

Sleep HealthCenters® Newsletter

Lawrence J. Epstein, MD, Editor

January 2007

Dear Colleague,

We are proud to announce that Sleep HealthCenters® is commemorating its 10th year of helping people get a better night's sleep!

In this issue of the Sleep HealthCenters® Newsletter, Sandra Horowitz, MD, FRCP(C) explores the relationship between sleep apnea and stroke. Sleep apnea is a known cause of hypertension. Dr. Horowitz discusses why sleep apnea is now being recognized as a preventable cause of stroke, as well. Dr. Horowitz, the Medical Director of Sleep HealthCenter® in Framingham, is a recognized expert in both sleep and epilepsy.

In the CEO Corner, we are pleased to announce that our first technologist training course, the Accredited Sleep Technologist Education Program (A-STEP), will be taking place this month. Sleep HealthCenters® is one of the first accredited A-STEP providers in the nation.

Our Newton facility has been relocated to Brighton and our Malden facility has been relocated to Medford. We have upgraded these facilities and added clinic space and beds in order to see more patients and reduce wait times.

We successfully held our second Sleep Apnea Awareness and Support Group Meeting for people who suffer from apnea, their families and support persons. Additional sleep apnea support group meetings are being planned for 2007.

If you have any questions about sleep disorders, our services, our affiliations or our locations, please feel free to contact us.



Sincerely,
Lawrence J. Epstein, MD
Medical Director
Sleep HealthCenters® LLC


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Better Sleep. Better Health.

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Obstructive Sleep Apnea and Stroke

By Sandra Horowitz, MD, FRCP(C)

Dr. Horowitz is the Medical Director of the Sleep HealthCenter® in Framingham. She is board certified in Sleep Medicine, Neurology and Neurophysiology and is an Associate Professor of Neurology at the University of Massachusetts. She is a member of the American Board of Clinical Neurophysiology. She continues to study the impact of neurological disease on sleep.



Is there a relationship between Obstructive Sleep Apnea and Stroke? How predictive is it? Can treating sleep apnea affect stroke risk?

Recent research has supported an association of these two common conditions. Stroke is the third most common cause of death in the United States and the leading cause of disability in adults, according to the American Heart Association 2005 (1). Obstructive Sleep Apnea (OSA) is highly prevalent, affecting 5% of men and 3% of women in the United States. When we think of the patho-physiology of stroke and sleep apnea, we can easily speculate an interrelationship.

As breathing diminishes during an apneic episode, there is an immediate effect of intermittent hypoxia and increasing negative intrathoracic pressure on heart rate and blood pressure. The arousal from sleep required to end an apnea causes changes in sympathetic activity and also affects blood pressure and heart rate. Nocturnal diastolic blood pressure, a strong predictor of cardiovascular risk, may be the first to rise in an apnea. Since the brain depends on a continuous supply of oxygen to function, even a temporary decrease in oxygen saturation may have far reaching physiologic effects. Cerebral autoregulation may be impaired by rapid swings in blood pressure. In the July Sleep HealthCenters® Newsletter, Dr. Douglas Kirsch explained that sleep apnea is a risk factor for impaired glucose tolerance, especially in patients with hypertension, and may be implicated in the recently described metabolic syndrome.

Common symptoms of OSA include habitual snoring, nocturia, unrefreshing sleep, dry mouth upon awakening, excessive daytime sleepiness, personality changes, morning headache and disturbances of mood. The most important risk factors are obesity, a large neck (>16 inches in women and >17 inches in men), adenotonsillar hypertrophy, habitual snoring, small chin and airway, as well as alcohol, sedative and opiate use. Family history plays a role, with studies focusing on inherited facial anatomy and on the genes that control receptor sensitivity in the pharyngeal muscles. Primary physicians should evaluate these symptoms in a clinical exam, even when the patient does not complain of excessive daytime sleepiness.

Hypertension and Stroke

Hypertension affects nearly 50 million people in this country. Effective recognition and treatment of hypertension has been credited as a key factor in the reduction of stroke rate. Elevated blood pressure, greater than 140/90 mm Hg, is a cause of shear stress in blood vessels, resulting in atheroma and arteriosclerosis. This can lead to damage of the heart, brain and kidneys. Cardiovascular risk doubles for every 20 mm Hg systolic or 10 mm Hg diastolic increase in blood pressure. Although patients who reduce their blood pressure have 28-38% fewer strokes, only 59% of known hypertensives are treated and only 34% achieve a blood pressure less than 140/90, according to the 1999 National Health and Nutritional Exam Survey.

Hypertension is a risk factor for all types of stroke, large vessel with atheroma and small vessel lacunar strokes with lipohyalinosis. Vascular cognitive impairment following stroke is greater in hypertensive patients and their risk of subsequent vascular dementia is elevated. Cerebral hemorrhage is a specific potentially devastating outcome of poorly controlled hypertension.

Apnea and Hypertension

OSA is a known risk factor for the development of hypertension (Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure, NHLBI, NIH Publication No. 03-5233, December 2003). Peretz Lavie, et al, prospectively examined 2,677 adults referred to a sleep center for any reason. Forty percent were hypertensive, and patients with an apnea-hypopnea index (AHI) >10 events per hour of sleep had significantly higher blood pressure compared to controls matched for age, body mass index and gender (2). Each additional apnea per hour increased the risk of hypertension by 1% (continued on page 2)

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Sleep HealthCenters®
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Sleep HealthCenters® is a network of sleep medicine centers staffed by experts in the field of sleep medicine. Our integrated care system provides all the services needed to diagnose and treat patients with the entire array of sleep disorders including obstructive sleep apnea, insomnia, narcolepsy and restless legs syndrome.

In this issue of the Sleep HealthCenters® Newsletter...

- ▶ Obstructive Sleep Apnea and Stroke by Sandra Horowitz, MD, FRCP(C)
- ▶ CEO Corner:
 - Sleep HealthCenters® relocates Newton and Malden centers
 - Accredited Sleep Technologist Education Program (A-STEP)
 - Sleep HealthCenters® welcomes Patrice Richardson, Nurse Practitioner
 - Sleep HealthCenters® implements automated appointment confirmation system
 - Sleep Apnea Awareness and Support Group Meeting
- ▶ Research Activities

Affiliations: Massachusetts – Beth Israel Deaconess Medical Center, Chadwick Medical Associates, Brigham and Women's Hospital, Faulkner Hospital, Hallmark Health, McLean Hospital, New England Sinai Hospital, UMass Memorial Medical Group
New York – Beth Israel Medical Center

Locations: Massachusetts – Bedford, Beverly, Boston, Brighton, Framingham, Jamaica Plain, Medford, Stoughton, Weymouth, Worcester
New York – Manhattan

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Requisition forms are available on our website.

Sleep HealthCenters® Newsletter

(continued from page 1) and each 10% lowering of the nadir of oxygen saturation due to apnea increased the risk of hypertension by 13%.

The Wisconsin Sleep Cohort Study (3) is a continuing study of state employees followed by serial polysomnography (PSG). It confirmed a dose dependent association between the frequency of apneas and hypopneas at baseline and the development of hypertension at follow up. The odds of developing hypertension were increased two-fold for an AHI of 5-14.9 and three-fold for AHI index >15. In the multicenter, NIH funded, Sleep Heart Health Study, younger subjects under forty years of age with an AHI >40 were at greatest risk, with four-fold increased risk of hypertension (4). Treatment of hypertensive OSA patients with continuous positive airway pressure (CPAP) alone has been reported to result in a decline of blood pressure of approximately 10 mm Hg in the first 4-8 weeks (5).

Clinicians confronted with unexplained or difficult to treat hypertension should think of sleep apnea, even in patients without typical symptoms or body habitus. Symptoms of

sleep apnea may be so insidious that patients are unaware of the lifestyle changes they have been forced to adopt. Chronic fatigue and apathy can become a personality style, the term "couch potato" is often appropriate. In the 6,000 patients of the Sleep Heart Health Study, only a minority of the patients with significant apnea complained of sleepiness. Often, the bed partner who insists on accompanying the patient to the clinic visit will give a more accurate account of the signs of sleep apnea and impact of night time activity on daytime functioning.

Apnea and Stroke

Shelden Kapen studied the relationship between stroke and sleep apnea in 1991 and found a high rate of OSA in patients with prior stroke (6):

47 Stroke Patients	
72%	AHI >10
53%	AHI >20
30%	AHI >40

Older age, sleepiness and obesity increased the risk of apnea. More recently, a group of

55 patients with stroke were studied in the sub acute phase, 2-5 weeks after the event. Seventy-seven percent of men had an AHI >10 compared to 23% of matched controls. Dysphagia is another common symptom in the early post stroke period that involves the oropharynx and interferes with stroke rehabilitation. In a different study, 53% of early post stroke patients had OSA (AHI >10) but only 29% had dysphagia. The authors concluded dysphagia was not a risk factor for OSA.

Given that strokes cause damage to the central nervous system, one might expect stroke to cause predominantly central apnea or Cheyne-Stokes respiration. However, Bassetti found that obstructive events predominate after a stroke or transient ischemic attack (8). He examined patients 3 days after the stroke and 6 months later, implementing CPAP therapy where indicated. Sleep apnea (AHI >10) was common in 58% of patients and was associated with increased mortality. Of 18 deaths, only 5 had an AHI <10. Patients with microangiopathic strokes had a higher AHI than those with cardio-

embolic ones. Age, diabetes, night time onset of stroke and brainstem location of lesion were all associated with sleep apnea.

CPAP is the treatment of choice for OSA and we are accumulating data for a possible preventive role of CPAP in stroke. CPAP was found to protect against future vascular events in a population of patients followed prospectively after a first vascular event. Ninety-five consecutive patients with stroke had PSG and 51 had AHI >20, but only 29% accepted CPAP. The patients were all followed for 18 months. There were 11 new cerebrovascular events, one episode of angina and one myocardial infarction. Overall, 36% of the apneics who were non-compliant with CPAP had another event versus 7% of patients using CPAP regularly. Failure to use CPAP in a patient with AHI >20 increased future stroke risk five-fold (9).

To decide whether sleep apnea was a risk factor for stroke independent of the effect on hypertension, H.Yaggi, et al, looked at 1,022 patients referred to their sleep center for evaluation for OSA and found that 68% had OSA (mean AHI = 35). Compared to the

control group (AHI = 2), the OSA group had a hazard ratio for first stroke or death of 2.24, with a 95% confidence interval of 1.86-3.86, p = 0.004. Adjustment was made for age, gender, race, smoking, alcohol consumption, body mass index, diabetes mellitus, hypertension, atrial fibrillation and hyperlipidemia. Most deaths were from vascular disease. The hazard ratios for the entire cohort were:

Stroke or Death After First Event	
AHI <3	Hazard Ratio: 1
AHI 4-12	Hazard Ratio: 1.75
AHI 13-36	Hazard Ratio: 1.74
AHI >36	Hazard Ratio: 3.3

The authors concluded that sleep apnea alone was responsible for the increase in hazard ratio (10).

The literature to date strongly supports that OSA is an independent risk factor for hypertension and cerebrovascular disease. Empirically it makes sense. In these studies, subjective sleepiness was not always present in patients with clinically significant apnea.

There is a need for further investigation with larger patient groups. To date, stroke size and location, the presence or absence of cerebral edema, source of stroke – cardiac versus carotid or small versus large vessel – have not been fully analyzed. Patients too ill for informed consent are often excluded from studies and these may be the ones most severely affected with OSA. Thus, we may be under representing the association of sleep apnea and stroke.

CPAP compliance continues to be a major issue in both acute and chronic settings. It is necessary to define, and then accommodate, the special needs of stroke patients with their varied disabilities if we expect to impact long term recovery of those patients with OSA. OSA is an independent risk factor for stroke. Treating sleep apnea with CPAP may improve stroke risk.

For a fully referenced version of this article, visit the Sleep HealthCenters® website at www.sleephealth.com.

Case Study

A 39 year old man was referred to the sleep center because of loud snoring that was disturbing his wife. He could be heard in other rooms of the house and it was a running joke with his camping buddies, who credited him with keeping the bears at a safe distance. They would turn him to his side, but that no longer controlled the symptoms. He worked as a computer analyst with long days in front of the computer fighting off sleep. He had gained 25 pounds in the last year for a BMI of 36.

His bedtime was 11:00 PM and wake time was 6:30 AM, but he regularly returned to bed to prolong sleep. Daytime tiredness was confirmed by an Epworth Sleepiness Index of 14/24 (index greater than 10 suggests excessive sleepiness). He commuted 45 minutes to work each way and to stay awake driving, he would drink mountain dew or coffee, amounting to 5 cups/day. More than that tended to result in palpitations. Snacks in the car aided alertness but contributed to weight gain. He consumed 4-6 beers/week and did not smoke.

His family history included a father who died at 69 years old of an intracerebral hemorrhage associated with poorly controlled blood pressure. He had two healthy younger brothers who both snored but had not been evaluated medically.

While sitting at his desk, he experienced three episodes of tingling in the left arm from the fingertips to the upper arm associated with mild heaviness and clumsy fine finger movements. The episodes lasted approximately one minute and the last episode was followed by residual numbness and slight clumsiness of the left hand. He was given aspirin. An MRI scan done within 24 hours showed a small lacune in the right centrum semiovale. MRA of the brain and carotid system in the neck and transesophageal echocardiogram were negative. Blood chemistry for homocysteine, anticardiolipin antibody, antithrombin III, were negative. The symptoms in the left arm resolved over a week.

He was hypertensive at the time of the stroke, with blood a pressure of 145/95 mm Hg. This was a new finding. Serum cholesterol was normal at 184 mg/dl, but LDL was elevated at 152 mg/dl. Thyroid function was normal. His primary care physician recommended exercise, weight loss and lifestyle changes to enhance relaxation and the elimination of caffeine and alcohol. A statin medication and a diuretic were started. When his blood pressure did not change, an ACE inhibitor was added and the pressure decreased to 145/90 mm Hg. He was unable to lose weight.

Due to the history of snoring and excessive sleepiness, he had an overnight polysomnogram. He snored loudly in all positions and there were frequent hypopneas, especially when supine, resulting in an apnea-hypopnea index of 24 events/hour of sleep. His lowest oxygen saturation was 84% with 3% of the time spent with a saturation <90%.

CPAP was applied and titrated to 8 cm H2O with good effect. The respiratory events and snoring were controlled. He used nasal pillows with a heated humidifier and was willing to use CPAP at home. He felt the same initially, but after instruction and 3 weeks of home use, he was feeling more rested. On follow up evaluation, his blood pressure had improved to 134/76 mm Hg. He was aware of the high risk in his family of cerebrovascular disease, and was relieved to be responding to therapy. His wife slept better from the first day of CPAP.

His blood pressure did not respond to medications until his OSA was diagnosed and treated with CPAP. The blood pressure remained under control once CPAP was added to his antihypertensive regime.



CEO Corner

Paul S. Valentine

President and Chief Executive Officer

Sleep HealthCenters® is pleased to announce our Newton center has been relocated to a new, 6-bed full service sleep medicine center in Brighton, located at 1505 Commonwealth Avenue. This new center includes an expanded clinic with 13 exam rooms. Our Malden center, affiliated with Hallmark Health, has also been relocated to a new, 6-bed center in Medford, located at 200 Boston Avenue. With the relocations to these new facilities, we will have more clinic space and beds to accommodate additional patients. All patients have been notified of the changes.

Our first Accredited Sleep Technologist Education Program (A-STEP) will be taking place this month. A-STEP is an 80-hour didactic course, the first of a two-step training initiative endorsed by the American Academy of Sleep Medicine (AASM). Sleep HealthCenters® is one of the first accredited A-STEP providers in the nation. This challenging program provides students with a comprehensive education and enables Sleep HealthCenters® to continually staff the most thoroughly trained sleep technologists.

We are please to welcome Patrice Richardson, Nurse Practitioner, to our staff. Patrice brings with her six years of nursing

experience in long term care, neurologic rehabilitation and medical-surgical telemetry. She will be based in our Framingham center.

As we continue to strive to provide efficient service for our patients, Sleep HealthCenters® has implemented an automated appointment confirmation call system. Two days prior to an appointment, a patient will be called with a personalized reminder of their appointment. Patients will also have an opportunity to speak with someone directly if they have questions or need to reschedule.

Finally, we are pleased to announce that Sleep HealthCenters® held its second Sleep Apnea Awareness and Support Group Meeting at Faulkner Hospital on January 16. CPAP patients, their families and support persons were able to talk with others who suffer from apnea and also take a look at the latest equipment. Douglas B. Kirsch, MD, was the featured speaker with a lively discussion about the medical consequences of untreated sleep apnea. The meeting was well attended and the feedback was once again incredible. We look forward to continuing our support group meetings throughout the region.

Thank you for allowing us to play a role in the care of your patients. Please contact us if there is anything we can do for you.

Research Activities

Sleep HealthCenters® is proud to work with some of the premier sleep researchers in the country. The following research studies are currently underway in conjunction with our partners:

Apnea Positive Pressure Long-Term Efficacy Study (APPLES) The Sleep HealthCenter® associated with Brigham and Women's Hospital is conducting a NIH-funded study that examines the long-term effects on quality of life, neurocognitive function, sleepiness and mood by using Continuous Positive Airway Pressure (CPAP) to treat sleep apnea.

Restless Legs Syndrome The Sleep HealthCenter® associated with Brigham and Women's Hospital is conducting two new research studies on treatments for Restless Legs Syndrome (uncomfortable sensations in the legs accompanied by the urge to move, which generally start during periods of rest and are worse at night).

Operation Healthy Sleep This innovative research project is funded by the National Institute of Justice and is designed to examine and evaluate the impact of sleep disorders and treatment of sleep disorders on the safety, health and performance of Massachusetts State Police and the City of Philadelphia Police.

Sleep and Menopause This unique study concentrates on understanding the role that hot flashes and sleep disruption play in the effect of estrogen replacement therapy on mood in perimenopausal and postmenopausal women.