

## Sleep Sage Predicts “Time of Huge Change”

At the 2009 Associated Professional Sleep Societies (APSS) meeting in Seattle earlier this year, David P. White, M.D. was the recipient of the William C. Dement Academic Achievement Award. We caught up with Dr. White to discuss a number of wide-ranging topics such as, home diagnostics, research priorities and his association with Philips Respironics.

With firm roots in the academic world, Dr. White brings clinical expertise and business acumen to any discussion about the past, present, and future of sleep medicine. In 1996, Dr. White began the clinical side of the sleep disorders program at Harvard-affiliated Brigham & Women’s Hospital (BWH). The American Academy of Sleep Medicine later named BWH’s Division of Sleep Medicine as a Comprehensive Academic Sleep Program of Distinction—an honor shared by just one other program at the University of Louisville, KY.

### CURRENT RESEARCH FOCUS

I have a research laboratory in Boston, and our focus there is to try to understand the pathophysiology of obstructive sleep apnea. We believe there are four or five traits that indicate why someone may develop sleep apnea. From that, we hope to develop focused therapies based on individual traits. If we understand more, we can individualize therapies. Philips Respironics is also looking at different approaches to define phenotyping.

From Philips Respironics’ point of view, we are always looking for better ways to help our customers diagnose and treat sleep apnea. We are striving to make PAP devices and patient interfaces better and more comfortable. We are also focused on making devices faster, quieter, with better algorithms for pressure relief and better focused on all different types of apneas and disorders. We are working on novel therapies, modifying air pressure and phenotyping. And, we are also looking at developing new products for a variety of other sleep disorders beyond obstructive sleep apnea.

### RESEARCHING THE CAUSES OF SLEEP APNEA

There is a lot of variability in what causes sleep apnea. For example, the anatomy of the pharyngeal airway is a big factor for a lot of people, but if you look at anatomy versus the severity of the disordered breathing, you find people with terrible anatomic abnormalities and no sleep apnea, and people with virtually no anatomic abnormality and severe sleep apnea.

If you look at the correlation between apnea severity and anatomy, the relationship is minimally or not statistically significant. We may someday approach sleep apnea similarly to the way we approach heart failure. With heart failure, we don’t treat patients using one therapy. We use beta-blockers, ACE inhibitors, diuretics, etc. This may one day be the case with sleep apnea where various therapy approaches may be used to influence the phenotypic traits.

### UNDERSTANDING LONG SLEEP AND SHORT SLEEP DURATION

Most data suggests that if you sleep under about seven hours each day, you begin to see performance defects, and there is an evolving body of literature, which suggests poor health outcomes as well. This can mean diabetes, hypertension, and heart attacks. Nobody has done—in the nonperformance arena—an intervention study. For example, freshman in college often do not sleep much and they gain weight pretty regularly. A colleague of mine was going to do a study of such freshman, putting them on actigraphs for the entire year, and pay half of them to sleep. They would get paid based on how much they slept without telling them the hypothesis of the study. This would be an intervention study assessing the association between sleep duration and weight.

The long sleep data is much more confusing. If you sleep over 8 or 9 hours each day, things start going south. We believe that long sleep in and of itself is not a cause of morbidity. We suspect that these patients have a disease that makes them sleep longer. You can make the same arguments about short sleep, but I think there are enough acute interventional studies that show that glucose regulation, blood pressure and similar things, result directly from short term sleep deprivation—but there is no definitive answer.

### EMERGING TRENDS

There is some clever surgical implantation technology that will emerge in the next three to four years and this phenotyping concept will also start to emerge in that same timeframe. A better way to titrate dental appliances may also come along. In general, I think a lot of forces are going to drive us to home diagnostics. Medicare is starting to pay for it, and Medicare said they’re going to reevaluate the whole reimbursement structure for PSGs. I don’t know if that will happen, but if changes in reimbursement occur then this would change the paradigm.

### THE GENETIC LINK TO SLEEP DISORDERS

I don’t think there is any question that there is a genetic link to sleep apnea—narcolepsy for sure, restless legs for sure—insomnia is not as well studied. But these are not likely single gene associated disorders. There are multiple traits that dictate who gets sleep apnea, as discussed above, making it certainly a multiple gene phenomenon. That being said, I don’t think that in my lifetime there will be a genetic application for taking care of sleep apnea patients. That is, I don’t think the genetics of sleep apnea will affect the care of sleep apnea patients in my lifetime.

To use an analogy, we know the exact cause of cystic fibrosis. It is one gene. Are we doing anything with that knowledge? Very little, and yet we have known the gene for at least 10 years. Genetics is getting there, but the practical applications are just beginning to pick up speed.

## ROLE WITHIN PHILIPS RESPIRONICS

My role within Philips Respironics is complex. I am involved with strategy; I help determine where we want to go scientifically, what type of projects and studies we want to take on, and what acquisitions to make. At a fairly high level, I oversee a lot of the research projects.

I also act as a liaison with the academic community. This has been a wonderful thing for me, because I can interact with academics thereby maintaining my academic status. This allows me to give scientific talks and participate in conferences. I also keep learning from the academic community, and in the long run I hope this makes me wiser in ways that will help continue to guide Philips Respironics in positive directions.

## BEST EDUCATIONAL TOOLS AVAILABLE TO CLINICIANS

It depends on what level you are. If your primary focus in sleep is clinical, scientific or academic, then you should be at SLEEP every year, and you ought to be attending the scientific sessions as much as possible. Reading the journals on a regular basis is essential. If you are an MD in training, you should consider a sleep fellowship. People can't just dabble in sleep the way they did for a long time. If you are really into sleep, the international conferences and the journals are also a good way to keep up.

## CARDIOLOGISTS AND SLEEP MEDICINE

Cardiologists have been slow to get involved because they have grown up in a culture where you do not believe something until you have read the results of a large-scale randomized trials. We have ongoing studies, which are not yet complete. Philips Respironics is the source of funding for the largest study that is currently underway. We made a substantial contribution to an investigator in Australia, who is also working with the Australian NIH equivalent, to fund part of the study. They are randomizing 5,000 patients who all have known obstructive sleep apnea. All participants will also have either known coronary artery disease or cerebrovascular disease. Half will be placed on CPAP, and the other half will not. Follow-up is in about 2 ½ years, and they are looking at heart attacks, strokes, and death.

Cardiologists will need a methodology by which they can diagnose and treat sleep apnea after they become convinced of its importance in their own practices. They will not likely just send people to a sleep lab and have the care of this

disorder delegated to the sleep physician. We have to get them involved, and I don't think we are going to do this until the data are firm and convincing.

## OPENING UP THE FIELD TO AMBULATORY MONITORING

The next three or four years are going to be a time of important change. Sleep labs have to work out a financial model based on in-lab polysomnography and apply it to ambulatory patients.

We are still monitoring sleep patients the same way as we did in 1963. Now we do it digitally and we measure nasal pressure, but other than that, it is pretty much the same. If you look at radiology, the only thing they could do in 1963 was an X-ray. There was no CT or MRI. They have made huge progress in radiology and now we need to apply this thinking to the future of sleep diagnostics. More change is required to identify new options and diagnostic tools.

There are all kinds of tests we need to be able to do, such as circadian monitoring and testing for insomnia. There are many other examples and areas we need to develop that will be valuable to patients. It won't be one size fits all approach and everyone gets the same test. I think Medicare is going to drive this, and home diagnostics, in my opinion, are quite capable of diagnosing routine obstructive sleep apnea.

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David P. White, M.D. is the Chief Medical Officer of Philips Home Healthcare Solutions. He joined the Company in May 2006. In this role, Dr. White is responsible for clinical research strategies and programs, advising senior management on key medical issues, and serving as a liaison between Respironics and the sleep and respiratory medical communities.

Dr. White is board-certified in sleep disorders medicine, internal medicine, pulmonary disease, and critical care medicine. Until recently, he served as Director of Clinical Sleep Disorders Program at Brigham and Women's Hospital and remains as a Professor of Sleep Medicine at Harvard Medical School, both in Boston. He has held many leadership roles within professional sleep and pulmonary societies, including serving as the Editor-in-Chief of the Journal SLEEP.

Dr. White holds a Bachelor of Science degree from Washington and Lee University in Lexington, Virginia and his Medical Degree from Emory University School of Medicine in Atlanta, Georgia. He did his postdoctoral internship and residency in Internal Medicine, as well as a pulmonary fellowship, at the University of Colorado Health Science Center.