

ResMed

Michael J. Farrell¹ and Drew Terry²

¹Vice President of Marketing, ResMed, Poway, CA and

²Sr. Market Manger, ResMed, Poway, CA

INTRODUCING THE REVOLUTIONARY VPAP ADAPT SV

The VPAP Adapt SV™ is an advanced and unique device that treats patients with complex sleep apnea, amongst other breathing disorders. Complex sleep apnea cannot be effectively treated with any other medical device. The VPAP Adapt SV is unique because it is the first and only product on the U.S. market with FDA clearance to treat central sleep apnea, mixed sleep apnea and periodic breathing, including Cheyne-Stokes respiration in the hospital and homecare environment. Probably the most compelling opportunity for the industry and its use of this new product is complex sleep apnea. Approximately 15% of patients going through the sleep lab environment have this type of sleep-disordered breathing, according to a study published by Dr. Timothy Morgenthaler, Mayo Clinic Sleep Disorders Center in the *SLEEP* Journal.¹ At the SLEEP 2006 conference in Salt Lake City earlier this year, Dr. Peter Gay of the Mayo Clinic and other physicians and researchers estimated slightly higher proportions: from 15% to as high as 25% of patients in sleep centers and sleep labs have complex sleep apnea.

COMPLEX SLEEP APNEA

Complex sleep apnea is a form of central sleep apnea that has only recently been formally recognized. Complex sleep apnea presents as obstructive sleep apnea during a diagnostic study; then during titration studies when the patient is treated with continuous positive airway pressure therapy, central apneas begin to appear in place of the obstructive events. This form of sleep-disordered breathing has been very frustrating for clinicians and patients and cannot be effectively treated with CPAP or bi-level therapies. The VPAP Adapt SV offers welcome relief with simple and effective treatment for complex sleep apnea. If complex sleep apnea afflicts only 15 percent of patients with sleep-disordered breathing, it is a huge unmet medical need. It is our pleasure to present sleep physicians and sleep technicians in the United States with the first and only device that effectively treats this underserved population of patients.

A STRONG HISTORY OF SUCCESS

The VPAP Adapt SV is ResMed's newest product in the U.S., having been available on a limited basis since February 2006 and now available nationwide. This latest addition to the VPAP family brings a strong foundation of experience from years of use in Europe and Asia-Pacific. In fact there are over 6,000 patients on Adaptive Servo Ventilation (ResMed's unique patented treatment algorithm) with well over 1,000,000 patient treatment hours in the field. Many of these patients are being treated for sleep disordered breathing associated with heart failure. Adaptive Servo-Ventilation has been shown to be superior to CPAP, bi-level, and oxygen therapy in reduction

of central apnea index and total arousal index in various patient populations.²

THE VPAP ADAPT SV IS SUPERIOR IN ALL OF ITS FUNCTIONS

Through the limited market release over the last 8 months, the VPAP Adapt SV has validated that the data from the scientific literature is replicated in the clinical setting: showing U.S.-based Sleep Physicians and Sleep Technicians that it treats patients more effectively than any other treatment modalities. Many patients who have been on CPAP and have tried bi-level therapy with and without oxygen therapy have found that such therapies do not resolve their complex breathing disorders. However, patients, physicians, and technicians are ecstatic when they finally find the device (VPAP Adapt SV) that treats these complex breathing disorders completely automatically.

As outlined in the previous section, an article by Teschler H, et al.² from the American Journal of Respiratory and Critical Care Medicine showed that in terms of treating the central apnea index and the respiratory arousal index, the Adaptive Servo Ventilation algorithm provided in the VPAP Adapt SV is clearly more effective than oxygen, CPAP and bi-level. Apart from being clinically more effective than bi-level, the best part for sleep technicians who have spent hours on bi-level titrations is that the pressure support titration is completely automated. The sleep technician must still titrate away obstructive sleep apnea events by adjusting the EPAP (designated as End Expiratory Pressure or EEP on the VPAP Adapt SV); the EPAP is titrated just like during a normal CPAP titration. The IPAP will be adjusted automatically by the algorithm as it matches pressure support to clinical need on a dynamic breath-to-breath basis targeting a ventilation rate that it has learned from the patient. The algorithm continues to learn on a 180-second-cycle rolling basis throughout each therapeutic session: it responds almost instantaneously, but retains memory and learns from the patient on an ongoing basis. This "learning ability" is an innovative advancement and many physicians are excited that this technology in the VPAP Adapt SV safely and effectively treats complex sleep apnea.

Although the clinical and engineering design aspects of the VPAP Adapt SV are very advanced, it is extremely simple for technicians to use. The MD and PhD team that created and designed the Adaptive Servo Ventilation algorithm used a variety of proprietary techniques including patented incremental flow-time curve analysis techniques, along with multiple fuzzy mathematical calculations: where the clinical answers are not binary (true or false, one or zero), rather there are "degrees of trueness and degrees of falseness" that better represent the real-world clinical environment. The result is a revolutionary device that delivers correct pressure support for the patient on an almost instantaneous basis. Nothing like it exists on the market.

IMPROVEMENTS SO FAR ARE SIMPLY AMAZING

In Europe, ResMed works with cardiologists and pulmonologists to identify central sleep apnea, mixed sleep apnea, and Cheyne-Stokes respiration amongst heart failure patients. Within that patient group researchers have seen great improvements in left-ventricular ejection fraction (LVEF), VO_2 Max, 6-minute walk, and quality of life improvements evidenced by Minnesota living with heart failure questionnaire improvements.^{3,4} Some of the most amazing improvements were witnessed by pulmonary and cardiovascular physicians as their patients moved from Class III or Class IV NYHA heart failure classification down to Class I or Class II after introduction of this algorithm. Pulmonary and cardiovascular physicians have provided examples of patients who were actually taken off the heart transplant waiting list with no other change to therapy other than the introduction of Adaptive Servo Ventilation: this is simply amazing!

FOCUS ON HEART FAILURE OR COMPLEX SLEEP APNEA?

Many patients with heart failure suffer from difficult-to-treat conditions. Clinical literature show that the prevalence of central sleep apnea in the heart failure patient population varies from 40% to 47%^{5,6} and when one includes mixed sleep apnea, the prevalence number increases further. Looking at the 5,000,000 patients in the United States with heart failure and the mortality association with Cheyne-Stokes respiration, there is clearly a huge unmet medical need. There is an important opportunity for sleep physicians to partner with cardiologists who specialize in heart failure to establish sleep apnea screening and referral pathways. One of the toughest barriers amongst the cardiovascular physician group is education and awareness: ResMed has been working with the American College of Cardiology and American Heart Association since 2001 as well as with the Heart Failure Society of America since 2002, to increase awareness of sleep apnea in the cardiovascular clinical community. Initially the focus was on obstructive sleep apnea and the use of CPAP, APAP, and bi-level devices with indications for use to treat obstructive apnea. Now, that we have a novel device that has an indication for use to treat central sleep apnea in the VPAP Adapt SV, we need to revisit our cardiovascular referral sources with the good news! We will be doing that and will partner with sleep centers and sleep physicians across the country to do so.

The VPAP Adapt SV has effectively treated both central sleep apnea and more recently has been used to treat complex sleep apnea. The key question is: will ResMed want to focus on central sleep apnea and the cardiovascular referral

pathway or on complex sleep apnea and growth of existing referral pathways? The answer is both. We want to partner with sleep physicians and sleep technicians to bring this unique therapy to these two important unmet medical needs.

WHERE THIS INNOVATIVE PRODUCT STARTED

In 1981, Dr. Colin Sullivan from the University of Sydney published the very first article on continuous positive airway pressure, and so CPAP was invented. During the late 1980's Sullivan and Dr. Michael Berthen-Jones first published together on AutoSet™, the first automated algorithm to treat obstructive sleep apnea. AutoSet is still the world leading auto-adjusting positive airway pressure algorithm and can be found in the commercially available S8 AutoSet Vantage™ device. In 2001, Dr. Helmut Teschler and Berthen-Jones published novel data on the clinical efficacy of the Adaptive Servo Ventilation algorithm.² Many other publications on the use of this technology have followed.^{7,8,9,10} Now in 2006, ResMed is pleased to bring this ground-breaking technology to the United States in the VPAP Adapt SV device. U.S. sleep physicians and sleep technologists now have the first commercially available product in this country to treat central sleep apnea and complex sleep apnea in a hospital and homecare environment.

ADVANCING THE FIELD OF SLEEP MEDICINE

ResMed continuously works on improving their products and looks to extend the advanced and automated treatment capabilities to treat broader patient populations. The VPAP Adapt SV is an important step in advancing the field of sleep medicine and it is an educational opportunity for ResMed and our sleep physician and sleep technician partners to learn more together about the emerging field of complex sleep apnea. We will take this technology to the next level in future product generations, but for now, our focus will be on the unmet medical need of treating central sleep apnea and complex sleep apnea amongst the more than 40 million Americans with sleep-disordered breathing

REFERENCES

1. Morgenthaler T, et al. *Sleep* Vol 29, No 9, 2006, 1203–09.
2. Teschler H, et al. *Am J Respir Crit Care Med* 2001; 164:614–19.
3. Philippe C. *Heart* 2005; Published online Jun 20.
4. Töpfer V, et al. *Pneumologie* 2004; 58(i):28–32.
5. Sin D, et al. *Am J Respir Crit Care Med* 1999; 160:1101–06.
6. Javaheri S, et al. *Circulation* 1999; 99:2711–12.
7. Kryger M, et al. *J Clin Sleep Med* 2006; 2:181–86.
8. Szollosi I, et al. *J Sleep Res* 2006; 15:199–205.
9. Zhang X, et al. *Chin Med J* 2006; 119:622–27.
10. Pepperell J, et al. *Am J Respir Crit Care Med* 2003; 168:1109–14.