

# Bibliography and Online Dental Sleep Medicine & Sleep Apnea References

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## **Knowledge, Education and Awareness**

1. **Predoctoral teaching of temporomandibular disorders A survey of U.S. and Canadian dental schools.** [Background. In the United States and Canada, there are no specific curriculum guidelines for predoctoral dental education in the field of temporomandibular disorders (TMDs). This situation has the potential to cause confusion for new graduates. Methods. The authors sent an 11-question survey regarding predoctoral teaching of TMDs to the appropriate faculty members in all U.S. and Canadian dental schools either electronically or via the postal service between June and December 2005. Results. predoctoral teaching of TMD—both didactic and clinical aspects—has progressed. Some schools, however, do not address these topics adequately, while others teach outdated concepts. Conclusions. Both qualitative and quantitative standards are needed to ensure that all predoctoral dental students learn about the diagnosis and treatment of nondental orofacial pain problems. Practice Implications. Owing to the lack of standardized predoctoral teaching of TMD, U.S. or Canadian patients with TMD or facial pain are at risk when seeking appropriate primary care for their problems.] Klasser GD, Greene CS. J Am Dent Assoc, Vol 138, No 2, 231-237.  
<http://jada.ada.org/cgi/content/abstract/138/2/231>

## **Introduction, Practice Parameters & Position Papers**

2. **American Sleep Disorders Association Standards of Practice Committee: Parameters for the treatment of snoring and obstructive sleep apnea with oral appliances.** [These clinical guidelines, which have been reviewed and approved by the Board of Directors of the American Sleep Disorders Association (ASDA), provide recommendations for the practice of sleep medicine in North American with regards to the use of oral appliances for the treatment of snoring and obstructive sleep apnea. Oral appliances have been developed for the treatment of snoring and have been applied to the treatment of obstructive sleep apnea, a syndrome associated with morbidity. Based on a review of the relevant scientific literature, the Standards of Practice Committee of the ASDA has developed guidelines describing the use of oral appliances for the treatment of snoring and obstructive sleep apnea in adults.] *Sleep* 18(6):511-513, 1995.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=PubMed&list\\_uids=7481422&dopt=medline](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=PubMed&list_uids=7481422&dopt=medline)
3. **Practice Parameters for the treatment of snoring and obstructive sleep apnea with oral appliances: An update for 2005.** [Oral appliances (OAs) are indicated for use in patients with mild to moderate OSA who prefer them to CPAP therapy, or who do not respond to, are not appropriate candidates for, or who fail treatment attempts with CPAP. CPAP is indicated whenever possible for patients with severe OSA before considering OAs. Oral appliances should be fitted by qualified dental personnel who are trained and experienced in the overall care of oral health, the temporomandibular joint, dental occlusion and associated oral structures. Follow-up polysomnography or an attended cardiorespiratory (type 3) sleep study is needed to verify efficacy, and may be needed when symptoms of OSA worsen or recur. Patients with OSA who are treated with oral appliances should return for follow-up office visits with the dental specialist at regular intervals to monitor patient adherence, evaluate device deterioration or maladjustment, and to evaluate the health of the oral structures and integrity of the occlusion. Regular follow up is also needed to assess the patient for signs and

symptoms of worsening OSA.] Kushida CA, Morgenthaler TI, et al. *Sleep Vol.29, No.2, p.218-221, 2006.*

[http://www.guideline.gov/summary/summary.aspx?doc\\_id=8774&nbr=004852&string=treatment](http://www.guideline.gov/summary/summary.aspx?doc_id=8774&nbr=004852&string=treatment) ;

4. **Position paper on the use of mandibular advancement devices in adults with sleep-related breathing disorders. A position paper of the German Society of Dental Sleep Medicine.** [Custom-made mandibular advancement devices are an effective treatment option for snoring, upper airway resistance syndrome, and obstructive sleep apnea (OSA). Evidence-based data indicates their efficacy, and international sleep societies recommend oral appliance (OA) therapy for patients with sleep-related breathing disorders. The following position paper by the German Society of Dental Sleep Medicine (DGZS) is to guide the interdisciplinary team (sleep physician and sleep disorder dentist) in detail when to prescribe oral appliances. This position paper supports the responsible use of OA as an effective treatment option for patients with sleep-related breathing disorders. The paper advises of proper indication regarding OSA severity, body mass index (BMI), and dentition. It emphasizes the interdisciplinary approach of oral appliance therapy and suggests treatment under the guidance of dentists trained in dental sleep medicine.] Schwarting S, Huebers U, et al. *Sleep Breath, Vol 11, Number 2 / June, 2007 p125-126.*  
<http://www.springerlink.com/content/k263413pu540q12r/?p=618d8c31efdf4004a24ec9c4ca41ac66&pi=8>
5. **The future of sleep medicine and the business of sleep.** [Over 12 years ago, an editorial in the *New England Journal of Medicine* asserted that untreated sleep-disordered breathing (SDB) and particularly its major manifestation, obstructive sleep apnea (OSA), was a major public health problem equivalent to smoking. Sadly, while this was an apparent clarion cry to action, there has been a marked reluctance on the part of the medical establishment to address this issue with the sense of urgency required.... We are promoting a Hub and Spoke Model as one sensible approach to "The Business of Sleep." ... Sleep specialists can have a tremendous impact on the progress and growth of the industry by educating fellow physicians and the public about the serious health consequences of untreated SDB, increasing the treatment capacity of their practices, and advocating better patient care by the caregivers with whom they deal. ] Farrell PC. *Sleep Breath (2006) 10:111-114.*  
<http://www.springerlink.com/content/h678675084634487/fulltext.pdf>

## **Education, Knowledge and Awareness**

6. **Knowledge and Attitudes of Primary Care Physicians Toward Sleep and Sleep Disorders.** [Purpose: To assess primary care physician (PCP) sleep knowledge and attitudes. Method: A sample of 580 PCPs practicing adult medicine in Northeast Ohio was selected, using a systematic random method (every 10th name on the American Medical Association mailing list). ... Of respondents, 94% were board certified with 76% certified in more than one area. When asked to rate their knowledge of sleep disorders, none rated themselves as excellent, 10% rated themselves as good, 60% as fair, and 30% as poor. The factors rated highest in influencing current practices regarding sleep and sleep disorders were articles in journals, continuing medical education courses, and discussions with specialists. Knowledge average was 34% (3 to 94%). Though virtually all agreed that prevention counseling should be a part of patient care, fewer agreed that they spend more time counseling patients on the

benefits of sleep than of diet or exercise. Conclusions: The majority of PCPs rated their own knowledge of sleep disorders as fair or poor. Knowledge testing and attitude assessment lend credence to these perceptions.] Papp KK, Penrod RE, et al. *Sleep and Breathing*, Vol.6, No.3, p.103-109.

<http://www.springerlink.com/content/m2b88c78k06anfc0?p=fb4cf0ea99c441229feda50db270f300&pi=0>

7. **Knowledge of Sleep Apnea in a Sample Grouping of Primary Care Physicians.** [The purpose of this pilot study was to examine four groups of primary care physicians' knowledge of sleep apnea. Methods: Using a 36-item questionnaire, we investigated how cognizant primary care physicians in Ontario, Canada, were of sleep apnea and its different symptoms. The questions covered incidence, diagnosis, treatment, and medical and social ramifications of sleep apnea. Sleep apnea surveys were administered to small groups of primary care physicians attending educational conferences or were distributed by mail to physicians who had previously referred patients to the sleep clinic. Results: A total of 151 physicians responded to the survey. An overall average score of 69% was obtained on the questionnaire. Conclusions: This score suggests that the physicians sampled in this pilot study are relatively underinformed about the clinical features and medical and social ramifications associated with sleep apnea.] Chung SA, Jairam S, et al. *Sleep and Breathing*, Vol.5, No.3, p.115-121.  
<http://www.springerlink.com/content/2bnlj4k5kb2gyp4j?p=c73069b7c5224d7095fb86ea65c2b5e3&pi=2>
8. **Knowledge, Opinions, and Clinical Experience of General Practice Dentists toward Obstructive Sleep Apnea and Oral Appliances.** [Undiagnosed obstructive sleep apnea (OSA) can contribute to hypertension, cardiovascular disease, stroke, and detract from overall quality of life. Dentists can play an important role in detecting, making recommendations for, and treating OSA with oral appliances (OAs). A survey of 18 questions of knowledge and opinion of, educational background for, and clinical experience with OSA and OAs was mailed to 500 general practice dentists in Indiana, United States. Two hundred survey returns produced 192 valid responses. Responders reported strong positive opinions toward OSA and OAs. However, 58% of dentists could not identify common signs and symptoms of OSA, and 55% of dentists did not know the mechanism for mandibular advance devices. Only 39% of dentists could identify snoring, mild OSA, and intolerance to continuous positive airway pressure as possible indications for OA treatment. Respondents reported a general lack of education about both OSA and OAs. Only 31 (16%) were taught about this issue in dental school; 77 (40%) knew little or nothing about OA treatment for OSA patients; 57 (30%) learned from postgraduate training. Cooperation and referrals between dentists and physicians were rated as "poor." Of the responders, 54% never consulted with physicians for a suspected OSA patient in their practice; 75% of dentists reported they have never been referred patients by physicians; and 80% of dentists never or less than five times prescribed OAs to OSA patients. Results suggest a need for increased education and training regarding OSA and OAs in dental school, as well as increased cooperation between dentists and physicians for better patient care. ] Bian H. *Sleep and Breathing*, vol. 8, No. 2, p.85-90.  
<http://www.springerlink.com/content/araq729er7x43q3y?p=491d42edd652406ba1c930b99226ed91&pi=2>

9. **Oral Appliance Therapy: The value of Dental Expertise.** [Oral appliances for the treatment of snoring and obstructive sleep apnea (OSA) have become an accepted therapeutic modality. Many medical providers involved in the diagnosis and treatment of this disorder have neglected the importance of involving a trained dentist and a dental facility in the process of providing treatment. The purpose is to point out the potential for unexpected dental conditions and avoidance of medical and legal complications encountered in a relatively straightforward clinical encounter for the fitting and construction of an oral appliance.] Strauss AM. *Sleep and Breathing, Vol.5, No.1, p.43-45.*  
<http://www.springerlink.com/content/lr1qd9awkqg06a8l/fulltext.pdf>

## **Diagnosis and Prevalence**

10. **A cephalometric and electromyographic study of upper airway structures in the upright and supine positions.** [Obstructive sleep apnea (OSA) is characterized by recurrent upper airway obstruction during sleep, usually in the supine position. To investigate the relationship between upper airway size and genioglossus (GG) muscle activity, upright and supine cephalograms were obtained in 20 OSA patients and 10 symptom-free control subjects. Tongue electromyographic (EMG) recordings were obtained with surface electrodes, and pressure transducers were placed in the 10 symptom-free controls. The tongue cross-sectional area increased 4.3% ( $p < 0.05$ ), and the oropharyngeal area decreased 36.5% ( $p < 0.01$ ) when the OSA patients changed their body position from upright to supine. No changes were observed in the tongue area, but soft palate thickness increased ( $p < 0.01$ ) when the control subjects changed from the upright to the supine position. Furthermore, the oropharyngeal cross-sectional area decreased 28.8% ( $p < 0.01$ ) despite a 34% increase ( $p < 0.05$ ) in resting GG EMG activity. Posterior tongue pressure increased 17% ( $p < 0.05$ ) with the change from upright to supine. On the basis of these findings, we propose that body posture has a substantial effect on upper airway structure and muscle activity. This postural effect should be taken into account when assessing upper airway size in the erect posture (conventional cephalography) and in the supine position (computed tomography). The vertical and anteroposterior position of the tongue and its relationship to airway size may be more important than soft palate size in the pathogenesis of OSA.] Pae EK, Lowe AA, et.al., University of British Columbia, Department of Clinical Dental Sciences, Vancouver, Canada. *Am J Orthod Dentofacial Orthop.* 1994 Jul; 106(1):52-9.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed&cmd=Retrieve&list\\_uids=8017350&Dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed&cmd=Retrieve&list_uids=8017350&Dopt=Citation)
11. **A community study of snoring and sleep-disordered breathing. Health outcomes.** [This report concerns the association between observed sleep-disordered breathing (SDB) and arterial hypertension and vascular disease. There were significant increases in the prevalence of hypertension, coronary artery disease, and occlusive vascular disease from nonsnorers, through snorers to subjects with SDB.] Olson LG, King MT, et.al., *Am. J. Respir. Crit. Care Med.*, Vol 152, No. 2, 08 1995, 717-720.  
[http://ajrccm.atsjournals.org/cgi/content/abstract/152/2/717?ijkey=8c28f378f9c5bbf26de94c3f6a1d6221f79acfaf&keytype=tf\\_ipsecsha](http://ajrccm.atsjournals.org/cgi/content/abstract/152/2/717?ijkey=8c28f378f9c5bbf26de94c3f6a1d6221f79acfaf&keytype=tf_ipsecsha)
12. **Diagnosis of obstructive sleep apnea syndrome.** (Article in Polish) [Symptoms and signs in 12 patients with severe obstructive sleep apnea (OSA) syndrome have been presented. The most common symptoms were snoring, increased motor activity during sleep and excessive daytime somnolence. The factors predisposing to OSA syndrome were obesity and anatomic

abnormalities of the upper airway structure. In some cases the signs of OSA syndrome included hypertension, right heart failure, chronic alveolar hypoventilation and polycythemia. Polysomnography showed sleep fragmentation and the prevalence of light sleep stages.] Brzecka A, Zukowska H, et.al, *Pol Tyg Lek.* 1992 Aug 18-31;47(34-35):722-5.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=1488356&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1488356&dopt=Abstract)

13. **Effects of age on sleep apnea in men: I. Prevalence and severity.** [The study shows that the prevalence of sleep apnea tends to increase with age but that the clinical significance (severity) of apnea decreases. On the basis of these findings, the sleep laboratory criteria used for diagnosis of sleep apnea should be adjusted for age.] Bixler EO, Vgontzas AN, *Am J Respir Crit Care Med.* 1998 Jan;157(1):144-8.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list\\_uids=9445292&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=9445292&dopt=Abstract)

14. **Health care utilization in the 10 years prior to diagnosis in obstructive sleep apnea syndrome patients.** [We conclude that by the time patients are finally diagnosed for sleep apnea, they have already been heavy users of health services for several years. It is possible that our findings reflect not OSAS per se, but the presence of some of the risk factors that predispose to OSAS, such as obesity, alcohol usage and perhaps tobacco consumption.] Ronald J, Delaive K, et.al., *Sleep.* 1999 Mar 15;22(2):225-9.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list\\_uids=10201067&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=10201067&dopt=Abstract)

15. **Higher Prevalence of Smoking in Patients Diagnosed as Having Obstructive Sleep Apnea.** [Nightly nicotine withdrawal as well as other respiratory and pulmonary effects of smoking may result in sleep-disordered breathing, especially obstructive sleep apnea (OSA). We hypothesize that there is higher prevalence of smoking in patients with OSA. We also hypothesize that smoking is an independent risk factor for OSA. The aim of this study is to determine whether there is a higher prevalence of smoking in patients with OSA compared with patients who do not have OSA. ...Adjusted for BMI, gender, age, and number of alcoholic drinks per week, former smokers were not more likely than never smokers to have OSA (odds ratio = 1.2, CI = 0.55–2.7, p = 0.64). We conclude that cigarette smoke may be an independent risk factor for OSA in this referral population.] Kashyap R, Hock LM, et al. *Sleep and Breathing, Vol.5, No.4, p.167-172.*

<http://www.springerlink.com/content/hhlq4j7tcj94v2b5/?p=e512b0829c4945449f3b741de968fb3b&pi=0>

16. **Increased Incidence of Cardiovascular Disease in Middle-aged Men with Obstructive Sleep Apnea.** [The incidence of a cardiovascular disease (CVD) was explored in a consecutive sleep clinic cohort of 182 middle-aged men (mean age, 46.8 ± 9.3; range, 30–69 years in 1991) with or without obstructive sleep apnea (OSA). All subjects were free of hypertension or other CVD, pulmonary disease, diabetes mellitus, psychiatric disorder, alcohol dependency, as well as malignancy at baseline. Data were collected via the Swedish Hospital Discharge Register covering a 7-year period before December 31, 1998, as well as questionnaires. Effectiveness of OSA treatment initiated during the period as well as age, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP) at baseline, and smoking habits were controlled. The incidence of at least one CVD was observed in 22 of 60 (36.7%) cases with OSA (overnight oxygen desaturations of 30 or more) compared with in 8 of 122 (6.6%) subjects without OSA (p < 0.001). In a multiple logistic

regression model, significant predictors of CVD incidence were OSA at baseline (odds ratio [OR] 4.9; 95% confidence interval [CI], 1.8–13.6) and age (OR 23.4; 95% CI, 2.7–197.5) after adjustment for BMI, SBP, and DBP at baseline. In the OSA group, CVD incidence was observed in 21 of 37 (56.8%) incompletely treated cases compared with in 1 of 15 (6.7%) efficiently treated subjects ( $p < 0.001$ ). In a multiple regression analysis, efficient treatment was associated with a significant risk reduction for CVD incidence (OR 0.1; 95% CI, 0.0–0.7) after adjustment for age and SBP at baseline in the OSA subjects. We conclude that the risk of developing CVD is increased in middle-aged OSA subjects independently of age, BMI, SBP, DBP, and smoking. Furthermore, efficient treatment of OSA reduces the excess CVD risk and may be considered also in relatively mild OSA without regard to daytime sleepiness.] Peker Y, Hedner J, et al. *American Journal of Respiratory and Critical Care Medicine* Vol 166. pp. 159-165, (2002).

<http://ajrccm.atsjournals.org/cgi/content/full/166/2/159> .

17.

18. **Obstructive Sleep Apnea Syndrome.** [OSAS is caused by an increased propensity for upper airway collapse during sleep. Much of the airway is supported by a bony or cartilaginous framework, but the dual function of the pharynx as both a conduit for deglutition and ventilation necessitates that its walls be muscular and thus compliant and collapsible. During inspiration, negative pressure is generated within the airway by the action of the respiratory muscles. Air flow is governed by the Bernoulli principle and the Venturi effect. The Bernoulli principle states that a column of air flowing through a conduit produces a partial vacuum or negative pressure at the margins of the column. This negative pressure increases as the rate of flow increases. The Venturi effect describes the acceleration of flow as a current of air or liquid enters a narrowed passage. These forces act upon the pharyngeal walls during inspiration to promote collapse of the airway. Obstructive sleep apnea syndrome is not only a disease that presents with symptomatology that is troubling to the patient and their family, but has severe complications which may be life-threatening. Despite new insight into the causes of the syndrome, treatment modalities remain suboptimal. Non-surgical treatments are limited by poor patient compliance, while surgical procedures have variable outcomes. Proper patient selection and long-term follow up may increase the effectiveness of the therapies and decrease the morbidity and mortality associated with the syndrome.] Stroud RH, Quinn FB, et al., Dept. of Otolaryngology, UTMB, Galveston, TX February 4, 1998. <http://www.utmb.edu/otoref/Grnds/OSA-980204/OSA-980204.htm>

19. **Obstructive Sleep Apnea Syndrome: Diagnosis and Management.** [Increased awareness that changes in sleeping habits and daytime behaviour may be attributable to obstructive sleep apnea syndrome (OSAS) has led many patients to seek both information and definitive treatment. The purpose of this article is to provide information to dentists that will enable them to identify patients who may have OSAS and to assist these patients in making informed decisions regarding treatment options. In patients who have identifiable anatomic abnormalities of the maxilla and mandible resulting in a narrow pharyngeal airway, orthognathic surgery appears to be an excellent treatment option. OSAS is a common condition associated with significant morbidity and mortality. It is therefore important that dental professionals be aware of the signs and symptoms of OSAS, so that the diagnosis can be confirmed and treatment initiated as soon as possible. As knowledge about the pathophysiology of OSAS improves, treatments may be designed to address the specific causes of the condition. In patients with identifiable anatomic abnormalities of the maxilla

and mandible resulting in a narrow pharyngeal airway, orthognathic surgery appears to be an excellent treatment option.] Goodday, RH, Precious DS, et.al. *Can Dent Assoc* 2001;67(11):652-8. <http://www.cda-adc.ca/jcda/vol-67/issue-11/652.html>

20. **Obstructive Sleep Apnea-Hypopnea and Related Clinical Features in a Population-based Sample of Subjects Aged 30 to 70 Yr.** [Apnea-Hypopnea Index AHI was associated with hypertension after adjusting for age, sex, body mass index, neck circumference, alcohol use, and smoking habit. This study adds evidence for a link between OSAH and hypertension.] Santiago JD, Esnaola S, et.al., *Am. J. Respir. Crit. Care Med.*, Volume 163, Number 3, March 2001, 685-689. [http://ajrccm.atsjournals.org/cgi/content/abstract/163/3/685?ijkey=02807714d1773ba16223a3bd0177591ee2684e3a&keytype2=tf\\_ipsecsha](http://ajrccm.atsjournals.org/cgi/content/abstract/163/3/685?ijkey=02807714d1773ba16223a3bd0177591ee2684e3a&keytype2=tf_ipsecsha)
21. **Periodic breathing and hypoxia in snorers and controls: validation of snoring history and association with blood pressure and obesity.** [In multivariate regression analysis, the hypoxic events were explained by obesity and apneic events. The diastolic blood pressure level was best explained by obesity, but not hypoxic or apneic events or snoring history.] Telakivi T, Partinen M, et.al., *Acta Neurol Scand.* 1987 Jul;76(1):69-75. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list\\_uids=3630648&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=3630648&dopt=Abstract)
22. **Predictors and prevalence of obstructive sleep apnoea and snoring in 1001 middle aged men.** [This study shows that snoring in this randomly selected population correlates best with neck size, smoking, and nasal stuffiness. Obstructive sleep apnoea, defined by nocturnal hypoxaemia, correlates best with neck size and alcohol, and less so with age and general obesity.] Stradling JR, Crosby JH, *Thorax*, Vol 46, 85-90. [http://thorax.bmjournals.com/cgi/content/abstract/46/2/85?ijkey=3ca55d3fcc72b165a55db44995273d7c5b5fc58&keytype2=tf\\_ipsecsha](http://thorax.bmjournals.com/cgi/content/abstract/46/2/85?ijkey=3ca55d3fcc72b165a55db44995273d7c5b5fc58&keytype2=tf_ipsecsha)
23. **Prevalence of concomitant sleep disorders in patients with obstructive sleep apnea.** [We determined the prevalence of concomitant sleep disorders in patients with a primary diagnosis of obstructive sleep apnea (OSA). ... We conclude that approximately one third of patients with sleep apnea have another identifiable sleep disorder, usually requiring treatment. This suggests that practitioners evaluating and treating sleep apnea ought to be prepared to deal with other sleep disorders as well. ] Scharf SM, Tubman A, et al. *Sleep and Breathing*, Vol. 9, No.2, p.50-56. <http://www.springerlink.com/content/h501104115467410?p=2e36b1fb445747e4952bfb3cb2b6b095&pi=1>
24. **Prevalence of sleep-disordered breathing in ages 40-64 years: a population-based survey.** [This survey indicates that sleep-disordered breathing is more common, especially among minorities, than had been previously believed, but less co-morbidity may be associated.] Kripke DF, Ancoli-Israel S, et.al., *Sleep*. 1997 Jan;20(1):65-76. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list\\_uids=9130337&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=9130337&dopt=Abstract)
25. **Prevalence of Sleep-disordered Breathing in Middle-aged Korean Men and Women.** [Logistic regression analyses showed that sex, body mass index, and hypertension were closely associated with the risk of SDB. Our findings show that SDB is a common problem in the Korean adult population. Understanding and treatment of SDB may be essential in terms of intervention to reduce the risk of related medical problems.] Kim J, In K, et.al., *American*

*Journal of Respiratory and Critical Care Medicine Vol 170. pp. 1108-1113, (2004).*  
<http://ajrccm.atsjournals.org/cgi/content/abstract/170/10/1108>

26. **Primary sleep apnoea syndrome.** [Polygraphic study in 18 men with the sleep apnoea syndrome showed central, upper airway obstructive, and mixed apnoeas. Fifty per cent of the total apnoea time was central, 33% was obstructive, and 17% was mixed. Apnoeic episodes were accompanied by oxygen desaturation, relative bradycardia and hypotonia of orofacial muscles innervated by ponto-medullary neurons. During regular breathing these muscles revealed tonic and phasic inspiratory EMG activities. The data suggest that the primary sleep apnoea syndrome results from a dysfunction of the central control of breathing.] Chokroverty S, Sharp JT, *J Neurol Neurosurg Psychiatry.* 1981 Nov;44(11):970-82.  
<http://jnnp.bmj.com/cgi/content/abstract/44/11/970>
27. **Public health and medicolegal implications of sleep apnoea.** [There is increasing evidence that sleep apnoea syndrome is associated with a considerable number of adverse sequelae, both behavioural and physical. Behavioural consequences include daytime sleepiness, impaired concentration and neuropsychological dysfunction, whereas physical consequences include cardiovascular disorders, particularly hypertension. Compared to the general population, OSAHS patients appear to have at least twice as much hypertension, ischemic heart disease and cerebrovascular disease. This population of patients has a high incidence of other co-existing cardiovascular risk factors such as obesity, hyperlipidaemia, increased age, male sex, smoking history and excessive alcohol intake, which makes the identification of a clear independent association of OSAHS with cardiovascular disease more difficult. A growing, but not yet conclusive, body of evidence points to an independent link between OSAHS and ischaemic heart disease, cardiac dysrhythmias and stroke.] McNicholas T, Krieger J et.al., *Eur Respir J* 2002; 20:1594-1609.  
<http://erj.ersjournals.com/cgi/content/full/20/6/1594>
28. **Relationship between sleepiness and general health status.** [Data suggest that 1) sleepiness has an important impact on general health and functional status, specifically influencing self-perceptions regarding energy/fatigue; 2) a more specific assessment of sleepiness in general health evaluations may help explain some of the observed variability in these measures across subjects; and 3) general health measures may be useful in the evaluations of patients with sleep disorders.] Briones B, Adams N, et.al. *Sleep.* 1996 Sep;19(7):583-8.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=8899938&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8899938&dopt=Citation)
29. **Sleep and Health Everywhere and in Both Directions.** [Sleep serves as an indicator of health and quality of life and therefore is highly and directly relevant to the practice of medicine. Indeed, numerous studies<sup>1-3</sup> have recently shown that sleep disorders are often comorbid with a broad range of medical and psychiatric conditions and also have a negative impact on health, mood, and quality of life. Increasing evidence also points to a bidirectional relationship between sleep and health; that is, sleep disturbances contribute to the development of or increase the severity of various medical and psychiatric disorders, and these same disorders result in poor sleep quality.] Zee P, *Arch Intern Med.* 2006;166:1686-1688. <http://archinte.ama-assn.org/cgi/content/extract/166/16/1686>
30. **Sleep apnea and mortality in an aged cohort.** [In the aged, sleep may be a vulnerable period for death from cardiovascular causes. Because of its high prevalence in the elderly, sleep apnea has been suggested to be one mechanism contributing to such sleep-related

mortality. "natural" death during sleep in the elderly may be associated with specific pathophysiological events during sleep.] Bliwise DL, Bliwise NG, et.al., *American Journal of Public Health*, Vol 78, Issue 5 544-547.

[http://www.ajph.org/cgi/content/abstract/78/5/544?ijkey=55374e74a851eec264c6369550aff6c8ba9b02e6&keytype2=tf\\_ipsecsha](http://www.ajph.org/cgi/content/abstract/78/5/544?ijkey=55374e74a851eec264c6369550aff6c8ba9b02e6&keytype2=tf_ipsecsha)

31. **Sleep apnea syndrome.** [Sleep apnea syndrome is estimated to affect as many as 2 to 3 percent of the adult male population. Excessive snoring and daytime sleepiness are but a few of the many clues to diagnosis. The hypoxemia occurring as a result of apnea may lead to pulmonary hypertension. Depressed respiratory center neural output or upper airway occlusion during sleep may cause the apnea. There are a number of treatment options available.] Waldhorn RE. *Am Fam Physician*. 1985 Sep;32(3):149-66.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=3898792&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3898792&dopt=Abstract)
32. **Sleep apnea, hypopnea and oxygen desaturation in normal subjects. A strong male predominance.** [Abnormal breathing and oxygen desaturation during sleep in subjects with chronic obstructive lung disease of the syndrome of hypersomnolence with periodic breathing may represent the superimposition of smoking or obesity on a normal tendency to snoring and oxygen desaturation in men.] Block AJ, Boysen PG, et.al. *NEJM* Vol 300:513-517, Mar 8, 1979 #10. <http://content.nejm.org/cgi/content/abstract/300/10/513>
33. **Sleep disordered breathing--a new component of syndrome x?** [Sleep disordered breathing (SDB) is a complication of obesity estimated to occur in about 4-6% of overweight individuals. These respiratory disturbances during sleep incorporate a number of conditions including snoring, upper airway resistance syndrome and obstructive sleep apnoea syndrome (OSAS). It is thought that as well as having deleterious effects on sleep quality these conditions may also promote cardiovascular and hormonal changes leading to an elevated blood pressure and an increased incidence of cardiovascular morbidity. Evidence reviewed here points to an alteration in sympathovagal balance, baroreceptor sensitivity, insulin resistance and leptin, growth hormone and lipid levels. Whether these changes are a consequence of the associated obesity or the SDB itself remains to be proven.] Coughlin S, Calverley P. et.al., *Obes Rev*. 2001 Nov;2(4):267-74.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?itool=abstractplus&db=pubmed&cmd=Retrieve&dopt=abstractplus&list\\_uids=12119997](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?itool=abstractplus&db=pubmed&cmd=Retrieve&dopt=abstractplus&list_uids=12119997)
34. **Snoring and breathing pauses during sleep: telephone interview survey of a United Kingdom population sample.** [Disordered breathing during sleep is widely underdiagnosed in the United Kingdom. The condition is linked to increased use of medical resources and a greater risk of daytime sleepiness, which augments the risk of accidents. Doctors should ask patients and bed partners regularly about snoring and breathing pauses during sleep.] Ohayon MM, Guilleminault C., et.al., *BMJ* 1997;314:860.  
[http://bmj.bmjournals.com/cgi/content/abstract/314/7084/860?ijkey=0e4016044bc1839bf01e76a408473c7c00b82a9&keytype2=tf\\_ipsecsha](http://bmj.bmjournals.com/cgi/content/abstract/314/7084/860?ijkey=0e4016044bc1839bf01e76a408473c7c00b82a9&keytype2=tf_ipsecsha)
35. **Snoring and obstructive sleep apnea.** [ ] Eckhart J, Veis R, et al. *J Cal Dent Assoc* 26:556-623, 1998.
36. **Snoring, hypertension, and the sleep apnea syndrome. An epidemiologic survey of middle-aged women.** [It is concluded that SAS is a relatively common occurrence among women, especially postmenopausal ones, and it is strongly related to hypertension.] Gislason T, Benediktsdottir B, et.al., *Chest*, Vol 103, 1147-1151,

[http://www.chestjournal.org/cgi/content/abstract/103/4/1147?ijkey=6da2aafa25d5c7419d22a8fd85aeab99b4426810&keytype2=tf\\_ipsecsha](http://www.chestjournal.org/cgi/content/abstract/103/4/1147?ijkey=6da2aafa25d5c7419d22a8fd85aeab99b4426810&keytype2=tf_ipsecsha)

37. **The Direct and Indirect Costs of Untreated Insomnia in Adults in the United States.** [Direct costs included inpatient, outpatient, pharmacy, and emergency room costs for all diseases, for six months before an index date. The index date for insomnia patients was the date of diagnosis with or the onset of prescription treatment for insomnia, sometime during July 1, 1999 — June 30, 2003. Non-insomnia patients were assigned the same index dates as the insomnia patients to whom they were matched. Indirect costs included costs related to absenteeism from work and the use of short-term disability programs. Propensity score matching was used to find insomnia and non-insomnia patients who had similar demographics, location, health plan type, comorbidities, and drug use patterns. Regression analyses controlled for factors that were different even after matching was completed. We found that average direct and indirect costs for younger adults with insomnia were about \$1,253 greater than for patients without insomnia. Among the elderly, direct costs were about \$1,143 greater for insomnia patients. Conclusions: Insomnia is associated with a significant economic burden for younger and older patients.] Ozminowski RJ, Wang S, et.al. *Journal SLEEP Volume 30/ Issue 3 - March 1, 2007.*  
<http://www.journalsleep.org/ViewAbstract.aspx?citationid=3163>
38. **The Effects of 53 Hours of Sleep Deprivation on Moral Judgment.** [These findings suggest that sleep deprivation impairs the ability to integrate emotion and cognition to guide moral judgments, although susceptibility to the effects of sleep loss on this ability is moderated by the level of emotional intelligence.] Killgore WDS, Killgore DB, et.al. *Journal SLEEP Volume 30/ Issue 3 - March 1, 2007.*  
<http://www.journalsleep.org/ViewAbstract.aspx?citationid=3172>
39. **The link between obstructive sleep apnea and heart failure: underappreciated opportunity for treatment.** [Obstructive sleep apnea (OSA) is a newly recognized risk factor for the development of systemic hypertension, ischemic heart disease and congestive heart failure. Mechanisms responsible for these links include OSA-related hypoxemia and arousal from sleep-induced increased sympathetic activity, large negative intrathoracic pressure-induced increased left ventricular transmural pressure gradient, and impaired vagal activity plus oxygen radial formation. Secondary phenomena include increased platelet aggregability, insulin resistance, and endothelial dysfunction with reduced endogenous nitric oxide production. Safe nonpharmacologic, nonsurgical therapy, namely continuous positive airway pressure, can attenuate OSA, and improve cardiac function and quality of life. Searching for signs or symptoms of OSA from the patient (or bed partner), namely loud habitual snoring, apneas, nocturnal choking, orthopnea, paroxysmal nocturnal dyspnea, excessive daytime sleepiness, or cardiovascular disease, which is difficult to control, may reward the curious physician with another treatment avenue.] Naughton MT. *Curr Cardiol Rep. 2005 May;7(3):211-5.*  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed&cmd=retrieve&dopt=abstract&list\\_uids=15865863](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed&cmd=retrieve&dopt=abstract&list_uids=15865863)
40. **The medical cost of undiagnosed sleep apnea.** [Obstructive sleep apnea is an under-diagnosed, but common disorder with serious adverse consequences. Regression analysis showed that the reciprocal of the apnea hypopnea index among cases was significantly related to log-transformed annual medical costs after adjusting for age, gender, and body mass index. We conclude that patients with undiagnosed sleep apnea had considerably higher

medical costs than age and sex matched individuals and that the severity of sleep-disordered breathing was associated with the magnitude of medical costs. Using available data on the prevalence of undiagnosed moderate to severe sleep apnea in middle-aged adults, we estimate that untreated sleep apnea may cause \$3.4 billion in additional medical costs in the U.S.] Kapur V, Blough DK, et.al., *Sleep*. 1999 Sep 15;22(6):749-55.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list\\_uids=10505820&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=10505820&dopt=Abstract)

41. **The occurrence of sleep disordered breathing in middle-aged adults.** [The prevalence of undiagnosed sleep-disordered breathing is high among men and is much higher than previously suspected among women. Undiagnosed sleep-disordered breathing is associated with daytime hypersomnolence.] Young T, et al. *N Engl J Med* 328:1230-1235., 1993.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=PubMed&list\\_uids=8464434&dopt=medline](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=PubMed&list_uids=8464434&dopt=medline)
42. **The Prevalence, Cost Implications, and Management of Sleep Disorders: An Overview.** [The International Classification of Sleep Disorders distinguishes more than 80 different disorders, which can be effectively treated. Problems with falling asleep or daytime sleepiness affect approximately 35 to 40% of the U.S. adult population annually and are a significant cause of morbidity and mortality. However, the *prevalence, burden, and management* of sleep disorders are often ignored or overlooked by individuals and society in general. This leads to an underappreciation and undertreatment of sleep disorders, making this group of illnesses a serious health concern. Sleep medicine is a young discipline, and as such the full implications of treating sleep disorders and the extent of sleep-related problems are not well delineated. As a result of high prevalence, severe complications, and concomitant illnesses in untreated cases, the cost implications are immense. The costs can be direct, indirect, related, and intangible. However, relatively little has been published on the economic implications of sleep disorders. Economic analysis can help evaluate available resources to set priorities and maximize management strategies for cost control without sacrificing safety, efficacy, or effectiveness. There has been considerable evidence of the cost-effectiveness of treating patients with obstructive sleep apnea, especially considering its high prevalence, morbidity, mortality, and concomitant health care consumption. We review the economic balance sheet of sleep disorders and conclude that sleep medicine education (among general population and health care professionals) and the availability of diagnostic and therapeutic facilities to treat sleep disorders will reduce ] Hossain J, Shapiro CM. *Sleep and Breathing*, Vol. 6, No.2, p.85-102.  
<http://www.springerlink.com/content/2baqhpubql1ml8qu/?p=1f5a83aa94b34ae5b1b5edabc637fc28&pi=4>
43. **The sleep hypopnea syndrome.** [We have observed patients who clinically have the obstructive sleep apnea syndrome but have no apneas, instead having recurrent nocturnal hypoventilation. There is disagreement about the definition and significance of such sleep-related hypopneas. Patients with recurrent hypopneas were clinically indistinguishable from and had a similar frequency of 4% desaturations and arousals to the patients with frequent apneas. This study confirms that hypopneas are clinically important and that the "sleep apnea syndrome" may occur in the absence of recurrent apneas.] Gould GA, Whyte KF, *Am Rev Respir Dis*. 1988 Apr;137(4):895-8.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list\\_uids=3354998&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=3354998&dopt=Abstract)

44. **Underdiagnosis of Sleep Apnea Syndrome in U.S. Communities.** [We hypothesize that clinical recognition rates for obstructive sleep apnea-hypoapnea syndrome (OSAHS) are influenced by comorbidity and demographic factors. ... We conclude that disparities (especially in women and in those with lower BMI) exist between current recognition rates for OSAHS and the estimated prevalence by symptom report across the United States.] Kapur V, Strohl KP, et al. *Sleep and Breathing, Vol.6, No.2, p.49-54.*  
<http://www.springerlink.com/content/2dpm6w631gwjxryy/?p=1f5a83aa94b34ae5b1b5edabc637fc28&pi=0>
45. **What Is a Necessary Knowledge Base for Sleep Professionals?** [Sleep medicine is multidisciplinary, and sleep medicine professionals should be trained to evaluate and treat all 88 sleep disorders. Sleep medicine specialists require a fund of knowledge that goes beyond what is obtained during a pulmonary fellowship. Skills required for a pulmonary sleep professional include: sleep medicine, neurobiology, psychiatry, neuro-psychology, neurology, pediatrics, and even limited exposure in otolaryngology, oral maxillofacial surgery, and dentistry. There is a paucity of published information concerning curricular requirements. Required skills for a sleep professional include proficiency in the clinical skills of sleep medicine as well as the technical skills of polysomnography. There is a very large knowledge content area requirement in both the basic sciences of sleep and the clinical aspects of sleep medicine. There are also important clinical skills content areas. As with all medical professionals, sleep professionals should have the highest ethical standards and a strong sense of responsibility toward their patients. A sleep medicine professional also has to be knowledgeable about administrative and legal aspects specific to sleep medicine. This essay reviews a sleep professional knowledge base model with emphasis on the requirements for a pulmonary sleep professional.] Harding SM, Hawkins JW. *Sleep and Breathing, Vol.5, No.3, P.101-107.*  
<http://www.springerlink.com/content/y9kyakatq9fnfght/?p=c73069b7c5224d7095fb86ea65c2b5e3&pi=0>

## **Oral Appliance Therapy & Dental Sleep Medicine**

46. **A Case Study Involving the Combination Treatment of an Oral Appliance and Auto-Titrating CPAP Unit.** [Treating severe obstructive sleep apnea can be a challenge. In this case it necessitated combining treatments to obtain the desired result. Now that oral appliances are a viable treatment of obstructive sleep apnea, they can be combined with continuous positive airway pressure or surgery to give the physician and patient more options.] Denbar MA. *Sleep and Breathing, Vol. 6, No.3, p.125-128.*  
<http://www.springerlink.com/content/9xdbfthmg18wuhx1/?p=a282040b48ec45558916ff2e95d8162e&pi=3>
47. **A crossover study comparing the efficacy of continuous positive airway pressure with anterior mandibular positioning devices on patients with obstructive sleep apnea.** [The AMP device achieved substantial success in most cases, but was less effective than CPAP, especially for the more severe cases. In general, the AMP device was strongly preferred over the CPAP by the subjects of this study.] Clark G, et al. *Chest 109:144-83, 1996.*  
<http://www.chestjournal.org/cgi/content/abstract/109/6/1477?maxtoshow=&HITS=10&hits=>

[10&RESULTFORMAT=&author1=clark%2C+G&fulltext=sleep+apnea&searchid=1&FIRSTINDEX=0&sortspec=relevance&resourcetype=HWCIT](#)

48. **A mandibular advancement device for the ENT office to treat obstructive sleep apnea.** [OBJECTIVE: To prospectively evaluate the efficacy of the mandibular advancement device (MAD) Somnoguard in the treatment of OSA patients. STUDY DESIGN AND SETTING: Forty-four patients with OSA and noncompliant to continuous positive airway pressure were enrolled in this case series. Somnoguard is made of thermoplastic material. Direct intraoral fitting was done by an otorhinolaryngologist. Polysomnographic data concerning sleep and respiration were assessed at baseline and after familiarization with the MAD. ...CONCLUSION AND SIGNIFICANCE: With Somnoguard 68% of the enrolled OSA patients could be cured or substantially improved. It is a simple MAD for the otolaryngologist.] Maurer JT, Huber K, et al. *Otolaryngol Head Neck Surg* 2007;136(2):231-5. <http://www.websciences.org/cftemplate/NAPS/archives/indiv.cfm?ID=20065042>
49. **A modified functional appliance for treatment obstructive sleep apnea.** [ ] George P. *J Clin Orthod* 21:171-175, 1987.. [www.jco-online.com](http://www.jco-online.com)
50. **A Prospective Randomized Study Comparing Two Different Degrees of Mandibular Advancement with a Dental Appliance in Treatment of Severe Obstructive Sleep Apnea.** [The objective of this study was to compare the effect of two different degrees of mandibular advancement (MA), 75% versus 50%, on somnographic variables after 6 months of dental appliance treatment in patients with severe obstructive sleep apnea (OSA). A further purpose was to compare the number of adverse events on the stomatognathic system and the effects of dental appliance treatment on the presence of daytime sleepiness. ... No significant difference was observed between the two groups. The results indicate that a dental appliance could be an alternative treatment for some patients with severe OSA. ] Walker-Engstrom ML, Ringqvist I, et al. *Sleep and Breathing, Vol.7, No.3, p.119-130.* <http://www.springerlink.com/content/cyretfm983phu8m9/?p=83cbec7cc4454ae4923f49acbd b8fc76&pi=3>
51. **A prospective randomized study of a dental appliance compared with uvulopalatopharyngoplasty in the treatment of obstructive sleep apnea.** [The enthusiasm for uvulopalatopharyngoplasty (UPPP) in the treatment of obstructive sleep apnoea (OSA) has declined in recent years, partly because of a lower success rate over time and partly because of adverse effects. Reports on the beneficial effects of dental appliances exist, but only one prospective randomized study has been published comparing dental appliances with nasal continuous positive airway pressure (CPAP) treatment. No study has been published comparing dental appliance treatment with UPPP. ... These findings suggest that the dental appliance technique is useful in the treatment of mild to moderate OSA. ] Wilhelmsson B, et al. *Acta Otolaryngol* 119:503-09, 1999. <http://www.informaworld.com/smpp/content~content=a713791936~db=all>
52. **A prospective study evaluating the effectiveness of a mandibular repositioning appliance (PM Positioner) for the treatment of moderate obstructive sleep apnea.** [ ] Parker J, et al. *Sleep* 22 (Suppl 1):S230-31, 1999. [www.journalsleep.org](http://www.journalsleep.org)
53. **A randomized crossover study of an oral appliance vs nasal-continuous airway pressure in the treatment of mild-moderate obstructive sleep apnea.** [We conclude that OA is an effective treatment in some patients with mild-moderate OSA and is associated with fewer side effects and greater patient satisfaction than N-CPAP.] Ferguson KA, Ono T, et al. *Chest* 109:1269-1275. <http://www.chestjournal.org/cgi/content/abstract/109/5/1269>

54. **A short-term controlled trial of an adjustable oral appliance for the treatment of mild to moderate obstructive sleep apnoea.** [Anterior mandibular positioner is an effective treatment in some patients with mild to moderate OSA and is associated with greater patient satisfaction than nasal CPAP. ] Ferguson KA, Ono T, et al. *Thorax* 52:362-368. <http://thorax.bmj.com/cgi/reprint/52/4/362.pdf>
55. **An individually adjustable oral appliance vs continuous positive airway pressure in mild-to-moderate obstructive sleep apnea syndrome.** [For the treatment of nonsevere obstructive sleep apnea syndrome (OSAS), mandibular advancement devices (MADs) are employed as an alternative to nasal continuous positive airway pressure (CPAP) therapy. Even in patients with mild-to-moderate OSAS, CPAP is the more effective long-term treatment modality. In the individual case, the better compliance seen with the intraoral sleep apnea device (ISAD) may be advantageous.] Randerath WJ, Heise M, et al. *Chest*. 2002;122:569-575. <http://www.chestjournal.org/cgi/content/abstract/122/2/569>
56. **An oral elastic mandibular advancement device for obstructive sleep apnea.** [Oral mandibular advancement devices are becoming an increasingly important treatment alternative for obstructive sleep apnea. The first aim of the study was to determine whether a new oral elastic mandibular advancement device (EMA) prevents pharyngeal airway closure during sleep in patients with OSA. The second aim of the study was to determine if the polysomnographic response to the oral mandibular advancement device was dependent on the site of airway closure. Overnight polysomnograms were performed in 28 untreated OSA subjects with and without EMA. A third polysomnogram was performed in 12 of the subjects to determine the site of airway closure without the device. Site of airway closure above or below the oropharynx was determined by measuring the respective presence or absence of respiratory fluctuations in oropharyngeal pressure during induced occlusions in non-rapid eye movement (NREM) sleep. Nineteen subjects (68%) had at least a 50% reduction in AHI with the device. The change in AHI with the device (AHI without device – AHI with device) was directly related to the AHI without the device. All three subjects with airway closure in the lower pharyngeal airway had a greater than 80% reduction in AHI with the device. Two of the nine subjects with airway closure in the velopharynx had a similar therapeutic response. The results show the effectiveness of EMA in the treatment of OSA. The results also indicate that polysomnographic severity of OSA and the site of airway closure should not be used to exclude patients from this oral device treatment.] Henke KG, Frantz DE, et al. *Am J Respir Crit Care Med* 161:420-425, 2000. <http://ajrcm.atsjournals.org/cgi/content/abstract/161/2/420>
57. **Cephalometric evaluation of pharynx, soft palate, adenoid tissue, tongue, and hyoid bone following the use of a mandibular repositioning appliance in obstructive sleep apnea patients.** [The aim of this study was to evaluate the pharynx, soft palate, adenoid tissue, tongue, and hyoid bone when a mandibular repositioning appliance was used for managing patients with obstructive sleep apnea. Lateral cephalograms of 45 adult obstructive sleep apnea patients from the Lancaster Cleft Palate Clinic were taken without the appliance and some days later with the device in the mouth. This device was used during sleep for improving patients' respiration. Twenty-four cephalometric variables were evaluated. When the appliance was in the mouth, significant alterations ( $P < .001$ ) were observed in the distances: (a) between anterior and posterior pharyngeal walls at the level of the second and third cervical vertebrae, respectively; (b) between the most superior point of the tongue and the maxillary plane; and (c) between the hyoid bone and the mandibular plane, ramus plane,

cervical vertebrae tangent, mandibular symphysis, gonion, and third and fourth cervical vertebrae. The results of this study indicate that significant changes in pharyngeal space, hyoid bone, and tongue positions take place in obstructive sleep apnea patients when a mandibular repositioning device is used.] Athanasiou AE, Papadopoulos MA, et.al., School of Dentistry, Department of Orthodontics, Aristotle University of Thessaloniki, Greece. *Int J Adult Orthodon Orthognath Surg.* 1994;9(4):273-83.

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58. **Comparison of two dental devices for treatment of obstructive sleep apnea syndrome (OSAS).** [We conclude that a dental device that advances the mandible and increases the vertical dimension to open the upper airway is more effective in reducing the number of apneic and snoring events during sleep than one which does not.] Hans M, et al. *Am j Orthod Dentofac orthop* 111:562-570, 1997.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9155816&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9155816&dopt=Citation)
59. **Dental and skeletal changes after 4 years of obstructive sleep apnea treatment with a mandibular advancement device: a prospective, randomized study.** [The aim of this prospective, randomized study was to analyze dental and skeletal side effects after 4 years of treating obstructive sleep apnea (OSA) patients with a mandibular advancement device (MAD) compared with uvulopalatopharyngoplasty (UPPP). ... Treatment of OSA with a dental appliance is probably a lifelong process, and long-term follow-up studies should therefore be undertaken to control both the treatment effect on OSA and the side effects on the masticatory system.] Ringqvist M, Walker-Engstrom JL, et.al. *Am J Orthod Dentofacial Orthop.* 2003 Jul;124(1):53-60.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=12867898&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12867898&dopt=Abstract)
60. **Dental appliances for the treatment of obstructive sleep apnea.** [Obstructive sleep apnea (OSA) is a syndrome in which the airflow created from breathing ceases through the upper airway although diaphragm movement continues. Resulting complications include severe daytime sleepiness, morning headaches, loud snoring, and disturbed nighttime sleep. Patients affected with OSA are frequently hypertensive and can have dangerous cardiac arrhythmias. The diagnosis of OSA requires an all-night polysomnographic recording; neither snoring nor other subjective complaints constitute adequate criteria for treatment. The treatment objective for OSA is to maintain airway patency. A potential treatment discussed here is temporary advancement of the mandible or tongue during sleep with the use of dental appliances.] Clark G, et al. *JADA* 118:611-619, 1989. <http://jada.ada.org/cgi/content/abstract/118/5/611>
61. **Dental considerations in upper airway sleep disorders: a review of the literature.** [Upper airway sleep disorders are becoming recognized as common medical concerns. Multiple treatment options have been advocated, including the use of dental devices. Dental practitioners are being asked by the medical profession to become a part of the treatment team. This may be a challenging task because of the large number of dental devices available, rapid advancement in the understanding of this disease, and numerous publications... Dental devices are indicated in snoring and mild-to-moderate obstructive sleep apnea patients after medical evaluation and referral.] Ivanhoe J, et al. *J Prosthet Dent* 82:685-98, 1999.  
<http://www2.us.elsevierhealth.com/scripts/om/dll/serve?action=searchDB&searchDBfor=ho>

[me&id=pr8,](#)

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=10588805&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10588805&dopt=Abstract)

62. **Dental side effects of an oral device to treat snoring and obstructive sleep apnea.** [Dental side effects occur in a significant proportion of patients using the MAS. In most cases these are minor and their importance must be balanced against the efficacy of the MAS in treating snoring and OSA.] Pantin C, et al. *Sleep* 22:237-40, 1999. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=10201069&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10201069&dopt=Citation)
63. **Diagnosing and co-managing patients with obstructive sleep apnea syndrome.** [Dentists cognizant of these signs and symptoms have an opportunity to diagnose patients with occult OSAS. After confirmation of the diagnosis by a physician, dentists can participate in management of the disorder by fabricating mandibular advancement appliances and performing surgical procedures that prevent recurrent airway obstruction. Obstructive sleep apnea syndrome, or OSAS, is typified by the periodic collapse of the upper airway during sleep and results in absent airflow (apnea) or diminished airflow (hypopnea) into the lungs despite persistent inspiratory effort. These episodes occur most frequently during rapid eye movement sleep when the geniohyoid, genioglossus and tensor veli palatini muscles—all of which usually dilate the upper airway—lose their tone. Obstruction of the airway follows as the negative pressure of inspiration draws the tongue, epiglottis and soft palate posteriorly against the pharyngeal walls. An epidemiologic study conducted in the United States estimated that 2 percent of women and 4 percent of men have OSAS. The problem is even more common among obese people, with 40 percent of men and 3 percent of women having the disorder.<sup>2</sup> Daytime sleepiness resulting from OSAS leads to auto- and work-related accidents, which cost the nation more than \$41 billion each year in medical care costs and lost productivity.] Friedlander AH, Walker LA, et al. *J Am Dent Assoc* 131(8):1178-4, Aug. 2000. <http://jada.ada.org/cgi/content/full/131/8/1178>
64. **Does two years nocturnal treatment with a mandibular advancement splint in adult patients with snoring and OSAS cause a change in the posture of the mandible?** [The aim of this pilot study was to investigate the effects of 2 years' nocturnal treatment with a mandibular advancement splint in adult patients with snoring and obstructive sleep apnea syndrome with respect to possible development of a forward position of the mandible or other dentofacial changes. ...None of the patients reported any permanent sense of altered occlusion, and the anteroposterior distance between habitual occlusion (intercuspal position) and centric relation (retruded position) did not exceed 1.0 mm in any of the patients either before or after the treatment. The change in mandibular position might be a result of a condylar and/or glenoid fossa remodeling or condylar position changes within the fossa as a compensatory reaction to the advancement of the mandible (bite jumping).] Bondemark I. *Am J Orthod Dentofac Orthop* 116:621-28, 1999. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=10587595&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10587595&dopt=Abstract)
65. **Effect of a prosthetic appliance for treatment of sleep apnea syndrome on masticatory and tongue muscle activity.** [This study examined the effect of the device on sleep apnea, and masticatory and tongue muscles. The apnea appliance activated masticatory and tongue muscles during sleep and prevented the upper airway from collapsing. The prosthetic appliance was useful in the treatment of sleep apnea syndrome.] Yoshida K. Department of

Oral and Maxillofacial Surgery, Faculty of Medicine, Kyoto University, Japan.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9597607&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9597607&dopt=Abstract)

66. **Effect of anterior mandibular position on obstructive sleep apnea.** [ ] Clark G, et al. *Am Rev Respir Dis* 147:624-629, 1993. [www.ajrccm.org](http://www.ajrccm.org)
67. **Effect of jaw position and posture on forced inspiratory airflow in normal subjects and patients with obstructive sleep apnea.** [These data document that when a patient is in a supine position, a 100% protrusive jaw position allows significantly more inspiratory airflow to occur.] Masumi S, Nishigawa K, et.al. *Chest*, Vol 109, 1484-1489. <http://www.chestjournal.org/cgi/content/abstract/109/6/1484?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&author1=clark%2C+G&fulltext=sleep+apnea&searchid=1&FIRSTINDEX=0&sortspec=relevance&resourcetype=HWCIT>
68. **Effect of a non-adjustable oral appliance on upper airway morphology in obstructive sleep apnoea.** [ BACKGROUND: To evaluate the effect of oral appliance (OA) on upper airway morphology and its relationship with treatment response in subjects with obstructive sleep apnoea (OSA). METHODS: Symptomatic OSA subjects were recruited. Non-adjustable OA was custom made. Variables examined at baseline and while wearing the device at 2 months included polysomnographic data, computed tomographic measurements of upper airway cross sectional area at level of velopharynx (VA) and hypopharynx (HA), upper airway volume, and cephalometric parameters. Treatment outcome was based on post-treatment apnoea-hypopnoea index (AHI). ... CONCLUSIONS: OA altered upper airway morphometry towards a profile consistent with decreased propensity to collapse, which may thus have contributed to improvement of OSA.] Sam K, Lam B, et.al. *Respir Med* 2006;100(5):897-902. <http://www.websciences.org/cftemplate/NAPS/archives/indiv.cfm?ID=20065150>
69. **Effect of the external nasal dilator Breathe Right on snoring.** [This clinical trial was designed to evaluate the efficacy of the external nasal dilator Breathe Right (nasal strip) on snoring. The assessment of snoring intensity and duration as well as the sleep quality without the Breathe Right nasal strip and after application was performed in 30 out-patients with primary habitual snoring. An all-night polysomnographic investigation including registration of a 17-channel EEG, EMG, respiration parameters such as breathing efforts and nasal/oral air flow, snoring vibrations, ECG, oxygen saturation, etc. was conducted in the sleep laboratory...Breathe Right is a safe and easily applied noninvasive method to reduce the maximum snoring intensity, especially in habitual mild snorers.] Todorova A, Schellenberg R, et al. *Eur J Med Res*. 1998 Aug 18;3(8):367-79. [http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=PubMed&list\\_uids=9707518&dopt=Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=PubMed&list_uids=9707518&dopt=Abstract)
70. **Effect of vertical dimension on efficacy of oral appliance therapy in obstructive sleep apnea.** [The aim of this study was to assess the effect of bite opening induced by a mandibular advancement splint (MAS) on efficacy and side effects in the treatment of obstructive sleep apnea. This study suggests that the amount of bite opening induced by MAS does not have a significant impact on treatment efficacy but does have an impact on patient acceptance.] Pitsis AJ, Darendeliler MA, et al. *Am J Respir Crit Care Med* 166:860-864. <http://ajrccm.atsjournals.org/cgi/content/abstract/166/6/860>
71. **Effects of a mandibular advancement device for the treatment of sleep apnea syndrome and snoring on respiratory function and sleep quality.** [In this study the fabrication of a

simplified mandibular advancement device for sleep apnea syndrome was described. Its effect on respiratory function and sleep quality variables was evaluated polysomnographically in 256 patients with sleep apnea syndrome and snoring. Polysomnographic recordings were performed twice, before and after insertion of the oral appliance. The mean apneahypopnea index (AHI) decreased significantly ( $p < 0.0001$ ) with the appliance to 18.2 from 43.2 without it. Responders defined by  $AHI < 10$  were 54% and those defined as a 50% decrease of AHI were 66%. Oxygen saturation, duration of apnea, sleep efficiency, and total arousal were improved significantly after treatment without major side effects. The device improved significantly the respiratory function and sleep quality in patients with sleep apnea syndrome. Compliance was about 90% followed for 2.5 years. This appliance offers some advantages over other therapies because it is noninvasive, easy to fabricate, and well accepted by patients.] Yoshida K. *J Craino Pract* 18:98-105, 2000.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=11202830&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11202830&dopt=Abstract)

72. **Effects of a Mandibular Protruding Device on the Sleep of Patients with Obstructive Sleep Apnea and Snoring Problems: A 2-Year Follow-Up.** [Objectives: To evaluate subjective discomfort and somnographic measures of patients with obstructive sleep apnea and snoring problems who had been treated for 2 years with a mandibular protruding device (MPD). ... Conclusion: MPD treatment is associated with a significant reduction in subjective complaints such as disturbing snoring, apneas, daytime tiredness, and poor quality of night sleep, and with a significant reduction in ODI values in the OSA group. In addition, favorable 6-month results were unchanged after 2 years. ] Fransson AMC, Tegelbert A, et al. *Sleep and Breathing*, Vol.7, No.3, p.131-141.  
<http://www.springerlink.com/content/wlgr35gl803jgk2n/?p=83cbec7cc4454ae4923f49acbdb8fc76&pi=4>
73. **Effects of a prosthetic appliance for the treatment of sleep apnea syndrome on masticatory and tongue muscle activity.** [The apnea appliance activated masticatory and tongue muscles during sleep and prevented the upper airway from collapsing. The prosthetic appliance was useful in the treatment of sleep apnea syndrome.] Yoshida K. *J Prosthet Dent* 79:537-44, 1998.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9597607&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9597607&dopt=Citation)
74. **Effects of Mandibular Posture on Obstructive Sleep Apnea Severity and the Temporomandibular Joint in Patients Fitted with an Oral Appliance.** [The purposes of this study were to assess the relationship between different increments of mandibular protrusion and a reduction of obstructive sleep apnea (OSA) severity and to use magnetic resonance imaging to assess temporomandibular joint (TMJ) morphology and condyle position after the insertion of an oral appliance (OA). Sequential polysomnographic studies facilitate OA titration. OA effects on the AHI seem to be dose-dependent on the amount of mandibular protrusion, and the OA proved over the period of one year to be innocuous for TMJ in the treatment of patients with OSA.] de Almeida FR, Bittencourt LR, et al. *SLEEP* 2002;25:507-13 <http://www.journalsleep.org/ViewAbstract.aspx?citationid=2140>
75. **Efficacy and comorbidity of oral appliances in the treatment of obstructive sleep apnea-hypopnea: a systematic review and preliminary results of a randomized trial.** [The obstructive sleep apnea-hypopnea syndrome (OSAHS) is a common sleep-related breathing disorder characterized by repetitive obstructions of the upper airway during sleep. The

modification of pharyngeal patency by oral appliance therapy has been suggested as an alternative to various treatment modalities for OSAHS. To determine the evidence base with respect to the efficacy and comorbidity of the oral appliance therapy in OSAHS, a systematic review of the available literature was conducted. In addition, the preliminary results of a randomized parallel trial are reported on the effectiveness and specific indication of, respectively, the oral appliance and continuous positive airways pressure therapy in OSAHS. ...oral appliance therapy is a viable treatment for, especially, mild to moderate OSAHS. ... Treatment with oral appliance and CPAP therapy was effective in, respectively, 77 and 83% of the included patients. Although CPAP is usually more effective than oral appliance therapy, results from the present study suggest that oral appliance and CPAP therapy are competitive in a substantial proportion of OSAHS patients.] Hoekema A. *Sleep Breath* (2006) 10:102-103. <http://www.springerlink.com/content/7773mq1806350685/fulltext.pdf>

76. **Evaluation of variable mandibular advancement appliance for treatment of snoring and sleep apnea.** [The role of oral appliances for treatment of nonapneic snoring and sleep apnea is currently being assessed. Most patients with sleep apnea are being offered nasal continuous positive airway pressure (CPAP) as the treatment of choice. However, compliance with nasal CPAP varies, and is particularly poor in nonapneic snorers and those with mild sleep apnea; this group of patients is notorious for poor acceptance of CPAP. That is why oral appliances constitute an attractive noninvasive alternative for patients with sleep apnea, provided the efficacy, compliance, long-term tolerance, and satisfaction with these appliances are established. Adjustable mandibular positioning appliance is an effective treatment alternative for some patients with snoring and sleep apnea.] Prancer J, et al. *Chest* 116:1511-1518, 1999. <http://www.chestjournal.org/cgi/content/full/116/6/1511> ;
77. **Four-Year Follow-up of Treatment With Dental Appliance or Uvulopalatopharyngoplasty in Patients With Obstructive Sleep Apnea.** [The dental-appliance group showed significantly higher success and normalization rates regarding the somnographic variables compared to the UPPP group, but the effectiveness of the dental appliance was partly invalidated by the compliance of 62% at the 4-year follow-up. However, the appliances had few adverse effects on the stomatognathic system and required only moderate adjustments. Use of a dental appliance with regular follow-up can be recommended for long-term treatment of OSA.] Walker-Engstrom M, Tegelberg A, et.al. *Chest*. 2002;121:739-746. <http://www.chestjournal.org/cgi/content/abstract/121/3/739>
78. **Mandibular advancement and obstructive sleep apnoea: a method for determining effective mandibular protrusion.** [The objectives of the study were to test the hypotheses that it is possible, during routine polysomnography (PSG), to prospectively identify favourable candidates for mandibular repositioning appliance (MRA) therapy in the treatment of obstructive sleep apnoea (OSA) and to accurately estimate an optimal protrusive distance at which to fabricate the MRA. ...In conclusion the remotely controlled mandibular positioner test outcome demonstrated a statistically significant association with mandibular repositioning appliance outcome. The target protrusion determined during the remotely controlled mandibular positioner test was the effective therapeutic protrusion in subjects with a successful remotely controlled mandibular positioner test.] Dort LC, Hadjuk E, et.al. *Eur Respir J* 2006; 27:1003-1009. <http://erj.ersjournals.com/cgi/content/abstract/27/5/1003>
79. **Mandibular advancement appliances and obstructive sleep apnoea: a randomized clinical trial.** [This randomized placebo-controlled cross-over trial assessed the effectiveness of a mandibular advancement appliance (MAA) in managing obstructive sleep apnoea

(OSA). When wearing the MAA, 35 per cent of the OSA subjects had a reduction in the pre-treatment ODI to 10 or less, while 33 per cent had an AHI of 10 or less. The MAA was less effective in the subjects with the most severe OSA (pre-treatment ODI > 50 and/or pre-treatment AHI > 50).] Johnston CD, Gleadhill IC, et al. *Eur J Orthod* 24:251-262. <http://ejo.oxfordjournals.org/cgi/content/abstract/24/3/251>

80. **Mandibular advancement devices and sleep disordered breathing.** [Overall, these data suggest that MADs should be carefully fabricated by dentists who work on a referral basis with sleep medicine physicians and patients using MADs must be monitored regularly for ongoing efficacy and for associated complications. The good news (with good data support for this conclusion) is that MAD's are a moderately effective treatment of snoring and mild to moderate OSA.] Clark G. *Sleep Med Rev* 2:163:174, 1998. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=15310499&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15310499&dopt=Citation)
81. **Mandibular advancement oral appliance therapy for obstructive sleep apnoea: effect on awake calibre of the velopharynx.** [The mechanisms of action of oral appliance therapy in obstructive sleep apnoea are poorly understood. Videoendoscopy of the upper airway was used during wakefulness to examine whether the changes in pharyngeal dimensions produced by a mandibular advancement oral appliance are related to the improvement in the severity of obstructive sleep apnoea. Following insertion of the oral appliance the reduction in AHI was related to the increase in cross sectional area of the velopharynx. A mandibular advancement oral appliance increases the cross sectional area of the upper airway during wakefulness, particularly in the velopharynx. Assuming this effect on upper airway calibre is not eliminated by sleep, mandibular advancement oral appliances may reduce the severity of obstructive sleep apnoea by maintaining patency of the velopharynx, particularly in its lateral dimension.] Ryan CF, Love LL, et al. *Thorax* 1999;54:972-977. <http://thorax.bmj.com/cgi/content/abstract/54/11/972>
82. **Nasal dilator strip therapy for chronic sleep-maintenance insomnia and symptoms of sleep-disordered breathing: a randomized controlled trial.** [To test the impact of nasal dilator strips (NDSs) on insomnia severity, sleep-disordered breathing (SDB) symptoms, sleep quality, and quality of life. Randomized, controlled trial of 4 weeks' duration. ...SDB education and NDSs demonstrated therapeutic efficacy in a select sample of insomnia patients with SDB symptoms. Replication of results requires placebo controls and objectively confirmed SDB cases.]. Krakow B, Melendrez D, et al. *Sleep and Breathing*, Vol.10, No.1, p.16-28, march 2006. <http://www.springerlink.com/content/t23w5n4071w47338/?p=11acb9090938418bad9a3108b40f4121&pi=4>
83. **Obstructive Sleep Apnea Patients with the Oral Appliance Experience Pharyngeal Size and Shape Changes in Three Dimensions.** [Pharyngeal size and shape differences between pre- and post trials of a mandible-protruding oral appliance were investigated using cine computerized tomography (CT). the cross-sectional area of these levels appeared to increase significantly ( $P < .05$ ) with the appliance in place during wakefulness. The oral appliance appears to enlarge the pharynx to a greater degree in the lateral than in the sagittal plane at the retropalatal and retroglossal levels of the pharynx, suggesting a mechanism for the effectiveness of oral appliances that protrude the mandible.] Kyung, SH, Park YC, et al. *The Angle Orthodontist: Vol. 75, No. 1, pp. 15–22.* <http://www.angle.org/pdfserv/i0003-3219-075-01-0015.pdf>

84. **Obstructive sleep apnea: oral appliance therapy and the severity of condition.** [Oral appliances have commonly been recommended only for mild obstructive sleep apnea. This study indicates that they may also have a role to play in selected cases in which the condition is more severe. There is a paucity of information about long-term success. This short-term (2-week) study should be followed by others evaluating the effect over longer periods.] Cohen R. *Oral Surg Oral Med Oral Path* 85:388-93, 1998.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9574946&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9574946&dopt=Citation)
85. **One-Night Mandibular Advancement Titration for Obstructive Sleep Apnea Syndrome.** [The efficacy of a DA can be evaluated during a single night of polysomnography.] Petelle B, Vincent G, et.al. *Am. J. Respir. Crit. Care Med.*, Volume 165, Number 8, April 2002, 1150-1153. <http://ajrcm.atsjournals.org/cgi/content/full/165/8/1150>
86. **Oral appliance therapy for the management of sleep disordered breathing: an overview.** [A burgeoning new arena in healthcare has opened to dental professionals with the potential to relieve the suffering of millions of people worldwide. Qualified dentists are increasingly being called upon to interface with the medical profession in an effort to manage the unstable upper airway during sleep. What has come to be called "oral appliance therapy" (OAT) involves the coordinated efforts of sleep physicians and the newly recognized sleep disorders dentist.] Rogers R. *Sleep and Breathing* 4 (2):79-84, 2000.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=11868123&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11868123&dopt=Abstract)
87. **Oral Appliance Therapy for Obstructive Sleep Apnea Syndrome: Progressive Mandibular Advancement During Polysomnography.** [Six patients diagnosed with obstructive sleep apnea completed titration of an adjustable oral appliance, called the Silencer, during a single night of polysomnography. This protocol allowed for rapid titration of the oral appliance and effective treatment of sleep apnea. Variables which showed improvement included frequency of obstructive events, oxyhemoglobin saturation and snoring. Dental appliance adjustments with the silencer device can be made within three minutes. We have demonstrated that incremental mandibular advancement and repositioning allow us to determine the most effective jaw position to treat sleep apnea and snoring, which is also most likely to be tolerated by the patient.]. Raphaelson MA, Alpher EJ, et al. *Cranio*. 1998 Jan;16(1):44-50.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9481985&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9481985&dopt=Abstract)
88. **Oral appliance therapy improves symptoms in obstructive sleep apnea: a randomized, controlled trial.** [The aim of this study was to evaluate the effect of a mandibular advancement splint (MAS) on daytime sleepiness and a range of other symptoms in obstructive sleep apnea (OSA). Other OSA symptoms were controlled in significantly more patients with the MAS than with the control device. MAS therapy improves a range of symptoms associated with OSA.] Gotsopoulos H, Chen C, et al. *Am j Respir Crit Care Med* 166:743-748. <http://ajrcm.atsjournals.org/cgi/content/abstract/166/5/743>
89. **Oral appliances for snoring and obstructive sleep apnea: A review.** [An evidence-based review of literature regarding use of oral appliance (OAs) in the treatment of snoring and obstructive sleep apnea syndrome from 1995 to present. ... The mechanism of OA therapy is related to opening of the upper airway as demonstrated by imaging and physiologic monitoring. Treatment adherence is variable with patients reporting using the appliance a

median of 77% of nights at 1 year. Minor adverse effects were frequent whereas major adverse effects were uncommon. In comparison to CPAP, OAs are less efficacious in reducing the apnea hypopnea index, but OAs appear to be used more, and in many studies were preferred over CPAP when the treatments were compared.] Ferguson KA, Cartwright R, et al. *Sleep* Vol.29, No.2, 244-262, 2006.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=16494093&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=16494093&dopt=Abstract)

90. **Oral Appliances for Snoring and Obstructive Sleep Apnea: A Review.** [We conducted an evidence-based review of literature regarding use of oral appliances (OAs) in the treatment of snoring and obstructive sleep apnea syndrome (OSA) from 1995 until the present. Our structured search revealed 141 articles for systematic scrutiny, of which 87 were suitable for inclusion in the evidence base, including 15 Level I to II randomized controlled trials and 5 of these trials with placebo-controlled treatment. The efficacy of OAs was established for controlling OSA in some but not all patients with success (defined as no more than 10 apneas or hypopneas per hour of sleep) achieved in an average of 52% of treated patients. Effects on sleepiness and quality of life were also demonstrated, but improvements in other neurocognitive outcomes were not consistent. The mechanism of OA therapy is related to opening of the upper airway as demonstrated by imaging and physiologic monitoring. Treatment adherence is variable with patients reporting using the appliance a median of 77% of nights at 1 year. Minor adverse effects were frequent whereas major adverse effects were uncommon. Minor tooth movement and small changes in the occlusion developed in some patients after prolonged use, but the long-term dental significance of this is uncertain. In comparison to continuous positive airway pressure (CPAP), OAs are less efficacious in reducing the apnea hypopnea index (AHI), but OAs appear to be used more (at least by self report), and in many studies were preferred over CPAP when the treatments were compared. OAs have also been compared favorably to surgical modification of the upper airway (uvulopalatopharyngoplasty, UPPP). Comparisons between OAs of different designs have produced variable findings. The literature of OA therapy for OSA now provides better evidence for the efficacy of this treatment modality and considerable guidance regarding the frequency of adverse effects and the indications for use in comparison to CPAP and UPPP.] Ferguson KA, Cartwright R, et al. *SLEEP* 2006;29(2): 244-262.

<http://www.journalsleep.org/ViewAbstract.aspx?citationid=2862>

91. **Oral appliances for the treatment of snoring and sleep apnea: a review.** [This paper, which has been reviewed and approved by the Board of Directors of the American Sleep Disorders Association, provides the background for the Standards of Practice Committee's parameters for the practice of sleep medicine in North America. The 21 publications selected for this review describe 320 patients treated with oral appliances for snoring and obstructive sleep apnea. The appliances modify the upper airway by changing the posture of the mandible and tongue. Despite considerable variation in the design of these appliances, the clinical effects are remarkably consistent. Snoring is improved and often eliminated in almost all patients who use oral appliances. Obstructive sleep apnea improves in the majority of patients; the mean apnea-hypopnea index (AHI) in this group of patients was reduced from 47 to 19. Approximately half of treated patients achieved an AHI of < 10; however, as many as 40% of those treated were left with significantly elevated AHIs. Improvement in sleep quality and sleepiness reflects the effect on breathing. Limited follow-up data indicate that oral discomfort is a common but tolerable side effect, that dental and mandibular

complications appear to be uncommon and that long-term compliance varies from 50% to 100% of patients. Comparison of the risk and benefit of oral appliance therapy with the other available treatments suggests that oral appliances present a useful alternative to continuous positive airway pressure (CPAP), especially for patients with simple snoring and patients with obstructive sleep apnea who cannot tolerate CPAP therapy. ] Schmidt-Nowara W, Lowe A, et al. *Sleep* 18(6):511-513, 1995.

<http://www.journalsleep.org/ViewAbstract.aspx?citationid=780>

92. **Oral appliances in the treatment of snoring and sleep apnea.** [Oral appliances have been developed that are effective in snoring patients and in patients with mild to moderate sleep apnea. This article reviews the types of appliances that are available, their possible modes of action, and their efficacy. In addition, the clinician is provided with guidelines on how to choose the appropriate patient for this therapy.] Millman r, et al. *Clin Chest Med* 19:69-75, 1998.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9554218&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9554218&dopt=Abstract)
93. **Oral Appliance Therapy for Obstructive Sleep Apnea - Finally Evidence You Can Sink Your Teeth Into.** [This study provides confirmation of the efficacy of adjustable mandibular positioner therapy in some patients with OSA. They had good results in patients with more significant OSA (AHI  $\geq$ 40) and many patients elected to continue on with MAS therapy as they had a good symptomatic response. Subjective response to the MAS was clearly superior to the objective response (reduction in AHI). The study suggests that the mechanism of action of oral appliances is mandibular advancement because the presence of an intraoral device without advancement showed no clinical benefit.] Ferguson K. *Am. J. Respir. Crit. Care Med.*, Volume 163, Number 6, May 2001, 1294-1295.  
<http://ajrccm.atsjournals.org/cgi/content/full/163/6/1294>
94. **Predicting response to the tongue retaining device for sleep apnea syndrome.** [Factors associated with increased severity of sleep apnea; obesity, the supine sleep posture, and age, were tested for their association with the effectiveness of the Tongue Retaining Device (TRD). Patients with substantial worsening of apnea index while in the supine sleep position were more responsive to the TRD than those who were equally affected in both sleep positions.] Cartwright R. *Arch Otolaryngol* 111:385-388, 1985. <http://archotol.ama-assn.org/cgi/content/abstract/111/6/385>
95. **Prospective evaluation of an oral appliance in the treatment of obstructive sleep apnea syndrome.** [The purpose of this study was to investigate the effects of an oral appliance (OA), with and without mandible advance, in the treatment of obstructive sleep apnea syndrome (OSA). ... Oral appliances, especially those that advance the mandible, offer an effective treatment for OSA. ]Zamarron BC, Pazos MTA, et al. *Sleep and Breathing*, Vol.9, No.1, p.20-25.  
<http://www.springerlink.com/content/9f5epp9rqhcrytnw/?p=79557596914542ecb5d44b30cb4a7be2&pi=4>
96. **Prosthetic therapy for sleep apnea syndrome.** [The Esmarch appliance is indicated for the treatment or diagnosis of sleep apnea syndrome.] Yoshida K, et al. *J Prosthet Dent* 72:296-302, 1994.  
<http://www2.us.elsevierhealth.com/scripts/om.dll/serve?action=searchDB&searchDBfor=home&id=pr>

97. **Randomized Crossover Trial of Two Treatments for Sleep Apnea/Hypopnea Syndrome.** [Mandibular repositioning splints (MRSs) and continuous positive airway pressure (CPAP) are used to treat the sleep apnea/hypopnea syndrome (SAHS). There are some data suggesting that patients with milder symptoms prefer MRS, but there are few comparative data on outcomes. Therefore, we performed a randomized crossover trial of 8 weeks of CPAP and 8 weeks of MRS treatment in consecutive new outpatients diagnosed with SAHS (apnea/hypopnea index [AHI]  $\geq 5$ /hour, and  $\geq 2$  symptoms including sleepiness). Assessments at the end of both limbs comprised home sleep study, subjective ratings of treatment value, sleepiness, symptoms, and well-being, and objective tests of sleepiness and cognition. Forty-eight of 51 recruited patients completed the trial (12 women; age [mean  $\pm$  SD],  $46 \pm 9$  years; Epworth  $14 \pm 4$ ; median AHI, 22/hour; interquartile ratio [IQR], 11–43/hour). Significant ( $p < 0.01$ ) differences between MRS and CPAP were observed for 7 of 21 variables (effect sizes, 0.3–0.6 SDs), all favoring CPAP, including AHI ( $15 \pm 16$  and  $8 \pm 6$ /hour, respectively), effectiveness rating, symptoms, Epworth ( $12 \pm 5$  and  $8 \pm 5$ , respectively), functional outcomes of sleepiness questionnaire, short-form 36 health survey mental component, and health transition scores. Objective sleepiness, cognitive performance, and preference for treatments were not different. In patients experiencing a mild form of the syndrome (AHI  $< 15$ ,  $n = 18$ ), symptoms, treatment efficacy and satisfaction, and subjective sleepiness were also better with CPAP than with MRS (effect sizes, 0.7–1.1 SDs). These results do not support these MRS devices as first-line treatment for sleepy patients with SAHS.] Engleman HM, McDonald JP, et al. <http://ajrccm.atsjournals.org/cgi/content/abstract/166/6/855>
98. **Randomised study of three non-surgical treatments in mild to moderate obstructive sleep apnoea.** [Patients with mild to moderate obstructive sleep apnoea (OSA) may be managed with different treatment options. This study compared the effectiveness of three commonly used non-surgical treatment modalities. ... CPAP produced the best improvement in terms of physiological, symptomatic and HRQOL measures, while the oral appliance was slightly less effective. Weight loss, if achieved, resulted in an improvement in sleep parameters, but weight control alone was not uniformly effective.] Lam B, Sam K, et al. *Thorax* 2007;62:354-359. <http://thorax.bmj.com/cgi/content/full/62/4/354>
99. **Recent developments in oral appliance therapy of sleep disordered breathing.** [Oral appliances are increasingly gaining a place in the treatment of sleep disordered breathing caused by upper airway obstruction. This review of publications since 1995 documents substantial progress in the scientific basis for this therapy. Imaging by several techniques has shown that mandibular advancing oral appliances open the airway in awake and anaesthetized subjects, creating the presumption that this effect is maintained in sleep. Three controlled cross-over treatment trials have shown that patients consistently prefer oral appliance over continuous positive airway pressure therapy, especially when the treatment effect is strong. Appliance design and use indicates a preference for adjustable mandibular advancing appliances. Complications of therapy appear to be infrequent, but evidence for safety of long-term use is still limited. Oral appliance therapy can be an effective therapy for sleep disorders caused by upper airway obstruction. Considering the accumulated evidence, it is no longer tenable to label oral appliance therapy an experimental procedure.] Schmidt-Nowara W. *Sleep and Breathing* 3(3):103-06, 1999. <http://www.springerlink.com/content/4cgbh2ptxbfgugt/>
100. **Review of oral appliances for treatment of sleep-disordered breathing.** [Between 1982 and 2006, there were 89 distinct publications dealing with oral appliance therapy

involving a total of 3,027 patients, which reported results of sleep studies performed with and without the appliance. These studies, which constitute a very heterogeneous group in terms of methodology and patient population, are reviewed and the results summarized. This review focused on the following outcomes: sleep apnea (i.e. reduction in the apnea/hypopnea index or respiratory disturbance index), ability of oral appliances to reduce snoring, effect of oral appliances on daytime function, comparison of oral appliances with other treatments (continuous positive airway pressure and surgery), side effects, dental changes (overbite and overjet), and long-term compliance. We found that the success rate, defined as the ability of the oral appliances to reduce apnea/hypopnea index to less than 10, is 54%. The response rate, defined as at least 50% reduction in the initial apnea/hypopnea index (although it still remained above 10), is 21%. When only the results of randomized, crossover, placebo-controlled studies are considered, the success and response rates are 50% and 14%, respectively. Snoring was reduced by 45%. In the studies comparing oral appliances to continuous positive airway pressure (CPAP) or to uvulopalatopharyngoplasty (UPPP), an appliance reduced initial AHI by 42%, CPAP reduced it by 75%, and UPPP by 30%. The majority of patients prefer using oral appliance than CPAP. Use of oral appliances improves daytime function somewhat; the Epworth sleepiness score (ESS) dropped from 11.2 to 7.8 in 854 patients. A summary of the follow-up compliance data shows that at 30 months, 56–68% of patients continue to use oral appliance. Side effects are relatively minor but frequent. The most common ones are excessive salivation and teeth discomfort. Efficacy and side effects depend on the type of appliance, degree of protrusion, vertical opening, and other settings. We conclude that oral appliances, although not as effective as CPAP in reducing sleep apnea, snoring, and improving daytime function, have a definite role in the treatment of snoring and sleep apnea.] Hoffstein V. *Sleep and Breathing Vol.11, Number 1 / March, 2007.*

<http://www.springerlink.com/content/j4w6r21256314131/>

101. **Sleep disordered breathing: orthodontics and sleep disorders dentistry.** Spiegel EP, Krahe JA. *Funct Orthod.* 2004 Winter-2005 Spring;22(1):24-32.
102. **Sleep disorders and oral devices.** [Many patients with upper airway sleep disorders can be successfully treated with oral appliance therapy. It is necessary for dentists to recognize these patients and refer them to a physician for further evaluation. Dentists must not become the primary care providers for these patients or attempt to treat a medical problem with an oral appliance without a proper diagnosis, which usually requires a sleep study and can only be diagnosed by a physician. Dentists must also be able to treat the patients referred by physicians and to follow accepted procedures when fabricating, inserting, titrating, and providing follow-up care for oral appliance therapy. In addition, the dental community needs to continue to heighten the awareness in their local medical community and in their patient population as to the possible contribution of oral appliance therapy to the management of snoring and some of the sleep-related breathing disorders.] Ivanhoe JR, Attanasio R. *Dent Clin North Am.* 2001 Oct;45(4):733-58.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?itool=abstractplus&db=pubmed&cmd=Retrieve&dopt=abstractplus&list\\_uids=11699239](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?itool=abstractplus&db=pubmed&cmd=Retrieve&dopt=abstractplus&list_uids=11699239)
103. **Snoring and obstructive sleep apnea: treatment with oral appliances.** [ ] Parker J. *Northwest Dentistry* 74:17-25, 1995. [www.mndental.org](http://www.mndental.org)
104. **The anterior mandibular positioning device for the treatment of obstructive sleep apnea syndrome: experience with the Serenox.** [Anterior mandibular positioning devices are seldom used at present in the treatment of obstructive sleep apnoea syndrome (OSAS).

The aim of our study was to evaluate the efficiency, the side-effects and the patient compliance with one type of device made in Switzerland, the Serenox. This device is designed to keep the mouth closed with the mandible forward, avoiding the vibration of the soft palate. ...In conclusion, 87% (13/15) of the patients were treated successfully. Indications for the use of a mandibular positioning device include snoring, upper airway resistance syndrome and light to mild OSAS without severe obesity. ] Pellanda A, et al. *Clin Otolaryngol* 24:134-41, 1999.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=10225160&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10225160&dopt=Citation)

105. **The effect of a modified functional appliance on obstructive sleep apnea.** [Six cephalometric measurements are presented to provide a means of assessing effects of the appliance on the oropharynx and associated structures. The modified functional appliance is a conservative, successful treatment alternative that could benefit patients with obstructive sleep apnea syndrome. ] Bonham P, et al. *Am J Orthod Dentofac Orthop* 94:384-392, 1988. <http://www2.us.elsevierhealth.com/scripts/om.dll/serve?action=searchDB&searchDBfor=home&id=od;>  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=3189241&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3189241&dopt=Abstract)
106. **The effect of anterior mandibular positioning on apneas and sleep in patients with obstructive sleep apnea.** [A mandibular advancement device reduces apneas and improves sleep quality in patients with obstructive sleep apnea, especially in those with mild and moderate disease. A follow-up sleep recording during treatment is necessary because of the risk of silent obstructive apneas without subjective snoring with the device.] Marklund M, et al. *Chest* 113:707-713, 1998. <http://www.chestjournal.org/cgi/content/abstract/113/3/707>
107. **The effect of the tongue retaining device on awake genioglossus muscle activity in patients with obstructive sleep apnea.** [Knowledge of how dental appliances alter upper airway muscle activity when they are used for the treatment of snoring and/or obstructive sleep apnea (OSA) is very limited. The purpose of this study was to define the effect of a tongue retaining device (TRD) on awake genioglossus (GG) muscle activity in 10 adult subjects with OSA and in 6 age and body mass index (BMI) matched symptom-free control subjects. The TRD is a custom-made appliance designed to allow the tongue to remain in a forward position between the anterior teeth by holding the tongue in an anterior bulb with negative pressure, during sleep. This pulls the tongue forward to enlarge the volume of the upper airway and to reduce upper airway resistance. It was concluded that the TRD has different effects on the awake GG muscle activity in control subjects and patients with OSA. The resultant change in the anatomic configuration of the upper airway caused by the TRD may be important in the treatment of OSA because such a change may alleviate the impaired upper airway function.] Ono, T, Lowe AA, et.al., Department of Clinical Dental Sciences, The Faculty of Dentistry, The University of British Columbia, Vancouver, B.C., Canada. *Am J Orthod Dentofacial Orthop.* 1996 Jul;110(1):28-35  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=8686675&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8686675&dopt=Citation)
108. **The effects of a non-surgical treatment for obstructive sleep apnea: the tongue retaining device.** [The tongue-retaining device (TRD) was designed to increase the unobstructed dimension of the nasal breathing passage during sleep. ... There was significantly improved sleep and significantly fewer and shorter apneic events on all nights

when the device was worn. On the first night of wearing the TRD for a half night only, there was a significant reduction in the number of obstructive and central apneic episodes. The mean apnea plus hypopnea index while wearing the TRD is comparable with the rate reported for patients who have been treated surgically by either tracheostomy or by uvulopalatopharyngoplasty, although the tracheostomy group contained more severe cases.] Cartwright R, Samelson C. *JAMA* 248:705-709, 1982. <http://jama.ama-assn.org/cgi/content/abstract/248/6/705>

109. **The effect of oral appliance therapy on blood pressure in patients with obstructive sleep apnea.** [The objective of the study was to investigate the effects of oral appliance (OA) therapy on ambulatory blood pressure in patients with obstructive sleep apnea (OSA). ... This study suggests that successful OSA treatment with an OA may also be beneficial to lower blood pressure in OSA patients, as previously suggested for nasal continuous positive airway pressure therapy.] Otsuka R, de Almeida FR, et al. *Sleep and Breathing, Vol 10, No.1, p.29-36.* <http://www.springerlink.com/content/7676wq7392856514/?p=11acb9090938418bad9a3108b40f4121&pi=5>
110. **The Effect of Posture and a Mandibular Protruding Device on Pharyngeal Dimensions: A Cephalometric Study.** [The objectives were to evaluate the impact of body posture on cephalometric measures and the level and the extent to which treatment with a mandibular protruding device (MPD) affects pharyngeal width. ... We conclude that the MPD significantly increased most pharyngeal measures except the linear distance between the hyoid bone and the third vertebra and decreased the area of the velum.] Fransson AMC, Svenson BAH, et al. *Sleep and Breathing, Vol. 6, No.2, p. 55-68.* <http://www.springerlink.com/content/c5h7cj5hhvpr2dl8/?p=1f5a83aa94b34ae5b1b5edabc637fc28&pi=1>
111. **The efficacy of a Herbst mandibular advancement device in obstructive sleep apnea.** [Treatment options for obstructive sleep apnea (OSA) may involve potential side effects or discomfort; nasal continuous positive airway pressure (CPAP) may not be tolerated by 25% of patients. We therefore sought to determine the efficacy of mandibular advancement as a treatment for OSA, and to investigate whether clinical and radiographic parameters can predict the response to this treatment. Comparison of pre- and post treatment cephalometric values revealed no significant change in the posterior airway space (PAS) despite a reduction in mean AHI. There was a significant decrease in the mandible-hyoid distance (MP-H) with treatment for the group as a whole. When the study population was evaluated on the basis of a successful response to mandibular advancement (post treatment AHI < 10), the baseline MP-H was found to be significantly shorter in the responders than in non responders. MP-H after mandibular advancement was likewise shorter in responders than in non responders. In addition, the soft palate length (PNS-P) showed a significantly greater shortening in responders after treatment.] Eveloff S, et al. *Am j Respir Crit Care Med* 149:905-909, 1994. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=8143054&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8143054&dopt=Abstract)
112. **The Efficacy of a Mandibular Advancement Splint in Relation to Cephalometric Variables.** [The efficacy of a titratable mandibular advancement splint (MAS) for the management of obstructive sleep apnea (OSA) was investigated in relation to supine cephalometric variables. ... We conclude that the MAS is an effective therapy for OSA and baseline HYML is an important predictor of improvement. Improvements in AHI may be

explained by the MAS maintaining the new or existing relationship of the hyoid and its surrounding structures, thus preventing obstruction in the upper airway during sleep.]

Skinner MA, Robertson CJ, et al. *Sleep and Breathing*, Vol.6, No.3, p.115-125.

<http://www.springerlink.com/content/j1vdpeu0mmmhg6b4/?p=a282040b48ec45558916ff2e95d8162e&pi=2>

113. **The efficacy of oral appliances in the treatment of persistent sleep apnea after uvulopalatopharyngoplasty.** [An adjustable oral appliance appears to be an effective mode of therapy to control OSA after an unsuccessful UPPP.] Millman R, et al. *Chest* 113:992-996, 1998. <http://www.chestjournal.org/cgi/reprint/113/4/992>
114. **The mandibular repositioning device: role in treatment of obstructive sleep apnea.** [This study suggests that the MRD is useful in the long-term treatment of patients with OSA of mild to moderate severity.] Menn S, et al. *Sleep* 19:794-800, [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9085488&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9085488&dopt=Abstract)
115. **The responsibility of the dental profession in recognizing and treating sleep breathing disorders.** [ ] Barsh L. *Compend Contin Educ Dent* 17:490-500m 1996.
116. **The role of oral appliances in treating obstructive sleep apnea.** [Dentists play an increasing role in managing the care of patients with sleep-related breathing disorders. With the advent of oral appliances, dentists are increasingly involved in managing the care of patients with sleep-related breathing disorders. Further studies are needed to determine the long-term complications of this type of intervention for the treatment of sleep-related breathing disorders.] Mohsenin N, Mostofi M, et.al. *J Am Dent Assoc*, Vol 134, No 4, 442-449. <http://jada.ada.org/cgi/content/full/134/4/442>
117. **The tongue retaining device and sleep state genioglossus muscle activity in patients with obstructive sleep apnea.** [The TRD reduces AH severity, normalizes the time lag, and counteracts fluctuating GG EMG activity.] Ono T, et al. *Angl Orthod* 66:273-279, 1996. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=8863962&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8863962&dopt=Citation)
118. **Titratable Oral Appliances for the Treatment of Snoring and Obstructive Sleep Apnea.** [The Klearway appliance is the most extensively researched appliance available today. It has been shown to effectively increase airway size, to be worn consistently and to have a significant effect on both snoring and OSA. The treatment of snoring and OSA can be a very exciting and rewarding part of any dental practice. Improving the quality of someone's life with an OA can significantly alter a practitioner's perspective on health care delivery. An international group of dentists with expertise in this area, the Sleep Disorders Dental Society, provides a newsletter, an annual meeting, a slide set and manual, and a library for member dentists. The Society also has a resource centre for use by both patients and dentists.] Lowe AA. *J Can Dent Assoc* 1999; 65:571-4. <http://www.cda-adc.ca/jcda/vol-65/issue-10/571.html>
119. **Toward a treatment logic for sleep apnea: the place of the tongue retaining device.** [ ] Cartwright R, et al. *Behav Res Ther* 26:121-126, 1988. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=3365202&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3365202&dopt=Citation)
120. **Treatment of sleep apnea with prosthetic mandibular advancement (PMA).** [Nine males with sleep apnea DOES syndrome and three males with sleep apnea DIMS syndrome were treated with prosthetic mandibular advancement (PMA). The method uses a prosthesis, which is designed to advance the mandible 3-5 mm to prevent upper airway occlusion during

sleep. The apnea index in the obstructive-type apnea and the percentage of time spent in obstructive apnea decreased significantly with PMA. Although the apnea index showed merely a tendency to decrease in central apnea ( $p < 0.1$ ), the percentage of time spent in central apnea decreased significantly with PMA. A marked improvement in sleep structures was observed with PMA; a significant increase was seen in total sleep time, percent slow wave sleep (SWS) and percent rapid eye movement (REM) sleep, and the time spent in intra-sleep awakening decreased remarkably. PMA had excellent effects on snoring, and daytime hypersomnolence was reduced in almost all patients.] Nakazawa Y, et al. *Sleep* 15:499-504, 1992.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=1475564&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1475564&dopt=Abstract)

121. **Treatment of Snoring and Obstructive Sleep Apnea with a Mandibular Protruding Device: An Open-Label Study.** [The study objectives were to describe the changes in signs and symptoms of obstructive sleep apnea (OSA) and snoring using a mandibular protruding device (MPD) and to define the group of responders. ...In conclusion, a 6-month perspective shows that the MPD could be an effective treatment in reducing signs and symptoms of OSA and/or snoring, the compliance was acceptable and only minor adverse events occurred.] Fransson AMC, Isacson G, et al. *Sleep and Breathing*, Vol.5, No.1, p.23-33. <http://www.springerlink.com/content/lvg1yf5rmqc78hpg/?p=d1348c60905348ff9d9644b1ef1d14bb&pi=3>
122. **Treatment of snoring and obstructive sleep apnea with dental orthosis.** [A dental orthosis, designed to increase the size of the upper airway by advancing the mandible, was used in 68 patients to treat snoring and varying degrees of obstructive sleep apnea. The orthosis increased the posterior airway space, as assessed by lateral cephalograms. Seven months (range 2 to 25) after beginning use, 75 percent of patients were using the orthosis regularly. Snoring, by report, was improved in all patients but one ( $p$  less than 0.001) and was eliminated in 42 percent (95 percent confidence interval 30 to 55 percent). Sleep quality and sleepiness were also reported improved. Apneas and hypopneas, measured before and after use in 20 patients with obstructive sleep apnea, were reduced from an average of 47 to 20 events per hour ( $p$  less than 0.001). Oxygenation and sleep disturbance were also improved. Apnea-hypopnea frequency was reduced with treatment to less than 20/h in 13 patients. Residual frequencies greater than 20/h were associated with higher initial frequencies of apneas and hypopneas. Side effects of orthosis use were minor, and no serious complications were observed. The dental orthosis is an effective treatment for the symptom of snoring and can also effectively treat obstructive sleep apnea of moderate severity.] Schmidt-Nowara W, et al. *Chest* 99:1378-1385, 1991. <http://www.chestjournal.org/cgi/content/abstract/99/6/1378>
123. **Treatment, airway and compliance effects of a titratable oral appliance for obstructive sleep apnea.** [The titratable adjustable mandibular advancement appliance, made from thermoelastic acrylic, significantly reduces RDI in moderate to severe OSA patients, has a direct effect on airway size and is well worn throughout the night.] Lowe A, et al. *Sleep* 23 (Suppl 3):S1-7, 2000. <http://cat.inist.fr/?aModele=afficheN&cpsidt=1414561>

## **Pathophysiology of OSA, Anatomy, Hypoxia-Inflammation, etc.**

124. **Activation of nuclear factor  $\kappa$ B in obstructive sleep apnea: a pathway leading to systemic inflammation.** [Apnea-induced hypoxia and reoxygenation, which generates reactive oxygen species, may activate the oxidant-sensitive, proinflammatory transcription

factor nuclear factor  $\kappa$ B (NF- $\kappa$ B), increasing systemic inflammation in obstructive sleep apnea. We measured NF- $\kappa$ B activity in circulating neutrophils and plasma levels of NF- $\kappa$ B-controlled gene products, soluble E (sE)-selectin and soluble vascular cell adhesion molecule-1 (sVCAM-1) in control subjects and in obstructive sleep apnea (OSA) patients. To confirm a causal link with OSA, we reassessed these parameters after nasal continuous positive airway pressure (CPAP) therapy. Twenty-two subjects undergoing evaluation for symptoms of sleep-disordered breathing were grouped by apnea hypopnea index: control, less than 5/h; mild to moderate OSA, 11–40/h; severe OSA, more than 40/h. A morning venous blood sample was obtained. Neutrophils were isolated, and NF- $\kappa$ B activity was determined by electrophoretic mobility shift assay. Plasma sE-selectin and sVCAM-1 were assayed by enzyme-linked immunosorbent assay. Neutrophils in mild to moderate and severe OSA patients showed 4.8- and 7.9-fold greater NF- $\kappa$ B binding activity compared with control subjects ( $p < 0.0001$ ). The degree of NF- $\kappa$ B activation was positively correlated with indices of apnea severity. In five severe OSA patients, 1 month of CPAP therapy decreased neutrophil NF- $\kappa$ B activation to control levels. sE-selectin and sVCAM concentrations were reduced by CPAP in four of these five subjects. OSA leads to NF- $\kappa$ B activation, which may constitute an important pathway] Htoo, AK, Greenberg H, et al. *Sleep and Breathing, Vol 10, No.1, p.43-50.*

<http://www.springerlink.com/content/v805310465670h68/?p=11acb9090938418bad9a3108b40f4121&pi=7>

125. **Anatomy of pharynx in patients with obstructive sleep apnea and in normal subjects.** [We conclude that the passive pharynx is more narrow and collapsible in sleep-apneic patients than in matched controls and that velopharyngeal Pc is the principal correlate of the frequency of nocturnal desaturations.] Isono S, et al. *Appl Physiol* 82:1319-1326, 1997.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9104871&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9104871&dopt=Abstract)

126. **Antioxidant capacity in obstructive sleep apnea patients.** [Obstructive sleep apnea syndrome (OSA) results in oxygen desaturation and arousal from sleep. Free oxygen radicals are highly reactive molecules, which can be produced by the OSA phenomenon known as hypoxia/reoxygenation. Hypoxic conditions, such as OSA, may also result in transient depletion of cellular reductants, which constitute a main line of antioxidant defense. Both apneas and hypopneas usually end in arousal, where reoxygenation causes the production of reactive oxygen species (free radicals). Living organisms have developed complex antioxidant systems to counteract reactive oxygen species and to reduce their damage. We evaluated the antioxidant capacity in serum from OSA patients and healthy people in order to confirm the hypothesis that there is a relationship between oxidative stress and OSA. Conclusions : Reduced antioxidant capacity in serum is an index of excessive oxidative stress. Patients with severe OSA have reduced values of antioxidant capacity.] Christou K, Moulas AN, et al. *Sleep Medicine, vol 4, Issue 3, Pp 225-228 (May2003).*

<http://www.sleep-journal.com/article/PIIS1389945702002538/abstract>

127. **Cephalometric evaluation of the upper airway in patients with complete dentures.** [Obstructive sleep apnea syndrome (OSAS) is a disorder characterized by repeated obstructions of the upper airway, with consequent episodes of apnea and hypopnea during sleep, snoring, and daytime sleepiness. Recently, a role of edentulism in the occurrence or in the worsening of this disorder was suspected. The aim of the study was to assess, through a

cephalometric analysis, if the removal of denture induces, and where, modifications that can favour the pharynx collapse. From the data obtained from the cephalometric analysis it seems that wearing denture induces modifications in the position of the tongue, of the jaw and of the pharyngeal airway space that can favour the reduction of apnea episodes.] Erovigni F, Graziano A, School of Dentistry and Prosthodontics, University of Turin Italy. *Minerva Stomatol.* 2005 May;54(5):293-301

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=15985983&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15985983&dopt=Abstract)

128. **Changes in breathing and the pharynx after weight loss in obstructive sleep apnea.**

[The effect of weight loss following dietary restriction on disordered breathing on the pharyngeal airway is controversial in patients with obstructive sleep apnea (OSA). We therefore prospectively studied eight patients before and after dietary-induced weight loss. Mean weight loss was 20.6 kg +/- 12.8 SD. After weight loss there were significant improvements in PO<sub>2</sub> and PCO<sub>2</sub> measured during wakefulness, and in the number of desaturation episodes per hour of sleep, average desaturation per episode, and number of movement arousals. The number of apneas and hypopneas significantly decreased in six of eight patients. There was a significant correlation between body mass index and number of disordered breathing events. Nasopharyngeal collapsibility and pulse flow resistance decreased in awake patients after weight loss. We conclude that moderate weight loss in obese patients with OSA improves oxygenation during both sleep and wakefulness, decreases the number of disordered breathing events in many patients, decreases the collapsibility of the nasopharyngeal airway.] Suratt PM, McTier RF, et al., *Chest.* 1987 Oct;92(4):631-7,

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=3652748&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3652748&dopt=Abstract)

129. **Circulating nitric oxide is suppressed in obstructive sleep apnea and is reversed by nasal continuous positive airway pressure.**

[Epidemiological studies have implicated obstructive sleep apnea (OSA) as an independent comorbid factor in cardiovascular and cerebrovascular diseases. The recurrent episodes of occlusion of upper airways during sleep result in pathophysiological changes that may predispose to vascular diseases, and we postulate that nitric oxide may be one of the mediators involved. This study investigates the levels of circulating nitric oxide (NO), measured as serum nitrites and nitrates, in the early morning in OSA subjects compared with control subjects, and the effect of overnight nasal continuous positive airway pressure (nCPAP) in OSA subjects.... This study demonstrates, for the first time, that circulating NO is suppressed in OSA, and this is promptly reversible with the use of nCPAP. The findings offer support for nitric oxide being one of the mediators involved in the acute hemodynamic regulation and long-term vascular remodeling in OSA.] Ip MS, Lam B, et al. *Am J Respir Crit Care Med.* 2000 Dec;162(6):2166-71.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list\\_uids=11112132&dopt=medline](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=11112132&dopt=medline)

130. **C-reactive Protein is Associated With Sleep Disordered Breathing Independent of Adiposity.**

[It is well established that medical conditions such as obesity and cardiovascular disease are associated with increased levels of inflammatory biomarkers such as C-reactive protein (CRP). Prior studies have produced inconsistent results regarding the association between sleep disordered breathing (SDB) and CRP, possibly due to the confounding effects of obesity or medical comorbidity. The present study examined the association between degree of SDB and level of CRP independent of prevalent medical conditions and obesity.]

The study sample consisted of 69 men (mean age 40 years; mean BMI of 31.2 kg/m<sup>2</sup>) free of prevalent medical conditions including hypertension, diabetes mellitus, and cardiovascular disease. Measurements of morning and evening CRP levels were performed along with full-montage polysomnography. Confounding due to obesity was assessed by adjustments for body mass index, waist circumference, and percent body fat. A strong association was found between degree of SDB and serum levels of CRP, with or without adjustment for age and several measures of adiposity. Between the lowest and highest quartiles of apnea-hypopnea index (AHI) the mean difference in adjusted level of CRP was 3.88 µg/ml (P < 0.001). Moreover, an independent association between serum CRP levels and nocturnal hypoxia was also observed, whereas no association was noted with parameters of sleep architecture. Conclusions: While more research is needed to elucidate causal pathways involving the effects of sleep-related hypoxia on low-grade systemic inflammation, the results of this study suggest that mechanisms other than adiposity per se could contribute to the inflammatory state seen in adults with SDB.] Punjabi NM, Beamer BA. *Journal SLEEP*, Volume : 30 Issue : 01 Pages : 29-34. <http://www.journalsleep.org/ViewAbstract.aspx?citationid=3115>

131. **Decreased plasma levels of nitric oxide derivatives in obstructive sleep apnoea: response to CPAP therapy.** [Reduced endothelium dependent vasodilation has been reported in patients with obstructive sleep apnoea (OSA) but direct measurements of the most potent naturally occurring vasodilator, nitric oxide (NO) or its derivatives (nitrate and nitrite, NO<sub>x</sub>), have not yet been performed in these patients. *CONCLUSIONS*—Plasma NO<sub>x</sub> levels are reduced in OSA and can be increased by short and long term CPAP therapy. Although the precise mechanism underlying this observation remains to be clarified, it may have important implications for the development of cardiovascular disease in patients with OSA and for the life saving effect of CPAP.] Schulz R, Schmidt D, et al. *Thorax* 2000;55:1046-1051. <http://thorax.bmj.com/cgi/content/abstract/55/12/1046>
132. **Dynamic Upper Airway Soft-Tissue and Caliber Changes in Healthy Subjects and Snoring Patients.** [Changes in airway dimension and lateral parapharyngeal wall thickness were significantly different between snorers and control subjects. Changes in parapharyngeal wall thickness and transverse oropharyngeal airway diameter changes were significantly related in those who snored but not in control subjects. Airway narrowing predominantly occurs in the lateral dimension in people who snore. Changes in the lateral pharyngeal wall are more important than the parapharyngeal fat pads in airway calibration. Narrowing of the upper airway area at the end of the expirium and the beginning of the inspirium is thought to be the cause of snoring and due to augmented muscle mass and prolonged laxity rather than inadequate activation of the pharyngeal dilating muscles.] Akan H, Aksöz T, et.al., *American Journal of Neuroradiology* 25:1846-1850, <http://www.ajnr.org/cgi/content/abstract/25/10/1846>
133. **Effects of sex on sleep-disordered breathing in adolescents.** [This study was conducted to determine the influence of puberty on features of sleep-disordered breathing (SDB) in adolescents. Males exhibited significantly higher neck circumference/height index and waist/hip index than females in both the peripubertal and postpubertal groups. In the postpubertal group, snoring and polygraphic alterations (respiratory events and oximetric parameters) were significantly more frequent in males than in females. Postpubertal adolescents showed sex differences in clinical and polygraphic parameters that were not observed at earlier pubertal stages. These findings support the influence of sex hormones on sex differences in sleep-disordered breathing.] Fuentes-Pradera MA, Sánchez-Armengol Á,

et.al., *Eur Respir J* 2004; 23:250-254.

<http://erj.ersjournals.com/cgi/content/abstract/23/2/250>

134. **Elevated C-Reactive Protein in Patients With Obstructive Sleep Apnea.** [Obstructive sleep apnea (OSA) has been increasingly linked to cardiovascular and cerebrovascular disease. Inflammatory processes associated with OSA may contribute to cardiovascular morbidity in these patients. We tested the hypothesis that OSA patients have increased plasma C-reactive protein (CRP). ...OSA is associated with elevated levels of CRP, a marker of inflammation and of cardiovascular risk. The severity of OSA is proportional to the CRP level.] Shamsuzzaman ASM, Winnicki M, et al. *Circulation*. 2002;105:2462.  
<http://circ.ahajournals.org/cgi/content/abstract/105/21/2462?ck=nck>
135. **Endothelin-1 Levels in Interstitial Lung Disease Patients During Sleep.** [Hypoxemia stimulates endothelin-1 (ET-1) secretion. The reduction in alveolar ventilation during sleep is considered sufficient to account for the hypoxemia observed in patients with respiratory diseases. ...Conclusions: According to our study, arterial ET-1 is markedly increased in ILD patients, especially in those with pulmonary hypertension.] Trakada G, Nikolaou E, et al. *Sleep and Breathing, Vol.7, No.3, p. 111-118*.  
<http://www.springerlink.com/content/9ft025egjyp87e07/?p=83cbec7cc4454ae4923f49acbdb8fc76&pi=2>
136. **Enhanced Release of Superoxide from Polymorphonuclear Neutrophils in Obstructive Sleep Apnea.** [Obstructive sleep apnea (OSA) is associated with increased cardiovascular morbidity and mortality. Free oxygen radicals have been implicated in the pathogenesis of cardiovascular disorders. Therefore, we aimed to test the hypothesis that increased oxidative stress constitutes one underlying mechanism for the connection between OSA and cardiovascular disease. In 18 patients with OSA the release of superoxide from polymorphonuclear neutrophils was determined after stimulation with the bacterial tripeptide formylmethionylleucylphenylalanine (fMLP) and the calcium ionophore A23. Superoxide production was measured as superoxide dismutase-inhibitable reduction of cytochrome *c*. Blood samples were obtained before and after two nights of CPAP therapy and after  $4.8 \pm 0.6$  mo of follow-up. Ten healthy young volunteers and 10 lung cancer patients without OSA but a similar spectrum of comorbidity served as controls. Before CPAP, neutrophil superoxide generation was markedly enhanced in OSA when compared with both control groups. Effective CPAP therapy led to a rapid and long-lasting decrease of superoxide release in OSA. In conclusion, OSA is linked with a "priming" of neutrophils for enhanced respiratory burst. The increased superoxide generation, which might have major impact on the development of cardiovascular disorders, is virtually fully reversed by effective CPAP therapy.] SchulzR, Mahmoudi S, et al. *Am. J. Respir. Crit. Care Med.*, Volume 162, Number 2, August 2000, 566-570. <http://intl-ajrcm.atsjournals.org/cgi/content/abstract/162/2/566>
137. **Evaluation of carotid artery wall thickness with high-resolution sonography in obstructive sleep apnea syndrome.**[ An increased intima-media thickness (IMT) in the carotid arteries is a marker of generalized atherosclerosis, and it has been associated with a high risk of stroke. The aim of this study was to investigate whether patients with obstructive sleep apnea syndrome (OSAS) have an increase in atherosclerotic indicators in the carotid arteries. This study shows that the carotid arteries' IMT is increased in patients with severe OSAS. This increase may predispose the patients to cerebrovascular disease. Additionally, the findings support the hypothesis that patients with OSAS are at risk of developing cerebrovascular disease regardless of the presence or absence of other vascular risk factors

(eg, hypercholesterolemia, diabetes mellitus, and hypertension). Altin R, Ozdemir H, et al. *Journal of Clinical Ultrasound, Volume 33, Issue 2, Pages 80 – 86.*

<http://www3.interscience.wiley.com/cgi-bin/abstract/109876456/ABSTRACT?CRETRY=1&SRETRY=0>

138. **Evidence for activation of nuclear factor kappaB in obstructive sleep apnea.** [Obstructive sleep apnea (OSA) is a risk factor for atherosclerosis, and atherosclerosis evolves from activation of the inflammatory cascade. We propose that activation of the nuclear factor kappaB (NF-kappaB), a key transcription factor in the inflammatory cascade, occurs in OSA. .... NF-kappaB activation occurs with sleep-disordered breathing. Such activation of NF-kappaB may contribute to the pathogenesis of atherosclerosis in OSA patients.] Yamauchi M, Tamaki S, et al. *Sleep Breathing, vol 10, No.4 / Dec 2006 p.189-193.* <http://www.springerlink.com/content/e017341122805424/?p=32bbd1a60c064ad5840e8c2164b39b69&pi=3>
139. **Exercise training prevents the inflammatory response to hypoxia in cremaster venules.** [Systemic hypoxia produces microvascular inflammation in several tissues, including skeletal muscle. Exercise training (ET) has been shown to reduce the inflammatory component of several diseases. Alternatively, ET could influence hypoxia-induced inflammation by improving tissue oxygenation or increasing mechanical antiadhesive forces at the leukocyte-endothelial interface. The effect of 5 wk of treadmill ET on hypoxia-induced microvascular inflammation was studied in the cremaster microcirculation of rats using intravital microscopy. In untrained rats, hypoxia (arterial Po<sub>2</sub> = 32.3 ± 2.1 Torr) increased leukocyte-endothelial adherence from 2.3 ± 0.4 to 10.2 ± 0.3 leukocytes per 100 µm of venule (P < 0.05) and was accompanied by extravasation of FITC-labeled albumin after 4 h of hypoxia (extra-/intravascular fluorescence intensity ratio = 0.50 ± 0.07). These responses were attenuated in ET (leukocyte adherence was 1.5 ± 0.4 during normoxia and 1.8 ± 0.7 leukocytes per 100 µm venule after 10 min of hypoxia; extra-/intravascular fluorescence intensity ratio = 0.11 ± 0.02; P < 0.05 vs. untrained) despite similar reductions of arterial (32.4 ± 1.8 Torr) and microvascular Po<sub>2</sub> (measured with an oxyphor-quenching method) in both groups. Shear rate decreased during hypoxia to similar extents in ET and untrained rats. In addition, circulating blood leukocyte count was similar in ET and untrained rats. The effects of ET on hypoxia-induced leukocyte-endothelial adherence remained up to 4 wk after discontinuing training. Thus ET attenuated hypoxia-induced inflammation despite similar effects of hypoxia on tissue Po<sub>2</sub>, venular shear rate, and circulating leukocyte count.] Orth TA, Allen JA, et al. *Journal of Applied Physiology, 2005, vol. 98, n<sup>o</sup>6, pp. 2113-2118.* <http://cat.inist.fr/?aModele=afficheN&cpsid=16796976>
140. **Fibro-optic study of pharyngeal airway during sleep in patients with hypersomnia obstructive sleep-apnea syndrome.** [Pharyngeal airway during sleep was observed with help of Fibro-optic flexible bronchoscope and cineradiography in 10 adult patients with Hypersomnia Sleep-Apnea (HSA) syndrome. The results of the study suggest that the structures involved in production of airway obstruction in the patients with HSA syndrome are the muscles of velopharyngeal sphincter and tongue. The laryngeal airway was not obstructed during the episodes of apnea.] Borowiecki B, Pollak, et.al. *Laryngoscope. 1978 Aug;88(8 Pt 1):1310-3.* [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=672363&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=672363&dopt=Abstract)

141. **Genioglossus and breathing responses to airway occlusion: effect of sleep and route of occlusion.** [We examined the effect of sleep state on the response of genioglossus muscle (EMGgg) activity to total airway occlusion applied at 1) nasal airway [and thus exposing the upper airway to pressure changes] and 2) tracheal airway. ... Results confirm the important role of the UAW in regulating breathing pattern and indicate that both immediate and progressive load-compensating responses during nasal occlusion are influenced by information arising from the upper airway.] Issa FG, Edwards P, et.al. *J Appl Physiol.* 1988 Feb;64(2):543-9.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=3372412&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3372412&dopt=Abstract)
142. **How and why should we stabilize the upper airway?** [This review focuses on the evidence for upper airway instability during sleep and on the methods used to correct this instability. Upper airway patency during sleep is determined by the balance between the forces tending to constrict the pharynx (i.e. negative suction force generated by the diaphragm) and those tending to dilate in the pharynx (i.e. force acting on the tongue, soft palate and pharyngeal dilator muscles). The evidence for reduction in genioglossus activity and tensor palatini activity, failure of compensatory mechanisms to maintain these activities, and increase in upper airway resistance during sleep is reviewed. Coupled with abnormal pharyngeal anatomy to start with, the above events lead to abnormal pharyngeal function and cause repetitive episodes of airway occlusion, that is, sleep apnea. It is concluded that abnormal airway function in sleep apnea is a diffuse, rather than a localized process, that may involve the entire airway from the nasopharynx to the larynx. Methods to improve abnormal pharyngeal anatomy and pharyngeal function, such as nasal continuous positive airway pressure (CPAP), oral appliances, posture, weight loss, medications, and surgery are discussed. Given the pathophysiology of sleep apnea, that is, diffuse abnormality of the upper airway, it is reasonable to expect that only those approaches that exert a beneficial effect on the entire upper airway, as opposed to the approaches that modify only a short segment of it, may be expected to be of benefit in treatment of sleep apnea.] Hoffstein V. St. Michael's Hospital, University of Toronto, Canada. *Sleep.* 1996 Nov;19(9 Suppl):S57-60.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9122573&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9122573&dopt=Abstract)
143. **Hypoxemia and obesity modulate plasma C-reactive protein and interleukin-6 levels in sleep-disordered breathing.** [C-reactive protein (CRP) and interleukin-6 (IL-6) are pro-inflammatory proteins and important risk factors for atherosclerosis. Plasma CRP levels in snoring children may or may not be elevated. Since obesity is prevalent among snoring children and is associated with elevated CRP levels, we aimed to investigate the relative contributions of sleep-disordered breathing (SDB) and obesity to the inflammatory processes in snoring children in this prospective study. Two hundred forty-four children (mean age  $8.9 \pm 3.4$  years) underwent polysomnographic evaluation. CRP was measured the following morning, and plasma IL-6 levels from 111 randomly selected children were also examined. Plasma CRP and IL-6 levels were elevated in children with SDB. Log plasma CRP levels were higher in the moderate-severe SDB group (apnea/hypopnea index, AHI  $\geq 5$ ) compared to the mild SDB group (AHI  $\geq 1$  and  $<5$ ;  $p < 0.0001$ ) or the control group (AHI  $< 1$ ;  $p = 0.0001$ ). Log plasma CRP levels correlated with AHI, arousal index, relative BMI, and SpO<sub>2</sub> nadir ( $r = 0.30$ ,  $p < 0.0001$ ;  $r = 0.21$ ,  $p = 0.002$ ;  $r = 0.39$ ,  $p < 0.0001$ ,  $r = -0.36$ ,  $p < 0.0001$ , respectively). Log plasma CRP levels were lower in children with SpO<sub>2</sub> nadir

$\geq 90$  ( $p < 0.0001$ ). Sub-analysis of the 116 non-obese children in the cohort revealed similar findings. Log plasma IL-6 levels were increased in children with moderate–severe SDB compared to controls ( $p = 0.03$ ) and correlated with AHI ( $r = 0.28$ ,  $p = 0.003$ ) and SpO<sub>2</sub> nadir ( $r = -0.24$ ,  $p = 0.02$ ). Children with SDB display significant severity-dependent increases in plasma CRP and IL-6 levels independent of obesity.] Tauman R, O’Brien LM, Gozal D. *Sleep Breath* (2007) 11:77-84.

<http://www.springerlink.com/content/q1431614v5215384/fulltext.pdf>

144. **Hypoxia inhibits expression of eNOS via transcriptional and posttranscriptional mechanisms.** [Normal blood vessel tone is maintained by a balance of vasoconstrictors and vasodilators produced by endothelial cells in the vasculature. Nitric oxide (NO) is a potent vasodilator that causes vascular smooth muscle cell relaxation by elevating intracellular guanosine 3',5'-cyclic monophosphate (cGMP) levels. The physiological mechanisms regulating NO production in the vasculature are not completely understood. We report here that production of this vasodilator by vascular endothelial cells can be significantly suppressed by hypoxia. Exposing human endothelial cells to low PO<sub>2</sub> results in 40-60% reduction in the steady-state mRNA levels of endothelial constitutive NO synthase (eNOS), the major enzyme responsible for NO production in these cells. The lower levels of eNOS mRNA result from decreased transcription of the gene as well as reduced message stability. In endothelial-smooth muscle cell co-culture experiments, hypoxic endothelial cells stimulated significantly less cGMP production by smooth muscle cells than the corresponding normoxic controls. This inhibitory effect of hypoxia on NOS production by endothelial cells occurs after 24 h of hypoxia and persists for at least 48 h. These new findings suggest that hypoxia might cause changes in blood vessel tone through compound mechanisms: by increasing the production of endothelium-derived vasoconstrictors and, as shown here, by suppressing the production of vasodilators like NO.] McQuillan LP, Leung GK, et al. *Am J Physiol Heart Circ Physiol* 267: H1921-H1927, 1994;  
[http://ajpheart.physiology.org/cgi/content/abstract/267/5/H1921?ijkey=135b138bbbad719bf2eeb7112a12741a3cc556a2&keytype=tf\\_ipsecsha](http://ajpheart.physiology.org/cgi/content/abstract/267/5/H1921?ijkey=135b138bbbad719bf2eeb7112a12741a3cc556a2&keytype=tf_ipsecsha)
145. **Inflammatory Ideas about Sleep Apnea.** [Intermittent hypoxia as occurs in sleep apnea has multiple physiological consequences, including increases in erythropoietin (EPO) and vascular endothelial growth factor (VEGF). Hypoxia has been shown to decrease the breakdown of a transcription factor, hypoxia-inducible factor-1, which triggers the induction of many genes like EPO and VEGF and which compensates for the reduction in blood oxygen levels by increasing red cell mass (EPO) or inducing the formation of new blood vessels (VEGF)... It is easy to understand how sleep apnea, by producing intermittent systemic hypoxia, increases VEGF. Even local hypoxia gives rise to increases in VEGF. VEGF is the major mediator of angiogenesis. Angiogenesis is an important factor in many diseases, including cancer, and it promotes tumor spread, retinopathies and rheumatoid arthritis.] Cherniack NS. *Respiration* 2004;71:20-21, editorial.  
<http://content.karger.com/ProdukteDB/produkte.asp?Aktion=ShowPDF&ProduktNr=224278&Ausgabe=229855&ArtikelNr=75643>
146. **Influence of Weight and Sleep Apnea Status on Immunologic and Structural Features of the Uvula.** [We conclude that (1) the amount of inflammatory markers is linked to obesity rather than to sleep-related breathing disorders, and (2) obstructive sleep apnea is associated with a structural alteration of the extracellular matrix of upper airway tissue.]

Sériès F, Chakir J, et.al., *American Journal of Respiratory and Critical Care Medicine* Vol 170. pp. 1114-1119, (2004). <http://ajrccm.atsjournals.org/cgi/content/abstract/170/10/1114>

147. **Lipopolysaccharide and interleukin 1 augment the effects of hypoxia and inflammation in human pulmonary arterial tissue.** [The combined effects of hypoxia and interleukin 1, lipopolysaccharide, or tumor necrosis factor alpha on the expression of genes encoding endothelial constitutive and inducible nitric oxide synthases, endothelin 1, interleukin 6, and interleukin 8 were investigated in human primary pulmonary endothelial cells and whole pulmonary artery organoid cultures. Hypoxia decreased the expression of constitutive endothelial nitric oxide synthase (NOS-3) mRNA and NOS-3 protein as compared with normoxic conditions. The inhibition of expression of NOS-3 corresponded with a reduced production of NO. A combination of hypoxia with bacterial lipopolysaccharide, interleukin 1 beta, or tumor necrosis factor alpha augmented both effects. In contrast, the combination of hypoxia and the inflammatory mediators superinduced the expression of endothelin 1, interleukin 6, and interleukin 8. Here, we have shown that inflammatory mediators aggravate the effect of hypoxia on the down-regulation of NOS-3 and increase the expression of proinflammatory cytokines in human pulmonary endothelial cells and whole pulmonary artery organoid cultures.] Ziesche R, Petkov V, et al. *Proc Natl Acad Sci U S A*. 1996 Oct 29;93(22):12478-83. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=8901607&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8901607&dopt=Abstract)
148. **Measuring nuclear factor-KB – who cares?** [A convincing body of evidence now exists that obstructive sleep apnea syndrome (OSAS) is associated with cardiovascular morbidity and mortality. OSAS has been specifically associated with hypertension, myocardial infarctions, stroke, and congestive heart failure. Apneic episodes and arousals cause surges in sympathetic tone with the release of vasoactive mediators including catecholamines. Intermittent hypoxia leads to hypoxic vasoconstriction and hypoxia reperfusion oxidative stresses. These metabolic stresses result in a systemic inflammatory response and vascular remodeling.] Eliasson AH, Lettieri CJ. *Sleep Breath* (2006) 10:p.4-5. <http://www.springerlink.com/content/y1p0403656853235/fulltext.pdf>
149. **Mechanical properties of the velopharynx in obese patients with obstructive sleep apnea.** Editorial. [Epidemiologic data indicate that the relationship between obesity and obstructive sleep apnea (OSA) is largely explained by variation in neck size. Fat deposits in the neck may predispose to upper airway (UA) occlusion during sleep by altering the mechanical properties of the UA, particularly at the level of the velopharynx (VP). Obese patients with large necks have a more collapsible velopharynx during wakefulness, which may predispose to upper airway obstruction during sleep.] Ryan CF, Love LL. Department of Medicine, University of British Columbia, Vancouver, Canada. *Am J Respir Crit Care Med*. 1996 Sep;154(3 Pt 1):806-12. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list\\_uids=8810623&itool=iconabstr&query\\_hl=1&itool=pubmed\\_DocSum](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=8810623&itool=iconabstr&query_hl=1&itool=pubmed_DocSum)
150. **Nitric Oxide (NO) and Obstructive Sleep Apnea (OSA).** [Nitric oxide (NO) and obstructive sleep apnea are inseparable. Obstructive sleep apnea could be described as the intermittent failure to transport the full complement of nasal NO to the lung with each breath. There NO matches perfusion to ventilation. NO is utilized by the efferent pathways that control the unequal, inspiratory battle between the pharyngeal dilators and the closing negative pressures induced by the thoracic musculature. Recurrent cortical arousals are a

major short-term complication, and the return to sleep after each arousal uses NO. The long-term complications, namely hypertension, myocardial infarction, and stroke, might be due to the repeated temporary dearth of NO in the tissues, secondary to a lack of oxygen, one of NO's two essential substrates.] Haight JSJ, Djupesland PG. *Sleep and Breathing*, Vol. 7, No.2, p.53-61.

<http://www.springerlink.com/content/0vqkque48lnwvqpn/?p=d50355ab561a40e998f1ae6110ac7b07&pi=1>

151. **Nuclear factor-kappa B is essential for up-regulation of interleukin-8 expression in human amnion and cervical epithelial cells.** [Interleukin-8 (IL-8) is a cytokine which recruits and activates neutrophils into tissue stroma... We conclude that the NF- $\kappa$ B binding site is essential for up-regulation of *IL-8* gene expression in these uterine cell types. An increase in IL-8 expression has been shown to occur in the uterus in association with parturition and NF- $\kappa$ B binding to the promoter may be of importance at this time.] Elliott CL, Allport VC, et.al. *Molecular Human Reproduction*, Vol. 7, No. 8, 787-790, August 2001. <http://molehr.oxfordjournals.org/cgi/content/abstract/7/8/787>
152. **Obesity and obstructive sleep apnea syndrome.** [We investigated the influence of obesity on upper airway obstruction, especially the relationship between obesity and the type of obstruction. The site of obstruction was identified by means of endoscopic examination and dynamic MRI during sleep. Many obese patients have the circumferential type of obstruction.] Nishimura Y, Nishimura T, et.al., Department of Otolaryngology, Fujita Health University School of Medicine, Nagoya, Japan. *Acta Otolaryngol Suppl.* 2003;(550):22-4. <http://cat.inist.fr/?aModele=afficheN&cpsidt=14707564>
153. **Obstructive sleep apnea, cardiovascular disease, and inflammation—is NF- $\kappa$ B the key?** [Obstructive sleep apnea (OSA) affects a large portion of the population and is associated with repeated airway collapse leading to chronic intermittent hypoxia, exaggerated swings in intrathoracic pressure and post apneic arousal. OSA is associated with heightened sympathoadrenal tone and is a risk factor for cardiovascular mortality and morbidity. In addition to well-known mechanical and autonomic effects, OSA appears to be associated with systemic inflammation. This could provide one mechanism leading to cardiovascular disease (CVD). A central factor in the inflammatory cascade is nuclear factor kappa B (NF- $\kappa$ B), which is involved in the transcription of numerous genes involved in the inflammatory cascade. The object of this article is to review recent literature on some of the aspects of OSA related to a proinflammatory state and the possible role of NF- $\kappa$ B as one mechanism providing a link between sleep apnea and CVD.] Williams A, Scharf SM. *Sleep Breath* (2007) 11:69-76 <http://www.springerlink.com/content/9154180v002w2321/?p=523ee98b5ef8482d853e5cff6049b645&pi=1>
154. **Obstructive Sleep Apnea Causes Systemic Inflammation and Metabolic Syndrome – Editorial.** [At the inflammatory point of view, the levels of TNF- $\alpha$ , IL-6, hsCRP, adhesion molecules, and monocyte chemoattractant protein-1 were markedly and significantly elevated in patients with sleep apnea than those in normal control subjects.8,9 IL-6 and hsCRP levels were independently associated with OSAS severity as indicated by the AHI. In addition, hsCRP level is associated with visceral adipose tissue and is significantly associated with the components of insulin resistance syndrome.5 These data support the belief that inflammatory processes and metabolic syndrome are activated in atherosclerotic lesions in patients with OSAS. C-reactive protein and other inflammatory cytokines accelerate the progression of

atherosclerosis in patients with OSAS. In addition, increase in circulating levels of adenosine and urinary uric acid in patients with obstructive sleep apnea are implicated with increased production of reactive oxygen species. Activation of redox-sensitive gene expression is suggested by the increase in some protein products of these genes, including vascular endothelial growth factor, erythropoietin, endothelin-1, inflammatory cytokines, and adhesion molecules.<sup>10,11</sup> These results implicate the participation of redox-sensitive transcription factors as hypoxia-inducible factor-1, activator protein-1 and nuclear factor- $\kappa$ B. Importantly, the elevated levels of atherogenic inflammatory mediators were improved by the OSAS-specific treatment such as nasal continuous positive airway pressure.<sup>8–11</sup> Thus, OSAS plays a crucial role in metabolic syndrome and systemic inflammatory disorders.] Teramoto S, Yamamoto H, et al. *Chest* 2005;127;1074-1075.

<http://www.chestjournal.org/cgi/reprint/127/3/1074.pdf>

155. **Oxidative Stress and Sleep Apnoea - A New Research Front.** [The association between breathing disorders in sleep and cardiovascular morbidity has been attributed to increased activation of the sympathetic nervous system; swings in intrathoracic pressure; altered blood coagulability; and, in recent years, acceleration of atherogenic processes that are uniquely triggered by the apnoea-related intermittent hypoxia and resultant oxidative stress. This latter explanation provides a better understanding of the natural evolution of cardiovascular morbidities in patients with breathing disorders in sleep and has major implications regarding the diagnosis and treatment of the disorder. The new understanding of the pathophysiology of cardiovascular morbidity in sleep apnoea opens a new research front. ... To prevent cardiovascular morbidity in OSA, diagnosis and treatment of breathing disorders in sleep should be made at the earliest age possible.] Lavie L, Lavie P. *European Respiratory Disease* 2006 - October 2006.

<http://www.touchrespiratorydisease.com/oxidative-stress-sleep-apnoea-a6192-1.html>.

156. **Oxidative stress and systemic inflammation in patients with sleep apnea: Role of obesity.** [Oxidative stress and systemic inflammation resulting from repeated hypoxia/reoxygenation cycles in obstructive sleep apnea-hypopnea syndrome (OSAHS) play a role in atherogenesis. It is unclear, however, if this association is independent of obesity. The aims of the present study were to compare markers of oxidative stress and systemic inflammation between patients with and without OSAHS independent of obesity, and to examine their interrelations. In experiment 1, 20 OSAHS patients, age  $42.1 \pm 10.0$  years, body mass index  $26.3 \pm 2.7$  kg/m<sup>2</sup>, and apnea-hypopnea index  $28.8 \pm 10.8$  events/h, were individually matched with 20 control subjects, age  $41.5 \pm 11.1$  years, body mass index  $26.0 \pm 2.9$ , and apnea-hypopnea index  $6.5 \pm 2.4$  events/h. In experiment 2, 15 OSAHS patients with body mass index  $> 27$  were individually matched with 15 OSAHS patients having the same age and similar apnea severity with body mass index  $< 27$ . In both experiments, blood was drawn at the end of the sleep study for determination of lipid peroxidation markers, thiobarbituric-acid-reactive substances (TBARS) and peroxides and the antioxidant enzyme paraoxonase-1, and the systemic inflammatory markers C-reactive protein (CRP), ceruloplasmin and haptoglobin. OSAHS patients had significantly higher concentrations of TBARS ( $P < 0.0002$ ) and peroxides ( $P < 0.03$ ) and lower paraoxonase-1 ( $P < 0.02$ ) than controls. No differences were found for the inflammatory markers but only in OSAHS patients there were significant correlations between the lipid peroxidation and inflammatory markers. There were no differences in lipid peroxidation between obese and non-obese patients, but CRP was higher ( $P < 0.03$ ) in the obese patients. We conclude that

sleep apnea is primarily associated with increased oxidative stress. Possibly, OSAHS influences systemic inflammatory pathways indirectly through oxidative stress.] Lavie L, Vishnevsky A, et al. *Sleep and Biological Rhythms Vol 5, Issue 2, P 100.*

<http://www.blackwell-synergy.com/doi/abs/10.1111/j.1479-8425.2007.00259.x?journalCode=sbr>

157. **Oxidative Stress in Obstructive Sleep Apnea.** [*Study objectives:* To investigate the relationship between the severity of obstructive sleep apnea (OSA) and oxidative stress, which plays an important role in the pathogenesis of cardiovascular disease, and to elucidate the factors contributing to this relationship. *Conclusions:* The severity of OSA is independently associated with oxidative stress. Among various sleep-disordered breathing parameters, ODI is most closely related to oxidative stress.] Yamauchi M, Nakano H, et al. *Chest.* 2005;127:1674-1679. <http://www.chestjournal.org/cgi/content/full/127/5/1674>
158. **Paradoxical glottic narrowing in patients with severe obstructive sleep apnea.** [Most patients with obstructive sleep apnea have increased pharyngeal collapsibility (defined in the present study as an increased lung volume dependence of pharyngeal area), which predisposes them to upper airway occlusion during sleep. However, there are patients with severe obstructive sleep apnea who have low-normal pharyngeal collapsibility. The factors leading to nocturnal upper airway obstruction in such patients have not been ascertained. We studied 10 overweight male patients with severe obstructive sleep apnea and low-normal pharyngeal collapsibility to determine the site of upper airway pathology in these patients. We found that all 10 patients exhibited paradoxical inspiratory narrowing of the glottis during quiet tidal breathing. This phenomenon was not observed in a matched group of 10 snoring, nonapneic male controls. We conclude that paradoxical glottic narrowing may be a contributing factor in the pathogenesis of upper airway obstruction in patients with severe obstructive sleep apnea who have low-normal pharyngeal collapsibility.] Rubinstein I, Slutsky AS, et al. Department of Medicine, St. Michael's Hospital, Ontario, Canada. *J Clin Invest.* 1988 Apr;81(4):1051-5. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=3350963&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3350963&dopt=Abstract)
159. **Pathogenesis of upper airway occlusion during sleep.** [ ] Remmers J, et al. *J Appl Physiol* 44:931-938, 1978. [www.jap.physiology.org](http://www.jap.physiology.org)  
<http://jap.physiology.org/cgi/content/citation/44/6/931>
160. **Pathophysiology of upper airway closure during sleep.** [While the upper airway normally remains patent during quiet breathing in wakefulness and sleep, patients with obstructive sleep apnea have repetitive periods of upper airway closure during sleep. The upper airway closures usually occur at various sites in the pharynx. The patency of the potentially collapsible pharynx during inspiration depends on the balance between subatmospheric pressure in the pharyngeal airway and airway dilating forces generated by pharyngeal muscles. The pressure required to collapse the upper airway in the absence of upper airway muscle activity, ie, closing pressure, is normally subatmospheric. In obstructive sleep apnea, positive pressures are required to maintain patency of the passive upper airway. The pathophysiologic mechanisms underlying upper airway closures during sleep form the basis for the treatment of obstructive sleep apnea. In general, these treatment modalities attempt to (1) raise the pharyngeal pressure above the closing pressure, (2) decrease the closing pressure, or (3) increase upper airway muscle activity.] Kuna ST, Sant' Ambrogio G.

JAMA. 1991 Sep 11;266(10):1384-9. <http://jama.ama-assn.org/cgi/content/abstract/266/10/1384>

161. **Pathophysiology of upper airway obstruction: a developmental perspective.** [The obstructive sleep apnea syndrome (OSAS) occurs in patients of all ages, from the premature infant to the elderly. Much remains unknown about the pathophysiology of the syndrome. However, research suggests that OSAS in all age groups is due to a combination of both anatomic airway narrowing and abnormal upper airway neuromotor tone. The anatomic predisposing factors for OSAS differ over the lifespan. However, a smaller upper airway is noted in all age groups and probably predisposes to airway collapse during sleep. Despite the known anatomic factors, such as craniofacial anomalies, obesity, and adenotonsillar hypertrophy, that contribute to OSAS throughout life, a clear anatomic factor cannot always be identified. This suggests that alterations in upper airway neuromotor tone also play an important role in the etiology of OSAS. Infants and children are less likely than adults to arouse in response to upper airway obstruction and do not compensate for prolonged increases in inspiratory resistive load. The overall ventilatory drive is probably normal in patients of all ages with OSAS. However, upper airway neuromotor tone and reflexes during sleep vary with age and are increased in normal infants and children compared to adults, perhaps as a compensatory response for their relatively narrow airway. This compensatory response appears to be blunted in children with OSAS. Further research is needed to fully understand the complexities of upper airway structure and function during both normal development and disease.] Arens R, Marcus CL, *Sleep*. 2004 Aug 1;27(5):997-1019 [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=15453561&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15453561&dopt=Abstract)
162. **Periodic sleep apnea: chronic sleep deprivation related to intermittent upper airway obstruction and central nervous system disturbance.** [Periodic sleep apnea may be due to repeated episodes of upper airway obstruction in patients who have a short thick neck and/or large jowls. Apnea due to complete cessation of breathing may occur to a lesser extent. Analysis of the sleep electroencephalogram shows that these patients rarely achieve deep sleep and have less stage 1-REM sleep than normal subjects of comparable age. They are chronically sleep-deprived, a manifestation expressed by daytime somnolence, chronic fatigue and often by personality disturbances marked by paranoia, agitated depression and hostility. The definitive diagnosis of this syndrome may be established by monitoring during sleep, the electroencephalogram, measuring abdominal excursions through a mercury-in-Silastic-strain gauge and recording air flow at the nose by means of a thermocouple. As demonstrated by other investigators, chronic hypoventilation during sleep leads to both pulmonary and systemic arterial hypertension, which may produce generalized cardiac enlargement and congestive heart failure. The abnormalities in the periodic sleep apnea syndrome are abolished by establishing a patent airway either through tracheostomy or weight reduction.] Sackner MA, Landa J, et al., *Chest*. 1975 Feb;67(2):164-71. <http://www.chestjournal.org/cgi/content/abstract/67/2/164>
163. **Pharyngeal narrowing/occlusion during central sleep apnea.** [We hypothesized that subatmospheric intraluminal pressure is not required for pharyngeal occlusion during sleep. ... Velopharyngeal narrowing consistently occurs during induced hypocapnic central apnea even in normal subjects. Complete pharyngeal occlusion occurs during spontaneous or induced central apnea in patients with SAH. We conclude that subatmospheric intraluminal pressure is not required for pharyngeal occlusion to occur. Pharyngeal narrowing or

occlusion during central apnea may be due to passive collapse or active constriction.] Badr MS, Toiber F, et.al., *J Appl Physiol.* 1995 May;78(5):1806-15  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=7649916&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7649916&dopt=Abstract)

164. **Pharyngeal size and shape during wakefulness and sleep in patients with obstructive sleep apnoea.** [Computed tomography has been used to study the pharyngeal airway during tidal breathing in wakefulness and during obstructive apnoeas in Non-REM sleep in patients with obstructive sleep apnoea. In supine subjects, contiguous transverse 10 mm sections were taken perpendicular to the posterior pharyngeal wall with a 2.1 s scan time. Studies during wakefulness showed that the narrowest section of the pharyngeal airspace was in the region posterior to the soft palate and that the minimal airway cross-sectional areas were significantly reduced in the group of patients with obstructive sleep apnoea.... The studies during sleep showed that in all patients, the airspace posterior to the soft palate was a site of obstructive apnoeas. Airway narrowing and obstruction was due to posterior displacement of the soft palate and the tongue in the majority of patients, although lateral displacement of the pharyngeal walls was also observed. The size of the oropharyngeal airspace during wakefulness did not predict the presence of airway occlusion below the level of the soft palate when asleep. The variability between patients in the site(s) of upper airway obstruction during obstructive apnoeas have important implications for the choice of appropriate treatment in patients with obstructive sleep apnoea.]. Horner RL, Shea SA, et.al. Department of Medicine, Charing Cross and Westminster Medical School, London. *Q J Med.* 1989 Aug;72(268):719-35.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list\\_uids=2602554&query\\_hl=1&itool=pubmed\\_DocSum](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2602554&query_hl=1&itool=pubmed_DocSum)
165. **Rapid Eye Movement-Related Disordered Breathing: Clinical and Polysomnographic Features.** [Neither clinical history nor daytime sleepiness differentiate patients with REM sleep-disordered breathing (SDB) from non-REM SDB patients. The disorder is more common in mild and moderate cases; there is an equal incidence in women and men. These findings may suggest that REM-related SDB is a part of the spectrum of SDB.] Haba-Rubio J, Jean-Paul Janssens, et.al., *Chest.* 2005;128:3350-3357.  
<http://www.chestjournal.org/cgi/content/abstract/128/5/3350>
166. **Reactive Oxygen Metabolites (ROMs) as an Index of Oxidative Stress in Obstructive Sleep Apnea Patients.** [Study Objectives: Obstructive sleep apnea syndrome (OSA) is accompanied by oxygen desaturation and arousal from sleep. Free oxygen radicals are highly reactive molecules which could be produced by the OSA phenomenon of hypoxia/reoxygenation: cyclical alterations of arterial oxygen saturation with oxygen desaturation developing in response to apneas followed by resumption of oxygen saturation during hyperventilation. On the basis of these considerations, it was hypothesized that OSA may be linked to increased oxidative stress. ...Results: Twenty-one out of 26 subjects had an apnea/hypopnea index greater than 5 (OSA group). The measurement of free radicals was high in OSA patients. Furthermore, ROMs values in OSA patients were linearly correlated with the apnea/hypopnea index ( $R = 0.426$ ;  $p = 0.042$ ). The predictive value of a positive D-ROM test is 81%. Conclusions: ROMs were elevated in patients with OSA. When OSA was severe, similarly the value of ROMs in blood samples was enhanced, and the probable underlying mechanism for these events is the hypoxia/reoxygenation phenomenon.] Christou K, Markoulis N, et al. *Sleep and Breathing, vol. 7, No.3, p.105-109.*

<http://www.springerlink.com/content/25rn92vhx17bj/?p=83cbec7cc4454ae4923f49acbdb8fc76&pi=1>

167. **Secretion of Tumor Necrosis Factor- $\alpha$  from Human Placental Tissues Induced by Hypoxia-Reoxygenation Causes Endothelial Cell Activation *in Vitro*.** [Preeclampsia is a hypertensive complication of human pregnancy characterized by generalized maternal endothelial cell activation. Circulating pro-inflammatory cytokines derived from the placenta are thought to play a key role. We recently demonstrated that hypoxia-reoxygenation (H/R) of placental tissues *in vitro* causes equivalent oxidative stress to that seen in preeclampsia. Our aim was to determine whether H/R also increases production of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and whether conditioned media from samples exposed to H/R causes activation of human umbilical vein endothelial cells (HUVECs). Concentrations of mRNA encoding TNF- $\alpha$  were significantly higher in placental tissues subjected to H/R compared to hypoxic or normoxic controls. Although there was no difference in the concentrations of TNF- $\alpha$  protein in tissue homogenates, levels of TNF- $\alpha$  protein in the medium were significantly higher after H/R compared to controls, indicating increased secretion. Furthermore, conditioned medium from samples subjected to H/R caused increased expression of E-selectin by HUVECs, and the addition of anti-TNF- $\alpha$  antibodies significantly reduced that activation. These results are consistent with our hypothesis that intermittent perfusion of the placenta, secondary to reduced trophoblast invasion, causes increased secretion of TNF- $\alpha$ , and that this contributes to the activation of maternal endothelial cells that characterizes preeclampsia.] Hung T, Charnock-Jones DS, et al. *American Journal of Pathology*. 2004;164:1049-1061.  
<http://ajp.amjpathol.org/cgi/content/full/164/3/1049>
168. **Selective Activation of Inflammatory Pathways by Intermittent Hypoxia in Obstructive Sleep Apnea Syndrome.** [Obstructive sleep apnea syndrome (OSAS), characterized by intermittent hypoxia/reoxygenation (IHR), is an independent risk factor for cardiovascular disease. We investigated the underlying molecular mechanisms of this association in a translational study. *Methods and Results*— In a novel *in vitro* model of IHR, we used HeLa cells transfected with reporter constructs and DNA binding assays for the master transcriptional regulators of the inflammatory and adaptive pathways (NF- $\kappa$ B and HIF-1, respectively) to investigate underlying transcriptional events initiated by repeated cell exposure to IHR. Furthermore, we prospectively studied 19 male OSAS patients (median apnea-hypopnea frequency, 48.5 episodes per hour; interquartile range [IQR], 28.5 to 72.9) and 17 matched normal control subjects. Circulating levels of the proinflammatory cytokine tumor necrosis factor- $\alpha$  and the adaptive factor erythropoietin were assayed in all subjects at baseline and again after 6 weeks of continuous positive airway pressure therapy in patients. Full blood count was measured as part of a detailed baseline evaluation. HeLa cells exposed to IHR demonstrated selective activation of the proinflammatory transcription factor NF- $\kappa$ B ( $P < 0.001$  by ANOVA), whereas the adaptive regulator HIF-1 was not activated, as demonstrated by luciferase reporter assays and DNA binding studies. Circulating tumor necrosis factor- $\alpha$  levels were higher in OSAS patients (2.56 pg/mL; IQR, 2.01 to 3.42 pg/mL) than in control subjects (1.25 pg/mL; IQR, 0.94 to 1.87;  $P < 0.001$ ) but normalized with continuous positive airway pressure therapy (1.24 pg/mL; IQR, 0.78 to 2.35 pg/mL;  $P = 0.002$ ). In contrast, erythropoietin levels were similar throughout. Furthermore, circulating neutrophil levels were higher in OSAS patients than in control subjects, whereas the hematocrit was unaltered. These data demonstrate selective activation of inflammatory over adaptive pathways in IHR and OSAS, which may be an important molecular mechanism of

cardiovascular disease.] Ryan S, Taylor CT, et al. *Circulation*. 2005;112:2660-2667. <http://www.circ.ahajournals.org/cgi/content/abstract/112/17/2660>.

169. **Serum Nitrite Levels in Obstructive Sleep Apnea.** [We read with great interest the paper by Ip and colleagues addressing serum levels of nitrite and nitrate in obstructive sleep apnea (OSA). These authors reported suppression of circulating nitric oxide (NO) derivatives in OSA, rapidly reversible upon onset of nasal continuous positive airway pressure (nCPAP) therapy. Our group has obtained similar results, which have been published in abstract form in 1998, and as an original contribution in *Thorax* at the same time as the article by Ip and coworkers appeared in *AJRCCM*. In addition to including healthy volunteers as a control group in our study, we also included a group without OSA, but which presented with a similar spectrum of comorbidity (keeping in mind that nitrite/nitrate levels might be influenced by a variety of confounding factors such as arterial hypertension, smoking, hypercholesterolemia, and diabetes mellitus). The subjects in this control group had intermediate levels of nitrite/nitrate compared with both other groups. This is a further argument for the assumption that the sleep-related breathing disorder by itself caused a reduction of NO. Moreover, in our study, the effects of nCPAP therapy on nitrite/nitrate concentrations were followed up for some months and were shown to remain constant after that time period. Thus, it might be hypothesized that nCPAP therapy will not only abolish the acute hemodynamic changes associated with decreased NO production, but will also exert beneficial effects on long-term processes such as vascular remodeling. Concerning the mechanisms of NO reduction in OSA, Ip and associates fail to mention some possibilities. First, as oxygen is a cosubstrate of NO synthase (NOS), OSA-related nocturnal desaturations might result in depressed synthesis of NO. Second, the nighttime hypoxia might suppress the transcription of the endothelial NOS gene and the stability of its mRNA as suggested by cell culture experiments performed under hypoxic conditions. Third, it has been demonstrated that NOS inhibitors are elevated in OSA and thus, might also contribute to lowered nitrite/nitrate levels. Finally, and perhaps most important, it is quite possible that NO is scavenged by free oxygen radicals generated under conditions of hypoxia-reoxygenation by circulating neutrophils.] Schulz R, Seeger W, et al. *Editorial. Am. J. Respir. Crit. Care Med.*, Volume 164, Number 10, November 2001, 1997a-1997. <http://ajrccm.atsjournals.org/cgi/content/full/164/10/1997a>
170. **Sleep Deprivation and Activation of Morning Levels of Cellular and Genomic Markers of Inflammation.** [Inflammation is associated with increased risk of cardiovascular disorders, arthritis, diabetes mellitus, and mortality. The effects of sleep loss on the cellular and genomic mechanisms that contribute to inflammatory cytokine activity are not known. Sleep loss induces a functional alteration of the monocyte proinflammatory cytokine response. A modest amount of sleep loss also alters molecular processes that drive cellular immune activation and induce inflammatory cytokines; mapping the dynamics of sleep loss on molecular signaling pathways has implications for understanding the role of sleep in altering immune cell physiologic characteristics. Interventions that target sleep might constitute new strategies to constrain inflammation with effects on inflammatory disease risk.] Irwin MR, Wang M, et al *Arch Intern Med*. 2006;166:1756-1762. <http://archinte.ama-assn.org/cgi/content/abstract/166/16/1756>
171. **Sleep-disordered breathing and hormones.** [Sleep-disordered breathing (SDB) is not only a problem of the upper airway but is a systemic condition with endocrine and metabolic interactions. The accumulating body of evidence shows that SDB induces changes in the

serum levels or secretory patterns of several hormones. Conversely, various endocrine disorders and hormone therapies may induce, exacerbate or alleviate SDB. Much of the understanding of the interactions between hormones and sleep-disordered breathing derive from intervention studies with nasal continuous positive airway pressure therapy. Better understanding of hormones and breathing may open new perspectives in developing strategies to prevent, alleviate or cure sleep-disordered breathing and its systemic consequences.] Saaresranta T, Polo O., *Eur Respir J* 2003; 22:161-172.

<http://erj.ersjournals.com/cgi/content/abstract/22/1/161>

172. Sleep disturbances, oxidative stress and cardiovascular risk parameters in postmenopausal women complaining of insomnia. [The aim of this work was to investigate cardiovascular risk factors and oxidative stress parameters as well as sleep disturbances in polysomnography recordings of 38 postmenopausal women with insomnia. ... CONCLUSIONS: Although all women complained of insomnia, 50% of them demonstrated apnea during polysomnography recordings. Of the parameters measuring oxidative stress, only TBARS levels were increased in our sample. Some clinical data, such as time of onset of menopause, may be associated with the oxidative stress status of these women, probably due to the lack of estrogen and to sleep disturbances, such as apnea.] Hachul de Campos H, Brandao LC, et al. *climacteric* 2006, Aug;9(4):312-9.

[http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=PubMed&list\\_uids=16857662&dopt=Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=PubMed&list_uids=16857662&dopt=Abstract)

173. **Soluble Interleukin 6 Receptor A Novel Marker of Moderate to Severe Sleep-Related Breathing Disorder.** [Given the previously described association between sleep-related breathing disorder (SRBD) and markers of inflammation, we assessed the relationship of SRBD with levels of both interleukin 6 (IL-6) and soluble IL-6 receptor (sIL-6R), a marker with more expansive physiologic effects than IL-6. The objectives were to explore the relationship between moderate to severe sleep apnea with IL-6 and sIL-6R levels and to examine morning and evening variability for each cytokine....Morning sIL-6R levels demonstrated stronger associations with moderate to severe SRBD than morning IL-6 levels. Associations with SRBD and morning sIL-6R levels persisted even after adjustment for waist circumference, cardiovascular disease, and evening sIL-6R levels, suggesting the potential utility of sIL-6R as a marker for measuring overnight SRBD stresses. Further investigation of this biomarker may provide insight into SRBD-related inflammation.] Mehra R, Storfer-Isser A, et al. *Arch Intern Med.* 2006;166:1725-1731. <http://archinte.ama-assn.org/cgi/content/abstract/166/16/1725>

174. **The effect of acute intermittent hypercapnic hypoxia treatment on IL-6, TNF- $\alpha$ , and CRP levels in piglets.** [Obstructive sleep apnea (OSA) is characterized by repeated episodes of upper-airway obstruction during sleep leading to significant hypercapnic hypoxic conditions. These conditions are associated with increased levels of proinflammatory cytokines (including interleukin [IL]-6, tumor necrosis factor [TNF]- $\alpha$ , and C-reactive protein [CRP]) and subsequent increased cardiovascular risk. It is unclear whether hypercapnic hypoxia itself causes inflammatory perturbations. ...IL-6, TNF- $\alpha$  and CRP levels were measured before and after IHH treatment sessions. Results showed an increase in IL-6 following the first session of IHH that was neither sustained, nor repeated, during a subsequent exposure. Using mixed-modelling, TNF- $\alpha$  changed between time points and groups. There were no changes in CRP over the duration of the study. These results suggest that acute hypoxia causes a transient increase in IL-6 levels and has implications for the

pathogenesis of increased cardiovascular disease in OSA, especially in childhood.] Tam CS; Wong M; Tam K et al. *SLEEP* 2007;30(6):723-727.

<http://www.journalsleep.org/Articles/300606.pdf>

175. **The hypotonic upper airway in obstructive sleep apnea: role of structures and neuromuscular activity.** [The structural properties of the upper airway determine its collapsibility during periods of muscle hypotonia. Both rapid-eye-movement (REM) sleep and increases in nasal pressure produce hypotonia, which persists even after nasal pressure is abruptly reduced. ...Hypotonic upper airway becomes most collapsible by the third breath after an abrupt decrease in nasal pressure, regardless of sleep stage and despite an increase in genioglossus-muscle activity. Our findings suggest that predominantly mechanical rather than neuromuscular factors modulate the properties of the pharynx after abrupt reductions in nasal pressure.] Schwartz AR, O'Donnell CP, et al. Johns Hopkins Sleep Disorders Center. *Am J Respir Crit Care Med.* 1998 Apr;157(4 Pt 1):1051-7.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9563718&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9563718&dopt=Abstract)
176. **The Relation Between OSA and Metabolic Syndrome: Role of Oxidative Stress.** [Obstructive Sleep Apnea/Hypopnea (OSAH) is associated with the Metabolic Syndrome. This Syndrome includes: insulin resistance, dyslipidemia, endothelial cell dysfunction, central obesity and hypertension. Since both OSAH and Metabolic Syndrome are associated with increased cardiovascular and cerebrovascular risk, it is plausible that this risk in OSAH patients is mediated through promotion of dysmetabolic features which are consistent with Metabolic Syndrome.] Univ. of Pittsburg, National Heart, Lung and blood Institute.  
<http://clinicaltrials.gov/ct/show/NCT00177892;jsessionid=C132ABE8C9699433F394E144761E96B4?order=46>
177. **The upper airway in sleep: physiology of the pharynx.** [The upper airway is the primary conduit for passage of air into the lungs. Its physiology has been the subject of intensive study: both passive mechanical and active neural influences contribute to its patency and collapsibility. Different models can be used to explain behavior of the upper airway, including the "balance of forces" (airway suction pressure during inspiration versus upper airway dilator tone) and the Starling resistor mechanical model. As sleep is the primary state change responsible for sleep disordered breathing (SDB) and the obstructive apnea/hypopnea syndrome (OSAHS), understanding its effects on the upper airway is critical. These include changes in upper airway muscle dilator activity and associated changes in mechanics and reflex activity of the muscles. Currently SDB is thought to result from a combination of anatomical upper airway predisposition and changes in neural activation mechanisms intrinsic to sleep. Detection of SDB is based on identifying abnormal (high resistance) breaths and events, but the clinical tools used to detect these events and an understanding of their impact on symptoms is still evolving. Outcomes research to define which events are most important, and a better understanding of how events lead to physiologic consequences of the syndrome, including excessive daytime somnolence (EDS), will allow physiologic testing to objectively differentiate between "normal" subjects and those with disease.] Ayappa I, Rapoport, et al. New York University School of Medicine, USA. *Sleep Med Rev.* 2003 Feb;7(1):3-7.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=12586528&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12586528&dopt=Abstract)

178. **Upper airway and its surrounding structures in obese and nonobese patients with sleep-disordered breathing.** [The objective was to understand the pathophysiological relationship between obesity and sleep-disordered breathing by using cephalometry with the Muller maneuver. The regression model generated for the nonobese group revealed that the apnea hypopnea index was significantly related to the pharyngeal length and the soft palate thickness. In contrast, the regression model generated for the obese group revealed that the apnea hypopnea index was significantly related to the soft palate length and dynamic position change, the hyoid position, the tongue dynamic position change, and body mass index.] Liao YF, Chuang ML et.al., *Laryngoscope*. 2004 Jun;114(6):1052-9  
<http://www.laryngoscope.com/pt/re/laryngoscope/abstract.00005537-200406000-00018.htm;jsessionid=FHWbG9sc9cn5gM1gfMcWLfs2vPV2B1TXyN6lhVdl9twvdRKf5dBH!2082300909!-949856145!8091!-1>

## **Diseases & Health Related Consequences of OSA**

179. **Acceleration of Cerebral Blood Flow Velocity in a Patient with Sleep Apnea and Intracranial Arterial Stenosis.** [Sleep apnea (SA) syndromes of different etiologies are known to induce complications including cardiovascular diseases and stroke. However, the exact mechanisms involved in cerebral ischemia remain obscure. We measured the cerebral blood flow velocities (CBFV) by means of transcranial Doppler sonography in an 81-year-old patient who presented with an acute ischemic stroke caused by an intracranial middle cerebral artery (MCA) stenosis in the presence of SA syndrome. During apnea episodes simultaneous recordings revealed reduced intra-arterial oxygen but increased carbon dioxide saturation. This resulted in an increased CBFV (220 to 320 cm/s) and suggested intermittent hemodynamic relevance of a structurally only moderate MCA stenosis. Intracranial artery stenosis can become hemodynamically significant due to episodic hypercapnia in patients with SA. This may cause ischemic infarction in the periphery of the related cerebral vascular territories.] Behrens S, Spengos K, et al. *Sleep and Breathing*, Vol.6, No.3, p.111-114.  
<http://www.springerlink.com/content/gabm19le7ng1jux3/?p=a282040b48ec45558916ff2e95d8162e&pi=1>
180. **Allergic Rhinitis and Its Consequences on Quality of Sleep** [Allergic rhinitis (AR) is common and has been shown to impair social life and sleep. Patients with severe symptoms may have more sleep disturbances than those with a mild form of the disease, but this has never been assessed using a validated tool. The objective of our study was to assess, in patients with AR, whether duration and severity of AR are associated with sleep impairment. These data underline the close relationship between AR and sleep and highlight the need for clinicians, particularly general practitioners, to be attentive in this respect.] Leger D, Annesi-Maesano IA, et.al. *Arch Intern Med*. 2006;166:1744-1748. <http://archinte.ama-assn.org/cgi/content/abstract/166/16/1744>
181. **Ambulatory blood pressure after therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised parallel trial.** [Obstructive sleep apnoea is associated with raised blood pressure. In patients with most severe sleep apnoea, nCPAP reduces blood pressure, providing significant vascular risk benefits, and substantially improving excessive daytime sleepiness and quality of life.] Pepperell JC, Ramdassingh-Dow S, et.al., *Lancet*. 2002 Jan 19;359(9302):204-10,  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list\\_uids=11812555&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=11812555&dopt=Abstract)

182. **Association of hypertension and sleep-disordered breathing.** [BACKGROUND: To our knowledge, the association between sleep-disordered breathing (SDB) and hypertension has not been evaluated in subjects from the general population with a wide age range while adjusting for the possible confounding factors of age, body mass index, sex, menopause and use of hormone replacement therapy, race, alcohol use, and smoking. ...RESULTS: Sleep-disordered breathing was independently associated with hypertension when potential confounders were controlled for in the logistic regression analysis. The strength of this association decreased with age and was proportional to the severity of SDB. In the best-fitted model, neither sex nor menopause changed the relationship between hypertension and SDB. CONCLUSIONS: In the results of this study, SDB, even snoring, was independently associated with hypertension in both men and women. This relationship was strongest in young subjects, especially those of normal weight, a finding that is consistent with previous findings that SDB is more severe in young individuals.] Bixler EO, Vgontzas AN, et al. *Arch Intern Med.* 2001 Nov 26;161(21):2634-5.  
[http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=PubMed&list\\_uids=10927725&dopt=Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=PubMed&list_uids=10927725&dopt=Abstract)
183. **Association of sleep-disordered Breathing and the Occurrence of Stroke.** [Sleep-disordered breathing has been linked to stroke in previous studies. However, these studies either used surrogate markers of sleep-disordered breathing or could not, due to cross-sectional design, address the temporal relationship between sleep-disordered breathing and stroke. *Conclusions:* These data demonstrate a strong association between moderate to severe sleep-disordered breathing and prevalent stroke, independent of confounding factors. They also provide the first prospective evidence that sleep-disordered breathing precedes stroke and may contribute to the development of stroke.] Arzt M, Young T, et al. *American Journal of Respiratory and Critical Care Medicine* Vol 172. pp. 1447-1451.  
<http://ajrccm.atsjournals.org/cgi/content/full/172/11/1447>
184. **Association of Sleep-Disordered Breathing, Sleep Apnea, and Hypertension in a Large Community-Based Study.** [Our findings from the largest cross-sectional study to date indicate that SDB is associated with systemic hypertension in middle-aged and older individuals of different sexes and ethnic backgrounds.] Nieto FJ, Young TB., et.al., *JAMA.* 2000;283:1829-1836. [http://jama.ama-assn.org/cgi/content/abstract/283/14/1829?ijkey=cafae293d137dc1943eb613993575cee15ee6227&keytype2=tf\\_ipsecsha](http://jama.ama-assn.org/cgi/content/abstract/283/14/1829?ijkey=cafae293d137dc1943eb613993575cee15ee6227&keytype2=tf_ipsecsha)
185. **Cardiac Rhythm Disturbances in the Obstructive Sleep Apnea Syndrome. Effects of Nasal Continuous Positive Airway Pressure Therapy.** [The data indicate that OSA syndrome predisposes to clinically significant cardiac rhythm disturbances that can be successfully controlled by nCPAP therapy.] Harbison J, O'Reilly P., et.al., *Chest.* 2000;118:591-595.  
[http://www.chestjournal.org/cgi/content/abstract/118/3/591?ijkey=b8471f2ba752b2c82ee0347537f8c451ffaf665c&keytype2=tf\\_ipsecsha](http://www.chestjournal.org/cgi/content/abstract/118/3/591?ijkey=b8471f2ba752b2c82ee0347537f8c451ffaf665c&keytype2=tf_ipsecsha)
186. **Cardiovascular aspects of obstructive sleep apnoea and their relevance to the assessment of the efficacy of nasal continuous positive airway pressure therapy.** [In conclusion, an objective review of the literature pertaining to the cardiovascular effects of OSA should have found that this disorder causes repetitive blood pressure rises at the end of each obstructive apnoea, that these rises are associated with an overall rise in nocturnal blood pressure, and that these changes are reliably normalised by CPAP. There are interesting but

mixed observations with regard to daytime awake arterial blood pressure, and whether there is truly an independent effect for OSA here (after allowing for obesity) remains uncertain. Even if there is an aetiological link with daytime blood pressure, there are no good data showing that this is improved by CPAP. ] Davies RJO. *Thorax* 1998;53:416-418. <http://thorax.bmj.com/cgi/content/full/53/5/416>

187. **Cardiovascular effects of sleep disorders.** [Normal sleep provides a period of physiologically reduced workload for the cardiovascular system for almost one third of the human life span. Snoring, the most common disorder of sleep, heralds the presence of an unstable upper airway and alerts perceptive clinicians to the possibility of OSA. Epidemiologic evidence has implicated snoring as an independent risk factor for the development of hypertension, ischemic heart disease, and cerebral infarction. However, many investigators would attribute these adverse cardiovascular effects to the substantial prevalence of OSA in habitual snorers. The detrimental effects of OSA on hemodynamics and cardiac rhythm have been well documented, and recent data have linked OSA with increased cardiovascular mortality. Worsening hypoxemia during sleep likely contributes to the nocturnal mortality observed in patients with severe COPD. Effective treatment to prevent nocturnal hypoxemia is available for OSA and COPD, with current evidence supporting beneficial effects on survival.] Parish JM, Shepard Jr JW. *Chest*, Vol 97, 1220-1226. <http://www.chestjournal.org/cgi/content/abstract/97/5/1220>
188. **Cardiovascular Manifestations in Obstructive Sleep Apnea.** [The acute hemodynamic effects of OSA include systemic hypertension and pulmonary hypertension, increased left ventricular (LV) and right ventricular (RV) afterload, and reduced cardiac output. Mechanisms causing these changes include increased sympathetic tone, physiologic responses to hypoxia, and generation of negative intrathoracic pressure during inspiratory efforts against an occluded airway. During hypoxia and termination of apnea, there is an increase in serum catecholamine levels that cause an increase in both systemic and pulmonary blood pressures. Hypoxia and hypercapnea increase sympathetic tone. Patients with OSA also exhibit an abnormal peripheral vascular response to hypoxia and increased vasoconstrictor sensitivity. Severe hypoxia during repeated episodes of apnea impairs myocardial contractility. Hypoxia contributes to the acute increase in systemic blood pressure, especially when the oxyhemoglobin saturation is less than 65%. Both hypoxia and hypercapnea can also cause acute pulmonary arterial vasoconstriction during episodes of apnea. The increase in the systemic blood pressure increases LV afterload, which reduces LV stroke volume during the course of apnea. The increase in pulmonary artery pressure also increases RV afterload during episodes of apnea. Reduced LV end-diastolic volume and increased LV afterload reduce stroke volume and cardiac output. During episodes of OSA, LV and RV outputs are reduced. Acute effects of OSA on the cardiovascular system also include reduced myocardial oxygen delivery, increased myocardial oxygen demand, nocturnal myocardial ischemia, nocturnal pulmonary edema, and cardiac arrhythmias. Chronic effects of OSA on the cardiovascular system include sympathetic nervous system activation, reduced heart rate variability, impaired baroreflex control of the heart rate, nocturnal and diurnal systemic hypertension, LV hypertrophy, LV systolic dysfunction, LV diastolic dysfunction, congestive heart failure (CHF), increased platelet aggregability, and increased susceptibility to thrombotic and embolic cardiac and cerebrovascular events. In a substantial per cent of patients with CHF, OSA may play a role in the pathogenesis and

progression of CHF through mechanical, adrenergic, and vascular mechanisms.] Aronow WS. *European Respiratory Disease* <http://www.touchbriefings.com/pdf/2001/aronow.pdf>

189. **Cardiovascular risk factors in patients with obstructive sleep apnoea syndrome.** [These findings indicate that obstructive sleep apnoea syndrome patients are at high risk of future cardiovascular disease from factors other than obstructive sleep apnoea syndrome, and may help explain the difficulties in identifying a potential independent risk from obstructive sleep apnoea syndrome. ] Kiely JL, McNicholas WT., et.al., *Eur Respir J* 2000; 16: 128-133. [http://erj.ersjournals.com/cgi/content/abstract/16/1/128?ijkey=f921aa7998e127fadd2bbfb39e5d2eb746011bbd&keytype2=tf\\_ipsecsha](http://erj.ersjournals.com/cgi/content/abstract/16/1/128?ijkey=f921aa7998e127fadd2bbfb39e5d2eb746011bbd&keytype2=tf_ipsecsha)
190. **Consequences of Comorbid Insomnia Symptoms and Sleep-Related Breathing Disorder in Elderly Subjects.** [The prevalence of sleep-related breathing disorder (SRBD) and insomnia symptoms increases considerably with advancing age, but little is known about their cooccurrence and their effects on daytime functioning when present together. Because insomnia comorbid with SRBD is associated with the greatest functional impairment, and SRBD is commonly found in the elderly population, health care providers should also consider SRBD in elderly patients with insomnia symptoms.] Gooneratne NS, Gehrman PR, et.al. *Arch Intern Med.* 2006;166:1732-1738. <http://archinte.ama-assn.org/cgi/content/abstract/166/16/1732>
191. **Day–Night Pattern of Sudden Death in Obstructive Sleep Apnea.** [The risk of sudden death from cardiac causes in the general population peaks from 6 a.m. to noon and has a nadir from midnight to 6 a.m. Obstructive sleep apnea is highly prevalent and associated with neurohormonal and electrophysiological abnormalities that may increase the risk of sudden death from cardiac causes, especially during sleep. *Results* From midnight to 6 a.m., sudden death from cardiac causes occurred in 46 percent of people with obstructive sleep apnea, as compared with 21 percent of people without obstructive sleep apnea ( $P=0.01$ ), 16 percent of the general population ( $P<0.001$ ), and the 25 percent expected by chance ( $P<0.001$ ). People with sudden death from cardiac causes from midnight to 6 a.m. had a significantly higher apnea–hypopnea index than those with sudden death from cardiac causes during other intervals, and the apnea–hypopnea index correlated directly with the relative risk of sudden death from cardiac causes from midnight to 6 a.m. For people with obstructive sleep apnea, the relative risk of sudden death from cardiac causes from midnight to 6 a.m. was 2.57 (95 percent confidence interval, 1.87 to 3.52). The analysis of usual sleep–wake cycles showed similar results. *Conclusions* People with obstructive sleep apnea have a peak in sudden death from cardiac causes during the sleeping hours, which contrasts strikingly with the nadir of sudden death from cardiac causes during this period in people without obstructive sleep apnea and in the general population.] Gami AS, Howard DE, et al. *NEJM Volume 352:1206-1214 March 24, 2005 Number 12.* <http://content.nejm.org/cgi/content/abstract/352/12/1206>.
192. **Hemodynamic Consequences of Obstructive Sleep Apnea.** [Summary: Patients with obstructive sleep apnea demonstrate both acute and chronic hemodynamic changes attributable to their disease. Acutely, these patients experience repetitive nocturnal hemodynamic oscillations. Sudden increases in heart rate and arterial pressure occur in association with decreases in left ventricular stroke volume immediately following apnea termination. These hemodynamic changes are likely attributable primarily to the effects of oxygen desaturation and arousal, an abrupt change in state. These acute changes occur against a background of altered cardiovascular control. Patients with sleep apnea, even when sleeping without obstructions, fail to display the normal nocturnal decline in arterial pressure

of 10-15% from the waking value. The absence of a nocturnal decline may have chronic consequences, such as development of left ventricular hypertrophy. Another chronic hemodynamic consequence of sleep apnea may be sustained diurnal hypertension. Epidemiologic studies suggest individuals with sleep disordered breathing are at greater risk of daytime hypertension, even after controlling for other risk factors. Although sleep apnea may contribute to pulmonary, as well as systemic hypertension, sleep apnea alone does not appear to be a cause of decompensated right heart failure. Although knowledge of the hemodynamic consequences of sleep apnea has grown in recent years, much remains to be learned.] Weiss JW, Remsburg S, et al. *SLEEP* 1996;19:388-97  
<http://www.journalsleep.org/ViewAbstract.aspx?citationid=651>

193. **High prevalence of hypertension in sleep apnea patients independent of obesity.** [Age, SA, and overweight represent both independent and additive risk factors for development of systemic hypertension. ] Carlson J, et al. *Am J Respir Crit Care Med* 150:72-77, 1994.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=PubMed&list\\_uids=8025776&dopt=medline](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=PubMed&list_uids=8025776&dopt=medline)
194. **Hypertension, cardiac arrhythmias, myocardial infarction, and stroke in relation to obstructive sleep apnea.** [ ] Shepard J. *Clin Chest Med* 13:435-458, 1992.  
<http://www.emedicine.com/neuro/topic419.htm>
195. **Insomnia and Hypersomnia Associated with Depressive Phenomenology and Comorbidity in Childhood Depression.** [Clinical profiles differ between depressed children without and with sleep disturbance, with those presenting insomnia plus hypersomnia being most severely depressed. Differentiating depressed children with different sleep disturbances may have important implications for research efforts on the etiology and therapeutics of child depression.] Liu X, Buysse DJ, et al. *Journal SLEEP, Volume : 30 Issue : 01 Pages : 83-90.*  
<http://www.journalsleep.org/ViewAbstract.aspx?citationid=3121>
196. **Insulin Resistance, Hyperleptinemia, and Obstructive Sleep Apnea in Launois-Bensaude Syndrome.** [ Patients with LBS demonstrated similar metabolic features in terms of insulin sensitivity and hyperleptinemia as patients with “simple” truncal obesity. LBS is not strictly associated with OSA.] Harsch IA, Schahin SP, et.al. *Obesity Research vol 10 No.7 July 2002. P.625-632.* <http://www.obesityresearch.org/cgi/reprint/10/7/625.pdf>
197. **Left Ventricular Dysfunction, Pulmonary Hypertension, Obesity, and Sleep Apnea.** [The purpose of this study was to determine the frequency of central and obstructive sleep apnea in adult patients who have echocardiographic evidence of left ventricular dysfunction and pulmonary hypertension. Subjects with left ventricular dysfunction, pulmonary hypertension (pulmonary artery systolic pressure >30 mm Hg) and no lung disease were evaluated for risk factors associated with pulmonary hypertension. ... We propose that a pulmonary artery systolic pressure of 35 mm Hg or greater in ambulatory patients with CHF may signify an increased risk of sleep apnea.] Blankfield RP, Tapolyai AA, et al. *Sleep and Breathing, Vol.5, No.2, p.57-62.*  
<http://www.springerlink.com/content/525ryldfh1x1w8na/?p=7cf73757247344b680c8872ce3cc09b3&pi=1>
198. **Long-term effects of nasal continuous positive airway pressure on vasodilatory endothelial function in obstructive sleep apnea syndrome.** [Obstructive sleep apnea syndrome (OSAS) is associated with a dysfunction of vascular endothelial cells. The aim of this study was to investigate long-term improvement of endothelial dysfunction in OSAS

with nasal continuous positive airway pressure (nCPAP) treatment. We investigated endothelium-dependent and endothelium-independent vasodilatory function in patients with OSAS using the hand vein compliance technique. ... These results suggest that regular nocturnal nCPAP treatment leads to a sustained restoration of OSAS-induced impaired endothelium-dependent nitric oxide-mediated vasodilation, suggesting an improvement of systemic endothelial dysfunction in patients studied. ] Duchna HW, Orth M, et al. *Sleep and Breathing*, vol 9, No3, p.97-103,

<http://www.springerlink.com/content/w2u582236876h067/?p=0d224b7ebd454c4180cefc276d076786&pi=1>

199. **Long-term outcome for obstructive sleep apnea syndrome patients. Mortality.** [Our data therefore encourage "aggressive" treatment for patients with OSAS.] Partinen M, Jamieson A, et.al., *Chest*, Vol 94, 1200-1204.  
[http://www.chestjournal.org/cgi/content/abstract/94/6/1200?ijkey=b55bb4ccf26da90d61cef21b15ec9ff3f52fe8b6&keytype2=tf\\_ipsecsha](http://www.chestjournal.org/cgi/content/abstract/94/6/1200?ijkey=b55bb4ccf26da90d61cef21b15ec9ff3f52fe8b6&keytype2=tf_ipsecsha)
200. **Mortality and apnea index in obstructive sleep apnea. Experience in 385 male patients.** [OSA patients with an apnea index of greater than 20 have a greater mortality than those below 20 and that UPPP patients be restudied after therapy. If the latter patients are found not to have marked amelioration of their AI, then they should be treated by nasal CPAP or tracheostomy.] He J, Kryger MH, et.al., *Chest*, Vol 94, 9-14.  
[http://www.chestjournal.org/cgi/content/abstract/94/1/9?ijkey=011c4b82da603a03f839144267d5a4d12dccd6e3&keytype2=tf\\_ipsecsha](http://www.chestjournal.org/cgi/content/abstract/94/1/9?ijkey=011c4b82da603a03f839144267d5a4d12dccd6e3&keytype2=tf_ipsecsha)
201. **Mortality in sleep apnea patients: a multivariate analysis of risk factors.** [ ] Lavie P, et al. *Sleep* 18:149-157, 1995.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=7610310&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7610310&dopt=Abstract)
202. **Obstructive Sleep Apnea and Heart Failure: Two Unhappy Bedfellows.** [Congestive heart failure is a major cause of morbidity and mortality and leads to one fifth of hospital admissions in those over 65 years. While the average age at diagnosis increased substantially between the 1950s and 1990s, and the death rate after diagnosis declined by approximately 30%, one-year mortality for all heart failure cases remains high at 25-30% . For symptomatic heart failure, one-year mortality is close to 45% . ACE-inhibitors, [beta]-blockers, and spironolactone have been shown to improve cardiac function, quality of life, and longevity without making major inroads into overall mortality. Cross-sectional data from the Sleep Heart Health Study showed an adjusted odds ratio of 2.2 for self-reported heart failure amongst subjects with obstructive sleep apnea (the upper quartile of apnea-hypopnea index greater than 11 as compared with lower quartile less than 1.3). Two clinical studies in the pre [beta]-blocker treatment era found the prevalence of sleep-disordered breathing (apnea-hypopnea index greater than 15 per hour) in severe systolic heart failure to be 50-60%; 11 to 37% of all patients had obstructive apnea-hypopnea. Others with sleep disordered breathing had mainly central apneas or Cheyne-Stokes respiration. These studies demonstrated associations, not causality. Sleep is normally a period of cardiac rest. Apart from brief bursts of sympathetic activity in REM sleep, sleep is characterized by decreased sympathetic activity and increased vagal activity, which lowers heart rate and blood pressure. This is not so for patients with obstructive sleep apnea. Large negative swings in intrathoracic pressure increase left ventricular afterload. Reflex sympathetic activation secondary to hypoxia and hypercapnia, and arousal from sleep, cause acute surges in blood pressure and heart rate,

further increasing left-ventricular afterload and wall stress. Increased venous return, plus acute hypoxic pulmonary vasoconstriction, increase right-ventricular volume and pressure, which may compromise left-ventricular filling. Vascular pressor responses to hypoxia are increased in patients with obstructive sleep apnea. Also, patients are more likely to have elevated daytime sympathetic activity and systemic blood pressure, which may further perpetuate heart failure. Thus, regardless of whether obstructive sleep apnea is sufficient to cause heart failure, there is ample reason to believe that it could adversely affect left ventricular function in those with an already failing heart.] *American Journal of Respiratory and Critical Care Medicine*, Feb 1, 2004.

[http://findarticles.com/p/articles/mi\\_qa4085/is\\_200402/ai\\_n9408307](http://findarticles.com/p/articles/mi_qa4085/is_200402/ai_n9408307)

203. **Obstructive sleep apnea syndrome is associated with metabolic syndrome rather than insulin resistance.** [OSAS is associated with metabolic syndrome rather than insulin resistance per se. Relatively high prevalence of OSAS is observed in Turkish women in whom it is significantly associated with CHD.] Onat A, Hergene G, et.al. *Sleep Breath* (2007)11:23-30.
204. **Obstructive Sleep Apnea: Implications for Cardiac and Vascular Disease.** [Obstructive sleep apnea is common, readily diagnosed, and usually treatable. It frequently coexists undiagnosed in patients with cardiovascular disease, activates disease mechanisms known to elicit cardiac and vascular damage, and may be implicated in progression of cardiovascular disease and resistance to conventional therapeutic strategies. In the absence of definitive evidence from large-scale trials and a better understanding of potential cost-effectiveness, the likely benefits of diagnosis and treatment of OSA are presently best appraised on an individualized patient basis.] Shamsuzzaman ASM, Gersh BJ, et.al. *JAMA*. 2003;290:1906-1914. <http://jama.ama-assn.org/cgi/content/abstract/290/14/1906>
205. **Obstructive sleep apnea syndrome is associated with metabolic syndrome rather than insulin resistance.** [The aim of this study was to investigate cross-sectionally the prevalence and covariates of obstructive sleep apnea syndrome (OSAS) and its relationship to metabolic syndrome (MS), insulin resistance (IR), and coronary heart disease (CHD) in a population sample of 1,946 men and women representative of Turkish adults. OSAS was identified when habitual snoring and episodes of apnea were combined with another relevant symptom. MS was diagnosed based on modified criteria of the Adult Treatment Panel III and IR by homeostatic model assessment (HOMA). ...Regression models controlling for sex, age, and smoking revealed that MS (and not IR per se) was associated significantly with OSAS (OR 1.94) in nondiabetic individuals. To conclude, abdominal rather than overall obesity in men and smoking among women are significant independent determinants of OSAS in Turkish adults. OSAS is associated with MS rather than IR per se. Relatively high prevalence of OSAS is observed in Turkish women in whom it is significantly associated with CHD.] Onat A, Hergenc G, et al. *Sleep Breathing Vol 11, Number 1 / March, 2007 p.23-30*.  
<http://www.springerlink.com/content/p201943r58m10j3r/?p=cb8b4a6ded8c432e8e9815768c6f94d0&pi=1>
206. **Obstructive sleep apnoea syndrome as a risk factor for hypertension: population study.** [Sleep apnoea syndrome is profoundly associated with hypertension independent of all relevant risk factors.] Lavie P, Herer P, et.al., *BMJ* 2000;320:479-482.  
[http://bmj.bmjournals.com/cgi/content/abstract/320/7233/479?ijkey=e5825615323d20cb715e6f42eddadfd9cf75ce78&keytype2=tf\\_ipsecsha](http://bmj.bmjournals.com/cgi/content/abstract/320/7233/479?ijkey=e5825615323d20cb715e6f42eddadfd9cf75ce78&keytype2=tf_ipsecsha)

207. **Obstructive Sleep Apnea Syndrome. More Insights on Structural and Functional Cardiac Alterations, and the Effects of Treatment With Continuous Positive Airway Pressure.** [The structural and functional consequences of OSA on the heart are influenced by the severity of apnea-hypoxia index. These effects are reversible if the apneic episodes are abolished.] Shivalkar B, Van De Heyning C, et al., *J Am Coll Cardiol*, 2006; 47:1433-1439, <http://content.onlinejacc.org/cgi/content/abstract/47/7/1433>
208. **Population-based study of sleep disordered breathing as a risk factor for hypertension.** [There is a dose-response relationship between sleep-disordered breathing and blood pressure, independent of known confounding factors. If causal, the high prevalence of sleep-disordered breathing could account for hypertension in a substantial number of adults in the United States.] Young T, et al. *Arch Intern Med* 157:1746-1752, 1997. <http://archinte.ama-assn.org/cgi/content/abstract/157/15/1746>
209. **Prospective Study of the Association between Sleep-Disordered Breathing and Hypertension.** [Sleep-disordered breathing is prevalent in the general population and has been linked to chronically elevated blood pressure in cross-sectional epidemiologic studies. We found a dose-response association between sleep-disordered breathing at base line and the presence of hypertension four years later that was independent of known confounding factors. The findings suggest that sleep-disordered breathing is likely to be a risk factor for hypertension and consequent cardiovascular morbidity in the general population.] Peppard PE, Young T., et al., *NEJM Volume 342:1378-1384*, [http://content.nejm.org/cgi/content/abstract/342/19/1378?ijkey=68f4871519be7c2f58b454e5b9d5dd15e48bec00&keytype2=tf\\_ipsecsha](http://content.nejm.org/cgi/content/abstract/342/19/1378?ijkey=68f4871519be7c2f58b454e5b9d5dd15e48bec00&keytype2=tf_ipsecsha)
210. **Pulmonary Hypertension and Sleep-Related Breathing Disorders.** [Pulmonary hypertension (PH), i. e. an increase of mean pulmonary artery pressure above 20 mm Hg under resting conditions, can be observed in different forms of sleep-disordered breathing (SDB). In obstructive sleep apnea (OSA) the apnea-associated triggers of hypoxia and intrathoracic pressure swings lead to repetitive rises of pulmonary artery pressure during sleep. In 20 - 30 % of these patients daytime PH occurs. PH in the setting of OSA is usually mild and rarely causes clinically evident cor pulmonale. Effective CPAP therapy has a beneficial influence on pulmonary hemodynamics in OSA. Severe congestive heart failure (i. e. with a LVEF < 40 %) might provoke pulmonary venous hypertension and thereby stimulation of pulmonary stretch and irritant receptors. The ensuing hyperventilation leads to a decrease of pCO<sub>2</sub> levels below the apneic threshold and thus contributes to the emergence of Cheyne Stokes respiration (CSR) in up to one half of the affected patients. Patients suffering from advanced idiopathic pulmonary arterial hypertension (IPAH) might show a similar breathing pattern while asleep. Possible pathogenetic factors of the nocturnal periodic breathing occurring in end-stage IPAH are prolonged circulation times and hypocapnia. In conclusion, SDB might cause PH (OSA-associated PH). On the other hand, PH might lead to the development of SDB (CSR in congestive heart failure, periodic breathing in IPAH).] Schulz R, Eisele HJ, et al. *Pneumologie* 2005; 59: 270-274. <http://www.thieme-connect.com/DOI/DOI?10.1055/s-2004-830189>
211. **Randomized Placebo-controlled Trial of Continuous Positive Airway Pressure on Blood Pressure in the Sleep Apnea-Hypopnea Syndrome.** [Arterial blood pressure rises at apnea termination, and there is increasing evidence that the sleep apnea-hypopnea syndrome (SAHS) is associated with daytime hypertension. CPAP can reduce blood pressure in patients with SAHS, particularly in those with nocturnal oxygen desaturation, but the decrease is

small.] Faccenda JF, MacKay JF, et.al., *Am. J. Respir. Crit. Care Med.*, Volume 163, Number 2, February 2001, 344-348.

[http://ajrccm.atsjournals.org/cgi/content/abstract/163/2/344?ijkey=c709783b300dd1045d424a6fa2ba1921b513233c&keytype=tf\\_ipsecsha](http://ajrccm.atsjournals.org/cgi/content/abstract/163/2/344?ijkey=c709783b300dd1045d424a6fa2ba1921b513233c&keytype=tf_ipsecsha)

212. **Respiratory Disturbance Index An Independent Predictor of Mortality in Coronary Artery Disease.** [Untreated OSA is associated with an increased risk of cardiovascular mortality in patients with CAD. Furthermore, it appears appropriate that RDI is taken into consideration when evaluating secondary prevention models in CAD.] Peker Y, Hedner J., et.al., *Am. J. Respir. Crit. Care Med.*, Volume 162, Number 1, July 2000, 81-86.

[http://ajrccm.atsjournals.org/cgi/content/abstract/162/1/81?ijkey=7d9a1df912a6cc1cd70d46060d6d4ebbab8432f8&keytype=tf\\_ipsecsha](http://ajrccm.atsjournals.org/cgi/content/abstract/162/1/81?ijkey=7d9a1df912a6cc1cd70d46060d6d4ebbab8432f8&keytype=tf_ipsecsha)

213. **Role of Sleep Duration and Quality in the Risk and Severity of Type 2 Diabetes Mellitus.** [Evidence from laboratory and epidemiologic studies suggests that decreased sleep duration or quality may increase diabetes risk. We examined whether short or poor sleep is associated with glycemic control in African Americans with type 2 diabetes mellitus. In our sample, sleep duration and quality were significant predictors of HbA<sub>1c</sub>, a key marker of glycemic control. Combined with existing evidence linking sleep loss to increased diabetes risk, these data suggest that optimizing sleep duration and quality should be tested as an intervention to improve glucose control in patients with type 2 diabetes.] Knutson KL, Ryden AM, et.al. *Arch Intern Med.* 2006;166:1768-1774. <http://archinte.ama-assn.org/cgi/content/abstract/166/16/1768>

214. **Self-reported sleep quality is associated with the metabolic syndrome.** [STUDY OBJECTIVES: To determine whether a simple, structured self-report of overall sleep quality is associated with the presence of the metabolic syndrome and its component risk factors. DESIGN: An observational, cross-sectional study comparing global scores on the Pittsburgh Sleep Quality Index with concurrently collected measures of the components of the metabolic syndrome and presence or absence of the syndrome. The metabolic syndrome criterion of the American Heart Association/National Heart, Blood, and Lung Institute was adopted. ... CONCLUSIONS: Self-reported global sleep quality is significantly related to the metabolic syndrome and several of its core components.] Jennings JR, Muldoon MF, et.al. *Sleep* 2007;30(2):219-23.

<http://www.websciences.org/cftemplate/NAPS/archives/indiv.cfm?ID=20065195>

215. **Serum amyloid a in obstructive sleep apnea.** [Patients with severe obstructive sleep apnea (OSA) may have increased risk for cardiovascular and cerebrovascular diseases. Serum amyloid A (SAA) protein has recently been linked to the development of atherosclerosis, stroke, diabetes, and dementia. Plasma SAA levels are more than 2-fold greater in patients with moderate to severe OSA compared with subjects with mild OSA or healthy controls regardless of gender. Elevated SAA may contribute to any increased risk for cardiovascular and neuronal dysfunction in patients with OSA.] Svatikova A, Wolk R, et.al. *Circulation.* 2003;108:1451. <http://circ.ahajournals.org/cgi/content/abstract/108/12/1451>

216. **Serum Cardiovascular Risk Factors in Obstructive Sleep Apnea.** [Obstructive sleep apnea (OSA) patients have increased cardiovascular morbidity and mortality. The cardiovascular markers associated with OSA are currently not defined. *Objectives:* The aims of this study were to determine whether OSA is associated with serum cardiac risk markers and to investigate the relationship between them. *Results:* There was no significant difference between group 1 and group 2 in total cholesterol, LDL-C, HDL-C,

triglyceride, apolipoprotein A-I, apolipoprotein B, and lipoprotein (a). All of the M-mode echocardiographic parameters were in the normal reference range. Serum homocysteine and CRP levels were significantly increased in group 1 compared to group 2 ( $p < 0.05$ ). Serum CRP values were increased in both group 1 and group 2 when compared with control subjects ( $p < 0.05$ ). Serum homocysteine values were higher in group 1 than in control subjects ( $p < 0.05$ ). *Conclusions:* Our results show that OSA syndrome is associated not only with slight hyperhomocysteinemia but also with increased CRP concentrations. Increased plasma concentrations of homocysteine and CRP can be useful in clinical practice to be predictor of long-term prognosis for cardiovascular disease and the treatment of OSA.] Can M, Acikgoz S, et al. CHEST. 2006;129(2):233-277.

<http://www.chestjournal.org/cgi/content/abstract/129/2/233>

217. **Sleep and cardiac diseases amongst elderly people.** [Poor sleep was associated with both an increase in angina pectoris and cardiac arrhythmias.] Ashland R. *J Intern Med* 236:65-68, 1994. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=8021575&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8021575&dopt=Abstract)
218. **Sleep apnea and hypertension. A population-based study.** [Our data indicate an association between hypertension and sleep apnea independent of obesity, age, and sex in a nonselected, community-based adult population.] Hla K, et al. *Ann Intern Med* 120:382-388, 1994. <http://www.annals.org/cgi/content/abstract/120/5/382>
219. **Sleep apnea and mortality in an aged cohort.** [Multiple regression with the Cox proportional hazards model suggested that cardiovascular death was most clearly associated with age in this cohort. These results raise the possibility that "natural" death during sleep in the elderly may be associated with specific pathophysiological events during sleep.] Bliwise D, et al. *Am j Public Health* 78:544-547, 1998. <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1349335>
220. **Sleep apnea in acute cerebrovascular diseases: final report on 128 patients.** [Multiple regression analysis identified age, BMI, diabetes, and SSS as independent predictors of AHI. Sleep apnea has a high frequency in patients with TIA and stroke, particularly in older patients with high BMI, diabetes, and severe stroke. These results may have implications for prevention, acute treatment, and rehabilitation of patients with acute cerebrovascular diseases.] Bassetti C, Aldrich MS., *Sleep*. 1999 Mar 15;22(2):217-23. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list\\_uids=10201066&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=10201066&dopt=Abstract)
221. **Sleep Disordered Breathing and Cardiovascular Disease.** [There is strong evidence for an association between sleep apnea and cardiovascular diseases, particularly OSA and hypertension. For other cardiovascular diseases, the evidence, although suggestive, remains circumstantial. Although the comprehensive diagnosis and treatment of OSA and CSA is determined by overnight polysomnography, a history of witnessed apneas during sleep, daytime somnolence, and evidence of oxygen desaturation on overnight oximetry should heighten the index of suspicion for significant sleep apnea. OSA should be considered in patients with refractory hypertension, particularly in obese subjects without the expected nocturnal decline in blood pressure, and in patients with nocturnal cardiac ischemia, nocturnal arrhythmias, and stroke. Both OSA and CSA should be considered in CHF patients who are poorly responsive to conventional treatment.] Wolk R, Kara T, et.al. *Circulation* 2003;108;9-12. <http://circ.ahajournals.org/cgi/reprint/108/1/9>

222. **Sleep-disordered breathing among patients with first-ever stroke.** [The prevalence of hypertension and coronary heart disease were higher among stroke patients with an RDI of 20 or higher than in those without SDB. We conclude that the prevalence of SDB among patients with stroke is high. Examination of stroke should include screening for SDB.] Wessendorf TE, Teschler H, et.al., *J Neurol.* 2000 Jan;247(1):41-7.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list\\_uids=10701896&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=10701896&dopt=Abstract)
223. **Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study.** [Disordered breathing during sleep is associated with acute, unfavorable effects on cardiovascular physiology, but few studies have examined its postulated association with cardiovascular disease(CVD). Sleep-disordered breathing was associated more strongly with self-reported heart failure and stroke than with self-reported coronary heart disease: the relative odds (95% CI) of heart failure, stroke, and coronary heart disease (upper versus lower AHI quartile) were 2.38 (1.22-4.62), 1.58 (1.02- 2.46), and 1.27 (0.99-1.62), respectively. These findings are compatible with modest to moderate effects of sleep-disordered breathing on heterogeneous manifestations of CVD within a range of AHI values that are considered normal or only mildly elevated.] Shahar E, Whitney CW, et.al. *Am J Respir Crit Care Med.* 2001 Jan;163(1):19-25.  
<http://ajrccm.atsjournals.org/cgi/content/full/163/1/19>
224. **Sleep-disordered breathing and cardiovascular disease: epidemiologic evidence for a relationship.** [Epidemiology studies of SDB and CVD to date do not provide a conclusive answer to the question of the degree to which SDB impacts CVD or mortality due to CVD. However, most of the studies seem to be consistent with a positive, but perhaps small, association. All the findings discussed or referred to in this review are likely to be biased to some degree. Bias can be both towards underestimation (e.g., from mismeasurement of SDB, and over-control for intermediate factors) and overestimation (e.g., from inadequate control of confounders and improper comparison groups), and the net magnitude of competing biases undoubtedly varies from study to study. Small associations were found in the prospective population-based studies, with one exception. The most obvious methodologic problem in these studies would be likely to result in underestimation of the associations. The case-control studies, in contrast, showed large associations, but serious biases in these studies would probably cause overestimation. Small associations of marginal statistical significance were reported from cross-sectional analyses; findings were limited by sample size. Although each individual study to date could be (and has been ) "dismissed" due to weaknesses, collectively they provide evidence that we cannot dismiss the hypothesis that SDB causes CVD. In many cases, the weak associations can be explained by problems that likely cause underestimation. In fact, finding any association with the limitations of most of the past studies is remarkable. Perhaps most important, the findings to date, in conjunction with biologically plausible mechanisms have sparked the interest needed to initiate the large undertaking of a population-based prospective study. The Sleep Heart Health Study (SHHS)<sup>15</sup> is a large multicenter prospective study specifically designed to investigate the role of SDB in incident coronary heart disease, stroke, increased blood pressure, and all-cause-mortality. A key feature of the study is that home polysomnography studies are performed on a sample of 6600 men and women, 40 years of age and older, drawn from the samples of other longitudinal studies. The new data collected by SHHS can then be linked to the large amount of data on cardiovascular risk factors available from the "parent" studies.

All baseline polysomnography studies have now been completed. Cross-sectional analyses of SDB and CVD history are now being analyzed, and collection of outcome data for longitudinal analyses is underway. Results from SHHS and other studies in the near future should greatly increase our ability to assess the association of SDB and CVD.] Young T, Peppard P. **1: Sleep.** 2000 Jun 15;23 Suppl 4:S122-6.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=10893084&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10893084&dopt=Citation)

225. **Sleep-Disordered Breathing and Cardiovascular Risk.** [Sleep-disordered breathing, broadly characterized by obstructive sleep apnea (OSA) and central sleep apnea (CSA), is an increasingly recognized public health burden. OSA, consisting of apneas or hypopneas associated with respiratory efforts in the face of upper airway narrowing or collapse, is a common disorder that can be effectively treated with continuous positive airway pressure (CPAP).1 OSA not only results in daytime sleepiness and impaired executive function, but also has been implicated as a possible cause of systemic disease, particularly of the cardiovascular system. CSA, which may coexist with OSA, has gained attention because of the association of Cheyne-Stokes respiration with an everincreasing prevalence of heart failure in an aging population. This article reviews some of the extensive literature on pathophysiologic mechanisms as they may relate to the development of cardiac and vascular disease and examine the evidence suggesting OSA as a specific cause of certain cardiovascular conditions. Available evidence regarding the implications of CSA in the context of heart failure is discussed.] Caples SM, Garcia-Touchard A, et.al. *Journal SLEEP Volume 30/ Issue 3 - March 1, 2007.*

<http://www.journalsleep.org/ViewAbstract.aspx?citationid=3166>

226. **Sleep-disordered breathing and stroke.** [Sleep-related breathing disorders are strongly associated with increased risk of stroke independent of known risk factors. The direction of causation favors sleep-disordered breathing leading to stroke rather than the other way around, although definitive proof of this awaits the results of prospective cohort studies. If causal, even a moderately elevated risk of stroke coupled with the high prevalence of sleep-disordered breathing could have significant public health implications. The relationship between sleep-disordered breathing and stroke risk factors is complex, and likely part of the risk for cerebrovascular events is because of higher cardiovascular risk factors in patients with increased RDI. The mechanisms underlying this increased risk of stroke are multifactorial and include reduction in cerebral blood flow, altered cerebral autoregulation, impaired endothelial function, accelerated atherogenesis, thrombosis, and paradoxical embolism. Because of the effects of sleep-disordered breathing on vascular tone, hypertension is believed to be a major mechanism by which sleep-disordered breathing might influence risk of stroke. Because sleep-related breathing disorders are treatable patients with stroke/TIA should undergo investigation, with a thorough sleep history interview, physical examination, and polysomnography. Treatment of sleep apnea has been shown to improve quality of life, lower blood pressure, improve sleep quality, improve neurocognitive functioning, and decrease symptoms of excessive daytime sleepiness [98]. Further treatment trials are needed to determine whether treatment improves outcome after stroke and whether treatment may serve as secondary prophylaxis and modify the risk of recurrent stroke or death.] Yaggi H, Mohsenin V. *Clin Chest Med.* 2003 Jun;24(2):223-37.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed&cmd=retrieve&dopt=abstract&list\\_uids=12800780](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed&cmd=retrieve&dopt=abstract&list_uids=12800780)

227. **Sleepiness and Sleep in Patients With Both Systolic Heart Failure and Obstructive Sleep Apnea.** [Adverse effects of obstructive sleep apnea (OSA), including sleep deprivation, can contribute to the progression of heart failure. The usual indication to diagnose and treat sleep apnea is subjective sleepiness. Previous studies suggest that patients with both heart failure and obstructive sleep apnea often do not complain of sleepiness, albeit their sleep time may be reduced. Therefore, we tested the hypothesis that patients with heart failure have less sleepiness and sleep less compared with subjects without heart failure for a given severity of OSA. . . . Patients with heart failure have less subjective daytime sleepiness compared with individuals from a community sample, despite significantly reduced sleep time, whether or not they have OSA. In patients with heart failure, the absence of subjective sleepiness is not a reliable means of ruling out OSA.] Arzt M, Young T, et.al. *Arch Intern Med.* 2006;166:1716-1722. <http://archinte.ama-assn.org/cgi/content/abstract/166/16/1716>
228. **Sleep-related myocardial ischemia and sleep structure in patients with obstructive sleep apnea and coronary heart disease.** [It is concluded that patients with CHD and obstructive sleep apnea are endangered by apnea-associated ischemia and that these ischemic episodes lead to activation of the CNS and additional fragmentation of sleep. Patients with nocturnal ischemia should be screened for underlying sleep apnea even if nitrate therapy fails.] Schafer H, Koehler U, et.al., *Chest*, Vol 111, 387-393. [http://www.chestjournal.org/cgi/content/abstract/111/2/387?ijkey=faac93b19298091f56b8102edade3fe270c9e794&keytype2=tf\\_ipsecsha](http://www.chestjournal.org/cgi/content/abstract/111/2/387?ijkey=faac93b19298091f56b8102edade3fe270c9e794&keytype2=tf_ipsecsha)
229. **Snoring and risk of cardiovascular disease in women.** [These data suggested that snoring is associated with a modest but significantly increased risk of CVD in women, independent of age, smoking, BMI and other cardiovascular risk factors. While further study is needed to elucidate the biological mechanism underlying this association, snoring may help clinicians identify individuals at higher risk for CVD.] Hu FB, Willett WC, et.al. *J Am Coll Cardiol.* 2000 Feb;35(2):308-1. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=PubMed&list\\_uids=10676674&dopt=medline](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=PubMed&list_uids=10676674&dopt=medline)
230. **Snoring and the Risk of Ischemic Brain Infarction.** [ Study indicates that snoring may be a risk factor for ischemic stroke, possibly because of the higher prevalence of an obstructive sleep apnea syndrome among snorers than nonsnorers.] Palomaki H. *Stroke* 1991;22:1021-1025.) <http://stroke.ahajournals.org/cgi/reprint/22/8/1021.pdf>
231. **Snoring every night as a risk factor for myocardial infarction: a case-control study.** [ ] D'Alessandro R, et al. *BMJ* 300:1557-1558m 1990. [www.bmjournals.com](http://www.bmjournals.com). [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=2372622&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2372622&dopt=Citation)
232. **The cardiovascular effects of obstructive sleep apnoeas: analysis of pathogenic mechanisms.** [Obstructive sleep apnoeas (OSA) exert immediate marked cardiovascular effects, and may favour the development of systemic and pulmonary hypertension in the long-term. As for the pathogenesis of the acute cardiovascular changes, the first studies highlighted the role of OSA-induced hypoxia and mechanical changes. However, more recent work pointed to the role played by the arousal reaction terminating OSA, and to the activity of the autonomic nervous system during apnoea and inter-apnoeic phase. As for the pathogenesis of chronic cardiovascular changes, recent findings suggest that the link between OSA and systemic hypertension may be through an abnormal function of the carotid body and underline the importance of chronic intermittent hypoxia versus continuous hypoxia in

the development of stable systemic hypertension. On the other hand, OSA do not appear to enhance strongly the development of stable pulmonary hypertension. In this review, we analyze OSA-induced cardiovascular changes with particular emphasis on to the interplay of the possible pathogenic mechanisms involved. Acute OSA-induced cardiovascular alterations during the apnoeic phase appear to result mainly from the mechanical effects of OSA, while during the interapnoeic phase they seem mostly determined by chemical factors (hypoxia, hypercapnia) and by the arousal reaction. In addition, the role of reflex changes elicited by resumption of ventilation should be reconsidered, since lung inflation seems to exert a positive effect on the cardiovascular changes occurring at the end of OSA. This would be in contrast with the inhibitory effects described as "lung inflation reflex", and deserves further study.] Bonsignore MR, Marrone O, et.al. *Eur Respir J* 1994; 7: 786-805.

<http://erj.ersjournals.com/cgi/content/abstract/7/4/786>

233. **The effect of continuous positive airway pressure on glucose control in diabetic patients with severe obstructive sleep apnea.** [Obstructive sleep apnea (OSA) is independently associated with glucose intolerance and insulin resistance, and recent studies have shown that continuous positive airway pressure (CPAP) improves insulin sensitivity. The objective of this study was to describe the change in glycosylated hemoglobin (HbA1c) after treatment with CPAP in patients with type 2 diabetes mellitus and OSA. ... Treatment with CPAP leads to a clinically significant drop in HbA1c in patients with type 2 diabetes mellitus and severe OSA.] Hassaballa HA, Tulaimat A, et al. *Sleep and Breathing, Vol.9, No.4, p.176-180. Dec 2005.*  
<http://www.springerlink.com/content/7p633037p0n1j2gh/?p=dff5c422b70a4a588776edec09f78be9&pi=4>
234. **Time Course of Sleep-related Breathing Disorders in First-Ever Stroke or Transient Ischemic Attack.** [Obstructive events seem to be a condition prior to the neurological disease whereas central events and CSB could be its consequence.] Parra O, Arboix A, et.al., *Am. J. Respir. Crit. Care Med., Volume 161, Number 2, February 2000, 375-380.*  
[http://ajrccm.atsjournals.org/cgi/content/abstract/161/2/375?ijkey=a5db0f35277e51d9f059f87a0b6a527347c9aa37&keytype=tf\\_ipsecsha](http://ajrccm.atsjournals.org/cgi/content/abstract/161/2/375?ijkey=a5db0f35277e51d9f059f87a0b6a527347c9aa37&keytype=tf_ipsecsha)
235. **Treatment of sleep apnea in congestive heart failure with a dental device - The effect on brain natriuretic peptide and quality of life.** [The aim of the present study was to investigate the effect of a mandibular advancement device (MAD) for the treatment of sleep apnea (SA) on plasma brain natriuretic peptide (BNP), left ventricular ejection fraction (LVEF), and health-related quality of life (HRQL) in patients with mild to moderate stable congestive heart failure (CHF). ... We conclude that SA treatment with a MAD on patients with mild to moderate stable CHF appears to result in the reduction of plasma BNP levels. Further studies to investigate if the observed reduction in BNP concentrations also result in improved prognosis are warranted.] Eskafi M, Cline C, et al. *Sleep and Breathing, Vol.10, Number 2 / June, 2006, p. 90-97.*
238. <http://www.springerlink.com/content/j70201646324g222/?p=150943e8bce04eb78e373382f8ffe8b5&pi=5>
239. **Vascular Dysfunction in Sleep Apnea: A Reversible Link to Cardiovascular Disease?** [In the past decade, obstructive sleep apnea has been increasingly recognized as an important and independent risk factor for cardiovascular disease. In addition, large cross-sectional and prospective studies have demonstrated that sleep-disordered breathing predicts hypertension, a major risk factor for cardiovascular disease, in a dose-dependent fashion.

Sleep apnea is associated with endothelial dysfunction and that it may be reversible with nocturnal continuous positive airway pressure. These studies add further weight to the concept that sleep-disordered breathing has profound adverse consequences on cardiovascular health.] Imadojemu, VA, Sinoway, L I, et al. *American Journal of Respiratory and Critical Care Medicine*, Feb 1, 2004. <http://171.66.122.149/cgi/content/full/169/3/328>

240. **Women with Sleep Apnea Have Lower Levels of Sex Hormones.** [Background: Low levels of sex hormones, especially progesterone, are suspected as a risk factor for sleep-disordered breathing (SDB). ... We conclude that reductions in female sex hormones are associated with an increased probability of SDB in women with daytime sleepiness.] Netzer NC, Eliasson AH, et al. *Sleep and Breathing*, Vol.7, No.1, p.25-29. <http://www.springerlink.com/content/5rjv8hr9mne7lerw/?p=8b14c9625fc64dfb9ded4de7dad5b9a8&pi=3>

## **Accidents**

241. **Accidents in obstructive sleep apnea patients treated with nasal continuous positive airway pressure: a prospective study.** [It is suggested that treatment with CPAP decreases the number of accidents occurring in OSA patients. This result may have important implications in the evaluation of the cost/benefit ratio when treating OSA patients.] Krieger J, Meslier N, et.al., *Chest*, Vol 112, 1561-1566. [http://www.chestjournal.org/cgi/content/abstract/112/6/1561?ijkey=bbf61a756fcad4beaa8173f427b2d8ab06ef4c7c&keytype=tf\\_ipsecsha](http://www.chestjournal.org/cgi/content/abstract/112/6/1561?ijkey=bbf61a756fcad4beaa8173f427b2d8ab06ef4c7c&keytype=tf_ipsecsha)
242. **Automobile accidents in patients with sleep disorders.** [Patients with a wide variety of sleep disorders appear to be at increased risk for sleep-related accidents. The severity and duration of hypersomnia are probably not the only factors that contribute to that risk. These findings have implications for the management of patients with sleep disorders.] Aldrich MS. *Sleep* 1989 Dec; 12(6):487-94. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list\\_uids=2595172&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=2595172&dopt=Abstract)
243. **Automobile accidents involving patients with obstructive sleep apnea.** [We compared the driving records of 29 patients with obstructive sleep apnea with those of 35 subjects without sleep apnea. The patients with sleep apnea had a sevenfold greater rate of automobile accidents than did the subjects without apnea (p less than 0.01). The percentage of persons with one or more accidents was also greater in the patients with apnea than in the control subjects without apnea (31% versus 6%, p less than 0.01). The percentage of persons having one or more accidents in which they were at fault was also greater in the patients with apnea than in the control subjects (24% versus 3%, p less than 0.02). The automobile accident rate of the patients with sleep apnea was 2.6 times the accident rate of all licensed drivers in the state of Virginia (p less than 0.02). In addition, 24% of patients with sleep apnea reported falling asleep at least once per week while driving. We conclude that patients with obstructive sleep apnea have a significantly higher frequency of auto accidents than do subjects without apnea. Impaired drivers with sleep apnea may cause many preventable auto accidents.] Findley L, et al. *Am Rev Respir Dis* 138:337-340, 1988. [www.agrcm.org](http://www.agrcm.org) [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=3195832&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3195832&dopt=Abstract)
244. **Drivers with untreated sleep apnea. A cause of death and serious injury.** [Because drivers with untreated sleep apnea may cause a large number of preventable automobile

accidents, physicians have specific duties involving these drivers.] Findley L, et al. *Arch Intern Med* 151:1451-1452, 1991.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=2064498&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2064498&dopt=Abstract)

245. **Prevalence of daytime sleepiness in a population of drivers.** [Our data confirm that daytime sleepiness is not only common in the general population, but also among drivers. Because daytime sleepiness is known to be a major factor in motor vehicle accidents,<sup>2</sup> it is critical that measures be taken to combat sleepiness at the wheel.] Benbadis SR, Perry MC, et.al., *Neurology* 1999;52:209.  
[http://www.neurology.org/cgi/content/full/52/1/209?ijkey=bca18d0644d42b95d88fc3ed40a072a9d8f0e4e3&keytype2=tf\\_ipsecsha](http://www.neurology.org/cgi/content/full/52/1/209?ijkey=bca18d0644d42b95d88fc3ed40a072a9d8f0e4e3&keytype2=tf_ipsecsha)
246. **Prevalence of risk factors for obstructive sleep apnea syndrome in interstate bus drivers.** [OBJECTIVE: To determine the prevalence of risk factors for obstructive sleep apnea syndrome in interstate bus drivers. ... CONCLUSION: The rate of stimulant use found in the group of drivers evaluated is alarming. The high prevalence of daytime sleepiness indicates that attentiveness is reduced in this population.] Viegas CA, De Oliveira HW. *J Bras Pneumol* 2006;32(2):144-9.  
<http://www.websciences.org/cftemplate/NAPS/archives/indiv.cfm?ID=20065048>
247. **Risk of traffic accidents in patients with sleep-disordered breathing: reduction with nasal CPAP.** [We conclude that treatment of sleep-disordered breathing by nasal continuous positive airway pressure is related to reduction in patient motor vehicle accident rates, probably due to the reversal of excessive daytime sleepiness.] Cassel W, Ploch T. et.al., *Eur Respir J* 1996; 9: 2606-261,  
[http://erj.ersjournals.com/cgi/content/abstract/9/12/2606?ijkey=38a7466967be0f28c57d82bf27957a64c3a809db&keytype2=tf\\_ipsecsha](http://erj.ersjournals.com/cgi/content/abstract/9/12/2606?ijkey=38a7466967be0f28c57d82bf27957a64c3a809db&keytype2=tf_ipsecsha)
248. **Simulated driving performance in patients with obstructive sleep apnea.** [We concluded that in laboratory driving performance skills are markedly impaired in over half our group with sleep apnea.] George CF, Boudreau AC, et.al., *Am. J. Respir. Crit. Care Med.*, Vol 154, No. 1, Jul 1996, 175-181.  
[http://ajrcm.atsjournals.org/cgi/content/abstract/154/1/175?ijkey=bae740dc4148d53c84acb407834e92700203e7b2&keytype2=tf\\_ipsecsha](http://ajrcm.atsjournals.org/cgi/content/abstract/154/1/175?ijkey=bae740dc4148d53c84acb407834e92700203e7b2&keytype2=tf_ipsecsha)
249. **Sleep related vehicle accidents.** [Sleep related vehicle accidents are largely dependent on the time of day and account for a considerable proportion of vehicle accidents, especially those on motorways and other monotonous roads.] Horne JA, Reyner LA, *BMJ* 1995;310:565-567,  
[http://bmj.bmjournals.com/cgi/content/abstract/310/6979/565?ijkey=405c352bcb0e25f4bdb360962be286184c97a74d&keytype2=tf\\_ipsecsha](http://bmj.bmjournals.com/cgi/content/abstract/310/6979/565?ijkey=405c352bcb0e25f4bdb360962be286184c97a74d&keytype2=tf_ipsecsha)
250. **The association between sleep apnea and the risk of traffic accidents. Driving with Sleep Apnea.** [Sleep apnea is not the only condition causing sleepiness that increases the risk of traffic accidents. Consumption of alcohol, sleep deprivation, working at night, driving between the hours of midnight and 6 a.m. or for long periods without a break, narcolepsy, and the use of sedating drugs all cause sleepiness and have been implicated in traffic accidents. The presence of any combination of these factors also substantially increases the risk of a traffic accident. Sleep apnea is most likely a factor in a substantial number of accidents.] Editorial, *NEJM* Vol.340:881-883, March 18, 1999.

[http://content.nejm.org/cgi/content/full/340/11/881?ijkey=cebd8c33162672ff538e1bb31996d00e9f7079cf&keytype2=tf\\_ipsecsha](http://content.nejm.org/cgi/content/full/340/11/881?ijkey=cebd8c33162672ff538e1bb31996d00e9f7079cf&keytype2=tf_ipsecsha)

251. **The Role of Sleep-Disordered Breathing, Daytime Sleepiness, and Impaired Performance in Motor Vehicle Crashes—A Case Control Study.** [Study Objective: To examine levels of sleep-disordered breathing, daytime sleepiness, and impaired performance in 60 motor vehicle crash drivers and 60 controls matched for age, gender, and body mass index. ... Conclusion: Crash drivers demonstrated significantly more driver sleepiness, slower reaction times and a trend for greater objective sleepiness compared with well-matched controls. However, the findings in crash drivers were independent of medical causes of sleep fragmentation, with both cases and controls showing moderate levels of unrecognized mild sleep-disordered breathing. Crash prevention strategies should focus on increasing personal awareness of the risks of sleepiness behind the wheel in all individuals. ] Kingshott RN, Cowan JO. Et al. *Sleep and Breathing, Vol.8, No.2, p.61-72.*  
<http://www.springerlink.com/content/25r39aeflf72479n/?p=491d42edd652406ba1c930b99226ed91&pi=0>
252. **Traffic accidents in commercial long-haul truck drivers: the influence of sleep-disordered breathing and obesity.** [We conclude that a complaint of excessive daytime sleepiness is related to a significantly higher automotive accident rate in long-haul commercial truck drivers. Sleep-disordered breathing with hypoxemia and obesity are risk factors for automotive accidents.] Stoohs RA, Guilleminault C, et.al., *Sleep. 1994 Oct;17(7):619-23.*  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list\\_uids=7846460&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=7846460&dopt=Abstract)

## **Polysomnography, Portable Monitoring**

253. **A comparison of clinical assessment and home oximetry in the diagnosis of obstructive sleep apnea.** [We concluded that home oximetry with CT90 < 1% practically excludes clinically significant OSA. Conversely, home oximetry with DI > or = 15 for 4% desaturations makes OSA likely: the positive predictive value for OSA is 83% if the pretest probability of OSA is 30% and over 90% if the pretest probability is at least 50%.] Gyulay S, et al. *Am Rev Respir Dis 147:50-53, 1993.*  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list\\_uids=8420431&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=8420431&dopt=Abstract)
254. **CPAP Compliance in Sleep Apnea Patients with and without Laboratory CPAP Titration.** [Advances in auto-adjusting positive airway pressure technology for obstructive sleep apnea now permit this treatment to be initiated outside of the sleep laboratory environment, bypassing the need for laboratory-based titration studies. Thus far, little research has addressed how such developments may affect compliance to continuous positive airway pressure (CPAP). ... These findings suggest that patients' sleep laboratory experience with CPAP and the support and education provided by sleep technologists are important factors in facilitating CPAP compliance. ] Means MK, Edinger JD, et al. *Sleep and Breathing, Vol 8, No.1, p.7-14.*  
<http://www.springerlink.com/content/c6cnyxd7hvx9h298/?p=8c13544087e8469cb0c4d7aad759870d&pi=1>

255. **Determining the site of upper airway collapse in obstructive sleep apnea with airway pressure monitoring.** [The site of airway collapse remained fairly constant through various sleep stages and positions.] Katsantonis G, et al. *Laryngoscope* 103:1126-1131, 1993. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=8412449&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8412449&dopt=Citation)
256. **Full polysomnography in the home.** [Using the DHSS, unattended full PSG can be performed in the home with reliable and high quality recordings. Full PSG can be extended to a larger patient population, because it is no longer limited by the number of beds, and there is a reduction in cost due to elimination of overnight staff and facility cost.] Fry J, et al. *Sleep* 21:635-642, 1998. [www.journalsleep.org](http://www.journalsleep.org) [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9779523&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9779523&dopt=Abstract)
257. **Portable computerized polysomnography in attended and unattended settings.** [Portable polysomnography is a viable alternative to laboratory-based polysomnography and may be improved further by better sensor attachment.] Mykytyn I, et al. *Chest* 115:114-122, 1999. <http://www.chestjournal.org/cgi/content/abstract/115/1/114>
258. **Portable recording in the assessment of obstructive sleep apnea. ASDA standards of practice.** [The objective assessment of patients with a presumptive diagnosis of obstructive sleep apnea (OSA) has primarily used attended polysomnographic study. Recent technologic advances and issues of availability, convenience and cost have led to a rapid increase in the use of portable recording devices. However, limited scientific information has been published regarding the evaluation of the efficacy, accuracy, validity, utility, cost effectiveness and limitations of this portable equipment. Attaining a clear assessment of the role of portable devices is complicated by the multiplicity of recording systems and the variability of clinical settings in which they have been analyzed. This paper reviews the current knowledge base regarding portable recording in the assessment of OSA, including technical considerations, validation studies, potential advantages and disadvantages, issues of safety, current clinical usage and areas most in need of further study.] Ferber R, Millman R, et.al. *Sleep* 17:378-392, 1994. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=7973323&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7973323&dopt=Citation)
259. **The usefulness of Sleep Apnea Syndrome screening using a portable pulse oximeter in the workplace.** [Sleep Apnea Syndrome (SAS) is a condition characterized by sleep-disordered breathing resulting in health impairment and sleep problems. From the viewpoints of the prevention of health impairment, accidents at work and traffic accidents, active implementation of screening for SAS in workplaces is necessary. Using a portable pulse oximeter, we conducted SAS screening for workers, who applied for the screening or who were instructed to participate by occupational physicians based on their symptoms at the time of medical check-up, in order to evaluate the effectiveness of a portable pulse oximeter as a screening device in the workplace. ... Therefore, in total, 65 subjects were diagnosed with SAS in this study and for 53 of them CPAP therapy was indicated. The simplicity of the SAS screening by pulse oximetry makes it easy to use for screening of workers, and this method was highly effective in detecting individuals with severe SAS for whom CPAP therapy was indicated.] Niijima K, Enta K, et.al. *J Occup Health* 2007;49(1):1-8. <http://www.websciences.org/cftemplate/NAPS/archives/indiv.cfm?ID=20065147>

260. **Utility of home oximetry as a screening test for patients with moderate to severe symptoms of OSA.** [Correlation between home oximetry and PSG was not high. Oximetry was more useful to confirm than to exclude OSA in our study. Qualitative assessment was not better than numerical analysis. The greatest value of oximetry in this setting seems to be as a tool to rapidly recognize and treat more severe OSA patients in waiting list for PSG.] Glope R, et.al., *Sleep* 22:932-937, 1999.  
<http://www.sogapar.org/public/utility%20of%20home%20oximetry.pdf>
261. **Utility of nocturnal home oximetry for case finding in patients with suspected sleep apnea-hypopnea syndrome.** [A negative home oximetry test result is helpful in ruling out the diagnosis of SAHS in patients clinically suspected of having this syndrome, because a negative test result reduced the probability from 54.1% to 3.1% in our patients. However, a positive oximetry test increased the probability from 46% to 61.4% in our group of patients.] Series F, et al. *Ann Intern Med* 119:449-453, 1993.  
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## **CPAP Treatment**

262. **A Case Study Involving the Combination Treatment of an Oral Appliance and Auto-Titrating CPAP Unit.** [Treating severe obstructive sleep apnea can be a challenge. In this case it necessitated combining treatments to obtain the desired result. Now that oral appliances are a viable treatment of obstructive sleep apnea, they can be combined with continuous positive airway pressure or surgery to give the physician and patient more options.] Denbar MA. *Sleep and Breathing, Vol. 6, No.3, p.125-128.*  
<http://www.springerlink.com/content/9xdbfthmg18wuhx1/?p=a282040b48ec45558916ff2e95d8162e&pi=3>
263. **Auto-adjusting versus fixed positive pressure therapy in mild to moderate obstructive sleep apnoea.** [STUDY OBJECTIVES: To determine if auto-adjusting positive airway pressure (APAP) would be better tolerated on the basis of delivering a lower mean pressure in patients with mild to moderate obstructive sleep apnoea syndrome (OSAS). ... CONCLUSIONS: APAP and CPAP are equally effective in managing patients with mild to moderate OSAS, but device preference may be influenced by fixed pressure requirements.] Nolan GM, Doherty LS, et.al. *Sleep. 2007 Feb 1;30(2):189-94.*  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&list\\_uids=17326544&cmd=Retrieve&indexed=google](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&list_uids=17326544&cmd=Retrieve&indexed=google)
264. **Can intensive support improve continuous positive airway pressure use in patients with sleep apnea/hypopnea syndrome?** [CPAP use and outcomes of therapy can be improved by provision of a nurse-led intensive CPAP education and support program. CPAP use is lower among patients whose partners ask them to seek treatment.] Hoy C, et al. *Am J Resp Crit Care Med* 159:1096-1100, 1999.  
<http://ajrcm.atsjournals.org/cgi/content/abstract/159/4/1096>
265. **Comparison of therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomized prospective parallel trial.** [Therapeutic nasal CPAP reduces excessive daytime sleepiness and improves self-reported health status compared with subtherapeutic control. Compared with controls, the effects of therapeutic N CPAP are large and confirm previous uncontrolled clinical observations and

- the results of controlled trials that used an oral placebo.] Jenkinson C, Davies RJO, et al. *Lancet* 1999;353:2100-5. <http://cat.inist.fr/?aModele=afficheN&cpsidt=1853911>
266. **Compliance with CPAP therapy in patients with sleep apnea/hypopnea syndrome.** [Patients with sleep apnoea/hypopnoea syndrome used CPAP for less than five hours/night on average with no correlation between severity of sleep apnoea/hypopnoea syndrome and CPAP usage. Patients who complained of side effects used their CPAP therapy less. It is recommended that, as a minimum, CPAP run time should be regularly recorded in all patients receiving CPAP therapy.] Engleman H, et al. *Thorax* 49:263-266, 1994. <http://thorax.bmj.com/cgi/content/abstract/49/3/263>
267. **Compliance with nasal CPAP can be improved by simple interventions.** [We conclude that simple, inexpensive efforts to improve compliance with CPAP can be effective, especially when applied at the start of CPAP treatment, but optimal intervention may vary with certain patient characteristics.] Chervin R, et al. *Sleep* 20:284-289, 1997. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9231954&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9231954&dopt=Abstract)
268. **Continuous versus bi-level positive airway pressure for obstructive sleep apnea.** [ ] Reeves-Hoche M et al. *Am J Respir Crit Care Med* 151:443-449, 1995. <http://ajrccm.atsjournals.org>
269. **Effects of continuous positive airway pressure on upper airway and respiratory muscle activity.** [The increase in mean inspiratory airflow for a given Pes despite the decrease in upper] Alex C, et al., *J Appl Physiol* 62:2026-2030, 1987. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=3298198&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3298198&dopt=Abstract)
270. **Nasal continuous positive airway pressure treatment: current realities and future.** [The AutoSet self-adjusting nasal CPAP system adequately treats obstructive sleep apnea syndrome on the first night under laboratory conditions.] Berthon-Jones M, et al. *Sleep* 19(9 suppl):S131-135, 1996. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9122570&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9122570&dopt=Abstract)
271. **Nasal CPAP in obstructive sleep apnea: mechanisms of action.** [These results are interpreted to suggest three potential mechanisms of action for nasal CPAP in OSAS: 1) reduced upper airway resistance due to prevention of sleep-induced collapse of the airway; 2) reduced upper airway resistance due to dilatation of the airway by nasal CPAP beyond its dimension in the awake state; and 3) possible stimulation of mechanoreceptors leading to an increase in airway tone while CPAP is applied.] Rapoport D, et al. *Bull Eur Physiopathol Respir* 19:616-620, 1983. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=6360256&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6360256&dopt=Abstract)
272. **Nasal CPAP therapy, upper airway activation and obstructive sleep apnea.** [We conclude that the elimination of apneas with CPAP is not attributed to increased EMG activity in the upper airway. The reduction in EMG activity observed with nasal CPAP was closely related to the improvement in hemoglobin oxygen saturation. Therefore, CPAP may act as a pneumatic splint and passively open the upper airway to prevent obstructive apnea.] Strohl K, et al. *Am Rev Respir Dis* 134:555-585, 1986. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=3530073&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3530073&dopt=Citation)

273. **Night-to-night variability in CPAP use over the first three months of treatment.** [Intermittent users continued to report significantly greater OSA symptoms (snoring, snorting, and apnea) posttreatment, suggesting that they continued to experience sleep disordered breathing.] Weaver T, et al. *Sleep* 20:278-283, 1997.  
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274. **Reversal of obstructive sleep apnea by continuous positive airway pressure applied through the nares.** [Continuous positive airway pressure applied in this manner provides a pneumatic splint for the nasopharyngeal airway and is a safe, simple treatment for the obstructive sleep apnoea syndrome.] Sullivan C et al. *Lancet* 1:862-865, 1981  
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275. **Treatment of obstructive sleep apnea syndrome with nasal continuous positive airway pressure.** [It is concluded that n-CPAP is a highly effective means of preventing upper airway occlusion in OSAS and, except for some patients with coexisting lung disease, it totally reverses the accompanying gas exchange disturbance. Long-term home-based n-CPAP therapy is acceptable to a majority of patients, is free of serious side effects, and appears to result in a partial reversal of the underlying breathing disorder.] McEvoy R, et al. *Sleep* 7:313-325, 1984.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=6440264&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6440264&dopt=Abstract)
276. **Treatment of obstructive sleep apnea with nasal continuous positive airway pressure, patient compliance, perception of benefits and side effects.** [Obstructive sleep apnea is a chronic disease whose treatment may require long-term nightly use of relatively cumbersome and expensive breathing equipment that provides continuous positive airway pressure (CPAP) via nasal mask. The majority of patients (81%) perceived CPAP as an effective treatment of the disorder, 5% were unsure, and 14% believed that CPAP was ineffective, despite the resolution of sleep apnea on polysomnography. Subjective improvement reported by the patients was also observed by the family members in 83% of the patients. The most common complaint, voiced by 46% of the patients, was nocturnal awakenings. Nasal problems, such as dryness, congestion, and sneezing, were the second most frequent complaint present in 44% of the responders. ] Hoffstein V, et al. *Am Rev Respir Dis* 145:841-845, 1992.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=1554212&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1554212&dopt=Abstract)

## **Surgery Procedures & Surgical Mandibular Advancement**

277. **A reversible uvulopalatal flap for snoring and sleep apnea syndrome.** [Velopharyngeal incompetence (VPI) is a recognized complication of uvulopalatopharyngoplasty (UPPP) for obstructive sleep apnea. A new uvulopalatal flap (UPF) technique that modifies the UPPP and reduces this risk is presented. The technique achieves the same anatomic results as the UPPP but is reversible. ... The new reported procedure is reversible and conservative and reduces the risk of VPI. Snoring is improved, which is consistent with a decrease in airway resistance or obstruction. ] Powell N, et al. *Sleep* 19:593-599, 1996.

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278. **An analysis of the evidence-practice continuum: is surgery for obstructive sleep apnoea contraindicated?** [Rationale, aims and objectives Currently there are multiple surgical interventions utilized in the treatment of adult obstructive sleep apnoea (OSA). The role of these operations remains controversial, with perspectives on treatment efficacy varying considerably. Despite this, their use is proliferating. Objectives In this paper, we present the degree of variability that occurs in the application of these procedures, and examine the effectiveness of surgical intervention as a treatment for OSA. Conclusions This case study demonstrates substantial procedural variability and limited effectiveness. This raises questions as to the quality of care, the treatment-derived health outcomes of this population and of efficient resource allocation. This issue requires greater policy attention.] Elshaug A. *Journal of Evaluation in Clinical Practice* Volume 13 Issue 1 Page 3 - February 2007 . <http://www.blackwell-synergy.com/doi/abs/10.1111/j.1365-2753.2006.00793.x>
279. **Bariatric Surgery for Obstructive Sleep Apnea.** [ The incidence of OSA has been shown to be almost 90% in severely obese patients. CPAP is strongly recommended before surgery. Only a small number of patients with sleep related breathing disorders succeed in maintaining their dietary achieved weight reduction. In general, reliable and substantial weight loss can be accomplished by gastric bypass surgery with accompanying major reductions in associated comorbidities.] Verse T. *Chest* 128:Vol 2 p.485-486. <http://www.chestjournal.org/cgi/reprint/128/2/485.pdf>
280. **Cephalometric parameters after multilevel pharyngeal surgery for patients with obstructive sleep apnea.** [Cephalometric studies have shown narrowing in the upper airway at multiple levels in patients with obstructive sleep apnea... The degree of collapse of the palate on modified Muller maneuver was highly correlated with the severity of sleep apnea as measured by the respiratory disturbance index; the collapse of the lateral pharyngeal walls was moderately correlated; and collapse of the base of tongue was not correlated. Cephalometric radiographs may reflect the anatomic changes that result from upper airway surgery for sleep apnea, but these changes are not useful for assessing surgical efficacy. The modified Muller maneuver, however, may represent a more predictive evaluation. ] Yao M, Utley DS, et al. *Laryngoscope* 108(6):789-95, June 1998. <http://www.laryngoscope.com/pt/re/laryngoscope/abstract.00005537-199806000-00003.htm;jsessionid=FhNKSDvQ9GhgsZZWSw40pz2TV6xR66fHfZntdNpSqtFLGnslqph8!2089961419!-949856144!8091!-1>
281. **Delayed muscle detachment after genial tubercle advancement in a patient with obstructive sleep apnea.** [ ] McAndrew BP, Strauss RA. *J Oral maxillofac Surg* 58(9):1040-3, Sept. 2000. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=10981985&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10981985&dopt=Abstract)
282. **Effects of uvulopalatopharyngoplasty on sleep architecture and patterns of obstructive breathing.** [In this retrospective study, 72 obstructive sleep apnea patients with polysomnograms taken before and after uvulopalatopharyngoplasty were evaluated. Postoperatively, there was a significant improvement of sleep architecture and respiratory indices. In addition, a second group of 17 patients also had position recordings with their polysomnograms. Time spent in supine and lateral sleep positions changed postoperatively. There was significant decrease of the apnea plus hypopnea index in the lateral position. This

study indicates that there is significant improvement of sleep architecture and respiratory indices in the majority of patients after uvulopalatopharyngoplasty, particularly in the lateral sleep position. ] Katsantonis GP, Miyashaki S, et al. *Laryngoscope* 100:1068-1072, 1990. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=2215038&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2215038&dopt=Abstract)

283. **Evaluation of effectiveness of uvulopalatopharyngoplasty.** [ ] Fujita S, et al. *Laryngoscope* 95:70-74, 1985. [www.laryngoscope.com](http://www.laryngoscope.com)
284. **Four-year follow-up after uvulopalatopharyngoplasty in fifty unselected patients with obstructive sleep apnea syndrome.** [The study resulted in the following conclusions: 1. The responder rate to UPPP in unselected patients is low. 2. Obesity and high indices of nocturnal respiratory disturbance are negative predictors. 3. The patients' subjective recovery alone must not be used for postoperative evaluation. 4. With regular follow-up and the use of the treatment alternatives available today, the majority of OSAS patients can receive effective treatment.] Larsson L, et al. *Laryngoscope* 104:1362-1368, 1994. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&list\\_uids=7968165&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&list_uids=7968165&dopt=Citation)
285. **Inferior mandibular osteotomy and hyoid myotomy suspension for obstructive sleep apnea: a review of 555 patients.** [Fifty-five patients with obstructive sleep apnea syndrome (OSAS) were evaluated following inferior mandibular osteotomy with hyoid myotomy and suspension. Patients were objectively examined by polysomnography before and 6 months following the surgical procedure. Thirty-seven patients (67%) had a good response from surgery, and 18 patients (33%) were considered nonresponders. Lung disease, mandibular deficiency, and obesity were factors found to affect the success of surgical treatment.] Riley R, et al. *Oral maxillofac Surg* 47:159-164, 1984. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&list\\_uids=2913251&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&list_uids=2913251&dopt=Citation)
286. **Mandibular distraction osteogenesis in the treatment of upper airway obstruction in children with craniofacial deformities.** [ ] Cohen Sr, Simms C, et al. *Plast Reconstr Surg* 101 (2):312-8, Feb.1998. <http://plasticreconsurg.com>
287. **Maxillomandibular advancement (MMA) in a site-specific treatment approach for obstructive sleep apnea: a surgical algorithm.** [Maxillomandibular advancement (MMA) is the most successful acceptable surgical treatment, excluding tracheostomy, for obstructive sleep apnea syndrome (OSAS). Nevertheless, the indications for and staging of MMA, with respect to the many procedures available, are unsettled and often limited to severe OSAS, dentocraniofacial deformities, and when other surgeries have failed. An algorithm is presented that defines the indications for MMA in an expanded role, based on a site-specific approach, according to proposed principles that include general goals and guidelines for governing the surgical treatment of OSAS.] Prinsell JR. *Sleep and Breathing* 4(4):147-54, 2000. <http://www.springerlink.com/content/pw0qej3cp1g4cw3j/>
288. **Maxillomandibular advancement surgery for obstructive sleep apnea syndrome.** [MMA is a highly successful and potentially definitive primary single-staged surgery that may result in a significant reduction in OSAS-related health risks, as well as financial savings for the health care system. The diagnosis and management of OSAS requires a multi-disciplinary team approach, including a working relationship between the dentist and sleep physician. General dentists and dental specialists who participate in the management of snoring and OSAS cases should have some knowledge of basic sleep medicine.] Prinsell JR.

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289. **Maxillomandibular Advancement Surgery in a Site-Specific Treatment Approach for Obstructive Sleep Apnea in 50 Consecutive Patients.** [MMA is highly successful and safe and may be a definitive primary single-staged surgical treatment of selected OSAS cases with diffusely complex or multiple sites of disproportionate velo-oro-hypopharyngeal anatomy.] Prissnell JR. *Chest. 1999;116:1519-1529.*  
<http://www.chestjournal.org/cgi/content/abstract/116/6/1519>
290. **Obstructive sleep apnea and maxillomandibular advancement: an assessment of airway changes using radiographic and nasopharyngoscopic examinations.** [The study aim was to evaluate the resultant changes in the upper airway after maxillomandibular advancement (MMA) for obstructive sleep apnea. MMA achieved expansion of the upper airway. In addition, MMA decreased the collapsibility of the airway, especially the lateral pharyngeal walls. These findings may explain the highly successful outcomes of MMA for the treatment of obstructive sleep apnea.] Li KK, Guilleminault C, et.al., Stanford University Sleep Disorders and Research Center, Stanford, CA. *J Oral Maxillofac Surg. 2002 May;60(5):526-30.*  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=11988930&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11988930&dopt=Abstract)
291. **Obstructive sleep apnea syndrome: a review of 306 consecutively treated surgical patients.** [Surgery was considered a success if it was equivalent to nasal CPAP or the postoperative RDI was less than 20 with normal oxygenation. The overall success rate, which included patients that dropped from the protocol, was 76.5%, with a mean followup of 9.3 months (SD, 6.7). The preoperative RDI, nasal CPAP RDI, and postoperative RDI were 55.8 (SD, 26.7), 7.2 (SD, 5.4), and 9.2 (SD, 7.5), respectively.] Riley R, et al. *Otolaryng Head Neck Surg 108:117-125, 1993.*  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=8441535&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8441535&dopt=Abstract)
292. **Overview of phase II surgery for obstructive sleep apnea syndrome.**  
[Maxillomandibular advancement enlarges the pharyngeal and hypopharyngeal airway dimensions by physically expanding the skeletal framework. In addition, the forward movement of the maxillomandibular complex improves the tension and collapsibility of the suprahyoid and velopharyngeal musculature. Most patients who undergo phase II surgery have failed to fully respond to the phase I protocol. These patients have already undergone reconstruction of the airways at the nasal, pharyngeal, and hypopharyngeal levels. Phase I surgical failure almost always involves persistent obstruction at the hypopharyngeal level (occasionally combined with pharyngeal-level obstruction). Maxillomandibular advancement creates more tension and physical room in the upper airway, relieving residual obstructions. In order to maximize airway expansion, a major advancement of the maxillomandibular complex is required. However, in doing so, it is important to maintain a stable dental occlusion and a balanced aesthetic appearance. Many patients who enter the phase II protocol have craniomaxillofacial abnormalities, such as maxillary and/ or mandibular deficiencies, that invariably are improved following surgery.] Li KK, Riley WR, et al. *Ear Nose Throat J 78(11):851-7, Nov 1999.* [www.entjournal.com](http://www.entjournal.com),  
[http://findarticles.com/p/articles/mi\\_m0BUM/is\\_11\\_78/ai\\_58062604](http://findarticles.com/p/articles/mi_m0BUM/is_11_78/ai_58062604)

293. **Postoperative airway findings after maxillomandibular advancement for obstructive sleep apnea.** [Although postoperative edema was expected after maxillomandibular advancement, hypopharyngeal hematoma was unexpected. Although none of our patients had evidence of airway difficulty, the possibility of an expanding hypopharyngeal hematoma should be considered in patients complaining of breathing difficulty after maxillomandibular advancement surgery.] Li KK, Riley RW, et al. *Laryngoscope* 110(2 Pt 1):325-7, Feb 2000. [www.laryngoscope.com](http://www.laryngoscope.com)  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list\\_uids=10680939](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10680939)
294. **Radio frequency volumetric reduction of the tongue: a porcine pilot study for the treatment of obstructive sleep apnea syndrome.** [ ] Powell N, et al. *Chest* 111:1348-1355, 1997. [www.chestjournal.org](http://www.chestjournal.org)
295. **Relief of upper airway obstruction by adenotonsillectomy.** [Adenotonsillectomy is often performed to relieve upper airway obstruction, even in children who do not present with severe apnea. Although adenotonsillectomy provides dramatic relief from obstructive sleep apnea, little evidence is available as to the efficacy of surgery in the far more prevalent cases of partial airway obstruction. We report the results of a prospective study of 100 children with adenotonsillar obstruction (without severe apnea) and 50 age-matched control children. The majority of patients exhibited appreciable sleep disturbances preoperatively, as compared to controls, and had substantial postoperative improvement, as demonstrated by parental questionnaire and sleep sonography--the computer-aided analysis of respiratory sounds. Mouth breathing and behavior problems were also prevalent preoperatively and were affected positively by adenotonsillectomy. It appears that surgery in such cases can have far-ranging benefits, even for the child whose obstruction does not demonstrate severe apnea.] Potts WP, Pasquariello PS, *Otolaryngol Head Neck Surg*. 1986 Apr;94(4):476-80. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list\\_uids=3086810&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=3086810&dopt=Abstract)
296. **Site-specific versus diffuse treatment/presenting severity of obstructive sleep apnea.** [ ] Moore K. *Sleep and Breathing* 4(4):145-46, 2000. <http://www.springerlink.com/content/cf0g4ln0fxr1yeqq/>
297. **Surgery and obstructive sleep apnea: long-term clinical outcomes.** [ ] Riley RW, Powell NB. *Otolaryngol Head Neck Surg* 122(3):415-21, Mar. 2000. <http://archotol.ama-assn.org>
298. **Surgical correction of anatomical abnormalities in obstructive sleep apnea syndrome: uvulopalatopharyngoplasty.** [Fujita first described the use of the uvulopalatopharyngoplasty (UPPP) for the treatment of OSAS in 1981 ] Fujita S, et al., *Otolaryng Head Neck Surg* 89:923-924, 1981. <http://archotol.ama-assn.org>
299. **Surgical treatment of severe sleep apnea syndrome by maxillomandibular advancing or mental transposition.** [Surgery of the facial skeleton or the tongue may be envisaged in case of failure of continuous positive pressure ventilation for severe sleep apnea syndrome defined by a apnea-hyponea index greater than 30/h. ... Maxillomandibular advancing is a major procedure which can be effective in sleep apnea patients with severe craniofacial skeletal anomalies. Its applications in apneic patients with no skeletal anomaly remains a subject of debate. Conversely, there would appear to be very few indications for mental transposition.] Wagner I, Coiffier T, et al. *Ann Otolaryngol Chir Cervicofac* 117(3):137-46, June 2000. [www.e2med.com/index.cfm?fuseaction=Revue&idxRevue=75](http://www.e2med.com/index.cfm?fuseaction=Revue&idxRevue=75)

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=10863198&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10863198&dopt=Abstract)

300. **The influence of craniofacial structure on obstructive sleep apnea in young adults.** [Highly significant craniofacial abnormalities were found in the upper and lower pharynx in young obstructive sleep apnea patients. Most of these patients (58%) had abnormalities in both the upper and lower pharynx, suggesting that palatal surgery alone may be an inadequate treatment. This information may define future investigations needed to determine how to more effectively treat this subgroup of young obstructive sleep apnea patients.] Johns FR, Stollo PJ, et al. *J Oral Maxillofac Surg* 56(5):596-602; discussion 602-3, May 1998. <http://www.websciences.org/cftemplate/NAPS/archives/indiv.cfm?ID=19981261>
301. **Three-dimensional changes in upper airways of patients with obstructive sleep apnea following maxillomandibular advancement.** [PURPOSE: The purpose of this study was to analyze the morphologic changes of the airway in obstructive sleep apnea (OSA) patients by helical computed tomography (CT) scanning following maxillomandibular advancement (MMA) surgery...RESULTS: There was enlargement of LAT and AP diameters for all patients at all levels. LAT dimensions were enhanced greater than AP in the retroglossal region. CONCLUSION: MMA results in significant increase in both AP and LAT airway dimensions.] Fairburn SC, Waite PD, et.al. *J Oral Maxillofac Surg* 2007;65(1):6-12. <http://www.websciences.org/cftemplate/NAPS/archives/indiv.cfm?ID=20065226>
302. **Tongue Base Reduction with Temperature-controlled Radiofrequency Volumetric Tissue Reduction for Treatment of Obstructive Sleep Apnea Syndrome.** [Daytime sleepiness and snoring improved significantly. Pre and postoperative morbidity was low; one severe complication occurred (tongue base abscess). We were able to achieve similar cure and responder rates to those reported in a recently published pilot study but with a reduced number of treatment sessions. We believe that this technique may improve patient acceptance and have beneficial cost implications.] Stuck BA, Maurer JT et.al. *Acta Oto-Laryngologica Vol 122 #5/2002 p.531-536.* [http://taylorandfrancis.metapress.com/\(ldtfvsrgximueq55s2t34a55\)/app/home/contribution.asp?referrer=parent&backto=issue,12,22;journal,58,107;linkingpublicationresults,1:102096,1](http://taylorandfrancis.metapress.com/(ldtfvsrgximueq55s2t34a55)/app/home/contribution.asp?referrer=parent&backto=issue,12,22;journal,58,107;linkingpublicationresults,1:102096,1)

## **Positional Therapy**

303. **A comparative study of treatments for positional apnea.** [Sixty male patients all with apnea plus hypopnea indices (A + HI) above 12.5, who met a criterion of positionality by having two or more times the rate of these events during supine sleep in comparison to their lateral sleep rate, were randomly assigned to one of four treatments for 8 weeks. All were restudied for two nights, one with and one without treatment devices. On treatment more than half the patients in each group reduced their A + HI to within normal limits and a third remained WNL without the use of devices.] Cartwright R, et al. *Sleep* 14:546-552, 1991. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=1798889&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1798889&dopt=Abstract)
304. **Cheyne-Stokes respiration during sleep: a possible effect of body position.** [Cheyne-Stokes Respiration (CSR) is a common finding in Chronic Heart Failure and Stroke patients. The body position effect during sleep on obstructive breathing abnormalities is well known. However, the effect of body position during sleep on breathing abnormalities of central type like CSR has not been well documented. The results of this study suggest that body posture may play a role not only in the prevalence and severity of obstructive breathing disorders, but

also in CSR, a central type of breathing abnormalities during sleep.] Oksenberg A, Arons E, et.al. *Med Sci Monit.* 2002 Jul;8(7):CS61-5.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list\\_uids=12118206&query\\_hl=2&itool=pubmed\\_docsum](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=12118206&query_hl=2&itool=pubmed_docsum)

305. **Effect of sleep position on sleep apnea severity.** [Sleep position adjustment may be a viable treatment for some nonobese sleep apnea patients. ] Cartwright RD. *Sleep* 7:110-114, 1848. [www.journalsleep.org](http://www.journalsleep.org).  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=6740055&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6740055&dopt=Abstract)
306. **Positional treatment vs continuous positive airway pressure in patients with positional obstructive sleep apnea.** [The aim of this study was to compare the relative efficacy of continuous positive airway pressure (CPAP) and positional treatment in the management of positional obstructive sleep apnea (OSA), using objective outcome measures. Positional treatment was highly effective in reducing time spent supine. The AHI was lower and the minimum oxygen saturation was higher on CPAP as compared with positional treatment. There was no significant difference, however, in sleep architecture, Epworth Sleepiness Scale scores, maintenance of wakefulness testing sleep latency, psychometric test performance, mood scales, or quality-of-life measures. Positional treatment and CPAP have similar efficacy in the treatment of patients with positional OSA. ] Jokic R Klimaszewski A, et al. *Chest* 115:771-781, 1999. [www.chestjournal.org](http://www.chestjournal.org)  
<http://www.chestjournal.org/cgi/content/abstract/115/3/771?ck=nck>
307. **Positional vs. nonpositional obstructive sleep apnea patients. Anthropomorphic, nocturnal polysomnographic and multiple sleep latency test data.** [In a large population of OSA patients, most were found to have at least twice as many apneas/hypopneas in the supine than in the lateral position. These so-called "positional patients" are on the average thinner and younger than "nonpositional patients." They had fewer and less severe breathing abnormalities than the NPP group. Consequently their nocturnal sleep quality was better preserved and, according to MSLT data, they were less sleepy during daytime hours. RDI was the most dominant factor that could predict the positional dependency followed by BMI and age. RDI showed a threshold effect, the prevalence of PP in those with severe RDI (RDI > or = 40) was significantly lower than in those OSA patients with mild-moderate RDI. BMI showed a major significant inverse relationship with positional dependency, while age had only a minor although significant inverse relationship with it. Body position during sleep has a profound effect on the frequency and severity of breathing abnormalities in OSA patients.] Oksenberg A, Silverberg DS, et al. *Chest* 112:629-39, 1997. [www.chestjournal.org](http://www.chestjournal.org).  
<http://www.chestjournal.org/cgi/content/abstract/112/3/629>

## **Children and Sleep Apnea**

308. **Adenotonsillectomy for obstructive sleep apnea in obese children.** [OBJECTIVE: To study changes in sleep behavior and quality of life in obese children after adenotonsillectomy for obstructive sleep apnea. Study design and setting Prospective study at the University of New Mexico Children's Hospital. RESULTS: The study population included 30 children. Twenty-six children (86%) were male. The mean age of the children at the time of inclusion in the study was 9.3 years; range, 3.0 to 17.2. The mean preoperative BMI was 28.6 (range,

19.2 to 47.1) and the mean postoperative BMI was 27.9 (range, 17.8 to 27.9). A 2-tailed paired t test showed that this difference is not statistically significant (P = 0.06). The mean preoperative RDI was 30.0 and the mean postoperative RDI was 11.6 (P < 0.001). The preoperative mean total OSA-18 score was 78.2 and the postoperative mean total score was 39.8 (P < 0.001). CONCLUSION: Obese children with OSA who undergo adenotonsillectomy show a marked improvement in RDI and in quality of life with no change in BMI. However, in the majority of children, OSA does not resolve.] Mitchell RB, Kelly J. *Otolaryngol Head Neck Surg.* 2004 Jul;131(1):104-8.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list\\_uids=15243565](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15243565)

309. **An association between symptoms of obstructive sleep apnea and hyperactivity in children.** [Last year we reported an association between symptoms of sleep-related breathing disorders (SRBDs) and hyperactive behavior in children attending a psychiatry clinic<sup>1</sup>. To further assess this association, we surveyed parents of children attending a general pediatrics clinic, combined it with data from the psychiatry clinic, and performed more detailed analyses.... This survey of children selected without regard to any sleep complaints or disorders identifies an association between hyperactive behavior and symptoms of SRBDs. Some of these symptoms could conceivably result from a hyperactive state, but snoring and waking up with a snort are difficult to attribute to the behavioral condition. An association may also exist, in our sample of children, between periodic leg movements during sleep and hyperactivity<sup>2</sup>; such an association has recently been suggested by other investigators<sup>3</sup>. We speculate that occult sleep disorders of different types may contribute to hyperactive behavior in a significant number of children, some of whom carry a diagnosis of ADHD.] Chervin RD, Ganoczy DA, et al. *Sleep Research* 1997; 26:190.  
<http://www.websciences.org/cftemplate/NAPS/archives/indiv.cfm?ID=19979110>
310. **Association Between Sleep Problems and Symptoms of Attention-Deficit-Hyperactivity Disorder in Young Adults.** [Results showed that, for both inattention and hyperactivity symptoms, the highly likely ADHD and probable ADHD groups were more likely than the non-ADHD group to have a variety of current and lifetime sleep problems. No significant difference in sleep problems was found between the highly likely ADHD and probable ADHD groups. Inattention, but not hyperactivity, was associated with greater sleep need and greater difference between sleep need and self-estimated nocturnal sleep duration. Hyperactivity, but not inattention, was associated with decreased nocturnal sleep duration. Conclusions: Consistent with prior findings from children and adolescents, ADHD symptoms in young adults are related to sleep problems. Further studies on adults with ADHD should help to refine our understanding of the causal basis for any implications of this association.] Gau SSF, Kessler RC, et al. *Journal Sleep, Volume : 30 Issue : 02 Pages : 195-201.*  
<http://www.journalsleep.org/ViewAbstract.aspx?citationid=3133>
311. **Characteristics of sleep-related obstructive respiratory disturbances in childhood.** [Sleep-related obstructive respiratory disturbances in childhood differ significantly from the adult's obstructive sleep apnea syndrome (OSAS). In contrast to adults, in children with OSAS the disturbance of the macrostructure of sleep, the increase of the number of apneas and hypopneas, and the diminution of oxygen saturation are not so prominent. Restlessness of the sleep, as reflected by movement arousals together with cortical (electroencephalograph-recorded) arousals, is important. The combination of clinical symptoms and polysomnographic parameters is necessary to diagnose OSAS in children. ]

Scholle S. *Sleep and Breathing*, Vol.4(1):17-21, 2000.

<http://www.springerlink.com/content/jm8uqwpu2tcg33tp/>

312. **Clinical analysis of 68 patients with obstructive sleep-disordered breathing in children.** [Upper airway obstruction caused by adenotonsillar hypertrophy were major reasons to lead to pediatric obstructive sleep-disordered breathing. The diagnosis and treatment must be combined clinical features with all kinds of examinations (cephalometric, endoscopic, polysomnography). Tonsillectomy and/or adenoidectomy with soft-tissue shavers were safe and effective in treatment of OSAHS children.] Huang Q., Wu H. et.al. *Lin Chuang Er Bi Yan Hou Ke Za Zhi*. 2005 Nov;19(21):971-3, 975. (Article in Chinese). Department of Otolaryngology-Head and Neck Surgery, Affiliated Xinhua Hospital, Shanghai Second Medical University, Shanghai, 200092, China.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=16494038&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=16494038&dopt=Abstract)
313. Craniofacial morphology in preschool children with sleep-related breathing disorder and hypertrophy of tonsils. [The purpose of this study was to examine craniofacial morphology, pharyngeal airway space and hyoid bone position in preschool children with sleep-related breathing disorder associated with hypertrophy of tonsils (SBDT). Thirty-eight preschool children, mean age 4.7 y, with SBDT and with an apnoea index (AI) of  $0 < AI < 5$ , were divided into two groups. One consisted of 15 children with sleep-related breathing disorder (SBD) and more than 75% of the tonsils visible (GUI) and the other of 23 children with SBD and 25–75% of the tonsils visible (Gil). The control group consisted of 31 children without ear, nose and throat disease and with GI (barely visible) tonsils. Compared with the controls, GUI children had a retrognathic mandible, a large posterior facial height, a large interincisal angle with retroclined lower incisors, a narrow pharyngeal airway space, an anterior tongue base position and a long soft palate. Compared with the controls, Gil children had a large anterior lower facial height and a short nasal floor. However, like the controls, Gil children did not have a retrognathic mandible. *Conclusion*: The findings show that children with SBDT display a characteristic facial appearance at an early age. Since the condition has an effect on growth, it needs to be prevented by controlling morphology and function at the preschool age.] Kawashima S, Peltomaki T, et al. *Acta Paediatrica*. Volume 91 Issue 1 Page 71 - January 2002. <http://www.blackwell-synergy.com/doi/abs/10.1111/j.1651-2227.2002.tb01644.x>
314. **Diagnosis and treatment of obstructive sleep apnea hypopnea syndrome in children.** [A discussion of the methods of diagnosis and treatment of obstructive sleep apnea hypopnea syndrome (OSAHS) in children. The major symptoms of patients with OSAHS are snoring in sleep, breathing opening mouth, apnea, hearing loss. 281/285 cases were diagnosed as adenoid and (or) tonsil hypertrophy. Two hundred- fifty five cases received surgery, adenoidectomy and tonsillectomy in 205, only adenoidectomy in 47, simple tonsillectomy in 3. The clinical symptoms of 248 cases improved evidently after operations. Improved rate is 97.2%. Children with OSAHS has significance itself; PSG is the major means for diagnosing. Surgery is main method for treating; CPAP can be as the method of treating for serious OSAHS in preoperative preparation and postoperative management.] Zhang YM, Zhao J, et.al. *Zhonghua Er Bi Yan Hou Ke Za Zhi*. 2004 Nov;39(11):654-7. (Article in Chinese). Department of Otorhinolaryngology, Beijing Children's Hospital Affiliated Capital University of Medicine Sciences, Beijing, China.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=15835814&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15835814&dopt=Abstract)

315. **Diagnostic approaches to childhood obstructive sleep apnea hypopnea syndrome.**  
[Obstructive sleep apnea hypopnea syndrome (OSAHS) is a common sleep disorder in adults that is increasingly recognized in children, affecting 1 to 3% of children. Children experience a spectrum of severity related to the degree of upper airway obstruction, the duration of the disease, and the presence or absence of hypoxemic episodes. Failure to diagnose and treat OSAHS can result in serious, but generally reversible consequences for the child including impaired growth, neurocognitive and behavioral dysfunction, and cardiorespiratory failure. Even mild OSAHS appears linked to reversible health consequences. Adenotonsillar hypertrophy is the major predisposing factor for OSAHS in childhood. However, enlarged tonsils and adenoids can be a normal finding in young children and are not diagnostic for OSAHS. The identification of children with OSAHS is often difficult because affected children may have no signs or symptoms when awake. Furthermore, clinical assessment cannot reliably distinguish between simple snoring and OSAHS. Adenotonsillectomy is the most common therapy for OSAHS in children, but surprisingly, only a small percentage of children undergo any diagnostic testing prior to surgery. Thus, the challenge is to develop new diagnostic strategies that effectively screen, identify, and treat children most likely to benefit from specific treatment.] Rosen C. *Sleep and Breathing, Vol.4(4):177-81, 2000.*  
<http://www.springerlink.com/content/dk4r72pbl095b0w9/>
316. **Increased Cerebral Blood Flow Velocity in Children With Mild Sleep-Disordered Breathing: A Possible Association With Abnormal Neuropsychological Function.**  
[OBJECTIVE. Sleep-disordered breathing describes a spectrum of upper airway obstruction in sleep from simple primary snoring, estimated to affect 10% of preschool children, to the syndrome of obstructive sleep apnea. Emerging evidence has challenged previous assumptions that primary snoring is benign. A recent report identified reduced attention and higher levels of social problems and anxiety/depressive symptoms in snoring children compared with controls. Uncertainty persists regarding clinical thresholds for medical or surgical intervention in sleep-disordered breathing, underlining the need to better understand the pathophysiology of this condition. Adults with sleep-disordered breathing have an increased risk of cerebrovascular disease independent of atherosclerotic risk factors. There has been little focus on cerebrovascular function in children with sleep-disordered breathing, although this would seem an important line of investigation, because studies have identified abnormalities of the systemic vasculature. Raised cerebral blood flow velocities on transcranial Doppler, compatible with raised blood flow and/or vascular narrowing, are associated with neuropsychological deficits in children with sickle cell disease, a condition in which sleep-disordered breathing is common. We hypothesized that there would be cerebral blood flow velocity differences in sleep-disordered breathing children without sickle cell disease that might contribute to the association with neuropsychological deficits. ... CONCLUSIONS. Cerebral blood flow velocities measured by noninvasive transcranial Doppler provide evidence for increased cerebral blood flow and/or vascular narrowing in childhood sleep-disordered breathing; the relationship with neuropsychological deficits requires further exploration. A number of physiologic changes might alter cerebral blood flow and/or vessel diameter and, therefore, affect cerebral blood flow velocities. We were able to explore potential confounding influences of obesity and hypertension, neither of which explained our findings. Second, although cerebral blood flow velocities increase with

increasing partial pressure of carbon dioxide and hypoxia, it is unlikely that the observed differences could be accounted for by arterial blood gas tensions, because all of the children in the study were healthy, with no cardiorespiratory disease, other than sleep-disordered breathing in the snoring group. Although arterial partial pressure of oxygen and partial pressure of carbon dioxide were not monitored during cerebral blood flow velocity measurement, assessment was undertaken during the afternoon/early evening when the child was awake, and all of the sleep-disordered breathing children had normal resting oxyhemoglobin saturation at the outset of their subsequent sleep studies that day. Finally, there is an inverse linear relationship between cerebral blood flow and hematocrit in adults, and it is known that iron-deficient erythropoiesis is associated with chronic infection, such as recurrent tonsillitis, a clinical feature of many of the snoring children in the study. Preoperative full blood counts were not performed routinely in these children, and, therefore, it was not possible to exclude anemia as a cause of increased cerebral blood flow velocity in the sleep-disordered breathing group. However, hemoglobin levels were obtained in 4 children, 2 of whom had borderline low levels (10.9 and 10.2 g/dL). Although there was no apparent relationship with cerebral blood flow velocity in these children (cerebral blood flow velocity values of 131 and 130 cm/second compared with 130 and 137 cm/second in the 2 children with normal hemoglobin levels), this requires verification. It is of particular interest that our data suggest a relationship among snoring, increased cerebral blood flow velocities and indices of cognition (processing speed and visual attention) and perhaps behavioral (Behavior Rating Inventory of Executive Function) function. This finding is preliminary: a causal relationship is not established, and the physiologic mechanisms underlying such a relationship are not clear. Prospective studies that quantify cumulative exposure to the physiologic consequences of sleep-disordered breathing, such as hypoxia, would be informative.] Hill CM, Hogan AM et al. *PEDIATRICS* Vol. 118 No. 4 October 2006, pp. e1100-e1108. <http://pediatrics.aappublications.org/cgi/content/abstract/118/4/e1100>

317. **Long-term effect of adenotonsillectomy on quality of life in pediatric patients.**

[HYPOTHESIS: Adenotonsillectomy improves general and disease-specific quality of life for properly selected patients suffering for upper airway obstruction secondary to adenotonsillar hypertrophy (UAO) and obstructive sleep apnea (OSA). RESULTS: CHQ-PF28 scores were improved in the Physical Summary parameter in long-term follow-up. Psychosocial scores did not improve significantly. OSA-18 scores showed improvement in both the short-and long-term scores. Physical findings and symptoms did not impact scores in any domain. CONCLUSIONS: Quality of life in children with OSA does improve after adenotonsillectomy. Disease-specific clinometric instruments show improvement in domains affected by the disease process. However, instruments used to assess general quality of life may show physical improvement but not psychosocial.] Flanary VA. *Laryngoscope*, 2003 Oct; 113(10):1639-44.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=14520088&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14520088&dopt=Abstract)

318. **Morbidity of Obstructive Sleep Apnea in Children: Facts and Theory.** [Sleep-disordered breathing (SDB) is a frequent, albeit underdiagnosed, problem in children. If left untreated, SDB may lead to substantial morbidities affecting multiple target organs and systems. This review provides a detailed and current description of the current status of our understanding of SDB-associated morbidity in children, and provides recommendations of future research directions necessary for increasing our knowledge and awareness on the

short- and long-term consequences of SDB during childhood.] Gozal D. *Sleep and Breathing*, Vol.5, No.1, p.35-42.

<http://www.springerlink.com/content/mqpmxrhfujjv2f3l/?p=d1348c60905348ff9d9644b1ef1d14bb&pi=4>

319. **Obstructive Sleep Apnea in Children** [Obstructive sleep-disordered breathing is common in children. From 3 percent to 12 percent of children snore, while obstructive sleep apnea syndrome affects 1 percent to 10 percent of children. The majority of these children have mild symptoms, and many outgrow the condition. Consequences of untreated obstructive sleep apnea include failure to thrive, enuresis, attention-deficit disorder, behavior problems, poor academic performance, and cardiopulmonary disease. The most common etiology of obstructive sleep apnea is adenotonsillar hypertrophy. Clinical diagnosis of obstructive sleep apnea is reliable; however, the gold standard evaluation is overnight polysomnography. Treatment includes the use of continuous positive airway pressure and weight loss in obese children. These alternatives are tolerated poorly in children and rarely are considered primary therapy. Adenotonsillectomy is curative in most patients. Children with craniofacial syndromes, neuromuscular diseases, medical comorbidities, or severe obstructive sleep apnea, and those younger than three years are at increased risk of developing postoperative complications and should be monitored overnight in the hospital.] CHAN J, EDMAN JC, et al. *American Family Physician* Vol. 69/No. 5 (March 1, 2004).  
<http://www.aafp.org/afp/20040301/1147.html>
320. **Orthodontic treatment in children to prevent sleep-disordered breathing in adulthood.** [The purpose of this article is to review human craniofacial growth and development, especially the growth of the mandible, to clarify the relationship between obstructive sleep apnea (OSA) syndrome and craniofacial abnormality, and finally, to propose the hypothesis that negative pressure produced in the chest of the OSA child inhibits the growth of the mandible. Recently, the development of diagnosis and treatment of OSA syndrome has progressed rapidly; however, the prevention of OSA syndrome was merely seen. Craniofacial abnormality is reported as one of the causes of OSA syndrome. If craniofacial abnormality is determined only by genetics, it is difficult to manage the craniofacial skeleton to prevent OSA syndrome. The role of epigenetic factors on craniofacial growth and development is still controversial. However, if we stand on the functional matrix hypothesis, we can manage not only growth of the mandible but also the craniofacial skeleton as a whole. The author proposes the hypothesis that the negative pressure produced in the chest prohibits the growth of the mandible even if the patients have a capacity for growth and development; therefore, if this negative pressure disappears because of the removal of the tonsil and/or adenoids or by an orthodontic treatment to make a patency of the airway, the mandible may grow normally, and we can prevent or reduce a number of OSA syndromes in the future.] Kikuchi M. *Sleep and Breathing*, Vol 9, No.4, p.146-158.  
<http://www.springerlink.com/content/f483157068812w7n/?p=168ff7289a624b55bc0c5dda9e19f6fb&pi=1>
321. **Sleep bruxism and behavioral disturbances in children: a population-based study.** [Bruxers and never bruxers had no significant differences found with respect to behavioural disturbance, emotional disturbance, and conduct problems, as assessed by teachers on the Rutter scale.] Azevedo MH, Clemente VM, et.al. *Actas de Fisiologia* 7, 2001.  
[http://72.14.253.104/search?q=cache:VFEBmqLGLQMJ:www.rau.edu.uy/universidad/medicina/actas7/pathologies\\_and\\_disorder.pdf+Compliance+and+effective+therapy+for+positional+apnea.+Freebeck&hl=en&ct=clnk&cd=3&gl=us](http://72.14.253.104/search?q=cache:VFEBmqLGLQMJ:www.rau.edu.uy/universidad/medicina/actas7/pathologies_and_disorder.pdf+Compliance+and+effective+therapy+for+positional+apnea.+Freebeck&hl=en&ct=clnk&cd=3&gl=us)

322. **Sleep-disordered breathing, behavior, and cognition in children before and after adenotonsillectomy.** [Most children with sleep-disordered breathing (SDB) have mild-to-moderate forms, for which neurobehavioral complications are believed to be the most important adverse outcomes. Subjects who had an adenotonsillectomy, in comparison to controls, were more hyperactive on well-validated parent rating scales, inattentive on cognitive testing, sleepy on the Multiple Sleep Latency Test, and likely to have attention-deficit/hyperactivity disorder (as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) as judged by a child psychiatrist. In contrast, 1 year later, the 2 groups showed no significant differences in the same measures. Subjects who had an adenotonsillectomy had improved substantially in all measures, and control subjects improved in none. However, polysomnographic assessment of baseline SDB and its subsequent amelioration did not clearly predict either baseline neurobehavioral morbidity or improvement in any area other than sleepiness. Children scheduled for adenotonsillectomy often have mild-to-moderate SDB and significant neurobehavioral morbidity, including hyperactivity, inattention, attention-deficit/hyperactivity disorder, and excessive daytime sleepiness, all of which tend to improve by 1 year after surgery.] Chervin RD, Ruzicka DL, et.al. *Pediatrics* 2006 Apr;117(4):e769-78. Sleep Disorders Center, Dept of Neurology, U. of Michigan, Ann Arbor, MI.  
<http://pediatrics.aappublications.org/cgi/content/abstract/117/4/e769>.
323. **Sleep problems and daytime somnolence in a German population-based sample of snoring school-aged children.** [Habitual snoring is associated with daytime symptoms like tiredness and behavioral problems. Its association with *sleep* problems is unclear. We aimed to assess associations between habitual snoring and sleep problems in primary school children. ...Habitual snoring was associated with several sleep problems in our study. Long-term habitual snorers were more likely to have sleep problems than children who had stopped snoring spontaneously.] Eitner S, Urschitz MS, et al. *J. of Sleep Research*, Vol. 16, Issue 1, P.96-101 March 2007. <http://www.blackwell-synergy.com/doi/abs/10.1111/j.1365-2869.2007.00560.x>
324. **Snoring and Sleep Disturbance Among Children from an Orthodontic Setting.** [Studies of snoring and sleep disturbance in the United States have been predominately in clinic-based settings of children suspected to have obstructive sleep apnea hypopnea syndrome. Therefore, the purposes of this study were to utilize an orthodontic setting in which healthy children were seen regularly to study the prevalence of snoring and sleep disturbance among 405 children aged 6 to 17 years of age and to identify specific sleep behavior patterns associated with the increased odds of snoring. ...The results indicated that 17% of the children habitually snored. The odds of snoring were approximately three times greater among mouth breathers and children who slept with their head tipped back and 1.5 times greater among those with morning headaches and frequent coughs and colds. In conclusion, snorers have significantly more sleep behavior problems than do nonsnorers.] Nelson S, Kulnis R. *Sleep and Breathing*, Vol. 5, No.2, p.63-70.  
<http://www.springerlink.com/content/y85gqeg500awj45h/?p=7cf73757247344b680c8872ce3cc09b3&pi=2>
325. **Symptoms of Sleep Breathing Disorders in Children Are Underreported by Parents at General Practice Visits.** [Sleep breathing disorders (SBD) in children are reportedly underdiagnosed in general practice. A contributory factor may be parental underreporting of symptoms. This possibility was examined by comparing the frequency with which snoring

was mentioned at general practitioner visits by parents with frequency that snoring was reported on questionnaire evaluation immediately prior to consultation. We also examined the effects of age and gender on SBD symptoms. ... We found that snoring was patently underreported by parents. In the children with a history of frequent snoring on questionnaire evaluation and where the reason for the consultation visit was documented, snoring was mentioned by parents at the current consultation visit in only 8% (8 of 100) of cases and at a prior consultation visit in only 15% (15 of 100) of cases. The present findings support a need for increased parental education regarding the symptoms and clinical significance of SBD. ] Blunden S, Lushington K, et al. *Sleep and Breathing*, Vol. 7, No. 4, p.167-176.  
<http://www.springerlink.com/content/akn0551d4x453abh/?p=5c02108d687741878cd0f5f617bce64a&pi=2>

326. **Treatment of Long-Standing Nocturnal Enuresis by Mandibular Advancement.** [Enuresis, the involuntary release of urine during sleep, is one of the most common disorders of childhood. More common in boys than girls, this condition is characterized by night-time wetting in the presence of normal urinalysis and physical examination. At present, treatment can be divided into behavioral modification and pharmacological therapy, despite which many enuretic children remain untreated or are treated ineffectively. Treatment of long-standing chronic enuresis by orthodontic appliances could be used more frequently to give relief to those not responding to conventional treatment. Mandibular advancement therapy is especially beneficial in the treatment of enuretic patients presenting with anteroposterior skeletal discrepancies. ] Robertson CJ. *Sleep and Breathing*, vol.8, No.1, p.57-60.  
<http://www.springerlink.com/content/vp5glr1chmjyadm/?p=8c13544087e8469cb0c4d7aad759870d&pi=6>

## **Bruxism and Sleep Apnea**

327. **Sleep Apnea and Bruxism in TMD Patients during Nocturnal Sleep** [Objectives: In order to clarify the appearance phase of sleep apnea in TMD patients the sleep apnea and bruxism of healthy subjects and TMD patients during sleep at night were analyzed. Methods: Twenty healthy subjects and 20 TMD patients, all females in their twenties were selected. Using a wireless telemeter system, the EEG, EOG, ECG, masseter EMG, mental EMG and respirogram were recorded simultaneously throughout the night. First the frequency of sleep apnea and the frequency of bruxism were compared between the healthy group and the patient group. Next the relationship between the frequency of sleep apnea and the frequency of bruxism was investigated. Sleep apnea was defined as cessation of respiration for over 10 seconds and bruxism was defined as those bursts that lasted more than 5 seconds or the burst between two bursts that was less than 5 seconds apart and the muscular activities were larger than the swallowing activities recorded prior to sleep. Results: Both the frequency of sleep apnea and the frequency of bruxism were larger for the patient group (bruxism : 8.2n/h, apnea : 1.6n/h) than for the healthy group (bruxism : 5.5n/h, apnea : 0.3n/h) and a significant difference was found between the two. There was no correlation between the frequency of sleep apnea and the frequency of bruxism in the healthy group, but for the patient group, when the frequency of bruxism increased the frequency of sleep apnea also increased and there was a positive correlation between the two ( $y=0.00187x^{3.12}$ ,  $R=0.809$ ,  $p<0.01$ , s.). Conclusions: From these results it was concluded that sleep apnea was intimately connected to bruxism and in TMD patient with high frequency of bruxism attention should be paid to the possibility of sleep apnea.] Y. KOBAYASHI, H. SHIGA, and M. YOKOYAMA, The

Nippon Dental University, Tokyo, Japan .

[http://iadr.confex.com/iadr/2002SanDiego/techprogram/abstract\\_13927.htm](http://iadr.confex.com/iadr/2002SanDiego/techprogram/abstract_13927.htm)

328. **Sleep bruxism and behavioral disturbances in children: a population-based study.** [Bruxers and never bruxers had no significant differences found with respect to behavioural disturbance, emotional disturbance, and conduct problems, as assessed by teachers on the Rutter scale.] Azevedo MH, Clemente VM, et.al. *Actas de Fisiologia* 7, 2001.  
[http://72.14.253.104/search?q=cache:VFEbmqlGLQMJ:www.rau.edu.uy/universidad/medicina/actas7/pathologies\\_and\\_disorder.pdf+Compliance+and+effective+therapy+for+positional+apnea.+Freebeck&hl=en&ct=clnk&cd=3&gl=us](http://72.14.253.104/search?q=cache:VFEbmqlGLQMJ:www.rau.edu.uy/universidad/medicina/actas7/pathologies_and_disorder.pdf+Compliance+and+effective+therapy+for+positional+apnea.+Freebeck&hl=en&ct=clnk&cd=3&gl=us)
329. **Sleep bruxism related to obstructive sleep apnea: the effect of continuous positive airway pressure.** [Several studies have reported that sleep bruxism rarely occurs in isolation. Recently, in an epidemiological study of sleep bruxism and risk factors in the general population, it was found that among the associated sleep symptoms and disorders obstructive sleep apnea (OSA) was the highest risk factor for tooth grinding during sleep. The purpose of this report was to evaluate the effect of continuous positive airway pressure (CPAP) on sleep bruxism in a patient with both severe OSA and sleep tooth grinding. Two polysomnographic (PSG) recordings were carried out. The first showed 67 events of sounded tooth grinding, most of them appearing as an arousal response at the end of apnea/hypopnea events in both the supine and lateral postures. During the CPAP titration night most breathing abnormalities were eliminated and a complete eradication of the tooth grinding events was observed. The results of this study suggest that when sleep bruxism is related to apnea/hypopneas, the successful treatment of these breathing abnormalities may eliminate bruxism during sleep.] Oksenberg A, Arons E. *Sleep Med.* 2002 Nov;3(6):513-5.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=14592147&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14592147&dopt=Abstract)

## **Psychiatric Conditions, Depression, Neurotransmitters, Endocrinology**

330. **Antidepressant treatment of the depressed patient with insomnia.** [Sleep disturbances are an integral part of depressive disorder. As such, they are a part of all contemporary sets of diagnostic criteria for major depression and of all major symptom-based rating scales for depression. Insomnia is a particularly frequent complaint, and it is reported by more than 90% of depressed patients. Although the "kindling" or "illness transduction" model of depression remains hypothetical, there is evidence that people with recurrent depression have more pronounced abnormalities of sleep neurophysiology than those experiencing a single or initial episode. Therefore, early relief of insomnia in a depressed patient, in addition to alleviating other symptoms, may increase adherence to treatment and increase daytime performance and overall functioning, while complete relief of insomnia may improve prognosis. Stimulation of serotonin-2 (5-HT<sub>2</sub>) receptors is thought to underlie insomnia and changes in sleep architecture seen with selective serotonin reuptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs). This is the reason why hypnotics or low-dose trazodone are commonly coprescribed at the initiation of the treatment with either the SSRIs or SNRIs. On the other hand, antidepressant drugs with 5-HT<sub>2</sub> blocking properties, such as mirtazapine or nefazodone, alleviate insomnia and improve sleep

architecture. In depressed patients, mirtazapine produces a significant shortening of sleep-onset latency, increases a total sleep time, and leads to a marked improvement in sleep efficiency. Antidepressants with preferential 5-HT<sub>2</sub> blocking properties are therefore a good treatment option for depressed patients with marked insomnia.] Thase ME. *J Clin Psychiatry* 1999; 60 Suppl 17: 28-31; discussion 46-8. <http://www.biopsychiatry.com/insomnia.htm>

331. **Increased norepinephrine variability in patients with sleep apnea syndrome.** [OBJECTIVE: To assess the plasma arterial catecholamine response to nocturnal desaturation in a group of patients with a history suggestive of sleep apnea. ... These results show that GABA(A) receptor stimulation at the hypoglossal motor nucleus suppresses both genioglossus muscle tone and activity in the presence of reflex stimulation produced by hypercapnia. Recruitment of such mechanisms may contribute to the major suppression of genioglossus activity observed with and without CO<sub>2</sub> stimulation in behaviours such as rapid-eye-movement sleep.] Liu X, Sood S, et.al. *Neuroscience*. 2003;116(1):249-59. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=12535957&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12535957&dopt=Abstract)
332. **Insomnia and Depression: Which Comes First?** [It has been well documented that depression can lead to insomnia. However, evidence from previous research and from clinical experience indicates that the reverse can also be the case: long-standing insomnia can often lead to depression. The aim of this study is to test the hypothesis that, for many people suffering from both depression and insomnia, treating the insomnia successfully without medication can lead the depression to lift as well. The sample consisted of 86 consecutive patients or clients who presented as suffering from chronic insomnia. Two thirds of these people were also suffering from depression at intake. During an initial hour-long interview, self-report estimates of key sleep parameters were recorded, and the Beck depression Inventory was administered. Subjects were then introduced to the “Sleep Better Without Drugs” self help program (a book and three audio cassettes), which they used at home to improve their sleep. At follow-up, six to eight weeks later, the sleep parameters were recorded again and the Beck Depression Inventory was re-administered. Results showed that 70% of the insomnia sufferers who were depressed before treatment and learned to sleep better were no longer depressed, or were significantly less depressed, once their sleep had improved. By contrast, among people who did not learn to sleep better, none experienced a significant reduction in depression. The conclusion is that, for many people who suffer from both depression and insomnia, treating the insomnia successfully without medication can eliminate or significantly reduce the depression.] Morawetz D. (Paper was first presented at the National Conference of the Australasian Sleep Association, Melbourne, 2000.) *Sleep Research Online* 5(2):77-81, 2003. [www.sro.org/2004/Morawetz/77/](http://www.sro.org/2004/Morawetz/77/)  
<http://www.sro.org/pdf/3344.pdf>
333. **Longitudinal Association of Sleep-Related Breathing Disorder and Depression.** [Sleep-related breathing disorder (SRBD) and depression have each been independently associated with substantial morbidity, impairment, and disability. The development of clinical strategies for screening and managing depression in patients with SRBD requires elucidation of the association between the 2 conditions. This population-based epidemiological study assesses SRBD as a longitudinal predictor of depression. ... Our longitudinal findings of a dose-response association between SRBD and depression provide evidence consistent with a causal link between these conditions and should heighten clinical suspicion of depression in patients with SRBD.] Peppard PE, Szklo-Coxe M, et.al. *Arch*

*Intern Med.* 2006;166:1709-1715. <http://archinte.ama-assn.org/cgi/content/abstract/166/16/1709>

334. **Obstructive sleep apnea and cognitive dysfunction.** [Obstructive sleep apnea (OSA) affects up to 5% of the population in Western countries, but as many as 80% of cases remain undiagnosed. Prevalence increases with age, peaking at approximately 60 years. Although 1 in 5 adults has mild OSA, only 1 in 15 has a moderate to severe case. Obesity is a significant risk factor, partly because layers of fat adjacent to the pharynx narrow its lumen. A 10% increase in weight leads to a six-fold risk of developing OSA. Thus, the incidence of OSA is expected to rise as the rate of obesity increases in the United States. Other risk factors for OSA include male sex and abnormalities of craniofacial morphology. Frequent alcohol use has also been considered a risk factor since it depresses the central respiratory drive and enhances muscle relaxation. Patients with untreated OSA may present with conditions such as hypertension, coronary artery disease (including MI), diabetes, heart failure, stroke, and cognitive dysfunction. Although these conditions are commonly treated without a search for underlying pathology, OSA can be a major contributor. Previous research has focused on the cardiac effects of untreated OSA, such as hypertension, stroke, and arrhythmias. However, a mechanism that causes cardiac dysfunction may also cause cognitive dysfunction resembling dementia. Failure to diagnose and treat OSA effectively may result in improper management of this dementia. With proper treatment, its progression may be halted—although the condition may not be completely reversed. At present, no optimal treatment options are available for OSA. Continuous positive airway pressure (CPAP) therapy is the first-line treatment, but patient adherence is only 46% to 70% because of discomfort caused by the mask.] Felmet KA, Peterson M. *May 2007, JAAPA – Official Journal of the American Academy of Physician Assistants.* <http://jaapa.com/issues/j20061101/articles/apnea1106.htm>