Volume 7 Number 1 February-March 2012

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The Journal of Pulmonary Technique

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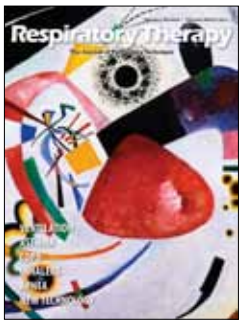

Respiratory Therapy™
The Journal of Pulmonary Technique

**Vol. 7 No. 1**
**February-March 2012**

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## DEPARTMENTS



## ARTICLES



# Editorial

## Breathless

A recent paper discussed the actual experience of breathlessness in COPD patients, as compared to breathlessness in other conditions, and I think the patients' comments are instructive.*

The authors wrote: For COPD patients, breathlessness was perceived as a self-inflicted symptom. Its insidious nature and response from services disaffirmed their experience and gradually led to greater disability in the course of illness. Breathlessness as a symptom affected 95% of patients with COPD, and lesser percentages in cancer, heart failure and ALS.

The salient observation the researchers made is that COPD sufferers tended to blame themselves for their condition, as opposed to cancer patients (except those who smoked), heart patients, and ALS sufferers. It should also be noted that some physicians did not adequately explain the condition to their patients, which caused the patients to be confused and anxious.

In the beginning breathlessness showed itself as hardly noticeable and it developed gradually. Patients easily adapted to its restrictions as they accepted them silently in everyday routines and conveniently explained them away. Patients said: "...It (breathlessness) is over time slowing down everything, and it wasn't until my daughter said: 'You're getting so slow mum you're like an old lady.' [...] I suppose that was when I became aware that it was having an effect on my everyday life."

Patients spoke about breathlessness in terms of the feelings associated with bad episodes: distress, anxiety, panic and fear of dying. They also told as frequently about the disability it caused, inhibiting every movement. Eleven of the 18 patients [in the study] evaluated it as their worst symptom.

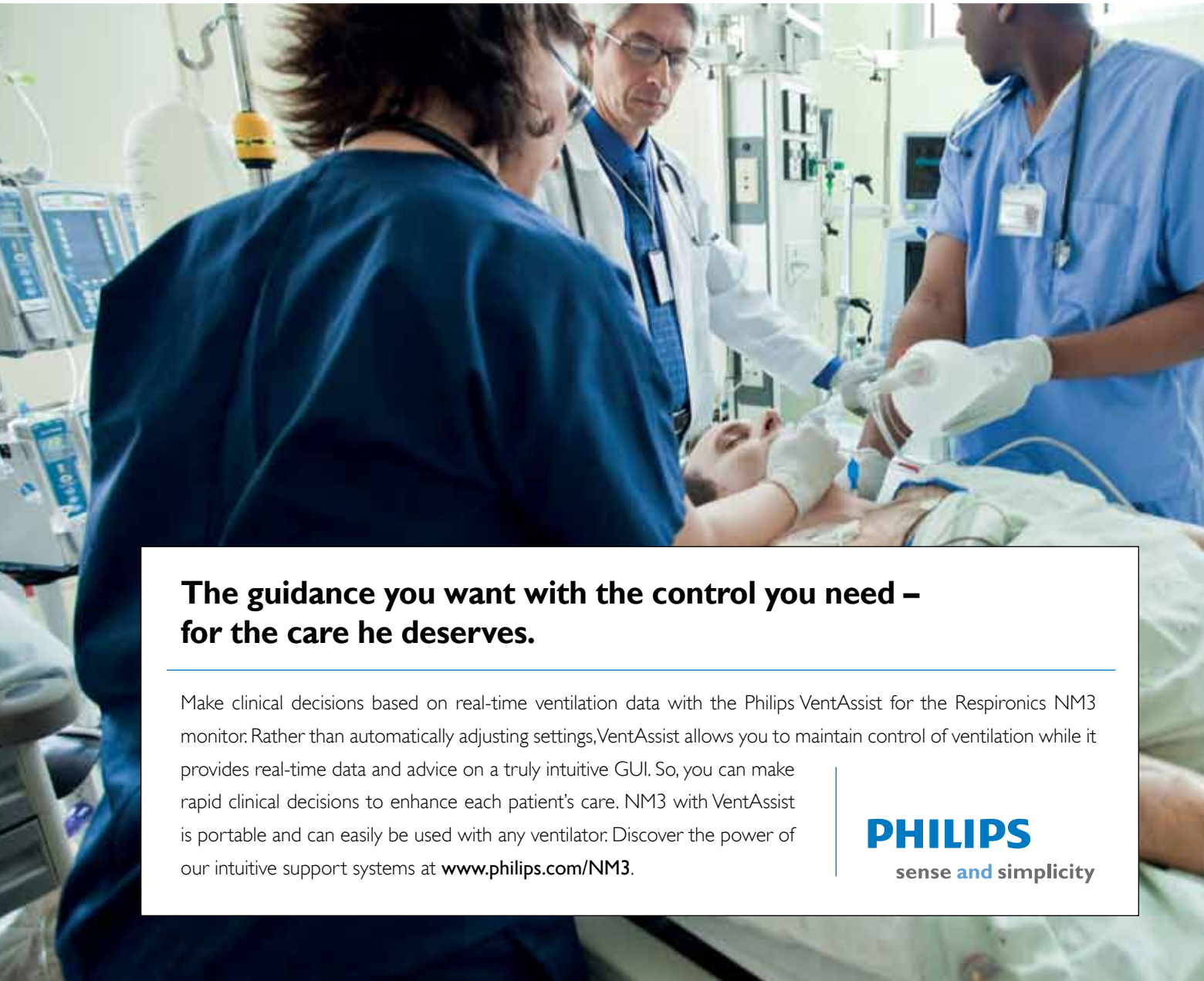
Patients only consulted health professionals after having lived for long periods with breathlessness. When they were confronted with a crisis, they were alarmed and they sought medical help. COPD derived its meaning from other diseases. Those with a smoking history feared to receive the news they had cancer: "I've been to the doctors and they've told me I've got COPD — what is it? Now the doctor hasn't even explained what those 4 letters mean and the worst thing about it is, it starts off with C, and first thing you think: Oh have I got cancer but this is the thing that is wrong, it's not a well known disease yet it's one of the greatest killers."

Instead of a definite diagnosis, patients received different labels: bronchitis, COPD, asthma, emphysema. The acronym of COPD starts with "chronic," implying a long-term and relatively manageable condition.

Over time, sufferers found out for themselves what breathlessness means: daily troubles with breathing, impaired mobility, anxiety restricting them to home, growing dependence. Patients started a quest for effective treatment once they realized the full extent of the symptoms. However, this proved to deliver little in terms of relief. Over time they built up knowledge, through personal experience, often without much expert advice. In the advanced stages of illness they re-evaluated the diagnosis and identified issues which had been left unaddressed. Patients found that full disclosure of the nature and course of breathlessness was crucial for its management: "At the time if I can remember rightly we weren't really told that [...] it would gradually get worse. We were just told this is what you've got, get on with it."

All 18 patients with COPD mentioned external causes for their diagnosis, one person added an internal cause. All patients attributed breathlessness to a

*Continued on page 37...*



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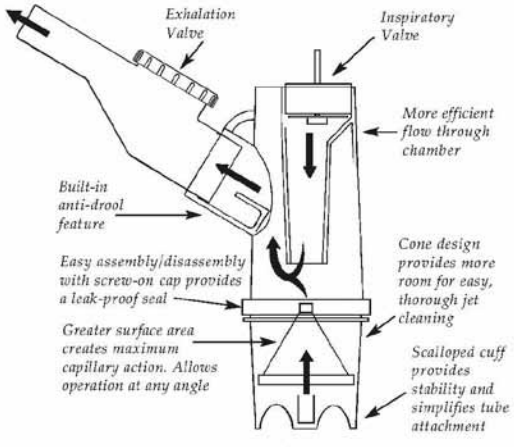


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# News

☐ February-March 2012

## LETTER

I want to commend you on your Respiratory Therapy magazine. I don't know how long it has been in circulation but I came upon it recently and thoroughly enjoyed reading all the articles and advertisements. It is, in my opinion, the best respiratory therapy magazine currently available and I recommended to all my students that they go to your website and make use of that rich source of information. I am the Director of Clinical Education for the US Army and Navy school for respiratory therapy and I try to stay abreast of all new technologies, therapies, and equipment. I found many interesting topics in your latest issue and even contacted some of the advertisers for information on their products.

*Oscar Lopez-Martinez MAEd, RRT, CPFT*
*Director of Clinical Education*
*Interservice Respiratory Therapy Program*
*Medical Education & Training Campus*
*Fort Sam Houston, TX*

## TINY TROUBLE

Nanoparticles of cerium oxide, a common diesel fuel additive used to increase the fuel efficiency of automobile engines, can travel from the lungs to the liver and cause liver damage, according to researchers at Marshall University. There is a dose-dependent increase in the concentration of cerium in the liver of animals exposed to the nanoparticles, which are only about 1/40,000 times as large as the width of a human hair. These increases in cerium were associated with elevations of liver enzymes in the blood and histological evidence consistent with liver damage. Cerium oxide is widely used as a polishing agent for glass mirrors, television tubes and ophthalmic lenses. Cerium oxide nanoparticles are used in the automobile industry to increase fuel efficiency and reduce particulate emissions. Some studies have found that cerium oxide nanoparticles may also be capable of acting as antioxidants, leading researchers to suggest these particles may also be useful for the treatment of cardiovascular disease, neurodegenerative disease and radiation-induced tissue damage.

## OPEN ACCESS

Open access to the latest research became even easier with the launch of BioMed Central's newly redesigned website (www.biomedcentral.com). The company, which pioneered the open access model and now publishes over 220 open access journals, has introduced a streamlined design and new look which makes the high-traffic website site much more straightforward to navigate. The redesigned site also introduces a range of new and enhanced features. Emphasizing the company's commitment to meeting the evolving needs of authors and readers, the new site includes: a greatly improved "My BioMed Central" section

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offering users convenient access to the latest research in their subject areas together with status updates on manuscripts which they are submitting or reviewing; enhanced navigation for archives, supplements and special article collections; additional RSS feeds and embedded social linking technologies and improved subject gateways, providing a central starting point to find research on particular scientific topics. In addition to the new appearance, the site is built using modern open-source java technologies, which provide a firm foundation for the enhancements and new services still in development.

## INFLAMED LUNGS

The bacterium that causes Legionnaires' disease manipulates our cells to generate the amino acids it needs to grow and cause infection and inflammation in the lungs, according to researchers at the University of Louisville. The researchers examined Legionella, which is an intercellular bacterium that exists in amoebae in the water systems and transmitted to humans through inhalation of water droplets. Cooling towers and whirlpools are the major sources of transmission. The bacterium uses the amoeba's cellular process to tag proteins, causing them to degrade into their basic elements of amino acids. These amino acids are used by the bacteria as the main source of energy to grow and cause disease. The same process occurs in a human or animal host who inhales the bacterium and is diagnosed with Legionnaires' disease, except that the the bacteria trick the host into tagging the proteins for degradation to generate the amino acids. The researchers found that by inactivating the bacterial virulence factor responsible for tricking the cell into tagging proteins in mice, the pulmonary disease was totally prevented, due to disabling the bacteria from generating amino acids. The researchers said that by interfering with the bacterium's sources of nutrients, they could stop it from thriving and causing disease.

## EXPOSURE

Metabolic syndrome biomarkers predict subsequent decline in lung function after particulate exposure, according to new research involving rescue personnel exposed to World Trade Center (WTC) dust. In a study of 327 non-smoking FDNY 9/11 rescue workers at NYU Langone Medical Center, metabolic syndrome biomarkers measured within six months of exposure to WTC dust predicted decline of forced expiratory volume in one second (FEV1) over the next six years. Study participants with dyslipidemia, elevated heart rate or elevated leptin levels had a significantly increased risk of developing abnormal lung function during follow-up. All subjects had normal lung function prior to 9/11. Biomarkers were available for 71 cases and 166 controls. Lung function in cases continually declined in the median 28 months between baseline and follow-up examinations, while lung function improved in controls. The findings suggested that systemic inflammation, a hallmark of the metabolic syndrome, may play a role in promoting lung function impairment in patients with particulate exposure.

## IN THE CUT, NOT

Pneumonia, not a deep incision surgical site infection, is the most common serious infection after heart surgery, according to new research at the University of Pennsylvania Medical Center. Researchers analyzed 5,100 patients in a heart surgery registry. The median time to major infection was 14 days after heart surgeries. Forty-two percent of all major infections occurred after hospital discharge. Half of these patients had no evidence

of infection before they were discharged from the hospital. Researchers found 742 infections, and 278 were classified as major. These included pneumonia in 2.4%; c. difficile colitis, in 1%, blood stream infections, and deep-incision surgical site infections.

## DUST-UP

Researchers at the Chinese University of Hong Kong reported that dust storms have an adverse effect on emergency hospital admission for COPD. They obtained data on daily emergency admissions to major hospitals for respiratory diseases in Hong Kong, and indices of air pollutants and meteorological variables over a five year period. Results showed that significant increases in emergency hospital admission due to COPD were found two days after a dust storm episode, with a 5% increase in risk. There is a link between the raised concentrations of coarse particles encountered during dust storms and a higher risk of hospital illnesses for respiratory illness, in particular, for COPD.

## NEW REGIMEN

Healthcare providers in the United States have a new way to treat latent tuberculosis infection, according to recommendations released today by the CDC. The new recommendations, published in CDC's Morbidity and Mortality Weekly Report, provide guidance on how to administer a new 12-dose regimen for TB preventive therapy that will significantly shorten and simplify the course of treatment from about nine months to 12 weeks. The recommendations are based on the results of three clinical trials, as well as expert opinion. A multi-national clinical trial conducted by CDC's TB Trials Consortium found that a once-weekly regimen of the anti-TB drugs rifapentine and isoniazid taken as directly observed therapy over a period of three months was as effective in preventing TB disease as the standard self-administered nine-month daily regimen of isoniazid alone, and was completed by more patients. The new regimen has a significant benefit over the previous standard of treatment by cutting the doses required from 270 daily doses to 12 once-weekly doses.

## FALLOUT

World Trade Center responders suffer from asthma at more than twice the rate of the general US population as a result of their exposure to the toxic dust from the collapse of the WTC towers, according to researchers at North Shore-LUK Health System and Hofstra School of Medicine. The study population consisted of a prospective cohort of 20,834 responders who received medical screenings from July 2002 to December 2007 at the WTC Medical Monitoring and Treatment Program. Eighty-six percent of WTC responders in this study population were men and the average duration of work at the WTC sites was 80 days. Forty-two percent of study participants were uniformed and other law enforcement and protective service workers. Other occupations of responders consisted of construction workers, installation, maintenance and repair workers, along with transportation and material moving workers, who were essential to service restoration and/or debris removal and clean-up efforts. Researchers found that 6.3% of WTC responders reported asthma symptoms or attacks, while only 3.7% of the US general population reported asthma symptoms or attacks. The asthma rates remained stable among the general population during the entire period, but there were large increases in 12-month asthma rates among WTC responders from 2000 to 2005. When comparing asthma rates of WTC responders in 2000 (one year before 9/11) to 2005, the 12-month asthma rate increased by 40 times. Furthermore, when comparing 2002 (one year after 9/11) to 2005, the 12-month asthma rate doubled among WTC responders.

## NOT WORKING

A Johns Hopkins Children's Center study of Baltimore City children with asthma shows that two programs designed to improve disease outcomes among those who may be affected the worst fall short of expectations. The Breathmobile, a mobile clinic that brings preventive asthma care and education to low-income, inner-city patients did not improve asthma outcomes, nor did home visits by asthma educators. The combination of the two had minimal and short-lived effects, the investigators report. The researchers say they believe each child treated by the mobile team benefited individually, but the cumulative, population-wide effects remained minimal because only a handful of those eligible for the services actually used them. Despite free care, multiple locations and many reminders to schedule a visit, only half of the families whose children qualified for mobile clinic care did so, and only 20% of those eligible to receive care showed up for their appointment.

## EITHER WAY

Pediatric asthma researchers at Washington University School of Medicine in St Louis and elsewhere found that daily inhaled steroid treatment was no different from preventing wheezing episodes than treating the child with higher doses of the drug at the first signs of a respiratory tract infection. They also found that daily treatment was comparable to use of the inhaled steroid intermittently at decreasing the severity of respiratory-tract illnesses, reducing the number of episode-free days or school absences, lowering the need for a rescue inhaler for acute asthma symptoms, improving quality of life or reducing visits to urgent care or the emergency room. The researchers studied nearly 300 preschool-age children with frequent wheezing and at high risk for future persistent asthma. The children in the trial were between 12 months and 53 months old, had recurrent wheezing and were at high risk for a worsening of asthma-like symptoms that could require treatment with oral steroids and/or a visit to urgent care or emergency room. During the trial, the children received either a dose of budesonide once a day through a nebulizer or an inactive placebo. At the first signs of a respiratory tract illness, those children who received the inactive placebo received a higher dose of budesonide twice a day, while those who received daily budesonide received a placebo twice daily and kept taking their regular budesonide. Neither the patients nor the physicians knew who received the active drug until the trial was over. Parents kept a daily diary of symptoms, medications, and visits to health care providers.

## STAY OUT OF THE HOSPITAL

Researchers from Boston University, Save the Children and the WHO found that young children treated at home for severe pneumonia by Pakistan's network of "lady health workers" were more likely to get well than children sent to health facilities. In the study, based in northern Pakistan, researchers found that home-based treatment of severe pneumonia by a corps of trained "lady health workers" armed with five days' worth of oral amoxicillin reduced treatment delays and failures compared to standard practice, which was to administer one dose of antibiotics and refer a child to a hospital or clinic for intravenous drugs. The researchers said their study was proof that trained community health workers can identify and manage a very complex disease. The researchers added that they hadn't suspected their study would show that the home care would produce better outcomes. The study authors noted that outpatient management of pneumonia offers significant cost-savings for families and health systems, while also reducing the risk that children with pneumonia will develop complications from infections in crowded hospital wards. The study compared outcomes between 1,857 young children treated at home with oral amoxicillin for five days, and 1,354 children in a control group who were given one dose of cotrimoxazole and referred to the nearest health center for treatment. Researchers looked at treatment failure at six days, as well as relapse within 14 days. With failure defined as the continued presence of fever or lower chest in-drawing on Day 6, the results were clearly in favor of home-based therapy: a 9% failure rate, versus 18%. The authors of the study credited the lady health workers, community members with basic training who are employed by the government, with accurately diagnosing severe pneumonia in 94% of the cases, which were validated by an independent assessor. Pakistan's network of 90,000 lady health workers was established in 1994 by then-prime minister Benazir Bhutto in an effort to improve maternal and child health and provide jobs for women, particularly in rural areas where three-quarters of the country's population lives. The health workers, who are required to have at least an eighth grade education, are each responsible for 150 families.

## STIMULATING

Hypoglossal nerve stimulation produced increases in airflow in OSA patients without arousing them from sleep, according to a new study from the Johns Hopkins Sleep Disorders Center. The study suggests the potential therapeutic efficacy of HGNS across a broad range of sleep apnea severity and offers an alternative to CPAP, the effectiveness of which is limited by poor patient adherence. Researchers enrolled 30 middle-aged patients with moderate and severe obstructive sleep apnea who were implanted with the HGNS system. The pacemaker-like device monitors breathing patterns and is activated during sleep to stimulate the hypoglossal nerve, which controls muscles in the upper airway. The device's current was increased stepwise during non-REM sleep. At each current level, stimulation was applied on alternating breaths so that responses in inspiratory airflow could be compared to adjacent unstimulated breaths, and maximal inspiratory airflow and IFL were measured. HGNS produced linear increases in VImax with increasing current. Mean VImax increased significantly from 215±21ml/s off stimulation to 509±37mL/s on stimulation. VImax increased in all patients, and IFL was abolished entirely in 17 (57%). Normal or near-normal levels of flow were achieved in all 30 patients.

## INTERMISSION

The FDA approved Intermezzo (zolpidem tartrate sublingual tablets) to treat insomnia characterized by middle-of-the-night waking followed by difficulty returning to sleep. Zolpidem tartrate was first approved in the United States in 1992 as Ambien. Intermezzo is a lower dose formulation. The recommended and maximum dose of Intermezzo is 1.75 milligrams for women and 3.5 mg for men, taken once per night. The recommended dose for women is lower because women clear zolpidem from the body at a lower rate than men. Intermezzo was studied in two clinical trials involving more than 370 patients. In the studies, patients taking the drug had a shorter time to fall back asleep after waking compared to people taking an inactive pill (placebo). The most commonly reported adverse reactions in the clinical trials were headache, nausea and fatigue. Intermezzo may cause serious side effects, including getting out of bed while not fully awake and doing an activity that you do not know you are doing or do not remember having done. Reported activities while under the influence of sleep medicines include driving a car, making and eating food, having sex, talking on the phone, and sleepwalking without knowing at the time or remembering later. Chances of such activity increase if a person has consumed alcohol or taken other medicines that make them sleepy.

## LIVING NIGHTMARES

Less than 8% of the general population experiences sleep paralysis, but it is more frequent in two groups — students and psychiatric patients — according to a new study by psychologists at Penn State and the University of Pennsylvania. Sleep paralysis is defined as a discrete period of time during which voluntary muscle movement is inhibited, yet ocular and respiratory movements are intact. Hallucinations may also be present in these transitions to or from sleep. Alien abductions and incubi and succubi, as well as other demons that attack while people are asleep, are implicated as different cultural interpretations of sleep paralysis. The Salem witch trials are

now thought possibly to involve the townspeople experiencing sleep paralysis. And in the 19th-century novel Moby Dick, Ishmael experiences an episode of sleep paralysis in the form of a malevolent presence in the room. Researchers looked at 35 published studies from the past 50 years to find lifetime sleep paralysis rates. These studies surveyed a total of 36,533 people. Overall they found that about one-fifth experienced an episode at least once. Frequency of sleep paralysis ranged from once in a lifetime to every night. Twenty-eight percent of students reported experiencing sleep paralysis, while nearly 32% of psychiatric patients reported experiencing at least one episode. Thirty-five percent of people with panic disorders surveyed reported experiencing these episodes. Sleep paralysis also appears to be more common in non-Caucasians. People experience three basic types of hallucinations during sleep paralysis — the presence of an intruder, pressure on the chest sometimes accompanied by physical and/or sexual assault experiences and levitation or out-of-body experiences.

## SLEEP WELL OR ELSE

Sleep-disordered breathing among older women leads to hypoxemia and thus raises the risk of dementia or cognitive impairment, according to researchers at UC San Francisco. Sleep disordered breathing is common among older adults and affects up to 60% of elderly populations. The researchers assessed 298 older females (average 82.3 yrs) who had no signs of dementia when the study began. Overnight polysomnography was measured over a three year period. Subsequently, they gathered data on the women's cognitive status. The researchers found that 35.3% of the 298 elderly females met the criteria for sleep-disordered breathing. After a follow-up period of about 4.7 years, 20.1% developed mild cognitive impairment and 15.8% developed dementia. Nearly forty-five percent of the women with prevalent sleep-disordered breathing developed dementia or mild cognitive impairment versus 31.1% of the women without the disorder. The researchers also found that an oxygen desaturation index of at least 15 and a high proportion of sleeping time in hypopnea or apnea was associated with a higher rate of dementia or mild cognitive impairment. Information is from Medical News Today, Christian Nordqvist, copyright Medical News Today.

## HOME ALONE

Children in single parent homes were 50% more likely to return to the hospital within a year for asthma than kids from two-parent homes, according to researchers at Cincinnati Children's Hospital Medical Center. Single-parent status, annual household income less than $60,000 and time constraints within the home were linked to this increased rate of readmission. Asthma is the most chronic condition of childhood, accounting for 12.8 million missed school days each year.

## FOOD FIGHT

Oral food challenges are rarely used by physicians to detect food allergies, according to researchers at Children's Memorial Hospital, Chicago. Researchers surveyed 40,104 children, identifying 3,339 cases of food allergy. Only 61.5% received a formal physician diagnosis. About 15% of children who received a physician diagnosis underwent an oral food challenge. Children with severe symptoms such as anaphylaxis, wheezing, trouble breathing, and low blood pressure were more frequently diagnosed by a physician, and more frequently confirmed by oral food challenge. The researchers noted that because a large proportion of children with convincing food allergy are not diagnosed by a physician and not given a food challenge, food allergy may be underdiagnosed in the US. When food allergy is suspected, it is recommended that patients be referred to an allergist who can determine which food allergy tests to perform, determine if food allergy exists, and counsel patients on food allergy management. About one in 20 children have food allergies.

### FAT KIDS AT RISK

Obese adolescents have an increased risk of sleep apnea or abnormal breathing during sleep, according researchers in Mexico, who compared overnight sleep studies of 27 obese teens with and without asthma to overnight sleep studies of 23 average weight adolescents with and without asthma. The study showed nearly 73% of obese children were diagnosed with sleep apnea/hypopnea syndrome (SAHS) while none of the adolescents at a healthy weight were diagnosed with SAHS. Children who are overweight are nearly 2-1/2 times more likely to have asthma than those who are not overweight.

### JADED TEXTERS

Research at Women and Children's Hospital in New York revealed that daily text message reminders can improve medication adherence for kids, but not teens. Researchers collected info on kids age 6 to 17 with asthma who used inhaled corticosteroids. They sent daily text messages to remind them to take their medication. Two of seven participants showed improvement and the text messaging was deemed valuable. But teenagers did not show improved adherence as a result of being texted, perhaps because they receive so many texts as a matter of course.

### LONELY AND SLEEPLESS

A study at the University of Chicago revealed that loneliness is linked to sleep disruption. People who scored themselves high on loneliness were also the ones whose monitored sleep patterns were most fragmented. The researchers found that lonely people slept the same amount of time, but woke up more during the night. The researchers recruited 95 adults of a traditional, close-knit farming community in rural South Dakota and asked them questions about their loneliness, depression, anxiety, and stress, as well as subjective sleep quality and daytime sleepiness. The participants were given wrist actigraphs. Higher loneliness scores were linked to significantly higher levels of sleep fragmentation. Information is from Medical News Today, Catharine Paddock, PhD, copyright Medical News Today.

## PRODUCTS

### EDUCATION ONLINE

CareFusion's Center for Safety and Clinical Excellence, built on the CareFusion campus, provides education and training on issues that are changing healthcare. With healthcare reform coming, the online Center for Safety will provide industry insights from CareFusion's C-Suite, including: weekly blogging from CareFusion clinical thought leaders on the latest healthcare issues; daily twitter feed with real-time updates on what's happening in healthcare; and access to the CareFusion clinical evidence repository, they can be searched by clinical focus and content type. To view the site, visit www.carefusion.com/centerforsafety or follow the company on Twitter @centerforsafety.

### LAWSUIT

Newport Medical Instruments Inc announced that it filed a patent infringement lawsuit in the US District Court for the Middle District of Florida against Flight Medical Innovations Ltd of Israel. The suit claims that Flight Medical's Flight 60 ventilator infringes upon a US patent owned by Newport Medical. "In our 30 year history, we have never filed a lawsuit. We had hoped to avoid litigation altogether," stated Hong-Lin Du, MD, President of Newport Medical. "Unfortunately, Flight Medical gave us no choice but to file this lawsuit in order to protect our valuable intellectual property rights." Newport Medical is a privately owned company based in Costa Mesa, CA. Newport ventilators, designed for use in hospitals, sub-acute facilities, medical transportation and homecare, are distributed in over 116 countries.

### APPROVED

3B Products, LLC announced FDA approval of its 3B Flex-Lite nasal mask, a light, flexible and comfortable alternative to standard CPAP masks. The Flex-Lite, patterned on a cannula design, comes with multiple sized nasal pillows for a perfect fit and increased patient compliance. The cannula design is often preferable for patients unable to tolerate standard 22mm CPAP air tubing on or near the face. Comfortable for both back and side sleepers. Contact 3Bproducts.com.

### EVOLVED

CHAD Therapeutics of Naples FL announced its Evolution OM-900. The company noted: "With a minimum of 2 years of operation using just two AA batteries, frequent battery changes are a thing of the past. Our highly sensitive technology can sense both weak and strong inhalation patterns. We offer a wide range of LPM settings, from 1-7 LPM equivalent as well as a continuous flow setting. The single-lumen design provides a 5:1 savings ratio at all settings, a uniform pulse delivery method, and operation between 200 – 3,000 PSI. These features, and our 2 year warranty, will provide an optimal return on your investment." Contact chadtherapeutics.com, (800) 423-8870.

### DRIVE, HE SAID

Drive Medical announced the acquisition of Inovo, Inc/CHAD Therapeutics ("Inovo"), a leading manufacturer of oxygen conserving devices, regulators and other respiratory products for the home care, long-term care, hospital and emergency markets. Inovo manufactures a broad line of patented oxygen conserving devices and regulators under private label for several leading manufacturers and distributors in the industry, as well as under its CHAD Therapeutics brand. Inovo acquired CHAD Therapeutics in 2008. Inovo will operate as a stand-alone division of Drive and will continue to manufacture its products from its ISO certified facilities located in Naples, FL. Contact drivemedical.com.

### PARTNERSHIP

Midmark Corporation, a maker of diagnostic devices for ambulatory care, announced a partnership with Cleveland Medical Devices, a leader in sleep diagnostics technology, launching the Midmark SleepView Monitor and SleepView Portal. The Midmark SleepView Monitor developed by Cleveland Medical Devices is the market's smallest and lightest portable home sleep monitor that meets the American Academy of Sleep Medicine's recommended channel set for Type III monitors. The Midmark SleepView Portal offers prescribing physicians secure, HIPAA compliant online access to registered polysomnographic technologists and board-certified sleep physicians who provide scoring, professional interpretation and treatment recommendations. Contact midmarksleepview.com, (800) MIDMARK, or clevemed.com.

### VAPOR-IZED

Uptake Medical announced the first commercial use of the InterVapor System for endoscopic lung volume reduction in a patient with severe emphysema. The patient successfully underwent treatment with InterVapor, the first endoscopic lung

volume reduction system for the treatment of severe emphysema that uses the body's natural healing processes without leaving foreign materials in the lung. The patient was treated by the team at the Thoraxklinik in Heidelberg, Germany, recognized as a leading institution for pioneering new therapeutic options for people with emphysema. The InterVapor System directly induces reduction of hyperinflation, a problem for patients with severe emphysema. InterVapor is a non-surgical procedure which treats hyperinflated parts of the lungs with heated water vapor. InterVapor triggers the body's natural healing process, gradually reducing the treated portion of the lungs and increasing the ability to breathe more fully. Unlike other approaches to lung volume reduction, InterVapor does not leave foreign materials in the lung, which may require additional procedures for adjustment or removal. Results from the VAPOR trial demonstrated clinically significant improvements in lung function and quality of life for patients with severe emphysema. In clinical studies, InterVapor has demonstrated clinically meaningful improvements in breathing function, exercise capacity and quality of life. Contact uptakemedical.com.

## NEW STUDIES

Covidien announced that 75 new clinical studies on the company's patient monitoring technology were presented at the American Society of Anesthesiologists (ASA) recent annual meeting in Chicago. Tong Gan, MD, and colleagues at Duke University Medical Center in Durham, NC conducted a study to evaluate the correlation between BIS technology and Ramsay sedation scores (RSS). They looked at whether BIS monitoring technology caused a change in depth of consciousness and reduced the risk of adverse events during nurse-administered moderate sedation. This prospective, observational study involving nearly 1,800 patients undergoing minor therapeutic and diagnostic procedures (eg, colonoscopy) found a significant inverse relationship between BIS values and RSS values. BIS technology-guided anesthesia administration enabled adequate sedation delivery and resulted in fewer sedation-related adverse events such as apnea, restlessness and significant desaturation ($SaO_2$<90%) compared to using RSS.[1] A separate study led by Dr Gan found the combination of three medical factors, mean arterial pressure (MAP), minimum alveolar concentration (MAC) and BIS value, can help anesthesia professionals determine who may be at risk for poor outcomes after surgery. Researchers evaluated data from nearly 19,000 patients who received an inhaled anesthetic during a non-cardiac surgical procedure. Patients with low MAP, MAC and BIS values ("triple-low") had 2.5 times higher risk of death in the first year after surgery compared to those with three normal values. The risk was significant even after adjusting for patient age and preoperative risk profile.[2] David Green, MB, BS, and Buzz Shephard, MB, BS, at King's College Hospital in London conducted a study to determine whether using BIS technology and regional oxygen saturation ($rSO_2$) monitoring, along with esophageal Doppler monitoring (EDM)-guided fluid replacement, can enhance fluid management during major abdominal surgery. Green and Shephard cited three previous clinical trials that found EDM use reduced hospital length of stay and incidence of complications in patients undergoing this type of surgery. The current study showed a regimen of BIS technology-guided anesthesia administration, $rSO_2$ monitoring (with INVOS cerebral/somatic oximetry) and EDM helped lower sodium and fluid requirements compared to EDM alone. The researchers recommended further investigation into using BIS technology and $rSO_2$ monitoring to improve patient outcomes during perioperative care.[3] In a study conducted at Hokkaido University Hospital in Japan, a research team led by Yosuke Uchida, MD, examined changes in cerebral oxygen saturation during pediatric heart surgery and the relationship of cerebral oxygen saturation to early postoperative outcomes. INVOS cerebral/somatic oximetry was used to measure $rSO_2$ in 69 children under age six who had undergone cardiopulmonary bypass (CPB) in the past 20 months. Patients were divided into two groups: those with cyanotic congenital heart disease (CHD), which is characterized by bluish skin discoloration due to a lack of oxygen in the blood, and those with non-cyanotic CHD. Investigators assessed early outcomes by the duration of intubation, length of intensive care unit and hospital stays, and the number of failing organs. The study found that in non-cyanotic patients, preoperative $rSO_2$ levels may be a predictor of clinical outcomes during CPB. There was no significant correlation between $rSO_2$ and postoperative early outcomes in cyanotic patients.[4] A study by Eric Mills, MSc, Buzz Shephard, MD, and David Green, MB, BS found that the LiDCO*rapid* PulseCO algorithm can access data directly from a noninvasive blood pressure monitor (CNAP* 500 blood pressure finger cuff) and provide continuous, clinically accurate feedback on hemodynamic changes in patients undergoing vascular surgery. Traditionally, hemodynamic parameters (eg, oxygen saturation levels, blood pressure and blood volume) have been gathered through pulmonary artery catheters threaded into a patient's heart. The results showed noninvasive CNAP monitoring can be successfully integrated into the LiDCO*rapid* monitoring platform.[5] [References: 1. Gan T, Hanna MA, Lu MY, Manberg P, Habib A. Bispectral Index Guided Moderate Sedation Resulted in a Lower Incidence of Sedation Complications. Study Abstract. ASA 2011. Presentation A241. 2. Gan T, White W, Hale B, Moretti E, Newman M. Mortality at One Year is Increased by a "Triple Low" Combination of BIS, Blood Pressure and Anesthetic Concentration. Study Abstract. ASA 2011. Presentation A1574. 3. Green DW, Shephard B. Influence of Depth of Anaesthesia (DOA) and Cerebral Oximetry (rSO2) Monitoring on Na and Fluid Requirements using the Oesophageal Doppler (ODM) for Targeted Fluid Replacement During Prolonged Major Abdominal Surgery. Study Abstract. ASA 2011. Presentation A277. 4. Uchida Y, Ito R, Ando S, Watabe A, Morimoto Y. Changes in Oxygen Saturation During Pediatric Cardiac Surgery with Cardiopulmonary Bypass and the Relation with Early Postoperative Outcomes – comparison Between Cyanotic and Non-cyanotic Children. Study Abstract. ASA 2011. Presentation A196. 5. Mills E, Shephard B, Green DW. A Comparison of Continuous Hemodynamic Monitoring by LiDCOrapid via Simultaneous Intra-arterial BP vs. Non-invasive BP Waveforms. Study Abstract. ASA 2011. Presentation A659.] Contact covidien.com.

## TRANSPORT CLEARANCE

Dräger has received FDA 510(k) Clearance for its Oxylog 3000 plus Emergency Transport Ventilator. With the Oxylog 3000 plus, critically ill or injured patients can be ventilated whether they are in emergency situations, during air-ambulance transport, or intra-hospital. New features previously only found on intensive care ventilators such as AutoFlow and integrated capnography are now available during transport. Dräger continues its leadership in advanced mechanical ventilation with the release of the Oxylog 3000 plus. A full range of ventilation modes such as VC-CMV, VC-AC, VC-SIMV, SPN-CPAP, PC-SIMV+, and now the addition of AutoFlow offers clinicians the continuity of care when transporting outside of the ICU. AutoFlow also allows for spontaneous breathing at the lowest inspiratory pressures as it

takes the patient's lung mechanics into account when delivering ventilatory support. Integrated capnography is now an available option with the Oxylog 3000 plus. For field clinicians, this can be an invaluable tool to recognize proper airway placement, as well as the ability to monitor a patient's change in metabolism especially in confined spaces such as the air ambulance. The Oxylog 3000 plus made its debut in the United States at the annual congress of the AARC in Tampa, FL. For more information, please contact Draeger Medical, Inc at (800) 437-2437 or email at info.usa@draeger.com.

**PRESTIGIOUS**

Masimo received the American Association of Respiratory Care's (AARC) prestigious Zenith Award for the fourth straight year. The company was honored at the 57th Annual International Respiratory Congress. The AARC's Zenith Award represents Masimo's unwavering commitment, dedication, and industry leadership in providing best-in-breed, innovative patient care solutions. The award is based on quality of products, truth in advertising, service, responsiveness, accessibility of sales staff, and support of the respiratory care profession. This year marks the fourth consecutive year that Masimo was voted to receive the award. More than 400 companies were eligible for one of five awards. Award winners were chosen by the association's membership of 52,000 respiratory care professionals. Contact masimo.com.

**CRITICAL ROLE**

The Passy-Muir Valve plays a very critical role in the rehabilitation of tracheostomy and ventilator patients of all ages across the continuum of care. Beginning in the intensive care unit, the valve is an essential component for achieving the multiple and complex rehabilitation goals of tracheostomy and ventilator patients. Clinicians who understand the importance of the multidisciplinary team shared their strategies for successful rehabilitation in Passy-Muir's fall newsletter, Talk Muir. Subjects include Developmental Therapy in the NICU, Pulmonary Rehab, Sensory Stimlation and TBI, and new products. For more about developmental therapy in the NICU, and the use of the Passy-Muir Valve, see our November/December issue. Passy-Muir also announced a new product, Passy-Muir Cleaning Tablets, made from a detergent used for other medical supplies because it leaves no residue as do some commercially available soaps. The tablets are biodegradable, and come with easy-to-read instructions for patients. Contact passy-muir.com.

**INNOVATIONS**

Philips Respironics showcased innovations for treating and managing the full spectrum of sleep and respiratory patients in the first interactive installation of its kind at Medtrade 2011. The debut of Philips Respironics "Pathway to Better Outcomes" was a dramatic departure from traditional HME exhibits. The interactive experience captured a day in the life of a home care provider in a dynamic 30' x 70' setting. The Pathway's multimedia installations, docent tours and hands-on demonstrations showed the latest sleep and respiratory solutions at work in physician, HME showroom and home environments. It followed three patients' journeys to better sleep and breathing at various points in the care cycle. The Pathway experience showed multiple solutions for the care and management of a sleep apnea patient, an asthma sufferer and a COPD patient. Philips Respironics' product releases range from the innovative HomeLox portable liquid oxygen system that enables patients to generate and store liquid oxygen right in their own home, to its newest entry in sleep therapy – REMstar Pro with AutoIQ. This fixed CPAP system tracks and delivers breath-by-breath therapy for up to 30 days, while it learns the patient's treatment needs, and checks back every 30 hours to see if the therapy pressure it established is on track. This occurs without the need to send someone from the care team to patients' homes, and it keeps the team informed of key patient data. Philips also offers TrueBlue, its first blue gel nasal mask with Auto Seal technology. For comfort and compliance, Philips Respironics built the new nasal pillows GoLife for Men and GoLife for Women, which has a distinctly smaller frame and headgear. Both have soft facial contour arms that gently hug the patient's face to maintain a secure seal and stability even when moving during sleep. In Respiratory Drug Delivery, Philips Respironics introduced OptiChamber Diamond valved holding chamber (VHC) for use with inhaled steroids, as well as long-acting and rescue pressurized metered dose inhaler (pMDI) medications. To help meet clinical and business challenges in a lab setting, the new Alice 6 sleep diagnostic system includes a choice of three head boxes ranging from the Alice LDE for routine sleep studies to the full-featured LDx base station with either the LDxS or LDxN head box. The systems combine flexibility with ease-of-use features, such as automatic Chin EMG referencing and integrated RIP drivers, to enhance the technician's ability to focus on the patient. In an ongoing effort to support compliance, broadband modem with oximetry is also now available. Patient compliance data, including oximetry, can be sent to Encore Anywhere, a web-based patient compliance management system, on a daily basis through the patient's in-home, high-speed Internet connection. Home healthcare providers can verify that compliance data has been successfully reported before the patient even comes into the office. Additionally, Philips Respironics' "Partners in Compliance Management" website offers essential tools to help home healthcare providers and their patients achieve sleep therapy compliance. The free website houses a resource center, best practices and protocols, clinical education and training materials, and reimbursement information. Contact healthcare.philips.com.

**OPTIMUM**

The OptiChamber Diamond valved holding chamber (VHC) from Philips Respironics is smaller than most conventional VHCs and incorporates a stepped mouthpiece, a clear, anti-static chamber, and a low resistance expiratory valve that helps measure breath count and breath hold. For use with inhaled steroids, as well as long-acting and rescue pressurized metered dose inhaler (pMDI) medications, OptiChamber Diamond's intuitive design enhances medication delivery and compliance for patients of all ages, at home or in the hospital. Designed for ease of use and to support compliance, OptiChamber Diamond's mouthpiece and anti-static VHC potentially allow more respirable drug to be delivered to the patient than with a pMDI alone. The stepped mouthpiece is intended to better accommodate smaller mouths and to help children more easily graduate from mask to mouthpiece. The VHC's flat bottom maintains stability and prevents it from rolling when not in use. OptiChamber Diamond's chamber is clear to allow visualization of medication, and its low resistance expiratory valve allows caregivers to count patient breaths to better facilitate medication delivery. OptiChamber Diamond is paired with the detachable LiteTouch VHC mask which is designed to provide comfort and an optimal facial seal. The mask uses a unique design that molds a clear, hard shell to an exclusive soft-seal interface that contours to the face with a minimum amount of pressure to promote aerosol therapy comfort and compliance. Contact philips.com.

## PARTNERS

Philips Respironics has launched the Partners in Compliance Management website. The website is designed for healthcare team members responsible for the compliance management of their sleep therapy patients. The website url is: www.sleepapnea.com/picm. As homecare providers, clinicians, and sleep lab staff deal with the challenges of patient compliance issues and managing patient compliance data, they are turning to manufacturers for related products, services, and expertise. Philips Respironics assists customers by providing a variety of materials to further their knowledge base through helpful tools such as training videos and tutorials, detailed product literature, reimbursement guideline documents, webinars, and interactive tools such as the recently released modem calculator. The Partners in Compliance Management website centralizes all of these materials in one convenient and easy-to-access online resource. The information is housed in three user-friendly sections: Resource Center, Best Practices and Protocols, and Training. As new therapy compliance tools and materials are developed, they will be posted on an on-going basis to the Partners in Compliance Management website.

## TRUE BLUE

The TrueBlue gel nasal mask from Respironics, Inc, is used in the treatment of obstructive sleep apnea (OSA). The TrueBlue gel nasal mask with Auto Seal technology offers a remarkably flexible seal designed to push the limits of performance and fit. The mask incorporates four distinct design features: a freeform spring that provides exceptional flexibility and a reliable seal; an intuitive forehead pad with a distinctly soft premium blue gel that delivers comfort as the freeform spring adjusts; angled exhalation micro ports that rotate 360° and redirect air away from a bed partner; and Respironics' premium blue gel that is thinner and lighter than ever before. Newly designed talon clips make it easy for patients to remove the mask and lock in the same fit, night after night. TrueBlue is available in five comfortable sizes: petite, small, medium, medium wide, and large. Two FitPacks also are offered: small/medium and medium wide/large. Used together with Philips Respironics System One Resistance Control, the mask helps to deliver optimum PAP therapy and comfort. Contact respironics.com.

## LADIES' CHOICE

ResMed Corp recently released their line of CPAP therapy products for women known as "Choices for Her." The offering includes three masks specially designed for women from ResMed's FX Series, as well as the S9 AutoSet for Her therapy device. While the focus of CPAP therapy products has traditionally been male patients, statistics show that there is a significant population of women with sleep apnea. In fact, almost 40% of newly diagnosed sleep apnea patients are women, and the risk of sleep apnea in women after menopause is equal to that of men. ResMed was the first company to design a mask for female patients, understanding that women have unique needs when it comes to CPAP therapy, particularly with mask choice and fit. The "Choices for Her" range allows healthcare providers to offer better fitting options and customized styling for their female patients. The popular FX family of masks, which boasts lightweight, unobtrusive design and comfortable cushion technology, offers a female-friendly version for all three mask categories. The Quattro FX for Her provides the coverage and stability of traditional full face masks with a clear field of vision. The Mirage FX for Her nasal mask is compact, lightweight and features ultra soft headgear with only four parts for easy wear and care. The Swift FX for Her nasal pillows system offers softness, simplicity and stability in a minimalist design. With the versatile headgear featured in all three FX masks, female patients who usually have trouble managing their hair while wearing their mask now have various options to accommodate a wide range of hairstyles. All masks also come in a stylish pink design to promote a softer, more feminine approach to therapy. ResMed also introduced the S9 AutoSet for Her. Offering the quiet comfort of the S9 Easy-Breathe motor and Enhanced AutoSet algorithm, the S9 AutoSet for Her ensures that her sleep environment remains quiet and peaceful. The H5i for Her heated humidifier with Climate Control, the only humidification system that prevents both dryness and rainout, integrates seamlessly with the S9 device to improve comfort and compliance. The S9 AutoSet for Her, paired with any of the FX for Her masks, offers the first complete therapy system designed specially for the female population. Contact resmed.com/choicesforher or (800) 424-0737.

## SINGLE SENSOR SOLUTION

Nonin Medical, Inc, the inventor of finger pulse oximeters and a 25-year leader in noninvasive medical monitoring, announced the European launch of an innovative pediatric sensor for use with the company's EQUANOX Regional Oximetry System. The EQUANOX Advance Model 8004CB Sensor* is the first and only single-sensor solution on the market for patients under 40kg, The 8004CB sensor is designed for use across neonatal and pediatric populations who require accurate oxygen saturation monitoring of cerebral and other tissues in diverse treatment settings. Nonin Medical's complete EQUANOX Advance sensor line, which also includes the Model 8004CA sensor for adults, provides inherent absolute accuracy, reducing the need for complex and time-consuming patient-specific setup. Highly portable and versatile, the EQUANOX Model 7600 Regional Oximetry System and the EQUANOX Advance Model 8004CB Neonatal/Pediatric Sensor provide comprehensive four-channel monitoring in cerebral and somatic positions. Nonin Medical's exclusive dual-emitter, spatially resolved sensor design isolates target tissue with consistent repeatability, and four-wavelength optics deliver rSO2 with absolute accuracy. Advanced signal processing ensures stability and responsiveness. The complete EQUANOX system provides key advantages, including: • Industry-Leading Accuracy** — Absolute accuracy that aligns to true patient physiology, indicating adequacy of perfusion; • Consistency and Reliability — Rapid, reliable, response to physiological change without signal instability and interruptions from ambient electrical and optical interferences; • Portability and Versatility — Lightweight and durable, with long battery life, allowing ease of continuous monitoring during patient transport within the hospital; • Sensor Optimization for the Patient — Unique optical spacing to isolate and target key tissues for neonatal and pediatric populations. [* 510(k) pending; ** Accuracy data based on 8004CA clinical results.] Contact noninequanox.com.

## ACQUISITION

Siemens Healthcare announced that the company has entered into a definitive agreement to acquire all issued and outstanding equity of MobileMD, Inc, of Yardley, PA, a provider of health information exchange (HIE) solutions. MobileMD's cloud-deployed HIE service liberates patient information across a community of providers, regardless of geographic, organizational, or health IT system boundaries. The HIE solution is in use by more than 110 hospitals and more than 2,000 physician practices. When hospitals and physician

practices connect through MobileMD they can engage in a clinical dialog that can better coordinate care by including results delivery, online ordering, referrals, scheduling, and more. The solution reduces providers' reliance on paper, phone and faxed information, and can lead to fewer duplicative or unavailable patient records, improved utilization, and a better patient experience. MobileMD has been active in the health information exchange space since 2005. The company markets the cloud-based 4D HIE, which addresses information sharing in four dimensions: care, service, economics and technology – providing physicians with near real-time, secure, clinical and administrative information regardless of location, affiliation, EMR technology or vendor. Contact medical.siemens.com.

**SMART MOVE**

Hamilton Medical has received 510(k) clearance from the FDA for INTELLICUFF, a new non-invasive automatic cuff pressure solution to reduce Ventilator Associated Pneumonia (VAP) and tracheal injuries. Following AARC Clinical Practice Guidelines, INTELLICUFF assists efforts to reduce VAP and tracheal injuries by continuously monitoring and automatically adjusting cuffed tracheal and tracheostomy tubes, providing a real-time optimization of cuff pressure. The controller module and software of INTELLICUFF are integrated parts of the Hamilton Medical Ventilator, controlled in the Ventilation Cockpit, the same unique user interface used to adjust and adapt ventilation therapy. The Ventilation Cockpit reduces complexity by graphically displaying the patient's status, current treatment, and the required support including current cuff pressure control and monitoring. It provides transparency by protocolized care so clinical staff can always be sure that INTELLICUFF optimizes cuff pressure at all times. By integrating INTELLICUFF within Hamilton Medical's unique intuitive user interface, ICU staff can now be focused on the patient. There is no longer a need to handle two different systems or learn additional user interfaces. INTELLICUFF is available for Hamilton-G5 and S1 Ventilators. Contact Hamilton-medical.com.

**IN AGREEMENT**

Hamilton Medical, Inc announced that they have signed a multi-year agreement with Amerinet, Inc, under which Hamilton Medical's advanced critical care and transport ventilation systems are now available to Amerinet's hospitals nationwide. The Amerinet agreement will provide Hamilton Medical's diverse ventilator system and advanced ventilation technology portfolio through December 31, 2014. Hamilton Medical provides neonatal through adult critical care and transport ventilators to hundreds of leading hospitals worldwide. Hamilton Medical ventilators have some of the industry's lowest cost of ownership as a result of our industry-leading reliability and warranty. With Hamilton Medical's award winning, unique graphical interface that is consistent across all ventilator platforms, a member facility will experience a reduction in training and implementation costs. All of Hamilton Medical's products include our proprietary closed loop technology, Adaptive Support Ventilation (ASV). ASV has proven to reduce ventilator length of stay and therefore improve care for patients and reduce patient care costs. Amerinet collaborates with acute and non-acute care providers – hospitals, surgery centers, longer-term care facilities, clinics and doctor offices – to create and deliver unique solutions through performance improvement resources, guidance and ongoing support. With better product standardization and utilization, new financial tools beyond contracting and alliances that help lower costs, raise revenue and champion quality, Amerinet enriches healthcare delivery. Hamilton Medical, Inc has produced critical care ventilators since 1984. Its ventilation products are routinely reviewed by the independent technology rating firm ECRI and independent customer satisfaction firm, MD Buyline. More information about Hamilton Medical, Inc can be found at http://www.hamilton-medical.com.

# COMPANY PROFILE

# Aerogen

**Describe your product and its unique features.**

Aerogen's vibrating mesh technology is a world leader in nebulization therapy. The company's leading product in the US market is the acclaimed Aeroneb Solo nebulizer which enables silent, efficient drug delivery for infants through to adults. The Aeroneb Solo is based on vibrating mesh technology and creates a fine particle, low velocity aerosol optimized for deep lung deposition. The vibrating mesh does not heat or degrade the medication, ensuring the drug integrity is maintained. It aerosolizes a broad range of formulations including suspensions, solutions, proteins and peptides. The Aeroneb Solo delivers more drug to the lungs than jet nebulizers or metered dose inhalers. The Aeroneb Solo is easy to install and intuitive to use, thereby making it a convenient device for the care giver to use.

**Tell us about the latest advances in the area your product serves.**

The intensive care setting is constantly evolving to better meet patients' needs. Aerogen works closely with respiratory therapists to ensure that its products help provide the best possible care. The company introduced its Continuous Nebulization Tube Set last year, which is customized for use with the Aeroneb Solo to ensure safe continuous nebulization and prevent tubing misconnection. This represents progress in meeting both the RTs' and the patients' needs.

**Discuss your R&D process, including clinical user input.**

Clinical user input is central to Aerogen's design process. At every stage of the R&D process Aerogen's focus is on the needs and requirements of the clinical experts. Through focus group meetings, one-to-one interviews with RTs and customer surveys, Aerogen endeavors to keep the customer at the center of all its product development decisions. This clinical user input is exemplified by the development of the Continuous Nebulization Tube Set. Clinical user input flagged the risk of misconnection. This feedback triggered the Aerogen R&D process, which resulted in the design, manufacture and launch of the Continuous Nebulization Tube Set to eliminate this risk.

**Discuss the educational services you offer for use of your product.**

Aerogen has recently launched the new look Aerogen website www.aerogen.com offering educational information about Aerogen products. In addition to this the website offers Continuing Respiratory Care Education programs. The programs available are: Aerosols & Children, Effects of Generator Type, Position and Humidity on Mechanical Ventilation, and Heliox and Medical Aerosols. All Aerogen programs are delivered by Dr Jim Fink, PhD, RRT, FARRC. All Aerogen CRCE programs are accredited by AARC and provide a one hour free CRCE credit for AARC members.

**What new technology do you see as having the greatest impact on your area of expertise?**
Aerogen's primary goal is to make nebulization therapy as easy to administer and as effective as possible. Aerogen has recently released an integrated module for the Maquet Servo-i ventilator. This module provides a complete aerosol delivery system which can be easily controlled through the Servo-i's user interface. The one-touch solution allows for mechanically ventilated patients to receive intermittent and continuous nebulization at the touch of a button. The Aeroneb module can be added to a new Servo-i or retro-fitted to an existing Servo-i.

# VENTILATION ROUNDTABLE

# Breathe Technologies, Inc

The Breathe Non-Invasive OPEN Ventilation (NIOV) System is an FDA 510(k) cleared, wearable ventilation system designed for adult patients with respiratory insufficiency. It is particularly well-suited to help patients who have difficulty breathing while performing everyday activities of daily living (ADLs). The NIOV System is designed to increase mobility and promote ambulation by helping patients to participate more fully in life.

The NIOV System is an easy-to-use, volume augmentation ventilator, delivering both ventilation and supplemental oxygen. The heart of the system is a small, one pound, battery-powered ventilator that can be easily worn at the waist while ambulating, exercising or performing activities of daily living. An external source of high pressure oxygen is required. The unique OPEN ventilation technology uses a small, nasal pillow interface that is open to ambient air.

The System senses the patient's spontaneous breath through sense ports in the nasal interface, and then delivers the selected volume of oxygen at up to 40 breaths per minute. As oxygen is delivered, ambient air is entrained through the entrainment ports, and positive pressure is developed within the mask to supplement the patient's spontaneous breathing, reducing the work of breathing, supplementing the volume of air inhaled and improving oxygen delivery. The NIOV System typically produces airway pressures of 2-8 cm $H_2O$, and is limited to a maximum of approximately 15 cm $H_2O$ lung pressure at maximum settings and conditions.

The NIOV System may be customized to each patient's needs using clinician customized settings. Volume delivery settings ranging from 50 ml to 250 ml are easily programmed by the clinician for three activity levels, and are accessed using a password protected clinician menu. Patients are then able to self-select which of the three activity settings best meets their breathing needs simply by pushing the desired activity level buttons. A user-friendly LCD touch screen is provided to allow both patients and clinicians quick access to ventilator functions and readouts.

Breathe Technologies, Inc has conducted multiple studies with the NIOV System. In its first randomized, controlled trial (NOVEL I), a mean improvement in six minute walk distance (6MWD) of 37 meters was observed (n=30), with a 43 meter improvement seen in a subset of patients with severe COPD. In a follow-up trial (NOVEL II), a mean improvement in 6MWD of 36 meters was observed (n=32), while a subset of patients with baseline 6MWD <300 showed a mean improvement of 73 meters. In a third trial (PRIDE), 18 subjects with severe COPD completed five consecutive, 6-hour clinic days in using the NIOV System during rest, ADLs, and while exercising. Study participants found the NIOV System to be comfortable and reported that the study device resulted in less dyspnea, reduced work of breathing, and greater mobility and exercise endurance compared to their current oxygen systems.

# Covidien

**Discuss your ventilation products.**
*Acute ventilation:* The **Puritan Bennett 840** ventilator is our flagship ventilation product. The Puritan Bennett 840 ventilator provides enhanced ventilation for critically ill, hospital-based patients, and can be customized with advanced technology to help maintain patient-ventilator synchrony.[1] Improving synchrony facilitates spontaneous breathing.[2] To enhance patient safety, the ventilator features alarm systems, high-efficiency filters, state-of-the-art flow sensors and self-diagnostic testing. A comprehensive suite of monitored and trended parameters helps clinicians assess and manage patient therapy. The **Puritan Bennett 840 Neonatal** ventilator delivers, manages and monitors ventilation for the smallest, critically ill patients. This ventilator enables clinicians to set a tidal volume as low as 2 mL for neonatal patients who weigh as little as 300 grams, without disconnecting the patient from the ventilator or interrupting ventilation. The **Puritan Bennett 840 Universal** ventilator is for a wide variety of patients, from neonates to adults. The ventilator offers a range of features, including noninvasive ventilation (NIV), and other advanced software options: NeoMode 2.0 software for neonatal ventilation, and Proportional Assist* Ventilation Plus (PAV*+), which improves patient-ventilator synchrony compared to pressure support ventilation.[1] *Portable ventilation:* The **Puritan Bennett 540** portable ventilator is lightweight and compact, providing mobility and flexibility to patients living at home in need of breathing support. The unit weighs less than 10 pounds and is quiet and easy to use. The Puritan Bennett 540 portable ventilator has a real-time battery life indicator that estimates remaining power in hours and minutes, and an audible and visual alarm to ensure that both patient and caregivers can track ventilation status.

**Tell us about the latest in your company's R&D efforts.**
Customers look to Covidien to excel in two areas: products and clinical evidence. Covidien is known for providing high-quality, innovative solutions that improve patient care, backed by scientific evidence that demonstrates our products' clinical value. Covidien continues to devote significant resources to fuel our research and development and pipeline of new products.

**What training and support services do your offer?**
Covidien offers one of the most comprehensive field service programs in the industry. Our field-based staff and service organizations provide extensive education and training to ensure healthcare providers and technicians know how to best use Covidien ventilation technologies and how to integrate clinical information into patient medical records. The Covidien Center for Clinical Excellence (www.ccexcellence.org) offers free online educational programs for nurses and respiratory therapists. It is accredited by the American Nurses Credentialing

Center (ANCC), the California Board of Registered Nursing and the American Association for Respiratory Care (AARC). Successful participants receive online certificates.

**Discuss your products' applications; that is, hospital, home care, etc.**
Covidien ventilation solutions cover the spectrum from the intensive care unit (ICU) to the general care floor to home care. The Puritan Bennett 840 ventilator, the Company's flagship critical care ventilation product, offers enhanced noninvasive ventilation for hospital-based acutely ill patients. The Puritan Bennett 540 portable ventilator provides mobile respiratory support to help patient transition from hospital to home care, and enables them to pursue daily activities.

References**:** 1. The PAV*+ ventilation mode, available on the Puritan Bennett 840 ventilator, has been shown to increase patient-ventilator synchrony compared to pressure support ventilation. Thille AW, Rodriguez P, Cabello B, Lellouche F, Brochard L. Patient-ventilator asynchrony during assisted mechanical ventilation. *Intensive Care Med.* 2006;32(10):1515-1522. 2. Xirouchaki N, Kondili E, Vaporidi K, et al. Proportional assist ventilation with load-adjustable gain factors in critically ill patients: comparison with pressure support. *Intensive Care Med.*2008;34(11):2026-2034. 

# Dräger

**Discuss your ventilation products.**
The Dräger ventilation portfolio has been transformed with newly released products to address each area of specialty care. Our newest critical care ventilator is the Evita Infinity V500, and our infant-specific ventilator is the Babylog VN500. In addition to the new V-series ventilators, Dräger introduced the new look of its turbine-driven ventilator, the Savina 300, and the newest transport ventilator the Oxylog 3000 plus, during the AARC this past November. The **Evita Infinity V500** is a comprehensive critical care workstation that can provide for the needs of neonatal, pediatric, and adult populations. Newest features include a "Smart Pulmonary View," standardized nomenclature, PC-APRV with auto-release, and customizable weaning protocols. The **Babylog VN500** is a neonatal-pediatric specific ventilator which offers a wide array of therapies including oxygen therapy, non-invasive ventilation, and invasive modes. Critical to ventilating premature infants is proper monitoring and compensation; the VN500 provides for effective leakage identification and compensation and has the option to volume ventilate small babies to a TV of 2 cc's. The **Savina 300** focuses on the essential elements of ventilation. Whether in volume or pressure ventilation, the Savina 300 provides for both adult and pediatric patients in settings such as acute, emergency, sub-acute, or post-operative care areas. Both invasive and non-invasive ventilation is available to provide clinicians a greater degree of flexibility for patient care. The **Oxylog 3000 plus** is a compact transport ventilator that can provide for adult and pediatric patients down to 50 cc's tidal volume. In addition to an array of volume, pressure, and spontaneous modes of ventilation, the Oxylog 3000 plus offers AutoFlow and integrated capnography and data management/export.

**Tell us about the latest in your company's R&D efforts.**
Generally speaking, Dräger invests approximately 7.3% of its revenue in research and development. We are constantly striving to develop new products to improve the lives of patients and the caregivers that work with them. Dräger remains in close collaboration with clinicians from around the globe to seek the best practice and be aware of current concerns in the health care arena. Prior to the new V-series, Savina 300, and Oxylog 3000 plus being released, various physicians' and respiratory therapists' opinions were sought to ensure clinical satisfaction.

**What training and support services do you offer?**
Dräger has an extensive team of sales representatives, sales managers, and applications specialists all of whom are either registered respiratory therapists or have extensive experiences/backgrounds in healthcare or engineering. Onsite clinical education and practical application training is offered to customers. Dräger customers also have access to a 24/7 clinical support hotline through ICON (Intensive Care Online) at 1-800-554-1312. The customer website is www.intensivecareonline.com. Here you can find complimentary CRCE courses, product resources, and a discussion board for peer-to-peer communication. Additionally throughout the year webinar training on contemporary issues is provided to all interested clinicians. The most recent web-training sessions included such topics as APRV by Dr Nader Habashi and Neonatal Ventilation by Dr Martin Keszler.

**What future developments do you foresee in ventilator products and applications?**
The healthcare delivery system has undergone many changes and hospitals face many challenges today. Technology has vastly grown over the past few years, especially in the health care environment. In the foreseeable future, we would expect future developments to be focused on improving safety in the ICU, closed-loop systems to automate weaning or decision making to ultimately reduce the length of stay, as well as a sharp focus on information technology and data sharing.

# Hamilton Medical, Inc

**Ventilation Products & Technology**
Hamilton Medical, Inc recently passed our 27th year in providing ventilator technology worldwide. We began in 1984 with the VEOLAR. The Hamilton G5 was introduced in 2007 and the Hamilton C2 soon followed in 2009. Hamilton Medical continues advancement of ventilator technology with the recent FDA 501(k) clearance IntelliCuff, NCPAP-ST, NIV and TRC on the G5 platform. In addition, we have three new ventilation systems currently pending 510(k) clearance, all anticipated this year. The clearance of IntelliCuff will provide our customers with Hamilton Medical's new non-invasive automatic cuff pressure controller for the Hamilton Medical G5. IntelliCuff assists the efforts of the clinician to reduce VAP and tracheal injuries by continuously monitoring and automatically adjusting cuffed tracheal and tracheostomy tubes, providing a real-time optimization of cuff pressure.

Hamilton Medical's extensive world-wide customer base speaks to Hamilton Medical's history and prior experience in meeting the ventilation needs of facilities throughout the world. All ventilation products are routinely reviewed by the independent technology rating firm ECRI and independent customer

satisfaction firm, MD Buyline. Hamilton Medical's continued preferred and high ratings with both firms show Hamilton Medical's success in both the quality of our ventilation products and the unsurpassed dedication and responsiveness of our support staff.

### R&D Efforts

Each of Hamilton Medical's ventilation platforms have an award winning interface that is consistent across all ventilators, making competencies for the staff simple and reducing the chance of error, regardless of the ventilator in use or the application. We continue to invest in R&D at much higher levels than our competitors. Hamilton currently invests over 25% of our OPEX into research and development. Economic conditions throughout the United States in the past five years have caused many manufacturers to reduce the size of their sales forces while Hamilton Medical has experienced growth. Our field staff shows a growth of over 140% in the past five years and additional clinical and sales support staff is currently being recruited.

### Training & Support

Hamilton Medical, Inc provides customers with our top rated Clinical Training, as noted by MDBuyline. This training includes CRCE credit courses, in conjunction with the American Association for Respiratory Care, course No. 212533000 – "Mechanical Ventilation Principles & Practice Series." This course is approved for a total of 14.0 CRCE credits; however, it is also approved for partial credit hours. In addition to the continuing education program noted, each facility automatically receives the following education for all clinicians: Training of Clinical Staff, Training Materials, Basic RN Introduction, Super user's training, and follow up with Continued Training requests/needs.

### Applications

By dedicating our efforts solely to ventilation technology, Hamilton Medical provides ventilation solutions that address ground and air transport ventilator needs for adult, pediatric and neonatal populations, MRI compatible ventilators and a dedicated neonatal ventilator.

### Future Developments

Hamilton Medical's patented ASV technology is advancing to Intellivent-ASV, integrated in the upcoming S1 Ventilator, the world's first fully closed-loop ventilation solution that automatically applies lung protective strategies. **PLEASE SEE HAMILTON MEDICAL'S ADVERTISEMENT ON PAGE 7 OF THIS ISSUE.**

## Resmed

**Noninvasive ventilation (NIV) is now available on ResMed's S9 platform.** ResMed recently expanded its award-winning line of S9 flow generators to include noninvasive ventilation (NIV) with the S9 VPAP ST. This new version of the ResMed VPAP ST adds Climate Control and substantially reduced noise levels to ensure that the patient's therapy is both effective and as comfortable as possible. Patients on NIV therapy often use their devices longer and at higher pressures than obstructive sleep apnea (OSA) patients, making good humidification critically important. Climate Control ensures a constant 80% relative humidity at the patient's preferred temperature – programmable between 60 and 86 degrees F. The exclusive ClimateLine tubing uses heated wire technology and an integrated sensor next to the mask to ensure that the temperature of the air is delivered to the patient at their set preference. The system also prevents condensation, further reducing therapy complications and inconvenience.

In addition to the great new features on the S9 VPAP ST, the platform continues to offer breath personalization technologies through TiControl, adjustable breath trigger, adjustable breath cycle (termination) and rise time. TiControl provides the clinician control of the time that the device remains at the IPAP pressure and can be used to extend the breath for patients who tend to cycle prematurely (restrictive patients) or terminate the breath in patients who tend to over-inflate (COPD patients). In addition to providing these guard-rails for breath length, TiControl also provides a window in which the patient can breathe spontaneously, thus maximizing patient comfort while providing the safety of a minimum or maximum breath length.

**Excellence in NIV through leak compensation:** As anyone who has worked with ICU ventilators knows, one of the most difficult aspects of providing effective NIV therapy is managing leak. If a device does not have good leak awareness and compensation, the ventilator soon gets out of sync with the patient. ResMed's Vsync technology actively measures flow rates and pressures from the ventilator and uses known characteristics of the mask, circuit and humidifier to quickly and accurately estimate the unintentional leak. Vsync works so effectively that it completely compensates for very large leaks in as few as two to three breaths. This is substantially faster than other noninvasive product options and critically important to maintaining good therapy.

**Stellar 100 – A new device in a new care setting:** With the recent introductions of the Stellar 100 and a new partnership with CareFusion, ResMed is well positioned to offer its unique advantages in NIV to more caregivers in more care settings than ever before. The Stellar 100 includes the TiControl breath personalization features and Vsync leak compensation, but adds many more features that are important in an institutional setting. The Stellar 100 treats a wide range of patients from pediatric (30lb and up) to adult, patients with high pressure requirements (up to 40 cm $H_2O$), and invasive and noninvasive interfaces. Stellar also includes many features that make it easier to treat and monitor patients in a hospital environment: • Integrated two-hour battery makes in-hospital transfers simple and convenient; • Live on-screen waveforms and patient trending information make it easy to review therapy effectiveness and make adjustments; • Innovative therapy defaults provide a simple starting point for a variety of disease conditions including restrictive disorders, obesity hypoventilation and COPD. With flow rates up to 220 liters per minute, the Stellar 100 provides a surprising amount of power in a very small and attractive package.

**Current tools and future innovation:** ResMed is currently supporting our NIV customers with several educational tools to make it easier than ever to set up patients quickly and effectively, while taking advantage of the powerful customization features that we offer. This includes a basic settings guide and online educational materials. As seen from the recent product releases in NIV, ResMed continues to invest in improving technologies and therapies. This stream of innovation will continue over the next several years as we expand our product offering in ventilation and related technologies. We look forward to working

with the respiratory therapy community to offer vital therapy solutions that complement the expertise and critical patient care services that you provide.

## SPOTLIGHT ON VENTILATION

### DOCUMENTATION & KNOWLEDGE

CareFusion announced the CareFusion Ventilation System, combining its industry leading ventilators with new interoperability and analytics software to better address clinical and operational challenges in patient care. The CareFusion Ventilation System includes the company's AVEA, VELA and EnVe ventilators and adds two new applications: **CareFusion Respiratory Documentation Application:** A handheld, positive patient ID application that automates the collection of ventilator documentation data at the point of care, and then wirelessly transmits it to a hospital's electronic medical records (EMR) system. Examples of documentation data include ventilator status, vital signs, breath sounds and clinical observations. This application enables more accurate and efficient documentation of therapy compared to manually entering the information into a computer. **CareFusion Knowledge Portal** for ventilator therapy: An analytics and reporting tool that measures clinical and process variability in ventilator therapy, and provides hospitals with actionable information to help clinicians improve patient care. The initial reporting capabilities focus on ventilator weaning and notifications on important patient trends to measure compliance with best practices. "Our focus is on delivering the safest and most effective care for our ventilated patients," said Michael Muth, director of respiratory at Good Samaritan Hospital in Los Angeles, which is the first limited release site for the new applications. "We've been impressed so far with how the CareFusion Ventilation System has helped us establish a better, more efficient workflow, so our respiratory therapists can spend more time with patients and less time on paperwork." Kevin Ketzel, general manager for Respiratory Technologies at CareFusion said, "It costs $4,900 per day to treat some of the most difficult-to-wean ventilator patients, and our customers are seeing decreasing reimbursement for these cases. Our new ventilation system helps address these pressures and provides capabilities to help our customers improve the quality of patient care, while reducing costs." (The CareFusion Knowledge Portal for ventilator therapy is currently an unreleased product and the company may not make it available for commercial sale.) Contact carefusion.com.

### USE ANYWHERE

Dräger announced the immediate availability of its new ventilator for adult and pediatric patients. The Savina 300 ventilator provides reliable ventilation therapy and is suitable for use nearly anywhere in the hospital. The Savina 300 provides invasive and non-invasive ventilation (NIV) capability which helps to reduce intubation and infection rates. The open breathing concept lets patients breathe freely at any time during the cycle and at any pressure level, increasing overall patient comfort levels and potentially helping to reduce weaning times. The large, color touch screen and intuitive operating system make configuration and operation very simple, requiring minimal training. "Developed in consultation with clinicians from the United States, and building on the success of the original Savina ventilator over the past ten years, the Savina 300 meets the growing demands of emergency rooms, recovery rooms, and other acute care settings" said Edwin Coombs, regional director of marketing for respiratory care at Draeger Medical, Inc. The Savina 300 was showcased at this year's AARC International Congress. Contact draeger.com.

### SIMPLIFIED DELIVERY

Discovery Laboratories, Inc released new data from a study showing that use of AFECTAIR resulted in as much as a 70% reduction in the amount of nitric oxide required to deliver the desired dose of the therapeutic gas when compared with current standard of care (SoC) ($p < 0.001$). AFECTAIR, the company's newest product candidate, has been developed by Discovery Labs to simplify the delivery of inhaled therapies for critical care patients requiring ventilatory support. The new AFECTAIR data were presented at the 2011 Hot Topics in Neonatology Congress, an internationally recognized medical meeting dedicated to advancing the practice of neonatology. Results from the study suggest that AFECTAIR may be an effective alternative to the SoC among ventilatory circuit devices used for the delivery of inhaled nitric oxide. The investigators also commented that the results of this study support further investigation of AFECTAIR in the delivery of other costly medical gases using various methods of ventilation. AFECTAIR is a series of proprietary ventilator circuit/patient interface connectors and related componentry. AFECTAIR simplifies the delivery of any inhaled therapies to critical care patients requiring ventilatory support. According to national health statistics and market assessment data, it is estimated that more than 1.3 million patients annually, in the United States and European Union, receive aerosolized medications while requiring ventilator support. Discovery Labs is implementing a regulatory plan that potentially will allow for the introduction of AFECTAIR in the United States and the European Union in 2012. The in-vitro study was supported by Discovery Labs and designed to compare the performance of AFECTAIR, a proprietary ventilator circuit patient interface connector, with a current SoC ventilator system in the delivery of nitric oxide under simulated neonatal ventilator conditions. The simulated breathing pattern was maintained within narrow ranges and the delivery of oxygen was not different between the study conditions. The investigators observed a 50 to 70% decrease in nitric oxide utilization requirements to achieve desired inhaled nitric oxide dose with AFECTAIR, compared with SoC ($p < 0.001$). Study investigators concluded that AFECTAIR significantly decreased the nitric oxide utilization requirements to achieve the desired inhaled nitric oxide concentration and that results of the study support further investigation of AFECTAIR in the delivery of other medical gases and with other ventilation methods. Contact www.discoverylabs.com.

# Pediatric Emergency Department Outcomes Comparing Levalbuterol vs Racemic Albuterol

Timothy R. Myers BS, RRT; Marsha Rogers, CRT; John C. Carl, MD; Carolyn Kercsmar, MD

**Background:** Pediatric asthma is a chronic condition of childhood with increasing prevalence. Emergency Department (ED) treatment of asthma constitutes a failure in outpatient management. Frequently, ED asthma treatment is unsuccessful and patients are admitted. Our ED data the past 5 years yielded an average admission rate of approximately 41%. The purpose of this study was to determine if levalbuterol resulted in improved clinical outcomes compared to racemic albuterol. Specifically, we sought to observe a decrease in admission rate.

**Methods:** An a priori analysis (powered at 80% (p-value <0.05)) indicated a need to randomize 552 children to detect a 10% decrease in admission rate. Patients who consented for participation were randomized in a double-blind fashion to receive either 2.5 mg albuterol or 1.25 mg levalbuterol delivered by a high-density NebuTech HDN (Salter Labs, Arvin, CA) nebulizer. We utilized our assessment-driven ED Asthma Carepath (ED-ACP) to control for treatment standardization between groups. Our ED-ACP standardizes assessments & therapy (oxygen, albuterol aerosols, corticosteriods) at prescribed intervals. Assessments and/or treatments were delivered every 20 minutes. Intensification of therapy was provided with either subcutaneous epinephrine (SQ Epi) injection (initially) and/or Ipratropium (during therapy). Treatment was discontinued when discharge criteria were met: good air exchange, mild/absent end expiratory wheezing, no accessory muscle usage, $SpO_2$ > 93%, and respiratory rate <40/min. Patients were observed for one hour after their last treatment, then discharged. Patients not meeting discharge criteria after 6 aerosols or 1 hour of continuous aerosols were admitted or transferred. A chronic asthma severity was assigned based on history, symptoms, and therapeutic drug usage. Fisher Exact Tests were used to compare race, gender, and administration of SC Epi & Ipratropium. A Pearson chi-square was used to compare chronic severity & admit vs. discharge status. Unpaired t-tests were used to compare age, ED LOS, initial $SpO_2$ & aerosols delivered. Significance was set at $p < 0.05$.

**Results:** This study randomized 552 children to treatment. Below are demographic and clinical outcome data reported as raw, mean (SD) or percentages with p-values.

| Demographics | Levalbuterol | Racemic Albuterol | p - Value |
|---|---|---|---|
| Number | 281 | 271 | |
| Age | 7.0 (4.0) | 7.1 (4.2) | 0.84 |
| Caucasian Race (%) | 12 | 15 | 0.27 |
| Male Gender (%) | 67 | 67 | 0.93 |
| Severe Chronic Severity (%) | 46 | 42 | 0.34 |
| **Outcome Data** | | | |
| Admissions (%) | 37 | 45 | 0.03 |
| Aerosols delivered | 3.8 (1.98) | 4.1 (1.97) | 0.05 |
| LOS (in hours) | 2.38 (0.84) | 2.38 (0.86) | 0.85 |
| Administered SC Epi (%) | 9 | 11 | 0.33 |
| Administered Ipratropium (%) | 23 | 30 | 0.10 |
| Initial $SpO_2$ | 94.8 (7.9) | 95.5 (5.1) | 0.25 |

**Conclusion:** Levalbuterol resulted in a clinical and statistical decrease in admission rate and treatments provided in our ED. An 8% decrease in hospital admission rate could result in a net savings of approximately $200,000 per year at our institution.

The authors are with Rainbow Babies & Children's Hospital, Cleveland, OH.
This article was provided by Salter Labs.

# INSPIRE YOUR PATIENTS

*Introducing the palm-sized, wearable Breathe Non-Invasive OPEN Ventilation (NIOV™) System. Designed to increase mobility and promote ambulation.*

The Breathe NIOV System — developed to ventilate patients with respiratory insufficiency. Opening the possibility to expand their daily activities at home, during pulmonary rehabilitation or to promote early mobilization while in the hospital.

- Wearable, one pound, battery-operated ventilator
- Delivers ventilation and supplemental oxygen*
- Unique OPEN nasal pillow interface
- Clinician customizable volume settings


*Actual Size*

Breathe NIOV™

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*An external source of oxygen is required.

# Non-invasive Open Ventilation System May Improve Activities of Daily Living – A Case Study

Robert McCoy, BS, RRT, FAARC; Kim Wiles, BS, RRT; Brian Carlin, MD

## Overview

Chronic obstructive pulmonary disease (COPD) is a leading cause of death in the United States. The prevalence of COPD is an estimated 10 million, or nearly 6% of US adults.[1,2] For many patients with COPD, exercise capacity is severely limited, and even performing normal activities of daily living (ADLs) can be difficult or impossible. Although supplemental oxygen is a therapeutic mainstay in COPD, it provides limited flow rates and does not assist with the work of breathing or in the clearance of carbon dioxide.

A portable device that can augment ventilation while supplying supplemental oxygen could improve patient mobility, enhance rehabilitation, and offset some of the functional impairment associated with advanced COPD.[3,4] In this regard, a wearable, non invasive open ventilation (NIOV) system that delivers oxygen therapy while augmenting ventilation has been developed by Breathe Technologies, Inc and cleared for use by the FDA. The ventilator is light enough (1 lb) to be carried by patients, and uses a proprietary "open" nasal pillow interface (Figure 1). Because of its portability and comfortable nasal interface, the NIOV System is uniquely positioned to provide patients with a means of receiving truly ambulatory supplemental oxygen plus augmented ventilation.


**Figure 1.** The portable Breathe Technologies NIOV System (note: model; patient not depicted).

## Managing expectations

Chronic lung disease is progressive and as a patient ages, anatomical and physiological changes occur that are distinctive to each individual. Therefore, prescribed therapies should ideally take into account the variables in product performance and the unique clinical characteristics of each patient. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines[5] describe four stages of COPD that help to segment patients based on their lung function measures (FEV1, FEV1/FVC). However, given that a patient's prognosis and activities may improve with early diagnosis and subsequent intervention, their level of activity and conditioning are important to consider in the overall management of the individual patient.

An example of managing expectations for long-term oxygen therapy (LTOT) would focus on the product's performance capabilities, the patient's acceptance of the device, and the patient's ability to effectively receive oxygen at all levels of activity. A patient whose supplemental oxygen requirements are assessed and deemed to be adequate while in the hospital might return home to find that the prescribed oxygen system does not meet their at-home needs. For activities of daily living, optimal oxygen use requires that its delivery be titrated based on the level of activity. So, when patients receive a "one-size-fits-all" standard 2 lpm, 24 hours/day prescription, an inherent outcome may be that the patient will be relegated to a very sedentary lifestyle. This, of course, is a formula for trouble, as ambulation and activity are critical to survival and to reducing healthcare costs as described by Petty and Bliss in 2000,[6] and more recently by Waschki, et al.[7] If a portable oxygen system is needed, weight and operating times must be in sync with the patient's physical capabilities, and in addition, be practical for activities outside the home. If nocturnal home oxygen is needed, all the variables that occur with sleep should be assessed to ensure that adequate oxygenation is provided throughout the night.

Managing expectations for patients using NIOV is somewhat different than LTOT, since augmented ventilation adds significant capability. Patients whose disease has progressed to a point of respiratory insufficiency may likely need both oxygenation and ventilation. With NIOV, the ventilator can be continuously adjusted to augmentation levels that are comfortable for patients, while reducing their work of breathing and enhancing their ability to perform activities of daily living with minimal dyspnea.

Another consideration in managing expectations are the patient's physiological capabilities. If a patient has been sedentary for a prolonged period of time, deconditioning and reduced stamina are certain to have occurred. While NIOV can provide an immediate boost to ventilation and oxygenation,

This article was provided by Breathe Technologies, Inc.

it cannot reverse the effects of long-term deconditioning. To regain increased functionality, patients will need to engage in a regular exercise (ie a comprehensive pulmonary rehabilitation program) and begin the process of conditioning to increase their strength and to bolster their ability to perform ADLs.

## Level of Physiological Capability (LPC)

NIOV may provide different benefit to patients with various levels of physiological capabilities. The following provides clinicians with a simple way to place patients with chronic respiratory insufficiency into categories that help delineate how augmented ventilation might benefit each patient.

**LPC-I:** This level includes patients who are currently on oxygen, are able to perform ADLs, and who may be participating in, or have recently completed a pulmonary rehabilitation program. In these patients, optimal performance of ADLs may be limited by oxygen desaturation and/or ventilatory insufficiency.

Potential Benefits of NIOV:
- Increased ability to perform ADLs with improved oxygenation and ventilation
- Increased endurance and conditioning
- Easier maintenance of current oxygenation/ventilation/ conditioning

**LPC-II:** Patients in this category include those who are independent at home but who can no longer perform the basic ADLs, and who may be unable to participate in a pulmonary rehabilitation program. Patients who have just entered LPC stage II without major loss of conditioning might be able to resume ADLs or pulmonary rehabilitation if NIOV is instituted.

Potential Benefits of NIOV:
- Help patients regain capability with improved oxygenation and ventilation
- Minimize or prevent deconditioning that would negatively impact muscle tone and the ability to exercise
- Help patients return to LPC-I status

**LPC-III:** Patients in stage III are unable to perform even low level ADLs due to poor oxygenation and ventilation and require significant assistance at home. In this category, patients may no longer have the ability to perform even the most basic ADLs, even while using NIOV.

Potential Benefits of NIOV:
- Allow patients to gradually improve from a completely sedentary lifestyle
- Establish a foundation of effective oxygenation and ventilation that allows patients to perform basic ADLs with the intent to engage the patient in a pulmonary rehab program intent upon improving cardiopulmonary function..
- Allow patients to build strength and stamina, regain mobility, and reduce exacerbations
- Help patients return to LPC-I or LPC-II status

## Patient Case Study

The Breathe NIOV System was evaluated in a 71-year-old, male patient with severe COPD and respiratory insufficiency. The severity of the patient's lung disease limited his ability to travel outside the home without incurring severe dyspnea, fatigue, and fear of a serious medical event. After conferring with the patient's physician and obtaining a prescription, evaluation of the NIOV System was undertaken to determine whether the patient could tolerate the device and gain benefit.

The patient was met in his home, where the purpose and procedures used in the evaluation were fully explained. The patient was allowed to ask questions and provided his informed consent to proceed with an evaluation of the device. Information was collected regarding the patient's current home oxygen system as well as his normal oxygen use patterns. Based on his very sedentary lifestyle over the prior six months, the patient was categorized as an LPC-III. After the patient was instructed on the use of the NIOV System, he was allowed to wear the ventilator for a 30-minute acclimation period.

Oxygen saturation and heart rate were collected every 30 seconds during the performance of in-home ADLs, first using the patient's standard oxygen therapy, followed by use of the NIOV System. In addition, Borg scores, comfort scores, and fatigue ratings were collected at the beginning, middle, and end of each of the ADL test runs.

## Summary of Results

The nasal interface was well tolerated and found to be comfortable by the patient. The positive pressure from the ventilator did not interfere with the patient's normal ventilation and he was able to immediately synchronize his breathing pattern with the equipment. While using his standard oxygen system, the patient was severely limited in his ability to perform ADLs. While using the NIOV system, the patient was able to complete the same activity with less desaturation and improved comfort. The patient's apparent and reported dyspnea, and also his fear of trying to do more exercise was reduced while using the NIOV device. During walking, the NIOV system was better able to maintain adequate $SpO_2$s compared to the patient's existing oxygen system. The patient was able to use the ventilator while moving about his home, allowing for its use during ADLs.

**Table 1.** Resting Data

| | Stationary Concentrator at 4 lpm (~36% $FiO_2$) | NIOV System at 100 ml Volume Setting (~38% $FiO_2$) |
|---|---|---|
| $SpO_2$ | 92 | 94 |
| HR | 74 | 74 |
| RR | 22 | 20 |
| $ETCO_2$ mmHg | 26 | 26 |

**Table 2a.** ADL – Walking using Standard Oxygen

| Concentrator 4 lpm,50 ft. tubing | Start | .5 min | 1 min | 1.5 min | 2.0 min Stop-rest | 2.5 min | 3.0 min | 4.0 min |
|---|---|---|---|---|---|---|---|---|
| $SpO_2$ | 91 | 90 | 88 | 85 | 83 | 81 | 86 | 91 |
| HR | 79 | 81 | 80 | 80 | 84 | 82 | 80 | 76 |

**Table 2b.** ADL – Walking using NIOV System

| NIOV System 100 ml | Start | .5 min | 1 min | 1.5 min | 2.0 min Stop-rest | 2.5 min |
|---|---|---|---|---|---|---|
| $SpO_2$ | 95 | 94 | 90 | 90 | 91 | 95 |
| HR | 82 | 80 | 80 | 81 | 77 | 76 |

**Table 3a.** Patient Borg, Comfort, and Fatigue Scores using Standard Oxygen

| Concentrator 4 lpm, 50 ft. tubing | Start | 1 min | End |
|---|---|---|---|
| Borg Score | 1 | 3 | 6 |
| Comfort Score | 0 | 3 | 7 |
| Fatigue Rating | 0 | 2 | 4 |

**Table 3b.** Patient Borg, Comfort, and Fatigue Scores using NIOV System

| NIOV System 100 ml | Start | 1 min | End |
|---|---|---|---|
| Borg Score | 0 | 1 | 2 |
| Comfort Score | 0 | 1 | 3 |
| Fatigue Rating | 0 | 2 | 4 |

The patient was allowed to wear the ventilation system for 20 minutes after the final ADL and provided his observations. Patient remarks regarding the NIOV device were all essentially positive and included:

- "The device felt smooth, not bad. I would walk to the mall."
- "Not bad, it's a little loud."
- "I feel better."

When asked if he would wear and use the NIOV device, the patient's responses included:

- "I'd be gone."
- "I'm good to go again, it feels easier to breathe."
- "When can I get one?"
- "I like this, it's good."
- "I'm going to be mad when you take it back."
- "It's like I felt 15 years ago. I feel like I could walk and exercise to build up my muscles."

## Discussion

Although this was a very limited evaluation of the NIOV System, it begins an exploration of a unique product. After using the device, the patient felt encouraged to return to pulmonary rehabilitation and to begin a program of structured exercise with appropriate provision of oxygenation and ventilation. If reconditioning allows the patient to increase his activity levels, a home exercise and maintenance program will be suggested.

In the past, this patient has experienced many exacerbations and complications due to the progression of his lung disease. His physician has suggested that if NIOV could overcome the patient's dyspnea and deconditioning, many of the complications associated with a sedentary lifestyle might be reduced, along with the patient's frequent need for hospital and doctor visits. Such patients (with frequent exacerbations) have remained a challenge to manage. While these patients often require intensive treatment in the hospital setting and at times require invasive ventilation, prior to now, they have not had the option of being discharged home with a lightweight, ambulatory, non invasive ventilation system.

## Conclusions

Non-invasive open ventilation in the home setting may provide the necessary oxygenation and augmented ventilation necessary to allow patients with chronic lung disease to more easily accomplish ADLs in their home and to participate in pulmonary rehabilitation programs. Ultimately a reduction in the overall associated complications in the management of these patients may occur. The experience of this case study, along with previous clinical trials[8,9] using the NIOV System seem to support this premise. Additional clinical studies in both the institutional and home environment are required to better define NIOV's applications, benefits, and its expected outcomes.

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# Advances in Awareness, Research and Optimal Treatment for COPD

Scott Cerreta, BS, RRT

As the third leading cause of death in the US, Chronic Obstructive Pulmonary Disease (COPD) affects 24 million Americans, with half remaining undiagnosed, and kills one person every four minutes in the US – more people each year than breast cancer and diabetes combined. Awareness of COPD remains a major obstacle in fighting the disease, especially for those who go undiagnosed.

In recent years, a number of awareness programs have been implemented to create a unified front against the disease, including the DRIVE4COPD – a multi-year public health initiative that aims to help people identify symptoms of COPD and take action; the National Heart, Lung, and Blood Institute's (NHLBI) "Learn More, Breathe Better" Campaign – the first national non-branded public awareness campaign, and other direct-to-consumer drug ads aimed at increasing awareness. The Centers for Disease Control and Prevention (CDC) brought out an Action Plan focused on prevention and awareness and has solicited support from Congress to fund its implementation and raise its research and prevention funding to a level comparable to that of other major causes of death, such as heart disease, cancer and diabetes.

Such initiatives mark a new era of progress to improve diagnosis and treatment, and coincide with a number of significant studies and registries.

## COPDGene Study

The COPDGene Study is one of the largest studies ever to investigate the underlying genetic factors of COPD. Through the enrollment of over 10,000 individuals, the study aims to find inherited or genetic factors that make some individuals more likely than others to develop COPD.

Clinical evaluations will be conducted physiologically and radiographically with a spirometry test, results of a six-minute walk test, and scores on a BODE scale (body mass index, degree of airflow obstruction, degree of dyspnea and exercise capacity). In addition, subjects will be given a chest CT scan, complete a set of questionnaires, and donate about 30cc of blood for genetic analysis.

Because not all smokers develop COPD, and only 15-20% of smokers develop severe lung impairment, researchers are looking for associations between genes across the entire human genome that affect the development of COPD.

Approximately 3,000 individuals (1,000 non-Hispanic white males, 1,000 non-Hispanic white females, 500 African American males, and 500 African American females) will be used in each of the first three phases. In the first phase, the first cohort of individuals will be stratified by their racial group. Their genome will be analyzed using an SNP screen (single nucleotide polymorphism) – identifying the differences in nucleotides at over 500,000 carefully selected positions across the entire human genome.

Once the SNP screen identifies portions of the genome associated with the development of COPD, the genome of the second group of individuals will be analyzed to confirm which of the genetic associations found in the first group of individuals carry through in the second group. This will allow researchers to narrow down the regions where the primary genes that affect the development of COPD are likely located.

At this stage, the study is expected to be able to identify about 50 genetic regions that may be important in both non-Hispanic white and African American study participants. To find the actual genes, the detailed genetic code of these 50 genetic regions will be mapped in the third group of study participants. The goal is to find the three to five specific genes that play a primary role in determining the risk of developing COPD in both non-Hispanic white and African American individuals.

In the fourth phase, each of the identified genes will be further analyzed in four different cohorts to confirm their association with, and importance in, COPD. Ultimately, the results of this study have the potential to lead to better treatments and improved outcomes for patients.

## COPD Registries

COPD Research Registry – This confidential database, comprised of individuals diagnosed with COPD or at risk of developing COPD, is designed to help researchers learn more about COPD and to help those interested in COPD research to

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find opportunities to participate. A committee comprised of leaders in the medical, ethical, scientific and COPD communities guide the Registry.

Bronchiectasis Research Registry – This registry includes patients with Nontuberculous Mycobacteria (NTM), and intends to enroll 1,500 NTM patients by 2013, many of whom are dually diagnosed with COPD and Bronchiectasis, in an effort to provide increased research opportunities and new clinical center site information for both diseases.

## Guidelines

Several professional organizations have compiled guidelines that are useful for medical professionals in diagnosing and managing COPD, including the American Thoracic Society (ATS), European Respiratory Society (ERS), Global Initiative for Chronic Obstructive lung Disease (GOLD), and American College of Chest Physicians (ACCP).

The treatment progression shown in Chart A below is intended to provide guidance:

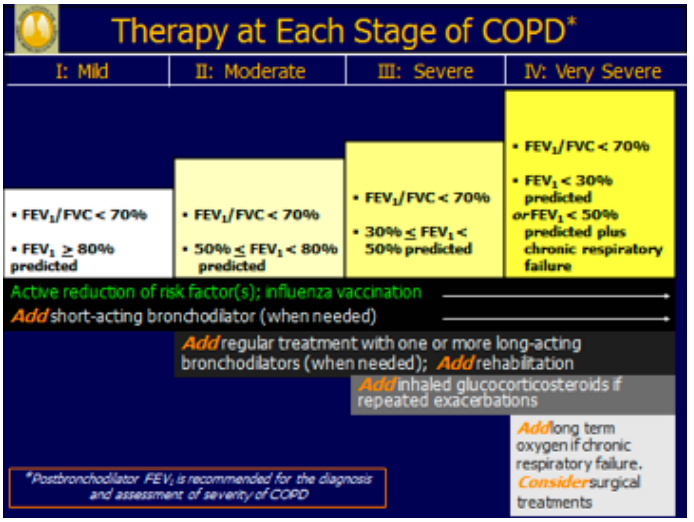



Chart A

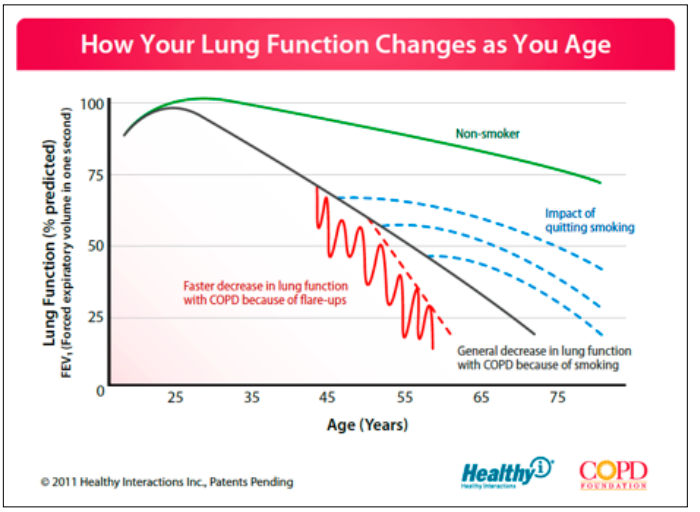
- Stage I: short-acting inhaled therapy as needed to control dyspnea or coughing spasms is usually sufficient.
- Stages II-IV: patients whose symptoms are not adequately controlled with as-needed short-acting bronchodilators should receive regular treatment with one or more long acting inhaled bronchodilators from each class (beta agonists and anticholinergics).
- Stages II-IV: patients who are on long-acting bronchodilator maintenance therapy may also use a short-acting bronchodilator as needed. Some patients may request regular treatment with high-dose nebulized bronchodilators, especially if they have experienced subjective benefit from this treatment during an acute exacerbation. However, once stabilized at baseline, maintenance therapy should resume and scheduled short-acting bronchodilators should be avoided.
- Stages III-IV: regular treatment with inhaled corticosteroids (ICS) is warranted in patients with a post-bronchodilator FEV1 <50% predicted and a history of repeated exacerbations. This should be added to regular bronchodilator treatment.
- Stage III-IV: COPD and a history of exacerbations and chronic bronchitis, the phospodiesterase-4 inhibitor, roflumilast, reduce exacerbations treated with oral glucocorticosteroids.

## Optimal Care for Management of COPD

Proper management of COPD requires a complex healthcare plan that treats the whole person, not just the lungs, going beyond medications and administration of oxygen. Treatment requires adherence to well-established guidelines and the following:

- smoking cessation
- annual well visit check which may include spirometry reassessment
- medication management
- oxygen therapy
- testing for Alpha-1Antitrypsin Deficiency
- pulmonary rehabilitation, which includes
  - exercise and nutrition
  - recognizing early signs of infection
  - coping skills
  - breathing techniques
  - making early decisions on end-of-life care

Optimal care demands a proactive approach. Therefore, RTs and other healthcare professionals should familiarize themselves with every aspect of COPD and serve as team leaders for others in order to ensure the best possible long-term results (see graph A).




What this graph does not show is the quality of life one suffers from when baseline FEV1 is below 50%, severe COPD.

## Pulmonary Rehabilitation

Evidence consistently reveals that long-term benefits of pulmonary rehabilitation (PR) (beyond 24 months) have not proven to be effective. The drop-off is multifactorial, with the two most significant factors being exacerbations of COPD and decrease in adherence to exercise and drug treatment. To remedy this, AACP and American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR) Pulmonary Rehabilitation Clinical Practice Guidelines suggest that pulmonary rehabilitation centers (PRCs) include strategies to promote long-term adherence.[1]

In order to maintain benefits after rehabilitation, RTs and healthcare professionals should encourage participation in Phase III maintenance rehabilitation and optimal care strategies.

The major roadblock here is that less than 20% of healthcare providers order pulmonary rehabilitation for their patients in the first place, despite the fact that it is the most critical resource for

## Spirometry

According to the ATS/ERS guidelines, spirometry should be obtained from all individuals who have symptoms as detailed below:

- A history of smoking with one or more symptoms
- Symptoms of coughing (with and without sputum), wheezing, and shortness of breath
- A history of exposure to environmental risk factors including second-hand smoke and occupational pollutants
- A family history of chronic lung disease

In order to maximize the quality of the test, these simple rules for administering spirometry should be practiced:

**1. Make sure the individual taking the test feels comfortable** – Explain the process of taking the test and the goals you both are trying to achieve. Reassure the individual that the test is simple. It is also best for the individual to take the test while they're seated.

**2. Breathe, Seal, Blast!** – Ask the individual to take in a very deep breath, hold their breath while they seal their lips around the mouthpiece, and to then exhale as fast and as long as they can. The goal is to empty out their lungs and to continue blowing for at least six seconds. During this time, they should try not to breathe in or stop exhaling. A demonstration before taking the actual test could be useful.

**3. Repeat** – Explain to the individual that they need three good quality and repeatable tests. It may take up to eight maneuvers to achieve those three good tests in order for the machine to take an accurate account of their measurements.

Spirometry will show the measurements of a Forced Expiratory Volume in the first second of the person blowing into a spirometer (FEV1) and the Forced Vital Capacity (FVC) for the total six seconds of the blow. If the FVC is 80% or higher and the FEV1/FVC ratio is between or above 70-80%, the person's lung health is normal. A ratio below 70% may indicate an obstruction. Note that the FEV1 is subject to the age, gender, height, and ethnicity of the individual being tested.

Recently, a new manuscript by the COPD Foundation has been accepted for publication, Case Finding in COPD: The Role of Peak Flow Testing. This study demonstrates a protocol for detecting COPD in a cost effective manner. It starts with a 5 question population screener, followed by peak flow for those at high risk for COPD. A peak flow of less than 70% warrants a spirometry test. Implementing this step-wise approach in primary care may prove beneficial as a case finding tool. Spirometry alone is not cost effective and can be difficult to perform in the primary care setting without first identifying those who are most likely to have an abnormal spirometry test.

### Endnotes


1 Ries AL, Bauldoff GS, Carlin BW, et al. Pulmonary Rehabilitation: Joint ACCP/AACVPR evidence based clinical practice guidelines. Chest 2007;131;4S-42S

2 Fiore MC, Bailey WC, Cohen SJ, et al. Treating Tobacco Use and Dependence. Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service. May 2008.


improving patient adherence and understanding of COPD. Clearly, more progress is needed in the development of new therapies that can slow the progression of COPD and improve quality of life. For now, RTs and other healthcare professionals can play a key role in raising awareness of COPD by educating patients about the disease, and providing them with tests, tools, resources and access to an appropriate therapy and treatment regimen.

### Promoting Long-Term Optimal Care

We have clearly identified the need to perform optimal care management. Optimal care management must be maintained lifelong so it's critical that participation in Phase III be encouraged, whenever possible. However, maintaining optimal care management when a patient is unmonitored may be more challenging. RTs and healthcare professionals should offer information about programs and resources, develop local programs for transitional care, and collaborate with other organizations. In particular, they should collaborate with local home care companies, the State Smokers' Quit Line and the COPD Foundation, which offers tools designed for the acute care and transitional care setting, along with educational tools for decreasing hospitalization through patient self-management. The Foundation also offers a Pulmonary Education Program (PEP), which is geared towards supporting PRCs' efforts to promote long-term benefits of rehabilitation by connecting patients to resources after graduation. This is especially helpful if the patient is unable to participate in a Phase III pulmonary rehabilitation program.

### Tobacco Cessation

Only two things have been proven to prolong life for those living with COPD: quitting tobacco and oxygen therapy for those who medically require it. Oxygen does not change lung function, but rather it improves cardiovascular performance, and improves exercise endurance by providing higher levels of oxygen to muscles and tissues during activity. Tobacco cessation is the only intervention that actually slows the progression of lung function loss for the susceptible tobacco smoker. While individuals cannot return lung function to normal after quitting smoking, they will get some restoration and ultimately slow the rapid progression of lung function loss. (See Graph A)

Average smokers do not develop COPD as determined by FEV1 values. However, they generally have lower FEV1 values than non-smokers of the same age (see Graph A).

"Susceptible Smokers" develop a decline in FEV1 at a very early age. Even at ages 35 to 45, a decline trend is observed. This group is just beginning to develop symptoms of COPD that become overlooked because they are mild, like chronic cough or mild dyspnea with heavy work or exercise. This age group will receive the most benefit from smoking cessation and may avoid development of COPD if caught early enough.

Dips in the "Susceptible Smoker" group represents severe decline in FEV1 from a small population of people that deviate from the normal because of multiple hits including: heavy tobacco use, other environmental exposures, co-morbidities, or Apha-1 Antitrypsin Deficiency. These groups have severe disease at early stages in life.

Disability usually appears with FEV1 values around 1.8 liters (50% pred), average age of 55. Death occurs with FEV1 values

*Continued on page 46…*

# Inhaler Techniques in COPD Patients: Avoiding Improper Use

Laura Baker, RN, BSN

**Abstract**
Improving inhaler technique in Chronic Obstructive Pulmonary Disease (COPD) patients is a challenge all healthcare providers need to address in their practice. As the number of people diagnosed with COPD continues to increase, the importance of symptom management becomes vital to increase the quality of life for COPD patients. Also, good treatment management will decrease the number of people disabled from this disease. This article describes a Capstone Project, which involved the development of ways to increase proper inhaler technique in COPD patients through a video, one-on-one counseling, and a brochure made by an adult nurse practitioner student in collaboration with a pulmonologist and graduate faculty.

Chronic obstructive lung disease affects 14.2% of people over the age of 65 and accounts for 19.9% of hospitalizations in people 65 to 75 years old (Gooneratne, Patel, & Corcoran, 2010). COPD is a disease of the lungs that causes dyspnea, exacerbations, and loss of ability to participate in life that can lead to depression and anxiety (Rozenbaum, 2008). COPD cannot be cured; therefore, the goal is to prevent the symptoms (Scullion, 2010). Inhalers are the best treatment because they target the lungs, allow a decreased dose, and have less systemic side effects. According to Barron, Pegram, and Borries, the best treatment for COPD is education about the disease and the rest is medication (2011).

## Types of Inhalers

**Metered Dose Inhalers:** Metered dose inhalers (MDI) are rescue inhalers or short acting beta agonists like Albuterol or Proair that act on the smooth muscles in the lungs to cause bronchodilation. MDIs are the most common type of inhaler prescribed and least expensive (Scullion, 2010). Common errors with these inhalers include not holding the inhaler upright, not shaking it before use, and not taking a breath in at the same time as pressing on the canister (Hesselink, Pennix, Wijnhoven, & Kriegsman, 2001). Also, there is not a dose counter on the MDI device, making it hard to know how many treatments have been used and when it will be time for a new one. Even with perfect technique, only about 10% of the medication is delivered to the lungs, so accuracy is crucial (Knowles, 2008). Patients with arthritis or dementia may not have the hand-eye coordination needed to use this type of inhaler. These people could use a spacer, allowing the patient more time to inhale more medication, and so that less crucial hand-eye coordination is needed (Scullion, 2010).

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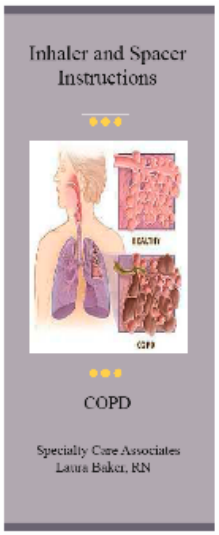
**Dry Powder Inhalers:** Dry powder inhalers (DPI) are maintenance inhalers or long acting beta agonists like Advair and Foradil that improve lung function for 12 hours or the whole day. Dry powder inhalers are breath actuated; therefore, timing is based on inhalation as opposed to timing when the canister is pressed for inhalation (Scullion, 2010). Some key information for the patients is not to swallow the capsule, hold a breath for 10 seconds after inhalation, and take two inhalations to make sure to get all of the powder out of the pill. Many people do not know this, which leads to a decrease in the amount of medication they receive, and symptoms persist. However, overall people seem to have a better technique with these inhalers (Hesselink, et al, 2001). Most DPIs provide a dose counter so patients know when it is time for a refill. Something a prescriber needs to keep in mind is these inhalers take a certain amount of inhalation force in order to use them correctly, so if the person has severe COPD, they may not have the force needed to use this type of inhaler. In DPI inhalers, 30% of the drug is delivered to the lungs if done correctly (Knowles, 2008).

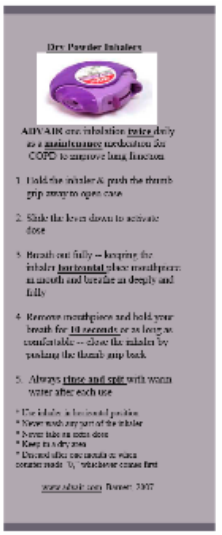
**Nebulizers:** Nebulizers or aerosol breathing treatments are easy to use but time consuming: 10 to 15 minutes. Nebulizers are relatively inexpensive; however, patients do have to rent a machine on top of getting the medication (Scullion, 2010). One advantage to nebulizers is patients can see the medication as they inhale. Disadvantages of the nebulizer are that there is a lot of equipment to clean and to take along when traveling (Barrons, et al, 2011). Nebulizers can be very useful for very severe COPD patients because these patients do not have sufficient force expiratory volume 1 (FEV1) to take a good breath. However, these patients may need help setting up the treatment if they are really weak.

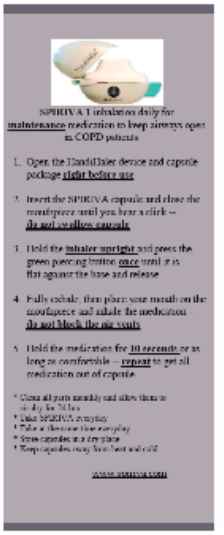
## Incorrect Inhaler Use

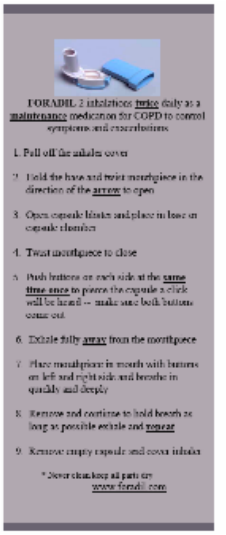
Inhalers are the best choice of treatment for COPD patients. However, studies have shown that 75% use MDIs incorrectly, and 43% use DPIs incorrectly, and it is important to figure out how to change these errors (Barrons, 2011). It has been found that many physicians themselves do not know how to use these inhalers. Also, many doctors do not have the time needed to give patients the proper e ducation. Continuity of care may also be lacking. For example, once the inhaler is prescribed, the patient may not get proper education because everyone else thinks the education has already been done (Hesslink, et al, 2001). One way for doctors to keep tabs on their patients' treatment success is by watching the increase in the number of rescue inhaler refills and decrease in maintenance inhaler refills (Barrons, et al, 2011). This should tell a physician that the patient is not using his or her medication correctly and needs more education. On the patient's side, they may have poor emotional or physical health, which

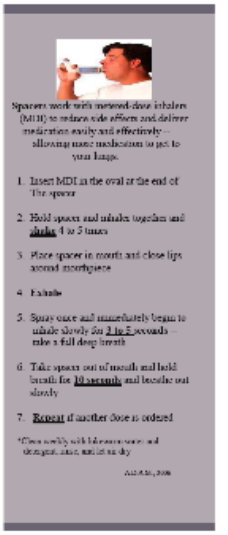







makes them less likely to be able to listen effectively, or they just do not care.

## Determining the Best Inhaler

A treatment plan for COPD needs to consider a patient's age, education level, co-morbidities, and if they are still smoking (Hesselink, et al, 2001). Also, consider the patient's symptoms; is the treatment for maintenance or acute symptom management (Scullion, 2010). It is also important to get a baseline FEV1 to make sure the patient has enough force to get the benefits from the inhaler. It is important to watch the patients use each inhaler before they leave the treatment center, to ascertain that they can use it correctly. A self-report questionnaire may also be helpful to see how patients view their disease, if they think their treatment is necessary, and if they can follow directions (Hesslink, et al, 2001). Last, but not least, cost has to be considered and discussed openly with the patient (Scullion, 2010).

## Improving Outcomes

Patients should be taught about the disease and how these inhalers are helpful in preventing its symptoms. Physicians need to explain when it is appropriate to use certain inhalers like the rescue versus the maintenance inhalers. If a patient is educated on why and when to use the inhalers, the chance of missing a dose or over-using an inhaler decreases (Hesselink, et al, 2001). Inhaler technique should be constantly monitored because a person who has been on an inhaler for several years may not continue to use it correctly. A nurse practitioner may find that the patient may be unable to use a previously prescribed inhaler because of physical reasons, or find that the inhaler is not preventing symptoms like it was.

Always be willing to change the treatment plan in order to best treat the patient (Hesselink, et al, 2001). Adherence to the treatment plan is better if the patient thinks it makes sense (Scullion, 2010). Also, caregivers need to be involved in how and when to use inhalers. Time taken initially with the patient teaching inhaler technique alleviates problems later on.

## Capstone Project

The Capstone Project is required in the Master's of Nursing program to evaluate the nurse practitioner student's ability to use synthesis and application of learning to make a project relevant and useful for the population the student will work with in the future. This project compiles all the previous courses of the program and emphasizes the need for evidenced-based practice to provide the best and up-to-date way of educating future patients. Since it seems that many of the COPD patients are not using their inhalers effectively or correctly, a project was developed to decide the best way to solve this problem. Scholarly research was done to see what literature existed that addressed the problem. Discussions occurred with a pulmonologist and her staff to decide what would help their particular patients.

The project member observed patients in the clinic using their inhalers and talked with them about their inhalers, finding that many did not use them correctly and were missing key information about them. The pulmonologist and her staff also showed concern that their patients needed more education and learning tools to take with them in order to have a guide once they went home. One obvious concern identified was that some patients were using the wrong inhaler for rescue and not using their maintenance inhaler routinely.

Because of this, the project was set into motion to educate these patients on why they were to use certain inhalers and when to use them. Also, they were taught the correct technique for using their inhalers and given the option of using a spacer. A video was made to demonstrate proper inhaler techniques and discuss the option of using a spacer. The video can be found at: http://www.youtube.com/watch?v=IjNo7AGIZy4&feature=email.

A brochure was developed so the patient had a take-home tool to remind them of how to use their inhaler and any key information about it. The pulmonologist decided which inhalers she wanted in the brochure and the video covered them as well.

## Planning Phase

To develop the best methods of increasing correct inhaler techniques, discussions were held with the pulmonologist, her staff, and her patients. Also, research was done to see what techniques were already available and being used. A point made in one of the articles was that the more time spent when the patient is first diagnosed and instructed to use an inhaler, the less likely they will need instruction down the road. Doctors themselves may not know how to use the inhaler correctly; therefore, they need to stay up to date or at least have the tools necessary to benefit their patients. Time is also a problem for doctors in that they are pressured to see so many patients a

day, leaving little time for education, and this is where a nurse practitioner could come into play and make sure these patients are instructed correctly.

It was decided that patients new to inhalers would be taught by the nurse and then instructed to watch the video that was developed in this Capstone Project. After the video, any questions would be answered by either the doctor or nurse, or the patients could go to websites on the video if they were comfortable with the internet. Finally, they would take home a brochure covering the same information in the video, giving them something they could refer to after the visit, which can be very overwhelming.

### Production Phase

Since the project member had no experience with video production, her parents volunteered their experience and equipment to help make the video. Her husband was the production manager and added key information and technical interest to the video. The video topic, inhaler techniques, was chosen because many people suffer every day from COPD, and the symptoms that go along with it cause patients to become debilitated. The goal was to help people learn proper technique and get back to living again. This topic is important to anyone diagnosed with COPD because these patients all need inhalers to help prevent their symptoms. The important information covered was written on cue cards, and the project member presented it to the camera. The inhaler video covered two different types of inhalers: dry powder and pressurized meter dose inhalers, how they work, adult dosing, step-by-step directions on how to use the inhaler, cleaning instructions, key information, and a website for each inhaler for more information. This information was gathered from the websites of Advair, Foradil, Spiriva, and Proair.

### Evaluation Phase

Evaluation of the video was done by the preceptor, a pulmonologist, and the professors. All evaluators agreed that the video was full of needed information. The video was easily understood, discussed clearly what each inhaler was used for, and included step-by-step instructions on how to use it. Feedback from the preceptor included statements such as, "very useful," and, "this video will be great for patients new to inhalers and anyone else that does not seem to understand how to use their inhalers." It was also noted that the written information included at the bottom of the video was helpful, so that people had two different ways of learning, and was an aid to the hearing impaired. The only suggestions were that the sound could have been louder and the lighting a little brighter. Overall, the video was well received and will be implemented into the preceptor's practice for new patients and anyone having problems with how to use inhalers. The message behind the video was to make sure that COPD patients are getting the most out of their medications, suffering less from their COPD symptoms, and in turn, enjoying a higher quality life.

The brochure was also evaluated by the preceptor and professors, and they thought that it was done professionally and included much needed information. The pictures included were good visual aids, and the step-by-step directions for each inhaler were clear, concise and easy to follow. The preceptor was very excited to implement the video into her practice as a teaching aide and as a tool for each patients who use an inhaler to take home and review. Proper cleaning of each inhaler was also included and this was an aspect of inhalers she felt many people did not know how to do correctly. Also, the brochure covered spacer use with metered dose inhalers, and she said she herself needs to do a better job using them with certain patients like the elderly or very ill, so that they can get as much of the medication inhaled as possible. She sent the brochure over to the print shop the same day to make sure she could implement it into her practice as soon as possible.

### Conclusions

The goal of this Capstone Project was to create a way to teach COPD patients proper inhaler techniques to improve symptom management. The number of people diagnosed with this disease continues to increase; therefore, teaching aids need to be available to help these people be as well as possible. The previous education these patients received was quick and done by a nurse. Now patients will be able to watch a video that describes the medication that they are taking, how to use it correctly, how to clean their equipment, and key information that they were not aware of before. Then they will be able to take home a brochure and review the information from the video. Having a condensed version of the video in the form of a brochure will be a great resource for COPD patients.

After developing this video and brochure, it is hoped that doctors like the preceptor recognize the need for nurse practitioners and how beneficial NPs would be for educating their patients. The idea of also making a video and brochure for asthma patients was also brought up and leads to many more educational paths for future nurse practitioners, demonstrating how helpful these teaching aides can be and how education is currently lacking. These patients need more education, and, unfortunately doctors are so strapped for time or out of practice themselves that a nurse practitioner could be the answer to closing the education gap for these patients.

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# Managing Obstructive Sleep Apnea with Provent Sleep Apnea Therapy

## 70 year-old woman diagnosed with obstructive sleep apnea and successfully treated with nasal expiratory positive airway pressure

Sarah Stolz, MD

### Introduction

Patient JV is a 70 year-old woman, with BMI of 33, diagnosed with obstructive sleep apnea (OSA) in 2008. She also has restless legs syndrome, hypertension and a history of thyroid disease and acid reflux.

A polysomnographic sleep study was performed showing an overall apnea-hypopnea index (AHI) of 28 events per hour, supine AHI of 52 events per hour and a nadir oxygen saturation of 77%. At this point, she was diagnosed with moderate severity obstructive sleep apnea, with moderate to severe oxyhemoglobin desaturations.

### Treatment Approach

Continuous positive airway pressure (CPAP) therapy was recommended to treat her OSA. The patient declined CPAP because she did not wish to wear the mask or carry the machine during her frequent air travel.

Provent Sleep Apnea Therapy, a disposable, nightly-use prescription, nasal expiratory positive airway pressure (EPAP) therapy was offered as an alternative treatment. The patient found this option more appealing because of its small size, ease of use, and portability.

A sleep study was performed on patient JV with Provent Therapy showing dramatic improvements in her OSA in all sleep positions. Overall AHI was reduced to 1.8 events per hour and supine AHI was 3.5 events per hour (Figure 2) versus the overall AHI of 28 events per hour and supine AHI of 52 events per hour prior to treatment (Figure 1). The patient spent roughly the same percentage of sleep time supine in both studies.

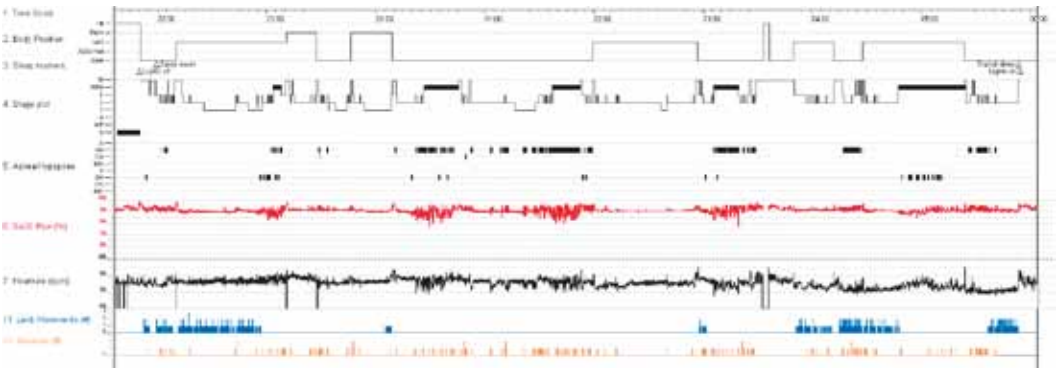

**Figure 1:** Patient's polysomnography hypnogram prior to treatment

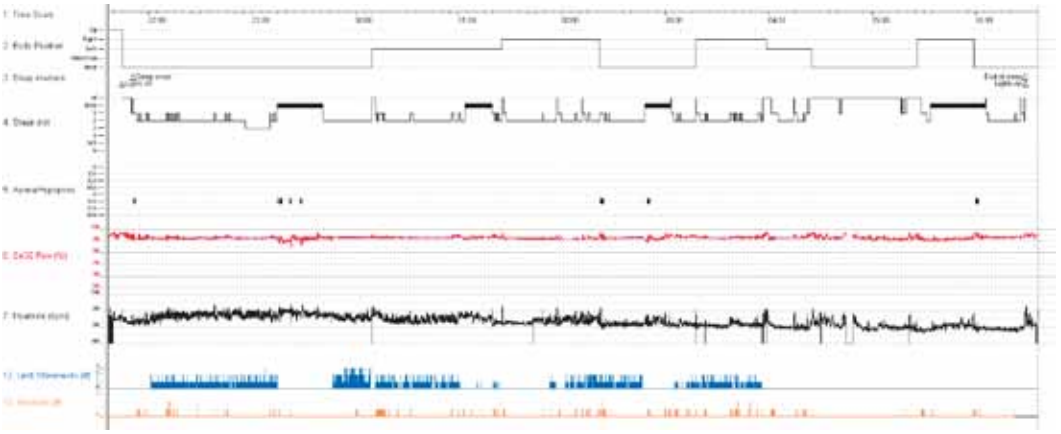

**Figure 2:** Patient's polysomnography hypnogram with PROVENT Therapy

### Patient Feedback Regarding Provent Therapy

Upon follow-up interview, JV reported an excellent overall satisfaction level, noting that she

- Likes the discreetness and dignity that it provides
- Finds it easy to use and very comfortable to wear when falling asleep and during sleep
- Appreciates being able to effectively treat her OSA while living an enjoyable lifestyle
- Plans to continue using it every night indefinitely

### Physician Summary

While nasal positive airway pressure is generally considered to be the gold standard treatment for patients with moderate to severe obstructive sleep apnea, some patients are unwilling or unable to use this therapy, and Provent Therapy provides a very welcome alternative treatment approach. In JV's case, this therapy turned out to be not only very well tolerated, but also very effective. JV currently reports a high level of satisfaction and compliance with the therapy after 10 months of use. Having this novel treatment provides physicians with an additional tool with which to treat apnea patients and allows patients to feel that they're not being "forced to use a machine."

Provent Therapy is a disposable, nightly-use, prescription device that incorporates a novel Micro-Valve design that is placed over the nostrils and secured with hypoallergenic adhesive. It is indicated for the treatment of obstructive sleep apnea (OSA) and works across mild, moderate, and severe OSA.

Sara Stolz, MD is a Diplomate of the American Board of Sleep Medicine and has been treating patients with sleep apnea for 19 years. She is Medical Director of Sleep Medicine Associates, which is based in the Seattle area and is the largest sleep medicine facility in the Pacific Northwest. This article was provided by Ventus Medical, Inc.

*Editorial…continued from page 4*

lifetime of smoking. They mentioned its detrimental effects: "I am poisoned," and "...it's a terrible condition but then it's self-inflicted with the cigarettes." Patients felt guilty about breathlessness; they felt responsible for having brought it onto themselves.

All patients had experience with inhalers and steroids, but inhalers offered minimal relief, and steroids caused side effects. Five patients relied on oxygen at home. Six had a nebulizer, two had purchased one on their own. They were unanimous that it helped their breathing and calmed them down.

Eight patients said they had never had any advice on how to manage their breathlessness: "I don't know what to do[...] you can't run to the doctor every 5 minutes, you can't run to casualty, you need to know how to deal with things yourself, [...] at least be discussing them..."

In the absence of professional advice one patient mentioned simple strategies: steam baths, a fan, open windows. Five patients went to PR classes. They learned the necessary skills and behaviors to self-manage and this gave them an acceptable quality of life. Only the patients who received PR said they cope reasonably well. Those who did not said that breathlessness inhibited every movement which led patients to reduce their activities even more, to the essentials. Gradual deconditioning made them realize that there is no "magic pill" for their suffering.

Disability was mentioned most frequently. They were often restricted to the home, leading to social isolation. Disability caused financial hardship as they lost their jobs, partners took on the role of carer over time. They spoke of having problems with access to care. Stigma added to patient suffering. Patients were not prepared to face the future and expressed only to be able to cope with one day at a time.

The paper concluded: Integrated palliative care is needed, that makes use of all appropriate therapeutic options, collaborative efforts from health, social care professionals, patients and caregivers, and therapies that acknowledge the dynamic interrelation of the body, mind and spirit.

Les Plesko, Editor

*The lived experience of breathlessness and its implications for care: a qualitative comparison in cancer, COPD, heart failure and MND [ALS]. Marjolein H. Gysels and Irene J. Higginson, BioMed Central, BMC Palliative Care 2011, © 2011 Gysels and Higginson; licensee BioMed Central Ltd.

# New Artificial Airway Monitoring Technology and Early Feedback from Deployment in the Adult ICU

### The SonarMed AirWave

The recently launched SonarMed AirWave brings a new respiratory tool to the Adult ICU that provides precise, real-time information about the ETT to support improved quality of care and patient safety. The AirWave uses acoustic reflectometry to help the clinician detect ETT obstructions, monitor ETT tip movement, and differentiate ETT placement (tracheal vs mal-positioned).

Using a disposable Adapter that resides in the respiratory circuit at the proximal end of the ETT and is connected via cable to a reusable Monitor, the AirWave translates reflected sound waves into easy to understand graphical/numerical feedback as well as acoustic waveforms. User-set alarms allow custom clinical parameters to be set for each patient, creating a 24/7 continuous monitoring tool. For more information about the AirWave system and how it works, see www.sonarmed.com.

### Clinical Issues

The AirWave was designed to give clinicians a tool to improve patient safety by reducing adverse events and complications, facilitated by the preventive actions the AirWave enables. While the list of complications associated with mechanical ventilation is long and serious, the areas of clinical and economic impact the developers of the AirWave focused on were:

- Reduction of unplanned extubations (UE). Study data from the 1980s through the last decade show an unchanging UE rate of approximately 10%.[1] Because a substantial portion of unplanned extubations require emergency reintubations (which are highly correlated to ventilator associated pneumonia, or VAP), the average cost of a single UE incident is approximately $35,000.[1] Even a modest reduction in UE will have a substantial impact on ICU costs and average length of stay.
- Reduction of undetected obstructions and subsequent extended weaning time. When weaning a patient, any additional work of breathing has the potential to extend the weaning process or even cause weaning failure. Undetected obstructions are a prime cause of additional work of breathing during weaning.
- Reduction of chest x-rays (CXRs). While there are many reasons to take a CXR, many times the sole reason is to verify ETT tip location, which creates the potential to instead use the tip position tracking of the AirWave.

This paper was provided by SonarMed.

There may also be other potential benefits to use of the AirWave, such as reduced malposition rates during intubation, reduced suctioning, reduced use of bronchoscopy for investigating suspected ETT constriction, and reduced aspiration.

### High Expectations

Based on respiratory clinicians surveyed after receiving an AirWave demonstration at the 2011 AARC,[2] expectations are high among clinicians that the AirWave will benefit patient safety and patient care. In fact, over 90% of all clinicians surveyed, and most notably over 90% of Respiratory Directors surveyed, indicated that the AirWave had "high potential" or "very high potential" to "reduce complications/adverse events" in ventilated patients. As well, over 90% of surveyed clinicians indicated that the AirWave had "high potential" or "very high potential" to "improve patient safety" and "improve patient care."

While quantitative outcomes studies to test those expectations are still some time away, early anecdotal feedback from routine use on approximately 20 ICU patients gives some promising indications that the AirWave delivers significant clinical value in the Adult ICU. In fact, clinical issues that might have otherwise been missed were identified in over 25% of patients.

### Adult ICU use – settings

With the cooperation of various sites using the AirWave in the Adult ICU, SonarMed has collected anecdotes and feedback shared by those clinicians using the system. A diversity of clinical settings was selected in order to represent a broad swath of the market, including:

- A Midwestern long-term acute care facility (LTAC)
- A single hospital of a large west-coast "ACO"-type healthcare system
- A very large (1000 beds,150 ICU beds) hospital on the east coast
- A single hospital of a large Midwestern traditionally structured hospital system

The anecdotes cited below are drawn from across these four institutions as they used the AirWave system.

### ETT obstruction insights

1) A respiratory therapist (RT) noticed a persistent high obstruction in a patient's ETT. After checking, it was clear that the ETT was not obstructed nor was it kinked. Upon closer inspection, the RT found that the patient's tongue was positioned such that it impinged the ETT and was creating a

20% obstruction. After repositioning the patient's tongue, the obstruction was relieved.

2) Another novel source of obstruction caught the attention of an attending intensivist. The AirWave had recorded a persistent 20% obstruction high on the ETT that lasted for many hours. The intensivist concluded that the ETT holder, which was of a type that involved a cinch, had been overly tightened to the point of creating a 20% ET obstruction. "Sometimes," the intensivist related, "the ETT holder is so tight I can't even pass a scope through it. Imagine if someone restricted your trachea 20%. Now I have the data I need to get the nurses and RTs to listen to me and change their practice on tightening the ETT holder."

3) An RT coordinator related his experience in fielding an inquiry about the AirWave from an RT. The RT had summoned him because she was convinced that the AirWave was showing a "false" obstruction in the lower regions of the ETT – she had suctioned and there was no change in the signal, leading her to conclude it was a false signal. Convinced by the AirWave's waveform screen that the obstruction was real and probably caused by mucus, the coordinator began to work with the suction catheter and lavage. He got the obstruction to move a couple of centimeters, thus confirming in his mind that the obstruction was in fact real. After several more minutes, he was successful in suctioning mucus out of the ETT – showing that even though obstructions can be very persistent, so can a determined clinician when they are equipped with the right tools.

4) An RT noted that a patient had a persistent high obstruction of 25%. When the ETT was re-taped, the obstruction went away, and it was discovered that the 25% obstruction was caused by the OG tube being taped too tightly to the ETT.

### Patient airway insights

The RT on duty was growing frustrated with the AirWave because the system was reporting "excessive noise" and was not providing monitoring information (the system requires a short quiet period between breaths to collect measurements). As the RT stood by the patient's bed, she noted that there were no significant sources of external noise, so she employed the AirWave's "listen to microphones" on-board quality control (QC) feature, which enables the user to hear both Adapter microphone inputs broadcast over the Monitor's speaker to confirm Adapter function. Not only was the Adapter functioning, but to her surprise and in her words, the patient's airways were "roaring" – the patient clearly needed suctioning, but there were no external signs of it – no coughing, no rasping. After a thorough patient suctioning, the AirWave returned to continuous monitoring mode.

Two other hospitals noted a similar occurrence – the AirWave indicated excessive noise, and when the RT investigated further, the patient needed to be suctioned. After suctioning, the AirWave reported normal results.

### ETT tip movement insights

One site reported an AirWave alarm indicating 4-5 cm of tube tip movement up, but the ETT was securely taped at the patient's mouth. When the disbelieving RT staff investigated, they found the patient had a very large throat and pharynx, and previous chest x-rays had shown "lots" of ETT tip movement. Further investigation revealed that immediately prior to the movement high alarm, the nursing staff had turned the patient. The conclusion was that the tip movement was real but in this case had not endangered the patient.

### Additional clinical utility?

While the airwave is currently FDA cleared for three indications for use – assisting clinicians in determining ETT placement, movement, and obstruction – feedback from the Adult ICU as well as an animal study hints at the potential for additional clinical utility that, if supported with data and cleared by FDA, could expand the value of the AirWave even further in the ICU.

At one site, RTs observed a steady decrease in the passageway size indication, with no significant movement at the tube tip. This particular patient shortly thereafter began to undergo significant clinical distress, and a chest tube was inserted. Immediately, the passageway size returned to normal. Unfortunately, as was discovered later, this patient had a hole in their heart and the ensuing severe internal bleeding resulted in patient mortality. The therapists speculated that the pressure on the pleural cavity from the internal bleeding was causing the trachea to contract, and when the chest tube relieved that pressure, the trachea returned to its normal size.

In addition to the ICU feedback, during an animal study using a pig, researchers were uncertain as to how much air to add to the ETT cuff, given their unfamiliarity with the size of a pig's trachea. They turned on the AirWave's "listen to microphones" on-board QC feature and used the "raspberry" sound of air escaping past the cuff to determine minimal occluding volume for cuff inflation. This raises the intriguing possibility of using the AirWave to determine minimum occluding volume and/or detect cuff leaks in human patients as well – after, of course, FDA clearance for such an indication.

### References


1 All referenced data are extracted from publications listed in SonarMed's White Paper "AirWave Health Economics," available for review or download at www.sonarmed.com.

2 n=46 for the AARC 2011 clinician survey. This survey was conducted after clinicians were given a brief demonstration of the system's functionality.

# High-Frequency Oscillatory Ventilation and Short-Term Outcome in Neonates and Infants Undergoing Cardiac Surgery

Mirela Bojan, Simone Gioanni, Philippe Mauriat, Philippe Pouard

## Abstract

**Introduction:** Experience with high-frequency oscillatory ventilation (HFOV) after congenital cardiac surgery is limited despite evidence about reduction in pulmonary vascular resistance after the Fontan procedure. HFOV is recommended in adults and children with acute respiratory distress syndrome. The aim of the present study was to assess associations between commencement of HFOV on the day of surgery and length of mechanical ventilation, length of intensive care unit (ICU) stay and mortality in neonates and infants with respiratory distress following cardiac surgery.

**Methods:** A logistic regression model was used to construct a propensity score, which accounted for the probability of being switched from conventional ventilation to HFOV, and included baseline characteristics, type of procedure and postoperative variables. It was used to match each patient in the HFOV group with a control. Length of mechanical ventilation, ICU stay and mortality rates were compared in the matched set.

**Results:** Overall 3549 neonates and infants underwent cardiac surgery from January, 2001 through June, 2010, and 120 were switched to HFOV. After matching and adjustment for delayed sternal closure, duration of renal replacement therapy, pulmonary hypertension and year of surgery, the probability of successful weaning over time was significantly higher in the HFOV group, adjusted hazard ratios and 95% confidence intervals (CI): 1.63, 1.17 to 2.26 (P = 0.004). The probability of ICU delivery over time was significantly higher in the HFOV group, adjusted hazard ratios and 95% confidence intervals: 1.65, 95% CI 1.20 to 2.28 (P = 0.002). No association was found with mortality.

**Conclusions:** When commenced on the day of surgery, HFOV was associated with shorter lengths of mechanical ventilation and ICU stay in neonates and infants with respiratory distress following cardiac procedures.

## Introduction

High-frequency oscillatory ventilation (HFOV) is an established treatment for acute respiratory distress in preterm neonates. However, there is no evidence that it improves outcome in term or near-term neonates with pulmonary disease.[1] HFOV is considered as a rescue therapy in children with severe acute respiratory distress syndrome (ARDS), but to date there is lack of evidence to support it.[2,3] HFOV is also used to achieve lung recruitment and improve oxygenation when recruitment maneuvers have failed, as part of the "open lung" and lung protective ventilation strategies in adults with severe ARDS, and early initiation of HFOV has been associated with improved outcome.[4-6] Mild acute lung injury occurs in 12% of adults following CPB, and more severe lung injury, indistinguishable from ARDS, in 0.4%,[7,8] as a result of accumulation of excessive extrapulmonary lung water, decreased lung compliance, atelectasis and increased shunting.

Experience with HFOV following cardiac surgery is limited, due to concerns about hemodynamic impairment in animal and human studies.[6,9-13] However, HFOV has been associated with a significant reduction in pulmonary vascular resistance (PVR) after the Fontan procedure in children.[14] Thought to be beneficial upon gas exchange and PVR, the present authors have used HFOV in neonates and infants with respiratory distress following cardiac surgery since January, 2007. The aim of the present study was to assess associations between commencement of HFOV on the day of surgery (day 0) and the length of mechanical ventilation and intensive care unit (ICU) stay, and mortality in this population.

## Materials and methods

This retrospective cohort study was conducted at the Necker University Hospital in Paris, France. It was reviewed and approved by the Ethics Committee of the French Society of Thoracic and Cardiovascular Surgery, which waived the requirement for consent to use anonymized records. All parents had provided informed consent to surgery.

Records of all neonates and infants who underwent cardiac surgery between January 1, 2001 and June 30, 2010 were reviewed, patients switched to HFOV on the day of surgery (day 0) were identified as the HFOV group. Those switched to HFOV after day 0, as a rescue therapy, were not analyzed. The remaining patients were included in the control group. Data for each patient were extracted retrospectively from a prospective database, which is updated daily by clinical staff. These concerned: demographics, surgical and cardiopulmonary bypass (CPB) techniques, short-term outcome variables accounting for

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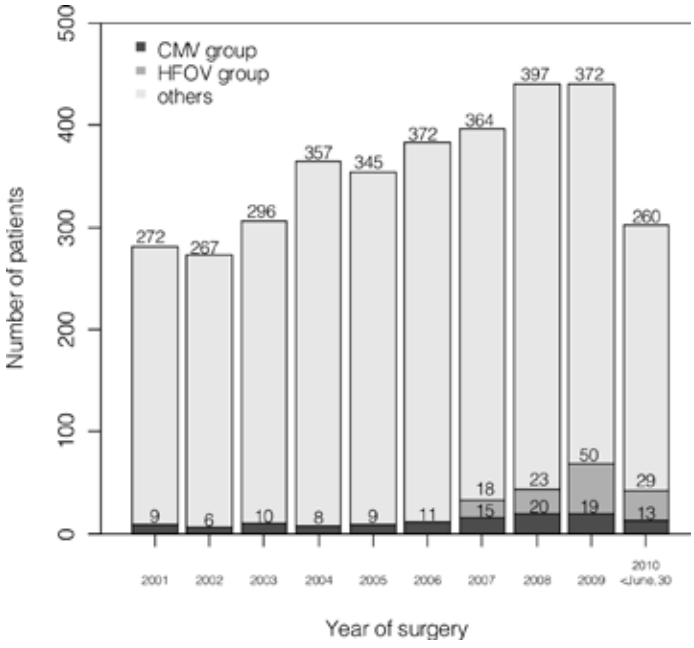


**Figure 1.** Number of neonates and infants who underwent surgery during the study period. The number of patients included in each group after matching is shown on the bottom of each column. High frequency oscillation was used since 2007. CMV, conventional mechanical ventilation; HFOV, high-frequency oscillatory ventilation.

the severity of the postoperative illness, such as re-operation, delayed sternal closure, extracorporeal membrane oxygenation (ECMO), acute kidney injury requiring renal replacement therapy (RRT), and hospital-acquired pneumonia, length of mechanical ventilation, length of ICU stay, and inhospital mortality.[15] Normothermic CPB with intermittent warm blood cardioplegia was performed in every patient during the study period, except in cases where deep hypothermic circulatory arrest (DHCA) was indicated.[16] Pulmonary arterial pressure was measured in every patient, either continuously by a catheter inserted into the pulmonary artery by the end of surgery, or by

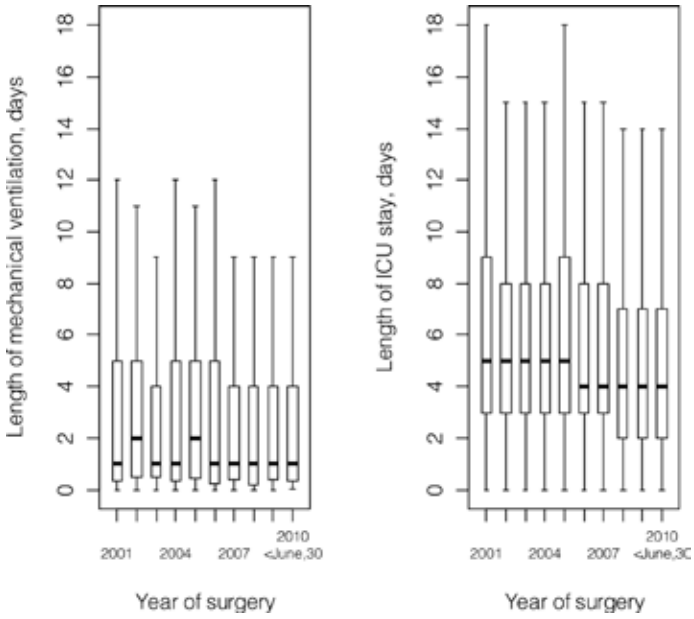


**Figure 2.** Length of mechanical ventilation and Intensive Care Unit stay across the study period. The median values and the inter-quartile ranges were used to construct the boxes. 10th and 90th percentiles are given as whiskers. Outliers are not shown. ICU, Intensive Care Unit.

serial echocardiography. Persistent pulmonary hypertension was noted whenever it occurred during the postoperative course, and inhaled nitric oxide was administered.[17]

All patients were initially commenced on pressure controlled conventional mechanical ventilation (CMV) using a SERVO-300 (Siemens – Elema AB, Sweden) before 2002, then a SERVO-i ventilator (Maquet GmbH&Co. KG, Rastatt, Germany). This was set to provide a positive end expiratory pressure of 2cm$H_2O$, a tidal volume of 6-8ml Kg-1, and a fraction of inspired oxygen which was dependent upon the underlying cardiac disease. In the event of severe respiratory failure, recruitment maneuvers by stepwise increase in the mean airway pressure were applied. The patients were switched to HFOV when hypoxemia and acidosis occurred despite increasing alveolar ventilation on CMV, when the tidal volume exceeded 10ml kg-1, or when there was evidence of pulmonary hypertension and right ventricular failure. The decision to switch was made by the attending intensivist. A SLE 2000 or a SLE 5000 HFO ventilator (SLE Ltd, South Croydon, UK) was used. This was set to a mean airway pressure (Paw) of 12cm$H_2O$, an inspiratory to expiratory ratio of 33%, and an oscillation frequency of 8Hz. Amplitude was adapted to achieve adequate chest wall vibrations. All parameters were adjusted to achieve optimal inflation, a $PaCO_2$ of 35-45mmHg and a pH >7.35. The adequacy of the $PaO_2$ level was judged according to the underlying cardiac disease. Patients were switched back to CMV when these conditions had been achieved with an oscillation frequency ≥ 10Hz and a mean Paw ≤ 10cm$H_2O$. Sedation was achieved through a continuous infusion of midazolam and morphine. Whenever possible, muscular relaxants were avoided and spontaneous breathing was maintained. Catecholamine support (milrinone and epinephrine), fluid support and diuretics were administered as appropriate to achieve hemodynamic stability and a negative fluid balance. All patients were weaned from mechanical ventilation when the underlying indication had resolved and following a successful 1-hours trial of spontaneous breathing with a continuous positive pressure of 2cm$H_2O$ and a pressure support of 10cm$H_2O$.

## Statistical analysis

After testing for normality, baseline characteristics of the two groups were compared using Student's t or Mann-Whitney tests for continuous variables and $\chi 2$ or Fisher's exact tests for categorical variables.

The hypothesis tested was that patients switched to HFOV had shorter length of mechanical ventilation and ICU stay and lower mortality rates. To control for the bias due to selection of patients switched to HFOV, 1:1 propensity score matching was carried out.[18] Logistic regression was used to develop a propensity score quantifying the probability for each patient undergoing surgery since January 2007 to be switched to HFOV. This included all baseline and post-operative variables accounting for severity of illness found to be

different between groups in univariate analysis ($P < 0.10$), and the HFOV index. Given the large number of surgical procedures and the absence of guidelines for HFOV in this context, an empirical HFOV index was attributed to each procedure. This accounted for the influence of each specific procedure on the probability to be switched to HFO, and was calculated as the prevalence of HFOV per procedure between January 2007 and

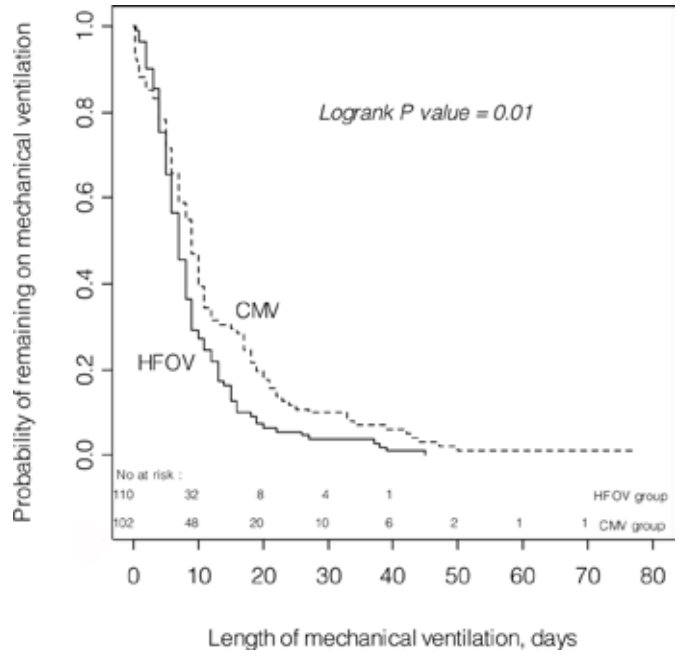


**Figure 3.** Kaplan-Meier plots of the probability of successful weaning over time for each ventilation group. The median length of mechanical ventilation was 7 days in the high-frequency oscillatory group, inter-quartile range 5 to 11, and 9 days in the conventional mechanical ventilation group, inter-quartile range 5 to 17, logrank test = 6.18, P = 0.01. CMV, conventional mechanical ventilation; HFOV, highfrequency oscillatory ventilation.

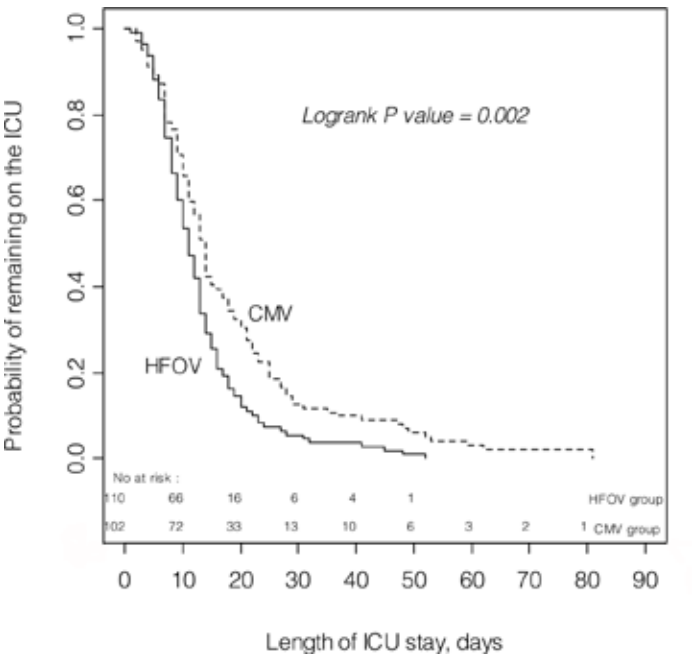


**Figure 4.** Kaplan-Meier plots of the probability of ICU delivery over time for each ventilation group. The median length of ICU stay was 11 days in the high-frequency oscillatory ventilation group, inter-quartile range 7.2 to 15.7 compared with 14 days in the conventional mechanical ventilation group, inter-quartile range 9 to 22, logrank test, 9.39, P = 0.002. CMV, conventional mechanical ventilation; HFOV, highfrequency oscillatory ventilation.

June 2010.

In accordance with previous authors, length of mechanical ventilation and length of ICU stay were modeled as censored variables in survivors, with weaning from mechanical ventilation and ICU delivery as censoring events.[19] The probability over time of successful weaning from mechanical ventilation and of ICU delivery for each group was calculated using the Kaplan-Meier method, and compared using the log-rank test. Results were confirmed using a multivariable Cox proportional-hazards model, controlling for variables related to length of ICU stay following pediatric cardiac surgery in a previous study,[20] variables unbalanced after matching (P < 0.10), for the propensity score and the year of surgery. Adjusted Hazard ratios (HR) were estimated.

The R statistical package, "Design" and "optmatch" libraries[21] were used for the analyses.

## Results

Overall 3549 neonates and infants with cardiac surgery were retrospectively enrolled. Life support was withdrawn from four patients with obstructed total anomalous pulmonary venous connection and one patient with severe pulmonary hypoplasia, with hopeless prognosis secondary to pulmonary lymphangienctasia. Another two patients died periprocedural, leaving 3542 cases to be analyzed. The number of patients, their length of mechanical ventilation and ICU stay across the study period are shown in Figures 1 and 2.

Patient characteristics are shown in Table 1. The 120 neonates and infants switched to HFOV on day 0 were younger and smaller, had undergone more complex surgery and had experienced more severe postoperative illness. Patients switched to HFOV had longer durations of both mechanical ventilation, median 7 days, inter-quartile ranges (IQR) 5-11 vs. 1 day, IQR 0.3-4 in controls (P < 0.001), and ICU stay, median 11 days, IQR 7-15.7 vs 4 days, IQR 3-7 (P < 0.001). The median duration of HFOV was 4 days, IQR 2-7. The inhospital mortality rates for the two groups were similar, 8.3% in patients switched to HFOV vs 4.8% in controls (P = 0.08).

Table 2 shows the most prevalent procedures and their HFOV indexes, range 0 - 0.82, median 0.04, IQR 0.03 - 0.08. Table 3 shows the variables included in the propensity score. When data was missing, the median of the respective variable was used (< 5% of all information concerning CPB technique was missing). The propensity score model was well calibrated (Hosmer Lemeshow test, P = 0.14) and discriminated well between patients on HFOV and the others (c index = 0.82). Patients were more likely to be switched to HFOV on day 0 if they were small, had undergone a procedure with high HFOV index, required CPB and DHCA, had hemodynamic impairment precluding closure of the sternum or required RRT on day 0. Patients commenced on postoperative ECMO were not matched due to their high mortality rate (39.1%).

Matching resulted in two well-balanced groups of 120 patients respectively: the HFOV and the CMV groups (Table 1). The HFOV group had shorter durations of mechanical ventilation, 7 days, IQR 5 - 11 vs 9 days, IQR 5 - 17 in the CMV group (P = 0.03), shorter durations of ICU stay, 11 days, IQR 5 - 17 vs 14 days, IQR 9 - 22 (P = 0.009), a higher prevalence of pulmonary hypertension, 36.7%, compared to 23.3% (P = 0.03) and a similar prevalence of hospital-acquired pneumonia, 49.2% in the HFOV group compared to 47.5% in the CMV group (P = 0.80). Ten patients in the HFOV group (8.3%) died during ICU stay, compared to 18 in the CMV group (15.8%) (P = 0.08). Median

**Table 1 Perioperative patient characteristics before and after matching**

| | Before matching | | | After matching | |
|---|---|---|---|---|---|
| | HFOV group (*n* = 120) | Overall controls (*n* = 3,422) | *P*-value[a] | CMV group (*n* = 120) | *P*-value[b] |
| Age (days) | 27, 7.7 to 100.2 | 58, 10 to 149 | 0.001 | 33.0, 7.0 to 89.5 | 0.83 |
| Weight (kg) | 3.4, 2.9 to 4.3 | 3.9, 3.2 to 5.4 | < 0.001 | 3.3, 2.8 to 4.2 | 0.93 |
| Surgery with cardiopulmonary bypass, n (%) | 109 (90.8) | 2560 (74.8) | < 0.001 | 110 (91.7) | 0.80 |
| Duration of cardiopulmonary bypass (min) | 128.0, 99.5 to 177.0 | 109.0, 77.0 to 134.0 | < 0.001 | 128.0, 90.0 to 165.0 | 0.64 |
| Conventional ultrafiltration rate (mL $kg^{-1}$ $h^{-1}$) | 93.3, 69.9 to 120.6 | 96.6, 66.9, 132.3 | 0.27 | 98.3, 87.2 to 127.3 | 0.40 |
| Aristotle score[c] | 9.0, 7.5 to 10.8 | 8, 6 to 10 | < 0.001 | 9.0, 7.3 to 10.8 | 0.99 |
| Surgery with deep hypothermic circulatory arrest, n (%) | 19 (15.8) | 251 (7.3) | < 001 | 21 (17.5) | 0.72 |
| Re-sternotomy, n (%) | 19 (15.8) | 406 (11.9) | 0.19 | 16 (13.3) | 0.59 |
| Requiring re-operation, n (%) | 13 (10.8) | 177 (5.2) | 0.007 | 16 (13.3) | 0.56 |
| Re-operated within 48 hours, n (%) | 3 (2.5) | 18 (0.5) | 0.03 | 2 (1.7) | 0.66 |
| Extracorporeal membrane oxygenation, n (%) | 0 | 23 (0.7) | | 0 | |
| Requirement for delayed sternal closure, n (%) | 56 (46.7) | 331 (9.7) | < 0.001 | 57 (47.5) | 0.85 |
| Delay to sternal closure (days) | 3, 2 to 4.2 | 4, 2 to 6 | 0.21 | 4, 3 to 7 | 0.08 |
| Acute kidney injury requiring renal replacement therapy, n (%) | 42 (35.0) | 127 (3.7) | < 0.001 | 39 (32.5) | 0.58 |
| Requirement for renal replacement therapy on the day of surgery, n (%) | 37 (30.8) | 89 (2.6) | < 0.001 | 32 (26.7) | 0.36 |
| Duration of renal replacement therapy (days) | 2, 1 to 4 | 3, 2 to 6 | 0.02 | 3, 2 to 7 | 0.09 |
| The propensity score | 0.07, 0.02 to 0.31 | 0.02, 0.01 to 0.03 | | 0.07, 0.02 to 031 | |

The "HFOV group" included all patients switched to high frequency oscillation on the day of surgery, "Overall controls" included all patients ventilated exclusively conventionally during the study period, and the "CMV group" included the patients ventilated exclusively conventionally in the matched set.

CMV, conventional mechanical ventilation; HFOV, high-frequency oscillatory ventilation.

[a]calculated before matching, using unpaired tests which compared the HFOV group with overall controls

[b]calculated after matching, using paired tests which compared the HFOV group with the CMV group

[c]accounting for the surgical complexity

Data are shown as medians and inter-quartile ranges, or as numbers and percentages.

follow-up was 411 days, IQR 32-3060, 18 patients (15.8%) died during follow-up in the HFOV group, compared to 22 in the CMV group (18.3%) (P = 0.66).

Kaplan-Meier plots of the probability of successful weaning over time are shown in Figure 3. The median length of mechanical ventilation was 7 days in the HFOV group, IQR 5- 11, and 9 days in the CMV group, IQR 5 - 17 (P = 0.01). Four patients in the HFOV group underwent mechanical ventilation for ≥ 30 days. Of these, one developed tracheal stenosis and underwent slide tracheoplasty, another required tracheostomy. Ten patients in the CMV group underwent mechanical ventilation for ≥ 30 days. Of these, two developed tracheal stenosis, one of whom died, one developed oeso-tracheal fistula and died, and seven developed chronic lung disease, of whom four required tracheostomy and two died. Kaplan-Meier plots of the probability of ICU delivery over time are shown in Figure 4. The median length of ICU stay was 11 days in the HFOV group, IQR 7.2 - 15.7 and 14 days in the CMV group, IQR 9-22 (P = 0.002). Differences between length of ventilation and ICU stay were found significant with a statistical power of 0.77 and 0.89 respectively.

Cox proportional-hazards regression analysis, adjusted for the delay to sternal closure, duration of RRT, occurrence of pulmonary hypertension and year of surgery, showed that patients in the HFOV group had a higher probability of successful weaning over time, adjusted HR 1.63; 95% confidence interval (CI) 1.17 - 2.23 (P =0.004) (Table 4). The probability of ICU delivery over time was also higher in the HFOV group, adjusted HR 1.65, 95% CI 1.20 - 2.28 (P = 0.002) (Table 4). Longer delay to sternal closure was independently associated with longer length of mechanical ventilation and ICU stay.

## Discussion

The present study reports experience with HFOV in a mixed pediatric cardiac surgery population of neonates and infants with respiratory distress. Previous findings reported from randomized trials of HFOV in term or near-term neonates with pulmonary disease showed no benefit in terms of 28-day mortality,[1] and our findings were similar. But, unlike previous research on elective use of HFOV, length of mechanical ventilation and hospital stay were reduced among patients with a similar severity of illness when they were switched to HFOV on the day of surgery.

HFOV and PVR: The most common reasons for late weaning from mechanical ventilation following congenital cardiac surgery are a low cardiac output state or a respiratory complication. Even when ventricular function is well preserved and no residual anatomical lesion is present, a low cardiac output may result from inadequate pulmonary blood flow, secondary to elevated PVR. Maintenance of cardiac output by fluid challenge, to ensure adequate preload, leads to extravascular fluid accumulation, pleural and pericardial effusions, pulmonary interstitial edema and decreased compliance. The loss of intravascular volume must be replaced to maintain cardiac output, which may initiate a vicious cycle, and should therefore be avoided.

PVR is multifactorial after CPB[22,23] and highly sensitive to changes in intrathoracic pressure[24] and acidosis.[25] Changes in intra-thoracic pressure have been extensively investigated in the Fontan procedure, where high-frequency ventilation has been found to be associated with an increase of up to 25% in cardiac output and lead to halve PVR and mean Paw.[14] Although HFOV is known to be effective in settings leading to hypoxemia, the use has been described in reports of asthma and severe bronchiolitis

**Table 2 Most prevalent procedures in the matched set, along with their "HFOV indexes"**

| Most prevalent procedures | HFOV group (*n* = 120) | CMV group (*n* = 120) | "HFOV index"[a] |
|---|---|---|---|
| Obstructed TAPVC repair | 14 | 12 | 0.82 |
| Unrestrictive VSD repair | 10 | 10 | 0.06 |
| Complete common atrioventricular canal | 9 | 7 | 0.11 |
| Aortic arch repair | 8 | 7 | 0.19 |
| Arterial switch operation, VSD repair | 6 | 9 | 0.08 |
| Truncus arteriosus repair | 6 | 7 | 0.30 |
| Arterial switch operation | 5 | 8 | 0.03 |
| Norwood operation | 6 | 6 | 0.41 |
| Modified Blalock Taussig shunt | 5 | 5 | 0.09 |
| Tetralogy of Fallot repair | 6 | 4 | 0.04 |
| Coarctation repair | 7 | 2 | 0.04 |
| Pulmonary atresia, VSD repair | 5 | 3 | 0.18 |
| Arterial switch operation, VSD, coarctation repair | 3 | 4 | 0.18 |
| Bidirectional Glenn | 2 | 4 | 0.05 |
| Konno Ross procedure | 2 | 4 | 0.50 |
| Aortic valvuloplasty | 3 | 3 | 0.10 |
| Other | 22 | 25 | |

CMV, conventional mechanical ventilation; HFOV, high-frequency oscillatory ventilation; TAPVC, total anomalous pulmonary venous connection; VSD, ventricular septal defect.

[a]accounting for the prevalence of HFOV from 1 January 2007 through 30 June 2010

to treat respiratory acidosis.[26,27] According to Babik et al,[23] CPB is responsible of an obstructive process in the bronchi, leading to bronchospasm and acidosis. Bronchospasm is also a frequent postoperative finding in patients with a large preoperative left to right shunt.[28] Thus, the use of HFOV to treat respiratory acidosis in an attempt to decrease PVR after CPB appears justified. In the present study, when switching to HFOV, ventilation frequency was initially set to 8 Hz to promote decarboxylation and, thus, rapidly increase pH. But the retrospective design of the present study rendered collection of reliable data concerning PVR, Paw and gas exchanges impossible. Nevertheless, documented pulmonary hypertension was more prevalent in the HFOV group (before or after transition to HFOV) even after propensity score matching, showing that the HFOV group was still more severely ill. Therefore, the shorter durations of mechanical ventilation in the HFOV group suggested beneficial effect of HFOV upon PVR.

Hemodynamic status: Usually, HFOV involves slightly higher mean Paw values than CMV, and low cardiac output may occur due to increased pleural pressure and reduced venous return. Studies of HFOV in animal models of ARDS have reported hemodynamic impairment when high airway pressures were applied.[9-11] Studies of adults[6,12,13] and infants[29,30] switched from CMV to HFOV have found effects such as increased pulmonary artery occlusion pressure, increased central venous pressure, and small decreases in cardiac output and stroke volume index, although it was unclear whether these changes were clinically relevant.

By contrast, sedation may lead to excessive venous vasodilatation and impaired venous return following cardiac surgery, whereas spontaneous breathing maintains a negative pleural pressure, facilitates venous return and improves cardiac output. Spontaneous ventilation can be maintained easily in neonates and small children on HFOV without increasing the work of breathing,[31,32] thus allowing reduced sedation.

**Table 3 Estimates and standard errors for variables included in the propensity score model**

| Variable | Coefficient estimate | Standard error | *P*-value |
|---|---|---|---|
| Intercept | -2.87 | 0.58 | < 0.001 |
| The "HFOV index"[a] | 3.94 | 0.48 | < 0.001 |
| Age (days) | 0.002 | 0.002 | 0.19 |
| Weight (kg) | -0.37 | 0.12 | 0.002 |
| Aristotle score[b] | -0.09 | 0.06 | 0.10 |
| Surgery with cardiopulmonary bypass | 0.87 | 0.37 | 0.02 |
| Surgery with deep hypothermic circulatory arrest | -0.97 | 0.33 | 0.004 |
| Re-operation | 0.59 | 0.34 | 0.09 |
| Requirement for a delayed sternal closure | 0.81 | 0.29 | 0.005 |
| Acute kidney injury requiring renal replacement therapy | 0.36 | 0.62 | 0.56 |
| Requirement for renal replacement therapy on the day of surgery | 1.82 | 0.63 | 0.004 |

The propensity score model included only patients operated from 1 January 2007 through 30 June 2010.

HFOV, high-frequency oscillatory ventilation

[a]calculated as the prevalence of HFOV from 1 January 2007 through 30 June 2010

[b]accounting for the surgical complexity

**Table 4 Independent predictors of successful weaning from mechanical ventilation and ICU delivery over time**

| | Successful weaning from mechanical ventilation | | | ICU delivery | | |
|---|---|---|---|---|---|---|
| **Variable** | **Adjusted Hazard Ratio** | **95% CI** | ***P*-value** | **Adjusted Hazard Ratio** | **95% CI** | ***P*-value** |
| HFOV | 1.62 | 1.17 to 2.25 | 0.004 | 1.65 | 1.19 to 2.28 | 0.002 |
| Delay to sternal closure (days) | 0.87 | 0.82 to 0.93 | < 0.001 | 0.88 | 0.82 to 0.94 | < 0.001 |
| Pulmonary hypertension | 0.74 | 0.54 to 1.02 | 0.07 | 0.73 | 0.53 to 1.01 | 0.05 |
| Duration of renal replacement therapy (days) | 0.95 | 0.89 to 1.02 | 0.19 | 0.94 | 0.87 to 1.01 | 0.08 |
| Year of surgery | 0.93 | 0.87 to 0.99 | 0.03 | 0.95 | 0.88 to 1.02 | 0.16 |
| The propensity score | 2.59 | 1.10 to 6.08 | 0.03 | 2.38 | 0.99 to 5.75 | 0.05 |

Adjusted Hazard ratios and 95% CI were estimated using Cox proportional-hazards regression analysis

CI, confidence interval, HFOV, high-frequency oscillatory ventilation

Reliable evaluation of hemodynamic consequences when changing ventilatory settings is impossible in a retrospective study. The low mean Paw strategy employed in the present study may have allowed preserve the hemodynamic stability on HFOV in our patients. Furthermore, if a long delay to sternal closure and a long duration of RRT were considered markers of hemodynamic impairment, then switching to HFOV may have resulted in hemodynamic improvement in the present cohort, since both the delay to sternal closure and the duration of RRT were slightly reduced in the HFOV group (Table 1).

Limitations: The present study was retrospective, and thus the validity of the results must be viewed with caution. Attempts were made to minimize bias related to selection of patients switched to HFOV through propensity score matching. Even though, and despite adjustment for the year of surgery, the choice of historical controls cannot rule out bias related to improvements in surgical and medical management of congenital heart diseases throughout the study period. Besides, the choice of transition to HFOV was made by the attending intensivist, and, despite the propensity score methodology employed, we cannot rule out residual bias related to pre-held beliefs about HFOV's performance. Furthermore, analysis of ventilation parameters and hemodynamic consequences were lacking. Because of the various intra-cardiac shunting patterns in the study population, oxygenation indexes were not analyzed. Future studies should address these limitations.

## Conclusions

When commenced on the day of surgery, HFOV was associated with a shorter duration of mechanical ventilation and ICU stay in this population of neonates and infants with respiratory distress following congenital heart surgery. No association was observed between HFOV and mortality.

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*Treatment for COPD…continued from page 32*
approaching 0.5 liters (15% pred), average age of 70.

Evidence also reveals that people with sub-optimal care are represented by the dips below the baseline. Poor care often leads to multiple exacerbations and a rapid decline in lung function progression in the last couple years of one's life. This is indicated by the RED line.

When it comes to tobacco cessation, learn how to perform a Brief Tobacco Intervention (BTI) by utilizing the 5As or AAR method, and connect patients who wish to talk to a professional about the benefits of quitting tobacco to a Tobacco Treatment Specialist (TTS), located at the State Smokers' Quit Line. This proactive referral approach is more effective than passive referrals. In fact, according to research conducted at San Diego State University, only three percent of clients receiving literature containing quit line information follow through and contact the quit line. A three minute or less tobacco intervention with a proactive referral will increase a person's likelihood of quitting tobacco by at least 30 percent.[2]

## Summary of Key Steps in Optimal Care Management

- Encourage patients to be more involved in their own lifelong care
- Know the patient's stage of COPD, and recommend annual well visit checks and encourage patients to learn their FEV1 and COPD stage
- Collaborate with others to maintain long term benefits of pulmonary rehabilitation

Ultimately, RTs and healthcare professionals hold the key to decreasing hospitalizations and improving patient outcomes.

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# Respiratory Support by Neurally Adjusted Ventilatory Assist (NAVA) in Severe RSV-related Bronchiolitis

Jean-Michel Liet, Jean-Marc Dejode, Nicolas Joram, Bénédicte Gaillard-Le Roux, Pierre Étrémieux, Jean-Christophe Rozé

## Abstract

**Background:** Neurally adjusted ventilatory assist (NAVA) is a new mode of mechanical ventilation controlled by diaphragmatic electrical signals. The electrical signals allow synchronization of ventilation to spontaneous breathing efforts of a child, as well as permitting pressure assistance proportional to the lectrical signal. NAVA provides equally fine synchronization of respiratory support and pressure assistance varying with the needs of the child. NAVA has mainly been studied in children who underwent cardiac surgery during the period of weaning from a respirator.

**Case presentation:** We report here a series of 3 children (1 month, 3 years, and 28 days old) with severe respiratory distress due to RSV-related bronchiolitis requiring invasive mechanical ventilation with a high level of oxygen ($FiO_2$ ≥50%) for whom NAVA facilitated respiratory support. One of these children had diagnosis criteria for acute lung injury, another for acute respiratory distress syndrome.

Establishment of NAVA provided synchronization of mechanical ventilatory support with the breathing efforts of the children. Respiratory rate and inspiratory pressure became extremely variable, varying at each cycle, while children were breathing easily and smoothly. All three children demonstrated less oxygen requirements after introducing NAVA (57 ± 6% to 42 ± 18%). This improvement was observed while peak airway pressure decreased (28 ± 3 to 15 ± 5 cm $H_2O$). In one child, NAVA facilitated the management of acute respiratory distress syndrome with extensive subcutaneous emphysema.

**Conclusions:** Our findings highlight the feasibility and benefit of NAVA in children with severe RSV-related bronchiolitis. NAVA provides a less aggressive ventilation requiring lower inspiratory pressures with good results for oxygenation and more comfort for the children.

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The authors wish to thank the patient Matteo's parents for permission to publish chest X-rays of their child, and to thank Dr Christer Siderby who helped improve the paper and to clarify its content. Reprinted from BioMed Central, BMC Pediatrics, 

## Background

Neurally adjusted ventilatory assist (NAVA) is a new method of assisted ventilation that can be used for children regardless of weight and age. This ventilation mode is controlled by diaphragmatic electrical signals through a gastric tube with specific electrodes on its surface. The collected electrical signals allow synchronization of ventilation to spontaneous breathing efforts of a child, as well as providing pressure assistance proportional to the electrical signal and thus to the output of the child's respiratory centers.

NAVA has mainly been studied in children who underwent cardiac surgery[1-3] during the period of weaning from a respirator. We report here a series of 3 children with severe respiratory distress due to respiratory syncytial virus (RSV) bronchiolitis for whom NAVA facilitated respiratory support.

## Case Presentation

Our unit is a 12-bed tertiary care university hospital pediatric intensive care unit. Recruitment is both medical and surgical. NAVA has been used in our unit for weaning children from a respirator who were operated on for congenital heart disease. The effectiveness of NAVA in these children led us to gradually expand the indications. We report a series of 3 children with severe respiratory distress due to RSV bronchiolitis for whom NAVA was used. The local ethics committee (groupe nantais d'éthique dans le domaine de la santé [GNEDS]) considered our report as non-interventional data research. The parents of all three children gave their written consent for publication.

Starting NAVA requires the initial correct positioning of the "NAVA" gastric tube. This commercially available feeding tube equipped with sensors (Edi catheter, Maquet Critical Care, Solna, Sweden) permits the recording of electrical activity of the diaphragm (Edi) via a Servo-I Ventilator (Maquet Critical Care, Solna, Sweden) using a standardized method.[4] Settings are relatively simple and include positive end-expiratory pressure (PEEP), fraction of inspired oxygen ($FiO_2$), and level of NAVA assistance.

The Edi was multiplied was multiplied by the NAVA level to adjust the pressure assistance delivered to the child. The delivered pressure is equal to: NAVA level × (Edi max -Edi min) + PEEP. In clinical practice we usually started with a NAVA level of 1 cm $H_2O$/μV that may have required adjustment if the Edi max signals deviated from a range between 5 and 20 μV. If the Edi signals turned out to be consistently greater than 20 μV, we

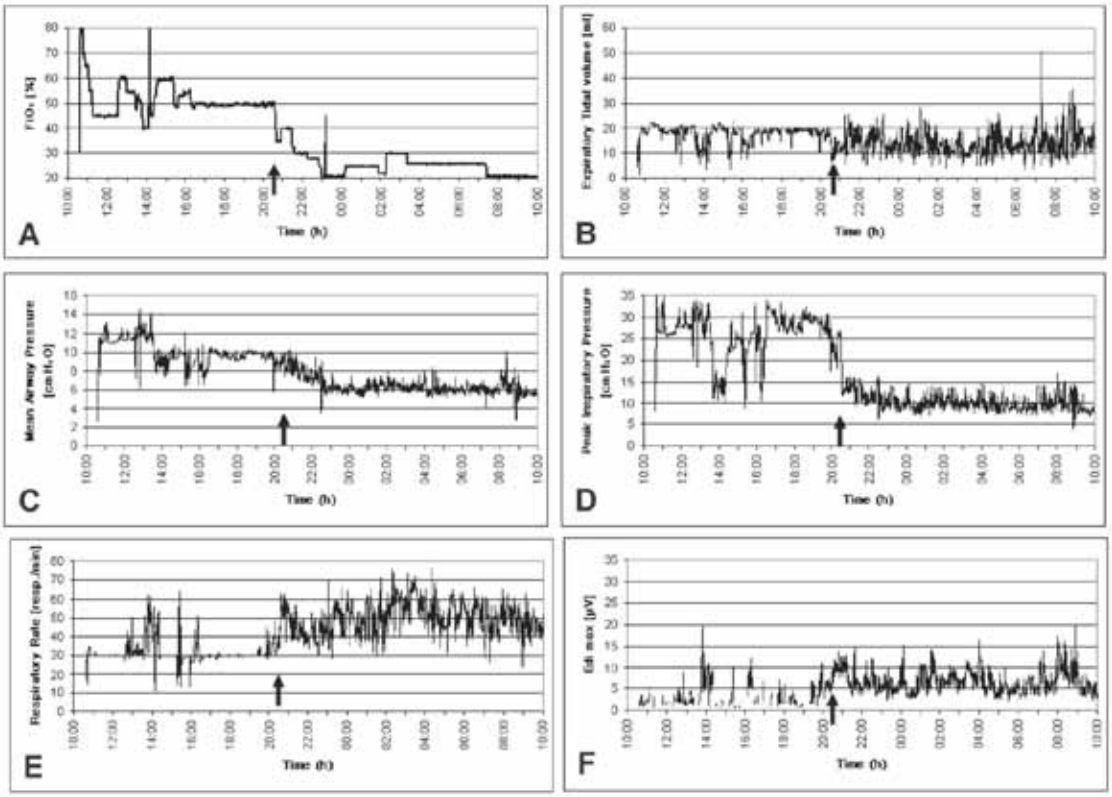


**Figure 1.** Continuous recording of ventilatory parameters for 24 hours (case 1). Figure demonstrates in the first patient the 24-hour evolution of FiO2 (Panel A), expiratory tidal volume (Panel B), mean airway pressure (Panel C), peak inspiratory pressure (Panel D), respiratory rate (Panel E) and Edi max (Panel F). The upward vertical arrows indicate the time point where the ventilator mode was switched from SIMV over to NAVA. (A first brief NAVA period was tested at 14:00). Upper panels: After starting NAVA, (A) FiO2 gradually decreased to 21% in 12 hours, and (B) tidal volume became much more variable from one cycle to another. Middle panels: One of the most remarkable changes observed with switching to the NAVA mode was the immediate reduction in the mean airway pressure (C) and in the peak airway pressure (D) which decreased from 30 to 10 cm H2O. Bottom panels: After starting NAVA, the respiratory rate became very variable over time (E). From a mandatory frequency set at 30 breaths per minute, respiratory rate increased to 40 and 60 breaths per minute. Clinically, the breathing became easier with harmonious chest movements. (F) Edi max that it is the sum of inspiratory Edi and Edi min corresponds to the peak of electrical activity of the diaphragm. In SIMV, this activity is depressed, and in NAVA, the inspiratory Edi (Edi max - Edi min) drives ventilation. Abbreviations: FiO2, fraction of inspired oxygen; Edi, electrical activity of the diaphragm; SIMV, synchronized intermittent mandatory ventilation.

increased the NAVA level until they are within this range. In the three reported cases, we did not need to do so. During NAVA, the ventilator is triggered when the deflection in the Edi curve exceeds 0.5 µV. The assist is cycled-off when the Edi decreases to 70% of its peak value. We assume that pressure support, which is pneumatically triggered, should remain a means of backup ventilation in case the Edi signal cannot be collected (eg if the child removes the Edi catheter). Therefore, we set the trigger of this pressure support high enough (typically 0 to -5 cm) so that this backup ventilation did not compete with NAVA ventilation.

We measured respiratory parameters ($FiO_2$, tidal volume, mean airway pressure, peak inspiratory pressure, respiratory rate, and Edi max) directly from data exported from the respirator. Nurses recorded vital signs and $SpO_2$. The oxygenation saturation index, OSI = ($FiO_2$ × mean airway pressure)/$SpO_2$, was used to provide a non-invasive method of oxygenation assessment. This index can be used for the diagnosis of acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) in children when $SpO_2$ values are ≤ 97%.[5] Diagnosis of ALI and ARDS required an acute onset of the process, bilateral infiltrates on a chest radiograph, no evidence of left atrial hypertension, and OSI > 6.5 (ALI) or > 7.8 (ARDS). Blood samples were also analyzed to provide blood pH and $PCO_2$ values.

## Case 1

Shemsy was one month old (3.8 kg) without any particular risk factors. Her parents referred her to the emergency room because of grunting and hypotonia. She had rhinitis for several days with a cough for 48 hours following a viral contamination 3 days prior. She presented with apnea, desaturation, bradycardia and altered consciousness. She was intubated and ventilated immediately, and then transferred to intensive care.

Ten hours later, respiratory parameters were as follows: synchronized intermittent mandatory ventilation (SIMV) with a tidal volume (VT) of 20 ml (5 ml/kg); rate, 30/min; PEEP, 5 cm $H_2O$; and $FiO_2$, 50%. Measured parameters (stable for 2 hours) included a $SpO_2$ of 91%, a mean airway pressure of 10 cm H2O, and a peak inspiratory pressure of 30 cm $H_2O$ (other parameters are also shown in Table 1). The OSI was 5.5. A chest X-ray showed poorly ventilated lungs with diffuse infiltrates. Since the child was agitated, the options for care were to increase sedation, or to attempt ventilation using NAVA. A brief test was undertaken to validate the use of NAVA, which proved successful. We chose to commence NAVA after a short period of decreased sedation (morphine was decreased to 8 µg/kg/h). Initial NAVA settings were PEEP, 5 cm $H_2O$; NAVA level, 1 cm H2O/µV; and $FiO_2$, initially 50% was then decreased by nurses to $SpO_2$ > 90%.

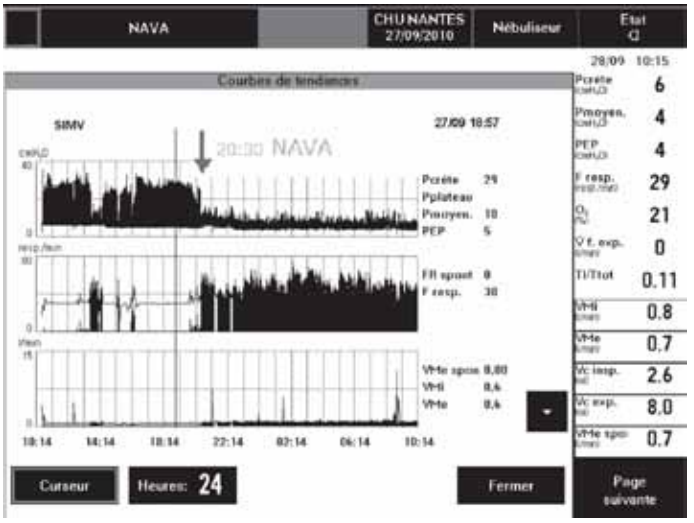


**Figure 2.** Screenshot with trends over 24 hours (case 1). In the window untitled "Courbes de tendances" (Trend curves), three panels report trends over 24 hours of peak inspiratory pressure (cm H2O), respiratory rate (resp/mn), and minute volume (l/min). On the right of these panels, the values of these ventilatory parameters were collected to the vertical bar (at 18:57 while the child was not receiving NAVA). The downward vertical arrow indicates the switch from SIMV to NAVA (at 20:30). Outside the window untitled "Courbes de tendances", on the right of the screnshot, ventilatory parameters were collected the next day at 10:15 while the child was receiving NAVA. The upper pannel showed a decrease in peak inspiratory pressure after the switch of ventilation. The middle pannel showed the extreme variability of the respiratory ratein NAVA (the white area under the curve corresponds to the mandatory respiratory rate, while the black area corresponds to the spontaneous respiratory rate). The lower pannel showed minute volume that remained unchanged. When comparing values of ventilatory parameters in SIMV (at 18:57) with those in NAVA (next day at 10:15), peak inspiratory pressure decreased from 29 to 6 cm H2O, mean airway pressure decreased from 10 to 4 cm H2O, spontaneous respiratory rate varied from 0 to 29 breaths/min. Abbreviations: SIMV, synchronized intermittent mandatory ventilation; PEP, positive end-expiratory pressure; P crête, peak inspiratory pressure; P moyen, mean airway pressure; FR spont, spontaneous respiratory rate; F resp, respiratory rate; VM, minute volume; FiO2, fraction of inspired oxygen.

We observed a dramatic decrease in inspiratory pressure with a reduced requirement for oxygen (Figures 1 and 2). Within several minutes, the child's breathing became much more harmonious and smoother, while her respiratory parameters showed large variations from one cycle to another. SpO2 was96%, mean airway pressure was 6 cm $H_2O$, peak inspiratory pressure was 10 cm H2O, and minute volume was 0.6 l/min.

Twelve hours later, $FiO_2$ was decreased to 21% with a mean airway pressure of 6 cm $H_2O$. Detailed ventilator parameters are reported in Table 1. Since respiratory parameters were very low (Peak inspiratory pressure < 12 cm $H_2O$ with $FiO_2$ < 25%) and blood gas values was normal, we extubated the child (10:30). She needed nasal continuous positive airway pressure for 3 days after which she was able to leave intensive care. Tracheal aspirate was positive for RSV and Streptococcus pneumoniae.

## Case 2

Matteo was 3 years old (14 kg), he was prematurely born (birth weight 1650 g) and he was mechanically ventilated in the neonatal period during 10 days for pulmonary hemorrhage. He was recently hospitalized because of subcutaneous emphysema, with signs of acute respiratory failure from RSV infection. Because of an increased need for oxygen, he was intubated and ventilated with an $FiO_2$ of 100%, and PEEP was 3. A chest X-ray did not show pneumothorax that could be drained. Tracheal

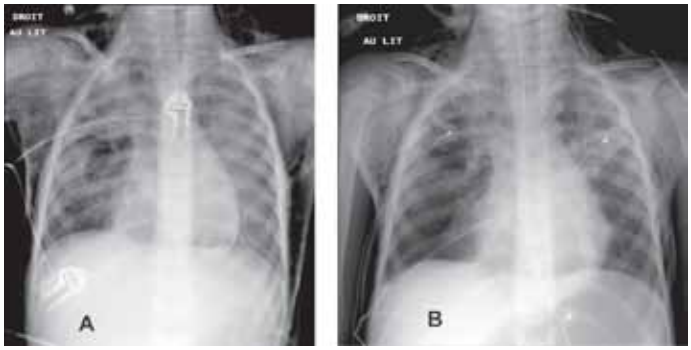


**Figure 3.** Chest radiographs of case 2. (A) The left X-ray shows bilateral infiltrates associated with diffuse subcutaneous emphysema. (B) Twenty-four hours after the onset of NAVA, the subcutaneous emphysema started to decline. Abbreviations: NAVA, neurally adjusted ventilatory assist.

aspirate was positive for RSV and Hemophilus influenzae. A few days later, because of emergence of an alveolar syndrome associated with persistence of subcutaneous emphysema, he was transferred to our unit for possible extracorporeal membrane oxygenation (ECMO).

Upon arrival, he had an oxygenation saturation index of 9.4 as well as with the other criteria for ARDS (bilateral infiltrates on a chest radiograph and no evidence of left atrial hypertension). Respiratory parameters were an SIMV with a VT of 85 ml (6 ml/kg), the rate was 25/min, PEEP was 6 cm $H_2O$, and $FiO_2$ was 70%. $SpO_2$ was 89%, mean airway pressure was 12 cm $H_2O$, peak inspiratory pressure was 28 cm $H_2O$, and minute volume was 2 l/min. Venous blood gas showed a pH of 7.32, and a $PvCO_2$ of 53 Torr (7.1 kPa). Because of a slight improvement, the child was not treated by ECMO. He underwent fibroscopy to eliminate the diagnosis of foreign body inhalation, which would have explained the subcutaneous emphysema. Forty-eight hours later, because of an increase in cough, cutaneous emphysema worsened and became diffuse (cervico-thoraco-abdominal) despite the reduction in PEEP to 4 cm $H_2O$ ($FiO_2$ 60%). We decided to use NAVA to improve the synchronization of mechanical ventilation with the child's spontaneous breathing. Sedation was reduced, midazolam was decreased to 80 µg/kg/h and sufentanil to 0.3 µg/kg/h. The child became alert. Initial NAVA settings were a PEEP of 5 cm H2O, NAVA level was 1.2 cm H2O/µV, and $FiO_2$ was 60%.

This change reduced the requirement for oxygen and normalized blood gases (Table 2). The next day, the subcutaneous emphysema started to decline (Figure 3). Peak inspiratory pressure was between 10 and 19 cm $H_2O$ with an FiO2 of 50% for a $SpO_2$ of 90%. The child's level of distress was scored with the modified COMFORT scale[6] and it ranged between 11 and 14 (adequately sedated, as confirmed by the child). This clear improvement allowed us to reassign the child to the original hospital 48 hours after initiation of NAVA. NAVA was continued at the second facility, permitting extubation 3 days later.

## Case 3

Leane was 28 days old (3 kg) and was born at term. She had a 2-year-old brother with bronchiolitis. After an episode of rhinorrhea, she presented with feeding difficulties and was referred to the emergency room of a local hospital. Four hours later, she progressively presented with low oxygen saturation, tachypnea, and chest retraction. She was placed under nasal CPAP with 30% $FiO_2$, and then transferred to our unit for severe RSV bronchiolitis. She was intubated on arrival because of

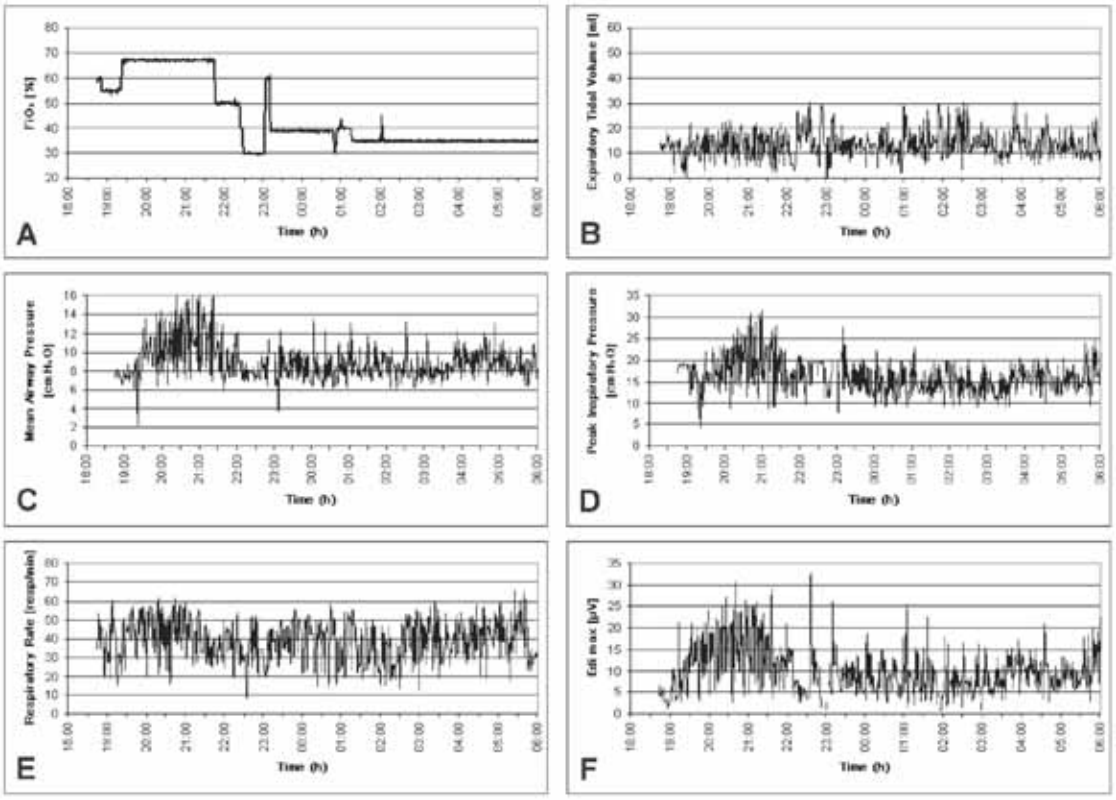


**Figure 4.** Continuous recording of ventilatory parameters for 12 hours (case 3). Figure demonstrates in the third patient the 24-hour evolution of FiO2 (Panel A), expiratory tidal volume (Panel B), mean airway pressure (Panel C), peak inspiratory pressure (Panel D), respiratory rate (Panel E) and Edi max (Panel F). Recording began with the establishment of NAVA. Upper panels: After starting NAVA, (A) FiO2 gradually decreased to 35%, and (B) tidal volume became variable from one cycle to another ranging from 5 to 30 ml. Middle panels: Variability was also observed in measurements of pressure: (C) mean airway pressure, (D) peak inspiratory pressure. Bottom panels: (E) After starting NAVA, the respiratory rate became very variable over time. (F) Edi max corresponds to the peak of electrical activity of the diaphragm. The highest Edi values (recorded between 19:00 and 22:00) drove assistance with the highest pressures. A decrease in signal intensity was accompanied by a decrease in pressure, corresponding to an improvement in lung function. The requirement for oxygen decreased at the same time. Abbreviations: FiO2, fraction of inspired oxygen; Edi, electrical activity of the diaphragm; NAVA, neurally adjusted ventilatory assist.

clinical signs of respiratory distress and collapse. Although we suspected concomitant bacterial pneumonia because of a major inflammatory syndrome, we did not have bacteriological confirmation. Her respiratory status deteriorated rapidly. The OSI was 6.8 (with other diagnosis criteria for acute lung injury). Her need for oxygen increased rapidly with bilateral infiltrates on a chest radiograph.

We chose to use NAVA after a short period of decreased sedation (morphine was decreased to 8 µg/kg/h). Initial NAVA settings were a PEEP of 5 cm $H_2O$, NAVA level was 1 cm H2O/µV, and FiO2 was initially 60% and was then adjusted by a nurse for a SpO2 > 90% and < 98%. Six hours later, FiO2 was 35%, while ventilatory pressures were lower than before starting NAVA (Table 3). As in the 2 other cases, ventilatory parameters were highly variable (Figure 4), while chest movements of the child were smooth as if the child was not mechanically ventilated. Twenty-four hours after starting NAVA, $FiO_2$ was 21%. The modified COMFORT scale ranged between 7 and 13.

At 36 hours of NAVA ventilation, the child was accidentally extubated during coughing. She immediately presented marked signs of respiratory distress (Silverman score: 7/10). We then used noninvasive ventilation with the NAVA option. Edi max values were initially very high (80 µV) and gradually decreased over 1 hour after the establishment of noninvasive ventilation. Thereafter, nasal continuous airway pressure was applied and the child left the intensive care unit 3 days later.

## Discussion

As in many pediatric intensive care units, our rate of intubation of children hospitalized for bronchiolitis is low (< 20%).[7] However, the severity of lung disease in some children still necessitates invasive mechanical ventilation. Our unit recruitment is both medical and surgical, and we therefore acquired expertise in NAVA through the weaning of children treated after cardiac surgery. We then expanded the indications of this mode of ventilation in children with severe respiratory disease.

The positive results in the present study may be explained by the specific selection of children to whom we applied NAVA. First, there should be no specific contraindication to the placement of a nasogastric tube. Second, there should be no alkalosis or hypocapnia (in such cases there would not be sufficient diaphragmatic electrical activity). During alkalosis, the ventilatory brain centers no longer stimulate the diaphragm, and the respirator works on a backup mode, which is simply conventional ventilation. Finally, the level of sedation should not be too high, so that it does not depress brain centers that control breathing. If the sedation is too high, the Edi signal cannot be collected and the respirator works again in a backup mode. Likewise, neuromuscular connection from the respiratory center to the diaphragm must be intact. For example, NAVA cannot be used in case of post-surgical lesion of the two phrenic nerves[3] or diaphragmatic paralysis secondary to botulism.[8]

**Table 1 Ventilatory parameters (case 1)**

| | Before NAVA | Twelve hours after the start of NAVA |
|---|---|---|
| **Ventilation mode** | **SIMV** | **NAVA** |
| Peak inspiratory pressure (cm $H_2O$) | 30 | (10)* |
| PEEP (cm $H_2O$) | **5** | **4** |
| Mean pressure (cm $H_2O$) | 10 | 6 |
| Tidal volume (ml/kg) | **5** | (4)* |
| Minute volume (ml/kg/min) | 0.6 | 0.7 |
| Respiratory rate (breaths/min) | **30** | (50)* |
| $FiO_2$ | **50%** | **21%** |
| $SpO_2$ | 91% | 92% |
| Edi max | < 5 | (10)* |
| NAVA level | - | **1** |
| pH | 7.38 | 7.41 |
| $PCO_2$, mmHg [kPa] | 48 [6.4] | 43 [5.7] |

Data in bold are prescribed settings. Other data are measured parameters that depend on the ventilatory settings and the respiratory status of the child.

* Data expressed in parentheses represent measurements that were very variable over time, and hence an estimate of the measured parameter is provided [see Figures 1 and 2].

Abbreviations: SIMV, synchronized intermittent mandatory ventilation; NAVA, neurally adjusted ventilatory assist; PEEP, positive end-expiratory pressure; $FiO_2$, fraction of inspired oxygen; Edi, electrical activity of the diaphragm.

The main benefit observed in our cases was an improvement in oxygenation associated with a normalization of blood pH. This was achieved with marked decrease in peak airway pressure. This effect has been previously found in crossover studies reporting NAVA in weaning children from a respirator who were operated on for congenital heart disease and comparing NAVA with pressure support.[1-3] Clinically, breathing becomes easier with harmonious chest movements. In one of our cases, NAVA was very effective for ventilation in a child who had both ARDS and extensive cutaneous emphysema. The excellent synchronization of mechanical ventilation with the spontaneous breathing of the child improved oxygenation without aggravating the emphysema.

Several factors could explain the beneficial effects observed with NAVA in these three children who had severe respiratory distress. First, asynchrony is associated with increased morbidity, a longer duration of ventilation, and a longer hospital stay.[9-11] There are few pediatric data published regarding the adverse effects of long-term asynchrony between mandatory ventilation and the respiratory efforts of children, but it has been shown that infant-ventilator asynchrony (both inspiratory and expiratory asynchrony) may affect more than 50% of the total breath duration.[12] Second, NAVA provides assistance in synchronization, as well as in pressure assistance in proportion to the measured electrical activity of the diaphragm. This helps to limit the periods of insufficient assist delivery that could induce respiratory muscle fatigue with increased oxygen consumption, and periods of overassistance that can generate intrinsic PEEP with an inadequate increase in intrathoracic pressure.[13] NAVA can also prevent air swallowing and gastric distension by optimization of patient-ventilator synchrony.[14] Third, it is likely that NAVA can help clinician avoiding inappropriate ventilator settings that overload (or underload) respiratory muscles, preventing recovery. Finally, improvements in pulmonary gas exchange, systemic blood flow and oxygen supply to tissues which have been observed when spontaneous breathing has been maintained during mechanical ventilation with clinical improvement in the patient's condition,[15] are assumed to occur in NAVA, when breathing efforts by the patient and the initiated breaths are in synchrony.

Cost effectiveness studies are required, as NAVA requires probes that are single-patient use. It is possible that improving comfort provided by better synchronization between spontaneous breathing and mechanical ventilation could reduce the sedation and thus shorten duration of ventilation.

## Conclusions

Based on three individual cases, NAVA appears to be a useful mode for weaning from a respirator and is an effective alternative treatment for children with severe respiratory distress. NAVA provides a respiratory support that is in harmony with the spontaneous efforts of breathing, allowing a decrease in inspiratory pressures and oxygen needs. Larger studies are required to compare NAVA with conventional respiratory support in children with various etiologies of respiratory distress.

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**Table 2 Ventilatory parameters (case 2)**

| | Before NAVA | Twelve hours after the start of NAVA |
|---|---|---|
| **Ventilation mode** | **SIMV** | **NAVA** |
| Peak inspiratory pressure (cm $H_2O$) | 28 | (15)* |
| PEEP (cm $H_2O$) | **4** | **5** |
| Mean pressure (cm $H_2O$) | 12 | 7.5 |
| Tidal volume (ml/kg) | **6** | (7)* |
| Minute volume (ml/kg/min) | 2.0 | 3.1 |
| Respiratory rate (breaths/min) | **25** | (30)* |
| $FiO_2$ | **60%** | **50%** |
| $SpO_2$ | 89% | 90% |
| Edi max | - | (10)* |
| NAVA level | - | **1.2** |
| pH | 7.35 | 7.48 |
| $PCO_2$, mmHg [kPa] | 64 [8.5] | 43 [5.7] |

Data in bold are prescribed settings. Other data are measured parameters that depend both on the ventilatory settings and the respiratory status of the child.

* Data expressed in parentheses represent measurements that were very variable over time, and hence an estimate of the measured parameter is provided.

Abbreviations: SIMV, synchronized intermittent mandatory ventilation; NAVA, neurally adjusted ventilatory assist; PEEP, positive end-expiratory pressure; $FiO_2$, fraction of inspired oxygen; Edi, electrical activity of the diaphragm

**Table 3 Ventilatory parameters (case 3)**

| | Before NAVA | Six hours after the start of NAVA |
|---|---|---|
| **Ventilation mode** | **SIMV** | **NAVA** |
| Peak inspiratory pressure (cm $H_2O$) | 25 | (15)* |
| PEEP (cm $H_2O$) | **5** | **5** |
| Mean pressure (cm $H_2O$) | 10 | 8 |
| Tidal volume (ml/kg) | **5** | (5)* |
| Minute volume (ml/kg/min) | 0.6 | 0.8 |
| Respiratory rate (breaths/min) | **40** | (40)* |
| $FiO_2$ | **60%** | **35%** |
| $SpO_2$ | 88% | 100% |
| Edi max | - | (10)* |
| NAVA level | - | **1** |
| pH | 7.40 | 7.44 |
| $PCO_2$, mmHg [kPa] | 52 [7.0] | 47 [6.3] |

Data in bold are prescribed settings. Other data are measured parameters that depend on the ventilatory settings and the respiratory status of the child.

* Data expressed in parentheses represent measurements that were very variable over time, and hence an estimate of the measured parameter is provided [See Figure 4].

Abbreviations: SIMV, synchronized intermittent mandatory ventilation; NAVA, neurally adjusted ventilatory assist; PEEP, positive end-expiratory pressure; $FiO_2$, fraction of inspired oxygen; Edi, electrical activity of the diaphragm


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# Short Women with Severe Sepsis-Related Acute Lung Injury Receive Lung Protective Ventilation Less Frequently

SeungHye Han, Greg S. Martin, James P. Maloney, Carl Shanholtz, Kathleen C. Barnes, Stacey Murray, Jonathan E. Sevransky

## Abstract

**Introduction:** Lung protective ventilation (LPV) has been shown to improve survival and the duration of mechanical ventilation in acute lung injury (ALI) patients. Mortality of ALI may vary by gender, which could result from treatment variability. Whether gender is associated with the use of LPV is not known.

**Methods:** 421 severe sepsis-related ALI subjects in the Consortium to Evaluate Lung Edema Genetics from seven teaching hospitals between 2002 and 2008 were included in our study. We evaluated patients' tidal volume, plateau pressure and arterial pH to determine whether patients received LPV during the first two days after developing ALI. The odds ratio of receiving LPV was estimated by a logistic regression model with robust and cluster options.

**Results:** Women had similar characteristics as men with the exception of lower height and higher illness severity, as measured by Acute Physiology and Chronic Health Evaluation (APACHE) II score. 225 (53%) of the subjects received LPV during the first two days after ALI onset; Women received LPV less frequently than men (46% versus 59%, $p < 0.001$). However, after adjustment for height and severity of illness (APACHE II), there was no difference in exposure to LPV between men and women ($p = 0.262$).

**Conclusions:** Short people are less likely to receive LPV, which seems to explain the tendency of clinicians to adhere to LPV less strictly in women. Strategies to standardize application of LPV, independent of differences in height and severity of illness, are necessary.

## Introduction

Acute lung injury (ALI) is a serious clinical syndrome with a high case fatality rate characterized by acute hypoxemia with bilateral infiltrates on chest radiography in the absence of clinical evidence of left atrial hypertension. Recent reports have suggested an increasing prevalence in the United States, up to 86.2 per 100,000 person-years and 2.2 cases per intensive care unit (ICU) bed per year. The use of a lung protective ventilation (LPV) strategy has been shown to reduce mortality rates in intubated ALI patients.

Men and women have different mortality rates in ALI. Several factors may explain this differential mortality rate. Women may have different incidence of ALI and thus different prevalence of ALI, or different case fatality rates from ALI than men. It has been reported that there is gender difference in genetic susceptibility to acute respiratory distress syndrome. It is also possible that treatment or response to therapy may differ by gender. It has been reported the differential care by gender in patients without ALI who received mechanical ventilation.

The aim of this study was to investigate whether gender is associated with the use of LPV, and to identify the potential confounding factors associated with the use of LPV in an ongoing observational study of patients with sepsis-related ALI. We hypothesized that gender is not associated with the use of LPV in patients with sepsis-related ALI.

## Materials and methods

Study population and design: As part of the Consortium to Evaluate Lung Edema Genetics (CELEG) study, invasively mechanically ventilated patients diagnosed with severe sepsis-induced ALI were prospectively enrolled from medical and surgical ICUs in seven academic medical centers between 2002 and 2008. Severe sepsis was defined according to Society of Critical Care Medicine/American College of Chest Physicians Consensus Definitions; ALI was defined as mechanically ventilated patients who met the American-European Consensus Definitions. Exclusion criteria were allogeneic bone marrow transplant and severe leukopenia (white blood count < 1,000/μL). All ICU patients were screened daily by specially trained research staff with previous experience in ALI trials and approached if they were eligible. The details of CELEG study have been described in elsewhere. The study was approved by the institutional review boards of all participating centers, and informed consent was obtained from the patients or surrogates. All severe sepsis-related ALI subjects with available heights were selected for our analyses.

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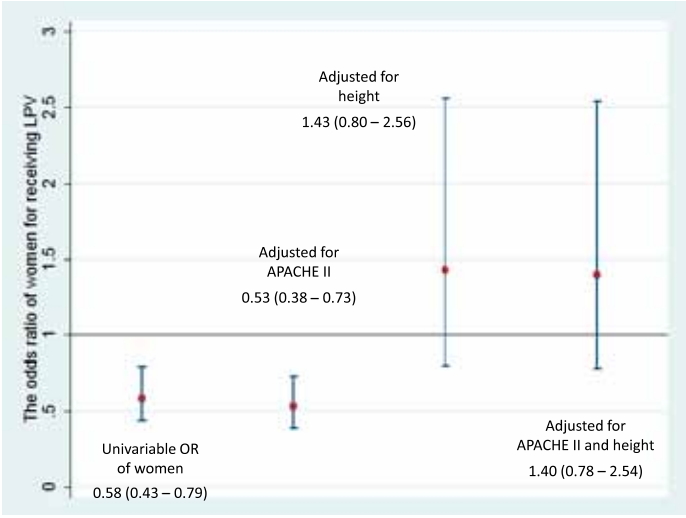


Association of gender (women versus men) with the use of LPV: OR (95% CI). APACHE II, Acute Physiology and Chronic Health Evaluation II; CI, confidence interval; LPV, lung protective ventilation; OR, odds ratio.

Outcomes and exposures: The primary outcome was the use of LPV during the first two days after developing ALI. We used an algorithm based on tidal volume (mL/kg of predicted body weight (PBW)), arterial pH and plateau pressure ($cmH_2O$) on the day of ALI onset, derived from the ARDSNet ventilation protocol. In constructing this algorithm, we chose the lowest arterial pH on the day of ALI onset to consider cases where the tidal volume would have been increased up to 8mL/kg of PBW to treat the patient's severe acidosis (49 patients). Patients who received LPV within two days of ALI onset were considered to have received LPV. All decisions regarding ventilatory strategy were made by primary treating teams.

The exposures we considered are: patient-related factors (age, gender, self-reported ethnicity, height, and body mass index) and severity of illness (Acute Physiology and Chronic Health Evaluation (APACHE) II score and the ratio of partial pressure of arterial oxygen ($PaO_2$) and fraction of inspired oxygen ($FiO_2$)). The first $PaO_2/FiO_2$ ratio at the time of ALI diagnosis was used for our analyses.

Statistical analysis: Descriptive statistics were reported with mean ± standard deviation (SD) for continuous variables and proportions for categorical variables, and were analyzed by Mann-Whitney and chi-square tests, respectively. We selected biologically plausible variables with p-values < 0.05 in univariable analyses, and estimated odds ratio (OR) of receiving LPV in multivariate models. To account for the possibility that the prescription of tidal volumes in the same hospital may not be independent, we ran a logistic regression model with robust and cluster options. Sensitivity analysis was performed to evaluate the potential variability of the results caused by missing data. All analyses were performed using Stata Statistical Software: Release 10 (StataCorp. 2007. College Station, TX: StataCorp LP).

## Results

Among 526 patients with sepsis-related ALI in the CELEG study, 24 patients were excluded because they were not on a fully controlled mode of mechanical ventilation with measured tidal volume: 21 subjects on airway pressure release ventilation and 3 subjects on high frequency oscillation ventilation. An additional 81 patients could not be evaluated as their heights were unavailable. Therefore, a final sample of 421 sepsis-related ALI subjects was used for our analyses.

Our study sample had a mean age of 54.9 ± 17.3 years, with 57% men and 68% European-Americans. The mean APACHE II score was 27.7 ± 7.9 and the mean $PaO_2/FiO_2$ ratio was 131 ± 63. Actual body weight (ABW) was 19 kg heavier than PBW (84 kg versus 66 kg, $p < 0.001$), and the majority (79%) of the patients had higher ABW than PBW. Women in our study were shorter and had higher APACHE II scores compared with men.

A total of 225 (53%) subjects received LPV. Women received LPV less frequently than men (46% versus 59%, $p < 0.001$). In contrast, 307 (73%) subjects were categorized as receiving LPV based on ABW, without gender difference (75% and 72% for women and men, respectively, $p = 0.416$). Height, gender and severity of illness as measured by APACHE II scores were significantly associated with the use of LPV in univariable analyses. In multivariable analysis, height and APACHE II score remained significantly associated with the use of LPV. However, gender was not associated with the use of LPV in multivariable analysis ($p = 0.262$).

In order to investigate further the association between gender and the use of LPV with its confounding factors, additional logistic regressions were fitted. In univariate model, the relative odds of receiving LPV comparing women to men was less than 1, which means women were less likely to receive LPV than men. Including APACHE II score in the model did not change the direction and significance of the association between gender and the use of LPV. However, after adjustment for height and/or APACHE II score, the gender was no longer associated with the use of LPV ($p = 0.231$ and 0.262, respectively).

In order to see how much our findings could be potentially biased by missing data, we performed a sensitivity analysis with two extreme scenarios: 1) all the subjects with missing height received LPV and 2) all the subjects with missing heights did not receive LPV, and saw how much results were changed in the two scenarios. Missing heights were replaced with average heights of men and women respectively in our study population. The results were similar with the exception of the OR for women versus men in a multivariate model under the assumption of no LPV. Height remained significantly associated with the use LPV throughout all the models.

## Discussion

Our prospective observational study at seven academic centers revealed that women were approximately 40% less likely to receive LPV compared to men during the first two days after ALI onset. This differential exposure may be explained by their height difference. According to our multivariable analysis, severe sepsis-related ALI patients were 20% more likely to receive LPV if they were one inch (2.54 cm) taller, while gender was not associated with the use of LPV. Our finding suggests that intensive care regarding mechanical ventilation in ALI patients may be influenced by patient-related factors such as height and severity of illness.

Several critical illnesses have different outcomes by gender. Women have higher mortality than men after developing acute myocardial infarction, respiratory distress requiring mechanical ventilation and nosocomial infections, while male patients with blunt trauma experience a higher risk of death than females.

Several potential explanations for these mortality differences include physiologic and hormonal differences, or differential exposure to intensive care and treatments. Men have been shown to be more likely to be admitted to ICU and undergo aggressive measures such as mechanical ventilation, vasoactive medication, renal replacement therapy, or central vascular catheterization compared with women, after adjustment for severity of illness. It has also been reported that the adjusted rates of reperfusion therapy and coronary angiography after myocardial infarction were higher in men than in women.

Our study showed the ventilatory care in intubated ALI patients was different by gender, likely from their height difference. On average, women are shorter than men and thus their calculated tidal volumes in mL would be smaller than men's, based on PBW derived from height and gender. If this factor is not considered in the ventilatory care of women with ALI and consequently women receive higher tidal volumes than men, this difference in treatment may contribute to the higher mortality seen in mechanically ventilated women compared with men. Another possibility is that women may be under-diagnosed with ALI and get LPV less often than men. Unfortunately this cannot be confirmed from our data. There was, however, no gender difference in the use of LPV if it was defined by ABW rather than PBW. This suggests the decreased use of LPV in women may be more related to the differential treatment itself rather than differential diagnosis.

We found that only 53% of severe sepsis-related ALI patients received LPV. This similar lack of compliance with the use of LPV has been reported in other studies. Several factors have been reported as barriers for initiating and maintaining LPV, including concerns about the patient's hypercapnia/acidosis and difficulty in calculating correct tidal volumes based on PBW. Even though our algorithm considered the cases where tidal volumes increased to treat severe acidosis, approximately half of ALI patients did not receive LPV during the first two days after ALI onset. Since height was not always available in our study population, it is likely that some patients received tidal volumes based on other factors such as actual body weight. Use of actual rather than predicted body weight may be associated with unintended larger tidal volumes since PBW has been reported to be smaller than ABW. The higher use of LPV based on ABW seen in our study also supports this possibility.

Our multivariate analysis showed that one-point increase in APACHE II score were associated with 6% higher using rate of LPV in severe sepsis-induced ALI patients. Less ill patients may be under-diagnosed or delayed-diagnosed and thus, received LPV less frequently for the first two days after ALI onset. In addition, clinicians may be more likely to prescribe LPV in patients with higher initial plateau pressures. Further, since oxygenation is a part of APACHE II score calculation, it is also possible that the degree of lung injury itself influenced the use of LPV. In our study population, lower $PaO_2/FiO_2$ ratio and higher APACHE II score were all significantly associated with higher using rate of LPV in both univariate and multivariate models. Patients with $PaO_2/FiO_2$ ratio < 200 were twice more likely to receive LPV than those with ratio of 200 or more (data not shown).

Our study additionally suggests that a written protocol alone, which has been reported to be associated with increased use of LPV in ALI patients, may not be enough to increase the compiance of LPV fully. Although most of our study centers except University of Maryland (n=41) implemented written protocols for LPV during the study period, the usage of LPV was not obviously satisfying (57% in the six centers with protocols). Extra-tools to enhance the use of LPV such as incorporating a reminder to record height and PBW may be necessary.

Our study has several limitations. We only have the ventilatory data during the first two days after ALI onset, rather than the repeated measures throughout the course of disease. It is possible that the first two days of data may not be enough to determine LPV as ventilator setting could be changed later. However, ventilatory settings within 48 hours after ALI onset are known to be important predictors for outcomes. Another limitation is that 16 % (81 out of 502) of the ALI patients who received conventional assist-control mode of mechanical ventilation in our CELEG study had missing heights, so that they were not included in our analyses. Patient characteristics such as age, gender and weight, and severity of illness such as APACHE II scores and $PaO_2/FiO_2$ ratio were similar between ALI patients with available heights and those with missing heights. However, outcomes such as 28- and 60-day mortality and ventilator free days were worse in the patients with missing height compared to those with available height, possibly because they were ventilated with higher tidal volumes calculated with actual weights or other factors rather than PBW. This suggests missing data of LPV might not be at random and thus potentially bias our findings. However, our sensitivity analysis with two extreme assumptions of LPV did not show any substantial changes in the results compared to our original analyses, and gives us the same inferences.

## Conclusions

In conclusion, women are less likely to receive LPV compared to men. However after adjustment for height and severity of illness, there is no difference between men and women in exposure to LPV. This is most likely from the differences in height, leading to the inaccurate selection of tidal volumes for women. Strategies to standardize LPV delivery, independent of differences in severity of illness and height, are necessary.

# Helium in the Adult Critical Care Setting

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## Abstract

Helium is a low-density inert gas whose physical properties are very different from those of nitrogen and oxygen. Such properties could be clinically useful in the adult critical care setting, especially in patients with upper to more distal airway obstruction requiring moderate to intermediate levels of $FiO_2$. However, despite decades of utilization and reporting, it is still difficult to give any firm clinical recommendation in this setting. Numerous case reports are available in the context of upper airway obstruction of different origins, but there is a lack of controlled studies for this indication. One study reported a helium-induced beneficial effect on surrogates of work of breathing after extubation in non-COPD patients, possibly in relation to laryngeal consequences of tracheal intubation. Physiological benefits of helium-oxygen breathing have been demonstrated in the context of acute severe asthma, but there is a lack of large controlled studies demonstrating an effect on pertinent clinical endpoints, except for a study reported only as an abstract, which mentioned a reduction in the intubation rate in helium-treated patients. Finally, there are a number of physiological studies in the context of COLD-COPD patients demonstrating a beneficial effect, mainly by a reduction in the resistive inspiratory work of breathing but also by a reduction in hyperinflation. Reduction of hypercapnia was mainly observed in spontaneously breathing and noninvasively ventilated helium-treated patients but not in intubated patients during controlled ventilation, suggesting that the decrease in $PaCO_2$ was mainly in relation to a diminution in $CO_2$ production, related to the diminution in work of breathing and not an improved alveolar ventilation. Moreover, there is little evidence that helium-oxygen could improve parameters of heterogeneity in such patients. Two RCTs were unable to demonstrate a reduction in the intubation rate in such setting, but they were likely underpowered. An adequately powered international multicentric study is ongoing and will help to determinate the exact place of the helium-oxygen mixture in the future. The place of the mixture during the weaning period will deserve further evaluation.

## Introduction

Helium is an inert gas whose physical properties are very different from those of nitrogen and oxygen. Such properties led to consider its use in various medical conditions since the first publication by Barach in the 1930s. The purpose of this review was to detail part of these clinical uses, focusing mainly on obstructive respiratory diseases in the adult critical care setting, and therefore excluding pediatric studies and also studies solely centered on helium-driven nebulization.

## Theoretical and practical considerations

Helium is the second element in the universe, after hydrogen. It is found in very high amounts in the stars. In the earth, helium can be found in very low quantities in the atmosphere and in natural gas fields, or it can be extracted from cleveite, a mineral found in uranium deposits. The main property of helium—compared with oxygen and nitrogen—is its very low density, as assessed by a volumic mass of 0.18 (in a gaseous state at 0°C) compared with volumic masses of 1.49 and 1.25 for oxygen and nitrogen, respectively. The low density of helium can exert important potential benefits with regards to the airway's dynamic of fluids: Mainly, transition of turbulent to laminar flows: as a theoretical example, the density (d) of the mixture is an important determinant of the Reynold's number; which indicates the type of flow in a perfect pipe: $R = (V.D.d) / \eta$; where V is the mean linear velocity, D is the diameter of the pipe, d is the density of the fluid, and $\eta$ is the dynamic viscosity of the fluid. When the Reynold's number falls below the 2000 limit, the flow becomes laminar. Because a laminar flow generates much less resistances, use of helium could be of benefit. Inspiratory flow is physiologically turbulent in the upper airways and in the proximal trachea, but in obstructive diseases, such as asthma and COLD/COPD, turbulent flow can be observed more distally in the bronchial tubing.

Reduction of resistances even in cases of persistent turbulent conditions of flow. Indeed, in cases of turbulent flow, resistances are linearly proportional to the density of the mixture and to the flow value and inversely proportional to the diameter of the pipe at the fifth power. Another important point to consider, although sometimes neglected, is the 14% higher viscosity of helium compared with nitrogen. In cases of pure laminar flow, such a property directly increases the resistances, as shown by the Poiseuille's law: $R = (8.l.\eta) / \Pi.r4$ (where R is the resistance, l is the length of the pipe, $\eta$ is the viscosity, and r its radius). This could potentially increase part of the respiratory resistances, because of a larger cross-sectional area flow is mainly laminar in the distal airways, even in obstructive diseases. Moreover, this might have additional clinical implications both for research purpose as well as for care and monitoring, because flow and volume are sometimes measured by methods that need a correcting factor for viscosity (ie, via pneumotachograph). More generally, useful publications are available that describe the consequences of the use of helium both for mechanical ventilators and for monitoring devices, such as capnometers.

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A third point to consider is the higher thermic conductivity of helium compared with to oxygen and nitrogen. Theoretically, this could favor thermic losses in helium-treated patients. However, to the best of our knowledge, such a complication has never been described in the adult clinical setting and has only been described in children breathing helium-oxygen via a Hood administration system. This also has consequences for some types of monitoring devices. From all the above-mentioned reasons, one can consider that the low density of the mixture could exert many beneficial effects in cases of airway obstruction, mainly by a diminution in the resistive inspiratory work of breathing but also by reducing expiratory resistances, leading to less hyperinflation and therefore diminishing elastic inspiratory work of breathing and putting inspiratory muscles in a more favorable geometric configuration, hypothetically by a redistribution of the gas throughout the lungs, in relation to modifications in time-constants and also by reducing arterial tension in $CO_2$ through different mechanisms: 1) diminution in $CO_2$ production, via a reduction in the total work of breathing; 2) hypothetically an increase in alveolar ventilation (through a reduction in $CO_2$ dead-space facilitated by a better diffusion of $CO_2$ in the low density helium-oxygen mixture; and 3) a reduction in the so-called pendelluft phenomenon, linked to heterogeneous parenchymal viscoelastic properties of the lung.

Importantly, the beneficial effects of helium are likely to be observed at low or intermediate $FiO_2$. As a consequence, the better candidates for a beneficial effect are patients with upper airways obstruction, severe asthma patients and decompensated COPD or COLD patients, all demonstrating very high respiratory resistances and usually requiring less than 50% $FiO_2$ under mechanical ventilation. For each of these situations, we will resume the available data, both from a physiopathological point of view but also with consideration of major clinical endpoints.

### Upper airway obstruction

Upper airway obstruction, especially if transient, is probably one of the better potential indications of helium-oxygen breathing. Some case reports are available that describe a beneficial use of the mixture in spontaneously breathing patients, mainly in the pediatric literature but also in adult patients: the potential indications are malignancies, bilateral vocal cord dysfunction complicating short-term intubation, or radiation therapy. Unfortunately, available data are generally limited to the description of clinical courses in small numbers of patients, without helium-free controlled periods and/or measurement of pertinent physiological parameters, such as the work of breathing or airway resistances.

Interestingly, Jaber and coworkers performed a physiological study during the postextubation period that compared short periods of air-breathing and helium-oxygen breathing in 18 non-COPD patients. They mainly found a helium-associated reduction in the transdiaphragmatic pressure inspiratory swings and in the pressure-time index (these two parameters are surrogates of the work of breathing) as well as an improvement in the comfort score of the patients. Such a benefit could be in relation to a beneficial effect of helium-oxygen breathing on clinically latent postintubation upper airway obstruction related to laryngeal injuries.

### Asthma

Numerous case studies have been published in the setting of acute severe asthma, reporting favorable outcomes. Unfortunately, no firm conclusion can be drawn from such cases with regard to the interest to add helium-oxygen breathing, systematically or as a rescue therapy, to the standard treatment of acute severe asthma. More rigorously, Manthous et al studied in the emergency setting 27 patients with acute asthma exacerbation who received standard treatment (beta-agonist aerosols and intravenously administered methylprednisolone); 16 patients were allocated to breathe helium-oxygen, whereas the remaining 11 patients acted as a control group. The authors documented in the helium-oxygen group a more marked fall in the pulsus paradoxus and a greater improvement in the peak expiratory flow (measured via a helium-oxygen calibrated peak flow meter) than in the control group. In another study, 23 patients with acute severe asthma were randomized in the emergency department to breathe air-oxygen or helium-oxygen in addition to standard treatment. The authors documented a more rapid improvement during the first hour (as assessed by the peak-flow and the dyspnea score) in the helium-oxygen group, without clinically significant differences between the two groups beyond this time-point. Finally, Sattonnet et al performed a randomized, multicenter, controlled study in the prehospital setting in 203 patients with acute severe asthma who needed hospitalization in the ICU. The authors reported in an abstract a significant difference in the intubation rate in favor of heliumoxygen: 7% versus 1%. They also reported a diminution in the ICU length of stay compared with the control group.

Altogether, there is to date no firm argument in favor of systematic administration of helium-oxygen therapy for acute severe asthma, as confirmed by a meta-analysis of ten randomized, controlled trials (seven involving adult patients), including 544 acute asthma patients. The helium-oxygen mixture could be of value in the more severe patients, who might be at risk of intubation, while awaiting the effects of standard therapy. However, the level of evidence seems too low to recommend firmly its administration in this setting. Interestingly, no data are available regarding the use of a combination of helium-oxygen and noninvasive ventilation in such a situation.

### COLD and COPD

The available amount of clinically relevant data is higher in COPD/COLD exacerbations than in the two previous situations, with well-performed physiological studies but also with published RCTs assessing pertinent clinical endpoints. We will discuss three different situations: 1) use of helium during spontaneous breathing and/or noninvasive ventilation in cases of acute exacerbation; 2) use of helium during invasive ventilation; and 3) use of helium during the weaning period.

### Use of helium during spontaneous breathing and/or noninvasive ventilation in cases of acute exacerbation

Gerbeaux et al reported provocative results obtained in 81 decompensated COPD patients in the emergency setting. Forty-two patients received standard treatment, whereas helium-oxygen during spontaneous breathing was administered in the 39 remaining patients. Unfortunately, the study was observational and the administration of helium-oxygen was not randomized but kept at the discretion of the physician in charge. However, no significant difference was found at admission between the two groups with regards to any of the relevant clinical parameters. The authors reported impressive results with regards to intubation rates (50% in the control group vs 8% in helium-oxygen group) compared with the mortality rates (24% and 3%

respectively) and finally with regards to the ICU and hospital lengths of stay for survivors. Unfortunately, the nonrandomized design of this monocentric study precludes any firm clinical recommendation in favor of the use of helium-oxygen breathing in such a situation. To date, no confirmation study of these results is available. Jolliet et al evaluated the interest of helium-oxygen in combination with pressure-support noninvasive ventilation in 19 decompensated COPD patients. They compared three different situations: air-oxygen while spontaneously breathing, air-oxygen pressure support, and helium-oxygen pressure support. They reported beneficial effects of helium-oxygen pressure support not only in comparison with the spontaneously breathing periods but also in comparison with the conventional pressure support period, mainly with regard to the dyspnea Borg scale.

Jaber et al extended these data in a comparable setting while studying ten COPD patients at two different levels of pressure support during noninvasive ventilation. They mainly reported a helium-oxygen associated diminution in the inspiratory work of breathing compared with air-oxygen periods. They also reported a beneficial effect in terms of $PaCO_2$ decrease during the helium-oxygen periods.

Finally, two multicenter RCTs were performed aiming to demonstrate a reduction in the intubation rate in exacerbation of COPD/COLD patients. Jolliet et al. included 123 COPD patients and Maggiore et al included 204 COLD patients. The intubation rates were 20.3% and 13.5% in the air and helium-oxygen groups, respectively, in the study by Jolliet et al. The intubation rates were 30.4% and 24.5%, respectively, in the study by Maggiore et al. These differences were not statistically significant. As secondary endpoints, the two groups of investigators reported a beneficial effect of helium-oxygen in term of improvements of pH and $PaCO_2$ values. Jolliet et al also performed a cost analysis, which favored the use of helium-oxygen, mainly because a shorter duration of mechanical ventilation and a shorter ICU and hospital length of stay. Finally, it is likely that the two studies were underpowered to demonstrate a difference in the principal endpoint.

## Use of helium during invasive ventilation

Tassaux et al. performed a study in 23 decompensated intubated COPD patients that compared two periods of air-oxygen ventilation to one period of helium-oxygen ventilation; all other parameters remained unchanged.[20] They mainly found helium-associated significant reductions in Pmax, static intrinsic PEEP (staticPEEPi), and trapped volume. There were no differences in oxygenation values, $CO_2$ value, or any hemodynamic parameter. Gainnier et al performed a study in 23 intubated COPD patients that compared two periods of air-oxygen and helium-oxygen. They reported a decrease in work of breathing, implying its resistive and elastic components as a decrease in staticPEEPi. These data were extended by a study of our group including 13 COPD patients. We used a similar design than in the study by Tassaux. We similarly found significant reductions in Pmax and in staticPEEPi, although the latest was less pronounced than in the study by Jolliet et al. Accordingly, we found no differences in oxygenation values, $PaCO_2$ values, as well as in physiological dead-space. Finally, we took the opportunity to test the hypothesis that helium-oxygen could improve the heterogeneity of ventilation in such patients. As previously reported in similar patients, we observed during air-oxygen ventilation major differences between staticPEEPi and dynamic intrinsic PEEP (dynPEEPi). Interestingly, helium induced a small diminution in each of these parameters, whereas the dynPEEPi/staticPEEPi ratio remained unchanged. The dynPEEPi/staticPEEPi ratio is thought to be related to regional differences in mechanical properties within the lung—a phenomenon often referred as pendelluft—and/or viscoelastic pressure losses. To date, there is no useful clinical way to appreciate separately the absolute magnitude and the relative contribution of each of these two factors, but one can reasonably consider that helium-oxygen had little influence on this global index of heterogeneity. Supporting this interpretation is the fact that we also observed no significant change in the difference in pressure between the pressure (P1) observed during an inspiratory pause after the rapid initial fall in pressure, at the first point of zero flow, and the pressure observed after 5 seconds of occlusion (Ppl). As for the dynPEEPi/staticPEEPi ratio, (P1 – Ppl) can be attributed both to pendelluft and stress relaxation.

Finally, Tassaux et al studied ten recovering intubated COPD patients while ventilated with pressure support. They consistently reported a heliuminduced reduction in PEEPi, in the number of ineffective breaths, in inspiratory effort, and in work of breathing for a given level of pressure support.

## Use of helium during the weaning period

We performed a study in 13 severe intubated COPD patients at the end of the weaning process, measuring ventilatory variables and work of breathing just before extubation during two periods of air-oxygen and helium-oxygen. Repetition of the measurements was possible in five patients after extubation. Before extubation, we observed mainly a diminution in the total work of breathing as well as in its resistive component. We also found a significant decrease in PEEPi during helium-oxygen breathing. Similar results were observed after extubation in the five patients who tolerated the repetition of measurements. Interestingly, we found that the absolute reduction in work of breathing was correlated with the basal value during air-oxygen breathing. We also observed that one of the patients exhibiting the lowest levels of WOB during air/oxygen breathing experienced an increase in WOB with the heliumoxygen mixture. This was perhaps in relation to a predominantly distal airway obstruction with a deleterious effect of the mixture possibly in relation with its higher viscosity compared with air-oxygen. Altogether, these results emphasized the need to search for predictors useful to identify responders to helium-oxygen breathing, because the physiological response could be variable for a patient to another, with possibility of detrimental effects.

## Conclusions and perspectives

Despite decades of reports and utilization, the exact place of helium-oxygen in the adult critical care setting is still not well-defined, although many studies suggest a potential benefit in upper airway obstruction, in severe asthma, and in exacerbations of COPD/COLD. The main body of evidence is found in COPDCOLD patients, with not only case reports or uncontrolled small series but also a consequent number of rigorous physiological study and RCTs. In the future, it will be important to consider the results of an international ongoing adequately powered RCT designed to evaluate helium-oxygen not only in combination with noninvasive ventilation, but also during the noninvasive free periods of spontaneous breathing. It also will be important to consider further evaluation of the clinical benefit of the mixture in the weaning period.

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