

## Something New in Apnea Treatment?

Is the next big thing in OSA treatment right under your nose? Officials at Ventus Medical believe the answer is yes, and they hope to prove it with their new PROVENT® Nasal Device.

Is it time to add “nasal devices” to the familiar sleep apnea treatments? While CPAP, oral appliances, surgery, and pharmacological approaches dominate the market, the folks at Belmont, Calif.-based Ventus Medical hope to crash the party with their PROVENT® Sleep Apnea Therapy. In case you didn’t catch it at the APSS show in Seattle, the PROVENT Nasal Device uses a MicroValve design that attaches over the nostrils and is secured in place with hypoallergenic adhesive. The valve opens and closes, redirecting air through small holes to create resistance upon breathing out. Because it’s a small, single use, disposable device, it is also discreet and convenient.

Philip Westbrook, MD first heard about the concept 3 years ago, and admits that at first he thought it would not work. After several studies, he has changed his mind. In his current post as Chief Medical Officer of Ventus Medical, Dr. Westbrook now adamantly believes that the PROVENT technology, which ultimately increases air pressure in the airway to help keep it open, could ultimately be a vital addition to other proven sleep apnea therapies. *Sleep Diagnostics & Therapy (SDT)* spoke with Dr. Westbrook about the future of PROVENT, and the technology’s exciting prospects as one of the 21st century’s first genuine innovations for sleep disordered breathing.

### **SDT: How was the Provent Therapy Developed?**

**Dr. Westbrook:** It was developed by the founder of the company, Rajiv Doshi, MD, who is both a physician and an engineer, and who is on the faculty at Stanford in both the medical school and the engineering school. Rajiv is really an inventor. He developed the idea, and there were some publications that supported this concept of creating a device that would impose an expiratory resistive load on the respiratory system. And this might change the subsequent tone of the upper airway at the moment of inspiration. So that was the idea. As with a lot of ideas, he tested it first in himself because he is a snorer, and indeed it worked.

That was the start. Subsequent to that, the company was formed. The company was called Ventus Medical, and the design of the device to impose the expiratory resistive load was improved, and continues to undergo improvement. Further studies were done to determine that it indeed worked.

The device works by imposing an expiratory resistance. The current device is actually an adhesive disc that is placed onto the nostrils. There are two discs, one for each nostril, and inside that adhesive disc is a valve, and this little microvalve opens up as a person breathes in, so that there is essentially no resistance to breathing in. When someone breathes out, the valve closes. Now the person is breathing out through two

small orifices, and a significant resistance to breathing out is created. This resistance translates into pressure on the inside of the airway. It is that pressure, and the slowing of expiration, which accounts for the effectiveness.

### **SDT: What is the Science Behind the Way the Product Works?**

**Westbrook:** In a way, it is counterintuitive. One always thinks of obstructive sleep apnea as being a problem of inspiratory collapse of the upper airway. And here we have a device which pressurizes the airway during expiration, but obviously not during inspiration. So why should that work? Well, we do not have all of the answers, and there may be more than one mechanism of action. But a couple of things we do know. First, it is the pressure on the inside of the airways that is required, because we did a sham study to make sure that it wasn’t something that we had done to the inside of the nose, or just the outside of the nose, that was causing the improvement. The sham study caused no improvement in the apnea hypopnea index (AHI) at all.

The mechanism requires pressurizing the airway during expiration. We know that when you impose this expiratory resistance that the expiration is slowed, and that the expiratory pause, which normally occurs—disappears. The result is that at the start of the subsequent inspiration, the airway is still pressurized. There is still a positive pressure on the inside of the airway indicating that the airway is still open. That alone might help the subsequent inspiration and prevent inspiratory collapse, because it takes less pressure to open the narrow airway that is already open than it takes to open an already closed airway. Part of this has to do with surface forces on the inside of the airway.

We think that because the airway—indeed the entire airway—is at a positive airway pressure at the end of expiration, that the lung volume at the time you start to breathe is increased. There is ample evidence that increasing expiratory lung volume, or functional residual capacity, causes a downward traction or “tugging” on the upper airway, and this actually increases its stiffness... It makes the airway less collapsible. We think that is the main mechanism of action. Research to document this mechanism of action is ongoing, primarily by David Rapoport’s group at New York University.

### **SDT: And this Product is Approved by the FDA, Correct?**

**Westbrook:** The product was cleared by the FDA in 2008 for all levels of OSA severity.

### **SDT: You presented posters at the recent APSS Meeting in Seattle. What were those About?**

**Westbrook:** One was on the proposed mechanism of action, and that was by David Rapoport’s group. We presented a poster that summarizes the clinical studies we have done to date.

And so far in three studies—first a pilot study with 24 subjects, and then a sham device study that also studied internal airway pressure that was on nine subjects. Then we did a 30-day sort of extension study to make sure that it continued to work after the initial placement of the device. We wanted to look at compliance and some downstream consequences, mainly the Epworth Sleepiness Scale. We summarized those three studies in this poster presentation to determine how well this really worked.

We found that 72% of all subjects achieved a reduction in their AHI to less than 10, or achieved a greater than a 50% AHI reduction. That is pretty good. People may say, “Gee, it’s not perfect.” I know it is not perfect. But one of the problems we have in pursuing perfection is that we may not actually treat patients as well as we could. There are very few treatments for chronic diseases that are perfect, be it diabetes, asthma, or hypertension. Interestingly enough, in those subjects with baselines AHIs between 10 and 60, 87% of subjects improved their AHI to a level of below 10, or had a greater than 50% AHI reduction. This puts us in the same ballpark, or better than, the other treatments if you also look at compliance during actual use with other treatments, including CPAP.

The results from our clinical studies are significant, and I would understand that they could be construed as controversial. This is a brand new therapy—really the first new therapy in 25 years. You have to put it in the context of what is available. And what is available now, of course, is CPAP. And in fact, one of the great myths is that treatment of sleep apnea means CPAP, and it should not.

CPAP can be spectacularly successful, and one can always verify that in the laboratory. You can almost always find a pressure which will prevent collapse of the airway, and lower the AHI close to zero. The problem is that in dealing with chronic diseases, it is not the physician that treats the patient, it is the patient who treats the patient. And unless you have a therapy that the patient will actually use, that therapy will not work very well. That is the problem with CPAP.

If you take it on an intention-to-treat-basis, probably less than half of patients actually use CPAP either at all or adequately. There are certainly those who use it each night and every night, and they get spectacular results. But at least for half the patients that is not the case. And the current standard for adequate treatment with CPAP seems a rather ridiculously low threshold—70% of the nights and 4 hours per night—that is equivalent to lowering the AHI from about 40 to 26. That is not terrific. That’s about a 36% reduction.

There are a number of other therapies that might do better than that, including oral devices. And now there is Provent. So we have this disease that is quite easy to diagnose. It is very prevalent, but it is really quite difficult to treat because patients have to treat it for the rest of their lives.

One of the things that we found that makes us optimistic about this as a treatment for chronic disease, is that the initial compliance figures that we got from the 30-day studies suggested that patients used it all night on 94% of all study nights. Now I don’t think that is going to hold up, because it is just too high. However, if it comes even close it will be a terrific addition to the armamentarium of treatments for this difficult-to-treat disease.

### ***SDT:* Who should Use Provent Therapy?**

**Westbrook:** One of the nice things about Provent Therapy is that it is so easy to try. And it is inexpensive to try. You do not have to manufacture a mandibular device. You do not have to send someone home with an expensive mask. And clearly, surgery carries with it not only initial expense and discomfort, but also some risk. With Provent, you can provide someone with a 5-day supply of these little devices, and know two things at the end of this time: 1) Are they going to use it?; 2) Does it work? Because it is easy to check on whether it is successfully managing the airway problems. That is a huge advantage.

One can say that we cannot accurately select which patients are going to respond to Provent, because not all of them do. We can not accurately pick those people out, but it does not make too much difference because we can accurately find out whether it works. Right now it seems to work in mild, moderate, and severe sleep apnea with AHIs up to 60. It works in all severity levels, and as far as we know right now, and we will certainly have more information on this in the next few months, it works in patients who are obese or not obese. It works in males, females, young people, old people. Right now, we can not accurately predict the people for whom it would not work. In that, we are not too much different from other therapies. Because with CPAP, we can not really predict who’s going to use it and who is not going to use it.

### ***SDT:* How will Provent Therapy Improve Patient Care?**

**Westbrook:** I think it will certainly improve patient care, because if we have something that patients will actually use, that will lead to a huge improvement. Again, the gold standard of treatment is CPAP. But too many patients do not use it, or do not use it adequately. And there is a huge pool of patients already diagnosed, and undiagnosed, and they need treatment. And too many of those folks just do not get any treatment at all. Here we have something that is simple to use, inexpensive to try, and if it works and they use it, it will be terrific.

It seems that because it is so unobtrusive, and so easy to use, that patients are more likely to use it. And if that is the case, it will be a huge advantage in treating this disease. It is so simple to use, you can carry a week’s supply in your pocket and go out hiking in the woods. You do not need any external power source. You do not need batteries. You just need these little adhesive devices that you stick on the end of your nose. Most people can tolerate it, and they get used to it rather quickly—3 to 7 days.

### ***SDT:* Can Compliance be Measured?**

**Westbrook:** we do not have a way of effectively measuring time on pressure, so we have to go by patient self report, and I’m sure you are aware of the problems with patient self reporting. But the other way we have of keeping track of compliance is the fact that these are prescribed items. So if someone gets a 30-day supply, and they do not order it again for another 60 days, it suggests that they are using it an average of every other night. If on the other hand, at the end of 30 days, they order another supply and get the prescription refilled, then they are using it daily. So this is, in a very real sense, an objective way of measuring use.