Volume 9 Number 5 October-November 2014

Respiratory Therapy™

The Journal of Pulmonary Technique

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DEPARTMENTS

ARTICLES

The Importance of Leadership Rounding

Today's respiratory care directors, educators, and even front-line coordinators are often inundated with a plethora of regulatory and institutional responsibilities and duties. Granted, in order to thrive, many of these responsibilities are critical to the development and function of today's respiratory care department. However, visible leadership is also crucial in maintaining a strong and thriving department. These administrative responsibilities and duties frequently contribute to extra office time and reduce clinician time availability.

Usually department leadership is composed of clinical experts with a cornucopia of clinical experiences. Many of these leaders were excellent bedside clinicians with expertise in patient management, technology utilization, and problem solving. Their expertise should not be subject to dormancy but available for staff to utilize to optimize patient outcomes.

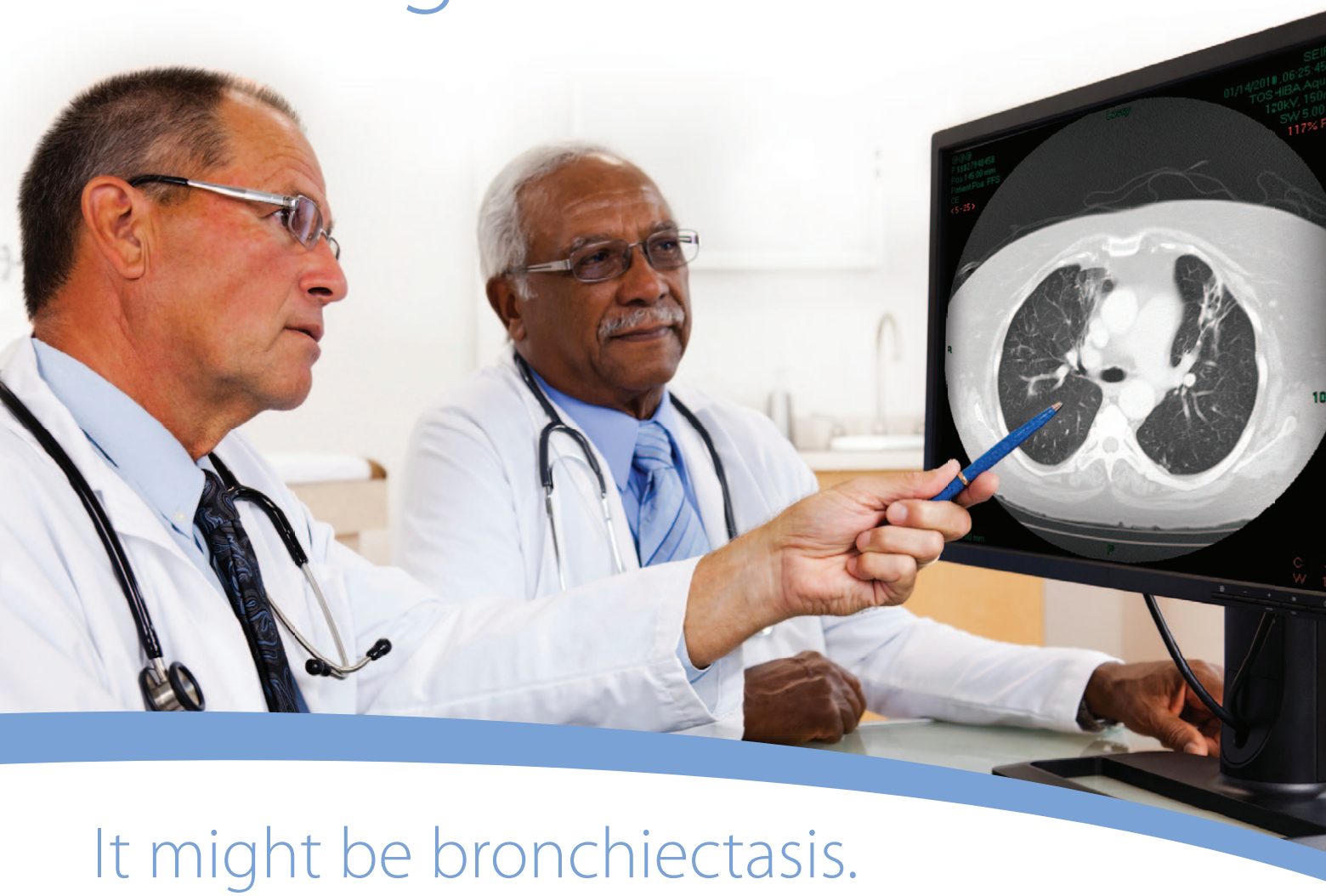
Currently the majority of respiratory care practitioners at the bedside are often new graduates or those who have limited clinical expertise or diverse experiences. The proficiency of care and knowledge of technology administration of department leaders can enhance and facilitate the learning processes of the "greenhorn" staff. As well as demonstrate the worth of the respiratory department in tough or unique clinical situations.

Other benefits from rounding with the clinical staff is it shows that the leaders understand the staff's working environment, what they are subject to and/or managing as well as the staff's responsibilities. This is vital for "seasoned" staff who often feel neglected. Rounding allows for the "teachable moment" which can be invaluable in the growth and learning of unseasoned clinicians. These bedside situations can strengthen the leader to staff relationships and help foster future communications. Leaders should incorporate daily rounding into their daily schedules, not just to collect QA data, but to engage and support their bedside staff.

Daily rounding should be a goal for all department leaders. Being prisoners to their offices will get assignments completed but a valuable part of being a leader will be squandered. The staff depends on leadership's expertise and knowledge, keeping it held captive in their offices, will prevent the department from reaching its highest summit of success.

Kenny Miller
Kenneth Miller MEd, RRT-NPS, AE-C
Educational Coordinator
Dean of Wellness
Respiratory Care Services
LVHN

Do you see it?
Look again.



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Targeted Neonatal Echocardiography (TNE) in the Neonatal Intensive Care Unit

Azif Safarulla, MD, Aysha Syed, MD, and Muhammad Aslam, MD

With advancements in neonatal care, the role of echocardiography has changed remarkably over the last few years. It has transitioned from echocardiograms being performed by pediatric cardiologists to diagnose and monitor congenital heart disease (CHD) and patent ductus arteriosus (PDA) to being used by neonatologists of late as a tool for assessment of hemodynamic instability. This wave of change has been spawned by an increasing awareness and desire to better manage neonates as well as due to the unavailability of pediatric cardiology services in certain remote areas in the United States and Europe.

Dr Mertens and associates published the following article in 2011, "Targeted Neonatal Echocardiography (TNE) in the Neonatal Intensive Care Unit – Practice guidelines and recommendations" in the European journal of echocardiography. This article examines the current trend of TNE being performed by non-cardiologists. It clearly defines what constitutes TNE and indications for the same, the practical applications, and more importantly establishes realistic guidelines on how to create and maintain quality in recording and interpreting data which is in accordance with standards set by the American Society of Echocardiography, European Association of Echocardiography and Association for European Pediatric cardiologists. These guidelines include a training period of 4 to 6 months dedicated to pediatric echocardiography with performance of at least 150 studies and interpretation of 150 additional studies to achieve core/basic training to perform TNE; and an additional period of 4 to 6 months dedicated to performance of 150 neonatal echocardiographic studies and review of an additional 150 studies to achieve advance training to perform and independently review TNE.

Understandably with the emergence of this new entity called TNE there is a lot of concern in the pediatric cardiology community in terms of potential to miss an infant with a critical CHD, maintaining quality of studies, losing exclusivity, challenge to income, medico-legal implications to name a few. The most important aspect of TNE is that it is NOT intended to be a substitute for evaluation of a neonate with a suspected CHD which rightfully should be assessed by a pediatric cardiologist and imaged by personnel trained in pediatric echocardiography. TNE should be viewed as an extension of clinical assessment which would enable the non-cardiologist to better understand and manage the changing hemodynamics in a neonate in the first few days of life which often is the most critical time. In addition, it has other applications in terms of assessing organ blood flow, suspected effusion (pleural, pericardial), position of central line, ECMO cannulae, etc. As our clinical knowledge expands, the applications will continue to evolve. In case of patient with a strong clinical suspicion of CHD, significant PDA, systemic hypotension, the initial assessment should be done by comprehensive echocardiography to rule out CHD. Once ruled out, follow up studies can be performed by personnel sufficiently trained in performing and interpreting TNE.

In conclusion, TNE has arrived at the scene and it is here to stay. TNE is an extremely useful tool which if utilized in the appropriate manner will enable clinicians to better manage neonates in an array of clinical situations. It represents an opportunity for the Neonatology and Pediatric Cardiology to work together to improve clinical care and for cardiology to take a leadership role in properly training and maintaining quality of information obtained via TNE.

Dr Safarulla is a Neonatal-Perinatal Medicine Fellow at University of California Irvine (UCI) School of Medicine and UCI Medical Center. Dr Syed is a Pediatric Resident at Sinai Children's Hospital, Chicago. Dr Aslam is an Associate Professor of Pediatrics at UCI School of Medicine and a staff Neonatologist and Director of Education and Scholarly Activities, Division of Neonatology, Department of Pediatrics at UCI Medical Center.

News

■ October-November 2014

Emergency Oxygen Helps Hikers Struck by Lightning

The important of emergency Oxygen was driven home during the summer after a group of three hikers were struck by lightning in Glacier National Park in Montana. Luckily, other hikers arrived quickly to find the trio unconscious and not breathing. The hikers began performing CPR and the first park personnel arrived to immediately administer emergency oxygen to all three victims before they were taken from the park by ambulance and helicopter to hospital. Observers believe emergency oxygen was crucial to the three hikers' survival, in addition to CPR. The American Heart Association recommends giving supplemental oxygen to victims in a wide variety of emergency situations, including shock. When a serious emergency occurs, the body's blood/oxygen concentration balance may be compromised, requiring the use of Emergency Oxygen to improve the victim's outcome. For 28 years, LIFE Corporation has manufactured superior emergency oxygen units, for all public places to be equipped with units available in time for use in an emergency.

Huge Growth for Home Medical Devices

US demand for home medical equipment is forecast to grow 8.2 percent annually to $12.6 billion in 2018, according to a new market research report by Reportlinker.com. Advances in the technological capabilities of products such as portable oxygen concentrators and remote telemedicine systems, will underlie growth. The introduction of new and improved devices and equipment will expand the number of medical conditions and patients adaptable to effective home treatment, management, and monitoring. Cost-saving advantages will promote the increasing substitution of home health care for hospital, ambulatory, and nursing home procedures whenever feasible. Among all types of home medical equipment, remote monitoring and real-time systems based on telemedicine technology will generate the fastest revenue growth as physicians, hospitals and other medical providers are pressured by health insurers to become more accountable for improving patient outcomes and controlling treatment costs. By contrast, demand for conventional patient monitors will expand at a below-average pace due to competition from telemedicine devices. A rising prevalence of chronic conditions, especially respiratory disorders, kidney failure, and cancer, will boost demand for home therapeutic equipment—the dominant product segment—up at a strong annual pace through 2018. Portable oxygen concentrators for treating chronic obstructive pulmonary disease (COPD), continuous positive airway pressure (CPAP) products for managing obstructive sleep apnea, and ventilators and accessories for alleviating severe breathing impairments will exhibit the fastest growing sales among home respiratory therapy equipment.

Improve Air Quality to Reduce Tuberculosis Transmission

Researchers are saying that increasing low-cost, WHO-compliant natural ventilation will result in healthy indoor environments and reduced risks of tuberculosis transmission. Scientists studying the role of room ventilation in tuberculosis transmission found that students in Cape Town, South Africa, spend almost 60 percent of their day in poorly ventilated rooms, at risk of transmission, according to results published in the open access journal PLOS ONE by Eugene Richardson from Stanford University School of Medicine and colleagues. Despite biomedical improvements to treat tuberculosis, the incidence in South Africa continues to increase. TB spreads through the air, and children attending school may be particularly vulnerable to the disease because they are required to spend large amounts of time indoors

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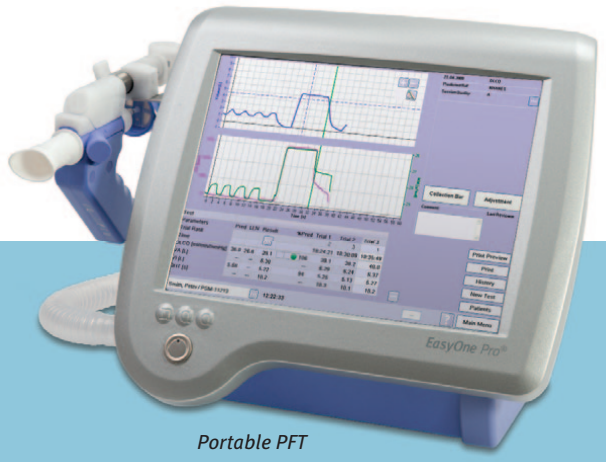

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in classrooms. Over one school year in a high school in Cape Town, South Africa, scientists assessed the role of schools and 'air hygiene' in TB spread or prevention by monitoring CO_2 in classrooms—using sensors carried around by students. In the study, the authors first calculated 1000ppm as the indoor CO_2 concentration threshold above, which indicates a high amount of rebreathed air and increased risk of TB transmission. This level falls in line with regulations in other industrialized nations.

Long-acting Inhaler Approved With Warnings

The FDA approved once-daily bronchodilator, olodaterol (Striverdi Respimat), for maintenance treatment of chronic obstructive pulmonary disease. Approved indications for the long-acting beta-adrenergic agonist (LABA) drug included long-term use in cases including chronic bronchitis and emphysema with airflow obstruction. The agency warned that olodaterol shouldn't be used in rapidly deteriorating cases or for rescue therapy in acute bronchospasm. It can cause serious side effects, including narrowing and obstruction of the respiratory airway (paradoxical bronchospasm) and cardiovascular effects, the FDA said. Olodaterol hasn't been proven or approved for treatment of asthma and carries a boxed warning that drugs in the LABA class increase the risk of asthma-related death, the FDA said.

Pulmonary Fellowships Made Available

El Camino Hospital and the Palo Alto Medical Foundation are collaborating with the UC San Francisco Fellowship Program to offer the first interventional pulmonology fellowships on the West Coast. Interventional pulmonology is an emerging field within pulmonary medicine that focuses on the use of advanced diagnostic and therapeutic techniques to treat patients with lung cancer, airway disorders and pleural (lung) diseases. The joint interventional pulmonology program is among the 15 nationwide that provide diagnostic and therapeutic services and cutting-edge treatment in pulmonary medicine. The National Resident Matching Program matches medical school students, residents and fellows with their preferred specialties based on a rank order list. There are 14 fellowship positions available in interventional pulmonology nationally.

Application Accepted by FDA

Boehringer Ingelheim Pharmaceuticals, Inc. has announced that the New Drug Application (NDA) for its investigational compound nintedanib has been accepted for filing by the US Food & Drug Administration and granted Priority Review designation. The application for nintedanib is currently under review for the treatment of people with idiopathic pulmonary fibrosis (IPF), a rare, progressive and fatal lung disease that affects as many as 132,000 Americans. There are currently no FDA-approved treatments for IPF. The efficacy and safety of nintedanib in the treatment of IPF has not been established.

VA Hospitals Add Device

Nonin Medical, Inc., the inventor of finger pulse oximetry, announced with distributor Jordan Reses Supply Company that the US Veteran's Administration (VA) has selected Nonin's PalmSAT Model 2500A handheld pulse oximeter for use in its hospitals. Nonin's PalmSAT Model 2500A is a portable handheld pulse oximetry system with alarms that measures a patient's arterial oxygen saturation (SpO_2) level and pulse rate. It

can be used for spot checking or continuous monitoring. Pulse oximetry measurements can provide clinicians an early warning of hypoxemia.

Medical Company Drives Forward

Drive Medical has announce the acquisition of the business of Medquip, Inc., a manufacturer of healthcare products located in South Carolina. Medquip manufactures nebulizers, respiratory disposable products, pulse oximeters, TENS units, breast pumps and digital blood pressure equipment. The company is perhaps best known for pioneering and developing its AIRIAL line of pediatric nebulizers.

Peer-reviewed Journal Launched

The COPD Foundation, a nonprofit devoted to finding cures for chronic obstructive pulmonary disease, has launched of its new open access, peer-reviewed journal: Chronic Obstructive Pulmonary Diseases: Journal of the COPD Foundation at journal.copdfoundation.org. Responding to the medical community's request for a new COPD journal, the publication will be guided by James D. Crapo, MD, editor-in-chief, National Jewish Health. The journal will feature original research articles, basic and clinical review articles, perspectives and practice guidelines.

COPD Website Revamped

GlaxoSmithKline has launched its redesigned copd.com website, which provides disease education, interactive tools, tips and inspirational testimonials from patients living with chronic obstructive pulmonary disease for an up-close and personal look at managing and living day-to-day with the condition. The revamped site offers user-friendly tools and helpful guidance to enhance patient awareness about COPD. It is uniquely designed to put first-hand accounts by patients at the center of the user experience.

Fixed-dose Combination Studied

Boehringer Ingelheim has presented results of the VIVACITO study, the first Phase 3 data to be reported from the TOviTO clinical trial program, evaluating the effect of the fixed-dose combination of tiotropium and olodaterol (T+O FDC) delivered via the Respimat inhaler on lung function in people with chronic obstructive pulmonary disease (COPD). These data were presented as a late-breaking poster at the American Thoracic Society (ATS) 2014 International Conference. Once-daily T+O FDC is an investigational treatment that combines the long-acting muscarinic antagonist (LAMA) tiotropium with olodaterol, an investigational long-acting beta agonist (LABA), delivered via the Respimat inhaler, a propellant-free inhaler that generates a soft, slow-moving mist. The Phase 3 clinical trial program for T+O FDC, TOviTO is a large global program that includes more than 8,000 patients with COPD. The improvement in lung function seen in the VIVACITO study suggests that T+O FDC has the potential to become a viable once-daily COPD treatment, according to Klaus F. Rabe, professor of Pulmonary Medicine at the University of Kiel and Director of the Department of Pneumology at Clinic Grosshansdorf in Germany. "This is good news as we have learned that not all patients respond to just one therapy and more options are needed, particularly considering the incidence of COPD is projected to increase worldwide in the coming decades."

Arizona Care to Help Propeller Fly

Propeller Health (formerly Asthmapolis), the FDA-cleared digital health solution for chronic respiratory disease, and Arizona Care Network, a physician and health system collaboration, jointly announced that ACN will be the first Accountable Care Organization (ACO) to offer the Propeller platform to its members with chronic obstructive pulmonary disease (COPD). Arizona Care Network was formed through collaboration between two of the state's largest health care organizations, Dignity Health and Abrazo Health (Tenet). Propeller is a digital therapeutic designed to help patients and their physicians better understand and control COPD, asthma and other respiratory disease to reduce preventable emergency room visits, hospitalizations and unnecessary suffering. With a novel combination of sensors, mobile apps, analytics and personalized feedback, the system encourages adherence to maintenance therapy and remotely monitors use of rescue medications to predict exacerbations and facilitate early intervention by care teams.

Fractional Exhaled Nitric Oxide Interpreted

Aerocrine AB announced that the results of a clinical evidence review conducted by a group of highly recognized experts were published in the medical journal Respiratory Medicine. The article outlines a guide for how to interpret the value of Fractional Exhaled Nitric Oxide (FeNO) in suspected asthma patients and in the management of asthma patients on anti-inflammatory treatment. What´s new from previously published FeNO guidelines is that for patients with values in the "grey zone", between 25 to 50 ppb, the authors now give clear treatment recommendations, based on newest clinical documentation. With this approach, measurement of airway inflammation becomes central in assisting with an accurate initial diagnosis of asthma and in the ongoing therapy monitoring and management to achieve the most successful outcomes. An important attribute of FeNO is its ability to potentially predict if a patient will respond to ICS therapy, thus avoiding the need to put patients on ICS therapy unnecessarily with a "see-if-it-works" approach. This new view on how to interpret the FeNO value will help general practitioners and other asthma treating physicians to optimize therapeutic control–step up and step down of inhaled corticosteroid, according to the amount of airway inflammation present.

Sound Waves Loosen Mucus

Westmed, Inc. has announced that the US Food and Drug Administration granted it 510(k) clearance to market the company's Vibralung Acoustical Percussor. The Vibralung is intended for use by patients with respiratory diseases and related conditions that involve increased mucus production, infection and inspissation of secretions, defective mucociliary clearance, and any other cardiorespiratory or neuromuscular diseases that inhibit effective cough, mucokinesis, airway clearance and expectoration. The Vibralung Acoustical Percussor applies vibratory sound wave patterns through a mouthpiece, during inspiration and exhalation, over a wide range of frequencies (5 to 1,200 Hz) to vibrate the column of air in the tracheobronchial tract at a multitude of resonant frequencies. As a result, mucus is loosened and mobilized by the principle of sympathetic resonance throughout the airways to promote safe, effective and gentle Airway Clearance Therapy (ACT). The Vibralung Acoustical Percussor can be used as either sole or adjunct therapy, depending upon the patient's needs and response. It is lightweight, portable and battery-powered, so it can go almost anywhere the patient goes. It also employs Positive Expiratory Pressure (PEP) that is applied simultaneously and it can be interfaced with Westmed's Circulaire II Hybrid high-efficiency aerosol drug delivery system to concomitantly deliver respiratory medications. Because the Vibralung Acoustical Percussor does not make contact with the external chest wall, it is a gentler form of ACT than vests or oscillatory PEP devices. It may be especially useful for airway clearance therapy when other means cannot be used, such as with patients that have chest wall injuries, burns, fresh surgical wounds or injured/broken ribs.

Once-daily Treatment Earns Approval

GlaxoSmithKline has announced that the US Food and Drug Administration gave approval for Incruse Ellipta (umeclidinium) as an anticholinergic indicated for the long-term, once-daily, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema. Umeclidinium is GSK's first once-daily anticholinergic, a type of bronchodilator also known as a long-acting muscarinic antagonist (LAMA), and is contained in the Ellipta inhaler. The FDA-approved strength is 62.5 mcg. GlaxoSmithKline, along with Theravance, Inc., also announced that Anoro Ellipta (umeclidinium and vilanterol inhalation powder), the first once-daily product approved in the US that combines two long-acting bronchodilators in a single inhaler for the maintenance treatment of chronic obstructive pulmonary disease (COPD), is now available to retail pharmacies in the US. Anoro Ellipta is a combination anticholinergic/long-acting beta$_2$-adrenergic agonist (anticholinergic/LABA) indicated for the long-term, once-daily, maintenance treatment of airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema. Anoro Ellipta is not indicated for the relief of acute bronchospasm or for the treatment of asthma. The FDA-approved strength is umeclidinium/vilanterol 62.5/25mcg.

Mask Series 'iVolves'

3B Medical, Inc. has introduced the iVolve mask series, consisting of the iVolve N2 Mini-Nasal, the iVolve Nasal, and the iVolve Full Face Mask. According to the company, these three new masks, together with the popular Willow Nasal Pillow Interface, it a new interface offering aimed at maximizing patient comfort at a comfortable price.

SleepVirtual Deal Reached

MGC Diagnostics Corporation has entered into an exclusive distribution agreement with Neurovirtual USA Inc. under which MGC Diagnostics will market and distribute the SleepVirtual BWII PSG and BWIII PSG Diagnostic polysomnography systems in the United States and Canada. The SleepVirtual products are used in the diagnosis and treatment of sleep apnea and sleep-related breathing disorders. The SleepVirtual BWII has a small, lightweight design and may be used as a stationary unit or a portable unit (fitting into a small briefcase), providing flexibility to use one device in several locations. The SleepVirtual BWIII PSG Plus is a larger device with combined sleep and neuro-diagnostics (EEG) capabilities.

AnchorFast Announced to Prevent Occlusion

Preventing occlusion just may have gotten easier as Hollister Incorporated announced the launch of the AnchorFast Guard oral endotracheal tube fastener with integrated tube protection. Recognizing the fact that every patient dependent on a ventilator is vulnerable and that ventilator-associated risks such as tube occlusions can result in increased length of stays and increased hospital costs, Hollister added this new product to the AnchorFast tube fastener line. Unlike separate bite blocks, the integrated tube protection sleeve is there before it's needed, helping to prevent occlusion without interfering with routine care. "AnchorFast Guard provides the potential to improve patient outcomes and may increase efficiencies at the same time," said Timothy Goedvolk, RN, BScN. With the addition of integrated tube protection to the trusted securement system, the AnchorFast Guard tube fastener can help to bring a new level of confidence to the ICU.

Michigan Lung Capacity Expanded

A new, sophisticated design modification from Michigan Instruments is expected to breathe new life into its Training and Test Lung—also known as the "Michigan Lung." The new design includes PneuView3, an innovative, intuitive software interface. The combination of the new software application and improved product design brings significantly improved user capabilities which further position Michigan Instruments as an innovative leader in the respiratory care industry. The new products will

be available in July 2014. Developed 40 years ago, the Michigan Lung embodies a mechanical "respiratory simulation" of the human pulmonary system capable of measuring airway pressure, lung pressure, tidal volume and 36 other parameters. It is the most versatile, reliable lung on the market and the latest fully-to-scale mechanical design allows for simulation of hundreds of patient scenarios. The system is comprised of a precisely engineered mechanical test lung (or lungs), a set of electronic sensors, a signal conditioning package, and an integrated micro control unit. The PneuView3 software application calculates and displays, in real time, numerous respiratory parameters and waveforms. This data can also be exported for later review. Michigan Instruments says it complies with Food and Drug Administration (FDA) and International Organization of Standardization (ISO) regulations for Good Manufacturing Practices. Both the FDA and ISO systems require continuous control over all activities that assure the quality of Michigan Instruments products and services. More information is available online at www.michiganinstruments.com.

Patent Invalidated

BMC Medical Co., Ltd says it has successfully invalidated a key ResMed patent on interfaces. BMC initiated invalidity proceedings in China against five ResMed's patents before the Chinese Patent Re-examination Board (PRB) in October 2013. The oral proceedings of five cases have taken place. One of the patents (No. 200680002169.4) entitled "Cushion for patient interface" has been revoked entirely by the PRB on April 22, 2014. Other cases are still pending. In addition, James Xu, President of BMC, also said that BMC was in the process of preparing similar IPR (Inter Partes Review) applications seeking to invalidate several ResMed patents in the US Patent and Trademark Office. Xu stated that BMC would initiate an "aggressive" new strategy with IPRs to invalidate a wide body of ResMed patents. "We did not ask for this fight, but we have no intention of backing down," said Xu.

Covidien a Guiding Light

Covidien has announced its support for the Centers of Medicare & Medicaid Services (CMS) guidance update emphasizing the need for post-operative electronic monitoring of patients receiving IV opioid medications, regardless of where they are located in the hospital. Opioids, frequently given to patients for pain management, may be associated with increased risk for dangerous complications from respiratory compromise, like respiratory depression, insufficiency, arrest or failure. The CMS updated guidance addresses the risk for respiratory compromise by urging hospitals to establish procedures for patient-risk assessment and appropriate electronic monitoring for earlier detection and prevention of oversedation and/or respiratory depression related to post-operative patients receiving IV opioids. Covidien said in a news release that it's committed to raising awareness of the dangers of respiratory compromise and the need for continuous monitoring of patients across the hospital. In fact, the company recently launched an awareness campaign around this patient safety issue. Respiratory compromise is all too common, costly and deadly. HealthGrades data shows post-operative respiratory failure occurred in more than 17 of every 1,000 patients. The cost per respiratory failure event was more than $53,000, totaling $1.9 billion dollars in just the Medicare population. Proactive prevention of respiratory compromise, leads to better patient outcomes, reduction in cost and reduction in reactive rescues. The CMS guidance further highlights recommendations of expert organizations regarding post-operative opioid monitoring, with organizations calling for continuous electronic monitoring of oxygenation, respiration and ventilation of patients receiving opioids postoperatively through pulse oximetry, respiration rate and/or capnography. Covidien offers market-leading respiratory function technologies and a complete portfolio of monitoring solutions that can help hospitals meet APSF and ISMP recommendations—in particular by implementing a continuous electronic monitoring solution, including $etCO_2$, respiration rate and SpO_2, that is tailored to each patient's unique needs.

Dispensers Aim to Prevent Mix-ups

NeoMed, a developer and manufacturer of neonatal enteral systems and oral dispensers, has launched its ISMP-compliant Oral Dispensers. The Institute for Safe Medication Practice (ISMP) published their 2014-15 Targeted Medication Safety Best Practices for Hospitals in January 2014. The ISMP recommends in Best Practice #5 to "use liquid medication dosing devices (oral syringes/cups/droppers) that only display volume using the metric scale (mL)". The ISMP hopes to reduce the risk of medication measurement mix-ups by standardizing the method for liquid measurement. In response to this best practice recommendation, NeoMed has removed all teaspoon gradient markings from their Pharmacy Oral Dispenser line. NeoMed offers a full line of amber and clear oral dispensers from sizes 0.5 mL through 60 mL that comply with the ISMP recommendations. NeoMed's oral dispensers feature an O-ring plunger design for smooth and accurate delivery, which aligns with distinct gradient markings for precise measurements. The plugged, hands-free, self-righting tip caps create an airtight and watertight seal to secure the dispenser's contents.

B&B Adds to Team

B&B Medical Technologies announced that respiratory sales and marketing management veteran Stu Novitz has joined its team as the company expands its growing international presence and strengthens its distributor network. Novitz brings with him a wealth of experience working with distributors within the hospital homecare and long-term care market, having recently spent the last four years at Clement Clarke spearheading the company's efforts to extend its reach into the North American medical markets. Joining in advance of B&B Medical's new product rollout, Novitz will make an immediate contribution to the company's continuing success. Novitz joins B&B Medical Technologies as Vice President of Sales and Marketing to advance B&B's reputation for providing specialty airway solutions to clinicians worldwide. "I look forward to working with the management team to further define our action plans that will ensure B&B's long-term growth strategy. I am fortunate to be joining such a respected company with enthusiastic goals for developing innovative, new products," said Novitz. B&B's newest product on the horizon is a solution for the Neonatal Critical Care market and that is only the beginning—the company's development plan is to launch new products each year.

Mask Maker Touts CPAP Comfort Solutions

When it comes to CPAP masks, many of the models are nearly complete replicas of the other models. According to Hans Rudolph, its V2 stands out with unique features that leave other models behind. Unlike other masks on the market, the V2 does not use a hard plastic frame to mount the seal to. Instead, the V2's seal and face piece are one molded piece of medical grade silicone. This allows for "unparalleled comfort at low and high

pressures and at varying strap tensions." Where other masks cause skin breakdown, lasting marks and even bruising—forcing many patients to rip off the mask during the night or ditching CPAP completely—the V2 rests and complies to the face comfortably. When you think of a CPAP mask, you almost always picture the intrusive forehead support as well. The V2 proves that a full face mask doesn't need this uncomfortable attachment in order to function properly. Instead of giving into the norm of the market, Hans Rudolph turned to its long history of quality engineering and design to solve this problem. A better mask with better seal technology and superior headgear use has allowed the V to be one of the only masks without a cumbersome forehead support. The headgear features five points of adjustment—four on the face piece connections and one Tri-Glide adjustment on the crown of the head. Achieving the right strap tension for a good seal is never a problem with the V2. Working your way to the front of the mask you will find that the V2 swivel port serves many functions as well. C02 ventilation, Anti-Asphyxia Valve, O2 titration ports and a detachment point can all be found on this Hans Rudolph port. For more information on the company's line of products, visit www.rudolphkc.com.

Instrumentation Systems Offer Multiple Flow Ranges
Respiratory therapy products manufacturer Hans Rudolph is promoting its complete line of linear pneumotachs to respiratory therapy professionals looking to ensure their equipment has state-of-the-art quality operation. Included is the RSS 100HR Research Pneumotach Instrumentation system with Windows-based software for. Pneumotachs are available in eight flow ranges for small animals through exercising adults, with other features that include LCD display, auxiliary pressure input, gas calculator, linearization and data acquisition. The company also offers its PA1—Pneumotach Amplifier—a low-cost instrumentation module with analog outputs for flow and pressure or 2 flows or 2 pressures. It provides the instrumentation necessary to produce an analog output proportional to flow when connected to any Hans Rudolph standard Pneumotachs, which are available in 8 different flow ranges. The PA1 will also provide an analog output of an independent auxiliary pressure signal for pressure anywhere in the circuit. The outputs can be configured for different voltage ranges to ease connection of your data acquisition system. Offset and gain adjustment pots are available. Other products offered by the company include the Series 1101 Breathing Simulator, which models a spontaneously breathing patient based on a computerized mathematical lung model. Airway resistance, lung compliance, breath rate and patient effort are adjustable parameters that simulate a wide range of patient conditions. Includes a large LCD display with real time graphics and data acquisition capability. The Series 1120 Flow/Volume Simulator is a servo motor driven piston pump that can be used for testing spirometry products and other respiratory devices. It is designed to be used in product development and manufacturing test applications. The Flow / Volume Simulator operates in three modes. The exhale waveform mode is used to test spirometry devices using the ATS waveforms, peak flow waveforms or custom waveforms. The steady flow mode can be used to generate steady state flows over a wide range of flow rates. This mode can be used to test and calibrate flow meters. The breathing waveform mode can be used to produce a continuous inhale exhale flow waveform that simulates breathing. All of the modes provide graphs for the flow and pressure signals. Data collected during the test can be saved to a file for additional analysis. Built-in pressure sensors measure the barometric pressure and cylinder pressure during the tests. The pressure data is used to correct the calculated flow for gas compression. For more information on the company's line of products, visit www.rudolphkc.com.

SPOTLIGHT ON SPIROMETRY

COSMED microQuark

The microQuark is a PC-based spirometer designed by COSMED for lung function screening. It can be used with any PC, either desktop or laptop, by simply installing the application software and connecting the USB cable to the USB port of the computer. Performing spirometry tests is extremely easy and intuitive with the microQuark thanks to OMNIA, the new generation software developed by COSMED, which is included in the standard package. Fast, simple and cost effective spirometry screening is now available to any user.

Full Spirometry Testing includes:
- Forced/Slow Vital Capacity
- Maximum Voluntary Ventilation
- Respiratory Pattern
- Bronchial Challenge Test (Pre-Post)
- Bronchial Dilator Test

NDD

EasyOne Pro ndd Medical Technologies' EasyOne Pro is a portable single breath DLCO device allowing physicians to provide their patients with prompt, accurate diagnosis and treatment. The EasyOne Pro performs PFTs in under 30 minutes all in on square foot. Some of the many features include Single Breath CO diffusion (DLCO), Spirometry, Flexible EMR capabilities, no warm-up time, challenge testing, no expensive service contracts along with a high-resolution color touch screen. With ndd's TrueFlow technology there are no moving parts, no codes to enter and no disposables to calibrate. The ultrasonic flow measurement is independent of pressure, temperature and humidity.

Easy on-PC ndd Medical Technologies' Easy on-PC is an easy to operate spirometer that uses the power of your PC, laptop, or tablet, leveraging premium ultra sound technology for a complete spirometry solution. The Easy on-PC offers challenge testing, pediatric incentives and inspiratory and expiratory real time curves. Some of the essential features of the Easy on-PC are flexible EMR capabilities, trending, selectable predicted values and interpretation, automated quality control, quick testing as well as being multilingual. With ndd's Easy on-PC you will receive point of care testing for fast, accurate and easy diagnosis.

SPOTLIGHT ON BLOODGAS

Roche

Roche Diagnostic's blood gas portfolio includes the **cobas b** 123 POC system, **cobas b** 221 system, and **cobas bge link** software for hospital point-of-care.

The **cobas b** 123 POC system is a mobile, near patient blood gas analyzer with a broad assay menu including COOX and lactate. The **cobas b** 123 POC system features an unparalleled system of four levels of clot protection to help prevent pack failures.

The **cobas b** 221 system was uniquely designed to help provide virtually uninterrupted performance. The **cobas b** 221 system configurable menu has options for blood gas (pO2, pCO2, and pH), electrolytes (Na+, K+, Cl-, Ca+, Hematocrit), metabolites (glucose, lactate, BUN), and Co-oximetry (O2Hb, HHb, COHb, MetHb, tHb, Bilirubin).

A variety of sample input devices including syringe, capillary, test tubes, and Microsampler PROTECT device can be used with both analyzers. The **cobas b** 123 POC system is FDA approved for analysis of whole blood samples. The **cobas b** 221 system is FDA cleared for analysis whole blood, serum plasma, dialysate solution and pleural fluid.

The **cobas bge link** software enables the user to remotely monitor and control multiple, decentralized units with true screen sharing, event logs, and e-reporting to enhance compliance.

Siemens

RAPIDPoint 500 Blood Gas System – The RAPIDPoint 500 Blood Gas System is a cartridge-based point-of-care analyzer for critical care testing available from Siemens Healthcare Diagnostics. With results in approximately 60 seconds, the RAPIDPoint 500 analyzer offers a comprehensive menu of critical-care tests for pH and blood gases, electrolytes, glucose, pleural fluid and lactate and full CO-oximetry, including neonatal total bilirubin and total hemoglobin, all from a single, whole-blood sample. Additionally, the measurement cartridges last up to 28 days and contain a full complement of tests, which reduces downtime.

Equipped with fully automated calibration and quality control (QC), the RAPIDPoint 500 system is designed to help POC professionals satisfy organizational and regulatory compliance requirements. Plus, the self-contained Automatic Quality Control (AQC) cartridge operates without manual intervention, helping reduce POC staff's administrative tasks. An integrated bar code reader—conveniently located on the front of the system—offers a wide scanning area to accommodate patient and operator identification to ensure overall data entry integrity.

The RAPIDPoint 500 analyzer can be integrated with the Siemens RAPIDComm Data Management System, which offers centralized management of multiple Siemens blood gas, urine chemistry, and HbA1c diabetes analyzers and operators. For more information visit www.usa.siemens.com/rp500.

RAPIDLab 1265 Blood Gas System – The RAPIDLab 1265 blood gas system is designed to enhance testing efficiency in the clinical laboratory and at the point of care. Delivering accurate results for all parameters in approximately 60 seconds, the RAPIDLab 1265 system enables clinical staff to make critical patient treatment decisions quickly.

Utilizing a unique hybrid system of ReadySensor and cartridge based technology, the RAPIDLab 1265 system is a high-volume, low maintenance solution that helps laboratories to increase throughput without increasing workload. Also, the RAPIDLab 1265 provides a comprehensive menu including blood gases, electrolytes, co-oximetry, and glucose and lactate metabolites. It also is equipped with an onboard automatic quality control cartridge that requires no operator intervention during the 28-day use life, allowing POC professionals to more easily satisfy organizational and regulatory compliance requirement.

The RAPIDLab 1265 offers testing efficiency, speed, and reliability to meet the escalating blood gas testing needs of busy clinical labs and clinicians in various hospital settings. It also can be integrated with the Siemens RAPIDComm Data Management System, which offers centralized management of multiple Siemens blood gas, urine chemistry, and hBa1c diabetes analyzers and operators. For more information visit: http://usa.healthcare.siemens.com/point-of-care/blood-gas/rapidlab-1200-systems/features-benefits.

RAPIDComm Data Management System – The RAPIDComm Data Management System allows centralized management of multiple RAPIDSystems blood gas testing instruments, as well as Siemens CLINITEK Status Connect urinalysis system and DCA Vantage analyzers for HbA1c testing. As a result of a major software upgrade, the RAPIDComm Data Management System now supports the new RAPIDComm Web Application, as well as an interface to PEP (Personalized Education Plan) Administrator, Siemens web-based learning management system.

The RAPIDComm Web Application allows POC coordinators to quickly view the status of their POC instruments and troubleshoot issues from a handheld device. It even enables customers who manage blood gas analyzers to remotely view and control their instruments directly from an iPad, regardless of where they are located.

The interface to PEP lets POC coordinators create and assign to instrument operators custom internet-based quizzes (e-quizzes), which must be successfully completed for training and certification. The RAPIDComm System can then automatically recertify operators and centrally manage and download their IDs and passwords to the appropriate POC testing instruments, ensuring secure access. This feature can help POC coordinators reduce the manual steps involved with the operator certification process. For more information visit: http://usa.healthcare.siemens.com/point-of-care/information-technology.

SLEEP ROUNTABLES

Circadiance

Tell us about the sleep products your company offers.
Circadiance provides the world's ONLY cloth masks for PAP and non-invasive ventilation. Our SleepWeaver line includes two nasal mask options (Advance and Élan) and one full face option (Anew). The clinical benefits of the SleepWeaver line of masks are unique due to the cloth-based construction. Not only do the masks seal well, meeting ISO criteria similar to traditional hard plastic masks, but they have a breathable component which wicks away moisture. There is no strap-related pressure (i.e. tightening the strap too tight) across the bridge of the nose

which makes them so light-weight and easy to wear. The masks come in a variety of sizes to provide a proper fit for practically anyone. We are particularly excited about our newest product, the Advance Small, which we will cover in more detail below.

What is the range of applications for your products?
The SleepWeaver line of masks can be used in a clinical setting or for long-term home use. One of the newer applications is for non-invasive ventilation and they can be used in patients who weight at least 66lbs (30Kgs), making them a good first line choice across a broad age range.

Discuss the training and support you offer to the users of your products.
While the use of SleepWeaver PAP masks is fairly intuitive, we offer both online and DVD instructional videos that take the patient and caregiver through the steps required to obtain a proper fit as well as appropriate cleaning and storage. For those with additional questions, Circadiance offers an excellent customer service team and clinical support. Downloads and a help section are also available for each product at www.circadiance.com. The company is planning to initiate a DME/Professional corner on the Circadiance website which will offer timely and relevant information with regard to customer and consumer trends in the field of respiratory care. In conjunction with these activities, a web-based educational series offering CEUs will launch in the last quarter of 2014.

How do users pay for your product?
SleepWeaver products are often reimbursed under the same codes as traditional hard plastic masks. However, in view of the fact that the SleepWeaver line of masks does not require a cushion replacement each month can equate to value-added savings for the patient and healthcare system.

Will you be offering any new products in the near future?
We have just released a new innovative nasal mask for patients with smaller facial features we called the "Advance Small". The Advance Small has a redesigned nasal interface with an enhanced seal that is simple and easy to use. Our research and development team is constantly exploring ways to make our masks better. One of the projects we hope to bring to fruition will fill a clinical gap with regards to pediatric masks for patients under 66lbs who require either non-invasive ventilation (NIV) or PAP for obstructive sleep apnea. Clinical research suggests that cloth masks may avoid the occurrence of hospital acquired pressure ulcers (HAPUs) and these young children are hard to fit with the traditional masks as they have small faces and heads. In addition, their facial structure is more malleable than adults, creating concern for facial mal-development. The cloth mask also provides the clinical team with a risk-management strategy with regards to mitigating the development of medical device pressure related ulcers. With appropriate crowd-funding, we hope to launch such a product in about a year.

3B Medical

Tell us about the sleep products your company offers.
3B Medical provides a full line of CPAP devices and interfaces. Our CPAP and Auto-CPAP line are an economical alternative that still provides users with all the bells and whistles of the pricier brands. Standard options such as RESlex, our exhalation relief feature, and one button daily compliance monitoring make this a higher end unit with a lower end price tag.

What really sets 3B Medical's PAP units apart is the free data compliance management. Every machine is equipped with iCode and iCodeConnect capability. Your home health company, sleep lab and physicians can have free, unencumbered access to users' data compliance monitoring anytime, anywhere as long as they have internet access.

iCode Connect is a cloud-based, HIPPA-compliant, secure way to store and view patient data. There is no software to install, no modems to juggle between patients, no special SD card readers needed. Patient information can be called into a provided number for patient convenience or iCode Connect can be set-up to automatically call patients on a pre-determined schedule. Then it's as easy as following the prompts to enter a 16 digit numeric string either through the phones key pad or using our IVR voice recognition.

Of course, 3B Medical also stocks a full range of CPAP interfaces. We are continually up-dating stock to give the customer the best flexibility in mask choices.

What are the range of applications for your products (that is, home, sleep lab or hospital)?
RESmart® CPAP and Auto-CPAP are marketed for in-home use by 3B Medical. Our units were designed to be rugged and have one of the lowest warranty failure rates in the industry.

The RESmart® CPAP devices are easy for patients to navigate at home. Most patient accessible applications are one touch or one button controlled. It is very user friendly for the vast majority of patients to learn to use.

Discuss the training and support you offer to the users of your product.
3B Medical has both a Tech Support and Clinical Education support department to address any patient training or support issues. Because we offer such an innovative compliance product with iCode and iCodeConnect we offer free weekly training webinars to any customers who are interested in learning the ins and outs of this powerful new product. In-depth assistance can always be had by calling our help line or scheduling a private learning session. This enables customers to learn to fully utilize iCode Connect in a way that is geared towards their individual compliance monitoring programs. All these services are of course free of charge, free compliance monitoring, free training, and free patient data storage.

How do users pay for your products; that is, is it reimbursable?
The RESmart line of products are reimbursable through insurance and Medicare following current guidelines. In fact the iCodeConnect cloud-based system was specifically designed to make reimbursement an easy, seamless, free alternative to current data compliance tracking and monitoring. iCode Connect uploads through a variety of means, including use of interactive voice recognition on inbound and outbound calls, SD card, smartphone apps for Android and iPhone. Our cloud-based portal populates simple, easy-to-read graphs that let you know exactly how well the patient is adhering to guidelines for PAP usage.

iCode and iCode Connect invite your patient to become active in their compliance and treatment. Helping Home Health Equipment providers to shrink out of pocket expenses in this new era of lowered reimbursement. iCode Connect is able to track and store your patient data no matter how stringent regulations become.

iCodeConnect offers DMEs the only FREE option to handle changing reimbursement schemes. If a payer changes the rules for reimbursement from 90 days to a full year of compliance reporting, iCodeConnect adapts to that change with a click of a mouse and not a penny more in expense.

Will you be offering any new products in the near future?
3B Medical is leading the industry in working to bring the latest technology to our customers, both in PAP therapy and data compliance technology.

3B will soon add an Auto-bilevel to our line of PAP products to offer additional modalities for patient therapy. We are hoping for a September product launch of our Auto Bi-Level device.

In addition our R&D teams are working on innovative new ways of capturing compliance data uploading at no cost. We expect to be first to market with devices that offer a host of options including use of QR Code scanning on a smartphone, inbound and automatic outbound IVR calling, Bluetooth and Wi-fi. Our approach is to find every FREE way of reporting compliance data and offer a variety of different options. We think that current use of cellular modems is unworkable moving forward as private payers begin to extend compliance data reporting requirements out to one year.

Philips Respironics

Tell us about the sleep products your company offers.
As a global leader in the Obstructive Sleep Apnea (OSA) marketplace, Philips Respironics has, for more than three decades, pioneered standards across the sleep care cycle. We focus on sleep-disordered breathing diagnosis, therapy and compliance. Our sleep products are designed to provide more natural therapy options to enhance patients' comfort and compliance.

What are the range of applications for your products (that is, home, sleep lab, hospital)?
Working as an ally throughout the entire care cycle, from awareness and diagnosis to long-term success, Philips Respironics' innovations are designed to enable greater patient compliance and care team success. We are a total solution provider, offering a range of sleep diagnostics, therapy devices, masks, and software to meet the needs of our customers and the patients they serve.

In today's evolving home healthcare environment, there's certainly no shortage of questions. And Philips Respironics is proud to be able to offer a much needed answer: a comprehensive portfolio of masks, services and support options that are just the right solution.

Discuss the training and support you offer to the users of your product.
Caregivers worldwide count on Philips Respironics for an unsurpassed level of service and support. Complementing our portfolio of products are programs and educational resources to helping providers deliver practical, ongoing care. Our technical/patient support line, which fields thousands of calls each day, offers best-in-class support.

How do users pay for your product; that is, is it reimbursable?
Most of our products that are distributed by homecare providers (HMEs) are reimbursed through Medicare, Medicaid, and commercial plans. The HME generally submits a claim for the patient to be reimbursed for the item they supplied to the patient. The patient usually has a co-pay, which is typically 20% of the amount the payer allows.

Will you be offering any new products in the near future?
We approach innovation with an intimate understanding of the needs of those who use our devices. In the sleep market, we're continuing to innovate our portfolio to provide solutions that streamline inventory for providers and promote quick acceptance and long-term use by patients.

MGC Diagnostics

Tell us about the sleep products your company offers.
MGC Diagnostics is the exclusive distributor of SleepVirtual products in the United States. Our mission is to provide the highest quality noise free diagnostic sleep products priced competitively. We currently have two sleep systems available. MGC is now able to offer both a pulmonary diagnostic and sleep solution to the pulmonologist. Patients with lung problems and sleep problems "overlap syndrome" can be seen by one physician prepared to handle both problems.

The BWII PSG has 29 Channels with 3 DC channels. It is the perfect solution for collecting sleep data. The BWII can be used in laboratory environments, or can be packed into a small briefcase for a no compromise portable lab solution. The software is intuitive that accumulates sleep statistics during both the acquisition and the scoring process such as the number of apneas and hypopneas, AHI, study duration, sleep efficiency, etc. Montages, filters, sensitivity, and chart speed can be adjusted real-time or after recording. The BWII report generator is powered with MS word which will handle almost 900 different parameters in a user formatted easy way.

The BW3 PSG and EEG offers 50 channels with 8 DC channels. It is a dual platform that allows both sleep and EEG, a perfect solution for a community hospital or when space is at a premium. Impedance can be checked at the bedside (as well as through the software) and the system has both photic and HV protocol capabilities (for full EEG capabilities).

Everything Virtual - with either system, there is exclusive technology allows you to have the system working anywhere when your team moves around to different locations. The system can be used for acquisition in one location, be scored somewhere else, interpreted by the physician in a third place and be archived
Continued on page 19…

Heliox Therapy in Bronchiolitis: Phase III Multicenter Double-Blind Randomized Controlled Trial

Chris Campbell

Sometimes having the right medicine or treatment is not enough—it's how this medicine or treatment is administered that makes all the difference for a patient.

Case in point: heliox therapy. A study out of the United Kingdom and Australia found encouraging evidence that this type of therapy could be effective in reducing the length of treatment (LoT) for infants with Bronchiolitis given the right delivery method. "Crucial" to its efficacy was if the heliox was given via a tight-fitting facemask or CPAP. The other conclusion was that nasal cannula (NC) heliox therapy is "ineffective."

The Bronchiolitis Randomized Controlled Trial Emergency-Assisted Therapy with Heliox—referred to as the BREATHE trial—was called the "largest multicenter randomized controlled trial to date" by its lead designers, who include Dr Mina M. Chowdhury and Dr Parviz Habibi, both of the Department of Pediatrics, Wright Fleming Institute, Imperial College, London.

Supportive care remains the mainstay of therapy in bronchiolitis. Acute viral bronchiolitis is a leading cause of infant hospitalization, with a rising incidence and health-economic burden in developed countries.[1-3] In the United States, about 75,000 respiratory syncytial virus (RSV)-positive bronchiolitic infants are hospitalized each year.[4,5]

Earlier studies suggest that helium-oxygen therapy may be beneficial. The BREATHE study, published in a 2013 edition of Pediatrics, aimed to compare efficacy of 2 treatment gases, Heliox and Airox (21% oxygen plus 79% helium or nitrogen, respectively), on LoT.

From 2005 to 2008, the BREATHE team studied 319 bronchiolitic infant subjects randomly assigned to either gas; 281 subjects completed the study (140 Heliox, 141 Airox), whose data was analyzed.

Severe bronchiolitics received CPAP from the start. Primary end point was LoT required to alleviate hypoxia and respiratory distress. Secondary end-points were proportion of subjects needing CPAP; CPAP (LoT); and change in respiratory distress score.

"Because many other variables can affect the length of hospital stay, we chose to measure total LoT as the primary end point, because it is directly linked to therapy," researchers wrote.

LoT was calculated from the start to successful stop of the trial gas, as defined by clinical stability (minimal work of breathing) for 1 hour breathing room air. Minimal work of breathing was qualified as having a normal respiratory rate, no cyanosis, no nasal flaring, no tracheal tug or grunting, no head bobbing, and no use of accessory muscles except for mild intercostal recessions.

Results

The BREATHE researchers said an analysis of data from all 281 subjects showed no difference in median LoT between treatment groups [Heliox 1.90 days (interquartile range 1.08-3.17) compared to Airox 1.87 days (interquartile range 1.11-3.34), P = .41]. However, LoT was significantly reduced in favor of Heliox for facemask (FM)-tolerant subjects [Heliox, 1.46 days (interquartile range 0.85-1.95); Airox, 2.01 days (interquartile range 0.93-2.86) P = .03]. A more notable reduction in LoT was seen in RSV+ subjects [Heliox, 1.31 days (interquartile range 0.61-1.91); Airox, 2.18 days (interquartile range 1.40-2.95) P = .004]. There was no difference in LoT for NC subjects [Heliox 2.51 days (interquartile range1.21-4.32), Airox 2.81 days (interquartile range 1.45-4.78) P = .53].

Analysis of data from all 281 subjects showed no reduction in proportion of cases progressing to CPAP [24 of 140 Heliox subjects (17%) vs 27 of 141 Airox subjects (19%); odds ratio 0.87 (0.47-1.60), P 5 .76]. However, for FM tolerant RSV1 subjects there was a 66% reduction in proportions requiring CPAP in favor of Heliox, at borderline significance [3 of 27 Heliox subjects (11%) vs 10 of 31 Airox subjects (32%); odds ratio 0.26 (.07-1.02), P 5 .76].

Heliox significantly reduced median LoT for severe bronchiolitic subjects who were started directly onto CPAP [Heliox 1,55 days (interquartile range 1.38-2.01), Airox 2.26 days (interquartile range 1.84-2.73); P = .02].

The BREATHE researchers said Heliox reduced respiratory distress in all 281 subjects across all time points and statistically significant at 8 hours onwards. MWCAS (mixed models estimate = 20.1298; 95% confidence interval 20.202 to 20.057, P < .001). Regardless of gas type, FM was more effective than NC (mixed models estimate 5 0.093; 95% confidence interval 0.005 to 0.181, P = .04).

Chris Campbell is the Senior Editor of Respiratory Therapy.

Conclusions

"The BREATHE study is the only RCT thus far to investigate the rate of CPAP use in Bronchiolitis," researchers wrote. "However, the observed 66% reduction only reached borderline statistical significance, which may be because of the relatively small number of CPAP subjects (n = 58)…The BREATHE study also enabled assessment of the impact of Heliox on CPAP efficacy. We analyzed data for subjects who were started on CPAP from the beginning of the trial because their pathophysiology had not yet been altered by previous therapy. We found that CPAP duration was significantly reduced if Heliox was the driving gas for CPAP."

According to the study's researchers, the clinical practice recommendations arising from the BREATHE study findings are as follows:

1) Heliox therapy should be started for bronchiolitic infants who require hospital admission for treatment of hypoxemia or respiratory distress.
2) If the use of Heliox therapy needs to be rationalized, it could be targeted to those who are RSV positive.
3) Heliox therapy should only be delivered via a tight-fitting non-rebreathing FM or CPAP, as per the protocol outlined in the BREATHE study.

"The BREATHE study showed that the delivery method of Heliox is critical to its efficacy," researchers wrote. "Heliox is effective if delivered via a tight-fitting non-rebreathing FM or CPAP but not via a NC at conventional flow rates. With effective delivery, Heliox reduces the LoT, alleviates respiratory distress, improves CPAP efficacy, and may reduce the need for CPAP. A more acceptable patient interface for effective delivery remains the challenge for industry if Heliox is to be more widely used in pediatric respiratory care."

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Sleep Roundtables…continued from page 17
in completely different location!

What is the range of applications for your products (that is, home, sleep lab, hospital)?

Sleep Virtual products cover all sleep lab and clinic needs, as well as hospital room coverage. The instrumentation can be used anywhere such as a hotel room for an attended sleep study.

Discuss the training and support you offer to users of your product.

Training is done on site. We know that excellent customer service is paramount. We have a 24 hour/day support line to solve problems whenever they occur. We proudly offer a two year replacement warranty with every system we sell.

How do users pay for your product; that is, is it reimbursable?

Reimbursement for all type one (CPT # 95810 Baseline PSG, 95805 MSLT, and 95811 Titration) and type two studies (HCPCS #G0398)

Will you be offering any new products in the near future?

We will soon introduce a whole new family of type III and type II sleep systems. A type III system can be expanded to a type II system so your hardware will always be able to meet your needs as your services expand. Most importantly, all SleepVirtual products use the same software platform for all systems to maximize simplicity and ease of use.

The Benefits of CPAP in the Post-Operative Environment

Chris Campbell

The impact of obstructive sleep apnea (OSA) is a subject that is gaining traction in today's media, with more and more outlets and publications raising awareness about how it is affecting the population.

The effects of OSA range from the annoyance of snoring for a spouse desperately trying to sleep to the more serious impact of dozing off while driving a vehicle, as well as the long-term and catastrophic health problems associated with the condition.

A more specific area impacted by OSA is when a person needs or elects to have surgery, with evidence is showing that OSA results in a raft of post-operative complications.

The good news is a growing list of studies and articles reveals that post-operative care is improved through the use of continuous positive airway pressure, known simply as CPAP.

Using CPAP in a hospital, however, isn't as easy as it sounds due to some hospital policies and the fact that, according to the evidence, most people with OSA don't even know they have it.

The Impact of OSA on Surgical Patients

Staff with the Department of Anesthesiology at the University of Rochester (Suzanne Karan, Shira Black and Falan Mouton) addressed this issue with an article published in 2011 in the Open Anesthesiology Journal called Perioperative Implementation of Continuous Positive Airway Pressure: A Review of the Considerations.

According to the article, "OSA occurs when a compromised airway collapses, disrupting the flow of air during sleep. With the ensuing hypoxia and hypercarbia, the respiratory drive is stimulated, a stronger inspiratory effort is made, and the cycle repeats itself throughout the night."

The article says that people with OSA are affected in a profound way when it comes to surgery due to the effects of anesthesia.

"Post-operative changes amplify the disease.[1-5] Residual anesthetics weaken the muscles of the upper airway[6,7] and depress the respiratory drive.[8,9] Thus, a mild pre-operative case of OSA can easily become a severe post-operative one. OSA patients require more monitoring, oxygen therapy, and unplanned ICU admissions.[10] When compared with controls, OSA patients have longer hospital stays and more adverse events than non-OSA patients.[11] Additionally, an OSA diagnosis is associated with increased post-operative complications, including, but not limited to: airway obstruction, cardiac arrhythmias, hypoxemia, encephalopathy and death.[10,12] Adverse outcomes related to respiratory events remains the largest class of injuries reported in the American Society of Anesthesiology Closed Claims study—in cases involving general anesthesia, sedation and monitored anesthetic care (MAC)."[13]

The Benefits of CPAP

According to the article, the use of CPAP can "reduce" some of the post-operative complications.

"In an unblinded study by Squadrone et al. (Continuous Positive Airway Pressure for treatment of Post-operative Hypoxemia: A Randomized Controlled Trial, 2005), CPAP application to treat hypoxemia after major abdominal surgery significantly reduced re-intubation rates, and correlated with a reduction in ICU length of stay, post-operative pneumonia, infection, sepsis, and death. Another review of 16 cases[14] reported a reduction in post-operative complications in patients who used CPAP therapy pre-operatively, upon extubation, and nearly continuously for 24 to 48 hours after surgery."

The article quoted the 2006 American Society of Anesthesiology (ASA), saying that the society's guidelines "regarding the perioperative care of OSA patients state that patients who use CPAP at night should use CPAP post-operatively."

In an article on obese patients and ambulatory surgery by Dr. Girish P. Joshi of the University of Texas, in the August 2013 edition of the ASA journal, it says that "patients with a known diagnosis of OSA (who are typically prescribed CPAP pre-operatively) may be considered for ambulatory surgery if their co-morbid medical conditions are optimized and they are able to use a CPAP device in the post-operative period. It appears that post-operative CPAP use may be protective against opioid-induced respiratory depression."

People with Undiagnosed OSA

CPAP, however, is often not used in hospitals because most people are not diagnosed with the condition.

John Davies, a clinical research coordinator at Duke University Medical Center, wrote about the issue in the May 2010 edition of the AARC Times. Davies warned about the risks of OSA

Chris Campbell is the Senior Editor of Respiratory Therapy.

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on surgical patients and from those not diagnosed with the condition.

"Complications from untreated OSA can lead to serious cardiac and respiratory complications that can endanger the patient's recovery. It is important for clinicians to recognize the potential for a patient to have undiagnosed OSA and be ready to use CPAP to optimize the clinical effectiveness of their hospital stay."

The University of Rochester article stated that OSA is "notoriously under-diagnosed" and that "recognizing patients with OSA is critical in determining who could potentially benefit from CPAP…If these patients are properly identified pre-operatively, the need for post-operative CPAP would be more easily implemented. Unfortunately, most of these patients are still being identified during post-operative quality improvement review of a poor outcome."

Using CPAP in a Hospital Setting

Dr. D. John Doyle with the Cleveland Clinic wrote an article in 2013 called Obstructive Sleep Apnea and the Surgical Patient in Anesthesiology News. It included a case study of a surgical patient previously diagnosed with OSA and one of the conclusions was that "the need for the patient to bring his CPAP system to the operating room and post-anesthesia care unit (PACU) should be emphasized."

That's because the patient is used to the fit of his or her CPAP mask, making it easier for them to use.

However, the Davies AARC Times article found that while CPAP is common in the home setting, "its use in the hospital is less well accepted and infrequently prescribed."

One fear of hospitals is with the possibility of infection from a patient's home CPAP system.

If this is the case, then a viable solution is with the use of a disposable CPAP system. If a hospital doesn't welcome a patient's home system, a disposable CPAP system offers an effective alternative because it is on site and can be quickly adjusted and fitted so it's easy to use.

And if clinicians suspect OSA in a patient before surgery—especially urgent surgery, when time is a factor—a disposable CPAP system can be used immediately to assist with recovery. It would then be up to the patient to be fitted for a long-term CPAP system.

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Benefits of Using a Portable Ventilator for Intra-hospital Respiratory Therapy

Chris Campbell

Why have two cumbersome devices, when one portable ventilator that achieves the same goals will suffice? That was the logic behind a change made by a Texas medical services provider that offers many in-hospital benefits when it comes to the equipment used in the Respiratory Therapy field.

Cooke County Emergency Medical Services, a provider of ground medical services in the Gainesville,TX area, added new ventilator technology—the Automatic Emergency Ventilator (AEV) from Impact Instrumentation, Inc.,—to its fleet of ambulances.

However, the AEV technology is also easily adaptable for RTs when transporting patients within a hospital setting because it is full-featured, lightweight, portable and runs on LiIon batteries for 10 hours on a single charge.

Kevin Grant, Emergency Medical Services Director, said that before buying into the AEV concept the Cooke County fleet—which completes about 3,500 transports annually—inefficiently used old Bird ventilators as well as CPAP machines.

"At Cooke County, we needed to replace the old technology in our rigs that we had been using for over 20 years. When we first saw the Impact AEVs we were impressed by the ease-of-use of the devices and that we could use this one piece of equipment for all of our ventilation needs. We accomplish both with the AEV. And the fact that they were designed specifically for the transport industry is impressive. They have been very reliable and offer one of the longest battery run times on the market at 10 hours. And they were very affordable."

Some key features of the new state-of-the-art Impact AEV Portable Ventilators include:

- Pressure and Volume Ventilation Modes — The modes you need for your most challenging patients: AC and CPAP/BiPAP with Automatic Leak Compensation and Pressure Support that can manage the needs of your infant, pediatric and adult patients without compromise.
- Rapid Charger — Battery run-time is important but how long it takes a device to recharge can be just as critical. The AEV has a built-in rapid charger, which brings battery life from virtually 0% to 90% capacity in just 2 hours.
- Lightweight — At ~9.5 lbs it is one of the lightest ventilators on the market. This makes transporting and maneuvering that much easier.

CPAP with automatic leak compensation — Impact's sophisticated software adjusts flow to compensate for leaks. SmartFlow is designed to provide the right amount of flow at all times to eliminate leak problems and not be a contributing cause of the problem. CPAP mode is oxygen efficient and allows delivered oxygen concentrations to be set anywhere between 21 and 100%.

"At Cooke County EMS we strive to provide the latest in medical technology in our mission to deliver the highest levels of quality patient care," Grant said. "These ventilators are yet another example of Cooke County EMS's commitment to continually enhancing patient care and providing the highest quality care on the ground. We look forward to improving the care of patients we transport with the addition of these new ventilators."

Additional features of the AEV include:

- Advanced Monitoring with On-Board Masimo SpO2 — Integrated on-screen continuous patient monitoring of oxygen saturation and heart rate. This allows the user to adjust the O2 levels as needed.
- Smart Help — This exclusive feature provides care givers with alarm resolution support by offering insight into possible reasons for the alarm and ways to address them.
- Ruggedness — The AEV incorporates a floating chassis mounting system that is designed to take a direct hit or a significant shock/drop.
- Powerful Compressor — The unique 12-valve rotary compressor operates with better control of flows, which optimizes patient comfort. In addition, it can deliver a very high flow up to 100 LPM into a very large load of 40 cm H2O.

The AEV Portable Ventilator is manufactured in the US by New Jersey-based Impact Instrumentation, Inc., a medical device developer and manufacturer of respiratory products and measuring instrumentation. Other portable ventilators by Impact are the EMV+, the Eagle II and Eagle II MRI for use in MRI suites. Visit Impact at www.impactii.com.

Chris Campbell is the Senior Editor of Respiratory Therapy.

Biphasic Cuirass Ventilation: An Approach Based On Normal Ventilation

Rick Leonard RRT, Gary Mefford RRT

Introduction

The primary purpose of the lung is to provide gas exchange in which oxygen will move from the ambient air into the arterial blood and carbon dioxide moved out of the venous blood and exhaled. A number of structures and functions of the lung, the musculoskeletal system, the central nervous system, the circulatory system, and other systems must efficiently work together to achieve this primary goal. Alterations to the normal function of any of these structures and systems may occur due to various insults, injuries, diseases, environmental changes, or medical interventions. When these functions and system relationships are altered, the primary purpose of the lung to supply oxygen and remove carbon dioxide may be compromised and may require intervention with various forms of support to sustain these systems until the underlying problems resolve and the function and purpose of these systems return to normal.

Interventions to support the various systems require an understanding of the normal function of these systems, what occurs when interventions are applied, and how normal functions may be restored such that gas exchange occurs in a normal manner. A brief review of normal ventilation and the impact of currently accepted interventions to restore normal ventilation may offer insights on how best to restore normal function with the least impact to the dynamics of providing oxygen to body and removal of carbon dioxide. Applying some basic principles and understanding how accepted interventions work will lead to successful application of these interventions with the best overall patient outcome.

Basic Principles of Medical Interventions

Three basic principles should be considered when determining the best possible interventions to restore normal physiological function and respiratory care. The first of these three principles is "First, do no harm". The phrase is often attributed to the ancient Greek philosopher and father of modern medicine, Hippocrates. Since the phrase is from the Latin, Primum non nocere, others have attributed its origin to the Roman physician Galen. Regardless of its origins, the principle has long standing considerations in the medical care of patients.

The second basic principle when considering ventilatory interventions and respiratory care is Isaac Newton's Third Law of Physics, and states "For every action, there is an equal and opposite reaction". This principle must be considered with interventions to ventilation and respiratory care because each activity undertaken to produce a desired result, also follows itself with an opposing reaction, which must be considered in the overall outcome of the care desired.

The third basic principle in the application of interventions to ventilation and respiratory care is "a respiratory care plan's interventions should in large part focus on the goal of recruiting and restoring to normal, the functional residual capacity (FRC) of the patient". Ironically simple, but true, if FRC can be recruited and restored for the patient, the respiratory care plan has usually succeeded.

Normal Ventilation

Normal ventilation is achieved by a series of complex interactions between the central nervous system and the thoracic musculoskeletal system, which creates airflow from the ambient atmosphere through conducting airways of the lung and to the lung periphery. The interface between the lung periphery and circulation system is referred to as the blood-gas interface and is the area where oxygen is delivered to the blood and carbon dioxide is removed from the blood. The process of moving the ambient air to the lung periphery is ventilation.

During normal ventilation, a neurological response sends a signal to the respiratory musculature which consists of the accessory muscles including the intercostal muscles, and the diaphragm. This signal causes the ribs to rise and the diaphragm to descend which increases the size of the thoracic cavity. The increase in size of the thoracic cavity creates negative pressure relative to ambient atmosphere, and air is drawn into the lungs. Usually, this intrapleural pressure creates a gradient of -5 to -8 cmH2O resulting in a tidal volume of 5-7 ml/kg ideal body weight of air pending no interference with airways resistance. The maximal transpulmonary pressure, the difference between intralveolar pressure and intrapleural pressure, which can be generated during spontaneous ventilation, is approximately 35 cmH2O.

Inspired air flows from the mouth, through the connecting airways of the trachea, bronchi, secondary bronchi, until it reaches the terminal bronchioles and alveoli or the area of the lungs where gas exchange occurs known as the respiratory zone. Once in the respiratory zone, diffusion of the inspired air provides oxygen delivery to the blood gas interface and carbon dioxide is removed for exhalation via reverse pathway by passive recoil of the lung and chest wall structures.

Rick Leonard is the Clinical Specialist at Hayek Medical Devices. Gary Mefford is the VPCO at Hayek Medical Devices .

As mentioned in the previous paragraph, a negative pressure gradient is created during normal ventilation to produce the tidal airflow into the lungs. This relative negative pressure also has an impact on the smaller airways, alveoli, and pulmonary extra-alveolar vessels of the thoracic cavity, by creating a pull on the external walls of these vessels. The pull of this negative pressure creates a slight dilatation to the lumen of these vessels. The slight increase in the lumen diameter reduces resistance to flow through these vessels, which include airflow to the smaller airways, blood flow to the pulmonary capillaries, and the vena cava, such that ventilation, perfusion, and venous return to the heart are naturally augmented and efficient.

Typically, the energy or work required of the respiratory muscles to provide normal ventilation at rest consumes less than 5% of the total oxygen consumption of the body assuming a normal minute volume. When these muscles are stressed, as in severe exercise, the oxygen consumption may increase to 30%. Should airway resistance increase, the compliance of the lung becomes low, and/or ventilation becomes inefficient due to ventilation and perfusion mismatch, as with frequently seen in various disease states and insult to the lung, the oxygen cost of breathing becomes dramatically increased. When the oxygen cost of breathing approaches 40% of the total oxygen consumption, the muscles of ventilation fatigue, become inefficient, and mechanical ventilation becomes necessary.

Indications for Mechanical Ventilation

Respiratory failure is simply defined as an inadequate delivery of oxygen and/or the removal of carbon dioxide to and from body tissues. Respiratory failure may be the result of low ambient oxygen, ventilation-perfusion mismatch, gas diffusion problems, shunting, inadequate circulation, or alveolar hypoventilation, in which the airflow into the alveoli is inadequate to provide adequate gas exchange. Typically, alveolar hypoventilation may result from increased airways resistance, reduced breathing efforts, decreased lung surface area for gas diffusion, neuromuscular problems or abnormalities to the chest wall due to disease, injury, or insult.

Clinical symptoms of respiratory failure include dyspnea, tachypnea, and increased work of breathing manifested by use of the accessory muscles of ventilation, patient confusion, possibly cyanosis, and a significantly increased PaCO2 and/or reduced PaO2 from arterial blood gas analysis. When respiratory failure is present, mechanical support of ventilation may become necessary to support the ventilatory functions of the patient until the underlying cause of failure is resolved.

Mechanical Ventilation of the Lung

Mechanical ventilation is used to support the delivery of oxygen to the alveoli and remove carbon dioxide from the body. Since the 1960s, mechanical ventilation uses a positive pressure applied to an airway to create a pressure gradient between the ambient atmosphere and the alveoli of the patient. Such positive pressure efficiently moves air into the alveoli to deliver oxygen and the passive recoil of the chest wall allows for exhalation and the removal of carbon dioxide.

As discussed earlier, during spontaneous or normal ventilation, a relative negative pressure is created in the intrapleural space as the thoracic cavity expands during inspiration. In positive pressure mechanical ventilation, the thoracic pressure gradients are the opposite of which occur during spontaneous ventilation and result in a positive mean intrathoracic pressure on inspiration. Positive intrathoracic pressure on inspiration means that venous return to the heart is greatest on exhalation. In spontaneous ventilation, the relative negative pressure facilitates venous return; therefore venous return may be reduced with the application of positive pressure ventilation. This becomes more apparent when exhalation time is reduced and PEEP is applied to the mechanical ventilator.

Due to the potential reduction in venous return and subsequent impact on cardiac output, other side effects are noteworthy. These include increased pulmonary vascular pressure, decreased urinary output, increased intracranial pressures and potential reduction in portal blood flow.

Other adverse effects of positive pressure ventilation are often associated with peak Inspiratory pressures to deliver the required tidal volume and minute ventilation. During normal positive pressure ventilation, airflow is essentially pushed into the airways. Airflow will take the path of least resistance such that areas of the lung which may be relatively well ventilated are those which receive a major portion of the tidal volume. Should peak Inspiratory pressures increase, as with increases in airway resistance, these well ventilated areas receiving the major portion of the tidal volume may over distend. Over distention of these alveoli may result in barotrauma leading to interstitial emphysema, pulmonary interstitial emphysema, pneumomediastinum, or pneumothorax, and significant inflammatory responses.

Positive pressure ventilation (PPV) can be applied as invasive positive pressure ventilation (IPPV) which requires the insertion of an endotracheal tube or tracheotomy tube to provide the interface between the ventilator and the patient. The insertion of these artificial airways also leads to complications. Damage to tracheal mucosa, laryngeal edema, loss of effective humidification from the upper airway, contamination of the lower airway, and loss of communication with the patient are concerns. PPV can also be applied as non-invasive positive pressure ventilation (NIPPV) which typically requires a facial mask type of interface. These types of interfaces can result in an extreme sense of claustrophobia particularly in patients with symptoms of dyspnea, as well as offering a potential of facial skin breakdown, oral pharyngeal moisture loss resulting in airway occlusion as well as decreasing the patient's ability to clear pulmonary secretions.

Biphasic Cuirass Ventilation

Negative pressure ventilation was the dominant method of mechanical ventilation for many years. The polio epidemics of the 1920s and early 1930s saw extensive use of negative pressure mechanical ventilation. Access to render patient care was a problem with negative pressure ventilation and the advent of positive pressure ventilation has been predominately used since the 1960s. Recent advances in ventilator technology and improvements in the patient-ventilator interface with a flexible cuirass shell designed to fit over the anterior surface of the chest and incorporation of an active expiratory phase has resulted in a revival of its use. The actual cuirass ventilators of today apply many of the ventilation patterns achieved with positive pressure ventilators and they can provide respiratory rates from normal to high frequency oscillation and cough assistance. The Hayek RTX Ventilator is one ventilator which uses a flexible cuirass shell attached to the anterior chest wall via chest straps and

a disposable seal mechanism to apply extrathoracic negative pressure to the chest wall in a non-invasive manner. When the negative pressure is applied by the ventilator to the chest wall, the chest wall rises and increases the space within the thoracic cavity, creating a negative pressure relative to ambient atmosphere and airflow into the lungs occurs. Negative pressure is applied to the chest wall either at a constant level to increase lung volume with spontaneous respiratory activity or in cycle with a positive phase to create the tidal volume desired. Usually this tidal volume is a calculated volume of approximately 6ml/kg. Ventilatory rate and tidal volume are used to achieve the required minute volume in a similar manner as with positive pressure ventilation. Various modes and controls allow many patterns to ventilation just as with positive pressure mechanical ventilation. Additionally, the Hayek RTX can apply extrathoracic pressure to chest during exhalation to provide exhalation assistance as needed while always maintaining a mean negative pressure delivery. This positive phase significantly decreases the potential of large end expiratory lung volumes and their negative effect on ventilation. The positive phase also allows use of I:E ratios in the inverse range better supporting oxygenation without the concern for high levels of intrinsic PEEP that can occur using PPV. Since the Hayek RTX uses an extrathoracic cuirass shell, it does not require an endotracheal tube or tracheotomy tube as a patient interface for airflow delivery. As such, it is considered a non-invasive approach to ventilation which reduces the adverse effects associated with artificial airways, maintains the humidification and filtration efficiency of the upper airway, allows patient communication, normal P.O. nutritional and fluid intake, and reduces the potential for ventilator-associated events.

The Hayek RTX Biphasic Cuirass Ventilator thus works very similarly to normal spontaneous ventilation. Airflow is created with expansion of the thoracic cavity due to the negative intrapulmonary pressure. The negative intrapulmonary pressure created by the ventilator simulates spontaneous ventilation and the benefits to venous return, airway dynamics approach that which are normal.

Modes of Biphasic Cuirass Ventilation

The Hayek RTX Biphasic Cuirass Ventilator can be used noninvasively by applying many different patterns of and modes in similar manner as with routine positive pressure ventilation. Additionally, the RTX provides a positive or active expiratory phase to facilitate complete exhalation. BCV has also been applied successfully as an adjunct to PPV to decrease the positive pressures required thus mitigating the side effects of positive intrathoracic pressures, and as a tool to decrease the duration PPV is required. The modes of ventilation which can be applied using the Hayek RTX are identified below.

• **Continuous Negative Extrathoracic Pressure (CNEP)** applies a continuous negative pressure to the chest wall. In this mode the patient can breathe spontaneously and the therapeutic goal is increase the functional residual capacity in the lung to a desired level. CNEP is similar to continuous positive pressure breathing in the therapeutic goals and desired patient outcomes without the side effects associated with positive intrathoracic pressure. CNEP can also be used effectively to decrease the positive MAP when used adjunctively with PPV as PEEP levels can be dramatically decreased or eliminated as FRC is maintained with CNEP improving venous return and decreasing potential lung damage from PPV. CNEP via the effects of small airway dilation and improvements in VQ matching makes an excellent weaning tool to facilitate spontaneous breathing trials for patients that are serially unsuccessful at weaning attempts from PPV.

• **Controlled Biphasic Cuirass Ventilation** provides a mandatory respiratory rate to the patient as necessary for the required minute volume. Tidal exchange is controlled by adjustment on the span or differential between the inspiratory and expiratory pressures. The patient is able to initiate unsupported spontaneous breaths when desired between the mandatory breaths. In the controlled mode, the Hayek RTX is very similar to intermittent mandatory ventilation using positive pressure devices.

• **Synchronized Biphasic Cuirass Ventilation** senses the spontaneous efforts of the patient and will deliver set negative and positive pressures to the chest synchronized with those efforts. Pressure changes of respiration are sensed either at the airway or from within the cuirass. Tidal exchange is affected by adjustment of the span or differential between the inspiratory and expiratory pressures in this mode. The patient sets the rate and tidal exchange increases or decreases based on patient effort during the respiratory cycle. A back-up rate is utilized to maintain support in the event of apnea. Synchronized biphasic cuirass ventilation is very similar to pressure support with positive pressure ventilators.

• **High Frequency Oscillation (HFO)** is applied to the chest wall with frequencies to 1200 cycles per minute. The therapeutic goal of HFO is to improve oxygenation and reduction of carbon dioxide through increased kinetic activity and gas diffusion at alveolar level and for secretion mobilization from the lung periphery. A separate secretion clearance mode setting utilizes a time cycled combination of HFO and cough assistance to provide a highly effective means of secretion mobilization and airway clearance of secretions from the larger airways.

Clinical Contraindications and Side Effects

BCV Exclusion Criteria

- Burned skin or draining wounds under shell or seal area.
- Indwelling lines or tubes that are located under seal. (Within shell is fine)
- Weight > 180 KG
- Patient's thoracic structure precludes establishment of good seal.
- Lack of viable airway either natural or artificial.
- Cardio/pulmonary arrest.

Actual side effects of cuirass ventilation are few. Use of BCV does require the patient have a patent airway. Use of the synchronized mode on the Hayek RTX is useful in preventing the increases in upper airway resistance and potential for upper airway obstruction that may occur rarely in control mode. Also use of CPAP in conjunction with BCV has been shown to assist with increasing airway patency if upper airway obstruction presents.

It is important to monitor the skin where the cuirass seal comes in contact. The cuirass foam seal in the RTX system is disposable and wears with use and will lose some of its padding ability over time. Routine removal q4-8 hrs to monitor patient's skin is recommended. It is important to monitor skin and seal integrity and change seals as indicated. The cuirass and seal should always be placed over a cloth barrier such as a cotton t-shirt to

hospital gown. Proper placement of the cuirass on the chest and maintenance of cuirass seals helps insure minimal potential of skin issues even with long-term continuous use.

Emesis or reflux is a rare side effect and can typically be avoided by basic reflux interventions of holding feeds or meals until after secretion clearance treatments, stopping continuous or bolus feedings until after BCV introduced and restoring rate gradually as patient becomes used to cuirass support, and close monitoring of residuals.

Patients with significantly misshapen thoracic structure may not be able to benefit from BCV. If the cuirass cannot be sealed to their thorax then BCV will not work for them. These patients can however often be supported with BCV through use of rolled towels or other means of providing a build up that helps match their thorax to the shape of the cuirass. Generally as long as the pressure changes in the cuirass can be brought to bear on the abdomen below the diaphragm then support can be accomplished.

Patients who feel they require being on their side or rolled forward or on their abdomen to sleep will often require a longer period of adjustment to cuirass ventilation and may need some pharmacologic assistance with achieving good sleep during the adjustment period.

A chill effect may occur in very small or very thin patients as some leak of gas occurs around the cuirass seal which room temperature air is flowing across a significant portion of the patient's body surface area. This can cause subsequent minor thermal losses. This is easily overcome in most cases. The cuirass and seal should always be applied over skin covered by cloth such as a t-shirt or hospital gown. In cases where thermal losses become an issue increasing the thickness or the insulating abilities of the cloth will usually resolve this problem. The chest and abdomen can be covered with a layer or two of a loose-fitting light blanket or towel and this will resolve in most cases.

Lines tubes and drains required in the area of anterior thorax and abdomen can pose a problem in some cases; however as long as the point of entry of the line tube or drain into the skin is within or outside the boundary of the cuirass seal there is generally no problems with any type of device. If the tube originates within the cuirass the seal is designed to absorb the shape of the tube without causing occlusion thus chest tubes, g-tubes or indwelling tubes and drains of any sort can be used without hindrance while BCV is being used. If the cuirass cannot be placed without the seal having to be over the point of entry of the tube into the skin then use of the cuirass is not recommended as irritation of the point of entry will often occur. The cuirass can be effective if placed slightly lower, higher, to the right or left and often the line tube or drain can be managed to the inside or outside of the cuirass seal so no problems occur.

Another very important consideration if BCV is being used to provide for full ventilatory support is availability of back-up support. For times that the cuirass needs to be removed for bath, skin assessment etc. an alternative means of support should be provided. All ventilators are manmade machines and can demonstrate loss of full function. At the least a Bag/Valve/Mask device should be present during use for these types of patients and support readily offered if the cuirass has to be stopped or come off for any period.

Clinical Considerations for the Hayek RTX Biphasic Cuirass Ventilator

The Hayek RTX Biphasic Cuirass Ventilator is a versatile non-invasive ventilator which can provide assisted ventilation to patients with acute or chronic respiratory failure. It provides such assisted ventilation in a manner that approaches normal ventilation. The advantages of the Hayek RTX over non-invasive positive pressure ventilation include minimal adverse effects on cardiac output and approaches the normal physiology of spontaneous ventilation compared to positive pressure ventilation. The extrathoracic cuirass shell serving as the patient ventilator interface may offer additional advantages over the mask serving as the patient interface with standard non-invasive positive pressure ventilation.

Successful use of the Hayek RTX has been documented in patients with multiple diagnoses with pulmonary symptoms. Severe, but stable COPD, and other respiratory illnesses where patients are experiencing respiratory muscle fatigue and reduced Inspiratory muscle endurance may see improvement in symptoms with use of BCV. Decrease work of breathing and intermittent respiratory muscle rest can occur with BCV resulting in improvement.

Similarly, patients with various neuromuscular disorders, muscular dystrophies, spinal muscular atrophy, amyotrophic lateral sclerosis, poliomyelitis, or spinal cord injury may benefit from the non-invasive use of the biphasic cuirass ventilator. BCV can provide an alternative that does not require a tracheostomy. Many of these patients can successfully have ventilation supported for long-term home care and maintain normal functions of airway clearance, eating, swallowing, and communication which would be compromised with invasive or non-invasive positive pressure ventilation.

Additional uses of the Hayek RTX Biphasic Cuirass Ventilator have been documented for short term use post-operatively for cardiac and abdominal surgery particularly cardiac procedures associated with single ventricle, arterial duct or tetralogy of Fallott repair. The ventilation with the cuirass often produces an increase in pulmonary blood flow and cardiac output in these patients. For patients prone to post op atelectasis CNEP is a very comfortable way to protect lung volumes until the patient recovers adequately to do on their own.

BCV in any of the modes offers a powerful tool to improve oxygenation. Hypoxemic respiratory failure will frequently respond using CNEP or one of the other support modes and adjusting to maintain a highly negative mean cuirass pressure. Whether the patient is on PPV at high FiO2s and PEEP levels or is on high flow O2 clinical progress will be severely hindered until oxygenation improves. BCV by supporting more naturally will improve O2 delivery by recruiting the lung and improving alveolar perfusion thus ventilation/perfusion matching.

There have been many other reported applications in the use of the biphasic cuirass ventilator. The application of biphasic cuirass ventilation should be considered in those case where respiratory muscle fatigue and the work of breathing is approaching ventilatory failure. Intervention with biphasic cuirass ventilation may avert the need for endotracheal intubation; assist in weaning from positive pressure ventilation, or assist with the prevention of re-intubation in the immediate post ventilation time.

Many clinical diagnoses which involve the lungs either directly or indirectly have common clinical problems present. Some of the problems which can be expected to respond to the interventions offered by BCV are:

- Need for ongoing recruitment of alveoli and small airways
- Conditions requiring non-invasive support for relief of increased WOB
- Small airways disease
- Need to improve oxygenation
- Need to decrease RV workload and improve function
- CO2 retention
- Low or absent respiratory drive
- Fatigued weak or poorly innervated pulmonary musculature
- Anomalous cardiac flow situations
- Restrictive pulmonary processes
- Obstructive lung processes
- Mixed obstructive and restrictive
- Muco-proliferative lung condition
- Reoccurring atelectasis/pneumonias
- Reoccurring pneumothoraces
- Other means of support have not worked or is not desired i.e. BiPAP due to skin issues, or desire to avoid trach and PPV

Returning to Our Three Basic Principles of Medical Interventions

1) First, do no harm

Any time an invasive intervention can be avoided it is better for the patient. Avoiding tracheal intubation or tracheostomy via use of BCV successfully will decrease ICU length of stay and eliminate any potential of a ventilator associated event. Mask ventilation is also stressful and can cause injury. An intervention such as BCV that provides support in a way that most mimics natural ventilation and preserves many cardio-pulmonary functions lost with PPV use offers a lower threshold of harm and should be offered as a first line treatment whenever it can. BCV can successfully replace CPAP, BiPAP, invasive PPV, Vest and Cough Assist in many cases with greater comfort while preserving the patient's ability to eat, drink and speak in many cases acutely and/or chronically.

2) For every action, there is an equal and opposite reaction

Air pushed into a patient's lungs by a ventilator even as carefully as possible can cause damage as over distension of the healthy and compliant lung units results. Positive pressure in the thorax decreases venous return and thus cardiac output. At no time in the natural physiology of respiration and cardiac function is there positive pressure present in the thorax for more than a very brief period if at all. These opposite reactions of cardio-pulmonary physiology to PPV make clear that a more natural intervention supporting ventilation such as BCV offers be applied whenever possible.

3) A respiratory care plan's interventions should in large part focus on the goal of recruiting and restoring to normal, the functional residual capacity (FRC) of the patient

Throughout the history of respiratory care interventions many means of restoring FRC and re-recruiting the lung have been proposed and attempted. Many involved positive pressure to little avail. Some sought to strengthen the patient's own ability to maintain full volumes, but many patients with lung volume loss lack the capacity to gain strength without assistance if at all. The best and most natural way to restore full lung volumes is to pull the gas into the lungs and maintain that pull until airway and alveolar re-inflation can occur while providing an effective means of secretion mobilization and clearance assistance if needed. BCV, because it is an approach based on normal ventilation, is simply the best way ever devised to do this, and provide ventilatory support more naturally.

To find out more about why they say "BCV It's Just Better" or to obtain information on how to bring BCV to your facility or to prevent readmission and provide it for your patients at home call 855-2-GETBCV. Authors Rick Leonard and Gary Mefford can be reached at rick.leonard@hayekmedical.com and gary.mefford@hayekmedical.com.

Resources

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Respiratory Compromise

Mary Erslon, Scott Stoneburner

Postoperative respiratory compromise is an umbrella term that includes respiratory insufficiency, arrest and failure. It is a serious issue that may increase patients' cost of care and length of hospital stay, as well as morbidity and mortality.[1]

In 2011, costs for hospital stays related to respiratory compromise exceeded $8.7 billion annually.[2] The cost of respiratory compromise in 2019 has been projected to reach $37.3 billion.[3] Respiratory compromise is one of the five conditions resulting in the most rapidly increasing costs for hospital stays in the United States.[2]

The Issue

Recent research reveals that up to 7 percent of all Medicare patients suffer from respiratory compromise, a number that is projected to increase by 31 percent by 2019.[3]

Respiratory compromise is a critical complication that can worsen patient outcome, increase hospital length of stay, and increase the cost of patient care. According to analysis by Kelley et al.[4], patients who developed respiratory compromise on the general care floor are 29 times more likely to die, are in the hospital seven days longer, are in the ICU almost three days longer, and cost hospitals an additional $18,208 per patient than patients who do not develop respiratory compromise.

Respiratory compromise is often preceded by clinical instability, most commonly elevated respiratory rate or progressive hypoxia.[5] Therefore, failure to prevent respiratory compromise events may be the result of inadequate early detection of abnormalities in patients' respiratory status. This may be especially prevalent in lower acuity settings such as the general care floor where patients' respiratory status is only periodically assessed.[6]

Approximately 74 percent of patients suffering adverse events have at least one undocumented respiratory rate measurement immediately preceding the adverse event,[7] which may lead to delayed intervention and worsened outcomes. Delayed interventions occur in 50 percent of patients with respiratory distress, with a median duration of delay of 12 hours.[8] Such delays in patients with respiratory distress are associated with an increase in mortality.[8]

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Given this context, medical manufacturers must create innovative monitoring technology that improves observation of the patient respiratory function and decreases the likelihood of this complication happening.

Continuous Patient Monitoring Solutions

Solutions do exist. With continuous monitoring solutions, caretakers may intervene earlier and identify this threat, improving the patient's health and safety.

Patient monitoring strategies encompassing respiratory rate, pulse oximetry and capnography may have the potential to reduce the likelihood and severity of postoperative respiratory compromise. In addition, these strategies not only have the potential to improve patient outcomes, but also may reduce the overall cost of care.

For instance, Nellcor Respiration Rate technology from Covidien—Respiration Rate software—may help clinicians meet the recommendations of the Joint Commission, ASA, APSF and other key standard bodies for continuous electronic monitoring of oxygenation and ventilation for adult patients receiving medication for postoperative pain management, who are at increased risk for respiratory complications and compromise.

This technology provides oxygen saturation (SpO_2), pulse rate and respiration rate using a single, integrated sensor. It also provides continuous, noninvasive measurement of respiration rate for adults in hospitals and hospital-type facilities and has an accuracy of ±1 breath per minute when compared to respiration rate derived from a capnography-based reference.[7]

Summary

In conclusion, postoperative respiratory compromise is a common, costly and often deadly complication that affects patients and caregivers throughout the healthcare environment. It is important that comprehensive and continuous patient monitoring strategies are developed that encompass pulse oximetry, respiratory rate and capnography. By implementing these solutions, caregivers have the potential to reduce the likelihood and severity of respiratory compromise, may improve patient outcomes and reduce overall cost of care.

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A Pilot Study of the Impact of High-Frequency Chest Wall Oscillation in Chronic Obstructive Pulmonary Disease Patients with Mucus Hypersecretion

Indranil Chakravorty, Kamaljit Chahal, Gillian Austin

Introduction: Chronic obstructive pulmonary disease (COPD) patients with mucus hypersecretion tend to demonstrate increased frequency of infective exacerbations and a steeper slope of decline in lung function. Enhanced mucociliary clearance with high-frequency chest wall oscillation (HFCWO) devices previously used in cystic fibrosis and bronchiectasis patients may offer the opportunity for community-based, self-managed therapy to improve quality of life and lung function.

Study design and methods: A randomized controlled crossover pilot study of HFCWO compared with conventional treatment was conducted in 22 patients with moderate to severe COPD and mucus hypersecretion. Patients spent 4 weeks using an HFCWO (SmartVest®) device and 4 weeks in a conventional phase with a 2-week washout. Eleven patients started with HFCWO and changed to conventional treatment, whereas the other eleven patients started conventional treatment and crossed over to HFCWO.

Results: The patients were elderly with a mean age of 71 (standard deviation [SD] 10) years and were at the upper end of the normal range of body mass index (25 [SD 4.2] kg/m^2). The majority of patients had moderate to severe COPD with a mean percentage predicted forced expiratory volume in 1 second of 41 (SD 15.6) and percentage predicted forced vital capacity of 73 (SD 17.7). Baseline sputum production was negatively correlated to lung function and positively to St George's Respiratory Questionnaire. Symptom scores and St George's Respiratory Questionnaire symptom dimension improved significantly (–8, P , 0.05). Sputum production showed a declining trend in the HFCWO phase, although not reaching statistical significance. The HFCWO device was well tolerated with good reported compliance.

Conclusion: This pilot study demonstrated that patients with advanced COPD and mucus hypersecretion at increased risk of declining lung function tolerated the HFCWO treatment well, leading to improvement in quality of life and reduced symptoms.

Background

Cough, sputum, and shortness of breath are cardinal features of chronic obstructive pulmonary disease (COPD). The natural history of COPD is characterized by a progressive reduction in exercise tolerance and health-related quality of life (HRQoL).[1,2] The rate of decline in lung function, which is a strong predictor of morbidity and mortality in COPD,[3] as well as health care utilization,[4] is higher in patients with mucus hypersecretion and recurrent exacerbations.[5-7]

There is currently a variety of methods to improve mucociliary clearance (MCC) that have been shown to be effective in chronic lung conditions associated with excess mucus production, such as cystic fibrosis (CF) and non-CF bronchiectasis. These include physical therapy techniques such as autogenic drainage, the active cycle of breathing technique,[8] and adjuvant mechanical devices such as the flutter device[9] and positive end-expiratory pressure.

High-frequency chest wall oscillation (HFCWO) is a technique utilizing automated pneumatic chest wall percussion delivered through a vest and transmitted to the airways that allows patients to manage their condition independently in their own homes, thus reducing health care costs. HFCWO delivers pressurized air pulses to the external chest wall via the vest, which results in transient cephalad bias airflow spikes in the airways to loosen bronchial mucus so that the patient can more easily expel secretions by coughing. Although HFCWO is well tolerated in children with CF[10-12] and has shown demonstrable improvement in MCC,[13] as well as in some institutionally managed adults with amyotrophic lateral sclerosis, there is currently very little evidence of usage or benefit in adults with COPD.[14] The in vivo benefit of HFCWO in improving MCC is based on the hypothesis that cyclical mechanical stress on the airway mucosa may improve hydration of the airway surface layer by activation of the P2Y2 receptors.[15] Intuitively, improved MCC may reduce airflow obstruction,[16,17] subsequent exacerbations,[18,19] and rate of lung function decline, leading to improvement in HRQoL.[20]

This pilot study aimed to explore the impact of improved MCC by application of HFCWO on symptoms and HRQoL in patients with advanced COPD and mucus hypersecretion.

Study design and methods

Ethical approval was obtained from the local research and ethics committee. A randomized crossover study design was used to compare HFCWO with conventional treatment. All COPD patients admitted to hospital or attending the emergency room in the preceding 12 months due to an exacerbation of their disease were invited to participate in the study. These patients were

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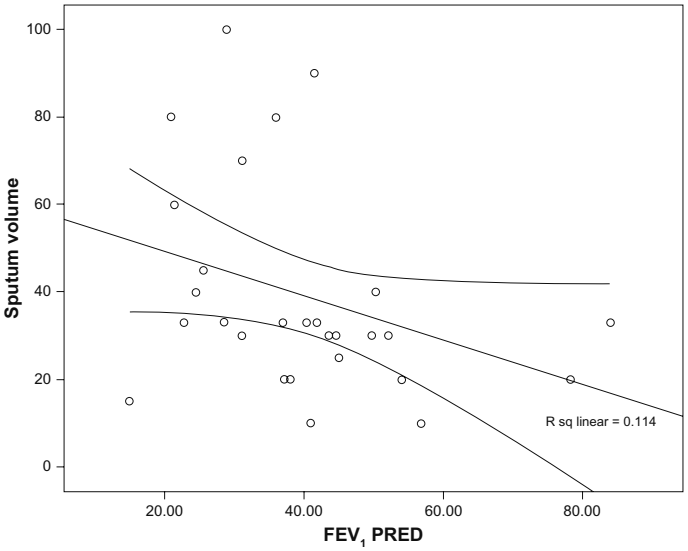

Figure 1 scatter plot demonstrating the relationship between sputum volume (mL) and lung function (forced expiratory volume in 1 second percentage predicted [FeV_1PreD]).

identified from the authors' COPD database. Patients who gave written consent attended for a screening visit. The minimum inclusion criteria were: forced expiratory volume in 1 second (FEV_1) , 0.8 predicted, ratio of FEV_1 by forced vital capacity (FVC) (FEV_1/FVC) , 0.7, and a daily wet sputum volume of .25 mL in the stable state for 3 consecutive days. Exclusion criteria included history of osteoporosis, significant gastro-oesophageal reflux, hiatus hernia, recent acute cardiac event (6 weeks), congestive cardiac failure, any significant musculoskeletal disorders, bronchiectasis, and asthma (excluded by reversibility testing).

Patients were randomized to receive either HFCWO or conventional treatment in phase 1 for 4 weeks, followed by a 2-week "washout" phase. Subjects then crossed over to the alternative phase for the final 4 weeks. Assessments were carried out at the beginning and end of each phase.

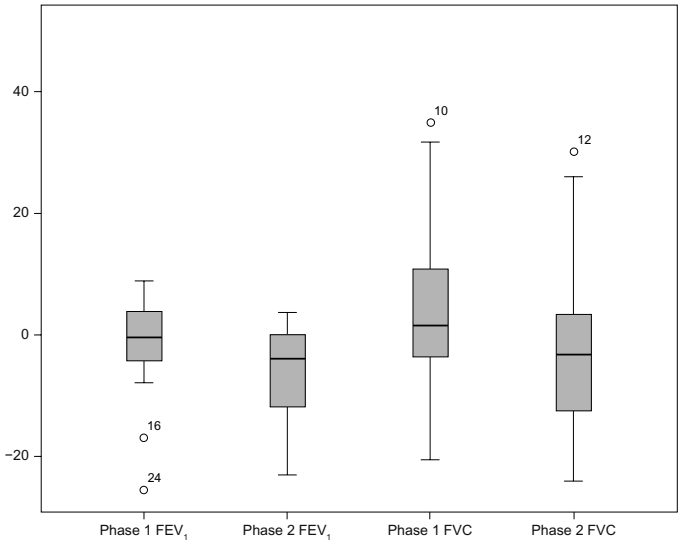

Figure 2 Boxplots representing median and interquartile range change in lung function (predicted forced expiratory volume in 1 second [FeV_1] percent predicted and forced vital capacity [FVC] percent predicted) from baseline after intervention in high-frequency chest wall oscillation (phase 1) and conventional arm (phase 2).

The SmartVest Airway Clearance System (Electromed, Inc, New Prague, MN) was used to deliver the HFCWO treatment for all patients in the HFCWO treatment group. The SmartVest system consists of an inflatable vest, which is worn over the torso, and an air pulse generator that produces and delivers the oscillating air pulses to the vest via a connecting air hose. The HFCWO group received two treatment sessions per day of 20 minutes each (morning and evening). The SmartVest air pulse generator was set at an optimum oscillating frequency of 13–15 Hz, based on individual patient tolerance during the "tuning procedure," and a pressure setting to achieve a tight but comfortably snug fit. Patients in the conventional treatment group followed their own COPD management regimen including all prescription medications, advice on the benefits of regular exercise, and cough clearance of sputum. Medication included a minimum of combination long-acting bronchodilator and inhaled corticosteroid as well as an acting anticholinergic inhaler.

Primary outcome measures included HRQoL, patient tolerability, and compliance of the SmartVest HFCWO device. Secondary outcome measures were spirometry and wet sputum volume. HRQoL was measured with the St George's Respiratory Questionnaire (SGRQ)[21] as well as with a nonstandardized symptom score measurement, which required subjects to rate five cardinal respiratory symptoms (cough, sputum, wheeze, shortness of breath, and exercise tolerance) as mild = 1, moderate = 2, or severe = 3.

A paired sample t-test was used to compare the results between the HFCWO and conventional phase. Baseline correlations were obtained using multiple linear regression analysis. An intention-to-treat analysis model was used for patients who dropped out during each phase of the study. Correction for type 1 errors for multiple statistical tests was not used.

Results

Thirty subjects (eight female) consented to participate in the pilot study. Twenty-two patients completed the trial. Eight patients developed exacerbations of COPD within the trial period and were consequently withdrawn from the trial.

The majority of patients had moderate to severe COPD with a mean FEV_1% predicted of 41 (SD 15.6) and percentage predicted forced vital capacity (FVC%) of 73 (SD 17.7). The baseline daily wet sputum volume was variable with a mean volume of 39 (SD 23) mL/day, based on a 72-hour collection. Daily sputum expectoration at baseline correlated with a lower FEV_1% predicted, as shown in Figure 1 (linear regression adjusted r^2 =−0.114, P , 0.05).

SGRQ scores at baseline were symptom score 72 (SD 18), activity score 77 (SD17), impact of disease score 51 (SD23), and total score 63 (SD19). Three of the SGRQ dimension scores showed a significant predictive relationship when modeled with FEV_1% predicted using a linear regression model: symptoms (coefficient β=−0.5, P , 0.016), activity (β=−0.7, P = 0.007), and total score (β=−0.4, P , 0.05). The SGRQ impact score remained nonsignificant.

There was no significant change in spirometry values (FEV_1 or FVC) with HFCWO baseline FEV_1 1.05 (SD 0.37) versus postintervention FEV_1 1.07 (SD 0.38) L or in the conventional phase (baseline FEV_1 0.97 [SD 0.37]) versus postintervention (FEV_1 1.01 [SD 0.36] L, P = not significant), as shown in Figure 2.

Table 1 Symptom and St George's Respiratory Questionnaire (SGRQ)[21] dimension scores before and after intervention in each arm of the study

	HFCWO before	HFCWO after	*P*	Conventional before	Conventional after	*P*
Symptom score	9.09 (3.3)	7.0 (4.7)	0.02	9.33 (2.3)	9.55 (2.0)	NS
SGRQ symptom score	72 (18)	64 (16)	0.02	70 (18)	68 (17)	NS
SGRQ activity score	77 (17)	78 (16)	NS	80 (14)	75 (19)	NS
SGRQ impact score	51 (23)	50 (19)	NS	49 (19)	53 (19)	NS
SGRQ total score	63 (19)	60 (17)	NS	62 (15)	62 (17)	NS

Note: Values in brackets indicate the standard deviation.
Abbreviations: FCWO, high-frequency chest wall oscillation; NS, not significant.

Sputum expectoration remained individually variable but showed a trend toward a reduction after HFCWO. In the HFCWO phase, the mean change in sputum volume was –2.6 mL (range –53 to +27 mL), and in the conventional phase the mean change was +6 mL (range –70 to +40 mL), P = 0.06.

The baseline sputum volume significantly predicted the change in sputum volume with HFCWO, in a model including age, sex, FEV_1% predicted, FVC%, and body mass index (linear regression model coefficient β= 0.7, P = 0.024), whereas in the conventional phase, none of the variables was found to be significant.

There was a significant improvement in the mean total score in the five-symptom self-reported questionnaire in patients on HFCWO, P = 0.03. SGRQ scores showed a significant improvement in the symptom dimension (∂=–8, P = 0.028), whereas impact of disease, activity, and total scores did not achieve a significant reduction (Table 1). There was no significant change in SGRQ scores in the conventional phase (Figure 3).

Discussion

Although the effect of HFCWO has been demonstrated to enhance MCC in children with CF,[22] as well as in adults with bronchiectasis and neuromuscular disease,[23] its use in COPD[24] is novel. In this pilot study, the authors set out to explore the suitability of using this modality to improve MCC in patients at the moderate to severe end of the COPD spectrum, where increased sputum production and retention can lead to increased exacerbations, hospital admissions, and a more rapid decline in lung function.[25] In addition to assessing the impact on HRQoL and sputum, another aim was to assess the tolerability and acceptability of this form of treatment in elderly patients with disabling COPD symptoms and often multiple comorbidities.

Toward this aim, it was found that patients demonstrated a significant improvement in HRQoL dimensions of SGRQ symptom control.The efficient daily clearance of sputum may have led to a decreased daily sputum volume at the end of the HFCWO phase. The HFCWO modality delivered by the SmartVest system was well tolerated in patients who often had significant disability including shortness of breath at rest. No subjects dropped out due to intolerance of the device.

The crossover study design was chosen to reduce the intersubject variability in physiological parameters, as each subject would act as their own matched control. It was decided to have two cohorts of patients, reversing the sequence of HFCWO/conventional versus conventional/HFCWO, to detect any residual effect on MCC after discontinuing the HFCWO treatment phase during the 2-week washout phase and none was detected. Placebo intervention for this study was deliberately not chosen, as the authors wished to compare HFCWO with "usual treatment," as is currently usual practice in a real-life setting. It was the authors' hypothesis that patients with severe disabling symptoms from COPD were likely to accept and comply with a treatment that involved setting up and using a vibrating vest around their chest for 20 minutes twice a day only if they experienced a detectable benefit. This has been demonstrated in several trials where compliance levels have been found to be below 50%.[26,27] However, it is theoretically possible that a proportion of the benefit demonstrated in HRQoL may indeed be due to a placebo "device" effect.

Although this pilot study was not statistically powered, a clinically significant improvement was found in the SGRQ symptom score as well as the SGRQ total score. The SGRQ dimension scores are considered to demonstrate a clinically relevant change if there is a mean reduction in the score of four or more units.[28] However, when the five-point clinical symptoms score was examined, there was a significant improvement in the HFCWO phase when compared with the conventional phase, which showed no change, although this symptom score was not standardized. When such disease-specific quality of life (QoL) outcomes are compared with generic QoL measures, the scores were found to demonstrate similar changes. Although in the conventional phase the five-point symptom scores were marginally worse, both of these outcomes improved in the HFCWO arm. Hence, it is likely that the size of improvement detected in the HFCWO phase is due to the intervention, rather than being entirely a placebo effect.

Analysis revealed a negative correlation between FEV_1 and sputum production and a positive correlation between FEV_1 and HRQoL. Not only did a low FEV_1 relate to a low HRQoL but also to increased sputum production.This would add credence to the current consensus that increased sputum production (and retention) may lead to an increased frequency of exacerbations and, in turn, to an increased rate of decline in FEV_1.[29] As FEV_1 decline is still the most reliable parameter of survival, this is a very powerful determinant of outcome in COPD patients.

A 25 mL/day mucus production threshold was chosen as a criterion for entry into the study after a comprehensive search of the relevant literature. Drawing on previous experience from trials in CF and non-CF bronchiectatics, the authors were keen to exclude these patients from this trial, intending primarily to focus on the phenotype of COPD[30] with airway obstruction and mucus hypersecretion as a novel area of use. The authors' hypothesis of improved MCC leading to a reduction in exacerbation of COPD and rate of decline of FEV_1 would be valid only in patients who exhibited both frequent exacerbations and increased mucus production. Patients who had at least one exacerbation in the last 12 months requiring a visit to hospital

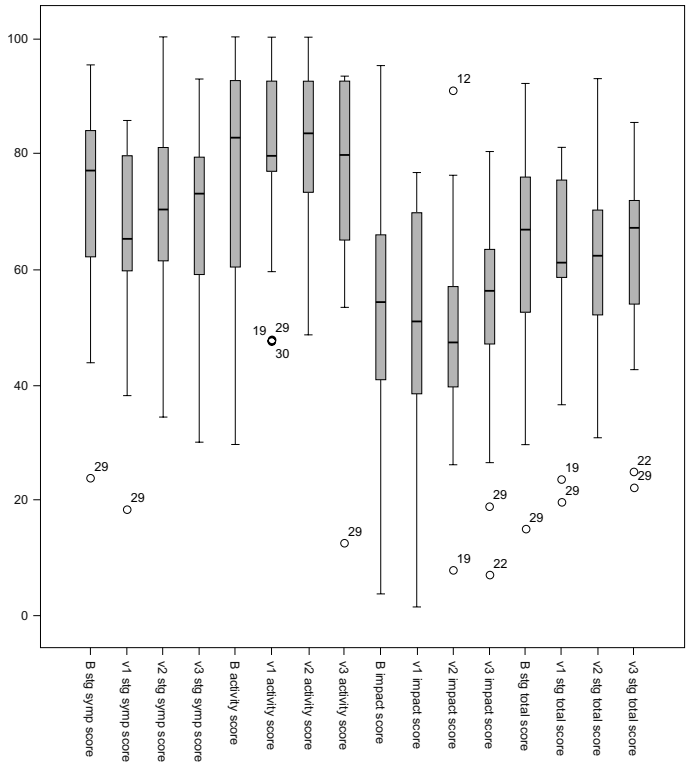

Figure 3 Boxplots demonstrating the st george's respiratory Questionnaire domain and total scores before and after intervention in both arms of the study (high-frequency chest wall oscillation B to v1 and conventional phase v2 to v3).

were invited to take part in this study. The subset of patients who were predominantly suffering from chronic bronchitis rather than having predominantly emphysema, where improved MCC may not be a relevant outcome, were especially sought for inclusion in the study. Clinical experience demonstrated that mucus production in generic COPD patients varied around 10 ± 10 mL/day. Hence, the minimum mucus volume was set at a consensus level of 25 mL/day. High-resolution computed tomography scans were not routinely undertaken in these patients to exclude mild bronchiectasis. It is recognized that a proportion of COPD patients with excess sputum production may have undetected areas of bronchiectasis in their lungs. However, clinical criteria of persistent sputum purulence (in the absence of a clinically detectable exacerbation) and chest radiographic examination were used to avoid patients with obvious bronchiectasis.

Mucus production was widely variable in the study subjects, reflecting the range of FEV_1 in this group. There was a consistent trend of reduction in mucus production in the HFCWO phase, when compared with the conventional phase, where the levels of sputum production remained stable or even increased. The baseline mucus production was the primary determinant in predicting the post-treatment mucus production during HFCWO treatment. Overall, there was a trend of reduction in sputum production by the end of the 4-week intervention period. This is likely to be due to efficient daily clearance, as well as a possible reduction in actual sputum production. Patterson et al explored sputum volumes in patients with bronchiectasis and also found significant variability, making this an unreliable measure of effectiveness of MCC modalities.[31]

In a Canadian study, with 15 severe COPD patients given a flutter device to improve MCC, the authors found an improvement in 2-hour postbronchodilator spirometry and exercise tolerance after 1 week of use.[9] Therefore, it is likely that effective MCC in COPD patients may have an impact on the rate of decline in lung function in the future, although this was not demonstrated significantly in this pilot study.

Conclusion

This study was designed to explore the feasibility of using the HFCWO modality of mucus clearance in patients with advanced COPD. It was found that that the SmartVest HFCWO device was well tolerated and that subjects demonstrated an improvement in symptom scores and QoL. A significant effect on lung function was not demonstrated, and the wet mucus quantities remained individually variable between patients. It is therefore feasible that HFCWO may have a role in enhancing mucus clearance in COPD patients with the "mucus hypersecretory" phenotype, and future studies may be able to explore the impact of MCC in lung function decline and prevention of exacerbations.

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Oxygen Therapy in the Management of Congestive Heart Failure

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Introduction

Congestive heart failure (CHF), also known as chronic heart failure, is a global term for the physiological state in which cardiac output is insufficient for the body's needs. Nearly six million Americans currently suffer from heart failure and there are about 670,000 new cases diagnosed each year. As the population ages, the incidence of CHF is rising dramatically; with estimates that it affects about 10 per 1,000 people after age 65. Heart failure is the most common reason for hospitalization in the elderly and carries an annual cost of approximately $39 billion.[1] In the Medicare fee-for service program, heart failure is also the most common reason for re-hospitalization within 30 days of discharge.

Section 3025 of the Patient Protection and Affordable Care Act mandates financial penalties for hospitals that fail to achieve federally determined reductions in 30-day readmissions of targeted conditions; including CHF. The financial penalties associated with this program can have significant consequences. As a result, acute care institutions are dedicating significant resources to establish a best-practices approach to managing these patients. These efforts include recruitment into rehabilitation programs, patient education and post discharge support with medications and follow-up telephone consultation. Central to these efforts is an eye to ensuring post-discharge patient stability. Unfortunately, these efforts may be undermined if attention is not also given to the destabilizing potential of nocturnal arrhythmias that may arise secondary to Cheyne-Stokes Respiration[4].

Cheyne-Stokes Respiration & CHF

Cheyne-Stokes respiration (CSR) is an abnormal respiratory pattern associated with CHF that is characterized by a crescendo-decrescendo alterations in tidal volume that is separated by periods of apnea or hypopnea. Studies by Javaheri[5] and Sin[6], consisting of 81 and 450 subjects respectively, reported prevalence rates of 40% and 33% in patients with a left ventricular ejection fraction (LVEF) of <40%. Patients with CSR generally experience sleep fragmentation and recurrent episodes of nocturnal hypoxemia that often result in marked daytime impairment. The presence of recurrent hypoxia triggers an increase in sympathetic tone through the cyclic release of catecholamines.[7,8] It has been suggested that such repetitious excitation of an already diseased heart may contribute to atrial fibrillation, ventricular arrhythmias and increased mortality.[9-11]

When a patient assumes a supine position to facilitate sleep, fluid that had accumulated in gravity dependent regions is redistributed. Aided by the negative intrathoracic pressure during inspiration, some of this fluid reaccumulates in the interstitial space of the lung where it acts to stimulate irritant receptors.[9,12] This stimulation triggers a vegally mediated hyperventilation and a resulting reduction in arterial carbon dioxide (P_aCO_2) and elevation of arterial oxygen (P_aO_2) levels. Eventually, the apnea threshold is reached and the drive to breath is abated. The resulting apnea is followed by progressive increases in inspiratory effort as peripheral chemoreceptors respond to the apnea triggered hypoxia.

The crescendo-decrescendo breathing alterations in CSR compensate for the changing serum partial pressures of oxygen and carbon dioxide. Sluggish circulation causes timing delays between the pulmonary artery and carotid and aortic chemoreceptors resulting in unstable swings in respiratory rate and depth of breathing[12]. Hypoxia has been shown to cause an enhanced sensitivity of peripheral chemoreceptors, which results in rapid compensatory changes in respiratory drive in response to small changes in serum oxygen and carbon-dioxide[12,13] (Figure 1). Although the carbon-dioxide level rises and falls in relation to changes in breathing depth and frequency, in the majority of patients the mean CO_2 level remains below normal. Hypoxia clearly plays a central role in the initiation of CSR as evidenced by the attenuation of periodic breathing following administration of supplemental oxygen.[12,14] Additionally, hypoxia appears to contribute to ongoing cardiac stress. Gottlieb and colleagues[8] studied the relationship of oxygen desaturation and hemodynamic stress in heart failure patients. By measuring the brain natriuretic peptide (BNP), a marker of ventricular stress and comparing it to blood oxygen saturation levels, they found a direct correlation between the time spent with a saturation below 90% and the rise in BNP level, concluding that prevention of hypoxia is especially important in this at risk population of patients.

Diagnosing Nocturnal Hypoxemia in CHF

There is strong evidence that nocturnal oxygen desaturation may be directly correlated to sleep disturbance and CSR in stable CHF patients with treated heart failure and no daytime evidence of hypoxemia[15]. Despite the evidence, the actual diagnosis of mild CSR often proves elusive. Since symptoms are rarely seen

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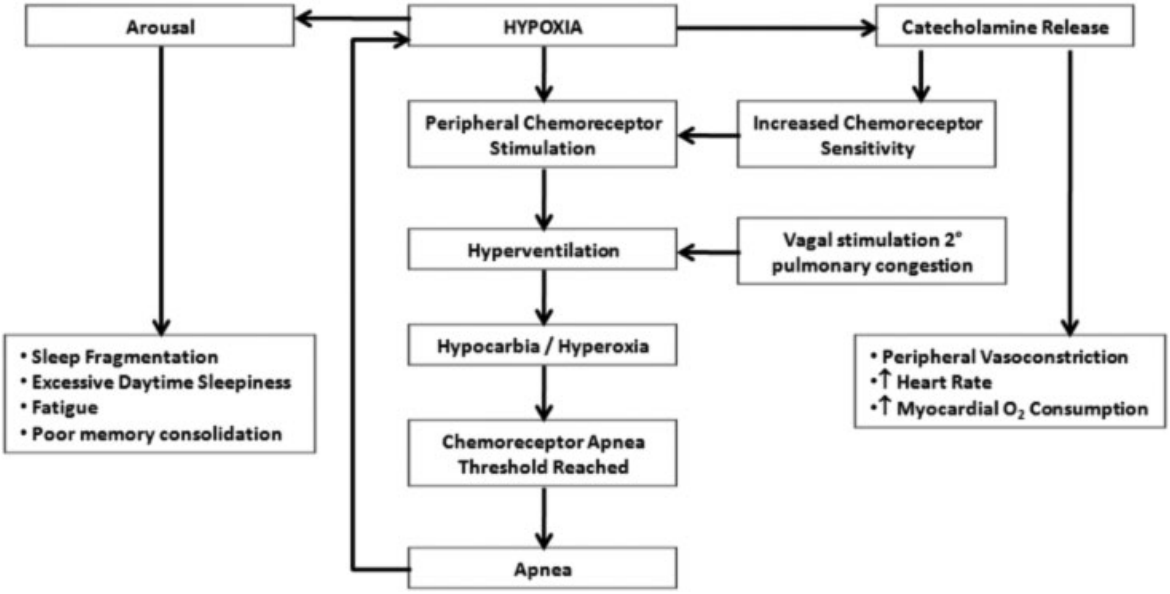

Figure 1. Cheyne-Stokes breathing results from a combination of hypoxia, up-regulation of peripheral chemoreceptor response and sluggish circulation. The crescendo-decrescendo breathing pattern is a product of oscillating peripheral and central chemoreceptor stimulation and trigger threshold overshoot. Apnea results from the hypocarbia that occurs during the hyperventilatory phase of breathing. Hypoxia is a resulting byproduct of the apnea. Preventing the onset of hypoxia removes a significant driver of CSR and results in reductions in the frequency and duration of events. Modified from references.[10, 11, 12]

at any time other than during sleep, clues to the presence of this pathology are typically not present during routine physical examination. Patient complaints of daytime sleepiness, morning headache and reduced cognition that can be suggestive of nocturnal hypoxemia may be easily confused with side-effect commonly associated with cardiac glucosides and other co-morbid symptoms and therefore, history and physical alone may be inadequate.

Diagnosing nocturnal hypoxemia in known, stable CHF is relatively simple, inexpensive and can be easily performed in the inpatient setting as well as in the patient's home. Although complete polysomnography will identify myriad sleep disturbances, the use of a single overnight pulse oximetry study can serve as an adequate screening test for identifying mild CSR with associated hypoxemia in patients with CHF[11]. There is no single definition of clinically significant nocturnal hypoxemia, as severity of desaturation and degree of impairment may be considered patient specific. However, the Medicare coverage policy for nocturnal home oxygen therapy[16] provides a reasonable definition: *"An arterial PO_2 at or below 55 mm Hg, or an arterial oxygen saturation at or below 88 percent, for at least 5 [cumulative] minutes taken during sleep for a patient who demonstrates an arterial PO_2 at or above 56 mm Hg or an arterial oxygen saturation at or above 89 percent while awake."*

Common Treatment Options

Oxygen therapy and various forms of positive airway pressure (PAP) are the common treatment options for stable CHF patients with documented sleep disturbances, CSR and hypoxemia. Many studies have demonstrated the clinical efficacy of low-flow nasal oxygen therapy as an effective treatment for CSR in patients with stable CHF, including studies that compare nocturnal oxygen therapy (NOT) to PAP.

An unrestricted Pub-Med search on the terms oxygen and Cheyne-Stokes yielded 234 citations. The use of oxygen to treat CSR first appeared in the literature over a century ago. Since then numerous studies have investigated the effectiveness of oxygen as a treatment for CSR. The beneficial effects of supplemental oxygen on CSR were first described by Pembrey[17] in 1907. By treatment and observation he reported that low-flow nasal oxygen reduced or eliminated CSR in patients with CHF.

Recent studies continue to confirm the findings of Pembrey. Sasayama and colleagues[18], in a randomized controlled trial studied the effects of nocturnal oxygen therapy on 56 stable CHF patients with CSR and nocturnal hypoxemia. Patients were randomized to receive either nocturnal oxygen or room air and were followed for 12 weeks. Respiration, airflow and oxygen saturation were monitored to quantify apnea-hypopnea index (AHI), angiography or echocardiography was used to determine left ventricular function and the Specific Activity Scale questionnaire identified quality of life (QOL) outcomes. There were significant improvements in all areas prompting the authors to conclude that NOT improves sleep disordered breathing (SDB), left ventricular function and quality of life scores.

To determine if NOT is effective in slowing the progression of CHF, Shigemitsu, et. al.[19] studied AHI and 24-hour urinary catecholamine levels in 93 patients with CHF that had demonstrated central SDB (AHI > 20), were hypoxemic and had left ventricular ejection fraction < 60%. Plasma markers for sympathetic activity along with cellular and oxidative stress were measured on successive days following nights where subjects were breathing room air and supplemental oxygen. Lower levels of all serum markers of stress were present on the day following the administration of supplemental oxygen. The authors concluded NOT significantly decreased apnea-hypopnea index (AHI) and suggest that NOT may prevent the progression of CHF in patients with SDB and hypoxemia.

Javaheri[14] and colleagues studied a group of 36 stable male CHF patients with an AHI >/= 15 and hypoxemia to determine the clinical effects of nasal NOT. Arterial blood gases, Holter

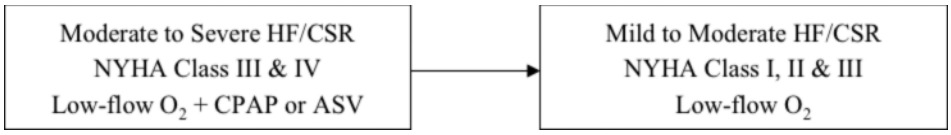

Figure 2. Step-wise treatment of Cheyne - Stokes respiration

monitoring and polysomnography were used before and after a night of sleep with low-flow oxygen therapy and the results were compared. AHI improved (49±19 vs 29±29), the central apnea index also improved (28±23 vs 13±18) and the percent of total sleep time below an arterial oxyhemoglobin saturation of 90% dropped from 23±21 to 0.8±2.3. However there was no change in the frequency of arrhythmias. An interesting finding was that patients with a higher mean $PaCO_2$ experienced a greater reduction in AHI than patients with lower $PaCO_2$ levels (39.3±5.4 vs 36.1±4.2 mmHg, p=0.03). The investigators concluded that in patients with stable heart failure, nasal NOT significantly improves periodic breathing and virtually eliminates clinically significant oxyhemoglobin desaturation.

More recently the use of positive airway pressure (PAP) therapies has gained popularity. PAP has the potential to increase pulmonary oxygen stores[20] by elevating the functional residual capacity (FRC) and by elevating mean intrathoracic pressure to diminish the accumulation of interstitial fluid. PAP therapies, in the forms of CPAP, bi-level and most recently adaptive servo-ventilation (ASV) have been used to treat mild to severe CSR. Studies focused on the effectiveness of these therapies have met with mixed results, although in advanced CSR there is a clear benefit, particularly for treatment with ASV. These mixed outcomes may, at least in part, be attributed to the targeting of therapy to treat the symptom, i.e. irregular breathing, rather than the arterial oxygen desaturation that is the cause of that symptom.

In the Canadian Continuous Positive Airway Pressure for Patients with Central Sleep Apnea and Heart Failure controlled trial (CANPAP), Bradley and colleagues[21] randomized 258 CHF patients with central apnea to receive CPAP or no CPAP and followed them for two years. CPAP therapy improved central apnea, nocturnal desaturation and left ventricular ejection fraction. CPAP also lowered norepinephrine levels. However, there was no difference in mortality in the CPAP and non-CPAP groups. In similar studies Buckle[22] and Davies[23] compared CPAP to room air and sham CPAP (respectively) in controlled randomized trials. Both studies found no difference in AHI, and Buckle found no improvement in nocturnal saturation or sleep efficiency.

Krachman and colleagues[24] compared oxygen therapy with nasal CPAP on CSR in patients with CHF. Polysomnography was performed on 25 stable CHF patients with 14 identified as having CSR. Those patients identified as having CSR were randomized to a night of oxygen therapy (2 L/min by nasal cannula) and another night on nasal CPAP therapy (9±0.3 cm H_2O). Nine of the 14 patients completed the study. When compared with baseline measurements, both oxygen and nasal CPAP significantly decreased the AHI (from 44±9 to 18±5 and 15 ±8 events per hour, respectively; $p < 0.05$), with no significant difference between the two modalities. The mean oxygen saturation increased significantly and to a similar extent with both oxygen and CPAP therapies (from 93±0.7% to 96±0.8% and 95±0.7%, respectively; $p < 0.05$). Total sleep time and sleep efficiency decreased only with nasal CPAP therapy (from 324±20 to 257±14 min, and from 82±3 to 72±2%, respectively; $p < 0.05$). The reduced sleep efficiency may be attributable to the greater degree of discomfort associated with the PAP interface as compared to a nasal cannula.

While the data for CPAP in CSR is mixed, there is growing evidence supporting adaptive servo ventilation (ASV), a form of noninvasive ventilation in the treatment of moderate—severe CSR. A number of recent papers have identified the effectiveness of ASV over CPAP or oxygen therapy alone in treating more severe SDB and CSR in CHF.[25-27] The greatest challenge to the clinician is not the effective application of this technology, but rather is effectively clearing the documentation hurdles imposed by CMS and other payers before insurance coverage will be allowed.

Compliance to Therapy

The best, most effective therapy is of no value if patients fail to adhere to it. No direct studies of either oxygen or PAP therapy adherence in the CHF/CSR population have been conducted, resulting in uncertainty regarding the most effective and appropriate therapy. Logically, it would seem that successful, effective treatment of CSR is an issue of practical comfort and convenience for the patient. Buckle[22] found that most of the CHF/CSR patients treated with CPAP did not tolerate the therapy and they would not have accepted long-term therapy even if it had shown some benefit to them. Indeed, much attention has been given in the sleep literature to the issue of compliance, with data suggesting about 50% of CPAP users are non-compliant[28, 29]. Although these studies are primarily directed at the treatment of obstructive sleep apnea, they highlight issues such as air leaks, nasal and sinus pain, pressure sores and other comfort related factors that drive patients away from adherence to therapy. CHF patients with CSR have the potential to encounter the same challenges. Conversely, it seems reasonable to assume that low flow oxygen therapy, provided by nasal cannula, is much more familiar, causes less discomfort and is less intrusive then PAP, particularly when it is administered as a nocturnal only therapy. However, studies of adherence to long-term oxygen therapy prescription in the COPD population have also met with results in the 50% range.[30-34] The difference however is that in this population the compliance standard is 15-16 hours of use per day, much of which is while awake as opposed to use only at night. The closest we come to an understanding of nocturnal oxygen compliance comes from a prospective randomized observational study that was focused on the oxygen delivery device. Costello[35] studied the nocturnal administration of oxygen by nasal cannula and Venturi mask in 99 hospitalized patients. He concluded that during sleep patients are more than twice as likely to dislodge or remove an oxygen mask than they are a nasal cannula. Unfortunately, the paucity of research on patient compliance leaves the clinician to rely on their experience, knowledge of the patient and best judgment to choose the most appropriate therapy.

Step Wise Approach to Therapy

The goal of any therapy is to relieve the severity of symptoms or mitigate progression of disease. The degree to which a therapy is successful in achieving these goals is largely dependent on the consistency of its application—in other words, adherence. Like many treatment protocols, an evidenced based approach that starts with the most practical, clinically appropriate, low intensity therapy may be received with the least reluctance by most patients. In a comprehensive review of the treatment of sleep disorders in heart failure, Arzt[13] evaluated eleven studies that reviewed either oxygen therapy or CPAP treatment or compared both and concluded that reduction in AHI was similar in the two therapies, but greater improvement in oxygenation was achieved when low-flow oxygen was the primary treatment. Similarly, Naughton,[12] in a review of the pathophysiology and treatment of CSR, concluded that CPAP improves cardiac function but fails to reduce the underlying hypoxemia that triggers CSR. In a small study of 9 patients, Buckle[22] found minimal improvement with CPAP and upon interview most patients expressed a subjective reluctance to use the therapy even if it had proven effective. Thus it would seem that a logical approach to treating nocturnal hypoxemia and CSR in stable CHF is to start conservatively with low flow nasal oxygen therapy. Assessment of the effectiveness of therapy and determination of appropriate dose can easily be conducted by overnight pulse oximetry under natural conditions in the patient's home. Patients should be periodically reassessed to ensure adequacy of oxygenation and minimization of CSR. In the presence of worsening disease or the need for progressive increases of oxygen dose, the addition of CPAP or ASV should be considered. Again, overnight oximetry should be used to validate settings and effectiveness of treatment.

Figure 3. New York Heart Association (NYHA) functional classification of heart failure[36]

Class	Symptoms
I	Patients with cardiac disease but without limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or angina pain.
II	Patients with cardiac disease with a slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or angina pain.
III	Patients with cardiac disease with marked limitation of physical activity. They are comfortable at rest. Less-than-ordinary physical activity results in fatigue, palpitation, dyspnea, or angina pain.
IV	Patients with cardiac disease with inability to carry on any physical activity without discomfort. Symptoms of heart failure or angina syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

Conclusion

Although easy to diagnose, the symptoms of CSR are often mistakenly attributed to age or medication side-effects. However, frequently stable CHF patients with no daytime symptoms may have undiagnosed CSR with associated nocturnal hypoxemia. Even during hospitalization evidence of CSR can be masked due to the regular administration of low-flow oxygen throughout the course of inpatient care. Given the high prevalence, the potential to contribute to decompensation and the negative effect on QOL, along with the ease and low cost of testing, all patients with a diagnosis of CHF should be screened for the presence of CSR. The diagnosis and treatment process is relatively simple and can be employed either during an inpatient stay or on an outpatient basis with the use of overnight pulse oximetry. Patient's with stable CHF demonstrating nocturnal desaturation may be ideal candidates for early treatment with low flow nasal oxygen therapy. As the disease progresses, it may be necessary to add PAP therapies, such as ASV into the treatment plan.

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Clinical Experience Using Inhaled Epoprostenol (Flolan) in Neonatal and Pediatric Patients at Children's Hospital Central California

Lawrence Nicol, AS, RRT

Prostacyclin (also called prostaglandin I2 or PGI2), is an arachidonic acid metabolite formed by a prostacyclin synthase in the vascular endothelium. Prostacyclin stimulates adenyl cyclase in vascular smooth muscle cells, which increases intracellular cAMP, resulting in vasodilation. As a drug, it is also known as epoprostenol or Flolan. These terms are often used interchangeably.

Intravenous epoprostenol (Flolan) is approved to treat Primary Pulmonary Hypertension (PPHN), but its use is limited by adverse effects including systemic hypotension and worsening of intrapulmonary shunting. When inhaled, epoprostenol (Flolan) may reduce pulmonary hypertension and improve oxygenation without decreasing systemic blood pressure. Aerosolized epoprostenol (Flolan) has been shown to be as effective as inhaled nitric oxide in reducing pulmonary vascular resistance in heart transplant candidates, in decreasing pulmonary artery pressures in primary and secondary pulmonary hypertension, and in improving right ventricular function in animals with hypoxic pulmonary vasoconstriction. It has also been shown to be as effective as a selective pulmonary artery vasodilator with improvement in oxygenation in patients with Acute Respiratory Distress Syndrome (ARDS).

Inhaled prostacyclin was first used in humans in 1978.[1] In 2004, based on the knowledge above and in journal articles written by Kelly in 2002, and Bindl in 1994, we started using inhaled epoprostenol or Flolan in the Neonatal Intensive Care Unit (NICU) at Children's Hospital Central California. Based on the recommendations of our Cardiologists in collaboration with the Medical Director of the NICU we used it on a limited basis initially with success to treat pulmonary hypertension. The nebulizers (Mini Heart) we used then were efficient, but sometimes created problems associated with the extra flow of gas that was added to the ventilator circuit. In pressure modes of ventilation the peak pressures had to be adjusted down once the nebulizer was running. Tidal volumes increased and could not be measured accurately because of the extra flow of gas into the circuit from the nebulizer.

Nitric oxide has been the standard of care for treatment of pulmonary hypertension in infants greater than 34 weeks of gestation. In April 2010, because of the rising costs associated with the administration of nitric oxide along with our previous experience with inhaled Flolan, we started a program using inhaled Flolan as an adjunct or alternative to nitric oxide, first in the Pediatric Intensive Care Unit (PICU), and then the NICU. We contacted 16 centers across the country for their advice and expertise. Specifically for the NICU, we researched the articles of Zwissler, Soditt, Lowson, DeLuca, Olmsted and Konduri/Kim. We purchased the highly efficient vibrating mesh type of nebulizers made by Aerogen. The Aerogen nebulizers are efficient and they do not add any additional gas to the breathing circuit so that peak pressures and tidal volumes are not affected. We also purchased Aerogen's proprietary syringes and tubing sets to further ensure patient safety. We used Medfusion IV pumps, and utilized a team approach with nursing in programming the pumps. Initially, we only introduced inhaled Flolan to the ventilator circuits after nitric oxide was already in use, and then tried to wean the nitric oxide if possible while closely assessing the patient. We have utilized inhaled Flolan successfully with patients on ventilators, SiPAP, high flow nasal cannulas, and oxygen masks.

To date in the PICU and NICU combined, we have used inhaled Flolan on fifty-six patients and have successfully weaned forty-two of them (75%) off of inhaled nitric oxide. The smallest patient was 870 grams.

We have used inhaled Flolan on twenty-two NICU patients. The majority were in the NICU itself but some were recovered and kept in the PICU after their cardiac surgery. Fifteen of these patients (68%) were successfully weaned off nitric oxide. Of the seven who were not, two of them had such an improvement in their oxygenation status after the initiation of inhaled Flolan (they were already receiving nitric oxide) that we were able to send them out for ECMO. One of the seven patients had hypotension that was thought to be caused by the Flolan so it was discontinued. Other than the one possible case of hypotension, we have not seen any untoward effects in using inhaled Flolan.

We use a high efficiency expiratory filter to prevent moisture and drug from getting into our ventilator exhalation valves. We have not observed any problems with the viscosity of the diluent in endotracheal tubes or ventilator systems even on patients less than 1000 grams. We have not observed tracheitis from the Flolan pH.

We started this program to see if we could provide the same safe level of care to our patients and cut costs at the same time.

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We were able to successfully and safely wean some patients off of nitric oxide. We did see a cost savings in decreasing our nitric oxide use especially when we ran out of contract hours with Ikaria. What we found was the benefit of having another biochemical pathway to treat pulmonary hypertension. In two instances the patients were already receiving nitric oxide and not improving significantly. The addition of inhaled Flolan did make a significant difference in improving their oxygenation status. The other advantage we observed was that some patients on low doses of nitric oxide had rebound reactions when coming off nitric oxide. These patients could be successfully weaned off nitric oxide by the addition of inhaled Flolan. Weaning the Flolan was accomplished without rebound pulmonary hypertension. Therefore, we feel that we have been able to safely provide an additional pathway for pulmonary vasodilation for our neonatal and pediatric patients.

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Application of the Breathe NIOV Device to Aid in Mobilization of the Patient on High Flow Nasal Cannula

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Background

The importance of mobilizing patients on mechanical ventilation has been successfully documented and many hospital ICUs generally support this program, but there is a gap when addressing patients on High Flow Nasal Cannula (HFNC). This patient population had not previously been mobilized regularly due to the limitation of the portability of the HFNC. The Respiratory Care Practitioners (RCP) in the Fletcher Allen Health Care FAHC's adult ICUs were becoming creative in attempting to solve this dilemma by strapping oxygen (O2) tanks on the base of the HFNC however, this was a safety concern. An additional issue was the rapid consumption of O2 on the HFNC which was a primary limiting factor to ambulation.

Our Respiratory Therapy department decided to trial the Breathe NIOV device to see if this was a solution for the patients on HFNC. The Breathe NIOV System is comprised of a one pound wearable device that uses a proprietary nasal pillow interface and requires an external source of compressed oxygen gas. The NIOV is a breath-actuated device that senses the patient's spontaneous breath through sense ports in the patient's nasal pillow interface. When the patient inhales, the device delivers a set volume of oxygen gas that is customized by the RCP. Volume delivery settings ranging from 50mL to 250mL are easily programmed to 3 levels of patient activity; low, medium and high. In addition to the volume of oxygen gas that is preset, ambient air is also entrained through two entrainment ports located on the interface. Delivering both ventilation and supplemental oxygen the NIOV System seems to effectively augment the patient's spontaneous breath and reduces the patient's work of breathing.

Often the patient was placed on a HFNC in an effort to avoid intubation or re-intubation. These patients were generally recovering from respiratory failure, in a weakened condition due to their disease process and at risk for further deconditioning.

Method

The ICU Physical Therapist (PT) would alert the RCP that there was a patient on HFNC that PT had been working with and was at a point that ambulation was a consideration. The RCP would titrate the volume settings on the Breathe NIOV to 3 activity settings. The augmentation volume are titrated to achieve the patients goal SpO2 and comfort levels. The low activity setting was titrated while the patient is in bed or doing any mild exertional activity. The medium activity setting is titrated to mild-moderate activity that may take place in and around the bed. The high activity volume is titrated during ambulation or during moderate-to severe exertional activity. The RCP would remove the patient from the HFNC and place them on the Breathe device and allow the patient time to become accustomed to the different "feel" of the device. Oxygen saturation (SpO2), Heart Rate, Respiratory Rate, and work of breathing (WOB) were observed as well as patient's subjective statements. Due to the unique configuration of the NIOV System, we were initially a bit concerned that we could not manipulate the fraction of inspired oxygen (FiO2) on the Breathe, especially since we had these patients on high liter flow as well as high FiO2.

Case Study

52 year old male admitted with atypical pneumonia (PCP), HX AIDS/HIV, HEP C, recent diagnosis of COPD, former smoker and had quit 3 weeks prior to admission.

1st Day – Hypoxic adult ICU patient on Optiflow HFNC set at 40 lpm and 40% FiO2. Patient was titrated on the Breathe NIOV with augmentation volumes set at: low = 70 milliliter (ml), medium = 180 ml and high = 250 ml. Patients SpO2 remained stable around 90-93% during the entire duration of the trial. Patient walked approximately 60 feet in 2 tries with PT assistance. The patient noted that the shape and fit of the cannula was much more comfortable to wear than the previous cannulas. He stated that the HFNC was difficult to tolerate because of the constant flow and the NIOV felt more natural and was synchronzied with his breathing. He also noted that the additional volume support he received during exertion helped his respiratory symptoms. He actually requested to remain on the Breathe device, however, he was returned to the HFNC at previous settings. Hours following this physical therapy session the patient's oxygen saturation improved and he was successfully weaned down to 6 lpm via nasal cannula.

2nd Day – In effort to continue his rehabilitation the patient was reevaluated by PT the following day. We reinitiated the NIOV on the previous settings and reattempted to mobilize the patient. Saturations remained above 90% for approximately 30-40 feet. Patient paused during a desaturation to 86% and then turned around to return to his room. Saturation increased to 93% and was returned to the 6 liter per minute NC. Saturation remained 92-93%. Again this patient stated how much he preferred the Breathe device, noting the shape and fit of the cannula.

The authors are with Fletcher Allen Health Care (FAHC), Burlington, VT.

Conclusion

Although we recognize that we would need to select patients carefully to confirm that their current FiO2 needs were being met, we do find a unique application for patient use in the ICU to mobilize patients. This portable system provides an option to those patients that were previously limited by their equipment in an effort to ambulate and regain muscle condition.

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5 Breathe Technologies—NIOV System Early Mobilization Protocol

Vibralung Acoustical Percussor: A New Paradigm in Airway Clearance Therapy

Michael McPeck, RRT FAARC

"If you wish to understand the universe, think of energy, frequency and vibration," so said Nikola Tesla (1856-1943), the Serbian-American inventor who is recognized for designing electrical supply systems based on alternating current, plus induction motors and wireless communication, along with other futuristic inventions.

Electro-Mechanical-Acoustical Airway Clearance (EMAAC)

Recently, a new device, the Vibralung Acoustical Percussor ("Vibralung"), has been introduced and, by virtue of its operating methodology, it creates a new paradigm in the spectrum of airway clearance devices, namely Electro-Mechanical-Acoustical Airway Clearance or EMAAC. EMAAC promotes mucokinesis by vibrating the column of gas in the airways with sound waves at different frequencies. This is a brief review of some of the technical considerations of EMAAC in general and the Vibralung Acoustical Percussor specifically.

The Vibralung, as its name implies, is an acoustic device that induces oscillatory sound waves by means of an electro-mechanical-acoustical transducer (audio loudspeaker), which is contained in an ergonomic hand-held audio reflex housing (Hand-held Transducer" or HHT). The HHT is interfaced to the patient's airway through a Y-adapter and mouthpiece. The Standard Y-adapter is a waveguide that directs the acoustical energy to the patient mouthpiece, while allowing separate gas flow pathways for inhalation and exhalation to minimize CO2 rebreathing and allow Positive Expiratory Pressure (PEP) to be applied. An Aerosol Y-adapter is also available to allow the Westmed Circulaire II high-efficiency aerosol drug delivery system to be used concomitantly with the Vibralung.

The HHT is connected to electronic frequency generator circuitry inside the Treatment Control Unit (TCU) via a thin cable. The TCU is battery-operated for safety and portability, and does not need to be plugged in to AC mains during use. The TCU is capable of producing audio frequencies between approximately 5 and 1,200 Hz to drive the speaker that is interfaced to the airway opening through the HHT.

Using the device is quite simple; the patient simply holds the light, ergonomically shaped HHT up to her lips and breathes normally through the standard mouthpiece. The Vibralung introduces sound waves into the patient's airways at, above and below the lung's various resonant frequencies, thereby vibrating the boundary between mucus and the airway surface in many different airways of all lengths and diameters. As with many ACT devices, this may be effective in mobilizing mucus accumulation, enhancing the lung's inherent mucociliary clearance mechanism and facilitating expectoration.

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Principles of operation

The Vibralung Acoustical Percussor uses acoustics (sound waves) as its fundamental operating principle. The sound generated by the Vibralung is specifically designed to resemble quasi-musical tones and "white noise." An electronic digitally controlled signal generator, using a unique software algorithm that sequences the tones in a reproducible pattern and tempo, generates these sounds and drives the loudspeaker.

Among the physical characteristics of sound is the fact that it can be transmitted through various media, such as air, and can also be conducted through tubes. Tubes that conduct sound from one location to another are known as "waveguides." Children talking onto one end of an empty garden hose, and listening at the other, are utilizing the waveguide principle for transmitting sound. The stethoscope we use for listening for lung sounds is essentially a waveguide. The tracheobronchial airways function as a series of waveguides inasmuch as they are capable of conducting sound bidirectionally. Recognizing that the airways comprise a series of waveguides, and that sound can be conducted bidirectionally within them, it is possible to transmit sound directly into and throughout the airways for therapeutic purposes.

The Vibralung Acoustical Percussor generates and couples sound energy to the column of gas in the patient's airways through a simple mouthpiece assembly. In turn, the sound energy vibrates the column of gas in the airways during both the inspiratory and expiratory phases of the patient's breathing cycle. As the patient breathes normally through the mouthpiece attached to the HHT, the acoustic sound waveforms are superimposed over the normal respiratory waveforms and travel throughout the lungs via the conducting airway system.

A useful analogy for the manner in which various waveforms superimpose themselves over each other would be the way multiple ripples form on a pond; even ripples emanating from different directions can readily pass through each other and continue along their intended pathway. Therefore, when using the Vibralung, its sound waves pass through the normal respiratory pressure waves and travel into the lungs through the "waveguides" that comprise the tracheobronchial airways. This

is effort-independent on the part of the patient, and requires the patient to only breathe normally with a mouthpiece.

Acoustic Resonance

In physics, resonance is the tendency of a system or structure to oscillate at greater amplitude at some frequencies than others. Acoustic resonance is the tendency of an acoustic system to absorb more energy when it is forced or driven at a frequency that matches one of its own natural frequencies of vibration (also known as resonant frequency, RF) than it does at other frequencies. The lung and system of conducting airways qualifies as an acoustic system for the purposes of this discussion.

The RF of the human respiratory system is not easy to measure and attempts at doing so typically render an "average" value when measured at the mouth rather than a discrete value for any specific airway segment. Bench testing of sound transmission through tubes of different lengths and diameters has revealed different resonant frequencies each time the length/diameter relationship of the tube changes. As a generalization, long and wide tubes tend to have a lower RF while short and narrow tubes have a higher RF. Presumably, each airway segment in the lung has its own distinct RF based upon its particular length and diameter. This is also confirmed using calculations of RF based on an electrical analog of the respiratory system.

Based upon well-accepted physiological treatises that describe the lungs in terms of their corresponding electrical circuitry, the airways of the lungs are essentially a series of impedances (multiple impedances in series). We know that there are 23 divisions in the normal adult human tracheobronchial tract, so there are 23 different "stages," and tens of thousands of actual airway segments of ever-diminishing length and diameter. This dimensional morphometry of the lung has been taught for decades through various versions of the classic diagram shown in Figure 1 below.

Essentially, this table describes a series of airways that are becoming ever-smaller over 23 generations. From this table, it can be understood that there are literally tens of thousands of individual airway segments in the 5th through 16th generations, and hundreds of thousands of individual airway segments in the 17th through 19th generations. Representative values are assigned for generational airway length and diameter, as well as quantity and the resulting cross-sectional area they would cover. Clearly, the vast variety of airway segment sizes can be appreciated.

In electrical nomenclature, the Impedance (L)-Conductance (C)-Resistance (R) or LCR circuit shown in Figure 2 simplistically represents an airway segment. Those familiar with elementary electronic circuits will recognize that this circuit also is a basic oscillator or tone generator.

The complete tracheobronchial tree can be modeled as a series of LCR circuits as shown in Figure 3, each one representing the particular dimensions and, hence, impedance, conductance and resistance, of any specific airway segment. Airway disease and regional nonhomogeneities can also alter RF. Therefore, treating the lung with a single RF, as so many contemporary ACT devices do, would likely fall short of providing therapeutic benefit to a large portion of the lung.

	Generation		Diameter, cm	Length, cm	Number	Total cross-sectional area, cm^2
conducting zone	trachea	0	1.80	12.0	1	2.54
	bronchi	1	1.22	4.8	2	2.33
		2	0.83	1.9	4	2.13
		3	0.56	0.8	8	2.00
	bronchioles	4	0.45	1.3	16	2.48
	terminal bronchioles	5 ↓ 16	0.35 ↓ 0.06	1.07 ↓ 0.17	32 ↓ 6×10^4	3.11 ↓ 180.0
transitional and respiratory zones	respiratory bronchioles	17	↓	↓	↓	↓
		18	↓	↓	↓	↓
		19	0.05	0.10	5×10^5	10^3
	alveolar ducts	T_3 20	↓	↓	↓	↓
		T_2 21				
		T_1 22				
	alveolar sacs	T 23	0.04	0.05	8×10^6	10^4

Figure 1. Divisions of the tracheobronchial tract (based on Weibel ER. Morphometry of the Human Lung. New York and Berlin: Academic Press, 1963).

Frequency Spectrum

The Vibralung Acoustical Percussor generates a sinusoidal waveform composed of a continuous spectrum of overlapping frequencies (quasi-musical tones) ranging from 5 to 1,200 Hz. Most of these tones are within the audible range of human hearing and can be heard by the patient and people close by although the volume is attenuated when the device is situated properly in the patient's mouth.

The frequencies are separated into five operating ranges that have been labeled as Low, Medium High, R2 and R5 to provide a simplified description. The tones emitted at the L, M and H settings deliberately resemble a series of staccato musical notes, at a tempo of about 360 beats per minute, to provide a predictable sequence of frequencies. The tones at the R2 and R5 (Random Noise) settings are described as "white noise" and cover the full available spectrum for either 2 or 5 minutes.

The therapeutic benefit from application of the Vibralung is through a mechanism known as "sympathetic resonance," not unlike the experience of having your car windows and rear-view mirror vibrated intensely by extremely loud music in an adjacent vehicle. Vibrating the column of gas in the tracheobronchial tract, progressively through all of its various RFs, vibrates the boundary between mucus and the airway surface through sympathetic resonance. Because the Vibralung works during both the inspiratory and exhalation phases of the breathing cycle, the therapeutic effect is applied for much longer than devices that work during exhalation only. For this reason, treatment times are quick and efficient with the Vibralung.

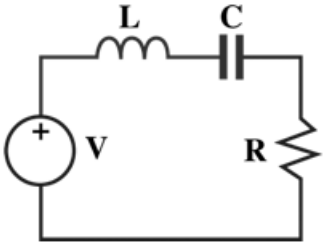

Figure 2. An LCR circuit is represented schematically by its 4 components in series, V = voltage, or pressure change, L = impedance, C = conductance (or compliance), and R = resistance.

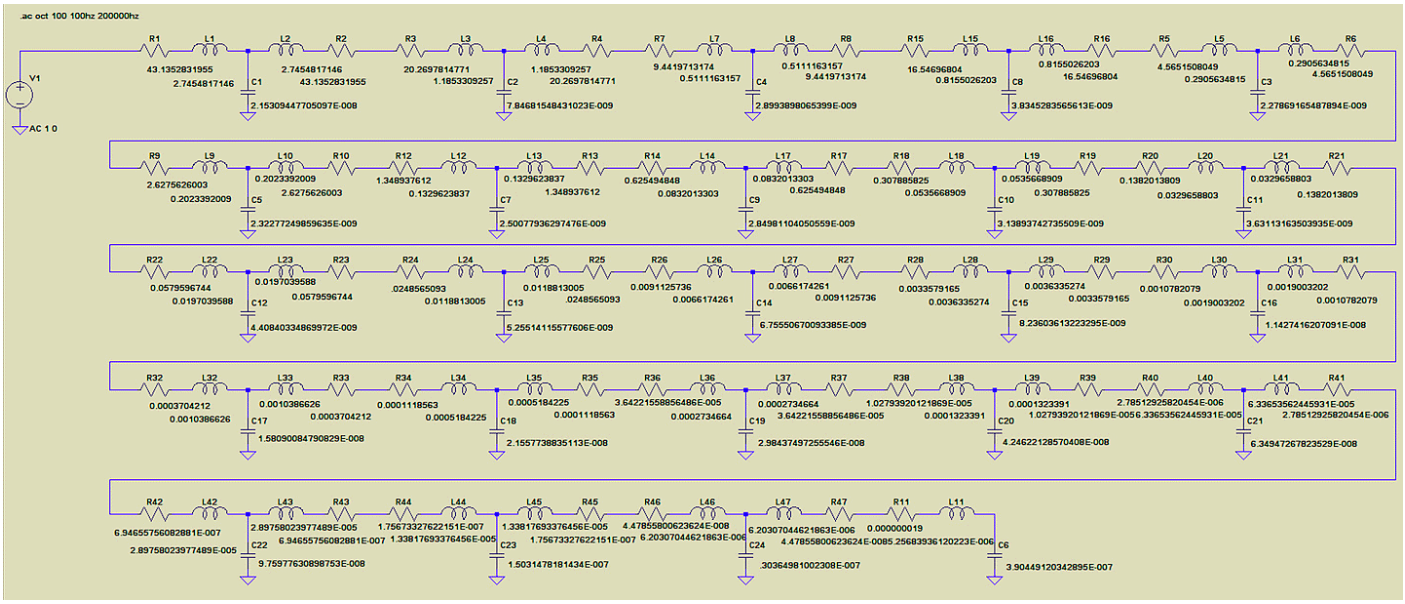

Figure 3. The 23 divisions of the tracheobronchial tree represented by a theoretical series of LCR circuits, each with different hypothetical values derived from the average dimensions of their airway generation.

Within its operating frequency range of 5 to 1,200 Hz, the Vibralung has two fundamental operating modes: sequential tones and random noise. In the sequential tone mode, it generates a sinusoidal waveform composed of quasi-musical tone bursts or pulses at a tempo of approximately 360 pulses per minute. The pulses are generated in groups of 4 sequential frequencies based loosely on note progression in music theory. For those who are musicians, or have some knowledge of music theory, think of playing four sequential notes in a row:

C – C# – D – D#

at a tempo of 360 beat per minute. Repeat that pattern about 20 times and then, while maintaining the tempo, move up a "half-step" and start a new 20-second sequence:

C# – D – D# – E

followed by yet another 20-second sequence:

D – D# – E – F

and so forth for approximately 7 minutes. Depending on the setting, a number of octaves will be achieved during the 7-minute period and the lung will be exposed to a broad span of sound frequencies designed to cause airway vibration at a multitude of different RFs. While this is a simplification of the actual frequency-sequencing algorithm, it will provide a basic understanding of the tone pattern that is heard when the Vibralung operates. In actuality, the sound emitted during the Low, Medium and High settings begins with 2 minutes of Random Noise, then transitions to 7 minutes of frequency sequencing, then ends with 1 minute of Random Noise. If only Random Noise is desired, there are setting for either a 2 or 5-minute session (R2 and R5).

Summary

The overriding operating assumption of the Vibralung Acoustical Percussor is that treating the lung with a single vibratory frequency is insufficient. Whether it is applied externally through the chest wall, or internally through airway interruption techniques, a single frequency will likely vibrate only a small number of airways whose resonant frequency happens to be at or near the particular frequency being applied. Therefore, the Vibralung Acoustical Percussor is designed to treat the lung with a multitude of frequencies between 5 and 1,200 Hz that incrementally advance over one of three ranges, from low to high, in a span of 7 minutes per treatment. The use of "random noise" spanning the same frequency range is also utilized at the beginning and end of the incremental advancing frequency sequence, or by itself, to provide yet another means of exposing the lung to the broadest possible range of acoustic frequencies.

And so, with apologies to Nikola Tesla, I would like to close by paraphrasing his prophetic statement:

"If you wish to understand Airway Clearance, think of energy, frequency and vibration."

Exhaled Nitric Oxide is Related to Atopy, But Not Asthma in Adolescents with Bronchiolitis in Infancy

Ingvild Bruun Mikalsen, Thomas Halvorsen, and Knut Øymar

Abstract

Background: The fraction of exhaled nitric oxide (FeNO) has been suggested as a non-invasive marker of eosinophilic inflammation in asthma, but lately rather as a biomarker of atopy than of asthma itself. Asthma after bronchiolitis is common up to early adolescence, but the inflammation and pathophysiology may differ from other phenotypes of childhood asthma. We aimed to assess if FeNO was different in children with former hospitalization for bronchiolitis and a control group, and to explore whether the role of FeNO as a marker of asthma, atopy or bronchial hyperresponsiveness (BHR) differed between these two groups of children.

Methods: The study included 108 of 131 children (82%) hospitalized for bronchiolitis in 1997–98, of whom 82 (76%) had tested positive for Respiratory syncytial virus, and 90 age matched controls. The follow-up took place in 2008–2009 at 11 years of age. The children answered an ISAAC questionnaire regarding respiratory symptoms and skin prick tests, spirometry, methacholine provocation test and measurement of FeNO were performed.

Results: Analysed by ANOVA, FeNO levels did not differ between the post-bronchiolitis and control groups ($p = 0.214$). By multivariate regression analyses, atopy, height ($p < 0.001$ for both) and BHR ($p = 0.034$), but not asthma ($p = 0.805$) or hospitalization for bronchiolitis ($p = 0.359$), were associated with FeNO in the post-bronchiolitis and control groups. The associations for atopy and BHR were similar in the post-bronchiolitis and in the control group.

Conclusion: FeNO did not differ between 11 year old children hospitalized for bronchiolitis and a control group. FeNO was associated with atopy, but not with asthma in both groups.

Background

Asthma in childhood is characterized by extensive heterogeneity regarding aetiology and natural history, and may present with various phenotypes probably related to different immunological, inflammatory and airway characteristics [1]. Chronic inflammation of the lower airways and bronchial hyperresponsiveness (BHR) are typical features of asthma, and markers of these factors are therefore used for diagnostic purposes and to guide treatment. The fraction of exhaled nitric oxide (FeNO) has been suggested as a non-invasive marker of eosinophilic inflammation [2], and thus a marker of asthmatic airway inflammation. Recently, FeNO has been suggested as a biomarker of atopy, and thereby a biomarker of atopic asthma rather than of asthma per se [3-5], although findings have been equivocal [6-8]. Associations between FeNO and BHR, but not between FeNO and asthma have been described in atopic children [5].

Bronchiolitis in early life is an established risk factor for subsequent asthma, although the mechanisms behind are complex and heterogeneous [9]. The risk of asthma is higher after RSV negative than RSV positive bronchiolitis [10], particularly after early wheezing or bronchiolitis due to Rhinovirus (RV) [11]. While atopic asthma is associated with an eosinophilic inflammation, asthma after bronchiolitis is less related to atopy and mainly associated with viral induced wheeze and bronchial inflammation mediated by neutrophils [12-14]. Thus, markers of inflammation such as FeNO could conceivably be different in asthma after bronchiolitis than in children with atopic asthma.

The primary aim of this study was to assess if FeNO was different in children with former hospitalization for bronchiolitis compared to a control group, and secondly to explore whether the role of FeNO as a marker of asthma, atopy or BHR differed between these two groups of children.

Methods

Study design and subjects

In this longitudinal prospective follow-up study, children below 12 months of age hospitalized for acute bronchiolitis at the university hospitals in Stavanger and Bergen (Norway) during the winter seasons 1997 and 1998 were invited to participate. Bronchiolitis was defined as an acute febrile episode of respiratory illness with tachypnea, dyspnoea, prolonged expiration and wheeze on auscultation of the chest. Exclusion criteria were previous hospitalization for wheeze or bronchiolitis, any previous use of systemic or inhaled corticosteroids, signs of bacterial infection or any other known lung disease [15]. Nasopharyngeal mucus was examined for Respiratory syncytial virus (RSV) by direct immunofluorescence

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in all patients (bioMèrieux, Marcy-l'Ètoile, France). Other viruses were not systematically tested for.

The children were invited to a follow-up in 2008–09 at 11 years of age. The follow-up included a questionnaire from the International Study of Asthma and Allergy in Childhood (ISAAC) [16], assessment of lung function and BHR, FeNO measurement and skin prick tests (SPT). An unselected age matched control group not hospitalized for bronchiolitis during their first year of life, reflecting the general population in the study area was recruited from 3 nearby schools.

We have previously published results showing that children in the post-bronchiolitis group had more asthma, lower lung function and higher BHR compared to controls [10].

The study was approved by the Regional Committee for Medical and Health Research Ethics West, and signed statements of informed consent were obtained from all parents.

Lung function measurements

Spirometry was performed according to established guidelines [17], using a Vmax Encore 229D spirometer (SensorMedics Inc., Anaheim, USA). Forced expiratory volume in first second (FEV_1), forced vital capacity (FVC) and forced expiratory flows at 25-75% of FVC (FEF_{25-75}) were recorded. Except for the ratio FEV_1/FVC, measurements were compared to values predicted by standard reference equations and expressed as percentages of predicted FEV_1% [18] and FEF_{25-75}% [19]. BHR was assessed with methacholine provocation test (MPT), by using an inhalation-synchronised, dosimetric nebulizer, Spira Elektra 2 (Spira, Hämeenlinna, Finland). The test was not performed if baseline FEV_1% was <65% predicted. Methacholine was administered in doubling doses until a 20% reduction in FEV_1 was obtained or until a cumulative dose of 11.54 µmol had been given. A dose response slope (DRS) was calculated as the ratio between the maximum percentage decline in FEV_1 from baseline and the total administered dose of methacholine (%/µmol), and the distribution regarded as ln-normal [20].

FeNO measurements

FeNO was measured online by the single breath technique according to published guidelines [21], with an EcoMedics Exhalyzer CLD 88sp with DENOX 88 (ECO MEDICS AG, Duernten, Switzerland). NO-free air was inhaled to near total lung capacity, followed immediately by full exhalation at a constant flow of 50 ml/s. FeNO was recorded as the mean value from 3 reproducible plateaus within 10% acceptability.

Skin prick tests

Skin prick tests (SPT) with the most common inhalant allergens (Dermatophagoides pteronyssinus, dog, cat dander, Cladosporium herbarium, birch, timothy, German cockroach) and food allergens (eggwhite, milk, peanut, codfish) (Soluprick, ALK Albello, Hørsholm, Denmark) for atopic sensitization in Norwegian children were performed [22]. Histamine 10 mg/ml was used as a positive control and a 0.9% saline solution as a negative control. A wheal diameter ≥ 3 mm larger than the negative control was defined as a positive result.

Definitions

Current asthma at 11 years of age was defined as a positive answer to the ISAAC question regarding "asthma ever" and a positive answer to at least one of the two questions:

1) wheezing or whistling in the chest or chest tightness during the preceding 12 months or 2) use of asthma medication (bronchodilators, inhaled corticosteroid, leukotriene antagonists) during the preceding 12 months.

The children in the post-bronchiolitis and control groups were divided into four sub-groups at the 11 year follow-up, according to their atopic and asthmatic status. 1) Healthy: No current asthma and no allergic sensitization. 2) Atopic non-asthmatic: Positive SPT for at least one allergen with the absence of current asthma. 3) Current atopic asthma: A combination of current asthma and atopy.4) Current non-atopic asthma: Current asthma without atopy.

Statistical methods

Means and standard deviations (SD), medians and quartiles were estimated and reported for normally and asymmetrically distributed data, as appropriate. Group comparisons were done with Student's t- test, Mann Whitney U-test or Pearson's chi-square exact test, as appropriate. FeNO (unit: parts per billion (ppb)) was regarded as ln-normally distributed and results

Table 1 Characteristics of 108 children hospitalized for bronchiolitis in their first year of life during 1997–98 at the university hospitals of Stavanger and Bergen (Norway) according to asthma and atopy at 11 years of age

	Healthy (n = 64)	Atopic non-asthmatic (n = 20)	P-value	Current non-atopic asthma (n = 15)	P-value	Current atopic asthma (n = 9)	P-value
Boys, n (% of group)	30 (47)	14 (70)	0.080	10 (67)	0.252	6 (67)	0.308
Age at hospitalization* (months)	3.5 (2.0, 6.0)	4.0 (1.0, 10.0)	0.603	6.0 (3.0, 9.0)	0.052	5.0 (4.0, 9.5)	0.083
Age at follow up* (year)	11.4 (11.0, 11.8)	11.3 (10.9, 11.5)	0.182	11.4 (10.9, 11.6)	0.745	11.6 (11.3, 12.2)	0.410
Weight at follow-up† (kg)	41.2 (9.3)	40.6 (8.2)	0.791	42.8 (7.5)	0.525	42.5 (8.3)	0.692
Height at follow-up† (cm)	149.0 (8.2)	147.2 (4.3)	0.206	149.3 (5.6)	0.888	148.9 (6.0)	0.963
ICS, n (% of group)	0	0		2 (13)	**0.034**	7 (78)	**<0.001**
FEV_1%†	93.9 (9.3)	99.7 (8.9)	**0.014**	97.8 (9.5)	0.145	95.8 (9.5)	0.555
FEF_{25-75}%†	89.9 (23.9)	88.6 (19.1)	0.819	86.0 (22.9)	0.568	84.4 (20.2)	0.514
FEV_1 /FVC ratio†	82.8 (7.5)	80.6 (4.9)	0.221	79.7 (7.7)	0.159	78.8 (7.3)	0.135
DRS to methacholine*	6.0 (1.7, 25.5)	4.9 (1.1, 13.4)	0.378	4.1 (1.5, 18.1)	0.910	4.4 (2.2, 13.8)	0.923

*Median (inter quartile range), †mean (standard deviation). ICS, inhalation corticosteroid last 12 months before follow up; FEV_1%, forced expiratory volume in first second as percentage of predicted; FEF_{25-75}%, forced expiratory flow between 25-75% of the forced vital capacity (FVC); DRS, dose response slope. For missing data, see text. P-values assess comparisons with the healthy group.
Bold values indicate significance at the 0.05 level.

Table 2 Characteristics of 90 children in an age matched control group at 11 years of age, according to asthma and atopy

	Healthy (n = 51)	Atopic non-asthmatic (n = 29)	P-value	Current non-atopic asthma (n = 5)	P-value	Current atopic asthma (n = 5)	P-value
Boys, n (%)	31 (61)	16 (55)	0.644	4 (80)	0.640	4 (80)	0.640
Age at follow up* (year)	11.8 (11.4, 12.2)	11.4 (11.0, 12.1)	0.081	12.3 (11.4, 12.8)	0.147	11.8 (10.9, 12.0)	0.502
Weight at follow-up† (kg)	41.7 (8.5)	40.9 (9.4)	0.677	47.9 (17.3)	0.472	51.4 (25.7)	0.449
Height at follow-up† (cm)	151.9 (7.6)	149.0 (7.0)	0.087	150.8 (10.2)	0.749	152.0 (17.1)	0.998
ICS, n (%)	1 (2)	0	1.000	3 (60)	**0.001**	4 (80)	**<0.001**
FEV_1%†	98.7 (10.6)	99.8 (7.9)	0.631	101.9 (10.7)	0.510	96.3 (28.3)	0.864
FEF_{25-75}%†	96.9 (22.9)	98.9 (16.1)	0.693	95.6 (18.9)	0.903	93.3 (45.7)	0.764
FEV_1 /FVC ratio†	84.3 (6.6)	84.2 (4.5)	0.969	79.8 (4.2)	0.146	80.8 (6.7)	0.269
DRS to methacholine*	1.7 (1.0, 6.8)	3.6 (0.8,17.6)	0.084	0.9 (0.3, 5.8)	0.292	4.7 (1.1, 24.5)	0.405

*Median (inter quartile range), †mean (standard deviation). ICS, inhaled corticosteroids last 12 months before follow up; FEV_1%, forced expiratory volume in first second as percentage of predicted; FEF_{25-75}%, forced expiratory flow between 25-75% of the forced vital capacity (FVC) as percentage of predicted; DRS, dose response slope. For missing data, see text. P-values assess comparisons with the healthy group.
Bold values indicate significance at the 0.05 level.

presented as back-transformed values given as geometric means with 95% confidence intervals (CI). To study overall associations with FeNO, a two-way ANOVA was performed for the post-bronchiolitis and control groups in one common analysis. To study associations with FeNO for each sub-group, the post-bronchiolitis and control groups were analysed separately and Dunnett's test was used for post-hoc comparisons between the sub-groups if the F-test was significant in the overall ANOVA analysis.

Linear regression analyses were applied to explore associations between putative explanatory variables and ln FeNO for the complete study group and for the post-bronchiolitis group separately. In both models, the following variables recorded at 11 years of age were assessed: Gender, age at follow-up, height, weight, atopy, current asthma, ln DRS, FEV_1%, FEF_{25-75}%, use of inhaled steroids the preceding 12 months and previous hospitalization for bronchiolitis in infancy. In the separate multivariate linear regression analysis including only subjects in the post-bronchiolitis group, RSV status (positive or negative) was also included in addition to those included for the complete study group. In all analyses, each variable was initially entered into a univariate model. Variables with p-values < 0.2 in univariate analyses were further analysed in a backward multivariate regression model. Analyses of interaction terms were used to explore differences between the sub-groups regarding associations between explanatory variables and FeNO. When ln transforming DRS, negative values were set to 0.001. P-values < 0.05 were regarded as statistically significant. All analyses were two-tailed and data were analyzed using the SPSS version 18.0 statistical package (SPSS, Chicago, IL, USA).

Table 3 Analysis of variance for fractional exhaled nitric oxide (FeNO) given as ln FeNO in children hospitalized for bronchiolitis (n = 105) during their first year of life and an age matched control group (n = 89) at 11 years of age

Variable	B*	95% CI	P-value‡
Main groups			
Control group	0	Reference	
Post-bronchiolitis group	−0.120	−0.309, 0.070	0.214
Sub-groups by atopy and asthma status			**<0.001**
Healthy	0	Reference	
Atopic non-asthmatic	0.745	0.522, 0.967	
Current non-atopic asthma	0.013	−0.308, 0.335	
Current atopic asthma	0.651	0.286, 1.102	
Intercept‡	2.131	1.970, 2.291	

No significant interaction effects were observed between the variables post-bronchiolitis/control group and the four subgroups of the study, i.e. the relationships between FeNO values measured in these four subgroups were similar in the post-bronchiolitis and the control group.
*Regression coefficient; represents the amount of change of ln NO induced by a change of 1 unit of the explanatory variable.
†P-values from F test. ‡Reference group (healthy children in the control group).
Bold values indicate significance at the 0.05 level.

Results

One hundred and thirty one children hospitalized for bronchiolitis during their first year of life were included, and 108 (82%) consented to the follow-up at 11 years of age. Of these, 82 children (76%) had tested positive for RSV. All completed the questionnaire and took part in SPT and lung function tests. MPT and FeNO were not performed in two and three children in the post-bronchiolitis group respectively, due to technical reasons.

In the control group, 91 of the 190 primarily invited children (48%) completed the questionnaire and agreed to SPT and lung function test; one was excluded as further investigations indicated chronic restrictive lung disease. One child was not able to perform neither spirometry, FeNO nor MPT. In addition, MPT was not performed in two children; one had FEV_1% < 65% and one was not able to cooperate.

In the post-bronchiolitis group, FEV_1% was lower in the healthy group compared to the atopic non-asthmatic group (Tables 1 and 2). There were no other differences between the four sub-groups regarding gender, age, weight, height, lung function and BHR at the 11 year follow-up within the post-bronchiolitis group and the control group, respectively (Tables 1 and 2).

Children in the post-bronchiolitis group (11.4 years; 11.0, 11.7) (median; quartiles) were slightly younger than the controls (11.7 years; 11.3, 12.1) at the 11 year follow-up (p < 0.001).

FeNO

The overall ANOVA analysis with all children included, revealed that FeNO levels did not differ between the post-bronchiolitis and control groups (p = 0.214) (Table 3). FeNO differed between the four sub-groups (p < 0.001). FeNO levels were higher in the atopic non-asthmatic and the atopic asthmatic children but not in the children with non-atopic asthma compared to healthy in

Table 4 Levels of fractional exhaled nitric oxide (FeNO) in children hospitalized for bronchiolitis and in an age matched control group, by asthma and atopic status

	Post-bronchiolitis group (n = 105)				Control group (n = 89)			
	N	FeNO	95% CI	P-values* vs. healthy	N	FeNO	95% CI	P-values* vs. healthy
Healthy	62	8.1	6.8, 9.6	Reference	50	7.6	6.4, 9.1	Reference
Atopic non-asthmatic	20	13.6	10.1, 18.4	**0.010**	29	19.5	15.6, 24.5	**<0.001**
Current non-atopic asthma	14	7.2	5.0, 10.4	0.920	5	9.7	5.6, 16.8	0.781
Current atopic asthma	9	12.3	7.8, 19.2	0.237	5	21.4	12.4, 36.9	**0.002**

Figures are geometric means and 95% confidence intervals (95% CI). FeNO values are given as parts per billion. *Dunnett's test.
Bold values indicate significance at the 0.05 level.

both the post-bronchiolitis group and in the control group (Table 3). Separate analyses for the post-bronchiolitis and the control group revealed that FeNO was higher in the atopic non-asthmatic children compared to healthy in both groups. Higher FeNO in children with atopic asthma compared to healthy was observed only in the control group (Table 4, Figure 1).

Regression analyses of potential explanatory factors for ln FeNO

Atopy, weight and height were positively associated with ln FeNO by univariate linear regression analyses including all participating children (Table 5). In the final multivariate model, atopy, ln DRS and height were independently associated with increased ln FeNO (Table 5). No interaction effects regarding ln FeNO were observed between the variables atopy and current asthma vs. no asthma, meaning that the associations between atopy and ln FeNO were similar for the asthmatic and non-asthmatic children and vice versa (Table 5).

Table 5. Linear regression model explaining fractional exhaled nitric oxide (FeNO) given as ln FeNO at 11 years of age in 105 children hospitalized for bronchiolitis and 89 children in an age matched control group, all children analysed together

Separate regression analyses were done for children in the post-bronchiolitis group. By univariate analyses, RSV negative bronchiolitis, height, FEV_1% predicted and atopy were positively associated with ln FeNO (Table 6). In the final multivariate model, ln DRS, height and FEV_1% predicted were positively associated with ln FeNO (Table 6). There was a significant interaction effect between RSV negative bronchiolitis and atopy, i.e. atopy was positively associated with FeNO in the RSV negative group (B = 1.005; 95% CI: 0.496, 1.513; p < 0.001), but not in the RSV positive group (B = 0.269; 95% CI: -0.071, 0.609; p = 0.120) Table 6.

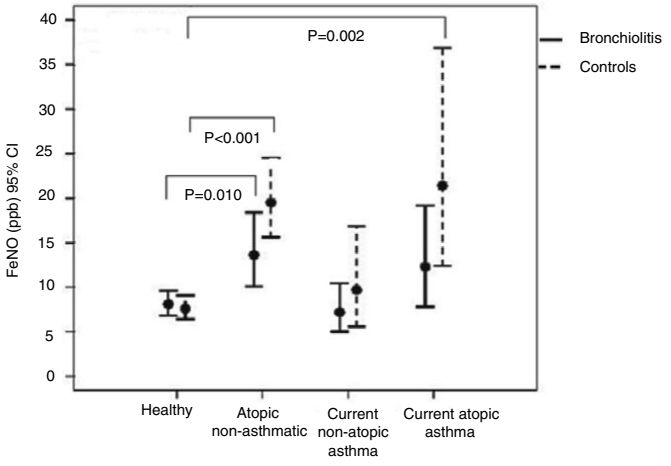

Figure 1. FeNO levels in four different sub-groups of children, split by bronchiolitis status in their first year of life. FeNO values are given as geometric mean with 95% confidence intervals (CI).

Table 6. Linear regression model explaining fractional exhaled nitric oxide (FeNO) given as ln FeNO at 11 years of age in 105 children hospitalized for bronchiolitis

There was no significant association between RSV negative bronchiolitis and atopy (Pearson's chi square exact test p =0.304), and there was no association between atopy and ln DRS (B = 0.173; 95% CI: -0.409, 0.755; p =0.558).

Discussion

In the present study FeNO did not differ between 11 year old children hospitalized for bronchiolitis in their first year of life and an age matched control group. Secondly, atopy and BHR, but not asthma were associated with FeNO, and these associations were similar in the post-bronchiolitis and in the control groups.

The guideline from the American Thoracic Society suggests that levels of FeNO below 20 ppb are less likely to indicate eosinophilic airway inflammation [2], as also reported by others [8]. In the present study, the majority of the FeNO measurements were below this limit. Infantile wheeze has been associated mainly with a neutrophilic inflammation, and a tendency for continued neutrophilic inflammation in this group of children could conceivably contribute to the findings of the present study [12].

The association between FeNO and atopy, but not between FeNO and asthma is in line with several other studies [3-5]. An association between FeNO and persistent wheezing has been reported for children less than 2–3 years of age [23,24], but we could not confirm that this association lasts until adolescence. One of these studies did not adjust for atopy [23], while another study observed that neither personal nor a family history of atopy was associated with increased FeNO [24]. Konstantinou et al. recently described an episodic increase of FeNO during viral wheezing in 4–6 year old children, independent of the atopic status of the test-subjects. The increase subsided after the episodes resolved, rendering wheezers comparable to non-wheezers outside the wheezing episodes [25]. This is consistent with the low levels of FeNO in the post-bronchiolitis group in the present study. Others have reported associations between FeNO and recurrent wheeze in infants with an atopic constitution [26] and in atopic children younger than four years of age [27]. The results from the present study suggest that also for older children with a history of infant and preschool viral wheeze, atopy should be considered as an independent risk factor for increased FeNO. This is in line with a study from the Netherlands showing that FeNO can differentiate between wheezing phenotypes, but only in atopic children [28].

Table 5 Linear regression model explaining fractional exhaled nitric oxide (FeNO) given as ln FeNO at 11 years of age in 105 children hospitalized for bronchiolitis and 89 children in an age matched control group, all children analysed together

	Unadjusted models			Fully adjusted model (N = 190)			Final model (N = 190)		
Risk factors	**B***	**95% CI**	**P-value**	**B***	**95% CI**	**P-value**	**B***	**95% CI**	**P-value**
Hospitalization for bronchiolitis	−0.200	−0.408, 0.008	0.059	−0.088	−0.276, 0.101	0.359			
Male gender	−0.131	−0.342, 0.080	0.223						
Age at follow up (months)	0.009	−0.006, 0.024	0.257						
Height (cm)	0.021	0.007, 0.034	**0.002**	0.025	0.008, 0.042	**0.005**	0.027	0.015, 0.038	**<0.001**
Weight (kg)	0.014	0.004, 0.025	**0.009**	0.001	−0.012, 0.014	0.849			
Atopy	0.736	0.539, 0.934	**<0.001**	0.757	0.562, 0.951	**<0.001**	0.773	0.583, 0.962	**<0.001**
Current asthma	0.035	−0.243, 0.313	0.805						
Ln DRS	0.053	−0.003, 0.108	0.062	0.056	0.008, 0.105	**0.023**	0.051	0.004, 0.097	**0.034**
FEV_1%	0.006	−0.004, 0.016	0.269						
FEF_{25-75}%	0.001	−0.003, 0.006	0.597						
Use of inhaled steroids preceding 12 months	0.200	−0.169, 0.568	0.287						

No interactions were found between current asthma and atopy, atopy and DRS, atopy and hospitalization for bronchiolitis or DRS and hospitalization for bronchiolitis.
*Regression coefficient, represents the amount of change of ln NO induced by a change of 1 unit of the explanatory variable.
CI, confidence interval; DRS, dose response slope; FEV_1%, forced expiratory volume in first second as percentage of predicted; FEF_{25-75}%, forced expiratory flow between 25-75% of the forced vital capacity.
Bold values indicate significance at the 0.05 level.

As previously published, lower FEF_{25-75}% predicted, consistent with small airway obstruction, was observed in children in the post-bronchiolitis group than children in the control group [10]. Except for a weak positive association between FEV_1% and FeNO in the post-bronchiolitis group, no associations between lung function and FeNO could be observed. FeNO may predict lung function decline in adults with severe asthma [29]. However, to our knowledge, few studies have found associations between lung function and FeNO in children [30]. Low levels of FeNO despite small airway obstruction could indicate structural explanatory mechanisms and not an ongoing eosinophilic inflammation [31].

RSV positive vs. negative bronchiolitis

Asthma after bronchiolitis in infancy is heterogeneous and likely to represent disease entities that differ from atopic asthma in childhood. RSV is the most common virus involved in bronchiolitis, but apart from one Swedish study [32], the risk of asthma after RSV bronchiolitis has not been linked to atopy [9,11]. An increased risk of asthma after RSV negative vs. RSV positive bronchiolitis has been reported [10], particularly after RV bronchiolitis [11]. Wheezing with RV infections has been associated with atopy [9,33], although we found no association between atopy and a history of RSV negative bronchiolitis. Temporarily reduced FeNO has been found in children hospitalized for RSV bronchiolitis. Although the explanatory

Table 6 Linear regression model explaining fractional exhaled nitric oxide (FeNO) given as ln FeNO at 11 years of age in 105 children hospitalized for bronchiolitis

	Unadjusted models			Fully adjusted model (N = 103)			Final model (N = 103)		
Risk factors	**B***	**95% CI**	**P-value**	**B***	**95% CI**	**P-value**	**B***	**95% CI**	**P- value**
RSV negative bronchiolitis	0.335	0.019, 0.651	**0.038**	0.010	−0.337, 0.357	0.957	0.009	−0.336, 0.354	0.958
Male gender	−0.112	−0.388, 0.164	0.423						
Age at follow-up (months)	−0.004	−0.277, 0.269	0.977						
Height (cm)	0.024	0.005, 0.043	**0.015**	0.025	0.000, 0.050	0.053	0.024	0.007, 0.041	**0.006**
Weight (kg)	0.015	0.001, 0.030	0.058	−0.001	−0.021, 0.020	0.946			
Atopy	0.510	0.219, 0.802	**0.001**	0.269	−0.073, 0.611	0.121	0.269	−0.071, 0.609	0.120
Current asthma	−0.033	−0.366 ,0.299	0.977						
Ln DRS	0.061	−0.025, 0.148	0.161	0.094	0.015, 0.173	**0.020**	0.094	0.017, 0.172	**0.018**
FEV_1%	0.015	0.000, 0.029	**0.044**	0.018	0.004, 0.032	**0.013**	0.018	0.004, 0.031	**0.012**
FEF_{25-75}%	0.002	−0.005, 0.008	0.610						
Use of inhaled steroids preceding 12 months	0.003	−0.494, 0.488	0.990						
Interaction									
RSV negative bronchiolitis × atopy				0.736	0.125, 1.346	**0.019**	0.736	0.128, 1.343	**0.018**

No interactions were found between current asthma and atopy, atopy and ln DRS or ln DRS and RSV negative bronchiolitis. There was an interaction between RSV negative bronchiolitis and atopy, and the final model therefor includes both the interaction effect and its main variables (atopy and RSV negative bronchiolitis).
*Regression coefficient, represents the amount of change of ln NO induced by a change of 1 unit of the explanatory variable.
CI, confidence interval; DRS, dose response slope; FEV_1%, forced expiratory volume in first second as percentage of predicted; FEF_{25-75}%, forced expiratory flow between 25-75% of the forced vital capacity.
Bold values indicate significance at the 0.05 level.

mechanisms are not known, it has been speculated if the absence of eosinophilic inflammation during the acute bronchiolitis may be involved [34]. The present study showed that previous RSV negative bronchiolitis was associated with higher FeNO, but not after adjusting for DRS, atopy and height.

The interaction effect observed between atopy and RSV negative bronchiolitis may suggest that the influence from atopy on FeNO is different for children with former RSV positive than RSV negative bronchiolitis. Our results could indicate that atopy was more linked to FeNO at 11 years of age in children with former RSV negative than RSV positive bronchiolitis. However, the number of participants was limited and there was a similar and near significant tendency also for children with a history of RSV positive bronchiolitis, suggesting that the results should be interpreted with caution.

FeNO and bronchial hyperresponsiveness

In the present study, DRS to methacholine was independently and positively associated with FeNO by the multivariate regression analyses including all children and also in the separate regression analyses including only children in the post-bronchiolitis group.

A similar association was found by Franklin et al., but only in atopic children [5]. The Copenhagen birth cohort study observed an association between FeNO and BHR, but underlined that this association was independent of asthma symptoms [35]. We found a similar association between DRS and FeNO for atopic and non-atopic children. In the present and in another recent study from the same population, asthma or atopy was not associated with BHR, although BHR was higher in the post-bronchiolitis group [10]. The relationship between NO metabolism and BHR in asthma is complex [36]. The ATS guideline underlines that studies report inconsistent associations and low correlations between FeNO and BHR, and that BHR, airway inflammation and FeNO belong to different domains [2]. A Norwegian twin study observed that common genetic effects could explain the association between FeNO and BHR, suggesting that FeNO is not related to BHR per se [37]. Moreover, BHR measured by direct provocation tests using methacholine or histamine reflects structural airway changes, compared to indirect provocation tests such as adenosine monophosphate or exercise which probably better reflects airway inflammation [38].

Strengths and limitations

The main strengths of this study were the prospective design, the long follow-up period and the high attendance rate of 82% of those originally included with bronchiolitis. However, the number of participants in the various sub-groups was relatively low, reducing the statistical power and complicating the interpretations of the results. This could impact the lack of interaction between the subgroups and between the post-bronchiolitis and control groups in the overall ANOVA analysis. In addition, the number of children in the RSV negative group was small and the results regarding this group must be interpreted with caution.

The children in the control group were slightly older than children in the post-bronchiolitis group at follow-up, but this should not influence the predicted values regarding lung function. However, a selection bias among those who consented cannot be excluded.

RSV was analyzed by direct immunofluorescence and not based on nucleic acid amplification such as reverse polymerase chain reaction (PCR). PCR is considered more sensitive and specific than direct immunofluorescence [39].

Conclusion

In this study, FeNO did not differ between 11 year old children hospitalized for bronchiolitis in infancy and an age matched control group. FeNO was associated with atopy, but not with asthma in both groups of children. This may suggest that FeNO may be unrelated to the pathophysiology of asthma after bronchiolitis. The results could also reflect that airway inflammation is rare in children 11 years after bronchiolitis.

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1. Wong, M et al. First National Survey of Patient Controlled Analgesia Practices. Physician-Patient Alliance for Health and Safety, 2013.