological causes, on the other hand, may result from apnea-induced daytime somnolence [25] or depressed mood commonly seen in patients with apnea episodes [26].

1.4. Treatment of ED Associated with OSA

The treatment of OSAS by continuous positive airway pressure (CPAP) is well established. To the best of our knowledge, there are only three studies addressing the effect of CPAP on ED in patients with OSAS [27-29]. Karacan’s [27], who reported an improvement in a third of his patients with impaired NPT after a single night of CPAP treatment. Another study was recently published by Perimenis et al [28]. The primary outcome in their study was successful for intercourse attempts. The authors reported a 25% success rate in sexual attempts of men with OSAS under CPAP therapy for 12 weeks. While both studies measured the effect of short-term CPAP treatment, our group [29] has extended their findings to long-term treatment.

The most important finding of our study is that in 20% of patient’s long-term CPAP treatment alone helped to alleviate ED. Interestingly, the same efficacy rates reported by Perimenis et al [28]. When considering these results clinically, it becomes apparent that one of every five patients with OSAS and ED will respond to CPAP therapy. Because of the apparently low response rate the identification of clinically useful predictors of improvement is essential. In our study [29], the most significant predictors of improved erectile function under CPAP treatment were severe pretreatment OSAS, higher RDI value and low oxygenation levels during apneic spells. The patients who benefited most were the ones who were most compliant and satisfied with CPAP therapy. The change in IIEF-5 score was negatively correlated with OxiMin values.

2. NOCTURIA AND OSA

2.1. Definition, Incidence and Impact on Quality of Life

Nocturia is a common, troublesome, and frustrating symptom for patients. It has been defined by the International Continence Society as “the complaint that the individual has to wake up at night one or more times to void” [30]. Schatzl et al. [31] reported that 10% of the general population over the age of 20 years awakens two or more times per night to void. They found that the prevalence of nocturia increases with age, from 3.4% in men under 30 to 32.4% in those aged 60 years or more [31]. Nocturia has been reported to be the most bothersome of all urinary complaints and the most frequently reported cause of sleep disturbance [32]. The presence of nocturia has been associated with a decrease in general state of health [33], a greater risk of falls in the elderly [34], and in those who void 3 or more times nightly, a greater mortality rate from all causes [35].
2.2. Nocturia and OSA- Association and Pathophysiology

Generally, nocturia occurs when there is a mismatch between nocturnal urine production and functional bladder capacity [36]. Nocturia can be a normal response to fluid intake, or a result of disordered fluid regulation (i.e. low levels of argentine vasopressin (AVP) production), bladder dysfunction (overactivity, benign prostatic hypertrophy or malignant disease), diuretic intake, or a general medical problem which leads to increased nocturnal urine production. Such medical conditions include diabetes mellitus, other hyperosmolar states, and congestive heart failure.

Recently, evidence has been assembled suggesting OSA may cause nocturia. Pressman et al. [37] in a sleep study, found that 79.4% of the awakenings that patients attributed to the need to urinate during a sleep study were in fact due to apnea, hypopnea, or other sleep disturbances. The authors suggested that patients with OSA were awakened by the primary sleep disorder and then felt an urge to void because of an abnormal pattern of urinary output. This assumption was in line with an earlier study showing that OSA was associated with higher fractional urinary flows and a lower percentage of filtered sodium reabsorption [38].

More recently Umlauf et al. [39] found both nighttime urine production and ANP excretion are elevated in subjects with a high RDI (>15). They proposed that the obstructive respiratory events combined with sustained ventilatory effort in OSA generate a negative intrathoracic pressure, causing the heart to receive a false signal of volume overload. The hormonal response to this signal is increased ANP secretion and, hence, increased urinary production. Thus, establishing the pathophysiologic mechanism of nocturnal polyuria associated with OSA.

Our group demonstrated [40] that the two main indicators of OSA severity, RDI and OxiMin were correlated with the number of nocturia events. In our study the number of nocturic events positively correlated with the RDI and negatively correlated with OxiMin. Adding further proof to the causal relationship between OSA and nocturia.

2.3. Treatment of Nocturia Associated with OSA

2.3.1. Desmopressin

Desmopressin, a structural analogue of vasopressin (an antidiuretic hormone), is well established as a treatment for children and adults with primary nocturnal enuresis. The role of desmopressin in the management of nocturia has been investigated in several studies [41-43]. A double blind, placebo controlled study of the elderly with nocturia (≥2 voids/night) and a urinary output of ≥0.9 ml/min showed that the treatment with oral desmopressin reduced nocturnal urine production, reduced nocturnal micturation and increased time to first awakening by 1.4h [43].

Whether desmopressin could change the sleep pattern of adults with nocturia was investigated in phase III studies [44]. Awakening to void occurred within 3h for 60% of placebo-treated patients, compared with 14% of desmopressin related patients. Importantly, 34% of patients receiving desmopressin achieved an undisturbed sleep lasting at least 5h, compared with just 4% of patients receiving placebo. However, desmopressin was not yet
studied specifically in patients suffering from nocturia related to OSA. We all await the results of such a trial.

2.3.2. CPAP

The treatment of OSAS by continuous positive airway pressure (CPAP) is well established. However only a few studies addressed the impact of CPAP treatment on OSA related nocturia. Since we consider the pathophysiology leading to nocturia in OSA are the negative intra-thoracic pressures during apnea spells. CPAP treatment eliminates the negative intrathoracic pressure and therefore should reduce secretion of ANP and consequently resolve the nocturia.

Krieger et al [45] were the first to demonstrate that nocturia decreased significantly in 25 patients with OSA treated with CPAP for at least one year. Our Group [40] recruited patients referred to a sleep laboratory with suspected OSA. After polysomnography, those found to have no OSA were excluded from the study, and the remainders were treated with CPAP. Nocturia was assessed at 4 time points: baseline (average number of awakenings to urinate per night over one week at home prior to polysomnography); diagnostic night in the laboratory; CPAP titration in the laboratory; and after 1 - 3 months of stable CPAP treatment at home (average number of awakenings to urinate per night for one week).

Ninety-seven patients (75 male, 22 female) completed the study. Mean (±SD) age was 55 ± 12 years; body mass index 33 ± 7 kg/m²; and respiratory disturbance index, 34±24/h. Mean number of awakenings to void at home prior to CPAP measured 2.5±2.4/night and during CPAP, 0.7±0.6/night (p<0.001); 73 patients reported improvement in nocturia. Mean number of awakenings to void in the laboratory measured 1.1 ± 0.9 prior to CPAP, with a decrease to 0.5 ± 0.6 during CPAP (p <0.001). Additionally, we found that CPAP is more effective in patients with severe than with moderate OSA. Interestingly, the reduction in nocturia was noted even after one night on CPAP treatment (in the laboratory), suggesting that this may be an acute effect rather than a chronic consequence.

These findings are further supported by FitzGerald et al [46], who in a retrospective analysis demonstrated that CPAP treatment significantly decreased the number of nocturic events in patients with OSA and nocturia. In addition they demonstrated that nocturia frequency in OSA patients is related to age, diabetes and severity of OSA.

CONCLUSION

Both nocturia and erectile function considerably affect patients’ quality of life. The linkage between these disorders and OSA is therefore essential to all physicians treating patients with nocturia, erectile dysfunction and/or OSA. It appears that both nocturia and erectile dysfunction may result from OSA, via several mechanisms. In many cases treatment of OSA alleviates or even cures the urological complaints. While non-compliance with CPAP is a major obstacle in treating OSAS, if patients realize it may improve their urological complications they may more easily accept and comply with the CPAP treatment.
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CHAPTER SOURCES

The following chapter has been previously published:

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INDEX

absorption, 134
academic performance, 72, 80, 145, 149
academic problems, 145
acceleration, 65, 111
acceptance, xii, 180
accidents, 118, 162, 163
accommodation, 55
accounting, 158
accuracy, 73
achievement, 72
achondroplasia, 119, 129, 143
acoustic, 136
acoustical, 147
acromegaly, 116, 169
activation, xii, 118, 179, 181
activity level, 145
acute, 114, 115, 184
adenoidectomy, 16, 27, 33, 53, 69, 74, 75, 79, 81, 84, 85, 127, 133, 134, 138, 147
adenoids, 16, 36, 53, 64, 68, 76, 78, 80, 116, 129, 130, 134, 138, 147, 148, 166
adenoma, 143
ADHD, 72, 145
adipose, 10, 11, 113
adipose tissue, 10, 11
administration, 18, 74
adolescence, 142
adolescents, 66, 71, 79, 80, 82, 132, 137, 138, 150
adult population, xii, 128, 132, 179
adulthood, 75, 142
adults, 4, 14, 16, 24, 25, 27, 32, 55, 57, 58, 61, 64, 68, 70, 71, 76, 104, 105, 106, 114, 115, 118, 123, 124, 132, 141, 144, 148, 150, 161, 170, 171, 178, 183, 187
air, 32, 45, 112, 113, 114, 122, 143, 148, 156, 161
airflow obstruction, 128, 143
airway inflammation, 67, 75, 80, 150
airway tissue, 67, 73, 143
airways, 13, 65, 124, 143, 148, 152, 153, 187
alcohol, 31, 33, 137, 143
alcohol consumption, 31
algorithm, 1, 32, 92, 102
allergens, 114
allergic rhinitis, 65, 66, 68, 76, 114, 143
allergist, 115
allergy, 114, 148
allometry, 115
alternative, 58, 92, 104, 131, 154, 160
alternatives, 55, 74
alters, 47, 132
alveoli, 112
Alzheimer's disease, 119
American Academy of Pediatrics, 70, 82, 128, 132, 135, 136, 141
amyloidosis, 116
analog, 98
anaphylaxis, 40
anatomy, 2, 5, 9, 10, 11, 16, 19, 20, 21, 23, 27, 51, 55, 65, 70, 75, 79, 88, 113, 177
aerodigestive tract, 97
affect, xii, 180, 184
agent, 39, 40, 109, 123
agents, 58, 148
aggression, 142
aggressive behavior, 68, 145
air, 32, 45, 112, 113, 114, 122, 143, 148, 156, 161
airflow obstruction, 128, 143
airway inflammation, 67, 75, 80, 150
airway tissue, 67, 73, 143
airways, 13, 65, 124, 143, 148, 152, 153, 187
alcohol, 31, 33, 137, 143
alcohol consumption, 31
algorithm, 1, 32, 92, 102
allergens, 114
allergic rhinitis, 65, 66, 68, 76, 114, 143
allergist, 115
allergy, 114, 148
allometry, 115
alternative, 58, 92, 104, 131, 154, 160
alternatives, 55, 74
alters, 47, 132
alveoli, 112
Alzheimer's disease, 119
American Academy of Pediatrics, 70, 82, 128, 132, 135, 136, 141
amyloidosis, 116
analog, 98
anaphylaxis, 40
anatomy, 2, 5, 9, 10, 11, 16, 19, 20, 21, 23, 27, 51, 55, 65, 70, 75, 79, 88, 113, 177
androgens, xii, 179, 181
anesthesiologist, 88, 103
aneurysm, 121
angina, 153
ANP, 179, 183, 184
ANS, 3
antagonist, 76
antagonists, 76
Antibodies, 114
antihistamines, 133, 148
anti-inflammatory medications, 63, 76
anxiety, 31
aorta, 121
aortic aneurysm, 121
apnea, xii, 1, 6, 7, 8, 10, 12, 18, 20, 32, 37, 42, 57,
60, 66, 68, 70, 71, 72, 73, 75, 76, 78, 79, 84, 90,
107, 111, 117, 118, 119, 128, 130, 132, 135, 137,
144, 145, 146, 147, 153, 159, 162, 166, 171, 179,
180, 181, 182, 183, 184, 185, 186, 187
appetite, 68, 130
arousal, 71, 72, 128, 132, 152, 153, 176, 185
arrhythmia, 67
arrhythmias, 118, 122
arteries, 181
arterioles, 181
Asia, 125
Asian, 26, 115, 124
aspiration, 48, 51, 143
aspirin, 114
assessment, 10, 15, 21, 26, 28, 32, 37, 61, 66, 73, 81,
87, 88, 92, 103, 108, 132, 153, 161, 163, 174, 180
assignment, 72
association, 180, 185
asthma, 141, 142, 148
Athens, 63
Atlas, 82, 125
atrial fibrillation, 118
atrial natriuretic peptide, xii, 179
atrophy, 119
attention, xii, 179
autoimmunity, 119
autonomic nervous system, 119
autosomal dominant, 119, 121
availability, 19, 20, 21, 146
avoidance, 58, 148
awareness, 173

babies, 130
back, 12, 18, 44, 45, 50, 121, 151, 158
backwardness, 67, 80
bacterial, 134

bariatric surgery, 79, 102
basal ganglia, 119
behavior, 53, 81, 119, 130, 141
behavioral difficulties, 64, 68
behavioral effects, 142
behavioral problems, 142
behaviours, 66
benefits, 74, 95
benign, xii, 114, 147, 179, 183
benign prostatic hypertrophy, xii, 179, 183
benzodiazepine, 137
biocompatible, 41
biomarker, 149
biomolecular, 123
biosynthesis, 120
bipolar, 74
bladder, xii, 179, 183
bleeding, 46, 50, 53, 54, 55, 133
blood, xii, 67, 100, 121, 147, 166, 179, 181
blood flow, 181
blood pressure, xii, 67, 137, 147, 179, 181
blood vessels, xii, 179
bloodstream, 118
BMI, 13, 33, 65, 92, 93, 94, 100, 102, 104, 171, 172,
173, 176, 177
body mass, 33, 116, 160, 166, 171, 172, 174, 184
body mass index, 33, 116, 160, 166, 171, 172, 174,
184
Body Mass Index, 92, 171, 175, 176
body weight, 68, 76
Boston, 149
boys, 128, 142
bradyarrhythmia, 118
bradycardia, 67, 71
brain, 117, 118, 119, 144
brainstem, 117, 118, 119
breathing, 1, 2, 4, 11, 22, 23, 25, 26, 27, 31, 35, 38,
56, 57, 58, 59, 60, 61, 63, 64, 65, 66, 67, 68, 70,
72, 73, 74, 75, 76, 78, 79, 80, 82, 83, 84, 87, 93,
117, 118, 119, 122, 127, 128, 130, 131, 135, 136,
138, 139, 141, 144, 145, 146, 148, 149, 150, 151,
153, 156, 161, 166, 168, 170, 174, 178, 180, 185
breathing disturbances, 168
bronchoscopy, 103
bubble, 40
buccal mucosa, 47
bulbar, 118, 119
butterfly, 57
bypass, 122
| C               | clinical examination, 32, 63, 69, 70, 95 |
|                | clinical heterogeneity, 121             |
|                | clinical symptoms, 93                   |
|                | clinical trial, 162                     |
|                | clinically significant, 147             |
|               | clinics, 65                             |
|               | closure, 43, 46, 48                     |
|               | Cochrane, 83, 159, 162                 |
|               | coding, 125, 161                        |
|               | cognitive function, 142                |
|               | cognitive impairment, 145              |
|               | coherence, 10, 26                      |
|               | cohort, 57, 70, 99, 144, 172           |
|               | collagen, 120, 121                     |
|               | community, 174, 178, 185               |
|               | co-morbidities, 118, 122               |
|               | compartment syndrome, 116              |
|               | compensation, 72, 129                  |
|               | complexity, 109, 121                   |
|               | compliance, xii, 1, 31, 38, 55, 56, 76, 101, 110, 115, 117, 122, 131, 154, 156, 159, 160, 161, 180, 184 |
|               | complications, 37, 38, 40, 44, 50, 55, 58, 60, 61, 62, 74, 75, 78, 100, 101, 103, 118, 121, 143, 153, 160, 162, 180, 184 |
|               | components, 109, 123                   |
|               | composition, 56                        |
|               | computed tomography, 2, 26, 59, 87     |
|               | Computed tomography (CT), 10           |
|               | concentration, 145, 147, 166           |
|               | confidence, 64, 66, 167                |
|               | confidence interval, 64, 66, 167       |
|               | configuration, 110, 115, 121           |
|               | confusion, 92                          |
|               | congestive heart failure, 183          |
|               | conjunctivitis, 121                    |
|               | connective tissue, 121, 129            |
|               | consensus, 63, 160                     |
|               | consent, 34, 37                        |
|               | constraints, 141                       |
|               | construction, 10                       |
|               | consumption, 31                        |
|               | continuous positive airway pressure, 19, 28, 56, 62, 84, 85, 107, 135, 137, 139, 148, 154, 159, 160, 161, 162, 179, 180, 182, 184, 186 |
|               | contracts, 117                         |
|               | contracture, 45                        |
|               | control group, 6, 166, 167, 168, 173, 177 |
|               | controlled trials, 99                  |
|               | conversion, 123                        |
cor pulmonale, 67, 127, 131, 137
coronal heart disease, 90
correlation, 7, 9, 13, 17, 19, 64, 73, 79, 145, 165,
  167, 172, 173, 175, 176, 177, 178, 180, 181, 186
correlations, 11
cortex, 118
corticosteroids, 76, 84
cost effectiveness, 161
cost-effective, 2, 73, 95
costochondritis, 121
costs, 19, 21, 74, 131
cough, 46, 127, 128, 134
covering, 47
CPAP, 15, 19, 21, 27, 28, 56, 76, 84, 101, 102, 104,
  113, 114, 115, 122, 135, 136, 148, 154, 169, 174,
  179, 180, 182, 184, 185, 186, 187
CPR, 122
cranial nerve, 118
craniofacial, 2, 4, 5, 7, 9, 11, 16, 21, 22, 53, 65, 67,
  73, 75, 80, 84, 109, 115, 116, 117, 119, 120, 121,
  123, 124, 126, 129, 136, 143, 167, 168, 169
cranium, 4
critical points, 145
criticism, 133
cross-sectional, 10, 11, 12, 13, 14, 17, 19, 21, 23, 25,
  46, 73, 101, 104, 112, 185
cross-sectional study, 73
CRP, 67, 73
CT, 2, 10, 11, 12, 13, 14, 21, 23, 25, 26, 73
curettage, 84
cyanotic, 66
cystic fibrosis, 66, 75
cysts, 36
danger, 168
data analysis, 14
death, 74, 121
decision making, 19
defects, 109, 121, 173
deficiency, 7, 52, 107, 115
deficit, 68, 72, 78, 149
deficits, 67, 166
definition, 64, 72, 98, 99, 100, 123, 161
deformities, 70, 93
degenerative disease, 119
degrees of freedom, 94, 156
dehydration, 74
delivery, 41, 42, 122, 142
dementia, 109
demographic characteristics, 22
demographics, 134
denial, 90
density, 111, 112
dental profession, 122, 156
dentists, 122, 162
deposition, 113, 117, 129
deposits, 27, 143
depressed, 179, 182
depression, 90, 166, 169, 186
depprivation, 137
desensitization, 31
destruction, 75, 119
detachment, 50
developing countries, 180
developmental delay, 64, 68
deviation, 101, 113, 114, 128, 143
dexamethasone, 83
diabetes, 121, 183, 184
diabetes mellitus, 183
diagnostic criteria, 151, 152
diaphragm, 113
diet, 133
dietary, 148
differential diagnosis, 66, 70
differentiation, 160
dilation, 113, 121, 123, 124
direct observation, 20
disabilities, 145
discipline, 104
discomfort, 31, 46, 122
discriminant analysis, 24, 94
discrimination, 6
diseases, 39, 100, 119, 135, 153
dislocation, 120
disorder, xii, 2, 21, 68, 72, 78, 95, 113, 119, 120,
  121, 122, 127, 128, 135, 137, 146, 148, 149, 151,
  152, 174, 179, 183
displacement, 5, 6, 29, 50, 53, 115, 116
distraction, 14, 26, 53, 54, 55, 120, 168
distress, 153
distribution, 79, 154, 172
diuretic, 183
Down syndrome, 16, 27, 63, 65, 73, 74, 77, 79, 83,
  116, 125, 136
drainage, 49
drugs, 66, 114, 117, 143
durability, 162
duration, 10, 68, 71, 75, 176
dust, 114
dynamic viscosity, 112
dyskinesia, 119
dysphagia, 38, 44, 46, 50, 51, 55
dysplasia, 119, 120
dysregulation, 119
<table>
<thead>
<tr>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>dystonia, 119</td>
<td>evaporation, 50</td>
</tr>
<tr>
<td>eczema, 142</td>
<td>evening, 145</td>
</tr>
<tr>
<td>edema, 28, 41, 50, 55, 100, 129, 143, 144</td>
<td>evidence, 183</td>
</tr>
<tr>
<td>EEG, 15, 18, 28, 71, 82, 146</td>
<td>examinations, 70, 166</td>
</tr>
<tr>
<td>effusion, 139</td>
<td>excision, 43, 74, 138</td>
</tr>
<tr>
<td>Ehlers-Danlos syndrome, 120, 125</td>
<td>excretion, xii, 179, 183</td>
</tr>
<tr>
<td>elastin, 121</td>
<td>executive function, 149, 166</td>
</tr>
<tr>
<td>elderly, 6, 117, 137, 182, 183, 186, 187</td>
<td>executive functions, 166</td>
</tr>
<tr>
<td>electrocardiogram, 70, 132</td>
<td>exercise, 31, 133</td>
</tr>
<tr>
<td>electrocautery, 38</td>
<td>exertion, 123</td>
</tr>
<tr>
<td>electrodes, 38, 39</td>
<td>eye, 71, 121, 132, 145</td>
</tr>
<tr>
<td>electroencephalography, 70</td>
<td>eye movement, 132</td>
</tr>
<tr>
<td>electrolyte, 66</td>
<td>eyelid, 109, 121, 125</td>
</tr>
<tr>
<td>electromyogram, 146</td>
<td>eyes, 114, 121</td>
</tr>
<tr>
<td>electron, 10, 121</td>
<td>factorial, 110, 122</td>
</tr>
<tr>
<td>electron beam, 10</td>
<td>failure, 24, 66, 68, 76, 93, 94, 96, 98, 116, 118, 145</td>
</tr>
<tr>
<td>electron microscopy, 121</td>
<td>failure to thrive, 68, 116, 118, 145</td>
</tr>
<tr>
<td>elongation, 68, 113</td>
<td>false positive, 70</td>
</tr>
<tr>
<td>EMG, 146</td>
<td>familial, 119</td>
</tr>
<tr>
<td>emotional, 90, 142, 148</td>
<td>familial dysautonomia, 119</td>
</tr>
<tr>
<td>encapsulated, 145</td>
<td>family, 65, 79, 129, 136, 141, 148</td>
</tr>
<tr>
<td>encephalitis, 109, 119, 125</td>
<td>family members, 79, 129, 141</td>
</tr>
<tr>
<td>endoscope, 36, 69, 110, 131</td>
<td>Far East, 65</td>
</tr>
<tr>
<td>endoscopy, 36, 69, 73, 96, 105, 127, 134, 160</td>
<td>fascia, 43</td>
</tr>
<tr>
<td>endothelial cell, 181</td>
<td>fat, 12, 16, 18, 27, 45, 56, 64, 79, 116, 117, 121, 129</td>
</tr>
<tr>
<td>endothelial cells, 181</td>
<td>fatigue, 90, 119, 145</td>
</tr>
<tr>
<td>endothelial dysfunction, 118</td>
<td>fauces, 69</td>
</tr>
<tr>
<td>endothelium, 181</td>
<td>FDA, 41</td>
</tr>
<tr>
<td>endotracheal intubation, 57, 88</td>
<td>females, 42, 175, 176</td>
</tr>
<tr>
<td>energy, 38, 57, 68, 153</td>
<td>FES, 121</td>
</tr>
<tr>
<td>England, 83</td>
<td>fiber, 118</td>
</tr>
<tr>
<td>enlargement, 9, 14, 19, 68, 70, 74, 128, 173</td>
<td>fiberoptic endoscope, 36</td>
</tr>
<tr>
<td>enuresis, 1, 54, 61, 68, 130, 144, 183</td>
<td>fibers, 43, 130</td>
</tr>
<tr>
<td>environment, 18, 131, 132</td>
<td>fibrillation, 118</td>
</tr>
<tr>
<td>environmental tobacco, 144</td>
<td>fibrinogen, 67, 73</td>
</tr>
<tr>
<td>EOG, 146</td>
<td>fibrosis, 38, 39, 41, 66, 75, 181, 186</td>
</tr>
<tr>
<td>cosinophilia, 114</td>
<td>finite element method, 126</td>
</tr>
<tr>
<td>epidemic, 65</td>
<td>fixation, 53</td>
</tr>
<tr>
<td>epidemiologic studies, 64</td>
<td>flora, 134</td>
</tr>
<tr>
<td>epidemiology, 66, 150</td>
<td>flow, 22, 23, 71, 72, 111, 112, 113, 114, 143, 145, 181</td>
</tr>
<tr>
<td>epiglottis, 3, 35, 36, 110</td>
<td>flow rate, 112</td>
</tr>
<tr>
<td>epinephrine, 41</td>
<td>fluctuations, 112, 119</td>
</tr>
<tr>
<td>epistaxis, 31</td>
<td>fluid, 40, 109, 111, 112, 183</td>
</tr>
<tr>
<td>epithelium, 43</td>
<td>fluoroscopy, 20, 21, 29, 70, 87</td>
</tr>
<tr>
<td>erectile dysfunction, 179, 180, 184, 185, 186</td>
<td>focusing, 101</td>
</tr>
<tr>
<td>estimating, 42, 66, 70</td>
<td>food, 148</td>
</tr>
<tr>
<td>estrogen, 117</td>
<td>food allergy, 148</td>
</tr>
<tr>
<td>ethnicity, 65, 80, 110, 115</td>
<td></td>
</tr>
</tbody>
</table>
foramen, 47, 119
fractal analysis, 114
fracture, 50
fragmentation, 82, 128, 146, 169
France, 172
freedom, 94, 156
frontal cortex, 144
functional changes, 19
functional imaging, 26

G

ganglia, 119
gas exchange, 67, 72, 128, 146
gender, 110, 118, 171, 172, 173, 176
gender differences, 118
gene, 121, 186
gene expression, 186
general anesthesia, 46, 49, 50
generators, 41
genes, 121
genetic abnormalities, 119
genetic disorders, 120
genetic factors, 33
genetic mutations, 119
genetic syndromes, 129
genioplasty, 107
Germany, 165
girth, 116
gland, 50
glaucoma, 121
globus, 48, 55
glottis, 110
glucocorticoids, 76
glucose, 81
gold, 1, 31, 52, 55, 70, 77, 127, 132, 135, 136, 141, 146
gold standard, 1, 31, 52, 55, 70, 77, 127, 132, 135, 136, 141, 146
gonadotropin, 186
gonadotropin secretion, 186
gravity, 109, 111
Greece, 63
groups, 6, 8, 12, 31, 71, 78, 90, 96, 97, 99, 116, 132, 134, 147, 155, 167, 168, 171, 177, 181
growth, 2, 53, 61, 63, 68, 75, 80, 81, 115, 118, 124, 134, 135, 145, 149, 168, 181
growth factor, 68, 81, 181
growth hormone, 68, 81, 118, 145
guidelines, 74, 96

H

aemostasis, 74
Haifa, 179
hands, 122
Harvard, 171, 175
hay fever, 114
headache, 151, 152, 153
healing, 55
health, 42, 125, 141, 142, 148, 160, 182, 186
health care, 142
healthcare, 122, 141
hearing, 130, 144
hearing loss, 130
heart, 71, 90, 104, 118, 121, 122, 178, 183, 185
heart disease, 121, 180
heart failure, 118, 122, 183
heart rate, 71
heart valves, 121
heat, 38, 48
height, 5, 6, 33, 46, 65, 67, 92
hematoma, 50
hemorrhage, 38
hemostasis, 46
heterogeneity, 109, 121
heterogeneous, 110
high risk, 53, 177
hip, 180
Hispanic, 142
Hispanic population, 142
histamine, 114
homeostasis, 72
Honda, 125
Hong Kong, 138, 174
hormone, 68, 81, 118, 145, 183
hormones, 117
horses, 123
hospital, 50, 74
hospitalization, 97, 100
hospitals, 20
human, 51, 116, 145, 181
human subjects, 51
humans, 120, 123
hydrate, 131
hygiene, 67, 145, 148
hyoid, 2, 3, 4, 5, 6, 7, 8, 9, 19, 21, 23, 24, 25, 28, 29, 50, 51, 52, 60, 75, 100, 106, 107, 108, 109, 115, 116, 124, 135
hyperactivity, 61, 64, 66, 68, 72, 78, 80, 82, 130, 142, 145, 149
hypercapnia, 72
hypercarbia, 128
hyperplasia, 76
hypersensitivity, 114
hypersomnia, 60, 119
hypertension, 33, 67, 90, 118, 121, 122, 131, 153, 180, 185
hypertrophy, 4, 39, 54, 57, 63, 64, 65, 66, 72, 74, 75, 76, 78, 81, 83, 84, 109, 113, 114, 116, 123, 127, 128, 129, 130, 133, 135, 138, 139, 142, 147, 179, 183
hypnotic, 10
hypoglossal nerve, 75, 117
hypoplasia, 65, 93, 119, 120, 129, 135, 139, 143
Hypopnea, 71, 92, 146, 147, 151, 152, 171, 172, 176
hypopnoea syndrome, 23, 82
hypothalamic, 134
hypothalamic-pituitary-adrenal axis, 134
hypothesis, 120, 123, 126, 156
hypothyroidism, 66
hypotonia, 129, 143
hypoventilation, 64, 72, 73, 119, 128, 133
Hypoventilation, 137
hypoventilation syndrome, 119
hypoxemia, 55, 72, 73, 180, 186
hypoxia, xii, 75, 128, 179, 180, 181
iatrogenic, 112
identification, 9, 35, 36, 90, 93, 116, 182
idiopathic, 119
IgE, 114
IGF-1, 118
IL-6, 67, 73
Illinois, 161
images, 10, 14, 15, 16, 21, 120
imaging, 2, 4, 10, 13, 14, 15, 16, 18, 19, 20, 22, 25, 26, 27, 28, 32, 34, 36, 37, 87, 123, 137, 168, 169
imaging techniques, 36, 37
immune response, 114
immunodeficient, 69
immunohistochemistry, 121
immunological, 133, 138
immunotherapy, 76
impairments, 78, 115, 145, 150
implants, 15, 41, 42, 58, 98, 102
impotence, 1
impulsivity, 72
inactive, 33
inattention, 61, 67, 82, 145
incidence, ix, xii, 33, 37, 38, 64, 66, 67, 87, 95, 96, 118, 122, 128, 168, 179
incisor, 50, 160
inclusion, 99, 159
indication, 75, 127
indicators, 71, 183
indices, 71, 94, 144
induction, 18, 119
inert, 41
infancy, 64, 117, 142
infants, 64, 66, 69, 71, 84, 85, 120, 139
infection, 41, 49, 50, 51, 53, 68, 84, 143
infections, 64, 65, 109, 118, 130, 166
infectious, 116, 130
inflammation, 50, 67, 75, 80, 114, 118, 129, 134, 143, 148, 150
inflammatory, 41, 63, 67, 73, 75, 76, 114, 116, 142
inflammatory mediators, 67, 73
inhalation, 113
initiation, 20
injection, 39, 40
injections, 41
injury, 48, 50
insertion, 41, 42, 50, 156
insight, 90
insomnia, 118, 119, 145
inspection, 33
inspiration, 70, 101, 144
instability, 117, 143, 158
instruction, 31
insulin, 68, 81, 90
insulin resistance, 90
insulin-like growth factor, 68, 81
integration, 109
intelligence, 72, 142
intelligence scores, 142
intensive care unit, 61
interaction, 109, 123, 146, 186
intercostal retractions, 130
interdisciplinary, 169
interference, 132
Internet, 83
interpersonal relations, 180
interpretation, 185
intervention, 2, 13, 14, 19, 21, 33, 37, 52, 53, 55, 75, 78, 90, 93, 102, 104, 119, 120, 156
interview, 129
intracranial, 121
intracranial pressure, 121
intravenous, 36, 50, 83
ionizing radiation, 69
ipsilateral, 114
irritability, 142, 153
irritation, 31, 114
ischemia, 118
ischemic, 121, 180
ischemic heart disease, 121, 180
isolation, 65
Israel, 179
Italy, 127, 151

JAMA, 56, 185
Japanese, 7, 22, 58, 119, 125
Japanese encephalitis, 119, 125
jaw, 55, 85, 156, 160
joint pain, 120, 158
judgment, 66

knowledge, 182
Korean, 124

macroglossia, 65, 69, 92, 116, 125, 129, 143
magnetic, 2, 14, 18, 22, 27, 28, 87, 168, 169
magnetic resonance imaging, 2, 14, 18, 22, 27, 28, 87, 168, 169
maintaining attention, 130
maintenance, 119, 134
males, 7, 9, 42, 112, 175, 176
malignant, 183
malocclusion, 53, 85, 109, 122, 130, 143
mammals, 123
management, ix, 1, 2, 8, 19, 31, 32, 33, 35, 37, 38, 40, 42, 43, 55, 59, 62, 70, 74, 76, 77, 82, 83, 85, 87, 90, 100, 103, 105, 107, 109, 111, 113, 116, 122, 123, 133, 136, 139, 148, 149, 150, 151, 154, 158, 162, 170, 183
mandible, 2, 3, 4, 6, 7, 9, 17, 25, 27, 34, 49, 50, 51, 53, 55, 60, 67, 115, 116, 122, 123, 129, 156
mandibular, 3, 4, 5, 7, 8, 9, 14, 19, 24, 25, 26, 28, 50, 52, 53, 54, 55, 56, 60, 65, 75, 76, 106, 107, 109, 115, 116, 122, 123, 135, 156, 157, 158, 160, 161, 162, 166, 167, 168
mandibular advancement appliances, 76, 162
manufacturing, 156, 158
Marfan syndrome, 120, 129
market, 155, 158, 159
mask, 31, 76, 135
mast cell, 114
mast cells, 114
maxilla, 2, 3, 4, 5, 8, 9, 34, 47, 53, 55, 65, 67, 75, 113, 122, 123, 129, 168
maxillary, 6, 7, 53, 55, 75, 76, 85, 111, 115, 123, 126, 156, 160, 166, 168
MDI, 162
measurement, 7, 8, 9, 10, 11, 37, 56, 59, 69, 161, 167
measures, 14, 32, 67, 78, 84, 101, 126, 166, 167, 174, 176
meat, 68
media, 130, 139, 142
mediators, 67, 73, 114
medication, 34, 76, 119
medications, 33, 36, 63, 75, 76, 148
Medline, 172
medulla, 109, 117
medulla oblongata, 109
membranes, 114
membranes, 114
memory, 72, 142
men, xii, 1, 4, 90, 104, 116, 174, 175, 176, 177, 179, 180, 182, 185, 186, 187
menopause, 178
meta-analysis, 64, 70, 93, 99, 149
metabolic, 116, 117, 118, 143
metabolic disorder, 143
metabolism, 66
microscopy, 121
midbrain, 119
middle-aged, 58, 104, 174
Minnesota, 41
minority, 119
misconception, 93
misidentified, 96
misleading, 69
mitral valve, 120, 121
mitral valve prolapse, 120, 121
mixed sleep apnea, 64
MMA, 52, 53
mobility, 17
modalities, 31, 63, 102, 153
modality, 14, 18, 20, 31, 38, 83, 90, 131, 138
models, 126
molecules, 134
monkeys, 67
monomers, 121
montelukast, 76
mood, xii, 169, 179, 182, 186
morbidity, 31, 37, 41, 53, 66, 74, 80, 97, 98, 100, 101, 102, 118, 162
morning, 1, 67, 151, 152, 153, 181
morphological, 112, 123
morphology, 22, 26, 27, 65, 67, 81, 109, 112, 115, 116, 122, 124, 154
mortality, 31, 74, 118, 119, 182
mortality rate, 119, 182
motion, 10, 111, 131
motivation, 31, 73, 97
motor neurons, 118
motor skills, 166
motor system, 156
movement, 55, 71, 122, 156, 168
MRA, 155, 159
MRI, 162
mucosa, 7, 38, 41, 43, 45, 46, 47, 114, 123, 129, 134
mucous membrane, 114
mucous membranes, 114
multidisciplinary, 63, 122, 142, 148, 153, 160
multivariate, 94
murmur, 121
muscle, 1, 15, 21, 43, 45, 46, 47, 49, 50, 65, 66, 101, 111, 113, 117, 118, 119, 128, 143, 144, 156, 181
muscle atrophy, 119
muscle relaxation, 21, 181
muscle weakness, 119
muscles, 14, 16, 38, 41, 45, 46, 51, 60, 65, 74, 113, 116, 117, 119, 129, 143, 144, 157, 160
muscular dystrophy, 65, 77, 129, 136
muscular tissue, 44, 113
musculoskeletal, 121
musculoskeletal system, 121
mutant, 121
mutation, 120
mutations, 119
myocardial infarction, 90, 122
nares, 84, 144
nasal cavity, 112, 113, 114, 123, 126
nasal polyp, 75, 113, 114, 130, 135, 143
nasopharyngeal carcinoma, 143
nasopharynx, 36, 48, 65, 110, 127, 133
natural, 10, 88, 131
nausea, 130
neck, 2, 12, 18, 33, 51, 69, 70, 73, 92, 116, 117, 143, 176, 177, 178
necrosis, 38, 39, 48
negative outcomes, 38, 93
neonates, 71
neoplasm, 143
neoplastic, 116
nerve, xii, 118, 143, 179, 180, 181, 185
neural function, 128
neural tissue, 181
Index

neurobehavioral, 72, 78
neurodegenerative, 109
neurodegenerative disease, 109
neurodegenerative diseases, 109
neurogenic, 31
neurological disorder, 137
neuromotor, 129
neuromuscular diseases, 119
neurons, 117
neuropathy, 121, 185
neurotransmitters, 110, 181
New England, 150
New York, 57, 78, 82
Newton’s second law, 109
Newton’s second law, 111
night terrors, 54, 68, 144
NIH, 180, 185
nitric oxide, 181, 186
nitric oxide (NO), 181
nocturia, xii, 179, 180, 182, 183, 184, 186, 187
nocturnal polyuria, xii, 180, 183, 187
noise, 15, 142
non-invasive, 4, 90, 95, 133
non-obese patients, 121
non-steroidal anti-inflammatory drugs, 114
normal, 4, 6, 7, 11, 12, 13, 15, 17, 18, 19, 20, 23, 25, 27, 37, 63, 70, 71, 72, 73, 82, 83, 110, 111, 116, 121, 128, 130, 132, 145, 146, 147, 148, 153, 170, 172, 183
normal children, 63, 70
normalization, 67
norms, 126
North America, 150
Northern Ireland, 83
nose, 33, 36, 37, 38, 67, 75, 76, 97, 102, 106, 112, 113, 114, 122, 123, 143
NPT, 181, 182
nucleus, 117
nurse, 148
obese patients, 7, 24, 27, 53, 56, 107, 129, 168, 174
obesity hypoventilation syndrome, 53
objective criteria, 37
obligate, 123
observations, 20, 35, 88, 144, 151
Obstructive Sleep Apnea, 5, 6, 11, 16, 42, 70, 78, 82, 136, 151, 171, 175, 176, 179, 180
Obstructive Sleep Apnea (OSA), 180
obstructive sleep apnoea, 22, 23, 24, 25, 26, 27, 28, 60, 79, 80, 81, 83, 84, 105, 106, 107, 124, 161, 162, 163, 165, 166, 169, 174, 178
occlusion, 34, 53, 122, 146, 166, 167, 180
occupational, 162
odds ratio, 66, 173
office-based, 40, 41
off-the-shelf, 156
older adults, 187
one dimension, 165, 167
online, 124, 125, 165
optical, 10, 26
optimal health, 142
optimization, 122
oral, 9, 10, 13, 14, 15, 21, 22, 25, 27, 28, 34, 38, 41, 46, 66, 76, 83, 84, 85, 103, 113, 116, 123, 124, 125, 126, 143, 156, 158, 159, 160, 161, 162, 183
oral cavity, 27, 41, 116, 143
organ, 79
organic, 135, 181
organic disease, 135
opharynx, 12, 14, 20, 25, 26, 36, 55, 65, 92, 95, 97, 101, 104, 116, 129, 160, 166
orthodontists, 76
osteotomy, 9, 24, 50, 51, 52, 53, 60, 107
ostium, 112
otitis media, 139, 142
otolaryngologist, 65
outpatient, 28, 38, 45, 65, 74, 132
output, 183
overload, 183
overproduction, xii, 179
overweight, 33, 67, 79, 166, 171, 172, 177
oxidative, 118
oxidative stress, 118
oxide, 186
oxygen, 9, 37, 71, 72, 99, 128, 132, 142, 147, 152, 180, 186
Oxygen, 186
oxygen saturation, 9, 72, 128, 132, 180
oxygenation, 149, 166, 182
oxyhemoglobin, 146, 176
pacemakers, 15
pain, 40, 44, 49, 50, 55, 57, 74, 83, 119, 120, 158, 160
palate, 2, 3, 4, 5, 6, 7, 8, 12, 13, 14, 16, 17, 18, 19, 20, 28, 33, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 53, 55, 59, 67, 75, 88, 89, 90, 93, 95, 96, 97, 98, 100, 101, 102, 104, 105, 110, 113, 115, 121, 129, 130, 144, 148, 156, 160, 165, 166, 167, 168, 169, 173
palpebral, 121
papilledema, 121
paradoxical, 147
parameter, 8, 72, 159
paraneoplastic, 119
parasympathetic, 181
parenchyma, 118
parental smoking, 129
parents, 68, 74, 75, 76, 129, 130, 131, 142, 144, 145, 166
Parkinson’s disease, 119
particles, 111, 114
passenger, 33
passive, 78, 136
pathogenesis, 14, 46, 101, 110, 117, 153
pathogenic, 64, 110
pathology, 34, 36, 37, 90, 101, 116, 119, 121, 128, 146, 147, 148
pathophysiology, 2, 15, 34, 110, 114, 118, 148, 153, 160
pathways, 118
patient care, 92
patient management, 2
pediatric patients, 29, 78, 127, 132, 135, 145, 147
peer, 142, 154
penis, 181
peptide, 179
percentile, 76, 166
perception, 53, 60, 100, 159
periodic, 117, 118, 120
peripheral, 185
permit, 74
personality, 1
perspective, 186
pH, 132
pharmacological, 55, 145
pharmacological treatment, 145
pharyngeal, 3, 8, 26, 27, 28
pharyngeal airway, 18, 25, 26, 27, 28, 46
pharynx, 1, 6, 12, 16, 27, 28, 35, 45, 49, 56, 65, 110, 114, 143, 144, 151, 152, 153, 156, 160
phenotype, 64
Philadelphia, 56, 125
phonation, 144
physical activity, 145
physical health, 1
physicians, 180, 184
physiological, 65, 158, 160, 166, 186
physiology, 26, 110
physiopathology, 162
pilot study, 58, 59
placebo, 107, 134, 183, 187
planning, 20, 32, 34, 50, 70, 134, 136
plastic, 156
platelet, 181
platelet derived growth factor, 181
play, 34, 76, 93, 112, 116, 118, 143, 153
plethysmography, 132
polio, 118
pollen, 114
polyethylene, 41
polyethylene terephthalate, 41
polls, 36, 65, 114
polysomnography, 1, 24, 26, 28, 32, 36, 37, 63, 70, 71, 72, 73, 77, 80, 82, 83, 93, 131, 137, 138, 141, 146, 148, 149, 150, 159, 181, 184
polyuria, xii, 179, 183, 187
poor, 8, 11, 32, 33, 66, 67, 68, 70, 72, 73, 93, 118, 130, 134, 142, 145, 153, 160
population, 20, 26, 57, 71, 96, 114, 118, 128, 132, 141, 142, 166, 169, 172, 173, 177, 178, 179, 182, 185
postmenopausal, 117, 172
postmenopausal women, 117, 172
postoperative, 8, 9, 14, 19, 28, 32, 37, 38, 39, 41, 44, 50, 54, 55, 58, 61, 83, 93, 97, 98, 99, 100, 101, 133, 135
posture, 114, 123, 130, 155
potato, 68
power, 84, 112
PPS, 119
precipitation, 112, 121
predictability, 159
prediction, 57, 138
predictors, 9, 20, 22, 24, 25, 65, 70, 104, 162, 182
predisposing factors, 64
prednisone, 75
preference, 37, 68
prematurity, 66
preschool, 82
preschoolers, 80, 149
Index

press, 124
pressure, ix, xii, 1, 19, 28, 31, 37, 55, 56, 62, 63, 65, 67, 70, 71, 76, 81, 82, 84, 85, 87, 101, 107, 110, 111, 112, 113, 114, 117, 121, 132, 135, 137, 139, 144, 145, 147, 148, 154, 159, 160, 161, 162, 179, 180, 181, 182, 183, 184, 186
pressure sore, 31
prevention, 138, 157
primacy, 114
primary care, 174
probability, 32, 114, 142, 145
problem behavior, 80
problem behaviors, 80
production, 121, 143, 148, 179, 181, 183
productivity, 159
prognosis, 33, 93
program, 97, 133
prolapse, 121
proliferation, 64, 144
protection, 53
protein, 121
proteins, 114
protocol, 98, 107, 115, 123, 160
protocols, 2, 10, 77, 122
pseudo, 120
PSG, 1, 6, 7, 9, 13, 19, 20, 36, 70, 71, 72, 73, 74, 75, 76, 77, 78, 98, 99, 102, 131, 132, 133, 135, 147, 159, 180, 181
psychological problems, 31
psychologist, 148
ptosis, 34
PTT, 73
puberty, 66
public, 33, 42
public health, 42
pulmonary hypertension, 118
pulmonologist, 148
pulse, 70, 73, 77, 83, 131, 132, 138, 147, 180
quality of life, xii, 53, 59, 63, 68, 74, 78, 81, 90, 149, 159, 169, 180, 184, 186
questionnaire, 32, 70, 125, 131, 138, 181
radiofrequency ablation, 38
radiography, 2, 6, 7
radiological, 69, 70, 76
radius, 112
range, 49, 99, 118, 122, 135, 147, 172, 176
reading, 33
recall, 165
receptors, 76, 84
recognition, 65
reconstruction, 10, 13, 37, 101, 124, 136
reconstructive surgery, 56
recovery, 40
recurrence, 74, 133, 138
reduced bladder capacity, xii, 179
reduction, 180, 181, 184
redundancy, 7
regional, 109, 147, 149
regression, 7, 16, 181
regression analysis, 16
regular, 31, 133, 145, 148
regulation, 67, 183
reinforcement, 168
relapse, 39, 53
relationship, ix, 9, 21, 23, 33, 35, 38, 51, 56, 66, 73, 87, 88, 93, 94, 145, 172, 173, 176, 177, 180, 183, 185
relationships, 4, 65, 72, 142, 177, 186
relaxation, 10, 21, 111, 181
relevance, 7, 136, 149
reliability, 71
REM, 68, 71, 111, 119, 129, 144
remodeling, 116, 123
renal, 118, 122
renal disease, 122
renal failure, 118
repair, 99
resection, 50, 55, 97, 99, 112
resilience, 168
resistance, 1, 13, 23, 31, 34, 64, 65, 66, 71, 72, 90, 101, 109, 112, 114, 122, 128, 129, 136, 137, 144
resolution, 10, 11, 14, 109, 122, 123, 135, 147, 148
respiration, 4, 13, 25, 80, 109, 117, 119, 129, 130, 144, 146, 173
respiratory, 1, 7, 10, 16, 33, 37, 54, 59, 64, 65, 67, 70, 71, 72, 78, 79, 80, 98, 110, 113, 114, 117, 118, 119, 123, 128, 129, 130, 131, 132, 136, 146, 147, 148, 150, 180, 183, 184
respiratory disorders, 131
respiratory failure, 119
respiratory problems, 79
respiratory syncytial virus, 64
respiratory therapist, 148
resuscitation, 122
sodium, 39, 183
soft palate, 2, 3, 5, 6, 7, 12, 13, 14, 16, 17, 18, 19, 20, 28, 33, 35, 36, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 55, 75, 88, 89, 90, 93, 104, 105, 110, 113, 115, 129, 144, 156, 160, 166, 167, 168, 173

software, 31
somatic complaints, 142
somnolence, xii, 32, 169, 179, 180, 182
sores, 31
sounds, 131, 142
spasticity, 143
specificity, 70, 71, 73, 131, 144, 158
spectrum, 1, 23, 31, 64, 66, 94, 109, 121, 127, 128, 146
speech, 48, 68, 125, 127, 128, 130, 166, 168, 169
speed, 10
spinal cord, 118, 119
spine, 3, 4, 7, 143
splint, 25, 161, 162
spontaneous pneumothorax, 121
SPSS, 176
SPT, 3
sputum, 67, 73
stability, 31, 34, 37, 55, 117, 125
stabilize, 50, 117
stabilizers, 156
stages, 88, 94, 100, 132, 141, 146
standard deviation, 172
standardization, 151, 186
standards, 70, 92
Standards, 82, 136
statistical analysis, 177
Statistical Package for the Social Sciences, 172, 176
steel, 74
stenosis, 44, 55, 101, 114, 170
stent, 103
steroid, 75, 127, 134, 135, 139
steroids, 75, 76, 84, 114, 127, 133, 134, 139, 148
stethoscope, 73
stimulant, 117
strategies, 58
stratification, 90
stress, 113, 118
stretching, 113, 156, 160
stridor, 66, 119, 144
stroke, 90, 118, 122, 180, 185
strokes, 118
subcutaneous tissue, 143
subgroups, 134
subjective, 98, 101, 104, 108, 159, 166
submucosa, 44, 45
substitution, 122
success rate, 8, 20, 36, 38, 40, 43, 49, 50, 51, 52, 53, 55, 93, 95, 96, 97, 98, 99, 100, 182
sudden infant death syndrome, 166, 169
suffering, 20, 21, 61, 119, 181, 184
sulfate, 39
superimposition, 20, 120
superiority, 158, 160
supply, 143
surface tension, 110
surgeons, 8, 33, 37, 44, 51, 52, 93, 98, 132
surgeries, 46, 101, 108
surgery, 1, 5, 7, 9, 10, 11, 13, 14, 15, 19, 20, 21, 24, 26, 28, 32, 33, 37, 38, 41, 43, 44, 45, 49, 50, 52, 53, 55, 57, 59, 60, 61, 62, 74, 75, 81, 82, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 133, 135, 138, 139, 143, 148, 162, 170
surgical intervention, 10, 14, 19, 21, 37, 53, 90, 93, 104, 120, 153
survival, 114
survivors, 119
susceptibility, 120
suture, 45, 48, 49, 59, 76, 107, 123, 126
swallowing, 46, 49, 68, 119, 130, 144
swelling, 40, 42, 114
symptomology, 90
symptoms, 1, 20, 64, 65, 66, 68, 73, 74, 75, 76, 78, 79, 80, 82, 90, 93, 98, 102, 114, 118, 119, 127, 128, 130, 131, 134, 135, 136, 145, 146, 147, 148, 151, 152, 153, 160, 162, 166, 169, 174, 185, 186
synergistic, 117
synergistic effect, 117

tachycardia, 118
tachypnea, 72
<table>
<thead>
<tr>
<th>Term</th>
<th>Page Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>teachers</td>
<td>145</td>
</tr>
<tr>
<td>technological advancement</td>
<td>74</td>
</tr>
<tr>
<td>teeth</td>
<td>50, 156, 160</td>
</tr>
<tr>
<td>Tel Aviv</td>
<td>179</td>
</tr>
<tr>
<td>temperature</td>
<td>59, 105, 107, 113</td>
</tr>
<tr>
<td>temporomandibular disorders</td>
<td>162</td>
</tr>
<tr>
<td>tension</td>
<td>43, 45, 46, 48, 49, 50, 110, 186</td>
</tr>
<tr>
<td>terminals</td>
<td>181</td>
</tr>
<tr>
<td>testosterone</td>
<td>117</td>
</tr>
<tr>
<td>TGF</td>
<td>181</td>
</tr>
<tr>
<td>thalamus</td>
<td>109, 119</td>
</tr>
<tr>
<td>therapeutic approaches</td>
<td>160</td>
</tr>
<tr>
<td>therapy</td>
<td>21, 25, 28, 32, 41, 55, 56, 58, 60, 61, 75, 84, 89, 91, 96, 104, 105, 113, 114, 122, 124, 126, 133, 134, 135, 137, 139, 147, 154, 161, 162, 168, 169, 174, 182</td>
</tr>
<tr>
<td>thoracic</td>
<td>113, 149, 184</td>
</tr>
<tr>
<td>threatening</td>
<td>147</td>
</tr>
<tr>
<td>three-dimensional</td>
<td>10, 13, 14, 26, 70, 112</td>
</tr>
<tr>
<td>three-dimensional reconstruction</td>
<td>10, 14, 70</td>
</tr>
<tr>
<td>threshold</td>
<td>72, 129</td>
</tr>
<tr>
<td>threshold level</td>
<td>72</td>
</tr>
<tr>
<td>throat</td>
<td>48, 148</td>
</tr>
<tr>
<td>thyroid</td>
<td>51, 116</td>
</tr>
<tr>
<td>time</td>
<td>183, 184, 185, 186</td>
</tr>
<tr>
<td>timing</td>
<td>100</td>
</tr>
<tr>
<td>tin</td>
<td>127</td>
</tr>
<tr>
<td>tissue</td>
<td>1, 2, 4, 10, 14, 16, 17, 19, 22, 27, 28, 34, 38, 40, 43, 47, 48, 53, 55, 57, 59, 64, 69, 70, 78, 79, 97, 98, 103, 105, 109, 110, 112, 113, 116, 121, 127, 129, 143, 148, 173, 177, 181, 185</td>
</tr>
<tr>
<td>titanium</td>
<td>50, 53</td>
</tr>
<tr>
<td>title</td>
<td>145</td>
</tr>
<tr>
<td>titration</td>
<td>184</td>
</tr>
<tr>
<td>tobacco</td>
<td>33, 142, 144</td>
</tr>
<tr>
<td>tobacco smoke</td>
<td>142</td>
</tr>
<tr>
<td>tolerance</td>
<td>31, 38</td>
</tr>
<tr>
<td>tongue</td>
<td>3, 48, 49, 50, 59, 87, 96, 103, 105, 108, 155, 156</td>
</tr>
<tr>
<td>tonsillectomy</td>
<td>16, 27, 33, 35, 43, 45, 46, 47, 53, 74, 75, 76, 79, 81, 83, 84, 85, 91, 93, 103</td>
</tr>
<tr>
<td>tonsilitis</td>
<td>74</td>
</tr>
<tr>
<td>tonsils</td>
<td>16, 34, 35, 43, 45, 46, 47, 53, 59, 64, 66, 68, 69, 76, 78, 80, 84, 88, 89, 90, 92, 93, 94, 95, 103, 104, 105, 116, 129, 130, 138, 147, 148, 166</td>
</tr>
<tr>
<td>trachea</td>
<td>73</td>
</tr>
<tr>
<td>tracheostomy</td>
<td>61, 75, 102, 148</td>
</tr>
<tr>
<td>traction</td>
<td>46, 121</td>
</tr>
<tr>
<td>traffic</td>
<td>33, 163</td>
</tr>
<tr>
<td>transforming growth factor</td>
<td>181</td>
</tr>
<tr>
<td>transverse section</td>
<td>111</td>
</tr>
<tr>
<td>trauma</td>
<td>43, 50, 75</td>
</tr>
<tr>
<td>trial</td>
<td>75, 78, 96, 102, 107, 108, 131, 134, 161, 162, 184</td>
</tr>
<tr>
<td>trial and error</td>
<td>96, 102</td>
</tr>
<tr>
<td>triggers</td>
<td>61</td>
</tr>
<tr>
<td>trisomy 21</td>
<td>119</td>
</tr>
<tr>
<td>tumor</td>
<td>113</td>
</tr>
<tr>
<td>tumors</td>
<td>143</td>
</tr>
<tr>
<td>turbinates</td>
<td>37, 53, 112, 114, 124, 135</td>
</tr>
<tr>
<td>turbulence</td>
<td>112</td>
</tr>
<tr>
<td>turbulent</td>
<td>111, 143</td>
</tr>
<tr>
<td>Turkey</td>
<td>1, 31</td>
</tr>
<tr>
<td>two-dimensional</td>
<td>10, 21</td>
</tr>
<tr>
<td>ulceration</td>
<td>38, 40, 49</td>
</tr>
<tr>
<td>uniform</td>
<td>72</td>
</tr>
<tr>
<td>United States</td>
<td>42</td>
</tr>
<tr>
<td>upper airways</td>
<td>27, 151, 152, 153, 154, 155, 156, 157, 160, 166</td>
</tr>
<tr>
<td>upper respiratory tract</td>
<td>10, 33, 65, 128, 130</td>
</tr>
<tr>
<td>urinary</td>
<td>182, 183</td>
</tr>
<tr>
<td>urine</td>
<td>xii, 179, 183</td>
</tr>
<tr>
<td>uvula</td>
<td>3, 9, 35, 39, 40, 43, 44, 45, 46, 47, 88, 89, 90, 102, 104, 113, 116, 144, 166, 167, 168</td>
</tr>
<tr>
<td>vaccine</td>
<td>118</td>
</tr>
<tr>
<td>validation</td>
<td>11, 95</td>
</tr>
<tr>
<td>values</td>
<td>4, 7, 23, 37, 71, 77, 82, 92, 94, 132, 133, 138, 147, 158, 172, 173, 182</td>
</tr>
<tr>
<td>variability</td>
<td>72, 82, 129, 132, 138, 153</td>
</tr>
<tr>
<td>variables</td>
<td>2, 3, 7, 9, 23, 25, 76, 132, 135, 146, 173</td>
</tr>
<tr>
<td>varicose veins</td>
<td>39</td>
</tr>
<tr>
<td>vascular endothelial growth factor</td>
<td>181</td>
</tr>
<tr>
<td>vasculature</td>
<td>181, 186</td>
</tr>
<tr>
<td>vasomotor</td>
<td>65, 114</td>
</tr>
<tr>
<td>vasopressin</td>
<td>183</td>
</tr>
<tr>
<td>vector</td>
<td>45</td>
</tr>
<tr>
<td>velocity</td>
<td>111, 112, 113</td>
</tr>
<tr>
<td>ventilation</td>
<td>76, 117, 128, 129, 132, 139</td>
</tr>
<tr>
<td>ventricle</td>
<td>121</td>
</tr>
<tr>
<td>ventricular tachycardia</td>
<td>118</td>
</tr>
<tr>
<td>venue</td>
<td>142</td>
</tr>
<tr>
<td>Vermont</td>
<td>171, 172, 175</td>
</tr>
<tr>
<td>vessels</td>
<td>179</td>
</tr>
<tr>
<td>vibration</td>
<td>128, 144</td>
</tr>
<tr>
<td>viral infection</td>
<td>64, 65</td>
</tr>
<tr>
<td>virus</td>
<td>64, 118, 119</td>
</tr>
<tr>
<td>viruses</td>
<td>64</td>
</tr>
<tr>
<td>viscosity</td>
<td>111, 113</td>
</tr>
</tbody>
</table>
visible, 41, 69
visualization, 35, 36, 88, 89, 90, 124
voice, 68
voids, 183
vomiting, 74, 83, 130
women, xii, 4, 90, 104, 116, 117, 121, 153, 172, 175, 176, 177, 178, 179, 186
working population, 185
wound healing, 39
wound infection, 50
walking, 68
warrants, 147
weakness, 119
wear, 76, 125
weight gain, 76
weight loss, 15, 31, 56
weight reduction, 133, 148
well-being, 186
Western Europe, 173
white matter, 118
Wisconsin, 144
x-rays, 70
yield, 72, 146
young adults, 4, 55
zygomatic, 123