Volume 5 Number 4 August-September 2010

Respiratory Therapy™

The Journal of Pulmonary Technique

SPIROMETRY
BLOOD GAS
COPD
BACTERIA
HISTORY
LIFE SUPPORT

HEMOGLOBIN

Noninvasive > Continuous > Immediate

THE FIRST AND ONLY TECHNOLOGY FOR NONINVASIVE AND REAL-TIME HEMOGLOBIN MONITORING

With Masimo's breakthrough total hemoglobin monitoring technology (SpHb®), you can noninvasively, continuously and immediately determine your patients' hemoglobin levels. Delayed and intermittent hemoglobin tests requiring invasive blood draws and time-consuming laboratory analysis do not provide the same level of real-time clinical decision-making data. When used with other clinical variables, SpHb may help you assess anemic status to determine treatment and additional test options. Noninvasive hemoglobin, along with oxygen saturation, also gives you the first and only technology for real-time and noninvasive oxygen content (SpOC™) monitoring, giving you a more complete indication of your patients' oxygenation status. SpHb and SpOC are part of the upgradable Masimo Rainbow® SET technology platform that includes carboxyhemoglobin (SpCO®), methemoglobin (SpMet®), and PVI in addition to the gold standard measure-through motion and low perfusion SpO_2 and pulse rate measurements of Masimo SET®.

To find out more about how noninvasive total hemoglobin monitoring with the Masimo Rainbow SET platform can help in your hospital's patient safety and "do no harm" initiatives, call 1-888-336-0043, or go to www.masimo.com

Masimo®

Aeroneb® Pro Aeroneb® Solo

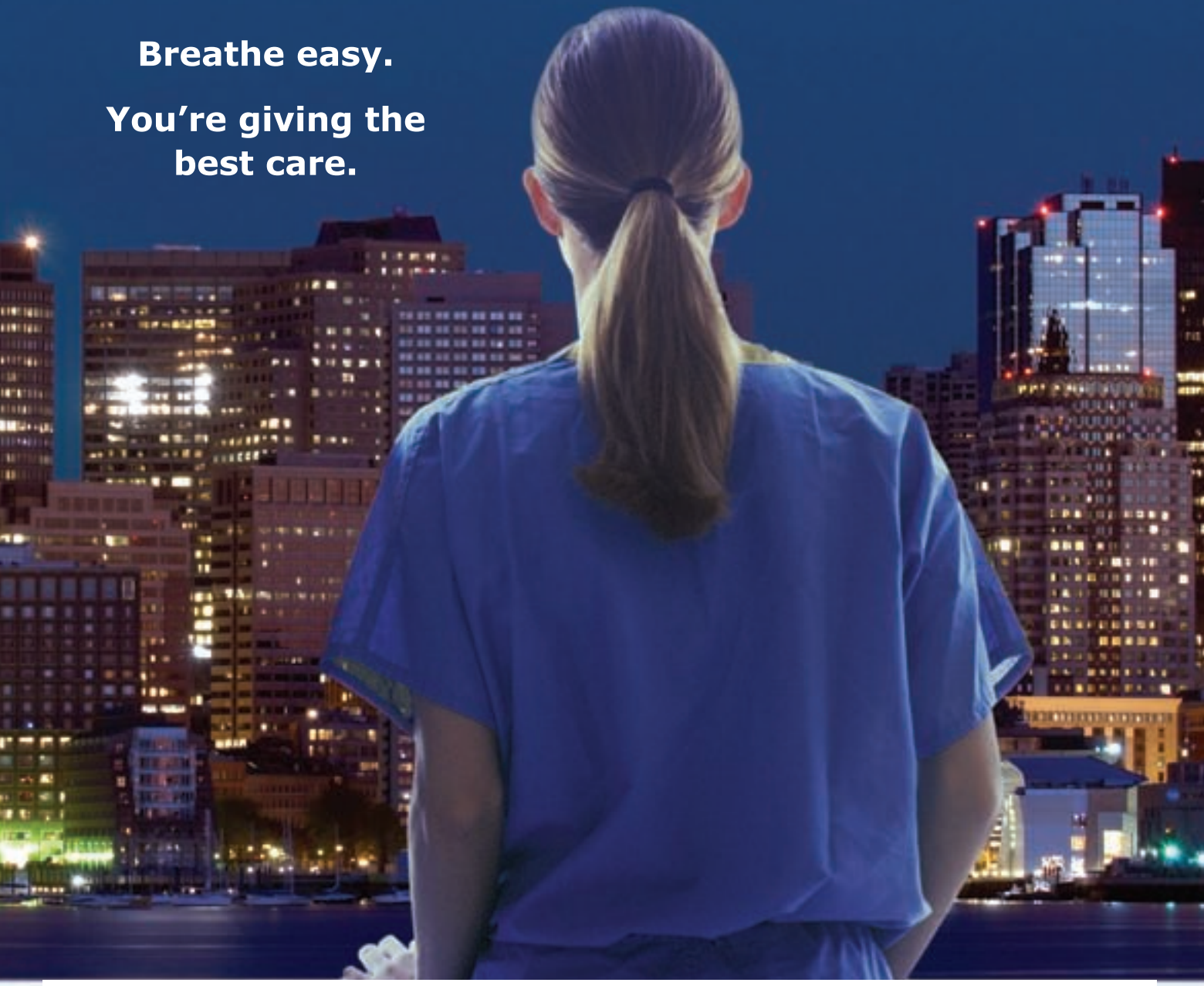
Aerogen nebulizers deliver an incredible four times more medication than traditional jet nebulizers, offering you unsurpassed efficiency and allowing you to give your patients the very best care available. They work independently to the ventilator settings meaning there's no added flow, no nuisance alarms, no loss of PEEP when opened for refill and no drug wastage. Aerogen truly sets a new standard.

Aerogen

We deliver best

Breathe easy.

You're giving the best care.



www.aerogen.com Phone USA (866) 423-7643 (toll free)

Respiratory Therapy™
The Journal of Pulmonary Technique

Vol. 5 No. 4
August-September 2010

Table of Contents

DEPARTMENTS

ARTICLES

Editorial

SARS, West Nile, 911, Bird Flu and H1N1—Positive Forces For Change

Dave Swift, RRT

Dave Swift is a member of Respiratory Therapy's Editorial Advisory Board.

For many years the professional associations (AARC, CSRT, provincial and state organizations), governments (federal, state and provincial) and respiratory care leaders/visionaries have attempted to encourage health care organizations to become more pro-active in preparing for mass casualty incidents. More often than not, the bottom line financial concerns limited the actual "buy-in."

Most organizations had disaster plans in place that were designed to deal with local disasters or MCI of limited scope. Most facilities had never actually been involved in an MCI, many had not carried out a full mock disaster response utilizing their plans but the majority had at least carried out a review of their plan. This formed the status quo for many years and most organizations had no reason to change their practice.

The first of many wake up calls came with the realization of terrorist activities occurring in the USA (Oklahoma City bombing, 9/11, etc). Although these MCI events were local, they elicited a national willingness to prepare and this helped spur on organizations to start reviewing their existing plans. However, the preparations continued to be in the context of local emergencies and this tone carried through to the planning. Facilities located in federal or state capitals often took this planning to heart as they were deemed to be of higher risk. In some cases, government(s) made special one-time funding available to facilitate the planning and in some cases actually conducted actual testing of their plans. However, most of these efforts continue to keep a "local" flavor, viewing planning, resources and coordination as a regional activity.

The next significant wake-up call came with SARS. This potiential pandemic MCI helped organizations and facilities to recognize that there needed to be more depth to their emergency response plans. One of the significant positives arising from SARS was the recognition and concerted effort to coordinate activities on a very large scale. Many levels of government focused their attention on the issues arising from SARS and offered resources, training and legislative direction to help facilitate the evolution of the MCI plans. For the first time, a serious review of resources available took place. This review triggered actions to update, replace and educate on existing resources. The expectation was that "there were more threats to come" and organizations were strongly encouraged (legislation, offers of additional funding, etc) to develop plans that could address the pandemic issues and forced facilities to look at developing a coordinated local, regional and national response. To varying degrees these efforts were successful. However, the litmus test was yet to come.

With the arrival of H1N1, many facilities found that their efforts were successful but quickly realized "when theory meets reality" that unanticipated results occurred. This was the latest and probably the most significant wake-up call yet. H1N1 demonstrated that during a pandemic there was really no known end point. Expected waves of casualties varied from region to region and the casualties, although low in numbers, required a disproportionate amount of resources that was not expected. The recovery phase was highly variable, with some patients taking months of critical care support before they could even enter the recovery phase. It was good fortune/luck (and efforts to provide mass inoculation) that the expected waves quickly became a "fizzle" and the numbers of casualties declined. This was a serious break for healthcare organizations as the potential for being overwhelmed had been recognized early on in the pandemic and preceded warnings from national health experts (ex CDC) and from WHO (World Health Organization). These warnings, although heard, had been discounted to some degree because of cost and previous experiences (the cry wolf

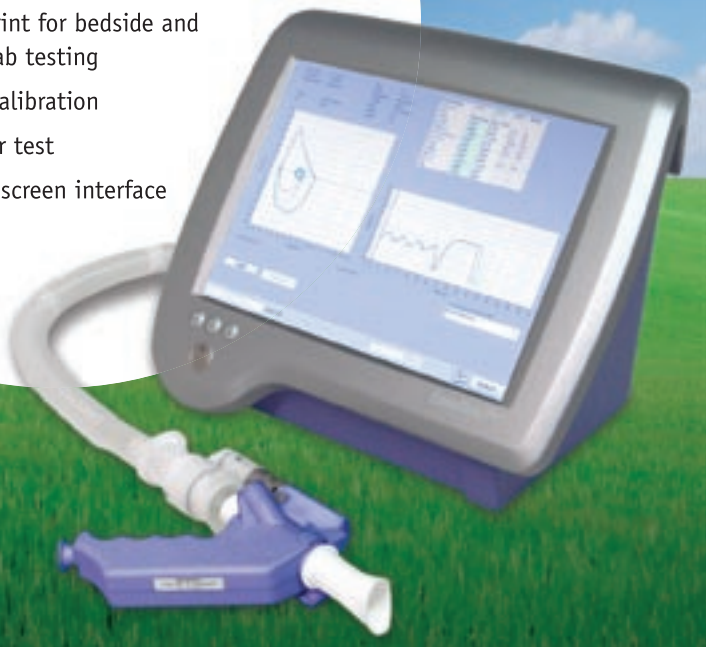
Continued on page 26…

Accurate diagnosis means accurate treatment

INTRODUCING THE **NEW**

EasyOne Pro™ single breath DLCO

- PFTs done in half the time
- Small footprint for bedside and stationary lab testing
- Automatic calibration
- Low cost per test
- Color touch screen interface



EasyOne™ Plus

- Great reimbursement
- Easy to operate menu
- Pictbridge compatible
- Not influenced by temperature, humidity, or barometric pressure
- No calibration, simple 3L cal-check
- No cleaning, no maintenance
- Single patient use spirette

The ndd Medical Technologies Advantage

Setting New Standards in Pulmonary Function Testing with Innovative Products

TrueFlow
makes the difference

www.nddmed.com

For further information contact ndd at **877-904-0090**

Respiratory Therapy™
The Journal of Pulmonary Technique

ISSN 2152-355X
Published six times each year by
Goldstein and Associates, Inc.
10940 Wilshire Blvd., Suite 600
Los Angeles, CA 90024 USA
Tel: 310-443-4109 · Fax: 310-443-4110
E-mail: s.gold4@verizon.net
Website: www.respiratorytherapy.ca
Video website: www.rttv.ca
Publisher Steve Goldstein
Editor Les Plesko
Senior Editor Carol Brass
Assistant Editor Laszlo Sandor
Design & Production http://accugraphics.net

Circulation, Coverage, Advertising Rates: Complete details regarding circulation, coverage, advertising rates, space sizes, and similar information are available to prospective advertisers. Closing date is 45 days preceding date of issue.

Change of Address notices should be sent promptly to Circulation Department. Provide old mailing label as well as new address. Allow two months for change.

Editorial Contributions will be handled with reasonable care. However, publishers assume no responsibility for the safety of artwork, photographs or manuscripts. All submissions may be emailed to s.gold4@verizon.net. Every precaution is taken to ensure accuracy, but the publishers cannot accept responsibility for the correctness or accuracy of information supplied herein or for any opinion expressed. Editorial closing date is the first day of the month preceding month of issue.

Editorial Advisory Board

Empowering the clinician to support VAP diagnostics

The Air*Life*™ diagnostic catheter's technology takes the mini-BAL to a new level of performance. Its standardized kit provides everything needed for a single clinician to conduct the procedure and achieve consistent, repeatable sampling with increased accuracy.

carefusion.com

CareFusion

BALANCING PAIN MANAGEMENT AND PATIENT SAFETY? YOU WANT MORE THAN A NUMBER.

Nellcor™
Puritan Bennett™
Airox™
Mallinckrodt™
DAR™
Shiley™

Know more than an SpO_2 reading—at a glance.

We give you warning about potentially harmful patterns of desaturation in your adult patients, so you can act sooner. With our alerts, you know that your patients may be experiencing repetitive reductions in airflow—even if they haven't crossed the SpO_2 alarm threshold.

That's just one feature of the new Alarm Management System for the Nellcor™ OxiMax™ N-600x™ pulse oximeter, offering more meaningful alarms and more pulse oximetry information, at a glance.

You live and breathe patient safety. And so do we.

Visit www.respiratorysolutions.covidien.com or call your Covidien representative at 800-NELLCOR for details.

COVIDIEN
positive results for life™

Miracles at Birth - Hamilton G5

The Hamilton G5 is designed to offer a choice of ventilation modes for neonatal, pediatric and adult patients requiring invasive or non-invasive ventilation.

With the unique features of Adaptive Support Ventilation (ASV) and the configurable user interface, the new neonatal option expands the G5 patient range down to the tiniest infants and premature babies. The proximal flow sensing provides the precise volume and leak monitoring with accurate, responsive triggering that your smallest patients demand.

Visit **www.hamilton-medical.com** for additional information or please send an e-mail to **info@hamiltonmedical.net**

25 YEARS

HAMILTON MEDICAL

My Name: Dr. Matson's Office

My Occupation: Family Practitioner

For my office staff, effective & reliable therapy is our utmost concern. We refer patients with a variety of respiratory needs and this versatile, clinical device gives my patients the confidence to lead active lifestyles.

MY PATIENTS
MY ECLIPSE

Created With You In Mind

With new and improved features, including variable rise time, adjustable sensitivity settings and pulse dosing up to 192mL, this robust system fulfills patients 24/7 oxygen needs at rest, during activities, during sleep and at altitude. A new, innovative large wheel cart design allows for easy battery replacement, and smaller AC and DC adapters make the E3 even easier for the patients to go anytime, anywhere.

One piece of equipment for both stationary and ambulatory use—the clear choice for a non-delivery business model. The Eclipse 3 reduces maintenance costs, increases productivity and lowers operating expenses.

The 3rd Generation has Arrived.

Saturate Patients at Rest • During Activities & Sleep • At Altitude

eclipse3™ with autoSAT™

SeQual®
www.sequal.com

YOU0410

News

☐ August-September 2010

KEEP YOUR COOL

According to a paper in Virology Journal, published on BioMed Central, winter temperate locations may be as susceptible to influenza as the humid tropics. According to the authors, it has been accepted for decades that international travel via jet aircraft is a major vector for global spread of influenza, and epidemiological differences between tropical and temperate regions have been observed. They wanted to study how indoor environmental conditions in the tropics and winter temperate zones contribute to the aerosol spread of influenza by travelers. To this end, a survey consisting of 632 readings of temperature (T) versus relative humidity (RH) in 389 different enclosed locations air travelers are likely to visit in 8 tropical nations were compared to 102 such readings in 2 Australian cities, including ground transport, hotels, shops, offices and other publicly accessible locations, along with 586 time course readings from aircraft. Using transmission risk contours and equations, transmission risk for each country's locations was compared with influenza reports from the countries. Higher risk enclosed locations in the tropics included new automobile transport, luxury buses, luxury hotels, and bank branches. Most temperate locations were high risk. The authors noted that accounting for differential aerosol transmission using T and RH can potentially explain anomalies of influenza epidemiology in addition to seasonality in temperate climates. See Aerosol influenza transmission risk contours: A study of humid tropics versus winter temperate zone, Brian P. Hanley and Birthe Borup, Virology Journal 2010.

THE EYES HAVE IT

The Huffington Post reported on Floppy Eye Syndrome and its relationship to Obstructive Sleep Apnea. FES manifests as rubbery-textured upper eyelids that may easily flip up during sleep, exposing the whites of the eyes, which can lead to dry, irritated eyes and discharge. While most people would awaken if their eyes became excessively dry and irritated during sleep, people with OSA may have a dysfunctional nervous system that prevents them from waking. Additionally, people with OSA tend to sleep on one side, which could result in intense, repeated pressure on the eyelid on that side of the face, contributing to or causing FES. But a British study reported on curing FES through CPAP, also used to deal with OSA. For more on this subject, go to the website of Michael Breus, thesleepdoctor.com.

JOBS JOBS JOBS

AOL's website Daily Finance reports that healthcare is the fastest growing job market, especially with the passage of The Healthcare Reform Act. Seventeen of the next decade's 30 fastest-growing occupations are healthcare-related. During the recession, healthcare added 600,000 jobs. In March, for instance, healthcare accounted for 27,000 new jobs: 16,000 of those in ambulatory health care services and 9,000 in nursing and residential care facilities. Growth is happening at all levels, from physicians to home health aides. The Labor Department projects 22% growth in the number of physicians; however, nursing will create the largest number of new healthcare jobs. Already, RNs constitute the largest occupation in the health industry, at 2.6 million. Another 581,500 new nurses will be needed over the next 10 years. The next fastest-growing area in terms of the most number of new jobs, at 461,000, is home health aides, an area predicted to grow by 50%. Healthcare technology is another growth area, what with government-mandated electronic medical record-keeping and new medical coding standards.

THE NERVE

The Plastic Surgery Center announced that a New Jersey medical team led by Dr Matthew Kaufman performed the fifth successful phrenic nerve decompression to reverse diaphragm paralysis. Immediately following the groundbreaking procedure, the patient, Julia Cooke, now breathes without complications. Ms Cooke, 57, was given six months to live due to her chronic pneumonia caused by a paralyzed right diaphragm, which lost function as a result of complications during a June 2009 surgery. She was previously told no treatment existed for diaphragm paralysis and suffered severe shortness of breath, chronic fatigue and incessant bouts of double pneumonia. In addition to allowing her to breathe normally, the procedure has also significantly improved Ms Cooke's mental and physical well-being, helping her to fully recover. In a highly complex procedure at Somerset Medical Center in Somerville, NJ, Dr Kaufman performed a microsurgical decompression of the phrenic nerve to restore function to Ms Cooke's right diaphragm, providing her immediate relief. As part of the process, the doctors also took the sural nerve from her leg and transplanted it to the phrenic nerve in her neck.

DON'T BREATHE

Don't hyperventilate before breath-holding underwater, said researchers at the Department of Neurology at Royal North Shore Hospital, NSW, who pointed to cases of two medical students who experienced seizure-like activity while competing in a breath-hold dive competition. In both cases, the students hyperventilated before the dive. The seizure-like activity that occurred was probably convulsions secondary to cerebral hypoxia induced by breath-holding, the researchers said. Swimmers often hyperventilate before breath-holding to reduce the urge to breathe from hypercapnia. This may result in prolonged breath-holds with consequent hypoxemia. Loss of consciousness may ensue without forewarning because the respiratory stimulus from hypoaemia is weak and easily overridden, and swimming may exacerbate hypoxia by increasing oxygen consumption.

SMALL-MINDED

Obstructive sleep apnea patients had reductions of grey-matter volume at baseline but showed significant grey-matter volume increase after three months of CPAP therapy, according to researchers at the University Vita-Salute in Milan. Obstructive sleep apnea patients showed focal reductions of grey-matter volume at baseline in the left hippocampus, posterior parietal cortex and right superior frontal gyrus. Significant grey-

matter volume increases were observed after three months of continuous positive airway pressure therapy in hippocampal and frontal structures. No further improvement in gray-matter volume was observed after one year of CPAP therapy. OSA patients showed cognitive impairment associated with neurostructural damage affecting specific cerebral regions. But most of the neuropsychological deficits were reversed after three months of treatment with CPAP and such cognitive improvements paralleled an increase of grey-matter volume in specific hippocampal and frontal brain regions. The increase of grey-matter volume in these regions was significantly correlated with the improvement at neuropsychological tests of executive functioning and short-term memory. The study involved 17 patients with an apnea-hypopnea index (AHI) greater than 30, indicating severe obstructive sleep apnea. They were compared with 15 healthy controls. Brain scans were conducted by MRI and VBM was used to characterize regional cerebral volume and tissue concentration differences. Results showed that specific neuropsychological measures are valuable tools for the assessment of therapy success and can offer to patients and physicians the evidence that adherence to treatment can lead not only to clinical but also to brain-structural recovery.

CARNIVORES

Children who eat at least three burgers each week may have a higher risk of developing asthma and wheeze, according to researchers from a number of European countries. The researchers said the risk was probably applicable worldwide, and definitely in developed nations. A Mediterranean diet, with plenty of vegetables, fruit and fish appeared to have the opposite effect. The findings were based on data on 50,000 children gathered over a ten-year period. Nearly 30,000 children were tested for allergic reactions, to determine whether diet might also influence their risk of developing allergies. While diet did not appear to be linked to sensitization to common allergens, it did appear to influence asthma and wheeze prevalence. High fruit consumption was linked to low wheeze rate among children in both developed and developing countries. In developed countries it was found that a diet rich in fish protected children, while a diet high in cooked green vegetables protected children in developing nations. The consumption of at least three burgers a week was associated with a higher lifetime prevalence of asthma and wheeze, especially among children in developed countries with no allergies.

A BETTER OPTION

Researchers at UT Southwestern and 19 other academic medical centers found that the use of CPAP might be a better option for preterm infants than the more conventional ventilator and surfactant therapy. Findings showed that patients who received the CPAP treatment required intubation less often both in the delivery room and neonatal intensive care unit. They also spent less time on ventilators and received fewer steroid drugs after birth. Researchers at the Neonatal Research Network randomly assigned 1,316 preterm infants to receive intubation and surfactant treatment within an hour of birth, or CPAP treatment in the delivery room followed by limited ventilation for two weeks. The infants, born between 24 weeks and 27 weeks, 6 days of gestation, also were assigned randomly to receive one of two ranges of oxygen saturation—either 85% to 89% or 91% to 95%. Infants treated with CPAP fared better, requiring less frequent intubation as well as fewer days on a ventilator. The rate of BPD or death, however, did not differ significantly between the two groups. Researchers sought to determine the range of oxygen saturation needed to minimize ROP or damage to the retina of the eye, while preserving life. Preterm infants who were in the lower blood oxygen saturation group did not have significantly less severe retinopathy of prematurity or death, but death before nursery discharge occurred more frequently. Among survivors, the risk of severe retinopathy was lowest among the babies who achieved between 85 and 89% percent oxygen saturation.

BMC NEWS

The **CONSORT 2010** statement has been co-published by eight journals, including Trials and BMC Medicine. Building on new evidence and experience, the revised guidelines are intended to improve the reporting of randomized controlled trials by providing a checklist of essential items for use by authors, reviewers and editors… A new thematic series in **Biology Direct** brings together cancer researchers and mathematicians to provide insight into the various roles of evolution in cancer… Research by Valerie Hu and colleagues, recently published in **Genome Medicine**, suggests that microRNAs have a role in the gene expression changes which can underlie autistic spectrum disorders… The journal **Herpesviridae** is now accepting submissions. It's a new open access journal dedicated to distributing knowledge of the role of herpes viruses in health and disease… **Critical Care** has co-published 10 free review articles as part of a joint effort with the Springer Yearbook of Intensive Care and Emergency Medicine, with each article selected for their relevance to healthcare professionals working in intensive care medicine… the Journal of **Biomedical Semantics** has now launched and publishes articles on all aspects of semantic resources used for data integration, modeling, interpretation and exploitation in biomedical research. **BMC Biology** and Journal of Biology are joining forces as a single journal committed to the publication of high-quality commissioned content and research articles of exceptional importance.

POC MEETING

The American Association for Clinical Chemistry announced its 2-day meeting commencing on September 24 in Boston. Topics include: Improving the Process of POC Tesing, Integrating POCT into Patient Care, Cardiac Markers at POC, Predictors of Patient Outcomes After Exposure to Respiratory Viral Pathogens, Implementation of POC Testing in the ED, Lessons from HIV, Rapid Testing for Influenza, Diagnostic Testing for Low Income Settings, and more. Among the "Gold" sponsors of the seminars are Abbot Point of Care, Biosite/ Inverness, Instrumentation Laboratory, Nova Biomedical, Quidel Corp, Radiometer, Roche Diagnostics and Siemens Healthcare Diagnostics. Contact aacc.org/events/meetings.

NEWS FEATURE

Endotracheal Tube Cuff Pressure—Let's Not Forget the Basics

Paul Garbarini, MS, RRT

Micro-aspiration of secretions past the endotracheal tube (ETT) contributes to the development of Ventilator Associated Pneumonia (VAP). New technologies such as continuous aspiration of subglottic secretions through the ETT, silver coated ETTs, tapered cuffs and new cuff materials have all been shown to potentially reduce aspiration or development of VAP.

However, the basic fundamental intervention with ETTs remains maintenance of adequate cuff pressure to prevent under-inflation which contributes to aspiration or over-inflation of the ETT cuff. Complications of over-inflation of the cuff include nerve palsy, tracheoesophageal fistula, tracheal wall damage, subglottic scarring or stenosis and hoarseness.

Cuff pressures are maintained in the 20-30 cm/H_2O range, most commonly utilizing the minimal leak technique in which air is added to the ETT cuff until no leak is heard, then a small amount of air is withdrawn until a small leak is noted. Cuff pressures are typically measured every 8-12 hours which may result in pressures being outside the recommended ranges. A pilot study continuously measured cuff pressures over a 9 hour period after initially inflating the cuff to 20cm. The results showed that 46% of cuff pressures over time fell outside the recommended pressure range with cuff pressure being low in 30% of patients and high in 16% of patients.[1] Another study found 30% of cuff pressures were too high and 15% were too low. Suctioning, coughing and patient position were noted to affect cuff pressure.

Continuous monitoring of cuff pressure and automatic maintenance of cuff pressure is feasible. An animal study using an automatic cuff pressure controller device showed that the automatic device maintained cuff pressure within prescribed limits 98% of the time versus only 65% of the time with manual fixed interval assessment of cuff pressure.[2] No animals had cuff pressures greater than 50cm with the automatic inflater, whereas 20% of control animals had a cuff pressure greater than 50cm. However, there was no difference in tracheal lesions during the 48 hour study period. Another audit of ventilated patients reported that 38% of cuffs were over inflated.

Some ventilators have the ability to monitor esophageal or tracheal pressures as they have a separate pressure transducer and port to attach catheters/tubing, (eg Hamilton GALILEO with a slight modification and the Hamilton G5). Thus, it is possible to continuously monitor cuff pressures using these devices. As ventilators can also control pressures, in the future it may be possible for the ventilator to automatically maintain cuff pressures in the desired range. [References: 1. 2009 American Association of Critical-Care Nurses; 2. http://ccforum.com/content/11/5/R109.]

COMMENTARY

Use of Patients' Medical Devices in the Hospital?

With the increasing use of CPAP therapy for Obstructive Sleep Apnea (OSA), there has come the recognition that these patients need to continue therapy while in the hospital. This is particularly important in the immediate post-operative setting in which respiratory drive may be diminished and/or upper airway muscles are relaxed. Many surgical services are implementing screening programs to identify patients with undiagnosed OSA. Additionally, patients on home mechanical ventilation need continued support in the hospital. Use of the patient supplied medical equipment in the hospital poses some challenges:

- Clinical staff is not trained or competent in all the potential types of CPAP/BIPAP or home ventilators available.
- Condition of and preventive maintenance of the equipment is not known.
- The patient may have been using the equipment for years and there's no documentation available of settings unless a home care provider is known and actively following the patient.

All of the above pose potential risk management issues. In light of this, the ECRI Institute, in a recent Health Devices Alerts Bulletin, published recommendations on the use of patient supplied respiratory care equipment. They noted patient deaths involving the use of patient supplied CPAP units. In these cases, there was no policy regarding use of patient equipment. Below are some of ECRI's recommendations on the use of patient supplied respiratory care equipment, along with some recommendations from personal experience in developing similar policies. The complete report can be found at: https://www.ecri.org/Documents/Esource/HT_Spring_2010/Alert_H0100_Patient-Owned_Equipment.pdf.

- Prohibit use of patient supplied equipment in the majority of cases.
- If patient supplied equipment is used due to unavailability of hospital supplied compatible devices, observe the following:
  1. Have an MD order for equipment.
  2. Respiratory Care notification of patient supplied equipment and assessment of the patient's ability to use the device. The assessment should include the degree to which the patient can self-administer the device and MD orders should subsequently reflect the level of clinical support needed, eg Respiratory Therapy to apply CPAP 10cm QHS (every night, at bedtime).
  3. Have Clinical Engineering perform a safety check (this may necessitate respiratory care to do a "functional" check if Clinical Engineering is not available 24/7).
  4. In the case of ventilators, standard ventilator checks in concordance with department policy are performed.

Paul Garbarini is Clinical Support Manager, Hamilton Medical, Inc.

COMPANY PROFILE

Salter Labs

Describe your product and its unique features.
Salter Labs, based in Arvin, CA, the provider of the broad line of Salter-Style cannulas—the worldwide standard for comfort and clinical efficiency, has also developed leading edge technology in the field of inhaled drug delivery. Its unique breath-enhanced NebuTech HDN high density small volume nebulizer provides superior clinical outcomes, faster treatment times (3 to 5 minutes), better patient compliance and reduced medication waste. The NebuTech HDN high density nebulizer accomplishes this by collecting and storing a plume of high density aerosolized medication in a patented 50cc tower during exhalation. Then, at the very beginning of inhalation this stored 50cc bolus of aerosolized medication is delivered very deep into the patient's lungs resulting in demonstrated superior aerosol deposition. With no moving parts to overcome, the HDN is appropriate for adults, as well as, pediatrics and is used in leading hospitals and institutions across the US and Europe.

How does your product directly affect patient care?
While providing patients with superior clinical outcomes, the NebuTech HDN high density nebulizer also can significantly improve patient compliance in the homecare environment by reducing treatment times to as little 3 to 5 minutes. In institutional settings, patient compliance is also improved as a result of the significantly reduced treatment times which have been demonstrated to also allow the elimination of concurrent SVN therapy.

Discuss your R&D process, including end-user input.
With the objective of supplying users with useful products that meet customers' specific needs, Salter Labs engages in continual, in-depth consultations with end users including physicians, therapists and patients while developing new products and modifying existing products. A prime example of this is the ongoing development of the NebuTech HDN high density nebulizer product line. The ongoing dialogue with users allowed the company, over time, to develop the NebuTech device and its various accessories into the most versatile aerosol product available. Initial customer feedback lead to the development of two different NebuTech HDN nebulizers—a cost effective reusable unit for homecare use and a less expensive disposable version for hospital use. These units were further modified so that they can deliver treatments either by a mouthpiece or via an aerosol mask. After much user feedback and consultation, a broad line of Salter aerosol masks were designed for use with the NebuTech HDN device. These masks are now available in a broad range of configurations to meet a wide range of specific patient and customer needs. Available are both over the ear and headband style masks in a variety of sizes ranging from infant through pediatric to adult and extra large adult sizes. Additionally in response to professional concerns regarding aerosolized medication depositing in the patients' eyes, Salter Labs developed a line of valved aerosol I-Guard masks. These unique valved aerosol masks direct any exhaled aerosol medication away from the patient's eyes and help with patient compliance and health by preventing unnecessary eye irritation.

Discuss the role of critical care providers in developing and upgrading your product.
Another example of designing products to meet specific customer needs is the company's aerosol filters. When Salter personnel, through consultations with respiratory professionals, became aware of concerns regarding long term occupational exposure to exhaled airborne aerosol particles, the company designed a special, inexpensive filter system for use with the NebuTech HDN nebulizer. These dual membrane filter sets capture 99.56% of all aerosol particles larger than 0.14 microns in size. The optional NebuTech filter sets and are currently being used by numerous medical facilities worldwide to significantly reduce the potential risks of cross contamination from patient exhalation and aerosol droplets.

Talk about how you test and evaluate your product in actual day to day use.
All of Salter Labs' products are subjected to intense bench and clinical testing both prior to and subsequent to their release. As part of Salter's continuing product testing and day to day evaluation, a very recent (2009) study was conducted on the NebuTech HDN high density nebulizer at a well known institution in Ohio. The results of this study provide new evidence of the superior aerosol deposition provided by the NebuTech HDN device. In this study, scintigraphic imagery was used to graphically show that the device provided uniform aerosol distribution in the lungs and periphery. Another example of the results of the day to day evaluation and testing of Salter products in a real world environment is a recently published study conducted at the Cleveland Clinic that demonstrated that the use of the NebuTech HDN high density nebulizer could significantly reduce SVN (small volume nebulizer) workload and associated costs without adverse events and demonstrated that the device would permit improved patient care and long-term cost savings over traditional T-piece nebulizers.

Tell us how you utilize conferences, seminars and such to promote your product.
To assist in educating clinicians about Salter products and their uses, the company employs a large staff of highly trained professional service representatives and independent reps to call on, work with and in-service the staffs of hospitals, alternate care facilities and homecare providers both in the US and abroad. To supplement these efforts Salter Labs participates in and attends over 175 national, international and regional professional meetings and trade shows each year. Patient educational materials, product data sheets, clinical reprints, etc. regarding Salter products are routinely provided to professionals by the Salter Labs' representatives or are available from the company's customer/professional service department by phone (800) 421-0024.

GUEST COLUMN

Spirit of Innovation

Catharine Johnson Tieck

The author is a respiratory therapist, innovator and peer. She will be writing a regular column, Product Review and Technology Watch, for this journal. Her goal will be to provide you information on innovative changes and trends in technology for our industry.

As the founder and CEO of Innovative Respiratory Concepts I have been involved in the innovative process for some time before starting IRC. Many years I worked nights 7P to 7A, sacrificing sleep and a personal life for the flexibility in my week in the pursuit of bringing my own innovation to market.

Like many therapists I was the "geek" in my field and loved the challenge of "rigging" to make things work, or pulling that rarely used technology out, for the challenging patient that needed something more. Like so many therapists I often thought, "Why don't they make things this way?" Or, "Why don't they make something that could do…" with no thought to all the process involved to make it the way they did.

This is how it began for me

Long before I invented my first device, an iconic inventor and forefather of our industry said that he saw an innovator in me. That someone was Dr Forest Bird. We met when attending a class he was giving on cardiopulmonary dynamics at his air lodge in Idaho. This changed my perception of pulmonary physics, ventilation and technology. I spoke to Dr Bird about a simple oxymoron in a device we use every day in respiratory care. It was then when he asked me how I would fix it and proceeded to tell me he saw the inventor in me. Little did I know this would evolve into a mentoring friendship and lead to the greatest passion in my life and career.

As many of you know, Dr Bird is the forefather to our profession, a highly awarded physician and innovator, but he is one of the most generous, kind and intelligent people a person could have the pleasure of meeting. Something many of us don't know in the respiratory world is that great person who is at his side, his wife Dr Pamela Riddle Bird. She is a fantastic success of her own, and a well known resource in the world of innovation, authoring Inventing for Dummies, which later became my "Eeagans" of inventing. Together the Birds have channeled their passion by helping future generations of innovators through sciences, math and innovation, including their own museum of innovation.

As my relationship continued with the Birds my passion for innovation grew. Eventually following in footsteps of Dr Bird and my father (who had passed more than 25 years ago), the day finally came where I had my first marketable invention. Little did I know the number of years of hard work and expenses that would follow. I believed I had a device that would really change the life of people who used it and the quality of the therapy. As I learned over time, many facets make

up the value, feasibility, and success of a potential device. As a result I created a value/feasibility scale, rating future devices with a grade of A, B, or C. The criterion was based on its effectiveness, uniqueness, time and cost to market and overall benefit to the caregiver and patient. Of course there are many additional considerations such as product life, research, regulatory and licensing and time window for market entry.

At a personal expense for this education I invested close to $60,000 on my first innovation in multiple prototypes, patent attorneys, peer evaluations, and research. Only to find out my device may never see the light of day in the US. This is where most are defeated. This is where I began, and my unusual sequence of events grew to the most amazing outcome.

Along the way, I began to receive what is now a priceless education that helped me build a model of "pay it forward," emulating what I saw in the Birds. This model was, "everything in the spirit of helpfulness." Many of the companies I met with liked my device, but wanted my opinions more. I began to have my eyes wide opened to what was a "realistic" expectation of bringing a device to market, in the "spirit of helpfulness" while meeting with manufacturers, distributors and our industry giants, in gratitude shared with them what I had to offer. Knowing this would be a long and difficult process that could take months and years to have a device evaluated, I sought out to meet all or most of the manufacturers in my industry traveling across the US relentlessly for the opportunity to personally demonstrate my device. During these travels relationships with these companies were built and this is where they provided me the education and explained the complexity and responsibility involved in creating a safe and effective device.

This stuff takes time

No one takes shortcuts or is on a fast track in this business. In the place where concepts meets the reality of the needs of the FDA, clinicians and market, most individuals and companies will have two to three generations of prototypes developed before it even comes to market. The cost with changes, specialists, and manpower is in the hundreds of thousands and some cases millions. Many devices are in development three to five years within a company and five to ten years privately.

So why do we do it?

As a clinical inventor, it is the passion to make something that is going to change the life of one of your patients and may end up on you some day... It is seeing the way technology should be, and striving to make that difference. I have found that most of the manufacturers are striving for the same thing. Over the years through my company I have met with, evaluated and consulted on many new innovative technologies and devices. These companies grow and thrive only if they make "the best device for the most competitive price." By the time you see a device, even a little adapter, millions have likely been spent to get it there.

There is definitely a David and Goliath in inventing clinical devices. The key is, you must have endless passion, dedication, preparation, and perseverance to make your invention a success. Be willing to take constructive criticism. Receive "no" with grace and most importantly, listen. With this you could someday see the fruits of your passion. Most importantly, never innovate with the foremost goal that it will be your key to riches. Instead, let your goal be to improve the outcome of at least one person with the knowledge that it may be you or your family.

Finally, as a therapist you see and have a vast choice of devices and technologies. All of those have undergone a rigorous process and high price to get there. Many devices look similar but in truth very few are. As an innovator, clinician, and consultant of developing respiratory care technologies, I have been involved in many stages and process of developing technologies that you will likely someday use. It is my experience, as my network of over 600 RTs grows, that this is because RTs are now more than ever highly valuable as innovators and resources for new developing technology. I invite you to consider this, when seeing new technologies in our publications, ads, and in your hospitals. Take the time to listen and read about it, it may change the outcome or quality of your care.

CLINICAL REPORTS

Masimo reported recent clinical findings:
Association of Carboxyhemoglobin Levels with Clinical Measures of Acute Asthma Severity, by Donald H. Arnold, et al, Vanderbilt University School of Medicine and Medical Center: Carboxyhemoglobin (COHb) is an indicator of both acute airway inflammation and second-hand smoke (SHS) exposure, both of which are known to be associated with worse asthma control. The objective of the study was to determine if COHb is associated with measures of acute asthma severity. The authors prospectively studied children ages 5 to 10 years of age with acute asthma exacerbations at a tertiary children's hospital emergency department (PED). COHb was measured using a Masimo multi-wavelength pulse oximeter (SpCO) at baseline and 2-hr after initiation of corticosteroid and bronchodilator treatment. SHS exposure was ascertained from the parent. Methemoglobin (SpMet) levels by multi-wavelength oximeter above 1.3% affects the accuracy of SpCO, and subjects with SpMet >1.1% were excluded. Univariate and multiple linear regression analyses were performed to assess the independent relationships between SpCO and measures of asthma severity, including exhaled nitric oxide (eNO), spirometry and clinical symptoms. Ninety subjects who had SpCO performed and SpMet <1.1% were included for analysis. Mean age was 9.3 yr (SD ±3.3), 59% were male, 62% were African-American, 50% had a parent with asthma, and 53% had SHS exposure. In multivariable analysis, SpCO was independently associated with presenting %FEV1 (n=47); for every 5% increase in SpCO, there was a 79 percentage decrease in presenting %FEV1 (p=0.015). SpCO level was not associated with the pediatric asthma score (p=0.38), airway resistance (p=0.25) or eNO level (p=0.83). The authors concluded that SpCO captured non-invasively during an acute asthma exacerbation in a PED population significantly correlates with %FEV1, such that as SpCO increases, the %FEV1 decreases. SpCO may represent a non-invasive, effort-independent measure of acute asthma disease severity as assessed by physiologic measures (%FEV1), but not symptom scores nor indirect measures of airway inflammation in this small study sample.

A new tool for the early diagnosis of carbon monoxide intoxication, by Piatkowski, et al, RWTH University Hospital, Aachen, Germany. Reported in Inhalation Toxicology, Vol 21, No 13,1144-1147. Invasive measurement of carboxyhemoglobin (COHb) by blood gas analysis (BGA) is accepted as the standard diagnostic procedure in diagnosis of inhalation injury and carbon monoxide (CO) intoxications. The main disadvantage of BGA with COHb testing is the unavailability in pre-hospital rescue conditions. The non-invasive SpCO analysis using pulse

CO oximetry (Rad57, Masimo Corp, USA) represents an easy-to-handle device to facilitate the diagnosis of CO intoxication. Between January 2006 and August 2008, 20 patients who were admitted with CO intoxication to our burn center were included in this study. Blood gas analysis including COHb testing was performed on the first day, hourly. At the same time, SpCO was determined using the Rad57 pulse CO oximeter. Patients received inhalative oxygen according to the parameters of blood gas analysis or hyperbaric oxygenation if COHb>10%. Five young healthy volunteers served as control group. The SpCO of the volunteers was cross-checked against their COHb levels, which were measured by blood gas analysis. Results of pulse CO oximetry revealed a mean error of approximately 3.15% from the results achieved by blood gas analysis. If COHb resulted in values higher than 10%, the bias remained approximately the same (3.43%/precision 2.362%). When different blood gas analyzers in our department were tested with the same patient sample, a mean error of 2.4% was found. This is only 1% lower compared to the mean error of pulse CO oximetry. Therefore, pulse CO oximetry represents a reliable measurement technique that is easy to handle and could facilitate the early diagnosis of CO intoxication in pre-hospital rescue conditions.

Plethysmography variability index: a new fluid responsiveness parameter, by M. Feissel, et al, France. From Critical Care 13 (Suppl 1), © 2009 Feissel et al; licensee BioMed Central Ltd. New predictors of fluid responsiveness have been obtained from plethysmographic waveforms displayed on pulse oximeters. However, they require recordings on a PC and offline operator-dependent analysis. A new parameter called the plethysmography variability index (PVI) has been proposed by a pulse oimetry manufacturer to be used for the purpose of fluid responsiveness. Its advantage is that it can be automatically calculated and displayed on the screen of the pulse oximetry monitor. The aim of the study was to test the accuracy of this parameter to predict fluid responsiveness in critically ill patients. Inclusion criteria were septic shock patients fully adapted to their respirator and on sinus rhythm. Methods involved simultaneous recording of the following tracings: invasive blood pressure, plethysmography pulse oximeter (Philips), ECG, airway pressure and digit values inscribed on the device (Masimo). Echocardiography was used to calculate the velocity–time integral (VTI). The authors infused fluid (500 ml saline) in patients with pulse pressure variation (ΔPP) ≥15% and performed passive leg raising (PLR) in patients with ΔPP <15%. The authors compared the PVI with ΔPP and with the variability of pulse oximeter wave amplitude (ΔPPleth) and sought the best threshold PVI value that predicted ΔPP >15%. Patients who increased their VTI by more than 15% in response to fluid or to PLR were defined as responders. The significance of the PVI threshold to distinguish between responders and nonresponders was examined. In the first step 25 patients were enrolled. Fifty paired values were analyzed. The r2 coefficients between ΔPP–PVI, ΔPPleth–PVI and ΔPP–ΔPPleth were 0.81, 0.79 and 0.74, respectively. A threshold PVI value of 20 identified patients with ΔPP >15% with a sensitivity of 84% and specificity of 90%. In a second step 18 other patients were enrolled. All patients with PVI >20 (n=8) were fluid responders and 10 patients with PVI <20 were PLR nonresponders. The authors concluded that the PVI automatically obtained from a pulse oxymetry device seems an accurate index of fluid responsiveness. The numerical value of 20 distinguished responders from non-responders with good sensitivity and specificity. Contact masimo.com.

COMPANY NEWS AND PRODUCTS

LABELING

The FDA released final label revisions for respiratory medications that contain an active ingredient known as a long-acting beta-agonist (LABA). This follows the FDA communication on 18 February 2010 requesting all manufacturers of LABA-containing medications to undertake class-labeling changes. The FDA made label revisions to both single ingredient and combination LABA-containing medications. For the treatment of asthma, single ingredient LABAs should only be used with an asthma controller medication such as an inhaled corticosteroid (ICS), they should not be used alone. SYMBICORT (budesonide/formoterol fumarate dihydrate) is an asthma combination medication that contains both an ICS (budesonide) and a LABA (formoterol). The updated label for combination asthma medications, including SYMBICORT, provides guidance on how these products should be prescribed to treat asthma, including: SYMBICORT should only be used for patients not adequately controlled on a long-term asthma control medication such as an inhaled corticosteroid or whose disease severity clearly warrants initiation of treatment with both an inhaled corticosteroid and LABA. Once asthma control is achieved and maintained, assess the patient at regular intervals and step down therapy (eg discontinue SYMBICORT) if possible without loss of asthma control, and maintain the patient on a long-term asthma control medication, such as an inhaled corticosteroid. In addition, the Boxed Warning, and other relevant sections of the label, have been revised to inform healthcare professionals and patients that LABAs, when used as single ingredient products, increase the risk of asthma-related death based on a large placebo-controlled study with salmeterol (a single ingredient LABA product). FDA considers this risk to be a class effect of all LABAs, including formoterol, one of the components of SYMBICORT. Currently available data are inadequate to determine whether concurrent use of inhaled corticosteroids or other long-term asthma control drugs mitigates the increased risk of asthma-related death from LABA. Contact astrazeneca.com or mysymbicort.com.

NEW EXEC

Neil Segil, PhD, has been named as Executive Vice President of Research at the House Ear Institute (HEI). Neil Segil joined the House Ear Institute (HEI) in 1996. In addition to his responsibility as a Scientist III, Segil currently holds two National Institute of Health RO1 grants. He also holds the position of Research Associate Professor in the Department of Cell and Neurobiology at the Keck School of Medicine of University of Southern California. Segil's research is focused on development and regeneration of the inner ear, as well as the problem of ototoxicity. The House Ear Institute is a non-profit organization dedicated to advancing hearing science through research and education to improve quality of life. Contact hei.org.

FULL DATA

Actelion announced that full data from the Phase II study of selexipag (proposed INN), the company's first-in-class, orally available, selective IP receptor agonist in patients with pulmonary arterial hypertension (PAH) were presented by Gerald Simonneau MD, PhD Chief of the Department of Pneumology, Hospital Antoine Béclère, Clamart, France, and lead investigator on the trial, during the American Thoracic Society's conference. Results of the 43-patient,

placebo-controlled, double-blind study, where patients were randomized in a 3:1 ratio receiving selexipag or placebo, showed a statistically significant reduction in pulmonary vascular resistance (PVR; primary parameter for the study). The treatment effect was shown to be 30.3% after 17 weeks of treatment (p=0.0045). Results also showed an encouraging numerical improvement in 6-minute walk distance (6MWD), which was a secondary endpoint of this trial. Selexipag was well tolerated and the safety profile was in-line with the expected pharmacologic effect. Treatment with selexipag was initiated at 200 microgram (mcg) b.i.d., which, if tolerated, was uptitrated to bid 400, 600 and 800 mcg on Days 3, 7 and 21, respectively. All patients enrolled in the trial were on background therapy with endothelin receptor antagonists and/or phosphodiesterase type 5 inhibitors before and during the course of the study. The primary efficacy endpoint of the trial was change from baseline to Week 17 in PVR. The secondary endpoints included 6MWD and other hemodynamic parameters. Safety and tolerability were evaluated in all enrolled patients. Selexipag is currently being evaluated in the Phase III GRIPHON, (Prostacyclin (PGI2) Receptor agonist in Pulmonary arterial Hypertension) trial, which is enrolling patients around the world. Contact actelion.com.

CEO APPOINTED

Philips Healthcare announced the appointment of Brent Shafer to lead Philips Home Healthcare Solutions as CEO of the global business. Since joining Philips in 2005, Brent Shafer has held a position as head of the Philips Healthcare North America Sales and Service organization, and as EVP and CEO of Philips North America. Prior to Philips, Shafer held executive positions at Hill-Rom and GE Medical Systems. Contact philips.com.

EXPANDED PLATFORM

Radiometer is expanding the TCM4 platform with several new transcutaneous modules and sensors. The **TCM TOSCA** module and the **TCM CombiM** module and sensors will increase patient safety, while promoting greater comfort. By linking patient and monitoring information, Radiometer's new TCM CombiM and TCM TOSCA monitors significantly decrease the risk of patient and data mix-ups during continuous transcutaneous monitoring of oxygen, carbon dioxide and saturation in adult, pediatric and infant patients. The new monitors allow the patient ID to be entered into the monitor, while linking monitoring data to a session. The TCM CombiM measures carbon dioxide and oxygen, whereas TCM TOSCA, compatible with the well-known **TOSCA 92** sensor, provides information on carbon dioxide and oxygen saturation. Information is provided continuously and non-invasively. With touch screen technology, the two new Radiometer monitors provide full connectivity to major patient monitoring systems and 48 hours of real-time data storage. The TCM CombiM configuration also includes two new transcutaneous sensors. The new **tc Sensor 84** is a combined oxygen/carbon dioxide sensor, whereas the new **tc Sensor 54** is dedicated for carbon dioxide measurements. To ensure optimal patient comfort during non-invasive monitoring, both sensors have a very small surface area and offer multiple choices of application-fixation ring, double-adhesive ring and ear clip. These sensors reduce the need for remembraning to once every other week. Radiometer also announced that its **NPT7** blood gas analyzer is retiring, and offers an upgrade to Radiometer's newest POC technology. Introduced in 2001, the NPT7 paved the way for a new generation of compact POC blood gas and CO-Ox analyzers, including the **ABL80 FLEX CO-OX**. The ABL80 FLEX CO-OX offers the same compact size, ease of use and maintenance of the NPT7, as well as a broader parameter profile, more intuitive user interface, onboard data management and full operation on battery. Contact Radiometer for special pricing and no-capital options. Contact radiometeramerica.com/tc.

FDA APPROVAL

Asthmatx Inc announced that the FDA has approved the Alair Bronchial Thermoplasty System for the treatment of severe persistent asthma in patients 18 years and older whose asthma is not well controlled with inhaled corticosteroids and long acting beta agonists, the current standard-of-care treatment for these patients. FDA approval of the Alair System was largely based on the promising results of the AIR2 Trial, a double-blind, randomized study designed to evaluate the safety and effectiveness of bronchial thermoplasty in adult patients with severe asthma. The trial demonstrated that patients treated with the Alair System improve their asthma quality of life over patients who rely solely on medical therapy after one year, but these patients also experience other clinically significant benefits, including: 32% reduction in asthma attacks, 84% reduction in emergency room visits for respiratory symptoms, 73% reduction in hospitalizations for respiratory symptoms,and 66% reduction in days lost from work/school or other daily activities due to asthma. In the period immediately following bronchial thermoplasty, there was an expected transient increase in the frequency and worsening of respiratory-related symptoms, which were of the type expected following bronchoscopy in patients with asthma. These resolved on average within seven days with standard care. In the long-term after treatment, fewer bronchial thermoplasty treated patients reported respiratory adverse events. Investigators in the AIR2 Trial concluded that the increased risk of adverse events in the short-term following bronchial thermoplasty is outweighed by the benefits, which persist for at least one year. Contact bronchialthermoplasty.com or asthmatx.com.

RIOCIGUAT

Bayer HealthCare Pharmaceuticals, Inc recently presented new data on the company's developmental compound riociguat (BAY 63-2521), an oral agent being investigated as a potential treatment for several different types of pulmonary hypertension. The company noted that despite improvement in patient care over the past few years, there is still a substantial unmet medical need in the treatment of different forms of pulmonary hypertension. Existing treatments are primarily indicated for pulmonary arterial hypertension and no non-surgical treatment is approved in the US for chronic thromboembolic pulmonary hypertension. A soluble guanylate cyclase (sGC) stimulator, riociguat has been shown in pre-clinical studies to directly stimulate soluble guanylate cyclase (sGC) and to enhance the action of nitric oxide (NO). A pathway involving NO is an area of investigational interest because the amount and effects of nitric oxide are thought to be impaired in patients with forms of pulmonary hypertention. Riociguat is being investigated in ongoing, randomized placebo-controlled phase III trials for chronic thromboembolic pulmonary hypertension (CTEPH) and pulmonary arterial hypertension(PAH), two life-treatening forms of pulmonary hypertension. Additional Phase II studies of riociguat in patients with other forms of pulmonary hypertension, including PH owing to interstitial lung disease (PH-ILD) and PH associated with chronic obstructive pulmonary disease (COPD), have been completed. Bayer HealthCare Pharmaceuticals also announced that the study "Riociguat for chronic thromboembolic pulmonary hypertension and

pulmonary arterial hypertension: a phase II study" was published online by the European Respiratory Journal. According to the published results, 96% of the patients enrolled completed the study, and the majority of patients (72%) were able to be titrated from the starting dose of 1 mg tid by 0.5 mg increments every two weeks to a maximum target dose of 2.5 mg tid. Sixty-five patients (87%) who received at least one dose of riociguat reported an adverse event (AE), including 11 serious adverse events (SAE). Adverse events were judged to be drug-related in 42 patients (56%), and most (96%) were considered mild or moderate in severity. The incidence of AEs was not considered related to the dose of riociguat. The publication also describes the effects of riociguat on secondary pharmacodynamic endpoints. Contact pharma.bayer.com.

CLOSED LOOP

CareFusion announced the launch of its Closed Loop Controller of Inspired Oxygen system or $CLiO_2$, the first automatic oxygen controller of its kind designed to keep the oxygen level in the blood within a safe range for newborns needing mechanical ventilation. This new software algorithm is an enhancement to the CareFusion AVEA ventilator. The $CLiO_2$ system noninvasively and continuously measures the oxygen level in a newborn's blood using Masimo SET Measure-Through Motion and Low Perfusion pulse oximetry technology to provide accurate and reliable oxygen saturation (SpO_2) measurements, even under challenging clinical conditions. The $CLiO_2$ system processes blood oxygen saturation levels by a computer algorithm that then anticipates trends and modifies the amount of oxygen delivered. If necessary, adjustments can be made on a second to second basis, something not currently possible with manual control. The $CLiO_2$ system is currently available in most Western Europe and Asian countries through CareFusion and its authorized distributors, with future availability in the US and Canada. Contact carefusion.com.

PORTABLE

COSMED announced the launch of the Spiropalm 6MWT, a new medical device incorporating the latest design for portable spirometry and a unique tool for the standardized Six-Minute Walk Test. The Spiropalm 6MWT provides the customer with a complete testing package with the ability to measure minute ventilation and breathing pattern during walking together with a fully integrated pulse oximeter to monitor SpO_2 and HR during the test. Spiropalm 6MWT allows full assessment of ventilation limitation due to dynamic hyperinflation and air trapping in patients with pulmonary disease. Fully complies with ATS/ERS guidelines for the 6MWT (2002). Contact cosmed.com.

REPORT CARD

At this year's AACN meeting, Covidien R&MS released a first year "report card" of its **Alarm Management System** (AMS), an upgrade to the company's flagship pulse oximeter, the Nellcor OxiMax N-600x, which was made available globally last spring. The AMS allows clinicians to detect desaturation patterns indicative of repetitive reductions in airflow in adults. The first year Report Card highlighted how healthcare systems across the nation have integrated the AMS into daily practice… The company also reports on independent studies validating the use of its **DAR Filters**. For patients who require mechanical ventilation, ventilator filters are a key to a good clinical outcome. Covidien's broad line of DAR ventilator filters and filter-HMES with either mechanical or electrostatic filtration have an N-A-C-L rating of greater than 99.97, providing high-performance filtration. That means they capture at least 99.97 percent of the particles most likely to penetrate the filter.[3] This level of efficiency exceeds the filtration capabilities of commonly used electrostatic filters.[1] Independent published studies have shown Covidien DAR filter-HMEs to be among the best HMEs in terms of moisture output.[4,5] A recently published study showed that out of 48 other filters and HMEs tested, three DAR Filter-HMEs ranked in the top 10 for performance. These three DAR filter-HMES are the Hygrobac, the Hygrobac S and the Hygroster filters.[4] [References: 1. Wilkes AR. Measuring the filtration performance of breathing system filters using sodium chloride particles. Anaesthesia. 2002;57(2):162-168; 3. Nelson Laboratories Inc. Sodium chloride aerosol testing of breathing system filters (BSF). Lab No. 399951A.1 Amended. Jan 2008; 4. Lellouche F, Taillé S, Lefrançois F, et al. Humidification performance of 48 passive airway humidifiers: comparison with manufacturer data. Chest. 2009;135(2):276-286; 5. Lucato JJ, Adams AB, Souza R, Torquato JA, Carvalho CR, Marini JJ. Evaluating humidity recovery efficiency of currently available heat and moisture exchangers: a respiratory system model study. Clinics (Sao Paulo). 2009;64(6):585-590.] Contact covidien.com.

SUCTIONED

Pulmodyne introduces the Blom Tracheostomy Tube System which has a unique Subglottic Suctioning Disposable Inner Cannula that gives the clinician the ability to suction secretions above the cuff of a tracheostomy tube, which should help them in their strategy to fight VAP. The Blom Tracheostomy Tube System is also an innovative solution for providing ventilator dependent patients with a tracheostomy the ability to speak regardless of cuff inflation. Included in the Blom Tracheostomy Tube System are the Speech Cannula and Low Profile Valve (LPV). Each has its own unique function by allowing the patient to speak in their own natural voice. The Speech Cannula is designed to allow speech for ventilator dependent patients that require a fully inflated cuff with a Blom Fenestrated Cuffed Tracheostomy Tube. The LPV is designed to allow tracheostomized, nonventilator dependent patients to speak without the use of finger occlusion, with the Blom Non-Fenestrated Uncuffed or the Blom Fenestrated Cuffed Tracheostomy Tube. Both the Subglottic Suctioning Cannula and the Speech Cannula can only be used with a Blom Fenestrated Tracheostomy Tube. The fenestration is located approximately 1mm above the cuff, so when inflated, fenestration contact with the tracheal mucosa is prevented. The Blom Tracheostomy Tube kits are available in four adult sizes: #4, 6, 8, & 10. This product is for Single Patient Use and is PVC and Latex Free. Contact pulmodyne.com.

INNOVATIONS

The **Rüsch Infant TruView EVO** from Teleflex Medical is an innovative optical view laryngoscope blade designed to provide indirect laryngoscopy with continuous oxygen insufflation more safely, clearly and easily. Indicated for use in both standard and difficult intubations, the Rüsch Infant TruView EVO illuminates and expands angular view of the larynx and adjacent structures, thereby facilitating endotracheal intubation. It is a cost effective solution for crash carts, emergency room and every day use in the OR. The Rüsch Infant TruView EVO uses an optical system within the viewtube which consists of prisms and lenses that extend vision beyond the distal end of the blade. It is designed to decrease laceration and bleeding of the pharyngeal-laryngeal mucosal tissue in addition to reducing the amount of force needed to successfully intubate a patient by greater than 30%.

This innovative approach protects patients and minimizes risk of esophageal intubation... **Sheridan Endotracheal Tubes**, part of the Hudson RCI line of products, includes a wide range of clinical solutions for adult and pediatric use. The Sheridan Ped-Soft line of uncuffed endotracheal tubes is made out of a soft PVC formulation which enhances the tube's compliance to a child's anatomy and makes it an ideal choice for short or long term pediatric intubation. The specially designed distinct black tip incorporated on the Ped-Soft endotracheal tubes aide in visualization during intubation. Additional depth markings are also included to assist in placement during nasal intubation… The **Comfort Flo Humidification System** is designed to comfortably deliver flow rates of 1-40 LPM of heated, humidified oxygen through a nasal cannula interface to a broad range of patients. A completely disposable delivery system and line of specialty cannula, the Comfort Flo Humidification System allows clinicians to maximize patient comfort, improve therapy compliance, and avoid more invasive and often more expensive therapies. The Comfort Flo Nasal Cannula is available in Premature, Infant, Pediatric, and Adult sizes… The **Hudson RCI Infant Nasal Prong CPAP System** is designed to reduce trauma associated with the delivery of infant nasal CPAP. The Hudson RCI Infant Nasal CPAP Prong System was specifically designed to minimize the problems associated with more invasive therapies. The soft, anatomically curved prongs enhance fit and minimize nasal septal necrosis. Additionally, the luer fitting on the expiratory connector allows proximal airway pressure monitoring. Available in six (6) prong sizes to allow greater choice for appropriate sizing of each infant, the Hudson RCI Infant Nasal CPAP offering can help improve clinical outcomes for the critical care infant. For optimal humidification in the NICU/PICU Teleflex offers the **ConchaTherm Neptune Heated Humidifier**. Adjustable airway temperature and gradient control features allow you to customize therapy--maximizing humidity delivered while minimizing circuit condensation. The Neptune can be used across the continuum of care, eliminating the need to change equipment as treatment advances (HFV, IMV, CPAP, and Oxygen Therapy). Teleflex Medical announced the introduction of a comprehensive education program in respiratory therapy, designed to provide an in-depth curriculum focused on maximizing humidification and minimizing challenges through the therapeutic levels outlined in the Respiratory Pyramid of Care. The courses are accredited by the American Association for Respiratory Care (AARC). The program's four modules cover humidification basics, passive humidification, active humidification and navigating the Respiratory Pyramid of Care and its five therapeutic levels that form the basis for effective, informed management of patients who require oxygen therapy and/or ventilatory support. Through the sponsorship of Teleflex Medical, an expert panel of respiratory therapy thought leaders was assembled to form the Council for Advances in Respiratory Therapy. Clinical contributors from this group were charged with the development of the content for this education curriculum based upon an extensive literature review to summarize current evidence and best practices. The program is designed to provide practical solutions for clinicians and joins other clinical education offerings from Teleflex Medical, including programs for vessel health and preservation and regional anesthesia best practices. Contact teleflexmedical.com.

INTELLIGENT

Hamilton Medical presents the world's first fully closed loop ventilation technology. INTELLiVENT-ASV opens the next era of intelligent ventilation. The company has launched universal ventilator HAMILTON-S1 with INTELLiVENT-ASV, the world's first fully automatic application for intensive care ventilation. Optimized ventilation therapy in intensive care requires permanent adjustment of setting parameters to wean and get patient off the device as quick as possible. Unfortunately therapists can't stay permanently with the patient at the bedside. Therefore in some situations settings are only adjusted as soon as some alarm threshold indicates physiologic lung changes to good or bad. This will become different with INTELLiVENT-ASV, with its fully closed loop ventilation technology for oxygenation and ventilation covering all applications from intubation until extubation. INTELLiVENT-ASV is based on the systematic evolution of ASV over the last decade and on scientific evidence. The automatic adjustments follow protocolized care measuring lung physiology, respiratory monitoring, capnography ($etCO_2$) and pulse oximetry (SpO_2). The INTELLiVENT-ASV is only available on universal HAMILTON-S1 ventilator. It is not yet approved in all countries. FDA submission is pending in the US. Contact hamilton-medical.com.

FDA RESPONSE

InterMune, Inc announced that the FDA issued a complete response letter for the New Drug Application (NDA) for Esbriet (pirfenidone) for the treatment of patients with idiopathic pulmonary fibrosis (IPF) to reduce decline in lung function. A complete response letter is issued by the FDA's Center for Drug Evaluation and Research when the review of an application is completed, but there are one or more reasons that preclude the approval of the NDA at this time. The FDA has requested an additional clinical trial to support the efficacy of Esbriet in IPF patients. InterMune intends to meet with the FDA as soon as possible to explore the best ways to address the points raised by the Agency and to discuss pathways to approval. The FDA Advisory Committee recommended the approval of the pirfenidone NDA by a 9-3 margin. The company stated that it was disappointed by this outcome, and would meet with the FDA to understand its points of view and to determine the most appropriate path forward to expeditiously make Esbriet available to the approximately 100,000 patients with IPF and their families who suffer from IPF. In Europe, the company has submitted a Marketing Authorization Application to the European Medicines Agency (EMA), seeking approval to market Esbriet for the treatment of IPF patients in the European Union. Esbriet (pirfenidone) has been granted Orphan Drug status for the treatment of IPF in Europe. Contact intermune.com.

NONINVASIVE

LungPoint helps bronchoscopists successfully navigate the lung airways and enables the patient to avoid more invasive procedures. The cutting-edge technology allows for pre-procedure mapping and visual guidance during bronchoscopy and helps physicians get to lung tissue that would have previously only been reachable through the chest wall or surgically. UC Davis Medical Center is currently using the LungPoint System. Similar to navigation systems used when driving, the LungPoint system allows physicians to select destinations and see the best routes to get there. With this application the "destination" is a suspicious spot in the lung and the "streets" are the lung airways. Once the best possible route is selected, the LungPoint system presents an animation of what the journey through the airways will look like, providing physicians with a full visual guide to the biopsy destination. The Hospital of the University of Pennsylvania has also been using the LungPoint System. Its software

allows for a shorter amount of time to get to a lesion in the lung and complete a biopsy procedure. Contact lungpoint.com.

ACQUISITION

Ohio Medical Corporation has acquired The MiniOX brand of handheld medical O_2 Analyzers and Monitors from Pittsburgh-based safety equipment manufacturer MSA. Ohio Medical is adding the MiniOX brand to its growing portfolio of suction and oxygen products. Ohio Medical Corporation has been a leading supplier of medical suction regulators, air and oxygen flowmeters, portable suction equipment and medical air and vacuum pumping systems, since 1958. The MiniOX Analyzers and Monitors will now be marketed and manufactured by Ohio Medical Corporation. Contact ohiomedical.com.

COST-EFFECTIVE

VORTRAN has introduced its new and most cost effective VAR Model PTM-5001 with special introductory price and the VAR-Monitor with an amazing 50% off list price (offers through 12/31/2010). Model PTM-5001 for adult and pediatric patients 10 kg (22 lbs) and above, delivers 100% FiO_2 only. VAR-Monitor designed to provide continuous monitoring for any non-cycling condition for current VAR. Contact vortran.com (800) 434-4034.

SAFETY STUDY

Pearl Therapeutics Inc, a company developing clinically differentiated double and triple combination therapies for the treatment of highly prevalent chronic respiratory diseases, reported on results of its Phase 1 safety and pharmacokinetics study of PT003. PT003 is an inhaled combination of glycopyrrolate, a long-acting muscarinic antagonist (LAMA), and formoterol, a well-known, established, long-acting ß2-agonist (LABA), delivered by metered dose inhalers (MDI), the most widely used inhalation drug delivery format. PT003 is the first and only dual long-acting rapid bronchodilator LAMA-LABA combination product in development as a pressurized hydrofluoroalkane MDI (HFA-MDI) formulation, and is currently being investigated in a Phase 2b study. Pearl has overcome fundamental chemistry, manufacturing and control (CMC) issues associated with MDIs via its proprietary porous particle technology. These particles have allowed the formulation of both formoterol and glycopyrrolate in the MDI format—in combination and as monotherapies—with highly stable, robust and aerodynamically efficient drug delivery. Pearl has developed a broad portfolio of high-performance combination and monotherapy MDI products, including PT003, PT001 and PT005, utilizing this formulation platform, without the need for complex drug delivery devices or manufacturing processes. Pearl also is developing PT010, a triple combination product that combines the LAMA and LABA components of PT003 with an inhaled corticosteroid (ICS) for twice-daily administration from an HFA-MDI for the treatment of severe COPD. Contact pearltherapeutics.com.

NEXT GENERATION

Siemens Healthcare offers the next generation of advanced visualization and agile PACS technologies. With **syngo.via**, Siemens' new imaging software for multimodality reading of clinical cases, the company is placing special focus on reading efficiency through automated case preparation and structured case navigation across multiple specialties, including cardiology, oncology, and neurology. Automated case preparation functionality automatically loads images into the appropriate application and sorts them into the corresponding layout—pre-processed according to the disease-specific requirements—thereby giving physicians more time to focus on image reading and diagnosis. When employing the software with syngo.plaza, users are presented with direct, no-click access between the two technologies and a unified user-interface, allowing for a smooth transition between different applications that helps speed up the reading workflow. Siemens Healthcare also announced that industry veteran **John Nosenzo** has joined the company as its new senior vice president of Zone Customer Relations. Nosenzo will oversee the US organization's business volume, responsible for the national sales organization. He was formerly with Quest Diagnostics. Contact siemens.com/healthcare.

EXTENDED

B&B Medical Technologies announced that its Sil.Flex Stoma Pad wear time has been extended up to 28 days for single-patient application. Per the manufacturer, the durability of the Sil. Flex Stoma Pad has been evaluated and meets the performance specifications required for extended wear. Sil.Flex is a soft, flexible pad that is placed between the tracheostomy tube and the patient's stoma site. The contoured surface provides a stable, comfortable interface between the flange and the patient's neck. Sil.Flex Stoma Pads are made of medical-grade silicone. Hypoallergenic and latex-free, each sterile pad is individually packaged, and is intended for single patient application. Once applied, Sil.Flex is easily removed for cleaning. The Sil. Flex Stoma Pad is available in four sizes, accommodating small infants to large adults. Contact bandb-medical.com.

EMERGENCY PLANNING/DISASTER PREPAREDNESS ROUNDTABLE

Draeger

On January 12, 2010 Haiti experienced a devastating earthquake that demonstrated that Draeger's motto,"Technology for Life" is more that just a tag line—it's a philosophy that is shared throughout the company's 11,000 employees. At the request of the University of Miami, Draeger Medical, Inc donated 16 Carina-home ventilators and two anesthesia machines to be immediately deployed to the field hospital that was being created at the Port-au-Prince Airport. Realizing the need to have on-site support, three field staff employees voluntarily offered their time and clinical expertise to support this mission which included:

- Setting up Narkomed and Tiro anesthesia machines so physicians could give general anesthesia.
- Setting up Carina-home ventilators and providing user training.
- Providing technical and clinical support as needed for the University of Miami medical team.

Prior to departing for this support mission, our team of volunteers, Frank Caminita RRT, Robert Dutruch RRT, and regional manager Dean Calderone were in close contact with the University of Miami staff to understand and prepare for the field hospital's needs as well as typical patients to be expected.

Over the course of the week-long mission, our volunteers were able to use their clinical expertise and provide for patients requiring simple and complex respiratory care. Regardless of job title, duties outside of traditional respiratory care included

everything from creating equipment rooms, establishing a makeshift RT department, and even occasionally shooting fluoroscopy.

The most critical patient that week was a 13-year-old child who required intubation and mechanical ventilation including 100% FiO_2 and +15 PEEP. Throughout the night, our RRTs worked tirelessly under a physician's direction to stabilize her and ultimately transfer the patient to the USS Comfort for continued care.

Supplies were scarce and in high demand; often times the team had to improvise in order to perform simple tasks such as the administration of Metered-Dose Inhalers or manual resuscitation with high PEEP. Frank and Robert's experience as RRTs were frequently put to the test.

In the middle of all of the destruction, pain, and death, the Haitian people found ways to uplift the human spirit with music and dance. Their amazing will to survive is what drove the volunteer staff to provide 24 hour support to over 300 people in this field hospital.

Left to right, Frank Caminia, RRT, Dean Calderone, Robert Dutruch

Smiths Medical

Tell us about the products you offer with emergency planning/execution applications.
In the chaos of disaster, people look to you for help. Before disaster strikes, look to Smiths Medical for your emergency preparedness supplies. Smiths Medical products are designed for ease of use, with minimal training, and are suitable for contaminated environments. All products are available for individual purchase, as part of pre-designed kits or your own custom-designed kit. Each kit contains the critical care items needed by first responders for scenarios requiring emergency and transport ventilation and resuscitation for adults, children and infants. Smiths Medical—we're ready.

- Pneupac VR1 Ventilator: Ventilator/resuscitator for medical personnel in the hospital, ambulance, fire, and police services, and also for use in industrial and commercial markets.
- paraPAC Ventilator: Designed specifically for use by respiratory therapists, paramedics, and trained emergency personnel, paraPAC enables greater control of breathing parameters. The dual controls allow easy selection of tidal volume and frequency to match your patient's ventilatory requirements. Suitable for ventilation during emergency or controlled transportation of adults, children and infants. MRI compatibility gives maximum flexibility for transport within the hospital.
- ventiPAC Ventilator: Suitable for the ventilation of adults, children and infants, ventiPAC covers the widest range of ventilation parameters. It operates reliably and provides alarms and monitoring similar to those found on more sophisticated ventilators. The clinician is able to alter the inspiratory and expiratory phases of ventilation to allow for critical patient requirements and can also provide essential ventilatory support options such as positive end expiratory pressure (PEEP). Portable, compact and lightweight ventiPAC has the flexibility and endurance to be moved with the patient providing optimum ventilation in both emergency situations and during the transport of the critically ill.
- babyPAC: specially designed to deliver ventilation to small, fragile lungs of patients ranging from neonates through pediatrics up to 20kg with precision and confidence. It has a sophisticated range of ventilation controls including CPAP, variable I:E ratio and variable oxygen concentration. The latter is particularly important in neonatal intensive care and transport since high oxygen concentrations over a prolonged period can be harmful. The babyPAC also incorporates a comprehensive range of alarms.

These ventilators are designed to take the guesswork out of providing respiratory support, and provide you with the feedback you need to make life-saving decisions. Visit the Smiths Medical website at smiths-medical.com to learn more about the Pneupac line of ventilators: VR1, paraPAC, ventiPAC, and babyPAC.

Describe the education you provide for users and staff about your emergency products.
Smiths Medical offers a wide variety of training opportunities for our Pneupac customers. Each Pneupac ventilator has an available training video in DVD format or available online at the Smiths Medical website at www.smiths-medical.com. Also, during our hands-on in-servicing, Smiths Medical sales specialists utilize detailed competency checklists to ensure proficiency in operating our vents. [Pneupac, paraPAC, babyPAC and VR1 are trademarks of the Smiths Medical family of companies. The trademark is registered in the US Patent and Trademark Office and certain other countries. All other names and marks mentioned are trade names, trademarks and service marks of their respective owners.]

Hamilton Medical

Tell us about the products you offer with emergency planning/execution applications.
The HAMILTON-C2 is a compact intensive care ventilator with high independence from gas and electrical supply. An internal turbine reduces oxygen gas consumption in comparison with single source emergency ventilators. It runs on low pressure oxygen (LPO) sources as well. Two hot swappable batteries give you up to six hours independence, which can be prolonged endlessly by battery exchange. An external charger supports battery supply. A very low self discharge allows long term storage (more than one year) of those Li-Ion batteries for a long time. HAMILTON-C2 runs virtually on any electrical AC or DC source—like a car or aircraft battery. Therapy setting is very easy and intuitive as well. Remarkably, the HAMILTON-C2 ventilates pediatrics and adults in invasive and non-invasive modes. Easy startup requires only body height and our self optimizing mode, Adaptive Support Ventilation (ASV), helps inexperienced staff in disaster situations to ventilate even critical patients. To avoid cross infections, our flow sensor is single patient use. A single patient use expiratory valve—to allow disposal of entire patient hose set in case of pandemic diseases—is under development. In Europe, a more compact "brother," the HAMILTON-C1 with similar attributes has been recently launched.

Tell us about instances where your products have been used in emergency scenarios.
HAMILTON-C2 was used during pandemic outbreak of influenza-A virus H1N1 in various countries like such as China and India.

Describe the education you provide for users and staff about your emergency products.
Our qualified staff and distributors provide product in-service, biomedical and optional application training for all Hamilton Medical ventilators. We also provide a 24/7 hotline for both biomedical and clinical support.

What contingency production plans do you have in place for an actual emergency?
All disposables used for the operation of Hamilton products (eg Flow Sensors) are produced both in Europe and in the USA. Therefore, in case of natural or man-made disasters, the supply of these products is ensured at any time.

Design, production and process documentation is stored in electronic systems for Hamilton. These electronic systems include data back up in regular intervals within the facilities (locked, safe internal archive) and in an external bank safe. Service for the Hamilton Medical products is ensured at any time due to many factory trained technicians at various locations all over the world.

Vortran Medical Technology 1, Inc.

Emergency Products: VORTRAN Medical Technology manufactures and markets a patented line of fully automatic disposable respiratory devices for patients in the hospital and other market segments (EMS, post acute and home care). Our latest advances in product development and applications have provided for a non-cycling alarm for the VAR (VORTRAN Automatic Resuscitator).

Emergency Product Applications: VORTRAN is able to help an area stricken by disaster or in an emergency situation by marketing our products to emergency service agencies and critical care providers. The VAR and E-vent Case products provide an inexpensive ventilation solution for any Mass Casualty Incident (MCI), whether man-made or natural disasters. The VAR being single patient and disposable eliminates contamination and equipment sterilization issues. The E-vent case is organized for rapid deployment and provides ventilatory support for seven patients simultaneously with the 7-port manifold. Connecting the manifold to a single oxygen source such as wall connection, "H" tank, or medical grade air compressors provides maximum clinical performance during an initial emergency medical response. Our experiences of dealing with man-made or natural disasters have involved communicating with end-users before and after the disasters. We recognized, through our communications with them, what invaluable resources the VAR and E-vent Case have proved to be.

Emergency Production: Our contingency plans for boosting production of our VAR and E-vent Case has remained the same since the 9/11 terrorist disaster situation. We continually monitor our raw materials, finished goods, stocking levels of our dealers and follow up with pending business. With this daily plan, we have been able to meet the demand and be prepared for future production.

Education: Because of the interest and widespread use of our (VAR), for Disaster Preparedness and ventilator shortage due to Pandemic Influenza, we have recognized the need for education and training. The 3 types of education and training we provide relevant to emergency services or disaster planning, are the interactive CDROM which contains a multi-medias presentation for PC platform, includes instructional video, brochure and user guide in PDF for all VORTRAN products. Second, is an online Educational Module Sponsorship for free CEUs. The programs provide online continuing education at no charge to medical professionals at accessce.com/courses.aspx. Third is VORTRAN'S website. We also maintain an informative intranet website at vortran.com with up-to-date information on the clinical research and outcome, product brochure and user guide in PDF format.

The VORTRAN mechanisms in place relevant to our VAR and E-vent Case product to assist hospitals, clinics and users in the event of the emergency use of our products is through annual training, daily utilization in transports, MRI/CT applications, publications and our network of dealers. The hospitals, clinics and users have created and adopted emergency response protocols providing a comfort level for use.

R&D: The role of critical care providers provides key communication links for defining goals in improved product development. VORTRAN'S processing program includes tracking and recording critical care provider comments, suggestions and complaint information that is continually analyzed for identification of corrective action if necessary and product improvement. For example, critical care providers commented that the VAR gas consumption was more than they realized would be needed to drive the pneumatic device and that an FiO_2 delivery option of 100% or 50% would be beneficial as not all patients require 100% FiO_2. VORTRAN launched the VAR RCM Model providing gas conservation utilizing the 50% FiO_2 delivery option. Other comments included addressing the pediatric patient population for disaster preparedness. VORTRAN launched the VAR-Plus PCM Model for patient body mass of 10 kg and above. This model can be used on both pediatric and adult patients as well as provide for the FiO_2 delivery options.

The testing and evaluation process of the VORTRAN products line for in-house and field use is an integral part of our commitment for continuous process improvement. Clinical trials with established standards and measurements, and the level of quality ensures customer expectations of product performance and features.

The R&D process for our team of mechanical engineers as it relates to disaster preparedness and day-to-day application provides for clinician and user input, patient safety, clinician comfort level and an affordable price tag allows us to assist public health emergencies and natural disasters in addition to meeting the demand for ventilator surge capacity. VORTRAN promotes our VAR and E-vent Case products through various avenues such as tradeshows, on-site visit and training, publication advertising, and our network of specialty dealer representatives.

SPOTLIGHT ON PULMONARY FUNCTION TESTING

ELITE

MEDGRAPHICS' Platinum Elite Series Plethysmograph offers complete spirometry, DLco, lung volumes by nitrogen washout and/or plethysmography, and airway resistance. Incorporating the strengths of the previous award winning Elite Series, the Platinum Elite's enhanced features represent the "Platinum Standard" for ease of operation, accuracy, and patient comfort to meet the most demanding clinician and patient needs. The Platinum Elite offers the largest seating capacity of any available plethysmograph and the new digital components offer maximum accuracy, reliability and serviceability. The Platinum Elite is easy to network and outputs a variety of file formats for EMR connectivity. Contact medgraphics.com, (800) 950-5597.

INTEGRATED

HDpft from nSpire Health provides industry leading spirometry, lung diffusion, lung volumes, and plethysmography in a powerful integrated package. HDpft incorporates the newest and most advanced technologies to deliver the best accuracy, fastest response time, and the lowest overall cost of ownership. Designed with upgradability and serviceability in mind, HDpft is built for the future-upgradable products and software technologies won't become obsolete. iFlow advanced flow sensor technology provides the industry's best flow and volume measuring accuracy and reproducibility at 300% better than the industry standard. Ultra-low resistance improves patient comfort and test compliance. Contact nspirehealth.com.

SPOTLIGHT ON VENTILATION

APPROVED

Draeger Medical Systems, Inc, US headquarters of DrägerMedical AG & Co. KG, an international leader in the fields of medical and safety technology and a worldwide leader in mechanical ventilation, announced that it has received 510(k) clearance from the FDA to market the **Babylog VN500** in the United States. The ventilator is Dräger's most advanced product for neonatal ventilation.The Babylog VN500 ventilator offers the latest technology in mechanical ventilation specifically designed for the special needs of neonates and infants. Its versatility and range of operation is well suited for special care nurseries and pediatric intensive care units. The Babylog VN500 combines important types of ventilation, such as conventional ventilation, nasal CPAP, and oxygen therapy in one medical device. The detachable control panel with 17" touch screen and rotary knob offers extended possibilities of device control and lung function monitoring. "Designed with the clinician in mind, the Babylog VN500 combines the latest in technology coupled with a simplified and easy to use user interface," said Ed Coombs, MA, RRT and Associate Director of Marketing for Respiratory Care Systems at Draeger Medical, Inc. "After over two decades of experience with the Babylog 8000+, our customers have led the development of the next generation in neonatal ventilation." With a company-wide focus to provide exceptional product support services, Dräger customers will continue to receive support from both our field support teams and Intensive Care Online Network (ICON). For more information, please visit our website at draeger.com or contact your local Dräger sales representative at (800) 437-2437… Other Dräger products:

Evita Infinity V500: Dräger continues to meet the challenges of critical care by working with respiratory therapists in the US with the development of the next generation of mechanical ventilation—The Evita Infinity V500. Designed with the clinician in mind, the Evita Infinity V500 is a highly advanced ventilator used for both acute care hospitals and university medical centers. The V500 offers a comprehensive array of invasive and non-invasive ventilation modes for adult, pediatric, and neonatal patients. Pulmonary monitoring features to provide a complete assessment at the bedside is also featured in the user interface. Contact info.usa@draeger.com.

HIGH-FLOW

High-Flow Nasal Oxygen Cannula and Humidification System, Salter Labs: In the past if adequate oxygen saturation levels could not be achieved, a face mask would be employed and delivery flow rates would be increased up to as much as 15 LPM. Oxygen masks are designed to be soft and comfortable, however by design are restrictive and uncomfortable to wear for lengthy periods of time. A nasal cannula is a cost effective way to deliver supplemental oxygen to patients in a hospital environment, at home or traveling, but saturation could only be achieved with flow rates from 1-6 LPM. Now, Salter Labs has a new 1600HF High-Flow Cannula that can deliver up to 15 LPM with a higher FiO_2 than simple masks, plus give the patient the ability to communicate with clinical personnel, family and visitors, take oral and aerosol medications, food and liquid intake without assistance. The new **Salter-Style Adult HF Cannula** features larger bore, safety channel head set tubing with an enhanced reservoir face piece to allow effective delivery of higher oxygen flows. Also available as part of our high-flow delivery system is our new 350 cc **Dry Bubble Humidifier** designed specifically for use with wall source oxygen, new high output oxygen concentrators, or other applications where higher flows are required. Contact salterlabs.com.

IMPROVED OUTCOMES

The Puritan Bennett 840 Ventilator from Covidien is yet another example of our commitment to working with you to improve ventilation outcomes. This flagship product in our line of critical care ventilators is highly responsive and offers superior patient comfort. It delivers sensitive, precise breaths to critically ill patients from neonatal to adults. The ventilator provides seamless electronic data transfer into a patient's medical record. As a result, it supports network communication with all major patient monitoring and hospital information systems. Contact covidien.com.

CONTINUOUS INNOVATION

Hamilton Medical stands for ease of use and improved patient outcomes in mechanical ventilation. Continuous innovations have boosted therapeutic efficiency with evidence. Hamilton Medical introduced the first microprocessor controlled ventilator in 1983. In 1998, Adaptive Support Ventilation was the first automated system ever to balance tidal volume and breathing rate according to the patient's lung physiology. Now various other inventions like the Dynamic Lung and the Vent Status Display help therapist to optimize mechanical ventilation. The most recent development launched in Europe—INTELLiVENT-ASV—is the first complete closed loop ventilation technology for oxygenation and ventilation covering all applications from intubation until extubation with the known simplicity from Hamilton Medical. Contact hamilton-medical.com.

25th ANNIVERSARY
Bunnell Incorporated is celebrating 25 years in the ventilator industry. The Life Pulse High-Frequency Jet ventilator has passed the test of time. Its therapeutic flexibility makes it an indispensable tool in many NICUs and PICUs. Jet pulse technology, passive exhalation, and an adjustable I:E ratio make this high-frequency uniquely effective. The most recent improvement has lowered the sound output from 56 to 41 dB. Constant improvement—Continued success. For more information or to arrange a free trial contact us at (800) 800.4358 or visit us at bunl.com.

WORLDWIDE
MAQUET SERVO ventilators are known worldwide for performance, reliability and adaptability. Neonatal to adult, the SERVO-i can be used for transport, Heliox treatments, and conditionally in the MR environment. The platform offers all conventional modes of ventilation, capnography, and the revolutionary NAVA technology (Neurally Adjusted Ventilatory Assist). NAVA allows the patient and ventilator to work in synchronous harmony. NAVA provides monitoring of diaphragmatic activity during all modes of ventilation allowing the clinician to evaluate dissynchrony and interpret effects of treatment. New for 2010, NAVA can also be used in non-invasive ventilation (NIV NAVA), which provides assist levels capable of matching the patient's neural demands regardless of leakage or user interface. For more information visit maquet.usa.com, criticalcarenews.com, or (888) 627-8383.

PORTABLE AND MORE
Philips Respironics introduces the **Trilogy 202** portable life support ventilator. In sub-acute and transitional care settings, a fully-featured critical care ventilator is seldom cost-effective or convenient. That's why Philips Respironics, an innovator of bi-level technology, developed the Trilogy 202 portable life support ventilator. The Trilogy 202 is both a volume-control and a pressure-control ventilator for invasive and noninvasive ventilation. The versatile breath delivery and setup options help to free clinicians from burdensome equipment exchanges and help to provide greater continuity of care for their patients. Because the Trilogy 202 has the unique ability to compensate for leaks in both pressure and volume control modes, using simpler passive circuits may support significant time and cost. Also from Philips: **Respironics V60** noninvasive ventilator. The V60 uses Auto-Trak auto-adaptive technology to help ensure patient synchrony and therapy acceptance. The six-hour internal battery supports emergency back-up and intra-hospital transport for continuity of care. The V60 is cleared for invasive and noninvasive treatment of pediatric and adult patients. Hospital ventilatory care is further supported with exclusive modes and features. The **Respironics V200** critical care ventilator provides state-of-the-art ventilation modes with synchrony options—Auto-Trak, Flow-Trak, and Baby-Trak—that reduce work of breathing and streamline patient care. The unique speaking mode allows appropriately selected tracheostomy patients to speak without an external valve. The V200 Ventilator has a range of treatment modalities for all patient populations and connects to Philips patient monitors and hospital information systems. The **Respironics AP111** nasal interface for noninvasive ventilation cushions contact only the outside of the nares, and the small frame allows patients to read with unobstructed vision. The **BiPAP AVAPS** is a noninvasive ventilator for home use, and features AVAPS (Average Volume Assured Pressure Support) technology. The AVAPS algorithm guarantees an average tidal volume by automatically adapting pressure support to meet the patient's needs on a breath-by-breath basis by estimating the patient's tidal volume over several breaths and calculating the change in pressure needed to achieve the target tidal volume. Trilogy100 is a highly versatile, lightweight (11 lb) life-support ventilator that has been developed to meet the needs of a wide range of patients in the home and alternative care settings. The **Trilogy100** portable ventilator features Respironics' proven BiPAP technology with leak compensation, volume and pressure control ventilation, and the ability to ventilate with either a mask or a tracheal tube. The display screens can be configured to show either detailed clinician information or simplified patient views. Contact respironics.com.

GO ANYWHERE
When transporting a critically ill patient you need a ventilator that can go anywhere in any situation. Smiths Medical Pneupac ventilators are lightweight, portable and durable gas powered alternatives to large or complex ventilators. Pneupac ventilators are MRI conditional, with an alarm option specifically designed for patient transports and noisy environments. These ventilators are designed to take the guesswork out of providing respiratory support, and provide you with the feedback you need to make life-saving decisions. Visit the Smiths Medical website at smiths-medical.com to learn more about the Pneupac line of ventilators: VR1, paraPAC, ventiPAC, and babyPAC. [The Pneupac and Smiths Medical design marks, Pneupac, paraPAC, babyPAC and VR1 are trademarks of the Smiths Medical family of companies. The trademark is registered in the US Patent and Trademark Office and certain other countries. All other names and marks mentioned are trade names, trademarks and service marks of their respective owners.] Contact smiths-medical.com.

EXECUTIVE PROFILE

SeQual Technologies

Describe your products and their unique features.
SeQual Technologies focuses primarily on the design and development of oxygen delivery devices used in homecare, emergency and industrial applications. We have engineered leading edge products in the field of gas separation which have been recognized as industry standards such as the Advanced Technology Fractionation system, Rotary Valve designs, and auto servo regulation of components to derive consistent delivery of oxygen in the most demanding conditions.

Tell us about the latest advances in the area your product serves.
We have been focused on a couple of key areas over the past few years which should prove to set new benchmarks in the field of long term oxygen care as well as emergency applications. We typically have been investing 8-9% of our revenues into research and development for the past 5 years, which in turn will yield some technologies that will leapfrog today's standards in care. Our work with the military along with leading medical researchers has provided us with new insights that have led to developing oxygen systems that will better match with patients clinical as well as lifestyle needs.

Discuss your R&D process, including clinical user input.
Our processes related to R&D are very disciplined and also

based on over 15 years of direct experience with end users across a spectrum of oxygen applications. We consider our company as one that balances art with science when it comes to oxygen products. Much of what we have accomplished has come about by focusing on being the best in this space and to date no company has surpassed the performance of our Eclipse portable oxygen systems. Clinically we have been co-developing the products with input from patients, key pulmonary physicians and home care providers and by approaching the market with an open mind we can gather data in a non biased manner and in turn via trial and experimentation execute quickly on features and benefits that first and foremost produce better outcomes and are efficacious. Basics always count in medicine so the product must be capable of meeting the demands of the patient and provide positive results or they simply won't comply with their therapy.

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

We pride ourselves in being clinically driven, not marketing driven, with our product designs. Marketing plays a key role in our company but the marketplace determines what we actually design. Many of the new features for instance in the new Eclipse 3 product are crossover modes being used on portable home care ventilators. We have designed the first portable oxygen concentrator that can be upgraded with software, adjustable rise times in pulse mode, a battery conservation mode to extend travel times and increased the bolus size in our pulse mode to 192 ml in order to address the clinical needs on a wider range of patients. Our clinical support staff consists of RTs with extensive experience in hospital and home care settings and we offer CEUs on many aspects of care for LTOT topics.

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

Again speaking to the needs of our patients and clinicians, we have been tasked to produce an equally powerful platform of oxygen systems that produce high levels of oxygen but in an even lighter weight and at lower costs. Reimbursement will continue to play a role in our decisions as well as the providers as to what technologies they adopt for their patients and business models but overall the trends look favorable towards portable oxygen generators. We are always looking at new battery options as well as adsorbents which are more efficient and at telemedicine components that can be coupled with our products to create better formulas for medicine. I think as we have seen in other sectors of the medical world, oxygen devices will become smaller - lighter and be able to provide better therapy for LTOT patients which in turn will increase adherence and reduce overall health care costs related to a disease which is the 4th leading cause on death in the world.

Editorial…continued from page 4

phenomenon). These warnings were similar to warnings for West Nile Virus that ended up producing minimal casualties so were viewed with skepticism. As facilities initiated their coordinated response plan, they quickly came to realize that even the most thorough plan would be severely tested and subject to day-by-day and week-by-week revision.

Unlike a natural disaster which has a finite number of casualties and lasts for a finite time, this pandemic seemed (initially) to have no end and severely tested each organization's ability to respond. The realization hit that there was, in reality, only a limited ability to predict how a pandemic MCI would play out and what resources were required to respond. This sudden realization helped galvanize governments, regulatory bodies and organizations to assess and, when possible, enhance their stockpiles. However, this resource pool remains limited and each healthcare facility must assess their own resources, and review and update their own resources and response plans.

The next MCI incident could be the avian flu (H2N5), volcanic ash fallout, industrial accident, localized flu outbreak, natural disaster or even a terrorist-caused event, but our ability to respond depends on the plan we have developed. Testing each new development/evolution in the MCI response plan is essential and should be carried out with each revision and at least semi-annually. The biggest challenge in developing the MCI response is the ability to triage our resources and maintain services—our staff, on-hand resources and physical space is finite so we have no choice but to work with what we have. The response to the need to triage resources must be developed within an ethical framework, with the support of all levels of administration, must be seen as fair and transparent to all staff, and there's a need to acknowledge that this will take a surprising amount of time. The government (municipal, state and federal) and regulatory bodies (AARC, etc) have resources to offer but the healthcare facility must be willing to tap into these resources. With H1N1, we seem to have dodged the bullet and have been given the opportunity to review our responses and revise our plans in preparation for the next MCI. Now is the time to regroup, re-assess, revise and educate to the updated MCI response plan.

Do You Have Gas?

Dave Swift, RRT

Many healthcare facilities are ill prepared to deal with the sudden loss of medical gases (oxygen, air or vacuum). In the last year there have been cases of the medical oxygen primary lines being cut at the bulk system by a backhoe, a contractor accidentally drilling a hole in the main pipeline, a fire in a pt room damaging the pipeline and a bulk system being undercut by running water and shifting. Medical air systems have been hit by desiccator failure resulting in water infiltration into the pipeline, compressor failure and contamination by high pressure oxygen back feeding through a blender into the air lines. Vacuum systems have failed by compressor failure or cutting of the primary line.

Faced with these potential failures, what is your response plan?
Last year a local hospital had its primary main line accidentally drilled into, resulting in a leak that disabled the whole system. It took 3 days to get the system up, purity testing done and the pts back on the oxygen system. Could you sustain your pts service for 3 days following loss of medical oxygen??

Do you have a plan to use large "K or H" cylinders or 250 lb liquid oxygen "mini" bulk tanks with 50 psi regulators to back feed units that are isolated (following closing of zone valves) and using this to support critical areas. This will buy you time to enact your full response plan. Will you be using an alternate gas source (portable liquid bulk oxygen trailers, large oxygen generators, mid sized liquid bulk systems, large cylinder manifolds)? This will get a large portion of your delivery system back up but may take hours to fully activate. However, if you are relying solely on small cylinders, your ability to sustain your service delivery will be very limited, as these resources are finite. There are mobile, mini emergency oxygen cylinder banks that can provide short term supply using existing delivery pipelines –they consist of 50 "E" sized tanks ganged together in a manifold. This system offers the advantage of being able to be turned off and stored for an extensive period of time.

Loss of medical air represents a critical failure (especially in neonatal care) but using large tanks (K or H size) can effectively maintain your service IF you have sufficient regulators and tanks. Have you tested your ability to respond and are aware of the time constraints to implement it? Oxygen/air blenders use 10 lpm of air (low flow blenders) or 13 lpm (high flow blenders) just sitting standby, once up and running add the gas you are using to this 10 -13lpm consumption to identify the biggest source of air "wastage". Ten blenders consume 100-130 lpm as standby losses. It is essential that during an air or oxygen failure that blenders not needed for essential service delivery be disconnected as part of your emergency gas conservation plan.

Emergency gas conservation plan: It is very common for the bedside care staff to leave flowmeters running when pts are out of the room. The simple act of turning off unused flowmeters contributes to oxygen conservation. Switching pts to MDI instead of SVN (small volume nebulizer) helps reduce gas wastage. Utilizing oxygen saturation monitors to rapidly titrate and wean oxygen also helps reduce gas consumption as well as monitoring the pts for safety during the emergency. Notifying the OR of the need for gas conservation will help make them aware of their role in this emergency and help the anaesthesia staff to make appropriate decisions in their clinical role, during an emergency.

It is very easy to test your ability to respond to a gas failure. Many staff will have additional ideas to help sustain your medical gas delivery and reduce its impact on your service delivery. The practice and review of your response plan carries many benefits beyond the immediate ability to respond to gas failure—it gets staff thinking. This results in the added benefit of helping to encourage staff to review other emergency response plans.

Dave Swift is a member of Respiratory Therapy's Editorial Advisory Board.

The Implications of the New 2009 ISO Spirometer Standard

Bernard R. Garbe

The International Organization for Standardization (ISO) recently published two standards (ISO 26782:2009[1] and ISO 23747:2007[2]) aimed at protecting the integrity of spirometry measurements for the assessment of pulmonary function in humans and supporting the accurate diagnosis and monitoring of lung disease.

These standards cover the essential technical operating characteristics of spirometers and peak flow meters and are endorsed worldwide, via CEN, BSI, DIN, ANSI and all the other national standards bodies.

Practical implications of the new ISO standards

The practical implications of these guidelines for spirometry can be summarized as follows:

- A routine daily accuracy check (sometimes confusingly called "calibration" in the guidelines) is required for all spirometers. A 3-L precision syringe is recommended, 3 pumps of a 1-L precision syringe are no longer recommended.
- The former distinction between monitoring devices (was a lower requirement) and screening spirometers (was a higher requirement) is removed. Now all diagnostic spirometers must conform to the same standards, whether they are used for monitoring, screening or any other purpose.
- MVV – The measurement of direct maximum voluntary ventilation is dropped by the standard, preferring an FEV1 factor (indirect MVV is usually taken as 37.5 x FEV1).
- Linearity – linearity checking is a new item. This is detailed for both volume displacement spirometers and flow sensing spirometers. This is intended as a periodic check, not a daily check. (Linearity assessment should be a part of the routine annual planned preventive maintenance service.)
- Back pressure – Formerly the term for the maximum allowable flow impedance (now called total resistance to airflow) must be <0.15kPa/L/s (1.5 cmH_2O/L/s). The total resistance must now be measured with all tubing, valves, bacterial viral filters, etc that are be inserted between the subject and the spirometer in normal use. Spirometers using moving vanes are most likely to fail this criterion.

The 2009 ISO 26782 Standard also includes new specifications for validation testing of spirometers which replace the ATS/ERS standard waveforms used previously, which were digitized analogue waveforms not suitable for high tech modern lung simulators.

The spirometer test methods are tightened up considerably with the variable start and ending in the protocol to prevent programming of the test waveforms in certain devices in order to be able to pass testing. The effect of this will be to make spirometers give much more repeatable readings. Spirometers which cannot measure low flows will fail the test as will devices which have a wide scatter in their readings, typical in ultrasonic measuring technologies.

Important new test protocols are also established for linearity and flow impedance testing. The latter is particularly important because a spirometer with excessive flow impedance will cause a reduced FEV1 and FVC value. The former ATS test protocol was very weak in this area allowing the marketing of many poorly designed devices, particularly turbine type devices, which had a real problem with flow impedance, or back pressure as it used to be called.

ATS/ERS

In 2005 the American Thoracic Society (ATS) and the European Respiratory Society (ERS) issued a series of joint Official Statements on standardization of lung function testing. These statements included: • ATS/ERS Standardization of Lung Function Testing: General Considerations for Lung Function Testing[3] • ATS/ERS Standardization of Lung Function Testing: Standardization of Spirometry [4] • ATS/ERS Standardization of Lung Function Testing: Interpretative Strategies for lung function tests.[5]

The 1994 BTS / ARTP spirometry guidelines[6] are pretty much in line with more up-to-date guidelines for spirometers.

Device testing

Rigorous device testing plays a vital role ensuring that spirometers deliver accurate measurements. Medical device manufacturers must subject sample spirometers and software to a whole series of testing protocols, including the accuracy check profiles in table 1.

Conducting good spirometry

Spirometry is a simple but highly sensitive test and a number of factors can affect the validity of spirometric results. These factors include:

- mastery of correct technique by both the medical professional and subject

B.R. Garbe is Managing Director, Vitalograph, vitalograph.co.uk.

Profile	Exp Vol	TC	Start	Ending	FEV_1	FEV_6	FVC
C1	7.0	1.00	Slow	Abrupt	4.894	7.120	7.120
C2	5.0	1.00	Fast	Smooth	3.272	5.168	5.179
C3	5.0	1.50	Fast	Smooth	2.489	5.027	5.119
C4	5.0	1.00	Bad	Smooth	4.090	6.636	6.652
C5	7.0	0.75	Slow	Smooth	5.889	8.025	8.027
C6	0.5	0.50	Slow	Smooth	0.526	0.609	0.609
C7	3.0	2.00	Slow	Abrupt	1.242	1.769	1.769
C8	0.5	1.50	Slow	Smooth	0.260	0.527	0.535
C9	4.0	1.50	Fast	Smooth	1.991	4.021	4.095
C10	6.0	0.75	Fast	Prolonged	4.627	6.311	6.438
C11	4.0	0.50	Bad	Smooth	5.588	6.639	6.639
C12	3.0	1.00	Slow	Prolonged	2.097	3.333	3.480
C13	4.0	2.50	Slow	Abrupt	1.374	2.406	2.406
Exp Vol is the volume for the single exponential.							
TC is the time constant used for the single exponential.							
Start is used for defined test profile: fast, slow or bad start.							
Ending is used for defined test profile: abrupt, smooth or prolonged.							

Table 1

- use of correctly functioning spirometers
- use of appropriate reference values
- Quality Assurance (QA) reviews.

Four elements contribute to accurate spirometer performance:

- Conformity to current safety and performance standards—the ISO and ATS/ERS recommend minimum performance-based standards for spirometers of all types.
- Correct maintenance. Spirometers must have annual calibration, certified and traceable to international standards. Also an electrical safety check is mandatory under UK law for mains powered devices. These elements plus other aspects such as hygiene procedures, linearity checking, performance check and reliability procedures will be a part of the routine annual maintenance service of the spirometer.
- User competence. Users must be able to recognise errors that occur during testing, even when the spirometer software does not pick up the error, and reject invalid tests.
- Daily accuracy checking. This verifies that the spirometer is measuring accurate and ensures prompt identification of defective devices.

Spirometer accuracy checks

The 2009 ISO 26782 Standard and the 2005 ATS/ERS Spirometry Statement state that the accuracy of both volume- and flow-type spirometers should be checked at least daily when a spirometer is in use. The acceptable spirometer response to a standard 3-L calibration syringe injection has been expanded to ±3.5% of the injected volume, ie 2.90-3.10 L.

The 3-L syringe also needs to have calibration certified annually and in addition a service is recommended every 3 years in normal use.

Calibration records should be saved indefinitely and the data transferred to a control chart. Also a log should be kept of technical problems found and solved, as well as all changes in standards, protocol, model and serial numbers of all equipment.

Peak Flow Measurements

The new standards for peak flow meters mean that you may need to replace old devices. This may be necessary for three important reasons:

1. The scale may be different on new units. The new ISO standard scale must now be used for all peak flow meters (not EU Scale). The standard now in force in the UK is ISO 23747:2007, which superseded the almost identical EN 13826:2003.
2. Low range peak flow meters are to be disposed of immediately. They are now considered dangerous since their 'stretched' scale can erroneously give the impression of a 'good' reading. Low range meters do not conform to ISO 23747:2007.
3. The design life of simple peak flow meters is only three years. Any devices older than this, whether manual or electronic, should be disposed of, unless annual certification is performed.

The ISO 23747:2007 standard applies equally to peak flow meters and spirometers, any device that measures and gives a reading of peak flow. This applies whether the units are L/min or L/s—either is allowed in the standard. This ensures that spirometers and peak flow meters will give the same 'peak flow' reading, except that spirometers are, of course, more accurate.

References

1 ISO 26782:2009 Anaesthetic and respiratory equipment—Spirometers intended for the measurement of time forced expired volumes in humans. http://www.iso.org/iso/catalogue_detail.htm?csnumber=43761

2 ISO 23747:2007 Anaesthetic and respiratory equipment—Peak expiratory flow meters for the assessment of pulmonary function in spontaneously breathing humans. http://www.iso.org/iso/catalogue_detail.htm?csnumber=41834

3 American Thoracic Society & European Respiratory Society: General Considerations for Lung Function Testing. Eur Respir J: 26 (1): 153-161, 2005. http://www.thoracic.org/sections/publications/statements/pages/pfet/pft1.html

4 American Thoracic Society—European Respiratory Society: Standardisation of spirometry. Eur Respir J: August 1, 2005; 26 (2): 319-338, 2005. http://www.thoracic.org/sections/publications/statements/pages/pfet/pft2.html

5 American Thoracic Society—European Respiratory Society: Interpretative Strategies for Lung Function Tests. Eur Respir J 2005; 26:948-968. http://www.thoracic.org/sections/publications/statements/pages/pfet/pft5.html

6 Recommendations of the British Thoracic Society and the Association of Respiratory Technicians and Physiologists, Guidelines for the Measurement of Respiratory Function, Respiratory Medicine 1994; 38, 165-194.

NIPPV in the Acute Care Setting

Melissa Turner, BA, RRT

For the past 20-plus years, Non-Invasive Positive Pressure Ventilation (NIPPV) has been used to avoid the risks that are associated with intubation. Since that time, it has transitioned to being standard first line of therapy in many situations. This review of Aboussouan and Ricaurte's[1] article in the Cleveland Clinic Journal of Medicine includes when to use NIPPV as first line therapy versus when clinicians should take a more cautious approach to its use. There are certainly several advantages to using NIPPV versus an invasive approach. NIPPV preserves the normal physiologic functions such as coughing, swallowing, eating, and speech, avoids the risk of tracheal and laryngeal injuries, and avoids the risk of respiratory tract infections. NIPPV has shown the best level of efficacy for conditions such as acute hypercarbia or hypoxemia in COPD patients, cardiogenic pulmonary edema, and immunocompromised patients.

While NIPPV can be advantageous for a myriad of conditions, it should not be applied indiscriminately for less established indications which include the following: • post extubation respiratory failure; • acute lung injury/ARDS; • severe hypoxemia or acedemia; • after failure to improve dyspnea or gas exchange.

Using NIPPV indiscriminately under the above conditions could delay intubation as well as increase delayed risks, including death. NIPPV is the first choice for ventilatory support in select patients which includes COPD exacerbation and cardiogenic pulmonary edema. NIPPV is not yet accepted universally and as Aboussouan and Ricaurte[1] report, is only used in 33% of COPD or CHF patients for whom NIPPV was indicated. Possible reasons are because doctors are not educated about NIPPV, respiratory therapists are not trained in its use, or equipment is lacking.

The use of NIPPV must be weighed carefully with particular attention to the indications and contraindications. Three main reasons to use NIPPV are to avoid complications of invasive ventilation, improve outcomes (by decreasing morbidity/mortality and hospital length of stay), and to decrease the cost of care. Indications for using NIPPV are as follows: • subjective dyspnea with a respiratory rate >25; • use of accessory muscles; • $PaCO_2$ >45mmHg with a pH <or=7.35; • PaO_2/FiO_2 <200mmHg; • Conscious and cooperative patient; • proper mask fit.

The contraindications to NIPPV include: • severe hypoxemia (PaO_2/FiO_2 <75mmHg); • severe acidemia; • multi-organ failure or slowly reversible disease; • upper airway obstruction; • anatomic abnormalities that interfere with gas delivery (ie, facial burns, trauma); • respiratory arrest/apnea; • cardiac arrest and hemodynamic or cardiac instability; • unconscious/uncooperative patient; • encephalopathy with the inability to protect the airway; • increased risk of aspiration (copious secretions, vomiting); • severe GI bleed; • recent airway or GI surgery; • inability to fit mask.

When making the decision to use NIPPV, always consider the specific disease and the expertise and skill of the staff. NIPPV is more likely to fail in patients with more severe disease and a lower pH.

NIPPV has now become the standard of care in patients with acute COPD exacerbation. The advantages of NIPPV over usual care include lower risk of treatment failure (defined as intubation, inability to tolerate the treatment, or even death), lower risk of intubation, lower mortality rate, lower risk of complications and shorter hospital stays. These benefits are realized for COPD patients because NIPPV is able to decrease work of breathing (WOB) and eliminate diaphragmatic work by unloading the respiratory muscles, lessening diaphragmatic pressure swings, decreasing respiratory rate and counteracting the threshold loading effects of auto-PEEP. Also, in this patient population, NIPPV helps to prevent post extubation failure and facilitates weaning from invasive ventilation. It is important to note that NIPPV should be tried early in the course of respiratory failure before severe acidosis develops. NIPPV has a failure rate greater than 50% for a pH less than 7.25, and shows that patients with mild exacerbation (pH >7.35) have no advantage over standard therapy.

NIPPV is also a first time line treatment for cardiogenic pulmonary edema. In a study named "Three Interventions in Cardiogenic Pulmonary Oedema (3CPO)",[3] NIPPV was applied versus standard oxygen therapy. NIPPV showed to be significantly better than standard oxygen therapy in the first hour of treatment in terms of dyspnea, heart rate, acidosis and hypercapnia. There was actually no significant difference between the group at day 7 or day 30 as far as mortality rates, rates of intubation, rates of admission to critical care units, or in rates of mean hospital length of stay. The mechanisms that make NIPPV beneficial for this group of patients is its positive hemodynamic effects, its PEEP effect on flooded alveoli, and its positive intrathoracic pressure which decreases preload and

Melissa Turner is Clinical Support Specialist, Hamilton Medical, Inc. This article is from Hamilton's newsletter.

afterload and therefore improves the cardiac index and WOB. Despite not showing any improvement in mortality or intubation rates, NIPPV does rapidly improve dyspnea, respiratory, and metabolic abnormalities. The available evidence also shows that NIPPV does not have any clear benefit as compared to CPAP therapy in this population.

For immunocompromised patients with acute respiratory failure, NIPPV has proved to be very helpful. Within this group of patients, the underlying pathophysiology of respiratory failure may not be reversible. The application of NIPPV should follow some clearly defined indications which one trial stated as follows: • immune suppression; • persistent pulmonary infiltrates; • fever (>38.3C; 100.9F); • respiratory rate >30; • severe dyspnea at rest; • early hypoxemic respiratory failure (defined as PaO_2/FiO_2 <200mmHg while on oxygen).

In this patient population, a study found that using NIPPV compared with conventional treatment, fewer patients were intubated (40% vs 77%), fewer suffered serious complications (50% vs 81%), fewer died in the hospital (50% vs 81%), and fewer died in ICU (38% vs 69%). In another randomized trial with 40 patients who had acute respiratory failure after solid organ transplant, the NIPPV group showed greater improvement in PaO_2/FiO_2 after 1 hour (70% vs 25%), or sustained improvement in PaO_2/FiO_2 (60% vs 25%), fewer needed intubation (20% vs 70%), fewer died of complications (20% vs 50%), shorter length of stay in ICU (mean 5.5 days vs 9 days), and fewer died in ICU (20% vs 50%).

Post extubation respiratory failure does not appear to respond favorably to NIPPV except in specific cases, namely COPD and hypercapnia. Two randomized controlled trials were conducted and compared NIPPV to standard care in patients who met extubation readiness criteria but developed respiratory failure post extubation. The NIPPV group showed a longer time to re-intubate, no difference in re-intubation rate and no length of stay difference in ICU. One study even showed a higher death rate in ICU for NIPPV (25% vs 14%) which could be due to delaying necessary re-intubation.

NIPPV can help to prevent respiratory failure post extubation. When NIPPV was used and initiated immediately on successfully weaned patients who were at risk for re-intubation, fewer intubations had to be made (8 v 24). Also, 10% fewer died in the ICU. Risk factors that were used for post-extubation failure risk were $PaCO_2$ greater than 45mmHg, greater than 1 consecutive weaning failure, CHF, or other co-morbidity, weak cough, or stridor. Another study showed a survival benefit of NIPPV post extubation limited to COPD and hypercapnic patients.

Using NIPPV to facilitate weaning has also shown positive results. In several studies, patients who failed spontaneous breathing trials (SBT) were randomized to undergo accelerated weaning, extubation, NIPPV, or conventional weaning with pressure support. Most patients developed hypercapnia during weaning and had COPD. NIPPV was shown to reduce the rate of death and VAP, as well as decrease the total duration of mechanical ventilation by a mean 7.33 days. These benefits are most significant with COPD patients.

NIPPV also shows a promise of positive outcomes for patients with asthma and status asthmaticus. One study showed NIPPV decreases respiratory rate and improves pH and $PaCO_2$ over 12 to 24 hours in asthma with acute respiratory failure. Another randomized trial with status asthmaticus was terminated early due to the physician's treatment bias which favored NIPPV. The preliminary results showed a 7.3% higher intubation rate in the control group. The trend for the NIPPV group was toward lower intubation rates, lower hospital length of stays and decreased hospital charges. The Conchrane Review says NIPPV use in status asthmaticus is controversial and can be used in patients with mild to moderate respiratory distress (defined as respiratory rate greater than 25, use of accessory muscles, difficulty speaking, pH of 7.25 to 7.35, and a $PaCO_2$ of 45 to 55mmHg).[4] It also states that patients with impending respiratory failure or inability to protect the airway should not use NIPPV.

To date, the use of NIPPV in acute lung injury and ARDS has been disappointing. NIPPV is unlikely to have any benefit for this patient population. An earlier study used CPAP, which showed some early physiologic improvement but no decrease in the need for intubation. There were also no improvements in outcomes and also a high rate of adverse events reported. Subsequent studies have shown that shock, metabolic acidosis and severe hypoxemia as predictors of NIPPV failure.

Besides the aforementioned uses of NIPPV, there are also a few other miscellaneous applications that can be beneficial. Percutaneous endoscopic gastrostomy (PEG) tube insertion, particularly for neuromuscular patients at risk of aspiration, poor oral intake and respiratory failure during procedures are starting to be done while using NIPPV. Experience with Duchenne's Muscular Dystrophy and ALS patients has shown NIPPV successful during this procedure. Some recent practice parameters show ALS patients with dysphagia may be exposed to decreased risk if PEG procedure is performed when the FVC is greater than 50% of predicted.

For patients undergoing bronchoscopy, randomized trials of CPAP showed that high risk hypoxemic patients fared better than those receiving oxygen alone. The patients on CPAP had better oxygenation during and after the procedure as well as a lower risk of post procedure respiratory failure. There was also an improvement in hemodynamics with a lower mean heart rate and stable mean arterial pressure.

NIPPV is also being used as palliative care for do not intubate (DNI) patients. NIPPV is most effective in reversing acute respiratory failure and improving mortality in COPD and cardiogenic pulmonary edema patients. There is some controversy surrounding the use of NIPPV in DNI patients, stating it could be a potentially uncomfortable life support technique. The Society of Critical Care Medicine has addressed this and recommends that NIPPV be applied only after discussion of the goals and care with patients and their families.[2]

Lastly, NIPPV is also used for pre-oxygenation before intubation. A prospective randomized study of oxygenation before rapid sequence intubation via either a non-rebreather bag-valve-mask or NIPPV found that the NIPPV group had higher oxygen saturations before, during, and after intubation.

In the last 20 years, the application of NIPPV has broadened and become more fine-tuned. It is certainly becoming a very important player in acute care today. It is important that doctors become aware of NIPPV and that respiratory therapists become well versed in its use. The use of NIPPV has shown a multitude

of benefits in many areas of acute care if it is applied properly.

Editorial note from Paul Garbarini MS, RRT, Hamilton Medical, Inc: I'd like to provide some pointers and clarifications on NIPPV for those not yet too experienced in its application. In the acute care setting, NIPPV (also referred to as NIV / non-invasive ventilation) is used as an alternative to invasive ventilation. As such, pressures significantly above the typical BIPAP settings used for treatment of obstructive sleep apnea are needed. It is not uncommon for inexperienced clinicians to set patients on 10 cm over 5 cm of pressure when starting NIV. If we note that the BIPAP devices typically used for NIV and the NIV modes on conventional ventilators are using pressure support as the mode of ventilation, a setting of 10/5 cm on a BIPAP device means that the peak pressure will be 10 cm and the CPAP pressure will be 5 cm, so the driving pressure or pressure support level is only 5 cm. Put in the context of what settings/ pressures we would start an intubated patient on, clearly 5 cm of pressure support will not provide adequate support during NIV for acute respiratory failure. It may seem obvious, but failure to titrate pressure adequately may result in NIV failure. As supported by studies, it is critical to assess patient response to NIV within 30-60 minutes and assess need to titrate therapy or consider intubation.

These same settings on an ICU ventilator would result in a pressure support of 10 cm, as unlike BIPAP/blower devices, pressure support settings in ICU ventilators are referenced as being above the PEEP/CPAP setting. As some facilities have both type devices, a policy to transcribe NIV pressure levels as pressure support level can avoid errors and confusion. Pressures up to ~25 cm can be tolerated by some patients and often a pressure of 10-15 cm is adequate even for patients with significant WOB.

Another common problem with those learning NIV is failure to size the mask properly. Often too large a mask is selected, the rationale being "I'm going to cover everything over" whereas most often the smallest size mask that sits not much higher than the bridge of the nose and just below the lower lip works best. Note, this is in reference to full face masks which are the interface of choice in acute applications of NIV. The transition to a nasal mask can be attempted in cooperative patients who can limit mouth breathing and/or who do not require significant pressure support levels.

One final comment is the importance of selecting a vented vs non-vented mask. Commonly used BIPAP devices that utilize a blower to generate pressures have a single limb circuit with no expiratory limb. Rebreathing of exhaled CO_2 is minimized by placement of vents or ports in the mask and/or end of inspiratory limb. Typically a minimum CPAP pressure of 4cm is used to ensure flushing of CO_2 during the expiratory phase. On the other hand, the NIPPV option on standard ICU ventilators almost universally requires the use of non-vented/non-ported masks to prevent autocycling of both the inspiratory and expiratory phases. Manufacturers such as Respironics and ResMed provide non-vent masks for ICU ventilator use that are color coded so as to differentiate them from vented masks.

References

1 Aboussouan SA, Ricaurte B. Noninvasive positive pressure ventilation: Increasing use in acute care. Cleveland Clinic Journal of Medicine 2010; 77(5): 307-316.

2 Curtis JR, Cook DJ, Sinuff T, et al ; Society of Critical Care Medicine Palliative Noninvasive Positive Ventilation Task Force. Noninvasive positive pressure ventilation in critical and palliative care settings: understanding the goals of therapy. Crit Care Med 2007; 35: 932-939.

3 Gray A, Goodacre S, Newby DE, Masson M, Sampson F, Nicholl J; 3CPO Trialists. Noninvasive ventilation in acute cardiogenic pulmonary edema. N Engl J Med 2008; 359: 142-151.

4 Ram FS, Wellington S, Rowe BH, Wedzicha JA. Non-invasive positive pressure ventilation for treatment of respiratory failure due to severe acute exacerbations of asthma. Cochrane Database Syst Rev 2005; CD004360.

College Station Finds Solution for High-Volume BGE Testing at POC

Networked control, minimal maintenance facilitate remote testing

Laszlo Sandor

Facility	College Station Medical Center, College Station, Texas
Profile	Full-service facility; official provider for Texas A&M athletics
Number of beds	150
BGE testing sites	ICU, NICU, ED, OR
Challenge	Expand POC blood gas testing; retain centralized control
Solution	cobas b 221, DataCare POC and cobas bge link software

Decentralized blood gas testing—running tests at multiple point-of-care sites vs the lab—became standard procedure several years ago at College Station Medical Center, located about 100 miles north of Houston. But as testing volumes grew, the respiratory care director wanted to add analyzers at various remote sites and yet be able to manage them all from a single location.

In conjunction with Roche Diagnostics, College Station implemented a comprehensive solution that provided centralized control and helped simplify regulatory compliance in the process.

Looking for remote control

Known locally as The Med, College Station Medical Center recently received the Texas Health Care Quality Award of Excellence, which recognizes hospitals that have improved initial baseline performance on specific national quality measures aimed at improving outcomes. Respiratory care is one of the areas in which it excels.

Michael Nibert, RRT, BSRT, who serves as the Respiratory Care Director, says he has always taken a decentralized approach to blood gas testing because it supports the often critical, time-sensitive nature of respiratory care. "Our decentralized structure for blood gas testing enables us to provide fast, reliable and accurate results that impact physicians' treatment decisions in critical situations where a second saved may mean a life saved," he says.

Laszlo Sandor is Associate Editor of Respiratory Therapy. For more information on the cobas b 221 system, contact your Roche Diagnostics representative, call 1-800-428-5076 or visit www.poc.roche.com.

A few years ago, College Station had two point-of-care (POC) blood gas analyzers, one in pulmonary and one in the OR. When the facility expanded recently, Nibert wanted to add analyzers to the neonatal ICU and the emergency department. But he was already having problems with instrument downtime, and the data management system required a lot of manual tasks and did not meet all his regulatory compliance needs. What he needed was a solution that could handle high-volume testing at the point of care, have less system downtime, and simplify data management. What he found was a solution that did all that and helped make compliance easier at the same time.

Delivering critical information with minimal downtime

College Station built its POC solution around the cobas b 221 blood gas system from Roche, a compact benchtop analyzer that provides full blood gas panel results in about two minutes and has a throughput range of 27-31 samples/hour. With "load-and-go" smart reagents, onboard QC and zero-maintenance electrodes, the system only requires brief instrument downtime about once every 42 days.

In addition, a recently updated firmware package (v7.02) offers Nibert's team a continuous self-monitoring feature that helps simplify regular maintenance in several ways: it tracks the status of electrodes, sensors, and consumables; provides real-time onboard maintenance logs; lists all scheduled maintenance activities to be performed; and provides advance notice of needed maintenance.

The cobas b 221 system offered Nibert and his 28-member respiratory care team benefits on the clinical side as well. It is the first blood gas system with FDA 510(k) clearance for testing pleural fluid pH, giving clinicians an excellent alternative to pH meters and pH litmus paper.[1] "Having this clearance as a moderate-complexity CLIA standard in particular has provided an additional diagnostic tool for our surgeons and critical care and pulmonary intensivists," Nibert says. His team is also reporting bilirubin in the neonatal areas (using the system's COOX module), as well as lactate, BUN, glucose, and electrolytes to complement basic panels of blood gas testing and co-oximetry in all age groups.

Managing instruments, data and compliance

One of Nibert's concerns about expanding the number of remote analyzers was keeping control and maintenance simple. Part of the solution was Roche's DataCare POC, a configurable software

Continued on page 38…

Saccharine Transit Time Test is Dependent on the Day Period in Nonsmokers

Naomi K. Nakagawa, Danielle M. Goto, Giuliana M. Torres, Janaina P. Oliveira, Adriana S. Santos, Sandra R. Wilson, Paulo H. N. Saldiva, Geraldo Lorenzi-Filho.

Abstract

Introduction: Mucociliary clearance is a basic mechanism to remove noxious agents from the respiratory tract. Saccharine test (STT) is a reproducible test that characterizes mucociliary clearance functions in normal and several pathological conditions and evaluates clinical interventions. We aimed to determine the STT-values in healthy young nonsmokers and smokers during the three periods of the day. **Material and Methods:** 195 subjects (18-45 years, 90 males, 69 smokers) were randomly assigned to have two STT-measurements carried out 2-4 hours apart, in one of the three periods of the day: (a) Morning: 6:01 am to 12 noon, (b) Afternoon: 12:01 noon to 6 pm and (c) Evening: 6:01 pm to 12 midnight. The individual clinical parameters were recorded. **Results:** Smokers and nonsmokers (27±8 years, 44% male) presented systolic blood pressure (121±14 and 115±10 mmHg, respectively, p=0.009), diastolic pressure (76±12 and 74±7 mmHg, respectively, p=0.03), respiratory rate (18±4 and 17±3 bpm, respectively, p=0.303), body temperature (36.4±0.4°C and 36.4±0.3°C, respectively, p=0.896) and heart rate (76±10 and 76±8 bpm, respectively, p=0.993). The two STT-measurements were similar in both groups. Smokers presented prolonged STT (16.6±6.3 minutes) compared with nonsmokers (12.1±5.1 minutes, p<0.001). Nonsmokers presented prolonged STT in the Morning compared with Afternoon and Evening (14.9±5.0, 11.3±4.6 and 11.2±5.5 minutes, respectively, p=0.012). **Conclusion:** STT is a reproducible test in smokers and nonsmokers in the three periods of the day. Smokers have prolonged STT during all daytime. Nonsmokers have normal STT-values in the Afternoon and Evening, except in the Morning when STT is prolonged. Therefore, STT to evaluate clinical interventions should be performed within the same period of the day.

Authors Nakagawa, Goto, Torres, Oliveira and Santos are with the Department of Physiotherapy, Communication Science and Disorders, Occupational Therapy, University of Sao Paulo Medical School; Nakagawa, Goto, Oliveira and Saldiva are with the Department of Pathology, Pulmonary Defense Group, University of Sao Paulo Medical School; Wilson is with the Palo Alto Medical Foundation Research Institute, Palo Alto, CA, USA; Lorenzi-Filho is with the Pulmonary Division, Heart Institute, University of Sao Paulo Medical School, Sao Paulo, Brazil. [Correspondence: Naomi Kondo Nakagawa, PhD, University of Sao Paulo Medical School—LIM 34 Av. Dr. Arnaldo, 455, Room 1150, Cerqueira Cesar, Sao Paulo, Brazil, CEP 01246-903 Phone: 55 11 3061-8529 Fax: 55 11 3068-0072, E-mail: naomi.kondo@usp.br.] The authors would like to thank Dr Julia Fukushima for helping us with the statistics, and the MECOR Course for the opportunity to discuss the present project.

Introduction

The respiratory epithelium is essential for defense of the airways against inhaled particles and microorganisms. Mucociliary clearance plays a pivotal role in this host defense from the nose and upper airways to the lower respiratory tract. The nose is the first barrier of this defense system, and is a safe and versatile locale to investigate the relation between cellular mechanisms and the mucosal functions and responses to local and systemic challenges. Several studies have used the nasal mucosa as a useful tool to assess inflammatory responses and events in the lower respiratory tract (Rutland and Cole, 1981; Stanley et al, 1986; Persson et al, 1992; Nakagawa et al, 2005). The nose has similar epithelium histology to the remaining airway (Kim and Rubin, 2008). Functional and structural alterations in the nose are common in many respiratory diseases, and impaired nasal mucociliary clearance has been related to a greater proneness to pulmonary diseases (Andersen et al, 1974; Puchelle et al, 1981; Konrad et al, 1994; Hogg et al, 2004; Murin and Bilelo, 2005; Nakagawa et al, 2005; Redding et al, 2008).

To study in vivo mucociliary clearance in humans is technically difficult. Several methods have been used to evaluate the efficiency of nasal mucociliary clearance. Studies based on direct observation of dyes or particles measured mucociliary clearance by estimation of the time between the moment of dye deposition on nasal mucosa and the moment of dyed mucus/particles appearance at the nasopharynx (Andersen et al, 1974). Saccharine transit time test (STT) is a simple, safe, non-invasive and low cost alternative screening test that can be used to determine the overall in vivo mucociliary clearance in subjects with normal and altered clinical conditions. STT was first described by Andersen et al (1974) and modified by Rutland and Cole (1974). Briefly, 5 mg particle of saccharine is placed 2 cm inside the non-obstructed nostril, on the inferior turbinate under visual control while the subject is quiet and seated. A timer is displayed to measure the transit time. STT is the elapsed time from the placement of the particle into the nasal mucosa until the subject reports the sweet taste of saccharine. Subjects are allowed to swallow freely, and oriented to maintain normal ventilation, avoiding deep breaths, talking, sniffing, sneezing, eating or coughing. The normal mean value reported for this assay is 11 minutes in healthy nonsmokers adults (Puchelle et al, 1981; Rutland and Cole, 1981; Deitmer, 1986; Stanley et al, 1986; Doyle and Van Cauwenberge, 1987; Salah et al, 1988; Yue, 1989; Moriarty et al, 1991; Middleton et al, 1993; Sachdeva et al, 1993; Mahakit and Pumhirun, 1995; Ho et al, 2001; Narozny et al, 2002; Çinar and Beder, 2004; Nakagawa et al, 2005; Rosen et al, 2005; Yadav et al, 2005; Oliveira et al, 2006; Karaman and Tek, 2009).

Table 1. Clinical parameters of 195 healthy young subjects at three periods of the day: Morning, Afternoon and Evening (*, p=0.002 vs Afternoon)

	Morning n=45	Afternoon n=115	Evening n=35
Systolic blood pressure (mmHg)	116.8 ±12.9	118.1 ±11.4	115.4 ±11.1
Diastolic blood pressure (mmHg)	73.2 ±12.8	75.1 ±8.3	74.3 ±7.2
Heart rate (bpm)	75 ±9	78 ±9	71 ±9*
Respiratory rate (rpm)	18 ±3	18 ±3	17 ±3
Body temperature (°C)	36.5 ±0.4	36.4 ±0.4	36.5 ±0.3

Table 2. STT-values of young nonsmokers and smokers during the three periods of the day (*, p=0.003 vs Afternoon; †, p=0.015 vs Evening)

	Nonsmokers	Smokers	P-value
Morning	13.4 ±4.6*†	16.6 ±4.9	0.187
Afternoon	11.6 ±5.3	15.9 ±6.3	<0.001
Evening	11.4 ±7.5	19.9 ±14.1	0.012

In a series of studies, we have used STT to characterize *in vivo* mucociliary dysfunctions in several pathological conditions and to evaluate the effectiveness of clinical interventions or medications in humans. Mucociliary clearance apparatus appears to be a dynamic structure, which readily and reversibly changes yield to the respiratory defense system. However, the circadian cycle of the nose may affect STT. The aim of this study was to evaluate the STT reproducibility during three periods of the day: Morning (6:01 to 12 AM), Afternoon (12:01 AM to 6 PM) and Evening (6:01 PM to 12 PM) and to compare STT-values of these three periods in young nonsmokers and smokers subjects.

Material and Methods

A hundred and ninety five young healthy subjects (aged 18-45 years) were recruited by telephone at University of Sao Paulo City from the records of students registered in 2007 and 2008. They were assigned to have two STT-measurements (two to four hours apart) in one of the three periods of the day: Morning, Afternoon, and Evening. Individual clinical parameters such as systolic blood pressure (SBP), dyastolic blood pressure (DBP) respiratory rate (RR), heart rate (HR), and body temperature (T) were recorded. The STT-measurements were performed in a quiet room, with temperature of 23°C and relative humidity of 63%.

Results

One hundred ninety five young volunteers (18-45 years, 86 male) were included in this study. Sixty nine volunteers (33%) were currently smokers (35 male) and 126 have never smoked (67%, 51 male).

Among all the subjects, there were no significant differences in clinical parameters among Morning, Afternoon and Evening periods (Table 1). However, heart rate was lower in the Evening group compared with the Afternoon group (p=0.002). Smokers presented higher systolic (120.7 ±13.7 mmHg, p=0.009) and diastolic blood pressure (76.0 ±12.4 mmHg, p=0.03) compared with nonsmokers (115.4 ±10.1 and 73.7 ±7.1 mmHg, respectively).

All the 195 subjects performed STT in two time points, and the results were similar (p=0.948). The STT-values did not correlate with gender (p=0.769), nor with the type of inhalation/exhalation (nasal vs oral, p=0.210).

STT-values of young smokers were different from nonsmokers (16.5 ±7.0 vs 11.9 ±5.7 minutes, respectively, p<0.001). The prolongation of STT in smokers was observed in all three periods of the day, with no differences between them (Table 2). On the other hand, nonsmokers presented prolonged STT-values in the Morning compared with Afternoon and Evening periods.

Discussion

STT is a reproducible test independently of the period of the day. Young smokers have prolonged STT-values compared with nonsmokers, during all daytime. On the other hand, nonsmokers have prolonged STT in the morning compared with afternoon and evening periods.

The efficiency of mucociliary clearance depends upon the balance of three components including volume and composition of the airway surface liquid, ciliary beating frequency and interaction between mucus and cilia (Puchelle et al, 1987; Matsui et al, 1998; Boucher, 2004; Kreindler et al, 2005; Nakagawa et al. 2005; Randell and Boucher, 2006; Rubin, 2007; Goto et al,2010). A mismatch in one or more of these components leads to mucociliary dysfunction, which is associated with inflammation and increased susceptibility of respiratory infection (Andersen et al, 1974; Puchelle et al, 1981; Konrad et al, 1994; Ho et al, 2001; Hogg et al, 2004; Murin and Bilelo, 2005; Redding et al, 2008). The use of STT to indicate the overall mucociliary clearance in the nose has been demonstrated in healthy subjects (showed in Table 3), as well as in asthmatics (Yadav et al, 2005), diabetics (Yue, 1989; Sadheva et al, 1993; Selimoglu et al, 1999), HIV positive patients (Rosen et al, 2005), COPD patients (Stanley et al, 1986) and also critically ill patients (Nakagawa et al, 2005).

The reproducibility of STT has been reported: (a) in children comparing two measurements in two consecutive days at the same nostril (Corbo et al, 1989), (b) in healthy adults comparing two measurements with 14 days apart (Valía et al, 2008), (c) in healthy adults comparing two measurements with at least 14 days apart at different nostrils (Stanley et al, 1984), and (d) in healthy young subjects comparing two to six measurements performed in different days (Doyle and Van Cauwenberge, 1987). In the present study, we performed STT measurements in the same day, two to four hours apart, in the free nostril. STT-values were similar during all three periods of the day in both, nonsmokers and smokers.

However, the potential of use STT to evaluate interventions as a biomarker of the overall mucociliary function, may be limited by variations. Some factors have been already

Table 3. STT values of healthy subjects

Author	N of subjects	Age (years)	STT (mean ±SD, minutes)
Puchelle et al, 1981	20	21	10.5 ±6.8
Rutland and Cole, 1981	10	15-29	10.1 ±2.1
Sakakura et al, 1983	64	20-74	13.1 ±6.3
Passàli et al, 1984	79	19-74	17.0 ±5.0
Deitmer, 1986	20	-	10.1 ±0.9
Golhar, 1986	150	18-35	7.1
Stanley et al, 1984	35	-	14.0
Doyle and Van Cauwenberge, 1987	10	20-34	8.3
Salah et al, 1988	11	17-38	11.9 ±5.3
Corbo et al, 1989	259	11-14	8 (median)
Yue, 1989	50	17-65	7.9 ±1.3
Moriarty et al, 1991	6	young students	8.0 ±2.0
Middleton et al, 1993	12	27	9.5 ±0.7
Sachdeva et al, 1993	50	15-49	7.5 ±1.1
Capellier et al, 1997	7	29	16 (9-21)
Selimoglu et al, 1999	10	12-57	7.19 ±2.3
Ho et al, 2001	41	21-40	9.8 ±5.0
Narozny et al, 2002	32	20-50	10.8 ±3.4
Çinar and Beder, 2004	38	23-49	11.0 ±3.2
Keojampa et al, 2004	22	-	13.2 ±5.2
Rosen et al, 2005	29	32	9.2 ±3.9
Yadav et al, 2005	25	26	7.9 ±0.3
Oliveira et al, 2006	11	26	10.5 ±6.8
Kesimci et al, 2008	60	40	7.2 ±3.6
Valía et al, 2008	249	10-49	15.3 ±6.8

Table 4. STT values of adults smokers and nonsmokers

Author	N of subjects	Age (years)	STT (mean ±SD, minutes)
Stanley et al, 1986	27	33	Nonsmokers: 11.1 ±3.8 Smokers: 20.8 ±9.3
Littlejohn et al, 1992	10	>18	Smokers: 11.7 ±3.3
Mahakit and Pumhirun, 1995	40	-	Nonsmokers: 12.0 Smokers: 12.4 ±3.0
Alfaro-Monge and Soda-Merhy, 1995	100	-	Nonsmokers: 10.3 Smokers: 13.6
Nakagawa et al, 2005	16	32 ±14	Nonsmokers: 10.5 Smokers: 22.0
Karaman and Tek, 2009	40	18-57	Nonsmokers: 12.1 ±1.9 Smokers: 26.4 ±1.8

pointed out to affect STT results that include allergic rhinitis (England et al, 2000; Vlastos et al, 2009), asthmatics (Yadav et al, 2005), chronic rhinitis (Deitmer, 1986), chronic sinusitis (Rutland and Cole, 1981; Sakakura et al, 1983; Alho, 2004), bronchiectasis (Rutland and Cole, 1981), Kartagener´s syndrome (Sakakura et al, 1983), laryngectomy (Sakakura et al, 1983); nasal surgery (Golhar, 1986; Kamani et al, 2006; Karaman and Tek, 2009), hypoxia (Barry et al, 1997), breathing dry air (Salah et al, 1988), and diuretics (Goto et al, 2010).

Among methodological issues, the period of the time of STT performance has not been evaluated. Circadian rhythms may influence mucociliary clearance. It has been suggested that ciliary beating frequency of human bronchial epithelial cells follows a cyclical pattern as a result of the influence of circadian rhythms (Rusznak et al, 1994). The study was conducted during three consecutive days from 8 AM to 8 PM. A significantly decreased maximal ciliary beating frequency was observed at 8:00 AM, and the maximal ciliary beating frequency at 12 noon. In the present study, nonsmokers present prolonged STT-values in the Morning compared with Afternoon and Evening, with no differences between measurements after 12 noon. On the other hand, smokers did not follow this behavior. They maintain prolonged STT-values along the daytime.

The STT results of smokers are still controversial (shown in Table 4). Some studies show 35 to 120% increase in STT-values in smokers (Alfaro-Monge and Soda-Merhy, 1995; Stanley et al, 1986; Nakagawa et al, 2005; Karaman et al, 2009). On the other hand, no significant differences between smokers and nonsmokers were found (Mahakit and Pumhirun, 1995, Littlejohn et al., 1992). In the present study, we observed a 37% increase in STT in young smokers compared with nonsmokers.

Conclusion

STT is a reproducible test independently of the period of

the day. Young smokers have prolonged STT-values that were maintained during the three periods of the day. On the other hand, nonsmokers did present differences along the daytime. STT-values were prolonged in the morning compared with afternoon and evening periods. Therefore, the use of saccharin transit testings to evaluate clinical interventions should be performed within the same period of the day.

References

1 Alfaro-Monge JM, Soda-Merhy A. The comparative test of nasal mucociliary functions in healthy subjects, smokers and non-smokers. Acta Otorrinolaringol Esp 1995; 46(3): 187-189.
2 Alho OP. Nasal airflow, mucociliary clearance, and sinus functioning during viral colds: effects of allergic rhinitis and susceptibility to recurrent sinusitis. Am J Rhinol. 2004; 8(6): 349-55.
3 Andersen IB, Camner P, Jensen PL, Philipson K, Proctor DF. Nasal clearance in monozygotic twins. Am Rev Respir Dis 1974; 110: 301-305.
4 Barry PW, Mason NP, O'Callaghan C. Nasal mucociliary transport is impaired at altitude. Eur Respir J 1997; 10(1): 35-37.
5 Boucher RC. New concepts of the pathogenesis of cystic fibrosis lung disease. Eur Respir J 2004; 23: 146-158.
6 Capellier G, Zhang Z, Maheu MF, Pointet H, Racadot E, Kantelip B, Regnard J, Barele F. Nasal mucosa inflammation induced by oxygen administration in humans. Acta Anaesthesiol Scand 1997; 41: 1011-1016.
7 Corbo GM, Foresi A, Bonfitto P, Mugnano A, Agabiti, Cole PJ. Measurement of nasal mucociliary clearance. Archives of Disease in Childhood 1989; 64: 546-550.
8 Çinar F, Beder L. Nasal mucociliary clearance in coal mine workers. Otolaryngol Head Neck Surg 2004; 130: 767-769.
9 Deitmer T. A modification of the saccharine test for nasal mucociliary clearance. Rhinology 1986; 24: 237-240.
10 Doyle WJ, Cauwenberge, PBW. Relationship between nasal patency and clearance. Rhinology 1987; 25: 167-179.
11 England RJA, Anthony R, Homer JJ, Martin- Hirsch DP. Nasal pH and saccharin clearance are unrelated in the physiologically normal nose. Rhinology 2000; 38: 66-67.
12 Golhar S. Nasal mucus clearance. J Laryngol Otol 1986; 100: 533-538.
13 Goto DM, Torres GM, Seguro AC, Saldiva PHN, Lorenzi-Filho G, Nakagawa NK. Furosemide impairs nasal mucociliary clearance in humans. Respir Physiol Neurobiol 2010; 170: 246-252.
14 Ho JC, Chan KN, Hu WH, Lam WK, Zheng L, Tipoe GL, Sun J, Leung R, Tsang KW. The effect of aging on nasal mucociliary clearance, beat, frequency, and ultrastructure of respiratory cilia. Am J Respir Crit Care Med 2001; 163: 983-988.
15 Hogg JC, Chu F, Utokaparch S, Woods R, Elliott WM, Buzatu L, Cherniack RM, Rogers RM, Sciurba FC, Coxson HO, Paré PD. The nature of small-airway obstruction in chronic obstructive pulmonary disease. N Engl J Med. 2004; 350(26): 2645-2653.
16 Kamani T, Yilmaz T, Surucu S, Turan E, Brent KA. Scanning electron microscopy of ciliae and saccharine test for ciliary function in septal deviations. Laryngoscope 2006; 116: 586-590.
17 Karaman M, Tek A. Deleterious effect of smoking and nasal septal deviation on mucociliary clearance and improvement after septoplasty. Am J Rhinol Allergy 2009; 23: 1-7.
18 Kesimci E, Bercin S, Kutluhan A, Ural A, Yamanturk B, Kanbak O. Volatile anesthetics and mucociliary clearance. M'inerva Anestesiologica 2008; 74: 107-111.
19 Keojampa BK, Nguyen MH, Ryan MW. Effect of buffered saline solution on nasal mucociliary clearance and nasal airway patency. Otolaryngol Head Neck Surg 2004; 131: 679-682.
20 Kim JS, Rubin BK. Nasal and sinus involvement in chronic obstructive pulmonary disease. Curr Opin Pulm Med 2008; 14: 101-104.
21 Konrad F, Schreiber T, Brecht-Kraus D, Georgieff M. Mucociliary transport in ICU patients. Chest 1994; 105 (1): 237-241.
22 Kreindler JL, Jackson AD, Kemp PA, Bridges RJ, Danahay H. Inhibition of chloride secretion in human bronchial epithelial cells by cigarette smoke extract. Am J Physiol Lung Cell Mol Physiol 2005; 288(5): L894-902.
23 Littlejohn MC, Stiernberg CM, Hokanson JA, Quinn FB, Bailey BJ. The relationship between the nasal cycle and mucociliary clearance. Laryngoscope 1992; 102: 117-120.
24 Mahakit P, Pumhirun P. A preliminary study of nasal mucociliary clearance in smokers, sinusitis and allergic rhinitis patients. Asian Pac J Allergy Immunol 1995; 13: 119-
25 Matsui H, Randell SH, Peretti SW, Davis W, Boucher RC. Coordinated clearance of periciliary liquid and mucus from airway surfaces. J Clin Invest 1998; 102: 1125-1131.
26 Middleton PG, Geddes DM, Alton EWFW. Effect of amiloride and saline on nasal mucociliary clearance and potential difference in cystic fibrosis and normal subjects. Thorax 1993; 48: 812-816.
27 Moriarty BG, Robson AM, Smallman LA, Drake-Lee, AB. Nasal mucociliary function: comparison of saccharin clearance with ciliary beat frequency. Rhinology 1991; 29: 173-179.
28 Murin S, Bilello KS: Respiratory tract infections: another reason not to smoke. Cleve Clin J Med 2005, 72: 916-920.
29 Nakagawa NK, Franchini ML, Driusso P, Oliveira LR, Saldiva PHN, Lorenzi-Filho G. Mucociliary clerance is impaired in acutely ill patients. Chest 2005; 128: 2772-2777.
30 Narozny W, Sicko Z, Stankiewicz CZ, Przewozny T, Sicko-Pegiel E. The effect of hyperbaric oxygen on nasal mucociliary transport. Clin otolaryngol 2002; 27: 140-146.
31 Oliveira LR, Yagi CSA, Figueiredo AC, Saldiva PHN, Lorenzi-Filho, G. Short-term effects of cpap on nasal mucociliary clearance and mucus transportability in healthy subjects. Respiratory Medicine 2006; 100: 183-185.
32 Passàli D, Bellussi L, Lauriello M. Diurnal activity of nasal mucosa. Acta Otolaryngol 1984; 110: 437-442.
33 Persson CG, Svensson C, Greiff L, Anderson M, Wollmer P, Alkner U, Erjefält I. The use of the nose to study the inflammatory response of the respiratory tract. Thorax 1992; 47: 993-1000.
34 Puchelle E, Aug F, Pham QT, Bertrand A. Comparison of three methods for measuring nasal mucociliary clearance in man. Acta Otolaryngol 1981; 91: 297-303.
35 Puchelle E, Zahm JM, Quemada D. Rheological properties controlling mucociliary frequency and respiratory mucus transport. Biorheology 1987; 24(6): 557-563.
36 Randell SH, Boucher RC. Effective mucus clearance is essential for respiratory health. Am J Respir Cell Molec Biol 2006; 35: 20-28.
37 Redding GJ, Kishioka C, Martinez P, Rubin BK. Physical and transport properties of sputum from children with idiopathic bronchiectasis. Chest 2008; 134(6): 1129-1134.
38 Rosen JE, Calhoun, KH. Alterations of nasal mucociliary clearance in association with HIV infection and the effect of

guaifenesin therapy. Laryngoscope 2005; 115: 27-30.
39 Rubin BK. Designing clinical trials to evaluate mucus clearance therapy. Respiratory Care 2007; 52: 1348-1361.
40 Rusznak C, Devalia JL, Sapsford RJ, Davies RJ. Circadian rhythms in ciliary beat frequency of human bronchial epithelial cells, in vitro. Respir Med 1994; 88(6):461-463.
41 Rutland J, Cole PJ. Nasal mucociliary clearance and ciliary beat frequency in cystic fibrosis compared with sinusitis and bronchiectasis. Thorax 1981; 36: 654-658.
42 Sachdeva A, Sachdeva OP, Gulati SP, Kakkar V. Nasal mucociliary clearance and mucus pH in patients with diabetes mellitus. Indian J Med Res 1993; 98: 265-268.
43 Sakakura Y, Ukai K, Majima, Murai S, Harada T, Miyoshi Y. Nasal mucociliary clearance under various conditions. Acta Otolaryngol 1983; 96: 167-73.
44 Salah B, Xuan ATD, Fouilladieu JL, Lockhart A, Regnard J. Nasal mucociliary transport in healthy subjects is slower when breathing dry air. Eur Respir J 1988; 1: 852-855.
45 Selimoglu MA, Selimoglu E, Kurt A. Nasal mucociliary clerarance and nasal and oral pH in patients with insulin-dependent diabetes. Ear Nose Troat J 1999; 78: 585-590.
46 Stanley P, MacWilliam L, Greenstone M, Mackay I, Cole PJ. Efficacy of saccharin test for screening to detect abnormal mucociliary clearance. Br J Dis Chest 1984; 78: 62-65.
47 Stanley PJ, Wilson R, Greenstone MA, MacWilliam L, Cole PJ. Effect of cigarette smoking on nasal mucociliary clearance and ciliary beat frequency. Thorax 1986; 41: 519-523.
48 Valía PP, Valero FC, Pardo JM, Rentero DB, Monte CG. Saccharin test for the study of mucociliary clearance: reference values for a Spanish population. Arch Bronconeumol 2008; 44(10): 540-545.
49 Vlastos I, Athanasopoulos I, Mastronikolis NS, Panogeorgou T, Margaritis V, Naxakis S, Goumas PD. Impaired mucociliary clearance in allergic rhinitis patients is related to a predisposition to rhinosinusitis. Ear Nose Throat J 2009; 88(4): E17-19.
50 Yadav J, Verma A, Gupta KB. Mucociliary clearance in bronchial asthma. Indian J Allergy Asthma Immunol 2005; 19: 21-23.
51 Yue WL. Nasal mucociliary clearance in patients Rhinological with diabetes mellitus. J Laryngol Otol 1989; 103: 853-855.

College Station…continued from page 33

program for managing and reporting patient information. The program offers Nibert's team the ability to capture temperature and respiratory settings with blood gas results and to flag patients with critical values, and they can customize it to help meet regulatory needs, spot areas needing attention and simplify workflow.

cobas b 221 blood gas system

The other part of the College Station solution was cobas bge link software, a network-level program that allows centralized control over multiple cobas b 221 systems from any PC on the hospital network. The program offers users the capability for remote diagnostics (through Axeda protected remote access software) and virtual 24/7 on-site technical support from Roche. It also provides a screen-sharing capability, enabling real-time data sharing between multiple users.

Nibert is now in the process of upgrading the system with a bidirectional data interface to further augment its capabilities. "With these programs, [lead diagnostic therapist] Stacey Howard can manage instruments, review QC information, do maintenance and training, and make sure all the instruments are up and running through her PC," explains Nibert. "It not only enhances the services we provide to physicians and clinicians, it also greatly simplifies our regulatory compliance process. The analyzer upgrades, along with interfaces into our health information management system, have allowed us to take our blood gas service line to another level."

Stacy Howard, RRT, Lead Diagnostic Therapist College Station Medical Center

[Reference: 1 Bowling MR, Chatterjee A, Conforti J, Adair N, Haponik E, Chin Jr. R. Perceptions vs. reality: measuring of pleural fluid pH in North Carolina. NC Med J. 2009;70(1):9-13.]

Evaluation of Psychological and Physiological Predictors of Fatigue in Patients with COPD

Agnieszka Lewko, Penelope L. Bidgood, Rachel Garrod

Abstract

Background: Fatigue in COPD impairs functional status; however there are few studies examining mechanistic pathways of this symptom. The aims of this study are to compare fatigue between COPD patients and healthy age-matched subjects, and to identify predictors of fatigue in COPD.

Methods: Seventy four COPD patients, mean age 69.9 (49-87) yrs, mean (SD) % predicted FEV_1 46.5 (20.0) % and FEV_1/FVC ratio 0.45 (0.13) and 35 healthy subjects, mean age 67.1 (50-84) yrs completed the Multidimensional Fatigue Inventory (MFI 20). Patients' assessment included Depression (HADS), lung function, BMI, muscle strength, incremental shuttle walk test (ISWT), exercise oxygen saturation (SpO_2), Borg breathlessness (CR-10) and exertion (RPE). Serum level of Interleukin 6 (IL-6) was recorded. Differences in MFI 20 between groups were examined and predictors of fatigue identified using logistic regression.

Results: Significant differences ($p < 0.01$) were found between the COPD and healthy subjects for all MFI 20 dimensions. There were significant differences when classified according to GOLD and dyspnoea stages for selected dimensions only. Predictors of General Fatigue were depression, muscle strength and end SpO_2 (R^2=.62); of Physical Fatigue: depression, % predicted FEV_1, ISWT and age (R^2=.57); Reduced Activity: % predicted FEV_1, BMI and depression (R^2=.36); Reduced Motivation: RPE, depression and end SpO_2 (R^2=.37) and Mental Fatigue: depression and end SpO_2 (R^2=.38).

Conclusion: All dimensions of fatigue were higher in COPD than healthy aged subjects. Predictive factors differ according to the dimension of fatigue under investigation. COPD-RF is a multi component symptom requiring further consideration.

Background

Fatigue, as a symptom in chronic obstructive pulmonary disease (COPD) may have diverse manifestations, such as physical or mental tiredness, loss of attention, concentration or motivation.[1,2] It is an important[3-5] and highly prevalent symptom[6,7] with data from one study suggesting that 90% of COPD patients may report fatigue.[6] Although fatigue in COPD is acknowledged by clinicians, it is often neglected. In fact, compared with cancer the predictors and patho-mechanisms of fatigue are poorly evaluated in COPD and there is a lack of understanding regarding the management of fatigue. There are evident associations between fatigue, impaired quality of life and increased depression.[8-10] Furthermore, fatigue and dyspnoea in COPD, whilst related, appear to be separate entities.[11,4] Using the FACIT-fatigue uni-dimensional scale, no association between disease severity and fatigue is noted.[8] However, the Multidimensional Fatigue Inventory (MFI 20),[12] which is well validated in COPD and shows moderate relationships with airflow obstruction.[10,13] The MFI 20 provides a multi-dimensional evaluation of fatigue, enabling investigation of the different components. Since several factors are likely to be involved in the development of COPD related fatigue (COPD-RF), the use of a multi-dimensional tool enables further elucidation of mechanistic pathways. For instance, whilst hypoxia and hypoxaemia, impaired fat free mass and loss of fatigue resistant muscle fibres are associated with fatigue,[14] it is not known if the variables relate to physical or mental fatigue specifically. In healthy subjects, acute exercise fatigue is associated with raised levels of Interleukin 6 (IL6); [15,16] possibly, this pathway is important in the development of COPD-RF.[17] There are few studies that comprehensively investigate predictors of the different domains of fatigue in COPD. This study attempts to draw together the psychological and physiological aspects of fatigue to develop working models of COPD-RF, by using comparative data from healthy age-matched subjects. This research hypothesises that increases in each component of fatigue in COPD may be predicted by differing factors. The aims of this study were firstly, to provide comparative data of fatigue, using the MFI 20, between COPD patients and healthy elderly subjects and secondly, to explore possible predictors of fatigue components of the MFI 20.

Methods

A total of 80 COPD patients (defined as FEV_1/FVC ratio <0.7 with a general practitioner or chest physician diagnosis) and 37 healthy elderly subjects were recruited to the study. Patients with stable COPD (no exacerbation or change of medication in last 6 weeks) were recruited from the chest clinic of St George's Hospital. Figure 1 shows the patient recruitment flow chart. Healthy subjects were recruited from the staff and volunteers of St. George's University, St George's Hospital and from an Open

Agnieszka Lewko is with the Faculty of Health and Social Care Sciences, St. George's University of London and also with Kingston University, Cranmer Terrace; Bidgood is with the Faculty of Computing, Information Systems and Mathematics, Kingston University, Kingston upon Thames, Surrey; Garrod is with Kings College NHS Foundation Trust, Dulwich Hospital, London, UK. Reprinted from BioMed Central, BMC Pulmonary Medicine,

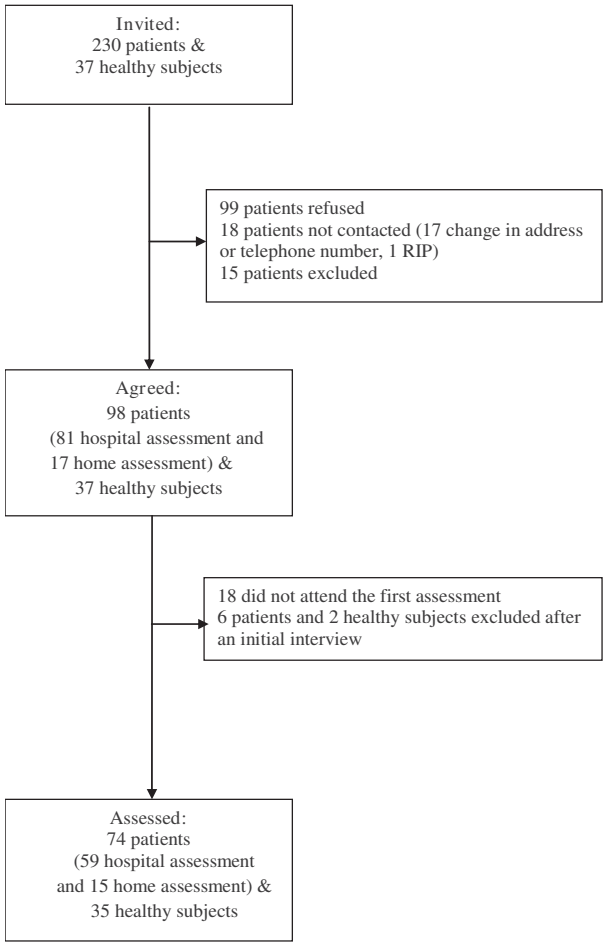


Figure 1. Flow chart of recruitment and assessment.

University group. Absence of airway obstruction was confirmed by spirometry. Additionally, patients and subjects were excluded if they had a history of significant inflammatory co-morbidities such as carcinoma, rheumatoid arthritis or stroke, unstable angina, a diagnosis of psychiatric disorders, or mobility limiting conditions.

Fifty nine patients included in the study attended the hospital for a baseline morning assessment of approximately 2.5-3.5 hours (transport available). Assessment was carried out over two days if necessary, for instance, when the patient was too tired to continue. A further 15 housebound severe COPD patients were unable to attend the hospital for assessment; for these patients an adapted home assessment was provided.

Fatigue was assessed in the morning prior to other assessments in patients and healthy subjects using MFI 20, a 20-item self-report validated instrument.[12,18] This tool has been previously used in COPD population and it is recommended as an outcome measure in clinical settings.[19] The questionnaire asks subjects to describe how they have been feeling lately. For issues of clarity this was specified as "within the last two weeks". The tool consists of five dimensions covering General Fatigue (GF), Physical Fatigue (PF), Reduced Activity (RA), Reduced Motivation (RM) and Mental Fatigue (MF). Each dimension has 4 items, each item scored from 1-5 with higher scores representing greater levels of fatigue.

All participants completed the Hospital Anxiety and Depression Scale (HADS). The HADS is a questionnaire designed to measure depressive moods and anxiety separately.[20] A score of 11 or higher indicates probable presence of the mood disorder, but it is not a synonymous of the diagnosis. Baseline breathlessness level was assessed using the Medical Research Council Dyspnoea Grade (MRC).[21] Health Related QoL was measured using Saint George's Respiratory Questionnaire (SGRQ).[22]

For all participants height (cm) and weight (kg) were measured. Body Mass (BMI) and Fat Free Mass (FFMI) indices were determined from body composition measurements using a non-invasive bioelectrical impedance technique (Body composition analyser, Tanita Ltd BC-418MA, UK). Baseline FEV_1 and FVC were assessed using a spirometer Micro Plus MS03 (Micro Medical Ltd, Rochester UK) and according to BTS recommendations.[23] GOLD classification was used to determine patients' airway obstruction severity.[24]

For all participants quadriceps maximal torque was measured using a Cybex Norm Testing and Rehabilitation System. The protocol consisted of 1 minute of consecutive concentric knee extensions and flexions, performed maximally at an angular velocity of 60°/sec, following a 10-repetition trial. The break between the trial and actual test was 20 seconds. Maximum torque was recorded as the best attempt during 1 minute isokinetic work of the dominant side (FtLbs) and as FtLbs/subject bodyweight (lb) *100.

For patients only, maximal exercise tolerance was assessed using the Incremental Shuttle Walking Test (ISWT), an incremental, externally paced exercise capacity test conducted according to standardised procedure.[25] Endurance exercise tolerance was then assessed using the Endurance Shuttle Walking Test (ESWT).[26] Prior to and after each test percutaneous arterial oxygen saturation (SpO_2) and heart rate were measured using a pulse oximeter (Pulsox-3i-Konika Minolta, Singapore) applied to the finger. Borg CR 10 (Dyspnea assessment) and Borg Rating of Perceived Exertion (RPE) scales were scored after each test.[27,28]

For patients only, a fasting, resting venous blood sample was obtained from the median cubital vein and Interleukin-6 (IL-6) was measured from serum. Blood samples were centrifuged within 2 hours of collection and serum was stored at -20°C until assay. The analysis was performed on an Immulite 1000 automated analyzer (Siemens Medical Solutions Diagnostics, formally Euro/DPC Ltd Gwynedd Wales, UK). The limit of detection for serum IL-6 was 0.2 pg/mL^{-1}. Patients' hemoglobin (Hb) levels were determined from their ear lobe capillary blood sample, using blood gas/electrolyte analyzer (model 5700; Instrumentation Laboratory, Lexington MA). Anaemia was defined according to WHO criteria.[29]

Home assessment: The 15 home assessments were as described above with the exception of measures of exercise tolerance, muscle strength and blood sampling. Summary statistics of the healthy subjects' and COPD patients' characteristics were reported. Independent sample t-tests or Mann-Whitney tests as appropriate were used to test for differences between the patients and the healthy subjects. The Kruskal-Wallis test was used to determine differences between fatigue dimensions according to the MRC score and GOLD classification with the significance level set at α=0.05. When significant differences were found, post hoc analysis was carried out using Mann-Whitney tests with Bonferroni correction. The data used to

Table 1: Characteristics and comparison of COPD and healthy subject groups

	COPD (n = 74)	Healthy (n = 35)	p value
MFI 20 General Fatigue	13 (5)	8 (4)	p < 0.001
MFI 20 Physical Fatigue	16 (5.25)	7 (5)	p < 0.001
MFI 20 Reduced Activity	13.5 (6)	6 (5)	p < 0.001
MFI 20 Reduced Motivation	10 (6)	6 (4)	p < 0.001
MFI 20 Mental Fatigue	8 (7)	6 (4)	p = 0.008
% FEV_1	46.5(20.0)	96.5(13.2)	p < 0.001
FEV_1/FVC ratio	0.44 (0.13)	0.78(0.1)	p < 0.001
Age (yrs)	69.9 (8.4)	67.11 (8.8)	NS
BMI (kg/m^2)	26.2 (5.4)	25.2 (3.4)	NS
FFMI (kg/m^2)	18.2 (2.6)	17.9 (2.2)	NS
Depression (HADS)	6 (5)	1 (3)	p < 0.001
Anxiety (HADS)	7 (6)	3 (4)	p < 0.001
Peak Tq (% BW)	38.6 (12.0)*	51.6 (14.5)	p < 0.001
ISWT (m)	343.3 (183.9) *	-	-
Post walk SpO_2 (%)	90.0(5.9)*	-	-
Borg exertion (RPE)	13(2.0)*	-	-
IL 6 (pg/mL) (n = 57)	5.4(5.9) *	-	-
MRC dyspnoea score	3 (2)	-	-
SGRQ	56.0 (27.4)	-	-

Data presented as median (IQR) for MFI 20-Multidimensional Fatigue Inventory, HADS - Hospital Anxiety and Depression scale, SGRQ - Saint George's Respiratory Questionnaire, total score, Borg exertion, MRC score or mean (SD) for % FEV_1 - % predicted forced expiratory volume in one second, FEV_1/FVC - Forced Expiratory Volume in one second/Forced Vital Capacity, BMI - Body Mass Index; FFMI - Fat Free Mass Index; Peak Tq (% BW) - quadriceps peak torque (% Body Weight), ISWT - Incremental Shuttle walk test, SpO_2 - Percutaneous arterial oxygen saturation. *not measured in home-assessed patients (n = 59).

measure fatigue are not metric and therefore multiple linear regression techniques are inappropriate. Due to the small number of subjects, logistic rather than ordinal regression was chosen to identify predictors of the 5 dimensions of fatigue; a backward elimination method was used. Therefore for each dimension of fatigue, a binominal category was defined using a cut-off point of the highest value of fatigue in the healthy subjects. Values above this point were considered as fatigued and values below as not fatigued. Explanatory variables that were independent of one another, according to appropriate correlation tests were included in the initial regression models. Other, clinically relevant variables, as identified from literature[9,10,13,14,17,30,31] were also included. The final models, presented here, are those where all the remaining independent variables are statistically significant predictors of the fatigue dimension under consideration and which have the highest R^2 value. The data from 15 home assessments were excluded due to the modified assessment. All analyses were performed using SPSS 15.

Results

Seventy four mild-to-severe COPD patients and 35 healthy subjects completed all assessments. There were no significant differences in fatigue according to gender in either the COPD (52 male vs 22 female) or the healthy group (12 male vs 23 female). Median scores for COPD patients were significantly higher than those of the healthy subjects in all dimensions of MFI 20. Table1 shows the scores for fatigue and other variables and differences between COPD patients and the healthy subjects.

Fatigue and disease severity: Statistically significant differences in fatigue when categorised according to the GOLD and MRC dyspnoea classifications were evident for selected dimensions of MFI 20 only (see figure 2 and figure 3).

Meaningful variables for fatigue dimensions: Regression analysis was performed on full data available from 59 patients (40 male) aged 68.7 (8.1), mean (SD) % predicted FEV_1 48.2 (20.9) and FEV_1/FVC ratio 0.45 (0.13). Clinically relevant variables were identified based on literature and results of correlations with fatigue dimensions. Following the initial regression analyses nine possible predictors were identified: % predicted FEV_1, depression, muscle torque, ISWT, end exercise SpO_2, IL6, Borg RPE, BMI, age. The final decision on which variables to include was determined by clinical relevance and by the best possible model of predictive variables.

Variables excluded from the analysis: The mean (SD)

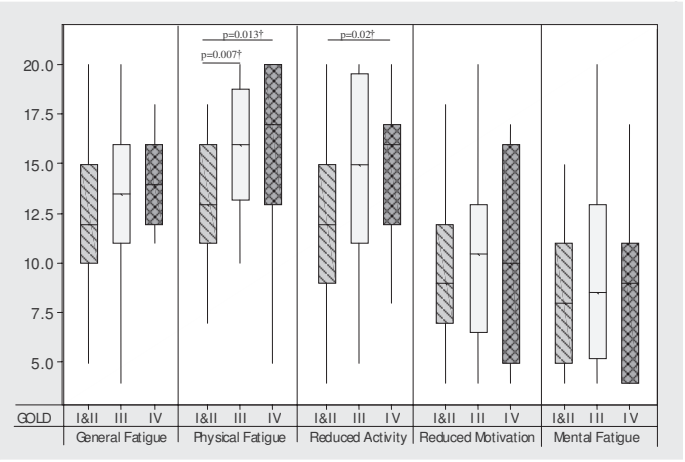


Figure 2. Box plots showing MFI 20 dimensions (median and IQR) in COPD patients for GOLD stages. GOLD stage I & II (n= 27), III (n=32) and IV (n=15). Kruskal Wallis tests: p=0.008 for Physical Fatigue and p=0.045 for Reduced Activity; p>0.05 for General Fatigue, Reduced Motivation and Mental Fatigue; †Mann-Whitney test (Bonferroni correction p=0.02).

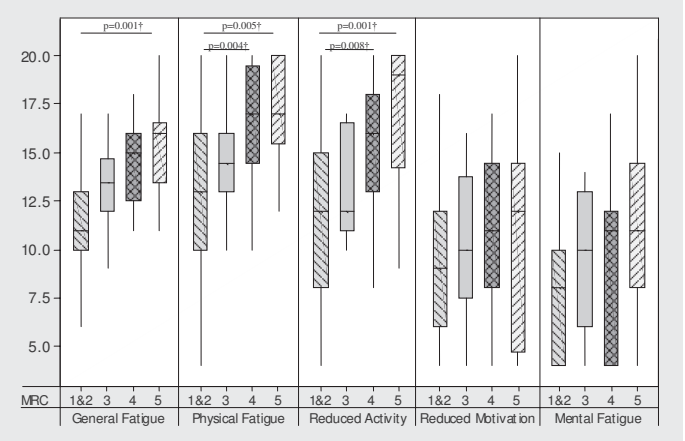


Figure 3. Box plots showing MFI 20 dimensions (median and IQR) in COPD patients for MRC scores. MRC score 1&2 (n=31), 3 (n=12), 4 (n=17), 5 (n=14). Kruskal Wallis tests: p=0.001 for General Fatigue, p=0.004 for Physical Fatigue, p=0.001 for Reduced Activity, p>.05 for Reduced Motivation and Mental Fatigue; †Mann-Whitney test (Bonferroni correction p=0.008).

hemoglobin level was 15.6 (2.9) g/dL in male and 14.6 (1.6) g/dL in female patients. Only 2 patients had values below normal. Anemia was therefore not a feature of the patient population and thus was not included in the regression analysis. There were high correlations between anxiety and depression, BMI and FFMI, ISWT and ESWT. Hence anxiety, FFMI and ESWT were not entered into the regression as independent variables as the others were considered more important clinically.

MRC score as a measure of dyspnea was initially considered as a predictor of fatigue. Although expected from literature and from the results presented in figure 3, it was not a significant predictor for any of fatigue dimension and it was eventually excluded in the final regression process. Measures of quality of life (SGRQ) were collected to enable baseline characterisation of the patients. Although quality of life has been shown to be associated with fatigue in previous studies,[8,9] direction of causality is unknown. It was felt that fatigue was more likely to be a mediator of impaired quality of life than the other direction, thus SGRQ data were not included in the regression as independent predictors.

Predictors of fatigue in COPD: For GF the following 5 variables were entered: depression, muscle torque, % predicted FEV_1, end SpO_2, IL 6; for PF: depression, ISWT, % predicted FEV_1 and age; for RA: depression, ISWT, % predicted FEV_1 and BMI; for RM: depression, end Borg RPE and end SpO_2 and for MF: depression, IL6 and end SpO_2. Table 2, 3, 4, 5, and 6 give the results of the logistic regression analyses. Table 2 shows, for instance, that the significant predictors of GF (as measured by Wald statistic) are depression, muscle torque and end exercise SpO_2. For every increase of 1 in the depression score a patient is approximately 1.5 times more likely to be fatigued and for lower end exercise SpO_2 there is a slightly higher chance of being fatigued; similarly lower muscle strength is associated with higher risk of fatigue.

Summary: Fatigue score was significantly higher in COPD compare to control group for all dimensions of MFI 20. After stratification for MRC and GOLD classifications there were significant differences only for selected dimensions of fatigue. Fatigue, when considered as a multi-component construct was explained by a different combination of variables.

Discussion

The results from this study show that subjective fatigue measured with MFI 20 was significantly higher in the COPD group than in healthy elderly people. Previous work supports these findings,[8,32] which suggests that the increased fatigue reflects disease entity and may therefore be considered as COPD-RF and it should be properly addressed in clinical practice. In contrast to other authors[8] differences were found in fatigue according to GOLD staging, however these differences were specific for selected dimensions of fatigue only. The difference in findings likely reflects the different fatigue tools used, with this study using a multi-dimensional tool compared with the FACIT-fatigue, a uni-dimensional tool.

Table 2: Logistic regression results for General Fatigue

MFI 20	Variables included	Wald χ^2	B (SE)	Odd ratio Exp b	95% CI lower-upper
General Fatigue (n = 48)	HADS depression	8.1	0.43 (0.15)	1.54	1.14-2.07
	Tq %BW	5.0	-0.13 (0.06)	0.88	0.79-0.98
	End SpO_2	2.9	-0.014 (0.08)	0.87	0.74-1.02
	Constant	3.4	13.9 (7.6)	1109057	

R^2 = .62 (Nagelkerke); HADS depression-depression score of hospital anxiety and depression scale, Tq%BM - quadriceps muscle torque % of body mass, End SpO_2 - percutaneous arterial saturation post walking test

Table 3: Logistic regression results for Physical Fatigue

MFI 20	Variables included	Wald χ^2	B (SE)	Odd ratio Exp b	95% CI lower-upper
Physical Fatigue (n = 57)	HADS depression	11.3	0.47 (0.14)	1.61	1.22-2.12
	%pred. FEV_1	9.9	-0.11 (0.04)	0.90	0.83-0.96
	ISWT	5.2	0.01 (0.003)	1.01	1.0-1.01
	Age	2.8	0.9 (0.06)	1.1	0.98-1.22
	Constant	2.6	-7.16 (4.48)	0.001	

R^2 = .57 (Nagelkerke). HADS depression-depression score of hospital anxiety and depression scale, %pred. FEV_1 - % predicted forced expiratory volume in one second, ISWT-Incremental Shuttle Walk Test

In line with this, it is demonstrated here that differing fatigue dimensions can be explained by different physiological and psychological variables associated with COPD and only depression was a common predictor. Although according to MRC dyspnea classification there were significant differences for Reduced Activities, General and Physical Fatigue, the regression analysis excluded dyspnoea score as a possible predictive variable of fatigue. Importantly, the cohort used in regression study differ from one used in MRC classification analysis and data from home-assessed most severe patients may have been more insightful. Previous studies also showed associations between dyspnea and fatigue.[8,30,31] Nonetheless, fatigue and dyspnoea are both subjective symptoms of COPD and some of the patho-mechanisms of fatigue may be common for those of dyspnea. Therefore, this may explain the close association between these symptoms. Since fatigue is not routinely assessed in current clinical practice, the models from this study may help to identify patients who are at risk of being fatigued and develop effective fatigue management strategies. Furthermore, the regression analyses revealed that each component could be explained by different variations. Hence, the multi-rather than uni-dimensional assessment should be considered. Over half of the variation in general fatigue was explained by a combination of depression, exercise de-saturation and muscle strength. These data then provide further support for the role of muscle training, depression management and use of supplementary oxygen in COPD. In this present study exercise de-saturation was also a significant predictor for the MFI 20 Reduced Motivation component. For Reduced Motivation; depression, post exercise saturation and exertion explained a little less than 40% of the variation. This component includes items such as "I dread having to do things" and "I don't feel like doing anything." Low oxygen levels may be associated with changes in cognitive function[33,34] and stimulate affective areas of the brain, mainly in the frontal lobe, which is associated with motivational process.[35,36] Feasibly, the administration of oxygen during exertion may be associated with lower fatigue levels and enhanced motivation. To date this application of oxygen has not been explored.

For physical fatigue the best model, a combination of depression, lung function and exercise tolerance, explained 57% of the variation. This provides some explanation as to how therapies that improve exercise tolerance and depression can have an impact on fatigue in COPD.[37] Muscle strength and exercise tolerance were significant predictors for general and physical fatigue, respectively. These two variables were highly correlated and therefore only one was used in the regression analysis. Muscle weakness and reduced exercise tolerance are well recognized in the COPD population[38,39] and may be important factors influencing COPD RF.

Around 40% of the variation in Reduced Activity was explained by the combination of lung function, BMI and depression. In this instance a higher BMI was associated with greater fatigue. This probably reflects the U-shaped curve nature of the association between BMI and outcomes, both low and high BMI is generally associated with poorer outcome.[40] Nutritional status remains an important therapeutic outcome in the management of COPD. Furthermore, in physically related dimensions of fatigue the severity of airway obstruction explained a significant amount of the variance, suggesting that treatments which affect airflow obstruction may also benefit the perception of physical fatigue. For mental fatigue few COPD patients were identified as fatigued and the results for this component should be treated with caution.

Anemia may be one of the causes of fatigue and can be present in COPD patients;[41] however, hemoglobin levels were generally

Table 4: Logistic regression results for Reduced Activity

MFI 20	Variables included	Wald χ^2	B (SE)	Odd ratio Exp b	95% CI lower-upper
Reduced Activity (n = 57)	%pred. FEV_1	7.5	-0.06 (0.02)	0.95	0.91-0.98
	BMI	4.5	0.19(0.08)	1.21	1.03-1.41
	HADS depression	3.9	0.19 (0.94)	1.20	1.0-1.45
	Constant	2.0	-3.12 (1.95)	0.04	

R^2 = .36 (Nagelkerke). %pred. FEV_1 - % predicted forced expiratory volume in one second, BMI - Body Mass Index, HADS depression-depression score of hospital anxiety and depression scale

Table 5: Logistic regression results for Reduced Motivation

MFI 20	Variables included	Wald χ^2	B (SE)	Odd ratio Exp b	95% CI lower-upper
Reduced Motivation (n = 56)	Borg exertion	5.8	0.54 (0.22)	1.71	1.11-2.66
	HADS depression	5.7	0.24 (0.10)	1.28	1.04-1.56
	End SpO_2	4.9	-0.13(0.06)	0.88	0.78-0.99
	Constant	0.3	2.69 (5.28)	14.67	

R^2 = .37 (Nagelkerke). Borg exertion (score) post walk test, HADS depression-depression score of hospital anxiety and depression scale, End SpO_2 - percutaneous arterial saturation post walking test.

Table 6: Logistic regression results for Mental Fatigue

MFI 20	Variables included	Wald χ^2	B (SE)	Odd ratio Exp b	95% CI lower-upper
Mental Fatigue (n = 52)	HADS depression	7.3	0.4 (0.15)	1.49	1.12-2.0
	End SpO_2	3.1	0.2 (0.12)	1.23	0.98-1.54
	Constant	4.3	-23.06(11.16)	0.0	

R^2 = .38 (Nagelkerke). HADS depression-depression score of hospital anxiety and depression scale, End SpO_2 - percutaneous arterial saturation post walking test.

within the normal range in the cohort, thus this factor could not be included in this analysis. Nevertheless, it is clear from this study, that COPD RF remains a significant problem even in patients with moderate disease and no anemia. Although some variables were not included in the final regression model, they may still play a role in the development of COPD RF. For example, there was a strong correlation between anxiety and depression, but it was decided only to include depression. Similarly, ESWT was strongly related to ISWT but only the maximal test was included. Although IL6 was considered a possible predictor, none of the final regression models included it, which may be due to its correlation with both muscle strength and walking distance[42] or reflects the need for other measures such as receptors.

Previous studies using a multiple regression identified depression as a predictive variable of uni-dimensional fatigue in COPD.[8,30] However, findings here reveal that depression is a predictor for all dimensions of fatigue.

Conclusion

This study shows that all dimensions of fatigue are greater in COPD than in healthy people of a similar age range. Increased fatigue in this population is therefore a feature of COPD and not of age per se. COPD-RF is a multi component construct and as such different aspects of fatigue are influenced by different clinical manifestations. Comprehensive treatment of COPD-RF includes management of depression, muscle weakness, optimization of BMI and exercise de-saturation levels. In contrast to other authors it was found that fatigue differs according to GOLD staging, however this is relevant only for Physical Fatigue and Reduced Activity. This study goes some way towards explaining the mechanistic pathway of COPD-RF and provides information to target hitherto neglected treatments.

References

1 Armes J, Krishnasamy M, Higginson IJ: Fatigue in cancer. New York, Oxford University Press; 2004.

2 Del Fabbro E, Dalal S, Bruera E: Symptom control in palliative care—Part II: Cachexia/anorexia and fatigue. Journal of Palliative Medicine 2006, 9:409-421.

3 Brissot R, Gonzalez-Bermejo J, Lassalle A, Desrues B, Doutrellot PL: Fatigue and respiratory disorders. Annales de Readaptation et de Medecine Physique 2006, 49 (6):403-412.

4 Small S, Lamb M: Fatigue in chronic illness: the experience of individuals with chronic obstructive pulmonary disease and with asthma. Journal of Advanced Nursing 1999, 30:469-478.

5 Yeh ML, Chen HH, Liao YC, Liao WY: Testing the functional status model in patients with chronic obstructive pulmonary disease. Journal of Advanced Nursing 2004, 48:342-350.

6 Kinsman RA, Yaroush RA, Fernandez E, Dirks JF, Schocket M, Fukuhara J: Symptoms and experiences in chronic bronchitis and emphysema. Chest 1983, 83:755-761.

7 Walke LM, Byers AL, Tinetti ME, Dubin JA, McCorkle R, Fried TR: Range and severity of symptoms over time among older adults with chronic obstructive pulmonary disease and heart failure. Archives of Internal Medicine 2007, 167:2503-2508.

8 Baghai-Ravary R, Quint JK, Goldring JJP, Hurst JR, Donaldson GC, Wedzicha JA: Determinants and impact of fatigue in patients with chronic obstructive pulmonary disease. Respiratory Medicine 2008, 103:216-223.

9 Breslin E, Schans C Van der, Breukink SO, Meek P, Mercer K, Volz W, Louie S: Perception of fatigue and quality of life in patients with COPD. Chest 1998, 114:958-964.

10 Breukink SO, Strijbos JH, Koorn M, Koeter GH, Breslin EH, Schans CP Van der: Relationship between subjective fatigue and physiological variables in patients with chronic obstructive pulmonary disease. Respiratory Medicine 1998, 92:676-682.

11 Gift AG, Shepard CE: Fatigue and other symptoms in patients with chronic obstructive pulmonary disease: do women and men differ? Journal of Obstetric, Gynecologic, & Neonatal Nursing 1999, 28:201-208.

12 Smets EM, Garssen B, Bonke B, De Haes JC: The

Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. Journal of Psychosomatic Research 1995, 39:315-325.
13 Oh EG, Kim CJ, Lee WH, Kim SS: Correlates of fatigue in Koreans with chronic lung disease. Heart & Lung 2004, 33:13-20.
14 Evans WJ, Lambert CP: Physiological basis of fatigue. American Journal of Physical Medicine & Rehabilitation 2007, 86:S29-S46.
15 Robson-Ansley PJ, De Milander L, Collins M, Noakes TD: Acute interleukin-6 administration impairs athletic performance in healthy, trained male runners. Canadian J Appl Physiol 2004, 29:411-418.
16 Spath-Schwalbe E, Hansen K, Schmidt F, Schrezenmeier H, Marshall L, Burger K, Fehm HL, Born J: Acute effects of recombinant human interleukin-6 on endocrine and central nervous sleep functions in healthy men. Journal of Clinical Endocrinology & Metabolism 1998, 83:1573-1579.
17 Gan WQ, Man SF, Senthilselvan A, Sin DD, Gan WQ, Man SFP, Senthilselvan A, Sin DD: Association between chronic obstructive pulmonary disease and systemic inflammation: a systematic review and a meta-analysis. Thorax 2004, 59:574-580.
18 Smets EM, Garssen B, Cull A, De Haes JC: Application of the multidimensional fatigue inventory (MFI-20) in cancer patients receiving radiotherapy. British Journal of Cancer 1996, 73:241-245.
19 Meek PM, Lareau SC: Critical outcomes in pulmonary rehabilitation: assessment and evaluation of dyspnea and fatigue. Journal of Rehabilitation Research & Development 2003, 40:13-24.
20 Zigmond AS, Snaith RP: The hospital anxiety and depression scale. Acta Psychiatrica Scandinavica 1983, 67:361-370.
21 Fletcher CM: Standardised questionnaire on respiratory symptoms: a statement prepared and approved by the MRC committee on the aetiology of chronic bronchitis; MRC breathlessness score. BMJ 1960, 2:1665.
22 Jones PW, Quirk FH, Baveystock CM, Littlejohns P: A self-complete measure of health status for chronic airflow limitation. The St. George's Respiratory Questionnaire. American Review of Respiratory Disease 1992, 145:1321-1327.
23 British Thoracic Society, BTS: Guidelines for the measurement of respiratory function. Respiratory Medicine 1994, 88:165-194.
24 Global Initiative for Chronic Obstructive Lung Disease (GOLD): Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. 2006 [http://www.who.int/respiratory/copd/GOLD_WR_06.pdf]. MCR VISION, Inc]
25 Singh SJ, Morgan MD, Scott S, Walters D, Hardman AE: Development of a shuttle walking test of disability in patients with chronic airways obstruction. Thorax 1992, 47:1019-1024.
26 Revill SM, Morgan MD, Singh SJ, Williams J, Hardman AE: The endurance shuttle walk: a new field test for the assessment of endurance capacity in chronic obstructive pulmonary disease. Thorax 1999, 54:213-222.
27 Borg GA: Psychophysical bases of perceived exertion. Medicine & Science in Sports & Exercise 1982, 14:377-381.
28 Borg GA: Borg's Perceived exertion and pain scales. In The Borg RPE Scale Champaign, IL, Human Kinetics; 1998:29-38.
29 World Health Organisation, WHO: Iron Deficiency Anemia. Assessment, Prevention, and Control. Geneva, Switzerland 2001. WHO/NHD/01.3
30 Kapella MC, Larson JL, Patel MK, Covey MK, Berry JK: Subjective fatigue, influencing variables, and consequences in chronic obstructive pulmonary disease. Nursing Research 2006, 55:10-17.
31 Woo K: A pilot study to examine the relationships of dyspnoea, physical activity and fatigue in patients with chronic obstructive pulmonary disease. Journal of Clinical Nursing 2000, 9:526-533.
32 Theander K, Unosson M: Fatigue in patients with chronic obstructive pulmonary disease. Journal of Advanced Nursing 2004, 45:172-177.
33 Grant I, Prigatano GP, Heaton RK, McSweeny AJ, Wright EC, Adams KM: Progressive neuropsychologic impairment and hypoxemia.Relationship in chronic obstructive pulmonary disease. Archives of General Psychiatry 1987, 44:999-1006.
34 Kozora E, Filley CM, Julian LJ, Cullum CM: Cognitive functioning in patients with chronic obstructive pulmonary disease and mild hypoxemia compared with patients with mild Alzheimer disease and normal controls. Neuropsychiatry, Neuropsychology, & Behavioral Neurology 1999, 12:178-183.
35 Incalzi RA, Marra C, Giordano A, Calcagni ML, Cappa A, Basso S, Pagliari G, Fuso L: Cognitive impairment in chronic obstructive pulmonary disease: A neuropsychological and spect study. Journal of Neurology 2003, 250:325-332.
36 Sari A, Oshiata S, Toriumi T, Yamashita S, Kojima S, Kakumoto S, Yonei A: Cerebral blood flow and cerebral oxygen consumption in patients with COPD on mechanical ventilation. Intensive Care Medicine 1992, 18:455-458.
37 Lacasse Y, Martin S, Lasserson TJ, Goldstein RS: Meta-analysis of respiratory rehabilitation in chronic obstructive pulmonary disease. A Cochrane systematic review. Europa Medicophysica 2007, 43:475-485.
38 Celli BR, MacNee W, The ERS Task Force: Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. European Respiratory Journal 2004, 23:932-946.
39 Gosselink R, Troosters T, Decramer M: Distribution of muscle weakness in patients with stable chronic obstructive pulmonary disease. Journal of Cardiopulmonary Rehabilitation 2000, 20:353-360.
40 Landbo C, Prescott E, Lange P, Vestbo J, Almdal TP: Prognostic value of nutritional status in chronic obstructive pulmonary disease. Journal of Respiratory and Critical Care Medicine 1999, 160:1856-1861.
41 Shorr AF, Doyle J, Stern L, Dolgitser M, Zilberberg MD: Anemia in chronic obstructive pulmonary disease: epidemiology and economic implications. Current Medical Research & Opinion 2008, 24:1123-1130.
42 Garrod R, Marshall J, Barley E, Fredericks S, Hagan G: The relationship between inflammatory markers and disability in chronic obstructive pulmonary disease (COPD). Primary Care Respiratory Journal 2007, 16:236-240.

Color of Sputum is a Marker for Bacterial Colonization in COPD

Marc Miravitlles, Alicia Marín, Eduard Monsó, Sara Vilà, Cristian de la Roza, Ramona Hervás, Cristina Esquinas, Marian García, Laura Millares, Josep Morera, Antoni Torres

Abstract

Background: Bacterial colonization in chronic obstructive pulmonary disease (COPD) contributes to airway inflammation and modulates exacerbations. We assessed risk factors for bacterial colonization in COPD.

Methods: Patients with stable COPD consecutively recruited over 1 year gave consent to provide a sputum sample for microbiologic analysis. Bronchial colonization by potentially pathogenic microorganisms (PPMs) was defined as the isolation of PPMs at concentrations of ≥102 colonyforming units (CFU)/mL on quantitative bacterial culture. Colonized patients were divided into high (>105 CFU/mL) or low (<105 CFU/mL) bacterial load.

Results: A total of 119 patients (92.5% men, mean age 68 years, mean forced expiratory volume in one second [FEV1] [% predicted] 46.4%) were evaluated. Bacterial colonization was demonstrated in 58 (48.7%) patients. Patients with and without bacterial colonization showed significant differences in smoking history, cough, dyspnoea, COPD exacerbations and hospitalisations in the previous year, and sputum color. Thirty-six patients (62% of those colonized) had a high bacterial load. More than 80% of the sputum samples with a dark yellow or greenish color yielded PPMs in culture. In contrast, only 5.9% of white and 44.7% of light yellow sputum samples were positive (P <0.001). Multivariate analysis showed an increased degree of dyspnoea (odds ratio [OR]=2.63, 95% confidence interval [CI] 1.53–5.09, P=0.004) and a darker sputum color (OR=4.11, 95% CI 2.30–7.29, P <0.001) as factors associated with the presence of PPMs in sputum.

Conclusions: Almost half of our population of ambulatory moderate to very severe COPD patients were colonized with PPMs. Patients colonized present more severe dyspnea, and a darker color of sputum allows identification of individuals more likely to be colonized.

Authors Miravitlles, Vila and Esquinas are with the Fundació Clínic Institut D'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS); Marin is with the Department of Pneumology, Hospital Germans Trias i Pujol. Autonomous University of Barcelona; Monso, Hervas, Garcia, Millares and Morera are with the Department of Pneumology, Hospital Germans Trias i Pujol; de la Roza is with the Medical Department, Bayer Schering Pharma, Sant Joan Despi, Barcelona; Torres is with the Department of Pneumology, Institut Clínic del Tòrax (IDIBAPS), Hospital Clínic. The authors are also with the Ciber de Enfermedades Respiratorias (CIBERES), Barcelona, Spain. The authors wish to thank Marta Pulido, MD, for providing an outline for this manuscript and support in editing and journal styling.

Background

Exacerbations are the main cost driver in chronic obstructive pulmonary disease (COPD), have a negative impact on the clinical course of the patients and are associated with increased mortality.[1-3] Around 70% of exacerbations are infectious in nature, either bacterial, viral or mixed.[4-7] It has been shown that airway bacterial load in the stable state contributes to airway inflammation and modulates the character and frequency of exacerbations.[8,9] There is also evidence that bronchial colonization influences the decline in lung function over time.[10] Different studies in which respiratory samples were obtained by the protected specimen brush (PSB) technique have shown a high prevalence of bronchial colonization in COPD patients.[5,11,12] However, the practice of bronchoscopy to assess bronchial colonization in routine clinical practice is not feasible and data that support the use of sputum samples to identify patients colonized by potentially pathogenic microorganisms (PPMs) are required.

Consequently, a cross-sectional study was designed to assess the frequency of bronchial bacterial colonization using sputum

Table 1. Clinical characteristics of the study population

Data	Frequency
Subjects, no.	119
Sex, men, no. (%)	112 (92.5)
Age, years, mean (SD)	68.1 (9.1)
Current smokers, no. (%)	11 (9.2)
Smoking, pack-years, mean (SD)	40 (21.1)
Cardiovascular morbidity, no. (%)	36 (29.7)
Exacerbations in the previous year, mean (SD)	1.3 (0.5)
Requiring hospital admission	0.3 (0.5)
Post-bronchodilator spirometry, mean (SD)	
FVC, mL	2790 (942)
FVC, %	68.9 (19.2)
FEV1, mL	1406 (493)
FEV1, %	46.4 (14.1)

Table 2. Potentially Pathogenic Microorganisms (PPMs) isolated in colonised COPD patients.

	No. (%)
Microorganisms isolated	
Haemophilus influenzae	21 (42)
Haemophilus parainfluenzae	15 (30)
Pseudomonas aeruginosa	5 (10)
Streptococcus pneumoniae	4 (8)
Moraxella catarrhalis	4 (8)
Staphylococcus aureus 1 (2)	
Mixed colonisations (from the above microorganisms)	
H. influenzae + S. pneumoniae	1
H. influenzae + P. aeruginosa	3
H. influenzae + H. parainfluenzae	2
P. aeruginosa + S. viridans	2

samples and to identify risk factors for colonization in stable ambulatory patients with COPD. The clinical characteristics of patients colonized and non-colonized with PPMs were compared as were those of patients with low and high bacterial loads in sputum samples.

Methods

A cross-sectional study was carried out to assess clinical characteristics associated with bronchial colonization in stable ambulatory COPD patients. These patients were visited at the outpatient respiratory clinics of two acute-care tertiary hospitals in Barcelona, Spain and were consecutively recruited over one year. After completing the collection of data for this study, patients with bronchial colonization were included in a randomized trial of antibiotic treatment the results of which have been reported elsewhere.[13] The protocol was approved by the institutional review board and all patients gave written informed consent.

Study population: Eligible patients were adults over 40 years of age, smokers or ex-smokers of at least 10 pack-years, with stable COPD, defined as a post-bronchodilator forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) ratio of <70%. A FEV1 of <60% of the predicted value higher than 0.70 litres and a negative bronchodilator test (increase in FEV1 <200 mL and <12% of baseline) was required for inclusion in the study as was a history of at least one documented exacerbation in the previous year. Clinical stability was defined by the attending physician on clinical grounds based on the absence of symptoms of exacerbation and use of any oral or systemic antibiotics or a course of oral corticosteroids in the 6 weeks prior to inclusion. The exclusion criteria were the following: (1) previous diagnosis of bronchial asthma, bronchiectasis demonstrated by a chest X-ray or computed tomography (CT) scan, or other relevant pulmonary diseases apart from COPD; (2) chronic treatment with oral corticosteroids at any dose; (3) formal contraindication for sputum induction or impossibility to obtain a valid sputum sample for analysis; and (4) participation in another clinical study concurrently or within the previous 3 months.

Study procedures: At the time of inclusion in the study, the investigator verified that the patient met the eligibility criteria and details of medical history were recorded. Information regarding comorbidities, particularly cardiovascular diseases, diabetes and liver or renal failure was collected. A forced spirometry was performed following criteria of the Spanish Society of Pneumology and Thoracic Surgery[14] and sputum samples were obtained. Patients unable to produce sputum were susceptible to reassessment for airway colonization at least one month after the initial investigation for a maximum of three consecutive visits.

Microbiological sputum study: A sputum sample was obtained and processed within 60 minutes on the day of the visit according to standard methods.[13,15,16] Patients who did not produce sputum spontaneously underwent sputum induction. In brief, patients were pretreated with an inhaled β2-agonist ten minutes before the nebulisation of isotonic saline (0.9%) with an ultrasonic nebulizer (Ultraneb2000, DeVilbiss Healthcare Inc), that was followed by increasing concentrations of hypertonic saline (3%, 4% and 5%), for 7 min with each concentration. After every induction, the patient attempted to obtain a sputum sample by coughing, and the nebulization procedure was stopped when the sputum volume collected was 1 mL or more.[17] In current smokers, sputum induction was performed after at least 6 hours of tobacco abstinence. The purulence of sputum was graded in a scale from 1 to 5 according to the color from white –1- to greenish –5-, always by the same researcher at each center. The sample was weighed and processed with a 4-fold volume of dithiothreitol (Sputasol, Oxoid Ltd., Hants, UK) and was cultured. Sputum samples were serially diluted and plated on chocolate agar enriched, chocolate agar with bacitracin, Hemophilus-selective agar, blood agar, and McConkey agar. Plates were incubated for 24–48 hours at 37°C and in 5% CO_2 atmosphere. Microorganisms were identified by colony morphology, Gram staining and specific culture conditions (eg, requirements for factors for growth, presence of oxidase and catalase, porphyrin synthesis). Cultures were considered positive for bronchial colonization if microorganisms considered as PPMs such as Haemophilus influenzae, Hemophilus parainfluenzae, Streptococcus pneumoniae, Moraxella catarrhalis, Pseudomonas aeruginosa, enterobacteria and/or Staphylococcus aureus were grown at loads of at least 100 colony-forming units (CFU)/mL according to previously defined criteria.[18,19] Colonized patients were then divided into high (>105 CFU/mL) or low (≤105 CFU/mL) bacterial load according to previous studies.[4,8] Sputum

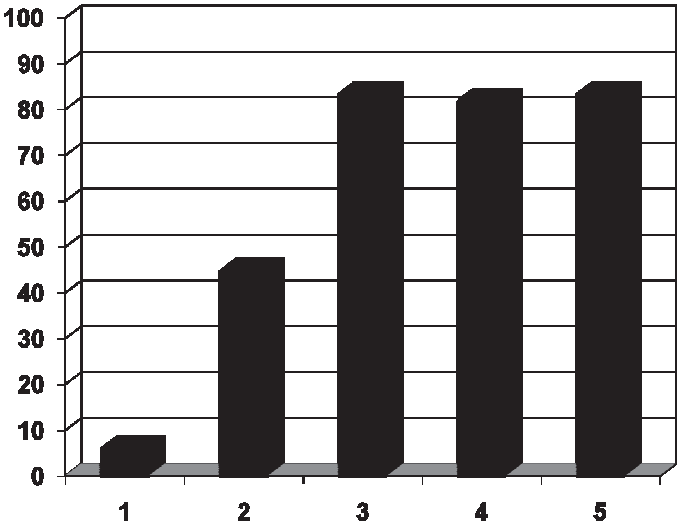


Figure 1. colour 1= white; 2= light yellow; 3= dark yellow; 4= light green; 5= greenish

Table 3. Differences between stable COPD patients with and without bacterial colonisation

Variables	Colonised (n = 58)	Not colonised (n = 61)	P value
Sex, men, no. (%)	54 (93.1)	55 (90.2)	0.74
Age, years, mean (SD)	68.3 (8.3)	67.6 (9.8)	0.67
Current smokers, no. (%)	7 (12.1)	4 (6.6)	0.35
Smoking, pack-years, mean (SD)	46.7 (25.1)	34.2 (23.4)	0.006
Cardiovascular morbidity, no. (%)	22 (37.9)	20 (32.8)	0.23
Comorbid conditions, mean (SD)	1.06 (0.99)	0.61 (1.02)	0.025
Use of inhaled steroids, no. (%)	46 (79.3)	47 (77.1)	0.83
Symptoms, no. (%)			
Dyspnoea	56 (96.5)	58 (95.1)	0.72
Cough	44 (75.9)	56 (91.8)	0.024
Expectoration	57 (98.3)	58 (95.1)	0.62
Grade of dyspnoea, mean (SD)	1.78 (0.92)	1.15 (0.54)	<0.001
Exacerbations in the previous year, no. (%)			
Number			0.021
≤ 2	31 (53.4)	47 (77.1)	
> 2	27 (46.6)	14 (22.9)	
Requiring hospital admission			0.007
None	36 (62.1)	51 (83.6)	
≤ 1	16 (27.6)	10 (16.4)	
> 1	6 (10.3)	0	
Lung function tests, mean (SD)			
FVC, mL	2852.7 (979.1)	2710.9 (911.5)	0.41
FVC, %	70.5 (19.5)	66.7 (18.9)	0.28
FEV1, mL	1411.4 (511.7)	1380.0 (433.1)	0.72
FEV1, %	47.4 (15.2)	45.1 (13.1)	0.38
FEV1/FVC	50.4 (11.8)	52.6 (13.9)	0.43
Sputum analysis			
Colour, mean (SD)	2.94 (1.0)	1.56 (0.8)	<0.001
Pro-inflammatory cytokines, median (IQR) in pg/mL			
IL-1, n = 53	14 (4-432)	168 (49-758)	0.82
IL-6, n = 53	258 (76-653)	112 (33-368)	0.62
IL-8, n = 61	13480 (1335-43400)	5390 (252-14335)	0.27
TNF-alpha, n = 54	45 (20-94)	35 (10-183)	0.12

FVC = forced vital capacity; FEV_1 = forced expiratory volume in the first second;
IQR = interquartile range; IL=interleukin; TNF = tumour necrosis factor.

concentrations of pro-inflammatory cytokines, including interleukin-1 (IL-1), interleukin-6 (IL-6), interleukin-8 (IL-8), and tumor necrosis factor-alpha (TNF-alpha) were measured using quantitative sandwich immunoassay techniques in processed supernatants as previously described.[20]

Statistical analysis: Variables were presented as mean values and standard deviations, those not following a normal distribution were presented as median and interquartile range (IQR, 25th–75th percentile). Categorical variables were compared with the chi-square test and continuous variables with the Student's t test or the Mann-Whitney U test when data departed from normality. Following univariate analysis, variables were included in two stepwise logistic regression models constructed as exploratory analysis to identify independent risk factors for bronchial colonization and factors significantly associated with high bacterial load as opposed to low bacterial load and sterile sputum cultures. The variables included in the models were: age, gender, active versus ex-smoker, packyears of smoking, FEV1 (% predicted), degree of dyspnoea, color of sputum, cardiovascular comorbidity and number of exacerbations and hospitalizations the previous year. Bilateral two-tailed hypotheses were formulated and 95% confidence intervals (CI) were calculated. Statistical significance was set at $P < 0.05$.

Results: A total of 119 patients (92.5% men) with a mean (standard deviation, SD) age of 68.1 (9.1) years were studied. The clinical characteristics of these patients are reported in Table 1. Induction of sputum was necessary to obtain a valid sputum sample in only 5 cases (3 in one centre and 2 in the other). Bacterial colonization was demonstrated in 58 (48.7%) patients,

Table 4. Differences between colonised and non-colonised COPD patients according to bacterial load

Variables	High bacterial load (≥105) (n = 36)	Low bacterial load (<105) and not colonised (n = 83)	P value
Sex, men, no. (%)	33 (91.7)	76 (91.6)	0.98
Age, years, mean (SD)	68.6 (6.9)	67.7 (9.9)	0.63
Current smokers, no. (%)	6 (16.7)	5 (6)	0.086
Smoking, pack-years, mean (SD)	48.5 (22.5)	36.7 (25.2)	0.017
Cardiovascular morbidity, no. (%)	11 (30.6)	31 (37.3)	0.34
Comorbid conditions, mean (SD)	0.86 (0.99)	0.83 (1.02)	0.88
Use of inhaled steroids, no (%)	29 (80.6)	64 (77.1)	0.81
Symptoms, no. (%)			
Dyspnoea	36 (100)	78 (93.9)	0.66
Cough	25 (69.4)	75 (90.4)	0.007
Expectoration	36 (100)	79 (95.2)	0.31
Grade of dyspnoea, mean (SD)	1.86 (0.83)	1.28 (0.73)	<0.001
Exacerbations in the previous year, no. (%)			
Number			0.32
≤ 2	20 (55.6)	58 (69.9)	
> 2	16 (44.4)	25 (30.1)	
Requiring hospital admission			0.003
None	20 (55.6)	67 (80.7)	
≤ 1	11 (30.6)	15 (18.1)	
> 1	5 (13.9)	1 (1.2)	
Lung function tests, mean (SD)			
FVC, mL	2936.9 (975.7)	2712 (927.6)	0.23
FVC, %	71.9 (21.0)	67.1 (18.4)	0.21
FEV1, mL	1423.9 (536.5)	1382 (443.1)	0.66
FEV1, %	47.3 (15.9)	45.8 (13.4)	0.61
FEV1/FVC	48.9 (11.2)	52.7 (13.5)	0.15
Sputum analysis			
Colour, mean (SD)	2.97 (0.94)	2.01 (1.08)	< 0.001
Pro-inflammatory cytokines, median (IQR) in pg/mL			
IL-1, n = 53	47 (5-593)	29 (4-255)	0.14
IL-6, n = 53	134 (39-381)	169 (34-415)	0.18
IL-8, n = 61	8060 (460-31400)	4890 (201-15025)	0.09
TNF-alpha, n = 54	76 (11-269)	38 (11-71)	0.96

FVC = forced vital capacity; FEV1 = forced expiratory volume in the first second;
IQR = interquartile range; IL=interleukin; TNF = tumour necrosis factor.

2 in samples obtained by sputum induction. Results of sputum microbiology are shown in Table 2. Colonization by a single PPM was recorded in 50 patients. Eight subjects yielded more than one PPM in their sputum. Hemophilus influenzae and H. parainfluenzae made up 72% of all bacterial isolates.

There were significant differences in cigarette consumption, cough, dyspnea, comorbidities, COPD exacerbations and hospitalizations in the previous year, and sputum color between patients with and without bacterial colonization (Table 3). The distribution of colonized patients according to sputum color is presented in Figure 1. Samples with color 1 (white) were predominantly sterile, whereas in the samples with colors 3 to 5 (yellow to greenish) the prevalence of colonization was higher than 80%. Color number two (light yellow) was not discriminative between colonized and non-colonized.

When colonized patients were divided according to bacterial load, 36 patients had a high bacterial load (>105 CFU/mL) and the remaining 22 had a low bacterial load (≤105 CFU/mL). The characteristics of colonized patients with a high bacterial load (n=36) were compared with a group formed by non-colonized patients (n=61) and those with a low bacterial load (n=22) considered together (n=83). Statistically significant differences between the two groups in smoking (pack-years), cough, grade of dyspnoea, hospitalizations in the previous year and sputum color persisted when patients with high bacterial loads were compared with the remaining patients (Table 4). Sufficient

sputum for inflammatory analysis was available from only 61 subjects, all from spontaneous sputum. Sputum concentrations of inflammatory markers showed a great inter-individual variability and did not follow a normal distribution. There were no significant differences in sputum concentrations for any of the inflammatory markers analysed between patients with or without bacterial colonization (Table 3). The lack of significance persisted when patients with high bacterial load were compared with those with low bacterial load and not colonized. However, in this last comparison, patients with high bacterial load presented consistently (but not significantly) higher concentrations of all pro-inflammatory cytokines except IL-6 (Table 4).

The results of the multivariate analysis were very similar when identifying the factors significantly associated with the presence of PPMs or on classifying the population according to bacterial load. In both cases, only the degree of dyspnea and sputum color were significantly and independently associated with the presence of PPMs and with high bacterial load. Sputum color was a stronger indicator of the presence of positive cultures for PPMs than its load (Table 5).

Discussion

In the present study, bacterial colonization of the airways by PPMs, mainly H. influenzae and H. parainfluenzae, was reported in 49% of patients with stable COPD. This finding adds evidence to a high prevalence of bacterial colonization of airways in stable COPD reported by others.[4,5,9-12] Interestingly, our results using sputum samples are quite similar to those obtained in other studies with the use of the PSB technique or bronchial lavage for microbiologic assessment of the lower airways in COPD.[4,5,11,12,20,21] The possibility of sputum collection along a maximum of three monthly clinical visits and the use of the induced sputum technique in selected cases may have accounted for this high diagnostic yield of the sputum. However, most of our patients were able to produce a valid sputum sample for microbiological examination and induction of sputum was necessary in only 5 cases. A previous study by our group demonstrated that spontaneous and induced sputum yielded equivalent results in terms of frequency of bacterial colonization and species recovered.[22] A pooled analysis of data from studies that used PSB demonstrated that a PPM load ≥102 CFU/mL should be considered abnormal and allowed the estimation that at least one quarter of the patients with stable COPD were colonized by PPMs.[5] Furthermore, most patients with exacerbated COPD had concentration of PPMs >105.[4,5] Since there is no universally accepted cut-off for high bacterial load in sputum samples, a 105 CFU/mL concentration was used in our study.[4,8] With this value, 30% of our total population and almost two thirds of the colonized patients in our study had a high PPM load.

Bacterial colonization in our study was related to cumulative consumption of cigarette smoking, history of exacerbations in the previous year and sputum color. Exacerbations in the previous year leading to hospitalization were associated with increased bacterial load, although this relationship disappeared on multivariate analysis. In other studies, current smoking and severe airflow obstruction have been identified as predisposing factors for bacterial colonization in stable COPD.[11,12] However, we did not observe significant differences in lung function between colonized and noncolonized patients. The relationship between lung function and frequency of colonization is not clear, since a lack of association between FEV1 and colonization has also been observed in other studies[8,12,21,23] and may be due, at least in part, to the under-representation of mild patients in most series as well as in the current study. Interestingly, the only two factors identified in multivariate analysis to be significantly and independently associated with both presence of bacterial colonization and high bacterial load were a more severe degree of dyspnea and a darker color of sputum. The degree of dyspnea is a marker of severity of COPD and being a categorical variable with a wider distribution in our population probably contributed to its demonstrated association with colonization, in contrast to the severity of FEV1 impairment.

Regarding bronchial inflammation, it should be noted that we did not find increased sputum concentrations of pro-inflammatory cytokines in patients with bacterial colonization. Different reasons may explain this finding, including a small number of patients with valid samples for analysis, the inter-individual variability in the sputum concentrations of the cytokines was very large,[24] and there was a large number of patients with low bacterial loads. In fact, Hill et al[8] have demonstrated that markers of inflammation increased progressively with increasing bacterial load in patients with stable COPD. Consequently, when our colonized patients were categorized according to high or low bacterial load, besides the persistence of the clinical differences already observed between the colonized and non-colonized groups (ie, cigarette smoking, hospitalizations in the previous year, grade of dyspnea and sputum color) a non-significant trend towards higher sputum concentrations of inflammatory markers (except IL-6) was observed in patients with high bacterial load. Our results concur with previous observations regarding the lack of association between colonization and increased IL-6[9,10] but are discordant with other works showing significantly increased bronchial IL-8 and TNF-alpha in colonized patients, particularly with H.influenzae.[9,10,21,23,25] Therefore, our data, if confirmed in a larger sample of patients, would also suggest a dose-response relationship between bacterial load and bronchial inflammation and that a threshold of bacterial load might be necessary to elicit a significant inflammatory reaction in the airways[5,6,26] In contrast, Sehti et al[27] examined whether the increase in bacterial concentrations functions as a separate mechanism of exacerbation induction, independent of a new strain acquisition. In a prospective longitudinal cohort of COPD patients assessed during exacerbations and stable disease, sputum concentrations of pre-existing strains of H. influenzae and H. haemolyticus were not significantly different in exacerbation versus stable disease. Concentrations of M. catarrhalis and S. pneumoniae were even lower during exacerbations compared with stable periods. However, concentrations of new strains of H. influenzae and M. catarrhalis were increased during exacerbations, but the differences were small. These authors speculate that change in bacterial load was unlikely to be a major primary mechanism of exacerbation induction in COPD.[27,28]

This hypothesis is a matter of debate, because the interpretation of what a significant increase in bacterial load is when measured in a logarithmic scale is not clear,[10] and when transformed to a non-logarithmic scale, the differences in absolute bacterial counts were of a very high magnitude.[29]

The identification of bronchial colonization has clinical implications. Patel et al[9] demonstrated that the presence of lower airway bacterial colonization in stable COPD was significantly related to exacerbation frequency and severity. In the study of Rosell et al,[5] again high bacterial loads were associated

Table 5. Results of multivariate analysis of factors associated with presence of bacteria in sputum and with high bacterial load.

	OR	95% CI	P value
Factors associated with bacteria in sputum			
Degree of dyspnoea	2.63	1.53 – 5.09	0.004
Sputum colour	4.11	2.30 – 7.29	<0.001
Factors associated with high bacterial load as opposed to no bacteria and low bacterial load			
Degree of dyspnoea	2.01	1.17 – 3.46	0.012
Sputum colour	1.99	1.32 – 2.99	0.001

with exacerbation and showed a statistically significant dose-response relationship between bacterial load and exacerbation after adjustment for covariates. In our study colonized patients had significantly more exacerbations and hospital admissions the year previous to the study compared with non-colonized patients, but the significance disappeared on multivariate analysis. It should be taken into account that our study was neither designed nor powered to demonstrate differences in exacerbation or hospitalization rates between colonized and non-colonized COPD patients. Therefore, the identification of patients colonized by PPMs using a non-invasive and relatively inexpensive technique such as the analysis of sputum may play an important role in the management of severe and very severe COPD, particularly if intervention studies with antibiotics demonstrate improved clinical outcomes.[13]

To facilitate the diagnosis of bronchial colonization the use of a surrogate marker could be of interest. Purulence (color) of sputum graded by the investigator with a simple scale from 1 to 5 revealed significant differences in color between colonized and non-colonized patients. Patients with color 3 or higher (dark yellow to green sputum) had a prevalence of bacterial colonization greater than 80%. The relevance of sputum color has been already described and validated for exacerbated patients in which yellowish or greenish sputum is significantly associated with a bacterial exacerbation compared with white (non-bacterial) sputum[30,31] but the relationship between sputum color and bacterial colonization in stable COPD has deserved little attention.[8]

The present results should be interpreted taking into account some limitations of the study, particularly the small sample size may not have allowed determination of sputum concentrations of inflammatory markers in all samples, in most cases due to the small recovery of sputum that did not provide enough supernatant for the quantification of inflammatory mediators. The cross-sectional design did not allow the dynamics and time course of bacterial colonization and airway inflammation during exacerbations to be examined. Patients with negative bronchodilator test were included to exclude individuals with asthma who are less likely to be colonized, but the results may not be extrapolated to partially reversible COPD patients. High concentrations of PPMs in sputum samples, however, is a simple parameter that may help to select candidates to participate in antibiotic trials of stable COPD in order to demonstrate bacterial eradication and potentially prolong time to exacerbation.[6,32,33]

Conclusions

Almost half of a population of ambulatory moderate to very severe COPD patients carry PPMs in their airways. Colonized patients had more severe dyspnoea, and sputum color allows the identification of patients most likely to be colonized by PPMs.

References

1 Miravitlles M, Murio C, Guerrero T, Gisbert R: Pharmacoeconomic evaluation of acute exacerbations of chronic bronchitis and COPD. Chest 2002, 121:1449– 1455.

2 Donaldson GC, Seemungal TA, Bhowmik A, Wedzicha JA: Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease. Thorax 2002, 57:847–852.

3 Soler-Cataluña JJ, Martínez-García MA, Román Sánchez P, Salcedo E, Navarro M, Ochando R: Severe acute exacerbations and mortality in patients with chronic obstructive pulmonary disease. Thorax 2005, 60:925–931.

4 Monsó E, Ruiz J, Rosell A, Manterola J, Fiz J, Morera J, Ausina V: Bacterial infection in chronic obstructive pulmonary disease. A study of stable and exacerbated outpatients using the protected specimen brush. Am J Respir Crit Care Med 1995, 152:1316–1320.

5 Rosell A, Monsó E, Soler N, Torres F, Angrill J, Riise G, Zalacaín R, Morera J, Torres A: Microbiologic determinants of exacerbation in chronic obstructive pulmonary disease. Arch Intern Med 2005, 165:891–897.

6 Miravitlles M: Exacerbations of chronic obstructive pulmonary disease: when are bacteria important? Eur Respir J 2002, 20 (Suppl 36):1s–11s.

7 Papi A, Bellettato CM, Braccioni F, Romagnoli M, Casolari P, Caramori G, Fabbri LM, Johnston SL: Infections and airway inflammation in chronic obstructive pulmonary disease severe exacerbations. Am J Respir Crit Care Med 2006, 173:1114–1121.

8 Hill AT, Campbell EJ, Hill SL, Bayley DL, Stockley RA: Association between airway bacterial load and markers of airway inflammation in patients with stable chronic bronchitis. Am J Med 2000, 109:288–295.

9 Patel IS, Seemungal TA, Wilks M, Lloyd-Owen SJ, Wedzicha JA: Relationship between bacterial colonization and the frequency, character, and severity of COPD exacerbations. Thorax 2002, 57:759–764.

10 Wilkinson TM, Patel IS, Wilks M, Donaldson GC, Wedzicha JA: Airway bacterial load and FEV1 decline in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2003, 167:1090–1095.

11 Zalacain R, Sobradillo V, Amilibia J, Barrón J, Achótegui V, Pijoan JI, Llorente JL: Predisposing factors to bacterial colonization in chronic obstructive pulmonary disease. Eur Respir J 1999, 13:343–348.

12 Monsó E, Rosell A, Bonet G, Manterola J, Cardona PJ, Ruiz J, Morera J: Risk factors for lower airway bacterial colonization in chronic bronchitis. Eur Respir J 1999, 13:338–342.

13 Miravitlles M, Marín A, Monsó E, Vilà S, de la Roza C, Hervás R, Esquinas C, García M, Millares L, Morera J, Torres A: Efficacy of moxifloxacin in the treatment of bronchial colonization in COPD. Eur Respir J 2009, 34:1066–1071.

14 Sanchis J y Grupo de trabajo de la SEPAR: Normativa para la práctica de la espirometría forzada. Arch Bronconeumol 1989; 25:132–142
15 Pin I, Gibson PG, Kolendowicz R, Girgis-Gabardo A, Denburg JA, Hargreave FE, Dolovich J: Use induced sputum cell counts to investigate airway inflammation in asthma. Thorax 1992, 47:25–29.
16 Pizzichini E, Pizzichini MM, Efthimiadis A, Evans S, Morris MM, Squillace D, Gleich GJ, Dolovich J, Hargreave FE: Indices of airway inflammation in induced sputum: reproducibility and validity of cell and fluid-phase measurements. Am J Respir Crit Care Med 1996, 154:308–317.
17 Aaron SD, Angel JB, Lunau M, Wright K, Fex C, Le Saux N, Dales RE: Granulocyte inflammatory markers and airway infection during acute exacerbation of chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2001, 163:349–355.
18 Angrill J. Agustí C, de Celis R, Rañó A, Gonzalez J, Solé T, Xaubet A, Rodriguez-Roisin R, Torres A: Bacterial colonization in patients with bronchiectasis: microbiological pattern and risk factors. Thorax 2002, 57:15–19.
19 Cabello H, Torres A, Celis R, El-Ebiary M, Puig de la Bellacasa J, Xaubet A, González J, Agustí C, Soler N: Bacterial colonization of distal airways in healthy subjects and chronic lung disease: a bronchoscopic study. Eur Respir J 1997, 10:1137–1144.
20 Weinreich UM, Korsgaard J: Bacterial colonization of lower airways in health and chronic lung disease. Clinical Respiratory Journal 2008, 2:116–122.
21 Soler N, Ewig S, Torres A, Filella X, Gonzalez J, Xaubet A: Airway inflammation and bronchial microbial patterns in patients with stable chronic obstructive pulmonary disease. Eur Respir J 1999, 14:1015–1022.
22 Marin A, García M, Badorrey I, Sabrià M, Morera J, Monsó E. Spontaneous sputum production as a marker of bacterial colonization in stable COPD. Eur Respir J 2005; 26 (Suppl 49): abstract 232.
23 Sethi S, Maloney J, Grove L, Wrona C, Berenson CS: Airway inflammation and bronchial bacterial colonization in chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2006, 173:991–998.
24 Sapey E, Bayley D, Ahmad A, Newbold P, Snell N, Stockley RA: Interrelationships between inflammatory markers in patients with stable COPD with bronchitis: intra-patient and inter-patient variability. Thorax 2008, 63:493–503.
25 Bresser P, Out TA, van Alphen L, Jansen HM, Lutter R: Airway inflammation in nonobstructive and obstructive chronic bronchitis with chronic Haemophilus influenzae airway infection. Comparison with noninfected patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2000, 162:947–952
26 Bresser P, van Alphen L, Habets FJ, Hart AA, Dankert J, Jansen HM, Lutter R: Persisting Haemophilus influenzae strains induce lower levels of interleukin-6 and interleukin-8 in H292 lung epithelial cells than nonpersisting strains. Eur Respir J 1997, 10:2319–2326.
27 Sethi S, Sethi R, Eschberger K, Lobbins P, Cai X, Grant BJ, Murphy TF: Airway bacterial concentration and exacerbations of chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2007, 176:356–361.
28 Sethi S, Evans N, Grant BJ, Murphy TF: New strains of bacteria and exacerbations of chronic obstructive pulmonary disease. N Engl J Med 2002, 347:465–471.
29 Abusriwil H, Stockley RA: Bacterial load and exacerbations of COPD. Am J Respir Crit Care Med 2008, 177:1048–1049
30 Stockley RA, O'Brien C, Pye A, Hill SL: Relationship of sputum color to nature and outpatient management of acute exacerbations of COPD. Chest 2000, 117:1638–1645.
31 Soler N, Agustí C, Angrill J, Puig de la Bellacasa J, Torres A: Bronchoscopic validation of the significance of sputum purulence in severe exacerbations of chronic obstructive pulmonary disease. Thorax 2006, 62:29–35.
32 Wilson R: Using antibiotics to delay exacerbations of chronic obstructive pulmonary disease. Hot Topics Respir Dis 2006, 2:21–26.
33 Chodosh S: Clinical significance of the infection-free interval in the management of acute bacterial exacerbations of chronic bronchitis. Chest 2005, 127:2231–226.

History

The History of Respiratory Therapy, by Dennis Glover, details the evolution of respiratory therapy, from the earliest beginning of the inhalational practice of medicine, vapors, and aromatherapy around 6,000 BC. Its roots are in Egypt, China, India, and the Middle East. From there, it spread to Europe and the Americas. But only in the past one hundred years has the major evolution of respiratory therapy been realized. The book is available through Author House, "The History of Respiratory Therapy Discovery and Evolution," by Dennis W. Glover, glover688@comcast.net.

Patient receiving oxygen therapy with full face mask. Note humidifier and oxygen (FIO2) controller attached to regulator.

John Weisledder, RRT explaining iron lung, with volunteer in the iron lung. The iron lung is from 1947. Picture from the March of Dimes.

Pragel infant transport incubator, c. 1940.

Lavoisier in his laboratory performing respiratory physiology experiments, c. 1666.

Advanced Medical Life Support Procedures in Vitally Compromised Children by a Helicopter Emergency Medical Service

Bastiaan M. Gerritse, Annelies Schalkwijk, Ben J. Pelzer, Gert J. Scheffer, Jos M. Draaisma

Abstract

Background: To determine the advanced life support procedures provided by an Emergency Medical Service (EMS) and a Helicopter Emergency Medical Service (HEMS) for vitally compromised children. Incidence and success rate of several procedures were studied, with a distinction made between procedures restricted to the HEMS-physician and procedures for which the HEMS is more experienced than the EMS.

Methods: Prospective study of a consecutive group of children examined and treated by the HEMS of the eastern region of the Netherlands. Data regarding type of emergency, physiological parameters, NACA scores, treatment, and 24-hour survival were collected and subsequently analyzed.

Results: Of the 558 children examined and treated by the HEMS on scene, 79% had a NACA score of IV-VII. 65% of the children had one or more advanced life support procedures restricted to the HEMS and 78% of the children had one or more procedures for which the HEMS is more experienced than the EMS. The HEMS intubated 38% of all children, and 23% of the children intubated and ventilated by the EMS needed emergency correction because of potentially lethal complications. The HEMS provided the greater part of intraosseous access, as the EMS paramedics almost exclusively reserved this procedure for children in cardiopulmonary resuscitation. The EMS provided pain management only to children older than four years of age, but a larger group was in need of analgesia upon arrival of the HEMS, and was subsequently treated by the HEMS.

Conclusions: The Helicopter Emergency Medical Service of the eastern region of the Netherlands brings essential medical expertise in the field not provided by the emergency medical service. The Emergency Medical Service does not provide a significant quantity of procedures obviously needed by the paediatric patient.

B.M. Gerritse is with the Department of Anaesthesiology, Amphia Hospital, Breda; Schalkwijk is with the Department of Epidemiology, Biostatistics and Health Technology Assessment; Pelzer is with the Department of Social Science Research Methodology; Scheffer is with the Department Anesthesiology, Pain and Palliative Medicine; and Draaisma is with the Department of Paediatrics, Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands.

Background

Advanced Life Support (ALS) for the pre-clinical management of vitally compromised children consists of endotracheal intubation and ventilation, intravenous or intra-osseous access with fluid replacement and administration of medication. The purpose of on-site advanced interventions is to stabilise the patient before transport to the hospital. These procedures are expected to reduce physiological deterioration, and thus to reduce mortality. However, this has never been proven on the basis of evidence. One of the confounding factors could be the (lack of) experience and the training required to perform the advanced interventions in a pre-clinical setting.

The Helicopter Emergency Medical Service (HEMS) was introduced in the Netherlands to provide optimal pre-clinical care for trauma patients by the Dutch government. The HEMS, consists of a physician (anesthesiologist or trauma surgeon), a flight nurse and a pilot/driver. When the HEMS became operational, the Emergency Medical Service (EMS) frequently asked for assistance in stabilizing vitally compromised children. There were no pediatric HEMS data available in the Netherlands, research in other countries could not be easily extrapolated due to the international differences in HEMS and EMS organisations. However, there was a necessity to characterize the children involved to ameliorate HEMS and EMS care. The objective of this study was to evaluate the advanced medical interventions performed by the EMS and the HEMS in vitally compromised children, and to examine how often the HEMS provided additional medical care which was not or could not be provided by the EMS.

Methods

Prospective cohort analysis of all HEMS calls for all paediatric emergencies for which the HEMS in the eastern part of the Netherlands (HEMS Netherlands-East) was called out, in the years 2001 to 2009. Only children under the age of 16 on the day of the emergency call were included. Approval from the ethical board of the Radboud University Nijmegen Medical Centre was obtained prior the onset of the study.

The HEMS Trauma Region Netherlands-East covers one of the four HEMS regions in the Netherlands, and covers an area of about 10,088 square kilometres in the eastern part of the Netherlands with 4.5 million inhabitants. Approximately 19.5% of

Table 1. NACA Score

Score Level	Patient status	Necessary intervention
I	Slight injury or illness	No medical intervention
II	Moderately heavy injury or illness	Ambulatory medical treatment
III	Heavy, but not life threatening injury or illness	Stationary medical treatment
	Heavy injury or illness, life threat cannot be	
IV	excluded	Emergency medical measures
V	Acute mortal danger	Emergency medical measures
VI	Acute cardiac or respiratory arrest	Emergency resuscitation
VII	Death	

The National Advisory Committee for Aeronautics (NACA) developed a simple scoring system for patients receiving air transport during the Vietnam War.[2]

the population in this area is under 16 years of age. The HEMS is called out either by the EMS dispatch centre (primary call) or by the EMS at the incident location (secondary call). The helicopter was active from January 2001 until September 2006 in daylight, and a physicians car was available during night and adverse weather. From September 2006 until today the helicopter crew is equipped with night vision goggles and fully operational 24 hours each day by helicopter. The physicians car is still available for foggy weather, and incidents close to the HEMS base (<10 kilometers).

HEMS physicians have received additional, extensive training (more than six months) in adult and pediatric emergency care, pain management and extrication techniques. The registered data include age, sex, type of incident, physiological parameters (respiratory rate, heart rate, blood pressure, capnography), Glasgow Coma Scale (GCS), the pre-hospital treatment given, diagnosis in the emergency ward and survival until 24 hours after hospital admission.

All data was recorded in an electronic patient data management system, custom made for the HEMS. The results were transferred into a data sheet (Excel, Microsoft Seattle, USA), after which all data underwent statistical analysis and graphical depiction with SPSS Statistics 16.1 (SPSS Inc, Chicago, IL). Pearson chi square was used for statistical comparisons, significance was defined as $p < 0.05$. Since the tables contain one or more cells with zero frequency, the exact significance of the obtained Chi square value was used instead of the asymptotic approximation.

Results

The HEMS had 803 calls involving children. In all cases the EMS was the first to arrive at the incident location. The average flight time of the HEMS was 9,6 minutes, ranging from 1 to 31 minutes. The time from HEMS alert to take-off of departure from the vehicle was an additional 2-5 minutes. Of these 803 calls, 245 (27%) were cancelled by the EMS before the arrival of the HEMS (199 children had normal physiological parameters, 27 children died and 19 calls were for other reasons). The HEMS examined and treated 558 children on scene with a mean age of 6.9 years (SD 5.3). Of these 558 children, 390 (70%) children had a trauma-related emergency and 168 (30%) children a non-trauma-related emergency. Of the children involved 115 (20.6%) had NACA scores of I-III, and 443 (79.4%) had NACA scores of

Table 2. Paediatric HEMS incident according to initial EMS call

Initial HEMS call	Incidents	Mean age (age range)	GCS (SD)	% 24-hour survival
	n	Years		
1. preclinical childbirth/neonatal	29	0.1 (0-0.25)	7 (5)	79
2. congenital	14	4.9 (0.25-15)	4 (2.4)	29
3. infectious	27	2.0 (0.25-15)	6 (2.8)	67
4. convulsions	18	3.4 (0.4-15)	7 (3.8)	94
5. asphyxia	35	5.5 (0.1-14)	10 (5.0)	71
6. CPR general (non-neonatal)	45	4.9 (0.1-15)	5 (5.7)	49
7. Near-drowning	40	4.3 (0.6-15)	7 (3.8)	80
8. Burns	12	4.5 (0.2-11)	13 (4.6)	50
9. Pedestrian versus motor vehicle	60	8.1 (0.2-15)	9 (5.0)	85
10. Cyclist versus motor vehicle	67	11.3 (0.3-15)	8 (4.7)	90
11. Passenger in motor vehicle	88	8.2 (0.3-15)	12 (4.9)	91
12. Moped	30	13.3 (1-15)	11.2 (5.3)	97
13. Fall	55	6.7 (0.3-15)	11.7 (4.7)	95
14. Equestrian	14	10.7 (4-15)	7.9 (5.2)	100
15. Other	24	7.5 (0.4-15)	12 (5.4)	92
Total	**558**	**6.9 (0-15)**	**8.9 (5.0)**	**83**

Table 3. Transportation of patients

	n	NACA I-III@	NACA IV-VII@
No transportation, dead on scene	64	0	64
Ambulance, with HEMS physician	273 20	253	
Ambulance, without HEMS physician	118 95	23	
Helicopter transport because of distance to hospital 25 0	25		
Helicopter transport because of condition of patient 76 0	76		
Interhospital transfer 2 0	2		

@NACA groups: Pearson chi square $p < 0.05$

IV-VII (medical cases 11% versus 89%, trauma cases 25% versus 75% respectively). (Pearson chi square $p < 0.05$). The youngest group of children (<1 year) had the relatively highest percentage of NACA scores IV to VII. (Figure 1).

Nine percent of all children were given cardiopulmonary resuscitation in the field (with a 24-hour survival rate of 26%). Ninety-five (17%) children died in the first 24 hours after the incident, of which 64 were at the incident location. The emergency types with above-average mortality were all the non-trauma emergencies (except convulsions), near-drownings and burns. The emergency type "congenital" includes all congenital disorders: cardiac, pulmonary or metabolic in a group of children with a wide variety of ages. The age range varied widely in the

Table 4. Pre-hospital medical procedures

Restricted to HEMS		HEMS more experienced	HEMS	EMS
	n		n	n
Hypnotics*	147	Unsuccessful endotracheal intubation®	0	20
Muscle relaxants#	146	Successful endotracheal intubation®	214	66
Chest tube	5	Peripheral venous canula	272	304
Central venous line	12	Intraosseous access	68	31
Hypertonic fluid&	104	Intraosseous access and CPR	19	27
Antibiotics∀	26	Pain management**	149	45
Physician transfer	376	Medication for ALS⊥	109	28
Venous cutdown	2			
Total	818		831	521

* Hypnomidate, midazolam, propofol, s-ketamine (hypnotic dose)
\# Suxamethonium, rocuronium
& Mannitol, hyperhaes
∀ Cefazolin, ceftriaxon
** Fentanyl, Alfentanyl, locoregional anaesthesia, s-ketamine (analgetic dose)
⊥ Amiodarone, atropine, dobutamine, epinephrine
® Successful versus unsuccessful endotracheal intubation: Pearson chi square p< 0.05

trauma related HEMS indications (Table 2). Of the 494 children who were transported from the incident location, 103 children (21%) were transported by helicopter. Children transported by ambulance without the HEMS physician had a significantly lower NACA score (Table 3).

A total of 1,649 advanced medical procedures were provided by the HEMS to the 558 children, an average of 3.0 procedures per child (table 4). Advanced medical procedures (n=818) restricted to the HEMS were given to 65% (n=365) of the children. Medical procedures (n=831) for which the HEMS is more experienced than the EMS were provided to 78% (n=438) of the children (Table 4). In 482 children (86%) a medical procedure from one or both of these groups was performed by the HEMS.

A medical procedure in which the HEMS is more experienced than the EMS is endotracheal intubation. EMS paramedics arriving at the incident location before the arrival of the HEMS intubated 86 children, with a success rate of 77% (n=66). A part

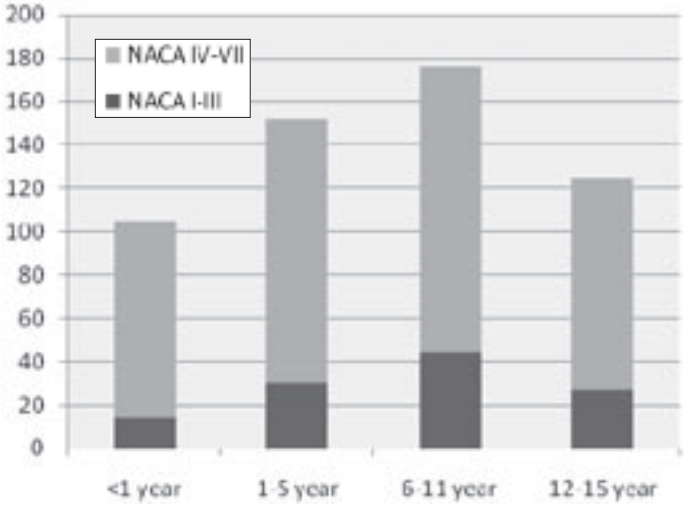


Figure 1. Age-dependent distribution of NACA scores, differentiated according to numbers of infants (<1 year), toddlers (1-5 years), schoolchildren (6-11 years), adolescents (12-15 years). Pearson chi square p<0.05

of these children have been further described in a previous publication by these authors. In twenty of these 86 children an emergency correction of the endotracheal tube or ventilator settings was performed by the HEMS upon arrival: oesophageal intubation (n=13), inappropriately sized endotracheal tube without cuff making positive pressure ventilation impossible (n=5) and potentially lethal ventilator settings (n=2) (>300% of recommended ventilator settings). The HEMS intubated 214 children with 100% success. Successful intubation was defined as symmetrical breath sounds by auscultation, and a positive mainstream capnography, followed by mechanical ventilation with normal airway pressures. These measures only partially eliminate the presence of bronchial intubation, but would make it more rare. An acknowledged and corrected primary esophageal intubation by HEMS was registered as a success. Oxygen saturation was often difficult to register during the medical intervention, and the fall of saturation was not registered during the endotracheal intubation. In cardiopulmonary resuscitation without any capnography reading, the endotracheal intubation was confirmed by repeat laryngoscopy. The difference in the number of successful endotracheal intubations by the EMS and the HEMS is significant (Chi square p <0.05). Twelve percent (n=39) of the children with a GCS >7 were intubated by the HEMS (compromised airway, pain management or to facilitate transportation by helicopter).

Intraosseous access was obtained in 99 children, 68 by the HEMS and 31 by the EMS. Eighty-seven percent (n=27) of all children provided with intraosseous access by the EMS were in cardiopulmonary arrest, versus 28% (n=19) in the HEMS group.

Pain management was given to 35% (194/558) of the children. The medication of choice was fentanyl or alfentanyl, occasionally lidocaine for infiltration anesthesia and levobupivacaine for peripheral nerve blocks. The youngest child provided with pain management by an EMS paramedic was four years old; by the HEMS two months old. No detrimental effects of the pre-clinical application of analgesics were recorded.

Discussion

There are no studies that show convincingly that a physician-

based EMS leads to a decrease in overall mortality or morbidity of pre-clinically treated patients. However, in those patients requiring advanced airway management or other invasive procedures, as well as fluid management and pharmacotherapy, adding a specialist physician to the pre-hospital emergency care can increase survival and improve outcome.

The children in this study who were examined and treated by the HEMS constitute a particularly compromised group. Nine percent of all children were given cardiopulmonary resuscitation in the field (with a 24-hour survival rate of 26%). Eich described 2,271 pediatric emergencies in a comparable study on EMS and HEMS in Germany. In this study, 72.7% of the children had a NACA score of I-III and 27.3% had a NACA score of IV-VII (versus 20.6% and 79.4% respectively in our study). (Pearson chi square $p < 0.05$). This discrepancy may be caused by profound differences between the Netherlands and Germany in the pre-clinical emergency care for vitally compromised children, due to differences in infrastructure, dispatching protocols, geography or training of EMS. Still, the conclusions stated in the study of Eich are even more valid to the HEMS in the Netherlands. The HEMS in our study encounters a high incidence of paediatric emergencies in children, therefore "...skills in paediatric airway management, cardiopulmonary resuscitation and intraosseous canulation in all age groups are essential..."

The youngest patients have the highest NACA scores. Certain causes of a preclinical vital threat occur only in early childhood, like unexpected childbirth and duct-dependent congenital heart disease. Other causes of life-threatening events, like sepsis, convulsions and near-drowning, occur especially in toddlers and younger children. These life-threatening events have a low rate of survival in this study. As advanced life support procedures are considered to be more difficult in younger children, special training in these cases should be provided for optimal performance of the HEMS. As shown in the age range variation in table 2, young children can be involved in any kind of trauma incident.

The number of 20 failed intubations or lethal ventilator settings is unacceptably high. The rate of failed endotracheal intubations by the EMS-paramedics has relatively diminished in the last years of this study in comparison to our previous publication on this subject. The reasons for this trend are unknown, still any not-recognized esophageal intubation can have catastrophic consequences.

It has been clearly shown that experience is crucial for successful preclinical endotracheal intubation. A far better option for the paramedics in the EMS would be the maintenance of oxygenation by bag-valve-mask ventilation until the arrival of an HEMS or arrival in the emergency ward. Theoretically, there are clear advantages to preclinical endotracheal intubation: facilitation of artificial ventilation, protection against aspiration, facilitation of transport by helicopter. This should, however, never compromise the application of supplemental oxygen and adequate ventilation.

Intraosseous access is recommended in vitally compromised children if intravenous access is difficult or impossible, and can also be effective in adults. As intraosseous access by EMS-paramedics is predominantly used in children in cardiopulmonary arrest, a potentially large group of vitally compromised children were left without this useful device. The HEMS in this study did provide intraosseous access to children outside the CPR group. Although the EMS paramedics are trained in intraosseous access, it is not widely applied: only 31% of all intraosseous access was provided by the EMS paramedics. The infrequent use of intraosseous infusion compared to other advanced life support skills in hospital and by paramedics and HEMS has been described. Still, several studies have shown that the placement of an intraosseous line is easy, fast and has a high success rate.

The number of children who needed pain medication but did not receive it from the EMS is high: 77%. No child under the age of four years (eg the burn victims) received any pain medication from the EMS. The safe delivery of adequate analgesia is a priority in pre-hospital care; ketamine is relatively safe when used by physicians. In a review by Thomas, clear evidence supporting the safety of pre-hospital analgesia was provided. Pain relief can be improved in an EMS or HEMS by balancing the desire to do no harm, and the unacceptable fact of allowing needless suffering. This clearly calls for additional education and standards to improve pre-clinical pain management. The potential fear of the EMS of causing ventilatory depression has to be addressed.

There are several limitations to this study. Due to the nature of the health care provided, a blind prospective study was not feasible. The added value of adding a HEMS to the EMS was quantified by the number of medical procedures, with special attention for the procedures for which the EMS is neither certified nor experienced. There was no follow-up after 24 hours of admission, so actual survival until hospital discharge was unknown. The reason for this was the transportation of patients to hospitals out of the primary HEMS region.

Conclusion

The HEMS of the eastern part of the Netherlands provides essential additional medical expertise not provided by the EMS. The only formal pediatric indication for HEMS at this moment is the pediatric cardiopulmonary resuscitation. This study calls for a lower threshold for HEMS activation in any serious incident involving children, preferably based on the type of primary emergency call.

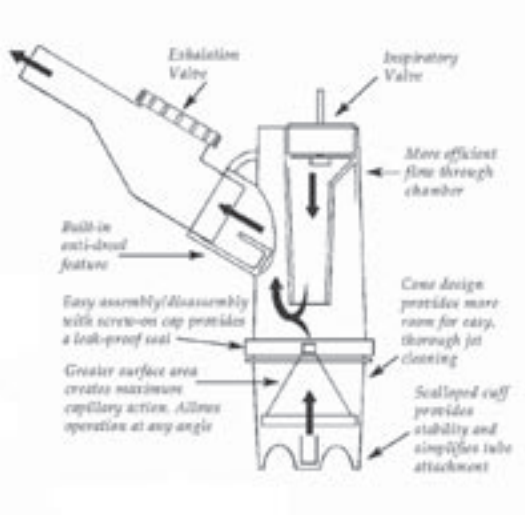
Sixty-five percent of the vitally compromised children received a preclinical medical procedure restricted to a physician, 78% received a medical procedure for which a physician was more experienced. The majority of all patients encountered by the HEMS had a NACA score of IV-VII. As the younger patients had a higher NACA score, special attention should be given to training and the provision of advanced life support procedures for younger children.

Successful endotracheal intubation and subsequent appropriate ventilation in children is a difficult task for EMS paramedics; preclinical endotracheal intubation of children calls for an experienced physician. The use of intraosseous access devices and the use of analgesics by EMS paramedics could be improved. Further investigation into the pre-hospital care for vitally compromised children is necessary.

IT LOOKS DIFFERENT BECAUSE IT IS DIFFERENT

One glance at Salter's NebuTech® HDN® design tells you that it is truly in a class by itself.

- Delivers a high density 50cc bolus on inspiration
- Faster Treatment Times
- Improved Outcomes
- Greater Versatility
- Eliminate Concurrent Therapy
- Eliminate Missed Treatments



Optional Disposable Filter Set:

- Reduces second hand aerosol exposure
- Exhalation filter minimizes occupational exposure
- Filters 99.56% of exhaled particles
- Attaches easily to existing one way valves on the NebuTech® HDN® nebulizer

For complete information, contact your Salter representative or call **1-800-235-4203**

Quality Care Begins With Quality Products
www.salterlabs.com

SALTER LABS®

cobas®

Life needs answers

Now you won't have to do backflips to meet regulatory compliance.

Why? Because the **cobas b** 221 blood gas analyzer:

- ☑ Is the only analyzer with FDA 510(k) clearance for pleural fluid pH testing
- ☑ Provides innovative and reliable IT solutions for remote control, patient data management and QC reporting
- ☑ Features an extensive, labor-saving AutoQC® module with automatic lot-to-lot comparisons
- ☑ Offers eQAP, online CEU programs and remote troubleshooting capability

To find out more, contact your Roche Diagnostics representative or call 800-428-5076.

Roche Diagnostics

http://us.labsystems.roche.com

Breathing circuit management takes time away from what really matters, the patient. Introducing OSMO™, a universal solution that allows for maintenance-free water removal from the expiratory limb during mechanical ventilation. An innovative approach to reducing circuit condensation, OSMO allows you to provide optimal humidification without significant clinician intervention.

To put it simply, OSMO manages condensate… so you don't have to.

TIRED OF?

draining condensate… water in the ventilator… interrupting ventilation… replacing filters… emptying water traps… depressurizing circuit spray… cross-contamination…

Visit teleflexmedical.com to learn more

OSMO: Maintenance Free Water Removal

Tel: 866.246.6990 Intl: 919.544.8000 **www.teleflexmedical.com**

Teleflex MEDICAL