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RESPIRATORY

Reader

For more than 20 years, UPMC's Sleep Medicine Center has been dedicated to helping to diagnose and treat a wide variety of sleep disturbances and disorders. Our physicians are recognized leaders in the field of sleep medicine.

In this issue of *Respiratory Reader*, we will highlight a number of clinical and research initiatives, in which our team is currently participating. We are proud of the accomplishments of the program, ranging from the development of new and innovative ways to diagnose and provide patient-centered treatment of sleep apnea, insomnia, disorders of excessive sleepiness, and circadian misalignment. We understand that many patients suffer from more than one sleep disorder and complete care requires not only addressing the primary sleep problem, such as sleep apnea, but also comorbid contributing sleep problems, such as insomnia, insufficient sleep, and mistimed sleep. Personalized and complete care involves a variety of interventions and assessments which we are well equipped to provide. We have titled this issue "Beyond CPAP" to illustrate some of our clinical and research programs that involve a variety of options we can provide, including advanced positive pressure modalities such as non-invasive ventilation, oral appliance therapy, innovative surgery such as upper airway pacing, cognitive behavioral therapy, and medication for daytime sleepiness.

The UPMC Sleep Medicine Center is accredited by the American Academy of Sleep Medicine. In addition, our ACGME fellowship in sleep medicine plays a critical role in the training of the next generation of sleep physicians and investigators who go on to careers in patient care and research. Research training is

(Continued on Page 2)

supported by our NIH Training Grant for physician scientists and PhD investigators.

We welcome any suggestions or comments on how we might support you in the care of your patients. Please enjoy this issue of *Respiratory Reader*.

With great enthusiasm and respect,



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2016 Pittsburgh-Munich International Lung Conference: Lung Immune Responses and Inflammation in Health and Disease

Thursday, Oct. 6 to Friday, Oct. 7
The University Club, Pittsburgh, Pa.

The objective of the 2016 Pittsburgh-Munich International Lung Conference is to bring together leading pulmonary, critical care, and infectious disease leaders and trainees from clinical, academic, and governmental organizations. This two-day conference will focus on a wide range of scientific disciplines including, pulmonary medicine, immunology, cell biology, computational biology, and translational and clinical science.

Rather than focusing on a single area of lung disease, our goal for this conference is to highlight the important role the immune system plays in preserving lung health, despite constant provocation by environmental insults, and its inappropriate engagement during disease. The conference will showcase cutting-edge basic and translational research to understand defenses against respiratory pathogens with utilization of immunological tools to develop a universal vaccine for flu, as well as immune mechanisms that incite and perpetuate different lung diseases. In addition, we will highlight innovative treatment strategies targeting the immune system to improve patient outcomes in lung diseases, ranging from asthma, bacterial and viral lung infections, COPD exacerbations, cystic fibrosis, sarcoidosis, acute respiratory distress syndrome (ARDS)/severe sepsis, and lung allograft rejection.

Conference topics will include:

- Immune tolerance in maintenance of lung health and loss in disease
- Immune response and inflammation in defense against respiratory pathogens
- Immune response and inflammation in promotion of lung diseases
- Cutting-edge technologies to probe immune cells and relevance in lung disease
- Targeting the immune system to treat lung diseases

For more information and to register,
please visit www.lungconf.pitt.edu.



New Frontiers in the Treatment of Sleep Apnea: Unilateral Hypoglossal Nerve Stimulation

Patrick Strollo, MD

What is It?

Unilateral stimulation of the hypoglossal nerve (the nerve that controls the movement of the tongue) is a new treatment for people with moderate to severe obstructive sleep apnea (OSA) who are unable to use CPAP. CPAP, oral appliances, and some surgeries work “from the outside in” to prevent the tissues from relaxing and blocking the upper airway (nasal and oral passages) [1]. This nerve stimulation therapy works “from the inside out” to move the muscles and keep the airway open. The device includes a nerve stimulator that activates the tongue muscle, causing it to open the upper airway. The device is implanted under local anesthesia after which it is turned on and tuned to adjust its settings to most effectively eliminate apneas (Figure 1). Patients then turn it on before going to sleep and turn it off when getting up. The device only treats apnea when it is turned on.

This therapy can prevent the collapse of the upper airway which occurs in obstructive sleep apnea patients. However, it cannot restore breathing which occurs as result of central sleep apnea.

Development

Unilateral hypoglossal nerve stimulation therapy was approved by the FDA in April 2014 as an implanted system that works with the structure of the patient’s mouth, throat, and tongue. The approval was the result of more than 20 years of research done with animals and humans on the role of muscle contraction in obstructive sleep apnea. About 10 years ago, Inspire Medical Systems and others formed and began sponsorship of clinical trials to first examine such factors as: what is the harm, and does it work? This investigation continued to smaller and then larger clinical trials [2]. The early trials helped to identify patient characteristics that best predicted a positive treatment response for the stimulator, known as Inspire. A larger study, consisting of 126 patients, was designed and conducted in collaboration with the FDA and published in the *New England Journal of Medicine* in 2014 [3]. Follow-up on this study group was conducted at regular intervals for five years after the original implant.

Does it Work?

There are three aspects of therapy to consider: the patient, the placement of the device, and the performance of the device.

This therapy is only recommended for certain patients. The FDA trial included patients who were unable to tolerate or use PAP therapy, had an apnea hypopnea index (AHI) greater than 20 and less than 60, had a body mass index of less than 32 kg/m², and had no obvious anatomic blockages during wakefulness; in a separate study, patients did not have a concentric camera shutter-like closure of the back of the throat. Patients had to have good heart and lung health, less than 25 percent of apneas as central, and no chronic conditions of the nerves or muscles.

Implantation, or the placement of the device, was generally uneventful with post-operative soreness, swelling, and skin infection cited as the majority of the side effects. Less than two

percent of the cases that were performed yielded serious results and there were no deaths related to the use of the device.

When evaluated after one year, it was found that significant improvements were made in many aspects of sleep apnea—including the AHI level, measures of sleepiness, and quality of life. The FDA trial reported that the AHI was lowered by more than 50 percent, and 80 percent of patients reported that sleepiness and quality of life also improved. Immediately after the 12 month visit, there was a group of 46 patients who responded well to the Inspire therapy and half of that group had their device turned off for a week. Those that had the device turned off, saw their sleep apnea return to a similar degree and all asked for their device to be turned on again. Both groups had identical positive responses 18 months after implantation. Treatment for patients within the Stimulation Therapy for Apnea Reduction (STAR) trial population continued three years post implantation.

Who Benefits from Stimulation Therapy?

Stimulation therapy is considered to be a “rescue therapy” because it is invasive and a permanent implant (like a hip replacement). Before patients consider stimulation therapy, they need to try alternative treatments, such as PAP or an oral appliance.

Since the device works by stimulating the tongue to move, the device may not work as well in patients who are obese since obesity may make the airway stiffer and smaller. The original trial used a BMI of less than 32, but the FDA permits consideration of patients with a BMI up to 35 (the level used in Europe).

Before stimulation therapy can be recommended for a patient, they must receive an ENT examination and undergo a drug-induced sedation endoscopy. This procedure will help determine how and where the upper airway might close during sleep. Specifically, the physician might look for a concentric collapse at the back of throat. If present, the chance for success appears to be lower.

Assessment for this Therapy

To determine candidacy for this study, a sleep study conducted within six to 12 months and an unsuccessful attempt at other sleep apnea treatments is required. It is important to remember that PAP therapy and oral therapy have made great advancements. Also note that the implantable system requires anesthesia and the potential for a lifetime with a device inside the patient’s body.

The Costs

Costs for this new therapy varies depending on the hospital. Insurance companies determine the implantation on an individual basis. Medicare regulates coverage at a regional level. Each hospital determines its pathways and this may vary across centers.

The assessments, the office airway examination, and the endoscopy are procedures that are generally covered by insurance; however, plans vary by co-pay, deductible, and health benefit accounts.

(Continued on Page 10)

Current Clinical Trials

Pragmatic Trial of Behavioral Interventions for Insomnia in Hypertensive Patients: Hush Trial

Dan Buysse, MD

This pragmatic, patient-centered, randomized controlled trial will compare two cognitive behavioral interventions for insomnia in patients with comorbid hypertension relative to online education in primary care. Recruitment will be conducted using alerts in the EpicCare EHR triggered by patient characteristics (hypertension; hypnotic medications or insomnia diagnosis/problem).

The primary outcome will be self-reported sleep at three months. Other outcomes include domains of symptoms, health, and patient/provider satisfaction obtained by self-report, and blood pressure control by home blood pressure monitoring.

For more information consult HUSH in the UPMC electronic health record or call 412-246-6445.

The Effect of Treatment of OSA on Diabetes Self-Management and Glycemic Control: DOTT Trial

Eileen Chasens, RN, PhD

Our goal is to improve understanding of the effect of OSA on diabetes self-management and to determine the efficacy of CPAP treatment in improving diabetes outcomes in adults treated with CPAP compared to those on sham-CPAP. We will enroll 210 adults (50 percent female; 40 percent minority) with T2DM and moderate-to-severe OSA (apnea + hypopnea index > 15) who have suboptimal glycemic control (A1C \geq 7.0 percent) for a double blind, randomized, placebo-controlled trial to determine if diabetes self-management outcomes and glycemic control are better in subjects with OSA who are treated with CPAP and receive diabetes education and counseling compared to control subjects who are on sham-CPAP and receive diabetes education.

We will compare the effectiveness of the intervention after six weeks and 12 weeks on measures of glycemic control, retention of information taught during the diabetes education sessions,

lifestyle behaviors required for optimal diabetes control, reported monitoring of self-management activities, physical activity, and diabetes-related distress. We will explore whether the average nighttime use (adherence) of CPAP, sleep quality, daytime sleepiness, mood, and vigilance mediate the effect of CPAP treatment on glycemic control and diabetes self-management outcomes. We will also explore if adherence to CPAP is associated with outcome measures of glycemic control and lifestyle behaviors in the entire sample after 24 weeks of therapeutic CPAP. This study uses objective measures to measure CPAP adherence, physical activity, vigilance, and glycemic control. After 12 weeks, subjects who were originally on sham-CPAP will be crossed over to active treatment.

For more information call 412-624-9380.

Sleep Disorder Breathing, Obesity, and Pregnancy Study: SOAP Trial

Francesca Facco, MD

Our central hypothesis is that SDB is an effect modifier that increases maternal cardiovascular risk and placental hypoxic injury in obese pregnant women, and that CPAP treatment during pregnancy will result in an improved cardiovascular risk and placental profile. To test this hypothesis we will identify a cohort of obese women both with and without SDB. We will examine SDB's impact on maternal vascular stiffness (uterine artery Doppler), angiogenesis (pregnancy specific angiogenic factors e.g., sFLT-1) and metabolism (insulin resistance) across pregnancy (Aim 1). We will perform a randomized controlled trial of autotitrating-CPAP versus sham-CPAP in pregnancy to examine the impact of CPAP treatment during pregnancy on cardiovascular risk (Aim 2) and we will explore the interplay between SDB, CPAP and evidence of maternal vascular disease and chronic fetal hypoxia by evaluating the placental profile of obese women with and without SDB (Aim 3).

For more information call 412-641-5406.

Weight Loss in the Management of Sleep Apnea



Sanjay R. Patel MD, MS

Obesity has long been recognized as an important risk factor for obstructive sleep apnea (OSA). Analyses from the Wisconsin Sleep Cohort study suggest that nearly 60 percent of all cases of moderate to severe OSA in the United States could be prevented by eliminating overweight/obesity. An increasing number of clinical trials have evaluated the role of weight loss in OSA. In one study of mild OSA, those able to lose just five percent of body weight had a 70 percent cure rate. With more severe diseases, the chance of a cure with behavioral weight loss is much lower but there are still improvements in disease severity. In the SleepAHEAD study, the apnea hypopnea index (AHI) fell by 10 events per hour with behavioral weight loss. A concern regarding weight loss interventions is that weight often rebounds after six to 12 months. Fortunately, several studies have shown the initial improvement in AHI persists long term despite partial weight regain.

In addition to treating OSA, weight loss helps address common comorbidities in this population. OSA is an independent risk factor for the development of cardiovascular disease as well as diabetes. Over five years, 15 percent of severe OSA patients will develop type 2 diabetes. There is very strong evidence that even a five-pound weight loss can lead to a substantial reduction in this risk. A recent trial comparing continuous positive airway pressure (CPAP), behavioral weight loss, or their combination found that both CPAP and weight loss alone reduce blood pressure, but the greatest reduction was in those receiving both treatments. In addition, weight loss, but not CPAP, improved insulin resistance and serum triglycerides.

Given that CPAP remains the mainstay of treatment for OSA, it is important that weight be addressed in the care of overweight or obese OSA patients because CPAP therapy itself causes weight gain. CPAP initiation is associated on average with a 1.1-pound weight gain compared to placebo. By preventing airway collapse, CPAP dramatically reduces the work of breathing during sleep. So aggressive weight loss interventions are needed to prevent weight gain when starting CPAP. Fortunately, studies suggest that CPAP does not interfere with the effectiveness of weight loss interventions.

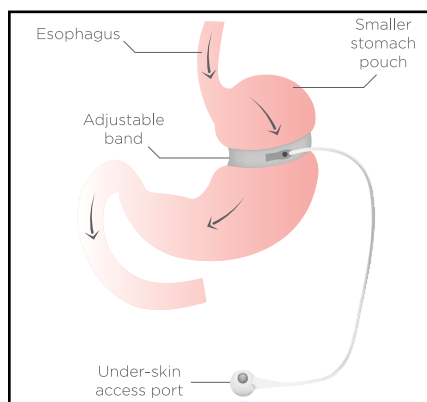
Behavioral Weight Loss

A wealth of clinical trial data has demonstrated that physicians can aid patients in losing weight. Guidelines for the management of overweight and obesity were published by the American College of Cardiology and the American Heart Association in 2013 and provide evidence-based recommendations on how to facilitate weight loss. Patients commonly want to know which diet works best. The evidence suggests that the key requirement for producing weight loss is creating a caloric deficit. A simple recommended weight loss prescription is to target dietary intake to 1200-1500 kcal/d for women and 1500-1800 kcal/d for men. There is no good evidence to support one type of diet (e.g., low fat, high protein, low carbohydrate, low glycemic load, Mediterranean diet) over another at a population level. At an individual level, patient preferences and ability to remain adherent will determine the most effective diet.

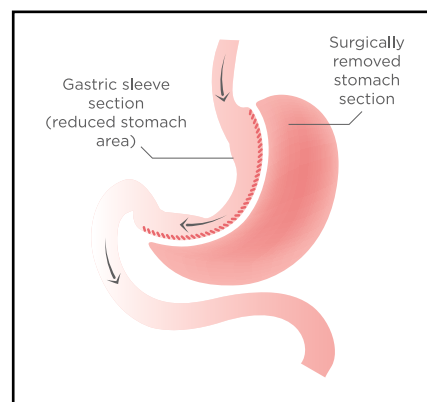
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Types of Bariatric Procedures

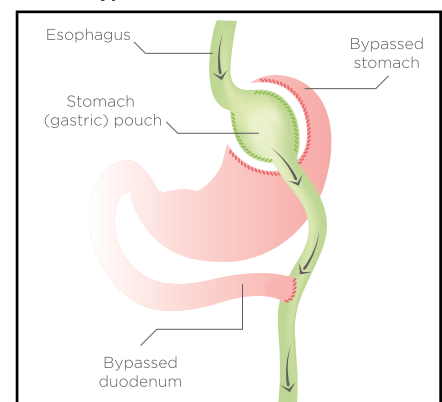
Gastric Band



Gastric Sleeve



Gastric Bypass



Case Presentation: Cognitive-Behavioral Therapy for Insomnia



Deborah A. Gillman, PhD

The Comprehensive Lung Center at UPMC is the optimal setting for a behavioral sleep medicine practice. Patients referred for CBT-I, or Cognitive-Behavioral Therapy for Insomnia, have already been evaluated and treated for conditions such as sleep-disordered breathing. With the medical screening complete, I am free to address what patients know or think about their sleep—cognitive factors—as well as what they do with respect to their sleep—behavioral factors.

CBT-I refers to an assortment of therapeutic techniques that offer an alternative to pharmacotherapy for insomnia and that have demonstrated lasting efficacy. Cognitive interventions include psycho-education about how the body regulates sleep and how insomnia can develop, challenging perceptions about sleep needs or the consequences of a poor night's sleep, and targeting sleep-related anxiety. Behavioral interventions include sleep restriction, or limiting a patient's time in bed to closely match their total sleep time, in order to increase sleep efficiency over time. We also recommend stimulus control, removing non-sleep activities such as computer use or TV from bed, so that the bed becomes conditioned as a stimulus only for sleep. Other behavioral strategies include relaxation, planning nighttime activities that support sleepiness, adjusting bedtime, and sleep hygiene. Here are two very different patients who both derived benefit from CBT-I:

Case 1: J is a healthy 34-year-old man, and a business executive in a highly competitive job requiring extensive travel. His chief complaints were sleep-maintenance insomnia of six-months duration and nocturnal ruminations about work performance. To compensate for poor sleep during the week, he would sleep past noon on weekends. His sleep had not improved with other efforts to manage stress (exercise, listening to music, and meditation). He worked on his computer until minutes before bedtime. Insufficient sleep had impacted his mood, patience, energy, and creativity.

Cognitive interventions for J included education about how the body regulates sleep and the value of a consistent wake-up time, even on weekends. We explored his competitive mindset and challenged sleep-interfering cognitions, also using imagery. Behaviorally, we developed a plan for winding down away from

screens. J would instead create a “to-do” or “worry” list each evening and set it aside. He was advised never to lie in bed awake, akin to opening a door and inviting one's worries into the room. As an alternative, J prepared leisure readings for when he could not sleep. He benefitted as well from eliminating evening drinking at work functions.

Case 2: R, in contrast, is a 58-year-old woman with obstructive sleep apnea and multiple chronic pain issues. Her chief complaint was worsening sleep-maintenance insomnia since leaving work on disability, but she had a history of poor sleep dating back 30 years. She reported a recent history of depression. She had tried multiple medications for sleep. She recently discontinued lorazepam at night and had started a low dose of doxepin. Her bedtime was determined by pain and the need to lie down, with the result that R was spending extended evening time in bed reading and watching TV. She was spending nearly 11 hours in bed but sleeping just five to nine hours per night. She was compliant with CPAP.

Behaviorally, we discussed ways to rest and treat pain at night while removing non-sleep activities from bed as much as possible. R planned activities for extended nighttime awakenings. Cognitively, we worked to reframe sleep as challenging, given her comorbidities, but to exchange frustration with sleep for a mindset of acceptance. No good can come from being on a vigil for sleep. I validated that loss of work identity and routine can impact sleep. Finally, we strategized about potential obstacles to R's change goals. She opted to remain on doxepin, but reported greatly reduced time in bed and reduced tension about sleep, even on the occasional “bad night.”

The Society for Behavioral Sleep Medicine is one resource for finding a CBT-I therapist. For more information, visit www.behavioralsleep.org.

Positive Airway Pressure for Sleep Apnea in Advanced Heart Failure



Ailia Ali, MD

An 88-year-old male was referred to the Sleep Clinic for evaluation. He reported loud snoring with witnessed apneas, fragmented sleep, morning headaches, and excessive daytime sleepiness. His average sleep duration was less than eight hours each night, and he was taking multiple unintentional naps throughout the day. His Epworth Sleepiness score was 15.

The patient was a former smoker. He reported no history of caffeine intake. His medical history included gastroesophageal reflux disease, open-angle glaucoma, hypertension, hyperlipidemia, atrial fibrillation, coronary artery disease (CAD), CABG, mitral valve replacement, sick sinus syndrome, and pacemaker insertion. His transthoracic echocardiogram was remarkable for mild concentric left ventricular hypertrophy, mild septal hypokinesis, and a left ventricular ejection fraction of 50 to 55 percent.

On physical examination, vital signs were normal and his BMI was 26.62. The exam was remarkable for a Mallampati class III airway. The remainder of the physical examination was unremarkable.

The patient had a home sleep study that showed severe obstructive sleep apnea with an apnea-hypopnea index (AHI) of 46/hour. He could not tolerate PAP therapy and opted for oral appliance therapy. Follow-up home sleep study with the oral appliance showed an AHI of 42/hour. Cheyne-Stokes Respiration (CSR) was present during 88 percent of the time monitored (Figure A).

How should we treat this patient with CSA and CSR?

Central sleep apnea (CSA) with periodic breathing, also known as Cheyne-Stokes Respiration (CSR), is commonly seen in patients with heart failure. It is characterized by episodes of hyperventilation followed by apnea or hypopnea and oxygen desaturation. Central sleep apnea has been shown to be an independent predictor of a poor prognosis and death in patients with heart failure. Intermittent hypoxia and arousal, with an increase in sympathetic tone, has been thought to be the mechanism for worsening cardiac function in CSA. Adaptive servo-ventilation (ASV) is a modality that works by providing servo-controlled inspiratory pressure support, in addition to the expiratory positive airway pressure. It has been the treatment of choice for CSA until recently when the results of the SERVE-HF trial were reported[1].

SERVE-HF was a multicenter randomized controlled trial that investigated the effects of ASV in patients who had heart failure with an ejection fraction of 45 percent or less, and predominantly CSA.



Rachel Givelber, MD

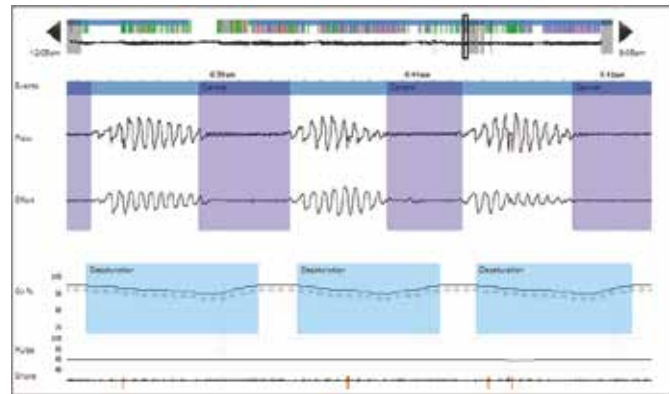


Figure A . Cheyne-Stokes Respiration, characterized by episodes of hyperventilation followed by apneas with the decrease in oxygen saturation.

This study was concluded at the first event of death from any cause, lifesaving cardiovascular intervention (cardiac transplantation, implantation of a ventricular assist device, resuscitation after sudden cardiac arrest, or appropriate lifesaving shock) or unplanned hospitalization for worsening heart failure.

There was no significant effect of ASV at the conclusion of this study. Surprisingly, the all-cause mortality and cardiovascular mortality at 12 months was significantly higher in the ASV group than in the control group. The reason for this unexpected increase in mortality is not currently known despite multiple hypotheses. Based on these findings, we have to reconsider the clinical practice of using ASV in patients with CSA and heart failure with *reduced ejection fraction*.

It is important to emphasize that these results are not applicable to patients with CSA due to heart failure with preserved ejection fraction, opioid use or stroke, and patients with predominantly obstructive sleep apnea regardless of the ejection fraction.

The patient presented in the case above, has heart failure with preserved ejection fraction. Given the patient's symptoms and severity of sleep apnea with predominantly CSR, he underwent positive airway pressure titration with ASV which led to successful abolition of CSR. The patient has since been using the ASV with significant clinical improvement.

Reference:

1. Cowie, M. R., H. Woehrle, et al. (2015). "Adaptive Servo-Ventilation for Central Sleep Apnea in Systolic Heart Failure." *N Engl J Med* 373(12): 1095-1105.

Non-invasive Ventilation for Neuromuscular Disease



David Kristo, MD

The Sleep Disorders Center supports patients with neuromuscular weakness through the Comprehensive Lung Center at Falk Clinic. Patients are typically referred by their neurologist, or other referring physician, following a diagnosis of neuromuscular weakness with associated concerns for respiratory insufficiency or failure and a need for noninvasive inspiratory positive pressure ventilation (NIPPV). We typically see patients with amyotrophic lateralizing sclerosis (Lou Gehrig's disease), muscular dystrophy, and Pompe's disease. Patients are readily seen with advanced neuromuscular weakness, but it is advantageous to see them at earlier stages of illness in an effort to preempt any acute loss of respiratory function that may occur as a result of insufficient home treatment resources.

First Visit

Our patients are initially assessed for spirometry, maximal inspiratory, and maximal expiratory pressures to assess the degree of respiratory muscle impairment. Medicare guidelines dictate that NIPPV cannot be initiated before the forced vital capacity (FVC) is below 50 percent or the maximal inspiratory pressure is below 60 cm H₂O. The initial evaluation includes pre- and post-bronchodilator assessment to identify all reversible causes for improving lung function. Pulmonary function results are reviewed with the patient and their candidacy for NIPPV is determined.

Additionally, cough assist and suction devices are also discussed. Patients are counseled about percutaneous enterogastrostomy (PEG), or feeding tubes, and their wishes concerning the need for mechanical ventilation. Overall efforts to minimize any chance of aspiration or respiratory failure are essential in patient care.

If the patient qualifies for NIPPV, we exclusively employ average volume assured pressure support (AVAPS) in an effort to maximally support those with neuromuscular weakness non-invasively. A "sip and puff feature" provides a convenient mouthpiece for daytime and as needed AVAPS use without requiring a traditional face mask and head gear. If the patient has short-term daytime needs for NIPPV, a brief rest on ventilator support can easily be achieved with "sip and puff." Additionally, if a patient qualifies for AVAPS support, we simultaneously order a cough assist and suction device for home delivery. Technical support is provided by sleep laboratory staff and the individual vendor to educate and aid our patients during all stages of NIPPV support. Whenever possible, family members and caregivers are included in the discussions about home care and ventilator support to minimize acute respiratory events.

AVAPS Initiation

Those that qualify are assessed for the correct AVAPS settings, ideally in a supervised overnight lab assessment in our sleep lab, or while awake if daytime assessment of AVAPS is needed. Patients who are in need of an urgent start of NIPPV are prescribed AVAPS by using an industry weight-based formula. AVAPS vendors are instructed to adjust settings to comfort and expedite AVAPS initiation. Patients are then provided an AVAPS unit and instructed to return quarterly with a data download, or computer memory card, to assess effects of AVAPS use at night. The data card is very helpful in identifying patients who are not readily accommodating to AVAPS and is often communicated directly from the vendor to physician for interventions as needed.

Repeat Visits

Spirometry is assessed through repeat visits and the results are tallied in an effort to track any changes in respiratory muscle weakness with neuromuscular disease.

It may be determined that a patient needs AVAPS or they may be alternatively assessed for any slowing in the progression of the disease or improvement in pulmonary function following AVAPS initiation. Our research in NIPPV includes a data download protocol that is designed to better identify complications with NIPPV compliance and to strategize efforts to improve AVAPS compliance and benefits. Patients are frequently reminded that timing, in regard to the placement of PEG feeding tubes, in relation to decrements in lung function and anesthesia risks is complex. Overall, patients are encouraged to receive PEG tubes when relatively stable in order to better tolerate the procedure and avoid respiratory complications that may occur later, after disease progression has severely compromised respiratory function. Patients are followed throughout the course of their illness. If needed, palliative care is incorporated to better suit their needs. Our goal is to provide for all patient needs within the home with high regard for maintaining dignity and autonomy.

The Sleep Disorders Center at the Comprehensive Lung Center is fully dedicated to the care and support of patients with neuromuscular weakness and strongly encourages all those at any stage in neuromuscular weakness to present for evaluation and support.

Awakening A.W.A.K.E.!



Matthew Anastasi, BS, RST

Sleep apnea presents a unique challenge to the physicians who manage it. Adherence to PAP, the gold standard treatment for sleep apnea, is poor. Research has shown that five to 50 percent of sleep apnea patients recommended for PAP either reject this treatment option or discontinue within the first week, and 12 to 25 percent of remaining patients can be expected to have discontinued PAP by three years [1]. A Cochrane Review of interventions to improve PAP adherence suggests that psychological and/or educational interventions may improve PAP usage, whereas mechanical interventions including Bi-PAP, self-titration, and humidification offer little benefit for increasing adherence [2].

Support groups may be a cost-free option for educating and assisting sleep apnea patients. In 1990, A.W.A.K.E. (Alert, Well, And Keeping Energetic) groups were formed by the American Sleep Apnea Association (ASAA) with the goal of enhancing the lives of those with sleep apnea by providing educational resources, patient-to-patient support, and real-life solutions. More than 100 A.W.A.K.E. groups are currently active across the U.S., with five groups in Pennsylvania. Pittsburgh was the first location to create an A.W.A.K.E. group; however, it is no longer active, leaving the closest active group more than two hours away.

With a growing population of sleep apnea patients in the Pittsburgh area, there is a need for the revitalization of the Pittsburgh A.W.A.K.E. group. Recently, an article in the Pennsylvania Sleep Society newsletter advocated for the creation of additional A.W.A.K.E. groups in Pennsylvania. The successful creation of a local A.W.A.K.E. group will require a city-wide effort from physicians and nurses, sleep technicians, sleep centers, home



Faith S. Luyster, PhD

healthcare companies, sleep researchers, patients, and families. The following are essential to reestablishing the Pittsburgh A.W.A.K.E. group:

1. Coordinators or leaders to organize, publicize, and facilitate the meetings.
2. Speakers to present on relevant topics.
3. Individuals and organizations to promote and support (refreshments, meeting space) the group once established.

Please consider joining the effort to “reawake” the Pittsburgh A.W.A.K.E. group so we can provide our sleep apnea patients the needed support to be diagnosed and treated successfully. If interested in supporting this effort, please contact Faith Luyster, PhD, at luysterfs@upmc.edu.

References:

1. Engleman HM, Wild MR. Improving CPAP use by patients with the sleep apnoea/hypopnoea syndrome (SAHS). *Sleep medicine reviews* 2003;7:81-99.
2. Haniffa M, Lasserson TJ, Smith I. Interventions to improve compliance with continuous positive airway pressure for obstructive sleep apnoea. *The Cochrane database of systematic reviews* 2004:CD003531.

New Frontiers in the Treatment of Sleep Apnea *(continued from page 3)*

After the Implant

Following implantation, there will be a follow-up visit with the ENT and a one-month visit to the sleep medicine physician to activate the device. Reassessment of the device's settings may occur one to two times before a sleep study is performed to verify and/or adjusting the settings. It is estimated that 80 percent of patients will need only one study after the device is implanted. Patients have a routine follow-up every three to four months for a year and then every six to 12 months.

Other Stimulator Devices

In addition to Inspire, other companies are now going through the process of development and clinical trials toward an FDA application. There are likely to be more options in the future.

References:

1. Jordan, A.S., D.G. McSharry, and A. Malhotra, Adult obstructive sleep apnoea. *Lancet*, 2014. 383(9918): p. 736-47.
2. Kezirian, E.J., et al., Electrical stimulation of the hypoglossal nerve in the treatment of obstructive sleep apnea. *Sleep Med Rev*, 2010. 14(5): p. 299-305.

Upper Airway Stimulation

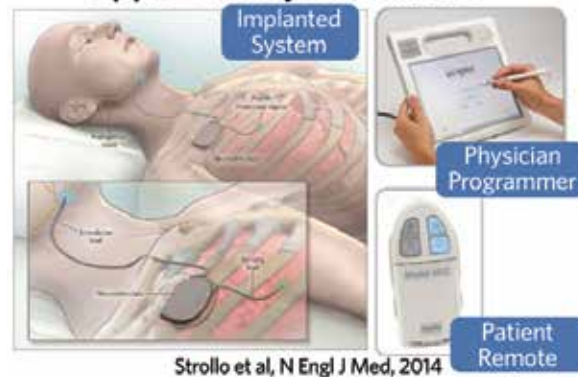


Figure 1

3. Strollo, P.J., Jr., et al., Upper-airway stimulation for obstructive sleep apnea. *N Engl J Med*, 2014. 370(2): p. 139-49.

Weight Loss in the Management of Sleep Apnea *(continued from page 5)*

In addition to diet, physical activity is a key component to an effective weight-loss plan. Although exercise is not as effective as diet in producing weight loss, regular aerobic exercise helps prevent weight regain. In addition, exercise has cardiovascular benefits beyond effects on weight. Similarly, OSA severity improves with exercise independent of any weight loss effects. The most effective behavioral weight-loss programs combine diet and exercise with behavior change counseling. Randomized trials have demonstrated that the optimal plan should include in-person counseling sessions with a trained interventionalist meeting individually or as a group. The frequency of meetings should be weekly at first. Weight loss will be maximized if meetings continue (even though less frequently) beyond six months.

Pharmacologic Therapy

Medications are increasingly being utilized to facilitate weight loss and recent data suggest they may help with OSA as well. Randomized trials have found both phentermine-topiramate (Qsymia) and liraglutide (Saxenda) improve but do not cure OSA. Among moderate to severe OSA patients, phentermine-topiramate and liraglutide produced AHI reductions of 15 and six events/hr respectively beyond that obtained from diet and exercise alone. Clinicians can also facilitate weight loss by reviewing medications and replacing commonly used sleep medications such as quetiapine, doxepin, mirtazapine, and gabapentin which promote weight gain with alternatives such as topiramate, zolpidem, or pramipexole.

Surgical Therapy

Bariatric surgery is growing in popularity as procedural complication rates have diminished and it has become clear that long term weight loss outcomes are substantially larger than with behavioral

or medical therapy. In addition, longitudinal studies demonstrate bariatric surgery reduces the incidence of diabetes, heart disease, cancer, and all-cause mortality. It is clear that obese OSA patients want to learn more about bariatric surgery. A recent study found that 35 percent of OSA patients presenting to sleep clinics would like to meet with a bariatric surgeon to learn more about surgical options. The most common bariatric operations currently are the gastric band, gastric sleeve, and gastric bypass procedures (see Figure). The gastric band is the least invasive and typically results in loss of 40 percent of excess weight at two years, while the gastric bypass is the most extensive procedure, typically resulting in loss of 60 to 70 percent of excess weight but also associated with more side effects. The gastric sleeve is the newest of the three procedures and provides an intermediate option with about 50 percent excess weight loss. Bariatric surgery can produce significant reductions in OSA severity, although some residual disease commonly persists. In one meta-analysis, the mean AHI fell from 55 to 16 events/hr with surgery. Two randomized trials have compared gastric banding to an aggressive dietary weight-loss program. Both studies found no statistically significant improvements; however, they were limited by small sample sizes. Further research is needed to better understand the potential role of the gastric sleeve and gastric bypass in OSA management.

Conclusions

Chronic disease management involves not just acute care but also treatment of underlying risk factors and prevention of common comorbidities. Just as we provide evidence-based treatments for smoking cessation to our patients with chronic obstructive pulmonary disease, we need to provide proven weight loss therapies as part of comprehensive sleep apnea care.

Department News

Announcing Our Newest Physician: Sanjay R. Patel, MD, MS



We are pleased to announce the appointment of Sanjay R. Patel, MD, MS, as director of the Sleep Medicine and Cardiovascular Outcomes Center and medical director of the UPMC Sleep Laboratory.

Dr. Patel received his medical degree from Harvard Medical School before moving on to the Hospital of the University of Pennsylvania where he completed an internship in internal medicine. Following a fellowship in pulmonary and critical care at Massachusetts General Hospital, he continued as a sleep fellow at Brigham and Women's Hospital and is recognized as the only person to win the American Academy of Sleep Medicine Young Investigator award twice.

In 2005, he obtained his master's degree in epidemiology from Harvard School of Public Health. In 2008, Dr. Patel received the James B. Skatrud Young Investigator Award from the American Thoracic Society.

Dr. Patel has developed a national reputation as an expert in the epidemiology of sleep and sleep disorders on the relationship between sleep and obesity. He brings a wealth of experience from his previous roles as associate professor of medicine at Harvard Medical School and the Division of Sleep and Circadian Disorders at Brigham and Women's Hospital.

Sally Wenzel, MD, honored with Breathing for Life Award

Sally E. Wenzel, MD, director of the University of Pittsburgh Asthma Institute at UPMC, was recently honored with the Breathing for Life Award at the annual American Thoracic Society Foundation Research Program Benefit. The award is the highest honor given to an ATS member for philanthropy.



"It's a great honor to be the first woman recognized by the foundation for the professional society (ATS) that has provided me so much during my career," Dr. Wenzel said. "I look forward to continuing my longtime commitment to the society as part of the global pulmonary community."

An internationally-recognized expert in severe asthma patient care and research, Dr. Wenzel gives back to the pulmonary community in many ways. Not only is she a sought-after clinician for treatment of severe asthma, she is also well recognized for her advocacy for women in science and mentoring of young scientists.

Dr. Wenzel is a global leader in the investigation of asthma phenotypes and in understanding the complexities of severe asthma. Her research has been dedicated to the investigation of asthma in humans, as opposed to mouse models. Dr. Wenzel has published more than 250 peer reviewed publications and has been funded by the National Institutes of Health for 30 years.

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Patrick J. Strollo, Jr., MD



Charles W. Atwood, Jr., MD



Rachel J. Givelber, MD



Paula M. Jernigan, MD



David A. Kristo, MD



Phillip E. Lamberty, MD



Deborah A. Gillman, PhD

UPMC Comprehensive Lung Center, Falk (in Oakland):

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*Professor of Medicine
Director, Sleep Medicine and Cardiovascular
Outcomes Center
Medical Director, UPMC Sleep Laboratory*

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