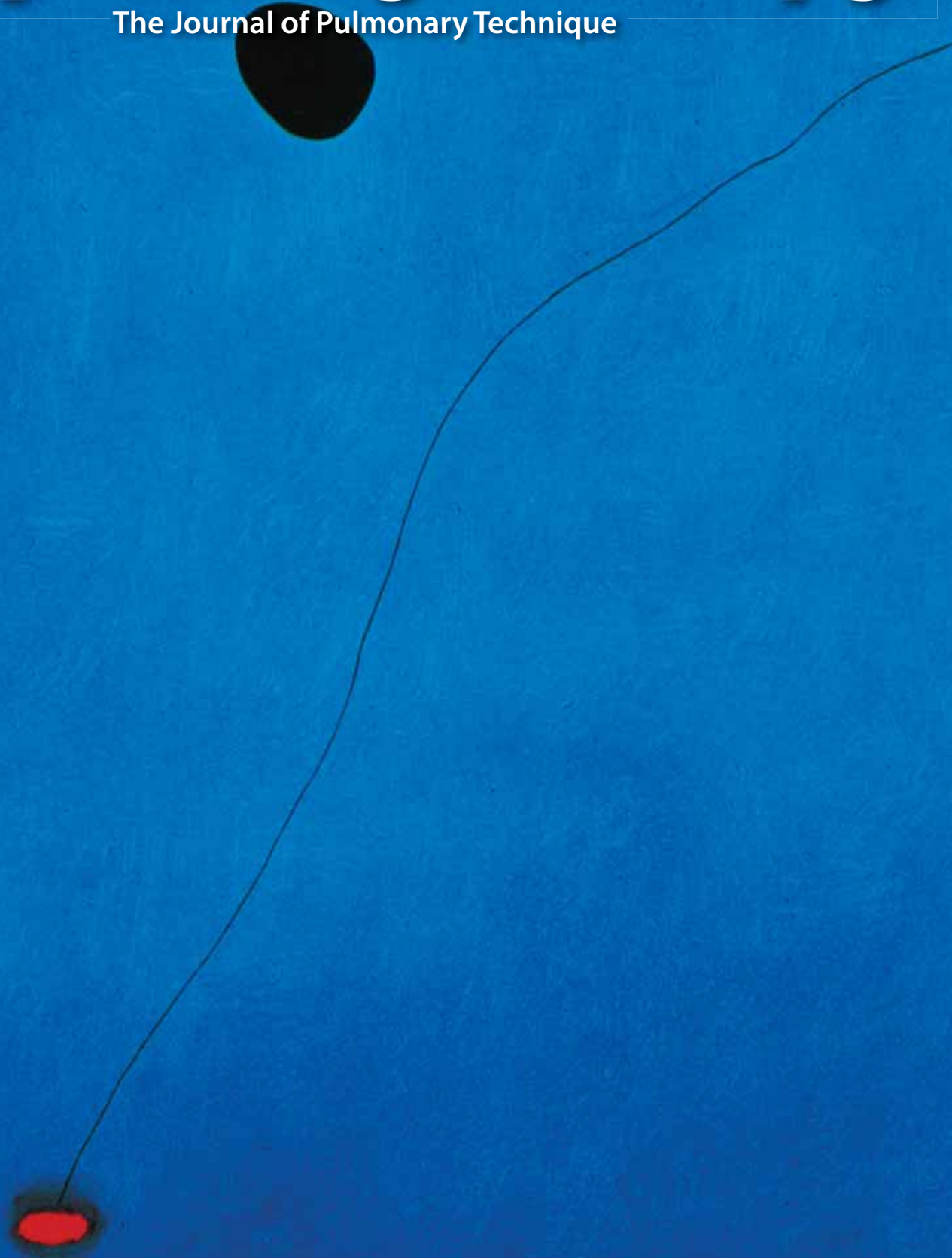


Volume 1 Number 5 August/September 2006

# Respiratory Therapy™

The Journal of Pulmonary Technique



# Intelligent Ventilation

**may mean the end of VENTILATOR-INDUCED LUNG INJURY. HAMILTON MEDICAL has started and continues to lead the quest for PATIENT SAFETY AND STAFF EFFECTIVENESS.**

Physicians, Respiratory Care Professionals and Nurses work hard every day to care for the patients that we all serve. Despite their best efforts, patients on ventilators are routinely harmed in the process. Ventilator-Induced Lung Injury is fact. Hamilton Medical wants to change that. We are leading the charge to create a standard of care where Intelligent Ventilation protects the patient from harm, reduces chances for errors and promotes better staff effectiveness.

Dear Friends and Colleagues,

Those of you who know me will understand the unconventional nature of my actions. Who gives some VP "suit" (a joke, since I rarely wear one) the idea that he should use valuable ad space as a bully pulpit? I do. I could not come up with a catchy, visually exciting marketing piece, so I decided to have a simple conversation with you. I consider the Hamilton Medical team on a quest to increase the safety of mechanical ventilation and increase the efficiency of the healthcare system.

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 better understand the mechanisms to provide the SAFETY and EFFECTIVENESS of Intelligent Ventilation to as many leading edge clinicians and facilities as possible.

What a huge success! Hamilton Medical would like to publicly thank those early adopters in healthcare that saw the benefits to the PATIENT and adopted the widespread use of Intelligent Ventilation. Their courage to look past inconsequential issues on a ventilator like touch screens (for example) and focus on what was the best for the PATIENT has created a new direction in healthcare that will benefit many.

Why do some very important non-biased industry sources rate Hamilton Medical as top in the industry? Why do some very prestigious health care professionals use Hamilton ventilators when it is far easier to buy "what everyone else does"? Why does my staff pride itself in working "Hamilton Half Days"; insane hours that keep them away from family and friends for extended periods in order to further our cause? Why are our key clinicians eager to offer their assistance in helping Hamilton make Intelligent Ventilation THE standard of care? We are on the right track, that's why. We are focused on the patient, that's why. We all agree that we can improve both the art and science of respiratory care, that's why.

We are looking for those clinical experts and leading edge facilities that want to join Hamilton Medical 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 over the next few years.**

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



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See full prescribing information on the following page.

\* IMS DDD Lung Surfactant Market Purchases July 1991 through December 2005, Ross Insights and Planning, data on file.

**SURVANTA CAN RAPIDLY AFFECT OXYGENATION AND LUNG COMPLIANCE.**  
During controlled clinical trials, the most commonly reported adverse experiences were associated with the dosing procedure: Transient bradycardia, 11.9% of doses; oxygen desaturation, 9.8% of doses; ETT reflux, fewer than 1% of doses.

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SURVANTA is indicated for prevention and treatment ("rescue") of Respiratory Distress Syndrome (RDS) (hyaline membrane disease) in premature infants. SURVANTA significantly reduces the incidence of RDS, mortality due to RDS and air leak complications.

### Prevention

In premature infants less than 1250 g birth weight or with evidence of surfactant deficiency, give SURVANTA as soon as possible, preferably within 15 minutes of birth.

### Rescue

To treat infants with RDS confirmed by x-ray and requiring mechanical ventilation, give SURVANTA as soon as possible, preferably by 8 hours of age.

### CONTRAINDICATIONS

None known.

### WARNINGS

SURVANTA is intended for intratracheal use only. SURVANTA CAN RAPIDLY AFFECT OXYGENATION AND LUNG COMPLIANCE. Therefore, its use should be restricted to a highly supervised clinical setting with immediate availability of clinicians experienced with intubation, ventilator management, and general care of premature infants. Infants receiving SURVANTA should be frequently monitored with arterial or transcutaneous measurement of systemic oxygen and carbon dioxide.

DURING THE DOSING PROCEDURE, TRANSIENT EPISODES OF BRADYCARDIA AND DECREASED OXYGEN SATURATION HAVE BEEN REPORTED. If these occur, stop the dosing procedure and initiate appropriate measures to alleviate the condition. After stabilization, resume the dosing procedure.

### PRECAUTIONS

#### General

Rales and moist breath sounds can occur transiently after administration. Endotracheal suctioning or other remedial action is not necessary unless clear-cut signs of airway obstruction are present.

Increased probability of post-treatment nosocomial sepsis in SURVANTA-treated infants was observed in the controlled clinical trials (Table 1). The increased risk for sepsis among SURVANTA-treated infants was not associated with increased mortality among these infants. The causative organisms were similar in treated and control infants. There was no significant difference between groups in the rate of post-treatment infections other than sepsis.

Use of SURVANTA in infants less than 600 g birth weight or greater than 1750 g birth weight has not been evaluated in controlled trials. There is no controlled experience with use of SURVANTA in conjunction with experimental therapies for RDS (eg, high-frequency ventilation or extracorporeal membrane oxygenation).

No information is available on the effects of doses other than 100 mg phospholipids/kg, more than four doses, dosing more frequently than every 6 hours, or administration after 48 hours of age.

### Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies have not been performed with SURVANTA. SURVANTA was negative when tested in the Ames test for mutagenicity. Using the maximum feasible dose volume, SURVANTA up to 500 mg phospholipids/kg/day (approximately one-third the premature infant dose based on mg/m<sup>2</sup>/day) was administered subcutaneously to newborn rats for 5 days. The rats reproduced normally and there were no observable adverse effects in their offspring.

### ADVERSE REACTIONS

The most commonly reported adverse experiences were associated with the dosing procedure.

In the multiple-dose controlled clinical trials, each dose of SURVANTA was divided into four quarter-doses which were instilled through a catheter inserted into the endotracheal tube by briefly disconnecting the endotracheal tube from the ventilator. Transient bradycardia occurred with 11.9% of doses. Oxygen desaturation occurred with 9.8% of doses.

Other reactions during the dosing procedure occurred with fewer than 1% of doses and included endotracheal tube reflux, pallor, vasoconstriction, hypotension, endotracheal tube blockage, hyperventilation, hypocarbia, hypercarbia, and apnea. No deaths occurred during the dosing procedure, and all reactions resolved with symptomatic treatment.

The occurrence of concurrent illnesses common in premature infants was evaluated in the controlled trials. The rates in all controlled studies are in Table 1.

TABLE 1

Concurrent Event	All Controlled Studies		
	SURVANTA (%)	Control (%)	P-Value <sup>a</sup>
Patent ductus arteriosus	46.9	47.1	0.814
Intracranial hemorrhage	48.1	45.2	0.241
Severe intracranial hemorrhage	24.1	23.3	0.693
Pulmonary air leaks	10.9	24.7	<0.001
Pulmonary interstitial emphysema	20.2	38.4	<0.001
Necrotizing enterocolitis	6.1	5.3	0.427
Apnea	65.4	59.6	0.253
Severe apnea	46.1	42.5	0.114
Post-treatment sepsis	20.7	16.1	0.019
Post-treatment infection	10.2	9.1	0.345
Pulmonary hemorrhage	7.2	5.3	0.166

aP-value comparing groups in controlled studies

When all controlled studies were pooled, there was no difference in intracranial hemorrhage. However, in one of the single-dose rescue studies and one of the multiple-dose prevention studies, the rate of intracranial hemorrhage was significantly higher in SURVANTA patients than control patients (63.3% v 30.8%,  $P = 0.001$ ; and 48.8% v 34.2%,  $P = 0.047$ , respectively). The rate in a Treatment IND involving approximately 8100 infants was lower than in the controlled trials.

In the controlled clinical trials, there was no effect of SURVANTA on results of common laboratory tests: white blood cell count and serum sodium, potassium, bilirubin, creatinine.

More than 4300 pretreatment and post-treatment serum samples from approximately 1500 patients were tested by Western Blot Immunoassay for antibodies to surfactant-associated proteins SP-B and SP-C. No IgG or IgM antibodies were detected.

Several other complications are known to occur in premature infants. The following conditions were reported in the controlled clinical studies. The rates of the complications were not different in treated and control infants, and none of the complications were attributed to SURVANTA.

**Respiratory:** lung consolidation, blood from the endotracheal tube, deterioration after weaning, respiratory decompensation, subglottic stenosis, paralyzed diaphragm, respiratory failure.

**Cardiovascular:** hypotension, hypertension, tachycardia, ventricular tachycardia, aortic thrombosis, cardiac failure, cardio-respiratory arrest, increased apical pulse, persistent fetal circulation, air embolism, total anomalous pulmonary venous return.

**Gastrointestinal:** abdominal distention, hemorrhage, intestinal perforations, volvulus, bowel infarct, feeding intolerance, hepatic failure, stress ulcer.

**Renal:** renal failure, hematuria.

**Hematologic:** coagulopathy, thrombocytopenia, disseminated intravascular coagulation.

**Central Nervous System:** seizures.

**Endocrine/Metabolic:** adrenal hemorrhage, inappropriate ADH secretion, hyperphosphatemia.

**Musculoskeletal:** inguinal hernia.

**Systemic:** fever, deterioration.

### Follow-Up Evaluations

To date, no long-term complications or sequelae of SURVANTA therapy have been found.

### Single-Dose Studies

Six-month adjusted-age follow-up evaluations of 232 infants (115 treated) demonstrated no clinically important differences between treatment groups in pulmonary and neurologic sequelae, incidence or severity of retinopathy of prematurity, rehospitalizations, growth, or allergic manifestations.

### Multiple-Dose Studies

Six-month adjusted-age follow-up evaluations have been completed in 631 (345 treated) of 916 surviving infants. There were significantly less cerebral palsy and need for supplemental oxygen in SURVANTA infants than controls. Wheezing at the time of examination was significantly more frequent among SURVANTA infants, although there was no difference in bronchodilator therapy.

Final twelve-month follow-up data from the multiple-dose studies are available from 521 (272 treated) of 909 surviving infants. There was significantly less wheezing in SURVANTA infants than controls, in contrast to the six-month results. There was no difference in the incidence of cerebral palsy at twelve months.

Twenty-four-month adjusted-age evaluations were completed in 429 (226 treated) of 906 surviving infants. There were significantly fewer SURVANTA infants with rhonchi, wheezing, and tachypnea at the time of examination. No other differences were found.

### OVERDOSAGE

Overdosage with SURVANTA has not been reported. Based on animal data, overdosage might result in acute airway obstruction. Treatment should be symptomatic and supportive.

Rales and moist breath sounds can transiently occur after SURVANTA is given, and do not indicate overdosage. Endotracheal suctioning or other remedial action is not required unless clear-cut signs of airway obstruction are present.

### HOW SUPPLIED

SURVANTA (beractant) Intratracheal Suspension is supplied in single-use glass vials containing 4 mL (NDC 0074-1040-04) or 8 mL (NDC 0074-1040-08) of SURVANTA. Each milliliter contains 25 mg of phospholipids suspended in 0.9% sodium chloride solution. The color is off-white to light brown.

Store unopened vials at refrigeration temperature (2-8°C). Protect from light. Store vials in carton until ready for use. Vials are for single use only. Upon opening, discard unused drug.

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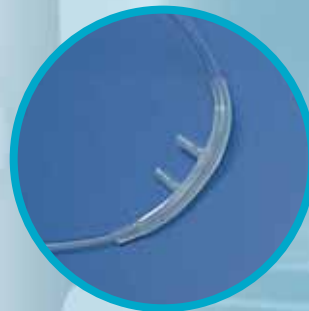
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## IN BED WITH BIG PHARMA

In a recent media advisory, Krystal M. Grube with Peppercorn, a public relations agency, wrote to us:

Recently, an article in JAMA called for an end to pharmaceutical involvement of continuing medical education (CME) courses. This significant change in direction will hurt both physicians and patients through the decline of quality education that is provided to physicians to enhance their care of patients.

Every physician is required to take a certain number of hours or CME credits per year (ranging from 50 to 80, depending on their individual practice areas) in order to be up to date on the latest medical procedures, medical devices, protocols, drugs, and so forth, to ensure that they are providing the best care possible for their patients. Each course on average lasts from one to four hours. The objective is for physicians to learn as much as they can so that they can make an informed decision about the appropriate course of treatment for their patients. In 2004, more than \$1 billion was provided by the pharmaceutical industry to sponsor these critical courses and, in general, approximately 90-95% of all CME courses are sponsored by the pharmaceutical industry.

### Background

According to the JAMA article, conflicts of interest occur when “physicians have motives or are in situations for which reasonable observers could conclude that the moral requirements of the physician’s roles are or will be compromised.” The authors say, “more stringent regulation is necessary, including the elimination or modification of common practices related to small gifts, pharmaceutical samples, continuing medical education, funds for physician travel, speakers bureaus, ghostwriting, and consulting and research contracts,” and propose that academic medical centers take the lead in eliminating such conflicts between physicians and pharmaceutical companies.

Says the JAMA article, “transgressions have prompted pharmaceutical firms to regulate themselves more stringently. That effort is commendable, but physicians’ behavior is a large part of the problem and industry efforts to date have not resolved the crisis... The serious threat that this state of affairs poses for professionalism, and for the trust that patients have in physicians, makes the need for effective guidelines on industry-physician relationships both apparent and urgent.” The authors of the article posit that “drug companies are attempting to promote the use of their products” through industry-sponsored seminars and related events... In our view, the guidelines produced by [professional groups for such events] are not sufficiently stringent and do not adequately uphold a professional commitment to patient welfare and research integrity.” The authors’ solution: “All gifts, free meals, payment for time for travel to or time at meetings, and payment for participation in online CME from drug and medical device companies to physicians should be prohibited. A complete ban on these activities by eliminating potential gray areas greatly eases the burden of compliance. It also frees physicians from deciding whether a gift is appropriate and removes a principal mode by which detail persons gain access to physicians’ offices and influence their decision making... The direct provision of pharmaceutical samples to physicians should be prohibited and replaced by a system of vouchers for low-income patients or other arrangements that distance the company and its products from the physician.” The study further suggests that drug and device companies be divorced from participation in CME programs.

However, the authors do note that AMCs should be “able to accept grants for general support of research from pharmaceutical and device companies, provided that the grants are not designated for use by specific individuals. As long as the institution stands between the individual investigator and the company making the grant, the likelihood of undue influence is minimized but certainly not eliminated.”



## Respiratory Therapy™

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The upshot of following these recommendations would be that, “decisions by physicians on which prescription to write and which device to use might become more evidence-based; medical societies’ practice guidelines might become less subject to bias. A greater reliance on objective sources for accurate and up-to-date information would also promote better patient outcomes. Total expenditures on prescription drugs might decline. An increased use of generic products, and, in some cases, a decreased reliance on pharmaceutical agents might be observed... The absence of industry representatives at AMC meetings and lunches and in corridors would increase the sensitivity among medical students and house staff to the values of medical professionalism and scientific integrity... Ultimately, the implementation of these proposals will substantially reduce the need for external regulation to safeguard against market-driven conflicts of interest, and the medical profession will reaffirm very publicly its commitment to put the interests of patients first.” (The foregoing appeared in JAMA, January 25, 2006—Vol 295, No. 4.)

pay for medical education certification. Neither is very likely to happen, given any number of financial and cultural factors. Physicians won’t want to pay, nor will medical educators, nor will the government. Perhaps the best that can be hoped for, an option the JAMA article brings up but dismisses as being of dubious ultimate value, is disclosure. That is, at the least, sources of educational information should be clearly labeled as manufacturer-influenced if that is the case. To a certain extent, this is already being done. Ultimately, then, it falls on the shoulders of caregivers to evaluate the information they receive, and make judgments about the value of the information accordingly.

Les Plesko  
Editor

### Can’t Live With ‘Em...

So what we have is a damned if you do or you don’t situation. Product manufacturers pay for educational courses, so they want to get something out of their investment. Medical practitioners need the courses for certification. You can’t expect the pharmaceutical companies to ante up the big bucks and get nothing in return, and you can’t really expect medical caregivers to home-school themselves. The only other alternatives would be for either caregivers or their educational institutions to pick up the whole tab, or for the government to



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# News

□ August-September 2006

## FOLLOW THE MONEY

Liquid ventilation could help save the lives of premature babies, but the patent-owning company will not market it, saying it lacks profitability, according to a recent report. Respirators don't always provide sufficient amounts of surfactants, so the Nautical School at the University of the Basque Country developed a liquid respiration respirator. The machine simulates placental respiration by filling the lungs of the premature baby with liquid and then the respirator introduces and extracts the required quantity of liquid at a suitable respiratory rhythm. The amount of liquid administered is usually in the order of 10 ml per kg of the baby's weight. Liquid respiration uses perfluorocarbon, since it has a suitable surface tension to maintain pulmonary structure and provides for good interchange. With the liquid ventilator, respirator syringes introduce the oxygenated perfluorocarbon to the last alveola. Here oxygen is released and carbon dioxide taken up in the same way as on the respiration surface. Then the respirator extracts part of the perfluorocarbon from the lungs and introduces the next oxygenated dose. The same machine carries out the removal of CO<sub>2</sub> from the perfluorocarbon and adds oxygen to it. Since liquid is used, pressure associated with conventional assisted respiration is avoided. The respirator, for the moment, is no more than a prototype. In the experiments carried out at the Cruces hospital in Bilbao with artificial lungs and with animals, the results have been very good. It has been applied successfully in more than 80 death-threatening situations in premature babies. But the perfluorocarbon for medical use is not available on the market. As premature babies need very small quantities and no commercial application for adults has been found, the patent-owning company has opted not to market it arguing that it lacks profitability. Thus, an industrial version of the liquid respirator is yet to be developed. (See our News Commentary on page 26. The news release for the foregoing can be found in Medical News Today, April 2, 2006, by Irati Kortabitarte, Elhuyar Fundazioa, iratik@elhuyar.com.)

## NO BRAINER

Hamilton Medical recently released its case study, Ventilator Auto-cycling on a Brain Dead Patient, by Tim France, RRT, Clinical Specialist, Sentara Careplex Hospital, Hampton, VA. An 80-year-old black male was admitted to the hospital's 32 bed ICU after MI post-massive GI bleed. The patient was resuscitated at the nursing home and brought to the ER where he was stabilized and transferred to ICU. He was diagnosed with a significant anoxic brain injury. The patient was ventilated for 4 days before being declared brain dead and removed from mechanical ventilation. This case study is intended to document an incidence of self-cycling while using flow triggering (FT) on a ventilator. The patient was admitted with anoxic brain injury s/p GI bleed and MI. The patient had a history of prostate cancer, hypertension and Alzheimer's Disease. On admission



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vital signs were HR of 130, BP 100/60. Vent settings were: AC/VC+ mode, Vt 500, FIO2 1.0, PEEP 5, Rate 12 and Flow Triggering of 3lpm. ABG results obtained at 2315 were pH 6.99, PCO2 56, PaO2 66, BE -18, HCO3 14 and O2 saturation 85%. Set RR was increased to 16. Blood gases obtained at 0310 were pH 7.31, PCO2 36, PaO2 505, BE -8 and HCO3 18 with saturation of 100%. EEG was obtained with a finding of severe hypoxic encephalopathy with severe grade 3 suppression. No response to photic stimulation. Electroencephalogram silence could not definitively be established. EKG showed sinus tachycardia with a HR of 139. Because of the inconclusive EKG and the presence of spontaneous respirations it was thought that the patient had some brain stem function left. Over the next two days the patient spontaneous rate averaged 24, 8 breaths greater than the set rate. On day four it was noted that the patient heart pulsations were visible through his chest. This coupled with the fact that he exhibited all the signs of brain death except for the presence of spontaneous breathing, prompted a switch from a flow trigger system to a pressure trigger system. After this change, the patient's RR dropped to the set vent rate; eg, spontaneous breathing ceased. The patient's chest was palpated to see if it was moving. It was ascertained from the exam that the patient was indeed apneic. An apnea test was performed that was positive. Shortly thereafter he was declared brain dead. Flow triggering is an extremely sensitive trigger system that enables a patient to initiate a breath with less work than pressure triggering. Pressure trigger systems sense the negative pressure drop caused by the patient's inspiratory effort. Flow trigger provides continuous flow of gas running through the vent circuit during the expiratory phase; when the patient inhales the equivalent of the flow trigger setting a breath is delivered. This small flow change at the airway requires less effort than a pressure trigger system. For this reason FT is widely used as the default triggering system for mechanical ventilation. This case study was completed to bring attention to the possibility that a brain dead patient was ventilated for 4 days because the ventilator was being cycled by the patient's heart palpitations which can cause sufficient pressure changes in the thorax to cause small flow changes in the airway. These pressure changes may be sufficient to cause false triggering. (This is possible, but less likely with a pressure trigger system). Because of this case the hospital instituted a policy that all patients suspected of being brain dead must be assessed for spontaneous breathing on a pressure trigger setting to rule out autocycling. For more information on this case, contact Hamilton Medical at [hammed1.com](http://hammed1.com).

### **DON'T SMOKE (IF YOU'RE A RAT)**

Exposure to nicotine the equivalent of smoking two packs of cigarettes a day produced complicated, abnormal breathing development during the first 18 days of newborn rats, University of Arizona researchers report. A research team found that the required increase in breathing in response to reduced oxygen supply was lower in nicotine-exposed animals compared to the controls over their first nine days, suggesting that prenatal nicotine exposure reduces the ability of a neonatal animal to respond to low blood oxygen, which can lead to prolonged and possibly lethal apneas. Between nine and 18 days, the situation reversed, and nicotine-exposed rats' response was actually higher than controls, showing an overall complicated, abnormal breathing development over the 18 days.

### **GET THE PAPER**

Clinical trials—and particularly randomized trials—are

critical in delivering reliable evidence about the efficacy of an intervention. Clinical trial data can also provide important information about the potential adverse effects of treatment. Currently, not all trials on human participants are reported in the peer-reviewed literature. PLoS Clinical Trials aims to fill this gap. The journal will broaden the scope of clinical trials reporting by publishing the results of randomized clinical trials in humans from all medical and public health disciplines. Publication decisions will not be affected by the direction of results, size or perceived importance of the trial. As an open-access journal, all articles published in the journal will be immediately and freely available online. Join us in supporting these goals, and get your paper read by the widest possible audience. To submit your trial results, contact <http://clinicaltrials.plosjms.org>.

### **RESEARCH AWARDS**

BioMed Central announced the launch of its BioMed Central 2006 Research Awards, which recognize ground-breaking open access research. Awards will be made to the authors of the most outstanding research articles published in BioMed Central's journals during 2006. One award will be made for biology and one for medicine. To be eligible for the awards, articles must be published during 2006 in one of BioMed Central's 150+ peer-reviewed open access journals. To nominate a published article for the award, send an email indicating the article you wish to nominate and your reasons to: [researchawards@biomedcentral.com](mailto:researchawards@biomedcentral.com). A panel of expert scientists and clinicians will choose the winners from a shortlist of nominated articles in January 2007.

### **BREATHE EASIER**

CNEP therapy has been vindicated in a recent study. Originally, the therapy was thought to lead to a small increase in deaths and disabilities of infants, but the study has shown that children treated in the standard breathing tube method face the same risks of long-term disabilities as CNEP-treated children. A couple whose daughter died after the CNEP trial brought suit against the doctors who treated her, claiming that they were not properly informed about the procedure. Their claims have been rejected so far, although the CNEP trial had been investigated by the hospital and the police and criticized by an investigative committee.

### **STIFLED BREATH**

Healthy preterm infants younger than 12 weeks were found to have a "noticeable reduction in expiratory flows compared with control infants and reference values," according to a study at the Hospital Ste Lucas in Brazil. After accounting for differences in body size, researchers noted that even infants who had not been diagnosed with any serious respiratory disease suffered from an increased incidence of wheezing and chronic cough. The study found that prematurity is a key factor in the development of persistent airway obstruction. Additionally, air flow was up to 30% lower in males. Researchers speculated that this might contribute to the increased neonatal morbidity and mortality related to respiratory illness for preterm male infants.

### **SNORE SCORE**

According to researchers at Cincinnati Children's Hospital, infants of parents who snore are three times as likely to snore themselves when compared to infants whose parents don't snore. They also found that children who have a tendency to develop allergies and atopy also have a higher likelihood of



being snorers. Black children seem to have the highest likelihood of being chronic snorers. The researchers studied 681 children, 45% girls, 80% white, who were just over one year old and whose parents were atopic. Twenty percent of the mothers and 46% of the fathers were habitual snorers. The incidence of snoring among infants who had at least one parent who was a habitual snorer was three times greater than infants whose parents did not snore.

## FREE INFO

The Federal Research Public Access Act, recently introduced to the US Congress, calls for every federal agency with a budget of more than \$100 million to implement a public access policy to ensure that articles resulting from the research funded by the agency are made openly available online within six months of publication. The legislation would make agencies require each agency-funded researcher to submit an electronic copy of the final manuscript that has been accepted for publication in a peer-reviewed journal and to ensure that the manuscript is preserved in a stable, digital repository maintained by that agency or in another suitable repository that permits free public access, interoperability, and long-term preservation. It also requires that free, online access to each taxpayer-funded manuscript be available as soon as possible, and no later than six months after its publication in a peer-reviewed journal.

## LYING IN PLAIN SIGHT

Pharmaceutical firms are inventing diseases to sell more drugs, researchers have warned. Disease-mongering promotes non-existent diseases and exaggerates mild problems to boost profits, the Public Library of Science Medicine reported. Researchers at Newcastle University in Australia said firms were putting healthy people at risk by medicalizing conditions such as menopause. But the pharmaceutical industry denied it invented diseases. Among conditions cited as “disease mongering” are irritable bowel syndrome, and menopause. Report authors David Henry and Ray Moynihan criticized attempts to convince the public in the US that 43% of women live with sexual dysfunction. They also said that risk factors like high cholesterol and osteoporosis were being presented as diseases - and rare conditions such as restless leg condition and mild problems of irritable bowel syndrome were exaggerated.

The report said: “Disease-mongering is the selling of sickness that widens the boundaries of illness and grows the markets for those who sell and deliver treatments. “It is exemplified most explicitly by many pharmaceutical industry-funded disease awareness campaigns - more often designed to sell drugs than to illuminate or to inform or educate about the prevention of illness or the maintenance of health.” The researchers called on doctors, patients and support groups to be aware of the marketing tactics of the pharmaceutical industry and for more research into the way in which conditions are presented. They added: “The motives of health professionals and health advocacy groups may well be the welfare of patients, rather than any direct self-interested financial benefit, but we believe that too often marketers are able to crudely manipulate those motivations.

## NOT SO FAST

Rapid lung function decline significantly increases the risk of death and hospitalization for individuals with COPD, according to a paper published in the American Journal of Respiratory and Critical Care Medicine, published by the American Thoracic Society. David Mannino, MD, of the University of Kentucky

Medical Center, and two associates found that patients with advanced COPD and rapid lung function decline are 10 times more likely to die than individuals with normal lung function. Over the course of three years, the investigators analyzed 13,756 middle-aged adults, all of whom participated in the 1986 Atherosclerosis Risk in the Communities Study and provided baseline information on respiratory symptoms and diseases. The researchers tested the participants’ lung function twice, once at the start of the study and during a follow-up three years later. The authors classified patients with the worst lung function as “rapid decliners.” Twenty-five percent of the entire study population (3,437 individuals) fell into this high-mortality category. Of the 720 subjects who died during the study, 273 (38%) were considered rapid decliners. In addition, patients in advanced stages of COPD who were also rapid decliners were hospitalized at a rate 40 times higher than those with normal lung function at baseline who had no rapid lung decline over the three-year period. Mean annual loss of lung function in the overall cohort was 62 ml. The mean loss of lung function as a percentage of the baseline value was 1.5 percent annually. Participants in the most rapidly declining quartile had a mean annual loss of 171 ml, which was 4.7% of the baseline level per year. The authors noted that the average annual loss of 62 ml in lung function was higher than that shown in other similar studies, including the Honolulu Heart Cohort at 26 ml, the Busselton Health Study at 30 to 40 ml, the Nottingham Study at 38 ml, and the Copenhagen City Heart Study at 22 to 38 ml. The authors acknowledged the limitations of their analysis. For example, they only measured lung function twice during the three-year investigation. “It is possible that people may have had a really good day or really bad day at either the baseline or follow-up examination, influencing our results,” said Dr Mannino. He noted that the group in which rapid decline showed the greatest predictive value for death and hospitalization was also the one least likely to be affected by any source of error. Although 461 rapid decliners were classified as having respiratory symptoms, none had either a lung abnormality or lung disease. The impact of rapid decline in adults with normal or near-normal lung function at baseline suggested that this group of people may need more frequent screening and interventions beyond what is typically recommended. Reported in Medical News Today.

## BAD BAD BAD

The New York Times reported that Federal officials reached a \$10 million settlement yesterday with Lincare Holdings, the maker of home oxygen and other respiratory equipment, over accusations that Lincare paid kickbacks to doctors. Lincare agreed to pay \$10 million to settle accusations by the Office of the Inspector General of the Department of Health and Human Services that it illegally paid doctors to recommend the company to patients. The settlement was the largest administrative recovery by the office. The company, based in Clearwater, FL, did not admit any wrongdoing. The federal officials accused Lincare of paying doctors to refer patients to the company from 1993 through 2000. Doctors were treated to sports tickets and gift certificates, taken on fishing trips and golf outings and given office and medical equipment, the officials said. Lincare was also accused of giving doctors kickbacks through payments disguised as consulting fees, like medical director agreements. Earlier in the year, the Inspector General reached settlements with two doctors accused of accepting kickbacks from Lincare. Other inquiries involved accusations that Lincare inappropriately sought payments under Medicare

and other government health care programs. The company said combined settlements totaled \$12 million.

## **BREATHE DEEPER**

Adults and children with asthma will breathe deeper and have better control over their asthma with inhaled corticosteroids than with the medicine cromolyn, according to a new review of recent studies comparing the two treatments. Researchers at the University of Pennsylvania School of Medicine noted that adult asthma patients using inhaled steroids such as Beclovent, Pulmicort and Flovent, had on average three fewer severe asthma flare-ups each year compared to patients using inhaled cromolyn, sold under the brand name Intal. Patients taking the steroids also scored significantly higher on tests of lung function and used their rescue inhalers less often than those taking cromolyn. The review appeared in the current issue of *The Cochrane Library*, a publication of The Cochrane Collaboration, an international organization that evaluates medical research. The consensus still leaves room for cromolyn treatment, according to William Storms, MD, an allergist at the University of Colorado Health Sciences Center and director of the William Storms Allergy Clinic in Colorado Springs. "Any expert would agree that inhaled corticosteroids are preferred first-line therapy for treatment of persistent asthma, which requires daily therapy. But we also will agree with the NIH asthma guidelines, which state that cromolyn and other drugs are alternative therapies," Storms said. Sodium cromoglycate and inhaled corticosteroids both block the action of certain inflammatory cells in the lungs. Physicians recommend both types of medication for persistent asthma, but individual studies disagree about which type of medication works best, the reviewers found. They noted that the safety of sodium cromoglycate has been well established, but the effectiveness of sodium cromoglycate in controlling asthma symptoms may be limited. The lack of effective control might be one reason cromolyn has fallen out of favor compared to inhaled corticosteroids since the 1990s. Cromolyn's manufacturer has changed several times during the past two decades, which may also explain why the drug's popularity has waned, Storms said. The succession of companies "did not spend one dollar in research in the past 20 years to study cromolyn. All of the data are old and most are forgotten." The Cochrane reviewers examined 17 studies involving 1,279 children and eight studies involving 321 adults with asthma. They found no differences in serious side effects between those using the steroids and those using cromolyn, but acknowledge that adverse effects were reported inconsistently. The study concluded that inhaled corticosteroids were superior to cromolyn regardless of the severity of the asthma, and suggest the results as so decisive that future studies comparing the two types of drugs may not be warranted. Storms said some patients may still prefer to stay away from inhaled corticosteroids. "We need to examine the total patient and treat the patient, not the disease. When I tell patients I am suggesting they take an ICS, many of them get that wide-eyed gaze because of the word 'steroid.' Then I discuss the fact that ICS are inhaled and not systemic but many patients would still prefer to try something else, if possible. That something else could be cromolyn."

## **BLACK, NO SUGAR**

A new study has found that caffeine therapy can help babies with apnea of prematurity breathe better, perhaps because of its stimulant effect on the respiratory system. The ongoing study, reported in the *New England Journal of Medicine*, involves 2,000 babies, born 27 weeks after conception. Some of them received

caffeine therapy while others had a placebo until apnea therapy was not required any more. They were all randomly selected. The babies were examined just before they left hospital and went home. If the babies still needed supplementary oxygen therapy it meant they still had BPD. Thirty six percent of the premature babies who had caffeine therapy still required supplemental oxygen when they were discharged from hospital, compared to 47% for the placebo therapy babies. The caffeine therapy group were on ventilator therapy for one week less than the placebo group. Brain injury and death rates were the same for the two groups. The group on caffeine therapy put on a bit less weight. The researchers will report follow up findings in two-years' time, and again when the babies reach the age of 5. (From *Medical News Today*.)

## **BEFORE THE MAST**

Researchers at Stanford University developed a mouse model of asthma that more closely mimics human disease than standard asthma models, in order to demonstrate that mast cells are key drivers of the most important inflammatory, structural, and functional changes observed within the lungs in chronic asthma.

The authors examined wild-type mice as well as mast cell-deficient mice to assess the role of mast cell receptors during chronic asthma. They demonstrated that mast cells are required for the development of airway hyperresponsiveness and airway inflammation. The critical novel finding was that allergen inhalation drives an expansion of mast cells in the airways of wild-type and reconstituted mice, which is associated with increased lung expression of the Fc receptor common gamma chain. Their studies reveal that Fc gamma receptor signaling is critical for this allergen-driven mast cell expansion, airway hyperresponsiveness, and the induction of airway inflammation. As such, the activation of mast cells via Fc gamma receptor-dependent mechanisms represents an attractive therapeutic target in asthma. (Reported by *Medical News Today*.)

## **PIPETTES**

Great Ormond Street Hospital for Children NHS Trust secured long term funding for its life saving tracheal service, which treats children suffering from extremely narrow windpipes (Long Segment Tracheal Stenosis). The surgery to correct LSTS has historically been very difficult and where surgeons have little experience in this rare condition, results are not always good. A new service offered by GOSH has produced better results and has now secured long term funding from government agency NSCAG. The tracheal team at GOSH is a group of health professionals who have been brought together to provide a range of expertise and includes specialists in ENT, interventional radiology, intensive care, cardiothoracic surgery and physiotherapy. The surgical technique the team used, tracheoplasty, involves making cuts into the narrowed part of the trachea, which can sometimes be only a few millimetres wide, and sliding the two sections over each other until the part of the trachea that is normal width is reached. The slide tracheoplasty technique was first described in 1990 by Peter Goldstraw and Victor Tsang, but it is only recently that it has become a widespread operation.

## **NOZONE**

In a small, poorly ventilated room, an indoor air purifier that produces even a few milligrams of ozone per hour can create an ozone level that exceeds public health standards, researchers at UC Irvine have found. Scientists also discovered that ozone

produced by air purifiers adds to ozone already present in any room, a prediction that had never been experimentally verified in a realistic indoor environment. The findings, published in *Medical News Today*, were presented in the *Journal of the Air & Waste Management Association*, and are being studied by officials deciding how to regulate the distribution of indoor air purifiers. The EPA has issued advisories discouraging use of air purifiers, but the devices remain on the market because no agency has the outright authority to regulate how much ozone they produce. Indoor air purifiers are advertised as safe household products for health-conscious people, but some purifiers produce ozone during operation. For example, certain widely used ionic air purifiers, which work by charging airborne particles and electrostatically attracting them to metal electrodes, emit ozone as a byproduct of ionization. Depending on the design, some ionic purifiers emit a few milligrams of ozone per hour, which is roughly equal to the amount emitted by a dry-process photocopyer during continuous operation. Ozone can damage the lungs, causing chest pain, coughing, shortness of breath and throat irritation. It can also worsen chronic respiratory diseases such as asthma and compromise the ability of the body to fight respiratory infections, even in healthy adults. For the current study, the researchers tested several types of air purifiers for their ability to produce ozone at 40 to 50% relative humidity in various indoor environments, including offices, bathrooms, bedrooms and cars. The largest increase in steady ozone levels occurred in small rooms with little ventilation, especially those containing materials that react slowly with ozone such as glossy ceramic tile, PVC tile and polyethylene, which is used in plastic. Ozone reacts quicker with materials such as carpet, cloth, rubber and certain metals, destroying itself in the process.

## ON THE DEFENSIVE

*Medical News Today* reports that for the first time, scientists have documented an organ-specific innate immune system. In research published in the April edition of the journal *Immunity*, scientists at the University of California, San Diego School of Medicine outlined the unique mechanism by which the lung shapes its defensive strategies against microbial invasion. It was found that the alveoli possess a complex immune system in which the macrophage is repressed in its steady state, activated when called upon to fight invading microorganisms, and then re-repressed, in a circuit that is unique to this microenvironment. The researchers' data outlines a complex circuit in which the alveolar macrophages circumvent the inhibition by TGF $\beta$  for a brief period of time, in order to perform their immune task. This is accomplished through regulation of TGF $\beta$  activity by integrins. This regulation allows the alveolar macrophages to take on their "killer" function - the ability of macrophages to engulf invading microorganisms - but only for a very limited period of time. The mediating role of TGF $\beta$ , briefly inactivated by the integrin, is then restored by one of the lung's own enzymes, the MMP9.

## OUTPATIENT REHAB

Pulmonary Rehabilitation and Respiratory Therapy Services in the Physician Office Setting, by S. Birnbaum and B. Carlin, Drexel University, is a study that details how pulmonary rehabilitation services benefit patients with chronic lung disease by reducing symptoms and restoring independent function. According to the paper's abstract, "With a multidisciplinary approach to individual patient care through education, exercise, and psychosocial interventions, healthcare costs and utilization

may be reduced. While pulmonary rehabilitation services have typically been provided in a facility setting, many respiratory care services can be safely provided and appropriately reimbursed in the outpatient physician office setting, with appropriate physician supervision. After reviewing the utility of pulmonary rehabilitation for patients with chronic lung disease, the supervision, documentation, coding, and reimbursement requirements for providing rehabilitative respiratory care services in the outpatient office setting are detailed." To find out more, type in the article name in Entrez Pub Med.

## TIME AND TIDE

Hamilton Medical's Newsletter recently highlighted the study, Lung-function tests in neonates and infants with chronic lung disease: Tidal breathing and respiratory control. (*Pediatr Pulmonol* 2006 May;41(5):391-419, by D.N. Baldwin, J.J. Pillow, J. Stocks and U. Frey, from the Centre for Child Health Research and Telethon Institute for Child Health Research, University of Western Australia, Perth, Western Australia, Australia.) The paper is the fourth in a series of reviews that summarize available data and critically discuss the potential role of lung-function testing in infants with acute neonatal respiratory disorders and chronic lung disease of infancy. The current paper addresses information derived from tidal breathing measurements within the framework outlined in the introductory paper of this series, with particular reference to how these measurements inform on control of breathing. According to the paper, infants with acute and chronic respiratory illness demonstrate differences in tidal breathing and its control that are of clinical consequence and can be measured objectively. The increased incidence of significant apnea in preterm infants and infants with chronic lung disease, together with the reportedly increased risk of sudden unexplained death within the latter group, suggests that control of breathing is affected by both maturation and disease. Clinical observations are supported by formal comparison of tidal breathing parameters and control of breathing indices in the research setting. *Pediatric Pulmonology* is published by Wiley-Liss, Inc., abstract © 2006 Wiley-Liss, Inc.

## PRODUCT NEWS

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## NEW AGENTS BEING STUDIED FOR COPD AND ASTHMA

Jeff Borrink, BS, RRT

Information was provided by Hamilton Medical's Intelligent Ventilation Newsletter.

New agents that are capable of suppressing the inflammatory response in COPD and asthma patients are currently being tested. It is hoped that they will have potential for both reducing symptoms of these diseases, as well as slowing down the



progression. One such agent that is being developed and studied by Altana Pharmaceuticals is Roflumilast, which would be marketed under the brand name Daxas. Roflumilast is being investigated for the treatment of both COPD and asthma, and has already been studied in more than 16 clinical trials involving more than 4,400 patients with COPD and asthma. Additional studies are currently underway. Roflumilast is a PDE-4 inhibitor, which is a nonsteroidal anti-inflammatory drug. Roflumilast is very specific for a certain enzyme that is involved in smooth muscle contraction, which is one of the features of bronchospasm. Although some analysts are intrigued by the principle of interfering with this pathway, many are skeptical about the value of these drugs. Some analysts have concerns about possible side effects, mainly those affecting the intestinal tract. Currently, no PDE-4 inhibitors have been approved by the Food and Drug Administration (FDA). It is hoped that the results of the current studies underway will open up a new class of drugs that can be used for the treatment of COPD and asthma. However, long-term studies are needed to fully assess the effect of these agents on health-related quality of life.

## THERAPIST-DRIVEN PROTOCOLS

Justin Tse, RRT-NPS

Information was provided by Hamilton Medical's Intelligent Ventilation Newsletter.

There have been many articles written to support protocols for weaning from mechanical ventilation; however, there have been some negative articles published as well. A 2002 study done at Johns Hopkins concluded that patients being weaned from mechanical ventilation by physician directed methods had a mean length of stay of 141.6 hours while therapist driven protocols had a mean of 146.3 hours. Although this seems to be a statistically small difference, researchers noted that therapist driven protocols varied with ICU routines and staffing levels. Therapist and physician directed protocols vary in many institutions but all depend on one main factor, staffing. Today, many ICUs are filled to capacity and there is more work than staff can reasonably handle. This can have an effect on weaning from mechanical ventilation.

Also, protocols are designed to help with a wide variety of patients, but not every patient can fit into every protocol. When patients do not fit into a particular protocol, they may end up being ventilated longer than is necessary. In a retrospective study, 36 patients were labeled as "patients who fail" in a hospital ICU; however, in the study, it was unclear whether these 36 patients were the overall number of mechanically ventilated patients or just those that failed to meet the weaning protocol criteria. The study reported that 7 of the 36 patients were subsequently extubated based on an individual assessment of their status. They concluded that "in some cases, physician judgment can improve the rates of successful weaning." This suggests that not all protocols work for every patient. Closed-loop control can be the answer to some of the limitations to implementing protocols. Closed-loop modes such as Hamilton's adaptive pressure modes (AVTS/ASV) are not just a set of rules or protocols that make the patients conform to the settings they are placed on, but continuously analyzes each patient's "individual status" and lets the patient and clinician work together to provide the best outcome for the patient. A protocol including AVTS/ASV can improve patient outcomes by decreasing ventilator days, decreasing sedation, decreasing length of stay, and decreasing overall cost to the hospital institutions. Adaptive modes can reduce the "human" factors

which often "trip" up actual implementation of, for example, daily assessment and implementation of a spontaneous weaning trial. There are several ways to correct flow limitation. Common solutions are to increase peak flow, set a decelerating waveform or increase tidal volume. An increasingly common intervention is to initiate variable flow modes such as pressure control or pressure support. These modes are able to respond to a patient's inspiratory demand by increasing the flow that is available to the patient. Unlike previously documented volume control/flow control waveforms, in the pressure control mode the ventilator will increase the flow available to the patient because flow is not fixed. As patient demand increases the flow rate increases while the pressure waveform stays fairly constant. While the benefits of pressure control are evident in flow limitation situations, pressure-based modes have an inherent problem in that any change in patient compliance or resistance can change tidal volume. Constant assessment of tidal volume while using a pressure-based mode is important and can be time consuming. For this reason there are modes that give clinicians the best of both worlds; a target tidal volume that is delivered to the patient with a constant pressure during the inspiratory phase instead of a constant flow. A "dual control" mode such as Adaptive Pressure Ventilation (APV) offered with the Hamilton Galileo Gold is able to achieve both goals. The clinician sets a target tidal volume and the ventilator titrates pressure up or down to maintain tidal volume. Clinicians also set alarms to limit the increase and decrease in pressure. The result is a patient can receive variable flow without the risk of lost tidal volume. Patients may be more comfortable and use less sedation, also therapists may spend more time doing other assessments besides tidal volume maintenance.

Commentary - Volume targeted pressure modes are commonly employed today. Modes such as APV, PRVC, autoflow and Volume + have similar characteristics. It is important for the clinician to understand the specific algorithms and limitations of these modes despite their advantages. Consider how the target volume is measured; is it proximal or from within the ventilator? Is the feedback loop measuring inspired volume vs expired volume (eg effect of leaks etc)? Is the targeted Vt corrected for circuit compliance? Are there safety features that prevent pressure from being titrated up to unsafe levels (eg until the high pressure alarms)? In fact, some ventilators will, often unbeknownst to the user, while in a constant flow volume mode (AC/IMV), switch to a variable flow to allow the patient to achieve more flow. Clinicians need to be aware of such differences between ventilator brands. I have not infrequently observed patients on "ARDSnetwork" with Vt set at 6cc/kg, yet the exhaled Vt reveals Vt's much higher. These "features" are marketed as beneficial, e.g. preventing flow starvation; however it's debatable whether we should allow the patient to take large Vts when trying to implement a protective lung strategy. One could argue that this might be better than having the patient flow starved etc. Another argument might be that the ventilator should respond in an easily discerned and predictable fashion—what you set is what you get. – Paul Garbarini MS, RRT Clinical Manager HMI

## INSTANT RECALL

Hamilton Medical, Inc recently announced that it is initiating a nationwide voluntary recall of 47 Raphael ventilators with older generation software. Current Raphael Color and Raphael XTC ventilators are not affected by this action. Only four customer facilities have been impacted by this action. Hamilton Medical, Inc has already contacted these facilities regarding



immediate field corrections. The voluntary recall was being conducted because the ventilator, under certain very specific conditions following an oxygen cell calibration without a compressed air supply, as instructed in the Raphael Operator's Manual, can be put into a state where no visible or audible alarms are triggered. Hamilton Medical investigated a single complaint and found that a software algorithm designed to suppress false positive alarms may preclude any alarm under this scenario. "It should be noted," states David Costa, Vice President for Hamilton Medical, Inc, "that the oxygen cell calibration is intended to be performed while the Raphael is connected to both air and oxygen high pressure gas sources. In the reported incident, this was not the case." The ventilators affected were those with software version 2.2x, Raphael Silver, 2.2xS and Color, 2.2xC and 2.2xCU. Those affected by this recall were instructed to verify the proper function of their devices as described in Section 3 of the Operator's Manual, attach a caution sticker to the ventilator advising the clinician to check the LowMinVol alarm after oxygen cell calibration and change in-house test procedures for oxygen calibration as indicated in the corrective action package supplied to each affected user. The ventilators may continue to be used after these steps are complete. Hamilton Medical also arranged for all customer units affected by this action to receive new current generation software at no charge; that will not only eliminate this problem but also provide noninvasive ventilation (NIV) and with tubing resistance compliance (TRC) along with a bi-directional apnea back-up among other enhancements. Contact Hamilton-medical.ch.

## SPACE LAUNCH

Spacelabs Medical announced the availability of its Ultraview line of patient monitors. The compact monitor supports the company's commitment to open standards and connectivity, including WinDNA, which brings workstation functionality for charting and other hospital applications to point of care monitoring. The monitor enables hospitals to augment their existing installation of Spacelabs monitoring. A wireless networking option supports central surveillance during patient transport, and the Clinical Event Interface connects to pagers and other handheld devices. For more contact spacelabs.com.

## STAR TRIP

Nova StatStrip from Nova Biomedical is a patented blood glucose monitoring system that incorporates new four-well glucose measuring strip technology. Current glucose strips use only one well, but Nova's Multi-Well system measures and corrects hematocrit interference as well as interferences from Tylenol, uric acid, ascorbic acid, maltose, galactose, xylose, and lactose. StatStrip eliminates oxygen interference to provide accurate glucose results. In addition, these strips require no calibration coding. StatStrip's six-second analysis time, color touch screen operation, and simple operating steps make bedside glucose testing fast and easy. Contact novabio.com.

## OMNI-POTENT

Roche Diagnostics announced that it has received clearance from the FDA for measuring pH in pleural fluid samples on the Roche OMNI blood gas analyzers. The Roche Diagnostics OMNI Modular 1-9, OMNI C, and OMNI S1-6 instruments are the only blood gas analyzers in the industry cleared by the FDA to run this test. Said Rod Cotton, Senior Vice President, US Point of Care Diagnostics, Roche Diagnostics, "With this new testing parameter on the Roche OMNI blood gas analyzers, hospitals

will be able to get quick results that are critical for diagnosis and treatment." A 1998 report by the ACCP determined that only pH values provided by blood gas machines are sufficiently accurate when pleural fluid pH is used for decision making (Cheng, DS et al. Comparison of Pleural Fluid pH Values Obtained Using Blood Gas Machine, pH Meter, and pH Indicator Strip. Chest 1998; 114:1368-1372). Roche Diagnostics OMNI blood gas analyzers provide point-of-care settings with additional time-saving features including a fully-automated Quality Control system (Auto QC) with up to 40 days of QC onboard, zero maintenance electrodes, and liquid calibration which eliminates the need for gas tanks, and basic blood gas and pH results in less than 60 seconds. The measurement of pH in pleural fluids is currently available on the Roche OMNI blood gas analyzers. There is no additional hardware or reagents required to perform pH testing on pleural fluid samples. Roche Diagnostics has also updated its software package for the OMNI S Blood Gas Analyzer. The onboard reagent stability has been extended from 28 to 42 days, providing 50% more user time. This improvement provides laboratories operational and flow efficiency that results in less reagent waste and less downtime from pack changes. The new Roche OMNI S onboard patient trending feature gives healthcare providers real-time and/or historical trending. For example, intensive care unit (ICU) caregivers have convenient access to a self-contained glycemic control platform for entering glucose results. Another application is for respiratory therapists who can trend any four blood gas and co-oximetry parameters to effectively monitor the efficiency of their therapies. Onboard patient trends can be accessed on the Roche OMNI S analyzer screen or from the report printout. For more information contact roche-diagnostics.com.

## SUCK IT UP

Boehringer Laboratories, Inc announces the New Platinum Series Suction Regulators, a line of higher performance suction control products. These products carry a 12 year warranty thanks to their workhorse design and durable materials of construction. Technological advances such as the Self Cleaning Technology air curtain feature and the patented, virtually indestructible XL gauge make the Platinum Series the next generation in suction regulators. No competitor can match the performance or durability. The Platinum Series products are available for a free 30 day evaluation. With superior performance and ground-breaking warranties that control costs, the Boehringer Laboratories, Inc has changed the way healthcare facilities shop for suction controls. The important clinical advantages built into each design have made these products the choice of healthcare professionals worldwide. Contact boehringerlabs.com, (800) 642-4945.

## REORGANIZED

Viasys Respiratory Care Inc, part of Viasys Healthcare Inc, is combining the Sales and Marketing organizations into three care specific areas: Sleep Diagnostics/Therapy, Critical Care, and Pulmonary Diagnostics. The restructuring will align Viasys Respiratory Care with its customers' specialties forming a more responsive and efficient organization on a global basis. Rebecca Mabry was appointed General Manager, Sleep Diagnostics and Therapy. She has global responsibility for the development and execution of the Sleep Diagnostics and Therapy business plan. Concurrently, she will manage Viasys Respiratory Care Marketing Communications as a Shared Service for Critical Care, Pulmonary Diagnostics and Sleep Diagnostics/Therapy.

Ruth Lundstrom was appointed Senior Vice President, Sales and Marketing—Critical Care. She has responsibility for worldwide ventilation products marketing, as well as her current responsibilities of directing the US Critical Care Sales team. Matt Margolies was appointed Senior Vice President, Sales and Marketing—Pulmonary Diagnostics. He has responsibility for worldwide pulmonary function products marketing, as well as his current responsibilities of directing the US Diagnostic Sales and National Accounts Purchasing Organization teams. The company appointed John Imperato as Senior Vice President, Business Operations. He will assume responsibility for Viasys Clinical Services (VCS), in addition to his current responsibilities for overseeing the business unit control and finance functions and his corporate responsibilities for financial planning and analysis. Imperato has held senior management positions with Rorer Pharmaceuticals, Rhone-Poulenc Rorer and Omnicare Clinical Research.

## SMART AND CEREBRAL

Somanetics offers its Invos Cerebra/Somatic Oximeter. Somanetics' Invos System is the only noninvasive oximeter to provide simultaneous cerebral/somatic monitoring of changes in regional blood oxygen saturation. Up to four noninvasive sensors may be used to gather real-time hemodynamic change data from the brain and body area under the sensors. This regional oxygen saturation (rSO<sub>2</sub>) value is like a vital sign that helps intensive care teams detect potentially harmful oxygenation issues such as those associated with seizures, neurologic damage, renal failure, low cardiac output and shock. When rSO<sub>2</sub> values dip toward or beyond threshold levels, the care team can intervene to potentially lessen or prevent complications. Contact [somanetics.com](http://somanetics.com).

## EXPANDED ACCURACY

The OxiMax N-600 Pulse Oximeter with LoSat Expanded Accuracy Range: Clinicians can more effectively monitor neonates with the OxiMax N-600 pulse oximeter from Nellcor. It delivers Nellcor's LoSat expanded accuracy range in conjunction with OxiMax adhesive sensors, to help clinicians better manage infants with congenital heart disease. The LoSat feature ensures the industry's widest specified accuracy range: 60% to 100% SpO<sub>2</sub> (vs. the standard 70% to 100% range) for improved patient assessment in the lower saturation ranges. The OxiMax N-600 pulse oximeter has Nellcor's latest digital signal processing technology to deliver accurate readings during low perfusion, patient motion and other forms of signal interference common in the NICU. It also incorporates Nellcor's unique SatSeconds alarm management technology, which offers a safe, practical way to reduce nuisance alarms. Together, these technologies assure efficient, reliable monitoring of challenging neonatal patients. The complete line of OxiMax sensors includes several models specifically for neonatal patients, such as the OxiMax SoftCare nonadhesive sensors designed to prevent adhesive-related skin trauma. SoftCare sensors are made of a soft, pliable foam material that wraps around the infant's foot and fastens with Velcro instead of adhesive tape, providing excellent fit even for micro-preemies under 1.5 kg. In addition to the OxiMax N-600 pulse oximeter and related monitors sold by Nellcor, most leading patient monitor manufacturers offer OxiMax compatibility in their products, making it easy to standardize on Nellcor OxiMax pulse oximetry in the NICU.

## WIRELESS

Nonin's Avant 4000 System is a wearable digital pulse oximeter that connects wirelessly to a tabletop display. Using Bluetooth technology, the Avant 4000 provides continuous monitoring for your smallest patients—even in a Kangaroo Care setting. The lightweight, durable system features PureSAT signal processing technology, 120 hours of battery life and 33 hours of memory. In addition, the Avant 4000 is compatible with Nonin's full line of PureLight sensors. For more information, contact Nonin Medical, Inc at (800) 356-8874 or [nonin.com](http://nonin.com).

## ALL CAPS

CAS Medical Systems, Inc introduced the first capnography/oximeter combining Masimo SET pulse oximetry and Oridion Microstream CO<sub>2</sub> technology. The CAS 750C, at 2 kg (4.4 lbs), is ideal where space is at a premium. Large digits, brightness control, color-coded fields and direction function keys facilitate operation and access to information. The unit can store up to 480 events for up to 24 hours and can be printed to an optional infrared printer. Accessories include a carry bag, roll stand, and various mounting solutions. Contact (800) 227-4414, [casmed.com](http://casmed.com).

## CAPITAL IDEA

Discovery Laboratories has entered into an agreement with Kingsbridge Capital in which the private investment group is providing up to \$50 million to support Discovery's future growth through the purchase of newly-issued shares of its common stock. The company said the financing will provide Discovery with the resources to develop Surfaxin through the final stages of US and European regulatory review. It will also allow Discovery to support its manufacturing and commercialization initiatives and develop its Aerosurf product. Kingsbridge will purchase up to 490,000 shares of common stock at about \$5.62 per share.

## DAILY DOSING

A study by researchers at UCLA and other universities looked at long-term evaluation of once-daily inhaled tiotropium in COPD. Patients with stable COPD were enrolled in two identical randomized double-blind placebo-controlled one-year studies. Patients inhaled tiotropium once daily as a dry powder. Tiotropium provided significantly superior bronchodilation relative to a placebo, and Tiotropium recipients showed less dyspnea, superior health status scores, and fewer COPD exacerbations and hospitalizations.

The study, published in ERJ, says Tiotropium is an effective, once-daily bronchodilator that reduces dyspnea and chronic obstructive pulmonary disease exacerbation frequency and improves health status.

## A NEW ERA

"A new era in patient respiration and oxygenation monitoring has begun," says Jim Brandt, Manager for Bemes, Inc, the newly appointed USA Master Distributor for SenTec AG. Bemes will lead a group of select regional dealers who will launch the SenTec Digital Monitoring System with the V-Sign sensor. The unique sensor provides continuous tcPCO<sub>2</sub>, SpO<sub>2</sub> and pulse from a single, non-invasive sensor! Early clinical tests have shown the V-Sign is unlike any cutaneous sensor of the past. The tiny 3-gram sensor uses twin thermistors to slightly warm the skin. Sensing gases in immediate proximity to the preferred central circulation of the cranium, the digital technology assures fast, reliable gas measurements and SpO<sub>2</sub> measurements even under

most low flow and systolic pressure conditions. Thus, this unique sensor improves the way ventilated, non-invasively ventilated, extubated and sedated patients can be managed. Contact [sentec.ch](http://sentec.ch).

## A SAFE PLACE

RF Technologies' new Safe Place 4.1 provides critical equipment monitoring in a single integrated, easy-to-use network system. Safe Place enables birthing and pediatric Units to meet new JCAHO standards for preventing infant and child abductions. In Emergency Departments, RF Technologies' network solution helps prevent elopements. On acute care floors, Safe Place reduces the risks and costs associated with wandering and patient falls. In addition, RF Technologies integrates its asset management system into Safe Place, creating the first total global healthcare facility enterprise solution. Features include network integration, remote monitoring, equipment management, nurse assistance, and fall management. Contact [rft.com](http://rft.com).

## CERTIFIED

Viasys Healthcare Inc announced today that Viasys Respiratory Care Inc has been audited by the British Standards Institution and awarded certification under International Organization for Standardization ISO 13485:2003. This certification covers a wide range of products including continuous positive airway pressure (CPAP) systems, gas blenders, accessories, cardiopulmonary diagnostics, sleep diagnostics, ventilators, oximeter products and respiratory care equipment. Contact [viasyshealthcare.com](http://viasyshealthcare.com).

## PRO-STAR

Respironics, Inc recently released its REMstar Pro M Series, the second model in its M Series line of sleep systems with C-Flex. The REMstar M Series is the only complete line of sleep therapy systems that provides proven patient comfort and ease of use in a sleek, modern design. The products are designed for the treatment of adults who have obstructive sleep apnea. With its small size, three easy-to-use primary control buttons and more lifestyle-oriented design, the REMstar M Series is targeted at improving the patient's acceptance to therapy. Comfort features such as ramp and integrated humidification are incorporated into the design. The optional ramp feature reduces the air pressure when a patient is trying to fall asleep and then gradually increases (or ramps) the pressure until the device reaches the patient's prescription setting. For patients using humidification, a less obtrusive humidifier chamber adds to the sleek appearance of the platform, and is easier to remove and fill. REMstar Pro is also able to automatically compensate for different altitudes. To help make therapy more comfortable, the REMstar Pro M Series features C-Flex technology. C-Flex tracks the patient's breathing and lowers the amount of pressure delivered during exhalation. With three settings, patients have the ability to select the level of pressure relief that's right for them, without altering the benefits of prescribed therapy. C-Flex helps to make exhaling against the CPAP pressure easier, providing a more comfortable treatment and ultimately increasing the likelihood of compliance. In a recent study involving both CPAP and C-Flex users, remarkably, after three months, patients using C-Flex technology used their therapy an average of one-hour and 42-minutes longer per night than patients on traditional CPAP. In a separate study, patients using C-Flex had a significantly greater satisfaction with treatment comfort and interface comfort, and greater overall satisfaction

with therapy at six months. The REMstar Pro M Series has also been designed with an improved data logging system to make data management more efficient. Reports are easily accessible to read and share among physicians/clinicians and homecare providers. Equipped with an Encore Pro SmartCard accessory module, the REMstar Pro records and reports advanced compliance information such as apnea/hypopnea index, snoring, and leaks. A self-management feature allows the proactive user to assess the therapeutic benefit of treatment. Contact [respironics.com](http://respironics.com).

## NOT NEBULOUS

In its recently released study of the global nebulizer market, Cambridge Consulting named PARI the market dominator for high-end, differentiated nebulizers in the United States and Germany. This follows the September Frost & Sullivan Product Differentiation Innovation Award for PARI's TREK compressor nebulizer system. Both the recognition as the market leader and the award for innovative technology speak to PARI's continuing commitment to improve the lives of people afflicted with respiratory disease. Cambridge Consulting's 2006 survey noted that global nebulizer market revenues are expected to grow from \$288.5 million to \$398.4 million in 2010. In the two largest markets in Europe and the Americas, PARI was named the market leader for differentiated nebulizers mainly used to treat asthma, COPD and cystic fibrosis. PARI Respiratory was also recognized with the Frost and Sullivan award for product differentiation for its TREK nebulizer system. The TREK is a lightweight, portable compressor system that can be used with PARI nebulizers and masks. Contact [pari.com](http://pari.com).

## AT ITS PEAK

Peak flow testing is now available with new flow/volume simulator. This is the only device of its kind for testing peak flow meters. It has been validated to meet the latest standards for generating flow/volume waveforms per the new peak flow meter EN Standard 13826. Hans Rudolph Inc's is the first and only computerized piston device that has been validated to meet these higher frequency waveform definitions. The device performs the ATS Flow and volume waveforms for spirometry testing as well. Static and sinusoidal flows, custom waveforms and heated and humidified deliveries are just some of the features available with this device. Worldwide engineering and biomedical departments in this industry and research labs all need this development and testing device. Contact Hans Rudolph, Inc at [rudolphkc.com](http://rudolphkc.com), (800) 456-1414.

## RESEARCH GRANTED

Nellcor announced that it has awarded a grant to the Baylor Research Institute in Dallas to support development of an information system that tracks oxygen saturation levels of neonates via pulse oximetry.

Baylor researchers hope by creating a system to track oxygenation levels of neonates, it will help to prevent the occurrence of retinopathy of prematurity. While several factors may contribute to developing ROP, some clinicians feel closer examination of current oxygenation standards could improve ROP outcomes.

"As clinicians, we already know to avoid saturation levels over 95% in high risk babies," said Cody Arnold, MD, epidemiologist and health services researcher at the Baylor Institute for Healthcare Research and neonatologist at Baylor University Medical Center at Dallas, who heads up the research team. "But by more closely evaluating those oxygenation levels



with an information system like the Neonatal Oxygen Therapy Information System (NOTIS), we have an opportunity to safely increase the amount of time patients spend in the desired saturation range and, hopefully, reduce incidence of ROP." When complete, the NOTIS system in development at BRI, will be available at no cost to any researcher or newborn intensive care unit (NICU) interested in studying oxygenation levels of premature infants in an effort to advance patient care. Arnold said he approached Nellcor for financial support to develop NOTIS because Baylor Dallas uses Nellcor pulse oximetry products in its NICU. "For Nellcor, supporting Dr Arnold and the NOTIS project offered us an opportunity to get involved in a meaningful way to support important research efforts aimed at improving the care of newborns," said Robert St. John RN, RRT, director of Clinical Research for Nellcor. For more information contact nellcor.com, Tyco Healthcare, Tyco International Ltd, tycohealthcare.com.

## A NEW HOME

Impact Instrumentation, Inc announces the purchase of 19 Fairfield Place, its third building in West Caldwell, NJ. This purchase increases Impact's total space to 62,000 square feet and follows closely Impact's 2003 purchase of a nearby property. The need for additional space was critical to accommodate the growing demand for Impact products and to bring under one roof capabilities that were previously sourced outside. Impact, now in its thirtieth year, is an industry leader in the manufacture of portable ventilators, specialized mounting systems, and portable, mobile and on-board aspirators. Contact impactinstrumentation.com.

## SPOTLIGHT ON VENTILATION

### MAKE AN IMPACT

The Model 73X from Impact Instrumentation is the first self-contained portable ventilator developed specifically for transport and mass casualty care. Impact's design team recognized the likelihood that limited oxygen supplies would deplete during a mass casualty incident and the need for an alternative gas source was imperative. As a result, the "X" may be used with external oxygen but more importantly it is operable via its own internal compressor. In addition, the "X" automatically switches to compressor operation should oxygen supplies become exhausted and simultaneously triggers an alarm to alert the caregiver. The "X" has a simple user interface that's easily managed by personnel with limited mechanical ventilation experience. It uses adult and pediatric disposable circuits, operates for about six hours between battery recharges, interfaces with industry-standard HEPA or chemical/biologic filters, and includes a digital airway pressure display, alarms suite, airway pressure limiting, continuous operation from external power, and more. Contact impactinstrumentation.com.

### PLUS FOR PULSE

The Bunnell Life Pulse High Frequency Ventilator provides improved oxygenation and ventilation of infants at lower mean and peak pressures than other high frequency or conventional ventilators. Jet pulse technology, passive exhalation and a wide range of I:E ratios are the keys to achieving the lowest therapeutic pressures. The Life Pulse is easy to use, with only three control settings, PIP, Rate, and I-Time. All other functions are controlled automatically. Bunnell's LifePort adapter has

eliminated the need to reintubate, with a special endotracheal tube, and the new WhisperJet inspiratory valve has significantly reduced noise levels. Contact (800) 800-4358, bunl.com.

## FLOW MOTION

The Infant Flow Nasal CPAP system was originally developed by EME as a single level nasal CPAP delivery system for the treatment of infants with respiratory distress. Since its introduction, the basic system has evolved into a bi-level device—Infant Flow SiPAP. Infant Flow SiPAP combined with the patented Infant Flow generator technology expands the clinician's noninvasive treatment options with Biphasic and Biphasic-tr (international only), at the lowest work of breathing with maximum pressure stability. EME is a Viasys Respiratory Care company. Contact viasyshc.com.

## GO WITH THE FLOW

Cardinal Health has developed a comprehensive solution for infant nCPAP applications—the AirLife infant nCPAP system. With a unique combination of advanced components and an innovative, patient-trending variable flow vortice technology, the AirLife has been engineered for maximum performance, reliability and patient comfort—because the less discomfort a patient experiences, the greater the opportunity for healthy growth and development. Developed with the assistance of clinical experts and designed to incorporate the best-in-class technology, the AirLife nCPAP system provides a superior solution for infant ventilation. Contact (800) 637-1500.

## ADVANCED VENTILATION

Dräger Medical presents SmartCare as an option for the EvitaXL critical care ventilator. SmartCare supports integrated, protocol-driven care, and uses a knowledge-based system to automatically wean the patient from the ventilator. By integrating protocolized care into a state-of-the-art ventilator, SmartCare is freeing the clinician for the "art of medicine." SmartCare/PS, a knowledge based weaning system, the first member of the new option SmartCare, contains automated clinical guidelines based on recognized medical expertise. A new standard in personalized patient care, this system has been shown to significantly cut average ventilation days, weaning times, and LOS. SmartCare will make use of Interactive Integration between Evita ventilators and the Infinity Patient Monitoring System to create additional knowledge-based ventilation protocols.

## INTELLIGENT VENTILATION

Hamilton Medical's premiere Clinical Expert's Workshop recently focused on the "Foundations of Respiratory Mechanics," presented by Paul Garbarini, RRT, Clinical Operations Manager. Attendees included MDs and RTs from across the United States. An international faculty presented in-depth lectures on pulmonary mechanics, PEEP titration, automated PV curve analysis, recruitment maneuvers and practical experience with Closed Loop Control of Mechanical Ventilation. Closed-loop control has been adopted in various industries over the last 20-plus years. Many industries such as airlines (auto-pilot), chemical, power and automotive (cruise control) have adopted closed-loop technology. Closed-loop control has helped improve quality of life today, yet to date has a modest effect on the healthcare industry. Healthcare is starting to see the benefits of closed loop control. It has been adopted in pharmacy, surgery, respiratory care and anesthesia areas. A paper presented to the 2004 American Control



Conference reported on the benefits of Closed-Loop Control in pharmacology and anesthesia. The paper concluded “open-loop control by clinical personnel can be very tedious, imprecise, time consuming, and sometimes of poor quality. Alternatively, closed-loop control can achieve desirable system performance in the face of highly uncertain and hostile environment of surgery and the intensive care unit.” Benefits associated with closed-loop control are improved safety, reduced errors and reduced cost of healthcare. Contact [hammed1.com](http://hammed1.com).

## PAV-LOVE

Proportional Assist Ventilation Plus (PAV+) is a revolutionary software option from Puritan Bennett. Designed exclusively for the 840 ventilator, PAV+ delivers positive airway pressure in direct proportion to a patient’s spontaneous effort to breathe. A sophisticated software algorithm dynamically adjusts ventilator pressure to maintain a clinician-set level of support. At a setting of 60%, for example, the ventilator performs 60% of the work of inspiration and the patient performs 40%. A unique “Work of Breathing” bar provides feedback on the adequacy of a chosen percentage support with assessments of patient and total work of inspiration. Proportional Assist and PAV are trademarks of The University of Manitoba and are used under license by Puritan Bennett.

## AT YOUR SERVO

The flexible and adaptable ventilator for all patient categories—SERVO-i from Maquet—meets today’s and tomorrow’s need for different treatment modalities and clinical situations. SERVO-i enables treatment of all patient categories, from neopeds to adults. It allows for transportation with no loss of treatment quality within and between hospitals, and it provides for investigation of different treatment options like Open Lung Tool and Automode. SERVO-i functionality can be easily added at any time because of its unique upward compatibility and flexibility. Visit [maquet-inc.com](http://maquet-inc.com).

## READY TO GO

The pNeuton Transport Ventilator (pronounced new-ton) provides adult/pediatric volume targeted ventilation and high performance CPAP for use in hospital, MRI and EMS environments. Pure pneumatic technology eliminates the need for batteries. A choice of 100% or 65% oxygen delivery lets you significantly extend transport times—up to twice what you might expect. The ventilator’s internal patient disconnect alarm system has audible and visual alarm indicators with a remote output for an external monitor. Contact [pneuton.com](http://pneuton.com).

## COMPACT & COMPREHENSIVE

Newport Medical Instruments, Inc announces availability of its newest ventilator, the Newport e360. The e360’s compact size, comprehensive features, safety management and low cost of ownership make it ideal for today’s hospital and sub-acute facilities. The Newport e360 Ventilator builds on the design and features of the 3500. Simple to use, the e360 provides comprehensive mode selections, with graphics and extensive monitoring built into a single compact package. The e360 can easily transition from invasive to noninvasive ventilation for adult, pediatric or infant patients. It provides the latest features with an intuitive user interface that makes training and setup fast and easy. Contact [ventilators.com](http://ventilators.com).

## EMERGENCY ONE

Distributed in the US by Smiths Medical PM, Inc, the

Wisconsin based manufacturer of patient monitors, the PneuPac products provide emergency support for patients in respiratory distress. The VR1 is a simple, safe, portable ventilator packaged into a lightweight, palm-sized unit. The paraPAC is a powerful, compact and rugged gas-powered, controlled ventilator. The ventiPAC is similar to the paraPAC, and specifically designed for use by paramedics and other qualified persons for adult, child and infant ventilation. The babyPAC is designed for delicate neonate and infant lungs. All of these ventilators are MRI compatible, and accessories/disposables used with them are available from Smiths Medical PM, Inc.

Smiths Medical PM, Inc is a designer, manufacturer, and distributor of the BCI brand of patient monitoring equipment and a distributor of the PneuPac brand of MRI-compatible transport ventilators. Located in Waukesha, Wisconsin, Smiths Medical PM, Inc. is part of Smiths Group plc, London. For more information or a demonstration, please contact Smiths Medical PM, Inc, (800) 558-2345, [smiths-medical.com](http://smiths-medical.com).

## THE NEXT GENERATION

Avea from Viasys was designed to be the next generation infant ventilator. With monitoring capabilities for proximal flows and volumes, the clinician has the choice between a heated wire or pressure differential flow sensor. A proximal pressure port is also available for up-close monitoring of the baby’s airway pressure. Volumes are monitored as milliliters per kilogram. Compliance and resistance measurements give dynamic as well as static readings of lung integrity. C20/C calculations give continuous monitoring of lung over-distension. Flow/Volume and Pressure/Volume loops can be saved, superimposed over real time loops and printed for archival. Screen images can even be saved as graphic files for slide presentations. Contact [viasyshc.com](http://viasyshc.com). Avea is an integrated ventilator and advanced monitoring system that meets the demanding needs of critical care practitioners. Bicore advanced pulmonary monitoring and Heliox administration provides clinicians with the tools to improve clinical outcomes. Innovative engineering is evident in Avea’s scroll pump compressor, the smallest, quietest medical air compressor on the market. Coupled with the ability to operate on battery power for up to two hours, this feature takes safety and wall independence to a new level.

The SensorMedics 3100A HFOV was first approved for use in 1991 and is the only HFV approved for early intervention treatment of neonatal respiratory failure. Use for pediatric patients failing conventional mechanical ventilation has been approved since 1995. The 3100A provides the ultimate in lung protection by inflating the lung with continuous distending pressure and superimposing very small pressure and volume swings. Numerous publications have reported improved benefits and outcomes associated with the use of HFOV. The 3100A is the standard of care in more than 90% of Level III nurseries and 75% of Pediatric Intensive Care Units in the US.

The SensorMedics 3100B signals the arrival of the next generation of High Frequency Oscillatory Ventilators. Based on the established technology of the Model 3100A ventilator, the 3100B HFOV adds the enhanced performance capabilities necessary for adult ventilation and is approved for the treatment of acute respiratory failure in adults and large children weighing more than 35 kilograms. The 3100B allows the application of continuous distending pressures up to 55 cmH<sub>2</sub>O to recruit and normalize lung architecture while ventilating the patient with near deadspace tidal volumes for the ultimate in low stretch lung protection.

Viasys is proud to include Bird Blenders in our family of

products. The quality, reliability and versatility of Bird Blenders have made them the blenders of choice for more than thirty years. The worldwide reputation for consistent durability of the Bird Blender is recognized and honored. Customers have remained confident in the steady accuracy of delivered gas from Bird Blenders. Viasys provides a diverse line of blenders to meet the needs for a variety of purposes. Specific units have been designed for M.R.I. facilities and nitrous oxide delivery. Our precise, low-flow blenders are essential for NICUs and labor and delivery applications.

The Vela ventilator exemplifies the term “seamless ventilation.” It has the ability to treat patients in any area of the hospital, a standard six-hour battery to transport patients between departments and considers an endotracheal tube to be an optional interface. Masks and speaking valves pose no problem for Vela. Advanced monitoring such as 24-hour trending, loops, waveforms and weaning parameters give Vela all of the tools demanded by today’s clinicians. Small in size, yet big on value and performance, Vela is the perfect choice for an all-round ventilator.

### ON BREATHING TRIAL

Viasys Healthcare—Pulmonetics Systems introduces the LTV 1200 Ventilator for ICU, PICU, ED, unified/military preparedness and patient transport. The newest addition to the LTV Series, the 1200 provides both invasive and noninvasive modes of ventilation for patients as small as 5 kg. Presets allow for quick patient setup, automatically configuring initial ventilation settings for the patient type selected. LTV 1200 also offers a Spontaneous Breathing Trial, which utilizes RSBI criteria to assess a patient’s ability to be weaned from mechanical ventilation. Clinicians can customize trial settings to ensure optimal levels of support throughout the weaning process. Contact (866) 752-1438, [pulmonetics.com](http://pulmonetics.com).

### THREE FROM GE

The Engstrom Carestation is the first critical care respiratory carestation to offer integration through the care process. From the ICU to the step-down unit, this artful expansion of our technology gives you the ability to integrate ventilation with monitoring modules capable of measuring advanced parameters—a first in ventilation and exclusively from GE Healthcare. The Engstrom’s features include: integrated ventilation and monitoring, plug and play modules to provide advanced monitoring parameters, familiar user interface, adaptability and flexibility to your environment, advanced aerosolized medication delivery with the Aerogen Aeroneb Pro, customizable screens, noninvasive ventilation, easy maintenance, and a focus on patient safety.

The Centiva/5 Critical Care Ventilator is your solution to the space and time demands of the critical care environment. The Centiva has been designed with the clinician in mind, combining a compact size with high levels of performance. The Centiva’s small size opens up valuable space around the patient’s bed and allows you the freedom to mount the entire system on the wall or remote mount the display unit while the ventilator engine is strategically placed out of the clinician’s way. Performance includes: seven modes of ventilation plus an apnea ventilation backup, airway resistance compensation, noninvasive ventilation, compliance and resistance compensation, automatic patient detection, automatic suction routine, and alarm autoreset.

The Aptaer Heliox Delivery System is user friendly and noninvasive. It offers an effective and consistent method for managing patients with severely compromised airways, from pediatrics to adults. The first of its kind, the Aptaer Heliox

Delivery System finally makes heliox therapy a viable option in critical care environments. The Aptaer is simple and effective therapy tailored to your patient’s needs. It is easy to use and calibrate, allowing you to begin therapy quickly. It’s highly automated, making gas delivery consistent and easy. The design is compact, for portability and ease of positioning in care areas. Aptaer integrates the Aeroneb Pro inline aerosol generator for delivery of medication within the breathing circuit. For all three products, contact [gehealthcare.com](http://gehealthcare.com).

## CORPORATE PROFILE

Hans Rudolph

### MOVING FORWARD

We grow and stay ahead of the other design and manufacturing companies by keeping focused on what we do best. Making patient interfaces for respiratory testing and therapy is our focus, and we continue to spend the time and money on product development and manufacturing so we can stay one step ahead of others in this market. We involve respiratory therapists in every phase of developing and marketing products for markets worldwide. We value their input and are very proactive in contacting and getting their feedback on everything from new product ideas, to the pros and cons of existing products, to essential and non-essential features they would like to see in a product, to warranty issues and more. To Hans Rudolph, the RT’s feedback is invaluable, since they are interfacing with patients in all the various markets where our products are used. This allows us to maximize our resources.

### AN ARRAY OF PRODUCTS

The lung simulators and instrumentation modules, along with our patented pneumotachs and calibration syringes, are innovative and necessary products for the development of respiratory therapy devices, research and comparative testing, production testing, and product training and demonstration. They also play a role in quality control in hospitals/labs and manufacturing facilities. We make three different types of lung simulators—breathing simulator, flow/volume simulator, and DLCO simulator—and due to the complexity of designing and making such devices, we are the leader in this technology. These products allow researchers, designers, developers, and trainers to simulate and measure human and animal breathing patterns under all conditions. Without accurate lung simulations and flow measurements, the respiratory therapy and pulmonary function testing markets cannot grow and develop. We have entered into two new markets in just the last couple of years. We now make nasal and oro-nasal CPAP and NIV masks for the obstructive sleep apnea and noninvasive ventilation markets. But even though our product line is wider than it was in the past, our focus on high quality has not changed. This is evidenced by the fact that our masks have become known as the most comfortable and best-fitting masks in these two very competitive markets in a very short time.

### THE FUTURE

Hans Rudolph began making valves and instruments in the early 1930s, drawing his designs on paper and then using old hand tools and manual lathes and mills to make the metal components to assemble the respiratory valves. We have been upgrading our manufacturing methods, equipment, systems, and people ever since. Today our management, manufacturing, and quality assurance systems have been certified and registered by

U.S., Canadian, and European legislation and standards, such as ISO 9001, ISO 13485, FDA, and GMP. We continue to develop our presence in the respiratory products field by designing, manufacturing, and marketing new and innovative products, such as better patient interfaces for full face (oro-nasal) and nasal CPAP/Bilevel/NPPV and NIV/NIPPV applications; masks and valves for pulmonary function testing; lung simulation and flow measurement solutions for researchers, designers, and manufacturers; and quality control devices for quality assurance in hospitals, labs, and design and manufacturing facilities. Hans Rudolph will continue to grow as a world-class designer and manufacturer for many years to come.

## BLOOD GAS ROUNDTABLE

### RNA MEDICAL

Daniel A. Mancuso

Daniel Mancuso is Director-RNA Medical, Division of Bionostics, Inc.

#### How has technology in blood gas measurement and reporting changed over the past 10 years?

Many of the newer instruments utilize automatic, electronic or equivalent QC methods, removing sample handling and introduction steps from the quality control process. RNA Medical believes that this is a shortcoming as it is critical to confirm that the entire process is in control and therefore, external run controls should be utilized. Point of Care (POC) testing is becoming more widely utilized in the hospital environment. Data collected from QC testing is typically analyzed in a statistical program such as RNA Medical's PeerQC service.

#### How has your company pursued R&D efforts to continue improving this technology?

RNA Medical specializes in developing liquid QC materials that evaluate the entire quality system including the important steps of sample handling and presentation to the instrument. Automatic or electronic QC removes the operator from this critical process and does not represent how patient samples are run in the real world. In addition, RNA Medical focuses its attention on creating aqueous based products that are safer and easier for the end user and offer longer shelf lives.

#### What efforts have you made in automation?

RNA Medical has been providing peer statistics since 1986 and was the first to offer real-time, web-based peer comparison reports. Our PeerQC, offered as a service to all RNA customers, was recently awarded a patent for this technology.

#### Where do you see your product used most?

Our blood gas, electrolyte, CO-Oximeter and linearity controls are used mainly in hospital central laboratories, clinical laboratories, respiratory care, cardiac catheterization labs and POC. Safe-Wrap blood collection tubes, which are Mylar-wrapped glass capillary tubes, can be used on virtually any blood gas analyzer. POC is the target for the Safe-Wrap tubes designed specifically for the Abbott i-STAT analyzer.

#### How prevalent is Point of Care testing vs. a centralized lab system?

In our view, many traditional laboratory tests are moving to POC. RNA is focusing a significant amount of effort to develop

controls and other quality products that address end-users' real-world challenges. Instruments such as the ITC IRMA TRUpoint, AVOXimeter, OSMETECH OPTI and i-Stat are becoming much more widespread as focus on reducing turnaround time (TAT) for test results becomes a higher priority.

#### What type of training and customer support programs do you have in place?

RNA Medical has a long history of providing top-notch customer service and technical support from people with hands-on experience in the field. RNA is focused on educating its customers in all areas of quality control and regulatory compliance. Over the last 3 months we have sponsored two POC educational events, most recently in the San Francisco area with over 50 of the area's leading POC coordinators and featuring Prof. Sharon Ehrmeyer a noted expert in the area of laboratory quality control and regulations.

#### Describe your customer assistance program for technical issues or compliance issues.

RNA is proud of its customer service and technical support functions. Technical issues are addressed directly by our product manager without the need to battle convoluted automatic phone systems or difficult e-mail exchanges.

#### How do you view your relationship with the end user of your product?

We view this relationship as a partnership, where neither party can be successful without the collaboration of the other. RNA is extremely proud of its reputation for providing superior products, customer service and technical support, and we will never compromise in these areas.

#### What in terms of cost-savings/benefits does your technology bring?

RNA Medical's external liquid quality control products offer the laboratory an opportunity to not only verify proper operation of their instrument, but critical feedback on operator proficiency not available when utilizing the internal "quality" controls of the instrument. RNA's products are always price competitive and we endeavor to develop products which offer the benefits of ease-of-use, non-human based formulations, longer shelf-life and non-refrigerated storage.



## NEWS FEATURE

### RESEARCH FINDINGS – PROTEINASE INHIBITOR FOR AAT DEFICIENCY

According to a new research study, Multi-Center Study: The Biochemical Efficacy, Safety and Tolerability of a New  $\alpha_1$ -Proteinase Inhibitor, Zemaira, augmentation therapy with a plasma derived  $\alpha_1$ -Proteinase Inhibitor ( $\alpha_1$ -PI) has been demonstrated to be effective in restoring serum Alpha<sub>1</sub>-antitrypsin (AAT) levels in individuals with AAT Deficiency. The study, by Stocks, Brantly, et al, was published in the Journal, COPD: Journal of Chronic Obstructive Pulmonary Disease. The objective of this study was to demonstrate that the steady-state trough serum  $\alpha_1$ -PI levels, achieved by a new plasma-derived  $\alpha_1$ -PI (Zemaira, study drug, ZLB Behring LLC, King of Prussia, Pennsylvania, USA), were bioequivalent to those achieved by the currently available  $\alpha_1$ -PI therapy, Prolastin (control drug, Bayer Corporation, Berkeley, CA), and maintained weekly trough serum antigenic  $\alpha_1$ -PI levels above the protective threshold of 11  $\mu$ M. The multicenter, controlled study randomized 44 subjects to receive either study or control drug for a 10-week double-blind phase. The control group was then crossed over to receive the study drug for the 14-week remainder of the study. The difference in mean trough serum antigenic  $\alpha_1$ -PI level between the treatment groups was 1.45  $\mu$ M, signifying bioequivalence. The mean trough serum antigenic  $\alpha_1$ -PI level in the study drug group was greater than the therapeutic threshold of 11  $\mu$ M, achieving a level of 17.7  $\mu$ M during the steady-state period. Treatment-related adverse events were seen in 7% and 21% of study and control drug treated subjects, respectively. No documented viral transmission occurred. The results demonstrate that the new plasma-derived  $\alpha_1$ -PI (Zemaira) is bioequivalent to the currently available product Prolastin, is well-tolerated, and safe with respect to the risk of viral transmission.

Alpha<sub>1</sub>-antitrypsin Deficiency ( $\alpha_1$ -PI Deficiency) is one of the most common chronic, autosomally inherited disorders that may pre-dispose to life-threatening lung and liver disease. Approximately 45% of  $\alpha_1$ -PI deficient patients also exhibit an asthmatic component to their lung disease, as evidenced by symptoms and/or signs of bronchial hyperreactivity. In addition, pulmonary infections, including pneumonia and acute bronchitis, are common and contribute significantly to the morbidity of the disease.  $\alpha_1$ -PI provides more than 90% of the lower respiratory tract's inhibition of neutrophil elastase (NE), a protease capable of destroying alveolar walls. Conditions that increase neutrophil accumulation and activation in the lung, such as respiratory infection and smoking, will in turn increase levels of NE. It is believed that this increase in uninhibited NE activity is the pathogenesis behind emphysema development in  $\alpha_1$ -PI deficient patients. Therefore, theoretically the most direct approach to therapy for  $\alpha_1$ -PI deficiency in patients with emphysema is to replace the missing protease inhibitor and thus re-establish anti-neutrophil elastase protection of the lower respiratory tract.

For almost 2 decades, the maintenance of blood levels of antigenic  $\alpha_1$ -PI above 11  $\mu$ M has been presumed to provide therapeutically relevant anti-neutrophil elastase protection. Previous research with the then only licensed  $\alpha_1$ -PI (Prolastin), has demonstrated that chronic  $\alpha_1$ -PI replacement therapy is safe and effective in raising serum  $\alpha_1$ -PI levels to the target levels while also significantly increasing  $\alpha_1$ -PI levels in lower lung epithelial lining fluid (ELF). Based upon current evidence,

augmentation therapy was recommended by the American Thoracic Society for individuals with established airflow obstruction from  $\alpha_1$ -PI Deficiency. Unfortunately, the supply of existing  $\alpha_1$ -PI products has not been able to meet the demands of the patient population, requiring the development and registration of newer  $\alpha_1$ -PI products.

Zemaira is a highly purified, lyophilized intravenous  $\alpha_1$ -PI product derived from human plasma, which undergoes dual viral inactivation/removal processes. A recent pilot study has suggested that the different manufacturing processes for each commercially-available  $\alpha_1$ -PI preparation may affect their purity, isoform composition and non-therapeutic protein content.

Zemaira is a highly purified, lyophilized intravenous  $\alpha_1$ -PI product derived from large pools of human plasma. Subjects for this study were randomized in a 2:1 ratio to receive either Zemaira or Prolastin for a 10-week double-blind phase. The control group was then crossed over to an open study phase where all subjects received Zemaira for the remainder of the study (14 weeks).  $\alpha_1$ -PI treatment with study drug or control drug was administered by weekly intravenous infusion at a dose of 60 mg/kg functionally active  $\alpha_1$ -PI. All subjects were followed for a total of 24 weeks. In a subset of 15 subjects with FEV<sub>1</sub>  $\geq$  50%, bronchoalveolar lavage was performed to evaluate levels of  $\alpha_1$ -PI in the epithelial lining fluid.

The primary objectives of this study were to demonstrate that the steady-state trough serum  $\alpha_1$ -PI levels achieved by weekly infusion of the study drug were bioequivalent to those achieved by weekly infusion of the control drug. In addition, weekly trough serum antigenic  $\alpha_1$ -PI levels were to be maintained above the protective threshold of 11  $\mu$ M. The secondary objectives were to compare the safety and tolerability of both drugs and to demonstrate increases of the antigenic  $\alpha_1$ -PI in the ELF of the lower lung. In addition the following exploratory analyses were to be performed: the weekly trough serum functionally active  $\alpha_1$ -PI levels during steady-state period (Week 7-Week 24) to demonstrate no significant downward trend and the serum functional  $\alpha_1$ -PI levels expressed as a percentage of antigenic levels.

A total of 44 subjects were enrolled in the study; 30 subjects were randomized to the Zemaira (study drug) treatment group and 14 subjects were randomized to the Prolastin treatment group. Nine subjects had participated in a previous clinical trial with the study drug. Forty-three subjects completed the blind phase; 1 subject died in the final week of the blind phase of the control drug treatment arm. Forty-two subjects completed the open phase; 1 subject voluntarily withdrew from the study and 41 subjects completed the viral safety follow-up phase. A subset of 15 subjects (10 in the study drug group and 5 in the control drug group) underwent bronchoscopy and BAL.

The primary objectives were met in this study. The mean trough serum antigenic  $\alpha_1$ -PI levels of the two groups were within 3  $\mu$ M (actual value 1.45  $\mu$ M) with the lower limit of the 90% confidence interval being -2.77  $\mu$ M. These results support the demonstration of bioequivalence of the two drugs studied. The difference between the two groups was statistically significant at a 2-sided  $\alpha_1$  level of 10%. The mean trough serum antigenic  $\alpha_1$ -PI level in the study drug group from Week 7 to Week 11 was 17.7  $\mu$ M (90% CI: 16.9, 18.5), greater than the therapeutic threshold of 11  $\mu$ M.

Within each treatment group, ELF levels of antigenic  $\alpha_1$ -PI demonstrated a statistically significant increase from baseline to Week 11; however, no significant difference was seen between the two products.

Examination of the steady-state trough serum antigenic  $\alpha_1$ -PI

level between Week 7 to Week 24 revealed a downward trend. Serum levels at steady state of functionally active  $\alpha_1$ -PI remained stable during the entire treatment period.

No serious or severe AEs were judged by the investigators to be related to either the study drug or control drug. In the blinded phase of the study, 90% of subjects in the study group and 100% of subjects in the control group reported at least 1 treatment emergent AE. The most frequently reported AEs were headache, sinusitis, upper respiratory infection, increased cough, sore throat, fatigue, fever bronchitis, bronchospasm, and flushing. No relevant differences were detected between the treatment groups. Various mild treatment-related AEs were reported.

There was a statistically non-significant lower incidence of serious AEs and of the overall AE rate in the study drug group compared to the control group during the blinded treatment phase. One death occurred during the blinded phase of the study of a patient with a history of COPD and osteoporosis, and the cause of death was judged as unrelated to study medication.

Analysis via an antigenic assay indicated a significantly higher level of antigenic  $\alpha_1$ -PI per unit of functionally active  $\alpha_1$ -PI in the control drug preparation, demonstrating a significant amount of inactive  $\alpha_1$ -PI protein. The potency of the products, as determined by functional assay was comparable and correlated well with the labeled amount. The mean specific activity of the study drug was 1.07, higher than that of the control drug (0.77).

This was a randomized, controlled, multi-center study, which compared the biochemical efficacy, safety, and tolerability of Zemaira, with that of Prolastin, in subjects with  $\alpha_1$ -PI Deficiency and emphysema. Based on previous clinical studies and consistent with the terminal half-life of approximately 5 days, all subjects were expected to have achieved steady-state trough serum  $\alpha_1$ -PI levels after 6 doses of study treatment (ie 42 days after the first dose). The study aimed to demonstrate the maintenance of a plasma level of 11  $\mu$ M  $\alpha_1$ -PI, in conjunction with the demonstration of an appropriately defined increment in ELF  $\alpha_1$ -PI analyte levels. The study results demonstrate the bioequivalence of Zemaira and Prolastin. Of greater clinical relevance was the mean level of serum antigenic  $\alpha_1$ -PI achieved during this period, which was significantly greater than the accepted therapeutic threshold of 11  $\mu$ M. These results also demonstrate that the treatment protocol of weekly infusions of 60 mg/kg of functionally active  $\alpha_1$ -PI delivers the therapeutically relevant anti-neutrophil elastase protection.

Although the trough serum antigenic  $\alpha_1$ -PI levels in the study drug group were not inferior to trough levels achieved after treatment with the control drug, the difference between the two groups was nevertheless statistically significant. Despite both treatment arms having received the same amount of functionally active  $\alpha_1$ -PI, analysis revealed a significantly higher level of antigenic  $\alpha_1$ -PI per unit of functionally active  $\alpha_1$ -PI in the control drug compared with the study drug. Due to the identified product differences and the dosing regimen, the subjects had received relatively larger amounts of antigenic  $\alpha_1$ -PI in the control drug group, which may have contributed to the higher antigenic  $\alpha_1$ -PI levels observed in the serum. Within each group, ELF levels of antigenic  $\alpha_1$ -PI increased from baseline to Week 11, providing direct evidence that intravenous administration of  $\alpha_1$ -PI delivers  $\alpha_1$ -PI to the target site in the lung, and supporting the hypothesis that intravenous administration of  $\alpha_1$ -PI confers antineutrophil elastase protection to the lung.

The study drug was well-tolerated. No statistically significant differences in AE rates were seen between groups in the blinded phase; however, there were a lower number of both total

reported and treatment-related AEs in the study drug group compared with the control drug group. One AE of particular interest and judged to be possibly treatment related, was the parvovirus B19 seroconversion in a patient who had received the control drug. In this subject no clinical symptoms of a parvovirus infection were reported and the source of infection was most likely community-acquired, as documented by the investigator. In summary, the primary and secondary objectives in this study were achieved demonstrating bioequivalence and comparability of Zemaira to Prolastin in treating patients with  $\alpha_1$ -PI Deficiency and emphysema. This means that Zemaira is a viable treatment option in  $\alpha_1$ -PI Deficient patients. This is especially important when considering the current ongoing screening efforts and the percentage of under-diagnosed patients in the population.

*Information for this article is from COPD: Journal of Chronic Obstructive Pulmonary Disease, 3:17-23, © 2006 Taylor & Francis Group, LLC, from the original research study: Multi-Center Study: The Biochemical Efficacy, Safety and Tolerability of a New  $\alpha_1$ -Proteinase Inhibitor, Zemaira, by Stocks, Brantly, Pollock, Barker, Kueppers, Strange, Donohue and Sandhaus.*

## NEWS COMMENTARY

### LIQUID VENTILATION

The impetus for this commentary is a news item from Basque Research (see page 11), which revealed the obstacle to a new treatment modality – not enough profit. Yet, much research has been carried out substantiating the viability of liquid ventilation, including total liquid ventilation. PubMed offers 548 papers on the subject, while BioMed Central lists 94. While experimental results vary, there's no doubt that total liquid ventilation is worth looking at.

#### Why Not Gas?

Conventional gas ventilation is often unsuccessful for RDS preemies. By eliminating the air-liquid interface in saccules, where scarce or absent surfactant production exists, pulmonary instability is avoided, lung compliance is improved, and atelectatic saccules are recruited, ultimately lowering the saccular pressure. Tidal LV involves administering a liquid tidal volume to the patient at each respiratory cycle, and therefore requires a dedicated circuitual setup to deliver, withdraw, and refresh the PFC during the treatment. One prototype liquid breathing system comprises two subcircuits managed by a pc-based control system. The ventilation subcircuit performs inspiration/expiration with two sets of peristaltic pumps. A system to evaluate the true inspired/expired volumes was devised that consists of two reservoirs equipped with pressure transducers measuring the hydraulic head of the fluid therein. The new apparatus has been used in preliminary animal tests on five newborn mini pigs with induced acquired RDS. The animals were successfully supported for 4 hours each.

#### A Partial Step

Partial liquid ventilation, on which much of the existing research has concentrated, requires partial filling of lungs with perfluorocarbons and ventilation with gas tidal volumes using a conventional mechanical ventilator. Various physico-chemical properties of PFCs make them the ideal media. It results in a dramatic improvement in lung compliance and oxygenation and decline in mean airway pressure and oxygen requirements. In an

experimental model of acute lung injury, partial liquid ventilation resulted in immediate and sustained increase in PaO<sub>2</sub> over 3 hours without significant change in lung mechanics or histological lung damage.

Total liquid ventilation has been explored as a potential therapy to mitigate ventilator-associated lung injury and acute lung failure. TLV is ventilation of the completely liquid-filled lung using tidal flow of oxygenated perfluorochemical liquid delivered by a liquid ventilator. Most TLV research to date has focused on small animal lungs, with primary relevance to its use in children. Although a simple scale-up of liquid ventilator components such as pumps, tubing, fittings, and gas and heat exchangers might be considered the most straightforward way to compensate for the increased demand, there are a number of practical problems with this approach, including the need to minimize priming volume and PFC evaporative loss, suppress flow-induced cavitation, maintain the accuracy of delivered breaths in a fluid mechanical environment, and maintaining PFC materials compatibility.

### Past Research

The concept of liquid ventilation has been investigated since 1962 when Kylstra evaluated the ability to sustain gas exchange in mice spontaneously breathing saline oxygenated at 6 atmospheres. Clark subsequently demonstrated that spontaneously breathing mice could survive when submerged in perfluorocarbon under normobaric conditions.

In "Liquid Ventilation Improves Pulmonary Function, Gas Exchange, and Lung Injury in a Model of Respiratory Failure," by Hirschl, et al (Ann Surg 1995 Jan;221(1)79-88), the authors evaluated gas exchange, pulmonary function and lung histology during perfluorocarbon liquid ventilation when compared with gas ventilation. They concluded that their study "documents the effectiveness of lung management with perfluorocarbon liquid ventilation in reducing alveolar pathology and inflammatory infiltration while improving pulmonary function and gas exchange in a model of severe respiratory failure."

In Total Liquid Ventilation, the lungs are filled with perfluorocarbon to a volume equivalent to the FRC, approximately 30 mL/kg, and a liquid ventilator is used to generate tidal breathing with perfluorocarbon. Optimal CO<sub>2</sub> clearance is achieved when ventilation is performed at a rate of 4-5 breaths/minute. Typical tidal volumes are in the 15-20 ml/kg range. One of the advantages of TLV is that exudate may be lavaged from the airways in the setting of respiratory failure. In addition, the distribution of perfluorocarbon within the lungs may be more uniform during TLV.

As far back as 1996, Critical Care Medicine published the article "Total liquid ventilation with perfluorocarbons increases pulmonary end-expiratory volume and compliance in the setting of lung atelectasis," by Tooley, Hirschl, et al (Critical Care Medicine. 24(2):268-273, February 1996).

The study's objective was to compare compliance and end-expiratory lung volume during reexpansion of normal and surfactant-deficient ex vivo atelectatic lungs with either gas or total liquid ventilation. The design was a controlled animal study using an ex vivo lung preparation on 36 adult cats. Normal lungs and saline lavaged, surfactant-deficient lungs were allowed to passively collapse and remain atelectatic for an hour. Lungs then were placed in a plethysmograph and ventilated for two hours with standardized volumes of either room air or perfluorocarbon. Reexpansion of normal atelectatic lungs with total liquid ventilation was associated with an 11-fold increase in end-expiratory lung volume when compared with the increase

in end-expiratory lung volume observed with gas ventilation. The difference was even more pronounced in the surfactant-deficient lungs, with an approximate 19-fold increase in end-expiratory lung volume observed in the total liquid ventilated group, compared with the gas ventilated group. Total liquid ventilation was associated with an increase in pulmonary compliance when compared with gas ventilation in both normal and surfactant-deficient lungs. The study concluded that end-expiratory lung volume and static compliance are increased significantly following attempted reexpansion with total liquid ventilation when compared with gas ventilation in normal and surfactant-deficient, atelectatic lungs. The ability of total liquid ventilation to enhance recruitment of atelectatic lung regions may be an important means by which gas exchange is improved during total liquid ventilation when compared with gas ventilation in the setting of respiratory failure.

"Evaluation of a Double-Piston Configured Total Liquid Ventilator in an Adult Animal Model of Acute Respiratory Failure" by Foley, et al (Annals of Surgery, Vol. 221, No. 1, 79-88), noted that total liquid ventilation with perfluorocarbon liquid had been associated with improvements in gas exchange and pulmonary compliance in animal models of acute lung injury. "The employment of this technique in the clinical setting has been limited, however, by the size and complexity of the mechanical liquid ventilators which have been developed to assist with both the tidal flow and regeneration of the liquid," the authors said. The efficacy of a double-piston configured liquid ventilator was tested in an adult animal model of the acute respiratory distress syndrome. All the animals survived the four hour treatment period, and no significant temperature or hemodynamic differences were noted between GV and TLV groups. TLV animals demonstrated significantly higher arterial oxygen tensions compared to GV controls at one hour after randomization and this difference was maintained for the rest of the experimental period. Gross examination of the lungs revealed less dependent atelectasis and hemorrhage in the TLV animals. The authors concluded that the double-piston pump total liquid ventilator is both easily used and effective in improving pulmonary function in an adult animal model of the acute respiratory distress syndrome.

### Possible Applications

The makers of Inolivent report that the overall market for liquid ventilation could easily be in the multibillion dollar range (according to Synthetic Blood International Inc). However, to perform an efficient liquid ventilation, a dedicated complex mechanical system is necessary, including the use of a total liquid ventilator, in order to ventilate completely filled lungs with a tidal volume of PFC. Inolivent reports that many studies involving various experimental models of acute lung injury suggest clear benefits from total liquid ventilation as compared to all other tested ventilation strategies, including conventional and high frequency gas ventilation and partial liquid ventilation without a liquid ventilator. At the Université de Sherbrooke, J-P. Praud, MD, PhD, initiated experiments on liquid ventilation several years ago, employing both PLV and TLV on normal lambs. Experimental results with newborn lambs show that the ventilator designed specifically for the experiments performed adequate ventilations. Pulsion Medical Systems provided support to study the hemodynamic consequence of tidal liquid ventilation. The final objective of the Inolivent group was to deal with the severe respiratory syndrome of the preemies and others who cannot be treated effectively by conventional gas ventilation. After many years of research, the group developed

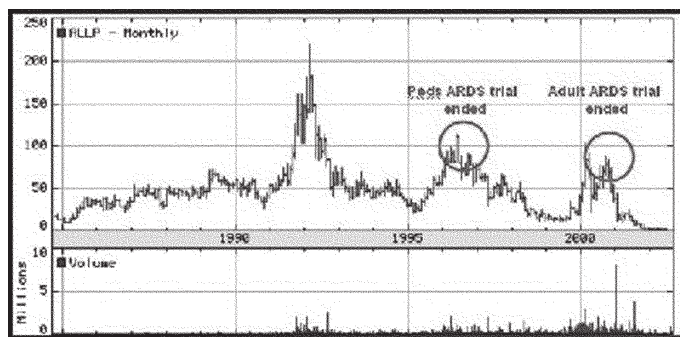


an original ventilator with an independent pumping system which allows the perfect control of the total liquid ventilation. Moreover, the patented ventilator is designed to be modular, giving the possibility to scale up from a newborn to an adult.

## ADDENDUM

Dennis Bing, RRT, Seattle, comments: The article in this issue, with information from Medical News Today, criticizes, but does not name, the company in question. The only clinical trials of Partial Liquid Ventilation (PLV) conducted in the USA were sponsored by the Alliance Pharmaceutical Corporation, of San Diego, California. The two initial phase 1 clinical trials were conducted in term infants, and preterm infants with severe RDS. These led to the phase 2/3 clinical trials in pediatric patients with severe ARDS. This trial was halted before it was complete because the subjects in the control group did not exhibit the mortality expected by history. The last clinical trial was in adults, also with severe ARDS. The PLV group however, did not differ from the control group's mortality. Curiously, that study's results were announced exactly 5 years ago today. That was, basically, the straw that broke Alliance's camel's back. See the image at right from one of my lectures in 2002.

Stock performance of Alliance Pharmaceutical Corp.



According to Alliance's 2004 annual report, investors are over \$2.7 M in the hole. I do still believe, based on the data published and my own experience, that liquid ventilation could offer infants, children, and adults with severe low-compliant lung disorders benefits that are not possible with gaseous ventilation. Unfortunately, it appears that no private medical company with sufficient financial resources to really do justice to another clinical investigation is willing to do so.

## EXECUTIVE PROFILES

### Draeger Medical Inc.

Dr. Christian Hauer

Dr. Christian Hauer is Vice President, DraegerService.

**Who is responsible within your company, by title or name or job description, for training and education of your staff and your customers?**

Within Draeger Medical Inc, we segmented the training efforts into three different departments to deliver the right content for different customer groups: We have biomedical training and training of Draeger Medical's Technical Service Reps. We have a manager for technical support and services. Draeger provides clinical application training for clinicians and end users of our product lines. We have a manager for clinical application support. The third department covers internal training for Draeger Medical's account managers and product specialists. We have a director for internal training.

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

Draeger Medical Inc provides technical service support via our 1-800 4 DRAGER phone number, and is available 24/7, 365 days a year. Our technical service support team is segmented into product areas to provide maximized expertise among the different modalities in Draeger's product portfolio. Technical service support is provided in Monitoring, Perioperative Care, Critical Care, Perinatal Care and Information Technology.

**What, if any, formal education programs does your company provide for biomedical training and service?**

Biomedical training is a core component of our DraegerService product portfolio. The Draeger training center provides courses

48 weeks a year, and offers a choice of more than 25 different programs for different skill levels.

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

People, communication, and service and parts are the most important items to support our customers. Draeger Medical offers a network of more than 100 highly trained and experienced Technical Service Representatives and a Technical Support Center operating around the clock, 365 days a year so that we can provide a short response time when issues arise. Service can be provided on-site or remotely via VPN connection, depending on the type of service required. Our world-class parts distribution center is located within 10 miles of the world's largest distribution hub (FedEx in Memphis, TN) and is able to deliver parts to the point of care in less than 24 hours, anywhere within the continental United States.

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

We at Draeger Medical use a variety of communications methods—from brochures, public relations, trade shows, and our sales and service teams, to marketing activities that communicate current product performance along with future technology breakthroughs that are changing the delivery of medicine at the acute point of care every day. It is important to note we see our communications with customers as a two-way street. We look to them for an exchange of ideas as we develop future solutions.

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

Draeger offers more than 25 biomedical courses as well as on-site education courses for clinicians to enable them to better utilize our products.

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

Whereas customers once looked only at the functionality of the device/box that they purchased, they are now interested in the entire solution, including the functionality, the impact of the network, and the integration of patient data with other devices and information technologies. We at Draeger Medical are well-positioned to address these needs with a product portfolio that provides solutions to the Perioperative, Critical, and Perinatal Care areas. While Draeger respiratory innovations will continue to lead the way in critical care, one cannot overstate the impact that the integration of the respiratory devices with information technology and monitoring will have on the workflow of our customers, and the delivery of care to their patients.

## Invacare

Bob Messenger

Bob Messenger, BS, RRT, is Clinical Manager, Invacare Corporation.

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

We have a variety of educational programs such as provider clinician training, continuing education (CEU based), and marketing/sales training. Formal education on positive pressure therapy and associated device performance are included in our "Current Concepts in Home Respiratory Care" continuing education program.

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

At Invacare, licensed, credentialed, respiratory care and sleep professionals provide clinical support via telephone on a 24-hour, seven-day-a-week basis. Our Technical Service Department provides support in the form of assistance in equipment programming, troubleshooting and supporting all service related questions.

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

A primary focus is provider training to ensure proper and appropriate application of therapy. This training incorporates both technical operation and the clinical rationale associated with device performance. Additional support is provided through our 24-hour clinical support line and our technical support team.

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

Direct marketing/sales efforts in sleep labs and to sleep physicians and medical equipment providers. Support of local, regional and national sleep seminars and symposia. Advertising in trade and professional journals.

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

Product performance is gauged on feedback obtained from users participating in satisfaction and evaluation programs. Feedback from providers is elicited by our territory business managers along with our clinical staff and incorporated in a quality database for monthly review. The resulting information is used to help identify performance and other characteristics of

future products.

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

A plethora of information is available on the Internet, which allows users to make informed decisions and to dictate which specific products they expect. This demands that providers, and manufacturers like Invacare, provide products that support the lifestyle, comfort and convenience expectations of the user. We see the development of product characteristics relative to user requirements as a progressive process. Evolving customer demands along with competitive pressures require ongoing product development to ensure appropriate therapy and end-user satisfaction.

## Respironics

Dick Ellis

Dick Ellis is with the Hospital Division, Respironics, Carlsbad, CA.

**Who is responsible within your company, by title or name or job description, for training and education of your staff and your customers?**

Technical Education Instructors (Service) and Education Format (Product/Clinical).

**What types of education do you provide?**  
Product, Clinical, and Service.

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

Standby Clinician on phone support. Field clinicians available on emergency basis.

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

Toll-free telephone support 24/7 on all products and remote diagnostics on Esprit Ventilator.

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

Formal classroom training on Vision, Esprit & NICO

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

Provide product, clinical and Service support along with product training that also involves CEU credits. Make the training available in a format convenient to the customer i.e. Web-based, interactive, CD, etc.

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

Advertising, tradeshow, workshops, user meetings.

## Teaching Outside the Box: A Constructivist Approach to Facilitating Critical Thinking in Respiratory Therapy Education

Kimberly Clark, MBA, RRT-NPS

### ABSTRACT

The current health care system is a rapidly changing and complex environment. Respiratory therapists are expected to access, interpret, and use information to make appropriate patient care decisions. Critical thinking skills are an essential component to effectively manage expanding professional roles and responsibilities associated with today's dynamic health care environment. Critical thinking is the ability to adapt and apply existing knowledge, previous experience, and new information to changing situations to effectively solve problems and make decisions. Respiratory educational programs are charged with the task of facilitating critical thinking by understanding adult learning principles, identifying learning styles among a diverse adult student population, and utilizing effective teaching and learning strategies in the classroom and clinical settings. Constructivism is an active view of learning in which learner knowledge is constructed by connecting new information to previous knowledge and experience. Constructivist approaches include inquiry-based, problem-based, and research-based learning methods. Reliance on textbook information and faculty expertise are not sufficient methods to stay current on new information and technology. As educators, we must help students learn how to ask the right questions that identify problems and conduct research to find possible solutions.

### INTRODUCTION

Over the last 15 years an explosion of technology, medication, and treatment advances has occurred in health care. Respiratory therapists (RTs) are expected to keep pace with the advances along with the vast amounts of available new information. Never before in the 60 year history of the respiratory care profession has the development of critical thinking skills been more important, which are an essential component necessary to effectively deal with increasing responsibilities and expanding professional roles associated with the rapidly changing and complex health care environment.

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Critical thinking is the ability to adapt and apply existing knowledge, previous experiences, and new information to specific situations to effectively solve problems and make appropriate decisions.

The respiratory care profession has continuously evolved since its beginning in the 1940s as inhalation therapy, and education was provided as on-the-job training in hospital-based programs. The length of the education process varied from a few weeks to several months. The majority of RTs receive education and training in associate degree programs based in community colleges. Baccalaureate degree programs are based in colleges and universities and seek to meet the demand for highly trained professionals armed with problem-solving and decision-making skills. The evidence is clear concerning the need to provide advanced level education for RTs which facilitates critical thinking in order to keep pace with the advances in health care.

Respiratory therapists are no longer passive receivers and initiators of physician ordered therapy. Instead, RTs actively participate in dialogue with physicians, nurses and other health care professionals to determine the appropriate course of action for patient care. In the current health care environment, RTs participate in advanced practices including emergency airway management and intubation; initiation and management of non-critical care therapist driven protocols (TDPs), ventilator weaning protocols, high frequency oscillation ventilation (HFOV), inhaled nitric oxide (INO), heliox, extracorporeal life support (ECLS), neonatal surfactant replacement therapy (SRT), hyperbaric oxygenation (HBO), indirect calorimetry, hemodynamic monitoring and the operation of the intra-aortic balloon pump (IABP); emergency ground and air transport; and assistance with bedside bronchoscopy and tracheostomy procedures. Additionally, RTs work in a variety of settings that extend beyond the acute care hospital including pulmonary rehabilitation, pulmonary function labs, skilled nursing facilities (SNFs), long-term acute care hospitals (LTACHs), pharmaceutical companies, case management, physician offices, sleep labs, home care, and educational institutions. To adequately function in the various settings, RTs must prioritize



**Table 1. Differences Between Pedagogical and Andragogical Learning Theories**

Six Assumptions	Pedagogy	Andragogy
Need to Know	Teacher-directed	Student-directed
Self-Concept	Dependent personality	Self-directed and autonomous
Prior Experience	Virtually irrelevant as a learning resource	Valuable learning resource
Readiness to Learn	Teacher-directed	Student-directed
Orientation to Learning	Subject-centered based on subject-matter content	Life centered, problem-centered, task-centered
Motivation to Learn	Extrinsic factors	Intrinsic factors, personal payoff

**Table 2. Socratic Seminar Structure**

Steps	Description
1	Prior to the seminar, students are given an assignment and establish criteria and ground rules for the discussion.
2	Students arrive and form a circle (with the teacher) prepared for the assignment.
3	The teacher presents a general open-ended question related to the topic.
4	Students respond to each other, not the teacher, with supported views or opinions.
5	The teacher may ask probing questions to stimulate deeper thinking or follow-up questions for clarification.
6	The teacher presents an open-ended core question to explore the main content.
7	The teacher presents an open-ended closing question, which is designed to personalize the discussion. Does the personal element bring about a change in students' previous position? Emotions personalize the discussion and tend to improve long-term memory.
8	Seminar Evaluation

Adapted from reference 30

**Table 3. RRT Credentialing Examination Pass Rate Comparison\***

Exams	1998-1999	2000-2001	2002-2003	2004-2005	Mean ± SD
WRRT†	77.4	84.5	73.5	78.8	78.6 ± 3.95
CSE†	46.6	66.1	64.0	61.6	59.6 ± 7.66

\*Data reported as percentages

†New candidate.

work assignments, anticipate problems, troubleshoot equipment, communicate effectively, negotiate responsibilities, make appropriate decisions, and engage in reflective thinking.<sup>1</sup> Are new respiratory therapy graduates ready to face this health care environment?

In many cases, new graduates lack the necessary critical thinking skills to adapt content knowledge and clinical experience received in school to new patient situations. Additionally, new graduates may become overwhelmed and intimidated by the volume of high acuity patients that require usage of complex problem-solving and decision-making skills in order to make appropriate and effective treatment decisions at the entry-level. Respiratory therapists are expected to perform patient assessments,<sup>2</sup> implement and modify treatment plans, and determine effectiveness of treatment plans<sup>3</sup> all of which requires critical thinking. Unfortunately, limited support is available to assist practitioners' ability to adapt and apply knowledge base, previous experiences, and new information to patient situations.<sup>4</sup> The ability to move beyond recall and application and move toward adaptation and application is essential. The ability to recall information does not translate into learning; it simply means that a piece of information was remembered. If the information is recalled, adapted, and applied

to a new situation, then it can be said that learning has occurred. Are respiratory education programs adapting course curriculum to create learning environments that promote critical thinking skills?

Mishoe and MacIntyre in 1997 recommended respiratory care educational reform to adequately prepare RTs to meet the demands of increasing responsibilities and expansion of roles in the current health care environment.<sup>5</sup> In 2003, Becker recommended the incorporation of liberal arts into respiratory education programs to provide additional opportunities to develop written and oral communication skills to prepare students for the changing environment.<sup>6</sup> The problem with these suggestions are that associate degree programs are hampered with limited available time to incorporate vast amounts of content information and clinical experience; and the addition of more courses into an already overloaded curriculum could spell disaster for faculty and students. Since the respiratory care profession recently mandated that an associate degree be the minimum standard for entry-level RTs, it is unlikely the profession will move toward mandating a baccalaureate degree as the minimum standard for entry-level RTs any time soon. However, baccalaureate and graduate degrees are recommended for RTs who conduct formal and continuing

education.<sup>7</sup> Currently, RTs who have baccalaureate and graduate degrees are approximately 32% and 13% respectively.<sup>8</sup> Even though a small percentage of RTs hold graduate degrees, a large percentage of those individuals conduct formal education. Approximately 13% of program directors, 5% of clinical directors, and 4% of other faculty members hold doctoral degrees.<sup>8</sup>

If it is not possible, at this time, to extend the length of respiratory education programs, other approaches are necessary to adequately prepare respiratory care students to enter the workforce.

The process in which respiratory education is conducted must change, which refers to the way course curriculum is taught. Traditional lecture methods do not facilitate critical thinking; therefore, students do not learn how to adapt and apply information to changing clinical situations.<sup>9</sup> Additionally, the lecture-based method promotes information memorization that can be quickly forgotten if it is not applied in practice. The process of learning is active, but lecture-based methods place students in a passive role which is contradictory to the very essence of learning. Even though sufficient evidence indicates that student-centered approaches in education enhance learning and critical thinking skills and that educators use the language of student-centered strategies,<sup>10</sup> teacher-centered approaches still dominate educational practices and strategies. A few reasons are offered to explain why educators have been slow to understand and use student-centered approaches including lack of exposure to student-centered strategies; the tendency to teach the way they were taught; and the tendency to teach according to their own learning preferences.<sup>11</sup> Student-centered learning approaches are most consistent with adult learning principles. College-level students are adults who come with different learning styles, different levels of knowledge, and different prior experiences which are all important factors to consider when planning educational strategies.

Educators must be facilitators of learning. Standing in front of a group of students and transmitting knowledge with the expectation of future recall and application of the information is not enough; teaching does not equal learning. Effective utilization of student-centered approaches based on adult learning principles promote learner independence, problem solving, decision making, and critical thinking.<sup>10,12</sup> Understanding adult learning principles provides the road map to the development of effective educational strategies. The following sections provide information regarding learning theories, learning styles, and teaching strategies consistent with adult learning used to facilitate critical thinking in respiratory care education.

## LEARNING THEORIES

### Pedagogy

Pedagogy is derived from the Greek words *paid* meaning “child” (paediatrics/pediatrics comes from the same stem) and *agogus* meaning “leader of,” which literally means the art and science of teaching children.<sup>12,13</sup> Six assumptions are made in the pedagogical educational model. The first assumption is that what learners need to know is teacher-directed. Second, the learner’s self-concept is a dependent personality. Third, the learner’s previous experience is practically irrelevant as a resource for learning. Fourth, the learner’s readiness to learn is

teacher-directed. Fifth, the learner’s orientation to learning is subject-centered according to the subject-matter content. Finally, the learner’s motivation is driven by extrinsic factors.

Pedagogy is predominantly a teacher-centered approach, in which the educator determines the course content, delivery method, and when and how much of it will be taught.<sup>13</sup> Why is this important? Ever since pedagogy’s inception, dated between the seventh and twelfth century, the pedagogical model has remained a dominant instructional approach in the educational system, including higher education. The pedagogical model ignores the fundamental concepts of adult learning; therefore, it impedes the development of critical thinking skills. However, many argue that a pedagogical approach is appropriate in situations when the learner has little or no knowledge base and no previous experience in a particular subject area. The differences emerge when the knowledge base is acquired. Andragogy proponents transition students toward independent learning or self-directed learning; in contrast, pedagogy proponents keep students in a dependent learning environment. Table 1 illustrates the differences between pedagogical and andragogical approaches to learning.

### Andragogy

Andragogy is derived from the Greek words *aner* with the stem *andra* meaning “man” or adult, and *agogus* meaning “leader of.” Andragogy means the art and science of helping adults learn.<sup>14</sup> Andragogy is described as a set of adult core learning principles, which mirrors pedagogical assumptions, that apply to all adult learning situations.<sup>12</sup> The first principle is that adults need to know the value of the learning experience. Second, the self-concept of the learner is self-directing and autonomous. Third, the prior experience of the learner is a valuable learning resource. Fourth, the readiness to learn depends on the relevancy of the information or situation. Fifth, the orientation to learning is life-centered, problem-centered, or task-centered. Finally, the learner’s motivation to learn is based on intrinsic value and personal value. In order for learning to take place, educators need to know how to apply the core adult learning principles to classroom and clinical situations.

Andragogical and pedagogical approaches are not mutually exclusive; each approach can be integrated into almost any learning situation regardless of the age group. The assumption that children cannot be self-directed or that adults are always self-directed is not wise. However, using a predominately pedagogical model does not promote adult learning principles. Even though there is an assumption that pedagogy came first, the concept of andragogy is dated back to the great teachers of ancient times including Socrates, Aristotle, and Plato; Confucius and Lao Tse; Cicero and Evelid; and Jesus.<sup>12</sup> These individuals were teachers of adults and believed that learning did not happen through passive transmission of information but that learning occurred through active inquiry, which is at the very root of critical thinking.

Additionally, understanding the relevance of adult learning principles can be directly applied to the increased enrollment of nontraditional students in higher education. Nontraditional students are categorized as students 25 years of age and older; and they make up approximately 50% of the new and returning student population currently enrolling in colleges.<sup>15</sup> Respiratory therapy students are no exception to this phenomenon. Nontraditional students begin an educational program with

prior knowledge and experiences, career opportunities, and economic and socio-cultural influences; and unfortunately, traditional instructional methods do not capture these key features. Consequently, the strength of the nontraditional student is lost. To capitalize on the strengths of nontraditional students, limited usage of traditional pedagogical approaches, such as lectures, and incorporation of andragogical approaches are recommended. Simply stated, usage of one predominant teaching approach is inadequate to reach the learning diversities of students.<sup>16</sup> Constructivism is an active view of learning consistent with andragogy and utilizes various instructional methods designed to promote the adult learning principles.

### Constructivism

Constructivism is a student-centered approach in which learner knowledge is constructed by connecting new information to previous knowledge and experiences,<sup>17</sup> and rejects the notion that knowledge is separate from the learner.<sup>18</sup> Students do not show up to class with empty minds ready to absorb new information.<sup>19</sup> Regardless of age, learning new information is easier when it can be connected to and built upon existing knowledge and experiences. Learning occurs best when information is learned in the context in which it is used. Additionally, learning is enhanced when information is relevant to the student and when the student understands why and how to use the new information,<sup>17</sup> which is consistent with the adult learning principles. A constructivist approach fosters open communication between students and the instructor that promotes interactive discussion and negotiation regarding relevant topics; therefore, it creates an environment of shared information.

Constructivism promotes self-directed learning in which learners assume responsibility for their own learning. This approach is consistent with Knowles' four phases of the adult learning process in which individuals are the driving force behind their own learning efforts by 1) determining their own learning needs, 2) creating a learning strategy and obtaining resources, 3) implementing the learning strategy and using acquired resources, and 4) evaluating the progress of achieving learning goals.<sup>12</sup> Constructivist approaches depend on the ability of learners to self-manage their learning situation and actively engage with peers.<sup>18</sup> Educators utilizing constructivist approaches become facilitators of learning and relinquish the roles of authority figures and primary resources for students. Essential to critical thinking, constructivism fosters the development of various perspectives in problem solving that requires students to look beyond arriving at a single correct answer.<sup>18</sup>

### LEARNING STYLES

Effective instructional strategies depend on the educator's ability to recognize and understand the characteristics of the adult learner. To enhance learning, educators must consider individual learning preferences when designing course content and delivery methods. Learning styles are the preferred methods and environments<sup>12</sup> in which individuals choose to participate in order to receive and understand information. Learning styles are not constant; but instead, they are subject to change depending on the learning environment and experiences.<sup>20</sup> Unfortunately, most educators only use a limited number of instructional methods<sup>21</sup> with the assumption that this approach is adequate in meeting the learning needs of students. Educators must use a variety of instructional methods to meet the needs of the

diverse learning styles among students. Additionally, usage of a variety of instructional methods facilitate retention and understanding of information, thus improving academic performance.<sup>21</sup>

David Kolb's learning theory is centered on four learning experiences of (a) concrete experience, which is experience-based; (b) abstract conceptualization, which is theory-based; (c) active experimentation, which is activity based; and (d) reflective observation, which is observation based.<sup>20</sup> These four learning experiences are used in combination to identify the four learning style preferences and they are described as (a) convergers (AC and AE), who tend to prefer learning by doing and thinking; (b) divergers (CE and RO), who tend to prefer learning by feeling and watching; (c) assimilators (AC and RO), who tend to prefer learning by watching and thinking, and listening; and (d) accommodators (CE and AE), who tend to prefer learning by feeling and doing.<sup>22</sup> Figure 1 illustrates the relationship between Kolb's learning experiences and learning preferences.<sup>11,16,20</sup> Learning style preferences among allied health students are varied and subject to change throughout the educational process, which is typical as students engage in different learning environments and gain experience.

In 2005, Russian reported that respiratory therapy freshmen students preferred the diverger and accommodator learning styles but senior students preferred the converger and assimilator learning styles.<sup>21</sup> Wessel and Williams indicated that physical therapy students preferred the converger and assimilator learning styles,<sup>23</sup> while Stradley et al reported that athletic training students preferred the accommodator and assimilator learning styles.<sup>16</sup> Additionally, critical thinking correlated with the preference for learning by active experimentation and abstract conceptualization.<sup>23</sup> However, learning style preferences are not indicators for determining students' abilities to develop critical thinking skills or for determining academic success. Lecture-based instruction alone will not adequately serve the diversity of learning style preferences among students; therefore, educators are charged with the task of creating learning environments that incorporate various instructional methods. The development of critical thinking skills requires individuals to move through the learning cycle using all four modes of learning; therefore, educators need to encourage students' engagement in all four modes of learning.<sup>11</sup> Since learning is a personal experience, educators should explore and develop their own learning styles and may require them to move outside of their preferred learning comfort zone.

There is so much more involved in teaching than just getting up in front of a group of students and lecturing on content material. A thorough understanding of learning theories and learning styles are required to adequately serve and prepare a diverse student population. As stated earlier, learning is active; learning requires active student and instructor participation. Student-centered instructional strategies not only encourage active participation but enhance the development of critical thinking skills. Additionally, active participation in learning enhances student interest, creates anticipation for future learning opportunities, and increases information retention.<sup>24</sup> Constructivism places the student at the center of instruction,<sup>25</sup> which is consistent with student-centered learning and adult learning. Constructivist approaches essential to learning in health care education include inquiry-based, problem-based, and



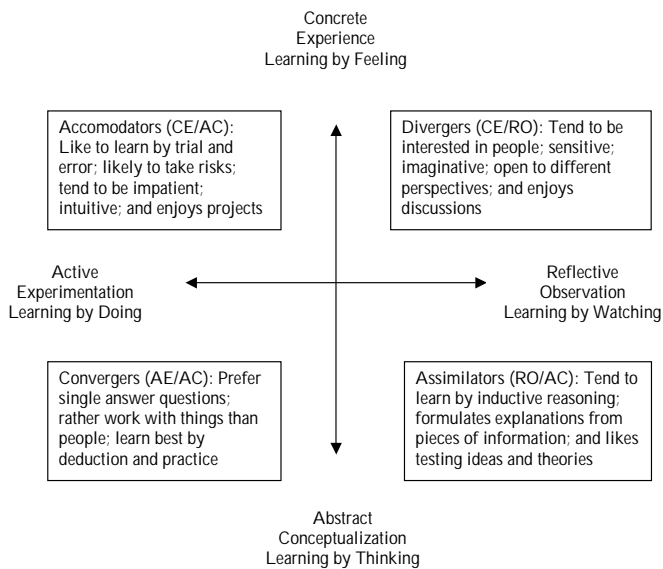


Figure 1. The relationship between Kolb's learning experiences and learning preferences. Each individual has a preference for a particular type of learning style. The development of critical thinking skills require individuals to move through the learning cycle using all four modes of learning.

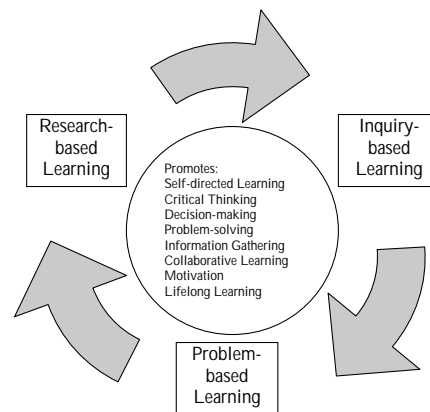


Figure 2. The active learning flywheel represents a continuous learning cycle that facilitates the development of attributes associated with self-directed learning and critical thinking.

research-based learning methods. Learning begins with a question or a problem that leads to research to find possible solutions.

## TEACHING AND LEARNING STRATEGIES

### Inquiry-based Learning

Inquiry is the art of questioning, and thinking begins with questioning. Inquiry-based learning (IBL) promotes critical and analytical thinking skills. Effective questioning strategies facilitate critical thought and assist students in the formulation of logical conclusions and supported points of view by integrating existing knowledge with new information.<sup>26</sup> Educators must help students formulate and ask meaningful and relevant questions, which stimulate thinking and creativity. "Teaching students how to ask critical questions improves critical thinking skills."<sup>27</sup> Additionally, IBL places students in the active role and educators assume the role of facilitators in the questioning process, which allow students to direct and construct their own learning. Inquiry-based learning can be used effectively in almost any learning situation including one-on-one learning, lecture-discussion formats, group learning, and clinical settings. Effective questions are open-ended and encourage students to question the instructor and each other, which mean that questions generate not only answers but more questions.<sup>28</sup> Examples of open-ended questions that generate more questions include: "How do you know? How did you come to that conclusion? What is the evidence? How do you know the evidence is reliable? What else should you consider?"

The Socratic method is a type of IBL that fosters group discussion, which can be preplanned or spontaneous. The questions are designed or adapted for the current level of student knowledge and then progress to higher levels of critical thinking.<sup>29</sup> "The art of Socratic questioning is important for the critical thinker because the art of questioning is important to excellence of thought."<sup>28</sup> The Socratic method frames essential questions that facilitate students' abilities to take information,

adapt it, and apply it to new situations; and therefore, it promotes critical thinking. The Socratic method attempts to get students to ask and analyze the "why" in situations, including "Why did that happen? Why do you feel that way? Why is it important?" The Socratic method is typically organized in a seminar or round table format, and it is usually preplanned. The purpose of preplanning informs students of the topic for discussion that allows for any sensitive issues to be addressed prior the seminar and to establish ground rules.

There are distinct differences between Socratic seminar and class discussion. The Socratic seminar has the following characteristics: (a) seating arrangement in a circle, (b) the instructor acts as a moderator, (c) discussion is peer driven, (d) average student response time is about 10 seconds, (e) the instructor does not provide any verbal or nonverbal feedback, (f) students provide supported opinions, and (g) students are accountable for contributions to the discussion.<sup>30</sup> On the other hand, class discussions typically have the following characteristics: (a) no particular seating arrangement, (b) the instructor is the primary discussion leader and contributor, (c) average student response time is less than 5 seconds, (d) instructor feedback is expected, (e) thinking ends with a correct answer, and (f) students see discussion as a small and sometimes unimportant part of course requirements.<sup>30</sup> The main difference between Socratic seminar and class discussion is the role of the instructor. The instructor is essentially hands-off in the discussion other than posing essential questions and acting as a moderator to clarify questions and keep the discussion on track. The students take ownership for most of the direction and flow of the discussion. In contrast, instructors are more involved and even control the nature of the class discussion, while providing students limited opportunity to contribute. Table 2 provides a brief overview of the Socratic seminar structure.

The Socratic method is an effective measuring tool to evaluate student comprehension of content material and critical thinking

skills; however, its use is limited by time constraints. Appropriate times for the Socratic seminar may be prior to examinations, or after covering essential or controversial content material. Preparation for conducting Socratic seminar is essential and usually requires building students up to a certain level to effectively and actively participate. Effective IBL approaches begin with open discussions, paired discussions, and group discussions which prepare students to engage in a structured Socratic seminar. Consistent with constructivist approaches and adult learning, IBL is student-centered; it promotes self-directed learning, fosters motivation, promotes active learning, values existing knowledge and previous experiences, includes peer interaction and peer teaching,<sup>31</sup> promotes collaboration; and supports research-based and problem-based learning environments.

### Problem-based Learning

Since the introduction of problem-based learning (PBL) to the McMaster Medical School in the 1960s,<sup>35</sup> PBL is gaining ground as an alternative teaching method for medicine,<sup>36</sup> nursing, and allied health care educational programs.<sup>5</sup> Problem-based learning is a student-centered, group-oriented<sup>32</sup> approach to teaching and learning that presents content material in the form of real-life problems, case studies, and simulations to engage students in active learning and problem-solving.<sup>9,33</sup> Consistent with the adult learning principles, PBL utilizes students' existing knowledge and previous experiences to solve problems. Students are responsible for directing their own inquiries<sup>33</sup> and conducting research on current topics related to the problem in order to make informed and appropriate decisions. Problem-based learning encourages students to assume responsibility for their own learning based on learning preferences and needs; therefore, it promotes lifelong learning, an essential element for personal and professional growth.<sup>5</sup> In 2004, Herron and Major suggested that PBL promoted peer collaboration, research skills, and provided opportunities for personal and professional networking,<sup>34</sup> which are necessities in the current health care environment.

How does PBL work? Typically, students work in small groups to develop possible solutions to a real-life problem. The instructor presents a case study and provides learning objectives for the problem; students are then expected to engage in independent study and participate in peer discussion to share their results.<sup>35</sup> This self-directed learning approach encourages students to choose what to learn and how to learn within the learning objectives. Unfortunately, much of the research on PBL does not provide strong evidence of a marked advantage over traditional teaching methods in achieving outcomes,<sup>37</sup> which may suggest that PBL is not a cure for what ails higher education. However, researchers indicate that PBL is at least as effective as traditional instructional methods,<sup>38,39</sup> and students experience benefits including better knowledge retention,<sup>24,40</sup> improved interpersonal and communication skills,<sup>40</sup> increased confidence in seeking and using information, and enthusiasm and enjoyment about learning<sup>38</sup> in a stimulating and challenging environment.<sup>40</sup>

Why is PBL so important to respiratory education? There are several reasons surrounding the need to incorporate PBL into the classroom setting. First, students need to learn information in the context in which it will be used. Students may forget memorized information obtained in lectures<sup>41</sup> when it is not applied to problem-solving and decision-making situations.<sup>9</sup>

Second, PBL provides a learning environment for students to practice information application to patient situations without causing potential harm to real-life patients. Computer simulations and patient simulator systems are excellent venues to practice critical thinking skills in realistic patient situations.<sup>42,43</sup> Third, the National Board for Respiratory Care (NBRC) Registered Respiratory Therapist (RRT) credentialing process requires two examinations. The written registered respiratory therapist examination (WRRT), consisting of multiple-choice questions, and the clinical simulation examination (CSE), which is based on a series of patient case studies requiring respiratory therapists to gather information and make appropriate decisions regarding patient treatment plans. The WRRT and CSE examinations measure problem-solving and critical thinking skills; and historically, the CSE pass rates are lower than the WRRT pass rates (Table 3).<sup>44-50</sup> Even though there are practice examinations available to help students and graduates prepare for the RRT credentialing examinations, the critical thinking process must begin before the test taking process. Fourth, PBL enhances student confidence by providing an environment that promotes problem-solving and decision-making proficiency. The lack of self-confidence may be a factor leading to low RRT examination participation rates. Finally, PBL utilizes the research process to promote effective information gathering of relevant evidence.<sup>38,51</sup>

### Research-based Learning

Research-based learning (RBL), also referred to as evidence-based learning (EBL), is an approach to teaching and learning that may involve different methods including incorporating relevant research results into the course content, teaching research concepts and methods, and involving students in the research process to facilitate the development of research skills. Research-based learning is not reserved only for graduate students; but instead, it can be incorporated into the curriculum at all levels. Just like the learning process, the research process begins with a question to identify a problem that leads to researching available literature and other sources to find possible solutions; and in return, it may lead to more questions that identify more problems that lead to more research. This active learning process is continuous and facilitates the development of attributes associated with self-directed learning and critical thinking (Figure 2). Unfortunately, most respiratory therapy students and practicing RTs rely on what they learned in school, experience gained in clinical situations, and information obtained from expert speakers to form their basis for decision-making in clinical practice. However, information and technology change so rapidly in the health care environment that it is virtually impossible to rely on those methods alone to stay current on new information. Depending on the textbook, new editions only appear every 3 to 5 years; and in today's healthcare environment, new textbooks are already outdated by the time they go to press. Additionally, information provided by expert speakers may be inadequate<sup>52</sup> or biased toward their own research.

Research-based learning is crucial to the development of good student learning practices that will carry over into their professional careers. Do students have adequate access to peer-reviewed medical journals? Do educators incorporate relevant research findings into course content? Do educators require students to engage in research activities? Do RTs subscribe to medical journals relevant to their practice to keep current on the latest research? Do respiratory care departments provide

opportunities for RTs to engage in research activities? These questions must be asked and addressed if the respiratory care profession is expected to grow and be recognized as a respected member of the health care team. Active involvement in research is the future of the respiratory care profession. Respiratory therapy students and practicing RTs should learn how to construct clinical questions;<sup>53</sup> locate relevant research literature from internet sources and electronic databases, including Medline, PubMed, MDCConsult, and Cochrane Library; critically appraise research studies for validity and relevance; and make appropriate decisions about the application of the study findings to specific clinical situations.<sup>54</sup> Additionally, students and practicing RTs should learn basic research concepts including understanding the difference between primary (original research) and secondary (literature reviews) sources of information, recognizing different types of research designs, and learning basic statistical analysis.<sup>55</sup>

## CONCLUSION

Research-based, inquiry-based and problem-based learning methods share common characteristics, benefits, barriers and criticisms. These methods are considered student-centered learning approaches that are consistent with the constructivist learning theory and adult learning principles. In 1999, Eitel and Steiner suggested that the type of instructional design can influence intrinsic motivation to learn.<sup>56</sup> Instructional designs that foster active learning and social integration correlate positively with student self-efficacy and competence, feeling of autonomy, and intrinsic motivation.<sup>56</sup> Of the seven characteristics of critical thinking identified by Mishoe, the ability to effectively communicate, troubleshoot clinical and technical problems, and prioritize work assignments were ranked as the most important characteristics of critical thinking in the respiratory care practice,<sup>57</sup> and the development of these characteristics are directly related to students' perceived self-efficacy, competence, and feeling of autonomy. Student-centered learning approaches foster the development of these essential attributes of critical thinking.

However, barriers and criticisms exist regarding the use of student-centered approaches in the classroom setting. Barriers to student-centered approaches include lack of trained and experienced faculty in the use of these methods, lack of available resources, time constraints, and limited understanding of adult learning principles and learning styles. Critics argue that insufficient empirical evidence exists to support the use of student-centered approaches over traditional teaching methods. It is true that more research is necessary to establish the degree of effectiveness that student-centered approaches have on improving objective student outcomes, but the lack of "enough" evidence should not be an excuse to avoid using these approaches. Student-centered approaches to learning are at least as effective as traditional methods<sup>38,39</sup> and foster independent learning and creative learning, which are important to lifelong learning because the learning process does not end with graduation.

Respiratory care educational programs are faced with many challenges to create effective and stimulating learning environments to help students develop necessary knowledge and skills to survive and thrive in today's healthcare environment, but with those challenges come opportunities to pave the way for innovative educational practices. As educators, we cannot wait until tomorrow to start. There is no better time

than now to get students engaged in developing critical thinking skills by helping them learn how to ask the right questions that identify problems and conduct research to find possible solutions. The respiratory care profession depends on it.

## REFERENCES

- 1 Mishoe SC. Critical thinking in respiratory care practice: a qualitative research study. *Respir Care*;48(5):500-516.
- 2 Wilkins R, Evans J, Specht L. A survey of physicians to identify their expectations of respiratory therapists in patient assessment. *Respir Care* 2002;47(5):583-585.
- 3 Hill T. The relationship between critical thinking and decision-making in respiratory care students. *Respir Care* 2002;47(5):571-577.
- 4 Greiner AC, Knebel E (editors). *Health professions education: a bridge to quality*. Washington DC: The National Academies Press; 2003.
- 5 Mishoe SC, MacIntyre N. Expanding professional roles for respiratory care practitioners. *Respir Care* 1997;42(1):71-91.
- 6 AARC Steering Committee of the Coalition for Baccalaureate and Graduate Respiratory Therapy Education. Development of baccalaureate and graduate degrees in respiratory care. *Respir Care Educ Ann* 2003;12:29-39.
- 7 Becker EA. Respiratory care managers' preferences regarding baccalaureate and master's degree education for respiratory therapists. *Respir Care* 2003;48(9):840-858.
- 8 Dubbs W. By the numbers: results from the AARC's 2005 human resources study. *AARC Times* 2006;30(6):36-43.
- 9 Mishoe SC, Welch M. *Critical thinking in respiratory care: a problem-based learning approach*. New York: McGraw-Hill; 2002.
- 10 Schaefer K, Zygmunt D. Analyzing the teaching style of nursing faculty: does it promote a student-centered or teacher-centered learning environment? *Nurs Educ Per* 2003;24(5):238-245.
- 11 Healey M, Kneale P, Bradbeer J. Learning styles among geography undergraduates: an international comparison. *Area* 2005;37(1):30-42.
- 12 Knowles M, Holton E, Swanson R. *The adult learner: The definitive classic in adult education and human resource development*. Houston, TX: Gulf Publishing Company; 1998.
- 13 Ozuah PO. First, there was pedagogy and then came andragogy. *Einstein J Biol Med* 2005;21:83-87.
- 14 John M. Geragogy: A theory for teaching the elderly. New York: The Hawthorn Press, Inc.;1988.
- 15 Back to College. Going back to college: frequently asked questions (FAQ). <http://www.back2college.com/library/faq.htm>. Accessed February 20, 2006.
- 16 Stradley S, Buckley B, Kaminski T, Horodyski M, Fleming D, Janelle C. A nationwide learning-style assessment of undergraduate athletic training students in CAAHEP-Accredited athletic training programs. *J Athl Train* 2002;37(4):S141-S146.
- 17 Spigner-Littles D, Anderson C. Constructivism: A paradigm for older learners. *Educ Gerontology* 1999;25(3):203-209.
- 18 Vrasidas C. Constructivism versus objectivism: implications for interaction, course design, and evaluation in distance education. *Int J Educ Telecom* 2000;6(4):339-362.
- 19 Lunenberg F. Constructivism and technology: instructional designs for successful education reform. *J Instructional Psychology* 1998;25(2):75-81.
- 20 McDonough J, Osterbrink J. Learning styles: an issue in clinical education? *AANA Journal* 2005;73(2):89-93.

- 21 Russian C. Preferred learning styles for respiratory care students at Texas State University – San Marcos. *IJAHP* 2005;3(4).  
<http://ijahsp.nova.edu/articles/vol3num4/russian.htm>. Accessed February 2, 2006.
- 22 Truluck J, Courtenay B. Learning style preferences among older adults. *Educational Gerontology* 1999;25:221-236.
- 23 Wessel J, Williams R. Critical thinking and learning styles of students in a problem-based, master's entry-level physical therapy program. *Physiother Theory Pract* 2004;20:79-89.
- 24 Chubinski S. Creative critical-thinking strategies. *Nurse Educ* 1996;21(6):23-27.
- 25 Karagiorgi Y, Symeou L. Translating constructivism into instructional design: potential limitations. *Educ Tech & Society* 2005;8(1):17-27.
- 26 Richetti C, Sheerin J. Helping students ask the right questions. *Educ Leadersh* 1999;57(3):58-62.
- 27 Loy G, Getula M, Vontver L. Teaching students to question. *Am J Obstet Gynecol* 2004;191:1752-1756.
- 28 Elder L, Paul R. The role of Socratic questioning in thinking, teaching, and learning. *Clearing House* 1998;71(5):297-301.
- 29 Rogge M. Transforming pathophysiology instruction through narrative pedagogy and Socratic questioning. *Nurs Educ* 2001;26(2):66-69.
- 30 Ball WH, Brewer P. Socratic seminars in the block. Larchmont, NY: Eye on Education: 2000: 11-12.
- 31 Plowright D, Watkins M. There are no problems to be solved, only inquires to be made, in social work education. *Innovations Educ Teach International* 2004;41(2):185-206.
- 32 Amos E, White M. Problem-based learning. *Nurs Educ* 1998;23(2):11-14.
- 33 Celia L, Gordon P. Using problem-based learning to promote critical thinking in an orientation program for novice nurses. *JNSD* 2001;17(1):12-19.
- 34 Herron JF, Major CH. Community college leaders' attitudes toward problem-based learning as a method for teaching leadership. *Community Coll J Res Pract* 2004;28: 805-821.
- 35 Chung J, Chow S. Promoting student learning through a student-centered problem-based learning subject curriculum. *Innov Educ Teach Int* 2004;41(2):157-168.
- 36 Antepohl W, Herzig S. Problem-based learning versus lecture-based learning in a course of basic pharmacology: a controlled, randomized study. *Med Educ* 1999;33:106-113.
- 37 Farrow R, Norman G. The effectiveness of PBL: the debate continues. Is meta-analysis helpful? *Med Educ* 2003;37:1131-1132.
- 38 Lusardi M, Levangie P, Fein G. A problem-based learning approach to facilitate evidence-based practice in entry-level health professional education. *JPO* 2002;14(2): 40-50.
- 39 Distlehorst LH, Dawson E, Robbs RS, Barrow HS. Problem-based learning outcomes: the glass half-full. *Acad Med* 2005;80(3):294-299.
- 40 Wood DF. Problem-based learning. *BMJ* 2003;326:328-330.
- 41 Eshach H, Bitterman H. From case-based reasoning to problem-based learning. *Acad Med* 2003;78(5):491-496.
- 42 Steadman RH, Coates WC, Haung YM, Matevosian R, Larmon BR, McCollough L, Ariel D. Simulation-based training is superior to problem-based learning for the acquisition of critical assessment and management skills. *CCM* 2006;34(1):151-157.
- 43 Rhodes M, Curran C. Use of human patient simulator to teach clinical judgment skills in a baccalaureate nursing program. *CIN* 2005;23(5):256-262.
- 44 Cullen DL, Van Scoder LI, Podgorski K, Elmerick D. Reliability of and correlation between the respiratory therapist written registry and clinical simulation self-assessment examinations. *Chest* 2003;123(4):1284-1288.
- 45 National Respiratory Care Board. Examination statistics. *NBRC Horizons* 2003;29(6): 1-8.
- 46 National Respiratory Care Board. Examination statistics. *NBRC Horizons* 2004;30(1): 1-8.
- 47 National Respiratory Care Board. Examination statistics. *NBRC Horizons* 2004;30(6): 1-8.
- 48 National Respiratory Care Board. Examination statistics. *NBRC Horizons* 2005;31(1): 1-8.
- 49 National Respiratory Care Board. Examination statistics. *NBRC Horizons* 2005;31(6): 1-9.
- 50 National Respiratory Care Board. Examination statistics. *NBRC Horizons* 2006;32(1): 1-8.
- 51 Ward J, Plevak D. An educational strategy: research methods and abstracting skills. *Respir Care* 1997;42(9):845-847.
- 52 Hess DR. What is evidence-based medicine and why should I care? *Respir Care* 2004;49(7):730-740.
- 53 Schilling LM, Steiner JF, Lundahl K, Anderson RJ. Residents' patient-specific clinical questions: opportunities for evidence-based learning. *Acad Med* 2005;80(1):51-56.
- 54 Kessenich CR, Guyatt GH, DiCenso A. Teaching nursing students evidence-based nursing. *Nurs Educ* 1997;22(6):25-29.
- 55 Landry MD, Sibbald WJ. From data to evidence: evaluating methods in evidence-based medicine. *Respir Care* 2001;46(11):1226-1235.
- 56 Eitel F, Steiner S. Evidence-based learning. *Med Teach* 1999;21(5):506-511.
- 57 Goodfellow, LT. Respiratory therapists and critical thinking behaviors: a self-assessment. *J Allied Health* 2001;30(1):20-25.



# Hospital-Based Tobacco Intervention: Seizing the Opportunity Supports Long-Term Smoking Cessation

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## ABSTRACT

A tobacco dependence intervention as brief as three minutes can increase smoking cessation rates significantly, and every patient who uses tobacco should be offered [at least] a brief intervention. Although the hospital setting offers a unique, opportunistic and effective environment in which to offer brief treatments for tobacco dependence, very few clinicians or hospitals offer practical, standardized interventions for their patients who use tobacco.

Our objective was to compare the effectiveness of different types of tobacco dependence interventions in hospitalized, adult smokers. Data was collected from a population of 800 hospitalized, adult smokers. We studied a variety of tobacco dependence interventions based on different time intensities, with two different types of non-physician clinicians delivering the intervention. The subjects who consented to treatment for their tobacco dependence received a treatment intervention that was either a highly intense or a moderately intense treatment (based on time) and delivered by a Tobacco Dependence Treatment Specialist. Subjects who did not consent to treatment received a 5-15 minute tobacco dependence intervention or a 5-minute or less intervention delivered by a Respiratory Therapist. Subjects who received the highly intense treatment quit smoking more often than those receiving the moderately intense treatment. Subjects receiving the 5-15 minute intervention quit more often than those receiving the 5-minute or less intervention, but neither of these intervention groups quit more often than those who consented to, and received treatment.

Our data supports that highly intense treatment delivered by a Tobacco Dependence Treatment Specialist is most effective in increasing long-term (6-months) smoking cessation success rates of hospitalized adult smokers, and shorter interventions

delivered by a Respiratory Therapist are also effective in increasing long-term smoking cessation success rates. Hospitals can increase the long-term smoking cessation success rates of adult patients who are smokers by using Tobacco Dependence Treatment Specialists and/or Respiratory Therapists to deliver a tobacco dependence intervention. Both types of clinicians and even a minimal contact intervention (5 minutes or less), will increase the success rates of long-term smoking cessation in hospitalized adult smokers.

## INTRODUCTION

Managing tobacco use and addiction is a complex process and minimal clinical interventions have been found to be effective in increasing tobacco users' motivation to quit. A tobacco dependence intervention as brief as three minutes can increase smoking cessation rates significantly, and every patient who uses tobacco should be offered [at least] a brief intervention.<sup>1</sup> Although the hospital setting offers a unique, opportunistic and effective environment in which to offer brief treatments for tobacco dependence, very few clinicians or hospitals offer practical, standardized interventions for their patients who use tobacco.

The significance of negative health outcomes associated with tobacco use is reflected in the top four medical causes of death in the United States (heart disease, cancer, stroke, and chronic obstructive pulmonary disease), and the associated financial burden of \$157 billion in annual health-related economic losses.<sup>2</sup> Smokers are in the hospital more often than non-smokers, and there is evidence that hospitalized smokers are receptive to smoking-cessation interventions.<sup>3</sup> The obstacles associated with getting healthcare delivery systems to adopt nicotine dependence treatment interventions are numerous and significant, and include time constraints limiting physicians' interaction with their patients, physicians are often reluctant to intervene, hospitals do not provide training and support to treat tobacco use, and healthcare facilities do not have systems in place to support consistent and universal identification of tobacco users.

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Individuals living in the community may not have otherwise sought help to quit, but may be receptive to assistance if hospitalized. According to Slade, "Those who have tobacco-caused illnesses and are struggling with nicotine dependence as a central issue have serendipitously advanced the treatment process among others who have not yet realized the significance of their smoking."<sup>4</sup> A hospital-based nicotine dependence treatment program may increase the number of non-smokers in the community. There is evidence to support the importance of offering some type of smoking cessation intervention to the hospitalized patient. The efficacy of hospital-based intervention may differ according to the type and intensity of the intervention method and the nature of the patient's illness. Results suggest that smoking interventions delivered during a period of hospitalization, with follow-up support after discharge, increase smoking cessation.<sup>5</sup> Since there is a need and desire for hospitalized smokers to quit smoking, we designed a program utilizing the respiratory therapy clinician's unique opportunity to provide a brief nicotine addiction intervention utilizing the bedside "teachable moment." We also instituted a Tobacco Dependence Treatment Program (TDTP) for admitted patients. This program utilized a Tobacco Dependence Treatment Specialist (TDTS) to provide intervention, and compared two treatment interventions with different time intensities. Employing a minimal-contact nicotine addiction intervention program in a hospital can turn mandatory, short-term abstinence into long-term (six months) smoking cessation.

## METHODS

### Subjects

Data was analyzed from a convenience sample of 800 adult smokers >18 years old, (400 from Year I and 400 from Year II) admitted to the hospital. Four hundred subjects consented to a tobacco dependence treatment assessment (intervention) and follow-up telephone contact, and 400 subjects did not consent to an intervention, but did consent to follow-up calls. The protocol was approved by the Saint Barnabas Medical Center Institutional Review Board. All subjects that were not contacted at the six month follow-up telephone call were counted as smokers. All subjects who expired were excluded from the data. The subjects were classified into two categories, smokers and non-smokers after a six-month period.

### Procedures

All hospital patients identified as smokers received an initial visit by a respiratory therapist (RT) who introduced the in-house TDTP and delivered educational and self-help material that included contact information for external community support resources. The RT facilitated intervention by attempting to motivate the patient, to commit to a quit attempt with assistance from a TDTS. The RT's intervention included education on smoking related disease process and lasted 5-15 minutes during Year I (n=200), and 5 minutes or less in Year II (n=200). The therapist asked the patient if they would like to see a TDTS. When the patient desired further assistance to quit the RT identified the patient to the TDTP.

The TDTS assessed each individual's stage of change in regards to a commitment to a smoke-free life-style, according to Prochaska and DiClemente.<sup>6</sup> Year I we offered a highly intense tobacco intervention lasting 1-3 hours for patients desiring to quit smoking and agreeing to treatment, collecting data from adult smokers (n=200) who had been admitted to the hospital. During Year II we offered a moderately intense tobacco

intervention lasting 30-60 minutes for patients desiring to quit smoking and agreeing to treatment, collecting data from adult smokers (n=200) who had been admitted to the hospital. For both groups of subjects a tobacco intake and assessment was conducted by the TDTS, which included previous and present tobacco usage, previous quit attempts, review of withdrawal/abstinent symptoms, the Fagerstrom Test for nicotine dependency, and recommendation of a quit method. The assessment addressed both the psychological, behavioral, and physical aspects to tobacco dependence. Behavioral modification and stress reduction techniques were also explored in the intervention session to address routine changes and psychological aspects to dependence. The interview took into consideration any pre-existing medical conditions or procedures before recommending pharmacotherapy or certain behavioral and/or stress reduction therapies. A TDTS may have (rarely) ordered a patient consultation with a dietician.

In addition to the length of the intervention, there were two more distinctions between the highly intense and moderately intense intervention. In the highly intense intervention there were additional brief counseling visits made by the TDTS after the initial intervention and the patient was given the opportunity to view a supplementary in-house nicotine dependency video. In the moderately intense intervention, multiple counseling visits were not made with the patient after the initial intervention, nor were additional motivational videos shown.

At the conclusion of each initial tobacco dependence assessment, patients were prepared with an action plan to maintain their smoke-free lifestyle upon discharge. After discharge, the TDTS followed-up with participants via telephone for a time period of six months to provide support and encouragement and answer any questions during the maintenance stage of change. These phone calls were made at the time intervals of 24-48 hours, one week, one month, three months, and six months post-discharge.

### Data Analysis

The measurement tool was self-report. Biochemical samples were not requested. In support of using self-reported data in smoking cessation research, the Surgeon General concluded that it is neither essential nor feasible to obtain biochemical validation in this type of study.<sup>7</sup>

## RESULTS

Year I revealed that 66 subjects (n=200) who had received the highly intense intervention reported that they were smoke-free at the time of the six-month follow-up phone contact. Also in Year I, 36 subjects (n=200) who declined treatment, but received a 5-15 minute intervention by a RT reported that they were smoke-free. Year II revealed that 54 subjects (n=200) who had received the moderately intense intervention reported that they were smoke-free at the time of the six-month follow-up phone contact. Also in Year II, 43 subjects (n=200) who declined treatment but received a 5 minute or less intervention by a RT reported that they were smoke-free. A total of 198 subjects (n=800) were smoke-free at the six month contact.

## DISCUSSION

Our findings support that a highly intense tobacco dependence intervention by a TDTS produced the highest rate of permanent cessation (six months abstinence). Another significant finding of our study is that a total of 79 hospitalized subjects who

declined treatment in our program, but did receive educational material and a brief motivational intervention from an RT, quit smoking within six months of their discharge. This data supports that although a highly intense tobacco intervention for hospitalized smokers is preferred to provide the best outcome, even a minimal-contact, nicotine addiction intervention program during hospitalization can help smokers turn mandated, short-term smoking abstinence into permanent cessation.

Our study examined three parameters, the length of intervention time (intensity) spent giving advice or counseling to quit smoking, the effectiveness of non-physician clinician advice through an RT to quit smoking, the effectiveness of non-physician clinician counseling through a TDTS to quit smoking. We then evaluated the effect of these parameters on successful smoking cessation among hospitalized smokers. Our study results support the findings of the meta-analysis by the Public Health Service (PHS) and the three key subsequent conclusions published in their 2000 Clinical Practice Guideline: Treating Tobacco Use and Dependence. These three PHS conclusions are, one, minimal clinician interventions lasting less than 3 minutes increase overall tobacco abstinence rates, two, "treatment delivered by a variety of clinician types increase abstinence rates, therefore all clinicians should provide smoking cessation interventions" and three, there is a strong dose-response relation between the intensity of tobacco dependence counseling and its effectiveness (the rate of abstinence). Additionally, our study's use of RTs to provide smoking cessation counseling underscores the importance of the finding within the PHS Guideline which supports that all clinicians should be educated and trained in effective tobacco dependence treatments.

Our data supports that telephone follow-up with patients post-discharge is effective in supporting successful long-term abstinence (also supported by the United States Department of Health and Human Services). We found that there was a higher abstinence rate at one month and three months than at six months, suggesting more time intervals in follow-up counseling by telephone (between 24 hours and 3 months post-discharge) is beneficial to support long-term abstinence.

An explanation for Year I subjects having a greater abstinence rate than Year II subjects can be due to different factors that include: more time spent counseling patients, multiple counseling visits and/or the viewing of additional motivational videos. The additional counseling time in Year I included more motivational enhancement and stress reduction therapy, as well as more behavior modification exploration.

We believe that the significance of a slightly higher cessation rate at six months in Year II subjects (43) who declined intervention compared to Year I subjects (36) who declined intervention, suggests that a minimal clinical intervention is all that is necessary to motivate smokers to quit in the future. For hospitalized adult smokers who are not ready to make a commitment to quit smoking, a brief intervention of just five minutes or less by a RRT is a minimum amount of time that can motivate a pre-contemplator or contemplator to abstinence within six months.

Our data can be important for hospitals or other healthcare institutions that desire to implement a smoking cessation program, but have limited resources that bar them from

implementing an intensive program for all admitted patients. More economical approaches are a five-minute or less intervention by an RRT for all admitted patients identified as smokers, or limited to only smokers of select diagnoses (ie cardiac, oncology, pulmonary).

A limitation of our study is that the majority of our patients attempted their quit attempt "cold turkey," as opposed to utilizing pharmacological means. In the hospitalized smoker, we found that, for different reasons, a smoker may decide, and/or we may recommend, initiating their quit attempt cold turkey. The patient may have quit a few days before admission, either because they felt too sick to smoke or because they abstained upon their physician's advice (ie before surgery). The patient's diagnosis may contraindicate pharmacological assistance, or the patient may recognize the opportunistic advantage of the hospitalization, having recently quit smoking pre-admission and desiring to sustain the quit attempt nicotine-free.

Another reason many of our patients quit cold turkey was a result of physicians' resistance to writing the TDTS recommended pharmacological intervention orders (NRT or Bupropion SR). Our TDTP was new and unfamiliar to physicians. Physicians may have also felt uncomfortable in their ability to address their patients' tobacco dependence due to their lack of training in treating this addiction.<sup>8</sup> Reviews of medical school curricula conducted during the late 1990's document suboptimal tobacco intervention education and training for medical students in medical schools across the United States.<sup>8</sup> Additionally, research has shown that physicians do not routinely and effectively counsel their patients to quit smoking and this may be a result of the lack of physician education, and possibly physician's own feelings of non-competence in tobacco dependence treatment.<sup>9</sup> Success rates may have been even higher at six months if physicians were more educated on the efficacy of pharmacotherapy relating to long-term nicotine abstinence.

Our data has limitations since we did not measure patients' motivation to quit smoking, which limited our ability to distinguish motivation levels of patients. Factors motivating a smoker to quit in the hospital setting are numerous. Some variables that can affect hospitalized smokers' motivation levels include: physicians' advice to quit (or lack thereof), timing of physicians' advice to quit (before, during, or after visit by TDTS or RRT), patient's perception of their illness in relation to the effects of smoking, patient's perception and/or understanding of the severity of their illness, other healthcare workers' advice to quit smoking, influence of family members to quit, patient's pre-planned intention to quit just before hospitalization (sometimes due to the request of their physician), or the patients themselves "feel" too sick, or are physically unable to continue smoking.

Future studies on physicians' openness to learn about the effectiveness of tobacco dependence treatment in the hospital setting are important. Cooperative physician attitudes towards clinician based smoking cessation efforts could highly influence the motivation of hospitalized smokers to quit and/or utilize assistance to quit (counseling and/or pharmacotherapy), with the possibility of favorably affecting their patients' long-term smoking cessation success rates. Although we have not measured their attitude change, anecdotally, we have seen positive changes in physicians' attitudes over the years. We attribute their acceptance of our role in treating tobacco

dependence with their increased familiarity with our TDTP. Physicians are now more accepting of the professional role of the TDTS/RRT in tobacco dependence treatment, and they are more aware of the availability of pharmacological interventions used in tobacco dependence treatment as medications have been added to, or changed on our pharmacy formulary. A large body of evidence supports the effectiveness of physician intervention in their patient's smoking cessation when physicians do intervene. Future studies are recommended to evaluate the effectiveness of more frequent telephone counseling between the third and sixth month period to gauge increased success in long-term cessation rates.

## CONCLUSION

By implementing a TDTP in the hospital setting we have accomplished the following: refined the identification of patient tobacco use in the hospital admission process, initiated a treatment process in this healthcare setting, created a protocol for tobacco dependence treatment, increased the number of ill tobacco users who initiate treatment of their tobacco addiction while hospitalized, and increased the number of ill hospitalized tobacco users who successfully quit smoking (become non-smokers within 6 months). We believe our data adds to the body of evidence which exemplifies that promoting the healthcare clinicians' role in tobacco dependence intervention for hospitalized smokers results in more adults quitting smoking. Our data also underscores that change in the healthcare systems' role as a proponent of preventative medicine promotes positive health behavior in individuals. Dedicating staff to provide tobacco intervention and assess the delivery of this service ensures the consistent delivery of quality treatment to the over 440,000 Americans who would die each year from a tobacco related illness.<sup>7</sup> Through the creation and refinement of a hospital-based TDTP, the promotion of hospital policies that support and provide tobacco dependence services are emphasized, facilitating a culture change among medical professionals in the way they view and treat seriously ill tobacco users. As a result of this system change, hospitals, and hopefully all healthcare institutions, will change their protocols to include the delivery of appropriate and effective tobacco dependence interventions among the defined duties of healthcare clinicians.

## REFERENCES

- 1 U.S. Department of Health and Human Services. Clinical Practice Guideline: Treating Tobacco Use and Dependence. Rockville: MD: USDHHS, 2000.
- 2 Dept. of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; Washington, D.C.: U.S. G.P.O., 2004.
- 3 Vernon JD, Crane LA, Prochaska AV, Fairclough D, Mackenzie TD. Smokers Hospitalized in an Urban, Public Hospital: Addiction, Stages of Change and Self-Efficacy. *Prev Med* 1999, 28, 488-495.
- 4 Hoffman AL, Slade J. Following the Pioneers: Addressing Tobacco in Chemical Dependency Treatment. *J Subst Abuse Treat* 1993,10, 53-160.
- 5 Munafo M, Rigotti N, Lancaster T, Stead L, Murphy M. Interventions For Smoking Cessation in Hospitalized Patients: A Systematic Review. *Thorax* 2001, 56, 656-663.
- 6 Prochaska J, DiClemente CC. Stages and Processes of Self-Change of Smoking: Toward an Integrative Model of Change. *J Consult Clin Psychol* 1983, 51,390-395.
- 7 U.S. Department of Health and Human Services. The Health Benefits of Smoking Cessation: A Report of the Surgeon General. Washington, DC: USDHHS 1990.
- 8 Spangler JG, George G, Long Foley K, Crandall SJ. Tobacco Intervention Efforts and Gaps in US Medical Schools. *JAMA* 2002; 288:1102-7.
- 9 Fiore MC, Epps RP, Manley MW. A Missed Opportunity: Teaching Medical Students to Help Their Patients to Successfully Quit Smoking. *JAMA* 1994; 271:624-626.



# Short Communications: Is There a Better Way to Set PEEP?

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How do we set PEEP today? Where do we start? When a patient comes to the ICU or ER, PEEP is set at 3-5 cm H<sub>2</sub>O and typically titrated upwards only if a high FiO<sub>2</sub> is required to maintain oxygenation. Many studies and clinicians advocate titrating PEEP based on individual patient lung mechanics to prevent derecruitment component of ventilator induced lung injury to improve oxygenation and adhere to a protective ventilation strategy.

Is there a better way to set PEEP? A recent study by Villar and associates may give us more insight into answering that question. Villar and associates hypothesized a high PEEP with a low tidal volume strategy improves outcomes in persistent acute respiratory distress syndrome (ARDS). The ventilatory strategy was based on setting PEEP above the lower inflection point on the pressure volume curve of the respiratory system (P<sub>flex</sub>). This was done in addition to a low tidal volume strategy. If 24 hrs after meeting ARDS criteria, the PaO<sub>2</sub>/FiO<sub>2</sub> remained ≤ 200 mm Hg on standard ventilator settings, patients were randomized into two groups: control and P<sub>flex</sub>/L<sub>Vt</sub>. Note, it appears the authors successfully weeded out patients who may not have had ARDS by reassessing the patients after 24 hrs to see if they still met ARDS criteria (eg had persistent ARDS.) Two-thirds of the patients were excluded due to this reassessment. This may have been done to avoid some of the criticism of previous ARDS trials in which patients were included whom many clinicians would not categorize or treat as ARDS patients. In the control group, tidal volume was 9-11 mL/kg of predicted body weight (PBW) and PEEP ≤ 5 cm H<sub>2</sub>O (smaller than the 12cc/kg in the ARDSnetwork trial). In the P<sub>flex</sub>/LTV group, tidal volume was 5-8 mL/kg PBW and PEEP was set on day 1 at P<sub>flex</sub> ± 2 cm H<sub>2</sub>O. (similar V<sub>t</sub> range as ARDSnetwork trial but different in that ARDSnetwork used the PEEP/FiO<sub>2</sub> table to determine PEEP setting). In both groups, FiO<sub>2</sub> was set to maintain arterial oxygen saturation >90% and PaO<sub>2</sub> 70-100 mm Hg and respiratory rates were adjusted to maintain PaCO<sub>2</sub> between 35 and 50 mm Hg. Main outcome measures were ICU and hospital mortality, ventilator-free days

and non-pulmonary organ dysfunction. Results: Control group had ICU mortality of 53.3% (24 of 45) vs P<sub>flex</sub>/Low V<sub>t</sub> group 32% (16 of 50), (p = .040), Control group hospital mortality 55.5% (25 of 45) vs P<sub>flex</sub>/Low V<sub>t</sub> group 34% (17 of 50), (p = .041). Control group ventilator free days at day 28 were 6.02 ± 7.95 vs. 10.90 ± 9.45 in P<sub>flex</sub>/LTV, (p = .008). All outcomes favored P<sub>flex</sub>/LTV. The mean difference in the number of additional organ failures post randomization was higher in the control group (p < .001). Also of note, plateau pressure on day 1 was almost equal, 32.6 ± 6.2 cm H<sub>2</sub>O for the control group vs. 30.6 ± 6 cm H<sub>2</sub>O for the P<sub>flex</sub>/LTV group. By day 6, plateau pressures for the control group were virtually unchanged while the P<sub>flex</sub>/LTV group had a drop in plateau pressure to 25.7 ± 7.2 cm H<sub>2</sub>O. FiO<sub>2</sub> was also shown to be lower in the P<sub>flex</sub>/LTV group than the control group. The authors concluded that a mechanical ventilation strategy with PEEP level set greater than P<sub>flex</sub> added to a low tidal volume improved outcomes compared with a higher tidal volume and relatively low PEEP strategy.

## COMMENTARY

This study could be considered a follow-up to the original Amato study which also used a low Vt/PEEP set to lower inflection point of PV curve but as the authors note, Amato included recruitment maneuvers in his trial and the patient population was atypical in that a lot of pneumonia patients were enrolled. However, this randomized controlled trial provides additional support for Amato's work. It is of interest to note that the ARDS network trial showed an absolute reduction in mortality of 9% (22% reduced mortality vs. control group) vs. the current Villar trial which showed an absolute reduction in mortality of 21% (a 38% reduction vs. control group.) So the absolute reduction in mortality by setting PEEP to the individual patient's PV curve was DOUBLE that of the ARDS network strategy. The authors in the discussion section state "We speculate that the use of PEEP P<sub>flex</sub> ± 2 cm H<sub>2</sub>O set on day 1 with a small VT in comparison with a ventilatory protocol with a higher VT and low PEEP level has the greatest impact on patients with persistent, established ARDS."

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# Short Communications: Learning Waveforms

Timothy France, BS, RRT

Ventilator asynchrony can be caused by a number of clinical situations. Common causes are pain, agitation, substance abuse withdrawal, increase in metabolic demands or inappropriate ventilator settings. This article will focus on the last reason, inappropriate ventilator settings. Flow controlled modes have an inherent limitation in that flow is fixed. Modes such as AC or SIMV have flow that is set and no matter what flow a patient may need, the ventilator will not respond to the patient's demand. If the patient's flow demand is 80 lpm and the ventilator is set to deliver the flow at 40 lpm, there will be a flow deficit that can cause patient-ventilator asynchrony and significant increased work of breathing. This phenomenon is demonstrated by the scooping of the pressure waveform as the patient tries to pull more flow from the ventilator. The flow rate however stays constant regardless of patient demand.

During volume/flow controlled breath delivery, there should be a linear rise in pressure. The rate of pressure rise will vary with compliance, resistance, autopeep and other factors. However the essential key concept is to identify any scooping or concavity in the pressure waveform at any point during the inspiratory phase. This indicates inadequate flow to meet patient demand and needs to be corrected. Corrective actions include increasing peak flow rate (decreasing inspiratory time), changing to a decelerating flow pattern if available, reassessing  $V_t$ . If the ventilator can measure peak spontaneous flow rate, it may be useful to switch to a low level of pressure support and directly measure the patient's inspiratory flow rate and then set the flow rate equal to or greater than the patient's flow rate. Additionally, it may be useful to note at the same time the patient's spontaneous  $V_t$ . If the set  $V_t$  is smaller than the patients desired  $V_t$ , manipulating flow rate settings will be fruitless. Other factors to consider are sedation and overall level of ventilatory support. Note: there are some ventilators on the market which, often unbeknownst to the user, switch from flow controlled breath delivery to variable flow delivery under some defined condition such as a drop in airway pressure below some threshold. The pros and cons of this 'feature' are beyond today's

discussion. One can ascertain this is occurring if one sees in A/C volume mode that the actual exhaled tidal volumes are much larger than the set  $V_t$  (assuming air trapping is not occurring). This certainly can confuse management, especially when trying to adopt a low  $V_t$  strategy in that it becomes difficult if the ventilator operating characteristics can vary. This makes it difficult to ascertain whether the ventilator or the patient is the source of the anomaly.

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# Pulmonary Interstitial Emphysema in a Premature Infant

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## BACKGROUND

Pulmonary interstitial emphysema (PIE) is an iatrogenic pulmonary condition of mechanically ventilated infants. It is manifested with air collection in interstitial, interlobar and peribronchovascular sheaths, as well as within the lymphatic channels. PIE is more frequent in premature infants who require mechanical ventilation for severe lung disease. The pressure and oxygen concentration required to keep the alveolar ducts open and maintain oxygen saturation may cause barotrauma of the immature lung. Once PIE is diagnosed, intensive respiratory management is required to reduce mortality and morbidity. We present a case of PIE in a premature infant with a brief review of the literature.

## CASE REPORT

**Prenatal History:** This preterm baby girl was delivered by caesarean section at 30 weeks of gestation due to complete placenta previa. Mother was a 31 year old, Hispanic female G4, P2012 who was generally healthy with no prior history of any medical illnesses. She was hospitalized at 28 weeks of gestation for vaginal bleeding secondary to complete placenta previa. During her hospital stay she received 4 blood transfusions with packed red blood cells due to a fall in hematocrit from 30 to 24. She received 2 doses of betamethasone, 3 doses of magnesium sulphate, 6 doses of Ampicillin and 5 doses of Gentamicin. She was Rh negative and received 2 doses of Rhogam prior to delivery. Her serology for hepatitis B virus, *Treponema pallidum* and HIV was negative and she was rubella immune. She had negative culture results for Group B streptococcus (*Streptococcus agalactiae*), *nisseria gonorrhoeae* and *chlamydia trachomatis*. She denied any use of tobacco, alcohol or illicit drugs. Her glucose tolerance test was borderline high and she was managed with dietary restrictions. A prenatal sonogram done at 28 weeks of gestation revealed no gross fetal anatomic abnormalities.

**Neonatal History:** The baby had an APGAR score of 7 and 7 at 1 and 5 minutes respectively. She received routine delivery room care. Positive pressure ventilation (PPV) with neopuff was used during transport of the baby to neonatal intensive care unit (NICU) where she was placed on nasal CPAP (nCPAP) with an initial FiO<sub>2</sub> of 0.40, which was decreased to 0.35 over the next 12 hours. Her weight (1455g), length (42cm) and head circumferenceHC (28cm) were appropriate for gestational age. The initial physical examination was remarkable for respiratory distress with decreased air entry bilaterally and subcostal retractions. She was kept NPO and IV fluids were started. An umbilical arterial (UA) line was placed. Bacteremic work up was done and she was started on Ampicillin and Gentamicin.

Initial arterial blood gas at 2 hours of age was normal (pH 7.32, PCO<sub>2</sub> 49, PO<sub>2</sub> 168, HCO<sub>3</sub> 24, O<sub>2</sub>sat 99, BE -2.3). Chest X-ray (CXR) showed bilateral hazy pulmonary granularity with air bronchograms, compatible with mild hyaline membrane disease (HMD) (Fig 1). By 20 hours of life the baby started to have low oxygen saturations with deterioration in the respiratory status requiring increasing oxygen concentrations. ABG prior to intubation showed pH 7.33, PCO<sub>2</sub> 46, PO<sub>2</sub> 45, HCO<sub>3</sub> 23, O<sub>2</sub> sat 77, BE - 2.7. She was intubated and 3 ml of intra-tracheal Curosurf was administered. Her clinical status improved but she continued to have fluctuation of oxygen saturations. A repeat CXR showed worsening changes of HMD with serpiginous lucencies overlaying the right base, consistent with PIE (Fi. 2). As the tip of the ET tube was at the carina, it was pulled back and the infant was placed in the right lateral decubitus position.

A CXR on 4<sup>th</sup> day of life showed improvement in the PIE. She was on mechanical ventilation with an IMV of 35, FiO<sub>2</sub> of 0.30, PIP/PEEP of 14/5. She improved symptomatically and was extubated on 5<sup>th</sup> day of life and placed on nCPAP with FiO<sub>2</sub> of 0.30 and later weaned to nasal canula with FiO<sub>2</sub> of 0.25 on the 6<sup>th</sup> day. A repeat CXR showed marked decrease in cystic changes in the right lower base. The respiratory distress resolved by 11<sup>th</sup> day of life and she was breathing room air and continued to have a stable respiratory status.

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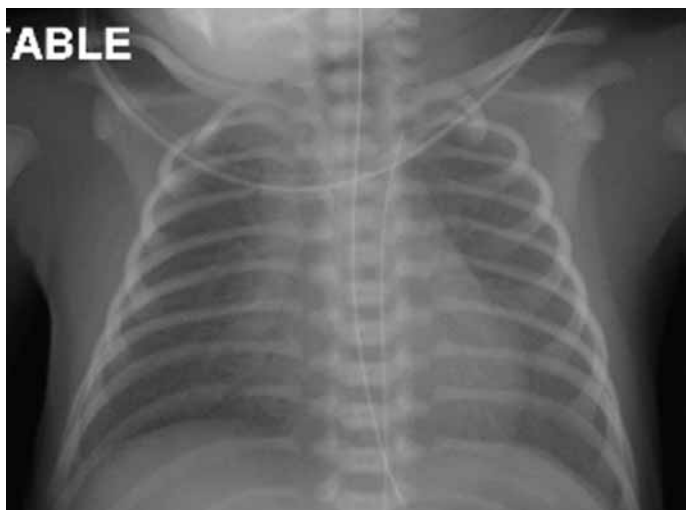


Fig. 1: An AP supine radiograph of chest shows tip of orogastric tube just passed GE junction in stomach and that of UA line at T2. The cardiothymic silhouette is normal. There is hazy granular pulmonary pattern bilaterally with air bronchograms consistent with mild hyaline membrane disease



Fig. 2: An AP slightly rotated radiograph of chest shows tip of endotracheal tube at carina, that of enteric tube in the stomach and that of UA line at T10-T11. There is increase in hazy pulmonary granularity with multiple serpiginous air filled structures at the right base consistent with pulmonary interstitial emphysema. Thymus is atrophied and cardiac size and configuration unremarkable.

## DISCUSSION

Several decades ago, PIE was a common occurrence in infants with severe respiratory distress on ventilators. Currently, it is an uncommon occurrence because of advances in respiratory care, use of pulmonary surfactant, improved conventional ventilation and use of high-frequency oscillatory ventilation for infants difficult to maintain with conventional ventilation.<sup>1</sup> In presurfactant era Gaylord et al, found that PIE developed in 3% of infants admitted to NICU.<sup>2</sup> In a randomized trial of surfactant replacement therapy at birth, in premature infants of 25-29 weeks' gestation, Kendig et al found PIE in 8 of 31 (26%) control neonates and 5 of 34 (15%) surfactant-treated neonates.<sup>3</sup>

Immature lungs of premature babies are underdeveloped and lack adequate surfactant to keep the alveolar ducts and early alveoli open on inspiration and expiration. This results in diminished surface for gas exchange and widespread atelectasis, requiring high levels of inhaled oxygen and PPV.<sup>4</sup> Excessive intra-airway pressure may lead to leak from the alveolar ducts into the lung interstitium. Once in the interstitium, the gas is absorbed into the rich lymphatic network of the neonate and carried toward the pleural and central bronchopleural lymphatics.<sup>5</sup>

Other risk factors for PIE include aspiration of meconium, fluid and blood, pneumonia, low APGAR scores, use of high peak airway pressures on mechanical ventilation and incorrect position of the ET tube.<sup>6</sup>

Studies have demonstrated the presence of free elastase and alpha 1-proteinase inhibitor as well as elastase-alpha 1-proteinase inhibitor in tracheal aspirate fluid of neonates with severe RDS who develop PIE.<sup>7</sup> This elastolytic damage and barotrauma in addition to infection play a major role in acute pulmonary injury and PIE in the early stages of RDS.

Currently, PIE is observed less frequently because of treatment of the immature fetus antenatally with steroids and postnatally with exogenous surfactant for RDS. Surfactant keeps the alveolar ducts open and also assists in the recruitment of

alveolar ducts to prevent areas of overinflation and underinflation.<sup>8</sup> Currently, PIE is seen more often in infants on long-term ventilator therapy with uneven aeration and bronchopulmonary dysplasia (BPD) leading to air trapping and potential airspace rupture.<sup>9</sup> PIE often occurs rapidly, usually within first 48-72 hours, being recognized in one region of the lung and quickly involving multiple lobes.

Different treatment modalities have been used to manage PIE. Lateral decubitus positioning has been successful and is most effective in infants with unilateral PIE.<sup>10</sup> Selective main bronchial intubation and occlusion of the contralateral bronchus is used to decompress the overdistended lung tissue and to avoid exposing it to high positive inflationary pressures.<sup>11</sup> Keszler et al studied use of high-frequency jet ventilation (HFJV) in 144 newborns with PIE. They concluded that HFJV was safe and more effective than rapid-rate conventional ventilation in the treatment of newborns with PIE.<sup>12</sup> Use of 3 day course of dexamethasone (0.5 mg/kg/d),<sup>13</sup> chest physiotherapy with intermittent 100% oxygen in localized and persistent compressive PIE have been studied. Lobectomy is indicated in a small number of patients with localized PIE when spontaneous regression is not occurring and medical management has failed.<sup>14</sup>

## CONCLUSION

PIE still occurs occasionally despite modern modalities of treatment and should be recognized early and treatment initiated to prevent further progress.

## REFERENCES

- 1 Nelle M, Zilow EP, Linderkamp O: Effects of high-frequency oscillatory ventilation on circulation in neonates with pulmonary interstitial emphysema or RDS [see comments]. *Intensive Care Med* 1997 Jun; 23(6): 671-6
- 2 Gaylord MS, Quissell BJ, Lair ME: High-frequency ventilation in the treatment of infants weighing less than 1,500 grams with pulmonary interstitial emphysema: a pilot study. *Pediatrics* 1987 Jun; 79(6): 915-21
- 3 Kendig JW, Notter RH, Cox C, Reuben LJ, Davis JM, et al:



- A comparison of surfactant as immediate prophylaxis and as rescue therapy in newborns of less than 30 weeks' gestation. *N Engl J Med.* 1991 Mar 28;324(13):865-71. PMID: 2000109
- 4 Campbell RE: Intrapulmonary interstitial emphysema: a complication of hyaline membrane disease. *Am J Roentgenol Radium Ther Nucl Med* 1970 Nov; 110(3): 449-56
  - 5 Wood BP, Anderson VM, Mauk JE: Pulmonary lymphatic air: locating "pulmonary interstitial emphysema" of the premature infant. *AJR Am J Roentgenol* 1982 May; 138(5): 809-14
  - 6 Morisot C, Kacet N, Bouchez MC: Risk factors for fatal pulmonary interstitial emphysema in neonates. *Eur J Pediatr* 1990 Apr; 149(7): 493-5
  - 7 Speer CP, Ruess D, Harms K: Neutrophil elastase and acute pulmonary damage in neonates with severe respiratory distress syndrome. *Pediatrics* 1993 Apr; 91(4): 794-9
  - 8 Soll RF: Prophylactic natural surfactant extract for preventing morbidity and mortality in preterm infants. *Cochrane Database Syst Rev* 2000; (2): CD000511
  - 9 Cochran DP, Pilling DW, Shaw NJ: The relationship of pulmonary interstitial emphysema to subsequent type of chronic lung disease. *Br J Radiol* 1994 Dec; 67(804): 1155-7
  - 10 Schwartz AN, Graham CB: Neonatal tension pulmonary interstitial emphysema in bronchopulmonary dysplasia: treatment with lateral decubitus positioning. *Radiology* 1986 Nov; 161(2): 351-4
  - 11 Weintraub Z, Oliven A, Weissman D: A new method for selective left main bronchus intubation in premature infants. *J Pediatr Surg* 1990 Jun; 25(6): 604-6
  - 12 Keszler M, Donn SM, Bucciarelli RL: Multicenter controlled trial comparing high-frequency jet ventilation and conventional mechanical ventilation in newborn infants with pulmonary interstitial emphysema. *J Pediatr* 1991 Jul; 119(1 ( Pt 1)): 85-93
  - 13 Fitzgerald D, Willis D, Usher R: Dexamethasone for pulmonary interstitial emphysema in preterm infants. *Biol Neonate* 1998; 73(1): 34-9
  - 14 Ahluwalia JS, Rennie JM, Wells FC: Successful outcome of severe unilateral pulmonary interstitial emphysema after bilobectomy in a very low birthweight infant. *J R Soc Med* 1996 Mar; 89(3): 167P-8P

# Defining New Procedures and Solutions in Ventilated Patient Transports

An interview with Liselott Järvinen, RN and Dr Kjell Olafsen

In-hospital transportation of the ventilated patient is usually one of the most difficult and challenging situations that ICU staff may encounter. The Intensive Care Department of Ullevål Hospital in Oslo, Norway, experienced a significant increase in ICU patient transports to the CT when it took over responsibility for neurosurgical ICU patients one year ago. Critical Care News spoke with registered nurse Liselott Järvinen, who has worked with establishing Quality Assurance standards and practices.

**How did ICU patient transports become a significant consideration of focus for defining your work routines?**

We have always had patient categories that must go for diagnosis and investigations; CT scans, ultrasound, MR investigations and X-ray examinations, so patient transports are a big part of our daily challenges in the ICU. One year ago, we took on the neurosurgery patients as well, which contributed to an increasing number of ICU patient transports as compared to the past; we went from one CT transport a day up to five times a day, a significant increase. So we have extensive experience of the challenges of transporting patients.

Some of these patients are extremely unstable, so a doctor may

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Liselott Järvinen is a registered nurse, with specialization in intensive care medicine and anesthesia. She has been working at Ullevål Hospital since 1996, and is responsible for medical technology within the ICU. She has worked with the establishment of Quality Assurance procedures for many years. Dr Kjell Olafsen received his degree in Intensive Care Medicine at the University Hospital of Tromsø, Norway. He has been the Director of Intensive Care at Ullevål Hospital since 2004. Critical Care News is published by Maquet Critical Care. The views, opinions and assertions expressed in the interviews are strictly those of the interviewed and do not necessarily reflect or represent the views of Maquet Critical Care AB. ©Maquet Critical Care AB, 2006. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any other means, electronic, mechanical, photocopying, recording, or otherwise, without the prior written permission of the copyright owner. Reprinted with permission of Maquet Critical Care News magazine.

accompany them. However, for the most part, it's the nurses that accompany the patient. We have two nurses, and a medic who coordinates arrangements for the elevator and other details within the facility.

**What was important when you started defining your requirements in transporting ventilated patients?**

In the past, we did not have respirators to do the job. We hand-bagged the patients for many years, and we observed that the patients' respiratory capabilities became diminished after transport. We had an older fleet of ventilators in the ICU at that time, and we were given permission to renew our ventilator fleet. We had one ICU ventilator that was dedicated for transport patients, but this had limitations from a practical perspective. When the neurosurgical ICU patients came to us a year ago and we were allocated additional funds, we started looking at SERVO-i, and decided to purchase it for transport purposes. It has been a great support to us and facilitated the patient transport situations. It enables us to use the same ventilator unit that the patient is treated with, simply connecting the O<sub>2</sub> gas trolley, without interrupting treatment. It is a complete system without any disruptions, so you don't need to disconnect or reconnect anything, and the patient treatment can continue as usual.

**What other ICU patients do you have, in addition to neurosurgical?**

We are a trauma ICU and an all-around ICU, and we support a broad spectrum of ICU patient categories. One main group is multitrauma patients. We also have patients from the heart/thorax surgery, gastroenterology, oncology and occasionally children down to 12 years, when the PICU needs to off-load.

We have a capacity of 11 patient beds, with a high acuity. There have been discussions about a need to increase to 17 beds in total. We have a staff of 70 ICU nurses, primarily full-time, and 9 ICU physicians. We welcome family members here 24 hours a day, especially during the acute phases.

**What are important aspects from a practical perspective, when transporting ventilated ICU patients?**

That it works, that it is safe. We need to provide stability in ventilation of the ICU patient, or trauma patient. That there are alarms that let us know if the gas supply is interrupted, that it has an extensive battery capacity, that it is simple to use and we can see quickly what the patient situation is. This enables us to focus on the patient, and not on the ventilator, from a more holistic point of view. We have trend information that allows us to go back and see if there were any events during the transport situation.

**How does the ventilator transport solution today compare to hand bagging in the past, in terms of the patient clinical situation?**

We are working on an evidence-based protocol, where we have seen the negative consequences of manual ventilation. We are in the process of this work, and have not yet made a summary of all of the negative consequences of hand ventilation. However, we have tracked patient blood gases throughout the years and have noticed that blood gases are stable in the current transport situation, and comparable to the levels we have measured before the patient has been transported. My own observation and experience is that patients who were hand-bagged required higher O<sub>2</sub> concentrations over a day or two after the transport had taken place, and often the lungs seemed to be more atelectatic. In certain cases, some very ill patients seemed to develop ARDS after the earlier transport situation with hand bagging.

The new solution with SERVO-i also enables us to monitor the patient in transport more carefully. It is easy to connect an additional capnography module, and the installation of the CO<sub>2</sub> module is an easy and simple procedure. We use this often with patients with head injuries, where it is important to have carefully regulated PCO<sub>2</sub> levels by means of stable tidal and minute volumes and expired CO<sub>2</sub>. Patients in the weaning process in pressure supportive modes can also be transported

with the ventilator, to maintain stable ventilation and to avoid extra work of breathing. This is helpful for patients in pressure-supportive modes, to see that there is no extra work of breathing, and to monitor tidal volumes without interruption in ventilation therapy.

**What is the most frequent disease or patient situation that you encounter in transport situations today?**

The most common situation is transports of neuro patients to the CT scan. In the periods where the patient is being monitored, with a control after three days, we can have up to five transports a day from the ICU. Two nurses always accompany the patient. The extremely sick intensive care patients require a certain amount of preparation before we can transport, and we always have a physician accompany us if the patient is unstable. We disconnect any infusion pumps that are not needed, for example TPN, but leave the necessary pumps including analgesia, if required.

But in an acute situation, with extra help we can prepare the patient and load and transport very quickly, within a few minutes if needed. As a final measure, we connect the oxygen trolley, set 100% oxygen on the machine, check battery status and alarm status, and take off with the patient in a safe manner in the acute situation. In these types of stressful acute situations, it is extremely important that we have followed the quality assurance transport protocol.

**You are in the process of establishing an evidence-based protocol for transport of ICU patients. What are the most important aspects you have defined in this process?**

We have learned that preparation is of utmost importance, along with a good communication with the treating physician. Any eventual complications during a transport of an ICU patient can be handled much more easily, if the preparation and communication work has been done in advance.

Transporting ICU patients is one of the most critical procedures.



Liselott Järvinen and Dr Kjell Olafsen.



Kari-Mari Tjelmeland, ICU nurse with a post-op cardiac patient on dialysis for kidney insufficiency. He has just returned to the ICU after transport for CT examination.

The risk for complications is evident, and when things go wrong, they do so in a hurry. For example, tubes can be dislodged, leakage may occur. Mental preparation of the staff accompanying these patients is therefore also very important. The protocol is focused on what steps to prepare for prior to a transport, and how to prepare the ventilator. We have established this protocol together with our ICU Director, Dr Kjell Olafsen.

**How much time does it take to transport an ICU patient to CT?**  
A controlled, follow-up neuro CT of a stable patient doesn't take long, since there are fewer infusion pumps. About 10 minutes for us to prepare, then a few minutes in the elevator, and the CT procedure takes a couple of minutes, or a total of 20 minutes.

We have another CT that is on the other side of the hospital, and that takes much longer. We need to mentally prepare ourselves when we transport the patients to the other facility. We usually have no waiting periods at the CT, when they know that we are coming with an ICU patient. However, the few times we have had to wait for some reason or another, it usually is not a problem, we have two oxygen cylinders with us, and plenty of battery power, where we can load 6 batteries in the SERVO-i ventilator. This is a big advantage.

Patient transports for X-ray examinations require other types of preparation. Will it be necessary to suction the patient? Is there oxygen, electrical supply for the infusion pumps if needed? The newer volumetric pumps are thankfully starting to have better battery capacity than in the past, but this is always a concern.

**If you summarize your current situation and solutions, what is important as you move forward?**

The arrival of SERVO-i in the ICU for patient transports is really an advantage, in our perspective. We save time and we ventilate safely in a closed system and without interruption to the patient. It is simple to use and clean. We feel from a nursing perspective that many of these details are important and were well designed.

In terms of our evidence-based protocol, it will be exciting to examine these main aspects of communication, safety, and

treatment strategies, and to summarize the results. We are also examining radiation levels in our staff members from patient transport situations. We want to challenge ourselves to continual improvement, in order to provide the best and most effective patient care in the transport situation. It is always better to act from a position of safety, than to end up in a situation where there are unnecessary risks. Patient safety and staff safety are foremost, and through preparedness, it is much easier to minimize potential risks.

Critical Care News spoke with ICU Director Dr Kjell Olafsen about the background and the need for the evidence-based protocol.

**How did you come to support the evidence-based protocol in ICU patient transports?**

I think that transporting the ICU patient is a big component of our every day challenges, as the technologies and opportunities for examining patients grow. It can be a risk-filled procedure if not done properly. The purpose of the evidence-based protocol is to examine all pre-requisites and conditions prior to transport, in order to plan and standardize, with the objectives of minimizing risks for safer patient transports, and offering more security for the staff in these conditions.

**Are evidence-based evaluations an increasingly important priority for this institution?**

Yes, if there are risks, we want procedures and routines to be standardized, in order to do them effectively. These evaluations will require a large amount of time, effort and resources to map out procedures in this respect, but we think it is an investment and significant in the long term to have this data in detail in the future. Evidence-based material is an important means of identifying the most effective routines, illuminating risk factors, and identifying the resources needed to carry out those procedures safely and effectively.



# Airway Clearance Requirements Among Patients With Mechanical Ventilation and Artificial Airways: An Overview

Jane M. Braverman, PhD

A mechanical ventilator is a device designed to augment or replace spontaneous respiration. It is used for recovery from an acute respiratory crisis and/or for long-term therapy for patients with chronic hypoventilation. For those patients for whom noninvasive ventilation is not appropriate, placement of an artificial airway is a necessary component of both short- and long-term mechanical ventilation (MV). For short-term use, endotracheal tubes are preferred. For long-term use, a tracheostomy is required. A tracheostomy may also be employed without the use of a ventilator to bypass the upper airway and maintain airway patency, to reduce the risk of aspiration, and to aid in clearing secretions from the central airways.<sup>1,2</sup>

In those patients who cannot be maintained adequately with noninvasive therapies, tracheostomy and/or MV may provide life-sustaining support. Mechanical ventilation facilitates alveolar ventilation and pulmonary gas exchange and assists thoraco-diaphragmatic dynamics.

Most commonly, MV is provided in the intensive care unit. The majority of patients receive short-term MV therapy until the cause of respiratory crisis resolves or death occurs, often within several days. Patients requiring long-term or permanent MV are referred to as chronic ventilator-assisted individuals (VAIs) or sometimes, when MV use must be permanent, as ventilator-dependent individuals.<sup>3</sup>

As MV technology continues to improve, a significant number of long-term MV patients are receiving treatment in extended care facilities, residential treatment centers, or in their homes,<sup>4</sup> thereby reducing hospital stays and costs. With the use of tracheostomies, management outside the hospital is now recognized as a feasible, cost-effective alternative.<sup>5,6</sup> However, because of the complexity of such care, the technical needs and medical issues associated with non-hospital MV utilization present major challenges to health care management teams.<sup>7</sup>

As the ventilator assumes the work of breathing, alterations occur in respiratory physiology, including changes in intrathoracic pressure, ventilation distribution, and cardiac output.<sup>8</sup> Significant pulmonary risks are associated with the use of both artificial airways and mechanical ventilation,<sup>9</sup> including, most commonly, aspiration and pneumonia. Bronchoconstriction can also occur, complicating the management of patients with underlying chronic obstructive pulmonary disease or asthma. Retention of lower airway secretions, common among VAIs, leads to atelectasis and poor gas exchange and provides an ideal medium for colonization by aspirated bacteria.

Although risks vary according to underlying pathology, patients who require an artificial airway and/or MV share the following risks of secretion retention and consequent pulmonary complications: impaired airway clearance; infection risks associated with bypassed upper airways; and immobility and associated risks of pulmonary compromise.

## IMPAIRED AIRWAY CLEARANCE MECHANISMS

Impaired airway clearance is both an indication for and a consequence of an artificial airway.<sup>10</sup> Frequently, translaryngeal intubation and/or tracheostomy are performed to clear secretions retained in the central airways.<sup>11</sup> However, the presence of such an apparatus can also cause mucosal inflammation and significant mucus hypersecretion,<sup>12</sup> predisposing to infection and encouraging atelectasis and hypoxia. When there is coexisting airflow obstruction or neuromuscular weakness, the work of breathing may be dramatically increased.

Moreover, the placement of an artificial airway bypasses the upper airway and the proximal trachea. As a consequence, certain physiological airway clearance functions are lost or impaired.

**Impairment of the mucociliary system:** Bypassed airways eliminate the humidifying, warming and filtering function of the upper airway. Breathing dry air significantly reduces mucus

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This article was provided by Hill-Rom.

transport velocity.<sup>13</sup> It is not known whether the effect of decreased humidification on mucus mobility is a result of impairment of the mucociliary transport system, moisture-related changes in mucus viscosity and elasticity, or both.<sup>14,15</sup> However, regardless of causes, increased viscosity and hyperproduction of mucus impairs ciliary function and exceeds the capacity for mucociliary transport.<sup>16,17</sup>

**Impairment of the cough reflex:** artificial airway placement may compromise the cough reflex.<sup>18</sup> Effective cough requires: inspirations sufficient to expand the airways and allow airflow to reach distal secretions; glottis closure and contraction of expiratory muscles to increase intrathoracic pressure; and sudden opening of the glottis to create a high air flow rate. Bypassing the glottis diminishes or eliminates its role in producing a forceful expulsion of air and secretions. Additionally, the reduced diameter and rigidity of an artificial airway increases airway resistance and contributes to restrictive lung disease, characterized by a reduced ability to exercise to maintain bellows function, lung volume, and aerobic capacity. Restrictive lung disease reduces the ability to generate airflow sufficient to produce an effective cough.<sup>19,20</sup> When secretion viscosity rises and elasticity falls, or when airway resistance is increased, ineffective cough may actually cause retrograde movement of secretions to the lung periphery or aspiration to the contralateral lung.<sup>21,22,23</sup>

**Structural damage to airway tissue:** An artificial airway may result in both acute traumatic injuries to airway tissue and long-term physiological responses to a foreign irritant.<sup>24</sup> The intubation procedure itself may precipitate laryngeal edema, inflammation, ulceration, or hematoma. High cuff pressures may induce mucosal ischemia and pressure necrosis of tracheal tissue. Risk factors associated with long-term or permanent tracheostomy include tracheal erosion, glottic and/or tracheal stenosis, tracheal dilation, and tracheomalacia.<sup>25</sup> Artificial airway may also be associated with denuded epithelium and ciliary damage.<sup>26</sup>

## INFECTION RISKS ASSOCIATED WITH BYPASSED AIRWAYS

In the United States, pneumonia, second only to urinary tract infections<sup>27</sup> as a common nosocomial infection, is the leading cause of death from community-acquired infection in hospitals.<sup>28</sup> Pulmonary infection is a common complication in patients treated with endotracheal intubation and mechanical ventilation. A recent international prevalence study involving more than 1,000 intensive care units indicated that ventilator-associated pneumonia (VAP) is responsible for approximately 90% of infections in patients receiving assisted ventilation.<sup>29</sup> Although the incidence of opportunistic infection varies greatly according to a number of underlying and contributing factors, the average rate of infection is approximately 25%.<sup>30,31</sup> The risk increases with the duration of invasive airway therapy.<sup>32</sup> Although debate exists regarding the mortality attributable to VAP among other causes of death, a substantial proportion of deaths result from VAP. Best estimates suggest that the crude mortality rate of VAP is 50%, with attributable mortality accounting for about 30% of total mortality.<sup>33</sup>

In patients with bypassed upper airways, the potential for infection is enhanced by a number of factors including: bypass of the filtering function of the upper airway; introduction of bacteria during aspiration; impairment of mucociliary transport;

hypersecretion of airway mucus; introduction of bacteria during intubation or suctioning; contaminated tubing, ventilator circuits, etc; and patterns of antibiotic use.

The presence of an artificial airway impairs normal airway protective reflexes. Endotracheal tubes prevent the aspiration of sizable particles, but they may permit pharyngeal secretions to enter the trachea via the interstices of the balloon cuff, resulting in tracheal colonization and increased risk of serious pulmonary infection.<sup>34</sup>

Aspiration can have dire consequences, especially for debilitated patients with underlying pulmonary disease. Deleterious consequences include chemical pneumonitis,<sup>35</sup> bacterial pneumonitis, mechanical obstruction, and transient hypoxia.

Most episodes of hospital-acquired pneumonia (which may be antibiotic resistant) are thought to derive from aspiration of pathogenic oropharyngeal bacteria into the distal bronchi.<sup>36</sup> The premise that nosocomial pneumonia in intubated patients develops from aspiration of colonized oropharyngeal or tracheal secretions is supported by studies showing that upper airway colonization usually precedes such infection.<sup>37,38</sup> The very high rate of endotracheal tube colonization may represent a persistent source of organisms causing pneumonia.<sup>39</sup>

In patients with impaired mucociliary clearance, secretions retained in the lower airways provide an ideal environment for colonizing organisms. Aspirated bacteria proliferate in the lower airways, stimulating a host inflammatory response. If the rate of bacterial proliferation exceeds the rate of host inflammatory clearance, the inflammatory response spreads to the contiguous bronchiole wall, leading to bronchiolitis, and may proceed to involve the alveoli and other interstitial tissues, leading to bronchopneumonia.<sup>40</sup> Patients who have impaired mechanical, humoral, or cellular lung defense mechanisms are especially vulnerable.

Aspiration of colonized gastric contents may also play a role in the etiology of pneumonia among patients with artificial airways. Although the role of gastric colonization and subsequent gastric aspiration as a risk factor for VAP remains controversial, most investigators agree that significant aspiration of contaminated gastric contents into the lower airway can lead to the development of VAP and may induce lung injury.<sup>41,42,43</sup> Although gross aspiration of large volumes of gastric contents is uncommon with artificial airways, the presence of invasive tubing can impair swallowing and esophageal motility, increasing the risk of aspiration.<sup>44,45</sup> Gastroesophageal aspiration may result in laryngitis, recurrent bronchitis, pneumonitis, and bronchiectasis. It may also lead to chemical pneumonia, increased secretion production, bronchospasm, and hypoxia.<sup>46</sup>

Pathogens may also be introduced directly during the intubation procedure during routine suctioning, or via contaminated tubing, ventilator circuits, etc.

Overzealous use of antibiotics, especially broad-spectrum agents, predisposes to the development of antibiotic-resistant infections.<sup>47</sup>

The pathogenesis of pneumonia associated with artificial airways and MV has been investigated extensively in the last

decade.<sup>48,49</sup> The roles of tracheal contamination from infected sinus and contaminated gastric secretions, bacterial adhesins and receptors, and other factors have received detailed attention.<sup>50,51,52</sup> Despite numerous studies, debate continues concerning the pattern and sequence of endotracheal tube colonization in intubated and MV patients. However, regardless of the precise sequence of events, significant colonization typically involves the lower part of the respiratory tract.<sup>53</sup>

## IMMOBILITY

Physical exercise is an important component of normal airway clearance, increasing mucus clearance by as much as 41% compared to quiet breathing at rest.<sup>54</sup> For those peripheral airways not effectively cleared by coughing, exercise is the most important component of the clearing mechanism.

Mechanically ventilated individuals with tracheostomies typically manifest both impaired mobility and absent or impaired cough function. As a consequence, they are prone to significant secretion retention and become vulnerable to bacterial colonization and a host of associated pulmonary complications, including recurrent infection leading to tracheitis, bronchitis, bronchiectasis, impaired gas exchange, and tissue damage.

## INDICATIONS FOR AIRWAY CLEARANCE THERAPY

Impaired mucociliary clearance is both an indication for and a consequence of the use of artificial airways. Artificial airways bypass important components of the normal airway clearance system and are irritants, which promote mucus hypersecretion and impair mucociliary clearance.

Poor secretion clearance disrupts the defense mechanisms of airway epithelium.

Retained airway secretions lead to: airway obstruction, inhibiting O<sub>2</sub>/CO<sub>2</sub> exchange; ineffective cough, resulting from mucus; accumulation in the airways; accumulation of particulate matter, including pathogens.

In individuals with bypassed upper airways, recurrent respiratory tract infections exacerbate lower respiratory tract secretion retention, frequently resulting in a vicious cycle of pneumonia, pulmonary atelectasis and respiratory failure.<sup>55</sup> During such events, existing pulmonary deficits are worsened by bronchial mucus plugging and further weakening and fatigue of respiratory muscles. Such episodes initiate a downward spiral involving recurrent or refractory pneumonia, emergency hospitalizations and, eventually, fatal respiratory failure. Prophylactic and therapeutic airway clearance is a very important component in optimizing outcomes for this patient population.

## REFERENCES

- 1 Shekleton ME. Ineffective airway clearance related to artificial airway. *Nurs Clin N Am* 1987; 22(1): 167-178.
- 2 Hess, DR. Indications for translaryngeal intubation. *Respir Care* 1999; 44(6): 604-609.
- 3 Currently, an estimated 6,800 Americans are classified as chronic ventilator-dependent patients. Stock MC, Perel A. *Handbook of Mechanical Ventilatory Support*, 2nd ed. Baltimore, MD: Williams and Wilkins; 1997; 294.
- 4 MacIntyre NR. Mechanical ventilation: the next 50 years. *Resp Care* 1998; 43(6): 490-493.
- 5 Annual costs of the hospital maintenance of VAIs is estimated to range between \$250,000-\$550,000. Although estimates vary, for patients with adequate education, motivation, and family resources to manage MV care at home, equipment and supply costs can be reduced to about \$20,000 yearly. *Ibid*, 294.
- 6 The largest part of home care costs for VAIs is allocated for skilled care, accounting for between 60-70% of total expenses. When such services are required, cost estimates are much higher than cited above, but remain well below the cost of hospital-based MV maintenance. For example, in a study of VAIs with amyotrophic lateral sclerosis (ALS), the mean yearly cost of home ventilation was \$153,252. Moss AH, Casey P, Stocking CB, Roos RP, Brooks BR, Siegler M. Home ventilation for amyotrophic lateral sclerosis patients: outcomes, costs, and patient, family, and physician attitudes. *Neurology* 1993; 43(2): 438-443. In a similar study of 38 ALS patients, yearly expenses for MV averaged \$136,000 annually compared to \$366,852 for hospital-based treatment. Moss AH, Oppenheimer EA, Casey P, Cazzolli PA, et al. Patients with amyotrophic lateral sclerosis receiving long-term mechanical ventilation. *Advance care planning and outcomes*. *Chest* 1996; 110(1): 249-255. See also, *inter alia*, Fields AI, Rosenblatt A, Pollack MM, Kaufman J. Home care cost-effectiveness for respiratory-technology dependent children. *Am J Dis Child* 1991; 147(7): 729-733; Gracy DR. Options for long-term ventilatory support. *Clin Chest Med* 1997; 18(3): 563-576; Bach JR, Intintola P, Alba AS, Holland IE. The ventilator-assisted individual. Cost analysis of institutional vs rehabilitation and in-home management. *Chest* 1992; 101(1): 26-30; Cohen IL, Booth FV. Cost containment and mechanical ventilation in the United States. *New Horiz* 1994; 2(3): 283-290.
- 7 Make BJ, Hill NS, Goldberg AI, Bach JR, Dunne PE, Heffner JE, Keens TG, O'Donahue WJ, Oppenheimer EA, Doninique R. Mechanical ventilation beyond the intensive care unit: report of a Consensus Conference of the American College of Chest Physicians. *Chest* 1998; 113(5 Suppl): 289S-344S.
- 8 For a detailed discussion of the physiological consequences of various MV modalities, see: Marini JJ, *Indications and options in mechanical ventilation*. *Eur Respir Mon* 1998; 8: 511-536.
- 9 For an outline of complications associated with intubation and mechanical ventilation, see: Weinberger Se, (ed.). *Principles of Pulmonary Medicine*, 3rd ed. Philadelphia: WB Saunders: 1998; 355-357.
- 10 Shekleton ME. *op cit* (n 1).
- 11 The placement of a tracheostomy to facilitate secretion clearance should be used only when other methods to maintain pulmonary hygiene have failed. In many cases, the use of an appropriate airway clearance modality and, if necessary, nasotracheal suctioning or artificial coughing may be sufficient. Ritz, R. *Methods to avoid intubation*. *Respir Care* 1999; 44(6): 686-699.
- 12 Wallis C, Prasad A. Who needs chest physiotherapy? Moving from anecdote to evidence. *Arch Dis Child* 1999; 80: 393-397.
- 13 Hirsch JA, Tokayer JL, Robinson MJ, et al. Effects of dry air and subsequent humidification on tracheal mucus velocity in dogs. *J Appl Physiol* 1975; 9: 242-246.
- 14 *Ibid*.
- 15 Wanner A. Clinical aspects of mucociliary transport. *Am Rev Respir Dis* 1977; 116: 73-125.

- 16 Siskind MM. A standard of care for the nursing diagnosis of ineffective airway clearance. *Heart Lung* 1989; 18: 477-482.
- 17 In one study concerning impaired mucociliary transport in intubated patients, such dysfunction was associated with a loss of cilia rather than to the development of ultrastructural abnormalities. Konrad F, Schiener R, Marx T, Georgeir M. Ultrastructure and mucociliary transport of bronchial respiratory epithelium in intubated patients. *Intensive Care Med* 1995; 21:482-489.
- 18 Although cough function is usually impaired by the placement of an artificial airway, some individuals remain able to cough quite effectively. Sant'Ambrogio G, Matthew O. Laryngeal receptors and their reflex responses. *Clin Chest Med* 1986; 7: 211-222.
- 19 Shekleton ME. Op. cite (n.1).
- 20 Newhouse M, Sanchis J, Bienenstock J. Lung defense mechanisms. *N Engl J Med* 1976; 295: 990-998.
- 21 Ibid.
- 22 Loudon RG, Shaw GB. Mechanics of cough in normal subjects and in patients with obstructive respiratory disease. *Am Rev Respir Dis* 1967; 96: 666-677.
- 23 Mucus viscosity increases and elasticity decreases most markedly if mucus is purulent. Dulfano MJ, Adler KB. Physical properties of sputum. VII Rheologic properties and mucociliary transport. *Am Rev Respir Dis* 1975; 112: 341-347.
- 24 Staffer JL. Complications of endotracheal intubation and tracheotomy. *Respir Care* 1999; 44(7): 828-844.
- 25 Slutsky AS. Mechanical ventilation. American College of Chest Physicians' Consensus Conference. *Chest* 1993; 104(6): 1833-1859.
- 26 Wanner A. Clinical aspects of mucociliary transport. *Am Rev Respir Dis* 1977; 116: 73-125.
- 27 National Nosocomial Infections Surveillance (NNIS) System Report, Data Summary from October 1986-April 1998. Atlanta, Georgia: Hospital Infections Program, National Center for Infectious Diseases, Centers for Disease Control and Prevention, U.S. Dept. of Health; 1998.
- 28 Grap MJ, Munro CL. Ventilator-associated pneumonia; clinical significance and implications for nursing. *Heart Lung* 1997; 26 (6): 419-429.
- 29 Vincent JL, Bihari DJ, Suter PM, Bruining HA, Nicolas-Chanoin MH, et al. The prevalence of nosocomial infection in intensive care units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC) study. EPIC International Advisory Committee. *JAMA* 1995; 274: 639-644.
- 30 Torres A, El-Ebiary M. Basis for the management and prevention of respiratory tract infections acquired during mechanical ventilation. *Eur Respir Mon* 1998; 8: 114-138.
- 31 Craven DE, Steger KA. Nosocomial pneumonia in mechanically ventilated adult patients: epidemiology and prevention in 1996. *Semin Respir Infect* 1996; 11(1): 32-53.
- 32 Although the risk of nosocomial infection is highest during the first two weeks of MV therapy, duration of ventilation is a risk factor exponentially related to the acquisition of ventilator associated pneumonia (VAP). The crude rates of VAP range from 1-3% per day of intubation and mechanical ventilation. Torres A. op. cite (n.30).
- 33 Ibid.
- 24 Slutsky AS. Op cit (n.25).
- 35 Acid-aspiration pneumonias carry a mortality rate of 60%-90%, depending on the extent of pulmonary involvement. Elpern EH, Jacobs ER, Bone R. Incidence of aspiration in tracheally intubated patients. *Heart Lung* 1987; 16(5): 527-531.
- 36 Valles J, Artigas A, Rello J, Bonsoms N, et al. Continuous aspiration of subglottic secretions in preventing ventilator-associated pneumonia. *Ann Intern Med* 1995; 122: 179-186.
- 37 Crouch TW, Higuchi JH, Coalson JJ, Johanson WG. Pathogenesis and prevention of nosocomial pneumonia and of patient and circuit colonization in a nonhuman primate model of acute respiratory failure. *Am Rev Respir Dis* 1984; 130: 502-504.
- 38 Dreyfuss D, Djedaini K, Weber P, Brun P, Lanore J, Rahmani J. Prospective study of nosocomial pneumonia and of patient and circuit colonization during mechanical ventilation with circuit changes every 48 hours versus no change. *Am Rev Respir Dis* 1991; 143: 738-743.
- 39 Feldman C, Kassel M, Cantrell J, Kaka S, Morar R, et al. The presence and sequence of endotracheal tube colonization in patients undergoing mechanical ventilation. *Eur Respir J* 1999; 13 (3): 546-551.
- 40 Estes RJ, Meduri GU. The pathogenesis of ventilator-associated pneumonia: I. Mechanisms of bacterial transcolonization and airway inoculation. *Intensive Care Med* 1995; 21: 365-383.
- 41 Kollef MH and Silver P. Ventilator-associated pneumonia: An update for clinicians. *Resp Care* 1995; 40(11): 1130-1140.
- 42 Noseworthy TW, Cook DJ. Nosocomial pneumonia, prophylaxis against gastric erosive disease, and clinically important gastrointestinal bleeding; where do we stand? *Crit Care Med* 1993; 21(12): 1814-1816.
- 43 In a recent study, investigators concluded that the stomach does not appear to be an important reservoir for gram-negative colonization in ventilator-dependent patients. Palmer LB, Donelan GF, Bellemore E, Greene W. Gastric flora in chronically mechanically ventilated patients: relationship to upper and lower airway colonization. *Am J Respir Crit Care Med* 1995; 151: 1063-1067.
- 44 Staffer JL. Op cit (n.24).
- 45 For a discussion and review of literature concerning gastric colonization, see: Torres A. Op. cite (n.30). *Chest* 1975; 68(4): 560-566.
- 47 Kollef MH. Op cit (n. 41).
- 48 Estes, RJ. Op cit (n.40).
- 49 Meduri GU, Estes RJ. The pathogenesis of ventilator-associated pneumonia: II. The lower respiratory tract. *Intensive Care Med* 1995; 21: 452-461.
- 50 Kollef MH. Op cit (n.41).
- 51 Palmer LB, Donelan SV, Fox G, Bellemore E, Greene WH. Gastric flora in chronically mechanically ventilated patients: relationship to upper and lower airway colonization. *Am J Respir Crit Care Med* 1995; 151: 1063-1067.
- 52 Estes RJ. op. cite (n.40).
- 53 Feldman C, Kassel M, Cantrell J, Kaka S, Morar R, et al. The presence and sequence of endotracheal tube colonization in patients undergoing mechanical ventilation. *Eur Respir J* 1999; 13: 546-551.
- 54 Wolff RK, Dolovich MB, Obminski G, Newhouse MT. Effects of exercise and eucapnic hyperventilation on bronchial clearance in man. *J Appl Physiol* 1977; 43(1): 46-50.
- 55 Wilson R. A vicious circle hypothesis operating during infective exacerbations of chronic bronchitis. *Monaldi Arch Chest Dis* 1994; 49(2): 159-164.



# Automatic Leak Compensation in the e500 Ventilator

Cyndy Miller, RRT

Nearly all patient-ventilator interfaces have variable amounts of gas leaks from either the ventilator breathing circuit/humidifier system or from around the endotracheal/tracheal tube. These leaks can lead to patient-ventilator dys-synchrony because ventilators are designed to work as closed systems (without leaks) and leaks can cause baseline pressure and flow to be unstable. A stable baseline pressure is essential for optimal patient triggering.

Automatic leak compensation is all about providing baseline pressure stability so that ventilator trigger sensitivity can be set to achieve optimal patient triggering synchrony. Optimal triggering synchrony is the basis for total breath synchrony.

Following is a discussion of how automating leak compensation, through the use of ventilator-selected bias flow, creates the stable foundation on which good patient ventilator synchrony is built.

## CHALLENGES OF TRIGGER WITH LEAK IN MAINTAINING PATIENT-VENTILATOR SYNCHRONY

Ventilators are designed to be connected to patients via closed systems. It is very uncommon in the real world to find a perfectly sealed interface between a patient and their mechanical ventilatory support system. With infants, in particular, it is common to have an air leak of approximately 15% of their tidal volume around an uncuffed endotracheal tube<sup>1</sup> (see Figure 1.) And patients ventilated via mask present an even bigger challenge. When these leaks are not compensated for, patient-ventilator dys-synchrony occurs.

## CLINICAL EFFECTS OF LEAKS IN A NON-LEAK COMPENSATED VENTILATORY SUPPORT SYSTEM

Poorly managed leaks can lead to both artifact and missed triggers. Leaks in a non-leak compensated ventilatory support system can interfere with the synchrony between the patient and the ventilator because the ventilator is designed to interact

with the patient through monitored pressure and flow (and time) signals and the leak of flow-and therefore pressure-may change these signals.

If the pressure and/or flow trigger threshold is set narrowly, it takes less change in those values to trigger the ventilator. This means that a small change in pressure and/or flow caused by a leak in the system will also trigger the ventilator, without patient effort. This is called artifact triggering. An artifact trigger can result in a mis-timed breath so when the patient's natural timing causes them to inhale, the ventilator misses the trigger effort due to the fact that it is in the middle of delivering a breath already.

If the pressure and/or flow trigger threshold is set very wide to avoid artifact triggering, it takes more change in flow and/or pressure values to trigger the ventilator.<sup>3</sup> This means that a small change in pressure and/or flow caused by a leak in the system will not trigger the ventilator but neither will a small patient effort. When a patient effort is recognized, there will be a significant delay in trigger, causing disruption in patient ventilator synchrony. See Figure 2.

## USER SET LEAK COMPENSATION

With the understanding that the presence of an unmanaged leak may consistently interrupt patient ventilator inspiratory synchrony, some manufacturers have introduced controls on their newest ventilators to allow the user to "make up for" gas escaping from the breathing circuit/humidifier system or patient airway in order to keep the pressure and flow signals stable. In most cases this is a user set flow. This method can work well but may also require frequent user adjustment to keep the system sensitive without artifact triggers. It is not practical to expect this of a busy bedside caregiver.

## THEORETICAL BASIS FOR AUTOMATING LEAK COMPENSATION

Optimal leak compensation requires:

- Correct identification of a leak as opposed to a patient effort;

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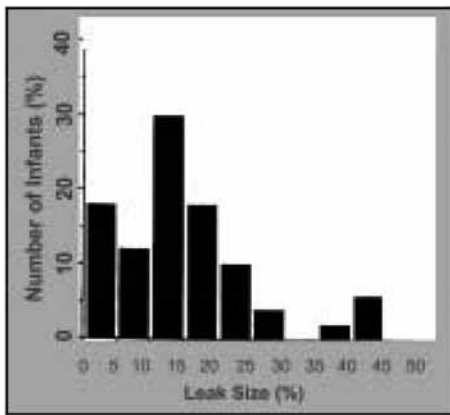


Figure 1. Distribution of airway leak size in 50 infants (n = 25 ± 11 ventilator breaths/infant). All infants were intubated with an uncuffed ET of appropriate size as recommended for body weight. 1

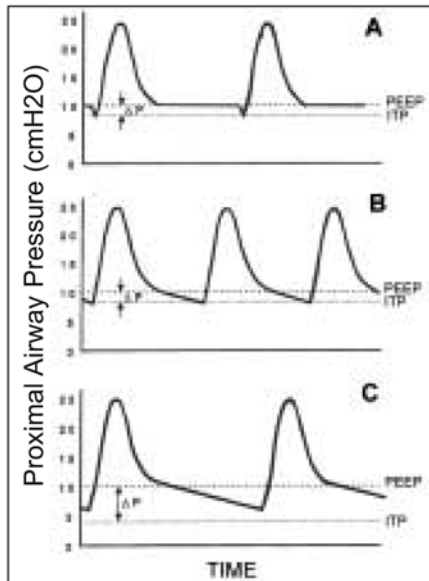


Figure 2  
ITP = Pressure Trigger Setting  
A = No. leak. Patient effort triggers breath.  
B = Leak resulting in auto triggering when ITP is set appropriately.  
C = Leak does not cause auto triggering because ITP is set very insensitively.<sup>3</sup>

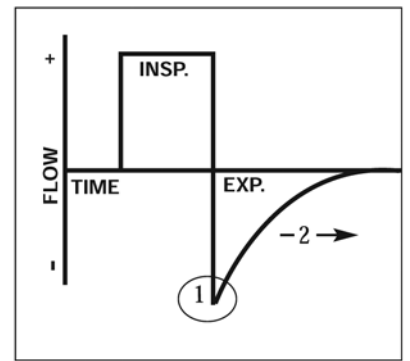


Figure 3: e500 Ventilator Base Flow Assessment

- Careful flow and exhalation valve pressure management to stabilize baseline pressure;
- Frequent re-analysis of the flow and pressure signals to accommodate changes that may occur due to wakefulness or patient position;

With correct programming the ventilator's microprocessor can do all of these things. The microprocessor already assesses flow and pressure continually. It retains this information in memory. The microprocessor can be "taught" to recognize the difference between a leak and a trigger and "taught" how to adjust flow delivery and exhalation valve pressure to compensate for leaks. The microprocessor can perform this leak compensation maneuver for the patient 24/7, for every breath, without user intervention.

### e500 VENTILATOR AUTOMATIC LEAK COMPENSATION

The e500 Ventilator is designed to automate leak compensation without user intervention. The e500 selects leak compensation flow and the exhalation valve pressure that will result in optimal leak compensation. Even when patient conditions are continually changing, this automatic leak compensation minimizes the possibility of artifact triggering when you set the flow and pressure trigger thresholds very sensitively.

When ventilating a patient with the e500 there is no need for the clinician to manually adjust a leak compensation mechanism since there is no user intervention required.

### GENERAL DESCRIPTION OF E500 VENTILATOR BASELINE PRESSURE, LEAK COMPENSATION ALGORITHM

Physically, baseline pressure is a function of the bias flow rate circulating through the expiratory limb of the breathing circuit and the pressure managed at the exhalation valve. At a given set PEEP level, baseline pressure can be stabilized by maintaining a

stable level of bias flow circulating through the expiratory limb of the breathing circuit.

**Definition of Bias Flow:** Flow delivered by the ventilator (and measured by the inspiratory flow sensor) into the breathing circuit during the exhalation phase of breathing.

**Definition of Base Flow:** Flow measured by the expiratory flow sensor at the end of the breathing circuit at end exhalation.

The e500 Ventilator delivers a bias flow of 3 L/min through the patient breathing circuit during exhalation to ensure the baseline pressure stability. As long as the measured base flow leaving the breathing circuit at end exhalation is equal to 3 L/min, baseline pressure should remain stable and therefore the e500 Ventilator does not change expiratory bias flow delivery. Leak Compensation refers to the mechanism by which e500 Ventilator adjusts delivered bias flow during exhalation to keep total flow (base flow) at end exhalation equal to 3 L/min and therefore keeps baseline pressure stable.

### HOW e500 BASE FLOW IS ASSESSED AND USED FOR ADJUSTMENT OF THE DELIVERED BIAS FLOW

Base flow is only assessed at end exhalation and used to adjust bias flow for the following exhalation time if a qualifying measurement can be made. To qualify, the following sequence must occur before measurement (see Figure 3):

1. A reversal of flow from inspiration to exhalation.
2. Minimum expiratory time of 250 msec. for Ped/Infant, 350 msec. for Adult patient selection followed by minimum of 80 msec. during which the change in flow is < 0.14 L/min/10 msec. In other words, safety against a false adjustment is ensured because base flow is only assessed at end exhalation and is used for adjustment of the delivered bias flow for the following

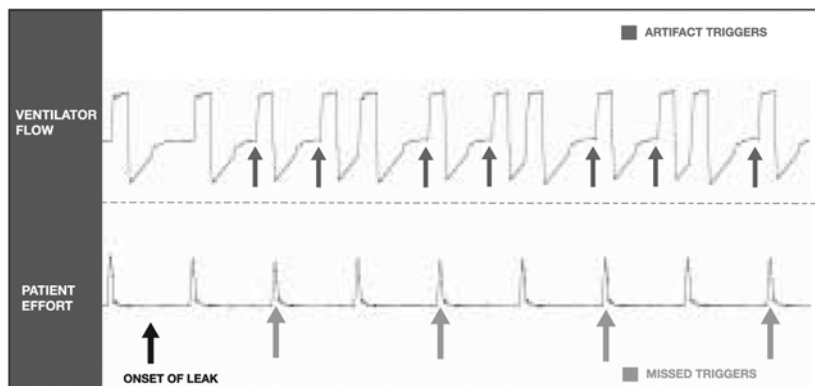


Figure 4. Ventilator with no Leak Compensation

Without leak compensation, the ventilator's flow and the patient's effort quickly fall out of synchrony resulting in missed triggers for the patient and artifact triggers on the ventilator.

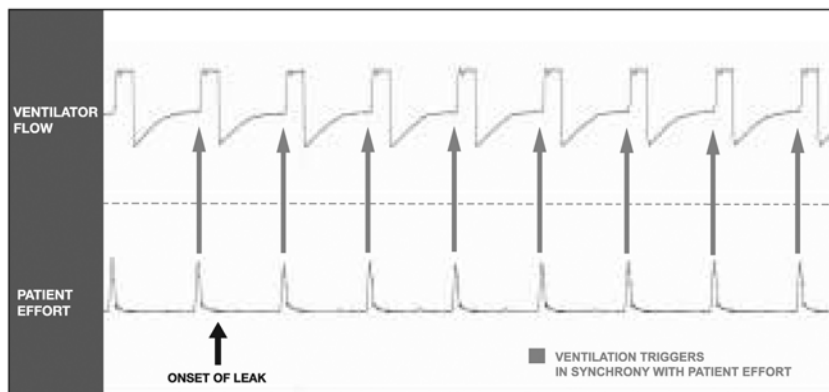


Figure 5. e500 Ventilator with Automatic Leak Compensation

With automated leak compensation, the e500 ventilator stays in synchrony with the patient's effort. Automated leak compensation is always engaged, managing baseline pressure and flow every breath, 24 hours a day.

breath if the minimum expiratory time is met followed by at least 80 msec. when flow is changing very little. If these conditions are not met, bias flow is not adjusted and remains the same for the following breath.

If a qualifying measurement of end-expiratory flow is lower than 3 L/min, it means that some flow is leaking from the patient/breathing circuit system. At the onset of the next exhalation, bias flow will be increased to bring the total up to 3 L/min. On the other hand, if a qualifying measurement of end-expiratory flow is higher than 3 L/min, bias flow for the following breath is decreased to bring the total to 3 L/min.

## EVALUATION OF THE E500 VENTILATOR AUTOMATIC LEAK COMPENSATION

The e500's automatic leak compensation was evaluated in a bench setup against a system offering no leak compensation.

### SETUP

The laboratory test setup was designed to simulate real patient triggering when a leak is introduced into the system.

### RESULTS

When a leak was introduced into the system of the ventilator offering no leak compensation, the ventilator exhibited both artifact and missed patient triggers. There was significant interruption of good inspiratory patient ventilator synchrony (see Figure 4).

In contrast, when the same exact leak was introduced into the system ventilated by the e500 ventilator with automatic leak compensation, patient triggering continued without interruption and there were no artifact or missed patient triggers (see Figure 5).

In other words, the e500 provided good leak compensation, without any user intervention when the system leak changed.

## SUMMARY

These theoretical and laboratory results suggest that the e500 ventilator is capable of managing leak compensation and baseline pressure management under changing patient conditions without user intervention. Since a ventilator's ability to compensate for leaks and manage baseline pressure affects inspiratory patient ventilator synchrony, we can conclude that the e500 is capable of successfully automating leak compensation to avoid the interruption of trigger synchrony. Managing leak compensation automatically, instead of with user selected controls, provides continual synchrony for every breath, 24 hours a day.

## REFERENCES

- 1 Bernstein G, Knodel E, Heldt G: Airway leak size in neonates and autocycling of three flow-triggered ventilators. *Critical Care Medicine* 1995, Vol. 23 No. 10, P1739-1744.
- 2 Tobin M, Jubran A, Laghi F: Patient-Ventilator Interaction. *American Journal Respiratory Critical Care Medicine*, 2001
- 3 Schwab R J, Schnader J: Ventilator Autocycling due to an Endotracheal Tube Cuff Leak. *Chest* 1991; 100:1172-73

# Lung Infection-A Public Health Priority

Joseph P. Mizgerd

**Abstract**  
Lung infections are a major public health priority because of the potential for pandemics. Recent examples include avian influenza and the severe acute respiratory syndrome (SARS). However, even in the absence of new pathogens or pandemics, lung infections have tremendous impact. Lung infections cause more disease than better-recognized threats to the public's health such as cancer, heart attacks, strokes, HIV/AIDS, tuberculosis, or malaria. This persistent and pervasive burden of lung infections receives proportionately little attention from the biomedical and public health communities.

Emerging lung infections capture the world's imagination because of the potential for pandemics. Recent examples include avian influenza and the severe acute respiratory syndrome (SARS). However, even in the absence of new pathogens or pandemics, lung infections have tremendous impact. Lung infections cause more disease than better-recognized threats to the public's health such as cancer, heart attacks, strokes, HIV/AIDS, tuberculosis, or malaria. This persistent and pervasive burden of lung infections receives proportionately little attention from the biomedical and public health communities.

## THE GLOBAL BURDEN OF LUNG INFECTIONS

The Burden of Disease Project<sup>1</sup> at the World Health Organization (WHO) collects statistics that can be used to determine the public health impact of different diseases. The metric of disability-adjusted life years (DALYs) lost takes into account the amount of otherwise healthy life lost to morbidity and/or mortality. Diseases were categorized according to the International Classification of Diseases (ICD) from WHO.<sup>2</sup>

The "lung infections" category includes "Influenza and pneumonia" (ICD-10 codes J10-18) and "Other acute lower respiratory infections" (ICD-10 J20-22), but it excludes "Tuberculosis" (ICD-10 A15-19) and "HIV disease resulting in infectious and parasitic diseases" (ICD-10 B20). By excluding respiratory tuberculosis as well as pneumonias in patients with HIV/AIDS, these statistics might be considered by some to underestimate the burden of disease due to lung infections. Even with these exclusions, lung infections accounted for more than 6% of the total global burden of disease in 2002. This disease burden is greater than that of other better-recognized causes of disease (Figure 1). This impressive burden is not an anomaly of that particular year, due to SARS or any other unusual epidemic or event, but is instead the norm. Since 1990,

when WHO began compiling and presenting such statistics, lung infections have consistently caused more burden than any of the diseases identified in Figure 1.<sup>3,4</sup>

## THE DISPROPORTIONATE BURDEN ON THE POOR

Lung infections are especially common and severe among the poor. When the relative burden of disease in communities is assessed by normalizing DALYs to population size, lung infections caused the loss of 2,983 DALYs/100,000 population in the poorest regions compared to 137 DALYs/100,000 population in the wealthiest. Thus, poverty is associated with a more than 20-fold increase in the relative burden of lung infections.

According to WHO, 2.6 billion people live in "Low Income" countries, with Gross National Income (GNI) per capita  $\leq$ US\$765, and 2.2 billion people live in "Lower Middle Income" countries, with GNI per capita of US\$766-US\$3,035. This single incremental improvement in income is associated with a dramatic difference in the relative burden of disease caused by lung infections. Lung infections caused the loss of 535 DALYs per 100,000 population in the "Lower Middle Income" population in 2002. Comparing this figure to the relevant figures listed above, it may be surmised that the vast majority (86%) of the difference due to income occurs between the lowest income group and the next-to-lowest income group. Thus, the poor are especially likely to suffer from lung infections, and relatively modest income improvements may substantially lessen their burden of lung infection. As with many infectious diseases,<sup>5</sup> fighting poverty and improving health care for the impoverished will greatly decrease the global burden of lung infections.

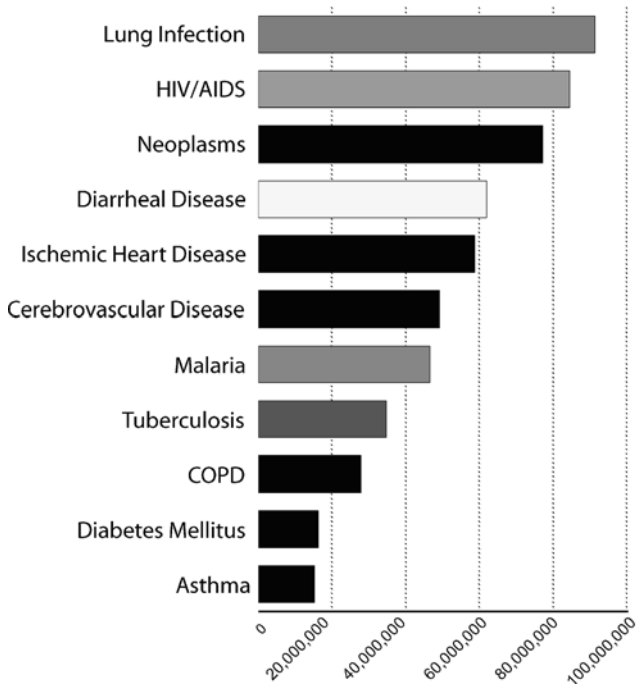
## LUNG INFECTIONS THREATEN ALL ECONOMIC GROUPS

Among those who live in wealthy societies, infectious diseases cause less of a burden than do chronic diseases such as cancers and cardiovascular diseases. However, even among advantaged populations, lung infections are remarkably prominent. In the wealthiest as well as the poorest regions of the world, lung infections cause a greater burden than any other infectious disease (Figure 2). Thus, while climbing the socioeconomic

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## Global burden of disease (DALYs lost in 2002, worldwide)



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**Figure 1.** The Global Burden of Selected Diseases in 2002, as Measured by Disability-Adjusted Life Years (DALYs) Lost Worldwide  
COPD, chronic obstructive pulmonary disease

ladder associates with a lesser burden, lung infections threaten across the economic spectra.

For those in wealthier populations, little further advancement is evident against lung infections. Focusing exclusively on the highest income populations ("Established Market Economies" or "High Income" groups in the WHO Burden of Disease Study), a comparison of the relative DALY losses due to lung infection shows little change from 1990 to 2002 (151 and 137 DALYs lost/100,000 population, respectively), whereas there have been dramatic improvements in the burdens due to other diseases within these wealthy communities. For example, among the wealthiest populations, HIV in 2002 caused less than half the disease it did in 1990 (from 159 to 72 DALYs lost/100,000 population). There are no DALY statistics available prior to 1990, but other indicators such as the US mortality rate due to pneumonia and influenza suggest that, for wealthy countries, there has been little or no progress against lung infections since the first half of the last century.<sup>6</sup>

For several reasons, lung infections in wealthy countries seem poised to become even more of a concern in the near future. First, in these populations, advancing age makes lung infections increasingly more prevalent and life-threatening.<sup>7</sup> Therefore, demographic shifts resulting in an expanding elderly community in wealthy countries<sup>8</sup> suggest that more and more people are likely to suffer severely from lung infections. Second, novel respiratory infections emerge frequently, some of which can be highly virulent. Recent examples include SARS<sup>9</sup> and avian influenza.<sup>10</sup> If and when these new infections emerge, globalization increases the likelihood that such respiratory infections will become rapidly widespread.<sup>11</sup> Third, microbes

that cause lung infections are increasingly resistant to previously effective antibiotics. While effective medical and public health practice will hopefully prevent the arrival of a "post-antibiotic" era,<sup>12</sup> the continuously diminishing number of drugs effective against *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, and other common agents of community and hospital-acquired pneumonias raises concern.

## EFFORTS AND RESOURCES

All diseases included in Figures 1 and 2, and many not listed, are critical targets of research and health care. All require more funding and more effort than they now receive. However, if some diseases (such as lung infections) are less widely recognized as critical threats to our health, then resources and efforts will be allocated suboptimally, resulting in poorly tailored responses to public health needs.

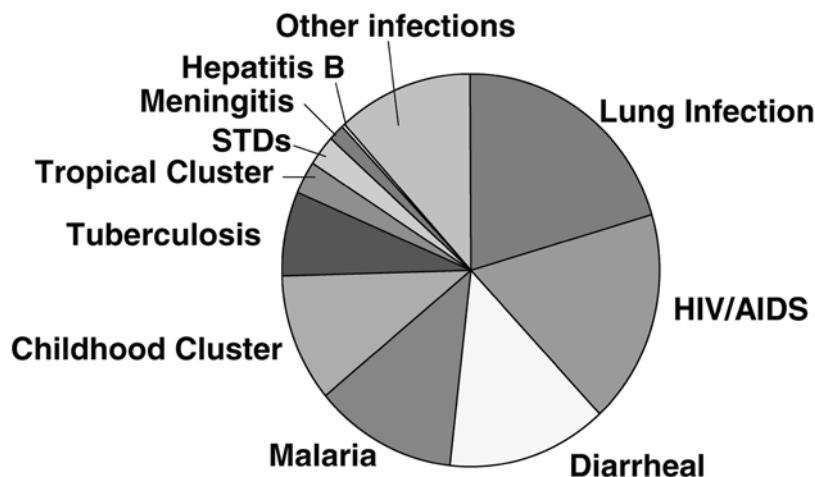
Determining whether funds are contributing to research against a given disease is horribly inexact. Furthermore, the conceptual advances with most promise against a particular disease may more likely result from basic research than from disease-focused research. However, substantial resources are allocated to understanding and fighting particular diseases, and biomedical progress against those diseases is influenced by these targeted efforts. While the greatest burdens of disease and the greatest threats to the public health might be presumed to receive the greatest shares of research funding, they do not.

The US National Institutes of Health (NIH) spent approximately US\$28 billion on health-related research in 2004,<sup>13</sup> of which US\$287 million was allocated to lung infections. This is substantive and laudable, but it must be considered in perspective. It pales in comparison with the US\$1.63 billion spent on biodefense. More NIH money is spent on smallpox research (US\$324 million) alone than on lung infection research. While it is essential to be proactive in recognizing, preventing, and preparing for looming or emerging threats to public health, it may be questioned whether funding for speculated risks should so overwhelm funding for diseases already causing such tremendous burdens.

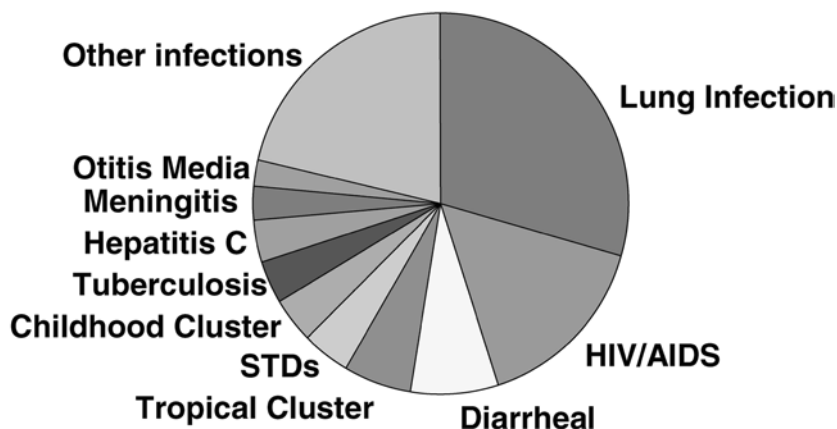
Lung infection research is also poorly funded when compared with other currently significant public health concerns. For example, US\$2.85 billion were spent on HIV/AIDS research, which is substantially improving prospects against this very important disease. It is remarkable, though, that lung infections cause a comparable or greater disease burden (Figures 1 and 2), yet they receive only one-tenth of HIV/AIDS research funding. In a similar vein, the NIH allocated comparable resources to lung infections as to sexually transmitted diseases (US\$237 million), even though in wealthy countries such as the US lung infections cause seven times more disease than do sexually transmitted diseases (Figure 2), with even larger differentials in poorer countries. These figures from the NIH are but a few examples demonstrating that lung infections are relatively under-represented.

Reacting to the pandemic threat of the recently emerging avian influenza virus (H5N1), the president of the US recently requested a lump sum totaling US\$7.1 billion.<sup>14</sup> The majority of requested funds in the president's plan, more than US\$5.3 billion, would be slated for the manufacture, purchase, and stockpile of vaccines and antivirals targeting influenza. An additional US\$0.8 billion would be allocated for research on

### Poorest regions of the world



### Wealthiest regions of the world



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**Figure 2.** The Ten Leading Infections of the Poorest and Wealthiest Regions of the World  
 These leading infections are represented as a fraction of the total infectious disease burden of that region, and are in clockwise descending order. (STDs, sexually transmitted diseases excluding HIV)

new vaccines and antivirals against influenza, US\$0.6 billion for influenza preparedness planning, and US\$0.3 billion to help countries detect and contain influenza outbreaks. It is this author's opinion that the immediate need for such immense resources results from the potential of a severe influenza pandemic combined with many years of inadequate attention to lung infections. As of the time of writing this essay, the US Congress has yet to approve funding, and it remains unclear how much will be approved and how it will be deployed if approved, but a discrete set of funds may soon become available for fighting influenza specifically.

It is more difficult to assess resources distributed by private organizations, but it is again evident that lung infections are underemphasized. US News and World Report identifies 20 charities as the largest to deal specifically with diseases and disease-related research.<sup>15</sup> Of these 20 leading charities, nine focus on cancer, two on organs (heart or kidney), two on classes of disease (mental illness or birth defects), and the rest

on six specific diseases (muscular dystrophy, diabetes, multiple sclerosis, cystic fibrosis, Alzheimer disease, and arthritis). Perhaps the most prominent philanthropy focused specifically on infectious disease is The Global Fund to Fight AIDS, Tuberculosis, and Malaria.<sup>16</sup> This fund reports that it has attracted commitments of US\$4.7 billion from national governments, private companies, and other contributors for fighting these three specific diseases. Such philanthropies perform wonderful services in improving health. Lung infections would similarly benefit from such a major philanthropic focus.

### INFECTIOUS DISEASE THROUGH THE PRISM OF MICROBIOLOGY

Why does the consistent burden of lung infections receive so little attention? It may result in part from our tendency to view infectious diseases from a microbiology perspective. Microbes can reasonably be portrayed and perceived as enemies to be attacked and defeated. Smallpox eradication is a powerful illustration of the potential of such an approach. Because AIDS

is caused by HIV, malaria by Plasmodia, tuberculosis by Mycobacteria, and so on, defeating HIV and Plasmodia and Mycobacteria are widely recognized as valid goals in virtually any informed community.

While the idea of fighting against a specific microbe is attractive, and such an "us-against-them" mentality is effective at mobilizing commitments, a microbe-specific focus is appropriate for some infectious diseases more than others. Lung infections do not result from one or a few extremely virulent microbes especially adapted to living in our lungs. Rather, a tremendous variety of microbes causes lung infections, and a strategy focused on the microbes is destined to be a game of catch-up. The physiology of breathing requires our lungs to be enormously exposed to microbes, both from the external environment (the air) and from a microbe-rich part of our anatomy (our upper airways). It is inevitable that microbes land in our lungs. In part for these reasons, respiratory infections are common, and new respiratory pathogens are likely to emerge frequently. Eliminating microbes in the lungs requires inflammatory responses that by their very nature compromise ventilation and blood-gas exchange. Thus, eliminating infection threatens physiology, and in part for this reason respiratory infections are often severe.

Tools are available for targeting some microbes causing lung infections (e.g., vaccines and antibiotics). Further research into reactive strategies directed specifically against individual microbes will likely improve our abilities to prevent or cure select lung infections. Few and marginally effective tools are available for targeting exposures of host responses to lung infection (e.g., ultraviolet germicidal irradiation or corticosteroids, respectively). Forward-thinking strategies might be directed at determinants of respiratory tract exposure, innate immune defenses against microbes in the lungs, and inflammatory injury resulting from lung infection. Advances in these areas will provide opportunities both to combat ongoing public health crises and to limit the potential threat from emerging pathogens.

## CONCLUSION

Like the proverbial elephant in the room, lung infections are a persistent problem not receiving the attention required. This may result in part from the nature of a disease lacking a single clear etiologic agent identified as a microbiological enemy. Whatever the reasons, it means that an important cause of human suffering is relatively underserved. Because the burden of disease is so substantial, greater efforts designed to elucidate the biology of lung infections, to generate novel therapeutic or prophylactic strategies, and to better deliver interventions to needy populations have the potential for tremendous public health impact.

## REFERENCES

- 1 World Health Organization (2005) Burden of Disease Project. Geneva: World Health Organization. Available: <http://www.who.int/healthinfo/bodproject/en/index.html>. Accessed 10 November 2005.
- 2 World Health Organization (2005) International Classification of Diseases (ICD). Geneva: World Health Organization. Available: <http://www.who.int/classifications/icd/en>. Accessed 28 November 2005.
- 3 Murray CJ, Lopez AD (1996) Evidence-based health policy- Lessons from the Global Burden of Disease Study. *Science* 274: 740-743.
- 4 Michaud CM, Murray CJL, Bloom BR (2001) Burden of disease-Implications for future research. *JAMA* 285: 535-539.
- 5 Jha P, Mills A, Hanson K, Kumaranayake L, Conteh L, et al. (2002) Improving the health of the global poor. *Science* 295: 2036-2039.
- 6 Armstrong GL, Conn LA, Pinner RW (1999) Trends in infectious disease mortality in the United States during the 20th century. *JAMA* 281: 61-66.
- 7 Janssens JP, Krause KH (2004) Pneumonia in the very old. *Lancet Infect Dis* 4: 112-124.
- 8 National Center for Health Statistics (2004) Population age. In: Health, United States, 2004, with chartbook on trends in the health of Americans. Hyattsville (Maryland): U.S. Government Printing Office. pp.20-21.
- 9 Peiris JS, Yuen KY, Osterhaus AD, Stohr K (2003) The severe acute respiratory syndrome. *N Engl J Med* 349: 2431-2441.
- 10 Aris B (2005) Avian influenza remains a cause for concern. *Lancet* 366: 798.
- 11 Osterholm MT (2005) Preparing for the next pandemic. *N Engl J Med* 352: 1839-1842.
- 12 Cunha BA (2001) Effective antibiotic-resistance control strategies. *Lancet* 357: 1307-1308.
- 13 National Institutes of Health (2005) Estimates of funding for various diseases, conditions, research areas. Bethesda (Maryland): National Institutes of Health. Available: <http://www.nih.gov/news/fundingresearchareas.htm>. Accessed 10 November 2005.
- 14 Kaiser J (2005) Pandemic or not, experts welcome Bush flu plan. *Science* 310: 952-953.
- 15 U.S. News & World Report (2005) Largest charities: Diseases and disease research. Available: <http://www.usnews.com/usnews/biztech/charities/lists/diseases.htm>. Accessed 10 November 2005.
- 16 The Global Fund to Fight AIDS, Tuberculosis, and Malaria (2005) How the fund works. Geneva: The Global Fund to Fight AIDS, Tuberculosis, and Malaria. Available: <http://www.theglobalfund.org/en/about/how>. Accessed 10 November 2005.

# Performance of a New Hand-Held Device for Exhaled Nitric Oxide Measurement In Adults and Children

K. Alving, PhD; C. Janson, MD, PhD; L. Nordvall, MD, PhD

## ABSTRACT

**Background:** Exhaled nitric oxide (NO) measurement has been shown to be a valuable tool in the management of patients with asthma. Up to now, most measurements have been done with stationary, chemiluminescence-based NO analyzers, which are not suitable for the primary health care setting. A hand-held NO analyzer which simplifies the measurement would be of value both in specialized and primary health care. In this study, the performance of a new electrochemical hand-held device for exhaled NO measurements (NIOX MINO) was compared with a standard stationary chemiluminescence unit (NIOX).

**Methods:** A total of 71 subjects (6-60 years; 36 males), both healthy controls and atopic patients with and without asthma were included. The mean of three approved exhalations (50 ml/s) in each device, and the first approved measurement in the hand-held device, were compared with regard to NO readings (Bland-Altman plots), measurement feasibility (success rate with 6 attempts) and repeatability (intrasubject SD).

**Results:** Success rate was high (84%) in both devices for both adults and children. The subjects represented a  $FE_{NO}$  range of 8-147 parts per billion (ppb). When comparing the mean of three measurements (n=61), the median of the intrasubject difference in exhaled NO for the two devices was -1.2 ppb; thus generally the hand-held device gave slightly higher readings. The Bland-Altman plot shows that the 95% limits of agreement were -9.8 and 8.0 ppb. The intrasubject median difference between the NIOX and the first approved measurement in the NIOX MINO was -2.0 ppb, and limits of agreement were 13.2 and 10.2 ppb.

The median repeatability for NIOX and NIOX MINO were 1.1 and 1.2 ppb respectively.

**Conclusions:** The hand-held device (NIOX MINO) and the stationary system (NIOX) are in clinically acceptable agreement both when the mean of three measurements and the first approved measurement (NIOX MINO) is used. The hand-held device shows good repeatability, and it can be used successfully on adults and most children. The new hand-held device will enable the introduction of exhaled NO measurements into the primary health care.

## BACKGROUND

Since the original reports of the presence of nitric oxide (NO) in exhaled breath of mammals including humans,<sup>1</sup> and of the increased levels in subjects with asthma,<sup>2</sup> there has been a rapidly increasing interest in the measurement of exhaled NO. The concentration of NO in exhaled breath relates to the degree of eosinophilic inflammation in the airways,<sup>3-5</sup> and NO measurement has been shown to be a valuable tool both to diagnose<sup>6,7</sup> and to monitor the therapy of patients with asthma.<sup>8,9</sup>

Up to now, a single type of NO analyzer has been used for nearly all measurement of exhaled NO: the chemiluminescence NO analyzer.<sup>10</sup> These instruments are based on a technology developed in the 1970's<sup>11</sup> and were originally used for environmental and atmospheric analyses. The chemiluminescence-based NO analysers are fast-responding, highly sensitive (detection limit 1 parts per billion (ppb) or lower) and specific for NO gas. However, they are also rather bulky and expensive, and they need to be calibrated on site, drawbacks that have been limiting factors for the introduction of exhaled NO measurements in routine clinical work. An alternative would be to use electrochemical sensors, but they have not been sensitive enough for analysis of NO in the low ppb range. Recently, however, a new electrochemical sensor has been developed, based on the amperometric technique (the production of a current when a potential is applied between two electrodes), which is suitable for NO analysis in exhaled breath.<sup>12</sup> This sensor has been incorporated into a hand-held measuring device that complies with international guidelines for exhaled NO measurements.<sup>13</sup>

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**Table 1: Device comparison. Some characteristics that are not identical in the two devices are given. Most other characteristics are similar, for example NO scrubbing of inhaled air and the exhalation flow control.**

	NIOX	NIOX MINO
Measurement range (ppb)	1.5–200	5–300
Accuracy	< 50 ppb: ± 2.5 ppb ≥ 50 ppb: ± 5%	< 50 ppb: ± 5 ppb ≥ 50 ppb: ± 10%
Visual feedback	Computer screen	Display via mirror
Calibration on site	Yes	No
Dimensions (cm)	50 × 30 × 40	24 × 13 × 10
Weight (kg)	40	0.8

In this study, the new hand-held device was compared to a chemiluminescence-based stationary device for exhaled NO measurements that has previously proven to provide repeatable results.<sup>14</sup> Both these instruments are now cleared for clinical use in Europe and the stationary device has also been cleared by the US Food and Drug Administration<sup>15</sup>. The two devices were compared with regard to NO readings, measurement repeatability and feasibility, in a sample of 71 children and adults with and without asthma.

## METHODS

Subjects were consecutively recruited at two separate clinics (adult and pediatric) at Uppsala University Hospital. A total of 75 subjects were invited; 34 adults (6 males, 38 ± 11 years; mean ± SD) and 41 children (30 males, 12 ± 3 years). The total age range was 6–60 years. Twenty-one subjects were non-atopic healthy controls, 52 subjects were atopic and 39 subjects had a diagnosis of asthma. None of the subjects had used any of the NO instruments over the preceding 6 months and were thus considered unexperienced with NO measurements. Subjects with a FE<sub>NO</sub> (fraction of expired NO) value of <8 ppb were excluded (tested with the chemiluminescence-based instrument). At the time of the study, the detection limit for the hand-held device was considered to be 8 ppb. This has later been corrected by the manufacturer (see Table 1). The study was approved by the regional ethics committee and all subjects gave written informed consent.

Experimental protocol: Under guidance of clinical personnel, all subjects inhaled NO-free air (built-in NO scrubbers) to close to total lung capacity and exhaled during 10 s at a flow rate of 50 ml/s to provide three approved FE<sub>NO</sub> measurements in each of

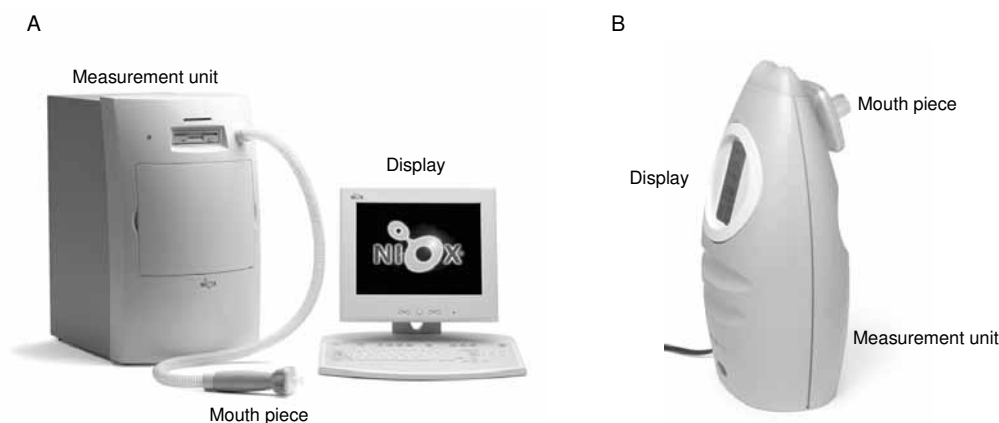
**Table 2: Success rate. Fraction of patients (%) that were able to achieve three accepted measurements out of at most 6 attempts under guidance (clinical setting), or one accepted measurement out of at most 3 attempts without guidance (simulated home use).**

Mode	Clinical setting		Home use
	NIOX	NIOX MINO	NIOX MINO
All subjects (n = 71)	94	92	92
Children (n = 37)	95	84	84
Adults (n = 34)	94	100	100

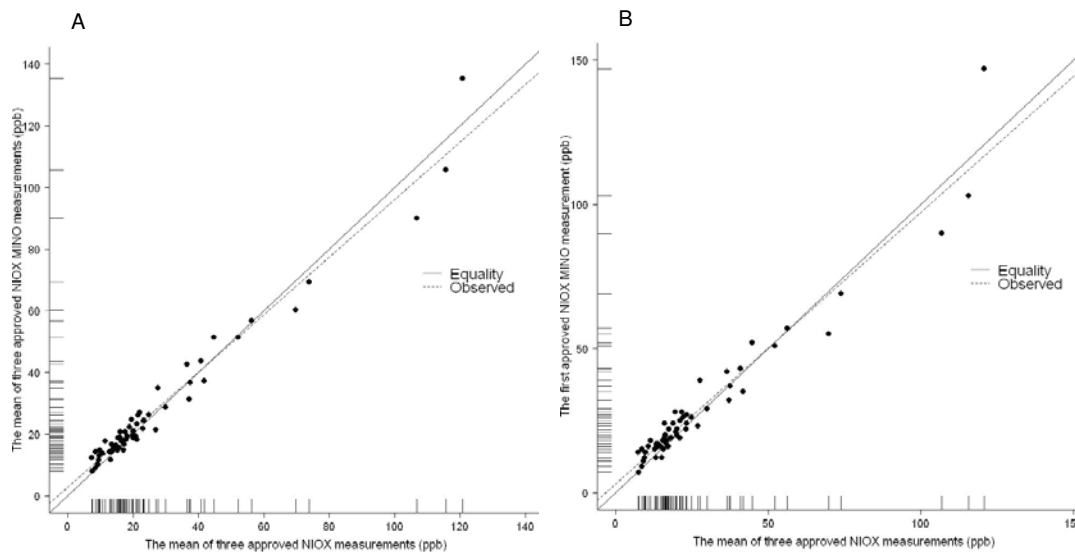
the two devices (NIOX Nitric Oxide Monitoring System (NIOX) and NIOX MINO Airway Inflammation Monitor (NIOX MINO); Aerocrine AB, Solna, Sweden). Oral pressure was measured and the subjects were instructed to keep the pressure between 12–18 cmH<sub>2</sub>O in both devices with the help of visual feedback (provided via a mirror in NIOX MINO). Exhalation flow rate was kept at 50±5 ml/s with calibrated dynamic flow resistors in both devices. In the NIOX, the mean NO concentration over the last 3 s of exhalation is calculated and the NO plateau is evaluated by linear regression, whereas in the NIOX MINO, the last 3-s portion of exhaled air is led into the measurement chamber containing the sensor. Analysis takes 100 s before a result representing the NO concentration in the mixed gas portion is presented. Sampling technique in both devices complies with current international guidelines.<sup>13</sup> The instruments are further described in Fig 1 and Table 1.

Measurements were performed in randomized device order (at most 6 attempts per device). The mean of three measurements in each device, or the first approved measurement in the NIOX MINO were used for agreement studies. After these measurements, subjects also attempted one valid FE<sub>NO</sub> measurement (at most 3 attempts) in the hand-held device in a simulated home-use environment where each subject performed the FE<sub>NO</sub> measurement without the assistance of clinical personnel.

Statistics: Data are presented as arithmetic mean ± standard deviation (SD), or median [interquartile range] when appropriate. For comparison between devices, interclass correlation coefficients (ICCs) were calculated and presented as reliability coefficients, and Bland-Altman plots were constructed. Repeatability was calculated from the intrasubject SD.



**Figure 1**  
**Appearance of devices.** Illustrations of (A) the NIOX and (B) the NIOX MINO. Note that the relative size is not proportional (see Table 1 for device dimensions).



**Figure 2**  
**Device agreement.** Scatter plots of the mean of three valid  $FE_{NO}$  measurements using the NIOX vs (A) the mean of three valid  $FE_{NO}$  measurements, or vs (B) the first valid  $FE_{NO}$  measurement using the NIOX MINO ( $n = 61$ ). Repeatability coefficients (ICCs) were (A) 0.97 and (B) 0.98, respectively ( $p < 0.001$  for both).

Student's paired t-test was used to compare the mean number of attempts in the two devices. The success rate was calculated as the proportion of subjects succeeding in obtaining three valid  $FE_{NO}$  measurements out of a maximum of six attempts in each device, or one successful measurement out of a maximum of three attempts using the NIOX MINO in the simulated home use. Differences in success rate was evaluated by Fisher's exact test.

## RESULTS

**Success rate for approved measurements:** Four subjects out of 75 had  $FE_{NO}$  measurements of  $<8$  ppb and were excluded from the study. They were all younger children (age  $\leq 13$  years). Of all subjects ( $n=71$ ) who made an attempt to use the NIOX or the NIOX MINO under guidance of clinical personnel, only a few failed to obtain three approved  $FE_{NO}$  measurements out of a maximum of 6 attempts (Table 2). These were primarily younger children (age  $\leq 13$  years) who failed when attempting to use the NIOX MINO (6 out of 7). The study subjects were similarly successful in a simulated home-use environment using the NIOX MINO where subjects were to obtain one approved measurement out of three attempts without guidance. There was no significant difference in success rate between the NIOX and the NIOX MINO, or between the clinical setting and the simulated home use, except for children being slightly less successful than adults when attempting to use the NIOX MINO ( $p < 0.05$ , Fisher's exact test).

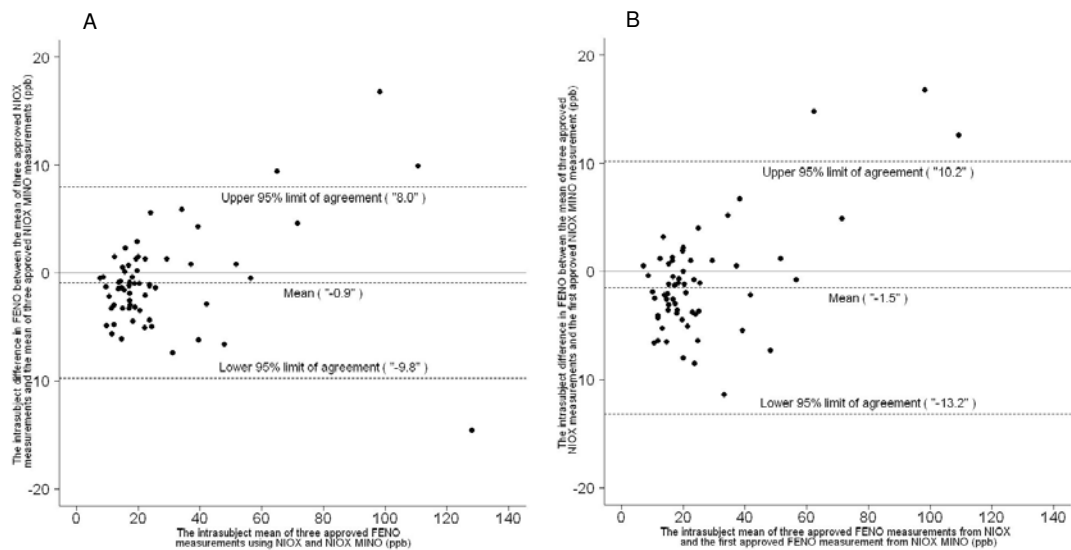
In subjects that were successful in all three sets of measurements ( $n=61$ ), the mean number of attempts required to obtain three approved measurements was  $3.8 \pm 1.0$  and  $3.4 \pm 0.8$  for the NIOX and the NIOX MINO, respectively. The number of attempts was significantly lower for the NIOX MINO ( $p < 0.05$ ; paired t-test). The mean number of attempts required by successful patients to obtain one approved measurement in the home-use environment was  $1.1 \pm 0.3$ .

Three adverse events were reported (mental stress, throat dryness, uncomfortable inhalation); they were all considered mild and were deemed unlikely to be caused directly by the study devices.

**Agreement between devices:** The subjects represented a  $FE_{NO}$  range of 8-147 ppb. The overall mean values for the NIOX and the NIOX MINO were  $26.5 \pm 24.2$  ppb and  $27.5 \pm 23.2$  ppb ( $n=63$  and 62, respectively). The reliability coefficient was high ( $r=0.97$ ) when comparing the individual mean values in the two devices (Fig 2A). The Bland-Altman plot shows agreement between the NIOX and the NIOX MINO when comparing the mean of three valid exhaled NO measurements (Fig 3A). The median of the intra-subject  $FE_{NO}$  difference was  $-1.2$  [ $-3.3, 0.8$ ] ppb, suggesting that the NIOX MINO gave  $FE_{NO}$  readings that were generally higher than the  $FE_{NO}$  measurements obtained using the NIOX. The 95% limits of agreement were  $-9.8$  and  $8.0$  ppb, which indicates that for 95% of all subjects the difference between  $FE_{NO}$  readings in NIOX and NIOX MINO is expected to lie in the interval  $[-9.8, 8.0]$  ppb. The Bland-Altman plot shows that the intrasubject  $FE_{NO}$  difference increased with increasing  $FE_{NO}$  level (Fig 3A).

In addition, we find the same degree of agreement between the NIOX and the NIOX MINO when comparing the mean of three approved exhaled NO measurements in the NIOX and the first approved measurement in the NIOX MINO in the clinical setting (Fig 2B, 3B). The median of the intra-subject difference was  $-2.0$  [ $-4.0, 1.0$ ] ppb, again suggesting that  $FE_{NO}$  measurements with NIOX MINO were slightly higher than  $FE_{NO}$  measurements using NIOX. The 95% limits of agreement were  $-13.2$  and  $10.2$  ppb.

**Measurement repeatability:** Repeatability was similar in the NIOX and the NIOX MINO. The 95th percentile for the distribution of repeatability (an estimate of the upper boundary of the repeatability for 95% of all subjects) in the NIOX was 3.3 ppb compared to 4.6 ppb in the NIOX MINO. The median repeatability for NIOX and NIOX MINO was 1.1 [0.6, 1.6] and 1.2 [0.6, 2.0] ppb, respectively. The real and estimated distribution of intra-subject SDs are shown in Fig 4. One extreme observation concerning the repeatability in the NIOX MINO was noted (seen in Fig 4B). However, this observation was not treated as an outlier in the population.



**Figure 3**  
**Device agreement.** Bland-Altman plots of the mean of three valid  $FE_{NO}$  measurements using the NIOX vs (A) the mean of three valid  $FE_{NO}$  measurements, or vs (B) the first valid  $FE_{NO}$  measurements using the NIOX MINO ( $n = 61$ ).

## DISCUSSION

Exhaled NO has been studied extensively over the past decade and reports of the clinical utility of this method in the management of patients with asthma are now appearing in the literature.<sup>8,9</sup> However, the introduction of the method into clinical routine has been restricted by the cost and complexity of existing NO analysers. In this study, the performance of a new hand-held device for exhaled NO measurements has been compared with that of a standard stationary unit.

When we compare the mean of three valid  $FE_{NO}$  measurements using the established chemiluminescence-based NIOX and the NIOX MINO, the results suggest clinically acceptable agreement between the two instruments. Measured  $FE_{NO} \pm$  levels obtained using the NIOX MINO were on average slightly higher than those obtained with the NIOX, and there was a tendency that the intrasubject  $FE_{NO}$  difference increased with increasing  $FE_{NO}$ . We believe that the difference between the two instruments is acceptable, considering the different measurement technologies and calibration procedures used in the two devices, and the results are in conformity with the declared accuracy for both the NIOX and the NIOX MINO. From a clinical point of view, accuracy will be more important in a  $FE_{NO}$  range close to a cut-off between health and disease (20-35 ppb) than at higher  $FE_{NO}$  levels. The NIOX MINO showed good agreement (within 95% limits of agreement) with the NIOX up to approximately 60 ppb, which indicates that the new hand-held device will be able to give clinical guidance with similar accuracy as the conventional chemiluminescence-based unit.

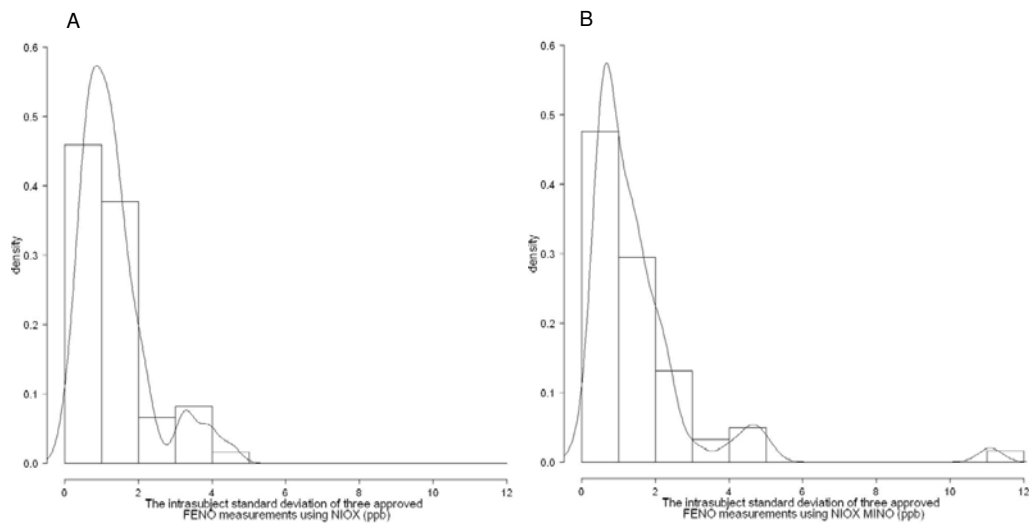
In general, the NIOX MINO and the NIOX had similar repeatability, except for one extreme observation with poor reproducibility in the NIOX MINO. However, this was seen in a subject with very high exhaled NO values (range 125-147 ppb in the NIOX MINO), and such variability at these high NO levels is of clinical importance. The repeatability agreed with the devices' technical specifications.

Success rates in achieving the required number of acceptable measurements were at least 84% for both devices and for both

subject groups. Since all subjects were considered unexperienced with NO measurements, this indicates that both measurement techniques are generally well accepted by the patients. However, younger children failed slightly more frequently than adults when attempting to use the NIOX MINO. Interestingly, the number of attempts needed for successful subjects to achieve three acceptable measurements was significantly lower in the NIOX MINO compared to the NIOX. This could at least partly be explained by the fact that some measurements in the NIOX may be discarded after a linear regression analysis of the NO plateau has been performed, even though the number of regression failures was not recorded in the present study. The linearized plateau must not deviate more than 10% from the horizontal axis according to current guidelines<sup>13</sup>. In the NIOX MINO, the NO level in the last 3-s portion of mixed exhaled air is analyzed. Thus, the need for an analysis of the quality of a real-time NO plateau is avoided in the hand-held instrument.

Four subjects were excluded because of a low exhaled NO value (<8 ppb). However, three of these subjects had a measurement above 5 ppb which is now the established lower detection limit of the NIOX MINO.

During the simulated home use, subjects were given the opportunity to use the NIOX MINO unassisted by study staff (children were assisted by their parents as they likely would be at home). This was performed after the clinical session, which would imitate what would normally happen, namely that the patient would receive training in the clinic prior to taking home the device. All subjects that succeeded in the clinical setting also succeeded in the simulated home environment. Using the mean of three measurements was advised in earlier guidelines,<sup>16</sup> but this was recently changed to two measurements.<sup>13</sup> We found essentially the same agreement between the two devices when comparing the mean of three valid measurements in the NIOX and the first valid measurement in the NIOX MINO. We thus suggest that one measurement is adequate when using the NIOX MINO, which would save valuable time in the clinic. The time for NO analysis in the NIOX MINO is 100 s, but since one



**Figure 4**  
**Repeatability.** Histograms of the intra-subject SD of three valid  $FE_{NO}$  measurements using (A) the NIOX ( $n = 63$ ) and (B) the NIOX MINO ( $n = 62$ ). The estimated distribution of SD is indicated with the line.

measurement seems to be adequate in most instances, the total measurement time will still be acceptable.

## CONCLUSIONS

The results show that there is clinically acceptable agreement between the stationary NIOX and the new hand-held NIOX MINO, when similar conditions were considered and examinations were made as consistently as possible. The repeatability of measurements done using the hand-held device was similar to the stationary device, and adults and most children were able to successfully use both instruments. In addition, subjects displayed ability to operate the new hand-held device in a simulated home-use environment. The new hand-held instrument will enable the introduction of exhaled NO measurements in the primary health care.

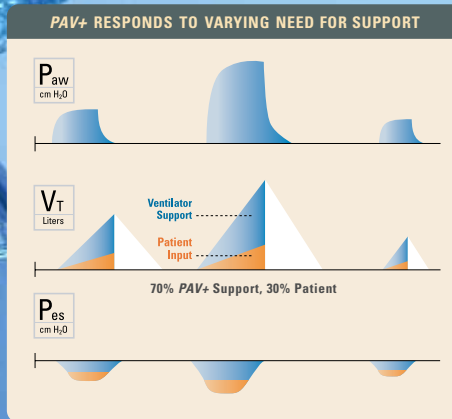
## REFERENCES

- Gustafsson LE, Leone AM, Persson MG, Wiklund NP, Moncada S: Endogenous nitric oxide is present in the exhaled air of rabbits, guinea pigs and humans. *Biochem Biophys Res Commun* 1991, 181: 852-857.
- Alving K, Weitzberg E, Lundberg JM: Increased amount of nitric oxide in exhaled air of asthmatics. *Eur Respir J* 1993, 6: 1368-1370.
- van den Toorn LM, Overbeek SE, de Jongste JC, Leman K, Hoogsteden HC, Prins JB: Airway inflammation is present during clinical remission of atopic asthma. *Am J Respir Crit Care Med* 2001, 164: 2107-2113.
- Mattes J, Storm van's Gravesande K, Reining U, Alving K, Thorst G, Henschen M, Kuehr J: NO in exhaled air is correlated with markers of eosinophilic airway inflammation in corticosteroid-dependent childhood asthma. *Eur Respir J* 1999, 13: 1391-1395.
- Jatakanon A, Lim S, Kharitonov SA, Chung KF, Barnes PJ: Correlation between exhaled nitric oxide, sputum eosinophils, and methacholine responsiveness in patients with mild asthma. *Thorax* 1998, 53: 91-95.
- Dupont LJ, Demedts MG, Verleden GM: Prospective evaluation of the validity of exhaled nitric oxide for the diagnosis of asthma. *Chest* 2003, 123: 751-756.
- Smith AD, Cowan JO, Filsell S, McLachlan C, Monti-Sheehan G, Jackson P, Taylor DR: Diagnosing asthma: comparisons between exhaled nitric oxide measurements and conventional tests. *Am J Respir Crit Care Med* 2004, 169: 473-478.
- Smith AD, Cowan JO, Brassett KP, Herbison GP, Taylor DR: Use of exhaled nitric oxide measurements to guide treatment in chronic asthma. *N Engl J Med* 2005, 352: 2163-2173.
- Pijnenburg MW, Bakker EM, Hop WC, De Jongste JC: Titrating Steroids on Exhaled Nitric Oxide in Asthmatic Children: a Randomized Controlled Trial. *Am J Respir Crit Care Med* 2005, 172: 831-836.
- Archer S: Measurement of nitric oxide in biological models. *Faseb J* 1993, 7: 349-360.
- Fontijn A, Sabadell A, Ronco R: Homogenous chemiluminescent measurement of nitric oxide with ozone. Implications for continuous selective monitoring gaseous air pollutants. *Anal Chem* 1970, 42: 575-579.
- Hemmingson T, Linaarsson D, Gambert R: Novel hand-held device for exhaled nitric oxide analysis in research and clinical applications. *J Clin Monit Comput* 2004, 18: 379-387.
- Anonymous: ATS/ERS Recommendations for Standardized Procedures for the Online and Offline Measurement of Exhaled Lower Respiratory Nitric Oxide and Nasal Nitric Oxide, 2005.
- Kharitonov SA, Gonio F, Kelly C, Meah S, Barnes PJ: Reproducibility of exhaled nitric oxide measurements in healthy and asthmatic adults and children. *Eur Respir J* 2003, 21: 433-438.
- Silkoff PE, Carlson M, Bourke T, Katial R, Oren E, Szeffler SJ: The Aerocrine exhaled nitric oxide monitoring system NIOX is cleared by the US Food and Drug Administration for monitoring therapy in asthma. *J Allergy Clin Immunol* 2004, 114: 1241-1256.
- Anonymous: Recommendations for standardized procedures for the on-line and off-line measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide in adults and children - 1999. This official statement of the American Thoracic Society was adopted by the ATS Board of Directors, July 1999. *Am J Respir Crit Care Med* 1999, 160: 2104-2117.



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