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The Journal of Pulmonary Technique

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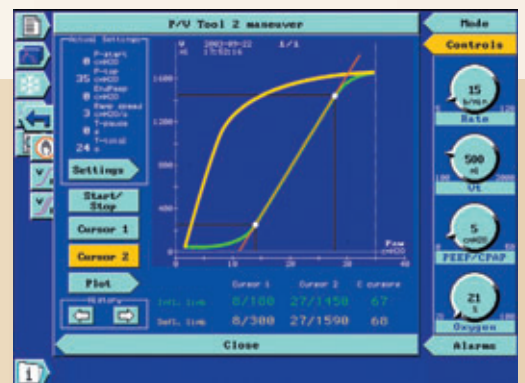
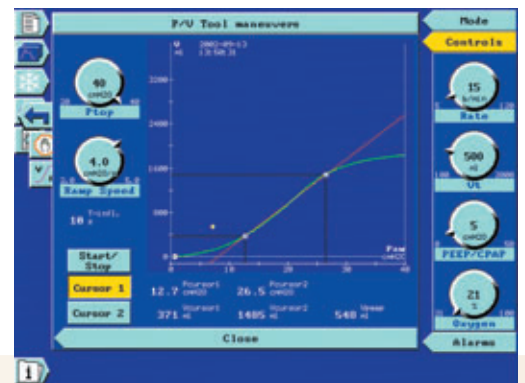
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As with other Alpha-1 therapies, Zemaira® may not be appropriate for the following adult individuals as they may experience severe reactions, including anaphylaxis: individuals with a known hypersensitivity and/or history of anaphylaxis or severe systemic reaction to A₁-PI products or their components and individuals with selective IgA deficiencies who have known antibodies against IgA.

In clinical studies, the following treatment-related adverse events were reported in 1% of subjects: asthenia, injection-site pain, dizziness, headache, paresthesia, and pruritus.

As with all plasma-derived products, the risk of transmission of infectious agents, including viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, cannot be completely eliminated.

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Please see brief summary of full prescribing information on the back of this page.

Zemaira®
alpha₁-proteinase inhibitor (Human)

www.Zemaira.com

Reference: 1. American Thoracic Society. American Thoracic Society/European Respiratory Society statement: standards for the diagnosis and management of individuals with Alpha-1 antitrypsin deficiency. *Am J Respir Crit Care Med.* 2003;168:818-900.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

Alpha₁-Proteinase Inhibitor (Human)

Zemaira®

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ZLB Behring

Rx only

Before prescribing please consult full prescribing information, a brief summary of which follows:

INDICATIONS AND USAGE

Alpha₁-Proteinase Inhibitor (Human), Zemaira®, is indicated for chronic augmentation and maintenance therapy in individuals with alpha₁-proteinase inhibitor (A₁-PI) deficiency and clinical evidence of emphysema.

Zemaira® increases antigenic and functional (ANEC) serum levels and lung epithelial lining fluid levels of A₁-PI.

Clinical data demonstrating the long-term effects of chronic augmentation therapy of individuals with Zemaira® are not available.

Safety and effectiveness in pediatric patients have not been established.

Zemaira® is not indicated as therapy for lung disease patients in whom severe congenital A₁-PI deficiency has not been established.

CONTRAINDICATIONS

Zemaira® is contraindicated in individuals with a known hypersensitivity to any of its components. Zemaira® is also contraindicated in individuals with a history of anaphylaxis or severe systemic response to A₁-PI products.

Individuals with selective IgA deficiencies who have known antibodies against IgA (anti-IgA antibodies) should not receive Zemaira®, since these patients may experience severe reactions, including anaphylaxis, to IgA that may be present in Zemaira®.

WARNINGS

Zemaira® is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses, that can cause disease. Because Zemaira® is made from human blood, it may carry a risk of transmitting infectious agents, e.g., viruses, and theoretically the Creutzfeldt-Jakob disease (CJD) agent. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating and/or removing certain viruses during manufacture. (See **DESCRIPTION** section of full prescribing information for viral reduction measures.) The manufacturing procedure for Zemaira® includes processing steps designed to reduce further the risk of viral transmission. Stringent procedures utilized at plasma collection centers, plasma testing laboratories, and fractionation facilities are designed to reduce the risk of viral transmission. The primary viral reduction steps of the Zemaira® manufacturing process are pasteurization (60°C for 10 hours) and two sequential ultrafiltration steps. Additional purification procedures used in the manufacture of Zemaira® also potentially provide viral reduction. Despite these measures, such products may still potentially contain human pathogenic agents, including those not yet known or identified. Thus, the risk of transmission of infectious agents can not be totally eliminated. Any infections thought by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare provider to ZLB Behring at 800-504-5434. The physician should discuss the risks and benefits of this product with the patient.

Individuals who receive infusions of blood or plasma products may develop signs and/or symptoms of some viral infections (see **Information For Patients**).

During clinical studies, no cases of hepatitis A, B, C, or HIV viral infections were reported with the use of Zemaira®.

PRECAUTIONS

General – Infusion rates and the patient's clinical state should be monitored closely during infusion. The patient should be observed for signs of infusion-related reactions.

As with any colloid solution, there may be an increase in plasma volume following intravenous administration of Zemaira®. Caution should therefore be used in patients at risk for circulatory overload.

Information For Patients – Patients should be informed of the early signs of hypersensitivity reactions including hives, generalized urticaria, tightness of the chest, dyspnea, wheezing, faintness, hypotension, and anaphylaxis. Patients should be advised to discontinue use of the product and contact their physician and/or seek immediate emergency care, depending on the severity of the reaction, if these symptoms occur.

As with all plasma-derived products, some viruses, such as parvovirus B19, are particularly difficult to remove or inactivate at this time. Parvovirus B19 may most seriously affect pregnant women and immune-compromised individuals. Symptoms of parvovirus B19 include fever, drowsiness, chills, and runny nose followed two weeks later by a rash and joint pain. Patients should be encouraged to consult their physician if such symptoms occur.

Pregnancy Category C – Animal reproduction studies have not been conducted with Alpha₁-Proteinase Inhibitor (Human), Zemaira®. It is also not known whether Zemaira® can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Zemaira® should be given to a pregnant woman only if clearly needed.

Nursing Mothers – It is not known whether Zemaira® is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Zemaira® is administered to a nursing woman.

Pediatric Use – Safety and effectiveness in the pediatric population have not been established.

Geriatric Use – Clinical studies of Zemaira® did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. As for all patients, dosing for geriatric patients should be appropriate to their overall situation.

ADVERSE REACTIONS

Intravenous administration of Zemaira®, 60 mg/kg weekly, has been shown to be generally well tolerated. In clinical studies, the following treatment-related adverse reactions were reported: asthenia, injection site pain, dizziness, headache, paresthesia, and pruritus. Each of these related adverse events was observed in 1 of 89 subjects (1%). The adverse reactions were mild.

Should evidence of an acute hypersensitivity reaction be observed, the infusion should be stopped promptly and appropriate countermeasures and supportive therapy should be administered.

Table 3 summarizes the adverse event data obtained with single and multiple doses during clinical trials with Zemaira® and Prolastin®. No clinically significant differences were detected between the two treatment groups.

Table 3: Summary of Adverse Events

	Zemaira®	Prolastin®
No. of subjects treated	89	32
No. of subjects with adverse events regardless of causality (%)	69 (78%)	20 (63%)
No. of subjects with related adverse events (%)	5 (6%)	4 (13%)
No. of subjects with related serious adverse events	0	0
No. of infusions	1296	160
No. of adverse events regardless of causality (rates per infusion)	298 (0.230)	83 (0.519)
No. of related adverse events (rates per infusion)	6 (0.005)	5 (0.031)

The frequencies of adverse events per infusion that were ≥0.4% in Zemaira®-treated subjects, regardless of causality, were: headache (33 events per 1296 infusions, 2.5%), upper respiratory infection (1.6%), sinusitis (1.5%), injection site hemorrhage (0.9%), sore throat (0.9%), bronchitis (0.8%), asthenia (0.6%), fever (0.6%), pain (0.5%), rhinitis (0.5%), bronchospasm (0.5%), chest pain (0.5%), increased cough (0.4%), rash (0.4%), and infection (0.4%).

The following adverse events, regardless of causality, occurred at a rate of 0.2% to <0.4% per infusion: abdominal pain, diarrhea, dizziness, ecchymosis, myalgia, pruritus, vasodilation, accidental injury, back pain, dyspepsia, dyspnea, hemorrhage, injection site reaction, lung disorder, migraine, nausea, and paresthesia.

Diffuse interstitial lung disease was noted on a routine chest x-ray of one subject at Week 24. Causality could not be determined.

In a retrospective analysis, during the 10-week blinded portion of the 24-week clinical study, 6 subjects (20%) of the 30 treated with Zemaira® had a total of 7 exacerbations of their chronic obstructive pulmonary disease (COPD). Nine subjects (64%) of the 14 treated with Prolastin® had a total of 11 exacerbations of their COPD. The observed difference between groups was 44% (95% confidence interval from 8% to 70%). Over the entire 24-week treatment period, of the 30 subjects in the Zemaira® treatment group, 7 subjects (23%) had a total of 11 exacerbations of their COPD.

HOW SUPPLIED

Zemaira® is supplied in a single use vial containing the labeled amount of functionally active A₁-PI, as stated on the label. Each product package (NDC 0053-7201-02) contains one single use vial of Zemaira®, one 20 mL vial of Sterile Water for Injection, USP (diluent), one vented transfer device, and one large volume 5 micron conical filter.

STORAGE

When stored up to 25°C (77°F), Zemaira® is stable for the period indicated by the expiration date on its label. Avoid freezing which may damage container for the diluent.

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Adapted from 19131-03
Revised: August 2004



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Editorial

Welcome to Respiratory Therapy, the Journal of Pulmonary Technique. We're bringing a new concept in presenting information to RT managers and supervisors, respiratory therapists, nurses, researchers and students. Our goal is to present a wide variety of papers in a clear, effective and familiar clinical format. Respiratory Therapy's international clinical focus will ensure that our readers receive, with every issue, the latest and best information about all aspects of respiratory therapy as actively practiced in a wide variety of clinical venues and modalities. The scope of our features and departments includes original clinical studies from around the world, papers from RT caregivers working in a wide variety of locales and types of facilities, works in progress from respiratory therapists, researchers, and scientists, and informative information about the latest products of RT caregivers worldwide. Special reports highlight RT management, legislative issues and the latest news, as well as practical technology updates and innovative approaches to respiratory therapy.



Les Plesko, Editor

PS: Respiratory Therapy, the Journal of Pulmonary Technique, aims to present its readers with an open forum for a non-biased discussion of respiratory therapy-related topics. As such, we will publish all relevant material in an easily-accessible format. And since we are an independent journal, we're able to publish submitted papers quickly and efficiently. All RT managers and supervisors, clinicians, techs, nurses, researchers, students, and suppliers of RT equipment and services are invited to participate in this international forum for pulmonary technique.

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*GC Smaldone. Facial and ocular deposition of nebulized budesonide - effects of facemask design. Poster #3537. ATS Conference 2004.



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Business Report

Navigating IT waters: The voyage to acquire (and keep) a respiratory information system

Donald A. Terpak

Donald A. Terpak is Director, Respiratory Services, St Elizabeth Health Center, Youngstown, Ohio, Member Humility of Mary Health Partners

With so many stakeholders fighting for capital IT dollars, getting organizational support for automating respiratory care departments can be both an exhaustive and exhausting process. The good news is that if you perform due diligence before, during and after system acquisition, the effort can pay off in installation success and significant department dividends.

Humility of Mary Health Partners (HMHP) consists of two acute care hospitals, St. Elizabeth Health Center and St. Joseph Health Center, and several community based rehabilitation clinics. St. Elizabeth Health Center first implemented its respiratory information system in September 1993. A decade later this project now spans 235 users across 37 cost centers in the HMHP system, encompassing Respiratory Care and Rehabilitation Services, as well as two outpatient Sleep Labs.

The struggle to obtain and retain HMHP's Respiratory/Rehab information system has been based on solid documentation of the system's benefits. Through using a system to standardize processes, monitor outcomes, and measure productivity, you will gain a wealth of data that is a constant reminder of project utility. Here are some hints on making the case for obtaining or retaining a system from the school of hard knocks:

Chart your department's course: build the business case

In making the case for a system, you will need to put together a cost/benefit analysis. Such an impact assessment will allow you to quantify the benefits over using paper, or designate the features that complement those already provided by the hospital-wide system. Getting this business case to decision-makers as part of the budget cycle is your best chance to influence budget approval and move to a Request For Proposal bid.

At HMHP, we articulated how the respiratory information system would complement a system in use for order entry and computerized electronic record functions. To make the case, we did a comparison of features, usability, configurability and reporting capabilities. Most importantly, we did a return on investment analysis of implementing such a system. This process culminated in a presentation to the information systems steering committee. You must be careful of how you present the benefits to your leadership. For example, if you show that you can save FTE's through automation, this is most likely a one-time benefit that may not be repeatable in the future! In today's reimbursement environment there is little to be gained by improving inpatient charge capture. Of particular benefit is our system's ability to capture outpatient type, activity and visits, especially in rehabilitation areas.

Challenge the crew

Turnover is an enemy of project success. Building a business case insulates you against changes brought about by turnover in the decision-making body of the hospital, and the resulting impact on a project's development. Recruiting champions as part of the business case process can energize your effort. Developing your own strong users who are also project champions is also key to retaining your system. When the excitement of a new system has faded over years, and you are still having upgrades and annual support fees analyzed by the hospital, these champions have first-hand knowledge of the system impact from project inception. Putting a historical face on the business case can work to your advantage.

In 1993, we had a huge learning curve as an early adopter for these kinds of systems. Today, with more PC literacy and more people filling the ranks who are comfortable with the use of keyboard and handhelds, it is almost as easy to find supporters as ...*continued on page 19*



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Here are a few AARC seminars that discuss therapies and technologies we are committed to or are exploring. Check the final AARC schedule for dates and times.

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Open Forum #1 – Monitoring

Open Forum #2 – Artificial Airways, Rehab and More

Open Forum #3 – Case Reports: Part I

The Utilization of NICO[®] in Conjunction with Mechanical Ventilation

Robert Lichstein RRT-NPS

Open Forum #7 – Neonatal and Pediatric: Part I

Open Forum #8 – Management of RC Departments: Part II

Reduction of Mechanical Ventilation Hours Using a Working Protocol with the Cardiopulmonary Management Center

Mikel W. O'Klock RRT

Open Forum #10 – Ventilatory Support: Part I

Results: Trial Use of Volumetric Capnography in Management of Mechanically Ventilated Patients

John W. Farnham RRT

Open Forum #11 – Neonatal and Pediatric: Part II

Continuous Monitoring of Volumetric Capnography Reduces Length of Mechanical Ventilation in a Heterogeneous Group of Pediatric ICU Patients

Donna Hamel RRT FAARC

Open Forum #12 – Ventilatory Support: Part II

Power of Breathing as a Predictor for Extubation from Ventilatory Support

Steve Bonett RRT

Open Forum #17 – Diagnostics

RTs at the Bedside

Ira Cheifetz MD FAARC, Duke University Medical Center, Durham NC

Closed-Loop Control of FiO₂ During Mechanical Ventilation

Sherry Courtney MD, Schneider Children's Hospital, Manhasset NY

Neonatal Pediatric Non-Invasive Monitoring: Transport to Bedside

Thomas J. Abramo MD, Dallas Children's Hospital, Dallas TX

Mechanical Ventilation and Cardiovascular Support

Ira Cheifetz MD FAARC, Duke University Medical Center, Durham NC

Invasive Therapies and Technologies

Unconventional Approaches to Mechanical Ventilation

Random Variable Ventilation

Robert M. Kacmarek PhD RRT FAARC, Massachusetts General Hospital, Boston MA

Transtracheal Gas Insufflation (TGI)

Robert McCoy RRT FAARC, Apple Valley MN

Technological Advances in Weaning the Long-Term Mechanically Ventilated Patient

Eric S. Yeager MD, Kindred Hospital, Denver CO

Noninvasive Therapies and Technologies

Open Forum #6 – Management of RC Departments: Part 1

Successful Implementation of a Non-Invasive Ventilation Program Using a Team Approach

Carol Spada RRT

Heliox with Non-Invasive Ventilation

Dean R. Hess RRT PhD FAARC, Massachusetts General Hospital, Boston MA

CPAP in the Delivery Room: What Do We Really Know?

Steven M. Donn MD, Mott Children's Hospital, Ann Arbor MI

CPAP vs. NPPV in Preventing Extubation Failure

Michael Tracy RRT, Rainbow Babies & Children's Hospital, Cleveland OH

Non-Invasive Ventilation in Adults

Nicholas S. Hill MD, Tufts-New England Medical Center, Boston MA

The Evidence for Nasal CPAP

Nicholas J. Macmillan AGS RRT FAARC, Rotech Healthcare, Greensburg PA

Critical Factor in Managing Work of Breathing in NICU Patients Receiving nCPAP

Khris O'Brien RRT, Children's Hospital of Wisconsin, Milwaukee WI

All Pressures Are Not Created Equal

Sherry Courtney MD, Schneider Children's Hospital, Manhasset NY

NPPV: An Important Adjunct to Palliative Care

Paul F. Nuccio RRT FAARC, Brigham and Women's Hospital, Boston MA

In-Home NPPV: Can Any Provider Do It?

Angela King RRT RPFT, Pulmonetic Systems, Cement City MI

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MAKING CONNECTIONS

Cyclophosphamide has been shown to be effective in treating lung disease associated with scleroderma. A higher portion of patients taking the drug also had significant reductions in breathlessness. The study included 162 patients whose scleroderma had caused significant impairment. The researchers did report some adverse effects, including five cases of pneumonia. Two patients died, but two also died in the placebo group, and the deaths weren't due to drug toxicity.

ROAD WORK AHEAD

Children living within 75 meters of major roads had a 50% greater risk of having asthma symptoms than kids who lived 300 meters away, according to a study by USC. Researchers studied 5,000 five and six years olds. California already has laws prohibits school construction within 500 feet of a freeway. The long-term effects are yet to be thoroughly investigated.

STROKE 'N SLEEP

Obstructive sleep apnea increases the risk for a stroke, according to a study from the University of Toronto. A study of 1,475 people found that those with significant sleep apnea were three to four times more likely to have a stroke in the four years subsequent to diagnosis. That's double the risk of other factors such as hypertension or diabetes. It's conjectured that interrupted sleep may cause high blood pressure. It was also posited that when a person stops breathing in sleep, lack of oxygen kicks in the fight or flight response, which makes the blood more clottable, and blood clots in the brain can cause a stroke.

VIRTUAL BREATHING

The University of Alberta in Edmonton has created an interactive online asthma management program that allows asthma educators to communicate with patients, provide feedback, and assist with asthma management. According to the program's creator, Irvin Mayers, MD, "This allows patients to be treated using the most up to date guidelines no matter where they

live, and to manage their asthma with minimal physician intervention. Sixty three patients enrolled in the initial program and used the website about 33 times, entering their peak flow data 27 times. Mayers said the program "allows patients to input their symptoms and peak flow rates, and forces them to recognize whether their asthma is controlled or not." Symptoms and rates are graphed and patients receive online recommendations about therapy. A study is now being prepared about the results of the program.

COUGHING UP SADNESS

Many people with chronic cough also suffer from depressive symptoms. According to a study with people who've had a chronic cough for about nine years, 53% also suffer from depression. As coughing slacks off, the depression tends to lift, according to the study at the Montefiore Cough Center in New York. Chronic coughing is typically caused by post-nasal drip, asthmatic cough medicines, and the use of proton-pump inhibitors. The coughers' depression was a result of social problems resulting from the coughing.

CONGRESS INFO

The European Respiratory Society Annual Congress will be held September 2 to 6 in Munich. Topics include integrated care, viruses, asthma and COPS, problems of the pleura, ventilatory strategies, sleep apnea, smoking, pharmacoepidemiology, tuberculosis, chronic respiratory illness, new pneumonia treatment, recurrent and multiple NSCLC, and lung resection. For info contact messe-muenchen.de or ersnet.org.

SAY NO(2) TO ASTHMA

Exhaled nitric oxide can help assess the severity of asthma, according to a study in the New England Journal of Medicine. After NO₂ analysis, researchers were able to reduce the amount of inhaled corticosteroids by an average of 40%. While the test equipment is currently quite expensive, cheaper machines are currently being developed. The final

average daily dose of fluticasone was 370 mg for the NO₂ test group vs 641 mg for the conventional group who used traditional tracking methods. The nitric oxide group also average 45% fewer exacerbations than the conventional group.

LEGAL DECISION

The United States Court of Appeals for the Federal Circuit denied a recent appeal by Nellcor and affirmed the findings of a Los Angeles court that Nellcor infringes two Masimo patents. The CAFC reinstated a jury verdict that Nellcor infringes two Masimo patents and a third Masimo patent. The products found to infringe are Nellcor's Oxismart XL, O5 and O5ci. These pulse oximetry products are found in the N-595, N-395, N-550 and NPB 40 pulse oximeters. The initial jury verdict included damages of over \$134 million for infringing products shipped through December of 2003. The final judgment from the Los Angeles court specified damages of over \$164 million. This information was provided by Masimo.

CONTINUED COMMITMENT

Regarding the Federal Court of Appeals ruling in the Nellcor patent litigation case, president David Sell said, "We are disappointed by this decision, yet as an organization have been preparing for this potential outcome. As one of the earliest pioneers in pulse oximetry, Nellcor has consistently delivered technology advancements along with value and choice." Sell said the company is launching a new product line in the near future as part of the OxiMax system that includes bedside and handheld monitors, as well as OEM oximetry circuit boards that Nellcor will provide to other manufacturers of multiparameter monitoring device systems.

QUICK TAKES

Here's a quick look at some news items relevant to respiratory therapy practitioners: **Asbestos consultation centers** have been launched at 22 hospitals across Japan after revelations that many people have died of asbestos

related causes... People with **IBD** are more likely to develop respiratory and nervous system disorders, and have shown a prevalence of asthma, among other complications. The study published in *Gastroenterology*, didn't say why... Middle and upper class **children** are less exposed to **asthma** since their houses and schools are cleaner and newer, and their parents are less likely to smoke, according to a Boston study. The results aren't surprising... **Asthma** patients struggle with **bills** when they have to get inhalers and such, as well as take care of home improvements, USA Today reports. **MedImmune** said it will begin marketing Synagis without partner Abbott Labs starting in 2006, a move said to boost the company's earnings in 2007. MedImmune plans to hire 125 sales reps... Growing up with **smokers** leads to **respiratory problems** according to a study by the NIEHS. "Secondhand smoke early in life has health consequences that can last a lifetime," said the NIEHS director... The study also said that those who had **fiber** in their diets had fewer health problems associated with exposure to tobacco smoke. They got the fiber from eating **apples**.

Emotions also trigger asthma attacks, according to researchers at the University of Wisconsin-Madison. Researchers said asthma-related words with negative connotations increased brain activity linked to body functions that triggered asthma. Researchers said certain brain areas were likely hyperresponsive to disease-specific emotions...

TO THE RESCUE

VIASYS supported the relief of Katrina hurricane victims by initiating an emergency shipment of 19 vents to Baton Rouge to support the increase in services the hospital there is facing. The vents were used to treat patients the same evening they were

received, on September 5. The company also matched dollar for dollar, all donations received from company employees. Its subsidiary, **Pulmonetics**, shipped an additional 20 ventilators... **AARC**, the American Association for Respiratory Care, activated its Disaster Relief Fund for members residing in Alabama, Louisiana and Mississippi. The fund has distributed more than \$25,000 to 60-plus AARC members since its inception in 1992. It has been used following hurricanes in Florida and Hawaii, earthquakes in California, flooding in the Midwest and tornadoes in the Southeast. For information contact (972) 243-2272... **MAQUET** contacted Lafayette General Hospital and Premiere purchasing group and worked out logistics to mobilize MAQUET's demonstration stock to aid storm victims... **Roche Diagnostics** contacted or attempted to contact all its customers in a 75 mile radius of New Orleans and Mobile. It established contact with FEMA and defined a process for deploying people into restricted areas should the need arise. It worked with Federal Express to make sure it could deliver emergency supplies. It expanded its customer list to include customers in the perimeter areas of New Orleans and Mobile. It contacted customers in Houston to ensure sufficient supplies and contacted blood centers across the nation to assess the need for additional supplies. The company assessed the feasibility of providing blood glucose meters and test strips to the Red Cross, and its Accu-Chek Customer Care Center fielded calls from consumers. Roche also assessed the feasibility of deploying loaner testing equipment. Priority status was given to all incoming calls from the hurricane region, and employees were encouraged to support charitable organizations directly... **Tyco** pledged \$500,000 to the Red Cross. The company worked with its customers and the government to evaluate ongoing needs

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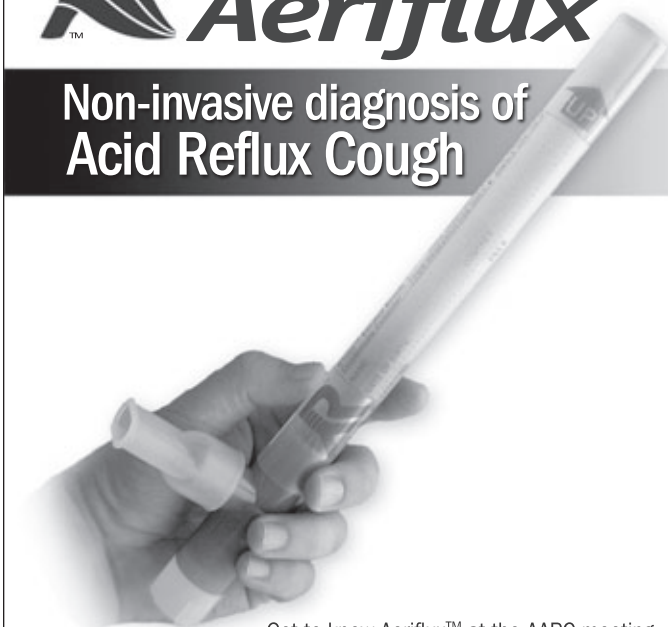
Respiratory Therapy

Invitation to Authors

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and provide assistance when possible and offer specific products and expertise. Tyco's Employee Matching Gift Program was available to match donations by employees... **Hamilton Medical, Inc** was contacted by Marie Easterling, Manager of Respiratory Care at St. Francis Medical Center in Northern Louisiana. Hamilton is providing Raphael and Galileo ventilators to assist with the needs of its patients. Hamilton was aided in this effort by UTI, United States, Inc, which provided the airfreight required to get the instruments to those in need, at cost... **Respironics** assisted with temporary housing, transportation and other needs. The company made a donation to the Red Cross and donated its products throughout the impacted areas. Respironics provided oxygen concentrators and pulse oximeters to a triage center at Louisiana State University and sent CPAP and other units, concentrators and oximeters to aid victims... **Bayer** announced that it shipped more than 45,000 Ascensia Brio blood glucose monitors and Ascensia Easyfill test strips to help meet the needs of Katrina's victims with diabetes. The portable hand-held monitors were shipped to Texas.

PRODUCTS

Editorial note: Respiratory Therapy, as a matter of editorial policy, does not capitalize the names of companies unless the name is a clearly identifiable acronym or the name represents the company's initials. We have instituted this policy because of the preponderance of companies and products capitalizing on capitalization strictly for graphic promotion, and to maintain graphic and editorial consistency and logic.

Respironics announced the release of its PLV Continuum updated version of the PLV-100. The Continuum offers options for daytime and nighttime comfort and it's smaller, lighter and easier to transport, designed for greater ambulation. The company also announced the release of its BiPAP S/T Ventilatory Support System which offers a straightforward user interface, integrated heated humidifier, and a SmartCard for use with other Respironics products. The company released its new ePOD, an electronic pulse oxygen device with a 4.25:1 conservation ratio in the pulse mode. Contact respironics.com... **Viasys Healthcare** announced the acquisition of Micro Medical Ltd for \$39 million. Micro Medical manufactures turbine spirometers and products for respiratory muscle measurement, smoking cessation, lactose intolerance and arterial measurement. Viasys also acquired Pulmonetic Systems, Inc, which makes portable mechanical ventilators for home healthcare for pediatric and adult patients. Contact viasyshc.com... **Masimo** debuted its Rad-57 Pulse CO-Oximeter, a handheld monitor that uses advanced signal processing to analyze data from a finger sensor. The Rad-57 is meant to replace traditional blood tests using expensive blood gas machines that aren't available outside the hospital. The product uses Masimo's SET technology. In other company news, a new study found that Masimo's SET perfusion index may help detect subclinical chorioamnionitis in newborns, alerting clinicians and speeding treatment. The company also continues to offer its online lecture series. Contact masimo.com... **MAQUET** introduced new neonatal ventilation functionality in its SERVO-i. New hardware allows near-patient measurements of pressure and flow with minimal dead space. The product allows for storage and viewing of FIO2 trend values, reference loops can be presented on screen, and the patient circuit can be tested independently of the per use check. The company debuted its SERVO-i Infant for neonatal patients at the ESPNIC conference in Brussels. The company announced a distribution

partnership for the Opus-RT clinical information management system tailored for the respiratory care department. MAQUET is sponsoring a book signing at the AARC Conference from December 3 through 6 in San Antonio. The book is The Clinical Practitioners Pocket Guide to Respiratory Care. Contact maquet.com... **Osmetech** offers its Opti R Blood Gas Analyzer with reusable sensor cassette available in a variety of sizes for different usage rates. The unit measures pH, blood gas, Na, K, iCa, and total hemoglobin and oxygen saturation. Contact Osmetech... **Nectar Therapeutics** announced a merger agreement with **Aerogen** valued at \$32 million. The acquisition broadens Nectar's pulmonary delivery capabilities by adding advanced inhalable liquid drug technology. Contact nectar.doc... **Spacelabs Medical** and **Nellcor** announced expanded pulse oximetry offering Ultraview Command Volume. The new configuration is the latest expression of the collaborative relationship between the two companies. Contact nellcor.com... **Puritan Bennett** unveiled its noninvasive ventilation capabilities for the 840 Ventilator. The 840 enhances noninvasive ventilation capabilities and makes it compatible with neonatal nasal CPAP prongs. NIV is designed for use on neonatal through adult patients with stable respiratory drives. Contact tycohealthcare.com... **Vortran Medical Technology** offers its VAR automatic resuscitator for single patient use. It provides hands-free ventilatory support via a mask or endotracheal tube using a continuous gas flow source. Contact vortran.com... **Draeger Medical AG & Co KgaA** offers its customized software version 3.05 of the Zeus anesthesia system. The rebreathing system has one of the world's smallest system volumes, and is adapted for ventilating children and newborns. The unit's automatic computer-assisted anesthesia control, TCA, has been available for adult anesthesia for a year. TCA control loop designs engage with the ventilation modes from Zeus and reduce user-initiated "control inventions." Draeger also received Frost & Sullivan Brand Development Strategy Leadership Award. Contact draeger.com... **Radiometer** offers the best-read articles on bloodgas.org. The compendium includes articles from each of the knowledge site's information racks offered in a magazine format. bloodgas.org has 6,000 registered users worldwide. Contact bloodgas.org. The company's new technology, the ABL0800 Flex allows operators to scan or enter their ID and link critical identifiers, reducing the risk of incorrect sample and patient identification. Contact radiometeramerica.com... **Hamilton Medical** introduced its new clinical website, IntelligentVentilation.org, designed to provide clinical information and innovative solutions for all medical practitioners treating patients for mechanical ventilation... **Boehringer Laboratories** offers the CASS Suction Regulator. Continuous Aspiration of Subglottic Secretions has been reported to be effective in reduced VAP. Contact boehringerlabs.com... **MAQUET** was awarded the manufacturer of the year award by the New Jersey State Society for Respiratory Care. Contact maquet-inc.com... **Maxtec, Inc.** introduced its MaxO2+ oxygen analyzer with one-touch calibration and 5,000 hour battery life. Contact maxtecinc.com.

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NEWS FEATURE: MONITORING OXYGEN LEVELS

The challenge of monitoring the oxygen levels of pediatric patients—due to movement and weak digital signals—has haunted doctors and nurses for years. Now, thanks to the accuracy of forehead sensors, there is hope. According to a recent study conducted by the Departments of Anesthesia Critical Care Medicine and Respiratory Care at the Children's Hospital Los Angeles and the USC Keck School of Medicine with children in the pediatric intensive care unit, reflective forehead oximetry performed as well as digital transmission oximetry with regard to obtaining a signal. Using the OxiMax MAX-FAST Forehead Sensor from Nellcor, a Tyco Healthcare company, researchers found that when digital sensors failed to work on poorly perfused and cold patients, the MAX-FAST Forehead Sensor provided accurate readings that correlated well to blood gases—leading to less false alarms.

Monitoring with advanced pulse oximetry technology that provides accurate SpO₂ level readings is critical to the safety of these patients and when there are a reduced number of false alarms, a nurse's time can be freed up to focus more on care-giving and patients' well-being.

Furthermore, forehead sensors are not the only pulse oximeters that benefit pediatric patient care. For example, the Children's Hospital of Illinois and University of Illinois College of Medicine at Peoria compared the Nellcor OxiMax N-595 Pulse Oximeter to the Masimo SET Radical and found the best monitoring performance in tracking the pulse rates of preterm infants from the N-595. Additionally, the N-595 reported significantly fewer false bradycardia events when compared to an ECG monitor. Again, with fewer false alarms, nurses can concentrate on what is really important: the patient.

ABSTRACT: Performance of Pulse Oximeters in Tracking Heart Rate Variability; Children's Hospital of Illinois, Peoria, IL

INTRO: The objective of the project was to determine the reliability of the latest generation of pulse oximeters for tracking heart rate changes in preterm infants.

HYPOTHESIS: We hypothesized that the Nellcor N-595 pulse oximeter was as reliable or superior as the Masimo Radical for tracking pulse rate in preterm infants.

METHODS: 2 pulse oximeter sensors (Nellcor MAX-N or Nellcor MAX-I and a Masimo LNOP Neo) were attached to separate distal extremities and their respective pulse oximeters (N-595, rev. 3.0, Nellcor, Pleasanton, CA; Radical, v 2, Masimo Corp., Irvine, CA). Both oximeters and an ECG monitor (Nellcor N-3200) were connected to a computer for continuous data recording during the 4-hour study per patient. True bradycardia events were defined as pulse rates < 100 bpm detected simultaneously by a minimum of 2 of the 3 monitors for ≥ 10 sec. False events were pulse rates < 100 bpm detected by only one of the monitors for ≥ 10 sec. A trained observer confirmed all events. A significant difference in true events, false events, and % time pulse rates undetected between oximeters was determined with chi square or Fisher's exact test. A p value < 0.05 was considered significant. Results: 19 infants, with median (range) age and weight, were studied in a NICU. There were a total of 57 true bradycardia events.

CONCLUSIONS: We conclude that the Nellcor N-595 and Radical pulse oximeters report significantly fewer false alarms than the N-3200, with the best performance coming from the N-595. Although there was a statistical difference between oximeters in pulse rate undetected, this accounted for less than one percent of the total monitoring time. All three monitors performed equally well in detecting true bradycardia events.

The information and the abstract above were provided by Nellcor.

Business...continued from page 11

detractors. Still, not everyone will be on board with paperless systems and handheld technology. Involve them early and expose them to people who have used similar technology before.

This strategy's success depends entirely on having a knowledgeable, committed multidisciplinary implementation team. We chose individuals proficient in clinical, billing and IT abilities. We also put them through a team/spirit building program entitled "The Ownership Spirit." This proved especially valuable as the project hit those inevitable bumps in the road.

All hands on deck

If your IT leadership is not responsive to the business case of your department, you can raise the stakes by making the case for a multi-facility and/or multi-department deployment. Such a tactic can allow you to avoid creating individual competitive capital presentations and lower both total acquisition and annual support costs.

While the initial effort in 1993 garnered St. Elizabeth Health Center a clinical information system for respiratory care, we made the case for bringing St. Joseph Health Center on board—and also expanding into the rehabilitation department. Aligning with the rehabilitation department gave us a stronger united voice to justify upgrades, add users, and add more system components. So in addition to supporting respiratory therapy, the HMHP system gained the benefit of automating inpatient and outpatient speech, physical, and sleep therapies.

Mid-course corrections

There can be both immediate, significant impacts of deploying the respiratory information system and ongoing/recurring impacts that are quantitative and qualitative in nature. First, you want to ensure your processes are developed and consistent enough to maintain your gains from initial implementation. Then the next strategic step is to use the system as a tool to

establish outcomes monitoring.

At St Elizabeth Health Center, we have ensured that we conduct ongoing checks to align evolving processes and evolving software. Now every RT and PT in the system is charting in the same way, as the system has created significant efficiencies in documentation and medical record coding time. To lay the groundwork for the next dimension of improvements, we examined our existing therapist driven protocols and care plans—and then had them reviewed by an external consultant. If you have 45 different sets of eyes on the same care plan, that care plan still should be carried out through a standard process. To make this work, it requires more than software, including training of key assessors on how to do an assessment. This is work in progress at St. Elizabeth's and St. Joseph's and we are excited at our interim progress.

We continually use the system to justify a quality size of our department for services delivered and quantify FTE complements for the budget cycle. These efforts help to answer the elusive question: "how many things should we be doing?" You can squeeze productivity and HR through skillful use of therapist productivity reports. Through measuring workload today you can predict workload tomorrow and assign FTE's by shift appropriately. Without the system to provide this level of granularity, the department functions without a rudder in planning both human and material resources.

At HMHP, we have strategically sought to create a data driven enterprise for human and material assets. Our goals are to manage clinical processes and leverage the productivity of clinical staff through automation, standardization, and outcomes monitoring. To successfully navigate the waters of top level IT, win finance approval, and acquire a system for your department, you must find the time to analyze your needs and continually measure your results. The voyage has been well worth the effort.



EDITORIAL POLICY

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Study of Personality Dimensions and Life Events of Bronchial Asthma Patients

Dr. P.P. Aravindan, Dr. M.S. Razeena Padmam

ABSTRACT

Objective

1. To study whether people with bronchial asthma and people without bronchial asthma differ in personality.
2. To study whether people with bronchial asthma and people without bronchial asthma differ in life events.
3. To study whether male patients with bronchial asthma and female patients with bronchial asthma differ in personality.
4. To study whether male patients with bronchial asthma and female patients with bronchial asthma differ in life events.

Design

Case control study

Setting

Secondary and tertiary care setting

Participants

128 patients diagnosed as bronchial asthma as cases and 128 persons not suffering from bronchial asthma as controls.

Main outcome measure

Personality dimensions such as extraversion/introversion, neuroticism/stability and life events score were assessed in 128 patients with bronchial asthma and compared with 128 persons without bronchial asthma and also compared between male and female patients with bronchial asthma.

Results

The first objective of the study mainly aimed at finding whether there was any significant difference between asthmatic and non-

asthmatic individuals in personality dimensions. Personality dimensions studied were extraversion/introversion and neuroticism/stability. From the mean scores it can be seen that the non-asthmatic group is 12.7188. This shows non-asthmatic individuals were more extraverted than the asthmatics. Bronchial asthma patients were more introverted. From Table 1 it is seen that there was a highly significant difference between the experimental and control group in terms of neuroticism. There was a high mean score of 14.5078 for the asthmatic group, as opposed to the mean score of the non-asthmatic group, 9.6875. The t-test value shows significance at 1% level for neuroticism. It clearly proves that bronchial asthma patients rated higher in the neuroticism dimension than the non-asthmatic group, which rated higher in the stability dimension.

Table 2 shows the significant differences between male and female patients in the personality dimensions, extraversion and neuroticism. The mean for males was 12.9018 and 11.6736 for females, for extraversion; the t-value was 2.565, which was significant at 1% level. Also, the mean for males was 10.6607 and the mean for females was 13.2153 for neuroticism; the t-value was -3.542, which was significant at 1% level. Hence, there is a significant difference between male and female asthmatic patients in extraversion and neuroticism.

From Table 1 it can be seen that the t-value shows a higher significant difference in terms of stressful life events in the experimental group than the score in the control group. The average mean score obtained for the experimental group was 29.0313 and 19.8359 for the control group. It is clear from the mean scores that the asthmatic patients have experienced a greater number of life events when compared to the non-asthmatic individuals.

From Table 3, it can be seen that there was no significant difference between male and female asthmatic patients in life events. The mean for males was 24.1161 and for females was 24.6806; the t-value was -0.349. There was no significant difference between male and female patients in relation to life events.

The authors are with the School of Behavioural Sciences, Mahatma Gandhi University, Kottayam, Karala. The authors express sincere thanks to Dr. M. S. Razeena Padmam, Professor and Director, School of Behavioural Sciences, Mahatma Gandhi University, Kottayam, who has supervised this research study. Acknowledge with gratitude to faculty members and staff of the Department of Respiratory Diseases at the medical college hospitals, Kottayam and Thrissur, and the superintendent, doctors, and staff of District Hospital, Palakkad.

Table 1

Mean, SDs and 't' value of Bronchial Asthma patients and controls on test variables.

Test Variable with bronchial asthma	Group	N	Mean	S.D	t' - Value
Extraversion	Experimental	128	11.7031	3.9272	* -2.130
	Control	128	12.7188	3.6992	
Neuroticism	Experimental	128	14.5076	5.3315	** 7.218
	Control	128	9.6875	5.3533	
Life events	Experimental	128	29.0313	13.6143	** 6.142
	Control	128	19.8359	9.8018	

* Significant at 5% level

** Significant at 1% level

Table 2

Mean, SDs and 't' value of Bronchial Asthma patients on Extraversion - Neuroticism with sex

Test Variable with sex	Sex	N	Mean	SD	t
Extraversion	Male	112	12.9018	3.6142	** 2.565
	Female	144	11.6736	3.9380	
Neuroticism	Male	112	10.6607	5.8287	** -3.542
	Female	144	13.2153	5.6434	

** Significant at 1% level

Table 3

Mean, SDs and 't' value of Bronchial Asthma patients on life events with sex

Test Variable with sex	Sex	N	Mean	S.D	t
Life events	Male	112	24.1161	12.6596	*** -0.349
	Female	144	24.6306	12.9656	

*** Not Significant

Conclusion

Bronchial asthma patients are more introverted than normal subjects. Bronchial asthma patients rated higher in the neuroticism dimension than normal subjects. Stressful life events were more frequent in bronchial asthma patients than in normal individuals. A significant difference was found between male and female bronchial asthma patients for extraversion and neuroticism. Male patients with bronchial asthma were more extraverted than female patients. Female patients with bronchial asthma rated higher on the neuroticism scale than male patients with bronchial asthma. Stressful life events did not vary with gender.

INTRODUCTION

Asthma is defined as a disorder characterised by chronic airway inflammation and increased airway responsiveness resulting in symptoms like wheezing, coughing, chest tightness, and dyspnea.¹ Inflammation of bronchial walls involving eosinophils, mast cells, and lymphocytes, together with the cytokine and inflammatory products of these cells, induce hyper-responsiveness of the bronchi so that they narrow more readily in response to a wide range of stimuli. The cardinal pathophysiological features of asthma include airflow limitation, airway hyperresponsiveness and airway inflammation. Bronchial Asthma is a common disease; 15% of children reported an episode of wheezing characteristic of asthma within the past year, 5% were diagnosed with asthma, and 1% had severe disabling asthma. In adults, 2-5% had a clinical diagnosis of asthma. Regarding the prevalence of diagnosed asthma, it may be around 2-6% and cumulative

prevalence around 3-9%. Approximately half of all subjects diagnosed with asthma started showing symptoms before the age of 10, though this varies from country to country.

Psychological factors can also affect health and well being. Exposure to stressful situations may produce feelings of anxiety, depression, anger, frustration, and so forth; these feelings may be accompanied by physical symptoms such as headache, palpitation, and sweating. These emotional states also produce changes in the endocrine, autonomic, and motor systems, which, if prolonged and in interaction with genetic and personality factors, may lead to structural changes in various bodily organs. The resulting psychosomatic disorders include conditions such as duodenal ulcer, bronchial asthma, hypertension, coronary heart disease, mental disorders, and socially deviant behavior.

The psychogenic effects on airway reactivity are presumably mediated by the autonomic nervous system. Furthermore, a whole class of medical problems, known as psychosomatic disorders, often result from stress. These medical problems are caused by an interaction of psychological, emotional, and physical difficulties.²

British trait theorist and psychologist Hans Eysenck's (1967) well known theory of introversion/extraversion³ proposes that introverts and extraverts have basic differences in the sensitivity of their nervous systems, which affects their emotional response and how they react to socialization.

Although bronchial asthma is triggered by allergens, psychological factors have long been implicated in this disease. Eysenck (1975; Eysenck and Eysenck, 1985) used factor analysis to identify patterns of traits.⁴ He found that personality could best be described in terms of just two major dimensions: extraversion/introversion and neuroticism/stability. At one extreme of the extraversion/introversion dimension are the extraverts (outgoing, sociable, and active), and the other are introverts (people who are quiet, passive, and careful). Independently of this dimension, people can be rated as neurotic (moody, touchy, anxious) versus stable (calm, carefree, even-tempered). By evaluating people with respect to these two dimensions, Eysenck has been able to predict behavior accurately in a variety of types of situations.

Research on life events attempted to demonstrate a connection between the onset of illness and the sheer number of life events that required adaptive responses. The effects of these events were assumed to be additive.

Stress is an important factor of psychosomatic diseases. Stress as conceptualized by Selye (1976) is a broad and general concept like anxiety describing the organism's total reactions to environmental demands. Stressful life events can evoke biochemical changes as well as changes in autonomic nervous system of the human body, thus leading to psychosomatic disease.⁵

Objectives

1. To study whether people with bronchial asthma and people without bronchial asthma differ in personality.
2. To study whether people with bronchial asthma and people without bronchial asthma differ in life events.
3. To study whether male patients with bronchial asthma and female patients with bronchial asthma differ in personality.

Diagram 1

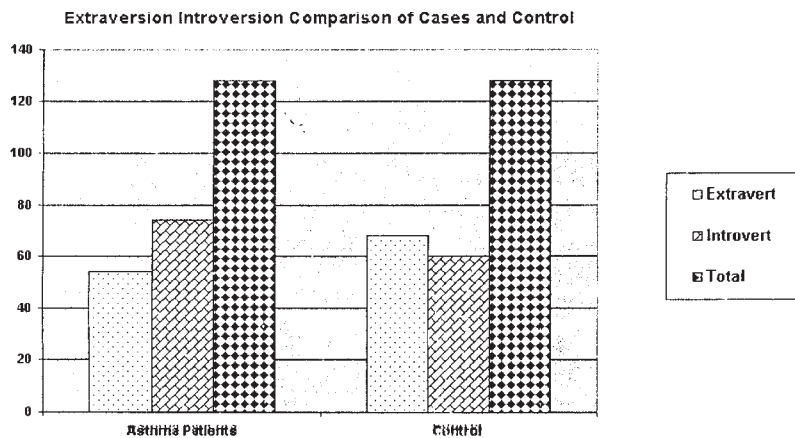


Diagram 2

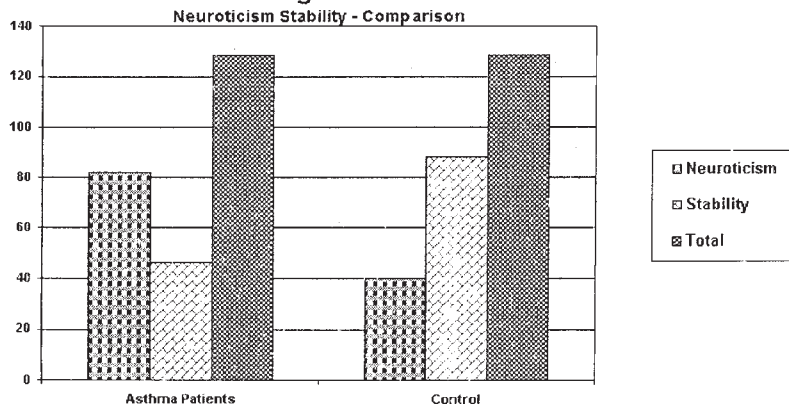
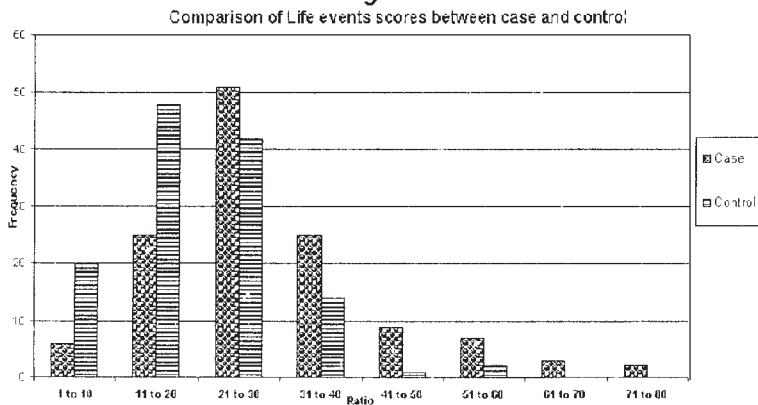


Diagram 3



4. To study whether male patients with bronchial asthma and female patients with bronchial asthma differ in life events.

Design

Case control study

Setting

Secondary and Tertiary care setting

Participants

128 patients suffering from bronchial asthma were selected from department of chest diseases of medical colleges Kottayam and Thrissur, and the medicine department of District Hospital, Palakkad. Both male and female patients were in the age group 15 to 65 years. One hundred twenty-eight persons without bronchial asthma were taken as a control group from the same institutions. Both male and female persons in the age group 15 to 65 years, preferably relatives and accompanying persons were taken as the control group. Patients with associated conditions like chronic bronchitis, emphysema, heart disease, pulmonary tuberculosis, pneumothorax, pleural effusion, and lung neoplasms were excluded from the study.

Tools

The following tools were used to collect necessary data for the study.

1. Eysenck Personality Inventory (EPI) Malayalam version—Sree Devi Ammal (1977)
2. Life Events Inventory (checklist) Razeena Padmam & Rajeev Kumar (1997)
3. Personal data sheet prepared by the investigator (2001)

The purpose of the study was explained to the patients and control group; after getting informed consent the tools were administered to both groups separately. The completed answer sheets were scored and subjected to statistical analysis.

Statistical analysis

The data so obtained was subjected to statistical analysis in the form of t-test and p-value was calculated.

Results

A total of 128 patients were selected from the Departments of Chest Diseases at medical college hospitals Kottayam and Thrissur, and from the Department of Medicine at District Hospital, Palakkad. Patients were both male and female and in the age group of 15 to 65 years.

The control group consisted of 128 individuals without bronchial asthma comprising the male and female relatives or acquaintances of respective patients in the age group 15 to 65 years.

The first objective of the study mainly aimed at finding whether there was any significant difference

between asthmatic and non-asthmatic individuals in personality dimensions. Personality dimensions studied were extraversion/introversion and neuroticism/stability. From the mean score it can be seen that the control group had a higher score in extraversion than did the experimental group. From Table 1 it is obvious that the mean score of the experimental group was 11.7031 and that of the control group was 12.7188. This shows non-asthmatic individuals were more extraverted than the asthmatics. Bronchial asthma patients were more introverted. From Table 1 it can be seen that there is a highly significant difference between the experimental and control groups in terms of the personality dimension of neuroticism. The mean score of 14.5078 for the experimental group is higher than the mean score of 9.6875 for the control group. The t-test value shows significance at 1% level for neuroticism. It clearly proves that bronchial asthma patients scored higher in the neuroticism dimension than the control group, which scored higher in the stability dimension. In the neuroticism dimension, the mean for males was 10.6607 and for females was 13.2153, and the t-value was -3.542 , which was found to be significant at 1% level. Hence there is a significant difference between male and female patients in extraversion and neuroticism.

Table 2 shows a significant difference between male and female patients in personality dimensions of extraversion and neuroticism. The mean extraversion score was 12.9018 for males and 11.6736 for females; the t-value was 2.565, which was found significant at 1% level. Also the mean neuroticism score was 10.6607 for males and 13.2153 for females; the t-value was -3.542 , which was found significant at 1% level. Hence, there were significant differences between male and female patients in extraversion and neuroticism.

From Table 1 it can be seen that the t-value shows a higher significant difference in terms of stressful life events in the experimental group than in the control group. The average mean score obtained for the experimental group was 29.0313 and 19.8359 for the control group. It is clear from the mean score that the asthmatic patients had experienced a greater number of life events when compared to non-asthmatic individuals.

From Table 3 it can be seen that there is no significant difference between male and female asthmatic patients in terms of stressful life events. It is obvious from the table that the mean for males was 24.1161 and 24.6806 for females; the t-value was .349. There was no significant difference between male and female asthmatic patients in relation to life events.

MAJOR FINDINGS

1. There was a significant difference for extraversion between the experimental and control groups. Bronchial asthma patients were less extraverted than patients in the control group. The control group scored higher in extraversion; therefore, the bronchial asthma patients were more introverted.

2. There was a highly significant difference between patients with bronchial asthma and those without, in terms of neuroticism. Patients with bronchial asthma were found to be more neurotic than non-asthmatic individuals.

3. There was a highly significant difference between patients with bronchial asthma and those without, in terms of the stressful life events score. More stressful life events were

reported by patients with bronchial asthma than non-asthmatic individuals.

4. There was a significant difference between male and female patients in extraversion and neuroticism.

5. There was no significant difference between male and female asthmatic patients in terms of stressful life events.

DISCUSSION

Traditionally, the medical profession has concentrated clinical and research efforts on understanding and controlling anatomical and physiological factors in disease. In psychopathology, on the other hand, interest has centred primarily on the discovery and remedy of psychological factors that are associated with mental disorders. Although a disorder may be primarily physical or psychological, it is always a disorder of the whole person, not just of the body or psyche.

Behavioral medicine is the broad interdisciplinary approach to the treatment of physical disorders thought to have psychological factors as major aspects of their causal patterns.

At the most general levels the influence of psychological variables on health is seen as excessive autonomic nervous system responses to stress or conditions sometimes resulting directly in organ damage. There is also increasing evidence to show that psychological challenges, including negative emotional states, can impair the immune system ability to respond, leaving a patient more vulnerable to disease producing agents. A common factor in most psychosocially mediated diseases is inadequacy of an individual's coping resources for managing stressful life circumstances. Psychological distress has been proven capable of altering the human ability to resist infections. It is also believed that emotional and psychosocial problems easily work on individuals with certain personality predispositions. Psychosocial and stressful life events play a major role in this aetiopathogenesis of bronchial asthma. They are among the multitude of factors leading to bronchial asthma, since the exact etiology is still unknown. Several research studies have substantiated the fact that certain personality dimensions, psychosocial factors and stressful life events can predispose or precipitate bronchial asthma.

The present study was an attempt to explore the personality and stressful life events experienced by bronchial asthma patients, and to compare them with those of non-asthmatic individuals.

Henry et al (1993) on reactive and adaptive phenomena in bronchial asthma⁶ found that psychological phenomena secondary to bronchial asthma play a relevant role in this disease influencing in a remarkable way in its clinical course in each patient.

In a Polish study conducted by Cesleska-Kopacz (1992) on evaluation of selected personality factors in patients with bronchial asthma,⁷ it was found that psychological factors play an important role in the development and clinical course of bronchial asthma.

In fact, the likelihood of the onset of any major illness seems to be related to the number and type of stressful events a person experiences. The effects of stress are best illustrated by a model developed by Hans Selye, a major stress theorist (Selye 1976).

This model, the general adaptation syndrome, suggests that the same set of physiological reactions to stress occurs regardless of the particular cause of stress.

CONCLUSION

Bronchial asthma is a multifactorial disease. Bronchial hyperresponsiveness to external allergens is the commonly documented cause. But several research studies have proved that psychological factors, personality dimensions, and stressful life events play a major role in precipitating or aggravating bronchial asthma. Findings of this study agree with the psychosomatic predisposition of bronchial asthma. These findings point to the role of psychotherapeutic interventions along with medical treatment as a better therapeutic response and recovery for bronchial asthma patients. Relaxation may help to reduce anxiety and hyperventilation. Anxiolytic agents help in reducing tension and stress of the asthmatic patients too. Hence, we must always consider the psychological factors including stress and the emotional state of the asthmatic patients. Reassurance, suggestions, and counselling may also help the patient to better prognosis and recovery.

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A Patient-Assisted Ventilator Treatment Program

From Critical Care News

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CoxHealth in Springfield, Missouri, has 9,000 employees and provides care to 750,000 people. In response to challenges in the high-risk, high-cost environment of mechanical ventilation, the institution set the goal of developing a method to improve clinical outcomes, decrease length of hospital stay, decrease health care costs, and increase clinician and patient satisfaction.

The solution was a Clinical Management Program from the ventilator manufacturer, based on the Open Lung recruitment concept. This was introduced in 2000. Within two years, the program achieved a 34% decrease in the number of ventilator hours, a 68% decrease in ventilator-associated pneumonias, and a 23% decrease in length of hospital stay for a selected group of non post-op patients. This represents a decrease in hospital costs of approximately \$US 4.5 million per year.

Critical Care News talked to David Tucker, Director of Respiratory Care Services at CoxHealth, and Martin Rohrer, Assistant Director, about the development of the program.

What factors led to the establishment of the Clinical Management Program?

David Tucker: Martin Rohrer, myself, and some other colleagues had been using the SERVO 900 ventilator for years. That was really the workhorse ventilator. We probably ended up using it longer than we should have, but we just weren't ready to give it up. But graphic monitoring was becoming prevalent, and we wanted a more comprehensive protocol; we only had a two-page protocol at that time. We wanted to use technology to optimize our therapy. When we saw the program we could get with SERVO-i, we thought that was an opportunity to streamline and provide a better protocol for ventilation care. It was a win-win situation.

Martin Rohrer: In 1995 and 1996, we were searching for better

ways to ventilate our patients. We knew we needed improvement in that area. Our ventilation management was inconsistent; physicians were doing things in different ways. Therapists had different ideas and concepts. We needed to bring people together, and we needed to utilize the technology that was out there. Graphic monitoring was coming along.

We knew from past experience that it can be hard getting everyone together and introducing new technology, and we didn't want to re-experience the failures of the past. We knew how hard it can be to change when you are accustomed to a specific ventilator. A program was needed to get everyone together—physicians, nurses, and respiratory therapists. We decided that the Clinical Management Program could accomplish that, and we committed to purchasing a fleet of SERVO-i ventilators, which had graphic monitoring capabilities and were responsive to patients. The manufacturer assisted us in setting up the program.

We presented a package to our physicians, and they loved it. Our medical directors have been extremely supportive to us over the years, and I think that is key. The administration approved budgets and meeting time. We utilized the Train the Trainer program, and things took off from there. We educated our staff in groups on the Open Lung concept, which was the focus of the Clinical Management Program.

When did you first become familiar with the Open Lung concept?

Martin Rohrer: In 2000. After reading the Clinical Management Program material from the manufacturer, we were really excited about what we could do, and we incorporated all of it into our education program. We gave classes during day and night shifts to get everyone on board. It just snowballed.

David Tucker: We had to convince hospital administration. I felt confident in the Open Lung concept, as did many others on the staff. We had to bring the program in, identify the appropriate patients, and see if we had success. Once you start having positive outcomes, shortened length of stay and other results, it's easy to get people's attention. In 2001, we adopted our department motto: "Open up the lung and keep it open."

What were the early staff experiences of Open Lung management? Were there learning thresholds to overcome?

David Tucker: Our staff started telling me that they were seeing wonderful results. After 12-18 months, I looked at the numbers

Roles and responsibilities of core members		
Members	Role	Responsibilities
VP Clinical Services	Administrative leader	Administrative approval
Pulmonary Physicians	Medical director and staff	Guide and monitor for best practice, medical approval and medical liaison
Respiratory Director/ Assistant Director	Department and project leaders	Administrative liaison
Respiratory Therapists	Clinical specialist	Researcher, patient advocate, implementation specialist
Data Analyst, QRD	Data analysis	Harvest and analyze data to evaluate opportunities
Director, QRD	Support	Provide resources for PI Process
Critical Care Nurse Manager	Member	Provide expertise and champion for nurse buy-in

Indicator	Pre-protocol	Post-protocol	% improvement
Ventilator-acquired pneumonia	2.7/1000 vent days	0.87/1000 vent days	68%
Ventilator hours/patient	200 hours	130 hours	34%
Average hospital length of stay	19.8 days	15.3 days	23%

VAP rates dropped 68%, from 2.7 to 0.87 pneumonias per 1,000 adult ventilator days, in CoxHealth Medical Intensive Care Unit (MICU). The US national average is 5.5.

in detail, and the benefits were evident. I sent the findings to the Quality Resource Department. They mapped the figures out, and the result was simply impressive. The staff motivation was just wonderful. The real winners here are the patients and the ICU staff.

Martin Rohrer: There were some key individuals who were able to grasp the concepts early on. They were working on the protocol while we were running the education. At the same time, our staff started applying some of the principles. The physicians tried the program, and they started to see patients getting better, and getting off the ventilators quicker.

We still didn't have our protocol finalized, but we were already utilizing the techniques and protective lung strategies of the Open Lung concept. It was just amazing. The conclusion was: "I know how to do this, how can we keep patients waiting and deny them these benefits while we are waiting for the protocol to be finalized?" In a way, this affected our data collection, starting our education before the protocol was out. A couple of months prior to rolling out the protocol, we were already using the method and getting good results.

From the Medical Directors' standpoint, we discussed the need for consistent ventilation management at CoxHealth. We wanted to incorporate evidence-based science at our institution. The Medical Directors saw the benefits of that and we received their backing. The administrators wanted to know the financial value to the institution, and we were able to show that if we decrease length of ventilator time, we decrease the medications and complications. The ground work showed the benefits, and it made sense to everyone.

The staff, including nurses, RTs, and pharmacists, quickly understood the benefits of applying a protocol to get the patients off the ventilators more quickly. The nurses are patient care oriented and loved the benefits.

How is the program coordinated?

Martin Rohrer: Once you have all the players on board, the management program and all of the functions, we believe it's important to establish a critical care supervisor with team leaders from all the ICUs. The supervisor is the point person for the program, for research, expert help, and for pulling all of the components together, between nurses, physicians, etc. That has been an integral part of the program and well worth the investment.

Have you had any special cases for which the protocol did not work?

Martin Rohrer: This is not a panacea. We are not curing patients from their disease—that is not the purpose of this program. The purpose is to protect the lungs and gain FRC so that other medical interventions can proceed. We want to

protect the lungs with protective therapy. Early on, we established that we could not do this in every situation. Once fibrosis starts, for example, you can't reverse it and you need steroids and the body's own mechanisms.

What we want to do is catch patients early on; we don't want to wait to intubate when too much damage has been done due to their disease process. Get them on early, maintain, and give the body and therapies a chance to work. Then get them off as quickly as possible. The longer they are on ventilation, the greater the chances of infection and other complications associated with ventilation therapy. Open them up, protect them, and then get them off.

David Tucker: Physicians have the option of managing the patient without the protocol. Within the protocol, they can manage individual parameters for individual cases. This allows the therapists to wean down on the FiO₂ as the SpO₂ improves, and adjust ventilation peak pressures as they improve.

Were the early indications in line with expectations?

Martin Rohrer: The results were above all of our expectations. But the early results also showed us areas where we needed to go back and improve. We did great when the patient was on the ventilator—we opened the lungs and saw improvement. But when we looked at the length of hospital stay, we saw that we needed to get better at weaning. It was a catalyst that led us to make improvements in other areas.

Will you be expanding or modifying the protocol in the future to include other patient categories or outcomes?

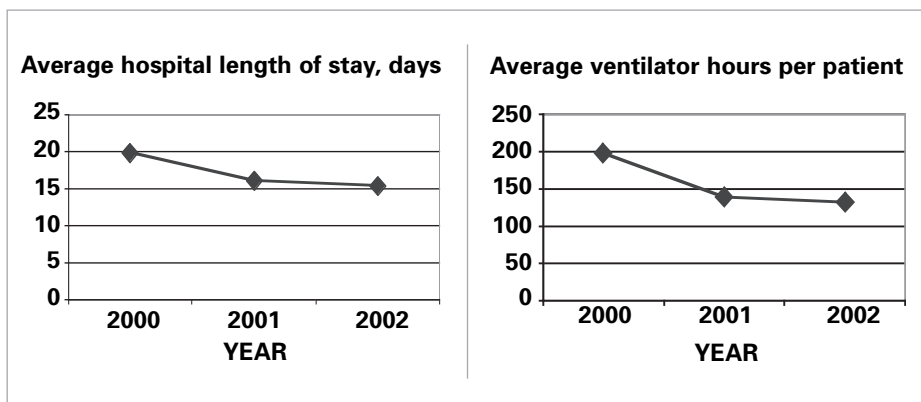
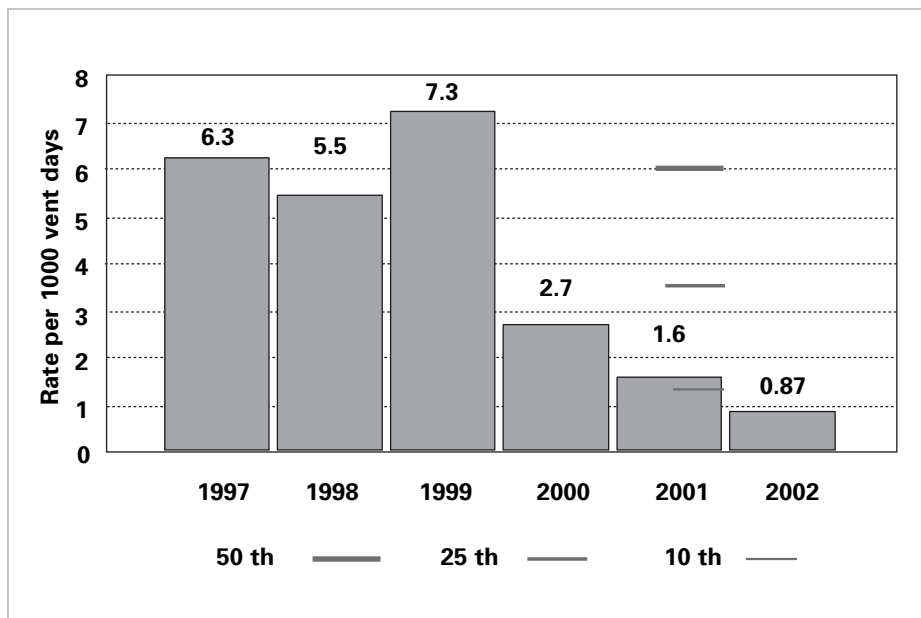
David Tucker: We are trying to move in the direction of allowing a bit more hypercapnia. We think greater use of hypercapnia will give better outcomes for some patients. Current literature indicates that you should look at the clinical situation for the individual patient. And we think we have some opportunities to allow for this in our current protocol version 4.0.

We have a standard protocol that allows us to tailor ventilation therapy according to need. It is critical to optimize each situation for the best outcome.

Martin Rohrer: Using non-invasive ventilation with SERVO-i is of great interest right now. We started this a few months ago, and have had great success. This ventilator is more responsive to the patient and their needs than other ventilators. We are looking further into comparison data for non-invasive therapy between SERVO-i and other ventilators.

What has been the financial impact for the ICU and the hospital as a whole?

David Tucker: We have a QRD department with statisticians, which has given us statistics on savings. These have gone far



Comparing baseline calendar year 2000 with 2002, the ventilator hours per set-up decreased from 200 to 130. CoxHealth Hospital LOS fell from 19.8 days to 15.3 days for a selected group of non post-op patients.

beyond the cost of the systems and start-up time. The savings from the most important clinical benefits, ie reduction in complications, ventilator hours, and length of stay, were calculated at \$US 4.5 million per year.

Both the ICU department and the hospital have benefited from the program. Our hospital administration always wants to do what is more appropriate for the patient. When we invested in the SERVO-i ventilator fleet, they were very supportive.

BIOGRAPHIES

David Tucker, BS, RRT, is Director of Respiratory Care Services at CoxHealth, where he has practiced for 30 years. He is head of the Respiratory Department and staff, and the administrative liaison between all functions involved in the Clinical Management Program. Martin Rohrer, BS, RRT, is Assistant Director Respiratory Care at CoxHealth, where he has practiced for 29 years. He is responsible for project leaders and administrative duties within the Clinical Management Program.

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High Frequency Chest Wall Oscillation for Individuals With Chronic Neuromuscular Weakness

Jan Tecklin

High frequency chest wall oscillation (HFCWO), also called high frequency chest compression (HFCC) and high frequency chest wall compression (HFCWC), is a mode of airway clearance used for more than a decade. It has been shown to be effective, safe, and cost efficient. Furthermore, HFCWO has increased airway clearance treatment acceptance and the quality of life for individuals and families who use the device regularly.^{1,2,3} HFCWO is different than traditional chest physical therapy that includes manual percussion, or “clapping” therapy, which was the standard method of airway clearance in the past. HFCWO utilizes an air pulse generator to deliver air pulses through a flexible hose to an inflatable vest worn by the patient. Once the vest is inflated, the pulses repeatedly compress and release the chest wall. The technique was initially developed for patients with cystic fibrosis, but over the past 5 years HFCWO has become an increasingly popular airway clearance technique for individuals not only with pulmonary diseases, but with respiratory consequences of many neuromuscular and neurological disorders as well. It is this group of patients about whom this briefing book is directed. Most specifically, we will demonstrate that HFCWO is an outstanding airway clearance modality for individuals with chronic, progressive neuromuscular diseases. Indeed, it should be the preferred approach for motor neuron disorders including amyotrophic lateral sclerosis (ALS) and spinal muscle atrophies, progressive myopathies such as Duchenne muscular dystrophy, and other diseases of a similar nature that result in major respiratory impairment. Because of the severity of respiratory

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manifestations of ALS and the universal recognition that treatment of those manifestations can reduce the morbidity and delay the mortality associated with ALS, we will focus on that disorder. Nonetheless, there is a large group of related disorders that will benefit from HFCWO as well.

AMYOTROPHIC LATERAL SCLEROSIS— A BRIEF OVERVIEW

Amyotrophic lateral sclerosis is a chronic and progressive neuromuscular disease that affects upper and lower motor neurons. The rate of progression is variable but approximately 50% of those diagnosed are dead within three to five years of diagnosis.⁴ The disease affects as many as 20,000 people in the United States with 5000 new cases being diagnosed each year. ALS strikes individuals of all racial and ethnic backgrounds and is more common among males and individuals in their 5th and 6th decade of life.

There are no predisposing risk factors in the vast majority of patients, and only 10% of individuals with ALS have some familial or genetic risk.⁵ There is no predictable pattern of onset for ALS. The earliest symptoms are often subtle and are frequently mistaken for clumsiness or awkwardness. The specific muscle groups first involved will be responsible for the presenting symptoms. Should a muscle group in the lower extremity be the first area affected, the individual may exhibit difficulty with gait, stair-climbing, and the ability to step up on curbs. A loss of a normal manual skill, such as buttoning a shirt or performing a particular task at work, often is indicative of early signs of upper extremity involvement. Yet other individuals exhibit difficulty with speech or problems with swallowing. This latter group is said to have bulbar involvement which is associated with increased risk of aspiration and related pneumonia which often lead to imminent respiratory failure.⁶ In addition, bulbar involvement is said to be responsible for the worst symptoms including speech, swallowing and respiration difficulty.⁷

Regardless of the body part first affected by the disease, muscle weakness and atrophy spread to other areas as the disease progresses. Patients have increasing problems with moving,

swallowing (dysphagia), and speaking or forming words (dysarthria). Symptoms of upper motor neuron involvement include increased muscle tone (spasticity) and exaggerated reflexes (hyperreflexia) including an overactive gag reflex. An abnormal reflex commonly called Babinski's sign (the large toe extends upward as the sole of the foot is stimulated in a certain way) also indicates upper motor neuron damage. Symptoms of lower motor neuron degeneration include muscle weakness and atrophy, muscle cramps, and fleeting twitches of muscles that can be seen under the skin (fasciculations).

RESPIRATORY MANIFESTATIONS OF ALS

Of the many manifestations of motor neuron disease, respiratory insufficiency leading to respiratory failure often poses the greatest challenge for both hospital and home caregivers. Progressing weakness of the inspiratory muscles, with primary emphasis upon the diaphragm, often instigates respiratory signs and symptoms. Dyspnea on exertion is one of the earliest symptoms of respiratory insufficiency and is followed by supine positional dyspnea and nocturnal dyspnea. The latter two forms of dyspnea often lead to impaired sleep patterns due to nocturnal hypoxemia.^{8,9} When the vital capacity falls to 50% of predicted value, respiratory symptoms are commonly encountered.¹⁰ A progression of vital capacity down to 1 liter or less is associated with impending respiratory failure.¹¹ When dyspnea and related symptoms are noted, it is common to find that maximum static inspiratory and expiratory pressures (MSIP, MSEP) measured at the mouth are significantly decreased from normal values.⁹ Recent research has demonstrated high sensitivity and specificity for sniff nasal-inspiratory force test as a good measure of respiratory muscle strength in ALS. In addition, sniff nasal inspiratory force can be performed by patients with advanced disease, and it gives prognostic information.¹² While inspiratory muscle weakness leads to low lung volumes and hypoventilation, expiratory muscles can also be severely diminished in their capacity to develop the necessary pressures to achieve a functional cough. The inability to generate adequate expiratory pressures to cough establishes the loss of a major pulmonary protective mechanism for a population which is often beset by lower and upper respiratory tract secretions, debris, and food.¹³

When bulbar involvement occurs with ALS, there is increased dysfunction with swallowing, and a heightened risk for aspiration of accumulated upper respiratory secretions, excessive saliva, and food.¹⁴ Inability to cough and thereby clear the larger airways adds to the probability of major aspiration and aspiration pneumonia. Aspiration can cause mechanical and chemical damage to the airway epithelium. When aspiration occurs, secondary lower respiratory infections including bacterial pneumonias will often develop. This sudden imposition of an acute obstructive phenomenon along with a bacterial infection can be sufficient additional stress that adds markedly to respiratory morbidity and mortality. Overwhelmingly, ALS patients die from pulmonary infection as a complication of progressive respiratory muscle weakness and eventual respiratory failure.¹⁵

MANAGEMENT OF SECRETIONS AND AIRWAY CLEARANCE IN ALS

The bulbar effects of dysphagia and chronic aspiration, along with expiratory muscle weakness and ineffective cough, result in a limited ability for patients with ALS to clear secretions from the respiratory tract. In addition, the lack of physical mobility

tends to cause accumulation of secretions and debris in dependent areas of the lungs.

Accumulated secretions disrupt the relative homeostasis that supports pulmonary defense mechanisms. A major issue regards harmful material in these accumulated secretions. This material may include environmental substances, debris from excessive saliva, micro-organisms, and others. This deleterious material causes liberation of more respiratory mucus, dysfunction in ciliary function, and the liberation of both primary and secondary inflammatory mediators.¹⁶ The net effect of this continuing series of events is to render the respiratory tree susceptible to on-going inflammation, periodic infection, and mechanical obstruction secondary to inflammatory debris.

Sialorrhea, excessive saliva, and the accumulation of secretions and foodstuff within the upper airways is a significant risk factor for aspiration and related aspiration pneumonias. Traditional non-pharmacological management of sialorrhea has included the use of suction machines, despite a lack of evidence of their effect,¹⁷ and the use of mechanical insufflation-exsufflation devices.¹⁸ When excessive secretions and dysphagia lead to choking on food, fluids, and secretions there is an increased probability of aspiration, aspiration pneumonia,¹⁷ and respiratory failure. Indeed Lechtzin et al clearly demonstrated that pneumonia and respiratory failure were major causes of significant morbidity and mortality in hospitalized patients with ALS.¹⁹ When these major respiratory events occur, more aggressive airway clearance becomes necessary both for upper and lower airway management.

Postural drainage, percussion and vibration (PDPV) has been the mainstay of airway clearance for as long as a century. PDPV used in an effort to remove excessive secretions in medically diverse patients has been commonly referred to as chest physical therapy or simply physiotherapy. The techniques of PDPV have been used for patients with pulmonary pathologies as well as for individuals with airway clearance encumbrance caused by inability to cough as commonly occurs with neurological, neuromuscular, and chest wall diseases and injury. When active coughing is not possible, secretion removal via airway suctioning and some type of assisted coughing are recommended.²⁰ The respiratory care literature has been replete with articles, studies, reviews, and commentaries about airway clearance. In fact the American Association for Respiratory Care has promulgated, published, and disseminated Guidelines for Postural Drainage Therapy that includes discussion of neuromuscular diseases.²¹

Another approach to airway clearance for individuals with ALS and related disorders has been supported in the literature in recent years. Mechanical insufflation-exsufflation (MIE) devices are often used along with the application of abdominal thrusting.²² A brief explanation of MIE is in order due to its common usage. MIE attempts to reproduce mechanically the forces generated in a normal coughing sequence. MIE is introduced via an electrical device which utilizes a blower and a breathing circuit. Flexible tubing, a bacterial filter and either a facemask, a mouthpiece, or an adapter to a tracheostomy or endotracheal tube complete the circuit. A valve system in the breathing circuit repeatedly applies first a positive inspiratory pressure of 40 cmH₂O or more followed rapidly by negative expiratory pressures of -40 cmH₂O.²³ MIE is a mechanical attempt to reproduce a cough in order to assist the patient in

clearing retained bronchopulmonary secretions. The expiratory pressures are often accompanied by an abdominal thrust timed to enhance expiratory flow.^{17,24} This approach has found favor in certain circles, because it improves cough peak flows²⁵ which, presumably, increase efficacy of this mechanically produced cough. The high inspiratory pressure and flow is necessary to inflate the lungs to provide for the mechanical cough. However, the focus on the expiratory phase ignores the effect of the high inspiratory pressures on secretions and other debris in the airways. One untoward effect of the inspiratory effort is the “muzzle loading” of debris and secretions distally in the respiratory tract. That is, the inspiratory force of the MIE cycle blows secretions and debris distally within the respiratory tree which is opposite of the desired direction. HFCWO always provides a strong distal to proximal movement of secretions as will be described below.

ADDITIONAL OPTIONS FOR AIRWAY CLEARANCE IN ALS

Prior to the development of commercially available HFCWO, most airway clearance was comprised of traditional patient positioning for gravity-assisted PDPV followed by deep breathing techniques and coughing or huffing to raise the sputum. This approach was effective for individuals with airway clearance encumbrance associated with both pulmonary disease and respiratory insufficiency secondary to neuromuscular disorders. Despite widespread use and acceptance the concerns with PDPV techniques for the individual with ALS are:

- 1) they are arduous and fatiguing for the patient
- 2) they require a trained, skillful and committed health care professional or caregiver at home to administer
- 3) treatment is very time consuming (up to one hour 2 or 3 times daily)
- 4) treatment is expensive when administered by a professional therapist
- 5) PDPV poses the potential for adverse events such as hypoxemia^{26,27} and hemoptysis.²⁸

NEWER APPROACHES TO AIRWAY CLEARANCE

Given these untoward consequences with traditional PDPV described immediately above, several new approaches were developed during the 1980's and into the 1990's. These approaches included autogenic drainage,¹ positive expiratory pressure,⁹ active cycle of breathing technique, Flutter device,ⁱⁱ intrapulmonary percussive ventilation,¹⁰ and HFCWO.¹⁰ Each of these techniques was effective and at least as efficacious as traditional PDPV for individuals with chronic lung disease such as cystic fibrosis and chronic obstructive pulmonary disease. However, HFCWO remains the singular technique that does not involve a specific coordinated breathing technique which would likely prove difficult, if not impossible, for an individual with neuromuscular disease and associated respiratory muscle weakness or dyscoordination. In addition, HFCWO can be easily carried out while a patient receives either invasive or non-invasive mechanical ventilation.¹⁰ These two issues of 1) difficulty coordinating respiratory efforts and the 2) need for mechanical ventilation mitigates strongly for airway clearance via HFCWO in patients with severe neuromuscular disorders such as ALS, spinal muscular atrophy, high spinal cord injury, acute Guillain-Barre syndrome, late stage Duchenne myopathy and others. These patients find it difficult and fatiguing when asked to perform the specific breathing maneuvers for most of the newer varied airway clearance techniques. In addition,

patients with ALS often require mechanical ventilation, thereby rendering all of the techniques, except HFCWO, unrealistic choices for regular periodic airway clearance. The choice of HFCWO seems obvious considering its method of operation and the acceptance it has achieved among many patient groups.

HIGH FREQUENCY CHEST WALL OSCILLATION

HFCWO operates by virtue of an air pulse generator that propels pulses of air through a large, flexible tube into inflatable bladders within a two-part vest-like garment. This garment is constructed of an inflatable inner bladder and a soft, washable external shell. The garment is worn over the torso and comes in varied sizes to fit most individuals. The bursts of air created in the air pulse generator may be delivered into the inflatable bladders at varied frequencies (commonly between 5-25 pulsations per second) and are produced at varied pressures. Each cycle begins with an air pulse that inflates the vest and causes compression of the chest wall. This compression creates a burst of air through the patient's airways which results in a brief cough-like response. At least one researcher has referred to this air movement as a “staccato cough.”³⁶ These rapidly recurring bursts of air, or staccato coughs, provide a shear force that cleaves the secretions from the walls of the airways. In addition to the shear forces, the air bursts reduce the viscosity of the secretions³⁷ and move the secretions upward where they can be coughed or suctioned out.³⁸ All lobes of the lungs are treated at the same time and the patient can sit upright throughout the entire treatment without having to assume the 10-12 different positions required for PDPV.³⁹ A HFCWO treatment typically requires 10 to 30 minutes, depending on the physician's prescription. The airpulses are delivered at a frequency of between 5 and 25 hertz, although frequencies around 13 hertz appears to provide the best results for secretion clearance.⁴⁰

HFCWO provides several physiological mechanisms by which secretions in the lower respiratory tract are both loosened from the airway wall and moved proximally in the respiratory tree. The four prominent mechanisms are:

- reduction in physical properties of mucus viscoelasticity and spinnability. Tomkiewicz et al were able to demonstrate an in vitro reduction in both spinnability of mucus and its viscoelasticity properties. That is, the mucus material became more fluid, and more easily cleared from the airway. The authors postulated that oscillating air flow as produced by HFCWO seemed to act as a physical “mucolytic” agent that augmented the cough clearability of the mucus.⁴¹
- shearing effects upon respiratory mucus. Chang and colleagues developed a model to examine mucus transport produced by non-symmetrical oscillatory airflow as seen in HFCWO. Their results showed increased tracheal transport of mucus and related this transport to shearing forces produced at the air-mucus interface.⁴²
- cephalad bias in flow during HFCWO. King et al found that enhancement of tracheal mucus clearance in the cephalad direction was most pronounced with HFCWO in the range of 11 to 15 Hz, reaching a peak value of 340% of control at 13 Hz.⁴⁰
- a “staccato cough” mechanism propelling mucus proximally

within the respiratory tract. Warwick reported that the volume of air expelled from the lungs during the compression phase of HFCWO was much greater than with active forced expiration alone. Warwick called this effect a “staccato cough” and noted that this high level of expiratory volume and the associated high flows can be sustained without effort or fatigue on the part of the patient.⁴³

The safety, efficacy, and acceptance of HFCWO have all been clearly demonstrated. Satisfaction and acceptance were demonstrated by Oermann et al using a validated instrument to measure treatment acceptance and satisfaction.⁴⁴ The authors documented fewer missed treatments with HFCWO than with other modes of airway clearance. Efficacy has been determined for two domains—improvement in pulmonary function and increased secretion removal.

Pulmonary function studies are a strong indication of the efficacy of HFCWO. Warwick and Hansen followed long-term pulmonary function changes in 16 subjects with CF used as their own controls. Patients received HFCWO at home for varied periods of time each day across a mean of 21.6 months (range 7- 26 months). 15 of 16 patients showed long-term improvement in forced vital capacity and forced expiratory volume in one second. In addition, those who improved showed a reduced slope of pulmonary function regression compared to the period prior to instituting HFCWO.⁴⁵ Arens et al compared short-term changes in pulmonary function in 50 patients with CF hospitalized for acute pulmonary exacerbations. Patients were randomized to either PDPV or HFCWO. Significant and important improvements at the end of hospitalization were seen in pulmonary function values and sputum production for both modalities. Of note is that 22 of 25 patients in the HFCWO group preferred this modality to PDPV which they had been using at home for years and made inquiry regarding its availability for use at home.⁴⁶

Increased sputum production is another good indicator of airway clearance efficacy. A four day randomized trial of HFCWO versus PDPV was performed by Kluff et al. They demonstrated greater wet weight and dry weight of sputum was produced in patients with cystic fibrosis (CF) who were hospitalized for acute exacerbation of their chronic pulmonary disease. Treatment was performed three times each day for a total of 30 minutes per session.⁴⁷ Braggion and colleagues also compared HFCWO versus PDPV and positive expiratory pressure breathing in 16 patients with CF hospitalized for acute exacerbations. There was a significant increase in sputum production for all of the airway clearance modalities.⁴⁸ In a prospective randomized short-term trial including 14 patients with CF who had stable disease, Scherer studied the effects of HFCWO, high-frequency airway oscillation delivered by mouth, and traditional PDPV. Each of the three modalities improved sputum expectoration. There was no change in oxygen saturation with any treatment.⁴⁹

HFCWO FOR PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS

As shown above, research, expert opinion, and experience have demonstrated that HFCWO is a safe, effective, and well accepted airway clearance modality. HFCWO does not require:

- patient positioning for gravity-assisted drainage

- manipulation of the thorax via percussion and vibration
- the availability of a skilled caregiver
- coordination of breathing techniques

HFCWO provides gentle oscillations which compress and relax the thorax in a non-invasive manner at frequencies of up to 25 hertz. These oscillations provide:

- reduced viscoelasticity of mucus secretions
- increased shearing force to loosen secretions and debris from the airway wall
- a cough-like pumping of loosened secretions in a cephalad direction towards the large airways

There are no published clinical studies of HFCWO for patients with any motor neuron disease or ALS. However, a series of brief reports and case studies support HFCWO as safe and effective in mobilizing secretions in individuals with neuromuscular weakness,⁵⁰ spinal muscular atrophy,⁵¹ Duchenne myopathy,⁵² and cerebral palsy.⁵³ The Plioplys presentation is of particular note in that HFCWO used in four subjects improved suctioning of pulmonary secretions and reduced hospitalizations and pneumonias that required antimicrobial therapy.⁵³

Despite lack of published evidence, the many factors noted in this paper strongly support the use of HFCWO for patients with ALS for the following reasons:

- HFCWO effectively reduces secretion accumulation by loosening and moving the secretions higher in the respiratory tree
- HFCWO improves pulmonary function
- HFCWO appears to reduce the incidence of pneumonia and hospitalizations
- Its use has found good acceptance
- Its use has improved adherence to airway clearance

The patient with ALS and the caregivers should find HFCWO a particularly helpful technique because:

- HFCWO is much less fatiguing than other modes of airway clearance
- HFCWO is much easier to use than all other modes of airway clearance
- HFCWO does not require a skillful and often expensive caregiver
- HFCWO is equally or MORE effective than other forms of airway clearance

These physiological benefits are provided by an FDA approved device called the MedPulse Respiratory Vest System (Electromed, Inc, New Prague, MN) This system has a number of attractive features:

- 1) The first HFCWO system designed to be portable
- 2) A single hose design that provides a high degree of mobility during therapy
- 3) Seven vest sizes and ample Velcro closures provide optimum fit and easy on / easy off fitting of the vest
- 4) Unique, garment-like vest design using soft fabrics enhance patient comfort; washable
- 5) A memory option that allows programming of treatment parameters for ease of use

Because respiratory care is often the most important feature in the day-to-day struggle for patients with ALS and their families, maintenance of respiratory health and prevention of potential threats to respiratory function is paramount. Accumulating secretions represents a formidable threat to the lungs from a mechanical, inflammatory and infectious point of view. It is apparent that airway clearance is a necessary part of this care, particularly as pulmonary function begins to decline in the face of declining respiratory muscle function. Early intervention with aggressive and effective airway clearance as provided by HFCWO will add to the quality of life of the patient and may enhance cost-effectiveness of early interventions as has non-invasive positive pressure ventilation.⁵⁴

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Developing New Neonatal Strategies and Improving Survival Rates

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How many neonatal cases does the unit treat each year?
Approximately 800 patients per year in Kagoshima, with about 70 patients weighing less than 1,000 grams, and about 80 patients in the 1,000 to 1,500 gram range. We have around 250 invasive mechanical ventilation cases. Only four to five babies are treated with ECMO per year.

What are your special ventilatory treatment considerations for infants weighing 1,000 grams or less?
For the past five years we have primarily been using SERVO ventilators, with SIMV and Pressure Support treatment. We have mostly SERVO 300 ventilators, but a few Babylog and Stephanie machines as well. We also have two SERVO-i ventilators from MAQUET Critical Care in this hospital, but these are shared between ICU departments.

You have conducted extensive research in the field of surfactant therapy. What is your experience of surfactant replacement in neonatal patients?
We use surfactant produced in Japan from calves. Before birth, we check amniotic fluid to establish whether or not the baby has surfactant. If the baby's surfactant is insufficient, we prepare the surfactant before birth. We intubate the baby immediately at birth, and administer surfactant supplement as quickly as possible. That is our "open lung" approach for the premature baby, to ensure there is no alveolar collapse. This way we prevent cycling opening and closing, and low volume injury. Extremely low birth weight infants, less than 1,000 grams, are mechanically ventilated long term, and need preventative measures for ventilator-induced lung injury (VILI),

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Kagoshima City Hospital has the largest NICU facility in Japan, and serves 1.8 million population of the Kagoshima prefecture. With 17,000 births per year, the neonatal death rate of 1.3 per 1,000 live births is one of the lowest in the nation. This article interviews Professor Satoshi Ibara, MD, chief of the hospital's neonatal division, to discuss the therapeutic strategies that have contributed to saving the lives of its very premature patients.

with respect to premature development of respiratory center and lungs, underdeveloped chest, respiratory muscles and circulatory system.

When did you establish this procedure, and what effect has it had on your survival rates?
We started following this procedure 13 years ago. It has had a very big impact on our survival rates. The average for the past three years looks like this: 57% at gestational age 22 weeks; 85% at 23 weeks; 61% at 24 weeks. But there are many here that include TTTS — 82% at 25 weeks; 88% at 26 weeks; 89% at 27 weeks. Last year, all patients born at 22 weeks gestation survived.

What method of suctioning does your NICU use?
Open suctioning systems are currently predominant in other NICUs in Japan. We started using a closed system here about ten years ago. Closed systems maintain the PEEP, which is very good for the lungs. If you use an open system, there is no PEEP during suctioning, which means that alveolar compartments will collapse. This can induce volume-related injury. Hasty insertion of an aspiration catheter in the trachea of these patients may complicate conditions. The catheter tip may hit the trachea and bronchi, generating damage to the airway mucosa. If it is grave, an ulcer is generated with formation of granulation.

Insertion of the suctioning catheter is very important. If done incorrectly, it can cause stenosis and injury to the trachea or main bronchi. This can result in atrophy, emphysema or atelectasis. The closed suctioning catheter should be introduced very slowly while watching the pressure drop, in order to minimize risk of injury. We avoid inserting it past the tracheal tube, but where this is necessary we do not pass it by more than 5 mm so as not to injure the bronchi. The number of cases using dexamethasone has been rapidly and significantly reduced.

How do you manage leakage in a clinical situation?
We use flow volume loops to monitor leakage. If the baby has a leak, we adjust the endotracheal tube. We have to reduce the leakage because we want to provide patient-triggered ventilation. We use slightly larger tracheal tubes for the tiny

Survival rates at Kagoshima NICU, 2002-2004											
2002											
Weeks	22	23	24	25	26	27	28	29	30	31	32
Number of patients	1	4	9	10	10	13	7	14	21	14	24
Survived	0	3	6	8	10	11	7	13	21	12	23
Died	1	1	3	2	0	2	0	1	0	2	1
2003											
Weeks	22	23	24	25	26	27	28	29	30	31	32
Number of patients	4	8	9	13	15	16	17	17	13	23	25
Survived	2	7	4	11	13	15	13	16	12	22	25
Died	2	1	5	2	2	1	4	1	1	1	0
2004											
Weeks	22	23	24	25	26	27	28	29	30	31	32
Number of patients	2	1	10	11	8	8	3	15	12	25	20
Survived	2	1	7	9	6	7	3	14	12	25	19
Died	0	0	3	2	2	1	0	1	0	0	1
2002-2004											
Weeks	22	23	24	25	26	27	28	29	30	31	32
Total	7	13	28	34	33	37	27	46	46	62	68
Survived	4	11	17	28	29	33	23	43	45	59	67
Died	3	1	11	6	4	4	4	3	1	3	1
Survival rate %	57	85	61	82	88	89	85	93	98	95	99

babies than other institutions, but we don't have many tracheal problems. Patient-triggered ventilation is part of our lung protective strategy. The weaning period is very short as a result of this strategy.

What are the key components of your ventilation therapy for neonates?

Our general lung protective strategy has many components: closed suctioning, humidification, early surfactant therapy, and reduction of oxygen toxicity. It also includes ventilator settings, especially PIP and inspiratory pressure.

Are there any special clinical cases where you are developing new strategies?

We are using a lung protective strategy for the diaphragmatic herniation baby. Almost all situations utilize hyperoxemia for the diaphragmatic herniation baby. We have just starting using a low O_2 , so lung damage is reduced. We keep saturation by pulse oximetry between 85 and 91, and measure SVO_2 (saturation central venous O_2). We measure pulmonary vascular resistance using ultrasonography.

We keep mixed venous saturation (SVO_2) above 70%, in contrast to the normal 80% or 90%, so the baby has no pulmonary hypertension. We think that SVO_2 is a very important pulmonary vascular consideration. The pulse oximeter indicates saturation from the heart to the organ. SVO_2 presents the net value. Pulmonary artery blood saturation is dependent on the SVO_2 , so we think pulmonary vascular resistance is affected by this as well. This is a very new approach to diaphragmatic herniation, and we have had very successful early results. I want to reduce pressure, inspiratory time and O_2 concentration as much as possible. This is our objective with every patient. We are also starting to measure a DNA marker (8 hydroxy-2 deoxyguanosine) that is attacked by the oxygen radical; we

measure this substance in urine. High concentration of O_2 results in a high marker. The baby's blood has many scavengers, so now we are checking the origination of these substances.

How are you weaning from invasive mechanical ventilation?

Our first activity is to establish that FiO_2 is less than 30%, and respiratory rate less than 20. If the baby has good activity and a good triggering response, we extubate. We have a success rate of about 80%. In the remaining 20%, we must reintubate or start nasal CPAP. After extubation, nasal CPAP therapy usually lasts three to five days, depending on the baby.

Can you tell us about the NICU facility and staff?

We have six physicians and eight residents, with 117 nurses in the NICU including CCU. We have two nutritionists, one clinical engineer, and one psychologist on staff for parents.

The babies are on three separate ward facilities on two stories of the building. We also have our own neonatal surgical theatre, as well as specially equipped NICU ambulance service. We encourage the infant's mother and father to be at the NICU between 2 pm and 8 am the next day. We have an average of 80 patients per day, and 32 mechanically ventilated babies.

Arterial Blood Gas Assessment: Managing Accuracy Issues and Improving Patient Management

Bruce Toben, RRT, NPS; Marcia L. Zucker, PhD; Frank M. LaDuca, PhD, FAHA

CLINICAL IMPORTANCE OF ARTERIAL BLOOD GAS ASSESSMENT

Frequent measurement of arterial blood gases (ABG) is a standard of care in the management of newborns suffering from acute respiratory failure, prematurity and congenital cardiac anomalies. In these critically ill patients, alterations in cardiopulmonary function can occur rapidly and ABG test results are used to guide the titration of oxygen, ventilatory support, hemodynamic resuscitation and acid-base balance. The successful administration of these therapies is essential in order to minimize morbidity and mortality in this subset of infants. Traditionally, the analysis of ABG has been conducted in a central laboratory using discrete blood samples, which are collected at the patient's bedside and transported to the lab for analysis. Recently, with the goal to improve patient care and expedite clinical interventions, ABG measurement has increasingly moved to point-of-care testing (POCT) using portable analyzers. The adoption of this technology has provided a means to isolate and eliminate sources of error in the testing, ultimately improving the quality of the clinical data.

PREANALYTICAL ERROR

Any variable which occurs prior to the actual analyte measurement is referred to as preanalytical error. In clinical practice, a number of these technical errors can lead to erroneous ABG measurements. Excess heparin in the collection syringe can reduce the pH of the blood and dilute the sample, resulting in lower PCO_2 and increasing the measurable PO_2 level (e.g., closer to 159 mmHg).¹ The presence of air bubble(s) within the specimen or the introduction of air during analysis will decrease PCO_2 , increase pH and drives the PO_2 closer to ambient air values. In the septic patient delay of analysis after collection, or inadequate cooling of the sample in the transport/storage phase can cause "leukocyte larceny" which will reduce the specimen's pH and PO_2 and increase the PCO_2 .²

PHYSIOLOGIC CONSIDERATIONS

Compounding the preanalytical issues of testing, ABG interpretation can be misleading due to alterations in the newborn's breathing pattern during sample collection. Tactile stimulation or the pain associated with heel sticks can cause hypocarbia from tachypnea or hypercarbia from breath holding. If the child is being supported by mechanical ventilation, abbreviated cycling due to pressure limiting with changes in functional positive end-expiratory pressure levels can also contribute to erroneous blood gas results. Most often, in remote lab testing, failure to record these conditions can lead to misinterpretation of ABG values and inappropriate interventions.³

ACCURACY OF ABG RESULTS

ABG values should be comparable between analytic systems showing little between system bias, and repeated measurements of the same sample should be reproducible. Manufacturers are required to report precision and accuracy performance specifications of their analyzers and laboratories routinely confirm these claims. Proficiency testing, a requirement for federal, state and independent accrediting agency certification, allows labs to periodically assess "blinded samples" and their performance compared to the reference "absolute" values. In addition, these results are also compared with values reported from other laboratories using the same reference instrument. Every analytical instrument has subtle variations in performance and differences of reported samples are expected. However, if significant variations outside of predefined limits are reported, identification of the cause and corrective action are required.

The Centers for Medicare and Medicaid Services (CMS) regulates all laboratory testing (except research) performed on humans in the US through the Clinical Laboratory Improvement Amendments (CLIA). The objective of the CLIA program is to ensure quality laboratory testing. CLIA has set guidelines defining the total acceptable variation for individual blood gas analyzers (Table 1). Based on these guidelines, the acceptable range of results for a single instrument can vary markedly. Laboratories may report differences for pH of 0.08 and PCO_2 of

The authors are with Clinical Affairs, International Technidyne Corporation.

Table 1 CLIA guidelines for individual blood gas analyzers and acceptable ranges for sample values (excerpted from reference 4)

Analyte	Standard variance for each individual analyzer	If a known sample has this value...	Then this is the acceptable reported range
pH	± 0.04 units	7.40	7.36 to 7.44
PCO ₂	± 5 mmHg or 8%*	40 mmHg	35 to 45 mmHg
PO ₂	± 3 SD	100 mmHg	73 to 127 mmHg**

* Whichever is greater

** Based on a 9% SD

10 mmHg on the same specimen using the same analyzer and still be within acceptable limits. Due to the volatility of the PO₂ measurement and the inability to consistently reproduce PO₂ data, CLIA has defined separate error limits for that analyte. Periodically, CLIA records the measured PO₂ values of the blinded samples sent to laboratories. Once all the results have been statistically tabulated, three standard deviations (SD) are calculated.⁴ This statistical method will result in acceptance of 98% of all PO₂ values measured from all participating institutions. Thus, individual blood gas analyzers may report significant differences from the same blood sample, even in the face of a stable clinical condition.

RELIABILITY AND INTERPRETATION OF ABG VALUES

Blood gas and acid-base stability are presumed at the time an ABG sample is drawn. Based on the analyzed values, diagnostic and therapeutic decisions are made. However, in an acute disease stage, or when interventions specifically intended to promote hemodynamic resuscitation or pulmonary recruitment are applied, is it appropriate to make this assumption? Consider the following series of questions. Once high frequency oscillation ventilation is instituted on a premature infant, when are ABG values stable enough for analysis? After instilling a bolus of surfactant down an endotracheal tube, when should an ABG test be performed to establish the effectiveness of the therapy? How often should ABGs be assessed when titrating nitric oxide? The absolute answers to these valid clinical questions are unknown because each patient responds at different rates to the interventions applied. In addition, most cardiopulmonary dysfunctions are a dynamic process.

Progressing pathophysiology and measuring the effective changes based on therapeutic interventions alter blood gases continuously. In many cases, estimating the physiologic status and monitoring disease management in the critically ill newborn is an attempt to hit a moving target.

IMPROVING ABG MEASUREMENT WITH POCT

Successful disease management necessitates that interventions are based on accurate diagnostic data which relates to the current physiologic condition of the patient. During periods of

acute physiologic change, delays in receiving test results can occur before therapeutic interventions are initiated. Such delays are often attributable to the process of ABG data collection. This time delay from sample collection to appropriate therapeutic intervention, referred to as the clinical turn-around-time (TAT) results from:

- Time to recognize the need to evaluate pH and blood gases
- Time to order an ABG test
- Time to summon technical staff to draw the blood specimen
- Time to acquire the blood specimen
- Time to transport the blood specimen to the laboratory
- Time to perform the ABG analysis
- Time to report the ABG results
- Time to interpret the ABG values and initiate a therapeutic intervention

The laboratory TAT (ie, time from receipt of specimen to reporting of test results) for blood gases has been reported to be 19 minutes, with a range from 5 to 48 minutes.⁵ It is obvious that the clinical TAT (ie, time from ordering an ABG to implementing intervention) must therefore be greater than 19 minutes, creating a significant challenge to our ability to react to sudden physiologic changes in a swift, decisive manner. In cases where rapid deterioration in pulmonary mechanics or hemodynamic function occurs, any delay to effectively intervene can contribute significantly to outcomes. With POCT, the improvement of TAT leads to a more rapid clinical intervention; especially important in the neonatal patient.

POCT also helps satisfy the concern that the measured newborn's pH and blood gases are reflective of the actual physiologic state, whereas with remote lab testing, delays in getting ABG results increase the likelihood that decisions on disease management are being made on "old data." If the ABG was drawn prior to physiologic stability or if the V/Q shifted after the sample was drawn, the resulting intervention could be too aggressive, not aggressive enough, or even altogether inappropriate. In such events, therapy would need further modification requiring another ABG sample to determine the



Photograph courtesy of Children's Hospitals and Clinics of MN.

effectiveness and the need for additional action. The above chain of events can be expected to occur most often in the population of highest acuity, ironically where ABG data is most crucial and relied upon.

One such POCT system, IRMA TRUpoint, is capable of providing ABG results in less than 90 seconds. This portable, self-contained system can be easily brought to the infant warmer or incubator for bedside testing. Trained nurses and respiratory therapists can operate the POC analyzer, thus eliminating many of the time consuming steps defined in the inherent laboratory testing model. By streamlining the results reporting aspect of the measurement, clinical interpretation and decision making can occur at one time, at the bedside, while observing the infant. This methodology of diagnosis and disease management can reduce staff resources, thus allowing more time to be allocated to patient care. The IRMA TRUpoint system also includes a complete CLIA compliant quality control program.

SUMMARY

ABG assessment is a vital diagnostic test, critical in the management of newborns with acute respiratory failure, prematurity and congenital cardiac anomalies. Erroneous values caused by preanalytic errors and/or delayed TAT can compromise the accuracy of the data, leading to misinterpretation and faulty decision making. Due to the known variations in ABG values across different instruments, adherence to a common system in a hospital-wide setting helps ensure that accurate and consistent clinical decisions are made. Minimizing TAT promotes prompt reaction to changes in patient status and potentially reduces co-morbidity. The use of POC

blood analysis systems can markedly reduce the time to intervene, preventing further physiologic stress on the infant's marginal condition and hopefully improve clinical outcomes.

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Choosing the Right Nebulizer

Angela D. Hedgman, BS, RRT-NPS

Small Volume Aerosol therapy for the administration of medication has long been a primary component in the care plan of patients with pulmonary disease. The use of the nebulizer to deliver drug therapy dates back to 1849, when Euget-les-Bains invented the atomizer. Many have studied this delivery system and deemed it an effective vehicle to deliver medication to the lungs. In the infant and pediatric patient population, this has proven challenging primarily due to the anatomical and physical characteristics of the airway.

In our Neonatal Intensive Care Unit, we were challenged with providing inhalation drug therapy to infants who also required Continuous Positive Airway Pressure (CPAP). Following extubation from mechanical ventilation, these premature infants received continuous positive pressure via High Flow Nasal Cannula humidified with the Vapotherm Humidification System. This constant pressure was needed to stent the airway and increase residual lung volume with the ultimate goal of decreasing work of breathing.

These patients were on a regime of inhaled bronchodilator therapy pre-extubation with post treatment response of improved exhaled tidal volume and increased inspiratory and expiratory flow rates as measured on the Dräger Evita Ventilator. Once extubated we were obligated to continue the therapy.

The following factors were considered in choosing the appropriate device to deliver inhalation aerosol therapy in conjunction with the Vapotherm High Flow Nasal Cannula:

- The power source of the device
- Aerosol particle size
- Interface with patient/Vapotherm High Flow Nasal Cannula system

These considerations were necessary as we needed to provide aerosol therapy without interrupting the continuous airway pressure of the Vapotherm High Flow Nasal Cannula system. This system is theorized to provide continuous positive airway pressure. However, there is no way to measure how much pressure is generated at any given flow. For this reason we did not want to add any additional flow to the system.

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Removing the nasal cannula during aerosol therapy, resulting in loss of CPAP, was not an option since patients quickly become distressed as evidenced by increased respiratory rate, increased heart rate, increased use of accessory muscles, and decrease in oxygen saturation. Irritability alone decreases drug deposition to the lung. Add to this the loss in volume associated with discontinuing CPAP and aerosol therapy becomes an exercise in futility.

Using the American Association for Respiratory Care guidelines and individual patient needs, we chose the Aeronex Professional Nebulizer System (Aerogen, Inc.). This nebulizer:

- Delivers an aerosol in the range of 1.9 to 2.5 μ m Mass Median Aerodynamic Diameter (MMAD) (optimal lung particle size)
- Can be placed inline with the CPAP system
- Does not require additional flow to generate the aerosol
- Delivers a higher volume of medication increasing the probability of delivering the prescribed dose
- Delivers the drug faster than the traditional Jet nebulizer (decreasing treatment time)

The Aeronex Pro nebulizer is placed inline between the modified nasal cannula tubing and the delivery tubing of the Vapotherm nasal cannula. Once in place, there is no need to remove the nebulizer. You simply open the medication filler cap and place the prescribed drug into the nebulizer without cessation to constant airway pressure. The electronic micropump creates a vibration, which sends the medication through holes in a domed aperture plate to create the aerosol without the addition of flow. The drug is delivered quickly; a volume of 3 mL is delivered in approximately 5 minutes with virtually no residual volume.

Though this is anecdotal, we have found the Aeronex Pro an effective, efficient, and optimal inhalation delivery system when providing aerosolized drug therapy to patients requiring High Flow Nasal Cannula. It does not alter flow to the system, nor cause the baby stress. Although we have no clinical data to support its use in this application, pre and post assessment suggests a positive patient response.

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Ventilator Alarms in the NICU

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A 2002 sentinel event alert was distributed by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) which reported that 65% of ventilator-related deaths and/or injuries involved ventilator alarms. Our ventilator policies were subsequently reviewed and rewritten to address ventilator alarm parameters in order to meet JCAHO recommendations. These recommendations are that alarm levels be sufficiently audible in the environment in which it occurs. Our policy covers alarm parameters and alarm volume in order to improve response to alarm conditions. Initially, alarm volumes were set to maximum levels throughout our institution, including the NICU. After receiving complaints regarding developmental and physiologic responses to alarm loudness levels in the NICU, we took a systematic approach to ascertain specific alarm volumes that could be heard within safety standards for distance and still be within acceptable decibel levels. Bremner, et al, demonstrated that NICU patients are adversely affected by excessive noise levels, producing tachycardia, tachypnea, and desaturation. These fluctuations can lead to increased numbers of apnea and bradycardia episodes and the sequelae to hypoxia. The Environmental Protection Agency recommendations for a hospital NICU is 50 decibels (dB) maximum with no more than sporadic spikes to 75 decibels (dB).

Decibel levels were measured from both incubators and open warmers at varying distances from the alarm source. These sources include the two mechanical ventilators we use in our NICU, the Bird VIP and the Drager Evita-4. Of note, the Bird VIP has no volume adjustment control, but the Drager Evita-4 was measured at varying volume settings and for moderate and severe alarm situations. Our ventilator policy was changed based upon our findings.

Our initial challenge involved getting buy-in to investigate, change, and enforce a new policy. We needed to evaluate frequent “nuisance” alarms, looking at proper alarm parameters that were safe yet not “too tight.” We also needed to look at environmental factors including our unit layout, the device location and proximity to the patient, and the minimal distance from the alarm source to facilitate intervention. Next, we needed to educate the staff as to our findings. By standardizing

alarm parameters, we were able to set safe standards while avoiding “nuisance” alarms and improve compliance to our policy.

We used the APT Instruments decibel monitor (model # SL2100) to test varying alarm conditions at varying distances from the patient. We tested from the patients’ vantage point in open warmers as well as closed incubators (the Ohmeda Medical Giraffe Omnibed). Our NICU is one large contiguous room so our noise level measurements were done during the normal “hustle and bustle” of the unit to ensure that alarms could be heard and responded to under “normal” conditions. By measuring decibel levels, we were able to demonstrate an alarm volume that was audible 15 feet from the patient, yet at a minimal decibel level. We ascertained that at any given time, staff was present within 15 feet of any patient location. That was our target distance.

Our findings concluded that alarms could be heard as well at less than full volume as at full volume at a distance of 15 feet with the Draeger Evita-4 ventilator. We also found that the Bird VIP alarm was within acceptable decibel range at 15 feet with its non-adjustable volume setting. We also ascertained that there was very little difference in decibel level at the patient on an open warmer compared to patients in an isolette.

In conclusion, we were able to rewrite our policy, increase patient safety, and increase staff compliance to intervene with ventilator alarms. Patient safety was increased by minimizing decibel levels to which the patient was exposed. Staff compliance was increased with better reaction time to ventilator alarms and minimizing “nuisance” alarm situations.

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Conservative Management of Pneumothoraces in Newborn Infants

H. Rowlands, A. Greenough

ABSTRACT

Small, symptomatic pneumothoraces in neonates may be managed by chest tube placement with underwater drainage, needle aspiration, or conservatively. Conservative treatment includes administering 100% oxygen to facilitate resorption of extra-alveolar air on observation. We report pneumothorax resolution after administering 100% oxygen for 18 hours or less to three consecutive term born infants. It is important to determine in a randomized trial if such management versus observation alone shortens the duration of NICU admission.

INTRODUCTION

Pneumothoraces are a common problem in newborn infants. Large, symptomatic pneumothoraces and those under tension should always be drained by placement of a chest tube connected to an underwater sealed drain. The management of small but symptomatic thoraces, however, is more controversial. In many textbooks, it is suggested that such a complication could be successfully treated by administering 100% oxygen. Theoretically, such a strategy would result in resolution of the pneumothorax without resort to a chest drain and resorption of the extra-alveolar air occurring via nitrogen washout. There are, however, no reports of the success of such therapy or how long infants should be maintained in 100% oxygen for resolution of the pneumothorax to occur. We therefore report three consecutive infants whose pneumothoraces resolved following administration of 100% oxygen and the time course of the resolution.

CASE REPORTS

Case 1

A male infant was born at term by forceps delivery; there had been failure to progress in the second stage of labor. He required no resuscitation, but at two minutes of age he started to grunt and was dyspneic. On admission to the neonatal unit he was tachypneic and his maximum inspired oxygen concentration requirement was 40%.

Case 2

A male infant was born at term by spontaneous vaginal delivery. The baby made poor respiratory efforts at birth, and the

midwife gave inflation breaths via a facemask. On transfer to the neonatal unit, the infant was tachypneic, had sternal recession and required 40% supplementary oxygen.

Case 3

A male infant was born at term by emergency cesarean section. The baby did not require resuscitation but at one hour, he was noted to be tachypneic with sternal recession. On admission to the neonatal unit, the infant was tachypneic and had an oxygen saturation of 92% in air.

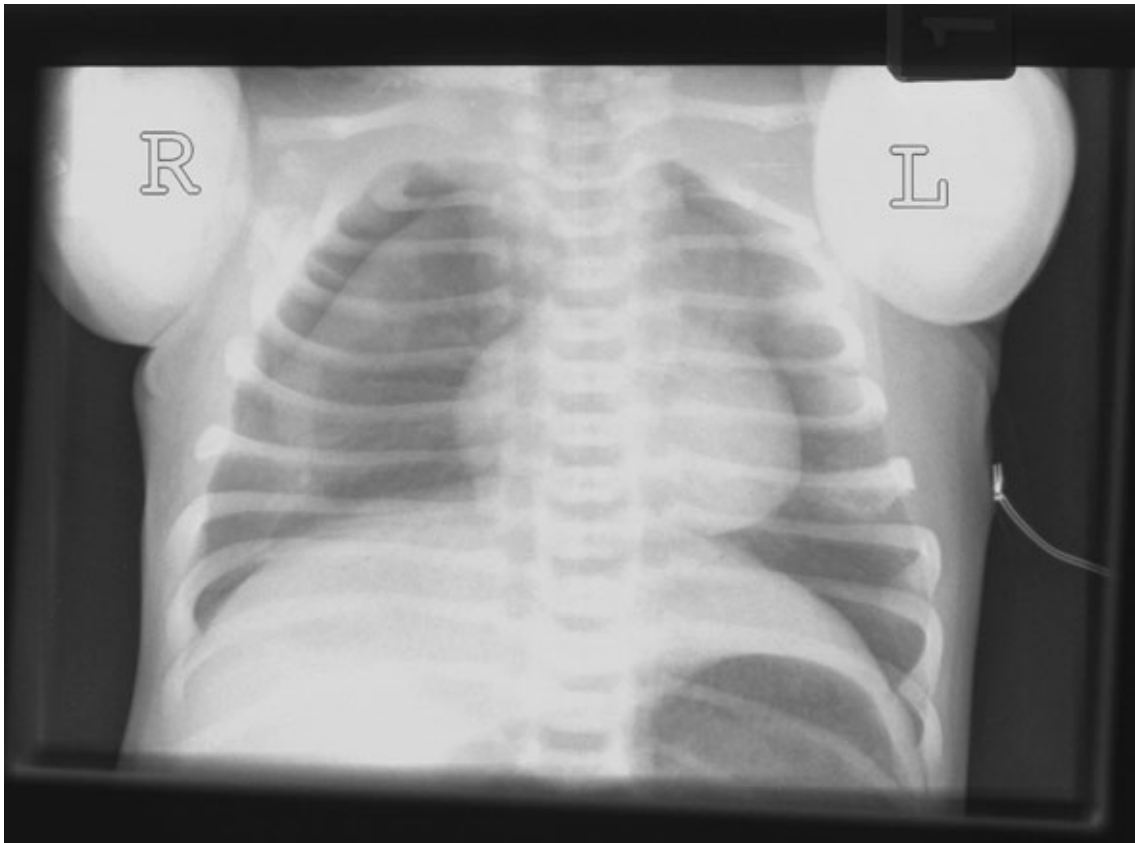
In all three cases, the chest radiograph on admission demonstrated a pneumothorax (figure), but no other pathology. As their respiratory status was not deteriorating and their maximum inspiratory oxygen concentration was 40% or less, they were treated conservatively and placed in an inspired oxygen concentration of 100%. Once their symptoms resolved, further chest radiographs were obtained at 12, 11 and 18 hours, respectively, which demonstrated in all cases the resolution of the pneumothoraces.

DISCUSSION

Small pneumothoraces can resolve spontaneously, but the infants we report became symptomatic shortly after birth and their symptoms only resolved some time after 100% oxygen was administered, suggesting that treatment had at least facilitated resolution of their pneumothoraces. It is likely that at least two of the three infants had spontaneous pneumothoraces. These may result from the high transpulmonary pressures which can be generated during an infant's first breaths. Pneumothoraces are more likely to occur if the infant requires respiratory support and in one of the three infants, bag and mask resuscitation was undertaken. The infants, however, had no underlying respiratory pathology, as demonstrated by their chest radiographs. It is in such infants that we report resolution of pneumothoraces in response to 100% oxygen.

The three infants were asymptomatic when their second chest radiographs were obtained, which was when they had received 18 hours or less of 100% oxygen. These results suggest that prolonged exposure to high concentrations of oxygen is not required to treat pneumothoraces. We emphasize that the infant we placed in 100% oxygen were born at term; such a strategy would not be appropriate for prematurely born infants at risk of retinopathy of prematurity.

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Chest radiograph of case two demonstrating a right-sided pneumothorax with free air seen both laterally and anteriorly. Note there is not complete collapse of the right lung.

Alternative strategies to treat small but symptomatic pneumothoraces are needle aspiration, chest tube placement, or observation without intervention. Drainage by aspiration is usually undertaken using a syringe and butterfly. The sharp end of the needle may traumatize the lung. Once the needle is inserted through the skin, it is important to move the needle and skin sideways (z-track) before advancing the needle through the underlying muscle. Otherwise, an open needle track will be left for the entry of air once the needle is removed. Alternatively, a chest tube connected to an underwater sealed drain may be placed, but there are many complications of chest drain placement. These include direct perforation of the lung.¹ At autopsy, perforation of the lung was found in 25% of cases.¹ This complication should be suspected if continuous drainage of air persists; a bronchopleural fistula is very difficult to treat. Trauma may also occur to the thoracic duct, resulting in a chylothorax,² or the chest drain may enter the pneumopericardium, causing a hemorrhagic pericardial effusion with cardiac tamponade.³ In addition, the phrenic nerve can be injured,^{4,5} particularly if the drain is placed deep in the chest and the tip impinges on the mediastinum.⁶

Conservative management avoids such complications but means that the infant must be observed on the neonatal unit until the pneumothorax resolves. As consequence, whether administering 100% oxygen to infants born at term who develop small, symptomatic pneumothoraces rather than just observing them results in a shorter duration of NICU admission and associated cost, merits testing in a randomized trial.

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Critical Care Testing: The Better Way

Long on dedication but often short on resources and time, NICU teams can face extreme demands caring for tiny, critically ill infants.

While in today's challenging healthcare environment employing additional staff often isn't possible, employing advanced technology that works as hard as your NICU team can provide a solution. Many hospitals are discovering that new state-of-the-art analyzers for blood gases, electrolytes and metabolites, in particular, can go a long way toward helping busy NICUs find more hours in the day, while realizing a host of additional benefits.

SPEED, ACCURACY AND RELIABILITY

"Fast, accurate and reliable analysis is extremely important for premature babies," says Terri Smith, MT, ASCP, NICU, Laboratory Supervisor for the Sheldon B. Korones Newborn Center at Regional Medical Center in Memphis, TN. Smith has been using a GEM Premier 3000 (Instrumentation Laboratory), cartridge-based critical care analyzer with fully automated quality control (QC) since mid-2004, and it has delivered significant improvements over previous technologies.

"Small metabolic changes have major impact in tiny, fragile babies. Immediately and precisely altering treatments based on accurate analyzer measurements is crucial," she says, adding that blood, electrolyte and metabolite testing in the NICU play a key role in guiding overall patient treatment.

At Albert Einstein Medical Center in Philadelphia, Lynn Pompa, RCP, Supervisor of Respiratory Care and Pulmonary Diagnostics, reports that the GEM Premier 3000 analyzer has provided similar benefits in his institution since 2003. He also notes that the dramatic decrease in QC and maintenance due to the automated Intelligent Quality Management (iQM) system has significantly improved the department's efficiency and performance.

"In our NICU, the respiratory therapist's brain is a very valuable commodity," says the highly experienced clinician, who oversees diagnostics services for respiratory services care throughout the entire hospital. "Our therapists really know their

patients and are involved in multiple aspects of care. Any technology that can allow them to spend more time with newborns rather than with equipment is invaluable. It just makes sense."

At Korones, Smith notes that job satisfaction among lab staff is of particular importance. Feeling the impact of the nationwide shortage of lab technologists, the NICU lab has operated with 1.5 FTE job openings for several years. "My staff has had to really pull together to make the department a success. The automation of the GEM Premier 3000 has taken a great deal of time and frustration out of the lab technologist's job, like constantly running controls. It has really helped us keep the department running smoothly."

CONSISTENT BENEFITS IN DIVERSE SETTINGS

These NICUs differ in size, ranging from 65 beds at Korones to 14 at Einstein's Level 3 unit. The professionals responsible for running blood samples include both respiratory therapists and laboratory technologists working in partnership with nursing staff. However, both units agree that blood gas analysis is crucial to neonatal care. And both have elected to channel significant financial and professional resources into creating dedicated NICU blood analysis sites located at the point-of-care.

Korones has a complete lab adjacent to the NICU that includes blood analysis. Working onsite, lab technicians are familiar with patients and can deliver results quickly and precisely. Einstein's analyzers are also situated directly adjacent to the NICU where therapists can conveniently run samples.

TRADITIONAL ANALYZERS—HIGH MAINTENANCE

Staff at both NICUs also agree that in the past their traditional analyzer's high level of maintenance was a significant detriment to their departments. Aware of advancing analyzer technologies, both sought a better solution and found one in the GEM Premier 3000 with iQM.

Pompa explains that daily QC with manual blood gas analyzers requires about an hour a day, with additional time spent on

Information for this article was provided by Instrumentation Laboratory.



Lynn Pompa, RCP, Supervisor of Respiratory Care and Pulmonary Diagnostics, and John Hurley, RRT-NPS, Albert Einstein Medical Center.

weekly and monthly maintenance and checks. Documentation and reporting all this for regulatory compliance involves even more hours.

Indeed, many hospitals report that routine analyzer QC takes up to 48 hours each month. Naturally, if calibration and corrective actions are needed—not unusual—they require even more attention.

Smith points out that with manual devices, analyzers can drift between checks, and the errors are not discovered until the next QC, up to eight hours later. Therefore, patient tests may be conducted under sub-optimal conditions and are routinely repeated, with costs in dollars, staff hours and quality of care. Moreover, at many hospitals, when staff is extremely busy, analyzers needing corrective action may run for some time without intervention, compromising results.

Providing a more efficient and accurate alternative to manual QC, iQM automatically and continually checks the GEM Premier 3000 to deliver real-time system diagnostics. Time to error detection and correction is just minutes.

iQM checks extend beyond analyzer electronics to include sensors and the chemical measurement process, which typically requires manual intervention, even on other advanced analyzers. The GEM Premier 3000 automates all corrective actions, freeing up therapists from labor-intensive manual trouble-shooting, as

well as eliminating lengthy equipment training and possible human error that might compromise test results. All regulatory compliance documentation also is automated.

Utilizing innovative Failure Pattern Recognition (FPR) software, the sophisticated and comprehensive iQM self-analysis system identifies any known failure patterns during cartridge operation. FPR enables real-time flagging of possible errors associated with clots, interfering substances or other issues which may produce erroneous analytical results. The GEM Premier 3000 also provides exceptional analytical performance with state-of-the-art planar sensors.

Routine analyzer maintenance is eliminated through the use of a single cartridge that contains everything needed for whole blood testing, including sensors, sampler, pump tubing, distribution valve, and waste bag and PC solutions. Every three weeks, a new cartridge is simply snapped into place and the analyzer is ready to function. A closed system, the GEM PAK maintains complete integrity of the testing process throughout the cartridge life. Changing electrodes, worrying about tanks and inventorying supplies are part of the past.

“With other analyzers, routine maintenance and QC disrupt therapists’ normal routines and take away from direct patient care,” says Pompa. “It’s easy to forget that total QC extends beyond the analytic process itself. Such pre- and post-analytic factors as inspecting samples for clots and contamination and

careful patient ID checks are vital. By unburdening clinicians from daily system checks, iQM allows them the time to focus on more critical responsibilities.”

“NICU lab staffs are under tremendous pressure to get it right,” adds Smith. “If samples are not run properly or the equipment malfunctions, precious time and blood is wasted. This has significant impact for tiny infants. The ease of use, as well as consistency and reliability of the GEM Premier 3000, helps relieve some of the pressure.”

GEM Premier 3000 also minimizes analyzer downtime. Both installations can count on the GEM Premier 3000 to be ready when needed. If a problem does occur, they say, it usually can be rectified in minutes by just swapping out the cartridge. Addressing problems with traditional analyzers generally demands much more time.

ULTRA-FAST TURNAROUND

In both NICUs, the GEM Premier 3000’s Point-of-Care-Testing (POCT) location and ultra-fast processing speed mean rapid sample turnaround—extremely important in the NICU. “Infants decompensate rapidly,” notes Smith. “When it comes to blood-gas and related measures, the faster the better. Readings also need to be precise because a small change in treatment has enormous impact in a tiny infant.”

“Another plus of the cartridge system is that it provides an extremely consistent platform for all measurements across analyzers,” notes Pompa. “We’ve tested them and found excellent correlation readings on every analyzer.” This precision is important for infants because a small discrepancy in measurement can drive unnecessary changes in treatment with major clinical repercussions.

Prior to the GEM Premier 3000, Pompa says that the hospital was using another manufacturer’s analyzer, with readings that were much more technique-dependant, creating inconsistent results that were complicated by clinical and data management problems.

Thanks to the unit’s web-based technology, it was easy to interface the analyzers to the hospital network at Einstein. Clinicians—wherever they are in the hospital—can access test results virtually in real time over the Clinical Information System hospital network. With Einstein’s GEM*web* interface in place, “I can review patient data directly on the analyzer from my office PC if necessary, follow corrective action logs, and even control the analyzer remotely,” says Pompa.

CONSERVING BLOOD

Blood conservation is another important issue for infants. Every drop of blood is important, and typically even the small volume removed for testing must be replaced through transfusions. “With the GEM Premier 3000 in POCT, we can use a single sample for a full panel of tests. We can get all the information needed quickly and accurately with just 140 or 150 micro-liters of blood,” says Smith.

In part because they do not need to draw extra blood and because results are so fast, many NICUs using automated analyzers now consistently run more comprehensive testing.

DELIVERING COST ECONOMIES

While delivering all these benefits, IL’s GEM Premier 3000 realizes important cost economies over manual monitors. Smith’s department at Korones has been able to handle a higher case volume with their limited staff size—representing a significant soft savings. “When really busy, we have been able to handle 1800 to 2000 blood-gas tests in a month,” says Smith. “Without the GEM Premier 3000, we likely would not have been able to handle the volume.”

Other GEM Premier 3000 users who carefully tracked budgets have reported economies due to elimination of up to 12 hours a week in QC and maintenance. Like Korones, these hospitals also have been able to boost patient volume with no increase in staff as well as cut *per diem* employment.

Pompa reports that based on supplies alone, Einstein’s previous analyzers cost more to operate and offered none of the convenience and reliability of the GEM Premier 3000.

Because the GEM Premier 3000 is fully automated, even the need for training was minimal. Most sites had the new analyzers up and running within a few hours.

THE BEST OF BOTH WORLDS

Pompa sums up his experience: “The GEM Premier 3000 analyzer represents the best of both worlds: point-of-care access and ease of use combined with benchtop analyzer stability and trackability. Everyone agrees it is a welcome change from the electrode-based systems of the past.

“With the GEM Premier 3000,” he adds, “therapists are not standing in front of an analyzer trying to do three things at once. Now, they’re focused on only doing one thing—patient care, based on reliable results.” And that makes a dramatic difference.

EXECUTIVE PROFILES

ITC

Lawrence Cohen

Lawrence Cohen is President of ITC

THE COMPANY

Subsidiary of Thoratec Corp, ITC was founded in 1968 and developed the first point-of-care coagulation test used for monitoring Heparin therapy during open-heart surgery procedures. Building upon that business, today we design, develop and manufacture as well as market and sell point-of-care diagnostic and monitoring tests and systems. We're the leading hospital point-of-care supplier for coagulation point-of-care systems, such as Hemochron, found in most operating rooms and cardiac cath labs throughout the world. Two years ago we purchased the IRMA Trupoint product line—a blood gas and electrolyte system for point-of-care testing. It's portable and like the Hemochron can be used at the patient's bedside. We are one of the only companies offering True Point-of-Care products that can be used conveniently at the patient's bedside. In addition to hospital point-of-care devices, we also develop products dedicated for use in alternate sites (ie, doctors' offices or at home).

PATIENT CARE

All our products are portable, self contained and are used to perform testing at the patient bedside—the true point of care. Point-of-care testing is important for the best patient care. It allows faster turn-around times of results and ensures that the clinicians remain in control during the procedure. This can result in a patient spending less time in an operating suite or in recovery.

For a respiratory therapist, point-of-care testing can provide ultimate productivity. It improves workflow and provides timely results at the patient's bedside. ITC point-of-care instruments are also self-contained and easy to use, requiring minimal training, maintenance and calibration. Everything is included in the disposable test cartridge. The Respiratory Therapist can draw a sample, analyze and adjust a patient's ventilation simply and quickly without ever leaving the room.

Both patients and respiratory therapists benefit when the patient is treated in a timely manner and can be moved to a "step down unit" instead of being in the operating room. Point-of-care testing improves the overall patient experience and adds more value to the clinical outcome.

TREATMENT MODALITIES

Treatment modalities depend on accessing the physiological condition of the patient and matching it with accurate diagnostic data. As a result, more testing is moving to the bedside and providing improved turn around time as well as reduced pre-analytical error. The use of the IRMA TRUpoint blood analysis systems for accurate diagnostic testing can reduce the time to intervene, resulting in reduced physiological stress on the patient's condition and improved clinical outcomes.

R&D

The ITC product development process utilizes five distinct phases including specific goals and milestones for each phase that must be met before the cross-functional product team can proceed to the next phase. During Phase 0, a product concept specification is developed by the program team. This usually starts with a list of features that has been collected by surveying customers over a period of time. We get feedback on the preliminary specification from customers through various means. A key component of Phase 1 is getting customer input to the product concepts. This can be done in a number of ways, however; recently we utilized customer focus groups to get unbiased feedback on the design concepts for the product. This has proven to be very valuable and

will definitely influence the final design of the product. Once prototypes are built, we may involve customers to run samples and get reaction to the customer interface. As the product design becomes more mature, we start conducting clinical trials where customers operate the product and run clinical samples. While they can not use these results they provide us with extremely valuable input and ultimately, we will use this data to file for regulatory approvals. We consider customers as a critical component of our product development process.

EDUCATION

Over thirty six years ago, ITC introduced point of care testing to the community. Our mission is to provide reliable tools to the healthcare community that will enable superior patient management, potentially leading to reduced healthcare costs and improved patient outcomes. We work actively with industry coalitions to promote education for clinicians and their patients. We sponsor and participate in many industry workshops and point of care coordinator workshops where end users learn about not only ITC products, but new regulations and requirements for testing and improving patient care. We are also involved with the pharmaceutical companies in developing and educating physicians on proper guidelines for monitoring anticoagulation therapies. ITC has developed an "Anticoagulation Clinic Primer" for clinicians to use in assisting them to set up a clinic for Coumadin patients. For training we provide educational product modules for the end user, training and implementation guides and utilize clinical specialists to train our hospital customers on the use of ITC point-of care devices. We also provide customers assistance with test performance verification through Analytical Measurement Range (AMR) Testing Analysis.

CLINICIAN INPUT

ITC sees the voice of the customer as a beneficial means to gain customer insight on the development and upgrading of our products. In fact our most recent product launches, the Hemochron Signature Elite and The IRMA Trupoint Creatinine test were as a direct result of feedback from our customers.

Our customers include many stakeholders involved in point of care testing. We solicit input from them in obtaining feedback on new product opportunities and improvements. Stakeholders can include the clinicians who will be using the test results and may even perform the test. This category may include respiratory therapists, perfusionists, surgeons, critical care physicians or nurses, an interventional cardiologist, etc. Other stakeholders include the laboratory. Each of these groups has different needs and it takes a special company to consistently deliver products that meet those needs. For example, end users want an easy-to-use product that produces accurate results. In addition to accurate results, the laboratory is also interested in quality control and connectivity—the ability of a device to automatically transfer the data to the laboratory computer.

ITC actively initiates involvement from these customers through a series of events which includes customer field visits, medical advisory council meetings, industry coalition meetings, point of care workshop forums and customer focus groups. Over the years, ITC has developed a great deal of sensitivity to each group's needs and as a result our products are modeled to address those needs.

NEW TECHNOLOGY

The use of new drug therapies in cardiac interventional procedures and post-interventional care, such as the low molecular weight heparins (LMWH) and direct thrombin inhibitors, will reduce the need for standard heparin monitoring in lower risk patient populations. However, ITC is working with the pharmaceutical companies to understand whether in some clinical applications and in some higher risk populations, monitoring of these new drugs will be required. We have tests under development that will be directed at some of these patient populations to help get better clinical outcomes.

ITC is an international company and we manufacture and sell our products worldwide. Each market we sell into has its unique characteristics, needs and

market drivers which are often influenced by governmental control and pricing policies. ITC additionally works closely with local country dealers to understand and meet the needs of each individual market we sell to. We invest in registering our products in many countries as well as translating software and operator instructions and complying to IVDD and CE requirements. By offering a full continuum of bedside instruments for coagulation, blood gas electrolytes and hemoglobin testing, we can offer our international customers options for their market place. In Asia and the Pacific Rim our POC coagulation testing customers select tube testing. In Europe, the microsample platform (i.e., cuvettes) is gaining rapid acceptance.

Osmetech

Alfred Marek

Alfred Marek is President, Osmetech Inc. Information was also provided by Gerri Priest, VP Global Marketing

PRODUCTS

Osmetech is focused on manufacturing and marketing portable analyzers for the measurement of time sensitive diagnostics tests such as blood gas, electrolyte and metabolite analysis. These portable analyzers are used in various locations within hospitals, emergency centers, ambulances, helicopters, airplanes, pulmonary centers, and in any location where time critical diagnostic testing is needed. The OPTI is the only analyzer of its size and portability to provide a measured total hemoglobin and measured oxygen saturation value along with the other traditional blood gas values.

PATIENT CARE

The OPTI analyzers utilize a sensor technology based on optical fluorescence sensors and the process of optical reflectance. The major advantages of this technology are reliability and stability, which makes the technology superior to electrochemical based systems.

Over the years, implementation of new technology has allowed both the complexity and cost of POC devices to be reduced, thus enabling the POC testing trend to grow, especially for tests where rapid intervention is needed and fast turn-around-time improves patient outcomes.

R&D

Our R&D process follows the Design Concept and Commercialization Guidelines (DCCG):

- Milestone 1—Design goals
- Milestone 2—Design input
- MS3—Design output
- MS4—Launch decision
- MS5—Product acceptance after launch

The decision regarding new features is created through end-user recommendations, trends in the marketplace and feedback from opinion leaders.

With every OPTI Analyzer is included a training and implementation package to facilitate and assist with regulatory compliance and getting on-line faster.

Osmetech is constantly listening to our customers and conducting customer satisfaction surveys, as well as hosting focus groups for customer feedback. After a new product is released for sale, its performance is carefully monitored through a program called PQM (Product Quality Monitoring), where every customer call is logged according to error codes. Monthly the data is analyzed and reviewed by the management team for trends and, if needed, action plans are implemented for the top occurring issues.

Our product portfolio is geared toward the point-of-care market where fast turn-around-time is critical and fast changing parameters are essential for patient outcome. New advances in microfluidics and PCR technologies, which allow speeding up of the DNA testing process, will make a difference in patient treatment/outcome. We have recently acquired a company in the U.K., Molecular Sensing, which is active in the research of DNA testing, allowing us to create a synergy with our current marketing/sales activities.

The features of the OPTI make it ideal for large hospitals with a POC program or that utilize decentralized testing in the ED, OR, and satellite labs. The flexibility of the OPTI also allows it to be successful as the primary analyzer in smaller hospitals, less than 200 bed, that have a low to moderate number of blood gas samples per day.

Since our market reach is global, the challenge is always to provide the best service for the lowest possible cost to our customers. There is no such thing as a global approach. Each country always has its own dynamics. Flexibility in being able to react swiftly is really the key element for success, especially for a small company like Osmetech.

We actively participate at a variety of conferences in both the respiratory laboratory and critical care areas. We provide corporate support of local, regional and national societies and are actively involved in committees, such as the American Association of Clinical Chemists (AACC).

I have personally been involved in the blood gas field for over 30 years. I was instrumental in building AVL Medical Instruments to a global company that was later sold to Roche Diagnostics. With my knowledge of the global marketplace and available technologies, I am actively involved in the development efforts at Osmetech.

Roche Diagnostics

Rodney D. Cotton

Rodney D. Cotton, Senior Vice President, Point of Care Diagnostics

PRODUCT PROFILE

The Roche OMNI S blood gas analyzer offers a significant advantage for both patient and care-giver by decreasing the sample size required. This is especially important in NICU. By offering Neonatal Bilirubin in or close to the NICU you can reduce the turn around times and improve the time it takes to deliver therapeutic interventions.

Roche Diagnostics' Auto QC system option helps to improve operator efficiency, thus resulting in additional time available for patient care. It also makes it easier to meet ongoing regulatory requirements. Roche Diagnostics' industry leading IT solutions help to regulate operator validation, quality oversight, help to manage cost and assure that clinical data is transferred to the LIS/HIS system for cost capture and reporting.

Roche Diagnostics' blood gas systems offer improved operator interfaces. This helps to improve operator effectiveness and efficiency thus providing for more time directly with the patient.

"MyLabOnline" service is a web portal for Roche Diagnostics product users. It empowers them to improve their operational efficiency via product and clinical information. In addition it provides real-time data on order status and peer-review QC statistical performance information.

eQAP – This is another Roche Diagnostics first. The eQAP program, available via "My LabOnline" permits customers to enter their QC results and have the data

analyzed and eQAP, as the Roche Diagnostics first, enhances customers' confidence in the results they are reporting by availability of real-time peer reviewed data on their QC results. This complimentary service facilitates our customers to compare their performance to others across the country in real-time.

ADVANCES AND IMPROVEMENTS

Major improvements in BGE testing include: NICU/ICU advantages—availability of neonatal bilirubin, and reduced sample size vs. lab method. The overall benefits of the Roche Diagnostics BGE portfolio are reduced complexity (operation and maintenance); and automated QC. Roche Diagnostics is the gold standard and the industry's first BGE analyzer with an Auto QC option. Today, we still maintain an advantage by offering 40 days of on-board QC material. For IT/data management, Roche Diagnostics provides hospitals with the industry's best blood gas work flow management solution with its Data Care software. Roche Diagnostics also launched the industry's first complete remote QC/Instrument status management software (OMNILINK).

Another first for Roche Diagnostics is that it has again led the industry by recently gaining the first 510k clearance for measuring pH in pleural fluids on blood gas analyzers. It is reported that over 1 million pleural effusions are diagnosed in the US each year. At present, the College of American Pathologists reports that over 68% of the analyses are performed via pH paper or pH meter. The American College of Chest Physicians reported in 1998, "When pleural fluid pH is going to be used for decision making, only pH values provided by blood gas machines are sufficiently accurate."

R&D & EDUCATION

Roche Diagnostics runs major R&D projects through a Global Portfolio Board for review approval and status update. Continued project improvements are evaluated and submitted for consideration on an ongoing basis. Input is strongly driven by input from customers (current and potential).

Roche Diagnostics' Annual Teleconference offers PACE & AARC accreditations. Its "My LabOnline" web portal provides on-line access to PACE & AARC accredited programs. Roche Diagnostics also offers educational workshops to national and regional meetings. At Roche Diagnostics, product upgrades, enhancement and new product designs are the combined result of input from advisory panels, visionary thought leaders and market research. For new product launches, Roche Diagnostics will run "Gamma Site" trials (these are beyond what is required for 510k submission). These studies provide us with greater insight as to work flow, positioning and impact to hospital patient care and hospital economics.

Roche Diagnostics is actively working on the development of new technology that will significantly reduce operator "hands-on time." We will broaden our IT portfolio and will deliver systems with the configuration flexibility to fit into all clinical areas where BGE is needed. All of the above will be delivered with continued focus on improved patient care and cost effectiveness.

NEW TECHNOLOGY

The most significant change that is currently occurring is the expansion of IT connectivity and DM. Also electronic miniaturization continues to drive reductions in size and weight while increasing reliability and reducing maintenance requirements and down time.

Examples of Roche Diagnostics' leading technology are: Omni Link (QC and device management software), DataCare (BGE data management and IT connectivity software), Smart Pack Technology (for reagent matching and expiration control), Auto QC (time saving automated QC option) and "O" Maintenance Electrodes (more time focused on patient care).

All hospitals and clinical sites can benefit from the Roche Diagnostics BGE technology. However, respiratory therapists in the ICU NICO can significantly

improve their patient care, work flow and operational efficiency by using the Roche Diagnostics BGE/IT portfolio.

Roche Diagnostics is clearly a global organization. However, we strongly believe that we must plan globally, yet deliver and implement locally. The US has a very strong input into global portfolio decisions with representation on the global portfolio book.

Roche Diagnostics will continue to use multiple methods to communicate our message and capture customer input. First, we will continue to have focused and dedicated sales teams for both BGE and IT. Second, we will continue to provide on-site training and technology support complemented by 24-7 telephone coverage. Third, Roche Diagnostics will continue to attend national and regional professional conferences. Fourth, we will continue to offer user centric web portals and services such as "MyLabOnline" and eQAP. Additionally we will utilize focus panels and advisory board to help us best formulate and deliver key product and service messages to our customers and market in general. (Roche OMNI, Auto QC, MyLabOnLine, DataCare POC and OMNILINK are trademarks of Roche.)

Nonin

Philip Isaacson

Philip Isaacson is Founder and Managing Director, Nonin Medical, Inc.

ABOUT NONIN

Nonin, a privately owned company, was founded by four engineers to produce noninvasive medical monitoring equipment. In 1986, we shipped our first oximeter and have since added a full line of proprietary pulse oximeters, sensors, accessories and software thereby providing effective and reliable solutions to medical professionals around the world.

HISTORY

Pulse oximeters were originally large heavy boxes, sometimes weighing 20 pounds or more. Nonin's first pulse oximeter was two pounds. Pulse oximeters have since evolved into handheld devices and then into fingertip devices providing smaller solutions with the same high performance. The performance of the latest Nonin fingertip pulse oximeter greatly exceeds that of the early pulse oximeters. Motion and low perfusion are now rarely a problem. False low readings are now very rare, although it is still possible to fool anybody's oximeter. The time it takes to acquire a first reading used to be in excess of 15 seconds. For most oximeters on the market, a reading can be obtained in under 5 seconds from the time the oximeter is turned on. Today's pulse oximeters offer convenience, performance, reliability, and versatility.

APPLICATIONS

Pulse oximeters can and are used everywhere these days. Some examples are:

Routing applications, operating rooms, critical care, patient wards, EMS, physician offices, and sleep studies. Home use can include oxygen titration, exercise, checking limits of exertion, eg for CHF patients, continuous monitoring, eg for sick infants. Non-medical applications include use by aircraft pilots, for exercise, and for high altitude hiking. Veterinarians can use pulse oximeters for measuring extended heart rates in the 18-450 BPM range, and for animal research. Pulse oximeters can be used in extreme conditions of low perfusion, for MRI, and fetal pulse oximetry where SpO2 down to 15% is common, as well as sleep studies where SpO2 may be down to 50% for short intervals.

NEW DEVELOPMENTS

The trend for new products is low power and small size with increased

performance. The trend for use is telemedicine—we see this as a way of reducing health care costs while patients are appropriately monitored in their home setting. The use of Bluetooth Wireless Technology in a pulse oximeter has created an awareness in the community that there is a way to continuously monitor patients while removing the cable between the patient and the bedside monitor. We see the usage in hospitals especially continue to grow year after year. Patients can be easily monitored anywhere. RTs, EMTs, doctors and nurses now can have their own personal oximeter to spot-check a patient anytime and anywhere.

Pulse oximeters will someday be more common than your standard thermometer. Patients will know their numbers and be able to modify their activities accordingly.

FUNDING AND CHALLENGES

There are funding issues at this time primarily in the homecare market. Insurance companies do not yet pay for home pulse oximetry.

The biggest misconception about the devices is that carbon monoxide (carboxyhemoglobin) causes pulse oximeters to read inaccurately. For judging the status of a patient, the SpO₂ reading is far more meaningful than the fractional oxygen saturation. The carboxyhemoglobin is transparent to pulse oximeters, as it should be to judge whether the cardiorespiratory system is able to provide adequate oxygen. If the pulse oximeter reads 97% and the subject has 10% carboxyhemoglobin the subject is getting sufficient oxygen. The heart may be working 10% harder to pump the extra blood and the exchange of oxygen in the lungs may not be as efficient. On the other hand, if a subject has 87% SpO₂, there are problems, regardless of the carbon monoxide levels.

MAQUET

Doug Smith, Ed Coombs

Doug Smith is VP Critical Care and Ed Coombs is Director of Marketing & Product Management, MAQUET.

PRODUCTS

The SERVO ventilator is the only ventilator system offering neonatal caregivers the ultimate flexibility to custom design a ventilator to meet specific clinical needs and requirements. This “platform” approach provides flexibility to configure it as an adult/pediatric ventilator, infant/neonatal ventilator or as an all patient population, universal ventilator. With this unique design the easy to use color touch screen provides a common user interface through all departments and clinical staff. In addition, the SERVO-i is easily upgraded with existing or new functionality using a simple PCMCIA software card. This scalability allows the ventilator system to grow as the customers’ needs or clinical practices expand providing a cost effective solution to maintaining state of the art technology. Combine these unique capabilities with our proven SERVO gas delivery system and new expiratory cassette and you have a ventilator system with the lowest work of breathing and fastest trigger response time. This creates a greater degree of patient comfort, less sedation, and improved patient outcomes.

GOLDEN MOMENTS

SERVO ventilators identify what are known as “golden moments” in mechanical ventilation. These golden moments are opportunities to improve lung protection and promote spontaneous breathing by providing timely ventilator assistance. Examples include: late inspiratory recruitment, breath initiation, inspiratory cycle off criteria, and patient-adjusted inspiratory flow. The ability to fine-tune a ventilator specific to patient requirements is of paramount importance.

ADVANCES

Other technological advances in ventilator technology unique to the SERVO-i ventilator include: the Open Lung Tool, which is a software tool used for effective lung recruitment; our new BiVent modality commonly used to actively recruit the lung on spontaneous breathing patients; the measurement of time constants (T_c) simplifies this application; MAQUET’s Automode feature speeds the weaning process lowering the length of stay of ventilator patients; and lastly, the SERVO-i features flow-adaptive volume control, where, if the patient requires additional inspiratory flow, the ventilator immediately responds to that need and remains dynamic to the patient.

R&D

When MAQUET Critical Care first began the R&D efforts for the SERVO-i ventilator, there was a major emphasis on user and clinician input to the design, functionality and ergonomics. Over a thousand clinicians provided input on our SERVO-i product during this process. This dedication to customer oriented improvement has continued since the introduction of the SERVO-i in 2001. Every 9 to 12 months we have released major new functionality, user requested improvements and enhancements to keep our SERVO products state of the art. We routinely engage customers to provide suggestions for improvements and product enhancements through site visits, our quality control processes, customer focus groups and product research forums.

MAQUET Critical Care invests over 9.7% of annual revenues in product research and development. Our R&D roadmap is constantly being examined to evaluate how advances in technology can improve patient outcomes and decrease costs. Our strong investment in research and development supports our goal to routinely bring new features and products to our customers. We strive to grow our market leadership position while entering into new market opportunities. Currently extensive research is being done in the area of lung recruitment, non-invasive application, and patient-ventilator synchrony as well as for new products for the transport and home markets.

EDUCATION

Our clinical applications specialists are all respiratory care practitioners who have years of critical care experience in all patient care areas—adult, pediatric, and neonatal. We offer onsite training to all members of the health care team including physicians, nurses, and respiratory therapists. This includes training sessions during the installation of equipment and updated training as necessary. Often, MAQUET will sponsor regional educational seminars pertinent to the field of mechanical ventilation. We also provide workshops at US and international research laboratories where clinicians can have hands-on training in the use of the Open Lung Tool and optimizing lung recruitment strategies.

NEW TECHNOLOGY

Much attention has focused on balancing quality care with cost-effectiveness in today’s hospitals. The open architecture design of the SERVO-i ventilator allows for clinicians to hot swap hardware modules such as CO₂ from one machine to another without interrupting ventilation. This allows clinicians to optimize treatment strategies based upon individual patient needs while providing administration with a cost-effective solution. The Open Lung Tool provides clinicians with an instrument to effectively determine the effect of a recruitment maneuver, identification of collapse point (PEEP titration) and provide breath by breath trends of vital parameters during and after the maneuver. Later this year, MAQUET will release the next new software version which is geared for the specific needs of neonatal patients.

MODALITIES OF USE

There are currently over 18,000 SERVO-i ventilators sold worldwide. Many hospitals are benefiting from the advanced technology the SERVO ventilator systems offer. Several hospitals in the US and abroad have been highlighted in MAQUET’s recent publication, Critical Care News. You may obtain a copy by sending a request to info@criticalcarenews.com. This year’s first edition highlighted the success of the Cox Health Medical Center in Springfield,

Missouri. By using a multi-disciplinary team approach, the hospital integrated new ventilator technology with patient-driven protocols. This resulted in operational cost savings of \$4.5 million.

MAQUET works closely with many renowned physicians and experts in mechanical ventilation, both in the US and around the globe. There are over 140 countries worldwide that utilize the SERVO ventilator technology. With over 200 dealers in countries worldwide, our service and support truly is a global "gold standard." This commitment has been recognized by Frost & Sullivan with its prestigious 2005 Market Leadership Award in Mechanical Ventilation. Our Ventilator Symposiums have brought together many US and internationally recognized experts in the field of mechanical ventilation to discuss ventilator related issues and topics with attendees.

As the global leader in mechanical ventilation, MAQUET is committed to advancements in technology and providing education to support these advances. We sponsor various local seminars and speakers throughout the year. The goal is to increase educational awareness of current therapeutic modalities or the latest advances in understanding a disease state. Additionally last August 2004 we sponsored a two day symposium in Monterey, California. This symposium, entitled "Current Trends in Mechanical Ventilation," included such speakers as Dr. Arthur Slutsky, Dr. Luciano Gattinoni, Dr. Marco Ranieri, Dr. John Marini, Dr. Mitchel Levy, Dr. Mark Heulitt, and Dr. Leonard Hudson. This year's 2005 conference, entitled "The Symposium on Acute Lung Injury—from Basic Science to Bedside Application," will be held in Strasbourg, France from September 12th to September 13th, 2005. MAQUET will continue this annual educational event in 2006 with a new venue back in the United States.

CLINICAL INPUT

Our roles within MAQUET, Inc provide us direct access to our counterparts and associates at the MAQUET Critical Care factory located in Solna, Sweden. We routinely communicate our US customers' needs, ideas, suggestions and future vision of ventilation and the respiratory care industry. Since the release of the SERVO-i, there have been a tremendous amount of product enhancements based on our customers' input. MAQUET's customer feedback and suggestion process is well defined. Feedback is sent to the appropriate manager at the factory including research & development, engineering, logistics, product steering committees and educational services. We work closely with our key clinical and reference sites to ensure that the products delivered meet their requirements and maintain our position of being the "Gold Standard" in the industry.

Draeger Medical

Bob Splane

Bob Splane is VP of Marketing, Global Business Unit of Perinatal Care, Draeger Medical, Inc. All information was provided by Draeger Medical.

PRODUCTS

Our products cover four key areas of perinatal care technology: ventilation, warming therapy, jaundice management, and monitoring. Mechanical ventilation for neonates is a critical aspect of neonatal care. Draeger Medical's Babylog ventilator is a product that was designed with the unique requirements of critically ill neonates in mind. The second area is thermoregulation devices, radiant warmers, incubators and transport systems, for which Draeger Medical offers the optimum thermal environment for the tiniest patients. The third area of perinatal care that Draeger has mastered is jaundice management, because the detection and management of this condition in both full-term and premature infants is critical. Finally, with Draeger Medical's joint venture with Siemens Medical Solutions, we have been able to bring our state-of-the-art patient monitoring products into the perinatal environment.

PATIENT CARE

Draeger Medical's product offerings include new modalities, new synergies and overall benefits resulting from our CareArea concept. This concept includes a comprehensive neonatal suite designed to create an optimal environment for the most fragile patients. Draeger Medical provides all the fundamental components essential to exceptional neonatal care, including innovative warmers, incubators, phototherapy lights, ventilators, vital signs monitoring and data management. These components work together to minimize stress and negative stimulation for the patient. Clinical staff will benefit from this integrated CareArea solution through increased quality of therapy and reductions in process costs. We can help customers to redefine the entire perinatal care process. The synergies of this union will enable customers to create a more nurturing environment for patients and their parents, as well as a more process-optimized solution for caregivers and the hospital.

ADVANCES AND TREATMENT

If I were to point out particular key advances in the perinatal care market that I have recently experienced, they would include the improvement of patient outcomes, which is a key driver in any care market, and the challenge of addressing caregiver shortages. Another key advance is integrated workspace and information solutions, which can reduce medical errors, improve the quality of patient care and increase hospital revenue. More specific to the perinatal market would be the concept of developmental care, moving from a micro to a macro environment. This also includes the expansion to family centered care. Another key driver in product development includes multiple births. Some other factors include services reimbursement reductions and total asset management, the latter being an area in which Draeger Medical provides support to its customers.

R&D

With more than 65 years of experience Draeger Medical has a true passion for perinatal care and an unwavering commitment to exceptional customer service and support. Our product support and development is on-going. It is targeted at providing the best possible infant care utilizing the latest technologies. Through frequent customer visits, we listen to our customers to better understand their needs, then design products to address those needs.

As a global company, Draeger Medical is represented in more than 190 countries worldwide. We have a total of 110 years of medical experience and continuous investment in research and development. Air-Shields products were recently merged into the Draeger Medical portfolio of anesthesia devices, critical care ventilation, patient monitoring, warming therapy and IT solutions.

The new Business Unit Perinatal Care, located in Hatboro, Pennsylvania, is dedicated solely to perinatal care and helping customers take perinatal care to a new level.

EDUCATION & TRAINING

Draeger Medical product training is provided to support the proper use and maintenance of our products to maximize the product's benefit to our customers. Included with the sale of each product is standard inservice training for the hospital staff. Additionally, DraegerService provides training for hospital service personnel and the Draeger Education and Training division provides advance training for hospital personnel.

COMMUNICATION WITH CAREGIVERS

Close dialogue with customers is ongoing at Draeger Medical. We have relationships with thought leaders throughout the world. By partnering with thought leaders in our market we continue to provide state of the art equipment. Prior to market release, our products are evaluated at key customer sites to gain customer validation.

NEW TECHNOLOGY

Wireless communications technologies will pave the way to eliminating many

of the annoying patient cables that our customers have to manage, allowing them to devote greater attention to their patient. Also, utilization of information technologies to integrate patient data from multiple infant care device sources can provide the caregiver a clearer picture of the patient's condition leading to better medical decisions.

FACILITIES, INTERNATIONAL, CONFERENCES

There are many hospitals having success using our products to provide quality infant care. These include birthing centers, transport teams, as well as NICUs in large clinical centers and teaching institutions.

Draeger Medical is committed to servicing its customers after the product sale. We provide a state-of-the-art service network and service engineers to help protect our customers' financial investments. We also help to ensure uninterrupted hospital productivity by maintaining our various types of medical equipment and enabling them to continue operating at peak performance levels. Draeger Medical annually supports several national organizations as well as regional forums and seminars. NANN, AWHONN, ANN are a few of the organizations Draeger Medical sponsors and supports.

Masimo Corporation

Joe E. Kiani

Joe E. Kiani is Chairman & CEO, Masimo Corporation & Masimo Laboratories

Our Vital, Shared Mission

Masimo designs, manufactures and sells pulse oximeters and Pulse CO-Oximeters with the largest selection of sensors, as well as remote alarm notification and central monitoring systems. No other pulse oximeter matches the performance and capabilities of our technology, and yet technology is not really the heart of our company. Our company mission states that our purpose is to "improve patient outcome and reduce cost of care." Our values dictate that we always "Do what is best for patient care." Viewed in this way, technology is a means to an end, an end that can only be accomplished in partnership with you, the caring clinicians who deliver and manage patient care.

Since our founding in 1989, we have always focused on solutions that attack the root of major problems for patients and clinicians. Masimo came into being because an engineer friend and I believed we could find a way to solve a serious, previously "unsolvable" problem that had always plagued pulse oximetry. When patients were in motion and/or experiencing low perfusion, pulse oximetry readings were unreliable. In fact, outside of the operating room, most of the alarms were false alarms. And in the OR, pulse oximeters often failed entirely due to low perfusion.

We invented Signal Extraction Technology (SET) to solve this problem, and we succeeded. The first version of Masimo SET reduced false alarms by over 90%, while, surprisingly, improving the detection of true alarms. We are now close to releasing version 5.0 of Masimo SET, which has further improved pulse oximetry's sensitivity and specificity. Over 70 independent clinical studies have demonstrated the superior performance of Masimo SET; no one has ever replicated our performance.

With this significant technological innovation, we are helping to improve patient outcome and reduce cost — with more accurate and reliable pulse oximetry. Studies show that clinicians using Masimo SET technology have reduced the incidence of Retinopathy of Prematurity (ROP), and have eliminated unnecessary blood gas measurements and overly high dosages of oxygen administration. You can find these studies on the Masimo website (www.masimo.com). Most rewarding, our customers tell us that we are helping them save and improve lives.

Our partnership with clinicians exists in our laboratories, as well as at the bedside. RT professionals, nurses, biomedical engineers and physicians were involved in identifying the needed and developing Masimo products such as our new LNOP Blue Sensor, the first device specifically designed to measure oxygen saturation in cyanotic infants.

Services Are an Important Part of the Masimo "Solution"

Every time a hospital converts to Masimo technology, we take the opportunity to provide education on the powerful capabilities of pulse oximetry, as well as on the use of Masimo products. Our educational programs are conducted in person by our clinical specialists, and are also available as convenient "e-inservice" learning programs offered by Masimo U through our web site. We delivered our first live, accredited Webinar, "Oxygen Transport and Neonatal Pulse Oximetry," in May and it can still be taken on the site for CE credit. We plan to continue our e-lecture series on a regularly scheduled basis.

The Rainbow Future: Continuous, Noninvasive Monitoring of Blood Constituents

Continuing to focus on "unsolvable" problems, Masimo and Masimo Laboratories have been working on non-invasive ways to monitor patients with our Rainbow technology, detecting potentially life-threatening problems that otherwise might have gone undetected, offering capabilities far beyond those traditionally available with pulse oximetry. By combining SET and Rainbow technology, we have introduced Pulse CO-Oximetry, which instantly and non-invasively measures carbon monoxide levels in the blood, as well as oxygen saturation, pulse rate and perfusion index. We are in the process of obtaining FDA clearance to add the capabilities of monitoring methemoglobin levels and fractional arterial oxygen saturation.

As our population ages, it will become increasingly important to identify at-risk patients before an emerging medical problem becomes critical. Noninvasive monitoring of vital physiological parameters will become an increasingly powerful tool to use in early intervention, both in the hospital and in outpatient care. It will significantly improve outcomes and reduce costs. As society confronts the challenge of an increasingly elderly and fragile patient population and a shortage of experienced clinicians, Masimo will be there to help you solve the "unsolvable" problems. I will continue to spend a large part of my time working with the clinical community to identify these problems and leading our product development efforts—doing "what is best for patient care."

Hamilton Medical, Inc.

David Costa

David Costa is Vice President, Hamilton Medical, Inc.

There are many very capable mechanical ventilators on the market today. At Hamilton Medical however, we are leading the paradigm shift toward closed-loop medical instrumentation. At Hamilton, we realize that the respiratory therapist has to manage a great deal of information and make ventilator changes based upon that information. Hamilton Medical asks, what if the ventilator could adapt to the patient on a breath by breath basis, make ventilator changes and therefore allow the clinician to perform at a higher level of efficiency and focus their expertise on more high-level patient care issues?

There is simply no way for the best and brightest clinician to be at a patient's bedside, 24 hours a day, 7 days a week. Hamilton Medical offers technology that is tireless in its protocol-based application of ventilator management. We perform closed-loop ventilation all over the world, where our Adaptive Support Ventilation (ASV) is becoming the mode of ventilation... except in the United States, where we have been required to make our technology "more manual." In the United States Hamilton Medical offers Adaptive Tidal Volume Support

(AVtS). AVtS is second only to our own ASV in being absolutely ground breaking in their technology. AVtS employs a lung protective strategy and automatically begins weaning when conditions allow. AVtS employs both protective ventilation and weaning goals using a sophisticated, continuous, on-line measurement of respiratory mechanics. AVtS manipulates the ventilatory pattern to maximize ventilation, minimize the work of breathing and likelihood of volutrauma. It does all of this while being extremely simple to operate.

Hamilton Medical's offerings support what we refer to as "intelligent ventilation."

- Superior performance in critical care environments, without overwhelming the clinician.
- Improved patient outcomes by having our devices do more of the work.
- Cost effective solutions and proof that the solution has provided a return on investment.

Automation in commercial aviation has made flying safer and has allowed the pilot of the modern airliner to focus on the critical tasks at hand, while having the ability to determine what tasks the automation should perform. Hamilton Medical intends to offer similar safety, reliability and systems management functions to the respiratory care professional.

CORPORATE STRUCTURE

Hamilton Medical, Inc is a part of the privately held group of Hamilton Company scientific instrument businesses that trace their history back to the early 1950s and now employs approximately 1,000 people. Clarke Hamilton, the founder of Hamilton Company, started the business in 1953 with the development and manufacture of precision glass syringes. Over the years, the Hamilton companies have developed an extensive line of specialty products combining the quality of Swiss manufacturing systems with global resources and the reliability of a focused organization. The collective companies are now in business with research, development, manufacturing and marketing worldwide. The world headquarters for Hamilton Company is Reno, Nevada.

First seen as a research company, Hamilton Medical emerged in 2003 as the fourth largest ventilator company in the world.

PRODUCTS

Hamilton's product offering is focused on three major platforms:

- Arabella Neonatal/Pediatric NCPAP
- Raphael Pediatric/Adult Critical Care Ventilator
- Galileo Gold Neonatal/Pediatric and Adult Critical Care Ventilation Suite

Hamilton Medical has a long history in perinatal care. We continue to consult with our neonatal physicians and clinicians to ensure that Hamilton Medical ventilation solutions are the appropriate ventilatory needs for even the smallest patients.

The Arabella system provides safe, effective delivery of NCPAP to infants, including those with very low birth weight (VLBW). The advantages of the system include no moving parts, small size, minimum dead space, quiet operation and decreased impedance to respiration. The Monitoring Gas Mixer is used with a Patented Universal Generator Set with interchangeable silicone Soft Prongs, a heated wire Delivery Circuit and an Arabella cap. Arabella disposables are compatible with all popular NCPAP delivery systems. Many neonatal clinicians prefer a mask to the more traditional nasal prongs and Hamilton Medical offers a wide selection of both delivery products.

The Raphael Color is the newest addition to Hamilton Medical's ventilator family. With its color screen, the full featured Raphael Color is a cost-effective and compact solution for ventilation needs for pediatric through adult patients.

It offers high-end critical care features at a highly competitive price. This ventilator is so simple to use which makes the RAPHAEL the ideal replacement for older generation ventilators and offers a rental alternative, since training is quick and easy.

The Galileo Gold is Hamilton Medical's highest performance intensive care ventilator. The Galileo Gold can ventilate all patient populations, from neonates to adults. It introduces all the closed-loop technology discussed in this summary. This platform has not reached its limit, and leads the industry in performance, capability and safety.

Hamilton Medical is also pleased to announce that we now offer EtCO₂ monitoring, SpO₂ monitoring and other patient monitors designed to complement our ventilation systems. Our EtCO₂ offering works extremely well on all patients, including neonates due to the micro sampling technology. We can also provide NIBP and soon will be offering ECG monitoring through our strategic partners.

Of course, rental programs and asset management programs are always available. These can be an ideal way to experience all the solutions that Hamilton Medical has to offer.

Hamilton Medical's innovative solutions adapt to the changing clinical environment allowing the clinician to focus on delivery of patient care. Its critical care systems enable the clinician to use evidence-based protocols in the care of the patient with our enhanced monitoring tools. Hamilton Medical provides unique solutions to optimize patient comfort with advanced adaptive modes of ventilation and proximal airway measurement for breath to breath assessment of the patient's changing condition. The company's proximal flow sensor is designed to provide accuracy in all critical care environments, providing the clinician reliable data for access of the patient's clinical condition.

Hamilton Medical's ventilation products provide ease of use for the entire staff and can be introduced with a minimal learning curve. Our superior product support ensures that the facility's investment is employed with maximum effectiveness.

EDUCATION, TRAINING AND INDUSTRY SUPPORT

Hamilton Medical, Inc. serves not only as a valuable training resource for education and training staff at the clinical site, but also as a clinical partner to the future trends in technology and ideas in health care. The Hamilton Medical education and marketing departments provide the following services to the clinician and health care providers within the Health System:

Ventilator Inservice Training programs have been designed for product-specific applications and are implemented at the hospital site. Multimedia educational tools for training and competency exams have been developed for each product and are available to the clinician. Continuing education credit programs can be given in coordination with the inservice program. Custom training and education programs have been developed to supplement the training resources of the hospital and medical education programs. Programs are available to evaluate product usage to recommend methods for improving efficiency and lowering overall operating costs.

The Ventilator Graphics and Pulmonary Mechanics Workshop has been developed for clinicians that have a basic knowledge of mechanical ventilators and now would like to advance into the measurements of respiratory mechanics and improve their understanding of the graphic display of the mechanically ventilated patient.

The Ventilator Graphics and Pulmonary Mechanics course has been divided into two sections, Basic and Advanced. The first workshop section introduces the clinician to the basics of pulmonary mechanics and ventilator graphics. The second workshop follows with the advanced application of pulmonary graphics

and mechanics to assist the clinician in fine tuning the ventilator to the patient's changing condition. The workshop has been designed to provide 3 hours of Continuing Education credit.

The goal of the Clinical Expert's Workshop is to offer the healthcare facility the perfect balance of clinical experience and technical expertise to build and reinforce the initial inservice platform. The first phase of the workshop is to provide an in-depth knowledge of the design philosophy of the ventilator, the second phase expands on the operating performance characteristics, and the third phase introduces best practice methods for implementing the Health System's ventilation protocols, policies and procedures. The workshop is intended for the individuals in the Health System that will be involved with direct patient care, physicians and clinical educators. Additional support information will be provided upon request.

INDUSTRY INNOVATIONS

Hamilton Medical was the first to introduce closed-loop ventilation in a production ventilator, and continues to lead the market today with thousands of ventilators using ASV worldwide. Josef Brunner, Hamilton Medical AG's CEO, is a published researcher in closed-loop mechanical ventilation and continues to drive the organization forward toward even more exciting technologies. It was the first to offer a P/V Tool Maneuver in a production ventilator and continues to lead the market with the best way to confirm that PEEP set is appropriate for the patient. Our P/V Tools allow the clinician to quantitatively assess the correct level of PEEP for the patient, under extreme safety. Hamilton Medical was the first to introduce the "Ventilation Cockpit," including the "Safe Ventilation Window," which provides the clinician instant assurance that the chosen ventilation settings are safe and appropriate for the patient. The Safe Ventilation Window clearly defines the lung protective rules strategy and defines limits for volutrauma, barotraumas, apnea and autoPEEP. This is accomplished through a very simple graphical interface that makes rapid assessment of ventilator setting simple, easy and safe.

Hamilton Medical was also the first to lead the perinatal market with NCPAP. We continue to offer patented elements to our disposable that allow us to continue this leadership in patient comfort for these tiny patients. The company will be the first ventilator manufacturer to use clinical and technical training methods, similar to those used by commercial pilots to focus on recurrent training, Advanced Qualification Programs (AQP), Scenario Based Training (SBT) and Formal Industry Training Standards (FITS). We are working with interested clinicians who are ready to take medical device training and competency to the next level. For more information contact Hamilton Medical at hammedl.com, (800) 426-6331.

Fisher & Paykel Healthcare

Chris Hutchinson

Chris Hutchinson is the Neonatal Product Manager, Fisher & Paykel Healthcare, Inc, based in Laguna Hills, California.

PRODUCT

Fisher & Paykel Healthcare utilizes our research capabilities, technical skills and clinical partnerships to design and develop innovative products and therapies which assist healthcare professionals to provide the best possible patient care and outcomes. Our four primary product groups include respiratory humidification, neonatal care, obstructive sleep apnea and the OR. Within the neonatal care area, we provide products for optimal thermoregulation, resuscitation, respiratory humidification, oxygen therapy and phototherapy.

All product lines are the result of ground-up development for specific neonatal applications, rather than "me-too" duplication of other products simply to expand an existing product line. Backed by clinical research, enhanced design and user ergonomics, all products are intended to provide superior clinical performance, ease-of-use for the caregiver and reliable day-to-day functionality

PATIENT OUTCOMES

Fisher & Paykel Healthcare's focus on specific products and their application within the neonatal environment is intended to provide optimal care and management of the healthy term baby in labor and delivery through to the critical ELBW baby in Neonatal Intensive Care.

From the perspective of the clinician through to the hospital administrator, the end-point of optimal care is obviously the growth and survival of all babies. Our clinical understanding is therefore fundamental to the success of our products and the delivery of optimal care, and we invest heavily in continued research and clinical partnerships throughout the world.

MARKETPLACE

The past five to ten years have seen a resurging importance in the fundamentals of initial patient care within the first 24 hours, with increasing focus on optimal resuscitation and thermoregulation in both the L&D and NICU. Fisher & Paykel Healthcare continues to lead the interface between physiology and physics to ensure optimal patient care.

For example, our ongoing clinical research and product development with neonatal resuscitation produced the Neopuff Infant Resuscitator in the late 1980s. This device continues to change the application of optimal neonatal resuscitation around the world; however, more importantly, the Neopuff safely improves the respiratory status and outcomes of the patient.

Our infant warmers are another example of the research and development process. Although the humble Infant Warmer was once considered as simply a "heat table," our advancements have resulted in many hospitals revising and amending their existing protocols and procedures to take advantage of what our new technology can provide their patients. With both of these examples, our focus is to ensure an optimal environment for the stability and growth of the baby, while reducing the environmental demands of stress and stimulation.

TRAINING & EDUCATION

An essential extension of our clinical and product knowledge is the education and training we provide through clinical workshops. Fisher & Paykel Healthcare is particularly proud of these invaluable sessions, which provide clinical, theoretical and hands-on training to nurses, physicians, respiratory therapists, educators and clinical engineering. This education philosophy extends further into support material for maintaining necessary skills and competency of end-users.

CLINICAL PARTNERSHIPS

Our worldwide clinical partnerships play two important roles during clinical research and product development. Firstly, these healthcare professionals provide essential due diligence as we work collectively to address the ever-changing needs of our patients. Secondly, as research becomes concepts and concepts become products, these partnerships provide an invaluable pathway for day-to-day incremental product evaluation and clinical validation, through to controlled randomized clinical studies.

THE FUTURE

As we mentioned earlier, the resurging importance of optimal resuscitation and thermoregulation is going to require products, processes and people that can respond appropriately to these new and unexpected demands. Our resuscitation and thermoregulation products have embraced these challenges through optimized design and assembly, and can be customized by the end-user day-to-day to fulfill these new changing clinical requirements. Future products will

continue to build on this customization and configuration concept as we continue to advance optimal patient care.

THE GLOBAL MARKET

Fisher & Paykel Healthcare is a global company with direct clinical sales and support in 12 countries and representatives in a further 90-plus countries, and our products have always been designed to meet the needs of the international marketplace. This international presence combined with a national focus in each market, provides an invaluable perspective during clinical research and product development. The end-result of such focus is numerous clinical studies, investigations, trials and evaluations underway throughout the world at any one time; these outcomes are integrated with the input from our clinical partnerships to lay the foundation for tomorrow's products.

CONFERENCES, FORUMS & MEETINGS

Fisher & Paykel Healthcare proudly supports the national conferences and annual meetings, as well as utilizing the regional, state and section meetings for sharing new clinical and product advancements. These meetings provide an ideal forum for customer input and feedback, and this opportunity to have "one-on-one" time with our customers provides further validation that our products are leading the marketplace. These meetings also provide an excellent opportunity to initiate new relationships and continue to build upon relationships formed over many years with our loyal and valued customer base.

Spacelabs Medical North America

Steve Hutchinson

Steve Hutchinson is General Manager of Spacelabs Medical North America. He joined Spacelabs as VP of Sales in 2004, having held various executive positions in his successful 16-year career at Datex-Ohmeda. Mr. Hutchinson is a graduate of RIT (Rochester Institute of Technology).

PRODUCTS

For fifty years, Spacelabs Medical has been a global manufacturer and distributor of patient monitoring systems. That, in itself, helps set us apart. Because we have chosen healthcare as our only focus, we have the advantage of being in constant, close communication with our customers – designing and manufacturing with the clinician in mind.

As a result, our intuitive, touch screen user interface is consistent across our entire monitoring line, so that a nurse can quickly learn one monitor and know them all. And Spacelabs monitors are modular, so the same monitor can be used for different acuity levels. NICU nurses especially like that Spacelabs' WinDNA technology brings charting, labs, radiology and the HIS to the bedside monitor so that they can have immediate access to vital information, yet stay with their patients. They also appreciate that our adjustable alarm settings and untethered remote can help keep things quiet in the NICU.

Other features and benefits include our Flexport system interfaces that integrate data and alarms from ventilators and other stand-alone devices into the Spacelabs patient monitor, and our barcode scanning feature that can save time and cut down on redundancy and errors. It's also important that Spacelabs monitors are backward compatible, meaning that a hospital's newer Spacelabs monitors will work with their existing Spacelabs monitors.

PATIENT CARE

Bringing information to the clinician, whenever and wherever it is needed, has tremendous value. For example, Spacelabs patient monitors with WinDNA can provide clinicians with immediate access to vital information such as

medication dosages and interactions, as well as patient labs and diagnostic test results. Nurses can even do their charting at the bedside – all without leaving their patients – thanks to Spacelabs' WinDNA technology. Taking this one step further, Spacelabs' Vital Signs Viewer allows access to all the latest patient data from any connected PC on the network, meaning that physicians can view live patient waveforms from their office and home PC. In providing clinicians with critical information, when and where they need it, Spacelabs is giving them more time to care for their patients.

R&D

A key contributor to our R&D process is our global development team, with representatives from many countries. This team travels constantly to hospitals around the world, collecting information from end users – including valuable feedback on our product iterations. The global development team is careful to solicit input from each care area, customers and non-customers alike, throughout the product design, development and launch processes. Our patient monitoring solutions are inspired also by what we learn as active members and sponsors of various healthcare organizations, through participation in conferences, and by conducting focus groups and product technology suites. Also, as mentioned earlier, Spacelabs has the advantage of being in close day-to-day communication with our customers, who are end users throughout various hospital care areas. We listen to their needs and develop solutions accordingly.

CLINICIAN INPUT

Spacelabs offers a wide variety of clinical support, including end user training, more advanced "Train the Trainer" sessions and customized programs such as "Advanced Clinical Concepts." All are presented by our Clinical Education Consultants, whose product knowledge and in-depth understanding of the various care areas are helping hospitals maximize the usefulness of their Spacelabs monitoring systems.

You might say that our products are designed by and for clinicians. We are in constant contact with clinicians in hospitals, at conferences, and in focus groups, worldwide, because they do play such a vital role in developing and upgrading our patient monitoring solutions. Our new product development process is very much a collaborative effort. We meet frequently to share input gathered from all disciplines within Spacelabs and from our customers – who are key contributors to this process. We are committed to making reliable products that make a difference and allow caregivers more time to care.

PRODUCT EVALUATION

Spacelabs adheres to rigorous guidelines for testing throughout the development process. Prior to releasing new or modified products, we perform field evaluations within the specialty care areas in hospitals. Fortunately, we have many customers who work with us to accomplish this. For example, for our upcoming SpO2 releases, we conducted field evaluations on Masimo technology and on Nellcor technology. Valuable input was brought back from nurses at the bedside to refine the product prior to final release.

TECHNOLOGY/MARKETPLACE/SPONSORSHIPS

Our smarter alarms and remote alarm notification capabilities both have a positive impact on the NICU. We are also introducing new, wireless portable monitoring.

The international marketplace and clinical community have a huge impact. Because we are a global company, we are very careful to design products that meet the needs of caregivers on all continents, not just North America. The members of our global development team represent the needs of their geographic areas and clinical expertise.

Spacelabs is a proud sponsor and/or advisory member of several organizations such as AACN, APSF, and HIMSS, to name just a few. We also provide educational sessions that offer CEUs at many of the dozen conferences where

we exhibit our patient monitoring solutions. Spacelabs also hosts regional "Medical Technology Fairs" where our goal is to keep hospitals up to date with the latest advances in patient monitoring technology.

Puritan Bennett

Dan Van Hise

Dan Van Hise is Director of Marketing for the Acute Care Ventilation Business of Puritan Bennett, a Tyco Healthcare Company

PRODUCTS

The Puritan Bennett 840 ventilator is the flagship product in our extensive line of critical care ventilators. It is highly responsive to patients, offering sensitive, precise invasive and noninvasive breath delivery to critically ill neonatal through adult patients. With the lowest 10-year cost of ownership in its class, according to MD Buyline, the 840 can be upgraded and customized with various software options to meet a variety of clinical needs today and in the future. The innovative design of the 840 ventilator makes it easy for technicians to set up and navigate, minimizing training time and giving hospitals the ability to train NICU and ICU clinicians alike on just one ventilator.

ADVANCES IN CARE

The NeoMode software options transforms the Puritan Bennett 840 ventilator into a highly effective neonatal ventilator system that is truly in tune with neonatal physiology. It allows clinicians to deliver sensitive ventilation tailored to critically ill patients, including micro-preemies. The recent release of an enhanced noninvasive ventilation software option for the 840 supports compatibility with neonatal and CPAP prongs. With these prongs, clinicians can now use the same ventilator on a neonate from first intubation through an infant's transition to more independent breathing.

R&D

The best innovations address clinician needs. Before launching any R&D effort, we look first to our customers for input to ensure that our next solution addresses developing needs in ventilation. Puritan Bennett routinely engages in clinician research on all product lines, and our R&D team prioritizes development efforts accordingly. Once the product development cycle begins, the teams continue to look to clinicians at each step along the way, from concept to prototype to beta testing, to help ensure that our advances continue to address challenges and support new technologies. In addition, as an international company, we develop products for use beyond the US. We actively seek input from international clinicians and regularly involve our international marketing team in product development cycles.

EDUCATION AND TRAINING

Puritan Bennett is committed to supporting education and training for all clinicians by providing various levels of outreach, from comprehensive product training to continuing education units, for all clinicians, not just our customers. For product training, most of our sales representatives are registered RTs and are available to answer detailed questions from their colleagues in the field about our ventilators, throughout the sales process and beyond. In addition, we offer one of the most comprehensive field service programs in the ventilator industry. Our extensive team of customer service engineers and technical support staff are dedicated to giving the highest quality service. Our service organization has consistently received top rating among all medical field service participants, ranked #1 for the last two years, according to monthly MedicalMetric Field Service survey results. Our field-based sales and service organizations work together to provide clinicians with everything from prompt warranty/repair service to education and insight into new or upgraded ventilator features and product options. Finally, Puritan Bennett offers a full complement of sales tools, computer-based training, and continuing education

units online through our Center for Clinical Excellence website and through such organizations as AARC and AACN. For more contact puritanbennett.com/educ/onlineed.aspx.

NEW TECHNOLOGIES

There are a number of new advances that promise to improve neonatal ventilation and overall care in the NICU.

Wireless: The technology we use every day is coming to NICUs to help increase staff efficiency. Wireless technology will enable clinicians to access patient data anywhere at anytime through the facility's secure network.

Smaller footprints: NICUs will see smaller ventilators. These ventilators will offer technology improvements, and will also fit better in the NICU's smaller space.

Automated and closed loop control: Through the use of devices such as pulse oximeters, capnographs and hemodynamic parameters, future ventilators will facilitate a faster response to patients' changing conditions.

SUCCESS AND MARKET VISIBILITY

Puritan Bennett contracts with most of the nation's largest group purchasing organizations, and is proud to count many of the world's leading medical institutions among its list of prestigious customers who use the 840 ventilator exclusively throughout their facilities. In addition, we proudly sponsor and attend leading industry conferences such as the AARC, SCCM, and NANN, and the AACN National Teaching Institute. We see conferences as an important opportunity to educate clinicians about new advances in ventilation, and they offer us another venue for gathering market feedback on our products while staying in touch with medical advances and trends in the industry.

CASE STUDY

Use Of A Micropump Nebulizer For Aerosolized Medication Delivery In A Ventilated Infant

Peggy Bartram, RRT-NPS, RCP

Successful aerosolized therapy in a mechanically ventilated patient depends on achieving adequate drug deposition in the lung, and is influenced by an array of factors that include aerosol device selection, drug formulation, ventilator circuit setup and ventilator settings, as well as the patient.

In the infant, this objective is further complicated by low tidal volume, low vital capacity and functional residual capacity and low I:E ratios. Combined, these result in a shorter period by which aerosol particles reside in the lung and lower rates of pulmonary deposition. A recent review indicates lung deposition of aerosolized medications in ventilated infants is less than 1% of the nominal dose compared with a range of 8-22% in ventilated adults.¹

In 2002, a novel micropump nebulizer (Aeroneb Professional Nebulizer System, Aerogen, Inc.) was introduced with the goal of improving the efficiency of inline aerosolized therapy without requiring adjustment to ventilator settings. This nebulizer works inline with all standard ventilator circuits and mechanical ventilators, including use with high-frequency oscillation.¹ A recent study of the Aeroneb Pro versus a conventional jet nebulizer in an animal model of infant ventilation documented a mean *in vitro* lung deposition of 14% of the nominal dose, versus a mean of 0.7% with the jet nebulizer.²

The case study that follows demonstrates the clinical utility of the Aeroneb Pro in this difficult to treat population.

CASE STUDY

A former 26-week PTAGA infant was transferred to the PICU at 8 months post-conceptual age. The infant was ventilator-dependent because of severe chronic lung disease. One week after transfer, the patient became septic, required increased ventilator support and was found to be wheezing with “tight” breath sounds bilaterally.



Ultrasonic nebulizer treatments were started with 2.5 mg racemic albuterol every 4 hours, and then increased to every 2 hours because of poor response, deteriorating blood gases, and overall worsening of clinical status. The infant was switched from racemic albuterol to 1.25 mg levalbuterol (Xopenex) treatments secondary to an increased heart rate. Ultrasonic nebulizer treatments were given with the humidification system bypassed to ensure that the maximum amount of drug was delivered to the airway; however, this required breaking into the ventilator circuit every two hours—putting the patient at risk for further infection and interrupting the patient's PEEP pressure.

The Aeroneb Professional Nebulizer System was placed inline with the ventilator circuit on the wet side of the humidifier (not possible with the ultrasonic nebulizer because of condensation collection in the nebulizer cup). Since a 1.25 mg dose of Xopenex was unavailable, two 0.63 mg ampoules were prepared for aerosolized administration. Upon aerosolization of the first 0.63 mg dose, within seven minutes of initiating therapy, the patient's oxygen saturation rose from 87% to 99%. Within 10 minutes of initiating therapy, the patient's peak inspiratory pressure (PIP) dropped from 36 to 27 cm H₂O, and it was determined that the second 0.63 mg dose of Xopenex would be held. The patient continued to receive 0.63 mg Xopenex every 6 hours until successfully weaned from ventilatory support three days later. The patient was subsequently discharged home.

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The author is Pediatric Clinical Specialist, UTMB, Galveston. This study was provided by Aerogen, Inc.

A Pilot Study Comparing the Purity, Functionality and Isoform Composition of alpha-1-proteinase Inhibitor Human Products

D.I. Cowden, G.E. Fisher and R.L. Weeks

ABSTRACT

OBJECTIVE: Alpha-1-proteinase deficiency predisposes affected individuals to early onset pulmonary emphysema and is treated with an alpha-1-proteinase inhibitor (A1-PI) from pooled human plasma. The objective of this pilot study was to assess analytical parameters of the three A1-PI products (Aralast, Prolastin, Zemaira) that may impact on clinical efficacy, safety, and convenience. These included: purity of the preparation, nature of impurities, functionality, and isoform composition.

METHODS: Purity was evaluated using reverse phase and size exclusion chromatography, high performance liquid chromatography (RP-HPLC and SEC-HPLC), capillary zone electrophoresis (CZE), sodium dodecyl sulfate polyacrylamide gel electrophoresis, sodium dodecyl sulfate capillary gel electrophoresis and Western blot analysis. The identity of protein impurities was determined by immunonephelometry, functionality by calculating the ratio of mg active A1-PI present (by anti-neutrophil elastase activity assay) to the mg antigenic A1-PI (by immunonephelometry), and normality of the A1-PI isoform pattern by isoelectric focusing (IEF). Three samples of Zemaira and one sample each of Aralast and Prolastin were available for analysis.

RESULTS: Zemaira had the highest specific activity. Using RP-HPLC analysis Zemaira averaged 99% purity, Aralast 70% and Prolastin less than 62%. Using SEC-HPLC, Zemaira was 95.98% monomeric, Prolastin 79% and Aralast 63.55%. Prolastin had lower activity/mg antigenic A1-PI than the other two products. A shift in isoforms in Aralast was suggested by the results of CZE and was confirmed by IEF.

CONCLUSIONS: Zemaira demonstrated greater purity compared

with Aralast and Prolastin. Prolastin had more inactive A1-PI than Zemaira or Aralast. Isoform ratios appeared to be altered in Aralast. The results from this pilot study warrant further investigation.

INTRODUCTION

In normal lung a delicate balance is maintained with alpha-1-proteinase inhibitor (A1-PI) present in sufficient quantity to protect the lung from degradation by neutrophil elastase, a serine proteinase.¹ For many, but not all individuals,^{1,2} low blood levels (< 11 μ m) of A1-PI are associated with progressive, severe pulmonary emphysema that becomes clinically apparent by the third to fourth decade of life.³ Non-smoking individuals may have delayed onset of symptoms.^{1,4}

First described in 1963,⁵ alpha-1-proteinase deficiency is now known to be an autosomally inherited hereditary condition, which may be associated with pulmonary emphysema, a major cause of disability and death.¹ Originally thought to be a rare disease solely of Caucasians, epidemiological data suggests that A1-PI deficiency may be one of the most frequent serious hereditary disorders in the world, with all racial sub-groups affected to varying extents. There may be at least 116 million individuals who are carriers (PiMZ, PiMS), and 3.4 million with deficient alleles in combination (PiZZ, PiSS, PiSZ).⁶ Ninety-five percent of A1-PI deficient individuals are of the severe PiZZ phenotype.

It is estimated that less than 10% of individuals with alpha-1-proteinase deficiency have been diagnosed.^{4,7} Those with A1-PI deficiency will often be diagnosed with emphysema, chronic obstructive pulmonary disease (COPD), or asthma without consideration of possible hereditary A1-PI deficiency. To increase consideration of this condition, the American Thoracic Society and European Respiratory Society have issued guidance that onset of emphysema, before age 46 years or in individuals without any known risk factors, should raise suspicion in the minds of physicians of A1-PI deficiency.¹

Augmentation therapy has been a primary treatment focus for hereditary emphysema since the FDA approved Prolastin (Bayer

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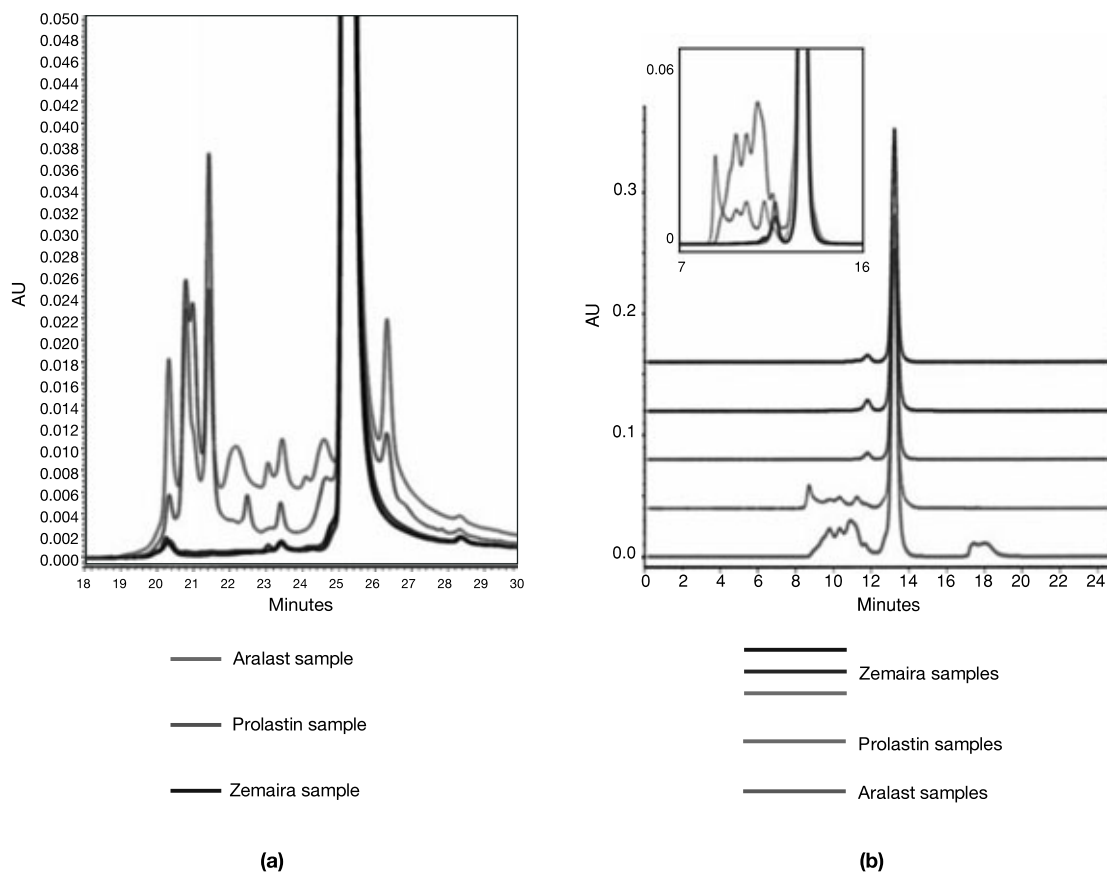


Figure 1. (a) Reverse phase high performance liquid chromatography (HPLC) comparison at 280 nm and (b) size exclusion chromatography HPLC comparisons of alpha-1-proteinase inhibitor products

Corporation, Pittsburgh, PA) in 1981, but product availability has been limited. Two new products, Aralast (Baxter International Inc, Deerfield, IL) and Zemaira (ZLB Behring, King of Prussia, PA) gained approval in 2002 and 2003, respectively, based on multi-centered, randomized, controlled, double-blind, clinical trials (versus Prolastin) in subjects diagnosed with hereditary A1-PI deficiency and emphysema. The primary objective of these clinical studies, was demonstration of “biochemical efficacy,” meaning that the products raise the A1-PI level in the serum and lung epithelial lining fluid.⁸⁻¹¹ The clinical effectiveness of A1-PI replacement therapy in reducing disease progression, however, remains to be determined.¹² While all three products elevate these A1-PI levels, there are clear differences in the purity profile and consequently, the non-therapeutic protein load patients may receive. Other differences, such as isoform composition and the presence of inactive A1-PI, exist between the products. This study was done to evaluate this product variability to provide clinicians with additional information for selecting a specific product to treat their patients.

Our current pilot study is an analytical comparison of the three A1-PI products available in the United States with respect to purity, nature of the impurities, functionality of the A1-PI protein, and isoform composition.

METHODS

Three samples of Zemaira and one sample each of Aralast and Prolastin were available for testing from stock available at ZLB Behring LLC (Lots C407505, 605, 705) and from a local hospital pharmacy (Arlast, Lot LH2010A; Prolastin, Lot 25N1T81). Each

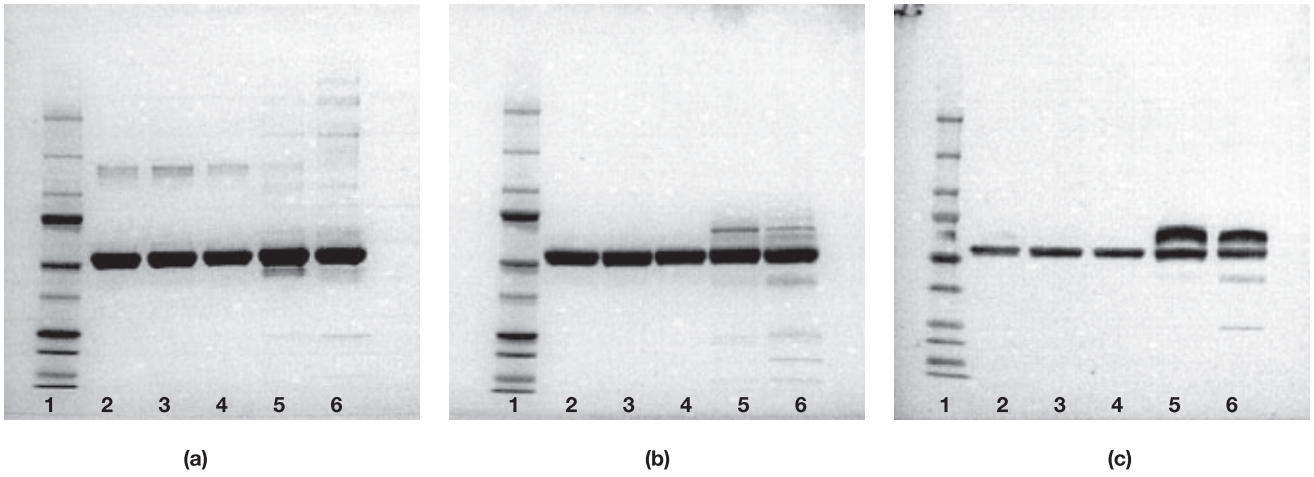
of the assays chosen provided a somewhat different insight into the purity profiles of each product. Sodium dodecyl sulfate-polyacrylamide gel electrodes (SDS-PAGE) and Western blots provide a qualitative view of overall purity. Size exclusion chromatography (SEC) and reverse phase high performance liquid chromatography (RP-HPLC) provided a quantitative evaluation of specific impurities in which proteins were separated by totally different methodologies.

Immunonephelometry quantified specific protein impurities and isoelectric focusing provided insight to isoforms and potential differences in glycosylation patterns. The potency assay determined functionality. This multi-assay approach is typically used in the evaluation of well characterized biologics, as is done in the biotechnology industry.

Purity

RP-HPLC was carried out on a Waters Alliance Chromatography System, model 2695, utilizing Empower Pro software. Columns used: (1) Phenomenex C-4 guard column with dimensions of 3 mm X 4 cm and a 5 µm particle size, part No. OOG-4167-EO. Mobile phase (A) 0.1% trifluoroacetic acid (TFA) in water; (B) 0.1% TFA in acetonitrile. Gradient: (1) 5 min at 80%A followed by increasing the %B to 100% in 40 min with a flow rate of 1mL/min.

SEC high performance liquid chromatography (SEC-HPLC) was carried out on a Beckman System Gold using a TSK3000SW_{XL} column (TosoHaas). The isocratic elution buffer was 50 mM potassium phosphate, 100 mM potassium chloride adjusted to pH 6.8 with sodium hydroxide. A flow rate of 0.7 mL/min was used and the column eluate monitored at 280 nm. A protein load



Lane 1 Molecular weight markers
 Lane 2 Zemaira sample 1
 Lane 3 Zemaira sample 2
 Lane 4 Zemaira sample 3
 Lane 5 Prolastin sample
 Lane 6 Aralast sample

Figure 2. Sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) comparison of (a) non-reduced alpha-1-proteinase inhibitor products, (b) reduced alpha-1-proteinase inhibitor products, and (c) SDS Western blot comparison of reduced alpha-1-proteinase inhibitor products probed with anti-whole serum antibody

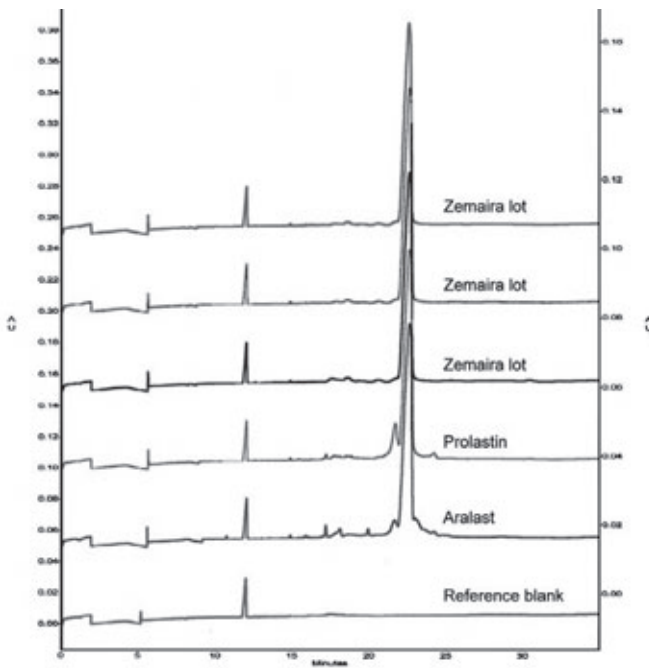


Figure 3. Sodium dodecyl sulfate capillary gel electrophoresis comparison of reduced alpha-1-proteinase inhibitor products

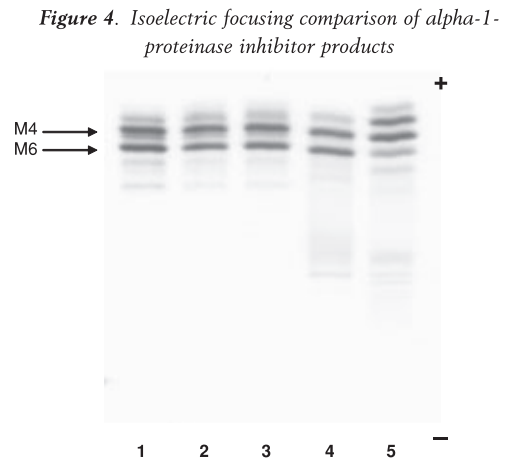


Figure 4. Isoelectric focusing comparison of alpha-1-proteinase inhibitor products
 From left: Lane 1 = Zemaira sample 1; Lane 2 = Zemaira sample 2; Lane 3 = Zemaira sample 3; Lane 4 = Prolastin sample; Lane 5 = Aralast sample

Table 1. Specific protein impurities in A1-PI products measured by immunonephelometry (mg/mg total protein)

	ALB	AAG	A2M	APO	ATIII	CER	HAPT	IgA	IgG	TRF
Zemaira sample A	< 0.007	< 0.001	< 0.001	< 0.001	0.001	< 0.001	0.003	< 0.001	< 0.001	< 0.002
Zemaira sample B	< 0.006	0.001	< 0.001	< 0.001	0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.002
Zemaira sample C	< 0.006	0.002	< 0.001	< 0.001	0.002	< 0.001	< 0.001	< 0.001	< 0.001	< 0.002
Aralast sample	0.032	< 0.002	0.004	0.012	0.004	< 0.001	0.043	0.076	< 0.002	0.009
Prolastin sample	0.068	< 0.001	< 0.001	0.005	0.006	< 0.001	0.011	0.014	< 0.002	< 0.003

ALB = albumin; AAG = alpha-1-acid glycoprotein; A2M = alpha-2-macroglobulin; APO = apolipoprotein A-1; ATIII = antithrombin III; CER = ceruloplasmin; HAPT = haptoglobin; IgA = immune globulin A; IgG = immune globulin G; TRF = transferrin

of 200 µg was used for each sample. Peak integration was performed using Beckman's 32 K Gold software.

Capillary zone electrophoresis (CZE) was performed on a Beckman P/ACE 5000 equipped with Beckman P/ACE Station software in a 50 µM, 57 cm Beckman bare silica capillary. The running buffer was 50 mM sodium borate pH 9.3. The applied voltage was 15 kV under normal polarity at 23°C. The detection wavelength was 214 nm. Prior to analysis, each sample was diluted to 4 mg/mL in 20 mM sodium borate pH 9.3. Samples were introduced into the capillary by 5s hydrostatic injections.

Sodium dodecyl sulfate-capillary gel electrophoresis (SDS-CGA) was performed on a Beckman P/ACE 5000 equipped with Beckman P/ACE Station software in a Beckman 100 µM, 47 cm eCAP SDS coated capillary. The running buffer was Beckman eCAP 14-200 gel buffer. The applied voltage was 14.1 kV under reverse polarity at 20°C. The detection wavelength was 214 nm. Prior to analysis, each sample was diluted to 4 mg/mL in Beckman eCAP SDS sample buffer in the presence or absence of DTT, and heated at 60°C for 20 min. Samples were introduced into the capillary by 99s hydrostatic injections.

SDS-PAGE was performed using BioRad Criterion gel units and 4%-15% Tris-Gly gels under reducing and no-reducing conditions. An 8 µg protein load was used for each sample. Gels were run at 200V for 0.9h. Gels were stained with Coomassie Blue.

For Western blots, separations were performed as described for SDS-PAGE. Samples were reduced and 1µg of protein loaded. Gels were transblotted onto nitrocellulose at 50V for 2.5h. Western blot membranes were probed with anti-whole serum and anti-alpha-1-antitrypsin (same as anti-alpha-1-anti-proteinase inhibitor).

Specific impurities were evaluated by immunonephelometry using a Dade Behring BN II nephelometer. The following proteins were assayed: albumin, alpha-1-glycoprotein, alpha-2-macroglobulin, apolipoprotein, antithrombin III, ceruloplasmin, haptoglobin, immune globulin A, immune globulin G and transferrin.

Functionality

A1-PI activity was measured with an anti neutrophil elastase activity assay and antigenic A1-PI by immunonephelometry. The ratio of mg active A1-PI present to the mg antigenic A1-PI was then calculated. Specific activity was calculated as the ratio of mg active A1-PI to mg protein as determined by Bradford assay using a Bio-Rad kit. Optical density was not used to determine protein concentration, because the suspected high levels of impurities in Aralast and Prolastin, with extinction coefficients

different from A1-PI, would have led to inaccuracies with this method.

The standard curve for the Bradford assay was constructed with the house standard A1-PI. The protein concentration for this standard was assigned by OD.²⁸⁰. The extinction coefficient was 4.33 and was a mean of determinations by four separate methods.

Isoform composition

Isoform composition of the A1-PI isoform pattern was evaluated by isoelectric focusing using a 1.25% agarose gel (IsoGel Agarose, Cambrex BioScience) with an ampholyte range of pH 4.2-4.9 (Amersham Biosciences). After focusing, the gel was placed in fixative solution, dried, and stained with Coomassie Blue R250.

RESULT

Purity of A1-PI Preparations

RP-HPLC and SEC-HPLC

The results of RP-HPLC demonstrated that the purity of Zemaira was 99%, Aralast 70% and Prolastin less than 62%. The lower values of Aralast and Prolastin were the result of numerous impurities, which are illustrated in the overlay of chromatograms shown in Figure 1a. Similarly the results from SEC-HPLC demonstrated that both Prolastin and Aralast exhibited numerous peaks not detected in the Zemaira samples (Figure 1b). Prolastin and Aralast also contained high molecular weight void volume eluting material, which was not present in Zemaira. Integration of the peaks revealed that Zemaira was the highest in percentage of monomeric A1-PI. Zemaira averaged 95.98% monomeric A1-PI for the three samples compared with 79% and 63.55% for Prolastin and Aralast, respectively.

SDS-PAGE and SDS-CGE

Results from both SDS-PAGE (Figure 2a) and SDS-CGE (not shown) of the non-reduced products demonstrated that Zemaira contained significantly less impurities than Prolastin and Aralast. Prolastin and Aralast exhibited similar patterns with some variation in quantitation. Multiple higher molecular weight species (ie > A1-PI) were more prevalent in Aralast than Prolastin. These multiple species were not present in the Zemaira samples at any appreciable levels.

However, all three Zemaira lots exhibited a single small higher molecular weight peak on SDS-CGE. Non-reducing SDS-PAGE was performed to demonstrate that it was not an artifact of the SDS-CGE system. In non-reducing SDS-PAGE, two bands were detected whose intensities correlated well with the absorbance of the SDS-CGE smaller peak for each lot of Zemaira. The

molecular weights of the bands were 12-140kDa and, as discussed below, are probably dimers of A1-PI.

SDS-PAGE (Figure 2B), and SDS-CGE (Figure 3) of the reduced products, like that of the non-reduced products, demonstrated that Zemaira contained less impurities than Prolastin and Aralast. Most of the high molecular weight species found in Prolastin and Aralast in the non-reduced SDS PAGE were reduced to lower molecular weights. None of the Zemaira lots exhibited the levels of impurities seen in the other two products. In addition, the single larger molecular weight species observed in Zemaira under non-reducing conditions (dimer) was no longer present under reducing conditions.

Western blot analysis

Western blots probed with anti-whole serum (figure 2c) showed a dark band in the Prolastin and Aralast lanes, which migrated above the A1-PI peak, between 50 and 75 kDa, when analyzed by reduced SDS-PAGE. This band corresponds to the position expected for albumin and haptoglobin and was not observed with the Zemaira samples. Numerous peaks of less intensity were also present in this region of the gel. Both Prolastin and Aralast exhibited the same impurity banding pattern below the A1-PI band, except that the bands were more pronounced for Aralast versus Prolastin. The Zemaira samples exhibited a barely visible band, which matched the molecular weight of the first impurity below the A1-PI band seen with the other two products. Reactivity to the lower molecular weight impurities in the Aralast and Prolastin samples was not as strong, especially for the Prolastin sample.

Identification of impurities

Specific protein impurities were measured by immunonephelometry. The quantity of impurities, normalized to mg/mg total protein, is detailed in Table 1. Aralast contained at least seven protein impurities. Some of these, namely albumin, haptoglobin, and immunoglobulin A (IgA), were found in relatively high concentrations. Prolastin contained five measurable proteins, one of which was also IgA. Zemaira contained the fewest impurities and those present were in low amounts. Zemaira did not contain measurable IgA.

Functionality of the A1-PI protein

The ratio of functional protein to antigenic protein (mg/mg) averaged 1.11 for the three Zemaira lots, 1.16 for the single Aralast lot, and 0.85 for the single Prolastin lot. This suggested comparable assay functionality for the A1-PI in Zemaira and Aralast, and that the Prolastin sample had considerably more inactive A1-PI than either of the other products.

Specific activity values (activity/mg protein) were 0.85, 0.65, and 0.56 for Zemaira, Aralast, and Prolastin, respectively, with pure fully functional A1-PI having an ideal ratio of 1.0.

Normality of the A1-PI isoform ratios

When compared by CZE the main Aralast peak migrated slightly slower than that of the other two products indicating a shift in charge to mass ratio and possibly in the isoform ratio. A shift in the isoform ratio was confirmed by isoelectric focusing (figure 4) which showed that in Aralast the M2 isoform band is enhanced and the M6 band diminished relative to those bands in the other two products.

DISCUSSION

With the availability of two new products on the United States market, a side-by-side comparison of the three available products was appropriate. Three findings from the present pilot study merit discussion: quantity and quality of impurities, presence of significant inactive material in Prolastin, and shift in isoform ratios in Aralast. Three samples of Zemaira were analyzed; however, only one sample each of Aralast and Prolastin were available for analysis, which is a major limitation of this study.

The quality of impurities was reflected in the lower specific activities of both Aralast and Prolastin. Our findings for Prolastin (specific activity of 0.56 and the list of impurities) are very similar to the original manufacturer's analysis conducted 20 years ago,¹³ with the exception of finding IgA (0.11 mg/mg protein), which was not originally evaluated. IgA may pose a risk of anaphylaxis to IgA deficient individuals with antibodies to IgA or the potential to stimulate their production. Aralast, a new product, seems to have a slightly higher specific activity of 0.65 but contains more IgA (0.76 g IgA/mg protein), and has more impurities, but less inactive A1-PI than Prolastin. The reduced Western blot probed for A1-PI (not shown) demonstrated that the extra bands observed with Prolastin and Aralast were not A1-PI but contaminants. Only a single A1-PI band was evident in all lanes. Zemaira is the purest (specific activity = 0.85) of the marketed products and does not appear to contain measurable IgA. Previous monitoring of Zemaira has revealed low levels of alpha-1-acid glycoprotein, antithrombin III and haptoglobin. However, because of the seriousness of anaphylaxis, all three products are contraindicated for IgA deficient individuals with known antibodies against IgA.¹⁴⁻¹⁶

For pure A1-PI, the maximum ratio of functional to antigenic A1-PI should equal 1.0. The immunonephelometric antigenic assay appeared to underestimate A1-PI levels when compared to functional units. Both assays utilize different standards for generating standard curves and entirely different technologies. A single standard in which potency and antigenic levels have both been calibrated would most likely reduce or eliminate bias in one or both assays.

The observation of a shift in isoform pattern in Aralast compared to that present in Prolastin, Zemaira and normal serum¹⁷ was unexpected. In normal plasma M4 and M6 are the most abundant isoforms constituting 40% and 34%, respectively, of the A1-PI,¹⁸ while M2, M7 and M8 are minor bands. With Aralast the two main isoform bands are M2 and M4. M2, M4 and M6 are closely related, differing in the degree of carbohydrate side-chain branching.¹⁷ As it is well known that protein glycosylation can affect the way the protein is handled by the body, this observed shift in isoform pattern merits further investigation.

CONCLUSIONS

Differences in manufacturing process have led to analytical differences in the A1-PI products. The results from this pilot study demonstrate that Zemaira is 99% pure, contains the least non-A1-PI contaminating protein and the A1-PI protein has high functional activity. Prolastin is about 60% pure and clearly contains detectable inactive A1-PI and several other protein contaminants. Aralast contains at least seven protein impurities, and the A1-PI isoform ratios appear to be altered, with M2 increased and M6 decreased relative to the other products and

to normal serum. The significance to the patient, if any, of this ratio shift is not known. Of the products, Zemaira has the lowest content of contaminating IgA (below the level of detection). The results from this preliminary study require further investigation.

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Sleep, Appetite, and Obesity— What Is the Link?

Patricia Prinz

There is a well-documented relationship between short sleep duration and high body mass index (BMI). In the largest study, a survey on sleep duration and frequency of insomnia in more than 1.1 million participants, increasing BMI occurred for habitual sleep amounts below 7-8 hours.¹ A recent prospective study found an association between sleep curtailment and future weight gain.² The mechanism linking short sleep with weight gain is unknown, but Mignot and colleagues' study in *PLoS Medicine*³ adds to the growing evidence implicating leptin and ghrelin, the two key opposing hormones involved in appetite regulation.

HORMONES THAT REGULATE APPETITE

Leptin, a peptide hormone secreted from white adipocytes, is implicated in the regulation of food intake and energy balance. The hormone acts on the central nervous system, in particular the hypothalamus, suppressing food intake and stimulating energy expenditure. Leptin production is primarily regulated by insulin-induced changes in adipocyte metabolism—its secretion levels correlate with adipocyte mass and lipid loads.

Leptin promotes inflammation. The hormone provides an interesting link between obesity and pathophysiological processes such as insulin resistance and atherosclerosis, and disorders such as autoimmune and cardiovascular diseases and the metabolic syndrome. Increased serum leptin levels in obesity and metabolic syndrome support the view that these disorders are in fact low-grade systemic inflammatory diseases, characterized by increased concentrations of proinflammatory cytokines like interleukin-6, tumor necrosis factor - α , and leptin. Leptin's proinflammatory role suggests that it may link energy homeostasis to the immune system.^{4,5}

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Ghrelin is a peptide hormone that stimulates appetite, fat production, and body growth, leading to increased food intake and body weight. It is secreted into the circulation from the stomach, but is also synthesized in a number of other tissues, including the kidney, pituitary, and hypothalamus, suggesting that the hormone has both distant and local (endocrine and paracrine) effects. These effects include stimulating the secretion of growth hormone, prolactin, and adrenocorticotrophic hormone, and a diabetogenic effect on carbohydrate metabolism.⁶

THE NEW STUDY

In this study of 1,024 participants in the population-based Wisconsin Sleep Cohort Study,⁷ Mignot and colleagues found that in persons sleeping less than 8 hours, increased BMI was proportional to decreased sleep.³ The researchers also found that shorter sleep times were associated with increased circulating ghrelin and decreased leptin, a hormonal pattern that is consistent with decreased energy expenditure and increased appetite and obesity.

These findings confirm earlier clinical reports on the effects of sleep deprivation and extend them to include naturalistic sleep in a large, community-based population. The study provides an exciting addition to the growing literature showing relationships between sleep curtailment, metabolic hormones, and metabolic disorders (including obesity). The data have important implications for our understanding of obesity and related disorders in the general population, with one caveat: the study population was enriched with snorers, making the results less applicable to a general population.

Mignot and colleagues' data are in accord with human and animal studies that show that experimental curtailment of sleep leads to lower levels of leptin^{8,9,10,11} and increased ghrelin.¹² The new study therefore lends some support to the interpretation that reduced sleep levels cause the hormonal changes.

But there is also evidence of opposite effects—that is, that administration of leptin¹³ and ghrelin can alter sleep. Ghrelin administration has been found to increase non-REM sleep in

humans and mice, possibly via its interactions with the sleep-inducing peptide growth hormone releasing hormone (GHRH). Ghrelin is an endogenous ligand of the growth hormone secretagogue receptor, making it a candidate for an endogenous sleep-promoting factor.¹⁴ Mignot and colleagues' study is congruent with the idea that inadequate sleep enhances ghrelin secretion, which in turn acts as an endogenous sleep factor in humans. This is an important new area of research that could conceivably lead to more physiological sleep aids than are currently available, with profound implications for improved public health.

Overall, the available studies suggest the presence of reciprocal interactions between metabolic hormones and sleep, relationships that are poorly understood at present. Does sleep interact with metabolic hormones directly or via intervening factors such as sleep-related breathing disorders? Patients with obstructive sleep apnea have impaired sleep and higher ghrelin levels than BMI-matched controls, and treatment with continuous positive airway pressure reduces ghrelin to control levels.¹⁵ Although sleep-disordered breathing (SDB) was measured in the present study, the SDB analyses were not shown, making it difficult to evaluate the influence of SDB on ghrelin and leptin in this population.

There is a clear need for well-controlled, population-based studies that allow us to examine multiple relevant factors simultaneously. The present study highlights the importance of shortened sleep in relation to obesity, leptin, and ghrelin, a good start toward this goal.

SLEEP AND PUBLIC HEALTH

Many other important questions remain, such as the roles that other hormones, cytokines, and SDB play in obesity. Many of the unanswered questions have important implications for public health. For example, diabetes, visceral obesity, hypertension, and hyperinsulinemia commonly aggregate together in large populations, and are considered a "metabolic syndrome" that has been linked to SDB¹⁶ and to inflammatory disorders.¹⁷ To what extent does long-term sleep curtailment contribute to these and related public health issues?

The possible role of sleep restriction in autoimmune and inflammatory disorders is of particular interest in light of recent findings linking immune function with ghrelin and leptin. Ghrelin and its receptor are expressed in human T-lymphocytes, where they can inhibit cytokine activation, including interleukins, tumor necrosis factor- α and leptin.¹⁸ Conversely, leptin stimulates cytokine activation and immune-cell proliferation, an effect that predisposes to inflammatory conditions.⁴ Is it possible, then, that sleep-related changes in leptin and ghrelin influence the development of metabolic and immune disorders? Can biologically restorative sleep reverse disease progression? Can biologically restorative sleep be defined on the basis of metabolic hormone responses? Future research may answer some of these and other questions, further elucidating the role of sleep in public health.

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Evaluation of the VapoTherm 2000i Humidifier for Delivery of Continuous-Flow Nasal CPAP in Infants

T.E. Bachman, MSHA

ABSTRACT

Nasal CPAP has become an important respiratory support modality in the acute care management of infants. Evidence supports its use as a standard of care for weaning infants from mechanical ventilation. Nasal CPAP is most effectively applied in neonates using systems that have been especially designed to optimize the stability of CPAP levels and reduce work of breathing by varying the flow rate during the respiratory cycle. Older approaches provide a continuous flow through nasal or nasopharyngeal cannula, but have been demonstrated to be less safe and less effective than variable-flow devices. Despite the strong evidence and corresponding practice recommendations, some practitioners continue to utilize continuous-flow nasal CPAP with neonates using cannula. A novel neonatal humidification system has recently become available from VapoTherm. Though not promoted by the manufacturer for this off label indication, anecdotal information suggests that the VapoTherm 2000i is being used to provide nasal CPAP to infants.

We compared the VapoTherm 2000i (CF) to the VIASYS Infant Flow system (VF), a commonly used variable-flow system. We used a bench nasal CPAP simulator at three different respiratory patterns and a CPAP level of 5 cm H₂O. The swings in pressures, a function of respiratory work, seen during the respiratory cycle were clearly larger for the continuous-flow device than the variable-flow device. The peak pressures during exhalation were significantly higher with the CF than the VF ($p < 0.01$), suggesting increased work of breathing for the CF approach. Likewise the pressures during inhalation were significantly less with the CF than the VF ($p < 0.05$), suggesting potential for de-recruitment during inhalation.

These tests confirm some of the established limitations of continuous-flow nasal CPAP application in infants and suggest

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that its application with the VapoTherm 2000i humidifier would result in suboptimum clinical outcomes as similarly reported for other continuous-flow nasal cannulas.

INTRODUCTION

First reported by Gregory over 30 years ago,¹ nasal CPAP has become an important respiratory support modality in the acute care management of infants. Evidence supports its use as a standard of care for weaning infants from mechanical ventilation.² In addition, nasal CPAP is also used by some neonatologists to avoid intubation.³ In 1988 Moa and Nilsson reported on the development of a novel variable-flow nasal CPAP system.⁴ Their device's instantaneous variation of flow during the respiratory cycle results in a significantly more stable CPAP level compared to the earlier approaches, which provide a continuous flow through nasal and nasopharyngeal cannula or prongs. This type of variable-flow nasal CPAP system has become widely used. Clinical studies have demonstrated the more stable CPAP level results in reduced work of breathing,⁵ better maintenance of lung volume⁶ as well as improved clinical outcomes.⁷ Despite this strong evidence and corresponding practice recommendations by the Cochrane Collaboration,⁸ some practitioners continue to utilize continuous-flow nasal CPAP in neonates through nasal cannulas.

A novel neonatal humidification system capable of delivering humidified gas at high flows has recently become available from VapoTherm.⁹ This system is only indicated for use for supplying humidified gas and is not promoted by the manufacturer for off label use for nasal CPAP.¹⁰ Nevertheless, anecdotal information suggests that it is being used for this indication. We decided to compare the VapoTherm 2000i (CF) to the VIASYS Infant Flow system (VF) using a bench nasal CPAP simulator.

METHODS

Tests were made at a set CPAP level of 5 cmH₂O and three different breathing patterns using a nasopharyngeal breathing simulator. The nasopharyngeal simulator interface was connected to a Harvard Apparatus Respiration Pump. Tidal volumes were monitored via a Florian NRM 200 infant ventilation monitor placed between the nasopharyngeal

nCPAP- Pressure Swing

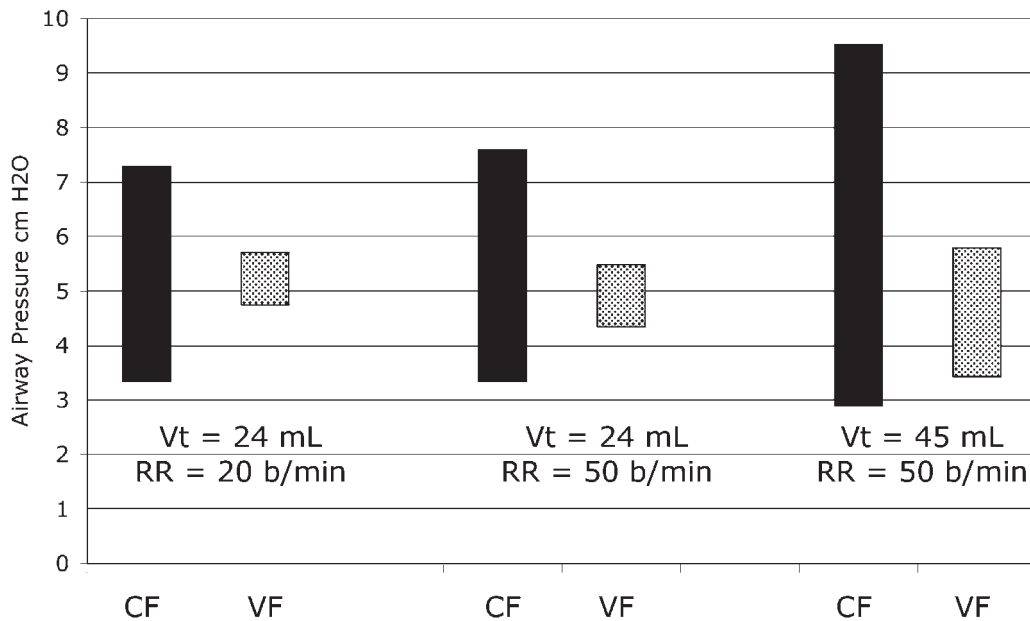


Figure 1: The chart reflects the pressure swings for the Continuous-Flow Vapotherm 2000i (CF) and Variable-Flow VIASYS Infant Flow (VF) systems at three different respiratory patterns. The differences between both the peak and trough pressures between the two devices at each of the three respiratory patterns were all statistically significant.

simulator and the Harvard Respiration Pump. Pressures were monitored with a Tektronix TDS 420A 4 channel oscilloscope.

During testing, a Vapotherm 2000i and an Infant Flow Nasal CPAP driver were set up per their respective operator's manuals. The Vapotherm 2000i was connected to the nasopharyngeal simulator using a Vapotherm infant nasal cannula. The Infant Flow Nasal CPAP driver was connected to the nasopharyngeal simulator via an Infant Flow Generator with nasal prongs. Baseline pressure measurements for each device were made with the Harvard Respiration Pump off. Flow was adjusted to achieve a CPAP level of 5 cmH₂O. Once a stable baseline pressure was achieved the Harvard Respiration Pump was actuated and adjusted to a tidal volume of 24 mL with a respiration rate of 20 breaths per minute. After obtaining data from each device the respiration rate was increased to 50 breaths per minute and data was collected. At the completion of these series of tests the tidal volume was increased to 45 mL and data collection was again repeated at a respiration rate of 50 breaths per minute for each device.

The mean and standard deviation of the pressures were calculated. Differences between means were evaluated with a pooled t-test. Differences in pressures were considered statistically significant if $p < 0.05$. The peak and trough pressures during the respiratory cycle were identified as the primary measure of effectiveness, as they reflect the respiratory work that the infant needs to add to the system to move gas in and out of their lungs. A higher resistance to exhalation from the incoming gas flow is reflected by higher pressures during exhalation that the infant would have to overcome to breathe out. The failure to meet the infant's inspiratory demand is reflected by a greater drop in airway pressure during inspiration. In addition to the changes in work of breathing and resultant respiratory failure, either of these conditions has the potential

for increasing the risk for adverse effects such as air leak, de-recruitment, and gastric insufflation.

RESULTS

The results of our bench tests can be seen in figure 1. Both the VF and CF devices showed some variation in the peak and trough pressure during the respiratory cycle for all three respiratory patterns. At the first setting (Vt= 24 mL, RR= 20b/min) the VF system had a pressure swing of 0.96 cmH₂O, while the CF pressure swing was 3.95 cmH₂O. Both increased slightly when the respiratory rate was increased to 50 (1.14, and 4.26 cmH₂O, respectively). Both systems showed a near doubling of the pressure swing when the tidal volume was doubled and the respiratory rate maintained at 50 (2.37 and 6.63 cmH₂O, respectively).

At all three settings, the peak pressures for the CF system (7.28± 0.39, 7.59± 0.60, 9.52± 0.27 cmH₂O) were significantly higher ($p < 0.01$) than the peak pressures in the VF system (5.70± 0.42, 5.48± 1.14, 5.79± 1.12 cmH₂O). At all three settings the trough pressures for the CF system (3.33± 0.28, 3.33± 0.38, 2.89± 0.28 cmH₂O) were significantly lower ($p < 0.01$, $p < 0.01$, $p < 0.050$ respectively) than the trough pressures for the VF system (4.47± 0.32, 4.34± 0.57, 3.42± 1.19 cmH₂O). Thus our hypothesis that the peak and trough pressures delivered by the two systems are significantly different was confirmed.

DISCUSSION

We found that the swing in pressures seen during the respiratory cycle are clearly bigger for the continuous-flow device than the variable-flow device. The peak pressures during exhalation were significantly higher with continuous-flow than the variable-flow device ($p < 0.01$), suggesting increased work of breathing for the continuous-flow approach. Likewise the pressures during inhalation were significantly less with the continuous-flow than

the variable-flow device ($p < 0.05$), suggesting potential for de-recruitment during inhalation. Our results are similar to bench¹¹ and clinical¹² results reported by others.

While differences in test results can be statistically significant, it is important to assess the clinical significance of that difference. There are no clinical standards for nasal CPAP stability or accuracy with which to compare these results. However, it is generally held that the therapeutic range for nCPAP is between 4 and 10 cm H₂O, and therapy is titrated in 1 cm H₂O increments. With the continuous-flow system, with large pressure swings across most of the therapeutic range, it is reasonable to assume that these differences are clinically important. That supposition is reinforced by the clinical studies showing that variable-flow nCPAP, when compared to constant-flow nasal CPAP results in less work of breathing,⁵ better lung volumes⁶ and improved outcomes.⁸ The much greater pressure on exhalation with the Vapotherm device may explain the similarly reported inadvertent PEEP during nasal cannula applied CPAP.¹²

Most of the evidence supporting the use of nasal CPAP over other approaches to weaning is based on a reduction in the need to reintubate. However, Stefanescu⁸ also reported important reductions in time to discharge, and days of supplemental oxygen.

Finally the large differences seen in this test were collected under really ideal conditions. The clinical environment would introduce more difficulties. The degree of respiratory effort of the patient would affect the leak around the cannula causing more unpredictable nCPAP levels, impossible to control, even if pressure monitoring were available.

CONCLUSIONS

These tests confirm some of the established limitations of continuous flow nasal CPAP application in infants and suggest that its application with the Vapotherm 2000i humidifier would result in the same suboptimum clinical outcomes reported for other continuous-flow nasal cannula approaches.

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Non-Invasive Diagnosis of Acid Reflux Cough Using Aeriflux

Brian Walsh, RRT-NPS, RPFT



Figure 1: Child using Aeriflux Collector

INTRODUCTION

Measurement of the pH of body fluids has a long and successful history in clinical diagnosis. Exhaled Breath Condensate (EBC) pH has recently been added to the list as a useful assessment relevant to lung disease diagnosis and management; proving particularly valuable in the diagnosis of gastric acid reflux into the larynx, retropharynx, and lower airways. The Aeriflux Diagnostic Breath Test from Respiratory Research, Inc (Charlottesville, VA USA) is the only commercially-available product using exhaled breath condensate sampling and analysis specifically for the diagnosis of acid reflux cough. This evolutionary diagnostic system, shown in figure 1, is the product of over six years experience in the emerging field of breath condensates.

Respiratory Research, Inc. has served the global research market including key academic, pharmaceutical, and military/government communities since 2000 with its initial products; the RTube Exhaled Breath Condensate Collector and the Gas-Standardized pH assay for Exhaled Breath. These technologies are being introduced into the clinical market with the Aeriflux Diagnostic Breath Test. This clinical diagnostic combines the proven RTube Collector with a patent-pending usage and interpretation model, all bundled with a gas-standardization and pH assay laboratory service. This unique combination of proven elements provides a robust diagnostic for acid reflux cough.

The Aeriflux opens the path for health care providers to accurately diagnose the underlying cause of cough/wheeze by

Brian Walsh, RRT-NPS, RPFT, has over the last decade served as a Senior Respiratory Therapist at the University of Virginia Children's Medical Center, Charlottesville, quickly becoming Team Leader and then appointed in 2002 by the governor of Virginia as a Respiratory Advisory Board Member, Virginia Board of Medicine. Recent honors include Neonatal/Pediatric Practitioner of the Year - American Association for Respiratory Care, as well as the James P. Baker Award - Virginia Society for Respiratory Care. With over 10 publications and active involvement in several research projects at the University of Virginia, as well as a full clinical schedule, Mr. Walsh continues to expand to the field of Respiratory Therapy.

differentiating acid reflux-induced respiratory symptomatology from airway inflammation in Asthma, Chronic Obstructive Pulmonary Disease (COPD), and Gastroesophageal Reflux Disease (GERD). After accurate diagnosis, proper treatment with anti-inflammatory and/or acid control therapies (such as proton pump inhibition (PPI)) then can be instituted. This new technology delivers diagnostic accuracy with comfortable and safe breath tests.

BACKGROUND

EBC consists primarily of water, with trapped aerosolized droplets from the airway lining fluid, as well as water-soluble volatile compounds. Volatile gases including acids and bases are absorbed by the condensing breath and alter its pH. Measurement of EBC pH after performing a gas-standardization process provides simple and accurate quantification of the acids in exhaled breath. The assay, which is performed by a central Respiratory Research laboratory, has very few and readily controllable confounders, and is immune to effects of sample storage duration or temperature. Importantly, EBC pH reflects changes in acidity of the airway lining fluid as measured by application of a standard clinical (esophageal) pH electrode to airway mucosa, but without subjecting the patient to the risks of an invasive procedure. Acidification of the airway caused by Laryngopharyngeal Acid Reflux Disease (LPRD), with or without aspiration through the vocal cords, readily can be identified with this non-invasive breath pH test. Notably, LPRD is not GERD, but a condition uniquely affecting the airway as summarized in Table 1.

There are strong and unequivocal associations of gastric acid reflux with respiratory symptoms,¹ and excellent data to support that gastric acid reflux frequently precedes respiratory symptoms.² According to a recent paper by Poe, gastric acid reflux-related cough was present in 31% of chronic cough patients, and in 43% of those patients, the gastric acid reflux was silent outside of the respiratory tract.³ Most physicians knowledgeable about gastric acid reflux consider it to be present in the majority of patients with asthma or COPD.

There are no particular history or physical exam characteristics

	GERD	LPRD
Symptoms	Gastrointestinal	Respiratory
Stimulus	Acid in the esophagus	Acid in the pharynx with or without microaspiration
Exposure	pH levels of 2-4 occurring infrequently (exposure time less than 6%) poses little erosive threat to the esophagus	pH levels below 6.5 for any duration can trigger cough, wheeze, hoarseness, airway inflammation, asthma and COPD exacerbations
Therapy	Proton Pump Inhibition (PPI)	Higher dose BID therapy with PPI
Diagnostic	Esophageal pH measurement	Airway pH measurement

Table 1: Comparison of GERD and LPRD

that confidently identify a cough as being caused by gastric acid reflux. The diagnosis of acid reflux triggered cough generally has been established by one or both of the following: presence of acid reflux as identified by esophageal pH probe and/or response to an empiric trial of proton pump inhibitor medications. These methods are compared with Aeriflux in Table 2.

Gastric acid reflux is so common in patients with obstructive airway disease that it is hard to determine causation of cough symptoms when it is present. In patients with respiratory symptoms and pH-probe proven gastric acid reflux, it was not possible to predict which patients would respond to PPI therapy based on esophageal pH probe results (and only 45% with documented gastric acid reflux did respond).⁴ Response to proton pump inhibition may have been the most useful tool. If a patient responds, their cough symptoms were probably caused by gastric acid reflux. However, this therapeutic challenge system is subjective, expensive, and exposes many patients to unnecessary or ineffective medication intervention. These medication challenges are intolerant of the reality that some

Diagnostic Technique	Points of Comparison				Result
	Specificity	Non-Invasive	Physician Preference	Patient Preference	
Esophageal or Nasopharyngeal pH probe					Low-confidence diagnosis, high therapeutic failure
Therapeutic Trial of PPI					Low-confidence diagnosis, high therapeutic failure
Aeriflux™					High-confidence diagnosis, high therapeutic success

LEGEND
 - High / Yes - Medium - Low / No

Table 2: Comparison of Current Diagnostics

patients need higher doses of PPIs to control their respiratory symptoms. It is unclear in the setting of PPI therapeutic failure whether the failure was caused by insufficient acid suppression or whether the cough was never gastric acid triggered in the first place. The varied success and occasional failure⁵ of PPIs in the treatment of respiratory diseases no doubt results from contamination of the study pools with many subjects who do not have gastric acid reflux as a cause of their symptoms.

THE AERIFLUX DIAGNOSTIC BREATH TEST

Aeriflux changes the paradigm of respiratory diagnostics by bringing the test to the patient “on demand” at the time and

place of symptomatic episodes. Aeriflux provides a unique way for physicians to link the occurrence of respiratory symptoms to airway acidification.

Aeriflux is used as follows:

- An Aeriflux kit is prescribed and brief instructions are provided on how to use the kit. Ideally the patient's first collection would be done in the clinician's office.
- The patient then collects six individual breath samples over the next 24-36 hours during symptomatic episodes using simple take-home collection kit. Two additional samples are collected during this period when the patient is specifically asymptomatic.
- Samples are sent to Respiratory Research central lab in the provided prepaid shipping carton
- The laboratory performs the assays and faxes the results with interpretation guidelines directly to the physician

Normative data on pH in the EBC are well-established in hundreds of subjects in the literature and these data are expanding. Any EBC pH below 7.4 is considered low and indicative of an acidified airway. If the patient was coughing or wheezing within the 10 minutes prior to starting the sample collection, a low pH measurement would then be temporally associated with respiratory symptoms. This result is considered “Aeriflux-positive” with a likely diagnosis of acid reflux cough.

The resulting temporal association of these symptomatic episodes with the pH of the gas-standardized exhaled breath condensate uniquely provides the high specificity and positive predictive value of this diagnostic test for acid reflux cough. The key elements of this diagnostic model have been used by EBC researchers for years and were rigorously exercised as part of a study aimed at determining the specificity and positive predictive value of the Aeriflux Breath Test for the diagnosis of acid reflux cough.

To emulate “real world” conditions, 15 patients with cough were enrolled from pulmonary and ENT clinics based on the physician's intention of prescribing proton pump inhibition as a therapeutic trial. Various evaluations of the patients had been performed seeking etiology of the cough. This enrollment criteria fit well with the expected practice in the field, where the test would be used as a targeted diagnostic. Prior to starting the PPI therapeutic trial, each patient performed an Aeriflux test. Neither the physicians nor patients were provided any Aeriflux results throughout the entire study.

The results demonstrated 88% specificity and 100% sensitivity for cough responsive to proton pump inhibition. Patients reporting 75% to 100% subjective improvement in cough symptoms with twice daily PPI at 1-2 months after initiation were considered positive PPI responders. “Aeriflux positive” test results predicted positive response to PPI therapy with high accuracy.

Two typical cases taken from this study illustrate how Aeriflux correctly predicts the outcome of therapeutic trials of proton pump inhibition. The first is an 8 year old boy with chronic cough for 6 months. There was no history of asthma or previous bronchitis, and no family history of asthma nor exposure to tobacco smoke. He had normal spirometry and a negative pertussis study. He had failed therapy with amoxicillin, azithromycin, prednisone, inhaled steroids, and montelukast.

This patient performed collections using the Aeriflux system in his home over 29 hours and express shipped the samples to the laboratory. He then began a planned intervention with the proton pump inhibitor omeprazole 20 mg twice per day. The results from the EBC pH assays are shown in Table 3, and reveal normal EBC pH values for both his “well” samples but 3 out of 6 low EBC pH values in his “cough” samples.

Within 10 days of initiation of omeprazole, the patient experienced complete resolution of his symptoms for the first time in half a year. A repeat Aeriflux sampling series was performed by the patient and revealed no episodes of EBC acidification. This demonstrates that EBC pH measurements normalize with successful intervention with proton pump inhibition (Table 4).

The second case is a 58 year old male with chronic cough. Acid reflux cough was suspected and an “empiric” course of PPI was prescribed as a therapeutic trial. An Aeriflux test was performed prior to initiating the PPI medication. Upon follow up at 2 months this patient revealed no improvement. In review of his initial Aeriflux data, however, we see why PPI did not help. His Aeriflux testing was normal indicating the absence of airway acidification with his coughing (Table 5). Acid reflux was unlikely to be contributing to his cough, and indeed the lack of responsiveness to PPI therapy substantiates the removal of acid reflux cough from the differential diagnosis.

PPI therapy has been successful in treating the substantial percentage of people who do indeed have acid-induced cough. But choosing the right patients in the absence of objective diagnostics such as Aeriflux is not possible. Directing that therapy appropriately is increasingly necessary because of the expense of the PPI medications. Furthermore, the recently elucidated increased risk of community acquired pneumonia occurring in patients on PPIs⁶, has certainly increased concern for more rational prescribing of this class of drugs⁷. EBC pH measures help to identify the patients who have acid-induced cough, by adding a rational, simple and safe tool to the acid reflux diagnostic armamentarium. Simply by measuring acid in the exhaled breath, we now can identify acid in the upper and lower airways.

Aeriflux Diagnostic Breath Test will help logically guide therapy by directing PPI therapy specifically to the appropriate patients, while allowing reduction and potentially elimination of other medication therapies such as steroids, thereby reducing the cost of care while increasing the patient’s quality of life.

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Date	Time	Symptom	EBC pH
12/26/04	1545	Cough	8.3
12/26/04	1745	Cough	5.0
12/26/04	1945	Cough	7.9
12/27/04	1015	Cough	6.0
12/27/04	1215	Cough	7.7
12/27/04	1730	Well	8.1
12/27/04	1930	Well	7.7
12/27/04	2130	Cough	5.8

Table 3: Aeriflux Positive Profile

Date	Time	Symptom	EBC pH
01/15/05	0945	Well	8.3
01/15/05	1630	Well	8.3
01/15/05	2000	Well	8.3
01/15/05	2145	Well	8.2
01/16/05	1015	Well	8.2
01/16/05	1315	Well	7.9
01/16/05	1800	Well	7.8
01/16/05	2045	Well	8.2

Table 4: Aeriflux Negative Profile at follow up.

Date	Time	Symptom	EBC pH
03/9/05	-	Well	7.8
03/11/05	-	Cough	7.9
03/12/05	-	Cough	7.9
03/12/05	-	Cough	7.9
03/13/05	-	Cough	7.8
03/13/05	-	Cough	7.8
03/13/05	-	Cough	7.9
03/13/05	-	Cough	7.9

Table 5: Aeriflux Negative (Normal) Profile

A New Noninvasive Parameter for CO Measurement

INTRODUCTION

Carbon monoxide (CO) is a colorless, odorless, and poisonous gas that kills or permanently harms thousands of people each year. It is the leading cause of accidental poisoning in the US. Approximately 500 people die annually from unintentional CO exposure, and there are more than 40,000 reported emergency department visits resulting from CO poisoning each year.

Carbon monoxide is a byproduct of combustion, with the most common sources including fire, exhaust from automobiles, gas furnaces and ovens, propane and kerosene heaters, and charcoal grills. Carbon monoxide is harmful when inhaled because it binds to the hemoglobin in red blood cells 200 times more strongly than oxygen carrying capacity of the blood, thereby reducing the amount of oxygen delivered to the tissues and vital organs.

Carbon monoxide poisoning can be very difficult to diagnose unless the poisoning is the result of exposure to an obvious incident such as fire or intentional exposure to exhaust fumes. The initial symptoms of CO poisoning are similar to other less critical conditions such as the flu or fatigue and include shortness of breath, chest pain, headache, fatigue, dizziness, drowsiness, and/or nausea. During prolonged or high exposures, symptoms can worsen and include vomiting, confusion, muscle weakness, and loss of consciousness. The symptoms of CO poisoning may occur sooner in those most susceptible: the elderly, very young, people at high altitude, people with existing heart or lung conditions, or those who already have elevated CO blood levels (COHb) for example, smokers. CO poisoning can be reversed if caught in time. However, even if the patient recovers, acute poisoning may result in permanent damage to vital organs and pronounced neurological deficits.

Methods for accurately measuring CO poisoning have been limited to invasive blood tests analyzed by blood gas machines with CO-Oximetry measurement capability. While many hospitals have blood gas machines with CO-Oximetry, many smaller hospitals do not, which makes confirmed diagnosis of CO poisoning in these situations impossible. Outside the hospital there is no method to measure CO poisoning, and pre-hospital clinicians have had to rely on a high degree of clinical

suspicion, general patient condition, and environmental factors to make treatment decisions. With lives and significant resources at stake, making the right decision is critical. A quick noninvasive measurement of COHb may direct, enhance, or alter medical treatment or transport decisions. From an Emergency Department worker treating a patient complaining of flu-like symptoms to the EMS clinician at a 911 call or firefighters at a fire scene, the immediate measurement of COHb will expedite treatment decisions that should lead to improved patient outcomes.

Masimo Corporation has responded to the need for quick, noninvasive measurement of COHb with the development of Masimo Rainbow SET Rad-57 Pulse CO-Oximeter. Many years of engineering research have gone into the development of Masimo SET Rainbow technology. Drawing upon years of pulse oximetry experience gained during the development of Masimo's revolutionary Signal Extraction Technology, Masimo utilized its expertise in sensor, algorithm, software and hardware design to create Masimo Rainbow SET Pulse CO-Oximetry. Rainbow technology's accuracy in measuring CO in the blood (COHb) was examined during a large clinical trial. The following sections will describe the study and its results.

METHODS

One hundred sixty (160) volunteers were tested for normal and elevated COHb levels. Levels of greater than 15% COHb were caused by very excessive smoking in volunteers with a substantial smoking history that has resulted in elevated COHb baseline levels. Each subject had Rainbow DC-I digit sensors attached to as many as 4 digits. The sensors were connected via patient cables to Rainbow SET Pulse CO-Oximeters. The data from the Pulse CO-Oximeters were fed into a laptop computer to continuously log oxygen saturation (SpO₂), Pulse Rate (PR), and carbon monoxide saturation (SpCO). [NOTE: SpCO is defined as COHb that is noninvasively measured via Masimo's Signal Extraction multi-wavelength pulse CO-Oximeter.] Once a stable baseline for SpO₂, Pulse Rate, and SpCO was achieved, a venous sample of blood was drawn. The blood was immediately analyzed on an ABL 700 series Blood analyzer with CO-Oximetry, which measures Hb, O₂Hb, COHb, and MetHb. All

were healthy volunteers, although many were enrolled in the study because of their significant smoking history and corresponding elevated COHb levels.

RESULTS

To help ensure that any subsequent statistics were unbiased, there was a need for an equal distribution of COHb data in the instrument's calibration range. To accomplish this, samples were entered into 5% bins for COHb. Each bin was filled to approximately the same number of samples. In this study, four hundred fifty-two (452) blood samples were analyzed for COHb and contrasted against SpCO measurements obtained by the Rainbow SET Pulse CO-Oximeters. The range of values was 0.9 to 39.9%. The bias and precision for the difference between SpCO and COHb were -0.2% and 2.8%, respectively.

CONCLUSION

The results show the Masimo Rainbow SET (Pulse CO-Oximetry) accurately measures COHb in the range of 0 to 40%. This accuracy, combined with the ability to place the technology in a small handheld device (the Rad-57), has the potential to change the way victims of CO exposure are diagnosed and treated. Because the Rad-57 is easy to use and provides accurate measurements of carbon monoxide saturation, oxygen saturation, pulse rate, and perfusion index, it is the ideal patient assessment tool for first responders, fire department personnel, and emergency department personnel, as well as safety personnel in areas of high industrial pollution and automobile exhaust.

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The Ferraris PiKo-1 Electronic Peak Flow/FEV1 Meter is a very small and easy to use device for measuring and monitoring a patient's expiratory performance. Powered by two button-style batteries, it provides a digital readout of Peak Expiratory Flow Rate (PEFR) and Forced Expiratory Volume in 1 second (FEV1). It also incorporates a Green-Yellow-Red scale on the display which can be used to correlate with an asthma action plan if a reference value is set for PEFR. Setting the reference value is simple once an appropriate reference value is determined.

The device arrived with the required two button batteries and English and Spanish instruction manuals. It also included an English Personal Asthma Plan to be completed by the patient's physician or health care professional (based on NAEP Guidelines). The front of this Personal Asthma Plan has definitions of the Green, Yellow, and Red zones and instructions for what action to be taken for each range. The reverse has a graph to track Peak Flow, symptoms, and sleep quality.

The device is simple to use, with only a single control button. To turn the unit on, press the button once and the digital display presents the last test values, alternating between PEFR and FEV1. To begin a test, press the button again (the unit will beep) and after a second beep, take a deep breath and forcefully blow into the mouthpiece. Results of the effort are immediately displayed in the results window, again alternating between PEFR and FEV1. An exclamation point (!) to the right of the results indicates a possible Quality problem ("Q factor"). This can be either a) a cough detected during the effort, b) the expiratory effort was too short, c) the expiratory effort had a slow start, or d) the result was suspiciously low or high for your reference value. A triangle-shaped marker is displayed along the green-yellow-red bar at the top of the display, indicating which NAEP asthma zone the effort falls into.

If you perform multiple efforts, the PiKo-1 will select and retain the best of all efforts performed within 3 minutes. The PiKo-1 can store and redisplay up to 96 tests. In addition, optional PiKoNET Asthma Management Software is available, with an installation CD, interface cradle, and manual. It requires a PC with a minimum Pentium III running Windows 98, Windows ME, Windows 2000, or Windows XP. The software was simple to install and transferring results from the PiKo-1 is straightforward using the infrared (IR) transfer cradle. The PiKo-1 has a small IR transfer window on the bottom which aligns with the IR receiver in the cradle. A couple of mouse-

clicks and pushes of the PiKo-1's only button, and the data is transferred to your PC for display.

The PiKo-1 is not designed or intended to be used as a diagnostic device, but rather as a monitoring device for detecting trends and dramatic changes. The manual indicates that its accuracy for PEFR is 6.5% or 15 LPM (whichever is greater) and for FEV1 is 4% or 0.1 Liter (whichever is greater). In a simple comparison study, the PiKo-1 was placed in-line downstream of the sensor of a diagnostic pulmonary function system. Ten simulated efforts, with PEFR ranging from 86 LPM to 605 LPM and FEV1 ranging from 0.75 to 3.04 Liters, were made. For PEFR, the PiKo-1 performed within its printed range of agreement in all ten simulated efforts. For FEV1, the PiKo-1 disagreed with the pulmonary function system by more than its printed range of accuracy in four of ten trials, even allowing for a possible 3% variance in the pulmonary function system results. The greatest disagreement was 6.9%. While I would have liked to see the unit always meet its printed accuracy ranges for both PEFR and FEV1, this modest shortcoming should not adversely affect the usefulness of the device for its intended use.

The mouthpiece can be removed for cleaning. The upper portion of the unit, through which the air flows, can be cleaned with low-pressure, cool water and mild liquid dish soap, although the unit should not be immersed in water. As far as toughness of the unit, be aware that a single fall from desk height to a tile floor rendered one of the two evaluation units inoperable; the other unit survived a similar drop to carpet and tile. The PiKo-1 probably should not be considered "rugged." Keep in mind this product is designed to replace Mechanical Peak Flow meters and it is in the same patient price range.

The manual (really a pamphlet) is quite small and some patients will have difficulty reading the tiny print. The size of the manual makes sense given the small size of the device, but it is a potential problem. Fortunately, the manual can be downloaded from the Ferraris website (<http://www.ferrarisrespiratory.com/usa/support/manuals>) and printed in full page size. Manuals in other languages can be found on the website by clicking "Support" and "Users Manuals."

In summary, the PiKo-1 is an easy to use device for measuring and trending expiratory performance for folks with asthma or other obstructive lung disorders. It is sufficiently accurate to allow meaningful trending and detect critical dramatic changes, especially in PEFR. Its small size makes it easy to take on a variety of travels for ongoing monitoring. The PiKo-1 is recommended the next time you are in the market for a Peak Flow monitor. The Ferraris Respiratory website is located at www.ferrarisrespiratory.com.

The author is Director of Respiratory, Neurology and Sleep Disorder Services, North Mississippi Medical Center, Tupelo. He recently took a look at the PiKo-1 Electronic Peak Flow/FEV1 Meter from Ferraris Respiratory.

Creating a Ventilator Management Protocol

A discussion about adult mechanical ventilation with Mikel O’Klock, RT, RCP, Staff Development Coordinator, and Dennis Harker, RRT, RCP, Manager, Respiratory Care, Genesis Medical Center, Davenport IA

What were the steps for developing a protocol in the respiratory department?

Over a year ago we formed a committee to look at convenience through accessibility for our patients. We had a lot of long-term patients on ventilators. This was identified as a costly service, a money-loser. We would have patients who would sometimes be on a ventilator for months at a time. Iowa doesn’t have many referral sites for long-term ventilation patients, so we formed a committee that included administrators, respiratory therapists, nursing staff, pulmonologists and other departments. The committee would look at developing an entire process to move these patients through the system more quickly, getting them out to referral sites, looking at what we could do to improve their quality of care. As respiratory therapists, our assignment was to research the protocols that are in use throughout the country and to come up with the best practice.

One element of writing a protocol is that you’re basically developing criteria for the therapists to operate within, and in addition you’re trying to hit a broad patient population. It’s one thing to write a protocol, but quite another to have a protocol that works over an extended period of time and that hits the majority of the patient base. As we started writing the protocol, we decided to call Mike Gentile at Duke University and Dr. Neil McIntyre, medical director for the respiratory department at Duke. Dr. McIntyre co-authored an article which presented scientific evidence about ventilator weaning and discontinuation. The challenges in developing a weaning protocol were presented to Mike Gentile, who informed us that Duke’s respiratory department had an adult ventilator protocol, as opposed to a weaning protocol. He was more than happy to send us the protocol so we could adapt it to our facility. The protocol was presented to our weaning committee, comprised of a majority of our pulmonologists and representing every department that handles ventilated patients. It was decided to adopt that protocol for the Genesis Medical Center, with a few minor changes, and we proceeded with a pilot program.

Why did you request the Respironics NICO monitor to assist in ventilator management?

We had to monitor CO₂, so we tried different monitors, and one feature of the Respironics Cardiopulmonary Management System is that it monitors hemodynamics noninvasively. As such, we can monitor cardiac output, cardiac index, stroke volume, and vascular systems, which allows you to see how outpatients are doing in terms of perfusion and hemodynamics. One of the problems a therapist has to assess is the severity of a patient’s condition when that patient is on the ventilator. The therapist knows when the patient’s condition is severe enough for intubation and placement on a ventilator, but they don’t know the degree of severity. The Respironics NICO

Cardiopulmonary Output monitors tells you how severe the patient is and whether you have a perfusion problem, a ventilation problem, or both. It also indicates if the patient’s condition is improving or becoming worse. The protocol states that you can’t begin the weaning process until you see improvement in the patient, which is indicated by chest x-rays. While therapists perform numerous functions, many are not proficient in reading x-rays, so the NICO has a graphic called “single-breath CO₂.” By plotting, it will actually show any improvement or worsening of the patient’s condition. It will also indicate if you have a perfusion or a ventilation problem. By entering blood gases, the NICO provides a VDT, a ratio of ineffective to effective ventilation, so you know how much ineffective ventilation you have to overcome, or how much work of breathing will have to be performed if you discontinue ventilation or extubate the patient. So not only does the NICO monitor cardiac output and hemodynamics, it also gives you a volume of CO₂ to blow off every breath, and end-tidal CO₂. It provides data on end-tidal CO₂, VCO₂, and a volumetric capnogram, and you can also calculate a patient’s calorie intake. Many end-stage COPD patients cannot be overfed or underfed, so a number of pulmonologists are requesting information about kcals per day. There is a quick formula the therapist can enter into the NICO to get the appropriate information. We chose the NICO over other end-tidal CO₂ products because it provides so much information to the therapist and physician.

What have been the benefits of the protocol?

From a department manager’s perspective, the benefits have been wonderful. First, we have improved staff satisfaction. Our employees feel that their skills are being valued and respected by the physicians, the nursing staff, the organization, and the patients. The nursing staff and physicians are very satisfied because they are part of a team approach. We work closely with nursing in adjusting sedation. We’ve been able to walk into a patient’s room, see changes on the monitor and tell the nurse, you need to come in, this patient is going to code, which the nurse did, two minutes later. There’s a lot of interest and excitement about the program. This is the first time in several years that we have no staff openings. Because of what we are doing here, as a result of such a high degree of quality and advanced technology, recruitment has been enhanced. Students and therapists are hearing about the program and they want to be here. As a result the department is fully staffed. The protocol has also reduced the amount of overtime, which is cost-effective for the department and the hospital.

Another advantage of using the NICO is that we’ve had to buy less equipment. Normally, on our ventilator replacement program, we buy one or two new ventilators each year, the idea being that we stay state-of-the-art: as equipment wears out, we

replace it. This year, because of the huge decrease in ventilator hours, many of our ventilators were sitting in the storage room. As a result, we didn't put them in our budget, which helped us get our requests approved to buy more NICOs. We now have ten, nearly one for every patient on a ventilator. In the next fiscal year we plan to request more, and we are looking to use the NICO as a prognostic indicator to perform some pre-op studies.

With regard to critical care beds, we didn't have any diversion this year because we were able to get our patients out of the ICU quicker. This meant we had more patients coming through; as a result, the fiscal line for the hospital has improved. Physicians are excited because they can contact the therapist and know exactly what's going on with a patient. We are also working with Respirationics on testing the capabilities of their product and working with its clinical experts on what we have discovered. We are also seeing the therapist's skills and attitude improve greatly. We have had ventilator-associated pneumonias, and we're seeing a decline in our VAPs, which is beneficial, as a VAP costs the hospital around \$25,000. Getting the patient off the ventilator sooner has resulted in a decline in VAPs.

Describe the pilot project in the ICU

We started in surgical intensive care. During a pilot program, you want to develop the therapist's skill and get the physicians, then the nurses, accustomed to the protocol. We covered the education with the RTs and educated the nursing and diet support staff. For the pilot program, we spent more than a month and a half in the surgical ICU, then we moved to the medical ICU. By July 2004 we had control over all three ICUs and the therapists became accustomed to the protocol. This protocol and the NICO completely changed how we looked at things. We no longer use SIMD, which was a popular mode here, so the therapists had to get accustomed to that. We were taking them from a control mode to a support mode. One problem is, when do you know when to do that? This was another element the NICO supplied us with. Then, we concentrated on understanding more about breathing: for instance, how is the patient tolerating what we are doing for them? This was also indicated by the NICO, which gives you an alveolar ventilation and a VCO₂ every minute, so you can see if the patient is tolerating the treatment. We also used a rapid self-breathing index to put a numeric figure on the breathing. As a result, after three months of the pilot program, all three ICUs had been monitored and statistics were recorded for the fiscal year.

What was the outcome of the pilot program?

The outcome was notable on many levels. One outcome was that the length of stay decreased dramatically for the patients on ventilators. We compared statistics with the year we started the protocol, July 2004 to July 2005, with statistics from the previous years. We went back and looked at the statistics for the past four years to see what kind of dramatic changes there were. We found that we were able to decrease the average length of time a patient was on a ventilator by 49%. The average number of hours all our patients were on vents in 2001 was over 105,000. Last year we decreased that to 48,000. From 2001 to 2005, that's a huge difference. We looked at cost savings to the patient, excluding ICU, nursing, equipment and supply charges, and we were able to save patients \$1.5 million for ventilation in one year. Estimates in the literature recommend about \$5,000 per ventilator per day as the hospital's cost. We had a total of 710 patients on ventilators. We cut out a huge number of days, so we figure we saved about \$7 million. Also, we used to have

many long-term patients, three to four at a time, and we have a step-down unit that takes ventilator patients. Though it's not long-term care, it's still acute care, and a money-loser for the hospital. However, after we started the protocol, the number of ventilator patients we transferred to that unit dropped to almost zero. Another outcome is, because of the value of the figures we were using and the criteria we were using to get patients off ventilation, our reintubation rate has dropped down to a little less than one percent. We've had patients who, in the past, given their negative inspiratory force, respiratory rate and forced vital capacity, we would never have attempted to get off the ventilator. Now we're seeing, from the data from the monitors, that we are able to get them off. We had one patient who had only a third of their lung capacity left, 67% was dead space ventilation—a COPD patient. That patient is now off the ventilator and in our pulmonary rehab program, which is just amazing. We're looking at getting patients off ventilation who wouldn't have had a chance before. We are finding that if we get them off sooner, they're in better condition, they haven't had muscle loss or atrophy, their nutrition is better. We have had referrals from other hospitals where the patients had been on a ventilator for two or three months, and within five days we had them off. Their families were ecstatic. So we can't measure some of the positive outcomes, but it has been great, and that's where we are with most of the outcomes we've had.



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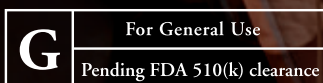
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