

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

- ▶ Obesity, Weight Loss, and Obstructive Sleep Apnea
- ▶ CEO Corner: Sleep HealthCenters® Opens NeuroSleep lab at Faulkner Hospital
- ▶ Research Activities

Sleep HealthCenters® is a network of sleep medicine clinics and labs 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. Sleep HealthCenters® has locations throughout eastern Massachusetts and is affiliated with the Brigham & Women's Hospital, Beth Israel Deaconess Medical Center, McLean Hospital, Faulkner Hospital, and Hallmark Health.

Sleep HealthCenter® locations include South Weymouth, Newton, Bedford, Malden, Boston, and Jamaica Plain.

For more information, please contact our scheduling office at: 1-877-SLEEPHC (1-877-753-3742) or visit our website at www.sleephealth.com.

Sleep Health Centers[®] Newsletter

David P. White, MD, Editor

January 2005

Dear Colleague,

In this issue of the Sleep Health Centers[®] Newsletter, we discuss the links between obesity, weight loss and sleep disordered breathing. Drs. Thomas, Robinson, and Fogel present an article and related case study discussing the epidemiology and treatment of obesity, including a recommendation that patients considering surgery for obesity be screened and, if applicable, treated for obstructive sleep apnea prior to surgery. If OSA is present, they also suggest that patients undergo a follow-up sleep study six to twelve months after surgery.

In addition, we introduce the opening of a dedicated neurophysiology and sleep evaluation laboratory at Faulkner Hospital. If you have any questions about sleep disorders or our services, please feel free to contact us.

Sincerely,

David P. White, MD
Corporate Medical Director
Sleep Health Centers[®], LLC




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Better Sleep. Better Health.

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Obesity, Weight Loss and Obstructive Sleep Apnea

Abraham Thomas, MD, MPH, Malcolm Robinson, MD and Robert B. Fogel, MD

Dr. Thomas is an Instructor, Division of Endocrinology-Diabetes-Hypertension and Medical Director, Program for Weight Management, Brigham and Women's Hospital. Dr. Robinson is an Assistant Professor of Surgery at Harvard Medical School and Director, Program for Weight Management, Brigham and Women's Hospital. Dr. Fogel is board certified in Sleep Medicine, Internal Medicine, Pulmonary Diseases and Critical Care Medicine and Associate Director, Respiratory and Allergy Division, Merck and Co. Inc.

Epidemiology: The prevalence of obesity has increased dramatically over the last few decades. Obesity is defined by the body mass index (BMI), which is calculated by dividing a person's weight in kilograms (kg) by the height in meters squared (m²). Normal weight is defined as a BMI of 18-24.9 and overweight is defined as a BMI of 25-29.9. Obesity is defined as a BMI of 30 or greater. Using these definitions, approximately 65% of adults in the United States are overweight or obese based on data from the most recent National Health and Nutrition Examination Surveys (NHANES). Children are also undergoing a dramatic increase in obesity. The obesity problem is not isolated to the U.S., but is occurring worldwide.

Obesity has a dramatic impact on an individual's health and mortality. Obesity is a risk factor for many chronic diseases, which may lead to premature death. Among the most serious are arteriosclerosis, hypertension, adult onset diabetes (type II) mellitus, certain types of cancer such as breast and prostate cancer, hyperlipidemia, and respiratory diseases such as obstructive sleep apnea (OSA). Other diseases commonly associated with obesity are osteoarthritis, gallbladder disease, gout, and reproductive disorders, such as polycystic ovary syndrome. Although these diseases might not decrease life expectancy, they clearly affect quality of life. In 1995, it was estimated that the financial burden of obesity was about 99 billion dollars with about 52 billion dollars going to direct medical care costs and 47 billion dollars going to indirect costs, such as loss of productivity at work. Americans also spend about 33 billion dollars a year on weight-loss products.

Obesity and OSA: OSA and obesity commonly occur together, with some studies suggesting that 25-75% of obese subjects suffer from OSA. Numerous studies have confirmed that obesity is the strongest risk factor for the development of OSA. A BMI >28 kg/m² is found in 60-90% of patients diagnosed with apnea (Dealberto et al, Chest 1994 105:1753) and obesity (BMI >29 kg/m²) may increase the risk of sleep apnea by as much as 10-14 fold (Young et al, NEJM 1993 328:1230). In addition, obese individuals with the greatest cardiovascular risk, those with the metabolic syndrome (the combination of visceral obesity, insulin resistance, hypertension and dyslipidemia), are those most likely to suffer from sleep-disordered breathing as well.

Although obese individuals are at increased risk for OSA, the relationship between measures of obesity and severity of OSA is only moderate and not linear. In fact, several studies of obese subjects have shown that the severity of apnea varies widely in these subjects. In a group of 250 morbidly obese men and women (mean BMI = 45 kg/m²) Vgontzas found there was no difference in mean BMI in the group with and without apnea (Arch Intern Med 1994 154:1705). Similarly, Rajala found no difference in mean BMI or neck circumference in a group of morbidly obese subjects (BMI = 50 kg/m²) with and without OSA (Arch Intern Med 1991 230:125). These data suggest that other factors must interact with obesity in the development of OSA, such as variability in upper airway anatomy (fat deposition), specific tissue characteristics of the upper airway, neuromuscular control of pharyngeal dilator muscles, lung volume, or ventilatory control mechanisms.

Only a small percentage of obese individuals with sleep apnea develop the syndrome of Obesity-Hypoventilation (Pickwickian Syndrome). This disorder is characterized by severe obesity, daytime hypoxemia and hypercapnia, signs of elevated Pulmonary Artery Pressure and, in severe cases, the development of right ventricular failure (Cor Pulmonale). While the etiology of this syndrome is incompletely understood, it is probably due to a combination of the intrinsic genetic variability in sensitivity to alterations in blood gases and the increased demand placed on the ventilatory system by severe obesity.

(continued on page 2)

Sleep Health Centers® Newsletter

(continued from page 1)

Treatment of Obesity: The treatment of obesity can be divided into two major categories: medical and surgical. The hallmark of medical treatment is lifestyle modification to reduce caloric intake and increase physical activity to cause higher energy expenditure. Although these changes in lifestyle can be quite successful in the short-term, long-term success for weight-loss and weight maintenance has been disappointing. Many different diets have been proposed to be more effective than others. In cases where diets have been compared to each other, such as the "Atkins" diet and the traditional low-fat diet, no differences in the ability to lose and maintain weight-loss have been seen at the end of one year.

Two medicines are approved for long-term (one year) use in weight-loss, sibutramine and orlistat. Sibutramine is a serotonin, norepinephrine, and dopamine reuptake inhibitor that causes decreased appetite and caloric intake. In those individuals who lost at least four pounds during the first four weeks of treatment, about 60% were able to lose 5% or more of their weight over six months. Orlistat is a reversible inhibitor of intestinal lipase and is presumed to cause weight loss by a 30% reduction in dietary fat absorption. Approximately 50-55% of subjects on orlistat lose 5% or greater of their weight at one year.

Surgical treatment for obesity in the U.S. is rapidly growing in popularity. However, even with surgery, lifestyle modification is an essential part of the treatment. Surgery is currently indicated for those individuals who have been unable to lose or maintain weight loss in a medically supervised setting, have a BMI >40 or >35 and have an associated co-morbid condition such as diabetes and OSA. Patients are evaluated for their risk from surgery, for their ability to comply with the changes in the diet because of the surgery and for any psychiatric or behavioral problems that would preclude them from following the appropriate diet post-surgery.

In the U.S. the two most common procedures are the gastric bypass (roux-en-Y) procedure and the laparoscopic banding procedure. There is greater experience with the roux-en-Y procedure in the U.S. The laparoscopic banding procedure has only been approved for a few years, but has been performed worldwide for many years. In U.S. studies, the gastric bypass procedure produces greater weight loss than the laparoscopic banding procedure. However, the risk of acute perioperative morbidity is greater for the gastric bypass procedure. Other complications from surgery are abdominal hernias, gallstones, dumping syndrome, abdominal adhesions, outlet obstruction, erosions secondary to the laparoscopic band, psychiatric illness, and nutritional deficiencies. The average excess weight loss with gastric bypass is about 55-70%. The average excess weight loss with laparoscopic banding is about 45-55% (Fobi et al, J Natl Med Assoc 2004 96:61).

Numerous studies have demonstrated that as little as a 5% weight-loss can improve medical conditions such as diabetes, hypertension and hyperlipidemia. A recent meta-analysis by Buchwald et al. in the Journal of the American Medical Association demonstrated that diabetes completely resolved in 76.8% of subjects, hypertension resolved in 61.7% of subjects, and hyperlipidemia improved in 70% or more of patients after surgical weight-loss procedures (JAMA 2004 292:1724).

Weight Loss and Sleep Apnea: Although well-controlled clinical studies have not been performed in large numbers of patients, there is

ample data supporting the idea that the weight loss associated with gastric bypass is quite effective in improving OSA in obese patients. In virtually all patients, the severity of sleep-disordered breathing is improved, as measured both by the RDI and severity of oxygen desaturation. Various studies have reported that sleep apnea is cured in 70-100% of patients, but these are largely based on the resolution of symptoms and few studies have systematically performed sleep studies on patients following surgery (6,7). We believe that all patients considering surgery should be screened for OSA and treated prior to surgery if significant OSA is present. Based on the available data, all subjects with at least moderate OSA (RDI >20 events/hour) should have a follow-up polysomnogram performed six to 12 months following gastric bypass surgery to assess for residual sleep-disordered breathing and need for additional treatment. Less data exist on the effects of gastric bypass surgery on the obesity-hypoventilation syndrome, although several reports document normalization of daytime blood gases following weight loss in patients with this syndrome.

Complete reference citations are available at our website; www.sleephealth.com

Research Activities

Sleep HealthCenters® and their related research affiliations are actively recruiting patients for the following studies:

Apnea Positive Pressure Long-Term Efficacy Study (APPLES)

A NIH-funded study examining the long-term effects on quality of life, neurocognitive function, sleepiness and mood of using Continuous Positive Airway Pressure (CPAP) to treat sleep apnea. The Sleep HealthCenter® affiliated with Brigham and Women's Hospital is recruiting patients age 18 or older who suspect they may have sleep apnea but have not been previously treated with CPAP or surgery. Subjects will be enrolled for six months (maximum of 7 months) and will receive extra medical attention as well as monetary compensation. *Study contact: Denise Clarke 617-527-3501 ext. 146.*

Heart Failure and Cheyne-Stokes Respiration

A research study investigating a new mode of positive pressure therapy for the treatment of Cheyne-Stokes respiration during sleep. The Sleep HealthCenter® affiliated with Brigham and Women's Hospital is recruiting patients age 21-80 with congestive heart failure (LVEF < 40%). The study involves one home study and up to four overnight studies in our sleep lab. *Study contact: Mary MacDonald 617-527-3501 ext. 162.*

Restless Legs Syndrome

A placebo controlled, double blind, crossover trial to investigate the effectiveness of levetiracetam (Keppra®) in the treatment of Restless Legs Syndrome. The Sleep HealthCenter® affiliated with Brigham and Women's Hospital is recruiting patients age 18-85 who suffer from Restless Legs Syndrome (achy, creepy-crawly sensations in the legs, which get worse at night). Participation in this study involves clinic visits and four overnight sleep studies over a 14-week period. Compensation is available. Other studies of Restless Legs Syndrome using other medication treatments are currently being run and do not require sleep studies. *Study contact: Lindsay Johnston 617-527-3501 ext. 115.*

Sleep HealthCenters® Newsletter



CEO Corner

Paul S. Valentine

President and Chief Executive Officer

We are pleased to announce that Sleep HealthCenters® recently concluded an agreement with Brigham and Women's/Faulkner Hospitals for a joint sleep medicine program. Sleep HealthCenter®, a collaborative program with Brigham and Women's/Faulkner Hospitals, is located within Faulkner hospital on the fifth floor at 1153 Centre Street, Jamaica Plain. This facility is a combined neurophysiology and sleep evaluation laboratory, making it unique among our six Boston area sites.

Patients coming to the Faulkner Sleep HealthCenter® can be evaluated for nocturnal seizure disorders as well as the standard sleep disorders such as obstructive sleep apnea, narcolepsy and periodic limb movements of sleep. The laboratory is equipped with state-of-the-art seizure detection capability in addition to standard polysomnography. This site is staffed by sleep specialists and epilepsy specialists from Sleep HealthCenters® and the Neurology department of BWH/Faulkner Hospitals. Physicians should consider referring patients specifically to this site who have unexplained behaviors during sleep or suspected nocturnal seizures.

Dr. David White is the facility medical director and Dr. Milena Pavlova, neurologist and sleep specialist, is the associate medical director. Elise

Franko, MS, RPSGT is the Lab Manager, and Kari Gale, RPSGT, is the Lab Coordinator.

The Faulkner Sleep HealthCenter® features comfortable, hotel-like bedrooms which offer patients privacy, a noise-free environment and the opportunity to get the best sleep possible while being tested. Each room has a private bath, a TV, and soft lighting. In the morning following sleep studies, patients are offered coffee and tea before going on their way. Comprehensive sleep-related services are coordinated through Sleep HealthCenters® Newton facility (only a few miles away), including physician clinics, Continuous Positive Airway Pressure (CPAP) clinics, oral appliances and behavioral therapies, such as relaxation techniques. Dr. Pavlova will be conducting her sleep clinics in the Newton facility.

Please contact us if you are interested in a tour of the facility or an introduction of the services we will be offering there. If you have a patient in the Greater Boston area that you would like us to see, you may contact our scheduling office at 1-877-SLEEPHC (1-877-753-3742). We look forward to continuing to service you and your patients from this new location.



OBESITY, WEIGHT LOSS AND OBSTRUCTIVE SLEEP APNEA: A CASE STUDY

Ms. J is a 42-year-old woman who presented to the Brigham and Women's Hospital Program for Weight Management. She stated that she has had a "lifelong" problem managing her weight. She is currently 5'3" and weighs 293 pounds (BMI = 52.3 kg/m²). She has attempted to lose weight in the past with several diet programs, and although she has lost as much as 40-50 pounds, she has never been able to sustain her weight loss for very long. She complains of chronic lower back and knee pain and was recently diagnosed with hypertension and Type II Diabetes. In addition, she complains of chronic dyspnea with exertion. Her current medications include lisinopril and atenolol for blood pressure control, simvastatin for hyperlipidemia and insulin for blood glucose control.

Upon further questioning, Ms. J revealed that over the last 4-5 years she has developed increasingly loud and disturbing snor-

ing and her husband recently mentioned that she occasionally gasps in her sleep. She has noticed increasing daytime sleepiness, which she initially attributed to "stress and working too hard". She has fallen asleep on the train several times both going to and from work and has missed her stop. An overnight sleep study revealed severe OSA with a Respiratory Disturbance Index (RDI) of 54 events/hour. Minimum oxygen saturation was 70% and O₂ saturation was < 85% for 45 minutes. Nasal CPAP at 8 cm H₂O eliminated all sleep-disordered breathing and she began therapy one week after the sleep study was completed.

Ms. J was deemed an appropriate candidate for weight reduction surgery on the basis of her elevated BMI and obesity-associated comorbid conditions. She underwent a complete pre-operative evaluation including medical, psychiatric and surgical consultation. Ms. J underwent laparoscopic gastric

bypass surgery and nasal CPAP was continued throughout the peri-operative period. Her hospital course was complicated by mild post-operative nausea and the development of an abdominal ileus, all of which resolved spontaneously. She was discharged on post-operative day five in good condition.

Over the next 12 months, Ms. J lost weight rapidly to 220 pounds at 6 months and then to 185 pounds at one year (BMI = 31.9). She was able to discontinue insulin as well as her anti-hypertensive medications. She denied any substantial snoring or sleepiness and a follow-up sleep study documented near complete resolution of the OSA with an RDI = 8, and minimum O₂ saturation of 90%. Nasal CPAP was discontinued, although Ms. J was cautioned that if she gained weight or symptoms returned she might very well need further evaluation.