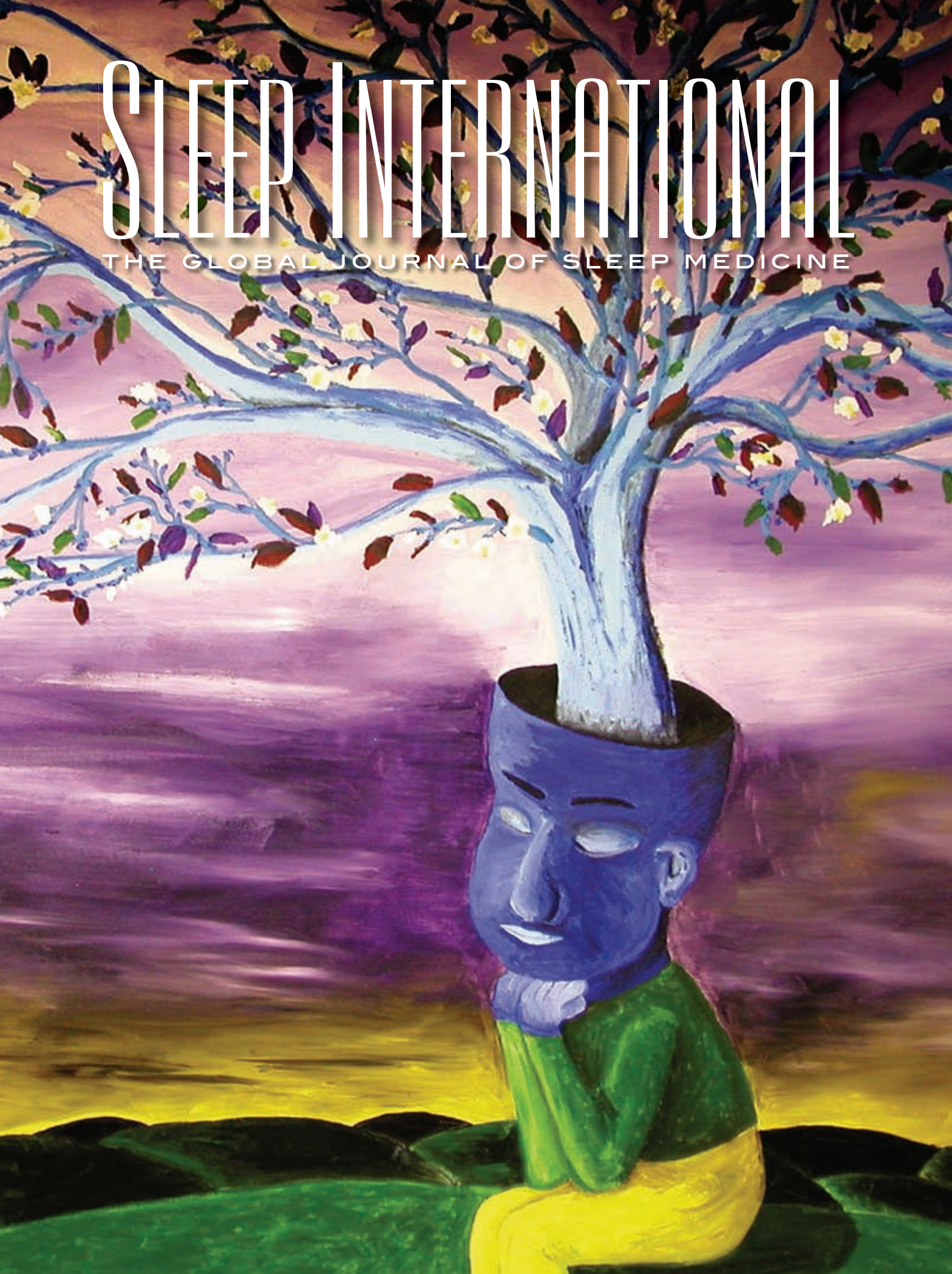


SLEEP INTERNATIONAL

THE GLOBAL JOURNAL OF SLEEP MEDICINE



EDITORIAL

Welcome to Respiratory Therapy's special section on sleep. According to the Institute of Medicine of the National Academies, it is estimated that 50 to 70 million Americans suffer from chronic sleep disorders, and hundreds of billions of dollars are spent on direct medical costs related to these disorders. The cumulative effects of sleep loss and sleep disorders represent an under-recognized public health problem and have been associated with a wide range of health consequences. As the public's awareness of sleep deprivation and sleep disorders increases, demand for treatment will multiply and require improved access to sleep diagnostic services and therapies. According to the Academies, "Investment in sleep-related research and training programs has grown dramatically over the past 10 years; however, it has not kept up with the rapid pace of scientific advances in sleep medicine."

Not to belabor the obvious, but one must breathe, perchance, to sleep. As such, respiratory therapists and related caregivers have a vested interest in keeping abreast of developments in sleep research and therapy as it relates to their practice.

According to the Institute of Medicine, "by its very nature, research and clinical practice in sleep is at the interface of many medical and scientific disciplines." Respiratory Therapy's Sleep Section aims to strengthen the interdisciplinary aspect of sleep medicine vis-a-vis respiratory care. Sleep International will address sleep-related issues and their significance for the daily practice of respiratory care, and will highlight original clinical articles about sleep research, education and training. We will also provide a forum for companies looking to introduce new products and preview the latest developments in approaches to sleep-related care.

In its aforementioned report, the Academies concluded that "although scientific opportunities and clinical activities in the field are expanding, the available human resources and infrastructural capacity to improve patient care and expand scientific research are insufficient... Increased awareness among healthcare professionals is required." Respiratory Therapy's sleep section, with the input of all our readers and those providing sleep therapies, and resources, will help fill this need by presenting the latest information about new and existing diagnostic, clinical, educational, and therapeutic resources and technologies related to sleep and respiratory therapy. Your comments and submissions are always welcome.



Les Plesko, Editor

Andrew DesRosiers, MS, RRT, RPSGT
Caritas Christi Health Care System
Program Director, Neuro/Ortho/ICU
Caritas Centers for Sleep Medicine
Methuen, MA

Marion Boyd Gillespie, MD, ENT Surgeon
Medical University of South Carolina
Charleston, SC

Roop Kaw, MD
Assistant Professor of Medicine
Section of Hospital and Perioperative Medicine
Cleveland Clinic Foundation
Cleveland, OH

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□ October-November 2006

GO TO SLEEP

A recent abstract in *Acta Med Okayama* (2006 Jun;60(3):191-5) discussed how continuous positive airway pressure ameliorated severe pulmonary hypertension associated with obstructive sleep apnea. Researchers Ogawa, Emori, Sumita, Watanabe, Fujio, Miyahi and Ohe, from the Department of Cardiovascular Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan, presented the following: A 52-year-old obese woman was admitted to our institution for evaluation of dyspnea and pulmonary hypertension (PH). Polysomnography revealed severe obstructive sleep apnea (OSA) with an apnea hypopnea index of 99.8. Treatment with nocturnal continuous positive airway pressure (CPAP) resulted in correction of daytime hypoxemia, hypercapnia, and near-normalization of pulmonary artery pressure. To our knowledge, this is the most severe case of OSA-associated PH (approximately 70 mmHg) reported to date, and it was successfully treated with nocturnal CPAP. This case demonstrates that OSA should be considered and polysomnography performed in all patients with PH, irrespective of severity, and that nocturnal CPAP has therapeutic effects on both OSA and daytime PH.

HAVE A HEART

Sleep Medicine 2006, June 30, presented the abstract, Obstructive sleep apnea-hypopnea and neurocognitive functioning in the Sleep Heart Health Study. The authors, Quan, Wright, Baldwin, Kaemingk, Goodwin, Kuo, Kaszniak, Boland, Caccappolo and Bootzin, are with the Department of Medicine, Arizona Respiratory, Sleep Disorders and General Clinical Research Centers, University of Arizona College of Medicine, Tucson. Obstructive sleep apnea-hypopnea (OSAH) is associated with sleep fragmentation and nocturnal hypoxemia. In clinical samples, patients with OSAH frequently are found to have deficits in neuropsychological function. However, the nature and severity of these abnormalities in non-clinical populations is less well defined. In Quan et al's study, one hundred and forty-one participants from the Tucson, AZ and New York, NY field centers of the Sleep Heart Health Study completed a battery of neuropsychological tests for 9-40 months (mean=24 months, SD=7 months) after an unattended home polysomnogram. Sixty-seven participants had OSAH (AHI>10) and 74 did not have OSAH (control (CTL), apnea-hypopnea index (AHI)<5). In addition to the individual tests, composite variables representing attention, executive function, MotorSpeed and processing speed were constructed from the neuropsychological test battery. There were no significant differences in any individual neuropsychological test or composite variable between the OSAH and CTL groups. However, when time spent with O(2) saturations less than 85% was dichotomized into those participants in the top quartile of the distribution and those in the lower three quartiles, motor speed was significantly impaired in those who were more

hypoxemic. In addition, poorer motor speed (model adjusted $R(2)=0.242$, $P<0.001$) and processing speed performance (model adjusted $R(2)=0.122$, $P<0.001$) were associated with more severe oxygen desaturation even after controlling for degree of daytime sleepiness, age, gender and educational level. The study concluded that mild to moderate OSAH has little impact on the selected measures of attention, executive function, motor speed and processing speed. However, hypoxemia adversely affects both motor and processing speed. These results suggest that in middle-aged to elderly adults the neuropsychological effects of clinically unrecognized mild to moderate OSAH are neither global nor large.

SAY AAAH

The International Journal of Otorhinolaryngology, July 17, 2006, reported on the effect of adenotonsillectomy on children suffering from obstructive sleep apnea syndrome (OSAS): The Negev perspective. The study's authors, Leiberman, Stiller-Timor, Tarasiuk and Tal are with the Department of Otolaryngology, Head & Neck Surgery, Soroka University Medical Center, Beer-Sheva 84101, Israel. The objective was to present the Negev perspective in recent decades as to the effect of adenotonsillectomy regarding clinical and polysomnographic features, cardiopulmonary morbidity, growth, neurocognitive function, health care services utilization, and enuresis by reviewing current related literature. All relevant published data by the Soroka University Medical Center and related community medical services were reviewed and compared to Medline linked literature regarding aspects of childhood obstructive sleep apnea published through November 2005. Published data support a significant effect of adenotonsillectomy on the associated co morbidities: adenotonsillectomy resulted in the reduction of pulmonary hypertension, improved growth as a result of an increase in growth hormone secretion, improvement of neurocognitive function to the normal range, reduction in nocturnal enuresis, as well as reducing general morbidities, as reflected by the reduction in health care utilization. However, there are still uncertainties relating to major aspects. There is no specific definition for OSAS grading, or for generating a guideline for surgical treatment and refinement of the indications of T&A. The authors concluded that adenotonsillectomy has a beneficial effect on children with OSAS, however, further research is required before recommendations for the treatment of OSAS in children can be formulated.

BIG HEARTED

Patients with obstructive sleep apnea have enlarged and thickened hearts that pump less effectively, but the heart abnormalities improve with use of a device that helps patients breathe better during sleep, according to a new study in the April 4, 2006, issue of the *Journal of the American College of Cardiology*. "Not only are the shape and size of the heart affected, the right side of the heart was dilated and the heart muscle on the left side was thicker in patients with obstructive sleep apnea, but the pump function was also reduced. The changes were directly related to the severity of the problem. Treating the problem brought significant improvements in the affected parameters, as well as in symptoms, in a relatively short period of time of six months," said Bharati Shivalkar, MD, PhD from the University Hospital Antwerp in Antwerp, Belgium. The study included 43 patients (32 men and 11 women) with obstructive sleep apnea. Sleep lab studies measured the severity and frequency of complete or partial interruptions of airflow.

The shape and pumping action of the participants' hearts was measured using ultrasound. The researchers also examined 40 similar control subjects who were healthy and did not report any symptoms that would indicate sleep apnea. Compared to the control subjects, the hearts of the sleep apnea patients were significantly enlarged on the right side and had thickened walls between the pumping chambers. The hearts of sleep apnea patients also pumped less blood per beat, and the velocity of wall motion was slower for both the left and right compared to the control subjects. The sleep apnea patients also had higher blood pressure and faster heart rates than the control subjects. The severity of the heart abnormalities was correlated with the severity of obstructive sleep apnea. The sleep apnea patients were then given continuous positive airway pressure (CPAP) devices to treat their breathing problems. An air pump that is connected by a tube to a face mask helped keep the patient's airways open during the night. The 25 sleep apnea patients who were evaluated after six months of CPAP treatment were not only sleeping better, and were more alert during the day, but there were significant improvements in the size, shape and pumping action of their hearts. According to Dr Shivalkar, "After treatment with CPAP, the antihypertensive medications could usually be substantially reduced... There should be a multidisciplinary approach to this problem, with a close association with cardiovascular physicians and sleep doctors in diagnosing and treating this problem." Nota bene, 18 of the 43 sleep apnea patients in this study did not complete the six months of CPAP treatment. Shivalkar said that although CPAP is a simple and noninvasive solution, a number of patients do not tolerate having the face mask on during the entire sleeping period at night.

KEEP IT DOWN

The publication *Nippon Rinsho* reported that the prevalence of gastroesophageal reflux disease (GERD) is increasing in Japan. Symptoms of GERD negatively affect quality of life and sleep. According to the report: there are several reasons for sleep disorder with GERD. Nocturnal GERD symptoms sometimes directly lead to loss of sleep. Sleep apnea syndrome and GERD are sometimes concomitant. Both share similar risk factors such as obesity and cause sleep disorder. When atypical symptoms of GERD are not diagnosed, patients are severely anxious about their physical condition. Then they feel stressful and sometimes get into a secondary depressive state, including sleep disorder. The authors of the article recommend, "we had better take care about patients' psychosocial factors and treat symptoms of GERD and sleep disorder together with holistic approach."

HOLD YOUR TONGUE

A University of Wisconsin research team has theorized that either the caudal raphe or the hypoglossal nucleus, or both together, play roles in sleep apnea. The researchers have turned their attention to these two areas of the brain because of the roles they play in controlling the tongue. Diminished tongue control is a major cause of obstructive sleep apnea, a serious condition which strikes men much more frequently than premenopausal women, said lead researcher Jessica R. Barker. She presented her findings in a paper presentation, "Sexual dimorphism in serotonergic input to the hypoglossal nucleus."

Previous research has found evidence that estrogen plays a role in respiratory control and may provide protection against hypoxia. Other research shows that post-menopausal women on hormone replacement therapy suffer less from sleep apnea than

post-menopausal women not on hormones, further strengthening the theory that estrogen plays a protective role. The unique theory could explain why men and post-menopausal women not on hormone therapy are much more likely to suffer from the condition than pre-menopausal women, Barker said. Estrogen is associated with serotonin, a neurotransmitter that helps control the tongue. The purpose of Barker's study is to determine if the difference in estrogen levels between men and women plays a role in serotonin expression in the caudal raphe and hypoglossal nucleus — leading to a difference in tongue control. The researchers hypothesized that females would have greater numbers of serotonin-activated neurons running between the hypoglossal nucleus and the tongue. They first looked at the caudal raphe because that is where serotonin — which plays a role in preventing the tongue from relaxing and blocking the airway — is manufactured.

Researchers used six young male rats and six females. They injected the rats' tongues under anesthesia with a tracer, Bartha pseudorabies virus (PRV). They examined the pathway of the virus into the brain and were able to "see" the path of the PRV and the serotonin-activated neurons projecting from the caudal raphe to the tongue. They looked at the number and distribution of neurons activated by serotonin in the caudal raphe, expecting there would be differences between males and females. Instead, they found male and female rats have the same number of serotonin producing neurons in this area of the brain. The study suggests the caudal raphe does not play a role, at least by itself, in obstructive sleep apnea. Researchers will next look at the neurons producing serotonin that run from the hypoglossal nucleus to the tongue. Also in the future: a look at the interactions among the caudal raphe, the hypoglossal nucleus and the tongue. The key may be in how these structures interact, she said. If this line of research eventually pans out, it may be possible to adjust hormone levels to relieve the sleep apnea and avoid the resultant health problems, Barker said. Patients with severe sleep-disordered breathing are two to four times more likely to experience complex, abnormal heart rhythms while sleeping than individuals without the problem, according to the Sleep Heart Health Study (SHHS). These findings appear in the April issue of the *American Journal of Respiratory and Critical Care Medicine*, published by the American Thoracic Society.

KEEP THE BEAT

Researchers at the University Hospitals of Cleveland at Case Western Reserve University in Ohio compared the prevalence of arrhythmias in 228 patients with sleep-disordered breathing and 338 with no sleep disorder. The individuals in both groups participated in the SHHS, a multi-center longitudinal study designed to determine the cardiovascular consequences of sleep-disordered breathing (SDB). In this study, participants with SDB had a respiratory disturbance index that averaged about 44 pauses per hour of sleep. The control subjects experienced only 2.8 interruptions per hour. No sex or race differences were observed between groups, but the SDB group was modestly older and had a higher body mass index than the control patients. The investigation included a detailed assessment of the existing cardiovascular risk factors and/or disease in all participants.

Researchers concluded that the study had potentially important clinical implications because it suggests an increased vulnerability to nocturnal cardiac arrhythmias in individuals with SDB and provides an explanation for the observed increase in sudden nocturnal death recently reported with sleep apnea.

PUMP IT UP

Patients with nighttime obstructive sleep apnea who receive air through a mask while they sleep can significantly reduce their blood pressure, according to a study to be presented at the American Thoracic Society International Conference. More than half of those with sleep apnea also have high blood pressure, and their blood pressure does not fall during sleep as it does in most people. Researchers studied 46 patients with moderate to severe sleep apnea. They were randomly assigned to receive either CPAP treatment, fake CPAP or supplemental nighttime oxygen through a face mask. All patients were hooked up to a 24-hour ambulatory blood pressure monitor. After two weeks, patients who received the real CPAP treatment had significant reductions in blood pressure during the day and night. Nighttime oxygen therapy did not affect blood pressure. The researchers noted that there has been some controversy over how sleep apnea causes elevated blood pressure. Doctors don't know if it is due to drops in oxygen levels or arousals from sleep. This study indicated that correcting drops in oxygen levels alone may not be enough to reduce blood pressure.

ON THE OTHER HAND

New research showed that short-term CPAP may have little affect on blood pressure in patients with OSAS and hypertension. Researchers from Spain compared blood pressure readings of 68 patients with OSAS and hypertension who were receiving treatment with antihypertensive medication. Patients were randomly assigned to receive therapeutic or subtherapeutic CPAP for four weeks. Antihypertensive treatment was not changed for either group. Baseline scores for sleep apnea, as well as comorbidities, blood pressure, and CPAP compliance, were similar between the groups. Results showed that there were no significant changes in systolic, diastolic, daytime, or nighttime blood pressure for either group. Researchers conclude that short-term CPAP has little impact on patients with OSAS and well-controlled hypertension. The study appeared in *Chest*.

PREPARE THE ICE CREAM

SDB and removal of tonsils is the subject of the paper, "Improved Behavior and Sleep After Adenotonsillectomy in Children with Sleep Disordered Breathing," by Julie L. Wei and her colleagues, recently presented at the American Society of Pediatric Otolaryngology meeting in Chicago. Within a pediatric otolaryngology practice, 117 consecutive children clinically diagnosed with sleep disordered breathing and scheduled for surgical removal of the adenoids and tonsils were enrolled as the research subjects. A convenience sample of caregivers of patients, age two to 17 undergoing adenotonsillectomy for SDB were eligible and asked to participate. Patients were excluded if the primary reason for adenotonsillectomy was recurrent infections. Data were collected on the day of the surgery and at six months following the surgery date. The results offered evidence that before surgery, the mean PSQ score for the 117 patients was 0.56, the scale is between 0 and 1, with scores approaching 1 representing the most severe disturbance in sleep. 112/117 (95.73 percent) had a PSQ score of >0.33 , which suggests high risk for SDB, and 5/117 (4.27 percent) had a PSQ score of <0.33 . At six-months after adenotonsillectomy, the mean PSQ score for the 71 patients who completed the study was 0.12[0.14]. Of these 71 patients, 7(9.86 percent) still had a PSQ score of >0.33 , while 64 (90.14 percent) had a PSQ score of <0.33 . For the CPRS-RS scores, a reduction was noted in aged and sexed norm T-scores for all four behavior categories

(oppositional, cognitive problems/inattention, hyperactivity, and ADHD index), close to one standard deviation from their preoperative score which is clinically significant. Also, the researchers found that the higher the baseline T-score, the greater the reduction in T-score after surgery. Correlations were found between behavior and sleep both before and after adenotonsillectomy. The study supported associations between adenotonsillectomy to alleviate upper airway obstruction and changes in both sleep and behavior, as evidenced by results in the PSQ and CPRS-RS surveys. At six months after adenotonsillectomy, patients experience improvement in both sleep and various behavior categories as measured by these instruments.

DON'T GET CHOKED UP

Deirdre Stewart, PhD, presented information to a crowded audience on a new patient-friendly device for detecting gastric reflux in the airway and its application in sleep medicine at the Association of Polysomnographic Technologists meeting, a segment of the SLEEP 2006 Associated Professional Sleep Societies (APSS). Stewart is Vice President of Clinical Affairs at Restech, the designer and manufacturer of the Dx-pH Measurement System(tm), which detects aerosolized upper-airway reflux, known as laryngopharyngeal reflux (LPR). (See our article on page 82 of this issue). "The miniature 1.5mm diameter catheter," Stewart explained, "is placed trans-nasally and is positioned behind the soft palate." This positioning has been deemed revolutionary in that patients are now exempt from larger catheters stretching uncomfortably to their lower esophagus. The Restech "plug & play" Dx-Sleep Adapter accessory allows sleep medicine professionals to track patients' airway pH events in real-time on their existing monitoring equipment. The system can be easily set up in a sleep clinic or physician's office. Since the device transfers data using wireless telemetry, there are no extra leads from the patient.

PRODUCTS

INNOVATION IS A TRADITION

Ambulatory Monitoring, Inc (AMI) of Ardsley, NY, is a pioneer and innovator in the design, development, and distribution of ambulatory instrumentation. AMI's products include the Inductotrace inductive plethysmograph, the instrument of choice for respiratory monitoring in sleep and pulmonary laboratories throughout the world; the PVT-192 Psychomotor Vigilance Task Monitor, the gold standard in reaction time measurement; and the Motionlogger Actigraph, the most sensitive and accurate actigraph on the market providing an approximate 88% correlation to polysomnography. Under the direction of its President Thomas Kazlauskys, AMI aims to educate the medical community and public at large with regard to the risks of poor sleep, whether caused by sleep apnea, insomnia, or conditions such as PTSD. By participating in numerous medical conventions annually AMI informs healthcare professionals and clinicians about the value of its products in sleep and sleep-related fields, and AMI encourages people to visit ambulatory-monitoring.com to learn more. Our pleasant staff of technicians, headed by Office Manager Joan Pellegrini, is available to answer clinical or technical questions regarding AMI equipment as well as to assist customers who may require product support. In the future AMI will strive to continue to live

up to its motto "Our Tradition is Innovation" by introducing new state-of-the art designs into the marketplace.

PAY ATTENTION

Within the past three years, about 4.4 million children have been diagnosed with ADHD, which now accounts for 30 to 50% of all child referrals for mental health services. Disorders such as sleep apnea and bi-polar disease can mimic ADHD symptoms, leading to possible misdiagnosis and unnecessary pharmaceutical intervention. In the past, ADHD diagnosis relied on subjective behavioral questionnaires, but lately, objective diagnostic criteria have been added to clinical diagnosis. Companies such as AMI have responded by offering actigraphic data collection to aid in diagnosis and track the effects of intervention strategies. By means of small, noninvasive wristwatch-like accelerometer devices, the long-term continuous sleep/wake patterns of children can be monitored and recorded. AMI's Motionlogger Actigraph, which provides an 88% correlation to polysomnography for sleep/wake determination, is worn by the child for three full days and nights, and recorded data is subsequently analyzed by a physician in the field, with careful attention to bi-polar disease and sleep apnea. AMI also designed a new Motionlogger called the BuzzBee, which aims to help children become their own control in reducing excess motor activity. For information contact AMI, ambulatory-monitoring.com.

TAKING THE PRIZE

Respironics' Sleep Diagnostic Group received this year's Frost & Sullivan Marketing Leadership Award in the sleep diagnostic device market, based on the company's continued market

leadership, strategic advancement, technology innovation, and ability to adapt. According to Frost & Sullivan, "[Respironics] continually demonstrates solutions for monitoring market changes and for implementing superior market strategies." The winner was selected by tracking revenue and market share within the industry and comparing rankings. Respironics' Sleep and Home Respiratory Group integrates technology in diagnostics, therapy and monitoring with strategic problems to help healthcare providers and sleep centers care for patients efficiently and cost-effectively. Contact respironics.com.

SNOOZE ANYWHERE

One of the newest products from Respironics is the REMstar M Series Sleep Systems. Smaller than a laptop, the new model packs stylish good looks in a compact, ergonomic design that goes from carry-on (if you could actually carry it on) to nightstand use with ease. Respironics' M Series devices weigh 2.2 pounds. At 7.5-inches long by 5 inches wide, the unit looks more like a high performance clock radio than a medical device. The REMstar is equipped with a universal power supply or adapters for international use. C-FLEX waveform technology tracks each breath and adjusts the amount of pressure delivered during exhalation for enhanced comfort. Advanced models, like REMstar Pro, automatically compensate for different altitudes. Optional accessories range from integrated heated humidifiers and pollen filters to convenient travel and battery packs. These modern sleep inventions also exhibit high IQs. Smart technology such as the Respironics Encore Pro SmartCard accessory module can capture critical data such as mask leak activity, allowing users and health care providers to monitor use and respond to treatment needs without a trip to the doctor's office. Available in three models, entry-level to premium, Respironics sleep therapy systems are designed for use in the home or favorite vacation spot. For information, visit mseries.respironics.com or call (800) 345-6443.

SLEEP CHIEF

Respironics named David White, MD as Chief Medical Officer of the company. White served as director of the Clinical Sleep Disorders Program at Brigham and Women's Hospital and as Professor of Sleep Medicine at Harvard Medical School. He has also served on the faculty at Penn State University and the University of Colorado Health Science Center. Dr White is board-certified in sleep disorders medicine, internal medicine, pulmonary disease and critical care medicine. He obtained his medical school training at Emory University and is past-president of the American Academy of Sleep Medicine, Chair of the Advisory Board of the National Center on Sleep Disorders Research, and Chair of the Task Force to write the latest NIH research plan in the area of sleep and sleep disorders. He is also currently the Editor-in-Chief of the Journal, Sleep.

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The Use of Polyvinylidene Fluoride (PVDF) Film Airflow Sensors: An Alternative to the Nasal Cannula for Measuring Respiratory Events

Suanne Goodrich, Maroun Tawk, William C. Orr

INTRODUCTION

The esophageal balloon is considered the ideal method for detecting respiratory effort in identifying sleep related breathing disorders (SRBD). The esophageal balloon is an invasive technique, so most sleep labs use thermistors, thermocouples, or an air pressure transducer (APT) with a nasal cannula. APTs coupled with cannulas perform better than thermistors¹ and correspond very well with esophageal balloons. However, a new device called a PVDF sensor is now available. It has a faster response time and greater sensitivity than conventional thermistors and thermocouples, and may present an attractive alternative to the cannula in sleep studies.

AIM

Fourteen individuals who had either symptoms of sleep apnea, or a previous diagnosis of sleep apnea, were included in the study. These individuals visited our laboratory on two occasions on the same day. In the late afternoon, the participants arrived and an esophageal balloon catheter was inserted into the mid esophagus. The participants were allowed to return home and instructed to eat a soft meal for dinner (eg, yogurt, soup). Later that evening, the participants returned for one night of complete polysomnography with the addition of the PVDF sensor and the APT with cannula. In the morning, the esophageal balloon was removed and the patient's participation was complete.

Respiratory events were analyzed in NREM and REM sleep separately. First, two raters judged respiratory events, including both apneas and hypopneas. There were two criteria for an event to be considered a "true event": there had to be at least a 3% oxygen desaturation, and at least one of the three measures (PVDF sensor, cannula, or balloon) had to reflect that an event had occurred. For both the PVDF sensor and nasal cannula, a

decrease in airflow of at least 30% was considered to be a hypopnea, whereas a flat or nearly flat airflow was considered to be an apnea. In the balloon, a pattern of at least three increasingly negative pressure points was required to be considered a respiratory event (either hypopnea or apnea).

Based on these criteria, 200 respiratory events were selected for analysis during NREM sleep, and another 50 events were analyzed during REM sleep. For each event, it was noted as to whether each of the three measures (PVDF sensor, nasal cannula, or esophageal balloon) did or did not detect the event. Both raters had to agree on all ratings or the event was thrown out.

RESULTS

There were 14 participants in the study (eight men, six women), ranging in age from 31 to 62 (mean age = 47). All participants were Caucasian. One participant could not complete the study due to equipment problems. Three of the participants did not have sleep apnea. There were difficulties with the esophageal balloon in several studies, also. Specifically, in one patient the balloon did not work at all, and in other patients the signal came and went periodically during the night. This can apparently be caused by changes in body position which may flatten out the signal. One participant had a small number of central apneas, but no obstructive apneas. This participant was a slender woman who did not have any significant oxygen desaturations associated with her central apneas. Since there was a requirement that all events have at least a 3% desaturation, her data were not included in the main analysis, but will be discussed separately. Due to the above issues, four studies were selected for analysis as the signals in these studies were good for all three measures of PVDF, cannula, and balloon (see Figures 1-4 for examples of respiratory events).

Out of the 200 NREM respiratory events, the PVDF sensor detected 90% (see Table 1). In comparison, the nasal cannula detected 86% and the esophageal balloon detected 82%.

During REM sleep, detection rates were 94%, 100%, and 68%, for

Authors Goodrich and Orr are with the Lynn Institute for Healthcare Research, Oklahoma City, Oklahoma; Tawk is with the University of Oklahoma Health Sciences Center. Research supported by Dymedix Corporation, Minneapolis, MN. These data reflect subsequent analyses of a larger data set than was presented in the abstract. For more information, contact Dr Suanne Goodrich (sgoodrich@lhsi.net).



Figure 1: Hypopneas detected by the cannula, PVDF sensor, and esophageal balloon, respectively

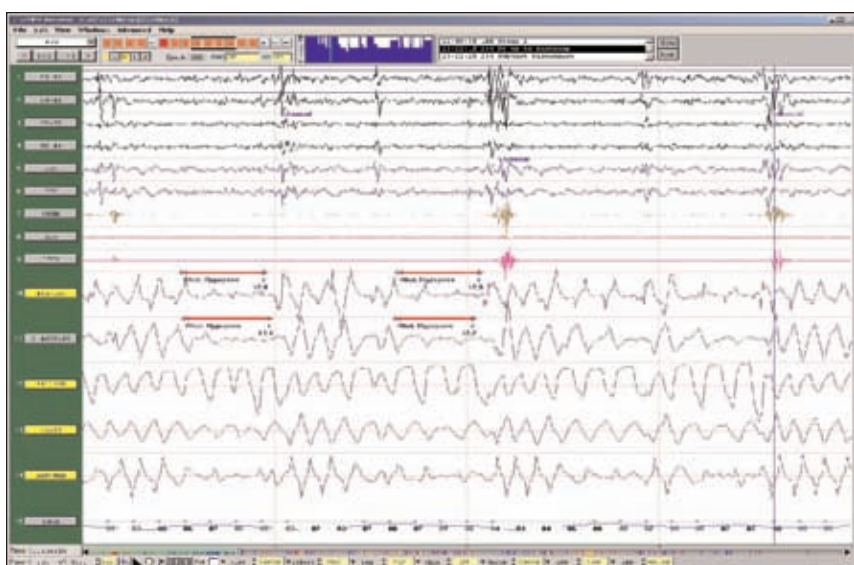


Figure 2: Hypopneas that were not detected by the esophageal balloon

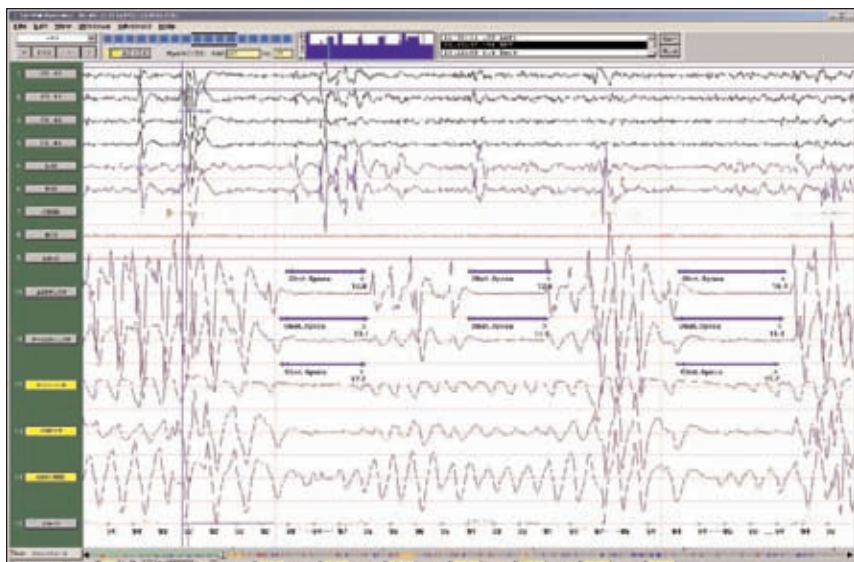


Figure 3: Apneas during REM sleep

the PVDF, cannula, and balloon, respectively. These statistics suggest that the PVDF sensor is quite good at detecting respiratory events in comparison to the cannula. The esophageal balloon, however, performed more poorly than expected.

Since the esophageal balloon is considered to be the gold standard for respiratory effort, the subset of events that were detected by the balloon was examined as well (see Table 2). Of these respiratory events that were confirmed by the balloon, the PVDF sensor agreed with 90%, while the nasal cannula agreed with 85%.

One participant had a small number of central apneas but no obstructive apneas or hypopneas. Due to the small number of respiratory events and the lack of a 3% oxygen desaturation to accompany the event, this participant's data was not included in the analyses above.

However, it can be noted that in this participant, the PVDF sensor, cannula, and balloon were all seen to become simultaneously flat during apneas.

CONCLUSIONS

The PVDF film sensor appears to be an accurate device for detecting respiratory events, as compared to the APT with cannula. Thus, it represents another alternative for measuring airflow. As compared to the esophageal balloon, the PVDF sensor was superior. In fact, in our analyses we did not find the balloon to be particularly accurate. This result was unexpected because the balloon has been referred to as the "gold standard" for detecting respiratory effort. In this study, however, we found the balloon to be somewhat unreliable. In several participants there were difficulties with the signal waxing and waning, and in one participant it did not work at all. Also, it has been well established that pleural pressure dynamics are notably different in REM vs. NREM sleep and our esophageal pressure measurements clearly reflect this. Yet the literature does not clearly establish how airway occlusion during REM should be identified with an esophageal balloon. Thus, judging balloon events during REM proved difficult. For that reason, NREM events were examined separately from REM events.

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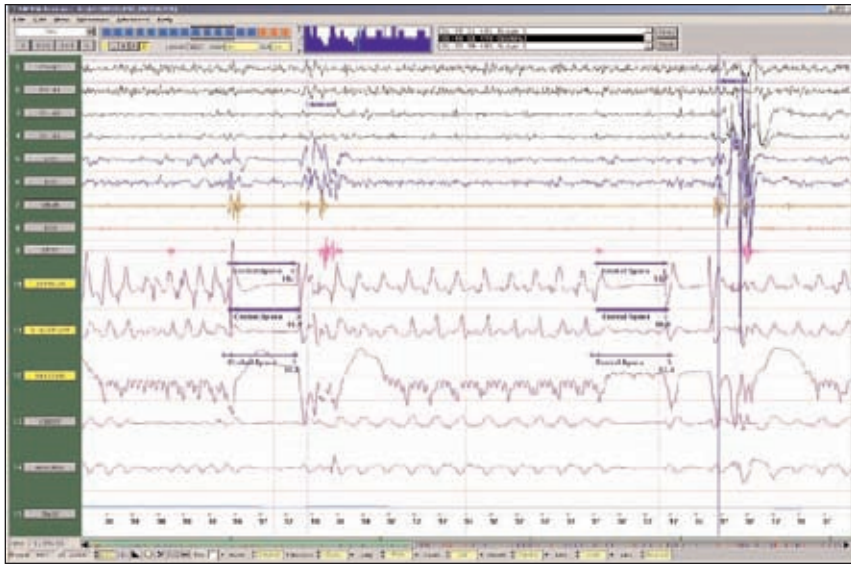


Figure 4: Central apneas during REM sleep

Table 1: Number of NREM Respiratory Events Detected for Each of Four Participants

	#1	#2	#3	#4
PVDF Sensor	45/50 (90%)	43/50 (86%)	45/50 (90%)	47/50 (94%)
Nasal Cannula	44/50 (88%)	31/50 (62%)	47/50 (94%)	50/50 (100%)
Esophageal Balloon	43/50 (86%)	35/50 (70%)	39/50 (78%)	46/50 (92%)

Table 2: Number of NREM Balloon-Confirmed Respiratory Events Detected for Each of Four Participants

	#1	#2	#3	#4	Overall
PVDF Sensor	40/43 (93%)	27/35 (77%)	34/39 (87%)	45/46 (98%)	146/163 (90%)
Nasal Cannula	38/43 (88%)	18/35 (51%)	36/39 (92%)	46/46 (100%)	138/163 (85%)

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¹ Todd Eiken, RPSGT- Sleep Review™ Sept. 2005
² Richard Berry, MD- CHEST Sept. 2005
³ William Orr, PhD- APSS 2003

Seeing the Trees *and* the Forest

Using Epoch-Based Trends with EEG Frequency Data to Assist in Sleep Staging

Pamela Minkley RRT, RPSGT, CPFT

INTRODUCTION

The traditional approach to sleep staging requires the technician to focus on a small segment of the sleep study. With any complicating signals in the sleep staging channels, such as alpha-intrusion, it is often more difficult, and more time consuming, to properly stage the study record. A number of commercial software packages include tools to assist the scorer with their task by providing global epoch based displays of the EEG frequency spectrum for the entire study. This article presents the advantages of using these tools to both improve the quality of scoring and improve the speed of scoring. In reality this provides a fly-over view of the forest of EEG signals while allowing the technician to zoom into the individual epoch trees (so to speak).

USEFUL TREND DATA

Most commercial PSG system software packages include epoch



Figure 1 Typical Epoch based Trend Analysis View

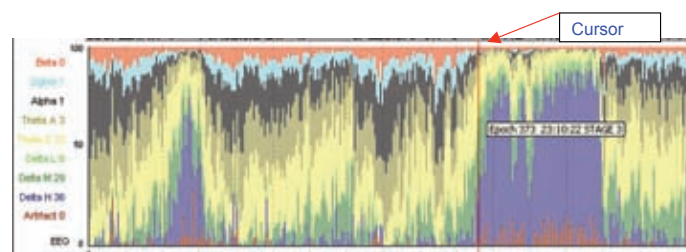
The author is the manager of Ingham Regional Center for Sleep & Alertness in Lansing, Michigan. She is a past-president of the APT and has served as chair of the examination development, curriculum and professional development committees. She is also a frequent speaker for educational seminars throughout the country.

based trend graphs for oxygen saturation levels, heart rate, body position and marked events. Many also provide epoch-based trends of EEG frequencies, automatically detected sleep spindles, K-Complexes, Delta waves, Rapid Eye Movements and chin-EMG amplitude.

EEG FREQUENCY ANALYSIS

A number of approaches are used for evaluation of EEG data in a sleep study including Frequency Power based FFT (Fast-Fourier Transformations), CSA (Compressed Spectral Array) and PAA (Period Amplitude Analysis).

Below is a representation of a system which uses Period Amplitude Analysis, each vertical band (colored line) represents one 30-second epoch. In this example the numbers on the left represent the percentage of each frequency band for the epoch under the cursor.



Description of Color-coded PAA frequency bands

EEG Spectrum Frequency Band Definitions	<p>The percentage of each epoch occupied by the frequencies in each band. The frequencies are calculated using the time between all minimum and maximum peaks.</p> <p>Beta – Red. > 16.0 Hz. Sigma – Light Blue. 12.0 to 16.0 Hz. Alpha – Black. 8.0 to 12.0 Hz. Theta A – Brown. 5.0 to 8.0 Hz. Theta D – Yellow. 2.0 to 5.0 Hz. Delta L – Light Green. 0.5 to 2.0 Hz. < 40 mV. Delta M – Dark Green. 0.5 to 2.0 Hz. 40 to 75 mV. Delta H – Dark Blue. 0.5 to 2.0 Hz. > 75 mV. Important for scoring Stage 3 (20 to 50%) and Stage 4 (>50%). Artifact – Dark Red. < 0.5 Hz, pen-blocking, flat lines, very sharp</p>
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SEEING THE FOREST

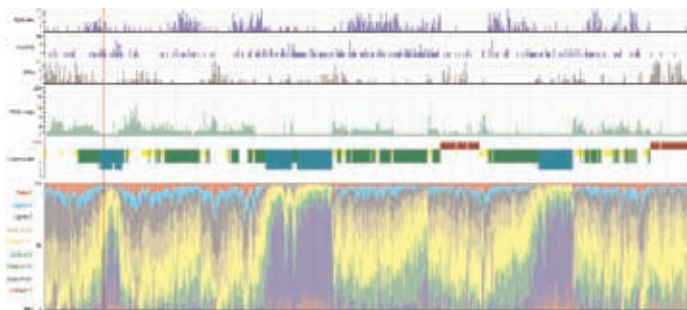
The main advantage of displaying and using tools like the EEG frequency analysis is that the epoch-by-epoch page display is placed in context of the surrounding data and the scoring technician can anticipate the changes that will occur in upcoming epochs. It also assists in decisions regarding transitional epochs (e.g., when is there enough Delta activity to move from Stage 2 to Stage 3 sleep).

Sometimes a “spot” or lesion on a chest x-ray is best seen from across the room, sometimes it is better seen up close with a magnifying glass and other “spots” are best appreciated from somewhere in between. This is not unlike our ability to view our data in 30 second to 30 minute epochs in the standard polysomnographic view or the summary graph, and the ability to sleep stage score using the EEG frequency graph as an assistant. You will have to decide to invest time in working with this tool provided by the manufacturer in order to gain the efficiency benefits from its use. Familiarity with the patterns presented by different conditions, disorders and artifacts will improve your ability to quickly score more complex studies and to identify staging transitions more accurately.

The following figures demonstrate patterns seen in the lab. Some are displayed with a “split window” showing the trend data and the epoch corresponding to the cursor location.

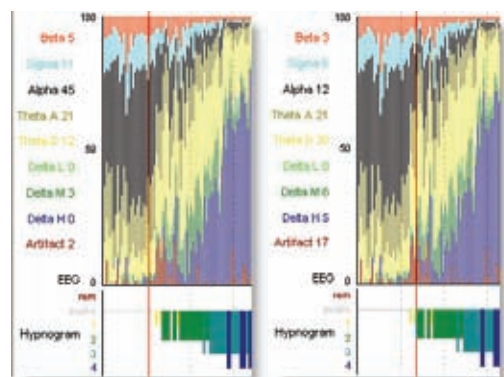
NORMAL SLEEP PATTERN

Normal sleep distribution with alpha frequency diminishing with onset of sleep, high amplitude Delta waves increasing with transition from Stage 2 to Stage 3/4 and low amplitude mixed frequency with corresponding rapid eye movements in REM.



Focus on Sleep Onset

On the two images below note the percentage of Alpha frequency EEG that occurs during wake (eyes closed) and the first few epochs of sleep. Seeing the Alpha percentage change from 30-50% to less than 10% assists in locating the onset of sleep. More useful is the forest view change in the spectrum that provides the context or in other words the multiple epoch transition into sleep.

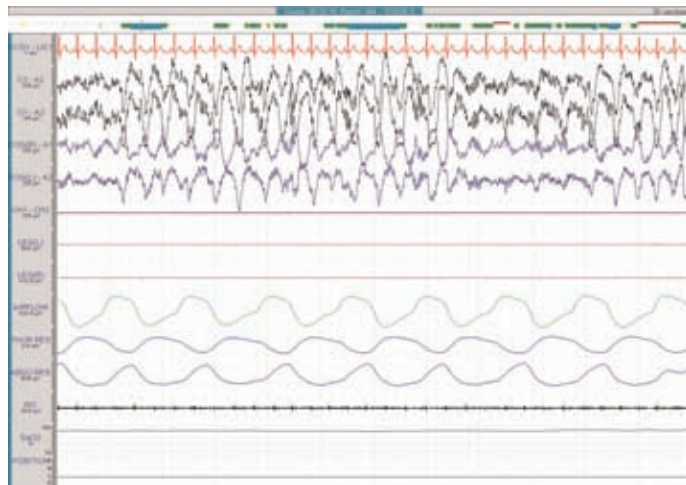


Alpha-Delta Sleep (aka Alpha Intrusion)

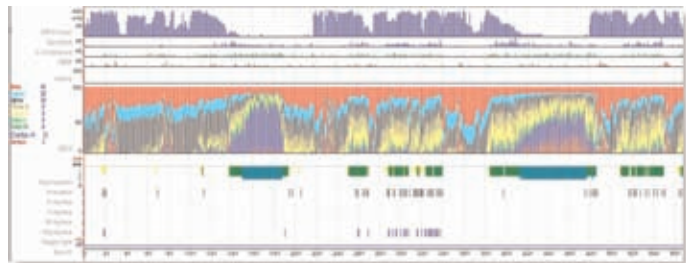
Alpha intrusion or Alpha-Delta sleep patterns tend to be more difficult and time consuming to accurately stage. These samples, from a patient with persistent alpha activity, were used to demonstrate the efficiency of using the frequency analysis display in my lab.

An experienced technologist scored this “ugly sleep” alpha-intruded recording. It took the technologist a long time; she did not use the frequency graph while staging the record. Because it took so long and was so miserable to score, the technician challenged another staff member who is an outspoken proponent of using the frequency graph to score it using only the frequency graph. Their reliability was better than the reliability between two technologists’ scoring with the raw data only AND given the “ugly sleep”, the scorer using the EEG frequency graph scored much faster. Note: It would not be appropriate to score using the EEG frequency exclusively. But using the frequency analysis as an aid to epoch waveform scoring we can quickly confirm the epoch scoring and stage the study appropriately.

Typical Epoch of study with alpha intrusion

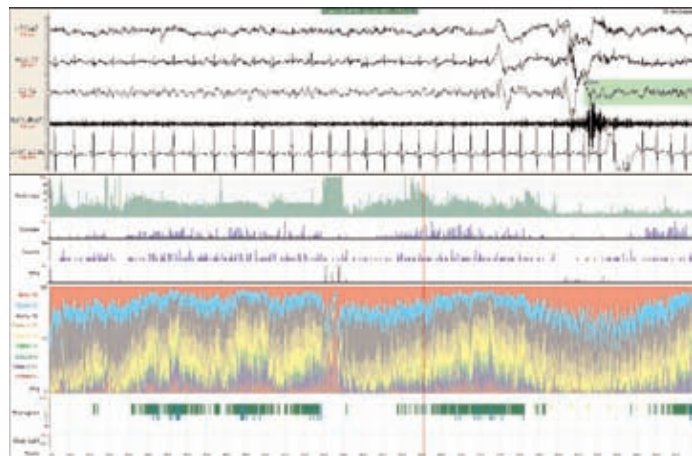


“Forest View” of the same study

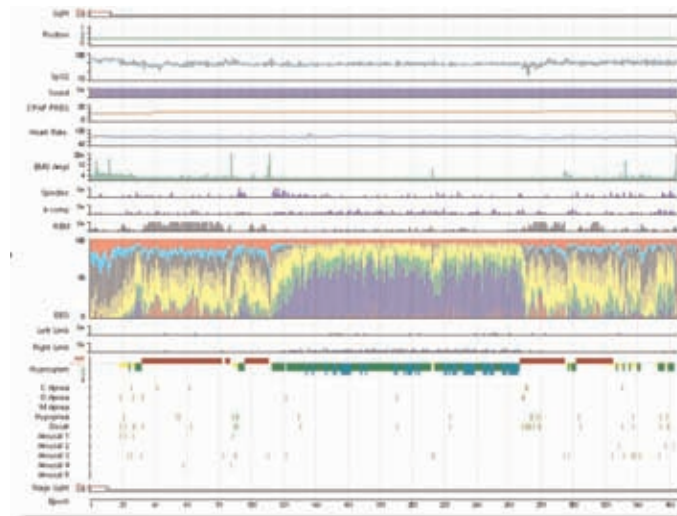


Note the increased alpha frequency throughout the night represented by the black color in the graph. Note also how there is very little black in the areas of delta sleep because although the alpha is very intrusive to our eyes looking at the waveforms, it is a very small percentage of the frequencies in the epoch. Therefore, the delta sleep is observed and scored much easier using the frequency graph.

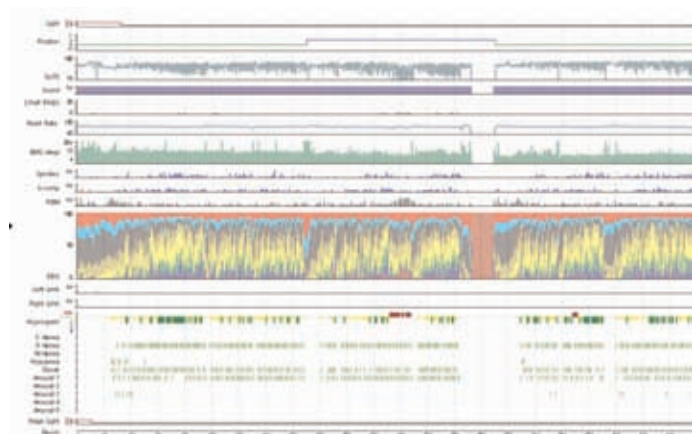
Pattern from subject with high AHI and interrupted sleep with view of expanded epoch within the context of the surrounding epochs



CPAP Titration – increased delta – less fragmentation of sleep in the same 60 year old female.



Sleep pattern with reduced Delta Sleep and sleep fragmentation due to obstructive sleep apnea in a 60 year old female.



Note the near absence of the dark blue color which represents delta sleep over 75 uV amplitude.

Using the entire forest (summary graph) is a good final check after sleep stage and event scoring is complete. Look at it; ask yourself if it makes sense. An example would be that you notice the patient has respiratory events all night but they are significantly worse in REM. You also notice that there is a section on the summary graph where there is a grouping of respiratory events but no REM scored. You review the frequency graph then go to the raw data to see if a REM period was missed, if respiratory events were over-scored in that section or if the scoring is correct. You can do the same thing with position related apneas to verify whether a position change may have been missed in an area of increased respiratory events where the position is graphed as right or left side but in other areas of the summary events are minimal on the sides but increased in the supine position.

CONCLUSION

The use of EEG Frequency Spectra and other signal analysis tools can enhance the efficiency of technologists scoring a sleep study by providing an overall view of the study, helping to clarify transitions in sleep state and confirming patterns

consistent with the 6 stages of sleep (wake, 1,2,3,4 and REM). It also helps in deciphering challenging studies such as Alpha-Delta sleep and fragmented sleep patterns. However, a commitment to learn a new pattern recognition process for the stages and events is needed to garner the benefits in improved scoring efficiency. The use of these “Forest View” tools can also serve as consistency and quality control checks.

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— **Dr. Bruce Corser, Sleep Management Institute**

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Treating Complex Patients with VPAP Adapt SV

Bruce Corser, MD

At the Sleep Management Institute, we have extensive experience with patients who continue to have high apnea-hypopnea index (AHI) with central events, despite our best efforts to titrate with continuous positive airway pressure (CPAP) and bilevel devices. Recently we have begun to titrate our most challenging patients with ResMed's VPAP Adapt SV, the new servo-ventilator recently cleared for the treatment of central sleep apnea. This device effectively normalizes breathing abnormalities in cases where CPAP and bilevel have failed. It is the first FDA-cleared device to treat complex forms of sleep apnea.

There is a subset of patients with a predominance of central components, and VPAP Adapt SV is very effective for this group. Typically, the people we feel benefit most are those with central sleep apnea (CSA) or a combination of obstructive sleep apnea (OSA) and CSA.

VPAP Adapt SV is designed to treat CSA in all its forms, including mixed apnea, periodic breathing and complex sleep apnea (CompSA). Mixed sleep apnea is fairly common and consists of both central and obstructive components. On the other hand, CompSA is a form of sleep apnea where central apneas persist or emerge while attempting to treat obstructive events with a CPAP device.

CompSA is characterized by the following:

- The persistence or emergence of central apneas or hypopneas upon exposure to CPAP when obstructive events have disappeared.
- CompSA patients have predominately obstructive or mixed apneas during the diagnostic sleep study occurring at least 5 times per hour.
- With use of CPAP, they show a pattern of central apneas and hypopneas that meets the Centers for Medicare Services (CMS) definition of CSA described below.

CSA is a form of sleep-disordered breathing (SDB) caused by a lack of signal from the central nervous system. A diagnosis CSA requires all of the following:

- An apnea index > 5
- Central apneas/hypopneas > 50% of the total apneas/hypopneas
- Central apneas or hypopneas occurring at least 5 times per hour
- Symptoms of either excessive sleepiness or disrupted sleep

Patients with CompSA cannot be adequately treated with CPAP. The clinical consequences are residual symptoms (fatigue, sleepiness, depressed mood) and intolerance to therapy.¹

About 50% of people with congestive heart failure (CHF) have nocturnal breathing abnormalities. These patients in particular have central & obstructive components. We had targeted CHF patients for titration with VPAP and often tried to titrate them on CPAP or bilevel ventilation. If they weren't responding, we brought them back for initiation on VPAP Adapt SV, which has been incredibly effective at reducing breathing abnormalities associated with SDB.

CASE STUDIES

The following case studies demonstrate patients' positive response to the VPAP Adapt SV.

H.F.

HISTORY OF PRESENT ILLNESS: H.F. is a 74-year-old man with a history of mild snoring and witnessed nocturnal apnea. He had marked excessive daytime sleepiness.

PAST MEDICAL HISTORY: Remarkable for low back pain and joint pain. He had a remote history of hepatitis.

SOCIAL HISTORY: He did not smoke cigarettes nor consume alcohol.

REVIEW OF SYSTEMS: Positive for hearing impairment and hypercholesterolemia.

The author is with the Sleep Management Institute.

PHYSICAL EXAMINATION: He is 6 feet 2 inches tall and weighs 195 pounds. His neck is 17 inches. The pertinent examination findings are notable for a low-lying soft palate with a resultant narrow posterior pharyngeal outlet.

An overnight polysomnogram performed in June 2006 revealed an AHI of 55 episodes per hour, with a central apnea index of 38 episodes per hour. The oxygen desaturation did not drop below 90%. Nasal bilevel titration was undertaken, but he continued to have CSA and remained markedly sleepy throughout the day. He returned for a trial of VPAP Adapt SV. VPAP Adapt SV with an EEP of 6 cm of water effectively reduced his AHI to one episode per hour. He had no snoring. His oxygen saturation remained about 90% throughout the night. His sleep quality was markedly improved. He stated that his excessive daytime sleepiness had resolved, and he tolerated the VPAP Adapt SV well. He used the device at least six hours every night and is committed to long-term use.

J. F.

HISTORY OF PRESENT ILLNESS: Jay F. is a 65-year-old man with a history of severe excessive daytime sleepiness. He snored loudly and episodically awakened with a gasping sensation. He had had intermittent atrial fibrillation and was referred by his cardiologist for the purpose of ruling out obstructive sleep apnea. His wife stated that he had prolonged apneic episodes while sleeping.

SOCIAL HISTORY: He did not smoke cigarettes but consumed approximately 10 alcoholic beverages per week.

PAST MEDICAL HISTORY: Positive for hypertension, osteoarthritis, and erectile dysfunction.

PHYSICAL EXAMINATION: He is 5 foot 11 inches and weighed 260 pounds. His blood pressure was 141/74 with a heart rate of 42. His neck is 20-1/2 inches. The pertinent examination findings included a narrow posterior pharyngeal outlet due to a low-lying soft palate. The cardiac examination showed a regular rhythm with no murmurs.

An overnight polysomnogram originally performed on August 15, 2004 demonstrated severe obstructive sleep apnea with an AHI of 55 episodes per hour and an oxygen desaturation as low as 79% during the night.

He was reluctant to pursue treatment with nasal CPAP. However, his sleepiness worsened to the extent that he had an episode of falling asleep while driving. This resulted in minor damage to his automobile. He returned for a trial of nasal VPAP Adapt SV on May 11, 2006. Titration with VPAP Adapt SV with the EEP set at 9 cm of water pressure effectively reduced his nocturnal breathing abnormalities to an AHI of 3.8 and eliminated his snoring. Furthermore, his oxygen saturation remained at about 90% through most of the night. He returned on July 13, 2006, stating that his excessive sleepiness is completely resolved. He felt awake and alert through the day. He tolerated treatment well and was delighted at his progress. He is admitted to the long-term use of the VPAP Adapt SV.

TREATING COMPLEX PATIENTS

The VPAP Adapt SV uses adaptive servo-ventilation to adjust to a patient's ventilatory needs on a breath-by-breath basis, to normalize breathing and completely suppress central sleep

apnea, mixed apnea, compSA and periodic breathing. The adaptive servo-ventilation algorithm automatically calculates a target ventilation (90% of the patient's recent average ventilation) and adjusts the pressure support to achieve it. In our recent experience with VPAP Adapt SV, we've had a very favorable response: patients like it and compliance is much better. We feel this device is an important addition to the repertoire of treatment tools available for the treatment of SDB. We're in business to take care of patients, so when patients come back struggling because of an inability to comply, that makes our lives difficult. When we have a therapy that helps patients comply, our lives are easier because our patients' lives are improved – that is very gratifying.

REFERENCE

- 1 Gilmartin GS, Daly RW, Thomas RJ. Recognition and management of complex sleep-disordered breathing. *Curr Opin Pulm Med* 2005;11:485-493.

Alternatives to CPAP in the Treatment of the Obstructive Sleep Apnea Syndrome

Konrad E. Bloch

SUMMARY

The obstructive sleep apnea syndrome (OSAS) results in excessive daytime sleepiness, impaired quality of life, and is associated with an increased risk of traffic accidents and cardiovascular disease. Nasal continuous positive airway pressure (CPAP), the standard treatment for OSAS provides immediate relief of symptoms and has only minor side effects. Nevertheless, an alternative treatment is needed if CPAP is not feasible for medical or psychological reasons. Removable oral appliances that advance the mandible when fitted to the teeth during sleep also improve nocturnal breathing disturbances, symptoms, quality of life, vigilance and blood pressure in OSAS patients. Their long-term effectiveness and side effects require further study. In morbidly obese patients suffering from OSAS bariatric surgery should be considered as a treatment that reduces obesity and at the same time improves OSAS. In selected patients including those with adeno-tonsillar hypertrophy, and cranio-facial malformations various surgical techniques that enlarge the upper airway may be a treatment option for OSAS.

INTRODUCTION

The obstructive sleep apnea syndrome (OSAS) is characterised by intermittent collapse of the upper airway during sleep resulting in hypopnoea, apnea, repetitive oxygen desaturation and sleep disruption.¹ Daytime consequences include excessive sleepiness, impaired cognitive performance, disturbed mood, and reduced quality of life.^{2,3} The increased risk of traffic accidents due to sleepiness is an obvious individual and public health concern.⁴ Furthermore, OSAS is an independent risk factor for hypertension,⁵ myocardial infarction⁶ and stroke.⁷ Epidemiological studies have suggested that 2 to 4% of the adult population suffer from OSAS⁸ but the prevalence may have increased with the epidemic of obesity.⁹ The diagnosis of OSAS

relies on typical symptoms including excessive daytime sleepiness and lack of concentration, habitual snoring, nocturnal choking, and witnessed apnea.¹⁰ Male gender, obesity, a large neck size¹¹ and certain cranio-facial characteristics further enhance the suspicion of OSAS.¹² The diagnosis is confirmed by a sleep study.

General treatment recommendations for patients with OSAS include sufficient and regular sleep hours (sleep hygiene), avoidance of smoking and alcohol consumption, and diet to reduce weight in obese patients. However, a persistent weight reduction is difficult to achieve and maintain and behavioral modification is only minimally effective.¹³ The current standard treatment for OSAS consists in nocturnal application of continuous positive airway pressure (CPAP) via a nasal mask.¹⁴ Several randomized trials have established the effectiveness of CPAP in patients with various degrees of OSAS severity.^{15, 16} Excessive sleepiness and other symptoms, quality of life, objective vigilance, driving simulator performance and other cognitive tasks are significantly improved by CPAP over baseline when compared to treatment with sham (placebo) CPAP or placebo medication.^{17, 18} The effect size achieved with CPAP for several clinical outcomes is large or moderate, and is largest in the most severe cases of OSAS.^{17, 19, 20} In addition to providing symptomatic improvement, there is evidence that CPAP reduces fatal and nonfatal cardiovascular events in moderate to severe OSAS,⁶ and modifies cardiovascular risk since it reduces blood pressure²¹ and circulating markers of cardiovascular risk such as cholesterol,²² C-reactive protein and interleukin-6.²³ Side effects of CPAP therapy are generally mild and reversible.¹⁶

Current guidelines suggest treatment of symptomatic OSAS patients with more than 5 to 30 apnea/hypopnoea per hour of sleep²⁴ depending on severity of symptoms and comorbidity. Generally, severely symptomatic patients with frequent apnea/hypopnoea (>30 events/hour) readily improve with CPAP therapy. Conversely, in asymptomatic patients even with a markedly elevated apnea/hypopnoea index (>30 events/h), there was no measurable benefit of CPAP therapy.²⁵ In practice, a trial

The author is with the Pulmonary Division, Department of Internal Medicine, University Hospital of Zürich, Switzerland. The author thanks Karsten Fritsch, MD, for careful review of the manuscript. Reprinted from *Swiss Med Weekly*, 2006 Apr 29;136(17-18):261-7, © 2006 Swiss Med Weekly.

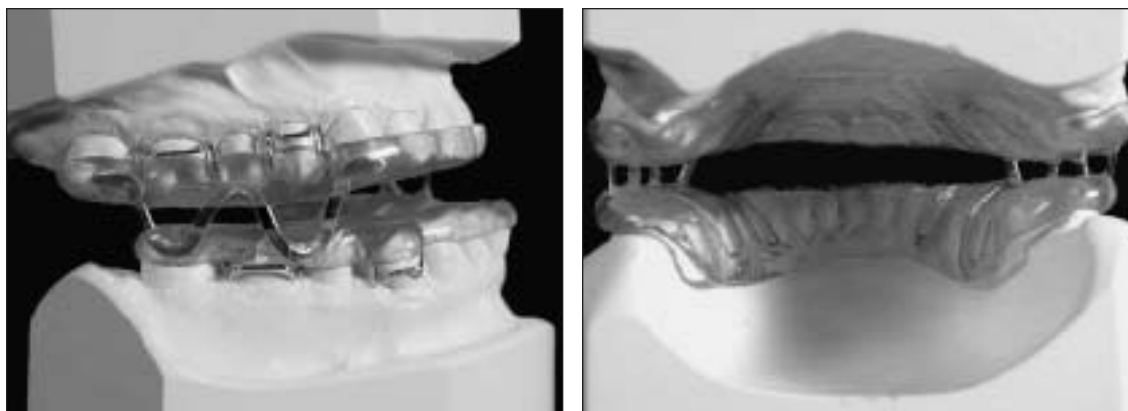


Figure 1 Monobloc mandibular advancement device as used at the University Hospital of Zurich. The custom-fitted appliance is snapped onto the dental arches for overnight treatment and held in place by metallic clasps. The protrusive forces acting onto the mandible are distributed over a large area of the alveolar process (modified from [33]).

of CPAP therapy over a limited time period may help to identify patients who might benefit from long-term therapy.²⁶ In a recent study we even found that a favorable response to a 2-week CPAP trial was more accurate in predicting OSAS patients successfully treated over >4 months than polysomnography, the conventional diagnostic “gold-standard” for OSAS.²⁷ In summary, OSAS therapy is performed to improve symptoms and quality of life, and to prevent sleepiness-related accidents. Treatment of asymptomatic patients solely for correction of a laboratory abnormality, ie, for reducing an increased apnea/hypopnea index, or for reduction of the cardiovascular risk or prevention of potential disease progression is not established.

Despite its effectiveness CPAP therapy is used less than prescribed.^{28,29} This may relate to the inconvenience of the therapy, psychological factors, discomfort due to pressure, skin irritation and other factors. In patients not able or not willing to perform CPAP therapy other treatment options have to be considered. The purpose of this article is to review the current alternatives to CPAP in the treatment of OSAS.

MANDIBULAR ADVANCEMENT DEVICES

Removable oral appliances are attractive treatment options for patients with OSAS not able or not willing to tolerate the standard CPAP therapy.³⁰⁻³³ This is because oral appliances are easy to apply, handy, not dependent on electricity and thus particularly suitable for use during travel. Furthermore, sleeping with an oral appliance is perceived as less socially disturbing than wearing a CPAP mask. The most effective oral appliances used today are designed to hold the mandible in an anterior position (protrusion). The so-called mandibular advancement devices (MAD) are fitted onto the lower and upper dental arches before going to sleep and removed in the morning (Figure 1). They increase the upper airway lumen during sleep by protrusion of the mandible and tongue,³⁴ increase the upper airway muscle tone,³⁵ and reduce the passive pharyngeal wall compliance.³⁶

Several randomised studies, some of them using a sham appliance without mandibular advancement or medication as a placebo control, have demonstrated that MAD are effective in controlling symptoms of OSAS, nocturnal breathing disturbances, oxygenation and sleep disturbances, and even

blood pressure.³⁷⁻³⁹ In one study, patients with mild sleep apnea (less than 30 apnea/hypopnoea per hour of sleep) were randomised to a sequence of 3 periods of 3 months with either a MAD, nasal CPAP or a placebo tablet.⁴⁰ At the end of each 3-month period, the outcomes were compared. CPAP and MAD significantly improved symptoms to a similar degree. CPAP was more effective in reducing sleep disordered breathing, while a reduction in blood pressure was achieved with MAD only. Patients rated CPAP to be more effective than MAD but the latter to be more convenient. This may have contributed to a higher treatment adherence with MAD.⁴⁰ In another study, MAD were shown to be effective in even severe cases of OSAS. The higher the number of apnea/hypopnea, the greater was their reduction by MAD.⁴¹ Side effects of MAD are relatively common but only rarely require discontinuation of therapy. They include tooth pain, hypersalivation, mucosal dryness, and occlusal changes.⁴² Potential limitations of MAD are the requirement of a minimal number of stable teeth (ie, at least 8 teeth in the upper and lower jaw), absence of gingival disease and temporomandibular joint pain. Individual adaptation by an experienced orthodontist in cooperation with a pulmonary physician is crucial for achieving an optimal therapeutic result. It may take several weeks and require repeated consultations to complete the construction of MAD and one or several follow-up sleep studies to establish the desired effect. Whether MAD remains effective over several years, and whether there are relevant and potentially irreversible side effects such as orthodontic changes and damage to the mandibulomaxillary joints requires further study. It is important to realise that the favourable results reported in the cited studies³⁷⁻³⁹ conducted with specific devices may not be extrapolated to the large number of other commercially available appliances which have not been subjected to a rigorous scientific evaluation. In conclusion, individually fitted and scientifically validated MAD are a valuable alternative for treatment of patients with mild and even severe OSAS if CPAP therapy is not feasible and if initial adaptation and long-term follow-up is performed by experienced professionals.

REDUCTION OF EXCESS WEIGHT

Obesity is a major risk factor for OSAS as well as for other diseases including hypertension and cardiovascular disease.⁹ Therefore, reduction of excessive weight is an important

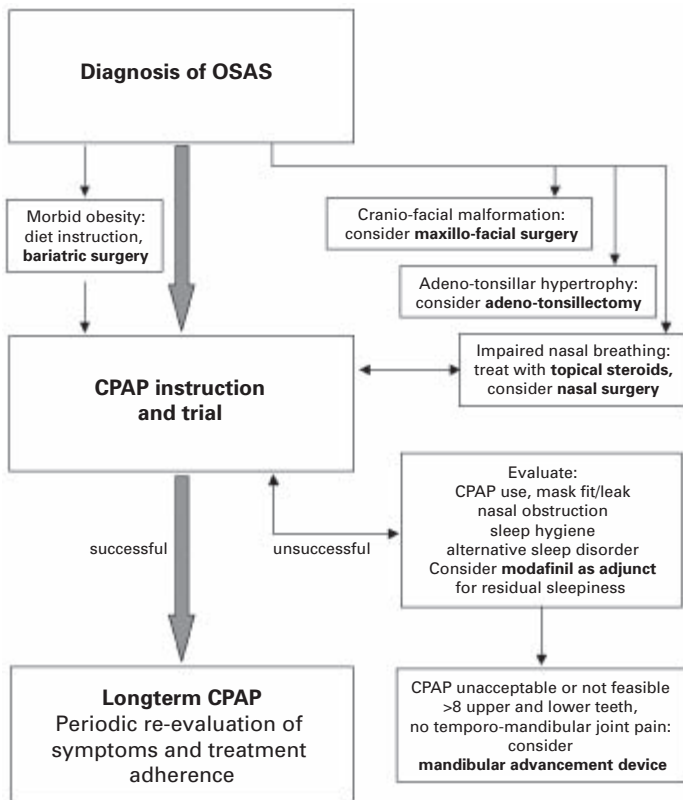


Figure 2 Treatment options for the obstructive sleep apnoea syndrome (OSAS). The standard therapy consisting of nasal continuous positive airway pressure (CPAP) and alternative treatment modalities along with suggested evaluations are outlined.

therapeutic goal independent of its beneficial effects on OSAS. While diet supported by pharmacological treatment has not resulted in major and persistent weight loss, favourable results have been achieved by bariatric surgery including adjustable gastric banding and gastric bypass surgery.^{43,44} A meta-analysis has evaluated the effects of bariatric surgery on OSAS.⁴⁵ Among 12,266 obese patients undergoing bariatric surgery and evaluated by sleep studies, OSAS was diagnosed in 2,399 (20%). In 1,636 of 1,921 (85%) in whom the information was available, OSAS improved or was resolved. In addition to the favourable effects on sleep related breathing disturbances, bariatric surgery improved diabetes mellitus, hypertension and hyperlipidaemia in a substantial majority of the patients. Therefore, bariatric surgery has an important role in the treatment of obese OSAS patients.

UPPER AIRWAYS SURGERY

Various techniques of soft tissue surgery for treatment of OSAS have been proposed but their role still remains controversial.⁴⁶⁻⁴⁸ An exception is adeno-tonsillectomy which is successfully performed in children and in adult OSAS patients with adeno-tonsillar hypertrophy.⁴⁹ Uvulopalato-pharyngoplasty (UPPP) performed by conventional techniques or with the use of laser⁵⁰ has provided inconsistent and unpredictable results in regard to improving OSAS and snoring. In one study, temperature-controlled radiofrequency tissue ablation applied in local anaesthesia to the tongue base and palate over the course of several weeks was compared to the effects of a sham procedure in patients with mild OSAS (mean apnea/hypopnea index 20/h). The verum surgery improved subjective sleepiness, quality of life and objectively measured reaction time more than the sham

procedure but the apnea/hypopnoea index remained unchanged. Side effects included haematomas, ulceration, pain and difficulty swallowing for several weeks in some patients. The follow-up time was not mentioned.⁵¹ Tongue base procedures including suspension or resection have been performed in small patient groups and the results require further confirmation.⁵² Tracheotomy and maxillo-facial surgery are considered too aggressive to be recommended routinely as first-line therapy. The Stanford step-by-step approach for surgery in OSAS is considered in patients not successfully treated with CPAP.^{46,53} The first stage comprises limited mandibular osteotomy (with or without UPPP, genioglossus advancement, hyoid myotomy, and hyothyroidopexy). Maxillo-mandibular advancement osteotomy, stage II surgery, is considered if stage I is not successful, or in the first place if cranio-facial dysmorphism is present.⁵⁴ In a single centre report on 51 OSAS patients treated surgically, stage I surgery was performed in 44 patients.⁵⁴ In only 10 of them satisfactory improvement was achieved while 34 were treatment failures. In 13 of these patients maxillomandibular advancement osteotomy was subsequently performed and an additional 7 patients with cranio-facial dysmorphias underwent maxillo-facial surgery in the first place. Maxillo-mandibular advancement osteotomy was successful in 15 of the 20 operated patients, 5 patients were treatment failures. Over the same time period in which the 51 OSAS patients underwent upper airway surgery, 939 patients were started with CPAP at this centre. Thus, the staged surgical concept seems to be successfully applicable in a very minor fraction of OSAS patients, namely those not successfully treated with CPAP or a MAD, and those with significant adeno-tonsillar hypertrophy, or cranio-facial dysmorphias and other anatomical obstacles amenable to surgery.

TREATMENT OF NASAL OBSTRUCTION

It has been a long-standing clinical observation that snoring is particularly common in patients with nasal obstruction, and early reports have shown that experimental nasal occlusion promotes obstructive sleep apnea.⁵⁵ Whether nasal obstruction due to chronic rhinitis, nasal polyposis or nasal septal deviation is a predisposing factor for OSAS is not clear. Epidemiological studies have shown that chronic rhinitis symptoms, and increased nasal resistance measured by rhinomanometry are associated with habitual snoring but a similar association was not demonstrated for OSAS.^{56,57} Nevertheless, treating OSAS patients with chronic rhinitis with fluticasone administered intra-nasally for one month improved sleepiness, and reduced the apnea/hypopnea index with statistical significance, though only to a minimal degree compared to placebo.⁵⁸ In another non-randomised study, 19 OSAS patients and 7 snorers with impaired nasal breathing underwent nasal surgery.⁵⁹ Sleep related breathing disturbances were not significantly changed but patients reported being less sleepy after the intervention. Nasal obstruction appears therefore to have a minor role in the pathophysiology of OSAS. Treating impaired nasal breathing may still be beneficial in selected patients since it improves subjective symptoms and sleep quality⁶⁰ and may contribute to successful nasal CPAP therapy in OSAS patients.

DRUG THERAPY, ADJUNCTIVE AND EXPERIMENTAL MEASURES

Unfortunately there are currently no drugs that allow effective pharmacological therapy of OSAS. Research in this field however is ongoing. Recently, interesting observations have been made in children with minimal adeno-tonsillar enlargement

and very mild sleep disordered breathing.⁶⁶ They were treated for 16 weeks with the leukotriene modifier montelukast achieving reductions in adenoid size and in sleep related breathing disturbances. Although these effects were modest, the results are promising. In compliant OSAS patients with residual hypersomnolence despite exclusion of other causes and effective CPAP treatment, modafinil, a drug prescribed to treat hypersomnolence in narcoleptics, has been used as an adjunct to improve alertness. In a randomized placebo controlled cross-over study with a 2 week period on modafinil no improvement in subjective sleepiness assessed by the Epworth score, no change in the multiple sleep latency test (MSLT) and only minor improvement in the ability to stay awake in a sleep-seductive environment (maintenance of wakefulness test) were found.⁶⁷ In another placebo-controlled parallel trial extending over 4 weeks with a final daily dose of 400 mg of modafinil, a statistically significant but clinically minor improvement in objective vigilance measured by the MSLT was demonstrated.⁶⁸ During extended open label use of modafinil over 4 months, patients continued to perceive an overall benefit in regard to improved sleepiness and quality of life.⁶⁹ Side effects of modafinil were generally mild and most commonly consisted of headache (28%), anxiety (16%), nervousness (14%), insomnia (11%), and nausea (11%).⁶⁹ Despite the relatively favorable results regarding residual sleepiness the use of modafinil is still controversial. Arguments in favour of modafinil in this setting are some subjective and objective improvements of alertness and of quality of life. Conversely, the use of a stimulant may reduce compliance with CPAP treatment as shown in the cited studies^{67, 69} and the stimulant drug may divert from inappropriate functioning of CPAP therapy and expose the OSAS patients to increased cardiovascular risk.

In mild positional OSAS, sleep in lateral position is often recommended. One randomised trial has evaluated the effect of 2 weeks of positional treatment consisting of a backpack with a soft ball inside. Thirteen patients with positional OSAS defined by more than twice the number of apnea/hypopnea in the supine as compared to the lateral position were included.⁷⁰ Positional training improved subjective sleepiness, maintenance of wakefulness time measured objectively, and psychometric test performance to a similar degree as CPAP but the latter was more effective in reducing apnea/hypopnoea and oxygen desaturations. Therefore, positional treatment is a reasonable therapy for selected patients with positional OSAS who are not tolerating CPAP. A nasal dilator⁷¹ and a number of other appliances have also been promoted for treatment of snoring and OSAS but have not revealed consistent effects and can therefore not be recommended.

Nocturnal electrical stimulation of the hypoglossal nerve by an implanted pace-maker has been thought to prevent sleep related upper airway collapse in OSAS patients by activating submandibular muscles.⁶¹ However, this treatment is still experimental and there is insufficient evidence to support its clinical use. In one randomised, placebo-controlled trial, tongue muscle training by electrical neurostimulation applied twice during daytime for 8 weeks has been found to reduce snoring but not sleep apnea in 33 patients.⁶² Whether this treatment modality is acceptable and effective in the long-term treatment of snoring remains open. The initial success achieved with atrial overdrive pacing as a therapy for OSAS patients treated with a cardiac pacemaker for other reasons has not been confirmed in subsequent trials, and this treatment is therefore not

recommended.^{63, 64} Whether biventricular pacing in heart failure patients with ventricular asynchrony improves co-existing sleep apnea requires further studies.⁶⁵

CONCLUSIONS

Figure 2 summarises the current options for treatment of OSAS and the suggested sequence of evaluations. CPAP remains the standard treatment for the vast majority of OSAS patients due to its immediate and persistent effectiveness and the lack of major side effects. For patients in whom CPAP therapy is not feasible because of mask intolerance or other reasons, a custom-fitted MAD may be a valuable and effective alternative treatment but long-term effectiveness and side effects need to be monitored. In morbidly obese OSAS patients, bariatric surgery should be considered as an option to treat both excess weight, and OSAS and to prevent cardiovascular consequences. Upper airway surgery has a role in children and adults with enlarged adenoids and tonsils, or with cranio-facial dysmorphism and other selected patients in whom CPAP is not an option.

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Dx-pH Measurement

INTRODUCTION

Restech's new Dx-pH Measurement System reliably monitors aerosolized pH events in the upper airway associated with gastric reflux for 24 to 48 hours. This system is the first to measure and record pH in the oropharynx for detection of laryngopharyngeal reflux (LPR) in real-time. Gastric reflux in the airway has been shown to exacerbate respiratory diseases such as asthma, chronic cough and sleep apnea, as well as throat disorders including chronic throat clearing and hoarseness.

The release of Restech's Dx-pH Measurement System has prompted interest from physicians and medical groups spanning several disciplines in conducting clinical studies using the airway reflux detection tool. Among the dozen studies either completed or currently in progress, three by preeminent institutions and physicians are reported.

Gregory Wiener, MD, a pioneer in pharyngeal pH testing, conducted a clinical study that confirmed the existence of supraesophageal reflux in the oropharynx and showed that it is detectable by Restech's Dx-pH Measurement System. Dr Wiener was invited to present the study at the international Digestive Disease Week (DDW) 2006 and received praise for the significance of his findings and for introducing the Dx-pH Measurement System's unequalled technology to the gastroenterology community (The study appears below).

University of Southern California's Keck School of Medicine is conducting a study (in Dr Tom DeMeester's lab) under the Principal Investigation of Dr Cedric Bremner, to determine the threshold at which significant damage to the airway occurs and establish what should be considered as "normal" values for upper airway reflux. This study will offer normative values as well as a justified closing argument to the debate on necessity of oropharyngeal pH measurement.

A third study is underway at Emory University's Voice Center in Atlanta, Georgia. Spearheaded by Dr. Adam Klein, the investigative team will examine the efficacy of the anti-reflux medication Nexium® in the treatment of laryngopharyngeal reflux. Dr. Klein has received a grant from Astra Zeneca to assist with the cost of the study, which is also confirming the Dx-pH Measurement System as a diagnostic modality for laryngopharyngeal reflux.

In recent years, awareness and recognition of LPR have fueled the development of an objective diagnostic test. There has been much debate amongst specialists who deal with this challenge. Impedance technology has shown that nearly all reflux above the esophagus is gas, not liquid. Consequently, Restech developed

the Dx-pH Measurement System to provide a reliable diagnostic tool that rests in the oropharynx in order to assist medical professionals in clarifying the causes and effects of LPR.

Like gastroesophageal reflux disease (GERD), the etiology of LPR is linked to esophageal sphincter dysfunction. In episodes of GERD, the lower esophageal sphincter (LES) is primarily involved, whereas in LPR, the pathology results from upper esophageal sphincter (UES) dysfunction. However, the diagnosis of LPR is more challenging than that of GERD as classic reflux-like symptoms of heartburn and regurgitation are often absent in patients with LPR.

This particular form of reflux that escapes the esophagus has been implicated in the pathogenesis of numerous laryngeal disorders including globus, dysphonia, chronic cough, laryngospasm, and benign vocal cord lesions, as well as granulomas, subglottic stenosis and laryngeal carcinoma.

In the pediatric population, LPR has been implicated in the development of asthma, sinusitis, otitis media and sudden infant death syndrome (SIDS). Common symptoms include chronic and intermittent hoarseness, vocal fatigue, globus pharyngeus, dysphagia, cough, postnasal drip and chronic throat clearing.

Prior to Restech's Dx-pH Measurement System, a minimally invasive, reliable objective test for LPR did not exist. The conventional test for diagnosing LPR involved a subjective laryngoscopy and sometimes a 24-hour triple-pH probe study, both invasive and cumbersome, all the while difficult to administer. Another diagnostic tool is the reflux symptom index (RSI), a validated nine-item questionnaire assessing LPR symptoms. However, LPR symptoms are fairly nonspecific and a definitive diagnosis of LPR is impossible without objectively measuring acid exposure. Therefore, the most widely used modality to diagnose LPR is symptomatic response to treatment, such as a daily proton pump inhibitor (PPI) or histamine receptor blocker therapy for several months. Still, the use of drug administration to make a diagnosis clearly carries disadvantages, including potentially unnecessary exposure to a drug's side effect profile, cost, and lengthy time to diagnosis.

In response to the afore mentioned limitations in diagnosing LPR, Restech's Dx-pH Measurement System has been shown to correlate strongly with 24-hour triple pH probe measurement of lower esophageal, upper esophageal, and lower pharyngeal pH. These reported studies, among others will further advance empirical data supporting the value of the Dx-pH Measurement System as the ideal diagnostic device for accurately assessing laryngopharyngeal reflux.

Dx-pH MEASUREMENT SYSTEM: A SENSITIVE DEVICE FOR DETECTING LIQUID AND AEROSOLIZED SUPRAESOPHAGEAL GASTRIC REFLUX (SEGR)

Gregory Wiener, Ross Tsukashima, Colleen Kelly, Erich Wolf, Molly Schmeltzer, Charles Bankert, Lauren Fisk

Gregory Wiener is in private practice in Chula Vista, CA. Wiener, Tsukashima, Wolf, Schmeltzer, Bankert and Fisk are with Restech Corp, Poway, CA. Kelly is with San Diego State University, San Diego, CA. Information was provided by Restech.

PURPOSE

Clinical and animal data have documented deleterious effects of acid pH < 4 (AGR) and weakly acid pH 4-7 (WAGR) gastroesophageal reflux, even in small amounts, when above UES. Despite recognition of multiple manifestations of SEGR, characterization, identification and response to therapy have evaded understanding due to lack of a suitable detection device.

AIM

Evaluate the Dx minimally invasive catheter (Restech) with ionic flow sensor, able to measure pH in liquid or aerosolized droplets at posterior oropharynx, for SEGR detection, using standard 24hr triple sensor pH catheter (24pH) for verification.

METHODS

Pts in a GI practice (GW) with chronic symptoms likely due to SEGR, off reflux meds 4-7days, underwent 24pH with 2 esophageal (E) and 1 pharyngeal (P) sensor (Sandhill PHI10-V) positioned with LES Indicator at 5 cm > LES, 5 cm < UES and 1 cm > UES. The 1.5 mm nasopharyngeal catheter placed at oropharynx behind uvula, above pts discomfort position. Tracings from all 4 synchronized pH inputs & pt diary were analyzed graphically on single screen, excluding meals +5 min. SEGR event definition: rapid pH drops at the Dx sensor, >3 S.D. from 60 sec baseline, sequential to drops in pH<4 in 24 pH sensors, then classified as AGR/WAGR. S.I. <50%+.

RESULTS

15 Patients, 5M, 10F, avg. age 57.5 (25-75): 11 cough, 1 loss enamel, 1 sleep apnea, 2 asthma. 4 had normal 24pH. There were 48 Dx SEGR events in 10 pts, being near vertical with gradual return to baseline & synchronous to E pH drops (see table 1). Increase in pH was 46% from E to P, 6% from P to Dx. These 48 SEGR events were 7.8% of 616 episodes with pH<4 at lower E. All 5 Dx negative pts had normal 24pH at E. CLINICAL FOLLOW UP (f/u): 11 pts took PPIs BID (f/u 3-8 mo., avg 6.5) or fundoplication (f/u 4 & 6 wks). 9 Dx + pts had 60% Chief Complaint Improvement (CCI), no worsening. 7 of these on PPI had CCI 48.6% (0,0,20,50,70,100,100), 2 had fundoplication with 100% CCI, post-op Dx without pharyngeal events. 2 Dx negative pts, 1 with CCI 0% on PPIs, the other 100% CCI on NO meds.

CONCLUSIONS

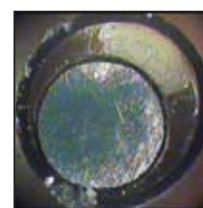
- (A) SEGR exists in oropharynx, detectable by Dx.
- (B) There is a gradient of increasing pH from E to oropharynx, the latter rarely <4.
- (C) Redefinition of significant pH events above UES as % or >3 S.D. pH drops merits consideration.
- (D) Clinical management may be influenced by Dx results, further studies should aid understanding of SEGR.

Table 1: Characteristics of Synchronous pH Drops-SEGR

pH SENSOR	AGR (pH≤4)	WAGR (pH > 4)	AVERAGE pH
Dx	6.25% Avg pH 3.67	93.75% Avg pH 5.65	5.52
Pharynx	25% Avg pH 3.8	75% Avg pH 5.69	5.22
5cm > LES	66.67% Avg pH 2.63	33.33% Avg pH 5.47	3.58



Dx-1 pH Probe and Dx-Transmitter



Dx-1 pH sensor with breath condensation

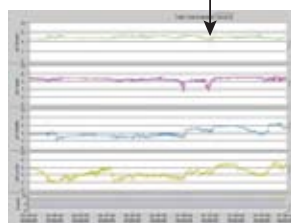


Dx-1 pH sensor tip/LED behind uvula



CT section showing Dx-1 and pharyngeal sensors

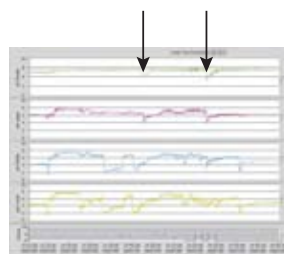
Examples of SEGR



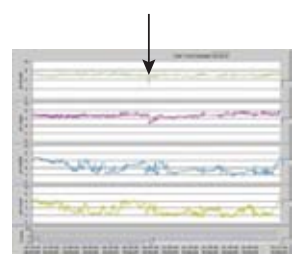
SEGR synchronous with drops < 4 on all [3] 24 hr pH Sensors (note: prior events that did not reach Dx-1 pH Probe)



SEGR event picked up at Dx-1 pH Probe and missed both P and mid E probes.



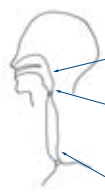
SEGR event synchronous pH drops in all 4 pH sensors associated with cough.

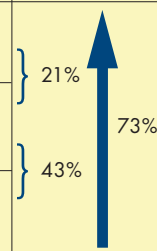


SEGR/AGR at Dx-1 pH Probe sequential to drops in 24 hr pH sensors (Pharyngeal sensor missed event by classical definition of pH<4)

CHART 1: Characteristics of synchronous pH drops (SEGR)

using pH < 4 as a conventional cut off for "acid reflux" in pharynx and 5cm > LES sensors. (N=14)



pH Sensors	AGR Events	WAGR Events	Avg. pH of All Events	Increase in Avg. pH
Dx-1 pH Probe	7 % pH 3.5	93% Avg pH 5.7 pH range: 4.5-6.5	5.54	
Pharynx	50% Avg pH 3.78 pH range: 3.1-4.0	50%* Avg. pH 5.34 pH range: 4.2-7.2**	4.53	
5 cm > LES	78.5% Avg pH 2.83 pH range: 2.0-3.38	21.5% Avg. pH 4.52 pH range: 4.17-5.0	3.20	

*3/7 events showed higher pharyngeal pH with no evidence of pH drop (missed event).
4/7 events showed pH drops that would have not registered using above criteria of pH<4. (true WAGR)
**Pharynx probe dried out.

DIAGNOSIS AND RESPONSE TO TREATMENT OF LARYNGOPHARYNGEAL REFLUX USING AN OROPHARYNGEAL AEROSOLIZED pH PROBE

Adam Klein, MD, et al

The author is with Emory University Voice Center.

Abbreviations: RSI (reflux symptom index), LPR (laryngopharyngeal reflux), GERD (gastroesophageal reflux disease), PPI (proton pump inhibitor), UES (upper esophageal sphincter), LES (lower esophageal sphincter)

HYPOTHESIS

Null hypothesis 1: There is no correlation between reflux symptom index (RSI) and oropharyngeal aerosolized acid reflux events and acid exposure time as measured by the Dx-pH measurement device.

Null hypothesis 2: Oropharyngeal aerosolized pH as measured by the Dx-pH measurement device cannot predict patient RSI response to esomeprazole 40 mg bid.

AIM

To conduct a randomized, controlled prospective study to determine the use of the Dx-pH Measurement System as a diagnostic modality for laryngopharyngeal reflux (LPR).

BACKGROUND AND SIGNIFICANCE

In this study, we investigate the use of a newly developed oropharyngeal aerosolized pH probe (Dx-pH Probe) as an accurate and minimally invasive diagnostic instrument for LPR. This device has previously been shown to correlate strongly to lower esophageal, upper esophageal, and lower pharyngeal pH as measured by a 24-hour triple channel bifurcated pH probe [reference/originally noted from Debra Krahel's e-mail]. The number of oropharyngeal aerosolized acid reflux events and acid exposure times will be compared to RSI before and after twice daily proton pump inhibitor therapy.

METHODS

Group Assignment:

1. Negative control group: "normal subjects" defined by RSI \leq 13 to receive:
 - 24 hour ResTech probe study.
2. Positive control group: Patients with RSI > 13 to undergo simultaneous standard triple pH probe study and Restech Dx-pH Probe study.
3. Experimental group: defined by RSI > 13 to receive:
 - Treatment (esomeprazole 40 mg bid x 8weeks). The pH probe and RSI will be administered before and after drug treatment.

Data Interpretation:

- The number of oropharyngeal acid reflux events and acid exposure times as measured by the Dx-pH Probe will be compared to the RSI.
- The number of oropharyngeal acid reflux events and acid exposure times as measured by the Dx-pH Probe will be compared to the RSI

ANTICIPATED RESULTS

It is anticipated that the Restech probe findings (oropharyngeal acid events and exposure time) will correlate with standard triple pH probe findings. It is anticipated that the RSI will correlate with oropharyngeal aerosolized pH acid reflux events and acid exposure times as measured by the Dx-pH probe. Specifically, higher RSI scores will be associated with lower pH levels and longer acid exposure times. In addition, it is expected that patients with abnormal oropharyngeal aerosolized pH levels will benefit esomeprazole 40 mg bid treatment as demonstrated by a reduction of their RSI score.

MEASUREMENT OF REFLUX IN THE UPPER AIRWAY: A NEW TECHNOLOGY

RESPIRATORY TECHNOLOGY CORPORATION Dx-UPPER AIRWAY pH MEASUREMENT SYSTEM STUDY

Colleen Gaughan, MD, et al.

The author is with the Keck School of Medicine of University of Southern California.

AIM

Introduce the use of a unique device designed specifically to record pH changes in the upper airway.

Examine the relationship of pH changes above the Upper Esophageal Sphincter (UES) with specific supraesophageal and respiratory symptoms.

Determine the threshold at which significant damage to the airway occurs and establish what should be considered "normal" values.

Confirm that pH changes in the upper airway are related to pH changes in the lower esophagus.

STUDY SUBJECT POPULATION

10 patients with symptoms indicative of GERD and Supraesophageal Reflux (SER) who are scheduled to undergo the Bravo study will, in conjunction with their Bravo, also test

the investigational device (Dx-pH Probe).

50 patients with symptoms indicative of GERD who are having the routine Bravo study.

50 asymptomatic volunteer patients will be tested after the completion of groups II and III.

METHODS AND PROCEDURES

Determine the appropriate placement of the Restech Dx-pH Probe sensor in the oropharynx of patients concurrently undergoing a standard Bravo procedure. (Group I).

Examine the relationship of distal pH to upper airway pH in GERD patients both with and without symptoms of supraesophageal and/or respiratory conditions. (Groups II and III, respectively).

GERD patients from group II will be assigned to a third group (III) if they exhibit symptoms of Supraesophageal Reflux.

By comparing the data obtained from control patients to that from patients with SER, normative data for both patient groups can be defined.

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