


Volume 6 Number 1 February-March 2011

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The Journal of Pulmonary Technique



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The Journal of Pulmonary Technique

Vol. 6 No. 1
February-March 2011

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Editorial

Ventilation: Shaggy Dog Stories

“If you take a dead animal and blow air through its larynx, you’ll fill its bronchi and watch its lungs attain the greatest distention.” So said the Roman physician Galen, offering the world the first description of mechanical ventilation. It wasn’t until 1908 that George Poe demonstrated the first mechanical respirator by asphyxiating dogs and bringing them back to life. But more on that later. The real history of mechanical ventilation began with the iron lung, a negative-pressure ventilator put into wide use during the polio epidemics of the early 20th century. The Drinker respirator came first in 1928, improved on by John Haven Emerson in 1931. Other forms of ventilation also have also cycled through their first and last gasp, including biphasic cuirass ventilation (not completely gone), the rocking bed, and primitive positive pressure machines. In 1949, Emerson and Harvard developed a mechanical assister for anesthesia. In the UK, an early model used a windshield wiper motor to drive its bellows. But employed in combination with flammable anesthetics, electrical motors were in danger of exploding in the operating room.

Modern positive-pressure ventilators are based on technical developments by the military during World War II to supply oxygen to fighter pilots in high altitude. In 1952, Roger Manley developed a gas-driven ventilator – much safer. A recrafted version drew on incoming gas to lift weighted bellows which rose and fell with gravity, forcing gases into the patient’s lungs, and its pressure could be carried by sliding a weight atop the bellows. A curved slider adjusted gas volume, and residual pressure was configurable. Thus positive pressure ventilation had fully arrived.

But what about that dog? On May 29, 1908, the New York Times published an article, “Smother Small Dog to See It Revived.* According to the Times: “An audience of thirty men and three or four women attended a demonstration of George Poe’s machine for producing artificial respiration in Brooklyn. They all applauded enthusiastically when the demonstrator, Dr William Harrison of Guadalajara, Mexico, smothered a small yellow dog gathered from the street and revived it by means of the respiration machine. The audience watched with eager attention the convulsive twitchings of the dog’s muscles and leaned forward when one of the assistants lifted the limp body to show that no sign of life remained. Finally, the machine did its work and the victim was brought back to life, although the little dog staggered as it tried to walk.” The machine’s inventor, Dr Poe was said to be a second cousin of Edgar Allen Poe, who did his own share of staggering. George Poe’s machine took thirty years to develop, and he got the idea when he saw a relative revive within two hours of the time set for his burial. To prepare for the dog demo, a small boy had been hired for a quarter and told to go out in the street and find a dog.

Laszlo Sandor, Associate Editor

*The New York Times article has been considerably edited. Information above is from Wikipedia and other sources.



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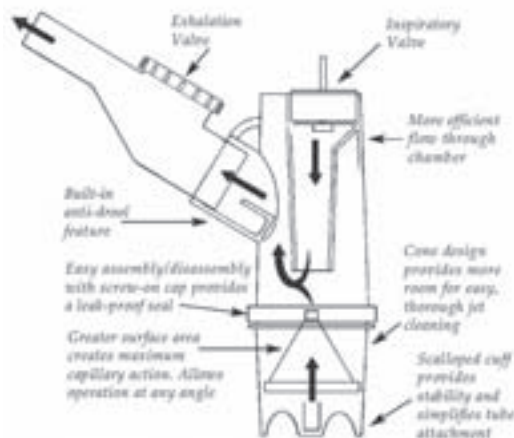
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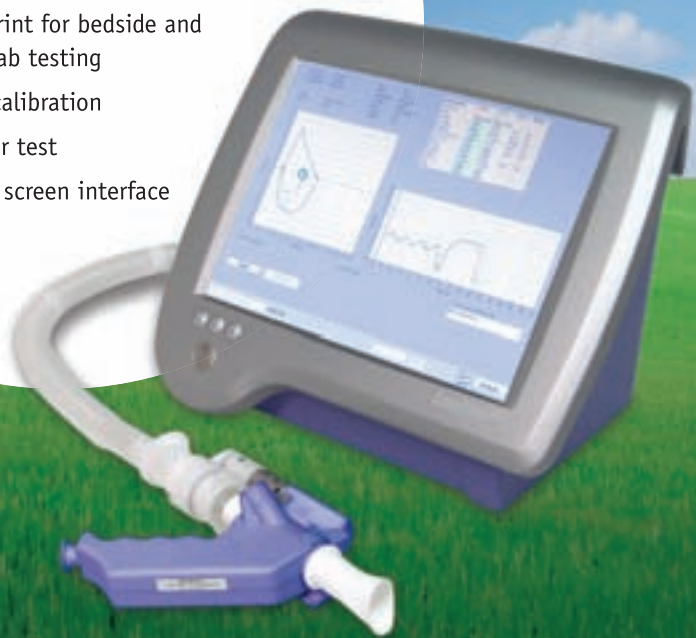
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News

□ February-March 2011

CORRECTION

The author of the article, "The Use of Non-Invasive Ventilation on COPD Patients" on page 29 of the October-November, 2010 issue is Michael Murray, MD.

SNOOZE ALARM

In our last issue we reported that nurses are moving into anesthesiology (see WAKE UP CALL.) The gist of the piece was that anesthesiology can be effectively provided by nurses, not necessarily by anesthesiologists, and that these nurses don't need a lot of supervision. Countering the argument, Douglas Farrago, MD, writes in *Placebo Journal*: "Forget the fact that an anesthesiologist has eight years of training after college, must complete a four-year clinical residency, and must pass several written and oral exams for certification, while a nurse anesthetist has about three years of training and must pass one three-hour certification exam. A bigger issue is the tension this will cause. What was meant as a relationship built on collaboration turns into one of competition. This is happening or has happened with nurse practitioners and nurse midwives as well. The attorney representing the CRNAs stated that this change 'ensures that California can continue to provide access to critical anesthesia services, particularly in rural areas.' Remember that line. It is the same line used by all the organizations trying to get solo privileges. In five years, you will see how few CRNAs will go into the country with the rural folk. This is about money not about access... The bottom line is that the training is not the same. And what seems like a good idea, practicing independently, I predict will lead to some bad blood which is not good for anyone." To read and subscribe to *Placebo Journal*, visit placebojournal.com.

BMC NEWS

Allergy, Asthma and Clinical Immunology has published the research articles from the Canadian Society of Allergy and Clinical Immunology Annual Scientific Meeting 2010. BioMed Central reported that its Open Access Week 2010 was celebrated by almost 900 participants in 94 countries, making it the most successful Open Access Week yet. October also recorded the biggest increase per month in OA mandates across funders, research institutions and universities, all showing support for OA publishing. In conjunction with its journals *Genome Biology* and *Malaria Journal*, BioMed Central hosted the conferences *Beyond the Genome* and *Parasite to Prevention* to mark the event. Open Access Africa, another OA Week 2010 initiative, ran from 10-11 November.

RISK IT

In a paper published in the journal *Anesthesiology*, a Cleveland Clinic-led research team announced the development of The Risk Stratification Index, developed using more than 35 million Medicare and Medicaid records, then validated on more than 100,000 patients at the Cleveland Clinic. The researchers used billing and procedure codes to develop an objective and

transparent system which allows for outcomes to be compared across institutions and among individual physicians. Cleveland Clinic worked with Covidien on interpreting the data for the Risk Stratification Index. The validity of the Index was confirmed by applying it to more than 100,000 Cleveland Clinic records. The system is statistically stable to as few as 5,000 patients. The investigators have put their Risk Stratification Index in the public domain; any entity can use it freely. Contact clevelandclinic.org or covidien.com.

E-BOOK, FROM US!

Respiratory Therapy has published its premiere full-length e-book, *Respiratory Therapy Ventilation 2011*. VENTILATION is the first in a series of comprehensive knowledge resource books that we plan to publish. It is now available from Amazon for download onto Kindle, iPad, PCs and other compatible e-readers. VENTILATION includes more than 200 pages of up-to-date papers about ventilation from renowned clinicians, researchers and scientists. The articles in this electronic textbook have been carefully selected and culled by Respiratory Therapy's editors for relevance to the readers of this journal. VENTILATION 2011 is the premier edition in an ongoing series, and will be updated each year, with the second edition, *Ventilation 2012*, to be available in December. The cost of this valuable educational and informational resource book is only \$29.99. To order, go to Amazon.com and type: *Respiratory Therapy Ventilation 2011*.

WHO'S YOUR DOCTOR?

The *Placebo Journal* reported: As per the *Wall Street Journal*, "health insurers are doing whatever they can to lower their costs... They are not talking about lowering premiums but instead are finding a way to keep their profits up." The *Placebo Journal* suggested: "check out how they are co-opting the newest and most ridiculous fads of accountable care organizations, quality performance payment plans and patient centered medical homes... Aetna's chief medical officer said, 'We're insinuating ourselves more and more in the actual care of the patient.'" *Placebo Journal* commented: "My god, they think they are the doctors now." The *Placebo Journal* is a humor magazine for doctors. Contact placebojournal.com for a newsletter or magazine subscription. You won't be disappointed.

ERS CONFERENCE NEWS

Online resources are available for ERS BARCELONA, including e-communications, abstracts, and webcasts. There are 600 sessions to choose from. Early bird registration is open for ERS/ESR International Sleep & Breathing Conference, coming this spring, in Prague. ERS also reported in its electronic bulletin: High fever and chills in patients presenting with pneumonia may be a good sign, according to a recent Swiss study. The findings suggest a better long-term prognosis for those patients suffering from pneumonia who exhibit more pronounced pro-inflammatory responses reflected by chills, high body temperature and high peak levels of the inflammatory blood marker C-reactive protein (CRP). In addition, a new serum biomarker, adrenomedullin, may be useful in identifying high-risk patients. ERS co-sponsored a symposium in the Indian Himalayas 3,500 meters up the mountain – a good spot, organizers said, for ERS's "Recent trends and future perspectives in high-altitude pulmonary research." Forty-five scientists from all over, and 75 from India, came to debate, schmooze, and hear from experts about new discoveries in high-altitude research likely to have an impact on the future of respiratory medicine. Contact ersnet.org.

AEROSOLIZED INFLUENZA

Aerosol transmission of influenza is possible, according to doctors in Hong Kong. Nine patients developed influenza A on a general ward in a Hong Kong hospital. The cause was traced to a patient who received non-invasive ventilation and was moved to the ward. His bed was next to the outflow jet of an air purifier, which blew the air across the ward. The tainted air caused a major nosocomial outbreak. According to physicians at the hospital, the spatial distribution of affected patients was consistent with the aerosol mode of transmission.

WHO KNEW?

Many people don't know the signs of lung cancer, according to a UK survey by the Royal Pharmaceutical Society, which interviewed 2,000 adults. Only 33% said that a persistent cough could be a warning sign. The actual warning signs are: a persistent cough or one that changes or gets worse, recurring chest infections, breathlessness, coughing blood, lethargy, weight loss, chest or shoulder pain, hoarseness or muteness, or sudden swelling of the face or neck. The authors added that not only smokers get lung cancer. Information is from Medical News Today.

OFFRAMP

Living near a freeway may be associated with increased risk of autism, according to a study published by a team of researchers from Children's Hospital Los Angeles, the Keck School of Medicine of the University of Southern California and the UC Davis MIND Institute. According to the study, children born to mothers living within 309 meters of a freeway appeared to be twice as likely to have autism. The study is the first to link exposure to vehicular pollutants with autism risk. Children between the ages of 24 and 60 months at the start

of the study who lived in communities around Los Angeles, San Francisco and Sacramento were matched to the autism cases by age, gender, and broad geographic area. The study examined the locations where the children's families' lived during the first, second and third trimesters of their mothers' pregnancies, and at the time of the baby's birth and looked at the proximity of these homes to a major road or freeway. The association between autism and freeway proximity was not altered by adjustment for gender, ethnicity, education, maternal age, or prenatal smoking. The emerging evidence that oxidative stress and inflammation are involved in the pathogenesis of autism supports the findings of this study.

SMOKE 'EM IF...

Seven major airport hubs still have smoking areas, according to a report by the CDC. Twenty-nine large airports, which account for about 70% of air passenger traffic, were smoke free. The largest airports that have smoking areas are Hartsfield-Jackson Atlanta, Dallas/Fort Worth, and Denver. About 80% of airports have outdoor smoking areas. Reported by Christian Nordqvist in Medical News Today.

GOOD MOVE

Taking cough and cold medicines for children under four out of stores has led to a decrease in overdoses, according to the CDC. Pharmaceutical companies stopped marketing cough and cold meds to kids about three years ago, because they typically contain decongestants and antihistamines. The researchers, using a large database, found that emergency room visits of under-two-year-olds dropped from 2,800 to 1,250. Nonetheless, the authors noted, two-thirds of ED visits are linked to cough and cold medications, and the total visits in the study period stayed about the same. The authors posited that unsupervised

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ingestion was the culprit. Information for the above was written by Christian Nordqvist, copyright Medical News Today.

NO SENSE

Stella Fitzgibbons, MD, reports to the Placebo Journal (placebojournal.com): “Recently, an asthma patient came to our free clinic – it seems she went to the local ER recently with pneumonia and was told the only way she could avoid hospitalization (and huge bills) was to take Levaquin. The bill? Over \$300. She found two family members with the discount cards we get at the clinic, borrowed money from neighbors and finally was able to buy the stuff. (Yes, I called the ER and gave them holy hell for prescribing Levaquin when Cipro would have cost her \$4 at WalMart). But what if this lady needs more than the rescue inhaler she can buy for \$9? The book says it’s standard of care to use steroid inhalers – does anybody know of one that costs less than \$30 a month? How about Singulair, \$136 wholesale for a month’s supply... Let’s stop dissing the Canucks and Brits for their two-tiered healthcare system. At least the people on their bottom tier get their meds, even if they’re not the latest heavily advertised ‘me-too’ drug.”

AUTOIMMUNITY

COPD may be caused by auto-antibodies, according to researchers in Spain, who found that a significant number of patients with COPD had five to ten times the amount of auto-antibodies as control subjects. Therefore, the researchers said, the pathogenesis of COPD involves an auto-immune component. The researchers tested blood samples for ANA, AT, AMA, LKM, SMA and PGC antibodies, as well as levels of C-reactive protein. Thirty-four percent of COPD patients had abnormally high levels of ANA titer-a prevalence, 11 times higher than seen in the control group, and 7 times higher than reported in healthy subjects in previous studies. Twenty-six percent were positive for AT, 4.5 times higher than controls. Patients with AT were typically younger, and smokers. The researchers said their studies and future studies could usher in new therapies like immunomodulators. Information is from Medical News Today, copyright Medical News Today.

FACE TO FACEBOOK

Logging into Facebook caused a guy to suffer asthma attacks, according to a report in the Lancet, as reported by Medical News Today. In fact, the man logged on to a specific page with the pictures of his ex girlfriend, then proceeded to hyperventilate. Though the swain had been deleted, erased, and defriended, he contrived to see her posts through a fake identity. On seeing her photo, he hyperventilated, and kept on doing it through repeated viewings. His mom contacted a doctor, who asked her to measure his peak expiratory flow before and after his Facebook adventures in melancholy. The post-Face value showed a variability of more than 20%. When he laid off the site, his problem disappeared. The authors said, “social networks could be a new source of psychological stress, representing a triggering factor [for asthma.]” See “Facebook: a new trigger for asthma?” in The Lancet. Information is from Medical News Today, written by Christian Nordqvist, copyright Medical News Today.

PRODUCTS

GOING GREEN AND MORE

Masimo recently debuted product enhancements to its Radical-7 and Patient SafetyNet, and presented a clinical review of real-

world use of the SafetyNet. A new clinical study offered results of Masimo’s Acoustic Respiration Rate technology (Accuracy of Acoustic Respiration Rate Monitoring in an Acute Nursing Unit, Jim Kumpula, Respiratory Care, Swedish Medical Center, Seattle, WA.) In other Masimo news, Kaiser Permanente recently converted its entire health system of 37 hospitals to Masimo oximetry technology, via Masimo Rainbow SET Pulse CO-Oximetry. Masimo is also actively going green. The company’s ReSposable Sensor solution has helped hospitals reduce sensor waste by more than 90%. The ReSposable Sensor system combines features of the LNOP, RNCS and Rainbow sensors into a design that allows the portion of the sensor that connects to the patient cable to be used on multiple patients, while the portion that attaches to the patient is used only once before disposing. The sensors measure hemoglobin, oxygen content, PVITM for fluid responsiveness, and methemoglobin, as well as oxygen saturation, perfusion index, and pulse rate – at a savings of 50% compared to single patient adhesive Rainbow sensors. In line with Masimo’s Green Initiative program, as part of Masimo’s manufacturing process, sensor and device packaging is made from 100% recycled material where applicable, cardboard waste is recycled, confidential documents are shredded on-site and recycled. Also recycled are batteries, CRTs and LCD displays, electronics, fluorescent lamps, metals and cables, plastic housings, and drink containers. The company is in the process of implementing ISO 14001 in its California facilities. Contact masimo.com.

DANNY TIES

The new Danny Ties tracheostomy holder from B&B Medical minimizes skin irritation under the collar and offers a softer and more comfortable fit around the patient’s neck. Danny Ties securely hold the artificial airway in place while maximizing comfort for infant, pediatric and adult patients. Danny Ties are made of a soft, absorbent cotton that lays smooth at the edges of the collar and significantly minimizes skin breakdown beneath the collar. Available in three sizes, the contoured collar holds its shape, does not fold in half around the neck and does not stretch when it absorbs moisture. The patent-pending design of the Danny Ties evenly distributes the padded collar material around the neck to minimize pressure points on the skin. The Danny Ties collar is easy and quick to apply, and is hypoallergenic and latex-free. If soiled, the Danny Ties may be washed, dried and reused for the same patient for up to 28 days, per institutional policy. Also available from B&B Medical Technologies are the Sil.Flex Stoma Pad and TrachStay, which may be used in combination with the Danny Ties. Sil.Flex Stoma Pads enhance patient comfort with all brands and styles of tracheostomy tubes. The TrachStay prevents accidental disconnects from the ventilator circuit. Contact www.BandB-Medical.com.

LAB NAVIGATION

The Illumination Webinar Series recently presented Navigating Laboratory Regulations and Implementing Quality Measures: Strategies to Enhance Patient Safety. It featured Sharon Ehrmeyer, PhD, MT(ASCP), Professor, Pathology and Laboratory Medicine, University of Wisconsin, and Mario Plebani, MD, FRCPath, Professor, Clinical Chemistry and Clinical Molecular Biology, and Chief, Department of Lab Medicine, University Hospital of Padova, Italy. The program covers the importance of lab and POC accreditation, quality requirements of ISO, CAP, JCI for accreditation; identification of opportunities to reduce errors and optimize quality assurance through accreditation, the role of technology and automation in reducing medical errors, and risk

management strategies to optimize patient safety. Contact www.ilus.com/illuminations.

SPECIAL DELIVERY

O2Delivery.net is a directory service enabling oxygen dependent patients and their caregivers to locate resources and services critical to their care, whether they are at home or traveling. The interface uses large, easy to read fonts. A very simple search form and geographical mapping display combine to create a frustration-free end-user experience. When the user initially goes to the site the system will display all the geographically relevant listings for selected services within twenty miles of the user's location. O2delivery.net also serves as a professional directory for oxygen providers, with geolocation markers, contact information and clear door-to-door directions from any listing, providing an invaluable resource to assist patients when they travel or relocate. O2delivery.net is in an advertising partnership with SeQual Technologies, Inc. Contact O2delivery.net.

NEW PLATFORMS

Covidien announced that three new platforms for its Puritan Bennett 840 ventilator – the Puritan Bennett 840 Neonatal ventilator, the Puritan Bennett 840 Universal ventilator and the Puritan Bennett 840 Pediatric-Adult ventilator – are now available in the United States. The Puritan Bennett 840 Neonatal ventilator helps clinicians safely deliver, manage and monitor a ventilation regimen tailored for even the smallest and most critically ill neonatal patients. It offers the ability to set a tidal volume as small as 2 mL for neonates weighing as little as 300 grams without having to change to another ventilator. The Puritan Bennett 840 Universal ventilator for every patient type, from neonatal to adult, includes a neonatal CPAP mode that enables clinicians to flexibly deploy noninvasive ventilation in neonates. It supports patient-ventilator synchrony, which has been shown to facilitate spontaneous breathing. The ventilator includes features that effectively match the patient's respiratory demand and adapt to changes in patient condition. The Puritan Bennett 840 Pediatric-Adult ventilator for pediatric to adult patients helps clinicians provide improved levels of ventilatory support by offering multiple therapies of ventilation, including invasive and noninvasive methods, as well as more advanced modes of ventilation.* [* Xirouchaki N, Kondili E, Vaporidi K, et al. Proportional assist ventilation with load-adjustable gain factors in critically ill patients: comparison with pressure support. *Intensive Care Med.* 2008; 34(11):2026-

2034; Alotaibi G, Kacmarek R, Scanlan C. Comparison of dual mode ventilation among selected adult critical care ventilators using a programmable lung simulator. *Respir Care.* 2004. (Abstract).]

WEB ENHANCEMENT

A new website featuring a wide range of acute and non-acute medical care products that has been upgraded to better serve hospitals and distributors is being introduced by Dale Medical Products, Inc of Plainville, MA. The new Dale Med-Surg Products Website for acute and non-acute care products is organized into three sections: "hospital," to provide education and product support; "distributor," to describe product issues; and a third one for home users to address product availability. Featuring

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SIL.FLEX™
STOMA PAD
Comfort for tracheostomy patients



BABI.PLUS™
BUBBLE PAP VALVE
0-10 CM H₂O
Focus on patient care, not the device



DANNY TIES™
Unique tracheostomy holder minimizes skin irritation under the collar



www.BandB-Medical.com

a new product spotlight section, this new website has a link to “Perspectives in nursing” which gives clinicians the latest information updates and the ability to earn CEUs sponsored by Dale. The Dale Med-Surg Products Website for acute and non-acute care products provides in-service videos for clinicians, showing how products are used. Standard website features include a search capability along with literature downloads and information about conferences where Dale will be exhibiting. Dale’s products include Foley catheter holders, abdominal binders, tracheostomy tube holders, and more. Contact dalemed.com.

TWO FROM SMITHS

The babyPAC emergency and transport ventilator from Smiths Medical is MRI compatible and allows for precise oxygen concentrations. Its variable gas mixing system extends cylinder life and allows precise selection of oxygen concentration. Calibrated inspiratory pressure control provides continuous adjustment of the end inspiratory pressure. Separate controls provide careful management of inspiratory/expiratory time and pressure to suit patient breathing requirements. It has four operating modes: CMV+PEEP; CMV+ Active PEEP, IMV+CPAP and CPAP. Adjustable pneumatic pressure relief with alarm provides a wide range of options. Dual function PEEP/CPAP control allows continuous adjustment of pressure... The PneuPac VR1 emergency ventilator offers a single control for setting the frequency and tidal volume, including a clock-stop setting at the recommended adult position. This portable ventilator enables rapid setup in demanding circumstances. Auto/manual controls, a patient demand system, MR compatibility, and other features provide the means to manage respiratory emergencies. Its oxygen powered unit eliminates the need for electricity. Linked manual controls allow it to be used in a variety of chest compression and ventilation options in cardiac life support. MR compatibility provides maximum flexibility for transport within the hospital. Contact smiths-medical.com/pneuPac.

eVent-FUL

eVent Medical announced that it will begin additional manufacturing of its Inspiration ventilators in the United States. The company chose California as the locale in order to access medical manufacturing resources, and “because of the beautiful weather,” said eVent CEO Kirk Inoue. eVent ventilators have a patented Swiss pneumatic design, are clinician-friendly, and employ a touch-screen graphic user interface, as well as graphic monitoring and trending software. The company is a division of Kobayashi Medical America, LLC. Contact event-medical.com.

GET SMART

Inspired Technologies, Inc, developers of SmartDose Auto-Adjusting technology, announced the availability of the SmartDose Mini+ Personal Oxygen Portable. In a lightweight (under 1 pound) package, the SmartDose Mini+ offers superior oxygen delivery, improved saturation rates, and batteries that last up to one year. The Mini+, and all SmartDose portables, feature state-of-the-art technology which allows the unit to continuously monitor the patient and auto-adjust the amount of oxygen delivered as the patient’s needs change, continually matching oxygen dose to exertion level. The Mini+ offers the added benefit of a unique valve system that allows patients to use the device up to 1,000 hours on one set of standard alkaline batteries. SmartDose Oxygen Dosing Systems, available in both gas and liquid versions, deliver the ideal balance of saturation and conservation, provide clinicians and HME dealers with vital,

patient-specific information, and improve the quality of life for people suffering from COPD. Contact smarterO2.com.

DICK TRACY

Nonin Medical, Inc announced the release of its second-generation wrist-worn pulse oximeter, the WristOx2, Model 3150. Engineered with Nonin’s PureSAT SpO₂ technology, the WristOx2, Model 3150 is the most versatile wrist-worn pulse oximeter available with proven accuracy in the widest range of clinical settings and challenging patient conditions such as motion and low perfusion. Ideal for daily activity monitoring to overnight study applications, the WristOx2, Model 3150 is a compact, wireless monitoring solution that delivers dependable readings in overnight oximetry and ambulatory settings. Featuring a new ergonomic design and large screen size, patients will enjoy increased comfort and ease of use, as well as greater independence due to the addition of Bluetooth wireless technology. The WristOx is built on a single platform to serve both standalone and OEM applications, replacing the WristOx 3100 and 4100 module. Performance upgrades to the WristOx2, Model 3150 include: increased connectivity with USB and Continua Certified Bluetooth technologies for real-time data transmission, enhanced non-volatile memory to ensure data won’t be lost during power loss or battery change, and up to 48 hours of battery life on two AAA batteries. Contact nonin.com.

VENT UPDATE

Early use of the Passy-Muir Valve with ventilator dependent patients has been shown to have many clinical and cost-savings benefits, including improved patient outcomes, improved quality of life, and expedited weaning. A visit to Passy-Muir’s website offers a variety of information. Linda Dean, RRT answers common questions about in-line ventilator application of the Passy-Muir Valve. Her answers provide insight into ventilator adjustments and therapeutic techniques to increase patient comfort and success. Passy-Muir recently completed a series of two Live Special Event Webinars featuring guest speakers and a variety of tracheostomy topics. These webinars were so well-received that the recordings are being offered as self-study courses for free CEUs. Currently there are 7 core self-study webinars. To register, contact passy-muir.com/ceu. Also featured on Passy-Muir’s website is a report about Madonna Rehabilitation, a long term acute care (LTAC) and rehabilitation facility located in Lincoln, NE, that has become a referral site for adult and pediatric patients. The facility uses the Passy-Muir Valve to expedite weaning and assess communication, voice, swallowing, and ability to manage secretions. Lastly, Passy-Muir has created a smaller version of its very popular anatomical model, Tracheostomy T.O.M. The new Pocket T.O.M. is ideal for hands-on demonstration, training for skills necessary for tracheostomy care, and discussion of tracheostomy and nasogastric tube placement issues. Contact passy-muir.com.

ON TRIAL

Pharmaxis announced significant results of pooled data from its two large scale six month Phase III trials of Bronchitol (inhaled mannitol) in people with cystic fibrosis. The two studies encompassed 643 patients from 11 countries. Over the 26 weeks of the two studies, patients treated with Bronchitol had an average 7.3% improvement in lung function (FEV1) compared to baseline and a highly significant improvement compared to patients in the control group. In the sub group of patients who were also on rhDNase, patients taking Bronchitol showed a 5.3% improvement from baseline, that was again

superior to the control group. In the sub group of patients who were not on rhDNase, patients taking Bronchitol showed a 9.44% improvement. The overall rate per annum reduction in exacerbations for patients on Bronchitol versus those on control was 25% (NS) and the number of patients experiencing an exacerbation was 29% lower for those taking Bronchitol (NS). This result was achieved in a well treated patient population who overall had a very low rate of exacerbations in the study. Overall adverse events on Bronchitol were similar to those experienced on control with 7% of patients taking Bronchitol withdrawing due to adverse events compared to 4% of patients on control. There was no increase in the numbers of bacteria present in the lungs. The most commonly reported adverse event related to treatment was cough, occurring in 6% of the Bronchitol group and 3.3% of the control group.

TIE ONE ON

One of the most frightening events of any ventilator dependent patient is an accidental ventilator circuitry disconnection. Pepper Medical offers a solution with its Vent-Straps (Product #403) trach tube holder with anti-disconnect straps (patent pending). The product is disposable and latex-free. Contact pepper-medical.com.

REDUCED MORTALITY

A recent analysis showed that the Novartis drug TOBI was associated with reduced mortality in cystic fibrosis patients. A review of data from a Cystic Fibrosis Foundation study showed a 21% mortality reduction in patients treated with TOBI, which is a widely used inhaled antibiotic for treating *P. aeruginosa*. The analysis of 12,740 US patients looked at whether they used

TOBI in any given year, and assessed the likelihood of mortality in the following year. The mortality reduction was especially apparent among patients who used TOBI every year. The analysis included patients aged six years and older with predicted FEV1 of 25-75% and four or more Pa cultures. Contact pharma.us.novartis.com.

DON'T HOLD YOUR BREATH

The Asthma Inhaler Holder is a form-fitting plastic case or holster for commonly used asthma inhalers that can be worn on a chain around the neck or clipped to a belt or inside of a handbag. The intent of this device is to make the inhaler more convenient to carry and to provide instant accessibility to the asthma sufferer or those with COPD, emphysema or other breathing conditions. It is an L-shaped lightweight durable injection-molded thermoplastic and has a hinge along the back side of the vertical leg of the "L" which opens to receive the inhaler. The Asthma Inhaler Holder comes in a variety of colors and eye-catching designs for younger users. Contact inventionpublicity.com or sellidea.com.

NEW MODULE

Roche announced the US introduction of the cobas e 602 analyzer, the latest addition to the cobas 8000 modular analyzer series for diagnostic labs with high-volume workloads. Labs will now be able to combine this new immunoassay module with two existing clinical chemistry modules to create an integrated platform with 24 unique system configurations to match their specific testing needs. The cobas e 602 module uses Roche's patented electrochemiluminescence (ECL) technology and includes more than 50 assays on its initial test menu. It offers a

VENTILATION is here. Respiratory Therapy's eBook, *Ventilation 2011* is now available for download from **Amazon.com**.

VENTILATION is the first in a series of comprehensive knowledge resource books from the publishers of Respiratory Therapy. It is now available from Amazon for download onto Kindle, iPad, Sony, PCs and other compatible e-readers.

VENTILATION includes 47 up-to-date papers about ventilation from renowned clinicians, researchers and scientists. The articles in this electronic textbook have been carefully selected and culled by Respiratory Therapy's editors for relevance to the readers of the journal – healthcare providers specializing in respiratory therapy.

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The cost of this valuable educational and informational resource book is only \$29.98. To order, go to Amazon.com and type:

Respiratory Therapy Ventilation 2011

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*Amazon content shown



throughput of up to 170 immunoassay tests per hour and when combined with the existing clinical chemistry modules. Ten unique configurations are available, which offer a throughput of 3,670 to 7,970 tests per hour. The cobas e 602 module is also available in 4 immunoassay-only configurations, which offer a throughput of 170 to 680 tests per hour. Contact roche.com.

GETTING SLEEEEPY

The Philips Respiroics System One sleep therapy platform features a host of innovative technologies and features that improve both the patient and provider/clinician experience: reduced sound levels, dual modes with remote switching, improved humidity output and control, mask fit and seal monitoring, easy night-time viewing, enhanced filtration design, 15 mm tubing option, and multilingual display. Reduced sound levels are achieved with WhisperSmart technology. Dual modes include bi-level and CPAP capabilities that can be switched between modes. Contact philips.com.

AGREEMENT

Roche and Medical Automation Systems, Inc (MAS) announced that they have signed an agreement under which Roche will acquire all MAS's assets associated with the RALS point-of-care information IT connectivity system, as well as the names "Medical Automation Systems," "MAS" and "RALS." As part of the transaction, Roche expects to retain substantially all of the MAS employees. MAS's RALS POC IT connectivity system is used in over 2,000 hospitals in the US. Contact roche.com.

VERSO VERSION

CareFusion announced the launch of the Verso 90 adapter, a component that enables uninterrupted access to a ventilated patient's airway without having to disconnect the patient from the ventilator. The new Verso 90 adapter is part of the AirLife Closed-Suction System, which is different from traditional closed-suction catheters because of its modularity. With this system, a clinician can change catheters or perform various airway access procedures through a single port without having to disconnect the patient from the ventilator. Clinicians also have the ability to replace the closed-suction catheter independent of the adapter, which may only need to be replaced when the ventilator circuit is changed. Contact carefusion.com.

SENTRY DUTY

CareFusion announced the launch of SentrySuite, a new set of software applications that improve the quality of patient data and increase clinician productivity and efficiency in pulmonary and cardiopulmonary diagnostic settings. The software focuses on data, organization, workflow and connectivity. SentrySuite runs on the CareFusion Jaeger and SensorMedics diagnostic devices. The SentrySuite software is backwards-compatible, allowing clinicians to transfer historical patient records to the new platform and complete patient data comparisons and trend analysis. The SentrySuite platform offers unlimited user access and user preference entry screens, animated operator coaching and guidance in real time during testing, disease classification and one single diagram that captures the quality of the diagnostics measurement performed on the patient. Contact carefusion.com.

NOTHING TO SNORE AT

Salter Labs offers an extensive line of sleep diagnostic products including: The BiNAPS Nasal Airflow Pressure and Snore Transducer, a wide array of *Salter-Style* Sleep Diagnostic

Cannulas, the ThermiSense Oral/Nasal Thermal Airflow Sensing System and cannula/holders, PneumoTHERM disposable and reusable thermocouples and unique and inexpensive SnoreTAC Snore sensing Adapters for use during patient titration. Recent changes to AASM guidelines call for both nasal pressure and oral/nasal thermal airflow sensing. Salter Labs has developed a solution to this with their ThermiSense and BiNAPS products. The concurrent use of Salter Labs' BiNAPS Nasal Airflow Pressure and Snore Transducer with its ThermiSense Oral/Nasal Thermal Airflow Sensing System or PneumoTHERM disposable and reusable Thermocouples allow sleep professionals to easily and inexpensively meet the new AASM guidelines requiring both nasal pressure and oral/nasal thermal airflow sensing. All of Salter Labs' sleep diagnostic products can be used in the hospital, in sleep labs, or during home testing and are specifically designed to function with most of the PSG systems available. Contact salterlabs.com.

ACQUISITION

RoundTable Healthcare Partners, a healthcare industry private equity firm, has acquired a majority interest in Salter Labs, which was founded in 1976 by Peter Salter. Salter is a manufacturer of disposable respiratory and sleep diagnostic products for homecare and acute care markets. Salter is RoundTable's first platform investment. It manages \$1.9 billion in capital. More info can be found at roundtablehp.com. Salter Labs develops, manufactures and sells single-use, disposable products for homecare and hospitals, and holds 31 patents, with numerous patent applications pending. Contact salterlabs.com.

SPOTLIGHT ON NEBULIZERS

GOING SOLO

The Aeroneb Solo nebulizer delivers silent drug delivery for infants through adults. Using the patented OnQ nebulization technology, the Aeroneb Solo creates a fine particle, low velocity aerosol optimized for deep lung deposition. Aerosolizing a broad range of formulations, the Aeroneb Solo maintains drug integrity as it does not heat, degrade or shear medications. Convenience is a key factor of this nebulizer, operating for both intermittent and continuous nebulization. The Aeroneb Solo does not effect ventilator parameters and can be refilled without interrupting ventilation, making its ease of use second to none. Contact aerogen.com.

SPOTLIGHT ON CAPNOGRAPHY

PORTABLE

The Oridion Capnostream 20 portable capnography bedside monitor enables effective, proven airway management by providing the earliest indication of airway compromise. The Capnostream 20's superior Microstream measurement technology provides an accurate and reliable assessment of a patient's breathing quality, whether intubated or non-intubated. The Capnostream 20 utilizes Oridion's newest Smart Capnography innovation – the Integrated Pulmonary Index (IPI). IPI improves clinical utility with a simple, clear and comprehensive indication of a patient's ventilatory status and trends, facilitating easier communication among clinicians. The IPI algorithm utilizes real time measures and interactions of four parameters (etCO₂, respiration rate, pulse rate, and SpO₂) to provide a single indexed value, enabling clinicians to instantly assess the patient's

ventilatory status sooner than the value of any of the four parameters individually. The Capnostream 20 also features the SARA (Smart Alarm Respiratory Analysis) alarm management algorithm, which recent studies have shown reduces clinically insignificant alarms by up to 80 percent. Contact oridion.com.

SAFETY FIRST

The Smart CapnoLine Guardian from Oridion, Inc is a new upper airway management system for breath sampling that significantly improves patient safety before, during, and after upper endoscopic and ultrasound procedures. The Guardian is highly efficient, simplifying work flow and providing optimal reliability of respiration rates and ventilatory status. Utilizing patented sampling technology, the Guardian's specialized cannula delivers continuous nasal and oral etCO₂ readings. Its unique design accepts a 60F dilator and allows oxygen delivery up to 10L/min without diluting the CO₂ sample. The Guardian's enhanced design greatly reduces the drag on endoscopes during the procedure, protecting them from damage. For denture wearers, a Gum Comfort Pad provides a gentle cushion for the patient and a more secure bite block fit for the physician. The CapnoLine Guardian is comfortable, easy to put on the patient, stays in place, and maintains exceptional scope maneuverability and stability, enhancing the patient experience and improving clinical outcomes. Contact oridion.com.

VENTILATION ROUNDTABLE

Bunnell Incorporated

Tell us about your ventilation products.

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. Jet pulse technology, passive exhalation, and an adjustable I:E ratio makes this high-frequency uniquely effective.

What is the scope of your company's current R&D efforts?

Sound reduction technology for the "**WhisperJet**" patient box continues to be a focus for R&D. The most recent sound reduction upgrade has lowered the sound output from 56 to 41 dBA. Bunnell is awaiting approval for a 3.0-mm LifePort Jet ET tube adapter and we continue to make incremental improvements in the reliability and durability of the Life Pulse High-Frequency ventilator.

What types of training and services support do you offer?

The Bunnell Hotline is by far the most valuable and effective service we offer our customers. Clinical specialist with years of clinical and technical experience answer questions 24/7 to support patient care efforts and minimize downtime. Bunnell has developed a three booklet pocket reference set that explains *what* high-frequency ventilation is, *why* the Life Pulse is uniquely effective, and *how* the Life Pulse is used to care for patients. These booklets provide a concise yet thorough overview of the Life Pulse. The Life Pulse HFV Training DVD contains a complete in-service video, a patient management video, an alarms and troubleshooting video, and more. It contains the information needed to understand how the Life Pulse works and how it should be used. The DVD is organized into chapters so clinicians

can focus in on the information that is most important to them. All of these training materials and much more are available on the Bunnell website at bunl.com.

Discuss the use of your products in various venues: ie hospitals, homecare, etc.

The Life Pulse HFV is used exclusively in the NICU & PICU environment to support critically ill infants.

Covidien

Tell us about your ventilation products.

Acute Care Ventilation: The **Puritan Bennett 840 Neonatal** ventilator helps clinicians safely deliver, manage and monitor a ventilation regimen tailored for even the smallest and most critically ill neonatal patients. It offers the ability to set a tidal volume as small as 2 mL for neonates weighing as little as 300 grams without having to change to another ventilator. The **Puritan Bennett 840 Universal** ventilator for every patient type, from neonatal to adult, includes a neonatal CPAP mode that enables clinicians to flexibly deploy noninvasive ventilation in neonates. It supports patient-ventilator synchrony, which has been shown to facilitate spontaneous breathing. The ventilator includes features that effectively match the patient's respiratory demand and adapt to changes in patient condition. The **Puritan Bennett 840 Pediatric-Adult** ventilator for pediatric to adult patients helps clinicians provide improved levels of ventilatory support by offering multiple therapies of ventilation, including invasive and noninvasive methods, as well as more advanced modes of ventilation.*

Portable Ventilation: Available in the United States, the **Puritan Bennett 540** portable ventilator is a quiet, lightweight ventilator that can be powered by a lithium-ion battery that provides up to 11 hours** (depending on settings and other factors) of power. A real-time battery life indicator displays remaining battery life in hours and minutes, instead of as a percentage of charge. This significant technical advancement eliminates guesswork about when the ventilator needs to be connected to a power source for recharging. The portability, long battery life and ease of use of the Puritan Bennett 540 ventilator enable a ventilator-dependent patient to pursue daily activities with confidence and peace of mind, ultimately enhancing quality of life. Available in Europe, the **Puritan Bennett 560** ventilator is designed for patient comfort, safety and maneuverability. Its lithium-ion battery provides up to 11 hours of power for extended time away from a power source. A real-time battery life indicator shows the remaining charge in hours and minutes and eliminates guesswork about when the ventilator needs to be recharged. A car adaptor also provides additional security when the patient is away from home. The Puritan Bennett 560 ventilator tracks patient data, which is essential for the clinician. The clinician can easily transfer data from the ventilator to a computer using a USB memory device. Data such as patient compliance, trend data and detailed waveforms can be analyzed using the Puritan Bennett Respiratory Insight software. Additionally, by using DAR filters with the Puritan Bennett 560 ventilator, patients can reduce the risk of transmission of airborne microorganisms that can cause respiratory illness. The filters help block the inhalation of infectious agents and also help prevent germs from being exhaled into the environment, lessening the risk to family members and caregivers.

Discuss the use of your products in various venues; ie hospitals, homecare, etc.

Healthcare providers and patients throughout the world depend on Covidien for state-of-the-art ventilation therapy. Whether healthcare provider's needs include acute care for critically ill patients with chronic respiratory failure or a solution to transition patients to homecare, Covidien has the right system for the task at hand. Healthcare professionals know all too well the range of issues that impact ventilation outcomes today. At Covidien, our innovations are systematically tackling the issues that truly matter—patient safety, healthcare efficiency and medical efficacy.

Tell us about the latest technological advances pertaining to your products.

The three new Puritan Bennett 840 Ventilator platforms, for neonates, pediatric-adult and the universal technology, provide clinicians with more flexible ventilation options than ever before. Covidien is committed to answering the needs of patients and clinicians in today's complex healthcare environment through advanced technologies and innovations.

[*Xirouchaki N, Kondili E, Vaporidi K, et al. Proportional assist ventilation with load-adjustable gain factors in critically ill patients: comparison with pressure support. *Intensive Care Med.* 2008; 34(11):2026-2034; Alotaibi G, Kacmarek R, Scanlan C. Comparison of dual mode ventilation among selected adult critical care ventilators using a programmable lung simulator. *Respir Care.* 2004. [Abstract]. **Fully charged battery at room temperature, set to $V_t=200$ ml (± 5 ml), PIP=10 cmH₂O (± 2 cm H₂O), R_{tot}=15 bpm. Level adjustments, environmental conditions and physiological characteristics of the patient affect battery life. Note: COVIDIEN, COVIDIEN with logo, the Covidien logo and *positive results for life* are US and internationally registered trademarks of Covidien AG. Other brands are trademarks of a Covidien company. Velcro is a trademark of its respective owner. © Covidien.]

Dräger

Tell us about your ventilation products.

Dräger offers specialized ventilation platforms for intensive care, neonatal care, chronic care, and noninvasive therapy. These ventilators are designed specifically to meet the wide-ranging needs of community hospitals as well as tertiary care centers. The current ventilator line includes our flagship product the **Evita Infinity V500**, a universal ventilator that can be utilized in the neonatal, pediatric, and adult critical care areas, and the **Babylog VN500** neonatal-specific ventilator that can perform both pressure and volume ventilation. Both of these devices received 510(k) clearance in April 2010. Our **Carina** ventilator provides both invasive and noninvasive ventilation and is well suited for areas outside of the ICU.

What is the scope of your company's current R&D efforts?

Dräger is constantly investing in R&D efforts with a goal of improving patient outcomes and facilitating efficiencies for healthcare professionals. Approximately 7% of revenues are dedicated to research and development – the Evita Infinity V500, the Babylog VN500, and the release of a new adjunct known as “Auto-Release” during APRV are examples of this commitment. The “Auto-Release” feature automatically adjusts the T_{low} based on the desired percent of peak expiratory flow to be retained.

Through customer feedback, Dräger has provided a customizable interface that can match the monitoring needs of the most critical patients as well as those requiring less diagnostic bedside care. Understanding how clinicians use our equipment to help improve patient outcomes gives us greater insight and inspiration to advance technology into the future.

What types of training and services support do you offer?

Dräger has a dedicated team of clinical applications specialists and ventilation sales executives, most of whom are respiratory therapists who work closely with customers to realize the current trends in respiratory care. This team provides on-site education (which is approved by the American Association for Respiratory Care for continuing education credits) and regional seminars that are open to all. Clinicians also have access to our newly released series of clinical workbooks on non-invasive ventilation, modes of ventilation nomenclature, protective lung ventilation, and spontaneous breathing. Dräger also continues to work cooperatively with Intensive Care On-Line Network (ICON) to provide customers with 24/7 access to online education, monthly webinars, and other clinical references 365 days a year. This coverage was recently extended to provide state-of-the-art support services to all Dräger ventilation customers. This enhanced clinical support gives clinicians the freedom to access information and continuing education at their convenience and provides the department manager with an online tool to view staff's educational progress.

Discuss the use of your products in various venues; ie hospitals, homecare, etc.

Dräger offers a wide range of ventilation products for the hospital setting that are designed to meet specific needs at many points of care. The Evita Infinity V500 is a highly advanced ventilation unit well-suited for use in acute care facilities and university medical centers. The V500 offers a complete array of invasive and non-invasive ventilation modes for adult, pediatric, and neonatal patients. Pulmonary monitoring and diagnostic tools featured in the user interface help to provide the clinician with a complete assessment at the bedside. Dräger's Babylog VN500 is an integrated ventilation solution for neonatal and pediatric patients and provides a comprehensive and dedicated mechanical platform for the special care nursery as well as the pediatric intensive care areas. Advanced new ventilation modes and options, such as Volume Guarantee (VG) and Mandatory Minute Ventilation (PC-MMV[®]) extend the clinician's therapeutic capabilities by offering an entire spectrum of modern neonatal ventilation therapy in a single device. With an internal battery, patients receive the same, high-quality respiratory support during intra-hospital transport or during power outages. The Evita XL is an advanced, multifunctional ventilator designed to deliver a comprehensive array of both controlled and assisted ventilation modes for the treatment of adults, children and neonates from the emergency room to intensive care to home. The ventilator combines a broad range of performance capabilities with many advanced application functionalities that can easily be configured to meet the needs of ICU staff and enables work processes to be tailored to a patient's individual needs. Additionally, for neonatal specific areas, Dräger offers the Babylog 8000 plus which provides pressure and volume ventilation specifically designed for neonatal patients. The Carina compact versatile ventilator is an innovative type of high-performance noninvasive ventilator that is ideally suited for emergency rooms, recovery rooms, or sub-acute facilities.

The ventilator offers the flexibility and performance to address a wide range of ventilation challenges. With battery back-up and the ability to utilize either high or low oxygen pressure sources, the Carina supports operational versatility for clinicians during transport or other adverse conditions.

Tell us about the latest technological advances pertaining to your products.

Dräger's Evita Infinity V500 and Babylog VN500 ventilators have been developed after years of experience and listening to clinicians from all over the world. Aspects of the latest technology focus on methods to improve workflow, clinical performance, ICU safety, and effective use of clinical information. Configurable data displays, smart views, and other closed-loop systems are examples of our latest products to support you and the patients you care for.

Hamilton Medical

Tell us about your ventilation products.

Hamilton Medical has produced critical care ventilators since 1984 and we continue to advance ventilation technology today. Our extensive world-wide customer base speaks to Hamilton Medical's history in meeting the ventilation needs of facilities throughout the world. By focusing on ventilation technology, Hamilton Medical is able to offer the **Hamilton G5, Hamilton C2, GALILEO GOLD, RAPHAEL XTC** and the Hamilton **ARABELLA Infant NCPAP System**. Within the next year, Hamilton Medical will be introducing ventilation technology within the US marketplace. Our original ventilator platforms, the VEOLAR and AMADEUS, can still be found in use in hospitals today. Hamilton Medical has developed all of our ventilation systems with our cornerstone closed loop ventilation technology, Adaptive Support Ventilation (ASV). ASV can be used as a default mode across a wide variety of patients, and more importantly, ASV supports evidence based medicine guidelines for weaning and protective lung ventilation, both of which reduce ventilator mortality and length of stay (LOS).

What is the scope of your company's current R&D efforts?

Hamilton Medical is in a unique position within the ventilation industry. We remain a privately held, family owned business that continues to make a difference in the medical field with our innovations. We continue to invest in R&D at much higher levels than our competitors. We have introduced three new ventilation products in the past 3 years and 6 new products to the European market by the end of 2010 with the intent that most will be available by early 2011 in the United States. This commitment to advancing ventilator technology is the reason Hamilton Medical continues to hold the honor of being the highest ranked ventilator manufacturer for 2010, as rated by the independent company, MD Buyline. Ventilator users have rated Hamilton Medical the top performer in all categories, including System Performance, System Reliability, Installation/Implementation, Applications Training, Service Response Time and Service Repair Quality. This rating is inclusive of all Hamilton Medical ventilators on the market today.

What types of training and services support do you offer?

Hamilton Medical has a dedicated Clinical Applications team, composed of experienced RTs, to provide direct on site clinical support for RTs, RNs and MDs. Our on-site clinical support

is provided with each ventilation purchase and can take several days or up to a week, dependent of the size of staff and schedules. Hamilton Medical's Clinical Applications Team is also available via Hamilton Medical's 24 hour support hotline, by calling (800) 426-6331.

Discuss the use of your products in various venues: ie hospitals, homecare, etc.

The Hamilton G5 and C2 are acute care ventilators, serving all patient populations, neonatal, pediatric and adult, with NIV capabilities. Not yet available in the United States, the Hamilton T1 is designed to ventilate adult or pediatric ICU patients at any place around the world and can accompany your patient within the hospital and between hospitals, either on the ground or in the air. The Hamilton C1 is unique in providing non-invasive performance in a full featured intensive care ventilator and the Hamilton MR1 is designed to ventilate the adult or pediatric ICU patient within the vicinity of an MRI.

Tell us about the latest technological advances pertaining to your products.

Currently under development, the Hamilton S1, features INTELLIVENT-ASV, the world's first fully closed loop ventilation technology for oxygenation and ventilation, covering all applications from intubation until extubation with the known simplicity from Hamilton Medical. Based on the systematic evolution of ASV over the last decade and on scientific evidence, it's in sync with daily clinical practice. The automatic adjustments follow protocolized care measuring lung physiology, respiratory monitoring, capnography (etCO₂) and pulse oximetry (SpO₂). INTELLIVENT-ASV reduces complexity by giving guidance on complex decision making, by visualizing complex information in an intuitive way.

Smiths Medical

Tell us about your ventilation products.

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.

What types of training and services support do you offer?

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 smiths-medical.com. Also, during our hands-on in-servicing, Smiths Medical sales specialists utilize detailed competency checklists to ensure proficiency in operating our ventilators.

Discuss the use of your products in various venues; ie hospitals, homecare, etc.

Acute Care (Hospital): Portable gas powered ventilators (PGPVs) have a wide use both inside and outside the hospital, providing artificial ventilation in both emergency situations and during the transport of critically ill patients. In many departments throughout the hospital, ventilation is carried out using sophisticated, semi-permanent machines. However, problems occur when the patient requires transportation from where they are being ventilated to another location. It is not feasible to move these ventilators with the patient, so portable transport ventilators are used. The Pneupac line of ventilators provide a level of ventilatory support comparable with larger ventilators, but also offer the flexibility to be moved with the patient for the length of the planned transport. This may be a few yards away in the same hospital, or a considerable distance by road or air. The Pneupac ventilators have a rugged design and offer the simplicity and reliability of operation that make the devices invaluable in all areas of clinical practice.

Alternate Care (Home Care): Breathing failure can happen anywhere, at home or in the street, at work or during recreation, and can affect adults and children alike. When breathing fails or stops completely in an emergency situation, it is essential that some form of artificial breathing is started to deliver oxygen to the lungs to help sustain life. Lightweight, quick to set up, accurate in their administration, and reliable in their operation, the Pneupac line of ventilators are ideal for use in emergency situations requiring basic or advanced life support. With their immediate ability to adapt to changing patient parameters, they provide essential breathing support and overcome many of the problems associated with manual ventilation methods. Emergency ventilation is a breath by breath situation and every breath matters. The Pneupac ventilators incorporate the essential features to provide the best quality emergency ventilation, at an affordable price. (Pneupac, paraPAC, babyPAC

and VR1 are trademarks of Smiths Medical, and are 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.)

COMPANY PROFILE

Oridion

Describe your product(s) and its unique features.

Oridion Microstream Capnography monitors adequacy of ventilation, providing the earliest, most accurate indication of respiratory distress. Neither respiratory rate nor pulse oximetry – alone or combined – can measure adequacy of ventilation. Microstream capnography has conquered the challenges common with virtually all other capnography monitors and patient CO₂ sampling lines. With its innovative FilterLine series of patient interfaces and superior measurement technology, Microstream capnography provides accurate, trouble-free monitoring effective for all patients in all environments. Microstream is the only CO₂-specific measuring technology; there is no cross sensitivity to other gases. Based on its patented Molecular Correlation Spectroscopy (MCS), Microstream delivers clear, crisp waveforms and accurate respiratory rates. Its rugged construction has no moving parts or expensive and damage-prone external sensors. The simplified etCO₂ monitoring that results from the Smart Capnography family of superior algorithms – Integrated Pulmonary Index (IPI), Smart Alarm for Respiratory Analysis (SARA), and Smart Breath Detection Algorithm (BDA) – reduces alarms, improves workflow and provides clinical utility for improved patient safety. Unique and patented design features in the Smart Patient Sampling Interface provides specialized products for use in varying patient conditions. These include sampling lines for intubated and non-intubated patients and oral/nasal sampling combined with oxygen delivery and high humidity environments. Utilizing a FilterLine patient interface with oxygen delivery eliminates the additional cost and inconvenience of an oxygen cannula while monitoring the patient. Other significant clinical advantages include no dilution with supplementary O₂ flow rate of up to 5 lit/min; capability to monitor patients with high respiration rates (above 100 bpm) and low tidal volumes (essential for monitoring infants and neonates); and moisture handling that provides extended duration patient sampling lines. Oridion patient monitors using Microstream capnography technology include the **Capnostream 20**, **Microcap**, and **Microcap Plus**. The Capnostream 20 is a portable bedside monitor, ideal for use in all clinical settings where there is a need to monitor and assess ventilatory adequacy or where patients are at risk for opioid-induced respiratory depression, especially for all sedation procedures and patient controlled analgesia (PCA). Capnostream 20 offers both capnography and pulse oximetry in one monitor. The Microcap is a hand-held portable monitor that provides accurate, continuous monitoring on intubated and non-intubated patients from neonate to adult in hospital and pre-hospital environments, including emergency transport. The Microcap Plus, also a hand-held monitor, combines Microstream capnography with pulse oximetry in a single device.

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

Smart Capnography is a family of superior algorithms that reduce alarms, improve workflow and provide clinical utility for improved patient safety. Today, Smart Capnography includes the

Integrated Pulmonary Index (IPI), the Smart Breath Detection Algorithm (Smart BDA), and the Smart Alarm for Respiratory Analysis (SARA). **Integrated Pulmonary Index (IPI)** helps caregivers manage four complicated monitoring parameters – end tidal CO₂, respiration rate, pulse rate and SpO₂ – with a single, simple number, providing an uncomplicated, inclusive assessment of a patient’s ventilatory status. IPI provides an early indication of changes in the patient’s ventilatory status that may not be indicated by the current value of any of these four parameters individually. Unlike traditional breath detection algorithms, the **Smart Breath Detection Algorithm (BDA)** rejects shallow, non-breath CO₂ excursions from being counted as breaths. Instead, the Smart BDA suite of proprietary filter and pattern recognition techniques screen out the low amplitude CO₂ changes superimposed on the CO₂ waveform. Only actual breaths are used to build the CO₂ waveform. **Smart Alarm for Respiratory Analysis (SARA)** is an alarm management technology that recognizes and reduces respiratory rate nuisance alarms while accurately reflecting the patient’s condition and preserving caregiver alarm vigilance. Preserving caregiver vigilance to alarms is essential for patient safety. **Smart Sleep Diagnosis (SSDx)**, another of the Smart Capnography family of algorithms, reports apnea and oxygen desaturation events and calculates the associated Apnea Index (AI) and Oxygenation Desaturation Index (ODI) for adult patients. By using Oridion SSDx algorithms—AI and ODI— we hope clinicians will be able to identify potential patient sleep apnea while patients are being monitored during their hospital stay (FDA 510k pending).

Discuss your R&D process, including clinical user input.

The R&D process at Oridion includes a comprehensive, multi-stage “Voice of the Customer” process, centering on the needs of clinical users. Prior to developing each product or technology, Oridion may conduct multiple focus groups, as well as interviews of individual nurses, respiratory therapists and physicians, to gather input on the challenges and needs of the clinical user. These interviews help provide or enhance products and technologies needed to improve patient care, patient safety and clinical work flow. Clinical data is collected to validate the clinical performance of each product. Upon completion of the product or technology and clearance by FDA, Oridion typically conducts a limited product release, allowing select customers and facilities to utilize the product to ensure it meets their needs. Oridion continues to gather input and make adjustments and improvements prior to a full market release.

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

Oridion recognizes that training and support are essential for a successful implementation of end-tidal CO₂ monitoring. To maximize the customer’s investment, Oridion has developed world-class educational materials and programs for medical professionals that are customized for the specific environment where capnography will be utilized. Its comprehensive educational programs include understanding the basics of capnography, as well as the use of capnography during procedural sedation, in the management of the critically ill patient, during opioid delivery, and during non-invasive ventilation. These programs are available in the Oridion Knowledge Center, a free online repository for educational support and long-term support, offering educational credits for nursing and respiratory therapy. Oridion also provides these electronic educational modules to hospital systems to upload onto their own educational intranet. Upon introduction of the

product to a facility or practice, Oridion provides a detailed implementation manual to guide users through the process. The manual includes a step-by-step implementation timeline, sample training materials, competency guides, sample policies, and other tools needed to introduce this technology into their organization. The manuals are customized for each clinical market. Augmenting the implementation manual, Oridion provides comprehensive “Go Live” support during the first critical days of use, as well as available short-term and long-term live support in training and project management.

FOCUS PRODUCT PREVIEW

Alere

Booth 710

What products will you be presenting at Focus?

Our goal is to create awareness of the new epoc system and to promote a next generation blood gas solution that brings testing cost effectively to the bedside in critical care areas throughout hospitals. We will be presenting the **epoc Blood Gas Analysis System**.

Discuss educational/training materials.

This is the first time we will be attending this show and educating the RT segment on the new epoc Blood Analysis System. Our goal is to create awareness and introduce the epoc Blood Analysis System which attendees can experience by stopping by our booth.

Why should Focus participants visit your display?

epoc Blood Analysis is healthcare’s first cost effective POC testing solution to leverage Smartcard Technology and the power of wireless communication providing caregivers with the real-time, laboratory quality blood gas, electrolyte and metabolite test results at the patient bedside. epoc improves the testing process and allows caregivers to maintain focus on their patients.

B&B Medical Technologies

Booth 210

Discuss the products you’ll be presenting.

B&B Medical Technologies will be showcasing our new **Babi.Plus** product line, which includes the Bubble PAP Valve 0-10 cm H₂O for noninvasive ventilatory support of neonates, premature infants and infants weighing ≤10 kg; Silicone Infant Nasal CPAP Cannula (prongs) for delivery of comfortable nCPAP; and a single or dual pole clamp for both the Bubble PAP Valve and humidifier systems; and Danny Ties for a soft, comfortable fit for tracheostomies. B&B Medical Technologies is the first company to offer an FDA-cleared, professional Bubble CPAP system specifically designed to deliver precise CPAP pressure for the very small infant population in the NICU through the 10 kg infant in the PICU. Babi.Plus Bubble Pap Valve and Infant nCPAP Cannula Kit eliminates the need for hospital personnel to invest time and money manufacturing and maintaining the “homemade” bubble devices previously used for nasal CPAP application.

Discuss the benefits of your products.

B&B Medical Technologies will introduce the new **Babi.Plus Pacifier Adaptor** for nebulized medication delivery via the

infant's own personal pacifier. The Babi.Plus Pacifier Adaptor is hypoallergenic, latex-free and phthalate-free. The Pacifier Adaptor has been designed to fit and adhere to a wide variety of non-silicone face plate pacifiers. The Pacifier Adaptor holds fast with a specialty adhesive but can be easily removed after treatment, even while the child still is sucking on the pacifier. The Babi.Plus Pacifier Adaptor provides a convenient and cost effective alternative to other methods of nebulized medication delivery for babies and young children. The new **Danny Ties** will be introduced at the booth. Danny Ties are made of a soft, absorbent material that lay smooth at the edges of the collar and significantly minimize skin breakdown beneath the collar. The collar holds its shape, does not fold in half around the neck and does not stretch when it absorbs moisture. The patent pending design of the Danny Ties evenly distributes the padded collar material around the neck to minimize pressure points on the skin. The Danny Ties collar is easy to apply with tapered ends to the collar straps. The ends thread easily through the eyelets of the tracheostomy tube allowing for quick application and changes of the collar on the smallest of infants and the large adult patient. Danny Ties are developed with special care by a Dad wanting to "make a difference" for his son and change the quality of life for tracheostomy patients. His engineering expertise and commitment to finding a better solution is found in the Danny Ties.

Discuss educational/training materials you'll be offering.

B&B Medical Technologies will have complete product brochures, clinical application guides to assist the clinician in the introduction and education for the complete line of B&B Medical Technologies specialty airway management products.

Why should attendees visit your display?

B&B Medical Technologies' "signature" giveaway – See's Candies Lollypops – will be available at our booth. Please stop by to see how our entire World of Products for Better Breathing will make your life easier in the clinical setting, and enjoy a lollypop from B&B Medical Technologies.

Dräger

Booth 609

What products will you be presenting?

Dräger will be presenting its newest generation in critical care and neonatal ventilation. Visitors to the booth will get a first-hand preview of the **Evita Infinity V500** ventilation system, as well as the new **Babylog VN500** neonatal ventilator. Both devices represent one of the most technologically advanced ventilation platforms with a comprehensive array of therapy options. The Babylog VN500 was designed with the neonatal respiratory therapist, neonatologist, and tiniest and most fragile of patients in mind. After over two decades of experience with the former device, the VN500 brings a wealth of technology in mechanical ventilation to the bedside. The Evita Infinity V500 enters the ventilation marketplace with new tools and options never before available. Features such as APRV with Auto-Release, Variable Pressure Support, Smart Pulmonary View, and configurable SmartCare/PS are some of the examples of new technology that the V500 brings to the respiratory therapist and critical care physician. Additionally, conference attendees will see the latest in non-invasive ventilation with Dräger's Carina high-performance ventilator, designed for patient comfort and ease of use for the caregiver.

Discuss the educational/training materials you'll be promoting.

Dräger will be promoting a variety of educational and training materials for respiratory therapists. These materials include a booklet on ventilation modes in intensive care and an interactive website for neonatal doctors, respiratory therapists and nurses. Launched in 2010, Babyfirst.com is an online resource where clinicians in Labor and Delivery and the NICU can share their expertise and experience across a range of neonatal care specialties, including respiratory care and infection control. The website also provides resources to assist clinicians in educating parents about the NICU for a healthy collaboration with professionals towards the growth of their babies. Visitors to the booth will also be able to request a copy of "Ventilation Modes in Intensive Care." The booklet is designed to improve the understanding of contemporary modes of mechanical ventilation. The revised nomenclature is an effort in standardizing common understandings of pressure, volume and spontaneous ventilation modes.

Why should participants visit your display?

Focus participants should visit our display to learn about the new and exciting activities at Dräger and to view our latest products. Dräger has been in the forefront of ventilation for over 100 years. Our knowledge and experience continues to bring the latest technological advances to caregivers worldwide. Forums such as the Focus Conference allow for sharing of expertise and of course fellowship amongst colleagues, customers and friends.

MedGraphics

Booth 305

What products will you be presenting?

Featured products from Medical Graphics include the **Platinum Elite Plethysmograph** and the **Ultima Cardio₂** gas exchange system. These systems lead the way in the diagnosis of cardiorespiratory diseases which affect millions of people.

Discuss educational/training materials you'll be promoting.

MedGraphics' annual Cardiorespiratory Diagnostic Seminar will be held in October this year in Las Vegas. Expert speakers in the field of cardiorespiratory diagnostics will present lectures as well as lead discussions in many areas of diagnostics.

Why should participants visit your display?

MedGraphics is a leader in cardiorespiratory diagnostics. Participants should visit our booth to see the latest innovations in hardware and software, and see how we can provide the best solutions for their diagnostic needs.

OPTI Medical

Booth 142

What products will you be presenting?

OPTI Medical will present the **OPTI CCA-TS** and **OPTI R Blood Gas Analyzers**, which both feature patented optical fluorescence and reflectance technology. Other products that will be presented are OPTI Medical's Rhythm Pulse Oximeter and ComfortSampler Blood Collection Kits.

Discuss educational/training materials you'll be promoting.

Brochures will be available, as well as interactive hands-on demonstrations on our products at the OPTI Medical booth.

What promotions will your company be featuring?

We will be offering our **Rhythm Pulse Oximeter** at excellent "trade show only" pricing. Each OPTI Rhythm comes with a one year warranty and is backed by OPTI Medical's excellent technical support. Also, we will hold have a raffle where participants can win prizes.

Why should participants visit your display?

Stop by the OPTI Medical booth to enter our raffle and/or purchase one of our OPTI Rhythm Pulse Oximeters at a special Focus Trade Show promotional price.

Pepper Medical, Inc

Booth 108

What products do you plan on presenting?

Pepper Medical Inc offers a full line of trach securement and ventilator antidisconnect products for both pediatric and adult patients. The focus is on ventilator dependent patients where circuitry disconnections are all too frequent and dangerous. The use of a commercially available ventilator Antidisconnect Device such as the patented **Vent-Tie** product lines for pediatric and adult ventilator dependent patients offers a margin of safety in today's litigious environment.

What training opportunities do you offer?

Pepper Medical is on a mission to reduce the number of ventilator associated injuries and deaths. One of the most frightening events of any ventilator dependent patient is an accidental ventilator circuitry disconnection. The FDA reports that approximately 200 deaths and numerous injuries and liability cases occur each year in hospitals alone due to accidental ventilator disconnections. Joint Commission states that "alarm fatigue" is a substantial issue in these injuries and the ECRI states, "We routinely see deaths associated with alarm fatigue problems." The use of the Vent-Tie product does not replace the need for ventilator alarms but by using in a supervised setting can reduce unintentional detachments.

Philips Respironics

Booth 503

What products will you be presenting?

The **Trilogy100** portable life-support home ventilator; **Trilogy200** portable life-support home ventilator; **BiPAP AVAPS** noninvasive home ventilator; and **CoughAssist** airway clearance in/ex-sufflator.

Discuss educational/training materials you'll be promoting.

We will be showcasing our latest Know How Webinars for clinicians. Know How Webinars are a series of live and on-demand presentations that help address key business and clinical issues faced by homecare providers and healthcare professionals. The webinars are hosted by experts from Philips Respironics or leading clinical professionals such as doctors or therapists.

Why should participants visit your display?

We will be featuring new disposable circuits designed specifically for use with our Trilogy ventilators. Combining disposable circuits with Trilogy's advanced technology helps to optimize patient ventilation synchrony and provides accurate leak compensation. The Trilogy series of ventilators support either passive or active exhalation breathing circuits, giving clinicians the flexibility to choose the appropriate circuit and interface for their patients. Trilogy circuits are lightweight, and available in adult and pediatric sizes for invasive and noninvasive applications.

Smiths Medical

Booth 403

What products will you be presenting at Focus?

Some of the key products we will be promoting at Focus include:

- Thermovent Heat and Moisture Exchangers;
- acapella Vibratory PEP Therapy;
- EzPAP Positive Airway Pressure System;
- Flo-Mist Continuous Medication Nebulizer;
- 1st Response Manual Resuscitators;
- Portex CO₂ Clip Carbon Dioxide Detector;
- Portex Arterial Blood Sampling Kits;
- Pneupac VR1 Ventilators;
- SPECTRO2 Pulse Oximeters;
- Capnocheck Plus CO₂ Detectors and
- Thera-Heat Heated Humidification System.

Why should focus participants visit your display?

The Building Blocks of Respiratory Care... Smiths Medical is a leading manufacturer of single-use disposables for respiratory care, devices for airway management and therapeutic systems. Our many brands, products and programs come together to help make every respiratory intervention successful. Visit us at Booth #403 and find out how Smiths' solutions can help you and your patients with: VAP reduction, percutaneous and customized tracheostomy, bronchial hygiene and lung expansion, and disaster preparedness.

Adherence and Inhaler Devices in COPD

James B. Fink, Richard Hodder

Introduction

Despite treatment advances that provide symptom relief, chronic obstructive pulmonary disease (COPD) poses a significant health challenge, with an estimated global prevalence of 210 million.¹ Deaths from COPD equaled 5% of global mortality for 2005 alone – an estimate that is expected to rise by 30% over the next decade unless adequate preventive strategies are employed.¹ The global disease burden is also reflected in the United States, where approximately 126,000 deaths were caused by COPD during 2005,² representing \$177 billion³ in total direct and indirect healthcare costs.

The 2009 updated Global Initiative for Chronic Obstructive Pulmonary Disease guidelines propose staged management of stable COPD and exacerbations, comprising both acute and maintenance pharmacotherapies to relieve airflow obstruction and lung hyperinflation, control complications and reduce the risk of exacerbations.⁴ The practice of adhering to recommended inhalation medications may be just as important as the efficacy of the drugs themselves. Evidence from two megatrials in COPD suggests that patients who adhere to their medications experience better survival, lung function improvement and a lower risk of hospital admissions due to exacerbations.⁵⁻⁷

COPD should be considered a treatable disease and much can be done with modern multimodality management strategies to help improve patients' lives. In addition to pharmacotherapy, non-pharmacotherapeutic treatments (including self-management education, exercise training and lifestyle alterations) are important for optimal management of symptoms and activity

James Fink is an independent consultant in San Mateo, CA. Hodder is with the Division of Pulmonary and Critical Care, University of Ottawa, Canada. Dr Fink is an advisor/consultant for Aerogen, Cubist, Novartis, Boehringer-Ingelheim, Aridis, Kalobios and Dance. Dr Hodder has received consulting and speaking honoraria, and research funding from several pharmaceutical companies including Boehringer-Ingelheim, GlaxoSmithKline, AstraZeneca, Nycomed and Novartis. This article was developed on the basis of the authors' presentations and discussions at the "Implications of Inhalation Delivery Systems for COPD Therapies" Advisory Board held in New York, NY, March 25–26, 2009. This meeting, the authors' participation, and manuscript preparation were supported by Boehringer-Ingelheim Pharmaceuticals Inc. and Pfizer Inc. Medical writing assistance was provided by Zeena Nackerdien, PhD, of Envision Scientific Solutions. The article reflects the concepts of the authors and is their sole responsibility. It was not reviewed by Boehringer Ingelheim Pharmaceuticals Inc, and Pfizer Inc, except to ensure medical and safety accuracy.

limitation associated with COPD. Adherence to both treatment modalities is necessary for optimal disease management; however, in general, adherence to therapy in COPD is often poor, and problems with inhaler use appear to be prominent in this regard. Multiple trials suggest that up to 60% of patients and providers are unable to use prescribed aerosol devices correctly,⁸⁻¹⁰ which seems to correlate with poor adherence rates in COPD patients. Similarly, difficulties associated with inhaler use may also contribute to poor adherence.¹¹ This article reviews the issues surrounding inhaler devices and adherence in patients with COPD, and how they can best be managed in primary care.

Magnitude and consequences of non-adherence with COPD management

Non-adherence is estimated to lead to a 10% excess in total hospital admissions in the United States.³ Non-adherence to medication in general is common,^{12,13} with up to 60% of patients with chronic diseases being poorly adherent.^{3,12} Non-adherence places a massive burden on healthcare systems, and contributes significantly to the overall burden of chronic illness including costly exacerbations and reduced quality of life.¹⁴ This appears to be particularly common in COPD, with poor adherence consistently reported in over 50% of patients with this disease.^{13,15-19} Examination of medication adherence and persistence among a cohort of 11,376 COPD patients during their last year of life showed that only half of the patients (5,913) used any medication.²⁰ Of the 3,436 patients on monotherapy, 40% discontinued medication within 30 days, and 70% discontinued within 90 days. The medication possession ratios (Σ # days of supply/total days), which were compared between regimens by quarterly periods, were 0.44 (standard deviation 0.32) during the last year of life. In a recent Swedish study of patients aged ≥ 60 years with COPD or asthma, only 28% of patients had "satisfactory" refill patterns (ie, dispensed refills covering 80-120% of the prescribed treatment time) of their inhaled corticosteroid, with 59% of patients under-supplied and 12% over-supplied with medication.¹⁷ Over-supply of medication indicated either drug stockpiling or overuse of the medication.

Adherence

Different medications, regimens and behaviors all have a varying impact on treatment adherence, which can be broadly defined as the degree of concordance between a patient's actual behavior and a provider's prescribed therapy. The primary methods for assessing adherence are: clinician estimates, patient self-reporting, pill counts/weighing, pharmacy records, biological markers and electronic monitoring.²¹ Adherence tends to

Table 1. Psychological predictors of poor adherence³²

Predictor (details)
• Denial
- Patient beliefs about illness and therapy
• Disruption
- Family and personal emergencies
• Depression
- Prolonged sadness, apathy and withdrawal
• Dementia
- Psychiatric impairment (loss of intellectual capacity) or related to substance abuse

decline over time with chronic medication use, making it an even larger problem with COPD and other chronic diseases. In one meta-analysis, analysis of the adherence to treatment pattern showed that good adherence (study definition: >80% use of prescribed medication) had a positive impact on exacerbations, hospitalizations and mortality in COPD patients.⁶

Non-adherence

Non-adherence has been broadly categorized as either unintentional or intentional.^{22,23} Unintentional non-adherence is associated with a patient's resources and ability to take medication which may include social, physical or psychological causes such as inability to afford medications, poor manual dexterity or eyesight, or simply forgetting to take prescribed medications.¹² When non-adherence is associated with a patient's beliefs and motivation, (eg, the need for a medication, the efficacy of a proposed treatment, concerns about side effects), the patient's unwillingness to accept a clinician's diagnosis or follow recommended treatment is viewed as an intentional action. In practice, patients frequently exhibit aspects of both intentional and non-intentional non-adherence.

Non-adherence can be further subdivided into "erratic," "unwitting" and "intelligent" non-adherence.²⁴ Erratic non-adherence occurs when the patient understands and agrees with therapy but has difficulty consistently maintaining the regimen. Forgetful, disorganized patients and complicated or changing management regimens promote this type of non-adherence. Unwitting non-adherence describes when both the patient and provider mistakenly believe that the patient is adherent.

Table 2. Properties of an ideal inhaler⁴¹

• Dose reliability and consistency
• High lung efficiency (>10–20%)
• Low oropharyngeal deposition
• Simple to use
• Easy to maintain
• Short treatment time
• Small size, easy to carry
• Multiple dose convenience
• Resistance to bacterial contamination
• Dose counter
• Cost effective
• Low ambient aerosol contamination
• Available with range of drugs required
• Clear instructions
• Functional placebo devices available for teaching
• Liked by patients!

Forgetful patients, cultural and language issues, level of patient education and reading level, as well as poor training and skills with inhaler technique can lead to unwitting non-adherence. Intelligent non-adherence occurs when patients deliberately alter or discontinue therapy based on reasoned decision-making about their perceptions of the drug's efficacy, likelihood of long-term harm, side effects and their social circumstances.²⁵ This type of non-adherence may be suspected when patients report that they do not see an obvious link between taking their medication and an immediate effect on their symptoms, express fear of side effects or long-term dependence on the medication, or acknowledge a dislike for taking medications in general; thus, non-adherence may appear to be an irrational act from the clinician's perspective, but completely rational from the patient's point of view.

General factors affecting treatment adherence

Many patients discontinue their medication in response to a decline in symptoms²⁶ or the complexity of the treatment regimen.¹⁸ Concerns by patients include worry that they will develop a tolerance to the inhaled medications if they take them regularly over the long term, so that the medication will be less effective when they really need it, eg, during an exacerbation.²⁷

In a recent study, COPD patients cited simply forgetting to use the inhaler (19%), cost (15%) and a perception that the prescribed inhaler did not help their breathing (20%) as reasons for inhaler misuse.²⁸ In addition, non-adherence to inhaler therapy by COPD patients can be a consequence of not filling the prescription (~30%), under-using the inhaler (>50%) or poor inhaler technique (30-70%).^{29,30}

It is important to understand that human behavior is a key consideration when evaluating what influences adherence.³¹ Several psychological factors may promote non-adherence including the patient's denial of his or her condition, disruption of daily living imposed by the necessity of taking drugs, depression and dementia (Table 1).^{31,32} Treatment-related factors include the method of drug administration, which in the case of inhaled medications can be particularly challenging for the older COPD patient. Other factors, such as dosing regimen, polypharmacy, and side effects of medications also impact adherence, and should be addressed by the prescribing clinician both upon initiation and regularly over the course of treatment.³³

The inhaler device and its role in patient adherence

Inhaled pharmacotherapy for COPD is delivered via a variety of devices that can be divided into four main classes: nebulizers, pressurized metered dose inhalers (pMDIs), dry powder inhalers (DPIs), and soft mist inhalers (SMIs).^{8,34,35}

Each type of medical aerosol delivery system has its advantages and disadvantages. In order to optimize chances for good adherence, these need to be assessed according to each individual patient's capabilities, lifestyle and preferences when prescribing treatment. Historically, nebulizers have been preferred for the treatment of infants or patients with severe exacerbations warranting treatment in the acute and critical-care settings. The extension of therapy with pneumatic small volume nebulizers to the ambulatory setting has been largely based on clinical practice patterns pre-dating the evolution of modern inhaler technologies. The liquid nebulizer has an advantage in administration with patients who cannot perform respiratory maneuvers, such as children less than 5 years of age

Table 3. Problems with inhaler use³⁹

pMDI	DPI
<ul style="list-style-type: none"> Inhale <ul style="list-style-type: none"> – too early – too late – too often – too many times Failure to shake Failure to prime Failure to hold breath Use in cold weather Cold freon effect High oropharyngeal deposition 	<ul style="list-style-type: none"> Inhale too slow Exhale into device prior to breath Failure to hold in proper orientation Failure to prime Failure to pierce capsule/ open blister pack Failure to empty capsule Failure to keep flow path open Failure to hold breath Humidity reduces dose High oropharyngeal dose

pMDI = pressurized metered dose inhaler; DPI = dry powder inhaler.

and older patients lacking hand-breath coordination required for use with inhalers. For the COPD patient there is a limited, albeit controversial, role for home use of liquid nebulizers.³⁶ The disadvantages associated with these devices include: size and weight (which limit mobility), expense, requirement for electricity (traditional nebulizers), time for administration (5–20 minutes), variability in aerosol and drug output characteristics (with choice of nebulizer/compressor combination) and contamination of the nebulizer medication reservoir during use, requiring extensive and frequent cleaning between treatments. Such considerations provided part of the impetus for the development of new inhalers that could more readily serve an array of ambulatory patient needs.³⁶

Both pMDIs and DPIs consist of small, light, portable containers designed to consistently deliver a specific drug formulation in a short period of time (often two breaths requiring less

Table 4. Considerations to facilitate improved adherence in COPD

<ul style="list-style-type: none"> Admit that poor adherence is often the norm Learn to recognize which patients have a high potential for poor adherence Recognize the different forms of poor adherence (eg, unwitting vs intelligent) Acquire communication skills that promote good adherence Avoid judgmental behavior when counseling adherence Practice collaborative self-management education principles <ul style="list-style-type: none"> – Use respiratory educators or case managers when available – Involve the patient and caregivers in treatment planning – Teach patients the rationale for various treatments, both pharmacologic and non-pharmacologic (eg, exercise) – Define expected outcomes and limits of therapy – Explain potential side effects – Teach the warning signs of impending exacerbations and provide written action plans – Explore potential barriers to poor adherence specific to individual patients Learn to write simple exercise prescriptions Learn and teach correct inhaler techniques and regularly re-assess Simplify drug dosing <ul style="list-style-type: none"> – use once-a-day medications and/or combination inhalers whenever possible – When multiple medications are necessary, try to synchronize them to one or two times in the day and link them to other regular activities such as brushing the teeth morning and night, or with meals if possible
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COPD = chronic obstructive pulmonary disease.

than a minute for administration). The pMDIs deliver drugs via active means ie, using a propellant under pressure. Chlorofluorocarbons (CFCs) propellants are being phased out in accordance with US Food and Drug Administration (FDA) regulations in favor of environmentally-friendly hydrofluoroalkanes (HFAs). Many devices also have a dose counter and offer multidose convenience. These inhalers pose less risk to the patient regarding contamination, with fewer critical requirements for cleaning between treatments.³⁶

Disadvantages for the standard “press and breathe” pMDI include requirements for hand–breath coordination. Due to the relatively short time (0.3 seconds) of aerosol generation, failure to actively inhale during actuation can drastically reduce the amount of dose inhaled by the patient. Prior to introduction of HFA propellants, pMDIs were greatly impacted by environmental temperature, with decreased output in colder weather. Many pMDIs have a “tailing off” effect ie, variability in the amount of drug dispensed towards the end-of-label claim for canister life, causing swings from normal to virtually no dose emitted from one breath to the next.³⁷ When this happens, the unit may still sound and feel as though it is working properly; therefore patients may continue using a pMDI after reliable dosing has ended – this was the basis of the FDA requiring new pMDIs to have a dose counter.

In contrast, the DPI is a passive device, in that it does not depend on pressurized gas to deliver medication but instead, relies on patient inspiratory flow to release the prescribed dose as a drug aerosol from the inhaler.³⁸ Many DPIs are impacted by effects of temperature and humidity. In the latter case, high humidity can reduce inhaled dose by up to 50%.³⁹ Most pMDIs and DPIs are associated with relatively low lung dose (10–20%) and high (up to 80%) oropharyngeal deposition.⁴⁰ While mouth rinsing has been recommended, it is difficult to sufficiently rinse drug from the hypopharynx to avoid potential adverse effects such as a hoarse voice with inhaled corticosteroids.

Next-generation portable inhalers, such as the Respimat SMI device (which is currently available only in Europe) combine some of the advantages of DPIs (propellant-free), pMDIs (inspiratory flow independence) and nebulizers (liquid formulations), while minimizing limitations such as low lung dose and high oropharyngeal dose.³⁵ Moreover, the drug aerosol emitted from this inhaler moves much more slowly when compared to aerosol clouds emitted from other inhalers such as pMDIs. The longer spray duration (~1.3 seconds) should enable many patients to properly execute the correct inhalation technique due to the timing of hand-breath coordination compared with the pMDI. However, the patient is still required to take a sufficiently long inspiration to inhale the complete dose. In theory, such a maneuver may be beyond the capabilities of some patients with advanced disease or those experiencing an acute exacerbation, although this has yet to be proven.

Inhaler design is a critical factor in the proper use of inhalers and patient adherence with prescribed medications. Portability, ease of use, multidose convenience, maintenance and priming requirements, can all impact patient willingness and ability to adhere to inhaler use. The characteristics of the long sought-after, but yet to be realized, “ideal inhaler” are shown in Table 2.⁴¹

There are several common misconceptions about inhaler use

Table 5. Key considerations for inhaler selection.

- Device/drug availability
- Clinical setting and environment
- Patient age and ability to use the device correctly
- Device use with multiple medications
- Cost and reimbursement
- Drug administration time
- Convenience in both acute and outpatient setting
- Physician and patient preference

that may conspire to promote inhaler misuse or non-adherence:

(1) “Inhalers are so simple to use, they do not require training”

The modern inhaler is one of the most complex drug delivery systems in common clinical use. The device, formulation and packaging must all come together to provide consistent and reliable dosing. Each device works differently with different instructions. Failure to perform each of the critical steps can greatly reduce efficacy. Typical inhaler errors are listed in Table 3 and include too rapid/slow inhalation, inability to coordinate actuation and inhalation, no breath-hold after inhalation, holding the device incorrectly, failing to open the capsule or package, multiple actuations during one inspiration, exhaling through the mouthpiece before, during or after activation, and failing to maintain a tight seal at the mouth.⁸ These errors can lead to suboptimal delivery of the medication, thereby affecting treatment adherence. Patient education is therefore a critical factor in the use and misuse of delivery devices and consequently, in the effectiveness of aerosol therapy.⁴²

(2) “The addition of a holding chamber or spacer device ensures adequate pMDI use”

The development of the valved holding chamber (VHC) has greatly expanded the clinical utility of the pMDI for use with infants, small children and others unable to sufficiently control their respiratory maneuvers and hand-breath coordination with the stand-alone device, while reducing oropharyngeal deposition to less than 1%. The use of an auxiliary device may facilitate optimal drug deposition by permitting a slowing down of the aerosol cloud emitted from a typical pMDI, and by allowing more time for propellant evaporation, thus increasing the fraction of drug particles in the respirable range (mass median aerodynamic diameter between 0.5 and 5 μm).⁴³ As is the case with the primary dispenser, auxiliary device design has a great impact on both function and the ability of the patient or clinician to effectively use the assembled device. Simple spacers help to reduce oropharyngeal deposition (<10%) but do little to overcome the need for proper hand-breath coordination. If used incorrectly, some VHC and spacer designs can even reduce the amount of drug available to the patient.⁴⁵

Unfortunately, auxiliary devices do not prevent incorrect pMDI use or inconsistent medication delivery. Despite use of such a device, patients may still fail to prime their inhalers prior to use, actuate multiple puffs into the device prior to breathing, and even forget to take the mouthpiece off of the pMDI actuator prior to inserting into the VHC. Add-on devices may also be associated with electrostatic charge build-up, which lessens drug delivery.⁴⁴ Replacement of a spacer or VHC made of electrostatic plastic with a similar device composed of non-electrostatic

materials may increase the inhaled dose by 4-fold above that delivered by the pMDI alone.⁴³ Whether this might have any clinical consequences has yet to be proven.

These devices also have limitations of added expense, complexity and size. Appropriately targeted pulmonary drug delivery and availability may also differ depending on whether an add-on device is used with either a CFC-propelled or HFA-propelled pMDI.⁴⁵ In summary, use of auxiliary devices does not provide a substitute for patient training and follow-up.

(3) “DPIs and nebulizers require less training than pMDIs”

The problems patients have with using DPIs and pMDIs are shown in Table 3, which indicates that there are as many potential user problems with DPIs as there are with pMDIs. In addition, patients who have been prescribed nebulizers (due to real or perceived benefits on the part of the patient), still need training to optimally use power-driven or battery-operated versions of these devices.³⁶ The basics of effective inhaler education and, consequently, effective treatment, are simplification, demonstration, and repetition of correct inhaler technique by the healthcare provider.³⁴

Unlike traditional pMDIs, DPIs offer substantial advantages in terms of bypassing the requirement for proper hand-breath coordination and emitting drug aerosols without the need for propellants.³⁶ However, the need for faster inspiratory flow rates to prevent clumping of drugs and some brand-specific requirements for a loading procedure for each dose³⁶ are factors that could negatively impact DPI technique and ultimately treatment adherence. COPD patients with very low inspiratory flow rates may not be able to inhale a sufficient dose from their DPIs; if the clinical response is poor for such individuals, an alternate delivery device should be considered.

(4) “Package inserts are self-explanatory to patients”

While consumer-friendly medication guides accompany prescriptions, it seems as if most package inserts detailing the prescribing information itself are written using language that is not easily understood by patients. The complex descriptions are often given in fine print and accompanied by small illustrations. This can be particularly daunting for patients with limited grasp of the English language or vision problems. It is wrong to assume that the patient or caregiver will learn how to use a given device by reading the package inserts.³⁴

No inhaler device is ideal; however, next-generation portable inhalers, such as the SMI appear to offer a mix of properties that might have an impact on patient use and adherence. The higher satisfaction rates reported by patients using this device versus pMDIs or DPIs imply a positive effect in terms of improved treatment adherence,⁴⁶ but this has yet to be proven. Indeed, the time-honored paradigm that use of a preferred inhaler leads to improved adherence and thus improved clinical outcome remains unproven.⁴⁷

Strategies to improve patient adherence with inhaled medications in COPD

General considerations to facilitate better adherence with drug and non-drug therapy in COPD are listed in Table 4. Crucial first steps to facilitate improved adherence are to acknowledge non-adherence as a reality and to learn to recognize the signs of

this problem, such as the previously discussed signs of erratic, unwitting and intelligent non-adherence. Clinicians should use the criteria listed in Table 1 as predictors of poor or non-adherence and take proactive steps to remedy the situation.³² These steps may include establishing a routine for drug therapy and increasing the patient's knowledge, education and faith in the prescribed treatment.³¹ An optimal management strategy needs to be flexible in nature and based upon factors that can impact treatment adherence, eg, effective communication with the patient, the patient's ability to cope with stress or illness, health beliefs, level of social support from family or caregivers, cost, reimbursement, treatment length, convenience, and continuity of care, as well as patient disease knowledge, inhaler device preference and capabilities.²²

Improving adherence with inhaled medication is fundamental to optimizing COPD management. Key approaches for facilitating good adherence include:

- Collaborative and mutually agreed decision-making between patient and clinician.^{22,31}
- The necessity for clinician and patient education about available drug/device combinations and correct use.⁴⁷ Although some medical personnel fare better than others in terms of inhaler knowledge,^{48,49} more clinicians and allied healthcare providers need to fulfill this ideal.
- Consideration should be given to patient-specific variables when selecting an inhaled medication (Table 5), including: patient age, factors affecting the ability to use the device correctly (eg, cognition, coordination, ability to generate adequate inspiratory flow rates with DPIs), use with multiple medications, cost and reimbursement, drug administration time, convenience, and patient preference.^{8,50,51}
- Fully informing the patient about the benefits of the treatment regimen; from the practicalities of administration to the rationale for taking the medication.^{23,52}
- Delivering simple and clear instructions.
- Assessing and discussing patients' illness with perceptions of prescribed therapies and attempting to bring perception in closer alignment with evidence. This has been shown to improve patients' adherence as well as their quality of life and clinical outcomes.⁵³

Tailoring treatment to fit the individual's needs, abilities, and preferences is a key element of all aspects of COPD management, and patients should be active participants in treatment decisions to augment optimal self-efficacy. Overall, COPD patients who collaborate with their clinicians to develop self-management plans tend to have better awareness and adherence.⁵⁴

Conclusions

Adherence to medication in COPD is crucial for optimizing clinical outcomes, and non-adherence results in a significant health and economic burdens. Suboptimal adherence is common among COPD patients and results from a complex interplay of medication, patient and provider factors. Optimal disease management should be an ongoing endeavor that includes regular inhaler technique assessment and training in order to optimize good adherence and, consequently, positive clinical outcomes.

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Clarifying Rise Time and Inspiratory Cycling Criteria Settings

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A thorough understanding of mechanical ventilation is vital to the daily job responsibilities of a critical care respiratory care practitioner. In recent years new advanced modes of mechanical ventilation and the non-descript nomenclature related to traditional and non-traditional settings continues to create misunderstanding among healthcare providers. Much of the confusion exists partially due to the general understanding of these advanced modes, but also from the variation in terminology between ventilator manufacturers. In most cases, proprietary reasons have created this wide spectrum of setting and mode terminologies. This article aims to clarify terminology and settings for two non-traditional settings, ie rise time and inspiratory cycling criteria, between five different ventilators.

Rise Time

Rise time (RT) is available in all pressure-based modes of ventilation, eg pressure support (PS), pressure-synchronized intermittent mechanical ventilation (PC-SIMV), and pressure-assist/control (PC-A/C). RT adjusts the rapidity with which airway pressure builds to a preset target pressure.¹ To achieve this rise in pressure the RT setting determines the level of initial flow delivery. For example, a rapid rise time value will increase initial flow delivery thus allowing the preset pressure target value to be reached more quickly compared to a slower rise time value.² Making adjustments in RT can meet patient requirements in flow demand and also aid in “fine tuning” the ventilator for patients with variable impedance conditions.¹

Some of the confusion with the RT setting is not due to its designed use but the variation in names when comparing different ventilator models. With no uniform name or setting range across ventilator manufacturers, identification and understanding of RT may present with some difficulty for all healthcare practitioners. Table 1 displays the various name and setting ranges related to five different ventilator manufacturers.

Besides the variation in names and setting ranges, there is also variation between the values indicating a minimum RT value and maximum RT value. For example, the Drager Evita’s RT setting provides a range of 0 to 2. On this ventilator, the smaller value, eg a setting of 0, will provide the faster initial flow and the larger value, eg setting of 2, will provide the lower slower initial flow. Compared to the RT settings on the Puritan Bennett 840 the 100% setting offers a faster initial flow and the 1% setting offers the slower initial flow.

Another potential area for confusion relates to the unit of measurement for each RT setting. For example, the Maquet Servo-i RT setting is expressed in seconds. The Hamilton G5 is expressed in milliseconds, the Puritan Bennett in percent, and the Viasys Avea lists no unit of measurement. The inconsistencies addressed above are testament to the potential level of confusion that may exist among practitioners. Table 2 displays the minimum and maximum RT values for the same five ventilators.

Inspiratory Cycling Criteria

Inspiratory cycling criteria (ICC) setting determines the percent of peak inspiratory flow at which the ventilator cycles from inspiration to expiration.³ Research has shown that adjustments in ICC can increase tidal volumes, decrease respiratory rates, and decrease work of breathing.⁴ Similar to RT, nomenclature for ICC varies in name and setting when comparing ventilator manufacturers.

In addition, not all ventilator manufacturers allow for adjustments in ICC. Four of the ventilators previously compared allow for variation in the ICC setting. Of the five ventilators; the Drager Evita is the only ventilator that does not allow a variable ICC setting. It maintains a fixed ICC value of 25%, meaning that the Drager Evita will cycle into expiration once the flow rate during a pressure supported breath declines to 25% of its peak inspiratory flow rate. Table 3 displays the various ICC settings and names on the same five ventilators.

Implications

With the wide acceptance of therapist weaning protocols, practitioners are more responsible than ever for knowing all aspects of mechanical ventilation as well as communicating the purpose of these setting to other providers. A complete understanding of RT and ICC has the potential to positively impact a weaning trial, the length of time on the ventilator, and patient-ventilator synchrony. Making minimal adjustments in RT and ICC may result in a beneficial change in inspiratory time, initial inspiratory flow, and patient work of breathing.

Another benefit of comprehensive knowledge relates to who determines the initial and subsequent settings for RT and ICC. The physician traditionally does not write an order for RT and ICC. Therefore, practitioners must rely on their own knowledge and understanding of these two settings when making adjustments. If the practitioner is well versed in RT and ICC function there is a higher likelihood that the settings will be

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Table 1. Rise Time settings and names

Ventilators	Rise Time Name	Settings
Drager Evita	Slope	0-2
Puritan Bennett 840	Rise Time %	0-100%
Maquet Servo-I	Inspiratory Rise Time	0-0.4 sec
Viasys Avea	PSV Rise	1-9
Hamilton G5	P-ramp	25 – 200ms

Table 2. Minimum and maximum Rise Time values.

Ventilator	Minimum RT	Maximum RT
Drager Evita	2 sec	0 sec
Puritan Bennett 840	1%	100%
Maquet Servo-I	0.4 sec	0 sec
Viasys Avea	9	1
Hamilton G5	200 ms	25 ms

Table 3. ICC settings and names.

Ventilator	ICC Name	ICC Setting
Drager Evita	N/A	25%
Puritan Bennett 840	ESENS	1-80%
Maquet Servo-I	Inspiratory Cycle-off	1-70%
Viasys Avea	PSV Cycle	5-45%
Hamilton G5	Expiratory Trigger Sensitivity	5-70%

adjusted when required. Also, the practitioner will understand when the RT and ICC may or may not benefit a particular patient in a particular situation. Often bedside solutions require minor adjustments in ventilator settings.

As the ventilator industry continues develop advanced modes and settings, practitioners must continue to educate themselves in the ventilator terminology. Practitioners must continue to stay educated with a broad spectrum of mechanical ventilators and not just the ventilators available at their respective workplace.

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Sound Measurement Comparisons of Two Manufacturers' Continuous Positive Airway Pressure (CPAP) Devices

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Abstract

Unwanted sound may delay or disturb sleep. Sound produced by a continuous positive airway pressure (CPAP) device may disrupt sleep or deter the use of the therapy. An evaluation of sound characteristics of two commercially available CPAP devices was conducted according to standardized test procedures. Sound was measured during simulated breathing. Differences in sound characteristics were confirmed depending upon the operating condition (with and without a humidifier, and with and without flexible expiratory pressure relief) and by the brand of CPAP device.

Background

Continuous Positive Airway Pressure (CPAP) treatment is the gold standard¹ for moderate to severe obstructive sleep apnea (OSA). Adherence to CPAP therapy involves many factors: perceived health benefit of CPAP therapy, ease of use of the mask and CPAP device, toleration of device blower noise, and bed partner's acceptance.^{2,3} CPAP is an effective therapy for OSA but only when it is used. Adherence is defined as a patient's use of CPAP therapy per night.

Sound from CPAP therapy includes sound from the CPAP unit and the mask (patient interface). The sounds from the mask are the result of unintentional and intentional air leaks from an opening that allows exhaled air to exit from the breathing circuit. As airflow changes with breathing (inhalation and exhalation), the characteristics of the sound changes as the motor in the therapy device makes adjustments to deliver the set pressure. These changes in sound may be disturbing to the patient or bed partner. Sound with undesirable characteristics is defined as noise. Undesirable characteristics may be the result of the sound intensity or volume or variations in the sound.

Due to the restorative function of sleep, noise-induced sleep disturbances may create alterations in sleep stage changes and sleep quality which may result in impairment of mood and performance. The extent of the reactions to noise depends on the characteristics of the noise and may vary by individual. Intermittent noise may be more disturbing than a constant sound. Sound variation produced by CPAP devices while in use has not been objectively tested.

An independent evaluation was undertaken to objectively

The authors are with Philips Respironics. This article was provided by Philips.

measure variations in sound produced by two commercially available CPAP systems. The testing evaluated breathing noise (the variation in device noise level during the breathing cycle).

Methods

Dynamic noise, or the noise level when someone is breathing (breathing noise), testing was completed by Orfield Laboratories Inc (an independent testing organization) on the System One REMstar Auto (Philips Respironics Inc, Murrysville, PA) and the ResMed S9 AutoSet CPAP devices (ResMed Corporation, San Diego CA). The test environment consisted of an open space above a reflecting plane in an anechoic chamber. A 10-microphone hemispherical measurement array was used to measure sound levels in multiple locations. Testing was conducted as required by ISO 17510-1:2007 and ISO 3744:1994 standards. See Figure 1, Test Set-up.

Three devices of the same make and model were evaluated. Devices were tested using various accessories and breathing comfort features and each was set to a standard pressure (Table 1). Each device was connected to a lung simulator generating a tidal volume of 500 cc, a breathing rate of 15 breaths per minute and an I:E ratio of 1:1. Recordings were made for a standard amount of time for each device in each condition. Breathing noise sound levels were calculated by taking the difference between the highest and lowest sound level measured over the period tested for each condition.

Results

Results are summarized in Table 2. In all cases, the System One device produced less sound level variation.

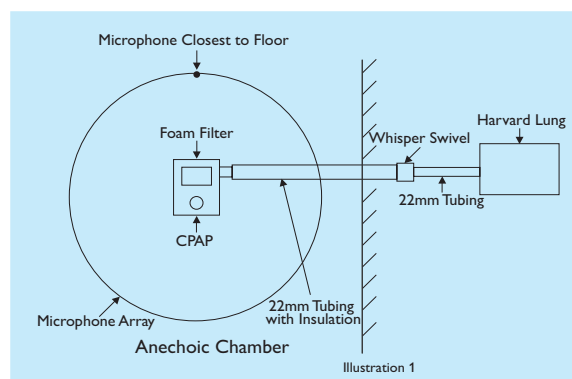


Figure 1. Test Set-Up.

Table 1. Four test conditions.

Device	Pressure	Humidifier	Pressure Relief
System One REMstar Auto	10 cm H ₂ O	none	0
S9 AutoSet	10 cm H ₂ O	none	0
System One REMstar Auto	10 cm H ₂ O	none	3
S9 AutoSet	10 cm H ₂ O	none	3
System One REMstar Auto	10 cm H ₂ O	yes, filled	0
S9 AutoSet	10 cm H ₂ O	yes, filled	0
System One REMstar Auto	10 cm H ₂ O	yes, filled	3
S9 AutoSet	10 cm H ₂ O	yes, filled	3

Table 2. Dynamic sound testing results.

Device set-up	Sound level variation (dBA)	Difference
System One REMstar Auto, no humidifier, Flex=0	2.6	
S9 AutoSet, no humidifier, EPR=0	4.3	1.7
System One REMstar Auto, no humidifier, Flex=3	3.4	
S9 AutoSet, no humidifier, EPR=3	4.5	1.1
System One REMstar Auto, full humidifier, Flex=0	3.5	
S9 AutoSet, full humidifier, EPR=0	4.6	0.9
System One REMstar Auto, full humidifier, Flex=3	4.2	
S9 AutoSet, full humidifier, EPR=3	4.8	0.6

Discussion

For some patients, the noise produced by a device while breathing may be a source of therapy complaints.⁴ However, the quality and properties of sound may be more of an issue than the absolute decibel level. A consistent sound will likely be less disruptive than sound that varies such as the comparison of a fan running to a dripping faucet.

Adherence is a major issue in the treatment of sleep-disordered breathing; device noise may present an obstacle to adequate therapy use. Minimizing sound variation, a therapy device producing a more constant sound may be less likely to disturb sleep and therefore less of a hindrance to compliance. Intermittent noise can impair sleep quality⁵ so the more consistent the sound property, the less likely a patient is to experience delayed or disrupted sleep.

This study demonstrates that the variation in sound differs by the type of device. The addition of a humidifier and the utilization of expiratory pressure relief affect the variation of the sound produced by the CPAP device. Smaller variation in sound level during breathing may be less noticeable to patients and may eliminate one obstacle to adherence.

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Research Review: Noninvasive Monitoring

Would you eat a 30-day-old steak that's been sitting in the refrigerator for dinner? Most people wouldn't dream of putting food that old into their bodies. But if you are one of the 10 million patients having surgery this year, chances are you may be putting blood that's over 30 days old into your body...with potentially deadly repercussions.

Mounting evidence has shown that blood transfusions significantly increase morbidity and mortality by up to 38%. When necessary, there is no question that blood transfusions can save lives. But unnecessary blood transfusions are causing unnecessary deaths and serious complications that burden our healthcare system... unnecessarily. Receiving stale blood and its physiological impact on body systems and health state are just two of the known risks that make blood transfusions seriously risky business. But according to the results of a new study, a new noninvasive medical technology could help significantly reduce the likelihood of receiving a blood transfusion altogether.

Using a new noninvasive and continuous hemoglobin (SpHb) monitoring technology developed by Masimo, researchers at MGH, Harvard Medical School, and Vanderbilt University Medical Center were able to dramatically reduce the need for and frequency of blood transfusions administered during surgery by 86%, proving that with the right technology, unnecessary blood transfusions and their risks can be safely avoided. And, when a transfusion was a lifesaving necessity during surgery, noninvasive hemoglobin monitoring helped researchers to transfuse more conservatively, reducing the amount of blood transfused by 90% to help lower the likely risk and impact of transfusion-related complications.

This is a major advancement in both science and patient care, as doctors have been waiting for a way to immediately, continuously, and noninvasively measure hemoglobin so that they would absolutely know when to transfuse and when not to – without having to guess or waste precious minutes waiting on lab results.

A first of its kind randomized controlled trial study on noninvasive and continuous hemoglobin monitoring technology showed it cuts the need for and frequency of blood transfusions by 86% and the amount transfused by 90% during surgery.

According to lead researcher, Jesse M. Ehrenfeld, MD, MPH,

This article was provided by Masimo.

recently appointed as Director, Center for Evidence Based Anesthesia at Vanderbilt University Medical Center, “Blood transfusions pose real risks to patients and are also a major contributor to the cost of surgical care. Very few monitoring technologies are subjected to the rigor of a randomized controlled trial, and even fewer are able to show a significant impact on clinician behavior and ultimate patient outcome. Our study has demonstrated that SpHb monitoring clearly changes clinician behavior and results in lower intraoperative blood transfusion rates and lower overall blood utilization. These findings have important clinical implications for hospitals around the world who are seeking to reduce surgical patient risk and costs.”

Traditional blood analysis has many drawbacks, including complexity, time-consuming turnaround times that can impact clinical decisions, and blood loss due to invasive blood draws that have been found to contribute substantially to the anemic conditions that commonly occur in critically-ill patients – thereby increasing transfusion rates. Published studies have shown that transfusion of just one or two units of blood significantly increases infection, pneumonia, sepsis, and mortality after surgery by up to 40%. These studies also suggest that transfusions and their associated risks could be “largely avoided” through implementation of better blood management techniques and “more appropriate indicators” for transfusions. The ability to continuously and noninvasively trend a patient's hemoglobin level with Masimo SpHb offers a breakthrough in blood management with the potential to improve clinical decision-making, reduce patient exposure to unnecessary blood transfusions, and preserve precious blood resources.

The full title of the study is: Impact of Continuous and Noninvasive Hemoglobin Monitoring on Intraoperative Blood Transfusions, Ehrenfeld, et al. According to the abstract: Blood transfusions continue to pose real patient risk in the form of adverse outcomes such as postoperative infection, cancer recurrence, impaired pulmonary function, as well as increased length of stay and mortality. Additionally, transfusion is a costly and a significant contributor to the expense of surgical care. Laboratory hemoglobin (Hb) values are a primary indicator of the need for blood transfusion, but testing is intermittent and results are often delayed. Continuous, noninvasive hemoglobin (SpHb) monitoring is now possible with a Pulse CO-Oximeter and multiwavelength adhesive sensor. We hypothesized that SpHb monitoring could reduce intraoperative blood transfusions. *Continued on page 48...*

An Evaluation of Exercise Tolerance in COPD Patients Using Six Minute Walk Test: a prospective study

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Abstract

Background: Functional exercise tolerance in patients with chronic obstructive pulmonary disease (COPD) is often assessed by the 6 minute walk test. Impairment of exercise tolerance is an important feature of COPD. Physical deconditioning and impaired lung function are main causes of decreased exercise tolerance. This study explored the evaluation of exercise tolerance in COPD patients using the simple six minute walk test.

Design: A prospective 4 week quasi-experimental study design.

Setting: Institute of Pulmonary Medicine and Research, Sri Ramakrishna Hospital, Coimbatore, India.

Patients: 10 patients with moderate and severe cases of COPD were included in the study.

Interventions: Patients who were admitted to the pulmonology general ward because of acute exacerbations and responded well to medical treatment were screened for Borg Scale Rate of Perceived Exertion and six minute walk test on 3rd day of hospital stay and the post test measurements were taken at 7th day. The statistical analysis was done using paired t test at the level of significance $\alpha=0.05$

Results: We compared the Borg Scale and six minute walk test on 3rd day of hospital stay and at 7th day. The result showed significant improvement in terms of reduced exertional dyspnea and increased six minute walk distance.

Conclusion: In light of assessing exercise tolerance in COPD patients, it has been concluded that six minute walk test was a useful tool in evaluating exercise tolerance in COPD patients, since it was easy to perform and very cost-effective.

Background

Functional exercise tolerance in patients with chronic obstructive pulmonary disease (COPD) is often assessed by the 6 min walk test (6MWT).¹ Impairment of exercise tolerance in COPD patients has important implications for health related quality of life, hospitalization rate and survival.² The impaired exercise tolerance may be due to peripheral muscle dysfunction characterized by atrophic muscle and reduced fatigue

resistance.³ As many as 70% of COPD patients may be affected by impaired exercise tolerance.³

Impaired exercise tolerance may lead to energy cost while doing activities of daily living in COPD patients.⁴ This may affect psychological well being and would increase sickness and absenteeism in the workplace. Recommendations on exercise testing in lung function laboratory settings are well established, and the role of incremental cardiopulmonary cycling exercise as the gold standard for evaluation of exercise tolerance is acknowledged.⁵ However, a widespread clinical use of simple exercise protocols are effective because of their simplicity, applicability and low cost.⁶⁻⁸ Moreover, timed walking tests have been shown to predict survival⁹ and utilization of health care resources¹⁰ in COPD. Based on this hypothesis we conducted this study to evaluate the exercise tolerance in COPD patients using the six minute walk test (6MWT). Therefore, it is suggested that simple exercise tests may be useful for staging of the disease.¹¹

The six minute walk test (6MWT) has been widely used and accepted as a simple, cost-effective means of clinically assessing the functional status of COPD patients. The 6MWT has proven reliable in providing reproducible data to serve as measures of pre and post treatment comparisons¹²⁻¹⁷ in the assessment of functional status¹⁸⁻²⁰ and in predicting morbidity and mortality for various disease states.²¹⁻²³ Distance testing was first advocated by Balke²⁴ in 1983 as a means of assessing physical fitness. McGavin²⁵ used a 12 min walk test to assess disability in patients with COPD. Subsequent work determined the effectiveness and reliability of shorter-distance walk testing and eventually the 6MWT became the most widely accepted protocol. The 6MWT is a sub maximal, self paced test used to evaluate the exercise tolerance in COPD patients in this study.

Materials and Methods

This study, in accordance with the research design as stated by C.R. Kothari,²⁶ was a prospective 4 weeks quasi-experimental study design in which a convenient sampling method was used.²⁵ Patients admitted to the Pulmonology General Ward at Sri Ramakrishna Hospital, Coimbatore, India were selected for the study, informed consent was obtained and 10 moderate and severe patients who were medically stable met with an inclusion criterion as follows: $FEV_1/FVC < 0.70$, $50\% \leq FEV_1 < 80\%$ predicted for moderate and $FEV_1/FVC < 0.70$, $30\% \leq FEV_1 < 50\%$ predicted for severe, pre bronchodilator to post response of $>20\%$, baseline dyspnea grade 2 using MRC, good left ventricular ejection

The authors are, respectively, Senior Lecturer, Lovely Professional University, Punjab and Head, Institute of Pulmonary Medicine, Sri Ramakrishna Hospital, Coimbatore, India.

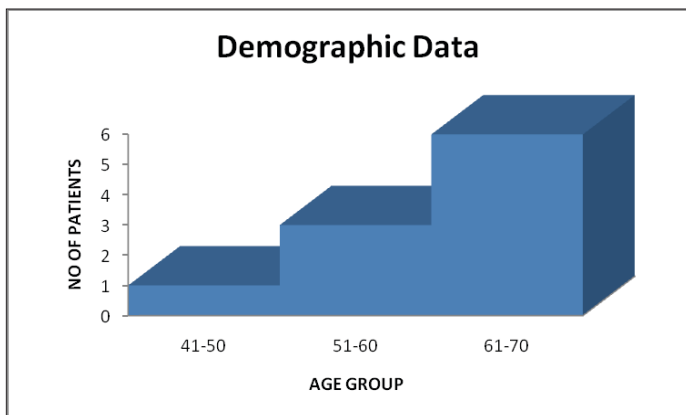


Figure 1. Demographic Data.

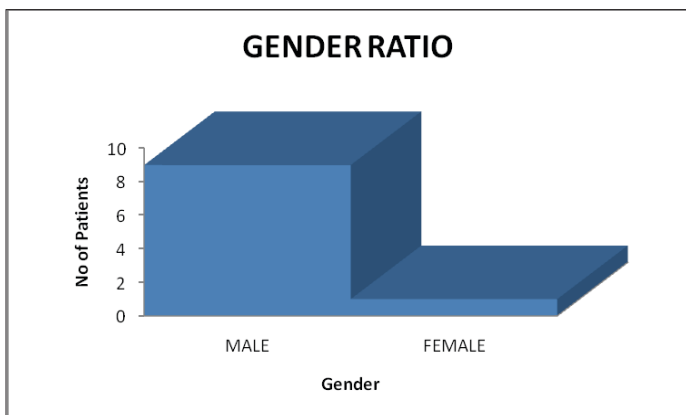


Figure 2. Gender Ratio.

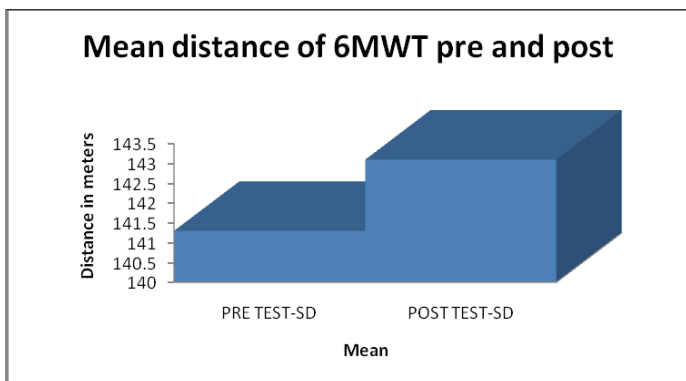


Figure 3. Mean Distance.

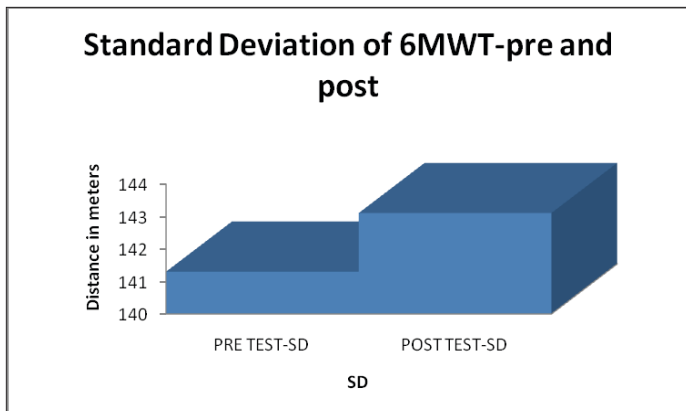


Figure 4. Standard deviation of 6MWT distance.

fraction and age group of 40-70 years, both male and female, ex smoker and stable vital signs.

The exclusion criterion were acute exacerbation not responding to medical treatment, intermittent claudication, associated cardiac failure, osteoarthritis, musculoskeletal pain, syncope and dyspnea at rest.

Baseline evaluation for Borg Scale of Rate of perceived exertion and 6MWT was taken at 3rd day of hospital stay since the subjects received conventional chest physiotherapy techniques such as repatterning techniques, breathing exercises, strategies to reduce increased respiratory rate, and relaxation techniques. The six minute walk test was carried out according to American Thoracic Society guidelines²⁷ 2002. The safety issues for conducting 6MWT as mentioned in American Thoracic Society guidelines was adopted. The patients were asked to take bronchodilator therapy^{28,29} 2 hours before walking. Pre and post test measurements were assessed using paired t test at $p=0.05$ and analysis was done using SPSS 17.

Measurements

Conventional chest physiotherapy was given to patients exactly two hours before the start of 6MWT to gain relaxation and to reduce respiratory rate and to gain confidence. The conventional chest physiotherapy was given twice daily for seven days. After the patients underwent chest physiotherapy, vital signs were checked including blood pressure, heart rate, respiratory rate, temperature and saturation of percentage of oxygen using pulse oximetry. The rate of perceived exertion was assessed using Borg Scale (20 point scale) before the commencement of 6MWT to assess exertional dyspnea. Six minute walk test was conducted after brief explanation to the patients. They were instructed to walk in a 100 m corridor where the Emergency Department was accessed easily to avoid any adverse effects. However, a trolley consisting of a defibrillator, emergency medications including atropine and a mobile oxygen therapy unit was kept in the corridor for safety. The rest periods were included in the study as per American Thoracic Society Guidelines²⁷ and the distance was measured in meters. Base line six minute walk distances were measured during 3rd day of hospital stay and post test measurements were taken at 7th day of hospital stay. A stop watch was used to record the time traveled by the patients and mechanical lap counter was used to record distance.

Results

The six minute walk distance in meters showed good improvement in terms of increased walking distance when we compared pre and post test readings, as mean distance was 243 ± 277 and standard deviation was 141.3 ± 143.1 ; the t value 10.854 was more than the critical value at $p=0.05$ level of significance. This ensured that the six minute walk test was a good indicator for measuring exercise tolerance in COPD patients.

The Borg Scale of perceived exertion also showed moderate improvement as compared to six minute walk distance in meters since its mean value was 11.4 ± 13.6 and standard deviation was 4.59 ± 4.42 and the t value 11 was more than the critical value at $p=0.05$.

Discussion

Reduced exercise tolerance is generally accepted as an unavoidable complication of advanced COPD; the presence

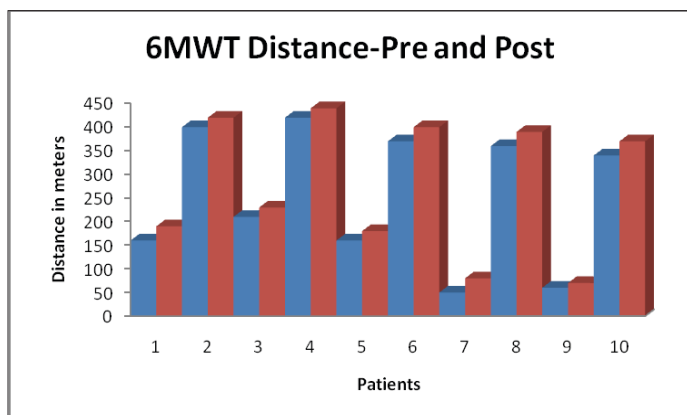


Figure 5. 6MWT Distance in meters.

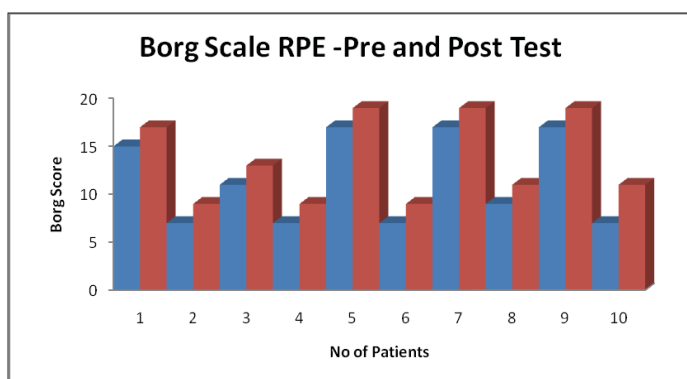


Figure 6. Borg Scale Pre and Post Test .

of different degrees of physical limitation in patients with comparable lung function impairment, however, suggests a multifactorial origin for this phenomenon. Although airway obstruction has classically been considered the most important of these pathogenetic factors, studies aimed at comparing lung function impairment and exercise tolerance in COPD failed to establish a clear correlation between the two parameters,^{28,29} probable difference in age groups or gender ratio, and also the differences in study population.

In this study, 9 male patients and 1 female patient participated, since males were more affected than females in India due to their personal habits of smoking and other socio-economic history. Jindal S.K. et al reported the prevalence of COPD³⁰ in males and females in India and they concluded that the disease is distinctly more common in males. The male to female ratio had varied from 1.32:1 to 2.6:1 in different studies with a median ratio of 1.6:1. In our study the total number of patients in age group of 41-50, 51-60, 61-70 were 1, 3, 6 respectively. This is shown in figure 1, and the gender ratio is shown in figure 2.

Killian J et al (1992)³¹ postulated that lower limb fatigue is another factor contributing to exercise intolerance, particularly in deconditioned elderly patients due to a variable degree of muscle atrophy leading to a significant reduction in muscle strength and endurance. Initially, the patients were uneasy about the six minute walk test because they thought it would exaggerate their symptoms, ie fatigue, but after careful explanation they realized that it would benefit their psychological well being and have other positive benefits. The self paced 6MWT didn't cause any exertional dyspnea while walking but after the test 75% of the patients experienced

dyspnea and light dizziness due to work load imposed on respiratory muscles, especially the age group of 51-60 and 61-70. This might not have altered the results, but was psychologically troublesome to some of the patients.

The use of the 6MWT as a single measurement of the exercise tolerance for COPD patients was widely accepted as stated by Redelmeier et al.³² In their study, they conducted 6MWT in 119 patients (mean age=67) and concluded that 6MWT was significantly correlated with patients' ratings of their walking ability relative to other patients ($r=0.59$, 95% confidence interval [CI] 0.54 to 0.63). They suggested that differences in functional status can be statistically significant but below the threshold at which patients notice a difference in themselves relative to others; an awareness of the smallest difference in walking distance that is noticeable to patients may help clinicians interpret the effectiveness of symptomatic treatments for COPD.

In this study, the mean age was 57.6 and the improvements in walking distance were quite significant. The mean distance was 243 ± 277 ; standard deviation was 141.3 ± 143.1 (figures 3 and 4). The determination of what constitutes a significant clinical change as a result of an intervention has been debated with generally well-accepted parameters for patients with COPD. The minimal important clinical difference in patients with COPD is reported to be approximately 55 m for cohorts,³³ and 86 m for individuals.³⁴ Our participants also showed significant differences in walking distance as compared to pre and post test measurements and the values were statistically significant at $p=0.05$.

The pre and post test measurements of 6MWT distance is shown in figure 5. Out of 10 patients, only 3 patients got less improvement in terms of walking distance. These belonged to the 61-70 age group. As such, age might be the limiting factor, as postulated by Killian³⁰ and his colleague in their research studies. There has always been a debate about the relationship between exertional dyspnea and 6MWT, since the speculation arises that submaximal exercise tests such as 6MWT also causes exertional dyspnea. In our study, we used the Borg Scale Rate of Perceived Exertion to evaluate exertional dyspnea.

Sue C. Jenkins³⁵ stated that dyspnea during activities of daily living is frequently reported by patients with COPD and can result in inactivity and the associated problems of deconditioning and muscle weakness. As far as we were concerned there was only one article that measured daily physical activity in COPD patients ($n=50$) and compared the findings to data obtained in age and gender matched healthy controls ($n=25$).^{36,37} Compared to the healthy controls, COPD patients spent significantly less time standing and walking during daily activities ($P<0.001$, for both).

The mean score of Borg Scale was 11.4 ± 13.6 and standard deviation was 4.59 ± 4.42 . Based on the mean value of Borg Scale we would state that patients were at the score of 11, which indicated fairly light and 13 indicating somewhat hard, with reference to the 15 point Borg Scale.³⁸ One of the potential reasons for exertional dyspnea is hyperinflation of the lungs with air trapping in the alveoli, which leads to an increased residual volume and as a consequence increases breathlessness on exertion. As a result of hyperinflation of the lungs, the natural dome of the diaphragm gets flattened. This requires more effort to breathe, which places a burden on the accessory

muscles during respiration. Consequently any activity such as walking, bending to tie shoelaces or shopping will worsen the breathlessness.³⁹

The pre and post test measurements of Borg Scale are shown in Figure 6. The reliability and reproducibility of Borg Scale had been investigated by many researchers. Wilson RC, Jones PW⁴⁰ stated that Borg Scale provides a reliable technique for studying the sensation of breathlessness in short and extended periods of time. O'Donnell, DE⁴¹ et al evaluated the reliability of Borg Scale and concluded that it was good indicator of measuring exertional dyspnea. Though numerous studies supported the reliability of the Borg Scale, its subjective nature would alter test results, and this could be one of the limitations in this study.

The possible mechanism for the improvement in walking distances using 6MWT would be the greater muscle mass, especially quadriceps involved in walking that increases muscular O₂ extraction thereby inducing a substantial decrease in venous pressure of O₂⁴² and also improved overall oxidative capacity of the individuals. Moreover, COPD patients are more dependent on anaerobic metabolism rather than aerobic metabolism during walking and other exercises.⁴³

Clinical recommendations for exercise training in COPD patients include a component of sub maximal intensity, at 60% peak exercise capacity, lower limb endurance training with the aim of eliciting some physiological training effects.⁴⁴ To achieve this, 6MWT was used in this study.

According to Frank I. Katch and Victor L. Katch,⁴⁵ several weeks of walking training at sub maximal intensity reduces the ventilator equivalent for oxygen (VE/VO₂) and lowers the percentage of the total exercise oxygen cost attributable to breathing. They also added that reduced oxygen consumption by the ventilator musculature enhances exercise endurance for two reasons: (1) it reduces the fatiguing effects of exercise on the ventilator musculature and (2) any oxygen freed from use by the respiratory musculature becomes available to the active locomotor muscles. This would support our hypothesis that 6MWT improves endurance and evaluates exercise tolerance in COPD patients. Since we didn't measure VO₂ Max to estimate the oxygen capacity, this might be one of the limitations in our study.

The reliability and validity of the 6MWT was well established in a number of studies. In one study, the validity of the 6MWT is demonstrated by the moderate to good relationship ($r \geq 0.5$) between 6MWD and peak oxygen consumption (VO_{2 peak}) measured during a laboratory-based incremental exercise test to peak work capacity in patients with COPD.⁴⁶⁻⁴⁹ The relationship tends to be strongest ($r > 0.7$) in patients with more severe functional limitation, because a self paced walking test for these individuals more closely represents maximal exercise performance.^{46,50} Absence of a control group in our study is considered to be one of the study weaknesses, as there are no published data in normal predicted distance of 6MWT in the Indian population.

Conclusion

Based on the available resources and our research experience in conducting 6MWT, the best rationale for use of the 6MWT lies in the practicality and simplicity of the test itself. The 6MWT is a cost effective procedure that may be performed in nearly any clinical location without the need for either direct physician

involvement or invasive, and often expensive, monitoring equipment. As a self-paced and sub maximal exercise procedure employing the familiar activity of walking, the 6MWT is well tolerated by patients over a wide span of fitness levels and debility. The 6MWT in comparison to other functional walking tests is felt to offer advantages that include established standards for testing, reference values, and correlation with the capacity to perform activities of daily living.¹⁷ In summary 6MWT is a reliable and valid method for evaluating exercise tolerance and also improving exercise tolerance for COPD patients owing to its simple method.

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Multidrug Resistant *Acinetobacter Baumannii*: a descriptive study in a city hospital

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Abstract

Background: Multidrug resistant *Acinetobacter baumannii*, (MRAB) is an important cause of hospital acquired infection. The purpose of this study is to determine the risk factors for MRAB in a city hospital patient population.

Methods: This study is a retrospective review of a city hospital epidemiology data base and includes 247 isolates of *Acinetobacter baumannii* (AB) from 164 patients. Multidrug resistant *Acinetobacter baumannii* was defined as resistance to more than three classes of antibiotics. Using the non-MRAB isolates as the control group, the risk factors for the acquisition of MRAB were determined.

Results: Of the 247 AB isolates 72% (177) were multidrug resistant. Fifty-eight percent (143/247) of isolates were highly resistant (resistant to imipenem, amikacin, and ampicillin-sulbactam). Of the 37 patients who died with *Acinetobacter* colonization/infection, 32 (86%) patients had the organism recovered from the respiratory tract. The factors which were found to be significantly associated ($p \leq 0.05$) with multidrug resistance include the recovery of AB from multiple sites, mechanical ventilation, previous antibiotic exposure, and the presence of neurologic impairment. Multidrug resistant *Acinetobacter* was associated with significant mortality when compared with sensitive strains ($p \leq 0.01$). When surgical patients ($N=75$) were considered separately, mechanical ventilation and multiple isolates remained the factors significantly associated with the development of multidrug resistant *Acinetobacter*. Among surgical patients 46/75 (61%) grew a multidrug resistant strain of AB and 37/75 (40%) were resistant to all commonly used antibiotics including aminoglycosides, cephalosporins, carbapenems, extended spectrum penicillins, and quinolones. Thirty-five percent of the surgical patients had AB cultured from multiple sites and 57% of the *Acinetobacter* isolates were associated with a co-infecting organism, usually a *Staphylococcus* or *Pseudomonas*. As in medical patients, the isolation of *Acinetobacter* from multiple sites and the need for mechanical ventilation were significantly associated with the development of MRAB.

Conclusions: The factors significantly associated with MRAB in both the general patient population and surgical patients were mechanical ventilation and the recovery of *Acinetobacter* from multiple anatomic sites. Previous antibiotic use and neurologic impairment were significant factors in medical patients. Colonization or infection with MRAB is associated with increased mortality.

Background

Acinetobacter baumannii, found ubiquitously in the environment, is an aerobic gram negative rod which is a non-fermenter of glucose. When stationary, AB appears as a coccobacillus, however during growth it takes on a rod form. Multidrug resistant *Acinetobacter baumannii* is an important cause of hospital acquired infection and has been shown in some studies to increase mortality and length of stay.¹

Multidrug Resistant *Acinetobacter baumannii* is often associated with co-infection by other virulent pathogens. Thus it is difficult to determine its attributable mortality. Though MRAB is considered to be a hospital acquired infection, patients occasionally present with community acquired colonization of chronic wounds. In order to provide timely and proper antibiotic therapy it is important to know the characteristics of those patients with colonization and invasive infection with MRAB. The purpose of this study is to determine the resistance patterns of AB in a city hospital and to examine the risk factors for colonization/infection in surgical patients. The source of infection and the prevalence of co-infecting pathogens will also be investigated.

Methods

Setting: This research was approved by Institutional Review Board of Meharry Medical College. The Nashville General Hospital (NGH) is a 200 bed teaching tertiary safety net hospital which serves a population of 1.5 million people. NGH also serves as a major provider of inpatient care for the Tennessee Department of Corrections. The medical/surgical intensive care unit has 18 beds and is a combined general medical and surgical semi-closed unit.

Study design: This study is a retrospective review of a city hospital epidemiology data base and includes 247 isolates of AB from 164 patients. For the period 2006 through 2008 a retrospective chart review was performed on all patients with AB isolates. The patients were identified through the hospital infection control data base. Documented patient demographics

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Table 1. Sources of 247 multi-resistant *Acinetobacter baumannii* isolates.

	N	%
Sputum	77	31
Urine	40	16
Extremity Wounds	32	13
Other	30	12
Blood	26	10
CVP Catheter	23	9
Decubitus Ulcer	19	8

and potential risk factors included diagnosis, length of stay, patient location, age, sex, race, previous institutionalization, previous antibiotic use, mechanical ventilation, tracheostomy, and underlying co-morbidity. The source of the AB isolates was also noted as well as the patient outcome.

Previous institutionalization included prior hospitalization, nursing home residency, or incarceration within 90 days of a positive AB culture date. Prior antibiotic use was noted for those patients who received an antibiotic within one month of the AB isolation. The resistance patterns of all isolates were included in the analysis; however patients with more than one isolate were counted only once. The source of the AB isolate is the anatomic site where the culture was obtained.

Identification and characterization of MRAB: The identification of the isolates as *Acinetobacter* and susceptibility testing of those isolates was performed using a Siemens microscan system, which is FDA approved for this use in clinical laboratories. Testing was performed according to manufacturer specifications for this instrument and was done in accordance with NCCLS recommended practices. This instrument makes use of broth microdilution methodology to determine resistance.

Table 2. Risk factors for 247 isolates of multi-resistant *Acinetobacter baumannii* (all patients, N=164).

Risk factor	MDRAB (N=122)	Control (N=42)	p-value ¹	Odds Ratio	95% C.I.2
Surgical admission	53	22	0.32	0.7	0.35 - 1.141
Age >55	49	12	0.18	1.68	0.78 - 3.59
Male Gender	90	27	0.24	1.56	0.74 - 3.30
Institutionalized <90 days prior to admission	91	32	0.84	0.92	0.41 - 2.08
Multiple Isolates	53	3	<0.01	9.98	2.93 - 34.08
Mechanical Ventilation	65	3	<0.01	14.82	4.35 - 50.57
Previous antibiotics	111	33	0.03	2.75	1.05 - 7.21
Quinolone	50	11	0.09	1.96	0.90 - 4.26
Co-morbidity ³	111	33	0.03	2.75	1.05 - 7.21
COPD ⁴	19	2	0.07	3.69	0.82 - 16.57
Neurologic impairment ⁵	27	3	0.03	3.69	1.06 - 12.89
Diabetes mellitus	35	19	0.05	0.49	0.24 - 1.00
Mortality	36	1	<0.01	17.24	1.70 - 83.33

¹ p-values derived from Fisher's exact test

² C.I. – 95% Confidence Interval

³ Congestive heart failure, chronic pancreatitis, peripheral vascular disease, coronary artery disease, chronic obstructive pulmonary disease, diabetes mellitus, end stage renal disease, asthma, cancer, obesity, hepatitis, human immunodeficiency virus

⁴ COPD – Chronic Obstructive Pulmonary Disease

⁵ Cerebrovascular accident, Traumatic brain injury, Alzheimer's disease, Spinal cord injury

Table 3. Risk Factors for multi-resistant *Acinetobacter baumannii* in surgical patients (N=75).

Risk factor	MDRAB ¹ (N=51)	Control (N=24)	p-value ²	Odds Ratio	95% C.I.3
Age >55	19	9	0.37	1.56	0.59 - 4.17
Male Gender	33	19	0.57	1.34	0.49 - 3.63
days prior to admission Institutionalized <90	32	20	0.96	1.03	0.38 - 2.82
Multiple Isolates	22	5	<0.01	4.4	1.43 - 13.54
Mechanical Ventilation	22	4	<0.01	5.73	1.72 - 19.09
Previous Antibiotics	41	25	0.73	1.31	0.32 - 5.35
Co-infection	26	8	0.64	1.09	0.76 - 1.56
Co-morbidity	41	23	0.32	2.14	0.59 - 7.79
Mortality	12	0	0.01	1.85	1.48 - 2.33

¹ Multi-resistant *Acinetobacter baumannii*

² p-values derived from Fisher's exact test

³ C.I. – 95% Confidence interval

An isolate was deemed pan-sensitive if it was sensitive to all commonly tested antibiotics except colistin and highly sensitive if it was sensitive to imipenem, amikacin, and ampicillin-sulbactam. The isolate was considered highly resistant if it was resistant to imipenem, amikacin, and ampicillin-sulbactam. An isolate was classified as pan-resistant if it was resistant to all commonly used antibiotics. Multidrug resistant *Acinetobacter baumannii* isolates are defined as those resistant to more than three classes of antibiotics. A distinction was made between carbapenems and the non-carbapenem β-lactam antibiotics because carbapenem resistance is a sentinel event for emerging antimicrobial resistance and in itself confers high resistance. This study is designed to document the risk factors for the isolation of MRAB in our surgical patient population, thus no attempt was made to distinguish between colonization and invasive infection. The differences between groups were determined by Student's T-test for continuous data or the Fisher's exact test for categorical data (2-tailed). The significance level threshold was a p-value of ≤0.05.

Results

Multidrug resistant *Acinetobacter baumannii* is defined as resistance to more than three classes of antibiotics. Of the 247 AB isolates, 177 (72%) were multidrug resistant. More than half of the isolates, 143/247 (58%) were resistant to imipenem, amikacin, and ampicillin-sulbactam; thus classifying these isolates as highly resistant. This is intriguing as these antibiotics were formerly very effective against AB. Only 42 (17%) of the isolates were sensitive to all three of the above antimicrobial agents. Forty-six percent (113/247) of the isolates were resistant to all commonly used antibiotics including aminoglycosides, cephalosporins, carbapenems, extended spectrum penicillins, and quinolones and therefore were classified as pan-resistant.

The sources of AB isolates in all patients are shown in Table 1. The major site of AB isolation in this study was the respiratory tract. Due to the inconsistency of obtaining quantitative cultures it was not possible to determine infection vs. colonization, however 32/37 (86%) of all patients who died had a positive isolate recovered from the respiratory tract. Among the positive wound isolates the majority were from chronic diabetic wounds, amputation sites, and decubitus ulcers. Using the non-MRAB isolates as the control group, the risk factors for the acquisition

Table 4. Co-infecting organisms in 75 surgical patients

Organism	N	%
MRSA1	18	24
MSSA2	25	33
<i>Pseudomonas aeruginosa</i>	11	14
<i>Proteus mirabilis</i>	6	8
<i>Escherichia coli</i>	5	7
<i>Enterococcus faecalis</i>	5	7
<i>Enterobacter cloacae</i>	5	7
<i>Staphylococcus epidermidis</i>	4	5
<i>Klebsiella pneumoniae</i>	4	5

¹ Methicillin resistant *Staphylococcus aureus*

² Methicillin sensitive *Staphylococcus aureus*

of MRAB were determined (Table 2). The factors which were significantly associated with multidrug resistance include the recovery of *Acinetobacter* from multiple sites, mechanical ventilation, previous antibiotic use, and the presence of co-morbidity (especially neurologic impairment). Diabetes mellitus and the previous use of quinolones trended toward significance.

Forty six percent of the total patients (75/164) were admitted to the surgical service and the analysis appears in Table 3. The sites of AB isolation in surgical patients were wounds 36 (47.4%), respiratory tract 17 (23%), urinary tract 14 (18%), blood 5 (7%) and vascular catheters 3 (4%). Thirty-five percent of the surgical patients had AB cultured from multiple sites and 57% percent of the AB isolates in surgical patients were associated with a co-infecting organism, usually a *Staphylococcus* or *Pseudomonas* (Table 4). While the finding of *Acinetobacter* in multiple sites was associated with increased likelihood of multidrug resistance ($p \leq 0.01$), no significant association was found for co-infecting organisms.

Among surgical patients 46/75 (61%) of isolates were MRAB and 37/75 (40%) were resistant to all commonly used antibiotics. The majority of surgical patients with positive AB isolates (69%) had been institutionalized as inpatients, nursing home residents, or inmates within 90 days prior to the positive AB culture. Peculiar to this hospital population, 18 (24%) of surgical patients had been incarcerated. Three patients (4%) had *Acinetobacter* recovered from chronic wounds without a history of prior institutionalization. Twenty six surgical patients (35%) required mechanical ventilation or tracheostomy. Mechanical ventilation ($p < 0.01$) was significantly associated with the development of MRAB.

The majority (92%) of surgical patients with AB colonization received antibiotics within 30 days of the positive culture. The most frequent antibiotics prescribed were non-carbapenem β -Lactams (39%), and fluoroquinolones (27%), aminoglycosides (15%), and carbapenems (13%). Overall prior exposure to antibiotics was not a significant risk factor in the development of MRAB in this group of surgical patients, however the previous use of non-carbapenem β -lactams trended toward significance ($p = 0.07$).

A co-morbidity was present in 63(84%) of surgical patients but overall was not a risk factor for MRAB in this study ($p = 0.32$). The most frequent co-morbidity associated with MRAB in this study is diabetes mellitus 27/75 (36%), followed by chronic obstructive pulmonary disease (12%), neurological impairment (9%), and cardiovascular disease (8%).

With regard to outcome, 41% of patients were discharged to home, 32% were discharged to nursing homes or transferred to other inpatient facilities, and 16% died. The mean length of stay for sensitive and multidrug resistant *Acinetobacter* (32 vs 29 days) was not significantly different ($p > 0.05$). Of the surgical deaths, all patients had MRAB and 9/12 (75%) were colonized or infected with pan-resistant AB. Overall, the presence of co-infection with other organisms did not contribute significantly to mortality ($p = 0.75$). The only organism that approached significance with respect to affecting survival was *Pseudomonas aeruginosa* ($p = 0.07$).

Discussion

Acinetobacter baumannii has become an important pathogen in recent years and has been shown to increase morbidity and mortality.¹⁻³ The definition of MRAB varies in the literature, but several authorities consider an isolate to be multidrug resistant if it is resistant to three or more classes of antibiotics.⁴ Resistant AB is a significant problem as seen in this study where 72% of isolates were considered multidrug resistant and 58% were resistant to imipenem, amikacin, and ampicillin-sulbactam, formerly very effective antibiotics. Nearly half (46%) of all isolates were resistant to all commonly used antibiotics including aminoglycosides, cephalosporins, carbapenems, extended spectrum penicillins, and quinolones. A distinction was made between carbapenems and the non-carbapenem β -lactam antibiotics because carbapenem resistance is a sentinel event for emerging antimicrobial resistance and in itself confers high resistance and therapeutic challenges.⁵

The factors associated with the isolation of AB in our combined medical and surgical patient groups include mechanical ventilation, previous antibiotic therapy, co-morbidity, especially neurologic impairment, and multiple *Acinetobacter* isolates. The significant factors for MRAB in the surgical group were mechanical ventilation, multiple isolates, and neurologic impairment. These findings are consistent with other reports.^{6,9} The most frequent antibiotics prescribed in this study population were β -lactams, followed by fluoroquinolones, aminoglycosides, and carbapenems. The prior exposure to quinolones trended toward significance which is documented in previous reports.¹⁰

Several investigators have found an association of MRAB with co-morbidities.⁷ Our patients had significant rates of diabetes mellitus, cardiovascular disease, chronic obstructive lung disease and neurological impairment. A co-morbid condition was found in 84% of our surgical cohort, however only neurologic impairment achieved significance. Neurologic injury, in particular paraplegia has been shown to be associated with the development of resistant *Acinetobacter*.¹¹ Our neurologically impaired population had a high prevalence of chronic wounds such as decubitus ulcers and most were nursing home residents. This most likely explains the significant increased risk of resistant *Acinetobacter* in this group.

Chronic obstructive pulmonary disease and diabetes showed a trend toward significant associations with the development of multidrug resistant *Acinetobacter*. It is well accepted that patients with chronic lung disease are at increased risk of airway colonization and pneumonia, especially when they require intubation.¹² Additionally, intubated patients with chronic pulmonary disease are often treated with prophylactic antibiotics which increase the risk of resistance. The association with diabetes is most likely related to the high prevalence of chronic

diabetic lower extremity wounds in this patient population.

As in several other studies, this descriptive study attests to the ability of AB to colonize/infect soft tissue and bone.^{13,14} Nearly half (47%) of our surgical patients had resistant AB in chronic diabetic wounds, amputation sites, or decubitus ulcers. Several of our patients had multiple positive cultures of their wounds over a period of several months. These patients are chronic carriers of resistant AB who may develop life threatening invasive infection or serve as portals of entry of resistant AB into the hospital. Whether routine surveillance and isolation of these patients may help to prevent outbreaks is unclear.¹¹

Previous institutionalization (hospital, prison, or nursing home) did not reach the level of significance ($p=0.07$) as a factor in the development of MRAB in this study. The reason for this finding is unclear since several studies have documented higher rates of MRAB in patients with a history of prior institutionalization.⁸ Our patient population is unusual due to the large number (24%) of incarcerated individuals. Three patients (4%) had multidrug resistant *Acinetobacter* despite having no history of being institutionalized. The existence of community acquired MRAB strains would present significant challenges to infection control.

As seen in Tables 1 and 2, MRAB was associated with a significant ($p<0.01$) increase in mortality. An increase in mortality for ventilator associated *Acinetobacter* pneumonia has been noted in several studies,^{2,15,16} however other investigators have not confirmed this finding.^{17,18} In the surgical group, a significant proportion (35%) had positive *Acinetobacter* cultures from multiple sites. Multiple isolates were associated with a significant increase in mortality. The finding of resistant AB isolates in more than one anatomic site most likely signifies an invasive infection rather than colonization. The majority of surgical patients (57%) had an organism other than AB identified on culture, usually a *Staphylococcus* or *Pseudomonas*. Co-infection with non-*Acinetobacter* organisms did not lead to a significant increase in mortality. *Pseudomonas* was the only organism that approached significance with respect to mortality ($p=0.07$).

There was no significant difference in the length of stay between patients with sensitive isolates vs multidrug resistant *Acinetobacter*. This finding was somewhat surprising given that some studies have shown an increase length of stay for resistant strains. The length of stay in patients with resistant organisms may be confounded by their increased mortality. The mortality rate in surgical patients was 16% and all had resistant *Acinetobacter*. Most of the surgical patients who died (75%) grew pan-resistant strains which were resistant to all commonly used antibiotics. Underlying co-morbidities and co-infecting organisms did not significantly impact mortality in this study, whereas the presence of a multidrug resistant *Acinetobacter* was associated with increased mortality (OR 1.6, 95% C.I 1.33-1.96). This suggests that colonization/infection with MRAB is a marker for severe illness or that the organism itself is responsible for poor outcome.

This study is limited because it does not identify patients with true infections versus those that are colonized. The goal was to determine the impact of MRAB in our hospital. The mortality rate in this study of 16% is consistent with a similar study reported by Mahgoub.⁹ Of note is that the rate of MRAB in our hospital was 122/164 (75%) which is higher than reported

elsewhere.¹⁹ The cause of the high rate of multi-resistance is not known and our study design does not enable us to answer this question. We are not certain what role our infection control procedures had on the high resistance rate. Standard infection control practices were followed (hand hygiene, personal protective equipment, environmental control, isolation, etc). Most of the resistant cases (75%) occurred in the ICU, however antibiotic susceptibilities and the anatomical sources varied greatly. We speculate that since different strains were involved, it is unlikely that a breakdown in infection control was the major cause of the high rate of resistance. Initially, the multi-resistant isolates were confirmed by an independent laboratory. Thus, we are confident concerning our determination of the antibiotic susceptibilities. We are planning a future study to determine the DNA fingerprinting of several of the more common resistant phenotypes in our hospital.

Conclusions

The factors associated with multidrug resistant isolates in this study were mechanical ventilation, previous antibiotic use, neurologic impairment, and the recovery of *Acinetobacter* from more than one anatomic site. This study also suggests that infection or colonization with MRAB is associated with increased mortality. The increasing presence of MRAB in wounds is particularly problematic in the surgical patient. Chronic wounds such as amputation stumps, decubitus ulcers, and diabetic wounds are portals of entry of *Acinetobacter* into the surgical intensive care unit. A small number of patients present with community acquired multidrug resistant strains, thus routine surveillance may be useful to guide hospital infection control measures. Vigilance is needed by the surgical team to prevent outbreaks of this opportunistic and deadly pathogen.

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Noninvasive Monitoring...continued from page 38

The researchers undertook a prospective, randomized, controlled trial to assess the impact of SpHb monitoring upon transfusions in patients undergoing elective orthopedic surgery during a six month period. Patients were randomized to receive either standard care alone or standard care plus SpHb monitoring (Radical-7 Pulse CO-Oximeter and R1-25 Rainbow Adhesive Sensor.) The frequency of intraoperative transfusions and mean number of blood units transfused were compared, along with the frequency of laboratory Hb testing and agreement between SpHb and laboratory Hb values. Complication rates for each group were assessed at 30 days post-surgery as a safety endpoint.

A total of 327 patients were enrolled (157 standard care, 170 SpHb). Procedures included hip replacement (31%), knee replacement (29%), and spinal surgery (14%). There were no differences between the standard care and SpHb groups in ASA physical status (2.2 vs 2.2), age (60.8 vs 61.9 yrs), male gender (54 vs 48%), pre-operative lab hemoglobin (13.6 vs 13.5 g/dL), surgical duration (127 vs 114 minutes), or surgical type. More patients received intraoperative transfusions in the standard care group compared to the SpHb group (4.5% vs 0.6%, $p=0.03$). The mean number of units of blood transfused was also higher in the standard care group compared to the SpHb group (0.10 vs 0.01, $p=0.0001$). No patient from either group received a transfusion during the immediate 12 hour post-operative period. The frequency of patients receiving intraoperative Hb testing and the mean number of Hb tests performed were similar in the standard care and SpHb groups (16.3% vs 11.8%, $p=ns$, and 0.21 vs 0.24 tests per case, $p=ns$, respectively). Intraoperative SpHb and laboratory Hb values showed good agreement (mean difference 1.1 ± 0.68 g/dL). There was no difference between groups in 30-day complication rates. The researchers concluded that the use of SpHb monitoring resulted in fewer intraoperative blood transfusions.

The Impact of Obesity on Walking and Cycling Performance and Response to Pulmonary Rehabilitation in COPD

Francesco Sava, Louis Laviolette, Sarah Bernard, Marie-Josée Breton, Jean Bourbeau, François Maltais

Abstract

Background: We examined the influence of overweight and obesity on pulmonary function, exercise tolerance, quality of life and response to pulmonary rehabilitation in COPD.

Methods: 261 patients with COPD were divided into three groups: normal body mass index (BMI), overweight and obese. Baseline and post rehabilitation pulmonary function, 6-min walking test (6MWT), endurance time during a constant workrate exercise test (CET) and St. George's Respiratory Questionnaire (SGRQ) scores were compared between all three classes of BMI.

Results: At baseline, obese and overweight patients had less severe airflow obstruction compared to normal BMI patients. There was no baseline difference in CET performance or SGRQ scores across BMI classes and 6MWT was reduced in the presence of obesity ($p < 0.01$). Compared to baseline, post-rehabilitation 6MWT, CET performance and SGRQ scores improved significantly in each group ($p < 0.01$), but 6MWT was still significantly lower in the presence of obesity.

Conclusions: Walking, but not cycling performance was worse in obese patients. This difference was maintained post rehabilitation despite significant improvements. Weight excess

may counterbalance the effect of a better preserved respiratory function in the performance of daily activities such as walking. However, obesity and overweight did not influence the magnitude of improvement after pulmonary rehabilitation.

Background

Chronic obstructive pulmonary disease (COPD) is associated with dyspnea and exercise intolerance, two major impediments to quality of life. Although low body weight and muscle wasting have traditionally been the focus of nutritional management in COPD, recent data indicate that obesity is becoming frequent in this disease. On one hand, a high body mass index (BMI) appears to convey a survival advantage to patients with COPD. On the other hand, obesity by itself may compromise lung function, decrease exercise tolerance particularly during weight bearing activities, and quality of life, leading to greater disability.

The effects of obesity in combination with COPD on exercise tolerance and dyspnea have received little attention. In one study, obese patients with COPD had a greater peak exercise capacity and reduced dyspnea perception at a standardized ventilation during incremental cycling exercise compared to their lean counterparts. These counterintuitive beneficial effects of obesity were felt to be related to reduced operating lung volumes during exercise in the obese individuals. Other studies showed that the 6-min walking distance, but not constant exercise cycling test time, was reduced in obese patients with COPD compared to non-obese patients highlighting the importance of taking into account the exercise testing modality before concluding about the impact of obesity on exercise capacity in COPD. Whether overweight may also influence exercise capacity in COPD has not yet been addressed.

Pulmonary rehabilitation addresses the systemic consequences of COPD, beyond the impairment in lung function. As summarized in a recent meta-analysis pulmonary rehabilitation improves dyspnea, exercise tolerance and quality of life. Because of the growing prevalence of weight excess in COPD, it is important to learn about the impact of overweight and obesity on pulmonary rehabilitation. A retrospective study showed that obesity did not adversely affect rehabilitation outcomes, although data obtained prospectively would be useful to confirm these findings.

Based on the existing data suggesting that overweight and obesity may interact with COPD, our hypothesis was that increasing BMI in COPD would reduce exercise tolerance,

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Table 1 Baseline characteristics of patients

	Normal BMI n = 88	Overweight n = 95	Obese n = 78	ANOVA p-value
Age, years	66.0 ± 9.4	65.7 ± 8.2	65.4 ± 8.0	NS
Sex, % of men	56	61	59	NS
Body mass index, kg/m ²	22.3 ± 1.8*	27.5 ± 1.5*	35.1 ± 3.5	<0.001
Height (cm)	164 ± 9.1	165 ± 9.2	163 ± 9.8	NS
Weight (kg)	61 ± 8.6*	75 ± 9.8*	91 ± 14.6	<0.001
BODE score	3.9 ± 2.0*	3.1 ± 2.0	3.2 ± 2.4	0.002
Pulmonary function				
FEV ₁ , L	1.02 ± 0.39*	1.18 ± 0.42	1.14 ± 0.38	0.002
% predicted	42 ± 15*	49 ± 15	49 ± 17	0.002
FVC, L	2.7 ± 0.8	2.6 ± 0.8	2.5 ± 0.9	NS
% predicted	86 ± 22	83 ± 21	82 ± 23	NS
FEV ₁ /FVC, %	40 ± 10*	45 ± 12*	49 ± 12	0.001
FRC, L	5.0 ± 1.6†	4.4 ± 1.5	4.1 ± 1.7	<0.001
% predicted	159 ± 42†	142 ± 41	135 ± 45	<0.001
RV, L	4.2 ± 1.4*	3.6 ± 1.4	3.5 ± 1.5	0.002
% predicted	178 ± 60*	157 ± 58	151 ± 64	0.006
TLC, L	6.8 ± 1.7*	6.3 ± 1.7	6.1 ± 1.8	0.01
% predicted	121 ± 22*	112 ± 21	110 ± 23	0.001
IC, L	1.8 ± 0.6	2.0 ± 0.6	2.0 ± 0.6	NS
% predicted	73 ± 21	77 ± 20	81 ± 19	NS
IC/TLC, %	28 ± 8*	32 ± 9	33 ± 8	<0.001
Incremental exercise test				
Peak $\dot{V}O_2$, L·min ⁻¹	0.85 ± 0.29*	1.02 ± 0.32*	1.12 ± 0.40	0.02
Peak $\dot{V}O_2$, % predicted	61 ± 36*	75 ± 56*	87 ± 69	0.01
Peak work capacity, Watt	59 ± 22	69 ± 29	65 ± 29	NS
Peak work capacity, % predicted	57 ± 28	64 ± 41	64 ± 37	NS
Constant exercise test				
CET time, s	367 ± 230	324 ± 201	338 ± 203	NS
6-minute walking test				
6MWT, m	407 ± 75	391 ± 78	342 ± 79*	0.001
Work-walk, m·kg	23296 ± 5902*	29590 ± 8045*	32779 ± 11078*	<0.001
Quality of life				
SGRQ total score	45 ± 17	45 ± 16	45 ± 18	NS
SGRQ symptoms score	53 ± 23	51 ± 22	50 ± 24	NS
SGRQ activity score	65 ± 20	65 ± 20	65 ± 22	NS
SGRQ impact score	32 ± 18	32 ± 17	32 ± 19	NS
Pulmonary rehabilitation				
Duration of rehabilitation (weeks)	8.5 ± 1.7	8.5 ± 1.7	8.4 ± 1.7	NS
Home based rehabilitation, n (%)	23 (26)	27 (28)	21 (27)	NS

Values are mean ± SD. Definitions of abbreviations: FEV₁: forced expiratory volume in 1 second; FVC: forced vital capacity; FRC: functional residual capacity; RV: residual volume; TLC: total lung capacity; IC: inspiratory capacity; $\dot{V}O_2$: oxygen consumption; CET: constant exercise test; 6MWT: 6-minutes walking test distance; SGRQ: St-George's respiratory questionnaire; NS: not significantly different. * = significantly different than the other two groups, p < 0.05. † = significantly different than obese group, p < 0.05.

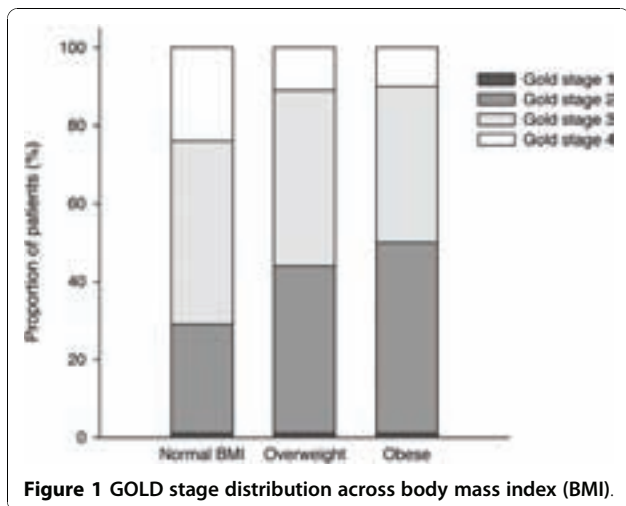
increase exertional dyspnea and reduce functional status during walking but not cycling and compromise the response to pulmonary rehabilitation in patients with COPD. This study was thus undertaken to investigate the effects of overweight and obesity combined with COPD on 1) resting pulmonary function; 2) 6-min walking distance and endurance time during a constant workrate cycling exercise test (CET time) 3) health-related quality of life and 4) improvement of these parameters following pulmonary rehabilitation. To address these issues, we took advantage of a prospective cohort of patients with COPD entering pulmonary rehabilitation in Canada.

Methods

Study participants: Patients with COPD about to take part in

pulmonary rehabilitation were recruited in 10 study centers across Canada. Inclusion criteria were: stable COPD, post-bronchodilator forced expiratory volume in one second (FEV₁) <70% predicted and FEV₁/forced vital capacity (FVC) <70%. Exclusion criteria were: participation to pulmonary rehabilitation in the preceding 12 months, living in a long term care facility and a diagnosis of asthma, congestive heart failure or dementia. All patients gave informed consent to participate in the study. Ethics committee from all 10 study sites approved this research project.

Study design: The data for this study was collected as a part of a prospective observational study of pulmonary rehabilitation in Canada. The main objective of this cohort was to compare home



versus hospital-based pulmonary rehabilitation. The secondary objectives were to identify possible predictors of the response to pulmonary rehabilitation, including obesity, and to evaluate the responsiveness of different evaluative tools to assess the effects of pulmonary rehabilitation. The participating centers agreed on a pre-established research protocol describing the evaluation process that was standardized and performed by qualified study personnel. Study monitoring was ensured by one of the author (SB). The length of the pulmonary rehabilitation programs (6 to 12 weeks) could not be standardized because of different rehabilitation capacity between centers. Patients' assessment included a medical history, pulmonary function tests, and CET, 6MWT and health status measured by the St. George's Respiratory Questionnaire (SGRQ). Dyspnea at rest was evaluated with the MRC dyspnea score. Data was collected at baseline and immediately after the pulmonary rehabilitation program. Patients were classified according to BMI classification of the World Health Organization into normal BMI (BMI 18.5-

24.99 kg·m⁻²), overweight (25-29.99 kg·m⁻²) and obese (>30 kg·m⁻²).

Pulmonary function: Spirometry and lung volumes were measured according to recommended procedures. Results were compared with predicted normal values from the European Respiratory Society. Disease severity was categorized according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification system.

Constant workrate cycling exercise test (CET)

CET was performed on a cycle ergometer with a workload set at 80% of peak work capacity achieved during incremental cycle ergometry. Patients were asked to cycle for as long as possible. The minimum clinically important difference (MCID) in exercise time was set at 100 s.

Six-minute walking test (6MWT): The 6MWT was administered in an enclosed corridor in accordance to the procedures recommended by the American Thoracic Society (ATS). The MCID in walking distance was set at 54 m. We also calculated the body weight-walking distance product in m·kg (walk-work) at baseline.

Health status: Health status was evaluated using French or English versions of the SGRQ. This disease-specific questionnaire has been extensively validated in patients with all grades of respiratory disease including advanced COPD. A score change of 4 points was considered clinically significant.

Symptoms assessment: Ratings of perceived exertion were reported by patients at the end of exercise tests (CET and 6MWT) on a 10-point Borg scale, for dyspnea and leg fatigue. The MCID for Borg scores was set at 1 unit.

Pulmonary rehabilitation: Rehabilitation program consisted of 6 to 12 weeks of tri-weekly 90-minute exercise sessions that

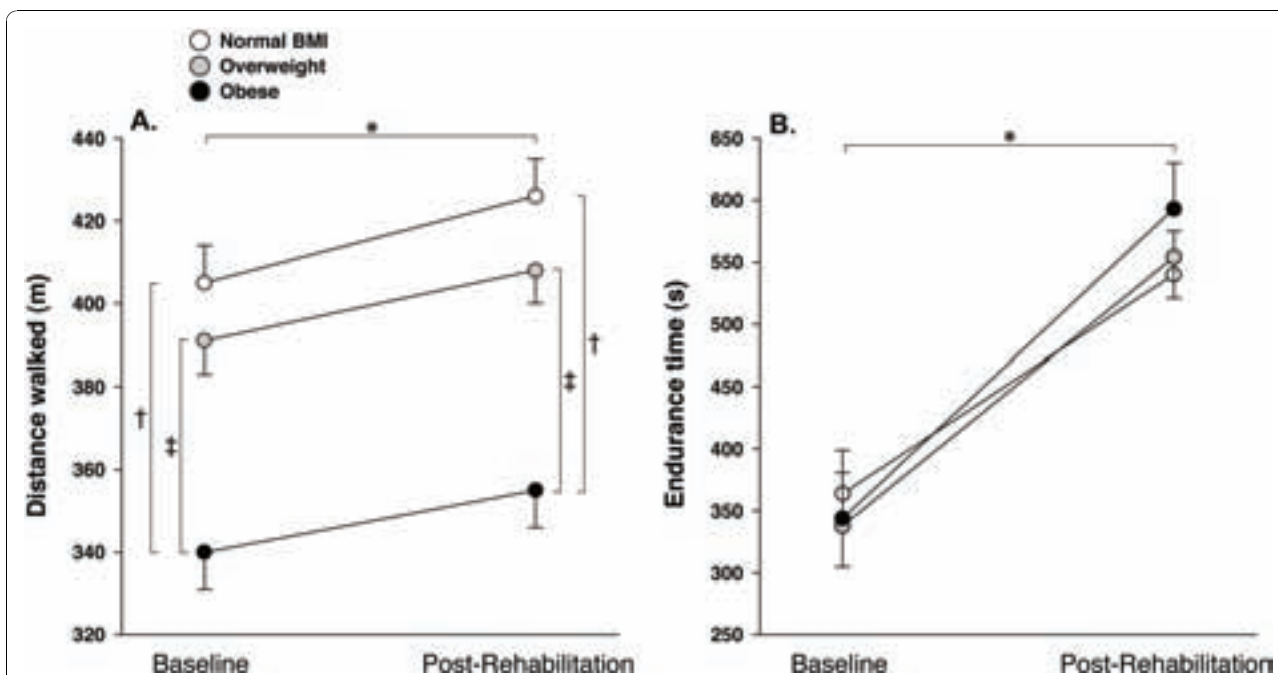
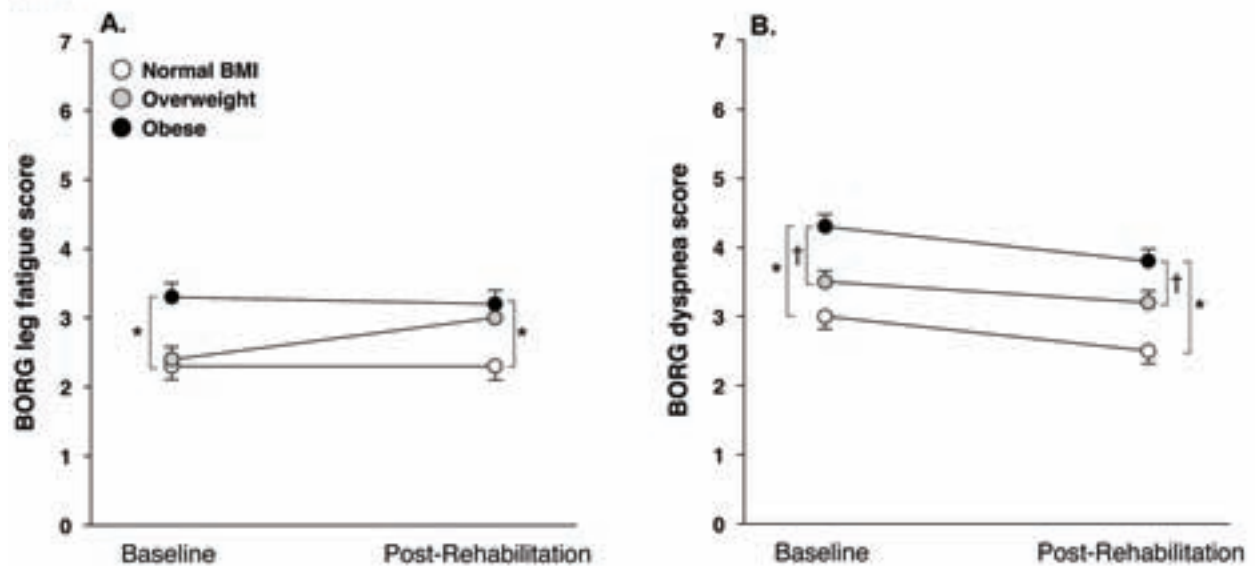


Figure 2 6-minute walking distance and endurance time to constant workrate exercise according to the 3 body mass index (BMI) categories, at baseline and after pulmonary rehabilitation. Values are mean (SD). * = p < 0.01 baseline versus after rehabilitation within each BMI group, † = p < 0.01 obese versus normal BMI, ‡ = p < 0.01 obese versus overweight.

6MWT



CET

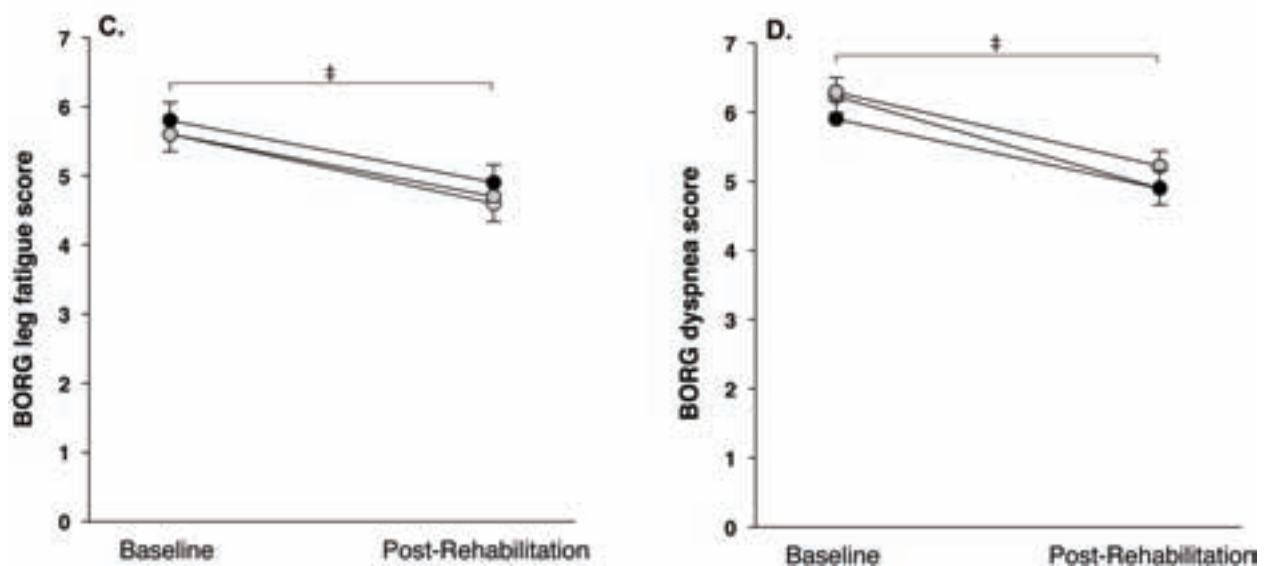


Figure 3 Dyspnea and leg fatigue Borg scores at the end of the 6-minute walking test (6MWT) and of constant workrate cycling exercise (CET) according to the 3 body mass index (BMI) categories, at baseline and after pulmonary rehabilitation. Values are mean (SD). * = $p < 0.01$ obese versus normal BMI, † = $p < 0.01$, obese versus overweight, ‡ = $p < 0.01$ baseline versus after rehabilitation within each BMI group.

integrated stationary bicycle endurance training, resistance exercises, and patient education, which has been described extensively elsewhere. The exercise training program was directly supervised ($n=190$) or was delivered at home ($n=71$). Since these two interventions gave similar results on dyspnea, quality of life and exercise tolerance, data from these two training strategies were combined in the present study.

Statistical analysis: Results are reported as mean \pm SD. A p value <0.05 was considered as statistically significant. One-way ANOVA was used to compare baseline characteristics, except gender for which we used the Pearson's chi-square. Post rehabilitation data was compared to baseline using repeated measures two-way ANCOVAs (group, intervention) using

baseline spirometric data and lung volumes as covariates ($FEV_1\%$ predicted, FEV_1/FVC ratio, functional residual capacity (FRC)% predicted, residual volume (RV)% predicted, total lung capacity (TLC), inspiratory capacity (IC)/TLC ratio). The normality assumption was verified using the Shapiro-Wilk's statistic while the homogeneity of variances was verified graphically with the residuals plot. Univariate and multivariate regression analyses were carried out to identify possible correlates of the response to pulmonary rehabilitation using age, sex, BMI, length of rehabilitation program and all the pulmonary function tests reported in table 1 as independent variables. All the analyses were done using SAS software, release 9.2 (SAS Institute Inc, NC).

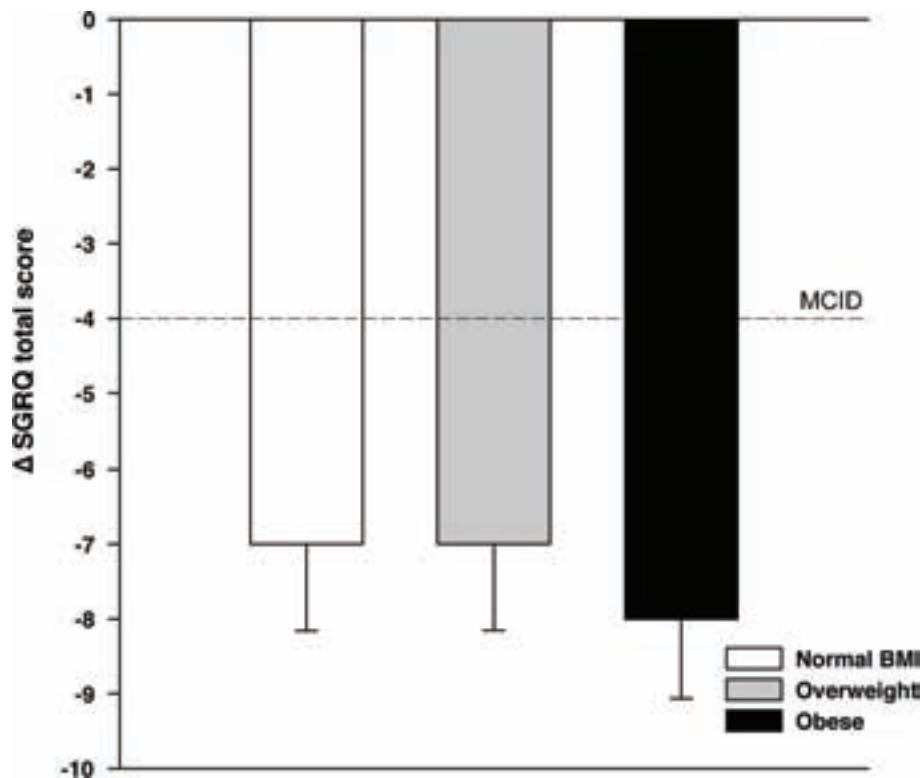


Figure 4 Changes in St. George's Respiratory Questionnaire (SGRQ) total score with pulmonary rehabilitation according to BMI categories. The horizontal dashed line represents the minimally important clinical difference (MCID) for this variable (Δ of 4 units). Values are mean (SD).

Results

Baseline characteristics: Three hundred patients were initially enrolled in the present study. A 13% drop-out rate was observed during pulmonary rehabilitation. The drop-outs were evenly distributed among the three groups. Reasons for dropping-out were: patient withdrawal (11%), lost to follow-up (1.5%) and death (0.5%). We report here data for the 261 patients who have completed pulmonary rehabilitation and whose baseline characteristics are presented in table 1. Patients had a mean FEV₁ of 46±15% of predicted value. GOLD stage distribution was as follows: stage 1, 1% of the total population; stage 2, 40%; stage 3, 44%; and stage 4, 15% (figure 1). Mean age was 65±8 years and 57% of patients were males. There were no patients with BMI under 18.5 kg/m² and only 5 patients with BMI >40 kg/m².

Table 2 Proportion of subjects reaching the MCID in each group for different outcomes

	Normal BMI	Overweight	Obese
6MWT, %	24*	18	15
CET, %	42	46	57
SGRQ, %	59	64	56
Dyspnea score at the end of 6MWT	46	37	46
Leg Fatigue score at the end of 6MWT	41	31	40
Dyspnea score at the end of CET	60	58	58
Leg fatigue score at the end of CET	56	51	60

Values are % of subjects reaching the MCID defined earlier on each group for three different outcomes. Definitions of abbreviations: 6MWT: 6-minutes walking test; CET: constant exercise test; SGRQ: St. George's respiratory questionnaire. * = $p < 0.05$ for normal BMI vs obese.

Sixty percent of the study population was either obese or overweight, a proportion reflective of the Canadian population aged 40 years or older. FEV₁ (L and %), FEV₁/FVC ratio and inspiratory capacity (IC) to TLC ratio (IC/TLC) were significantly lower in the normal BMI group than the other two groups ($p < 0.05$). Residual volume (RV, L and %), total lung capacity (TLC, L and %), and BODE scores were significantly higher in the normal BMI group than in the other two groups ($p < 0.05$). Functional residual capacity (FRC, L and %) was significantly higher in the normal BMI group than in the obese group. There was a larger proportion of GOLD stage II patients in the overweight and obese groups (figure 1).

At baseline, 6MWT distance in the obese group was 65 m shorter compared to normal BMI ($p < 0.01$) and 49 m shorter compared to overweight ($p < 0.01$) (table 1 and figure 2). Work-walk at baseline was significantly higher in the obese group (32779±11078 m·kg, $p < 0.01$) compared to the other two groups and was higher in the overweight group (29590±8045 m·kg) compared to normal BMI (23296±5902 m·kg, $p < 0.01$). At baseline, CET time was similar across all BMI categories ($p = 0.8$) (table 1 and figure 2).

Borg dyspnea and leg fatigue scores after 6MWT were higher in the obese group at baseline ($p < 0.05$) (Figure 3a and 3b). During CET, Borg dyspnea and leg fatigue scores were similar between groups. Baseline SGRQ total scores were not significantly different between groups (table 1).

Effects of pulmonary rehabilitation according to BMI: The duration and modality (home versus hospital-based) of pulmonary rehabilitation programmes were similar across the three BMI categories (table 1). Albeit small, the pre versus post

rehabilitation difference in the 6-min walking distance were statistically significant ($p < 0.01$) and of similar magnitude within each group (mean 15-21 m, $p = 0.92$) (figure 2). Improvement in CET time following rehabilitation was also similar in the 3 groups and reached the clinical and statistical thresholds within each group (mean 175-216 seconds, $p < 0.01$) (figure 2). There was no significant reduction in 6MWT Borg scores with rehabilitation within the 3 BMI categories (figure 3a and 3b). This is in contrast to CET Borg scores and SGRQ scores which were significantly reduced (1.0-1.3 points, $p < 0.01$ and 7-8 points, $p < 0.01$ respectively) after rehabilitation in all three BMI groups (figure 3, panel c and d, and figure 4). In univariate and multivariate regression analyses, the changes in 6MWT distance, CET time and SGRQ scores as dependant variables were not statistically associated with BMI nor with any of the potential correlates of the response to rehabilitation that are outlined in the statistical analysis section.

MCID for the 6MWT, CET and SGRQ was reached by 19%, 46%, and 60% respectively in the entire study population. Table 2 shows the proportional MCID attainment according to BMI category. This proportion for the 6MWT was smaller for obese than normal BMI (15% vs 24%, $p < 0.01$) but was similar across groups for CET, SGRQ and Borg scores.

The changes in BMI after rehabilitation were small and not statistically significant averaging -0.03 ± 0.98 kg/m² (range: -6.26 to 3.94 kg/m²). There was a significant reduction in BODE scores in the 3 groups with rehabilitation with a post-rehabilitation BODE scores of 3.1 ± 1.8 , 2.5 ± 1.6 , 2.6 ± 1.6 , for normal BMI, overweight and obese, respectively, $p < 0.01$ versus pre-rehabilitation.

Discussion

This study reports on the impact of obesity and overweight in a large prospective cohort of patients with COPD participating in pulmonary rehabilitation. The results can be summarized as follow: i) obese and overweight patients had higher FEV₁, lower static lung volumes and higher peak incremental exercise capacity at baseline, ii) despite this, their CET time was not longer than that of patients with normal BMI, iii) obese patients had a reduced walking capacity compared to overweight and normal BMI patients, iv) BMI did not seem to affect SGRQ scores in the present population, finally v) overweight and obesity did not reduce the magnitude of improvement in exercise capacity and quality of life after pulmonary rehabilitation and BMI had no effect on outcomes on univariate or multivariate regression analyses taking account differences in baseline pulmonary function.

It is interesting to observe that, in this cohort, the proportion of overweight and obese patients was greater than normal BMI patients, a likely reflection of the obesity epidemic that afflicts industrialized countries. These results underscore that the study of the impact of obesity and overweight in patients with chronic respiratory disorders will be a topic of interest in the coming years.

Obese and overweight patients had higher FEV₁ and FEV₁/FVC ratio than their lean counterparts, an observation that was previously reported. One possible explanation is that patients with weight excess tend to be more dyspneic for a given FEV₁ as illustrated by the higher Borg dyspnea and leg fatigue scores found in the obese patients during 6MWT. Therefore, obese patients with COPD might attract medical attention at an earlier

stage of their disease. It is intriguing to consider that obesity may influence the natural history of COPD; in a subanalysis of the TORCH trial, BMI > 25 kg/m² was associated with a slower decline in FEV₁. Another possibility for the differences in baseline lung function relates to the influence of obesity on ventilatory function. Decreased chest wall and lung compliance in obesity would tend to increase expiratory flows and decrease resting lung volumes.

At baseline, resting hyperinflation was reduced and the IC/TLC ratio increased in the obese population. This finding is consistent with those of Ora et al. One novel finding of our study is that overweight was also associated with reduced lung volumes in comparison with patients with normal BMI.

We found that obesity had a significant impact on walking capacity but not on the endurance time during cycling exercise. This is likely the result of the increase in energy expenditure associated with weight bearing exercise as shown by higher body weight-walking distance product. From a functional point of view, walking better represents daily activities than cycling. Taken together, these data suggest that obese COPD patients might have more important functional impairments. It would be interesting to study the impact of weight reduction strategies on walking capacity in obese patients with COPD.

As indicated by similar SGRQ total scores, there was no difference in health status between groups, both at baseline and post-rehabilitation, even though patients in obese group had a more limited walking capacity. This could be related to the fact that obese patients might compensate by adapting their environment and diminishing the amount of activity they perform.

In a retrospective analysis, Ramachandran and colleagues reported that the improvement in 6-min walking distance and quality of life improved to a similar extent after rehabilitation in obese patients with COPD when compared with patients with a BMI < 30 mg/kg². One limitation of that study is that it did not include overweight patients. This appears to be relevant given that overweight is even more common than obesity. Our prospective study therefore adds to this information in showing that dyspnea, quality of life and exercise tolerance improve as much in the obese and overweight COPD patients as their normal BMI counterparts. BODE scores improved significantly in our population within each group to an extent that is consistent with the literature.

We did not observe significant reductions in BMI after pulmonary rehabilitation. Exercise in itself is usually not sufficient to adequately manage obesity and it should be done in conjunction with nutritional counseling which was not offered here. In the future, it will be important to learn how to intervene efficiently with COPD patients in their goal of losing excess fat.

This study provides some novel information. First, it is, to our knowledge, the only study looking prospectively at the effect of BMI on pulmonary rehabilitation outcomes. We also report on improvements in terms of MCID for 3 different outcomes, the 6 MWT, CET and SGRQ. Although it is generally suspected that walking capacity is compromised in obese COPD patients, this study is the first to systematically investigate the impact of obesity on specific exercise modalities. Finally, the number of patients enrolled in our trial also provides sufficient statistical

power to make valid conclusions.

The impact of comorbid conditions on rehabilitation outcomes is currently being investigated. In general, it is felt that comorbidities do not prevent pulmonary rehabilitation from being effective although some conditions such as metabolic diseases and osteoporosis may reduce the chances of success. The present study extends these results by showing that obesity reduces the likelihood of a patient achieving the MCID of improvement in distance walked during the 6MWT after rehabilitation. In contrast, the proportion of patients reaching the MCID for cycle exercise and SGRQ was not influenced by BMI. The proportion of our patients reaching the MCID for the SGRQ is similar to what has been reported. Although we did not record the amount of aerobic and resistance training that was performed during rehabilitation, BMI was not a factor in the choice of the training strategies and modalities (home versus hospital-based) used in the three groups. It is thus unlikely that intrinsic differences in the design of the training programs were the main factors in explaining the lower proportion of obese patients reaching the MCID for the 6MWT.

Although the improvement in 6MWT following pulmonary rehabilitation was less than typically reported, we felt that the CET data was reassuring about the exercise enhancing effects of our rehabilitation programs. Measuring the cycling endurance time is a better test of the functional effect of pulmonary rehabilitation than the 6MWT. The modest gain in the distance covered during the 6MWT probably reflects our program's emphasis on the bicycling component of the training intervention since the training modality is known to impact on specific outcomes. For example, patients training solely on stationary bicycle have less improvement in walking capacity compared to patients performing walking exercises.

Our study has potential limitations. First there were only 3% of morbidly obese patients (BMI >40 kg/m²), it would be important to see how such patients fare in the context of pulmonary rehabilitation. Secondly, it is well recognized that reduced fat free mass is associated with muscle weakness, decreased exercise tolerance and poorer survival in COPD. Reduced fat-free mass may occur despite normal BMI. Thirdly, the CET and 6MWT dyspnea and leg fatigue Borg scores were collected only at the end of exercise. Dyspnea and leg fatigue scores obtained at isotime would have been useful to assess the effects of pulmonary rehabilitation on these variables in a more complete fashion. Finally, the impairment in baseline FEV₁ was greater in patients normal BMI and the question may be raised as to whether this difference in disease stage between groups could explain our results. We do not believe that this is the case for the following reasons: i) the main analysis consisted in an analysis of covariance that took into account any differences in FEV₁ and lung volumes at baseline; ii) since obese patients had milder airflow obstruction and resting hyperinflation, their performance during the 6MWT should have been better, not worse; and iii) the magnitude of improvement following pulmonary rehabilitation is independent from baseline lung function.

Conclusion

Obesity and overweight are frequently associated with COPD. As the prevalence of excess weight is increasing, this association will be more and more frequent in clinical practice. Obese patients with COPD, despite having less severe airflow obstruction, resting hyperinflation and better peak VO₂ than

normal BMI patients, had more severe walking impairment. Pulmonary rehabilitation was still beneficial in improving several clinical outcomes despite the presence of excess weight. It would be of great interest to study the impact of weight reduction strategies in conjunction to exercise training in this specific patient population.

Outcome of Children with Life-Threatening Asthma Necessitating Pediatric Intensive Care

Kam-Lun Hon, Wing-Sum Winnie Tang, Ting-Fan Leung, Kam-Lau Cheung, Pak-Cheung Ng

Abstract

Objective: To report the outcome of children with life-threatening asthma (LTA) admitted to a university Pediatric Intensive Care Unit (PICU).

Methods: Retrospective study between October 2002 and May 2010 was carried out. Every child with LTA and bronchospasm was included.

Results: 30 admissions of 28 patients (13 M, 17 F) were identified which accounted for 3% of total PICU admissions (n=1033) over the study period. The majority of patients were toddlers (median age 3.1 years). Few had past history of prematurity, lung diseases, or neuro-developmental conditions. Approximately half had previous admissions for asthma and one-fourth with history of non-compliance to recommended treatment for asthma. One patient had parainfluenza virus and one had rhinovirus isolated. None of these factors were associated with need for mechanical ventilation (n=6 admissions). Comparing with patients who did not receive mechanical ventilation, ventilated children had significantly higher PIM2 score (1.65 versus 0.4, $p<0.001$), higher PCO_2 levels (9.3 kPa versus 5.1 kPa, $p=0.01$) and longer PICU stay (median 2.5 days versus 2 days, $p=0.03$). The majority of patients received systemic corticosteroids, intravenous or inhaled bronchodilators. There was one pneumothorax but no death in this series.

Conclusions: LTA accounted for a small percentage of PICU admissions. Previous hospital admissions for asthma and history of non-compliance were common. Approximately one quarters required ventilatory supports. Regardless of the need for mechanical ventilation, all patients survived with prompt treatment.

Introduction

Asthma is a very common childhood condition worldwide and in Hong Kong. Acute asthmatic attacks cause significant morbidity and account for a significant number of emergency department consultations and hospital admissions.¹⁻⁴ Most children admitted to the hospital because of acute asthma do

not require intensive care treatment. Nevertheless, a small percentage of children with life-threatening asthma (LTA) would develop progressive respiratory failure refractory to treatment and require admission to the pediatric intensive care unit (PICU).⁵⁻⁷ In those who are admitted to the ICU, approximately 10 to 33% need intubation and mechanical ventilation, with a risk of worsening bronchospasm and hyperinflation, barotrauma, and cardiovascular depression.^{8,9} If not promptly managed, severe asthmatic attacks may occasionally result in death.¹⁻¹⁰ The purpose of this study was to report the clinical pattern and outcome of all children with LTA and severe bronchospasm admitted to the PICU.

Methods

We retrospectively reviewed the medical records and analyzed data from all children with LTA admitted to the PICU of a tertiary care university hospital (Prince of Wales Hospital) in Hong Kong during the period October 2002 and May 2010. LTA was defined as all children with asthma who required ICU admission and care. The initial diagnosis was made clinically by the admitting physicians. Final diagnosis was confirmed on chart review and subsequent evaluations. The hospital provides PICU care to a catchment population of approximately 1.1 million. The following data were collected: age, sex, duration of admission, treatment of the LTA, clinical condition, blood gases, the incidence of barotrauma, and outcome. Respiratory viruses and bacterial pathogens were routinely screened for by standard examination of nasopharyngeal aspirate and cultures. The Pediatric Index of Mortality 2 (PIM2) score based on admission data was used as severity score.¹¹ Numerical data were compared with Mann Whitney U test and categorical data with χ^2 or Fisher exact test. All comparisons were made two-tailed, and p-values less than 0.05 considered statistically significant.

Results

There were 30 admissions (13 boys and 17 girls; median age, 3.1 years; IQR 2.0 - 6.8 years; Table 1) with LTA which accounted for 3% of total PICU admissions (n=1033) over a study period of 7 years and 8 months. Two male patients were admitted twice because of a recurrent episode of LTA. Indications for admission to the PICU were severe dyspnea, worsening or failure to improve on nebulized bronchodilators, and need for administration of intravenous salbutamol or mechanical ventilation. The decision for PICU admission was determined clinically together with blood gas as well as pulse oximetry parameters by the admitting physicians.

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Table 1: Clinical data of children with status asthmaticus admitted to PICU

Case	Total (n = 30)	Ventilated (n = 6)	Non-ventilated (n = 24)	P*
Male (%)	13 (0)	5 (75)	8 (40)	0.06
Median age (IQR), yr	3.1 (2.0-5.4)	3.3 (2.0-5.5)	3.1 (1.9-6.8)	0.84
Median (IQR) PIM2, %	0.50 (0.30-1.00)	1.65 (1.45-1.95)	0.4 (0.3-0.5)	< 0.001
Relevant risk factors				
Family history of atopy	12	1	11	0.36
Prematurity < 36 weeks (%)	4 (14)	0 (12)	4 (15)	0.57
History of chronic lung disease, bronchiolitis, pneumonia, or pneumothorax (%)	7 (17)	0 (0)	7 (25)	0.29
Neurodevelopmental delay (mental retardation, cerebral palsy, neuromuscular disease) (%)	2 (14)	0 (25)	2 (10)	1.00
Previous asthma admission (%)	16 (50)	4 (62)	12 (45)	0.66
Maintenance inhaled CS (%)	12 (35)	3 (37)	9 (35)	0.66
Non-compliance (%)	7 (25)	2 (25)	5 (25)	0.60
1 st PaCO ₂ in PICU, kPa	5.5 (4.3-7.9)	9.3 (6.4-10.9)	5.1 (4.3-5.9)	0.01
1 st PaO ₂ in PICU, kPa	9.9 (7.8-13.2)	10.1 (9.4-13.5)	9.3 (7.5-13.3)	0.40
Viral isolation (%)	2 (3)	0 (0)	2 (5)	1.00
Treatment at PICU				
Systemic CS (%)	30 (100)	6 (100)	24 (100)	N/A
Inhaled salbutamol (%)	22 (73)	5 (83)	17 (71)	1.00
Inhaled ipratropium (%)	7 (23)	0 (0)	7 (29)	0.29
Inhaled adrenaline (%)	2 (7)	1 (17)	1 (4)	0.37
Intravenous salbutamol (%)	22 (73)	5 (83)	17 (71)	1.00
Intravenous magnesium sulphate (%)	4 (13)	2 (33)	2 (8)	0.17
Systemic antibiotics (%)	19 (63)	5 (83)	14 (58)	0.37
Outcome				
Median (IQR) PICU stay, day	2.0 (1.0-2.5)	2.5 (2.0-4.5)	2.0 (1.0-2.0)	0.03
Median (IQR) hospital stay, day	5.0 (3.0-7.5)	6.5 (3.0-20.0)	5.0 (3.0-6.8)	0.27
Pneumothorax (%)	1 (3)	0 (0)	1 (4)	1.00
Died in PICU	0	0	0	N/A

CS: corticosteroid; IQR, interquartile range; N/A, not applicable.

* Analyzed between ventilated and non-ventilated patients by Fisher exact test or Pearson χ^2 for categorical variables and Mann-Whitney U test for numerical variables.

In terms of risk factors, 'smoker(s) at home' were present in 5 of the admissions, 'history of atopy in 1 st degree relative' in 11 admissions, and 'personal history of atopy' in 20 admissions. Few had past history of prematurity (n=4 admissions), lung diseases (1 neonatal pneumothorax, 1 pneumonia, 1 chronic lung disease, and 4 recurrent bronchiolitis), neuro-developmental condition (Rasmussen's encephalitis plus epilepsy \times 2 admissions). Half had previous admissions for asthma and one-fourth with history of non-compliance to recommended treatment for asthma. In the ventilated group, three patients were on inhaled corticosteroid but compliance to corticosteroid was reportedly poor in two. In the non-ventilated group, 9 patients were on inhaled corticosteroid. One patient also received oral montelukast. Poor-compliance to asthma management was reported in 5 patients. One patient had parainfluenza virus and one had rhinovirus isolated. None of these factors were associated with need for mechanical ventilation which was required in 6 patients. Ventilator modes included Synchronized Intermittent Mandatory Ventilation (SIMV) or Pressure Regulated Volume Control mode

(PRVC), with low Positive End-Expiratory Pressure (PEEP) and low inspiratory to expiratory (I:E) ratios. Comparing with patients who did not receive mechanical ventilation, ventilated children had significantly higher PIM2 score (1.65 versus 0.4, $p < 0.001$), higher first PaCO₂ levels measured at PICU (9.3 kPa versus 5.1 kPa, $p = 0.01$) and longer PICU stay (median 2.5 days versus 2 days, $p = 0.03$) but no differences in other factors evaluated in Table 1. These patients received systemic corticosteroids and intravenous or inhaled bronchodilators. Some received intravenous magnesium sulphate. There was one pneumothorax but no death in this series. A 7-year-old girl with asthma but no previous asthma hospitalization, presented with sudden dyspnoea following a 2-day history of blocked nose and cough. Her private practitioner prescribed inhaled and oral bronchodilators. However, dyspnoea was not relieved and chest radiograph at the emergency department revealed left apical pneumothorax, which was drained with a chest drain. CT scan of the thorax showed subcutaneous emphysema, pneumomediastinum, and pneumothorax. Her symptoms

Table 2: The incidence of PICU admissions for LTA during the study period

Year	PICU admissions	PICU for LTA (%)
2002 (partial data)	33	1 (3)
2003	122	7 (6)
2004	155	3 (2)
2005	111	2 (2)
2006	127	3 (2)
2007	144	5 (3)
2008	138	3 (2)
2009	140	3 (2)
2010 (partial data)	63	3 (5)

Median of 2% of annual PICU admissions were due to LTA (average absolute deviation from Median = 1.0%)

resolved at the PICU following corticosteroid and inhaled salbutamol. Mechanical ventilation was not required. The chest drain was removed three days later. Regardless of mechanical ventilation, all had very brief PICU stays (median 2 days; range, 1 to 7 days). Furthermore, there did not appear to be any increase in incidence of PICU admissions for LTA between 2003-2009 (median 2% of PICU admissions; Table 2).

Discussion

Incidence of PICU admissions: Asthma is a common disease and its frequency of occurrence sometimes detracts from its potential seriousness.¹² Severe asthma in children is a frequent cause of hospital and pediatric ICU admissions in reported series.¹²⁻¹⁴ Globally, morbidity and mortality associated with asthma have increased over the last 2 decades.^{1,2,4} This increase is attributed to increasing urbanization and undertreatment of asthma especially among the high risk pediatric population with low-socio-economic class.¹⁵ Despite advancements in our understanding of asthma and the development of new therapeutic strategies, the morbidity and mortality rates due to asthma reportedly increased between 1980 and 1995.^{2,4,13} In the United States, the mortality rate due to asthma has increased in all age, race, and sex strata. From 1975-1993, the number of deaths nearly doubled in people aged 5-14 years.² In Hong Kong, data about severe asthma hospitalizations are lacking. In a previous study, we reported that asthma accounts for approximately 10% of general pediatric admissions.³ In the present study, the admission rate was only 3% of PICU admissions. It appears that LTA is a relative uncommon cause of PICU admission in our locality. The reason for this is unknown. It might reflect that treatment received at the emergency department is prompt and effective to halt PICU admission.⁶

PICU treatment: Status asthmaticus is severe asthma that does not respond well to immediate care and is a life-threatening medical emergency.⁵ Ensuing respiratory failure results in hypoxia, carbon dioxide retention and acidosis.¹⁶ Patients require aggressive treatment with oxygen, bronchodilators, and corticosteroids.^{5,17-19} Rapid reversal of airflow obstruction is achieved by using repeated or continuous administration of an inhaled beta2-agonist. Early administration of systemic corticosteroids (oral or intravenous) is indicated in children with LTA.^{5,19} In severe cases, alveolar hypoventilation requires mechanically assisted ventilation.^{1,5,8,16} In our study, the only

significant difference between ventilated and non-ventilated group is the presence of CO₂ retention. LTA can be associated with metabolic acidosis, which reduces the effectiveness of β -agonists.⁹ In a prospective randomized trial, continuous nebulization of albuterol is safe and results in more rapid clinical improvement than intermittent nebulization in children with impending respiratory failure due to status asthmaticus.²⁰ In severe LTA attacks, intravenous salbutamol was found to be a safe and effective bronchodilator capable of reversing severe bronchospasm in most children who would otherwise require mechanical ventilation.²¹ Mechanical ventilation compromises active expiration with increased air trapping and hypercapnia, and should therefore be delayed as long as possible by using medical therapy.¹ Noninvasive positive pressure has also been advocated but further evaluation of its efficacy is required.²²

Co-infections: One of the clinical problems facing pediatric intensivists is the differentiation between viral and bacterial infections when an acutely ill child with LTA is admitted. Empirical course of antibiotics were often used in the initial management in order to avoid missing any treatable bacterial co-infections. Rapid diagnosis of respiratory viral infections in children is important because prompt diagnosis may result in significantly reduced antibiotic use and unnecessary strict isolation for respiratory viruses. In this study, there was no bacterial isolation and viral co-infection was only found in two cases (parainfluenza and rhinovirus).

Complications and morbidity: Status asthmaticus is one of the most common causes of admission to a pediatric intensive care unit (PICU). There have been published data examining the complications associated with the treatment of status asthmaticus in children in the PICU. In one study of children admitted to PICU, there was a 22% complication rate, increased by intubation.¹⁴ The risk of death is increased where there is delay in getting treatment, particularly time to starting steroids. Another retrospective review showed 8% of children admitted to the ICU with status asthmaticus experienced one or more complications during their treatment. The most common complications were aspiration pneumonia, ventilator-associated pneumonia, pneumomediastinum, pneumothorax, and rhabdomyolysis.²³ Intubated children were significantly more likely than non-intubated children to experience a complication (RR 15.3; 95% CI 6.7-35). Intubated children experiencing a complication also had significantly longer duration of mechanical ventilation, ICU length of stay, and hospital charges than intubated children not experiencing a complication, suggesting that intubation and mechanical ventilation itself may increase the risk of developing a complication in this population.^{7,14} Asthma patients have variable resolution of airway obstruction during mechanical ventilation and controlled hypoventilation can be a safe therapy for the patients with more severe obstruction.⁸ Prompt treatment with corticosteroid, bronchodilator (intravenous route if needed), magnesium sulphate, permissive hypercarbia, and the avoidance of mechanic ventilation together might have accounted for the satisfactory outcome seen in our patients. Indeed mechanical ventilation has not been needed for the past 3 years in our unit.

Conclusions

Near-fatal asthma continues to be a significant problem despite the decline in overall asthma mortality. Two distinctive phenotypes of near-fatal asthma have been identified: one with eosinophilic inflammation associated with a gradual onset

and a slow response to therapy and a second phenotype with neutrophilic inflammation that has a rapid onset and rapid response to therapy. In stable condition, near-fatal asthma frequently cannot be distinguished from mild asthma. Diminished perception of dyspnea plays a relevant role in treatment delay, near-fatal events, and death in patients with severe asthma. Reduced compliance with anti-inflammatory therapy has also been associated with fatal or near-fatal asthma.²⁴ The sudden-onset patients were older and they more commonly presented to the emergency department between midnight and 8:00 am with severe exacerbations that required intubation and intensive care unit admission. Nevertheless, this sudden-onset group was discharged from the hospital earlier.²⁵ The preventable factors included inadequate assessment or therapy of prior asthma, poor compliance with therapy, and delay in seeking help.¹⁰ In our series, history of previous asthma admissions and noncompliance were also relevant factors. Nevertheless, we report no fatality and the majority required brief PICU stay regardless of need for mechanical ventilation.

Approximately one third of patients were on maintenance inhaled corticosteroid; many of these patients were on inhaled salbutamol on a prn-basis and had been asymptomatic for a number of months, but some were non-compliant to prescribed therapy. The limitation of this study is the small sample size and there was high chance of type II error with regard to different parameters studied.

In conclusion, LTA and bronchospasm accounted for a small percentage of PICU admissions following initial stabilization at the emergency department. Approximately 20% required ventilatory supports. Ventilated patients appeared to have higher PIM2 severity score, higher PCO₂ and longer PICU stays. Regardless of the need for mechanical ventilation, all patients survived with prompt treatment, and only required brief PICU stays.

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Association of Residential Dampness and Mold with Respiratory Tract Infections and Bronchitis

William J. Fisk, Ekaterina A. Eliseeva, Mark J. Mendell

Abstract

Background: Dampness and mold have been shown in qualitative reviews to be associated with a variety of adverse respiratory health effects, including respiratory tract infections. Several published meta-analyses have provided quantitative summaries for some of these associations, but not for respiratory infections. Demonstrating a causal relationship between dampness-related agents, which are preventable exposures, and respiratory tract infections would suggest important new public health strategies. We report the results of quantitative meta-analyses of published studies that examined the association of dampness or mold in homes with respiratory infections and bronchitis.

Methods: For primary studies meeting eligibility criteria, we transformed reported odds ratios (ORs) and confidence intervals (CIs) to the log scale. Both fixed and random effects models were applied to the log ORs and their variances. Most studies contained multiple estimated ORs. Models accounted for the correlation between multiple results within the studies analyzed. One set of analyses was performed with all eligible studies, and another set restricted to studies that controlled for age, gender, smoking, and socioeconomic status. Subgroups of studies were assessed to explore heterogeneity. Funnel plots were used to assess publication bias.

Results: The resulting summary estimates of ORs from random effects models based on all studies ranged from 1.38 to 1.50, with 95% CIs excluding the null in all cases. Use of different analysis models and restricting analyses based on control of multiple confounding variables changed findings only slightly. ORs (95% CIs) from random effects models using studies adjusting for major confounding variables were, for bronchitis, 1.45 (1.32-1.59); for respiratory infections, 1.44 (1.31-1.59); for respiratory infections excluding nonspecific upper respiratory infections, 1.50 (1.32-1.70), and for respiratory infections in children or infants, 1.48 (1.33-1.65). Little effect of publication bias was evident. Estimated attributable risk proportions ranged from 8% to 20%.

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Conclusions: Residential dampness and mold are associated with substantial and statistically significant increases in both respiratory infections and bronchitis. If these associations were confirmed as causal, effective control of dampness and mold in buildings would prevent a substantial proportion of respiratory infections.

Background

Dampness and mold in buildings have been associated in many studies with adverse respiratory health effects. A number of qualitative summaries of this literature are available. In their review, the Institute of Medicine (IOM) of the National Academy of Sciences found sufficient evidence to document an association between qualitatively assessed indoor dampness or mold and upper respiratory tract symptoms, cough, wheeze, and asthma symptoms in sensitized persons. A later review by the World Health Organization (WHO), including additional studies, expanded the documented associations to include asthma development, current asthma, dyspnea, and respiratory infections. While both reviews concluded that excessive indoor dampness was an important public health problem meriting prevention and remediation, neither review produced quantitative summaries of association between dampness or mold and specific health outcomes.

Two prior quantitative meta-analyses have been published on indoor dampness and mold and selected health effects. In 2007, Fisk et al quantitatively summarized the associations of home dampness and mold with a set of respiratory and asthma related health effects, based on available studies published in peer-reviewed journals in English. Health outcomes included were upper respiratory tract symptoms, cough, wheeze, asthma diagnosis ever, current asthma, and asthma development. The meta-analyses produced central estimates of ORs ranging from 1.34 to 1.75 for these health outcomes, with 95% confidence intervals (CIs) excluding the null in nine of ten instances. Antova et al analyzed pooled data from 12 European cross-sectional studies of visible mold in residences and respiratory or allergic health outcomes of children. Outcomes included bronchitis, wheeze, asthma, nocturnal dry cough, morning cough, sensitivity to inhaled allergens, hay fever, and "woken by wheeze." Central estimates of ORs ranged from 1.30 to 1.50, with all 95% CIs excluding the null.

Thus while prior non-quantitative reviews have reported consistent associations between dampness or mold and respiratory infections, no quantitative meta-analysis of this

Table 1. Health outcomes from reviewed studies, grouped into outcome categories used in meta-analyses.

Category in Meta-Analysis	Number of studies	Outcomes from Individual Studies Included in Each Category
Bronchitis (all: acute or chronic)	13	bronchitis, bronchitis in the prior year, current bronchitis, obstructive bronchitis, chronic bronchitis; doctor diagnosed bronchitis in the past year; bronchitis indicated by cough and phlegm \geq 3 months for at least two consecutive years, bronchitis times per year
Respiratory infection group	19	airway infection last month; sinus or ear infection with antibiotic use; cold; common cold; $>$ 4 (or $>$ 6) colds in last 12 months; frequent childhood respiratory infections; sinusitis; tonsillitis; acute upper respiratory tract infection in past 12 months; tonsillopharyngitis, croup, bronchitis, or bronchiolitis diagnosed by doctor; chest cold; consulting general practitioner for acute respiratory tract infection (with wheeze); sum of episodes of tonsillitis, sinusitis, otitis, bronchitis; one or more episodes of bronchitis or pneumonia; tonsillitis, otitis media, sinusitis, bronchitis, or pneumonia at least once; chest cold with wheeze; otitis media; pneumonia; bronchitis times per year
Respiratory infections excluding otitis media	17	same as listed in cell above excluding otitis media
Respiratory infection group excluding nonspecific upper respiratory infection	15	sinus or ear infection with antibiotic use; sinusitis; tonsillitis; tonsillopharyngitis, croup, bronchitis, or bronchiolitis diagnosed by doctor; sum of episodes of tonsillitis, sinusitis, otitis, bronchitis; one or more episodes of bronchitis or pneumonia; tonsillitis, otitis media, sinusitis, bronchitis, or pneumonia at least once; otitis media; pneumonia; bronchitis times per year

relationship has been reported. A substantial number of epidemiologic studies on dampness or mold and respiratory infections are available for this purpose. Respiratory (tract) infections are generally considered to include infections of the lower and upper respiratory tract, and otitis media. Lower respiratory tract infections include pneumonia, acute bronchitis, and acute exacerbation of chronic bronchitis. While acute bronchitis is generally caused by an infection, chronic bronchitis is generally non-infectious in origin. Upper respiratory tract infections are acute infections of the nose, sinuses, and throat. Otitis media, an infection or inflammation of the middle ear often resulting from a prior upper respiratory tract infection, can be bacterial or viral in origin.

The burden of morbidity and mortality and the financial costs of respiratory tract infections are enormous. Little effective prevention is currently possible outside of two strategies: attempting to avoid contact with or spreading of infectious

agents in aerosols, droplets, or surfaces, such as by hand washing, avoiding infected individuals, avoiding face-touching, and covering sneezes; and vaccination for influenza and pneumococcal pneumonia. It is important to determine whether avoidance of dampness and mold can provide another means of reducing respiratory tract infection. As a step toward that goal, we performed a quantitative meta-analysis to summarize findings in the peer-reviewed medical literature on associations between dampness or mold in residences and respiratory tract infections or bronchitis.

Methods

Our search for published articles involved several strategies: an online search of PubMed, an online search of the journal *Indoor Air*, and a manual search of the reference list in the publication "World Health Organization Guidelines on Dampness, Mold, and Health."

Table 2. Studies included in the meta-analyses

Study		Health Outcomes	Study Type	Number of Subjects	Controlled for Age, Sex, Smoking and Socioeconomic Status
Bakke et al. 2007	[29]	RI	cross sectional	173	Yes
Biagini et al. 2006	[10]	RI	birth cohort	585	Yes
Brunekreef et al. 1989	[30]	B	cross sectional	4,625	Yes
Dales et al. 1991	[31]	B	cross sectional	13,495	No
Diez et al. 2003	[32]	B	birth cohort	172 - 178	No
du Prel et al. 2006	[33]	RI, B	cross sectional	5,757 - 20,059	Yes
Ekici et al. 2008	[34]	RI, B	cross sectional	9,610 - 9,853	Yes (BR) No (RI)
Haverinen et al. 2001	[8]	RI, B	cross sectional	1,017	Yes
Karevold et al. 2006)	[35]	RI	cross sectional	275 - 737	Yes
Kilpelainen et al. 2001	[36]	RI	cross sectional	9,765 - 10,504	No
Koskinen et al. 1999	[37]	RI, B	cross sectional	57 -147	No
Li and Hsu 1996	[38]	RI, B	cross sectional	1,340	Yes
Pettigrew et al. 2004	[39]	RI*	birth cohort	806	No
Pirhonen et al. 1996	[40]	RI, B	cross sectional	1,460	Yes
Rylander and Megevand 2000	[41]	RI, B**	cross sectional	304	No
Spengler et al. 1994	[42]	B	cross sectional	12,842	No
Spengler et al. 2004	[43]	RI, B	cross sectional	5,951	Yes
Stark et al. 2003	[7]	RI	birth cohort	499	Yes
Strachan 1988	[44]	RI	cross sectional	873	No
Sun et al. 2009	[45]	RI	cross sectional	3,436	Yes
van Gageldonk-Lafeber et al. 2007	[9]	RI	case-control	626	No
Yang et al. 1997	[46]	RI, B	cross sectional	4,164	Yes
Yang et al. 1999	[47]	RI*	case control	438	Yes

RI=respiratory infection group, B=bronchitis (acute, chronic, or uncharacterized as acute or chronic), *Outcome is otitis media, most often accompanied by an upper respiratory infection ^used for inputs to meta-analyses **Bronchitis times per year assumed to be acute/infectious bronchitis.

Table 3. Key results of the meta-analyses, with results of tests for heterogeneity.

Health Outcome	All Studies		Studies Controlling for All Four Key Confounders		
	Summary Estimate OR (95% CI)	p-Value Heterogeneity	Summary Estimate OR (95% CI)	p-Value Heterogeneity	Attributable Risk Proportion#
Bronchitis	1.45 (1.34 - 1.56)	<0.0001	1.45 (1.32 - 1.59)	0.12	8.3 - 18.4 %
Respiratory infection group	1.44 (1.32 - 1.58)	<0.0001	1.44 (1.31 - 1.59)	<0.0001	
Respiratory infections excluding otitis media	1.43 (1.31 - 1.56)	<0.0001	1.40 (1.29-1.52)	<0.0001	
Respiratory infections excluding common cold and nonspecific upper respiratory infections	1.42 (1.26 - 1.60)	0.01	1.50 (1.32 - 1.70)	0.07	9.1 - 20 %
Common cold or acute upper respiratory infection	1.38 (1.21 - 1.57)	0.009	1.38 (1.13 - 1.67)	0.002	
Respiratory infections (children or infants)	1.48 (1.34 - 1.62)	0.16	1.48 (1.33 - 1.65)	0.09	8.8 - 19.4%
Respiratory infections (adults)	1.50 (1.22 - 1.83)	<0.0001	1.49 (1.14 - 1.95)	<0.0001	

#estimated for findings restricted to studies controlling for four key confounders and assuming a range of 20-50% of houses with dampness or mold; provided only for estimates with p-value for heterogeneity >0.05.

We performed one set of analyses including only results from studies that controlled for potential confounding by the following factors via study design or analysis method: age, gender, smoking (eg, active smoking, smoking in home, smoking by mother during pregnancy), and some measure of socioeconomic status (SES). We considered studies with populations limited to home owners, university students, or university employees as adequately controlled for SES. We also considered the reporting of no significant association between an outcome and a potential confounder as equivalent to controlling for that confounder. In another set of unrestricted analyses, we did not require control for these potential sources of confounding, although most of the added studies controlled for all but one of these factors.

For papers which reported strength of association as RRs instead of ORs, we included RRs as if they were ORs for the primary analysis. RRs approximate ORs well when outcome prevalence is low; however, we also performed an analysis excluding RR values.

Ideally, a meta-analysis would utilize input data only from studies with the same precisely defined risk factor, health outcome, and population. As this was not possible, we used input data from studies that were as similar as practicable, all in residences. The following risk factors were accepted: dampness, water damage, visible mold, mold odor, or flooding - all in the whole home, main living area, or bedroom. We did not distinguish among dampness, mold, dampness or mold, and dampness and mold as risk factors. Our rationale - visible mold is always considered the result of excess dampness whether or not the dampness is reported, and excess dampness is very often accompanied by mold, although the mold may not be visible. Thus, it was not possible to make a clear distinction among these risk factors. Excluded as inputs were ORs for condensation (a less certain indication of potential microbial contamination), ORs per unit area of visible mold or water damage, ORs for "suspected moisture problem," and ORs for higher measured airborne concentrations of molds, bacteria, ergosterol, glucan, or endotoxin. The included studies had either adults or children as subjects. Presence of dampness and/or mold was determined in each study by either the occupants or the researchers. We did not distinguish between occupant-reported dampness and/or mold and researcher-reported dampness and/or mold.

The categories of health outcomes constructed for meta-analyses were respiratory infection group, respiratory infection group excluding otitis media, and bronchitis (acute, chronic, or not

clearly characterized as acute or chronic). The respiratory infection group outcomes involved viral or bacterial infections; we excluded from consideration respiratory infections by fungi which occur primarily in people with compromised immune systems. The respiratory infection and bronchitis outcome categories overlap, with some studies of respiratory infections including bronchitis or episodes of bronchitis within their definition of a respiratory infection. We included separate bronchitis outcomes in the respiratory infection group only if the definition stated or suggested acute bronchitis. The category of bronchitis includes acute bronchitis, normally the result of an acute respiratory infection, and chronic bronchitis, which may be unrelated to an infection. Most papers did not provide sufficient information to allow classification of the bronchitis as acute or chronic.

For respiratory infections, we also produced summary estimates separately for studies of children and of adults (omitting the one study that included both). In addition, we produced a summary estimate for the respiratory infections group after excluding findings for a set of relatively nonspecific upper respiratory outcomes that seemed most susceptible to inclusion of allergic or irritant symptoms. This excluded findings such as for common cold, chest cold with wheeze, acute upper respiratory infections, acute respiratory tract infections, respiratory infections, and airway infections. We did not exclude throat infections, sinusitis, tonsillitis, otitis, or the various lower respiratory infections.

We applied random effects models to derive central estimates and confidence limits for associations of the health outcomes with dampness and mold as reported by the multiple published studies which varied in symptom definitions, subjects, and locations.

Results based on the models were compared to those obtained from secondary analyses using fixed effects models that assumed independence of multiple ORs within individual studies. Additional models were constructed that omitted the reported RR values. For final models, we assessed heterogeneity of study-specific effect estimates using the meta command in STATA to estimate the Q statistic and associated p-value. Where the p-value for heterogeneity was <0.05 for both the full and restricted sets of findings, we further explored possible sources of heterogeneity by conducting sensitivity tests, and performing tests of heterogeneity for various subsets of findings, as feasible.

Funnel plots were produced to check for evidence of publication bias. If the plot for an outcome showed asymmetry only among

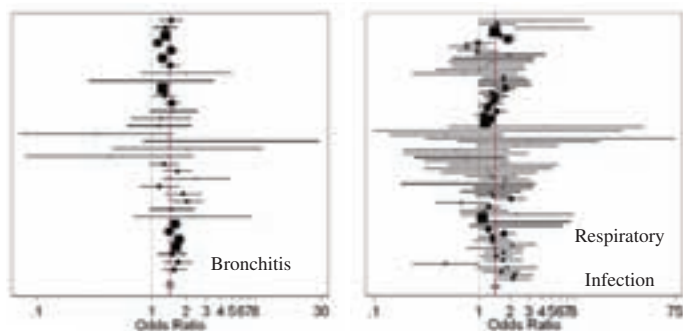


Figure 1. Odds ratios and confidence intervals from all studies meeting the less restricted eligibility criteria and from a meta-analysis of these studies performed using the random effects model and assuming dependent estimates within studies.

The width of the boxes (some so small they appear as points) is proportional to the precision of the study and the ends of the horizontal lines represent lower and upper 95% confidence limits. The left vertical line marks an odds ratio of 1.0, corresponding to no increased risk, while most of the reported odds ratios are greater than unity indicating an increase in risk with dampness and mold. The central estimate from the meta-analysis is indicated by the right vertical line and the left- and right-side points of the diamond at the bottom of the figure indicate the lower and upper 95% confidence limits from the meta-analyses.

less precise (generally smaller) studies, suggesting that smaller studies without positive findings were less likely to have been published, then an alternate analysis was performed. This excluded the set of smaller studies exhibiting asymmetry, in order to produce presumably less biased summary estimates based only on the more completely reported, more precise studies.

Results

Overall, 23 studies were selected for inclusion in these meta-analyses. Table 1 provides the number of studies for each health outcome category and the specific outcomes from reviewed studies included in each category. Table 2 identifies the studies in each health outcome category. It was not possible to summarize findings for acute bronchitis separately, as too few studies reported findings for an outcome clearly restricted to acute or infectious bronchitis

Major results from the meta-analyses of all eligible studies, regardless of control for confounding, are provided in column 2 of Table 3. For the two primary outcomes, bronchitis and respiratory infections, central estimates of ORs were 1.44 and

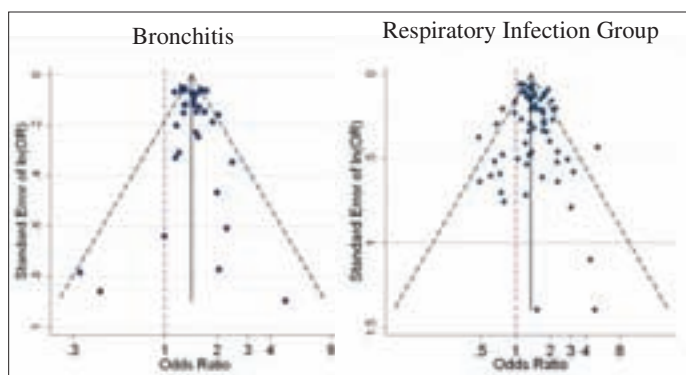


Figure 2. Funnel plots for bronchitis and the respiratory infection group. The horizontal line in the plot for the Respiratory Infection Group indicates the line (Standard Error=1) below which asymmetric data points were omitted in a secondary analysis.

1.45. For these and all other subcategories in Table 3, 95% CIs excluded the null. P-values for heterogeneity for both were <0.0001 . For bronchitis and the respiratory infection group, central estimates changed little (by less than 0.01) when the models were restricted to studies that controlled for age, gender, smoking, and socioeconomic status (column 3); however, with this restriction the p-value for heterogeneity for bronchitis increased to 0.12. Estimates (not shown) derived from fixed effects models were also very similar to the estimates in Table 1 – the maximum change in central estimate OR was 0.04. For the respiratory infection group, excluding RR values reported by two studies changed the central estimate by less than 0.01 and confidence interval endpoints by 0.03 or less.

A series of models excluding each finding sequentially did not identify highly influential single findings. The two most extreme findings (ORs of 0.48 and 5.1) were not from large studies, and did not have major influence. Additional models were constructed with specific subgroups of respiratory infection outcomes (Table 3). For these subgroups, when restricted to studies with control of at least the four key confounding factors, modeling outcomes of respiratory infections excluding otitis media did not much change the estimate or decrease heterogeneity. Modeling outcomes of respiratory infections excluding common cold and nonspecific upper respiratory infections increased the central estimate to 1.50 and decreased heterogeneity ($p=0.07$). Restricting the model to only common cold or acute upper respiratory infection (excluding several findings of unspecified respiratory infections), the central estimate was 1.38, but with high heterogeneity. Constructing separate overall respiratory infection group models for children/infants and for adults led to similar ORs of 1.48 and 1.49, with decreased heterogeneity ($p=0.09$) only for children/infants. Other study factors potentially contributing to heterogeneity included statistical adjustment for subject atopy, parental atopy, or presence of furry pets, and whether assessment of environmental dampness was conducted by researchers or participants. Numbers in these subgroups were small, and inspection of estimates revealed no clear potential to influence heterogeneity.

Figure 1 shows forest plots with adjusted ORs and 95% CIs for the associations of respiratory infections and bronchitis with dampness and mold as reported in the original studies. Figure 1 also shows the summary estimates produced in the metaanalyses using random effects models with all studies listed in Table 2.

Funnel plots for the respiratory infection group and bronchitis are shown in Figure 2. No asymmetry was evident for bronchitis. The asymmetry in data points for the respiratory infection group, i.e., the absence of published ORs less than 1.0 produced by less precise (generally smaller) studies, suggested possible publication bias. When we excluded study results with standard errors greater than 1.0 (the set with asymmetric estimates), the revised estimate for this outcome differed by only 0.01 from the estimate in Table 1, suggesting that publication bias had little effect on the central estimates.

Discussion

The results of these meta-analyses indicate that building dampness and mold are associated with moderate but statistically significant increases in respiratory infections and bronchitis. The central estimates and confidence limits for these associations were stable across different modeling strategies: adding studies that controlled for fewer confounding variables,

assuming independence of multiple estimates from the same studies, and omitting included RRs. Also, analyses suggest that publication bias likely had little impact on these estimates.

The statistical associations reported here do not document that dampness and mold are causally related to the bronchitis and respiratory infections. Building dampness itself is unlikely to directly cause adverse health effects. If these associations are confirmed as causal, exposure to one or more dampness-related agents, either microbiologic or chemical, is likely to be ultimately implicated. However, the consistent evidence of adverse health effects from a substantial number of studies that have controlled for key potential confounders, along with the moderately strong associations and the limited evidence of publication bias, provide initial evidence for causal links between these health effects and some dampness related agent(s).

Evidence for relationships of dampness or mold with respiratory infections and bronchitis has strengthened – initially anecdotal, now documented in multiple observational studies. Within the past decade, there have been at least three major qualitative reviews of the associations of dampness and mold with health outcomes. An interdisciplinary Nordic review panel in 2001 concluded “There also seems to be an association between dampness and...airway infections.” but this review provided no conclusions pertaining to the association of dampness with bronchitis. The IOM review in 2004 made no conclusions relative to the association of dampness or mold with respiratory infections or bronchitis, but stated “Healthy persons exposed to dampness or moldy indoor environments sometimes report that they are more prone to respiratory infections...” The most recent review, by WHO in 2009, concluded that there is sufficient evidence to document an association of dampness and dampness-related agents with respiratory infections, but only limited or suggestive evidence of an association for bronchitis. The results of the present quantitative meta-analyses are consistent with the WHO findings for respiratory infections, but imply more strongly that dampness and mold are associated with bronchitis.

Prior quantitative meta-analyses on health effects of dampness and mold have not included a category for respiratory tract infections overall. The meta-analysis by Antova et al. on visible mold in residences and bronchitis in children, based on a set of similar European studies, reported an OR (95% CI) of 1.38 (1.29-1.47). This compares well to the summary OR reported here for dampness or mold in residences and bronchitis, based on the larger medical literature, of 1.45 (1.32-1.59).

The outcome categories included in this review contain a variety of specific diseases, with all but chronic bronchitis caused by a range of infectious organisms. We will consider biologic plausibility of the associations reviewed here separately for the infectious and non-infectious mechanisms.

Respiratory infections include upper and lower respiratory tract infections and otitis media. Upper respiratory tract infections include common colds, pharyngitis (sore throat), and sinusitis. Most are caused by viruses such as rhinovirus, coronavirus, adenovirus, or respiratory syncytial virus, although a minority of cases is caused by bacteria. Otitis media, an infection or inflammation of the middle ear often resulting from a prior upper respiratory tract infection, can be bacterial or viral in origin.

Lower respiratory tract infections, including pneumonia, acute bronchitis, and acute exacerbation of chronic bronchitis, can result from a variety of causal organisms, including *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Moraxella catarrhalis*. Pneumonia is an inflammation of the lung, caused usually by an infection from bacteria, virus, or fungi, but sometimes by accidental inhalation of other substances. Bronchitis, an inflammation of the mucus membranes of the bronchi, can be acute or chronic. Acute bronchitis often occurs in conjunction with viral infections such as common cold (e.g., rhinovirus, adenovirus), respiratory syncytial virus, or influenza, with a minority of cases caused by bacterial infections. In contrast, chronic bronchitis is generally caused not by respiratory infection, but by recurring injury or irritation to the lining of the bronchi, such as from tobacco smoke or irritating dust or fumes.

An evident increase in respiratory infections in association with dampness or mold could occur from increased numbers of infections, or from more serious infections that are more clinically apparent; either might result from impairment of immune defenses. Although the specific exposures occurring in the reviewed studies are not known, and although it has not been demonstrated that exposures to microbial toxins in typical damp or moldy houses can suppress immune response in humans, potential underlying mechanisms can be suggested. Studies both *in vitro* and *in vivo* have demonstrated inflammatory and immunosuppressive responses to the spores, metabolites, and components of specific microorganisms found in damp buildings. Repeated activation of immune responses and inflammation from microbiologic exposures may contribute to inflammation-related diseases, and the resulting inflamed mucosal tissue may provide a diminished barrier to respiratory infections. Observed synergistic interactions in toxicologic studies among microbial agents present in damp buildings, including specific fungi, actinomycetes, and amoebae suggest that immunotoxic effects of fungal and bacterial strains typically found in damp buildings may be potentiated during joint exposures. This could explain lack of evident associations for specific exposures. Thus, some biologic plausibility is evident even in the absence of consistent associations between human exposures to specific microorganisms or microbial components or products and respiratory infections in healthy individuals.

For chronic bronchitis, more often caused by chronic exposures to irritants and inflammatory agents, the immunostimulatory and inflammatory agents and allergens in some molds and other dampness-related microbial agents may explain or contribute to the associations. Also, dampness in building materials can increase the emission rates and indoor concentrations of some chemicals, such as formaldehyde, which could cause irritation or inflammation. Our analysis is subject to multiple limitations. Publication bias in the selection of available studies remains a possibility despite the limited evidence of publication bias effects described above. Estimates from random effects models should be interpreted with caution when the number of observations is small, as in some sub-analyses reported here. The test of heterogeneity used here has low power to reject the null hypothesis when the number of included findings is small.

The respiratory infections category used in this analysis is broad, including outcome definitions of various types of lower respiratory infections that include acute bronchitis; common cold; mixes of lower and upper respiratory infections; and upper respiratory infections including otitis. There were not

sufficient numbers of most outcomes for separate analyses. We have separately estimated summary measures of effect for bronchitis (acute or chronic), respiratory infections overall, and various subsets of respiratory infections. It is possible that some disease caused by allergy or irritation, especially in the upper respiratory tract, was classified erroneously as respiratory infection. Since allergy and irritation are known to be associated with damp indoor spaces, this could have resulted in erroneously linking dampness and mold with respiratory infections. To check this possibility, we estimated risks for a restricted set of respiratory infections: including lower respiratory infections plus specific upper respiratory infections of tonsillitis, pharyngitis, sinusitis, and otitis, but excluding common cold and less specific upper respiratory infections (e.g., acute upper airway infections, airway infection, and frequent childhood respiratory infections), with the highest potential of being allergic or irritant outcomes misclassified as infections. Because this restriction of the respiratory infection outcomes increased the summary OR slightly from 1.44 to 1.50 (and reduced heterogeneity of findings), this potential misclassification is not likely to explain the elevated risk of infections found here with dampness or mold. Regarding the summary OR of 1.38 for common cold and acute upper respiratory infections, it is not clear how much allergic and irritant effects have been included with true upper respiratory infections. We did not estimate effects for a category of lower respiratory infections because these findings were mostly for acute bronchitis. There were only seven findings for pneumonia from three studies (ORs 0.79, 1.30, 1.33, 1.71, 1.77, 1.85, and 2.3), too few to allow confidence in a meta-analysis (estimated summary OR=1.57), but suggestive of increased risk.

The substantial diversity of findings in the studies reviewed here was evident in the initial low p-values for heterogeneity. When acute bronchitis findings were restricted to studies adjusted for the four key confounding variables, the p-value for heterogeneity increased to 0.12. This suggests that heterogeneity for the unrestricted findings may have been due to scattered estimates from less well-adjusted studies. That the central OR estimate, 1.45, remained unchanged with this restriction suggests scatter in the unrestricted findings rather than systematic bias.

For the respiratory infection group, restriction to findings from more consistently adjusted models omitted many of the most extreme estimates (eg, 0.48, 0.49, 4.4, 4.8), but did not decrease heterogeneity of the remaining findings. Exclusion of relatively nonspecific upper respiratory infections, which might be misdiagnosed allergic or irritant effects, increased the central estimate to 1.50 and decreased heterogeneity ($p=0.07$), whereas the estimate for common cold or acute upper respiratory infection was 1.38. While substantial heterogeneity remained within many of the subgroups listed in Table 3, for those subgroups with little heterogeneity within, differences in OR were not large.

Because of the small number of available studies and the frequent use of outcomes containing multiple diseases, clear conclusions cannot be drawn about even associations with specific infectious diseases such as influenza. While the central estimate for common cold or acute upper respiratory infection of OR=1.38, the lack of homogeneity in the included findings and the uncertain diagnosis makes this estimate only suggestive.

Most studies included here relied on occupant reporting of dampness and mold, a possible source of both systematic

bias and error. However, two prior reviews have considered whether biased subjective response by building occupants in dampness studies might have positively biased the findings. The prior comparison by Fisk et al. of occupant-reported versus independent researcher-based assessments of dampness and mold in six studies concluded that it is “very unlikely that the observed association of respiratory health effects with dampness and mold is a consequence of over-reporting of dampness and mold by occupants with respiratory symptoms.” Bornehag et al reported that findings of studies with independent assessment of both dampness and health effects were similar to findings of studies with more subjective information sources.

The use of subjective, qualitative assessments of dampness and mold, even if not systematically biased, will misclassify actual causal exposures. However, these subjective metrics are currently the most useful correlates of health effects. Direct causal exposures related to dampness and mold have not yet been documented. Many quantified assessments of microbial exposures have been studied, and they have not shown consistent associations with specific health effects in healthy individuals. This is likely because the specific causal exposures involved have either not yet been identified or not been well measured. Also, as Antova et al say, visible molds “may better represent long-term exposure to moulds than direct measurements during a short sampling time.”

The majority of underlying data are from cross sectional studies that are subject to confounding and other limitations inherent in that study design, despite the attempts to control for known confounders. The resulting estimates are all less than 1.5, making their elevations especially susceptible to alternate explanation by unmeasured confounding factors and other biases rather than by dampness- or mold- related exposures. It is not clear what additional confounding variables might explain these findings consistently across studies. On the other hand, since the risk factors assessed in these studies are likely to be surrogates for unmeasured indoor dampness-related causal exposures, ORs for the true causal exposures would be higher.

The primary summary estimates reported here required that studies controlled at least for age, gender, smoking, and SES (although many included studies also controlled for other factors). If studies did not adequately control for all important confounders, biased estimates may have resulted. Evidence suggesting that substantial residual bias was unlikely comes from the paper by Antova et al. Only two of the 23 studies included here were among the 12 included in Antova et al. Yet findings for bronchitis here and in the pooled data analysis of over 58,000 children by Antova et al were very similar, even though Antova et al. adjusted for 13 potential confounding factors – age, gender, current smoker in household, maternal smoking during pregnancy, maternal and paternal education, household crowding, nationality, gas cooking, unvented gas/oil/kerosene heaters, birth order, “ever had a pet,” and study area. Also, the analysis by Antova et al, when adjusted only for age, gender, and geographic area, gave similar estimates as when adjusted for many factors. Although the estimates included in Antova’s summary for bronchitis had significant heterogeneity, estimates from all included studies exceeded 1.0, and CIs for nine of the 10 exceeded 1.0. Furthermore, Antova et al. performed a sensitivity analysis on potential heterogeneity on other variables such as season of questionnaire, age of subject, year of study, and response rate, and found little effect other

than a significantly higher ORs for bronchitis in studies with above 80% response. Overall, this suggests that the relationships of bronchitis and various other respiratory outcomes to mold are not much confounded by the most obvious variables, and are not modified substantially by other key variables.

Respiratory tract infections, the most common infectious diseases in humans, have large health and cost consequences for individuals and for the public. Acute lower respiratory infections are the leading cause of death in children below five years old worldwide. Community-acquired pneumonia (e.g., not hospital-acquired or in the immunosuppressed) is a major cause of hospitalization and morbidity and costs more than \$17 billion dollars annually in the U.S. Otitis media is the most common bacterial infection in children, and is a major cause for antibiotic prescriptions. Estimates of the prevalence of dampness or mold problems in houses are available from multiple sources, and include the following: at least 20% in European countries, the U.S., and Canada; 14-40% in Europe, Russia, and North America; and 50% in the U.S.

Little effective prevention is currently possible for human respiratory infections outside of attempting to avoid contact with or spreading infections, vaccination for influenza and pneumococcal pneumonia, and possibly specific nutritional supplementation. The few documented environmental risk factors for respiratory infections include environmental tobacco smoke, wood or biofuel stoves, and low building ventilation rates. If prevention and remediation of dampness and mold in houses and other buildings were documented to substantially reduce some or all types of human respiratory infections, this would be good and important news.

The attributable risk proportion (ARP) of respiratory infections in the population associated with dampness or mold exposure would be estimated, assuming no confounding and that RRs approximate ORs, with formula (2):

$$\text{ARP} = [\text{Pe} (\text{RR}-1)] / [\text{Pe} (\text{RR} -1) + 1] \quad (2)$$

where: Pe is the proportion of the population exposed.

Based on a proportion of damp/moldy housing in the population of 20-50%, and selected ORs in Table 3, approximate ARPs would be: for acute bronchitis, 8-18%; for respiratory infections excluding common cold and nonspecific upper respiratory infections, 9-20%; and for respiratory infections in children or infants, 9-19%. Thus, if exposures related to residential dampness or mold directly caused respiratory infections, then preventing or remediating all this dampness and mold would reduce the prevalence of various respiratory infections by approximately 8-20%.

Thus, this review provides evidence that preventing or remediating dampness and mold in residences, a very common condition, may substantially reduce the burden of respiratory infections. This could be one of the few available preventive environmental strategies for these common diseases, now considered mostly inevitable. In addition, most exacerbations of asthma have been shown to occur in the presence of viral respiratory infections, and hospitalizations for severe exacerbations of asthma are strongly associated with viral infections. This agrees with the finding that dampness and mold in buildings are associated consistently with asthma

exacerbation. Thus, reduction in viral respiratory infections may have important dual benefits.

Conclusions

Dampness and mold in buildings are associated with moderate but statistically significant increases in respiratory infections and bronchitis. If these associations were causal, reducing dampness and mold in buildings would reduce the occurrence of respiratory infections, the most common human infections. The results of these meta-analyses provide support for recommendations by the Institute of Medicine and WHO to prevent building dampness and mold problems in buildings, and to take corrective actions where such problems occur. Additional focused research is necessary to document whether these associations are causal, and to develop more objective assessment tools for dampness, mold, or various other microbiologic factors that correlate with human health effects.

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