

Volume 1 Number 7 December-January 2006/2007

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The Journal of Pulmonary Technique

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This is recommended by the ARDS Network's publication, funded by the National Heart and Lung Institute, which showed a 22% lower mortality with low TV ventilation strategy in patients with ALI or ARDS.<sup>(1)</sup>

Fig 1 - Rate Automatically Changes [with Changing Compliance (VAR-Plus with in-line PEEP Valve)

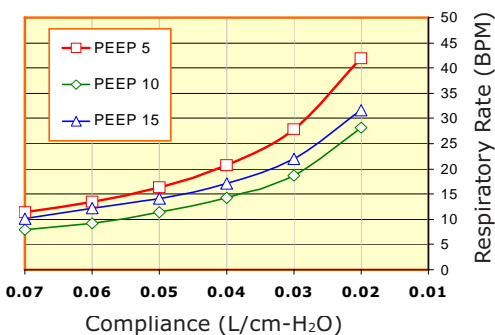
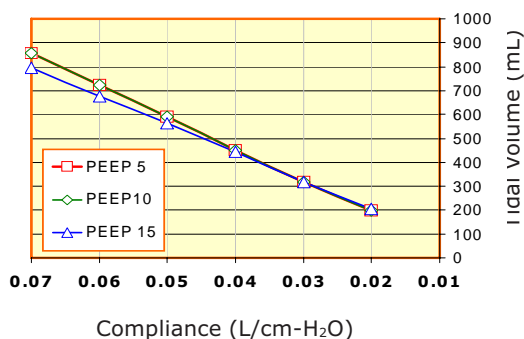


Fig 2 - TV Automatically Changes with Changing Compliance



The VAR automatically delivers a lower TV and a higher rate and is ideal for ARDS patients with decreasing compliance.

[1] Kallet, Richard H MS RRT: Implementation of a Low Tidal Volume Ventilation Protocol for Patients with Acute Lung Injury or Acute Respiratory Distress Syndrome. *Respir Care* 2001;46(10):1024-1037

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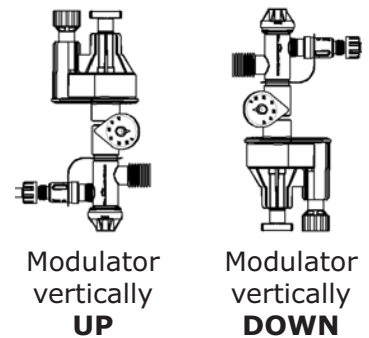


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\* E.Wesley Ely, New England Journal of Medicine (1996), Vol. 335:1864-9

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## TIMING IS EVERYTHING

Let's hear it for pragmatism in respiratory care, especially when it comes to the limits of treatment. Here's a case in point: According to Jewish religious law, caregivers are not allowed to withdraw medical treatment once it's begun; however, one can withhold treatment at a patient's request. To put it bluntly, you don't have to start, but once you start, you can't stop. This caused a particularly vexing problem for ventilator treatment. According to Vardit Ravitsky, writing in the British Medical Journal, "The withdrawal of treatment is perceived as forbidden even if the death of the patient...is an ethically appropriate outcome. In this cultural context withholding is acceptable but withdrawing is not. Consequently, an individual's request to withdraw life sustaining treatment, such as mechanical ventilation, is perceived by many as conflicting with this traditional approach." To put it simply, patients may request not to be connected to a ventilator, but they cannot be disconnected once treatment has been initiated. This approach delineates limits imposed even on the autonomy of competent adult patients. Says Ravitsky, "Israel thus faces the challenge of respecting personal autonomy and the right of individuals to choose how and when to end their lives, while taking into consideration traditional values that sometimes demand limits on these choices." The ethical/religious quandary has led to a debatably elegant solution. "Jewish religious law considers human intervention to end the life of dying patients unethical. Timers on ventilators are... a solution to prevent unnecessary suffering." Ravitsky notes that the Israeli solution offers an approach that sticks to the letter of the law, yet provides a practical methodology for those who wish to end their lives with dignity. Ravitsky writes, "The committee studying the problem suggested a distinction between continuous and discrete treatment as a way of translating the traditional distinction between withdrawing and withholding into clearly defined terms... 'Not continuing discrete treatment' is perceived as withholding, whereas 'not continuing continuous treatment' is perceived as withdrawing." The solution was a delayed response timer, which allows a ventilator, "to be set for a limited time (such as a week), at the end of which it [can be] turned off without human intervention. This would allow time for appropriate discussion among patients, family members, and healthcare providers. The discussion may result in a decision to extend the operation of the ventilator for a time determined by medical need or by the wishes of the patient or the family, or in a decision to let it turn off at the set time, providing the patient is under appropriate sedation." Such timers have been used to resolve other aspects of Jewish law, for instance, for using electrical devices during the Sabbath. As for the ethical hairsplitting, Ravitsky writes, "Timers are not a ruse to an unethical outcome. According to Jewish religious law, even if the outcome is ethically desirable, the procedure leading to it may still be forbidden. Hence, the termination of continuous treatment is perceived as ethically prohibited not because it leads to an ethically wrong outcome but because it uses an ethically questionable procedure to achieve that outcome, as in the case of using tainted evidence to achieve a justified conviction. The difficulty of accepting withdrawal is not based on a belief that the life of a suffering dying patient should be prolonged at all costs but on a cultural approach that is ethically opposed to human intervention to terminate life. Consequently, creating an alternative procedure allows the legislator to overcome the obstacle and proceed towards achieving the desirable outcome. By converting 'commissions into omissions,' timers are meant to enable healthcare providers to overcome a procedural obstacle to achieve an ethically justified outcome."



Les Plesko, Editor

The article quoted above is by Vardit Ravitsky, a bioethics fellow with the Social and Behavioral Branch, National Human Genome Research Project, Bethesda, MD. The full paper can be found in *BMJ* 2005;330:415-417, © 2005 British Medical Journal.



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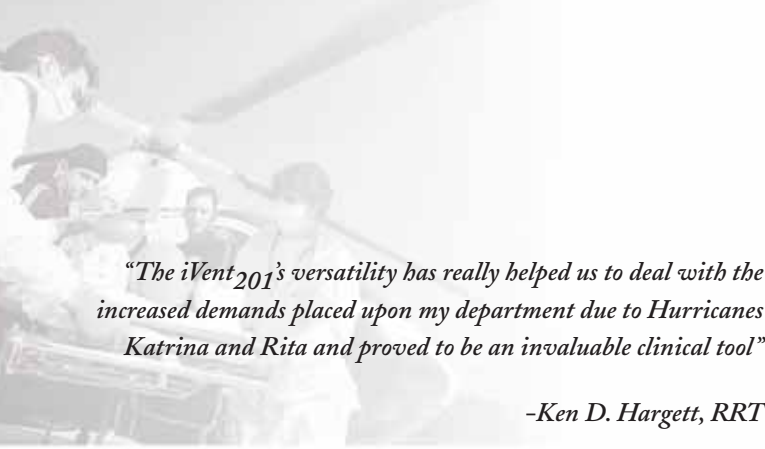
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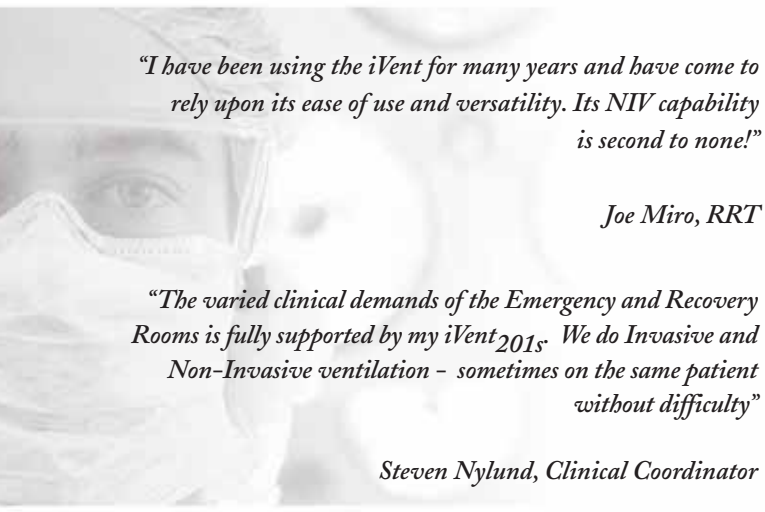
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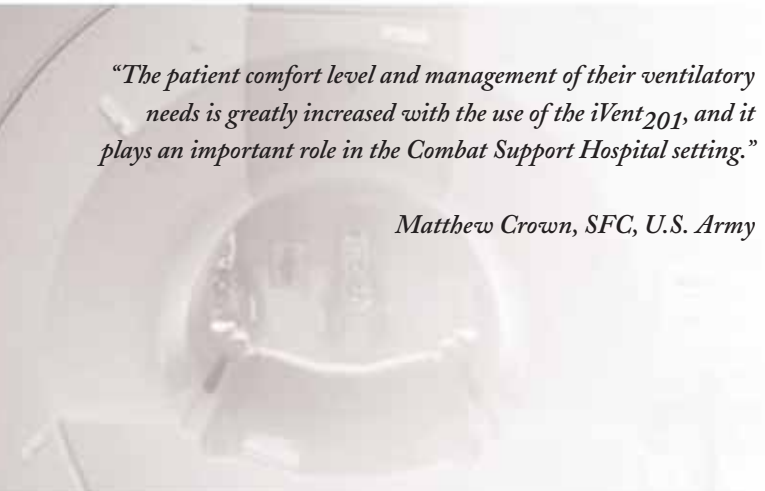


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**PUBLICATION NOTE:** Re the article, Utilization of an Automatic Mode of Ventilation (ASV) in a Mixed ICU Population: Prospective Observational Study, by J-M Armal, C. Nafati, M. Wysocki, Y-S Donati, I. Granier and J. Durand-Gasselin: The authors have requested that this paper be withdrawn from publication in *Respiratory Therapy*. The paper and information contained in the article was provided by Hamilton Medical and not from the authors, without explicit permission provided to *Respiratory Therapy* by the authors.

## CORRECTION

In the article, Pleural Fluid pH Analysis in the Blood Gas Laboratory, which appeared on page 7 in the Supplement to our October-November issue, the author should have been identified as Michael Nibert, RRT, BSRT. Michael Nibert is Director Respiratory Care & Heart Station/Neurodiagnostics, College Station Medical Center, College Station, TX. He can be contacted at (979) 764-5256. We apologize for the error.

## LETTER

I just finished reading the article entitled "Alternatives to CPAP in the Treatment of the Obstructive Sleep Apnea Syndrome" in Vol 1 No. 6 Oct/Nov issue of *Respiratory Therapy* by Konrad E. Block MD. I thought it was very well written and especially well referenced.

My comments are confined to the fact that with the obvious literature search done by the author, there isn't *any* mention of the use of transtracheal oxygen therapy in selected patients who failed multiple conventional treatment methodologies, and simply refuse to consider full tracheostomy. Studies were done in a small number of patients as far back as 1985, by Spofford and Christopher in Denver.<sup>1</sup> The use of TTOT to treat OSA was further studied by Chauncey and Aldrich at the Univ of Michigan Medical Center in 1990,<sup>2</sup> by Farney and Walker at LDS hospital as early as 1991 and 1992,<sup>3,4</sup> and a few years ago, by Hartmut Schneider with Philip Smith and Alan Schwartz at Johns Hopkins Hospital in a pilot study published in the *AJRCCM*.<sup>5</sup>

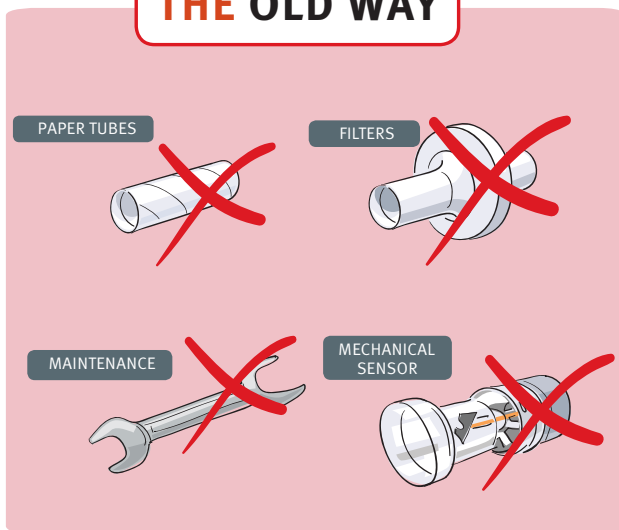
For many OSA patients who are either unable or unwilling to use their CPAP or BiPaP equipment on a consistent basis, TTOT may offer an attractive alternative to traditional tracheostomy, especially when all other options have been tried and exhausted. OSA is a complex disorder and it is not unusual to use a "trial and error" approach to treat it such that the best clinical benefit is combined with the highest rate of compliance. Compliance with TTOT is virtually 100%. Can the same be said for the more "conventional" alternative therapies presented?

*John R. Goodman BS RRT*

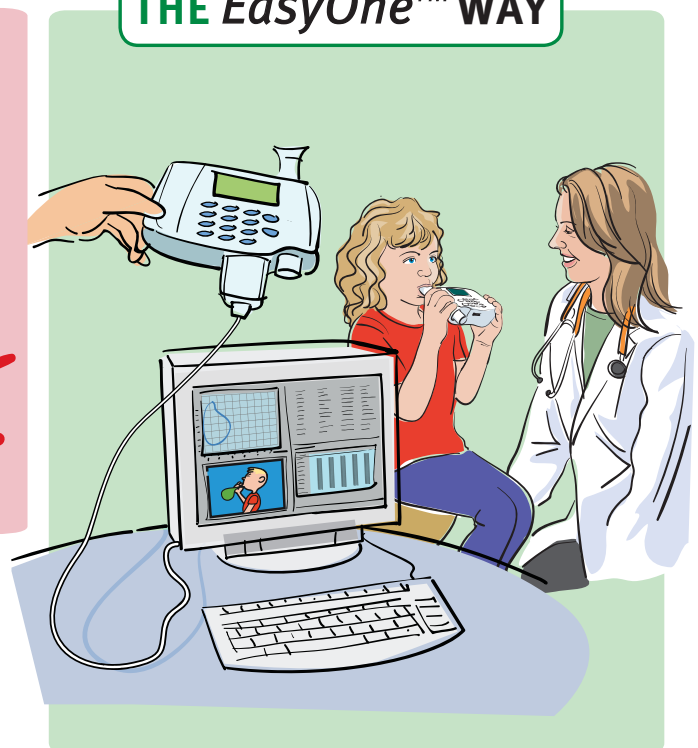
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## KATRINA COUGH

Nearly a year after the hurricane, some New Orleans residents say they have "Katrina cough," and they blame the storm and its aftermath for their respiratory problems. USA Today reports that doctors are still debating whether the symptoms are related to the hurricane, and no one knows exactly how many patients have respiratory problems. The American Lung Association of Louisiana has screened about 1,600 people since the hurricane. About 25% had mild to moderate reduced lung function. AmeriCares, a relief agency, awarded the lung association \$100,000 to help people with hurricane-related respiratory problems.

Pulmonologists said they saw many patients with coughs and other symptoms, and that some patients developed a cough right after the hurricane. Others with asthma, emphysema or lung diseases noticed that their symptoms have worsened. Patients who live or work in flooded or moldy areas appear most at risk.

"Katrina left a long time ago, and people are still coughing," says Parada, a specialist who sees patients who don't get better after seeing their primary-care doctors. Patients' problems could have many different causes, including allergies, environmental irritants such as dust or mold, or even gastroesophageal reflux, which can be made worse by stress. Paul Timmons, who works for the American Red Cross, said his asthma was under control until October, when he arrived in New Orleans. By December, Timmons, 38, was waking up with night sweats and coughing up sticky phlegm. His fevers went away with treatment. But he says he still wakes up at night unable to breathe.

## PAINT IT BLACK

Despite laws aimed at limiting the amount of coal dust in mines, coal miners are still coming down with black lung or pneumoconiosis, according to a report from the CDC. From March to May of this year, the Coal Workers' Health Surveillance Program identified 30 miners with pneumoconiosis out of a total of 328 miners who were screened. Of these, 11 had advanced disease. Thirty-one percent of the estimated 1,055 underground coal miners employed in southwestern Virginia underwent screening at mobile examination units. Nine percent of those screened had evidence of rapidly progressive pneumoconiosis. The 11 most advanced cases had worked in the mines for an average of 31 years.

The authors of a related editorial estimate that 5.5 cases of advanced coal workers' pneumoconiosis would be expected if dust levels had not exceeded the current limits. In contrast, 11.9 cases would be expected if miners' exposure averaged double

the limit. The report suggested that mandated levels of dust are too high, and should be lowered to the "recommended exposure limit" of 1 milligram per cubic meter suggested by the National Institute for Occupational Safety and Health.

## COME FLY WITH ME

A little over a year ago, the FAA approved two portable oxygen concentrators for use onboard commercial airlines. The AARC, which worked hard to promote the ruling along with other groups and organizations interested in opening up the skies to oxygen users, applauded the move as a definite step in the right direction. Now the Association and its colleagues have something new to celebrate: the FAA has just expanded the list of approved POCs to include three new devices and removed an earlier provision requiring approved POCs to use pulse technology only, opening the door to approval of the first device to allow both pulse dose delivery and continuous flow. "This is good news for oxygen users everywhere," says AARC Director of Government Affairs Cheryl West. "Now patients can choose from five different devices, including a device that allows for continuous flow, an important factor for patients who cannot maintain adequate oxygenation on pulse technology alone." The newly approved devices include the AirSep FreeStyle and Respironics EverGo, along with the SeQual Eclipse, which offers both pulse and continuous flow technology.

## BY ANY OTHER NAME

Asthma is unlikely to be a single disease, so we should abolish the term altogether, states an editorial in a recent issue of *Lancet*. The word asthma originates from a Greek word that means "to breathe with mouth open or to pant." Asthma includes a range of different symptoms, such as wheezing, coughing, and difficulty breathing. People with asthma can have a range of different triggers, symptoms, and responses to treatment, and the general consensus now emerging is that asthma is unlikely to be a single disease entity. The *Lancet* states: "So why wait? Rather than confusing scientists, doctors, and patients even further, is it not time to step out of the straightjacket of a seemingly unifying name that has outlived its usefulness? The conclusion should surely be that it is best to abolish the term asthma altogether."

## LAST GASP

Critical care physicians with the University of Pennsylvania Health System address a newly-emerging ethical dilemma in medicine: what should healthcare professionals do when faced with a request from a patient to end the use of life-sustaining supplemental oxygen? Scott Halpern, MD, PhD, a fellow in the Division of Pulmonary, Allergy and Critical Care Medicine and senior fellow with the Center for Bioethics at Penn, along with John Hansen-Flaschen, MD, chief of the Division of Pulmonary, Allergy and Critical Care Medicine at Penn, have co-authored a guide for physicians faced with such requests. The commentary, which examines concerns physicians may have in removing such a minimally invasive and potentially palliative therapy, and suggests strategies for physicians to overcome them, appears in the September 20th issue of *JAMA*. According to Halpern, "Informed patients with decision-making capacity have well-established rights to forgo any and all forms of life-sustaining therapy. However, there is no clear definition of what constitutes a life-sustaining therapy. When administered by face mask or nasal prongs, high flow oxygen is not at all invasive, yet it clearly serves a life-sustaining role for an increasing number of patients with advanced lung, heart, or cancer-related

diseases. Many of these patients would lose consciousness and die within hours or even minutes if their supplemental oxygen was withdrawn.” Both Halpern and Hansen-Flaschen have received requests from patients to stop their flow of supplemental oxygen, resulting in death. Halpern first grappled with the difficulty of withdrawing oxygen from an awake and alert patient when, as a first year medical resident, he was treating a hospitalized patient suffering from advanced lung disease and cancer. One morning, the patient said he’d “had enough” and tugged on his mask but was too weak to remove it and asked for Halpern’s help. Halpern debated this request with the attending physician who was concerned that the patient would experience air hunger and fear after oxygen was removed, necessitating high doses of sedating drugs. He worried this might constitute a form of euthanasia. Hansen-Flaschen received a similar request from an outpatient who suffered from an advanced lung disease and was living at home. He could no longer get out of bed and his quality of life had seriously deteriorated. The patient wanted to stop his oxygen therapy and asked Hansen-Flaschen to help him avoid a sense of suffocation afterwards. “I had to ask myself, is this participating in a patient’s death or is it simply respecting a patient’s request? Plus, there’s no way to predict an individual’s response to removing supplemental oxygen and how much they will suffer.” The authors’ commentary addresses specific concerns physicians may have about withdrawing oxygen, including how to balance the burdens and benefits of supplemental oxygen; whether withdrawing oxygen might appear neglectful; how to determine whether patients retain decision-making capacity; when it is acceptable to use sedation in lieu of oxygen; and concerns about patients’ motivations for discontinuing oxygen. A four-step approach is recommended: 1) Physicians should assure themselves, and other healthcare professionals involved that supplemental oxygen is a form of life-sustaining medical treatment. As such, requests to discontinue oxygen should be honored with the same judiciousness as requests to withdraw other forms of life support. 2) Physicians should ensure that patients requesting the terminal withdrawal of oxygen are free from undue influences, including family member’s wishes, economic considerations or treatable depression. 3) Physicians should ensure that the patient has the capacity to make medical decisions by documenting that patients show consistency, understanding, and rationality in making such requests. 4) Physicians should ensure that patients and their family members understand the difficulty of predicting patients’ experiences after oxygen withdrawal.

## BREATHE IT IN

Patients with COPD who use inhaled corticosteroids may have a significantly decreased mortality risk, according to a new study published in a recent issue of CHEST. New research shows that patients who received inhaled corticosteroids within 30 days of hospital discharge had a 25% reduced all-cause mortality rate. Cardiovascular-related death alone in patients using steroids paired with beta-agonists was reduced by 38 percent. Controversy still exists with respect to the effect of inhaled corticosteroids on mortality. This latest research examined the effect of inhaled corticosteroids on survival, and results suggest that the survival is longer in patients using inhaled corticosteroids. From 1995 to 2000, researchers from the University of Manitoba, Winnipeg, assessed the influence of inhaled corticosteroids on mortality in patients, 90 to 365 days posthospital discharge for COPD. Researchers collected patient information from a comprehensive database, excluding those

who died within 90 days. In total, 4,987 patients were split into two groups: those between the ages of 35 to 64 (965) and those 65-years-old or older (4,002). Within those groups, patients who received inhaled corticosteroids within 90 days of hospital discharge were compared with those who did not. Results showed that the mortality rates in patients 65 and older who received inhaled corticosteroids were 11.7%, compared with 13.1% for those who did not. Patients in the younger group showed even greater results, with a mortality rate of 3.0% for patients receiving inhaled corticosteroids within 90 days, compared with 6.0% for those who did not, providing a mortality reduction rate of 53%. Researchers also found a 23% reduced risk of death when comparing the effects of inhaled steroids with bronchodilators in patients in the 65-plus group. In all cases, the most significant results were found when inhaled corticosteroids were administered within the first 30 days following hospital discharge.

## PLACE YOUR MARKERS

Scientists have devised a new way of detecting TB infection, by looking for unique biomarkers in serum blood samples. The test is 94% accurate and will be further developed into a simple serum test for use in the developing world. The current TB diagnosis method involves careful examination of sputum using a microscope. Away from a clinic in rural areas in developing countries, this test has only 40-60% accuracy. Sputum culture, which takes between 2 to 6 weeks to produce a result, is not routinely carried out in countries with a high prevalence of TB but improves rates of diagnosis. The research by scientists at the Medical Research Council National Institute for Medical Research (NIMR) and at St George’s Hospital, University of London, is published in *The Lancet*. The TB serum signature was detected using a mass spectrometer and statistical methods were used to uncover complex patterns known as biomarkers, within samples from people infected with TB. They then used this signature to work out a simpler way to diagnose TB infection.

## BF DEAL

New health economic data presented today at the European Respiratory Society 2006 Annual Congress (ERS) add to a growing body of evidence demonstrating a further benefit of budesonide/formoterol in COPD. An analysis of switching patients from LABA-therapy to ICS/LABA combination therapy showed that when compared with the respective LABA, budesonide/formoterol (Symbicort) is more cost-effective than salmeterol/fluticasone (Seretide) in the treatment of severe COPD1. A computer simulation was performed with 4,000 patients over one year to compare the reduction in exacerbations frequency and difference in drug costs for formoterol versus budesonide/formoterol and salmeterol versus salmeterol/fluticasone. The relative cost-effectiveness of budesonide/formoterol and salmeterol/fluticasone was then examined showing that switching patients from formoterol to budesonide/formoterol rather than from salmeterol to salmeterol/fluticasone, results in a saving of 138 Euros per patient in healthcare costs per year. When epidemiological data were applied, total annual savings for the Swedish healthcare system were estimated at 7,565,394 Euros.

## THEY REALLY LIKE IT

The results of an observational study presented today at the 16th Annual Congress of the European Respiratory Society in Munich, Germany show that patients with asthma and chronic



obstructive pulmonary disease (COPD) are highly satisfied with the novel Respimat Soft Mist Inhaler (SMI) from Boehringer Ingelheim. In a 12 week observational cohort study in respiratory specialist practices in Germany, the handling, including device assembly, inhalation satisfaction and technique were assessed with a clinical questionnaire. 2006 patients from 695 centers in Germany were interviewed after 4, 8 and 12 weeks of 2-4 times daily administration of ipratropium bromide/fenoterol in the Respimat Soft Mist Inhaler. Most patients (66%) received treatment with the Soft Mist Inhaler for the first time. After 4 weeks, feedback from both physicians and patients was very positive, with 79% of patients and 87% of physicians very satisfied or satisfied with the ease of the set-up for use of the inhaler. Reactions to the soft mist inhalation were even more positive: 92% of patients and 97% of physicians were very satisfied or satisfied. The rating for the inhalation technique was also high: 86% of patients and 91% of physicians were very satisfied or satisfied. The ratings improved further over time.

### **BAD IS GOOD**

The University of Cincinnati has received \$2.4 million to study whether environmental toxicants can stimulate the body's natural defense system to stop additional damage in people with chronic lung diseases. It's believed that some long-term exposure to certain environmental toxicants may activate the receptor NKG2D in lung cells that causes the immune system to attack stressed and damaged lung tissue. However, when lungs experience chronic, low-level damage, at some point that damage exceeds the body's natural ability to repair tissue. UC scientists say when this happens repeatedly, such as through environmental tobacco or workplace exposures, it may cause the immune system to attack the damaged tissue in the same way it would if the tissue were infected with bacteria or a virus. By blocking the NKG2D receptor, researchers believe they can stop the immune system response and minimize damage to delicate tissue in the lung. Lymphocytes continually survey the epithelial cells lining the lungs to identify and destroy diseased cells. If the lymphocyte recognizes the tissue, it simply continues its survey for problems. But if the cell receives a signal that the tissue is infected, it will automatically destroy it to protect the body from disease. The immune system thinks it's eradicating disease from the body when it destroys cells that have been damaged by environmental toxins, but in chronic lung disease that destruction may be doing more harm than good. For the study, using an animal model, researchers will expose surface cells in the lung to two environmental toxins, *Pseudomonas aeruginosa* and acrolein, an air pollutant found in tobacco smoke, smog and diesel exhaust, to determine how cells respond to infection and toxicant-induced cell damage. This will help scientists determine which lymphocytes are important for regulating damage in the lungs, so they can develop ways to tweak the immune system and prevent the lymphocytes from causing additional damage to already-injured tissue.

### **LADIES' SPECIAL**

Women on long-term oxygen therapy for COPD are more likely to die from the disease than men, according to a study by the State Public Hospital of Sao Paulo in Brazil. Researchers assessed 435 oxygen-dependent patients with COPD. Of the group, 184 women and 251 men were observed while on long-term oxygen therapy over a seven-year period. After considering such factors as age, pack-years smoked, lung function test results and weight, investigators found females to be at a

significantly higher risk for death from the disease. Women had a 54% increase in the risk of death after initiating long-term oxygen therapy compared with the men. Researchers found that men and women exhibited similar survival rates during the initial follow-up period. Differences in survival became more apparent only after three years of follow-up. The clinical management for COPD for both groups was similar and was based on the latest treatment guidelines. One explanation for worse survival among women might be that some of the systemic complications of COPD, such as muscle dysfunction or depression, are more common in women and that these lead to worse outcomes. In two recently published studies of COPD, women had almost three times the prevalence of depression as men and twice the prevalence of fat-free body mass depletion.

### **HIGH COST OF BREATHING**

Patients with persistent asthma incur high medical costs as well as indirect costs for employers, reports a study in the August Journal of Occupational and Environmental Medicine. Researchers used a large insurance database to analyze costs associated with persistent asthma. Patients were classified as having persistent asthma if they suffered from asthma attacks at least twice weekly. The analysis included nearly 3,000 patients with persistent asthma, including employees and dependents covered by insurance plans at 17 US companies. Direct medical costs for patients with persistent asthma averaged about \$6,500 per year, compared to just over \$2,000 for patients without asthma. Data on 443 employees with persistent asthma also showed high indirect costs from disability and missed work days. On average, annual indirect costs were \$924 higher for workers with persistent asthma. Costs were highest for patients with severe persistent asthma who have continual asthma symptoms causing significant limitations in physical activity. There was no significant difference in costs between patients with moderate persistent asthma, who have asthma attacks at least twice weekly, and those with moderate persistent asthma who have daily attacks. This probably reflected the low rate of treatment with inhaled steroids—the most effective medications for controlling asthma—by patients in the mild group. Less than 10 percent of patients with mild persistent asthma used inhaled steroids on a daily basis, compared to 80 percent or more of those with moderate to severe persistent asthma.

### **STRAIGHT FROM THE GUT**

Researchers at the University of Pennsylvania School of Medicine have helped develop a technique in animal models for using the abdominal cavity to exchange gas, supplementing the function normally performed by the lungs. The goal is to provide a way to support patients who are on a mechanical ventilator but who need extra time and support to heal, beyond what a ventilator can provide. The only other alternatives that can rest the lung involve variations of bypass machine technology, all of which require anticoagulation. A technique that appears nontoxic and does not require anticoagulants could have huge implications for patients suffering from potentially reversible pulmonary failure. The system developed involves recirculating a gas-carrying liquid through the abdomen to deliver oxygen. The system was tested in adult pigs that were put to sleep and ventilated with low concentrations of oxygen to simulate lung failure. Using this technique, researchers observed an increase in arterial oxygen saturation from 73% to 89%. Doctors generally aim to keep the oxygen saturation of patients in the 90% range. The idea was inspired by peritoneal dialysis, already used for patients suffering from kidney failure, in which a catheter is

placed into the abdominal cavity and the blood is cleansed by using the lining of the abdominal cavity to exchange toxins and electrolytes.

## QUICK DEATH

The risk of death due to stroke is associated with exposure to high concentrations of air pollution about 2 hours before death, Japanese investigators report. Because this risk appears to be independent of 24-hour particulate matter levels, they suggest that air quality standards be based on hourly data, as well as 24-hour levels. Epidemiologists at Kyoto University collected data from the 13 largest cities in Japan regarding concentrations of suspended particulate matter 7  $\mu\text{m}$  diameters or higher, ambient temperature, plus other components of air pollution, from 1990 to 1994. During that period, 17,354 residents age 65 or older died due to hemorrhagic or bleeding stroke, and 46,370 died from ischemic stroke, the type caused by blood clots. According to their analyses, reported in the journal *Occupational and Environmental Medicine*, the OR of death from ischemic stroke was increased with temperatures above 30 degrees centigrade in the warmer months compared with moderate temperatures of 15 to 22 degrees (OR 1.333). In contrast, the risk of death due to bleeding in the brain was increased in cold weather (0 to 8 degrees, OR 1.225). However, during warmer months, high 1-hour mean concentrations of PM7 increased the risk of death from hemorrhagic stroke nearly 2.4-fold, an association independent of 24-hour mean PM7 concentrations. In contrast, death due to ischemic stroke was not associated with 1-hour PM7 levels. The researchers suggested that this discrepancy may be due to the longer interval from ischemic stroke onset to death, or to the fact that inhaled particles raise blood pressure, a risk factor for bleeding in the brain. The authors noted that during the 4 years covered by this study, there were 443 hours in which the concentration of PM7 was over the 1-hour air quality standard in Tokyo, and that 49 of those hours occurred on days when the 24-hour mean concentration of PM7 was within the air quality standard for 24-hour periods. Reported by Reuters.

## AOP: A PRIMER

In utero a fetus begins to make breathing movements during the second stage of lung development. After birth breathing starts intermittently and then becomes continuous. When a baby is born prematurely, the central nervous system is underdeveloped and can interfere with stimulating normal breathing patterns. When there is cessation of breathing for more than 20 seconds, this is considered apnea. In the premature infant it is called apnea of prematurity (AOP). AOP may be due to an immature breathing control center but there are other reasons that can cause apnea. These include bleeding or damage in the brain, respiratory diseases, hypothermia, unstable calcium or glucose levels, infections and vagal stimulation during suctioning or positioning of the neck. Apnea is also seen in the term infant, but often these episodes are self limited and do not create physiological changes. In the premature infant apnea is usually followed by a bradycardic episode. When breathing slows so does the heart rate. It is important to identify the difference between apnea and periodic breathing which is seen in both term and premature infants. Periodic breathing is a pause in breathing that lasts less than 15 to 20 seconds followed by several rapid shallow breaths. There are no other associated symptoms and the infant resumes normal regular breathing without stimulation. An apneic episode lasts greater than 20 seconds with a change in facial color (bluish) usually around the mouth. There may be other

symptoms such as bradycardia and limpness. In the case of apnea the infant may self stimulate back to normal breathing or need stimulation from a caregiver. When an infant is diagnosed with AOP, there are several different treatment options. One such treatment is stimulation via motion (bumper bed). This treatment is where the neonate is physically stimulated at regular intervals preventing apnea. It is effective with patients who respond well to stimulation. Trials without stimulation are done to observe if apnea reoccurs. Another treatment option is to provide low flow oxygen. This prevents the patient from becoming hypoxic. With some patients FIO<sub>2</sub> is weaned to room air. The stimulation from just the flow is enough to initiate breathing. Flow is then weaned as apneic episodes decrease. The above option can be carried further through the use of nasal continuous positive airway pressure (NCPAP). This is effective in providing both the oxygen requirements of the neonate as well as to augment ventilation. AOP can also be caused by obstructive sleep apnea. NCPAP helps prevent obstruction through the use of pressure. NCPAP is indicated when drug therapy has not worked. The medication, caffeine citrate, is another treatment option. Caffeine citrate is administered with a loading dose of 20 – 40 mg/kg IV or PO. This is followed up 24 hours later with maintenance doses of 5 – 7 mg/kg every 12 hours or once a day. Caffeine citrate is weaned over a two to three month period as patient gains weight as long as there are no apneic episodes. If apneic episodes persist the dose of caffeine is adjusted to the patient's weight. When the above options fail, intubation of the neonate becomes necessary. The length of time on the ventilator varies but usually not more than a few days. This gives the caffeine level in the blood time to rise to therapeutic levels. Support is decreased immediately after intubation to let the neonate do most of the work. Another cause of AOP may be gastroesophageal reflux (GER). If GER is suspected pH probe studies are often conducted. These studies note changes in pH associated with reflux in the esophagus. Anti-reflux medications are also provided to help decrease reflux. Radiological findings may indicate a need for surgical intervention. Patients are placed on their sides to help prevent aspiration from occurring, thus reducing the chances of apnea. Most babies should be apnea free 2 – 10 days before discharge. Many are discharged with apnea monitors. The data from these monitors are downloaded once or twice a month and read by a pulmonologist. If frequent alarms occur the infant is admitted for further observation and tests. Many premature babies will "outgrow" AOP by the time they reach 36 weeks gestation.

Apnea of prematurity is a common occurrence in the NICU. This can be a stressful event for healthcare workers who are not familiar with this patient population. Training and education on neonatal stabilization will help practitioners intervene appropriately. There will be further newsletter articles discussing stabilization of the neonate and how to get these patients ready for transport to another facility that specializes in neonatal care. Reported by Justin Tsze, RRT-NPS, in Hamilton Medical's Newsletter.

## COMPUTER-DRIVEN

For patients with acute respiratory failure, a computer-driven system can significantly reduce the duration of mechanical ventilation and length of stay in the intensive care unit, as compared with the traditional physician-controlled weaning process. Doctors at the Hôpital Henri Mondor in Creteil, France weaned 74 patients using the computer-driven system and 70 with the usual process. They found the computerized system

reduced the duration of mechanical ventilation from 12 days to 7.5 days and cut patients' ICU stay from 15.5 days to 12 days. According to the researchers, the total number of ventilator-related complications such as reintubation, self-removal from ventilator assistance, need for noninvasive ventilation, mechanical ventilation longer than 21 days, and tracheotomy, was reduced by 30 percent in the computer-driven weaning group. The system was designed to perform several tasks comparable to a ventilator weaning protocol 24 hours a day, seven days a week. It automatically and gradually reduced the ventilatory assistance to the patient; it performed the equivalent of a spontaneous breathing test; and it displayed an incentive message for the doctor and technicians when the patient was deemed ready to breathe spontaneously. The computer-driven weaning protocol did not depend on the willingness or availability of the staff, and full compliance with the weaning protocol was therefore ensured, the researchers noted. Reported in Medical News Today.

### THE WINNER

Frost & Sullivan has named Spacelabs Healthcare its 2006 North American Patient Monitoring Company of the Year, citing the company as "a leading innovator of patient monitoring products" and the medical community's praise for the connectivity and reliability of its devices. Frost & Sullivan made special mention of Spacelabs' commitment to a "customer first philosophy," particularly its open architecture, ease of connectivity and compatibility for hospital systems concerned about managing multiple technologies. The Award also singled out Spacelabs Healthcare as an innovator for extending its capabilities to integrate directly with anesthesia delivery systems, pulse oximetry technologies, diagnostic cardiology and other medical products and services. For more contact the company at [spacelabshealthcare.com](http://spacelabshealthcare.com).

### VITAMIN WHEEZE

Children whose mothers consume more foods containing vitamin E during pregnancy are less likely to develop wheeze or asthma by the age of five, according to researchers. Those born to mothers who had the lowest vitamin E intake were 3.47 times more likely to have persistent wheeze and five times more likely to have early-onset persistent asthma than those born to mothers with the highest levels, according to researchers at the University of Aberdeen. Higher maternal dietary vitamin E intake, assessed at 32 weeks gestation on a dietary questionnaire and nonfasting blood sample, was associated with less wheezing in their children after five years of follow up, even after adjustment for a full range of variables including breast feeding. Dietary vitamin E rather than supplements containing the antioxidant appeared to be key.

Children of mothers who had more intrapartum vitamin E intake were also less likely to have asthma outcomes at age five. The 2,000 mothers who were recruited at Scottish antenatal clinics were also measured for other antioxidant levels including vitamin C, beta carotene, alpha tocopherol, and zinc. Of these, zinc had the strongest associations with early respiratory function. Late onset asthma (after age 2) was correlated with lower maternal zinc intake during pregnancy. The children's own nutrient intake had no impact on their asthma, wheezing, eczema, or other outcomes. While breastfeeding was not associated with wheezing or asthma outcomes at the five-year follow-up overall, breast fed children (74.6%) had greater magnitude associations between maternal antioxidant intake and outcomes than those who had not been

breast fed. The researchers said their results were consistent with the notion that early life nutrient intake, both in utero and in the early postpartum period, modifies the risk of developing childhood asthma. Other studies have found that supplementation with antioxidants including vitamin C and E and trace elements like selenium and magnesium does not consistently improve asthma outcomes for adults. Dr. Devereux and colleagues said that their study may offer an explanation for the inconsistencies between epidemiologic and dietary intervention studies.

### COMO SE LLAMA, "AWARD?"

The prestigious Hospes Hotels & Moments Group, in collaboration with the Asociacion Iberica de Patologia del Sueno, the Iberian Association of Sleep Pathology, announces its second Hospes Suenos International Award for the best scientific study of sleep habits. Submitted papers must be publications studying the influence of medical, scientific, psychological, environmental, nutritional, cultural, social or other aspects on population sleeping quality. The amount of the award is 6,000 Euros. All studies must have been published or accepted for publication during 2005, and can be submitted in Spanish or English. They must include a three to five page abstract and no more than two figures. Each author may submit up to two papers. Works must be sent by e-mail to [suenos@hospes.es](mailto:suenos@hospes.es) before April 30. A CV should be included.

### POINT OF CARE CONFERENCE

The Bay Area Point of Care Coordinators (BAPOCC) recently held their Spring meeting in Walnut Creek, CA. Striving to offer an event that delivered significant value to its members and avoid another "dry" seminar, Robyn Medeiros, QA/POCT/Education Manager at El Camino Hospital and Susan Woo, CLS, MT(ASCP)M of Kaiser Permanente collaborated with RNA Medical to secure quality control industry renowned professor, author and AACC speaker, Sharon L. Ehrmeyer, PhD as the keynote speaker to anchor the day's event. Professor Ehrmeyer delivered two very interactive and informative presentations, the first on recent updates in POC testing regulatory requirements and the second on building a quality control program for POCT. She emphasized the need for all laboratories and POC testing areas to develop a rigorous quality control program and to approach electronic and automatic QC programs with caution. In her presentation, Ehrmeyer stated that "there is a very important role for external liquid QC and that will never go away." Also presenting topics were Howard Koo, Regional Director of Laboratory Quality and Compliance, from Kaiser Permanente and Jackie Coleman, PhD, Senior Clinical Scientist, for Accumetrics. Koo talked about the unique requirements of the state of California with regard to laboratory quality and regulatory requirements. He also emphasized that quality control is more than a matter of compliance; it is critical to patient safety. Dr Coleman presented a lively discussion of how the Accumetrics VerifyNow assay is used to determine the level of patient response to aspirin or Plavix therapy. Peer-reviewed studies were presented that show by assessing a patient's level of platelet inhibition, therapies can be adjusted, as well as bleeding levels predicted, providing an improved outcome for the patient. Rounding out the day's events was a panel discussion that featured Professor Ehrmeyer, Mr. Koo, Valerie Ng, PhD, MD, Director of the Clinical Laboratory at Alameda County Medical Center and Randy Byrd CTO/VP R&D from Bionostics, RNA Medical's parent company. Many of the questions focused on gaining an understanding of how to

reconcile CLIA, CAP, JCAHO, COLA and California state requirements. A significant number of questions surrounded the quandary of when, where and how to employ electronic and automatic QC offered on many of the newer blood gas analyzers. The general consensus was that there is still a significant amount of interpretation required by the laboratory, but that patient safety is paramount. During the meeting, RNA Medical announced its newest quality control offering, the Safe-Wrap Combo Blood Collection Tube, used for the collection of capillary blood samples for use with i-STAT blood gas, electrolyte, and chemistry cartridges requiring either 95 µL or 65 µL of sample. These tubes are Mylar-wrapped glass capillaries that have been treated with calcium-balanced lithium heparin. Also sponsoring this fast moving and well-attended event were Abbott POC, Accumetrics and Triad Associates. Attendees received continuing education credits for Dr. Ehrmeyer's and Mr Koo's presentations. For information on this or future events contact Paul Shea, Director of Sales and Business Development at RNAMedical.com.

## BOOK REVIEW

### TO ERR IS HUMAN: BUILDING A SAFER HEALTHCARE SYSTEM

*(Institute of Medicine Washington D.C.; To Err Is Human: Building a Safer Healthcare System. National Academy Press, 2000. 287 pages.) Tim France, BS, RRT. Tim France is with Hamilton Medical. This review is from the company's newsletter.*

The Institute of Medicine (IOM) has as its main focus a concentration on quality care and best practice within healthcare. Over the last five years the IOM has tried to bring attention to the epidemic rate of adverse events related to medication errors within healthcare, and to put forth recommendations for change. The catalyst for this change was the groundbreaking book, *To Err is Human: Building a Safer Healthcare System*. This book is a very important piece of research literature that should be read by all healthcare leaders.

The IOM works from the assumption that most errors are caused by flawed processes and not flawed healthcare providers. The IOM is attempting to accomplish several aims within this text. Each chapter covers a specific aspect regarding adverse events related to medications. The executive summary outlines the intent of the book and gives a brief overview of the strategy recommended by the institute. The summary also disseminates the current state of healthcare as it relates to errors and also compares healthcare with businesses that work in similarly chaotic environments. The book examines what errors are and how they are caused. It uses statistics and supportive data to illustrate the problem. For example, in two large studies, one done combining Colorado and Utah and another in New York, it was found that adverse events occurred in 2.9 and 3.7 percent of hospitalizations (1). In the Colorado/Utah study, 6.6 percent of patients died from adverse events while 13.6 percent died from adverse events in the New York study. If you were to take those percentages and apply them to the more than 33.6 million admissions across the country, the total deaths range from a low of 44,000 to a high of 98,000. The IOM report goes on to say that medical errors cause more deaths than motor vehicle accidents (43,458), breast cancer (42,297), or AIDS (16,516). The IOM's focus is on

convoluted processes rather than blaming healthcare providers for adverse events. I agree that most healthcare providers want to do a good job, but because of complicated equipment or policies, doing that job can be very difficult. *To Err is Human* outlines the issues that cause medical errors and then goes into recommendations for improvement. Also, IOM does a great job in comparing what other industries have done to improve safety. They make the point that other high profile industries have had years to correct their problems, whereas healthcare has just begun their safety awareness.

My overall evaluation of the book was very positive. Having worked in the healthcare field for 23 years, I can appreciate the important need for safety. The ideas presented in the book are well thought out, concise and to the point. The IOM took great pains to explain their rationale for each recommendation. They would explain how the recommendation was arrived upon, and ways to implement a recommendation.

*To Err is Human* is a book I feel all healthcare providers should read. However, the book is heavy into processes, and bedside clinicians may feel that they would have little impact changing policy. I feel it is very important that a bedside clinician should pay attention to the message that is being relayed and not so much the process. Leadership within an organization should pay attention to the recommendations and be able to disseminate the processes to bedside clinicians. *To Err Is Human* is a passionate plea for healthcare to change its processes and make patient safety more than their number one priority. I say that because when you prioritize initiatives, they can move up and down the priority list according to what is important at that moment. Healthcare needs to make patient safety a part of their culture. Patient safety has to be second nature, something that is just done and doesn't need to be thought about. Before this change happens, there will need to be a lot of thinking about patient safety and practicing the initiatives that make it part of your culture. That is the message that I acquired from *To Err is Human*. In the five years since *To Err is Human* has been published there has been an increased awareness regarding patient safety. Organizations such as JCAHO have mandated accredited hospital initiated programs to improve patient safety. The Institute for Healthcare Improvement (IHI) has started a 100,000 lives campaign. In-hospital programs such as Rapid Response Teams have been instituted in an effort to improve safety. Ventilator companies such as Hamilton Medical have developed Intelligent Ventilation technology that can respond to a patient's changing pulmonary status and give clinicians valuable information that can help optimize ventilator settings.

## CLINICAL TRIALS REVIEW

### CICLESONIDE VS BUDESONIDE

*Pulm Pharm Ther 2006 Jul 11 (Elsevier)* reports that ciclesonide is more effective than budesonide in the treatment of persistent asthma. The objective of the study by Ukena et al was to compare the efficacy and safety of once-daily ciclesonide versus once-daily budesonide in patients with asthma. A total of 399 patients with asthma were randomized to receive once-daily doses of ciclesonide or once-daily budesonide for 12 weeks. Both ciclesonide and budesonide significantly increased FEV1 from baseline. The increase in FEV1 was significantly greater in ciclesonide-treated patients. Ciclesonide and budesonide

significantly improved FVC and PEF and significantly greater increases occurred with ciclesonide versus budesonide. Analysis of morning PEF revealed an earlier onset of action for ciclesonide versus budesonide; a significant improvement was seen by day 2. The authors concluded that once-daily ciclesonide was more effective than once-daily budesonide in improving FEV1, FVC and PEF. Ciclesonide also had an earlier onset of action than budesonide in patients with persistent asthma.

## PERSISTENT ASTHMA

Respiration 2006 Sep 6 (Karger) reports on the effects of salmeterol in patients with persistent asthma receiving inhaled corticosteroid plus theophylline. The purpose of the study by Inoue et al was to investigate the efficacy and safety of salmeterol combined with high-dose ICSs plus theophylline in severe asthma. The researchers undertook a randomized, placebo-controlled, crossover study to compare the effect of a single dose of inhaled salmeterol or a placebo in patients with severe asthma whose conditions were not being adequately controlled by therapies with high-dose ICSs plus oral theophylline with or without leukotriene receptor antagonists. Twenty patients took part in the trial. Compared with the placebo, the inhalation of salmeterol significantly increased the FEV(1). Even in the 9 patients treated with high-dose ICSs plus theophylline plus a leukotriene receptor antagonist, the FEV(1) increased significantly more after salmeterol than after the placebo. Inoue et al concluded that patients with severe asthma receiving high-dose ICSs plus theophylline may benefit from the addition of salmeterol. (© 2006 S. Karger AG, Basel.)

## OBESITY AND ASTHMA

Chest 2006 (Sep;130(3):890-95) reports that the association between obesity and asthma is stronger in nonallergic than allergic adults. The cross-sectional survey of 86,144 Canadians by Chen, Dales and Jiang sought to determine the modifying effects of sex and allergy history on the association between body mass index and asthma prevalence. The adjusted odds ratios for obesity associated with asthma was 1.85 for women and 1.21 for men. One unit of increased BMI was associated with an approximate 6% increase in asthma risk in women, and 3% in men. A stronger association between obesity and asthma was observed in nonallergic women than in allergic women, with the adjusted ORs being 2.53. For men, the corresponding ORs were 1.30 and 1.18, respectively. The authors concluded that obesity is likely to have a larger effect on nonallergic asthma. The greater prevalence of nonallergic asthma in women may explain the stronger obesity-asthma association seen in women compared with men and children who have a greater prevalence of allergic asthma.

## NEWS FEATURES

### NEW SEDATION DRUG MAY HELP FACILITATE EXTUBATION

*Melissa Turner, BA, RRT. Reprinted from Hamilton Medical's Intelligent Ventilation Newsletter.*

Patients requiring mechanical ventilation often require sedation due to agitation, which is caused by delirium. Patients may be sedated for a variety of reasons such as to prevent self-destructive behavior, improve patient ventilator synchrony by

decreasing excessive central respiratory drive, and to alleviate patient discomfort. Once a patient's condition improves to a point where weaning and extubation can be considered, sedation is usually reduced. Reducing sedation can provoke a stress response, catecholamine release, and agitation, resulting in tachypnea, tachycardia, and hypertension. Sedation is often resumed or increased as a result of the stress response. Inevitably, mechanical ventilation is prolonged in these patients who would otherwise be weaned and extubated. The main reason that patients requiring sedation can not be weaned and extubated is the patient's decreased respiratory drive caused by the sedation.

One drug currently being studied, dexmedetomidine hydrochloride, also known as Precedex, is both a sedative and analgesic. An alpha-2 receptor agonist, its stimulation in the central nervous system "inhibits sympathetic activity and reduces plasma epinephrine and norepinephrine levels." Dexmedetomidine has proven helpful for hemodynamic stress caused by agitation that is associated with delirium and may help to facilitate weaning and extubation of ventilated patients since alpha-2 receptor stimulation does not cause respiratory depression. In a study by Siobal et al, dexmedetomidine was studied in a small uncontrolled trial where five patients in a trauma/surgical ICU failed previous wean attempts. These patients were infused with dexmedetomidine which allowed weaning of other sedation and successful extubation without cardiopulmonary instability or agitation which had caused earlier failed weaning attempts. Only one of the five patients required reintubation for upper airway obstruction. This study was a small, unblinded, single-arm trial which does leave some room for bias.

Further studies need to be done on dexmedetomidine facilitation weaning and extubation, but this study by Siobal et al. does provide a good preview of what could be expected. The FDA has approved dexmedetomidine for use of less than 24 hours duration in postoperative patients, but there are some reports of the drug being used for longer periods of up to 7 days. It appears that dexmedetomidine is successful in maintaining adequate sedation without diminishing respiratory drive or causing hemodynamic instability and therefore may be a useful tool in facilitating extubation in patients who are difficult to wean due to agitation. Dexmedetomidine certainly deserves a closer look and further investigation.

#### Sources

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## PRODUCTS

### TIME AND TIDE

Mercury Medical is pleased to introduce the StatCO<sub>2</sub> and Mini StatCO<sub>2</sub> disposable, colorimetric CO<sub>2</sub> detectors. These devices offer a quick visual breath by breath reading to detect the presence of CO<sub>2</sub> by color comparison assisting in the verification of proper tube placement. The StatCO<sub>2</sub> is available for patients weighing over 15 kg and the Mini StatCO<sub>2</sub> is available for those patients weighing 1-15 kg. From intensive care uses to the operating room and recovery, these single-patient use carbon dioxide detectors will perform continuously for up to 24 hours, keep working in 100% humidity and have a packaged shelf life of up to 2 years. Contact Customer Service for more information at (800) 237-6418.

### CHILDPROOF

An innovative device for detecting gastric reflux in the airway was put to the test as Chris Landon, MD, Chief of Pediatrics at Ventura County Medical Center, conducted a clinical study to test the efficacy of Restech's Dx-pH Measurement System on infants and children. The study features six patients, five of whom range in age from three months to nine years old, and the sixth a 20 year old with severe muscular dystrophy. Each patient was experiencing pulmonary manifestations of gastroesophageal reflux disease (GERD) including: Sleep apnea, asthma, hoarseness of the throat, pulmonary fibrosis and chronic cough, among others. GER occurs when acid from the stomach flows up through the lower esophageal sphincter (LES) and into the esophagus. Reflux that rises even higher and escapes the upper esophageal sphincter (UES) into the oropharynx is deemed laryngopharyngeal reflux (LPR). In the pediatric population, LPR is known to be implicated in the development of asthma, sinusitis, otitis media and sudden infant death syndrome. The need for a device that can detect reflux in the airway tied to manifestations of GER and LPR inspired Restech to develop the Dx-pH Measurement System. "What's exciting about this [Dx-pH Measurement System] device is that it is the first to measure and record pH in the oropharynx, and its positioning is ideal for detecting LPR in real-time," asserts Dr Landon. Each patient was objectively assessed; depending upon symptoms and conditions, they were administered either a 24 or 48 hour test. The miniature 1.5mm diameter Dx-pH Probe was visually guided by a blinking light emitting diode (LED) to a comfortable location in the airway posterior to the uvula. Thanks to a streamlined placement process, the children tolerated the test with minimal discomfort, a welcome refinement from conventional pH measurement catheters. The youngest patient in the study, at three months, unknowingly became Restech's poster child by displaying the most definitive results and proving an explicit need for the test. The child was admitted with cystic fibrosis, cough symptoms and posed a failure to thrive in his current state. An upper gastrointestinal (UGI) evaluation revealed no signs of GERD or anatomic obstruction, at which time Dr. Landon administered the Dx-System test for 24 hours. While the infant tolerated the test exceptionally well, the results showed dramatic reflux events with dangerously low (acidic) pH levels. With sufficient evidence to go forth, Dr. Landon advised that the infant undergo fundoplication surgery, the standard surgery for treating patients with severe GERD. After the procedure, the infant underwent a post-fundoplication Dx-System test and revealed

healthy results, with pH levels remaining constant around pH 7. These results show the Dx-System test led to differential diagnosis of symptoms missed by the initial UGI. Dr Landon concluded, "The Restech Dx-pH Measurement System is an advanced ambulatory monitoring tool that fills a distinct void in the diagnosis of acid reflux." For more information on the Dx-pH Measurement System, call Debra Krahel or Wal Flicker at (800) 352-1512 or visit [restech-corp.com](http://restech-corp.com).

### AEROSOL DELIVERY

Monaghan Medical Corporation recently released its newest product, the AeroEclipse II Breath Actuated Nebulizer. The AE II incorporates a more sensitive breath-actuator diaphragm so patients will require less effort to actuate the device. A user-friendly mode selector switch on top can easily toggle between breath actuation and continuous modes. The device enables caregivers to provide fast, assured patient dosing, since the AE II BAN delivers an optimal particle size and customized dosing. It also delivers less drug into the environment during administration, protecting RTs from the risk of exposure. Contact [monaghanmed.com](http://monaghanmed.com).

### NEW MANAGEMENT

A new team has assumed ownership and management of B&B Medical Technologies, a leading designer of specialty airway management devices and nebulizers for infants, pediatrics and adults. Continuing B&B's legacy as a respiratory therapist-owned company are David Thompson and Beth Keifer, who together bring more than 50 years in clinical, educational and technical expertise in the respiratory care field. Thompson and Keifer teamed up with Robert Sprowls, a successful CA businessman, to manage the B&B Medical Technologies team. B&B products are designed for easy, one person application, helping to minimize risk of accidental disconnects and unplanned extubations. B&B's StabilTube, LockTite, E.T.Tape for Adults and Infants and Bite Block provide clinicians simple solutions for comfortably securing the endotracheal tube, prevention of ventilator disconnects and a convenient answer to prevent ET tube biting. B&B's TrachGuard and TrachStay comfortably secure the ventilator circuit to the tracheostomy tube while preventing accidental disconnects. B&B's patented Hope nebulizer technology provides efficient delivery of continuous medication combined with the ability to blend gases such as Heliox without affecting medication delivery. The Hope Nebulizer is the first nebulizer specifically cleared by FDA for Heliox administration. Contact [bandb-medical.com](http://bandb-medical.com).

## SPOTLIGHT ON NEONATOLOGY

### NO LEAK

Passy-Muir Tracheostomy & Ventilator Swallowing/Speaking Valves (PMVs) are the only patented closed position "no leak" swallowing/communication valves. This unique design restores natural physiology and reduces tracheostomy complications. Interchangeable for use on/off the ventilator, the PMVs provide a cost-effective treatment for tracheostomized and ventilator-dependent neonates, with the goal of decreasing aspiration, improving oral feedings, facilitating secretion management and expediting weaning and decannulation. The PMV has been successfully used on ventilator dependent neonates as young as five days old. Early intervention with the PMV in the NICU

population allows for natural development of speech and feeding skills, improving quality of life.

## BLOOD TUBE

RNA Medical, division of Bionostics, Inc, Devens, MA, announces the introduction of Safe-Wrap Combo Blood Collection Tubes for use with i-STAT blood gas, electrolyte, and chemistry cartridges. These capillary tubes have been treated with calcium-balanced lithium heparin. The Mylar wrapping minimizes the risks associated with broken glass capillaries by containing both the glass and the sample in the event of accidental breakage. Safe-Wrap Combo tubes may be used for cartridges requiring either 95 or 65 µL of sample and feature a plunger for dispensing the sample into the cartridge. They are packaged in cylinders containing 50 capillaries and plungers. (800) 533-6162, RNAMedical.com.

## EXECUTIVE PROFILES

### lapyx Medical

Chris Whelan

Chris Whelan is with lapyx Medical.

#### What led you to develop your products?

Cliff Wright, our founder and chief product designer, is a biomedical engineer, who spent fifteen years working in the hospital environment. Most of his early designs were inspired by the needs he witnessed first-hand. For instance, he designed the Iso-Line Holster System for Yankauer wands because he noticed the inconsistent and often questionable storage of these devices. A few of the products we are preparing to launch have predicates in the market, but we believe we can offer significant improvements while still being price sensitive.

#### What level of user input has gone into the design and development of your product?

Iapyx Medical designs products with extensive user input. We take design ideas directly to end users so that we get meaningful feedback. By visiting hospitals, clinics, and professional meetings, we gather a wide array of candid feedback from experts and end users. And as a small company, we have the ability to keep a designer, engineer, and product manager focused on customer needs, design challenges, and adoption sensitivities.

### Bunnell

David Platt, MS, RRT

David Platt is Marketing Director, Bunnell.

#### Who is responsible for training and education of your staff and your customers?

Evan Richards is the Director of Education and Clinical Services at Bunnell. He is a respiratory therapist with eight years of neonatal and pediatric experience. Evan has worked at Bunnell

Incorporated for 17 years. During that time, he has written and illustrated most of the educational and training materials used to train clinicians and Bunnell's clinical specialists.

#### What types of education do you provide?

Bunnell has always had a strong commitment to training and education. Our clinical specialists lecture on a variety of ventilation topics at hospitals and at regional and national conferences. They also provide two to three days of on-site clinical training for the Life Pulse High-Frequency "Jet" ventilator. Initial and ongoing training are provided to hospitals at no charge.

#### How do you manage "off-hours" assistance for clinical questions?

"Off-hours" clinical support is a service that Bunnell has offered since day one. For the first few years the hotline number was Dr Bunnell's home phone number. Since the commercial release of the Life Pulse in 1988, the same three people, two respiratory therapists and Dr Bunnell, have staffed the hotline. This consistent and high level of support is unusual in the medical industry. We believe the fastest way to get a question resolved is to call our hotline. A clinical specialist is available, 24 hours a day, 7 days a week. When you call (800) 800-HFJV, you get a call back in five minutes or less.

#### Do you provide technical service support, and of what nature?

Bunnell's service department is staffed by biomedical technicians and engineers. They provide technical support, via the phone, Monday through Friday, 9 am to 5 pm MST. All service is done at our factory in Salt Lake City. Off-hours technical support is supplied by clinical specialists via our hotline.

#### What formal education programs does your company provide for biomedical training and service?

Bunnell has a two day service training program for biomedical technicians. It covers routine maintenance and calibration procedures for the Life Pulse ventilator. The theory of operation and clinical troubleshooting are also emphasized. If we can help biomed techs evaluate and troubleshoot reported problems at the hospital, we can limit downtime and save the hospital money.

#### What do you feel is important to support the customer/end-user of your product?

Thorough product training and real-time support of clinicians are the most important services Bunnell provides its customers. To be successful treating critically ill patients, clinicians have to understand how the ventilator works and how to apply it for the maximum benefit. If questions arise during a clinical application, getting an answer or resolving a problem must happen quickly. That's why Bunnell has a toll free hotline. Customer support begins with manufacturing a quality product. Having a friendly professional staff that provides excellent customer service is also a critical ingredient.

#### What activities does your company undertake to promote the product?

High-frequency ventilation is a niche market focused primarily on neonatal and pediatric intensive care units. As a result, our product promotion is highly targeted. We use a combination of direct mail, print advertising, and direct marketing at

professional conferences. We market to respiratory therapists, nurses, and physicians. Encouraging and supporting clinical studies is also an important component of our marketing effort. With the current emphasis on evidence-based medicine, it is important to generate data about the benefits of your product.

#### **How does your company reach out to its customers regarding product performance and R&D?**

Bunnell tracks customer input regarding product performance through a formal program that records all customer comments and complaints. Quarterly, we summarize and analyze this information to look for trends. If problems or weaknesses are identified, the information is used by R&D and product engineering to develop solutions and implement improvements. We use this same mechanism to improve our training materials and educational practices. Focus groups are conducted throughout the product development process to ensure customer preferences are incorporated into every new product.

#### **What mechanisms are in place to assist hospitals in their educational requirements and ongoing education?**

The Bunnell website, [www.bunl.com](http://www.bunl.com), has a wealth of information on the Life Pulse and high-frequency ventilation. Our In-service Training Manual, Operator's Manual, and Quick Reference Guide are available, in their entirety, on our website. The In-service Training Manual is our best resource for ongoing education. It is divided into 12 short chapters, each with objectives, post tests, and answers for the post tests. Bunnell provides ongoing training for all its customers. The Bunnell website includes a form that allows hospitals to request training. We also have a large library of articles published on HFJV and PowerPoint slides that explain every aspect of HFJV on a password protected site.

#### **Where do you see the future of your product in relation to end-user requirements?**

Our goal for the Life Pulse is to continue to refine its features to make it the most effective ventilator possible. Current plans include making it smaller, quieter, and more user friendly.

## **B&B Medical Technologies**

David Thompson, Beth Keifer

David Thompson is President and Beth Keifer is Vice President, Sales & Marketing, B&B Medical Technologies.

A new team has assumed ownership and management of B&B Medical Technologies. Continuing B&B's legacy as a respiratory therapist-owned company are David Thompson and Beth Keifer, who together bring more than 50 years in clinical, educational and technical expertise in the respiratory care field. Thompson and Keifer are joined by Robert Sprowls, a Carlsbad, CA businessman with over 40 years in business development, manufacturing and distribution experience. Stephen Briggs III along with Dr. Ernie Bodai created B&B Medical Technologies in 1985 to ensure that specialty airway related products had a pathway to the clinical community. The foundation formed by Briggs through his lifetime in the respiratory therapy community will be carried on in the new ownership and management.

#### **Describe your product(s) and their unique features.**

Since 1985, B&B Medical Technologies has been a leading designer of specialty airway management devices and nebulizers for infants, pediatrics and adults. B&B products are designed for easy, one person application, helping to minimize the risk of accidental disconnects and unplanned extubations. B&B's StabilTube, LockTite, E.T.Tape for Adults and Infants and the Bite Block provide clinicians simple solutions for comfortably securing the endotracheal tube, prevention of ventilator disconnects and a convenient answer to prevent endotracheal tube biting. B&B's TrachGuard and TrachStay comfortably secure the ventilator circuit to the tracheostomy tube while preventing accidental disconnects. B&B's patented Hope nebulizer technology provides efficient delivery of continuous medication combined with the ability to blend gases such as Heliox without affecting medication delivery. The Hope Nebulizer is the first nebulizer specifically cleared by FDA for Heliox administration.

#### **How do your products directly affect patient care?**

B&B's airway management product line offers a complete package for rapid access to stabilizing the airway. The "all-in-one package" solution provides the tools necessary for the clinician to rapidly secure the endotracheal tube and tracheostomy tube to the patient and ventilator circuit, saving time for patient assessment and care. The B&B products take into account the need for patient comfort with our selection of materials used to manufacture our products.

The B&B ET Tapes comply with the new AHA guidelines recommending the use of a commercial device for "securing the endotracheal tube for preventing accidental tube disconnects when compared with traditional methods of securing," ie, tape. B&B specialty products have been incorporated into many hospital based quality improvement processes to economically minimize the incidence of sentinel events in the ventilated patient.

The HOPE Nebulizer has become the gold standard for continuous medication and Heliox therapy in respiratory care. The patented supplemental gas delivery port for the delivery of specialty gasses, such as Heliox, in a closed dilution nebulizer greatly enhances the performance of the nebulizer providing a significant amount of medication in the respirable range for the moderate to severely compromised patient. The utility of Heliox has potential as supportive therapy, allowing time for other medications to take effect. The HOPE Nebulizer can achieve cost savings during continuous nebulization and provide a useful clinical adjunct for non-intubated patients.

#### **What sets your products apart from others in the field?**

The value of our products is in the economic design, manufacturing processes and time savings provided by a packaged product ready for use when the clinician needs it most. B&B products provide efficient solutions to allow the clinician the ability to provide patient focused care at the bedside, in the emergency department and by first responders in the field. Our convenient kits are both time and cost saving.

#### **Discuss your R&D process, including end-user input.**

The original founders as well as B&B's new team began in the bedside trenches and we believe the best ideas continue to come from our colleagues working day in and day out in the clinical arena. Taking the ideas and fine tuning them with B&B's engineering, production and clinical staff results in the quickest,



most economical way to get the solution to the problem. We call on both domestic and international resources to provide a steady stream of product ideas and recommendations for materials and technologies required to provide the highest quality and most cost effective products.

**What are your goals for R&D in the near future?**

From the onset of the company, B&B has always valued the clinical and engineering input from the end-user. B&B's first products were conceived from bedside experience in critical care units. The lack of useful tools for patient safety in maintaining a closed airway started the process for product development and still drives a division of the company. We continually work with clinicians and our clinical and engineering consulting team to provide feedback for us on the impact and ease of use of B&B products. We plan to increase communication throughout the health care community and we invite existing and new users to contact us with ideas for new products and suggestions for improving current ones. We have several new products in development that we expect to introduce in early 2007. Each one bears the stamp of end user input.

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

We believe that supporting the respiratory therapy schools is the key building block for smooth transition of new technologies into the clinical area. With the simplicity and ease of use of the B&B specialty airway management devices, we have found that multimedia tools, such as educational CDs and DVDs with tutorials provide a consistent method for training today's health care practitioners. These tutorials are developed with input from B&B's team of clinical consultants who provide the educational support tools needed by the clinician. On the CD, each B&B product is identified with a separate training module. Each module provides a visual display of the applicable training material along with an audio portion to allow the clinician to view the material at the clinicians' own speed. A basic competency program has been developed as an adjunct to the product CD with a focus on application of each product. As part of the B&B Value Add program, Policy and Procedure Protocols that focus on patient care are provided to the hospital clinical education department.

Clinical, technical and educational materials are available upon request and many of the support documents can be downloaded from the B&B Medical Technologies website at [www.bandb-medical.com](http://www.bandb-medical.com).

**Discuss the role of critical care providers in developing and upgrading your product.**

B&B was founded over 30 years ago by critical care clinicians interested in finding a solution to everyday problems that needed an easy to use tool. All of the current B&B products have imprints from clinicians worldwide that have allowed us to continue to manufacture cost effective and time efficient products for clinicians with the primary focus of patient comfort and safety.

**Talk about how you test and evaluate your product in actual day to day use.**

Long before a product is released into general distribution it will go through a series of end user practical tests and evaluations to ensure that it will safely and effectively meet its intended use

claim. This testing encompasses a wide variety of clinical settings from major teaching institutions to community based hospitals and clinics to first responders. After release, product performance is an ongoing process. This process includes technical performance assessment as well as operator errors, effectiveness of labeling and training materials. Corrective action plans, if required, are implemented as a standard course of business.

**What new technology do you see as having the greatest impact on your area of expertise?**

Necessity is the mother of invention and this applies to our area as well. The development of new materials to combat skin allergies, for instance, brought about new materials with characteristics that have allowed cheaper, smaller, higher quality components for fields such as our airway security and medication nebulization devices. The rising price of petroleum based materials has resulted in an entire new class of plastics that will soon result in a "green" solution to the current discarding and recycling problems of many medical consumable products.

**Discuss the international scope of your testing/marketing/development efforts.**

Thomas L. Friedman's book, "The World is Flat" stated that thanks to fiber optics and high speed digital networks the difference in communicating and doing business around the corner or around the world now amounts to about 630 milliseconds. This has greatly impacted how we are able to take advantage of worldwide resources and meet the growing demands of our customers. This includes intellectual and academic resources, unique and specific research, engineering, availability of materials, manufacturing, international testing, certification, distribution and an almost instantaneous link to and from our customers. The development, supply and distribution chains now go around the world the way they did around the neighborhood at the beginning of the previous century.

**Tell us how you utilize conferences, seminars and such to promote your product.**

Conferences, seminars and other off site gatherings without the pressure of the clinical schedule are unique venues for exchange of ideas with clinicians to focus on new products and new applications of current products. We have found that the time invested in gathering market research prepares B&B for assuring that our current and future products meet the needs of the users. These meetings allow us to also look at the post market assessment of our products, training tools and support and at our distribution channels to ensure quality customer care. We look forward to meeting you at the next congress.

## Versamed

Kevin Plihal

Kevin Plihal is VP of Marketing and Business Development for VersaMed

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

The iVent201 is a fully featured ICU grade ventilator that happens to be MRI compatible and transportable as well. It is the first product with such a rich feature set, that includes:

Static mechanics measurements, nebulization and the ability to monitor additional parameters like SpO<sub>2</sub> all in one small package.

**How does your product directly affect patient care?**

A typical patient with respiratory disease is subject to several ventilator related risks, especially during transport: Being removed from a ventilator, ventilation by ambu bag, transition to a time cycled pressure limited ventilator, then back to the bag and finally back to their volume or pressure control mode on their ventilator in their hospital room or ICU. Each of these transitions brings about instability in blood gases and airway mechanics. Each of these transitions involves loss of PEEP and the concomitant loss of recruitment that clinicians fight so hard to obtain. A hospital ventilator should be versatile enough to accompany the patient throughout his stay in a hospital, regardless of where this may take the patient. This is one way in which the iVent201 helps to improve patient care.

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

Ventilation is forever changing. Clinicians find new modes or modifications of modes that can be of assistance to patients. The best of the latest generation of ventilators are software driven and do not rely on knobs and buttons to set and control their modes. These ventilators can be updated when new software is loaded and therefore they are guaranteed to never become outdated. For example, typically, when a customer desires to add SpO<sub>2</sub> monitoring capability to the iVent201 ventilator, it is a matter of loading new software! All of the controls and displays are handled by software on the standard VGA display.

**What sets your product apart from others in the field?**

Our product is uniquely suited to serving all the needs of a ventilated patient in any hospital setting and during transport. We are the only fully transportable ICU ventilator to offer so many features in such a small wall gas independent package.

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

User input defines the goals of our product development process. Whether through focus groups, through user feedback and the feedback of our own clinical specialists and our sales people, all input is fed to the R&D group so that their efforts are targeted to features and enhancements that benefit the end user. We employ experienced clinicians and we rely on them throughout the product specification process. Our process is software intensive so a lot of our development process is based on sound (software) architectural planning and laying out ground rules for defining tasks and "entities" so that our object oriented approach remains flexible as the product ages.

**What are your goals for R&D in the near future?**

R&D is the soul that drives our company. We have learned that retaining the right people is key to our success in R&D so one goal is to make our company a dynamic and fun place to work. VersaMed plans to release a new product in 2007 and R&D is working intensively on this. Following on are additional products based on this new platform. We will be busy for the foreseeable future. In addition, the R&D group constantly works to enhance the performance and features of the current product line.

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

**product.**

Again, VersaMed is a thought leader in this part of the business. Our marketing group has created an interactive online clinical training program that is truly unique in the field. We also offer an interactive CD for training. Let us not forget though that we also offer the traditional on-site clinical training that is normal in this business. For customers seeking additional technical training, we also provide biomedical service training sessions here on our campus in Pearl River, NY.

**Discuss the role of critical care providers in developing and upgrading your product.**

VersaMed appreciates that it would have no market without close collaboration with critical care providers. VersaMed frequently attends scientific sessions to understand their needs, we establish relationships with researchers and contribute in funding their research to better understand the clinical issues. VersaMed relies on their candid feedback and does its best to incorporate their suggestions. In essence, all enhancements made in the VersaMed ventilator line have been implemented based on such advice and guidance.

**Talk about how you test and evaluate your product in actual day to day use.**

VersaMed manages an efficient and comprehensive QA system that ensures constant, day to day communication with the field. As there are thousands of VersaMed ventilators installed worldwide, there are countless interaction points between the end-user and VersaMed. VersaMed's customer support personnel is not only attuned to product performance feedback coming from the field but in fact initiates and encourages such feedback. This feedback is being fed to the R&D and QA groups and when required, enhancements and corrections are made.

There is a saying in the software development world – "The probability of detecting a bug decreases exponentially with time but never reaches zero." Similarly, in the product development world you have to be open to discovering unmatched expectations with your product's performance and be able to quickly address it with the help of your customers. VersaMed believes in this philosophy and does its best to implement it.

**What new technology do you see as having the greatest impact on your area of expertise?**

Fundamentally, everything that is driving the whole electronics industry is driving us as well. These technologies include multimedia compatibility and wireless technology. Of course technologies related to manufacturing and the ever continuing miniaturization of semiconductors has helped us to reduce the cost of manufacture. Advanced software and mechanical innovations also effect VersaMed's product development. A solid platform incorporating these technologies is what VersaMed strives to accomplish.

**Discuss the international scope of your testing/marketing/development efforts.**

VersaMed has an extensive international presence. We sell in over 90 countries around the world with sales and support offices in every continent. Our international scope gives us a very good perspective on the marketplace. The international regional offices work closely with elaborate networks of distributors and independent sales representatives in their respective regions. The feedback collected through this close interaction with the international user base, is funneled to the

R&D and QA groups who, in conjunction with Marketing, work to implement the necessary product enhancements.

**Tell us how you utilize conferences, seminars and such to promote your product.**

VersaMed exhibits in numerous trade shows both domestically and internationally. These conferences are a main venue for meeting both current and prospective customers and for promotion of current and new products. Those who drive marketing and business development decisions in our company are attending scientific sessions that we think may be "leading edge" in order that we may be better informed in our product development process.

## INTERNATIONAL Q&A

# nnd Medical Technologies

Todd Austin

Todd Austin is VP Sales and Marketing, nnd Medical Technologies.

**Are there publications that support and/or endorse your claim?**

Yes, there are numerous publications, peer reviewed articles and abstracts that independently investigated nnd's ultrasound sensor technology and concluded the sensor to be calibration free. Below are just a couple of references.

1 Buist, AS, Crapo, RO, Jensen, RJ, Burney, PG. The Burden of Obstructive Lung Disease Initiative (BOLD): Rationale and Design. COPD: Journal of Chronic Obstructive Pulmonary Disease, June 2005; 2:227-283

"To optimize quality control in the BOLD Study, sites are required to use the nnd EasyOne Spirometer, which was chosen because it provides a high degree of accuracy and requires no calibration with a 3-liter syringe."

2 Julia A. E. Walters, Richard Wood-Baker, Justin Walls, David P. Johns, Cardio-Respiratory Research Group, School of Medicine, University of Tasmania, Hobart 7001, Stability of the EasyOne Ultrasonic Spirometer for use in General Practice. *Respirology* 2006; 11: 306-310.

"These results provide strong evidence that the EasyOne spirometer is accurate and maintains its accuracy during routine clinical use for at least 26 weeks. This has practical implications in general practice, as it implies that this spirometer does not require a daily calibration check as recommended by the ATS/ERS."

**Is nnd's ultrasound technology used for other lung functions test besides spirometry?**

Yes, the ultrasonic flow sensor provides not only calibration-free flow measurements, but the sensor can also detect concentrations of gasses in the exhaled breath. We call this measurement UPG (ultrasound pneumography). Briefly described, nnd's ultrasound sensor measures the transit time differences between upstream and downstream ultrasound

pulses, the bigger the differences in transit times, the higher the velocity of flow. The speed of sound in a gas is dependent upon the molar mass (molecular weight x concentration) of the gas mixture. The differences between inspired and expired air molar mass is largely due to carbon dioxide and in essence, the nnd flow sensor can produce volumetric 'capnography' exhaled profiles without an additional CO<sub>2</sub> sensor. This has been demonstrated in many abstracts and presentation at the ATS and ERS (Jensen R, Buess C, Crapo R, Goldman M, Gappa M, Fuchs S) and has promise to provide an effort-independent test that will diagnose airway obstruction in children and adults. Additionally, the ultrasonic molar mass measurement is used for traditional lung function measurements such as FRC (Gappa M, Buess C, Fuchs S) and DLCO (Buess C) further simplifying these measurement by replacing traditional side-stream analyzers with a single ultrasound sensor.

**Are there any European public health programs that use nnd products?**

Yes, in Switzerland, a country-wide Pharmacy based COPD Screening Program sponsored by the Swiss Society of Pharmacy, the Swiss Society of Pneumology, AstraZeneca, Boehringer Ingelheim, and Pfizer, screened over 38,000 people. In total, 80% of the spirometry tests met acceptability criteria. The screening identified 20% of the participants to have abnormal results, resulting in 7,000 physician referrals. Once again, the nnd EasyOne spirometer was chosen for this program because of its accuracy, robustness, and ease-of-use.

Also, the European Respiratory Society hosts a yearly Public COPD Screening in the Congresses host city town center. This year in Munich 1,800 people participated where they were provided COPD Screening and Smoking Cessation education. NDD has been the spirometer of choice for this event four year's running.

**What new products and technology will we see from nnd?**

We are in the final stages of development of our EasyOne Pro. The EasyOne Pro is a portable, maintenance free DLCO system that allows point-of-care, bedside and other ambulatory applications outside the confines of the traditional lung function laboratory. Using our ultrasound technology, we will introduce the first completely self-contained DLCO system packaged as a portable, touch screen, fully functional PC. Look for the EasyOne Pro to be introduced in Europe this year, followed by the US in 2007.

Our continued collaboration with key opinion leaders will provide many more endorsements and validations of our technology. Even now, we see major lung function companies adopting our original ultrasound technology replacing old style flow sensors, further confirming our leader position in the lung function market.

## More Benefits of NIV in Critically Ill Patients

Melissa Turner, BA, RRT

The use of noninvasive ventilation (NIV) certainly has its niche in the critical care arena. The venues in which NIV can be used are now expanding. Baillard et al did a study to find whether the use of NIV for preoxygenation during endotracheal intubation (ETI) held an advantage over the usual method of preoxygenation. Usual method of preoxygenation is defined as the use of a bag valve mask driven by 15 l/m oxygen to provide a  $FiO_2$  of 1.0 while allowing patients to breathe spontaneously with occasional assistance.<sup>1</sup> Complications associated with ETI are met more frequently in the ICU than in the controlled environment of scheduled surgery. "Approximately 10 to 30% of rapid sequence intubations are associated with transient oxyhemoglobin desaturation ( $SpO_2 < 90\%$ ). Moreover, profound oxyhemoglobin desaturation ( $SpO_2 < 70\%$ ) is encountered in 2% of such procedures and these desaturations have been shown to increase mortality in specific populations."<sup>1</sup> Is it possible that NIV used as a preoxygenation method during ETI could improve oxygenation?

Farmery and Roe showed that it only takes a critically ill post-op patient 23 seconds to desaturate below 85% during an apneic period in comparison to 502 seconds in a healthy adult.<sup>2</sup> From this information one can see the importance of effective preoxygenation preceding ETI. The usual method of preoxygenation was shown to be only "marginally effective in critically ill patients."<sup>3</sup> There is clearly enough evidence to show that there is a great need to optimize preoxygenation techniques prior to intubation in critically ill patients.

The study by Baillard et al showed that the NIV technique used for preoxygenation was superior to the usual method of preoxygenation in that it was safe and more effective. "NIV was more effective than the usual method in reducing the decrease in  $SpO_2$  and allowed enhancement of  $PaO_2$  up to 30 min after ETI."<sup>1</sup> In Baillard's study, NIV was engaged using pressure support with PEEP. No one in the NIV study group received a peak inspiratory pressure level, through the utilization of pressure support and PEEP, greater than 20 cm  $H_2O$ . It is assumed that

critically ill patients have full stomachs and positive pressure ventilation may increase gastric air content in these patients. Along with the increase in gastric air content is the risk of pulmonary aspiration. That risk is increased with positive pressure ventilation greater than 20 cm  $H_2O$  which is easily attainable via manual resuscitation with a bag valve mask. The risk can be minimized through the use of NIV by limiting the insufflation pressure at 20 cm  $H_2O$ . In addition to limiting the risk of pulmonary aspiration, NIV also helps with recruitment of collapsed alveoli which allows for an increase in oxygenation via the decrease in perfusion without ventilation. As stated previously, the  $PaO_2$  was enhanced up to 30 minutes after ETI in patients preoxygenated using NIV. Baillard et al states that this could be due to the "residual effect of NIV in recruiting alveoli and increasing lung volume before ETI."<sup>1</sup> Mort also concludes, "NIV improves oxygenation by delivering high oxygen concentration, by unloading respiratory muscle, by recruiting alveoli, and by increasing lung volumes."<sup>3</sup>

Presently, NIV has found its niche in the ICU. It is commonly used to avoid ETI as well as to facilitate weaning and extubation. Baillard et al has also shown its value in being used as a preoxygenation technique for ETI. Baillard also points out that since the need for ventilation equipment is already identified for hypoxemic patients, there should be no delay to limit the use of NIV as a preoxygenation technique. Furthermore, now that ventilators have an NIV option available, it makes it very easy to provide NIV and transition to invasive ventilation and back to NIV if necessary.

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# Tidal Volume Reduction in Patients with Acute Lung Injury When Plateau Pressures are Not High

Tim France, BS, RRT

There is evidence to support the use of volume and pressure limited ventilation in patients with ALI/ARDS. ARDSNET proved that mortality can be reduced by employing a low tidal volume and PEEP high enough to prevent lung derecruitment injury. Plateau pressures less than or equal to 30-35 have been cited as the “safe zone” to target when ventilating ALI/ARDS patients. The evidence according to this article suggested that any further reductions in plateau pressures were unnecessary and yielded few benefits. The thesis for this article was to review the evidence and find if there was a safe upper limit for plateau pressures and if there was any evidence to suggest that further reductions in plateau pressures would yield better patient outcomes. This review will only address the animal studies included in this article. The article itself goes on to review the ARDSNET data and other trials of lung protective strategies in an effort to answer the thesis question.

The investigators first reviewed animal data to see if there was any evidence there. Rats were ventilated at different pressures and examined to see the extent of lung damage that was created. All the intact rats ventilated for 60 minutes at pressures of 30 cm H<sub>2</sub>O developed lung damage. Three of six rats ventilated at pressures of 14 cmH<sub>2</sub>O developed lung damage. In isolated rat lungs, lung injury was seen at PIP of 13 cm H<sub>2</sub>O. Rats that had induced ALI, ventilating at a lower Pplat of 21 cm H<sub>2</sub>O demonstrated a 55% decrease in lung injury than rats ventilated at a Pplat of 30 cm H<sub>2</sub>O. Further reductions were noted when Pplat was reduced to 16 cm H<sub>2</sub>O. Another study examined the PIP change in rabbits with *Pseudomonas pneumonia* after being ventilated at 6 ml/kg and 15 ml/kg. After being ventilated for 8 hours the 6 ml/kg groups PIP increased from 17 to 21 cm H<sub>2</sub>O and the 15 ml/kg groups increased from 22 to 35 cm H<sub>2</sub>O. Lung damage was 30% lower in animals that received the lower VT and lower PIP.

In dogs ventilated for 20 to 30 minutes, lung damage was not seen unless the ventilating pressures exceeded 42 cm H<sub>2</sub>O. In

dogs with open chests, lung damage did not occur until after 30 minutes of mechanical ventilation at pressures of 64 cm H<sub>2</sub>O, but not at a lower pressure of 22 cm H<sub>2</sub>O. In lambs lung damage did not occur until after four hours of ventilating at PIP of 61 cm H<sub>2</sub>O. This was after being ventilated for four hours at pressures of 33 and then 43 cm H<sub>2</sub>O.

In summary, there is evidence to support the strategy of keeping Pplat below 35 cmH<sub>2</sub>O. In some animal studies lung damage does not occur until after the lungs have been subjected to PIP above 40-60 cm H<sub>2</sub>O. However, because of the reduction in lung damage noted in the animal studies there may be evidence to support further reductions, if possible in plateau pressures below 30-35.

## EDITORIAL NOTE

There is evidence to suggest that lowering VTs to achieve minimal plateaus can actually cause derecruitment and decreased oxygenation. In practice most clinicians strive to reduce Pplat as low as possible without causing increased work of breathing (WOB) for patients because of either low volume delivered to the patient in volume controlled modes or low flow availability in pressure controlled modes. Decreasing Pplat to very low levels should accompany an assessment of WOB to insure patients are not struggling to breath or being subjected to atelectasis caused by low VT being delivered.

Reference: Hager DN, Krishman JA, Hayden DL, Brower RG. Tidal Volume Reduction in patients with Acute Lung Injury When Plateau Pressures Are Not High. *Am J Respir Crit Care Med* Vol 172 pp 1241-1245, 2005.

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# Noninvasive Ventilation Use During Palliative Care

Tim France, BS, RRT

An issue that has come up with increasing frequency is the use of life support during palliative or comfort care. Palliative treatment to relieve dyspnea for patients dying from terminal diseases has mostly been achieved with the use of narcotics or anxiolytics.<sup>3</sup> The problem with the use of drugs is the negative side effects that accompany their use. Side effects include respiratory depression and decreased level of consciousness. Non-Invasive ventilation (NIV) has been increasingly employed since the 1980's. NIV with positive pressure replaced the iron lungs (NIV negative pressure) which were used during the polio epidemics.<sup>1</sup> Today NIV is mainly used for chronic or acute lung impairments such as Amyotrophic Lateral Sclerosis (ALS) or Chronic Obstructive Pulmonary Disease (COPD). NIV has enabled ALS and COPD patients the ability to live longer and also improve their quality of life.

NIV use in acute lung Injury/ARDS is highly controversial and recent studies have shown negative outcomes in this patient population, especially if NIV failure leads to delays in intubation. Noninvasive ventilation has been increasingly used as a treatment for dyspnea in the terminally ill. A controversial issue evolves, because though NIV can relieve dyspnea, it may concurrently prolong life. Palliative care is an issue that most hospitals deal with on a regular basis. And as the population ages it will become an even greater issue. Caregivers are asking themselves, "What is the role of NIV in end of life issues"? There are clear guidelines for the use of NIV.<sup>4</sup> Patients must be able to breathe on their own and they must be able to take the mask off if needed. Reasons for this are if a patient stops breathing, NIV becomes an unsafe mode of ventilation and if the mask is not able to be removed, a patient could vomit in the mask and aspiration and/or asphyxia could occur. During palliative care or comfort measures several questions need to be asked. First, does the patient want this intervention; second does the patient meet criteria for its use and third is it appropriate for the situation. If a patient is awake, alert and oriented then their

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wishes must be met. So if they want the intervention then we are required to use the technology.<sup>3</sup> There may a situation where an end stage COPD patient may need a few extra days to clean up end of life issues. This is a patient that is cognitively intact and can still make his or her own decisions. The gray area is the patient who has hours to live, but the family or physician wants to use the technology to relieve the patient's dyspnea. There may be family coming from out of town or even out of the country, but normally when the decision has been made to end the suffering, we should let the dying process proceed naturally. The problem with using NIV is that it can actually prolong the dying process. There has been the situation where families keep their grandmother on NIV for days before they would make the decision to let her go. Another situation is the end-stage COPD patient who has been on NIV for years with a low quality of life.

With the advent of sophisticated ventilation equipment we have been able to treat a variety of pulmonary illnesses. In the past most patients would have died an early death and some cases an appropriate death. However, there are times when ventilation technology actually prolongs the dying process. In a society where resources, be it human or financial, are becoming scarce, prolonging the inevitable can put a huge burden on everyone.

## ADDITIONAL COMMENTARY

The August 2006 RT – The Journal for Respiratory Care Practitioners, pages 38-45 features a point/counter point article on the use of NIV in palliative care, do not intubate/do not resuscitate situations. The article is available on-line at <http://www.rtmagazine.com/toc.php>. The contrast in the two positions taken is very thought provoking, but my empirical experience with NIV in these patients is more in line with the "Con" author's experience. I believe most RT's would agree that the reality is that patient's end up placed on general floors on NIV which is sustaining life. More often than not the patient is increasingly uncomfortable is at risk of acute decompensation as typically there is no one able to closely monitor NIV therapy on the 'floors'. These patients are often 'triaged' out of the ICU. I would also note, as pointed out in the RT magazine article, there is good evidence to support the use of NIV in patients with terminal immunocompromised disease. I believe the issue of NIV in 'palliative' care is separate from use of NIV in terminal diseases where application of NIV is intended to treat a revisable complication such as an acute pneumonia. (eg, if I had cancer and had 6 months to a year to live and develop an acute pneumonia that is not part of the natural terminal progression my cancer, I would not consider this to be "prolonging" my life.)

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# The Continuing Development of Neonatal and Pediatric Ventilation Therapies

The very first pediatric intensive care unit in Germany was established at the Children's Hospital of The Johannes Gutenberg University in Mainz in 1965. Ever since that milestone, the center has been involved in great advances in neonatal and pediatric research and patient treatments, which has led to rapid expansion and the establishment of the current interdisciplinary pediatric intensive care facilities. The institution recently celebrated its 40<sup>th</sup> anniversary by means of a two-day symposium with international experts. Critical Care News met with some of the staff members of this remarkable ICU, including Ralf G. Huth, Director of Pediatric Intensive Care.

**Can you tell us about your 40th anniversary celebrations?**

**Ralf Huth:** The background story is quite simple: in 1965, the Director of Pediatrics had a job offer at the University Hospital in Frankfurt, and in the negotiating period, he established an emergency department here. This building was only intended as a provisional solution for five to ten years, but it grew and became well established over the years. This was the first pediatric intensive care unit in Germany, and the fifth in Europe. Our recent anniversary symposium was not only a celebration, but also an overview of what pediatric intensive care is all about, from disease and therapeutic perspectives. We reviewed not only disease situations but also the therapy options we have today, compared to the past and with a view to the future.

**What has been your experience of ventilation therapy, in regard to past history as well as your future requirements?**

If we review our own experiences in mechanical ventilation, we always used as a standard ventilator the old SERVO 900 device. But the problems with weaning meant that ventilation with infants was not that easy with this device. We were looking for another device. At that time there were only the old Draeger Babylog devices available. We then tested other ventilators;

such as the Infant Star, the Engström ventilator and the Sechrist. We decided to go with the Infant Star, which in those days had the combination of flow-interrupted neonatal ventilation with the possibility of High Frequency Oscillation (High Frequency Flow Interruption HFFI). We had four devices aboard for neonates, and for older children we had Servo Ventilator 900 C.

This worked well in the early days. But when we moved to this new facility, we needed to redesign and that was the time that the Servo 900 C was getting older, and the Servo Ventilator 300 came on the market, so we would have a combination of treating even neonatal patients with the Servo Ventilator 300. The issue of weaning was important, especially when we started with pediatric cardiac surgery here in 1985. At that time it was necessary in controlled ventilation to start up with the Servo 900 C, and when it was time for spontaneous ventilation we would switch to a neonatal ventilator. The subject was almost solved with the Servo Ventilator 300 as a very good device covering a large range of patients.

Non-invasive ventilation was not regularly in use at that time. We were the first center in Germany to try out HFO with the Sensormedics 3100A. Oscillation came from neonates, as well as high frequency jet ventilation. It was transferred to Europe, and increasingly used in neonatal and pediatric ventilation, but never connected with the adult patient population. As there was some interest in our anesthesia department, I tried to show the benefits of oscillating flow. At that time, we had a sophisticated system that provided nitric oxide in combination with HFO. In the adult departments, we came to help out with our equipment for the especially difficult cases, like the ARDS patients. I had an opportunity to take part in one of the first scientific and education symposia on HFO, and convinced some of my colleagues in the adult department to come with me. In a workshop with lung lavage model in a big pig, HFO was initiated and you could see improvement and we almost understood how HFO could work. Normally technology comes from the adult sector to the pediatric, but in this case it was the other way around.

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Dr. Ralf G. Huth, Director of Pediatric Intensive Care.

After this experience, we were then focusing on the neonatal and pediatric noninvasive ventilatory care. We found one device that was ready to do this at that time, the Hamilton Gallileo that offered noninvasive ventilation and also automated ventilation or adaptive support ventilation (ASV) for bigger children, for weaning after operations for instance. A little later, we started looking at SERVO-i since this device offers the possibility of noninvasive therapy in addition to controlled ventilation, even in the neonatal age group. Different ventilation

treatments for all age groups combined in one device was the goal. Currently we have a problem with too many models for different therapies. We need to define how to reduce to fewer devices, but providing the same treatment performance.

**How large are the children's intensive care units, and how many staff members do you have to run them?**

We have up to 150 patients in the pediatric department, including 10 pediatric ICU beds, 10 neonatal beds and up to eight intermediate care beds, all arranged on the same floor, in two wings. For nursing staff, we have 33 regular full time positions which means 44 people including part time staff. Many of our pediatric ICU nursing staff have longstanding experience. We have very high standards in terms of professional intensive care nursing education. Over 90% have not only pediatric specialty, but also pediatric ICU nursing certifications. So this is a very special background, which contributes to a true team effort together with the physicians.

In regard to the number of physicians here, we share the facilities between neonatology and pediatric intensive care, and all together we have 18 fulltime physicians, including consultants. Some of the consultants working in cardiology and neonatology also have duty during the night shifts here, which comprises a total of 22 people. We have a focus on pediatric intensive care, especially the surgical cases, and a focus in neonatology on the perinatal problems. Our patient occupancy

is roughly 90% with a changing turnover of nearly 500 a year.

**What types of patients do you most frequently encounter?**

Dr Jan-Helge Höpner, pediatric intensive care physician: Our main focus is on pediatric post-cardiac surgery, or post-neurosurgery. We do have general surgical cases, and everything that comes

otherwise: infections, oncology patient with ALI or ARDS, trauma patients (fortunately decreasing rates over the past years), orthopedic surgery, urological surgery, oro-facial deformities, and other birth defects. We have a separate burn unit for two patients.

**How long have you been doing nasal CPAP therapy here?**

Ralf Huth: Since the introduction of this therapy, Nasal CPAP therapy had a big impact on controlled ventilation with all the complications. We were among the first to introduce transcutaneous CO<sub>2</sub> measurements and transcutaneous O<sub>2</sub> measurements. Being early involved with nasal CPAP therapy, we then gathered additional information by noninvasive monitoring to know when to reduce invasive ventilation therapy and change to noninvasive ventilation. Previously, we were flying blind. I can remember in the past how we did blood gas analysis. I started at bed number one, finished at bed number ten and went back to bed number one again. What has changed from that time is the add-on information from noninvasive monitoring; like saturation monitoring and CO<sub>2</sub> monitoring. This gives us a sense of security when it's possible to reduce invasive ventilation therapy and go over to noninvasive support.

**Based on your experiences, when is nasal CPAP therapy best indicated? Which types of patients and which types of situations?**

I think the question is rather when do you indicate invasive ventilation? Ventilatory support is something that is needed if you have an additional oxygen requirement, if you have exertion and exhaustion. In the early years, we would say, "this child needs ventilatory support," which automatically implied invasive ventilation. We were not secure about interfaces: masks, nasal prongs and the like. Gradually we got experience and saw that it could work. By introducing PEEP and opening the lung, we could also give these children support that was feasible by noninvasive measures, with less oxygen requirement, fewer ventilatory problems, and less exertion.

**So is noninvasive ventilation therapy generally always preferred over invasive therapy?**

Yes, generally, we go for noninvasive when we can, and if this doesn't work, we apply invasive therapy. In some cases, such as post-op patients, they are intubated anyway and need invasive therapy to start out with. But in other cases we want to avoid invasive ventilation when possible; for example, oncology patients, patients with chronic respiratory problems needing support due to oxygen requirement and CO<sub>2</sub> retention.

**In light of some of your experiences with nasal CPAP, is there an advantage of being able to provide nasal CPAP and invasive ventilation therapy with the same equipment?**

Yes – right now we have too many devices, and the storage rooms are too small. Offering combined therapies with the same ventilator is an advantage.

Susanne Frey, pediatric intensive care nurse: When there is a new patient coming, we have to decide which ventilator to use. If you have too many devices, you almost have to decide before you see the patient, which is difficult because we need to know if they will need noninvasive or invasive ventilation. If you have too many machines, it is difficult and time-consuming. Now we see the chance of choosing one device and doing pretty much everything with it. In Mainz we are looking for everything in one unit, from the newborns to the ninety kilo children, for the







Susanne Frey, pediatric intensive enteral nutrition and pneumonia care nurse.

noninvasive and the invasive support.

**Dr Höpner:** It's an advantage to have a unit mounted behind the bed, with the interface at the head of the bed. You can start with noninvasive and go to invasive if needed, or scale down from invasive to noninvasive without having to move the whole unit.

**How many different ventilators have you had in inventory, and as a nurse what are the**

**challenges in training on these different devices?**

**Susanne Frey:** Plenty of models: the Infant Star, the Servo Ventilator 300, the Hamilton Galileo Gold, the SensorMedics 3100 A and B with HFO, the Breas transport ventilator LTV 1000 and a CPAP device Vital Flow. This is a problem because if you get new staff members you have to teach them all different devices. Each model functions a little different, in terms of modes, and user interface. It is a challenge for the nursing staff. And each device model has special tubing, which requires training and logistical management as well.

**Dr Höpner:** It is also a challenge for the doctors. We need to decide which therapies the nurses should monitor. The other thing is that we physicians have to rotate between the different wards as well, which means that it is easier if there is some standardization – not only within the unit, but in our neighboring units too.

**Ralf Huth:** The difference between the devices is a problem, which we are trying to overcome by finding one device that suits all. There are not only the technical aspects, but also how the user interfaces for these devices are designed for easy understanding and operating.

**What are your experiences of combined invasive ventilation and nasal CPAP in the same ventilator? Can you share some of your patient experiences?**

**Susanne Frey:** We have treated neonatal patients with ALI or respiratory distress using nasal CPAP and we have treated pediatric patients with muscular disease. We have treated post-



PICU nurse Connie Zander and volunteer Frau Diehl, with a 5-month-old heart failure patient, treated with nasal CPAP therapy.

op surgical patients with atelectasis, which have started out on invasive ventilation, before we have switched them over to nasal CPAP, as well as oncology patients with pneumonia. Different types of noninvasive therapy have been provided depending on the situation. For instance, in some cases we only needed CPAP to maintain PEEP. In another situation, we needed pressure support too. There

is much that can be done with noninvasive therapies, and we have different patient interfaces available: nasal prongs, nasal masks and full-face masks.

**What are the most important practical aspects for nasal CPAP therapy? Is it early application, fixation, or the fitting of the patient interface?**

**Susanne Frey:** The system should be easy to use. The patient interface should fit the patient comfortably but avoid leakage as much as possible. We used a helmet in one girl with chronic myeloid leukemia, who in the course of chemotherapy had leucopenia and ALI/ARDS due to pneumonia with PEEP up to 15cm/ H<sub>2</sub>O. Initially she had an oxygen requirement of up to 100%, recovering under NIV. Oxygen was reduced to 30%. The noninvasive therapy with the helmet worked quite well in the acute situation.

**Do you have a preference for the types of patient interfaces you are using with nasal CPAP?**

**Connie Zander, pediatric intensive care nurse:** For the small patients (up to 5-6 kg), we use the prongs, which work very well in combination with the pacifier, which manages leakage nicely. For the larger children (bigger than 6 kg), we prefer to use a nasal mask, and in some cases a full-face mask is needed, depending upon the individual facial morphology. Or in cases where they are not fully awake and can keep their mouths closed, we use a full-face mask. We have used the Fisher Paykel nasal CPAP interfaces, and they worked very well since you have different sizes to fit the actual patient, no problems with long or short nostrils.

**Susanne Frey:** We did have one tricky interface problem with a patient on the SERVO-i. She had been intubated for a very long period, and after extubation, we saw a big difference in the size of the nostrils. This was one specific case that was a little tricky to manage, but we did it.

**Ralf Huth:** It may not be a matter of which of the interfaces to use, but whether we have the right interface for this new kind of ventilatory support? I would say that a center might want to re-investigate which types of interfaces they are using, since this new combined device for invasive and noninvasive therapy probably gives you some new necessities and possibilities.

I think that we are not yet at the end of discussions on how the patient interfaces between ventilators and children are designed. But hopefully we will see continued interface development. Having a new ventilator on the market, providing different kinds of support, from invasive to noninvasive therapy and back again, may challenge development of interfaces with quality and ease of use, alarm management and patient comfort in terms of application for neonates and small children.

**Dr Höpner:** I think patient comfort is a very important issue



Dr Huth and Susanne Frey with a patient soon to be discharged. The baby was born a metabolic birth defect requiring enteral nutrition and pneumonia.

equal to the ease of use. If it is easy to start up a device, but you need to go back and readjust it every half hour because the patient is awake and moving, you have really gained nothing.

How long have you had the latest combined ventilator for invasive and nasal CPAP therapy?

Ralf Huth: For about six months, in the recent version which we have been evaluating. We have just decided to purchase these units, which we consider an investment into the future. In my point of view, the development of SERVO-i was a straight line in development from the Servo Ventilator 300. It offered the same type of ventilation opportunities, but it was not a re-introduction of ventilation concepts; rather you could see a natural continuation in development. It was significant to us that SERVO-i included the combination of PRVC with SIMV, so that you have the possibility of this mode, which was not available before. This was something we were really looking for. I think the user interface was straightforward, with the easy access knobs to the most interesting parameters. The calibration of the O<sub>2</sub> cell facilitated ease of use. So I think that the development was going in the right direction, and it was very easy to introduce this device after long experience with Servo Ventilator 300, compared to other devices we had been testing before. It was a logical continuation of development, which eased the acceptance of introducing SERVO-i into the ward, compared to other models.

We have one infant patient here who has been extubated after an operation, he was treated with SERVO-i for a long time. He has spinal muscular atrophy with pneumonia, which needed long time support. I think without the SERVO-i we would have had to switch to intubate him. But we were able to easily switch from nasal CPAP to noninvasive ventilation. So we were able to keep him totally on noninvasive support, which is unimaginable with any other device we have had so far.

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# Demystifying Methemoglobinemia: A Clinically Pervasive Disorder with Ambiguous Symptoms Masking Prevalence, Morbidity, and Mortality

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## SUMMARY

Dysfunctional hemoglobins are among the most confounding compromises to patient health and safety. Dyshemoglobins impede the ability to deliver oxygen to the tissues. Methemoglobin (MetHb) is a dyshemoglobin that normally exists in small concentrations in blood, accounting for less than 2% of the total available hemoglobin. Methemoglobinemia is defined as elevated levels of methemoglobin in the blood, is commonly induced (acquired) within virtually all acute care settings, presents with ambiguous symptomatology, and can be lethal at high levels. Because increases in MetHb often go undetected until dangerous levels are reached, the rapid diagnosis and treatment of methemoglobinemia have both quality and cost of care implications.

Patients presenting to the Emergency Department with equivocal flu-like symptoms should be evaluated for elevated MetHb levels as well as for carbon monoxide poisoning (carboxyhemoglobinemia, COHb). Nitrogen-based cardiac medications (eg nitroglycerin), Dapsone for immunosuppressed patients, and many common local anesthetic agents (eg benzocaine, prilocaine, lidocaine, EMLA creams for neonatal applications) are common MetHb inducing agents. Patients treated with inhaled nitric oxide (NO) are also candidates for continuous methemoglobin monitoring.

Published studies imply a relationship between elevated levels of MetHb and the onset of sepsis, suggesting that continuous measurement of MetHb may prove valuable in the ability to predict the onset of sepsis.

The conventional method for MetHb determination, blood CO-Oximetry, is invasive, noncontinuous, and is subject to significant delays in reporting. It is estimated that CO-Oximeters are available in only 50% of the hospitals in the United States. The advent, market clearance, and validation of Pulse CO-Oximeter technology permits instantaneous, noninvasive and continuous MetHb and COHb monitoring. Pulse CO-Oximetry is an advancement and extension of Masimo SET technology that measures arterial oxygen saturation through motion and low

perfusion. The focus of this paper is on acquired methemoglobinemia, and its clinical consequences.

## THE PHYSIOLOGY OF DYSHEMOGLOBINS

Methemoglobin (MetHb) is a dysfunctional form of hemoglobin that is incapable of transporting oxygen, thus reducing blood oxygenation and potentially inducing tissue hypoxemia. In healthy subjects, blood methemoglobin levels are low, typically < 2% of the total hemoglobin in the blood. When MetHb concentrations are increased (a condition called methemoglobinemia), there is less available functional hemoglobin to carry oxygen for systemic delivery. The 'functional anemia' induced by increased levels of methemoglobin is exacerbated by the fact that MetHb induces a leftward shift of the oxyhemoglobin dissociation curve. This leftward shift impedes the unloading of oxygen from the normal hemoglobin. Thus, methemoglobinemia has a dual impact on blood and tissue oxygenation. MetHb reduces the amount of oxygen that can be bound for delivery to the tissues, and at the tissue level, MetHb influences the behavior of the normal hemoglobin, forcing it to bind more tightly to oxygen, thus releasing less oxygen to the tissues.

## ACQUIRED METHEMOGLOBINEMIA

Exogenous agents can produce methemoglobinemia either by accelerating the production of methemoglobin or by inhibiting the protective enzymatic systems that normally maintain MetHb at low levels. The exogenous causes of methemoglobinemia, including commonly prescribed drugs, chemical fume inhalation, and clinical use of inhaled nitric oxide, are ubiquitous in the inpatient and outpatient settings. The Institute for Safe Medical Practice concluded in 2002 that "methemoglobinemia is unlikely to be a rare occurrence." Unfortunately, elevations in methemoglobin levels are often unrecognized until symptoms become extreme. Because the symptoms are ambiguous and similar to those associated with general disorders like cold, flu, and viral infections, proper diagnosis is often delayed. While treatment efficacy is high, failure to treat or treatment delays may cause significant morbidity and mortality.

Table I

Select Drugs documented to contribute to Methemoglobinemia	
Benzocaine, Cetacaine, Prilocaine (the 'caines')	Anesthetic – endotracheal intubation, transesophageal echocardiography, bronchoscopy, topical for hemorrhoids and dental/teething preps.
Celecoxib	Arthritic Pain
Dapsone	Prophylaxis for pneumocystis carinii in patients with human immunodeficiency virus (HIV). Also dermatologic applications.
EMLA Creams	Eutectic Mixture of Local Anesthetics.
Flutamide	Prostate Cancer
Nitrates	Food additives, well water, by-product of fertilizer run-off and incorporation into foods. Preservative.
Nitric Oxide	Pulmonary vasodilatation
Nitroglycerin	Cardiac vasodilatation
Sodium Nitroprusside	Intravenous Antihypertensive, Vasodilator
Sodium Nitrate	Preservative salt used in meat and fish
Sulfonamides	Broad spectrum antibiotics

## Drugs

From Table I, note that among the most common culprits contributing to generation of high levels of methemoglobin are local anesthetic agents such as benzocaine, lidocaine, prilocaine, etc., which are regularly used in “scoping” procedures such as endoscopy, laparoscopy, etc. In February 2006, the Veterans Health Administration issued an alert and a call to all VA facilities to discontinue the use of benzocaine on the perilaryngotracheal regions and other airway structures due to several cases of severe and/or fatal methemoglobinemia. The FDA announced an ongoing review of the risk shortly thereafter.<sup>1,2</sup> The popular EMLA cream, an epidermal anesthetic agent used primarily on children, contains 2.5% lidocaine and 2.5% prilocaine and has been linked to methemoglobinemia.<sup>3</sup> The antibiotic dapsone, used to treat Hansen’s Disease (leprosy) has been found to produce methemoglobinemia.<sup>4</sup>

## Nitrates, Nitrites, and Nitric Oxide

Nitrates and nitrites are powerful oxidizing agents that can cause methemoglobinemia. Ingestion of barbecued foods containing nitrites has caused patients to present to the emergency department with methemoglobinemia.<sup>5,6</sup> The fumes of carbon compound combustion (wood burning stoves, forest fires, etc.) contain variable levels of carbon monoxide, a hemoglobin poison. These fumes also produce nitric oxide (NO), which is a potent inducer of methemoglobin. When nitric oxide is inhaled, 85-90% goes to the direct formation of MetHb.<sup>7</sup>

Methemoglobinemia has been reported by several investigators as a result of ingesting nitrates in drinking water. A study of five residential regions in India with high nitrate levels in the water found that in the 178 people sampled, methemoglobin levels were significantly elevated, ranging from 7-27%.<sup>8</sup> A University of Iowa review of nitrate toxicity and methemoglobinemia in rural America suggested that nitrate levels are increasing in the US because of the use of nitrogenous fertilizers. Baby foods containing fennel, or prepared with rural well-water containing high nitrate levels associated with fertilizer run-off, have caused methemoglobinemia in infants.<sup>9</sup> Newborns (to 6 months of age) are particularly susceptible to foods and water with high nitrate levels because fetal hemoglobin is more readily oxidized to methemoglobin when contaminated well water is unwittingly mixed with infant formula.<sup>10</sup> A study of commercial baby food found that many have nitrate levels of greater than 45 ppm. The amount of nitrate in one four-ounce jar of beets contained the equivalent nitrate to 5.5 liters of water at 45 ppm raising concern for methemoglobinemia in infants.<sup>11</sup>

## Other Exogenous Sources of Acquired Methemoglobinemia

In the Emergency Department, methemoglobinemia has been linked to a wide array of substances, ranging from pesticides and insecticides, herbicides, automobile and boat engine exhaust fume inhalation, and inhalation of industrial chemicals such as nitrobenzene, nitroethane (commonly found in nail polish), common resins, and rubber adhesives. Dehydration is also associated with increased methemoglobin production. Infants suffering from diarrheal disease are particularly likely to become victims of methemoglobinemia associated with dehydration.<sup>12</sup>

## METHEMOGLOBIN AS A POTENTIAL PREDICTOR OF SEPSIS

Small but measurable MetHb increases have been shown to occur prior to the onset of sepsis or septic shock. Because relatively large amounts of nitric oxide (NO) are released into the blood in patients who are septic or are transitioning into a septic state, the conversion of NO to methemoglobin contributes to elevated MetHb levels.<sup>13</sup> During infection and other inflammatory processes, transient levels or “bursts” of NO occur within the patient. While the relationship is not completely understood, it is thought that the purpose of these rapid NO elevations is to destroy invading bacteria.<sup>14</sup> The body converts most blood-based nitric oxide into MetHb. While further investigation is needed to fully understand the relationship between methemoglobinemia and sepsis, continuous methemoglobin monitoring as a sepsis predictor may offer a significant opportunity to impact healthcare quality, cost, and total efficacy.

## THE JOHNS HOPKINS STUDY: ACQUIRED METHEMOGLOBINEMIA.<sup>15</sup>

In a major study by researchers at the Johns Hopkins University School of Medicine, a retrospective analysis was performed at two tertiary care hospitals and affiliated outpatient clinics over a period of 28 months. The Johns Hopkins study had several key findings. Patients characterized by elevated MetHb levels were found in every clinical department of the hospital system. Nearly 20% of all patients evaluated with traditional CO-Oximetry had elevated methemoglobin levels and 25% of the cases were accidentally found. Over 25 drugs that are frequently used in hospitals caused methemoglobinemia, including local anesthetics, nitroglycerin, EMLA cream for neonates, inhaled nitric oxide, and Dapsone. The study concluded that elevated MetHb in the sample population resulted in one death and three near deaths during the period of evaluation. When consideration is given to the fact that only 1.5% of all blood gas samples drawn in this study were subjected to CO-Oximetry analysis, the authors suggest that the actual number of patients afflicted with methemoglobinemia can be expected to be greater than captured by this retrospective analysis. If the ratio of CO-Oximetry evaluations to mortality outcomes due to methemoglobinemia in this study is applied to all US hospital admissions, up to 18,000 patients are potentially at risk annually for early mortality associated with untreated MetHb. Finally, the cost of traditional invasive testing for methemoglobin was \$25 for each evaluation. Despite the cost, the authors recommended measurement of MetHb each time blood was drawn for serial evaluations of MetHb during treatment.

The frequent occurrence of sources of acquired methemoglobinemia within the clinical setting is emphasized by the study. The use of the drug Dapsone (prescribed for

immunocompromised patients and for dermatologic disorders) was the primary source of acquired methemoglobinemia in this study, followed by surgery (anesthetic-related). "Unknown" was listed as the third most common cause of methemoglobinemia as the condition often went unrecognized and untreated. Pediatric dehydration and others (fume inhalation, sepsis, and sickle cell crisis) completed the list. In the same study, methemoglobinemia did not discriminate by gender or age, with the exception of a higher rate in diarrheic infants.

A critical finding of the study: *"Methemoglobinemia does not discriminate significantly throughout areas of hospital care, with the operating room, outpatient clinics, and the intensive care units receiving similar distributions."*<sup>15</sup> (See Table II, created from various literature citations.)

Table II

Diagnosis of Methemoglobinemia in the Hospital	
Hospital Department	Why is CO-Oximetry Ordered?
Intensive Care Units, including NICU	Evaluation of Cyanosis/Dyspnea, iNO Therapy
Inpatient Surgery	Evaluation of Cyanosis/Dyspnea
General Med/Surg Floors	Evaluation of Cyanosis/Dyspnea
Pediatric Medicine	Dehydration with Gastroenteritis, sepsis
Outpatient Dermatology	Dyspnea secondary to Dapsone treatment
Rheumatology	Dyspnea secondary to Dapsone treatment
Human Immunodeficiency Virus Clinics	Dyspnea secondary to Dapsone treatment
Anesthesiology (intra and post operatively)	To obtain immediate hemoglobin status updates and/or to evaluate cyanosis
Cardiology/Cardiac Catheterization Labs	Serial CO-Oximetry tests to calculate Fick cardiac output
Respiratory Care: PFT Lab, Pulmonary Stress Lab; Bronchoscopy	Dyspnea on exertion related to methemoglobin. Bronchoscopy: local anesthetics may induce MethHb
Imaging, including gastrointestinal procedures	Transesophageal echocardiography - patent foramen ovale/intracardiac shunt. GI imaging - local anesthetic
Neurology	Changes in mental status/headache
Emergency Room	Cyanosis/Dyspnea that does not resolve with 100% oxygen treatment. Suspected acquired/toxin-induced methemoglobinemia

## METHEMOGLOBINEMIA SYMPTOMATOLOGY

The signs and symptoms of methemoglobinemia are problematic because they are ambiguous and nonspecific. At levels of 20%-30%, symptoms include changes in mental status, headache, fatigue, exercise intolerance, dizziness, and syncope. Greater levels of methemoglobinemia are associated with dysrhythmias, seizures, and comas. (See Table III). Comorbidities such as sepsis, cardiac and lung disease, or the presence of other dyshemoglobins such as carboxyhemoglobin, will often cause significant symptoms to appear at lower levels of methemoglobinemia.<sup>15</sup> Gross inspection of blood samples taken from afflicted patients reveal blood that is thick and "chocolate brown" in color.

Table III

Clinical Levels of Methemoglobin and Associated Symptoms <sup>15</sup>		
Methemoglobin %	Symptoms	Notes
< 15%	Asymptomatic	Symptomatic with Anemia
20 - 30%	Cyanosis, headache, fatigue, mental status changes, syncope, dizziness, and exercise intolerance	Comorbidities: Anemia, cardiovascular disease, cardiopulmonary disease, sepsis, or the presence of other dyshemoglobins amplify the hypoxic impact of methemoglobinemia.
30 - 50%	Shortness of breath and headache	
50 - 70%	Lethargy, stupor, dysrhythmias, seizure, coma	
Over 70%	Death	

## TREATMENT

Mild methemoglobinemia symptoms can be adequately treated with supplemental oxygen therapy to maximize the oxygen carrying capacity of the remaining normal hemoglobin. Methylene blue is the most commonly prescribed treatment for moderate to severe methemoglobinemia.<sup>16</sup> Interestingly, methylene blue therapy has also been shown to induce methemoglobinemia. In addition, repeated methylene blue treatments may be indicated in some cases, as rebound methemoglobinemia has also been reported up to 12 hours post-methylene blue.<sup>17</sup> In extreme cases, a blood transfusion may be indicated to rapidly decrease MethHb levels that have escalated to near-fatal levels.

While serial methemoglobin measurements through CO-Oximetry can be used to monitor adequate response to treatment, continuous noninvasive monitoring may speed accurate diagnoses with faster therapeutic interventions when necessary.

## COST, CLINICAL YIELD AND LIMITATIONS OF CURRENT DIAGNOSTICS

The diagnostic dilemma is that the traditional detection of methemoglobinemia, CO-Oximetry, is costly and requires an invasive procedure - an arterial blood sample with subsequent laboratory analysis. In the Ash-Bernal study at Johns Hopkins, the authors state "if CO-Oximetry tests had been performed on every blood aliquot sent for arterial blood gas analysis during the 28-month study, the incurred cost at \$25.00 per test could have been approximately \$9 million."<sup>15</sup>

Obtaining an arterial blood gas evaluation requires a physician order. Therefore, the single methemoglobin spot-check value obtained from each ABG evaluation is rate-limited not only by the availability of CO-Oximetry devices, but also by the frequency of the physician order for serial blood gas evaluations. It has been estimated that less than 50% of US hospitals do not offer CO-Oximetry evaluations because they do not have immediate access to the device. When CO-Oximetry evaluations are indicated and ordered in hospitals with CO-Oximetry, delays average only about 10 minutes from the time the blood is sampled. Nonetheless, the test is ordered only a fraction of the time. In hospitals without CO-Oximetry samples are sent to laboratories outside the hospital for evaluation, with diagnostic delays averaging about 15 hours, providing a disincentive to order the test because of long delays.

Methemoglobinemia causes pulse oximetry technology devices to report different oxygen saturation than calculated by arterial blood gas measurement.<sup>18,19</sup> Elevated methemoglobin 'pushes' the SpO<sub>2</sub> value to 85%, and the relationship between SpO<sub>2</sub> and actual arterial oxygen saturation during methemoglobinemia is disproportionate. When elevated methemoglobin is present, the SpO<sub>2</sub> values reported by conventional pulse oximetry are suspect, and may significantly misrepresent the actual clinical status of the patient.

## NON-INVASIVE, CONTINUOUS PULSE CO-OXIMETRY

In 2005, Masimo Corporation (Irvine, CA) developed a new multi-wavelength Pulse CO-Oximetry technology called Rainbow SET, that continuously and non-invasively measures the percentage of hemoglobin saturated with oxygen (SpO<sub>2</sub>), as well as the percentage of

methemoglobin (SpMet), the percentage of carboxyhemoglobin (SpCO), Pulse Rate and Perfusion Index (PI), all through a single sensor typically placed on the finger. This allows clinicians to perform simple and inexpensive spot-checks and/or continuous monitoring with clinician-set alarms for detection of elevated MetHb and COHb levels. Clinicians can, with confidence, perform sound clinical protocols by actively monitoring MetHb during treatment and reacting appropriately before methemoglobin escalates to dangerous levels. Continuous monitoring also allows clinicians to monitor for sufficient periods to ensure that the inciting etiologic agent has been fully removed and effects have completely abated.

## CONCLUSION

Methemoglobinemia is a pervasive and significant clinical condition. Although treatable, its detection and proper diagnosis has been problematic due to:

- lack of awareness in the clinical community of its prevalence
- process limitations associated with the prescription of CO-Oximetry
- limited availability of current laboratory standard of measurement, invasive CO-Oximetry
- process limitations associated with spot testing, or MetHb “snapshots” derived from blood CO-Oximetry

The cost of misdiagnosis of this condition can be significant, with ramifications for almost all hospital departments and specialty areas.

Masimo Rainbow SET Pulse CO-Oximetry provides the validated ability to noninvasively and continuously measure methemoglobin and carboxyhemoglobin levels that have been clinically proven to impact the reported morbidity, treatment costs, and mortality of many hospital patients. Because Pulse CO-Oximetry provides immediate measures of the dyshemoglobins MetHb and COHb, without a blood sample, it has value in settings with and without on-site CO-Oximeters. The ability to noninvasively and continuously evaluate methemoglobin becomes a powerful diagnostic tool in the armamentarium of methods used to evaluate the pervasive nature of methemoglobinemia in the acute care setting. The potential to trend changes in a patient’s methemoglobin profile as an early marker for sepsis is an exciting possibility that warrants further investigation and clinical study.

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# Surge Capacity, Pandemic Ventilator Alternatives – Patient Safety in Selection

Dave Swift RRT, RRCP

The Federal, Provincial/state, and municipal governments have been encouraging Health Care institutions to prepare for a probable flu pandemic.<sup>1</sup> The projected statistics are a definite wakeup call, with 15-35% (35% being the expected total) of the population infected and 7.5% of the infected population requiring ventilatory support.<sup>2</sup>

The Ottawa Hospital (TOH) is a three campus, 1,200 bed tertiary and trauma center serving the nation's capital and eastern Ontario (Champlain Health District). In a "normal" week TOH would treat approximately fifty (50) patients requiring ventilatory support.

During a pandemic, the Ministry of Health and Long Term Care (MOHLTC) is estimating an additional 350 patients per week (representing 7.5% of flu patients) would require ventilatory assistance in the Ottawa region. The total is over and above the normal patients that require ventilatory support. It is estimated that 1.5-2% of all patients acquiring influenza will need hospitalization. It is further predicted that pandemic patients will use 74% of all ventilatory supported beds for up to 10 days.<sup>3</sup>

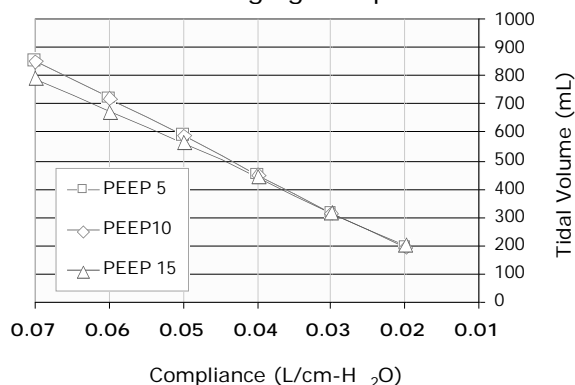
Surge Capacity has become a hot topic as these surges of flu related ventilated patients are expected in repeated 3-9 month waves.<sup>2,4</sup> Most hospitals do not have the ventilatory capacity to handle these surges and have turned to alternative sources of ventilation. It is expected that during a flu pandemic approximately 30% of clinical staff will be absent, so at any one time, skilled clinicians will be available in limited numbers.<sup>2,5</sup>

Historically, pressure-time cycled Bird Ventilators<sup>6</sup> (ex. Bird Mark 7, 9 & 10) were used successfully for decades to ventilate patients in emergency/mass casualty situations and in critical care settings. The role and success has been well documented. With the advent of volume ventilators the pressure-time cycled ventilators had a limited role. Today, pressure controlled ventilation has become an essential part of positive pressure ventilation options – advances in technology has allowed better controls and monitoring capabilities.

The VORTRAN Automatic Resuscitator (VAR) is a pneumatically powered, disposable ventilator that has become the emergency and disaster ventilatory support device for many institutions.<sup>7,8,9,10</sup> However, selecting the appropriate device in the emergency is critical for patient safety. Knowing the characteristics of the VAR is essential for safe and appropriate clinical implementation. The rapid changes in lung compliance and pulmonary resistance experienced during the evolving pathology of the flu are very similar to those experienced in the early stages of acute respiratory distress syndrome (ARDS).<sup>11,12,13</sup> Historically, ventilatory management utilized low rates and high tidal volumes (10 mL/kg body weight) but has now given way to higher rates and lower tidal volumes (5 mL/kg body weight) with the same minute volume. The higher rate with lower tidal volume is believed to decrease ventilator associated lung injury or volu-trauma.<sup>14,15</sup>

As the VAR is a "pressure cycled, continuous flow" unit, it is well suited to deliver small volumes at higher rates. The safety in using the device is knowing its performance characteristics in clinical applications and selecting the device for specific clinical situations.<sup>16</sup> It is essential that the clinician recognize that the

Figure 1 - TV Automatically Changes with Changing Compliance



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Figure 2 - Rate Automatically Changes with Changing Compliance

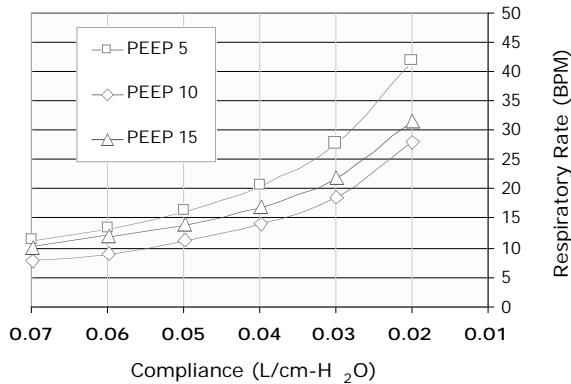
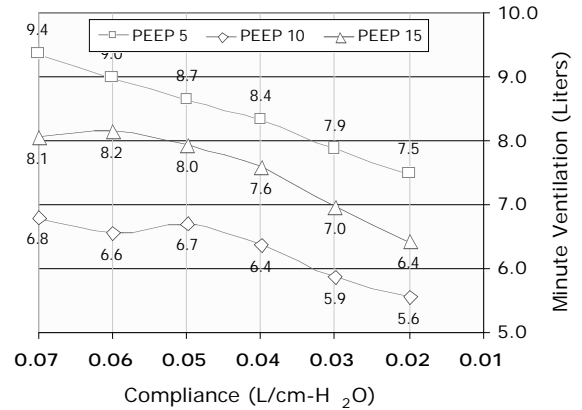


Figure 3 - Delivered Minute Ventilation (MV) with Changing Compliance



VAR is not a full feature ventilator but an automatic resuscitative device.

Knowing that the delivered tidal volume (Figure 1) and rate (Figure 2) will alter as lung compliance and pulmonary airway resistance changes is essential to selecting the appropriate ventilatory support. The VAR is able to maintain the desired minute volume (Figure 3) as the pulmonary mechanics change. The clinicians using the device must be aware of how to monitor the patients and to anticipate the changes in the performance characteristics in the dynamic clinical picture experienced with the flu. Understanding the effects on arterial blood gases allows the clinician to adjust the parameters to maintain stability in the dissolved gases and pH.

It is important to note that during a “flu surge” ventilatory resources will be taxed and that the “normal” number of ventilated patients will continue to happen. By selecting the appropriate ventilatory device (conventional ventilator vs VAR) the limited resources can be used to optimize the number of ventilated patients that can be cared for. A patient with a more stable respiratory clinical presentation would be more appropriate for use with the VAR. Patients with rapidly changing pulmonary compliance and resistance would be very labour intensive to manage using the VAR. By screening your patients and assessing the appropriate support device the limited resources can be maximized. However, in the end, when all of the resources have been utilized and a patient requires ventilatory support, the VAR offers a viable clinical alternative to manually bagging patients for a prolonged period of time if it were only a limited number of patients for a prolonged period of time. If it were only a limited number of patients it might be possible but with the numbers expected during the flu pandemic there will be a finite number of clinicians available to carry out this task. Utilizing one trained clinician to supervise a number of patients using the VAR may provide the only alternative to not offering any positive-pressure support.

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# Management of Neonatal Hyperbilirubinemia: Pediatricians' Practices and Educational Needs

Anna Petrova, Rajeev Mehta, Gillian Birchwood, Barbara Ostfeld, Thomas Hegyi

## ABSTRACT

**Background:** Early detection and treatment of neonatal hyperbilirubinemia is important in the prevention of bilirubin-induced encephalopathy. In this study, we evaluated the New Jersey pediatricians' practices and beliefs regarding the management of neonatal hyperbilirubinemia and their compliance with the recommendations made by the American Academy of Pediatrics (AAP) in 1994.

**Methods:** A survey questionnaire was mailed to a random sample of 800 pediatricians selected from a list of 1623 New Jersey Fellows of the AAP initially in October 2003 and then in February 2004 for the non-respondents. In addition to the physicians' demographic characteristics, the questionnaire addressed various aspects of neonatal hyperbilirubinemia management including the diagnosis, treatment, and follow up as well as the pediatricians' beliefs regarding the significance of risk factors in the development of severe hyperbilirubinemia.

**Results:** The adjusted response rate of 49.1% (n = 356) was calculated from the 725 eligible respondents. Overall, the practicing pediatricians reported high utilization (77.9%) of the cephalocaudal progression of jaundice and low utilization (16.1%) of transcutaneous bilirubinometry for the quantification of the severity of jaundice. Most of the respondents (87.4%) identified jaundice as an indicator for serum bilirubin (TSB) testing prior to the neonate's discharge from hospital, whereas post-discharge, only 57.7% felt that a TSB was indicated ( $P < 0.01$ ). If the neonate's

age was under 72 hours, less than one-third of the respondents reported initiation of phototherapy at TSB levels lower than the treatment parameters recommended by the AAP in 1994, whereas if the infant was more than 72 hours old, almost 60% were initiating phototherapy at TSB lower than the 1994 AAP guidelines. Most respondents did not regard neonatal jaundice noted after discharge and gestational ages 37-38 weeks as being significant in the development of severe hyperbilirubinemia. However, the majority did recognize the importance of jaundice presenting within the first 24 hours and Rh/ABO incompatibility.

**Conclusion:** The pediatricians' practices regarding the low utilization of laboratory diagnosis for the quantification of jaundice after discharge and underestimation of risk factors that contribute to the development of severe hyperbilirubinemia are associated with initiation of phototherapy at lower than AAP recommended treatment parameters and recognition of neonatal hyperbilirubinemia as an important public health concern.

## BACKGROUND

Management of hyperbilirubinemia remains a challenge for neonatal medicine because of the risk for serious neurological complications related to the toxicity of bilirubin.<sup>1</sup> The neonatal hyperbilirubinemia practice guidelines published in 2004 by the American Academy of Pediatrics (AAP) expresses the pediatric community's concern regarding bilirubin-induced neurological pathology.<sup>2</sup>

The prevention of bilirubin encephalopathy is based on the detection of infants at risk for developing significant hyperbilirubinemia and the early treatment of this condition.<sup>3</sup> Newman and Maisels<sup>4</sup> have questioned the compliance with the existing guidelines in the neonatal hyperbilirubinemia cases associated with an adverse outcome. Therefore, understanding the pediatricians' practices and beliefs towards the management of neonatal hyperbilirubinemia is of particular importance. A survey conducted more than ten years ago showed wide variation in neonatal hyperbilirubinemia management practices among the pediatricians and neonatologists.<sup>5</sup> Approximately 66% of the pediatricians reported an awareness of the neonatal

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hyperbilirubinemia clinical practice guidelines published in 1994.<sup>6</sup> Atkinson et al<sup>7</sup> showed that only 54% of the pediatricians initiated treatment in accord with the recommended parameters.<sup>7</sup> However, none of the previous studies investigated the pediatricians' preferences regarding management of hyperbilirubinemia in term infants before and after hospital discharge. Moreover, no study has clearly assessed the pediatricians' beliefs regarding the risk factors for severe neonatal hyperbilirubinemia.

In the present survey study we evaluated the New Jersey pediatricians' practices and beliefs regarding management of neonatal hyperbilirubinemia and their compliance with the 1994 AAP recommendations.

## METHODS

We designed a mailing survey study. The survey questionnaire was mailed to a random sample of 800 pediatricians selected from a list of 1,623 New Jersey Fellows of the AAP. The list obtained from the AAP did not specify the physicians' area of practice. The questionnaire was mailed twice to the pediatricians, initially in 2003 (October 27-29) and then in 2004 (February 24-28) for the non-respondents. A letter that assured the participants of the voluntary nature of the study, complete anonymity, and confidentiality of data accompanied the questionnaire.

All respondents were classified as those: (i) who completed more than 80% of questions; (ii) who completed 50% to 80% of questions; (iii) who did not return survey; and (iv) others (questionnaire returned by postal services for the non-availability of a forwarding address). The categories that were not eligible for inclusion in the analysis included: residents in training; retired pediatricians; pediatricians who did not provide services for newborn infants; and pediatricians who answered less than 50% of the questions. The technique of the Council of American Survey Research Organization (CASRO) was used to classify the survey respondents and calculate the response rate.<sup>8</sup>

### Study Instrument

We designed a two-page (four-sided) survey questionnaire that included 25 questions. The questions addressed various aspects of neonatal hyperbilirubinemia management such as pre-discharge bilirubin testing and follow up of infants who were jaundiced at discharge, the diagnostic and treatment approaches used for the management of neonatal hyperbilirubinemia, and the public health significance of these conditions. The physicians were also asked about their practice type, the population area covered by their service, years in practice since completing residency, annualized number of neonates seen in their practice, and experience with cases of kernicterus. All questions were designed using a yes/no and either single or multiple-choice format. A scale type format (hardly at all, to a small degree, to a moderate degree, to a very high degree, and not applicable) was used to assess the pediatrician's beliefs regarding the risk factors for severe hyperbilirubinemia. We assessed the following risk factors: jaundice presenting in first 24 hours, jaundice noted at discharge, previous siblings with jaundice, gestational age between 37 and 38 weeks, breast feeding, bruising/cephalohematoma, Rh and ABO incapability, and glucose-6-phosphate dehydrogenase (G-6-PD) deficiency.

We asked the pediatricians questions regarding the hour-specific TSB (at 25-48 hours, 49-72 hours and >72 hours) that they used for the initiation of phototherapy and/or exchange transfusion, and the TSB they considered as high risk for the development of kernicterus in term neonates. We also asked about diagnostic

approaches (transcutaneous bilirubinometry, cephalocaudal progression), and pre- and post-discharge neonatal hyperbilirubinemia management. Additionally, we sought their opinion on whether severe hyperbilirubinemia and kernicterus should be considered a public health concern and made reportable conditions in New Jersey.

The questionnaire was pre-tested among seven pediatricians from the university hospital and private practice setting in order to reduce redundancy and increase the clarity of the questions. The Institutional Review Board of the UMDNJ-Robert Wood Johnson Medical School approved the study.

### Statistical analysis

The statistical analysis was performed using STATISTICA 6.0 for Windows (StatSoft, Inc., Tulsa, OK) to identify the significance of the observed differences in proportion (Chi-square test) and the continuous variables (analysis of variance). We reported results for the overall sample and for groups that were determined by the type of pediatric practice (university hospital, community hospital, private group, and private solo). Age-specific total serum bilirubin (TSB) levels published by the AAP in 1994 for the initiation of phototherapy and/or exchange transfusion were used for assessment of the pediatricians' preference in the treatment of neonatal jaundice.<sup>9</sup> Significant differences were accepted if the P value was less than 0.05 (2-tailed).

## RESULTS

### Response rate and demographic characteristic of the respondents

Among the 431 returned questionnaires, 24 were received incomplete from retired pediatricians, 13 from pediatricians in residency training, and 17 from pediatricians who did not provide neonatal services. Twenty-one questionnaires were returned because of lack of a forwarding address. The rest of the respondents (n=356) completed more than 84% of the survey questions and were included in the analysis. The adjusted response rate of 49.1% was calculated by dividing the number of completed survey questionnaires (n=356) by the 725 eligible responders [800-(24+13+17+21)].

The majority of the respondents (90.7%, n=323/356) were board certified. The demographic and practice characteristics of pediatricians by the type of practice are presented in Table 1. Most of the respondents practiced in private groups and provided services for children from the suburban area of New Jersey. University and community hospital-based practices that most often provided pediatric services for children from urban and rural areas involved only 19.9% of the respondents. Private pediatricians in solo practice were older, had been in practice much longer and provided services for a lesser annual number of neonates.

### Pediatricians' practice preference for neonatal hyperbilirubinemia management

Overall, a higher proportion of pediatricians checked TSB levels in jaundiced neonates prior to their discharge from the hospital as compared to jaundiced neonates noticed at the infant's post-discharge visit (87.4% vs. 57.7, P<0.01). Table 2 indicates that pediatricians from the university hospitals showed lower TSB testing activity prior to the jaundiced neonate's discharge from the hospital as compared to pediatricians in private practice. In cases where the mother called for advice regarding the baby's jaundice, the majority of pediatricians asked the mother to bring the infant to

Table 1. Demographic and other characteristics of the pediatricians by the type of practice

Characteristics	Type of Practice					
	Total* (n=356)	University Hospital (n=29)	Community Hospital (n=42)	Private Group (n=219)	Private Solo (n=66)	P** value
Male	175(49.2%)	18(62.1%)	16(38.1%)	105(47.9%)	36(55.4%)	.108
Age (years) †	45.3±11.5	39.9±12.8	43.3±10.9	45.4±10.8	49.8±12.7	.01
Years after residency*	14.3±1.4	11.3±9.8	12.1±10.1	14.6±9.3	16.5±9.8	.05
Neonates per year††	150	245	300	170	60	.01
Practice area***						
Suburban	302(84.5%)	20(69.0%)	24(57.1%)	203(92.7%)	55(83.3%)	.01
Urban	110(30.9%)	19(65.5%)	27(64.3%)	44(20.1%)	20(30.3%)	.01
Rural	56(15.7%)	5(17.2%)	11(26.2%)	33 (15.1%)	7(10.6%)	.07

\* Total number of respondents (University and Community Hospitals, Private Groups and Solo)

\*\* P-values represent Chi-square test (for proportion) and analysis of variance (for continuous variables)

\*\*\* Check all that apply

† Mean age ± Standard Deviation (years)

†† Median

Table 2. Pediatricians' preferences regarding the management of neonatal jaundice

	Practice Type					
	Total*	University Hospital	Community Hospital	Private Group	Private Solo	P** value
TSB testing with clinical jaundice before discharge	306/350 (87.4%)	16/24 (66.7%)	39/42 (92.9%)	195/218 (89.5%)	55/64 (85.9%)	0.012
TSB testing with clinical jaundice post-discharge	196/340 (57.7%)	12/24 (50.0%)	28/37 (75.7%)	116/214 (54.2%)	39/64 (60.9%)	0.302
Using cephalocaudal assessment†	271/348 (77.9%)	21/28 (75.0%)	34/41 (82.9%)	170/217 (78.3%)	46/62 (74.2%)	0.645
Using TcB assessment†	56/349 (16.1%)	5/27 (18.5%)	10/42 (23.8%)	34/216 (15.7%)	7/64 (10.9%)	0.017
Recommendations to the mother regarding the baby's jaundice						
1. Bring baby to the office	284/335 (84.8%)	20/25 (80%)	35/40 (87.5%)	175/210 (83.3%)	53/60 (88.3%)	0.426
2. Put baby in the sunlight	3/335 (1.1%)	-	1/40 (2.5%)	2/210 (0.95%)	-	
3. Refer baby for TSB measurement	38/335 (11.4%)	3/25 (12.0%)	3/40 (7.5%)	26/210 (12.4%)	6/60 (10.0%)	
4. Stop breastfeeding	-	-	-	-	-	
5. Other	9/335 (2.7%)	2/25 (8.0%)	-	7/210 (3.3%)	1/60 (1.7%)	

\*Total number of respondents (University and Community Hospitals, Private Groups and Solo)

\*\* P-values represent Chi-square test (for proportion)

†To quantify the severity of jaundice

Table 3. Pediatricians' answers to the question: "Do you believe that following factors are associated with severe hyperbilirubinemia in term neonates?"

Risk factor and number of respondents	Response				
	Hardly at all	To a small degree	To a moderate degree	To a very high degree	Not applicable
Jaundice presenting in the first 24 hours (n=348)	2.3%	3.5%	17.2%	77.0%	-
Jaundice noted at discharge (n=345)	14.2%	52.5%	29.3%	2.9%	1.2%
Gestational age between 37 and 38 weeks (n=346)	25.1%	45.7%	26.0%	2.0%	1.2%
Breastfeeding (n=343)	12.0%	42.0%	40.2%	5.8%	-
Bruising and/or cephalohematoma (n=345)	2.6%	38.6%	50.4%	8.4%	-
Rh incompatibility (n=347)	4.0%	6.9%	25.9%	61.9%	1.2%
ABO incompatibility (n=342)	0.9%	8.8%	46.5%	43.6%	0.3%
G-6-PD deficiency (n=339)	5.9%	17.4%	40.4%	34.2%	2.1%
Previous sibling with jaundice (n=346)	15.6%	45.1%	34.4%	4.3%	0.6%

Table 4. Demographic characteristics of the total population of AAP Fellows in the United States versus respondents

Demographic characteristics	AAP data for the U.S. *	Respondents†	P value
Gender			.328
Male	52.3%	49.2%	
Female	47.7%	50.8%	
Age			
<34 years	24.2%	19.4%	.071
35-44 years	34.5%	31.8%	.550
45-54 years	25.3%	30.0%	.100
55-64 years	11.9%	13.5%	.444
>65 years	4.2%	5.3%	.405

\* N=820 AAP fellows (Socioeconomic Survey of Pediatricians: Part 1 2000, Response rate 52%)

† N=356 respondents

the office and only 12% of them preferred to directly refer the infant to a laboratory in order to obtain a TSB level. None of the pediatricians advised the mother to stop breastfeeding. Most respondents used cephalocaudal progression of jaundice and a significantly low number of pediatricians (mainly in solo practice) used transcutaneous bilirubinometry (TcB) for the quantification of neonatal jaundice.

**Treatment pattern of neonatal hyperbilirubinemia**  
 Pediatricians' practices regarding phototherapy use in neonates with respect to age-specific TSB levels are revealed in Figure 1. Initiation of phototherapy at TSB levels lower than recommended by the AAP at 24-48 ( $\geq 15$  mg/dL), 49-72 ( $\geq 18$  mg/dL), and >72 hours ( $\geq 20$  mg/dL) were reported by 21.8%, 26.4% and 57.2% of the pediatricians, respectively. As shown in Figure 2, exchange transfusions at TSB levels lower than recommended by AAP at the age of 24-48 ( $\geq 20$  mg/dL), 49-72 ( $\geq 25$  mg/dL), and >72 hours ( $\geq 25$  mg/dL) were reported by 6.7%, 32.7%, and 34.2% of the respondents,

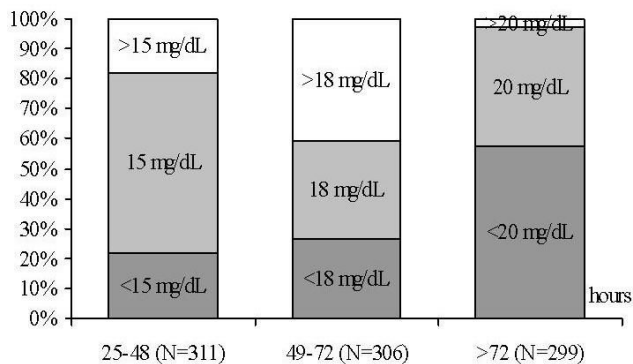


Figure 1

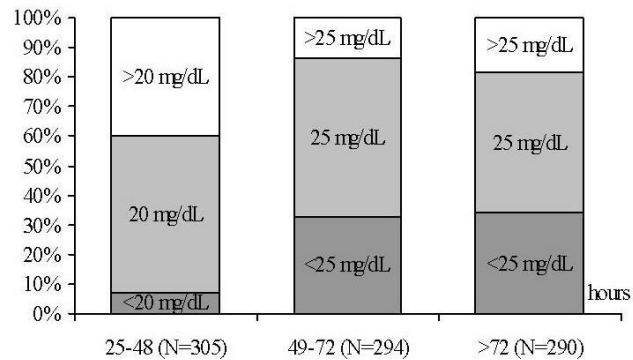


Figure 2

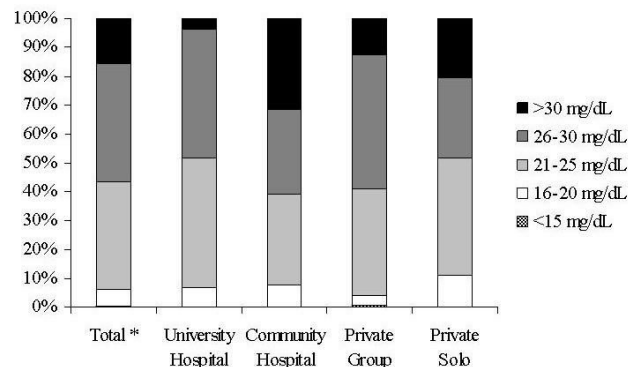


Figure 3

respectively. The pediatrician's preference for using age-specific thresholds of TSB for phototherapy and exchange transfusion was not associated with the type of practice.

### Risk factors for hyperbilirubinemia and kernicterus

The pediatricians' response regarding risk factors for the development of severe neonatal hyperbilirubinemia is presented in Table 3. The majority believed "to a very high or moderate degree" that jaundice presenting in the first 24 hours and Rh/ABO incompatibility were significant risk factors for the development of hyperbilirubinemia in term infants. More than 70% of the pediatricians stated that "hardly ever or to a small degree" would they consider gestational age between 37-38 weeks and jaundice noted after discharge from the hospital as significant risk factors for the development of severe neonatal hyperbilirubinemia. Breast-feeding, bruising/cephalohematoma, and previous siblings with jaundice were rated by more than 80% of pediatricians as risk factors for hyperbilirubinemia with only a small or moderate degree of belief. The pediatricians' belief regarding the relationship between these risk factors and severe hyperbilirubinemia was not associated with the practice type.

Only 48 of the 351 respondents (13.9%) reported firsthand

experience with one or more patients with kernicterus. These pediatricians were older (50.7+/-11.5 vs. 44.5+/-11.3 years,  $P < 0.03$ ) and had been in practice much longer (18.0+/-12.4 vs. 13.8 +/-12.4 years,  $P < 0.01$ ) as compared to those who had not seen a single case of kernicterus. A large number of pediatricians believed that a TSB more than 20 mg/dL was a significant risk factor for the development of kernicterus (Figure 3). Among these, a higher proportion of pediatricians from community hospitals regarded bilirubin >30 mg/dL as a risk factor for kernicterus. The vast majority of respondents (more than 88% in each practice group) rated kernicterus as a public health concern and about 50% agreed that severe hyperbilirubinemia and kernicterus should be made laboratory based reportable conditions in New Jersey.

### DISCUSSION

The result of our population-based survey of practicing pediatricians in New Jersey showed overall uniformity with the 1994 AAP recommendations<sup>9</sup> in the management of neonatal hyperbilirubinemia prior to discharge but significant heterogeneity in the post-discharge follow up and treatment practices. Although the majority of respondents preferred to see infants with jaundice in their office, most did not consider post-discharge jaundice as an indicator for a follow up TSB level. Such post-discharge follow up practices may contribute to the development of undiagnosed pathological neonatal hyperbilirubinemia because of the practice of early discharge and the presentation of jaundice mostly after the third day of life.<sup>10, 11</sup> However, almost all of the respondents were concerned about bilirubin-induced neurological complications and recognized the importance of post-discharge TSB monitoring. Therefore, the lack of outcome expectancy that is often classified as the major factor influencing physicians' compliance with existing recommendations<sup>12</sup> could not be considered. In addition, approximately 60% of the pediatricians reported the initiation of phototherapy in neonates more than 72 hours old at TSB levels lower than recommended by the AAP.<sup>9</sup> Gartner et al (although the age of the infants was not reported) previously revealed this general tendency for the initiation of phototherapy at lower TSB levels in a pediatrician's survey in 1992.<sup>5</sup> Concern has been expressed regarding negative outcome in association with the use of lower threshold bilirubin levels for the initiation of therapy for neonates with hyperbilirubinemia.<sup>13, 14, 15</sup> The initiation of phototherapy at TSB lower than the AAP recommended levels by some pediatricians may reflect the insufficiency in our understanding of the biology of neonatal jaundice.<sup>16</sup>

The majority of respondents reported using cephalocaudal progression of jaundice to quantify the severity despite the inaccuracy of this methodology especially in darkly pigmented infants.<sup>2, 17</sup> The low utilization of TcB for assessment of the severity of neonatal hyperbilirubinemia that was reported by the majority of pediatricians may reflect their uncertainty regarding the diagnostic accuracy of this methodology<sup>18, 19, 20, 21, 22</sup> or the cost of the equipment. It is possible that the disagreement that exists in the literature<sup>23, 24, 25, 26, 27, 28, 29</sup> alters the practicing pediatricians' perception regarding the importance of some significant risk factors in the development of severe hyperbilirubinemia.

Certain aspects of our study such as the response rate of 49.1%, may limit the interpretation of the results. However, this response rate may actually represent a higher proportion of the general pediatricians because the mailing list of the New Jersey Chapter of the AAP included pediatricians who were in specialty practice and the likelihood of a response from these physicians was rather small. Moreover, studies have shown that non-responder bias is not

strongly related to the survey response rate and therefore it is unlikely that a greater survey response rate would have significantly altered the results.<sup>30,31</sup> The demographic composition of our respondents is no different from that of the AAP Fellows in the rest of the United States (Table 4). Secondly, we did not review records to confirm actual practices. However, previous studies have shown that surveyed physicians are able to characterize their actual practices with reasonable accuracy.<sup>32</sup> Thirdly, junior fellows in residency programs and family practitioners who may provide neonatal services were not included in the study, but that is a relatively small group.

## CONCLUSIONS

In conclusion, the apparent low threshold of bilirubin level for the pediatrician's concern regarding kernicterus and their willingness to initiate phototherapy or exchange transfusion at TSB levels well below those recommended by the AAP are the most important results of this study. The pediatricians are aware of the message regarding the importance of preventing severe hyperbilirubinemia and hyperbilirubinemia-related neurological complications as articulated in the AAP guidelines published in 2004.<sup>2</sup> However, the result of this survey indicates the pediatricians' uncertainties about the utilization of diagnostic approaches and risk factor identification, and their significant tendency for lower utilization of bilirubin levels post-discharge for the initiation of phototherapy. This suggests the need for greater education in order to promote evidence-based practices for the prevention and management of neonatal hyperbilirubinemia and kernicterus.

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# Maximum Static Inspiratory and Expiratory Pressures with Different Lung Volumes

Christopher G. Lausted, Arthur T. Johnson, William H. Scott, Monique M. Johnson, Karen M. Coyne, Derya C. Coursey

## ABSTRACT

**Background:** Maximum pressures developed by the respiratory muscles can indicate the health of the respiratory system, help to determine maximum respiratory flow rates, and contribute to respiratory power development. Past measurements of maximum pressures have been found to be inadequate for inclusion in some exercise models involving respiration.

**Methods:** Maximum inspiratory and expiratory airway pressures were measured over a range of lung volumes in 29 female and 19 male adults. A commercial bell spirometry system was programmed to occlude airflow at nine target lung volumes ranging from 10% to 90% of vital capacity.

**Results:** In women, maximum expiratory pressure increased with volume from 39 to 61 cmH<sub>2</sub>O and maximum inspiratory pressure decreased with volume from 66 to 28 cmH<sub>2</sub>O. In men, maximum expiratory pressure increased with volume from 63 to 97 cmH<sub>2</sub>O and maximum inspiratory pressure decreased with volume from 97 to 39 cmH<sub>2</sub>O. Equations describing pressures for both sexes are:

$$P_e/P_{\max} = 0.1426 \ln(\%VC) + 0.3402 \quad R^2 = 0.95$$

$$P_i/P_{\max} = 0.234 \ln(100 - \%VC) - 0.0828 \quad R^2 = 0.96$$

**Conclusions:** These results were found to be consistent with values and trends obtained by other authors. Regression equations may be suitable for respiratory mechanics models.

## BACKGROUND

While maximum respiratory pressures at the mouth have been measured in numerous subjects, less data exists to characterize maximum pressures as they vary with lung volume. Maximum pressure is volume dependent because muscle tension is length dependent, because muscle tension produces higher pressure with a smaller radius of curvature, and because respiratory tissue is elastic. Rahn et al<sup>1</sup> first produced static pressure-volume diagrams from a group of adult men, and later, Cook et al<sup>2</sup> produced pressure-volume diagrams from a larger group of subjects including women and children. These diagrams were useful in modeling the energetics of respiration<sup>3</sup> and in monitoring the progress of respiratory muscle training.<sup>4</sup> Yet the total number of subjects tested remained small, particularly regarding females. The present paper provides additional static pressure-volume data obtained from adult volunteers, both women and men.

## METHODS

**Subjects:** Forty-eight normal subjects agreed to participate in the study. The subjects were recruited from students and staff at the University of Maryland. The study was approved by the Institutional Review Board and all subjects gave informed consent. The subjects' characteristics are shown in Table 1.

**Protocol:** Subjects were first acquainted with the spirometer and the test protocol. They were instructed in the definition of functional residual capacity (FRC) as the resting volume of the lung and given time to practice finding FRC. The subjects were then measured for inspiratory capacity (IC) and expiratory reserve volume (ERV) relative to FRC. Volume measurements were repeated until three consecutive maneuvers produced volumes within a 100 ml range. The average of the three volumes was recorded. Vital capacity (VC) was calculated as the sum of IC and ERV. Maximum pressure measurements were taken from occlusions occurring at nine predetermined target volumes. The volumes were randomly ordered and ranged from 10% to 90% of VC by 10% increments. Subjects began each maneuver at FRC. Subjects were instructed to inhale or exhale, as necessary, to the desired volume. When the target volume

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**Table 1.** Age, height, weight, and lung volume data in the two groups tested shown with standard deviations.

Group	Number of Subjects	Average Age (Range)	Average Height, cm	Average Mass kg	Average Vital Capacity, L
Females	29	25.5 ± 3.7 (18 to 31)	164 ± 6	60.5 ± 13.3	3.58 ± 0.63
Males	19	26.5 ± 4.3 (19 to 34)	177 ± 7	74.1 ± 8.8	4.72 ± 8.4

**Table 2.** Maximal inspiratory and expiratory static pressures at different lung volumes for the female subjects.

Expiratory Volume (%VC)	Pressure		Inspiratory Volume (%VC)	Pressure	
	Positive Pressure (cmH <sub>2</sub> O)	P <sub>e</sub> /P <sub>max</sub>		Negative Pressure (cmH <sub>2</sub> O)	P <sub>i</sub> /P <sub>max</sub>
8.9 ± 0.7	38.7 ± 25.0	0.5864	12.1 ± 0.9	65.9 ± 31.6	0.9985
18.4 ± 1.0	44.2 ± 25.9	0.6697	22.5 ± 1.3	65.0 ± 31.6	0.9848
27.6 ± 1.3	53.4 ± 30.7	0.8091	33.0 ± 1.8	59.6 ± 32.0	0.9030
37.3 ± 1.5	53.7 ± 28.8	0.8136	43.3 ± 2.0	55.0 ± 32.0	0.8333
46.8 ± 1.9	53.3 ± 28.9	0.8076	53.5 ± 2.2	53.0 ± 32.9	0.8030
56.2 ± 2.2	55.4 ± 29.6	0.8394	63.8 ± 2.6	47.6 ± 28.3	0.7212
65.7 ± 2.6	57.3 ± 33.2	0.8682	73.6 ± 2.6	42.3 ± 28.6	0.6409
74.7 ± 3.2	61.7 ± 38.5	0.9398	83.1 ± 2.7	34.2 ± 27.4	0.5182
84.4 ± 3.2	61.2 ± 39.0	0.9273	92.6 ± 2.4	28.0 ± 29.0	0.4242

Volumes are expressed in percent of vital capacity at ambient pressure. All values are shown with standard deviations. P<sub>max</sub> for females was determined to be 66 cmH<sub>2</sub>O.

**Table 3.** Maximal inspiratory and expiratory static pressure at different lung volumes for the male subjects.

Expiratory Volume (%VC)	Pressure		Inspiratory Volume (%VC)	Pressure	
	Positive Pressure (cmH <sub>2</sub> O)	P <sub>e</sub> /P <sub>max</sub>		Negative Pressure (cmH <sub>2</sub> O)	P <sub>i</sub> /P <sub>max</sub>
8.2 ± 1.0	63.2 ± 32.6	0.6196	13.5 ± 2.0	96.7 ± 45.5	0.9480
17.2 ± 1.3	75.3 ± 39.0	0.7382	24.2 ± 2.8	95.3 ± 49.8	0.9343
26.2 ± 1.6	84.1 ± 39.9	0.8245	35.2 ± 3.2	97.3 ± 52.2	0.9539
35.2 ± 2.2	91.6 ± 38.3	0.8980	45.9 ± 3.6	87.2 ± 42.3	0.8549
44.8 ± 2.6	89.6 ± 41.3	0.8784	55.7 ± 3.2	77.9 ± 36.9	0.7637
53.5 ± 2.7	93.3 ± 36.3	0.9147	66.7 ± 4.2	75.4 ± 42.2	0.7392
62.6 ± 3.4	94.6 ± 44.3	0.9275	76.5 ± 4.5	69.4 ± 40.4	0.6804
72.1 ± 3.8	94.2 ± 43.3	0.9235	85.5 ± 4.9	51.4 ± 38.4	0.5039
80.8 ± 4.2	97.2 ± 41.5	0.9529	94.2 ± 5.1	38.9 ± 38.8	0.3814

Volumes are expressed in percent of vital capacity at ambient pressure. All values are shown with standard deviations. P<sub>max</sub> for males was determined to be 102 cmH<sub>2</sub>O.

was obtained, the occlusion valve automatically closed. The subject was told to inhale or exhale, as necessary, for two seconds. After two seconds of effort, the valve was released. This gave the subject access to fresh air for at least one minute of rest. More time was given, if desired. After all 18 measurements were taken, the test was repeated. The stronger effort, or higher maximum pressure, at each measurement was saved.

**Measurements:** A commercial spirometry system (Collins, Braintree, MA) was used for all the measurements. Lung volumes were monitored by the dry-seal bell spirometer. The occlusion valve and pressure transducer utilized were those located in what Collins refers to as its "universal breathing valve." Collins "Research Assistant" (RA) software controlled the occlusion valve and collected pressure and volume measurements. For the experiment, a supervisory program, "PV," was authored in Microsoft Visual Basic for Applications to

configure RA and provide feedback to the experimenters. PV was designed to fill the spirometer with an appropriate volume of fresh air prior to each measurement. It then calculated the spirometer volume corresponding to the target lung volume, taking thermal expansion into account. Occlusion was triggered automatically when the subject reached the target lung volume. As target lung volumes were randomly ordered, a randomization feature was built into PV. After each occlusion, RA returned pressure and volume data, which PV analyzed and saved to disk. The spirometer was calibrated each test day with a three-liter syringe and the pressure transducer was calibrated each day with a 10 cmH<sub>2</sub>O manometer.

**Data analysis:** The maximum inhalation or exhalation pressure magnitude (P<sub>i</sub> or P<sub>e</sub>) at each lung volume (V<sub>i</sub>) was recorded by the computer. The average pressure for the last one second of each effort was calculated. This pressure was then used to correct V<sub>L</sub> using the method by Cook et al.<sup>2</sup> Absolute lung volumes were not measured and volumes were calculated based on the assumption that residual volume was 26% that of TLC.

## RESULTS

Average maximum pressure values for all of the female subjects tested appear in Table 2 and values for all of the male subjects appear in Table 3. Observations were grouped according to the lung volumes at which occlusion occurred and actual volumes within each group were averaged to produce the tabled values. The pressures produced by the men were typically 64% higher than the women in expiration, and 53% higher in inspiration.

Data were then scrutinized in an exploratory manner to see if they could be easily and universally fit by a simple mathematical expression.<sup>5</sup> It was found that both men's and women's data could be described by an expression of the form:

$$P_e/P_{max} = A \ln (\%VC) + B \quad \text{for exhalation}$$

and

$$P_i/P_{max} = C \ln (100 - \%VC) + D \quad \text{for inhalation}$$

Here, P<sub>max</sub> is the asymptotically maximum pressure that could be developed by the respiratory muscles at any lung volume and P<sub>i</sub> is the maximum inspiratory pressure that can be developed at specific lung volumes. The average value of P<sub>max</sub> found by determining the limit of the nonlinear P-V curve for the group of subjects was found to be 102 cmH<sub>2</sub>O for males and 66 cmH<sub>2</sub>O for females, and was found to be the same for both inhalation and exhalation directions. Least squares regression using Microsoft Excel yielded the following two equations:

$$P_e/P_{max} = 0.1426 \ln (\%VC) + 0.3402 \quad R^2 = 0.9549$$

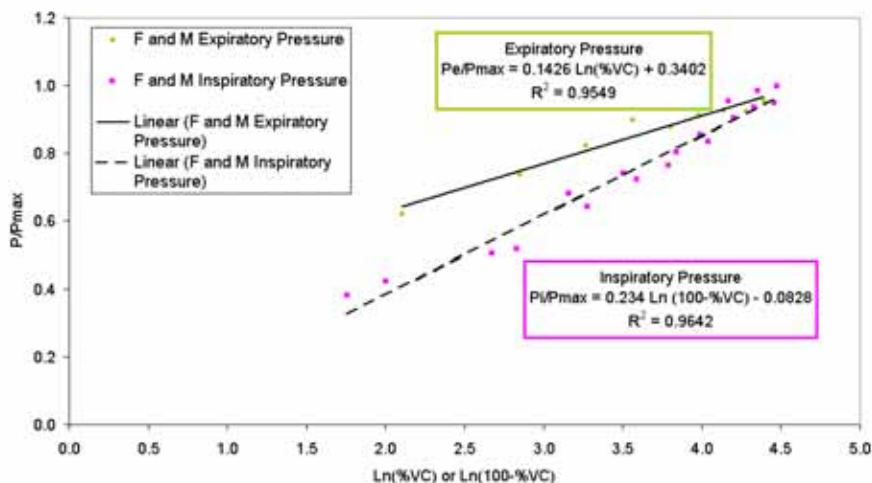
and

$$P_i/P_{max} = 0.234 \ln (100\% - \%VC) - 0.0828 \quad R^2 = 0.9642$$

These equations are graphed in Figure 1.

## DISCUSSION

Greater (more positive) expiratory pressures were developed at higher V<sub>L</sub>, while greater (more negative) inspiratory pressures were developed at lower V<sub>L</sub>. In women P<sub>e</sub> increased with volume from 39 to 61 cmH<sub>2</sub>O and P<sub>i</sub> decreased with volume from 66 to



**Figure 1.** Graph of empirical equations determined to describe relative expiratory and inspiratory pressures for men and women. Some data points are coincident. Symbols: F = female; M = male; other symbols as in text.

28 cmH<sub>2</sub>O. In men, P<sub>e</sub> increased with volume from 63 to 97 cmH<sub>2</sub>O and P<sub>i</sub> decreased with volume from 97 to 39 cmH<sub>2</sub>O. These trends occur primarily for two reasons. First, respiratory muscles work both with and against respiratory tissue elastance to produce pressure. Expiratory efforts are aided by tissue elastance (lung recoil effects) at high V<sub>L</sub> and inhibited at low V<sub>L</sub>. Inspiratory efforts are inhibited by tissue elastance at high V<sub>L</sub> and aided at low V<sub>L</sub>. Second, respiratory muscles exert greater tension when they are stretched to greater lengths. Expiratory muscles are stretched when the lung is inflated, while inspiratory muscles are stretched when the lung is deflated. Both of these factors describe the general trend of the data.

The volume dependence of P<sub>i</sub> was much more pronounced than the volume dependence of P<sub>e</sub> in both women and men. This can be seen as a higher slope of the inspiratory equation compared to the expiratory equation in Figure 1. This may reflect a combination of strength differences between diaphragm (largely responsible for inhalation) and abdominal muscles (largely responsible for exhalation) recruitment of intercostal muscle (largely responsible for posture maintenance), and different mechanical advantages of each type of muscle as the lung volume varies.

The Laplace equation may be relevant here. This equation states that enclosed pressure is proportional to the product of wall tension and wall thickness and inversely proportional to the radius of curvature. The Laplace equation for a sphere differs from that of a cylinder by a factor of two. Pressure in a sphere is twice that of a cylinder, all other things being equal.

The diaphragm is positioned under the lungs and curves upward in a somewhat spherical shape. As it contracts, it becomes flatter, meaning that its radius of curvature increases. Lung volume increases as the diaphragm contracts. If the Laplace equation can be applied to the respiratory system, then it would show that inspiratory pressure should decrease as radius, and thus lung volume, increases (P<sub>i</sub>, as long as wall tension and thickness remain steady).

The abdominal muscles are arranged differently, more like wrapping around a cylinder. The abdominal muscles flatten at smaller lung volumes instead of larger lung volumes, and the Laplace equation indicates that higher pressures should be developed at larger lung volumes (PV)

Both effects have been observed. Inspiratory pressures increase as lung volume decreases and expiratory pressure increases as lung volume increases. There is roughly a factor of two between the dependence of pressures upon lung volumes for inspiration and expiration. This could well be related to the difference in the Laplace equation for a sphere and a cylinder.

The pressure-volume data obtained in this study are of the same general magnitudes as those previously reported.<sup>1,2,6</sup> Rahn et al<sup>1</sup> studied P<sub>i</sub> in 11 men and P<sub>e</sub> in 12 men using similar methods. The highest pressures from three efforts at each of six starting volumes were recorded. Measurements were read from a mercury manometer connected to the subjects' noses. Pressure-volume data closely match the results of the present study. Craig<sup>6</sup> produced pressure-volume diagrams from 10 men using methods similar to the present study. Pressures were taken from a mercury manometer connected to the subjects' mouths. These data also closely match the results of the present study. Cook et al<sup>2</sup> studied 17 males and 9 females using two techniques. One technique was a conventional occlusion maneuver. The other technique involved subjects breathing into or out of large, fixed volumes. The compressibility of the air in differently sized containers provided for various ultimate lung volumes. The volumes were calculated from Boyle's Law using peak pressures that could be sustained for 1-2 seconds. Five volumes were used. It was concluded that the results of the occlusion method and the compression method were the same. In women, the compression-method P<sub>i</sub> values were similar to those of the present study at high volumes, but slightly higher at lower volumes. The P<sub>e</sub> values were similar at low volumes, but much higher at higher lung volumes. In men, the compression-method P<sub>i</sub> values agree well with those of the present study. However, the P<sub>e</sub> values are much higher than those of the present study at the higher volumes. Cook et al<sup>2</sup> suggested that their P<sub>e</sub> values



might have been higher than the Rahn et al values because of the use of mouth pressure measurements rather than nose pressure measurements. It was also hypothesized that these  $P_e$  values exceeded Craig's values due to better mouthpiece sealing.

As the results of this study are more in agreement with work of Rahn et al and Craig, it is more likely that there is another reason for the discrepancy. Aside from muscle strength alone,  $P_e$  and  $P_i$  are highly effort dependent. Subjects may limit their maximum pressures due to factors such as pain in the ear or general discomfort. During some maximum pressure maneuvers, researchers have observed changes in hemodynamics leading to loss of consciousness.<sup>7</sup> It is possible that the subjects of the Cook study were more highly motivated. It is also possible that these subjects were of above average strength.

Numerous authors have collected maximal pressures at a single  $V_L$ . Most recently, Wilson et al<sup>8</sup> measured maximal  $P_e$  and  $P_i$  in 87 women and 48 men using partial occlusion and Bourdon gauges. The women were found to have  $P_e = 93 \pm 17$  cmH<sub>2</sub>O and  $P_i = 73 \pm 22$  cmH<sub>2</sub>O and the men were found to have  $P_e = 148 \pm 34$  cmH<sub>2</sub>O and  $P_i = 106 \pm 31$  cmH<sub>2</sub>O. It could be expected that the  $P_i$  and  $P_e$  values from a single volume study would exceed the values from a multiple volume study because more efforts are made at the optimal  $V_L$  in the single volume study, while muscle fatigue can be a factor in the multiple-volume study.

Judging from inspiration values, this does not appear to be the case. In the present study, women were found to have  $P_i = 66 \pm 32$  cmH<sub>2</sub>O at  $V_L = 12\%VC$  and men were found to have  $P_i = 97 \pm 46$  cmH<sub>2</sub>O at  $V_L = 14\%VC$ . These values are virtually identical to the Wilson et al<sup>8</sup> data. On the other hand, women in this study were found to have  $P_e = 61 \pm 39$  cmH<sub>2</sub>O at  $V_L = 84\%VC$  and men were found to have  $P_e = 97 \pm 42$  cmH<sub>2</sub>O at  $V_L = 81\%VC$ . These values are considerably smaller than the Wilson et al data. The  $P_e$  values of the single volume study fall in between the maximum  $P_e$  values of the present study and the maximum  $P_e$  values of the Cook study.

Satisfactorily describing maximum lung pressures with mathematical expressions can be helpful for respiratory mechanical modeling.<sup>3</sup> It is not likely that maximal pressures would be developed in young, healthy adults during quiet breathing. During exercise, and especially during expiratory flow limitation, however, maximum pressures may well be developed. For example, modeling the effects of respiratory masks during hard work could use these equations to calculate respiratory work rate. These equation forms are good because pressures and lung volumes both appear as relative rather than absolute values. That way, both men's and women's pressures could be determined with the same equations despite large differences in absolute pressures developed. Respiratory models for those conditions could well use the equations developed here.

Although we have no data to support the notion, it is possible, if their respiratory mechanics changed proportionally, that maximum pressures developed by patients with respiratory impairments could be described by the same equations as developed here. That is because these equations are in relative pressure and volume form. One would expect that  $P_{max}$  could be much lower in diseased patients, but  $P/P_{max}$  could be scaled the

same. If this were so, then equations developed here could have more universal value.

## CONCLUSION

Maximum pressures at the mouth have been determined to depend on lung volumes. Equations to describe these pressures have been developed, and these are in a form that may be useful for modeling and predictive purposes.

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# Pleural Fluid pH Analysis in the Blood Gas Laboratory

Michael Nibert, RRT, BSRT

This article is specifically addressing the role of the Respiratory Care Practitioner (RCP) in the role of body fluid analysis and specifically pleural fluid pH. Before we take an in depth look at this analyte we must first look at the pathophysiology of this pneumonic process.

Pleural effusion is the accumulation of fluid in the chest between the lung and the chest cavity. Normally there is no space between the parietal pleura, which covers the chest wall, and the visceral pleura, which covers the lung. The normal fluid that is present facilitates the mechanics of ventilation that maintains a negative intrapleural pressure therefore allowing the lungs to remain expanded. For a diagnosis of pleural effusion, 75% of those patients will have a diagnosis made at the onset of the clinical findings presented. 25% of those patients will have a positive cytology or positive culture of the aspirate analyzed. Fifty percent of those patients have a presumptive diagnosis prior to the laboratory findings. Fifteen to 20% of the patients will not have a diagnosis made prior to diagnostic studies. The history and physical (H & P) exam are critical in guiding the evaluation of the pleural effusion and it is imperative that an extensive H & P be obtained from the patient. Chest examination demonstrates dullness to percussion and diminished breath sounds, which may be, but are not necessarily gravity dependent. Confirmation of a pleural effusion may include an Anterior-Posterior radiograph, lateral decubitus whereby the patient lays on their side, and/or CT of the chest and abdomen. The interpretive physician is looking for clear radiographic findings that suggest a pleural space infiltrate. The definitive diagnosis is a thoracentesis whereby the physician performs a needle aspirate to a local anesthetized area of the chest wall and inserts the needle into the pleural space now occupied by an infiltrate. The sample must be obtained under anaerobic conditions, iced, and analyzed within two hours preferentially through the "gold standard" Blood Gas Analyzer (BGA). If the sample is not iced, in vitro glycolysis will

occur resulting in a false low pH. If the sample is exposed to room air, then a false high pH will occur due to gas equilibration. The sample, by most clinical standards of medical practice, should include a diagnostic order for LDH, Protein, Glucose, Amylase, Cell Count, Cytology, and cultures in addition to pH analysis. There are about 1 million cases per year of pleural effusions and primarily are subcategorized as transudate (movement of fluid into the pleural space due to imbalance of hydrostatic and oncotic pressures) or exudative (caused by inflammation of the lung or pleura) effusions. Transudative effusions normally have a pH 7.40-7.55 and exudative effusions normally have a pH less than 7.45. Categorically, most of the effusions are by congestive heart failure, malignancy, infections, and pulmonary emboli, requiring urgent evaluation and treatment. It is interesting to note that 25% of the pleural effusions are resolved within 48 hours with aggressive diuretic therapy. Cirrhosis, pulmonary embolus, infection, malignancy, immunologic disorders, lymphatic abnormalities, non-infectious inflammation and nephritic syndrome are other common etiologies of transudative pleural effusions. Decreased glucose in the pleural fluid may indicate a malignancy, empyema, and a complicated parapneumonic effusion, or tuberculosis to name just a few disease entities. Normal pH of pleural fluid is 7.60. American College Chest Physicians (ACCP) and the British Thoracic Society agree that pH values less than 7.20 are a critical value with a parapneumonic infection and will require immediate drainage via chest tube insertion. 20-25% of pneumonia patients have a parapneumonic infection and will resolve with aggressive antibiotic therapy. Decreased glucose with a decreased pH signals the possible diagnosis of a malignant pneumonic process. A pH less than 7.28, with a malignant pneumonic process, has a 39% mortality after 3 months. Two negative cytologies with a low pH indicate possible tuberculosis or rheumatoid pleurisy.

Several analytical methods have historically been performed over the years. The methods that have been and currently are being utilized are the pH meter, pH indicator strips, and the Blood Gas Analyzer (BGA). In studies reported in Chest (1998), pH meters and pH indicator paper reported significantly higher

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mean pH than the BGA; therefore the clinical and research findings as stated earlier in this article were that the BGA is the gold standard for pleural fluid pH analysis. Blood Gas Laboratories must meet regulatory standards as set forth by CLIA and other regulatory agencies such as College of American Pathologists (CAP). The method of testing falls into three CLIA classifications of waived, moderately complex, and highly complex categories. The BGA fall into either the moderately complex or high CLIA complexity category depending upon whether the BGA has undergone 510K FDA clearance for analyzing pleural fluid pH. It is each laboratory's responsibility to determine if their BGA has met the FDA clearance for analyzing pleural fluid pH. If your instrument is 510 K FDA cleared, then CLIA recognizes this instrument's analyte as a moderately complex instrumentation. If the BGA is not FDA cleared which is referred to as "off-label," then the analyte is considered to be reported from high complexity instrumentation and must meet the 6 point high complexity CLIA category. Pleural fluid pH analyte reported from a moderate complex BGA has less regulatory requirements from CLIA as opposed to an "off-label" BGA that must meet more CLIA regulations. CLIA does not recognize the waived category for pleural fluid pH so to use litmus paper you must meet CAP guidelines of proficiency testing, daily QC, method validation, and personnel training and competency validations. The use of litmus paper is compromised by the fact that the test results cannot be reported in hundredths (X.XX) and the accuracy needs to be reported to this mathematical expression, as accuracy is the critical factor in reporting pleural pH. Litmus paper relies on colorimetric determinations and has a falsely reportable high value as previously mentioned in CHEST. PH meters expose the anaerobic sample to room air and have falsely high reportable pH as well. Pleural fluid samples when analyzed through the BGA should be cautiously analyzed with the addition of a clot catcher between the syringe and the BGA sample inlet port or an internal clot catcher as the pleural sample presents a small risk of BGA clotting contaminates much like other blood samples introduced into a BGA such as neonatal or patients with polycythemia. Critical values must be determined to meet CAP standards and documented like any other critical value in your laboratory. We have established any value less than 7.20 as a critical result and must be called and read back to the ordering physician to meet CLIA, CAP, JCAHO, and other accreditation standards.

Body fluids must meet proficiency testing just like any other analyte and can be ordered from the CAP web site. These are performed twice a year and reported using similar proficiency testing methodologies.

In summary, pH pleural fluid testing provides the physician with a valuable diagnostic test that complements the clinical decisions necessary to provide excellence in patient outcomes. Not only does the diagnostic testing provide a diagnostic tool, but also from the financial aspect it is a revenue stream within your departmental operations.

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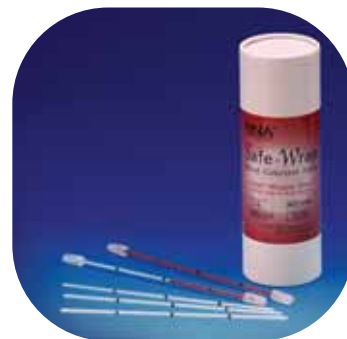
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- For use with most blood gas systems
- Variable fill volume (220 µL maximum)
- Fill lines at 55, 110, and 165 µL

*Please contact us for more information...*

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QMS-MKT0087

# Intelligent Ventilation

**IT IS ALL ABOUT THE PATIENT, THAT'S WHY!**

**FIRST**, do no harm. Does this sound familiar? Then why consider any ventilator that does not have an **AUTOMATED**, patient-driven, lung-protective strategy? Habit? Resistance to change? **READ ON** for Part 2 in a series designed to explain the changing paradigm in mechanical ventilation.

Dear Friends and Colleagues,

**To those of you, who responded with positive comments regarding my last editorial, THANK YOU. I am humbled by the support from the health care professionals that truly understand how important this concept is for the patients that we all serve. The ranks of patient care professionals embracing technology that improves patient safety and staff effectiveness is growing daily.**

The Institute of Medicine has published that medical errors are the eighth leading cause of death among Americans, with error-caused deaths each year in hospitals alone exceeding those from motor vehicle accidents, breast cancer, or AIDS.

I am a former airline pilot (in addition to 25 years in this business). What other industry is more keenly aware of safety than the commercial airline industry. Automation is a fact of life. Is this because the pilots aren't highly skilled and qualified? Consider the years of experience in that cockpit. Consider the thousands of hours of experience required before even being allowed the privilege of stepping into that cockpit. Yet, automation is routinely used to **REDUCE ERRORS, IMPROVE CREW EFFECTIVENESS** and to **PROTECT THE LIVES OF THE PASSENGERS**.

Now consider this. Despite the recent focus on the Institute of Medicine facts, the 100K Lives Initiative by the Institute for Healthcare Improvement and others, experts assure us that the health system in the United States is safe; but the safety record is a far cry from the enviable record of commercial aviation, which is equally complex and often used as a benchmark against health care. Recent airline statistics suggest that a person would have to fly nonstop for 438 years before expecting to be involved in a deadly airplane crash. That, says the Institute of Medicine, places health-care at least a decade behind aviation in safeguarding consumer's lives and health.

Hamilton Medical was the first company to offer closed-loop control mechanical ventilation and we still lead the market today. The last year has been a turning point for Intelligent Ventilation. Hamilton Medical has been working with key experts in the specialty of respiratory care to best understand the mechanisms to provide the **SAFETY** and **EFFECTIVENESS** of Intelligent Ventilation to as many leading edge clinicians and facilities as possible.

We are looking for those clinical experts and leading edge facilities that want to join us at the forefront of the industry. I want to combine the power of like minds to help patients. Contact me. I will send you a book on Closed Loop Control Mechanical Ventilation and a complete set of clinical documentation that proves our point. You will also receive a voucher valid for free tuition to a 2007 Clinical Experts Workshop that Hamilton Medical offers to our clinical leaders. That's OK... not all of you will agree with me. We are looking for the top 10% who "get it".

**Look for Hamilton Medical to continue to introduce new elements to INTELLIGENT VENTILATION. If you think we are ahead of the curve now, wait until you see what develops next...**

Sincerely,  
**David Costa**  
Vice President, Hamilton Medical, Inc.  
[Dave.costa@hamiltonmedical.net](mailto:Dave.costa@hamiltonmedical.net)

**See Intelligent Ventilation:**  
**AARC at Booth 256**  
**SCCM at Booth 411**