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Respiratory Therapy™
The Journal of Pulmonary Technique

Vol. 3 No. 6
December-January 2008/2009

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Editorial

Humidification and VAP: Myths & Practical Realities

Paul Garbarini, MS, RRT

The author is with Hamilton Medical.

Meta-analysis on studies examining the effect of passive vs active humidification systems have not demonstrated any clear advantage of HMEs (passive humidification) vs heated humidifiers (active humidification) in reducing VAP rates.[1] Nevertheless, clinicians often have strong opinions over the choice of humidification devices. Indeed, there are international differences in practice. The vast majority of European hospitals employ HMEs for humidification whereas heated humidification is commonly utilized in North America.

Unfortunately, the choice of humidification device at times appears not to be based on evidence-based medicine or recommendations of agencies such as the CDC. Rather, users of HMEs cite convenience, low cost and the assumption that a dry circuit reduces the potential for patient contamination. Devotees of heated humidification cite the need to provide 100% relative humidity to maintain normal secretion viscosity, avoid plugs, etc. Others take a protocol approach such as utilizing the AARC clinical practice guideline for ventilator humidification. This approach typically calls for switching to a heated humidification after so many days or if certain criteria or contraindications are met.

I'd like to try and punch some holes in the above "myths" with some questions we might ask ourselves and provide insight on some practical/empirical realities.

• Clinicians infer cause and effect too easily: "Our VAP rates are 0 because we use HMEs." One could also conclude there's a correlation between your alarm clock ringing and the appearance of the sun. Such conclusions about cause and effect must be evaluated in the light of available studies.

• "Having no water in the circuit prevents the patient from getting contaminated." On the contrary, studies have shown that the patient contaminates the circuit. I'm not aware of any studies showing the reverse. (Assuming use of molecular high humidity (eg, steam), not heated aerosol type humidifiers). The real problem is more likely the clinician cross contaminating patients after draining secretions from the circuit, then moving from patient A to patient B while not adhering to universal precautions.

• "We don't need to drain circuits because we use heated wire circuits." "Our heaters automatically regulate the heated wires so as to eliminate water in the circuit." Well, you can't fool Mother Nature (defy the laws of physics in regards to absolute and relative humidity): If there's no condensate in the circuit, by definition, you cannot be delivering 100% relative humidity at the set temperature. In reality, if one looks at on real patients, the temperature is often set lower so as to get rid of too much water in the circuit (whether manual or automatic temperature adjustment). Heated wire systems reduce but don't eliminate the need to drain circuits. The only way eliminate water in the circuit would be for the heater to allow a range of temperatures, which defeats the goal of maintaining 100% RH. In both of these scenarios, I'd suggest you may be delivering no more humidity than a high performance HME.

• "We have a protocol" for HMEs vs heated humidification. "Probably the best approach. But as with all protocols, compliance with the protocol is an elusive goal. When your taking care of 10 ventilator patients, the time required to set up an active humidification system including the need to change the circuit may delay adherence to the protocol.

Continued on page 54…

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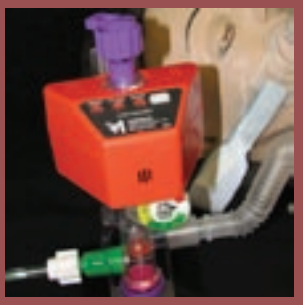

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[a] HCPCS, Healthcare Common Procedure Coding System.
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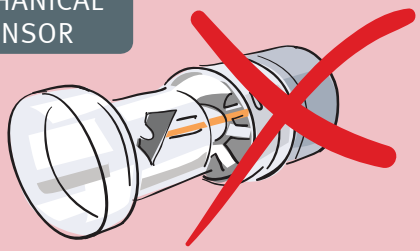

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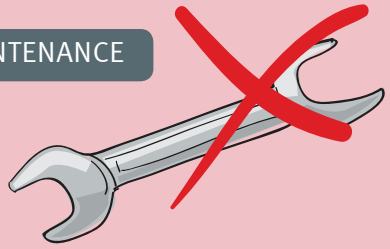

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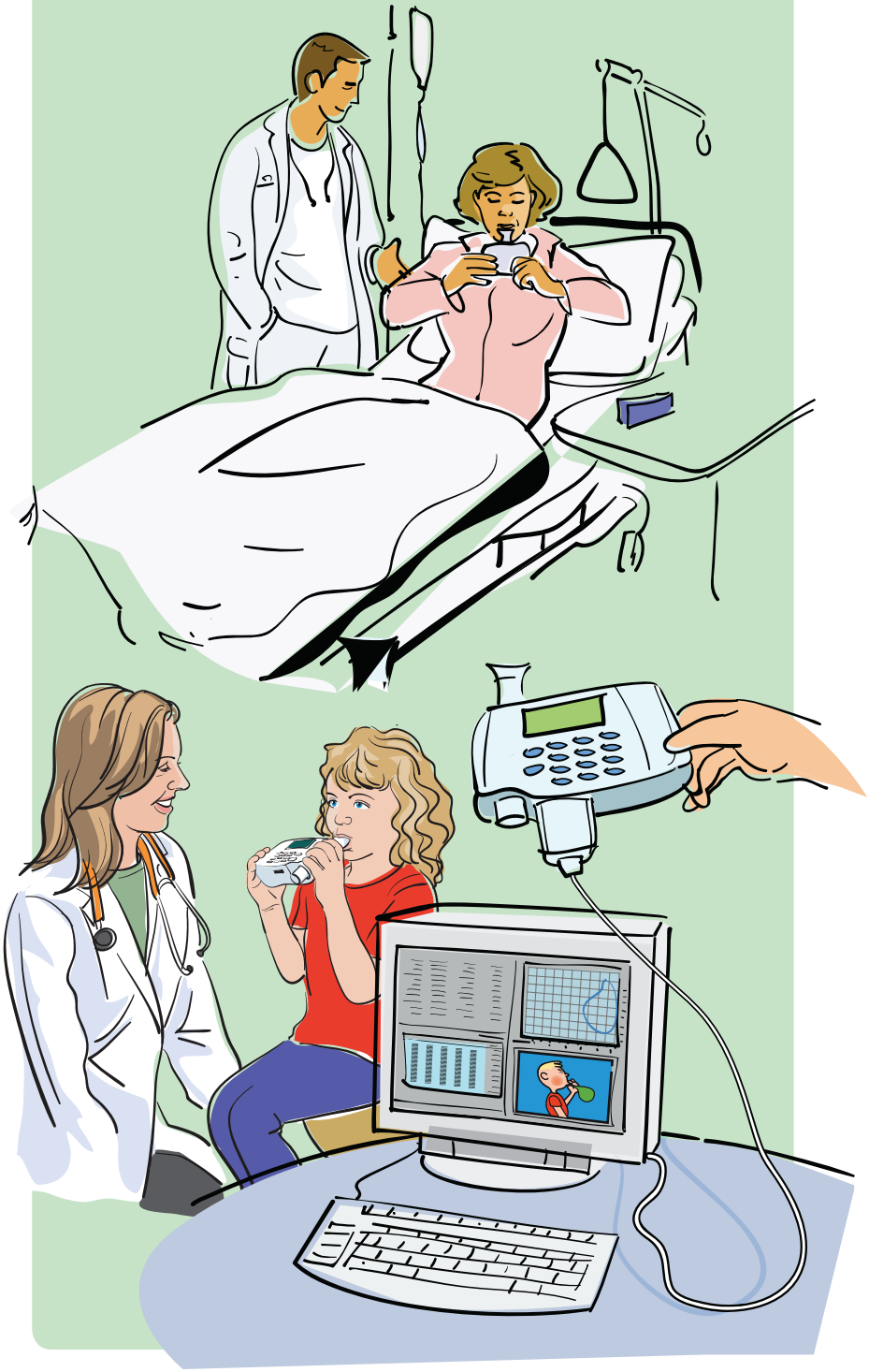

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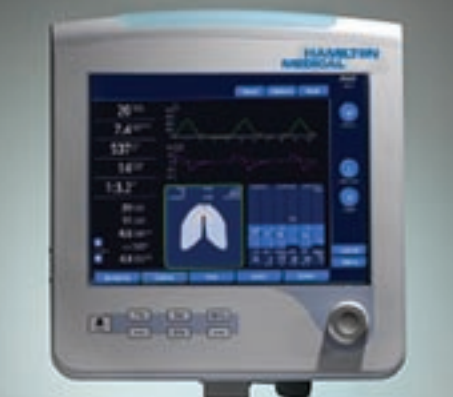

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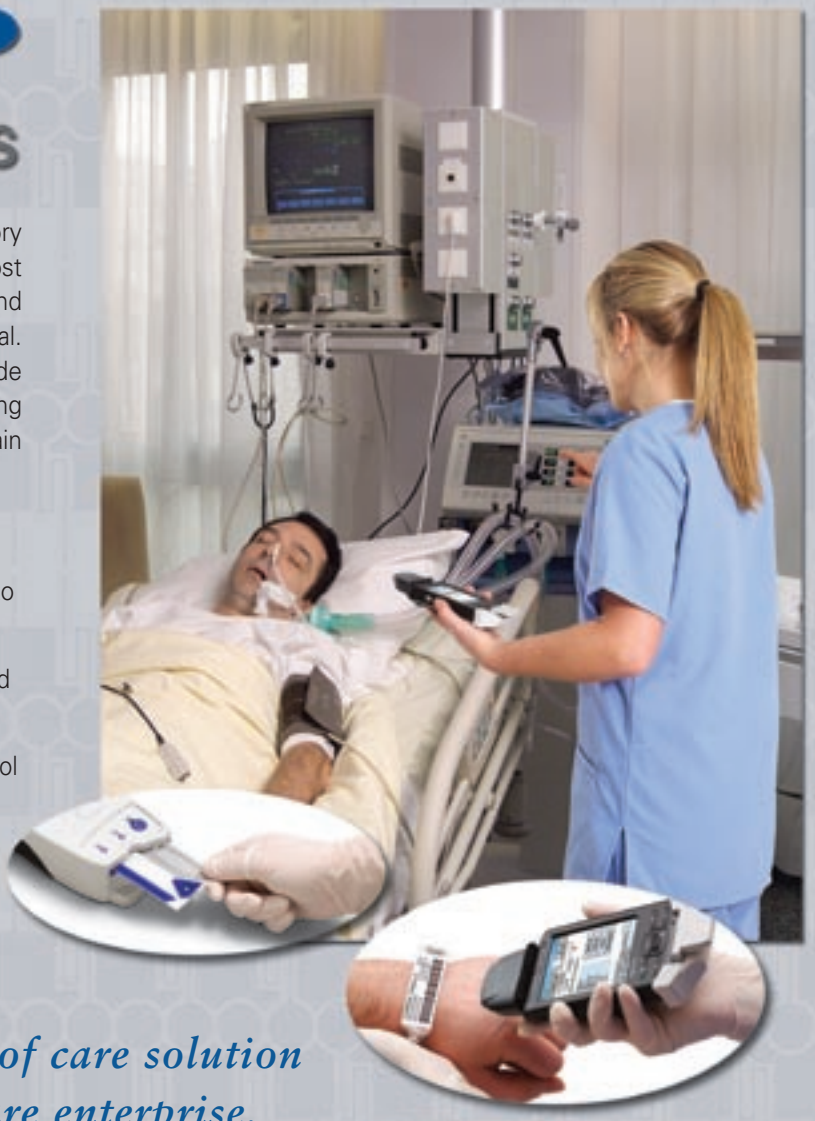

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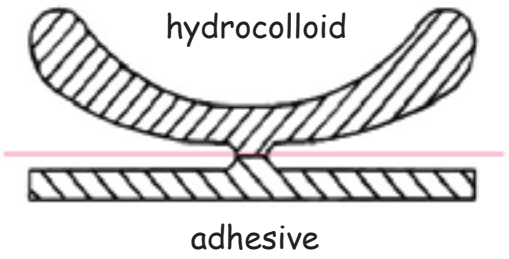

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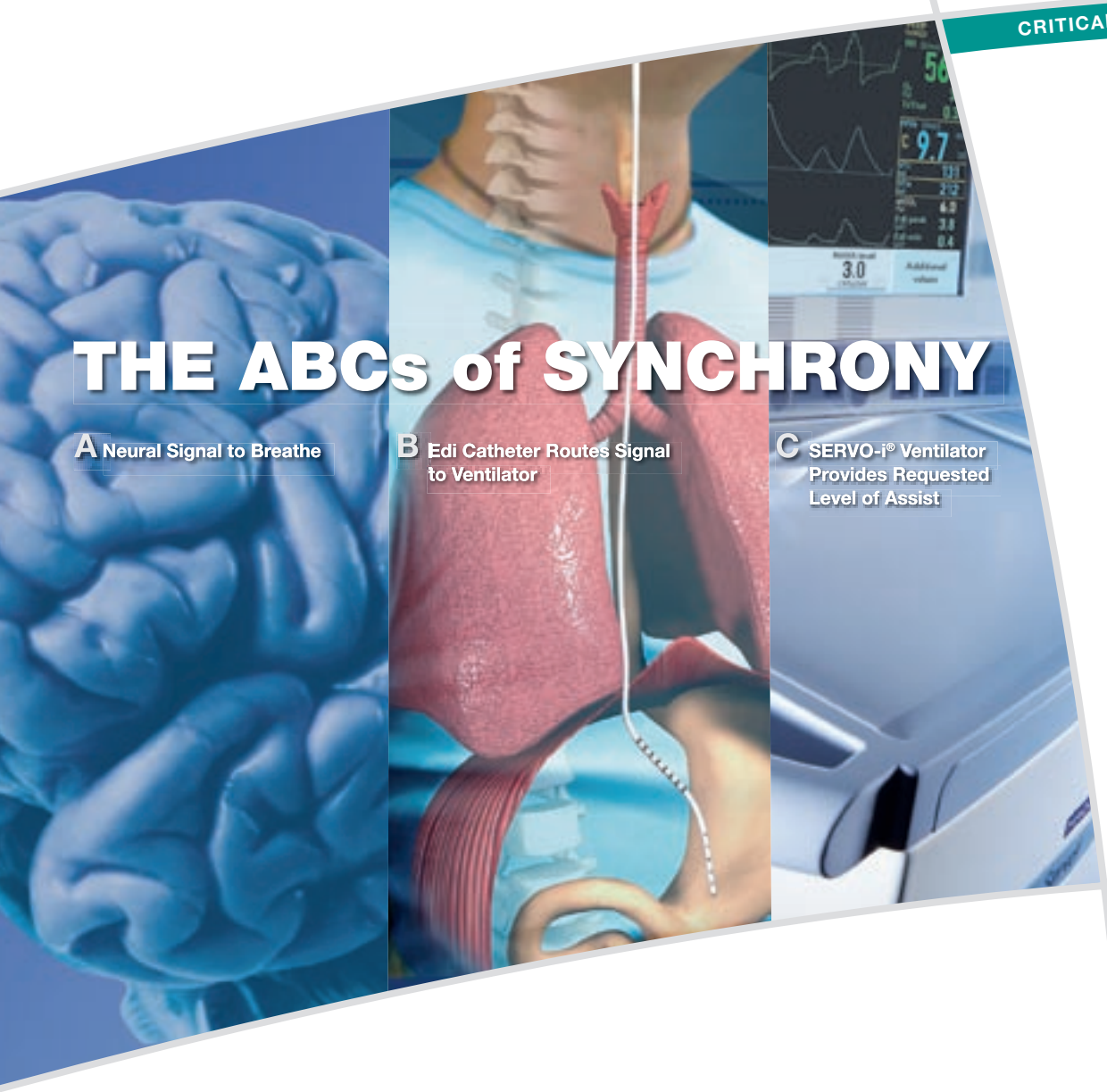

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News

☐ December-January 2008/2009

A FEW GOOD WO/MEN

The New York Times recently reported on the growing need for midlevel healthcare providers. In her article, Christine Larson wrote about the increasing opportunities, and lack of, qualified physician assistants, profiling Adam Kelly, who works in the neonatal unit of Hartford, CT's St Francis Hospital and Medical Center. Ms. Larson wrote, "In an aging population, a shortage of doctors has created new demand for care providers like physician assistants and nurse practitioners — nurses with advanced training who can also examine and treat patients, make diagnoses and write prescriptions. From 2001 to this year, the number of nurse practitioners in the United States has grown to 125,000 from 82,000, and the number of PAs to 68,000 from 43,000." The average income of a full-time PA in clinical practice is $86,000; and $92,000 for an NP. Physician assistants practice under a physician's supervision, while nurse practitioners are licensed as independent healthcare providers, though some states require them to work under a supervising or collaborating physician. PAs are typically generalists, while NPs specialize. Ninety percent of PA schools now offer master's programs, and candidates have to pass a certifying exam. These programs cost about $46,000. Nurse practitioners are licensed by state boards of nursing, and are typically registered nurses who must then earn a master's in nursing science or a can earn a doctorate in nursing practice, a growing trend. Reported in the New York Times, August 9, in the column, "Fresh Starts."

DEATH RATES REVEALED

Jeff Borrink, BS, RRT, writes in the latest Hamilton Medical newsletter: For healthcare consumers, information is power, and knowing a hospital's death rates can give health care consumers more power to influence the quality of their medical care. However, until recently, this information has not been readily available. Last year, the US Centers for Medicare and Medicaid Services released a broad comparison of death rates for heart attacks and heart failure, noting how hospitals compared against the national average -better, worse or no different- without releasing the death rates themselves. This year the agency decided to disclose the rates to consumers through a government website called Hospital Compare. Hospital Compare was created through the efforts of CMS, the Department of Health and Human Services, and other members of the Hospital Quality Alliance, a national public-private collaboration to encourage hospitals to voluntarily collect and report hospital quality performance information. CMS posted their new mortality estimates on the Hospital Compare website, along with more than two dozen other measures of how well hospitals meet patients' needs. On this website, healthcare consumers can find information related to hospital death rates, how often a hospital gives recommended treatments for certain conditions or procedures, what patients say about the care they received during a recent hospital stay, and more. The hospital quality measures on this website show recommended care for some of the most common and costly conditions that hospitals treat. The Hospital Compare website can be used as a tool when trying to determine which hospital to choose for certain surgeries or procedures. A general search of a hospital can be done by looking up a hospital by name, zip code, city, state, or county. The general search provides information on hospital process of care measures, hospital outcome of care measures, and survey information of patients' hospital experiences. More specific searches can be done by choosing a specific medical condition or surgical procedure. Data can be viewed and compared from up to three hospitals at a time. Using the information from CMS, USA Today created another tool that is easy to use and can quickly show how any local hospital compares with one across town, across the state or across the nation. It is a 50 state interactive map that gives the mortality death rate data for hospitals across the United States in regards to heart attack, heart failure and pneumonia compared to the national average. Using this map, data can be viewed by condition, state, year, and even ranking (100 highest and 100 lowest mortality rates). Being able to monitor and track hospital death rates, among other things, not only helps health care consumers make more informed choices regarding their medical care, but provides valuable information to hospitals and health care providers with regard to their performance against their peers, which can be used to assess and improve the quality of care being delivered. [Reference: Sternberg S., DeBarros A. Hospital death rates unveiled: Patients can compare care for the first time. USA TODAY. August 20th, 2008; sect 7B-8B.]

PLOUGHING AHEAD

Schering-Plough Corp has received approval from the European Commission for the drug Bridion. Bridion allows the anesthesiologist to rapidly reverse both moderate and deep levels of muscle relaxation. Neuromuscular blockade is commonly used for surgeries requiring paralysis of the abdominal and thoracic areas. This requires intubation and mechanical ventilation until the paralysis is reversed or the drug wears off. The company reports: A muscle relaxant plays several critical roles in general anesthesia. Anesthesiologists use muscle relaxation to improve surgical conditions and to facilitate intubation and mechanical ventilation. Reversal agents reverse the effects of muscle relaxants, enabling patients to regain normal muscle function sooner and breathe on their own. Current reversal agents are slow and are associated with certain undesirable side effects, including cardiac rhythm disturbances and gastrointestinal and pulmonary side effects... Bridiron has a rapid onset and, in addition to routine reversal, can be used in critical situations when immediate reversal of rocuronium is needed. In Bridiron clinical studies, the median time to reversal of rocuronium was about three minutes. Bridiron is indicated for routine reversal of the commonly used muscle relaxants rocuronium or vecuronium and for immediate reversal of rocuronium in adults, and for routine reversal following rocuronium in children and adolescents (2-17 years of age). Reference: Bridion (sugammadex) Injection—First and Only Selective Relaxant Binding Agent—Approved in European Union, Schering-Plough News Release. Reported in Hamilton Medical's newsletter by Justin Tse, BS, RRT-NPS.

WHY WHITES?

A gene variant known to raise the risk of childhood asthma in European and American children doesn't plays a similar role in African American children. A current study, from The Children's Hospital of Philadelphia and the University of Pennsylvania School of Medicine, showed that the gene ORMDL3 plays a role in asthma of any severity level, but data suggest that other genes outside the region occupied by ORMDL3 might have important

roles in raising susceptibility to asthma. Drawing on patients from the Children's Hospital network, the study team analyzed DNA from 807 white children with asthma, compared to 2,583 white children without the disease. Another cohort consisted of African American children, of whom 1,456 had asthma and 1,973 were healthy controls. Researchers said continued investigations may shed light on how genetic knowledge could be used to develop more effective treatments.

REDUCING VAP

Hamilton Medical reports, in an article from the company's newsletter by Melissa Turner, BS, RRT: Ventilator Acquired Pneumonia is a topic frequently on the mind of critical care clinicians everywhere. Institutions all over the world have implemented certain guidelines and practices in the hopes of effectively reducing or wiping out their occurrence of VAP. For clinicians to participate in the efforts to reduce VAP, it is important that they understand the guidelines and practices set forth by their institution and how effective those practices are against VAP. Nosocomial infection rates among critically ill patients average forty percent (40%) and could be as high as sixty percent (60%) for patients that remain in the ICU for longer than five (5) days. For ventilated patients, VAP has become one of the leading contributors to morbidity and mortality. As for the prevention of VAP, there is no single method to address this problem. There are, however, several identified interventions that can be used and are widely accepted as being effective. Prevention of VAP must also be a collaborative team effort. The RN and RT play a very important role in VAP prevention as they are the clinicians that spend the most time at the patient's bedside. Kaynar et al[1] surveyed both RNs and RTs to determine the self reported rates of various measures to prevent VAP. There were a total of 325 surveys administered and 278 responses were received. Of those responses, 172 were from RTs and 106 from RNs. There were 20 different measures surveyed; 11 proven effective measures, 4 undetermined effectiveness measures, and 5 ineffective measures.

Of those surveyed, 83% of RNs and RTs reported adhering to effective measures. The lowest reported adherence rates for effective measures were for continuous subglottic suctioning and scheduled drainage of condensate from ventilator circuits. Some of the reported reasons for the non adherence were clinical convenience for scheduled drainage of condensate in ventilator circuits and that most heated wire ventilator circuits do not include a drainage port. Also cited was lack of availability and cost for continuous subglottic suctioning. Other than the two aforementioned measures, there was indeed a greater than 85% adherence rate for the rest of the listed effective measures. There was also, however, a greater than 62% adherence rate to ineffective measures. It is certainly possible that performing these ineffective measures could cause undue harm by increasing the risk of VAP, although the measures are being performed with good intentions. These particular measures are inclusive of routine changes of ventilator circuits, dedicated use of disposable suction catheters, routine changes of in-line suction catheters and chest physiotherapy. As one would conclude, most of these therapies interrupt a closed circuit. With the reported greater than 62% adherence rate for those ineffective measures, one suggestion would be that perhaps the evidence is not translated into practice. The survey also asked

questions about the respondents' knowledge of VAP-related data in their institution. A high percentage of RTs and RNs were unaware of the VAP rate at their facility. It is possible that a lack of formal infection control programs could account for this, as well as the fact that many centers are still trying to decide on a reliable VAP diagnosis method. If clinicians were aware of the VAP rate at their facility, it is thought that they would be more willing to facilitate efforts in the prevention of VAP. It is important to identify VAP rates at all facilities and employ various effective measures to try and prevent VAP. Clinicians should take a closer look at all measures they currently employ and determine if they are effective or ineffective. Perhaps building more effective measures into the arsenal while deleting non-effective and potentially harmful measures could be the first step in bringing VAP rates even lower. Reference: Kaynar AM, Mathew JJ, Hudlin MM, Gingras DJ, Ritz RH, Jackson MR, Kacmarek RM, Kollef MH. Attitudes of Respiratory Therapists and Nurses About Measures to Prevent Ventilator-Associated Pneumonia: A Multicenter, Cross-Sectional Survey Study. Resp Care 2007; 52(12): 1687-1694.

Removal of nasogastric or ETT as soon as clinically feasible	Effective
Use of a formal infection-control program	Effective
Adequate hand-washing between patient contacts	Effective
Semi-recruitment positioning of the patient	Effective
Avoidance of unnecessary reintubation	Effective
Oral (non-nasal) intubation	Effective
Scheduled drainage of condensate from ventilator circuits	Effective
Continuous subglottic suctioning	Effective
Maintenance of adequate pressure in ETT cuff	Effective
Use of protective gowns and gloves	Undetermined
Humidification with heat-and-moisture exchanger	Undetermined
Humidification with heat-and-moisture exchanger with bacteriologic filter	Undetermined
Postural changes	Undetermined
Routine changes of ventilator circuit	Ineffective
Dedicated use of disposable suction catheters	Ineffective
Routine changes in in-line suction catheters	Ineffective
Daily changes of heat-and-moisture exchangers	Ineffective
Chest physiotherapy	Ineffective

CALLING THE CODE

Paul Garbarini, MS, RRT, writes in Hamilton Medical's recent newsletter: Will Respiratory Therapists be "Calling the Code"?—One of the responsibilities of the Respiratory Therapist is monitoring of inspiratory and expiratory gases. This includes $ETCO_2$ monitoring. $ETCO_2$ is routinely monitored to confirm endotracheal tube placement. ETCO2 is also utilized as a surrogate for arterial CO_2 measurement. If ventilation/perfusion matching (V/Q ratio) is normal, the $ETCO_2$ will be ~3-5 torr less than the arterial CO_2. However, only the minority of ventilated patients have normal V/Q's, whether it be due to inequalities in ventilation and/or perfusion. For example, an asthmatic patient who has autopeep high enough to decrease blood pressure and cardiac output will have an increased arterial to $ETCO_2$ gradient with typically an elevated arterial CO_2 and a decreased $ETCO_2$. A cardiac arrest represents extreme V/Q mismatch as there may be no or very little perfusion. This technically represents deadspace ventilation, eg ventilation without perfusion (assuming we're ventilating the patient, whether it be with a resuscitation bag or mechanical ventilator). Back in the 90's, I recall setting up an $ETCO_2$ monitor on cardiac arrest patients in the emergency department. My observations were that few patients with an $ETCO_2$ less than 10 torr were ever resuscitated. On the other hand, if I saw the $ETCO_2$ level suddenly rise, I'd ask the person doing compressions to stop and check for a pulse. Invariably, there would be a pulse as spontaneous circulation had resumed. A recently published study on over 700 cardiac arrest patients now provides good evidence for the prognostic value of monitoring $ETCO_2$ during cardiac arrest. The study revealed that an $ETCO_2$ level of 14 torr after 20 minutes of CPR differentiated between survivors and non-survivors. The sensitivity, specificity, positive predictive value, and negative predictive value of the $ETCO_2$ level at 20 minutes were all 100%. No patient with an initial, average, final or maximum p $ETCO_2$ value of less than 10 torr was resuscitated. The authors recommend that $ETCO_2$ monitoring be routinely monitored and used as a criteria in determining when to end resuscitation efforts. So, RT's may indeed provide the critical objective measurement to "call the code." [Reference: Partial pressure of end-tidal carbon dioxide predict successful cardiopulmonary resuscitation—a prospective observational study. Critical Care 2008, 12:R115, http://ccforum.com/content/12/5/R115.]

FIRST PRIZE

The European Society for Intensive Care Medicine has awarded the first Bernhard Dräger Award for Advanced Treatment of Acute Respiratory Failure to Dr Hermann Heinze, from the Clinic for Anesthesiology and Intensive Care Medicine at the Schleswig-Holstein University Hospital. The research prize, which is worth 15,000 Euros and was donated by Draeger, was presented during the Society's annual conference. The annual prize was created to support research projects relating to intensive care medicine that are dedicated to the progressive treatment of acute respiratory insufficiency. This year the focus was on improving respiration therapy using noninvasive monitoring, and Heinze was awarded the prize to investigate the functional residual capacity guided alveolar recruitment strategy in patients with acute respiratory failure after cardiac surgery. By monitoring the FRC using electric impedance tomography (EIT) for the first time, it should be possible to carry out recruitment maneuvers in a more targeted manner since this technique provides a continuous, radiation-free and spatial depiction of lung ventilation. Heinze works in the Anesthesiology Clinic at Lübeck University.

MISDIAGNOSED

Current clinical guideline definitions for airflow obstruction are leading to middle-aged and elderly people being misdiagnosed with COPD, according to Dutch researchers, who compared the diagnostic outcome when two recommended but different definitions for FEV1/FVC were applied in a large population of patients without a prior diagnosis of chronic respiratory disease. Guidelines recommend a fixed cut-off point of 0.70 for the FEV1/FVC ratio to decide on whether or not airflow obstruction is present, regardless of the age and gender of the person involved. Researchers used a gender- and age-specific lower limit of normal cut-off point for comparison. Using spirometry tests from 14,056 respiratory patients, the researchers calculated a sensitivity of 97.9% for the fixed cut-off relative to the lower limit of normal cut-off point for COPD, a specificity of 91.2%, a positive predictive value of 72.0% and a negative predictive value of 99.5%. The discrepancy between the recommended fixed cut-off and the gender- and age-specific lower limit of normal cut-off became more pronounced as the age of the patients increased. In patients 50 years or older, at least 33% were misdiagnosed with airflow obstruction when the fixed cut-off point definition was used. Reported in the European Respiratory Journal, "Current clinical guideline definitions of airflow obstruction and COPD overdiagnosis in primary care."

GET OUT OF THE POOL

Summers over, so save this tip for next year: outdoor pools can pose similar asthma and allergy risks to indoor pools, according to Belgian researchers. Chlorine vapors floating at the surface of outdoor pools and chlorinated water penetrating the upper airways are the suspected cause. Researchers examined 847 secondary school students and found that asthma risk increased almost linearly with the number of hours adolescents had spent in outdoor pools. Children with the highest outdoor attendance (more than 500 hours, the equivalent of one hour per week for 10 years) were five times more likely to be asthmatic than those who had never swum in an outdoor pool. Asthma risk stemmed from an interaction between pool attendance and atopic status, as evaluated on the basis of total IgE. Researchers also found that children who swam regularly in outdoor pools before the age of seven were more likely to be allergic to cat or dust mites.

MAKING A CONNECTION

COPD is often associated with other serious illnesses, according to researchers at the University of Kentucky, who set out to determine the linking factor of COPD to cardiovascular disease, hypertension and diabetes, and to assess to what degree comorbidity could affect hospitalization and mortality rates. More than 20,000 patients were classified according to the severity of their COPD, and researchers analyzed the presence or absence of diabetes, arterial hypertension, or cardiovascular disease, including angina pectoris, antecedents of myocardial infarction, heart failure, stroke and TIA. They also noted the levels of hospitalization and mortality. A total of 530 patients were in one of the more severe COPD categories, with another 2,076 suffering from moderate COPD and 2,892 for whom the disease was just beginning. Just over 4,500 subjects were considered as potentially at risk and 2,868 others were found by functional respiratory testing to be suffering from restrictive syndrome. As such over half of the COPD patients were suffering from an associated condition. For patients at GOLD stage 3 or 4, the risk of diabetes was increased by 50%, hypertension by 60% and cardiovascular disease by 140%. The risk of hospitalization during the five-year study period was significantly higher for those with one or more comorbidities. However, researchers found that the association with cardiovascular disease appeared to be independent of the severity of the respiratory condition. The article appeared in the European Respiratory Journal, "Prevalence and outcomes of diabetes, hypertension, and cardiovascular disease in COPD."

BAD FOR YOUR HEART

Ipratropium, sold under the names Atrovent and Combivent, used for more than a decade by patients with COPD, has been linked to a one-third higher risk of cardiovascular-related deaths. A study from Northwestern University's Feinberg School of Medicine found that veterans with recently diagnosed COPD using ipratropium were 34% more likely to die of a heart attack or of arrhythmia than COPD patients using only albuterol or patients not using any treatment. Researchers said the medication may be having some systemic cardiovascular effect that is increased the risk of death in COPD patients. The study looked at the cause of death of 145,000 veterans with newly diagnosed COPD from 1999 to 2003.

BAD FOR BREATHING

Adults who take paracetamol weekly were nearly three times more likely to have asthma than those taking paracetamol less often, according to a study organised by GA²LEN, the

Global Allergy and Asthma European Network. Use of other painkillers was not significantly related to asthma. In the GA²LEN-SARI study, published in the European Respiratory Journal, researchers across Europe compared the frequency of analgesic use in 500 adults with asthma and 500 controls. Their results suggest that the risk of asthma symptoms is increased by frequent paracetamol use. This may be the consequence of the action of paracetamol that reduces levels of glutathione in the lungs. Researchers noted that several publications have reported this association.

TOO TUBBY

Researchers at National Jewish Health have shown that glucocorticoids are 40% less effective in overweight and obese asthma patients than in those of normal weight. The findings identify a potential mechanism involved in the resistance, which suggests therapeutic targets for future medications. The study identifies what could be a significant issue for the 10 million Americans with asthma who are classified as either overweight or obese, with a body mass index (BMI) of greater than 25. Obese people often have higher levels of inflammatory molecules in their bodies; asthma is characterized in part by inflamed airways. The study sought to understand why glucocorticoids might be less effective. Researchers enrolled 45 nonsmoking adults, 33 of whom had asthma, and measured the response of cells in the blood and the lungs to dexamethasone. Steroids interfere with inflammatory signaling pathways by raising the level of MAP kinase phosphatase-1 (MKP-1). When the researchers applied dexamethasone to cultures of the participants' blood cells, they found that steroids did not increase MKP-1 as effectively in overweight and obese asthmatics when compared to lean asthmatics. Dexamethasone increased the levels of MKP-1 by 5.27 times in cultured blood cells from lean asthma patients, whereas MKP-1 levels in overweight and obese asthmatics increased by only 3.11 times, a 41% smaller response. The heavier a person was the less their cells were likely to respond to dexamethasone. This negative relationship between weight and response to steroids did not occur in participants who did not have asthma. The researchers cautioned, however, that inhaled steroids were still effective in overweight and obese asthmatics, and that if patients are concerned that their asthma controller medication isn't not working, they should discuss this with their physician rather than simply quit taking it or increasing their dosage.

NOW IN PRINT

A summary of current papers from international journals.

BIOFEEDBACK

The objectives of a study by Barbiero et al were to assess the effect of re-expansive respiratory patterns associated to respiratory biofeedback (RBF) on pulmonary function, respiratory muscle strength and habits in individuals with functional mouth breathing (FMB). Sixty children with FMB were divided into experimental and control groups. The experimental group was submitted to 15 sessions of re-expansive respiratory patterns associated to RBF, which provided biofeedback of the thoracic and abdominal movements. The control group was submitted to 15 sessions using biofeedback alone. Spirometry, maximum static respiratory pressure measurements and questions regarding habits (answered by parents/guardians) were carried out before and after therapy. The Student's t-test for paired data and non-parametric tests were employed for statistical analysis at a 5% level of significance. Significant changes were found in forced vital capacity, Tiffeneau index scores, maximum expiratory pressure, maximum inspiratory pressure and habits assessed in FMB with the use of RBF associated to the re-expansive patterns. No significant differences were found comparing the experimental and control groups. The results allowed the conclusion that RBF associated to re-expansive patterns improves forced vital capacity, Tiffeneau index scores, respiratory muscle strength and habits in FMB and can therefore be used as a form of therapy for such individuals. Source: Influence of respiratory biofeedback associated to re-expansive ventilation patterns in individuals with functional mouth breathing, E.D. Barbiero, et al, Int J Pediatr Otorhinolaryngol. 2008 Sep 23.

PHYSIOTHERAPY DOESN'T HELP

Australian researchers set out to investigate the effect of respiratory physiotherapy in an ICU on the prevention and treatment of VAP for adults with an acquired brain injury. A total of 144 subjects with ABI were admitted, with a Glasgow Coma Scale ≤ = 9, requiring intracranial pressure monitoring, and invasive mechanical ventilation for > 24 h; 33 subjects were subsequently diagnosed with VAP. Respiratory physiotherapy comprised six treatments (positioning, manual hyperinflation and suctioning) in each 24-h period while on MV. The control group received standard medical/nursing care but no respiratory physiotherapy. There were no significant differences between groups for incidence of VAP, duration of MV, length of ICU stay or clinical variables such as requirement for re-ventilation. In adults with ABI, regular respiratory physiotherapy in addition to routine medical/nursing care did not appear to prevent VAP, reduce length of MV or ICU stay. Due to small numbers, it was not possible to draw any conclusions as to whether or not respiratory physiotherapy hastens recovery from VAP. Source: Physiotherapy does not prevent, or hasten recovery from, ventilator-associated pneumonia in patients with acquired brain injury, S. Patman, et al, Intensive Care Med. 2008 Sep 24.

HARD TO SWALLOW

Researchers in Ireland reported on the unusual case of a 32-year-old HIV-positive man requiring ventilation for seizures secondary to viral encephalitis. He had a prolonged care unit stay and had percutaneous tracheostomy performed on day 14 of his admission. He subsequently developed persistent right basal infiltrates and atelectasis on chest radiographs that were slow to respond to antibiotic treatment. Fiberoptic bronchoscopy revealed the cause of his infiltrates to be a 14-cm tip section of closed suction catheter tubing that had presumably fractured during suctioning and became lodged in his trachea and right main bronchus. The researchers noted that foreign body aspiration should be considered in the differential diagnosis of persisting lung infiltrates or atelectasis in all patients, and concluded that medical staff required education about the importance of ensuring that suction catheters and other airway adjuncts are intact following use to prevent possible airway foreign bodies. Source: Fractured closed suction catheter: an unusual cause of endobronchial obstruction in a ventilated patient, M.P. Morgan, B. Marsh, Ir J Med Sci. 2008 Sep 24.

FAT AND WHEEZY

Researchers at the University of Genoa aimed to analyze the relationship between BMI and allergic diseases, including allergic rhinitis and asthma, and functional parameters, such as nasal airflow, FEV(1), and non-specific BHR to methacholine,

in a cohort of navy army subjects. The study included 100 patients with moderate-severe persistent allergic rhinitis alone, 100 with intermittent allergic asthma alone, and 100 healthy controls. All subjects were evaluated performing skin prick test, spirometry, and bronchostimulation test with methacholine. Rhinomanometry was performed in patients with rhinitis. BMI values were significantly lower in control subjects with respect to patients with rhinitis and with respect to patients with asthma. BMI was also significantly higher in males with respect to females. A significant relationship has been observed between some categories of BHR and BMI either in patients with rhinitis or in patients with asthma, whereas there was no association between BMI and functional parameters. The study provided the first evidence of a significant relationship between BMI and allergic rhinitis and between BMI and BHR in both allergic disorders. Source: Body mass index, respiratory function and bronchial hyperreactivity in allergic rhinitis and asthma, G. Ciprandi, et al, Respir Med. 2008 Sep 23.

PRODUCTS & COMPANIES

READY TO WEAR

Draeger Medical, Inc's Infinity M300 patient-worn monitor system provides the performance of a full-size patient monitor, packaged in a compact patient-worn telemetry device for adult and pediatric patients. In addition to monitoring ECG and SpO_2, the device has built-in algorithms to enhance ECG processing and reduce false alarms, such as pacer detection software and ACE, (Arrhythmia Classification Expert), an arrhythmia analysis tool. The Infinity M300 addresses the three major challenges of telemetry monitoring: viewing patient information at the patient's side, hearing and responding to alarms, and eliminating the cost and effort associated with disposable batteries. The Infinity M300 provides continuous standalone monitoring, even if the patient moves out of the hospital's wireless network coverage area. Bidirectional communication between Infinity M300 and Draeger's Infinity CentralStation facilitates wireless data exchange and signal integrity. Working together, the Infinity CentralStation and Infinity M300 enhance patient care management by providing fast data access, rapid assessment, decision support, and clinical reporting.

Draeger Medical also announced the release of Version 7.0 of Software for its Evita XL ventilator. The new Evita XL 7.0 Software can help to address some everyday challenges faced by Respiratory Therapists. With its easier ventilation setting, clinicians can find the appropriate expiration time and apply a constant I:E ratio as well as realize better recruitment maneuvers via standard QuickSet and PressureLink features. A new measured value called "f trigg" indicates the frequency of all triggered breaths to help with the patient weaning process. The more breaths triggered by the patient, the more active the patient is. The software offers easier ventilator screen information access and visibility, and users can use one device, a ventilator, for both O_2 therapy and ventilation. No O_2 flowmeter is needed. For patient safety, this Evita offers online help text in case of alarm messages. With Evita XL 7.0 software, clinicians can provide a direct backup for O_2 therapy for quicker reaction time and therefore enhanced patient safety for patients when ventilation is needed again.

The company announced its enhanced and exclusive partnership with Intensive Care On-Line Network (ICON) to provide 24x7 clinical and educational support for Draeger ventilation equipment now including the Babylog 8000+. ICON has supported Draeger Evita Series ventilator customers in the US and Canada beginning in September 2001 and has since extended support to Savina and Babylog ventilator customers. ICON uses telephone and broadband technology to connect subscribers to their Critical Care Resource Center, which provides immediate live support for users of Draeger Evita, Savina and, now, Babylog 8000+ ventilators. ICON clinicians are certified and trained in the use of these Draeger ventilators and are available 24x7 to answer questions about the equipment, assist in troubleshooting alarms and help guide ICU staff through critical ventilation issues. ICON clinicians can even be contacted via live video, enabling uni- or bidirectional visual and audio interaction between ICU staff and the support team. ICON is staffed with a multi-professional group including intensive care physicians, pulmonologists, critical care nurses, respiratory care practitioners, critical care pharmacists, registered dieticians and information technology specialists. Draeger customers can receive around-the-clock support from ICON clinicians while continuing to manage patients at the bedside. ICON provides customer care packages through their website's "members only" section. Subscribers also have access to on-line clinical documents and case studies as well as educational web conferences, symposiums with continuing education units and respiratory care modules for RCPs and registered nurses. "This relationship enables Draeger to provide a detailed level of clinical assistance and support that is not typically available to customers. ICON provides the 24x7 clinical support from simple troubleshooting to the most critical of issues" said Ed Coombs, MA, RRT, and Director of Marketing for Ventilation, Draeger Medical, Inc. ICON provides Draeger customers a support system and resource center that increases patient safety by reducing the number of errors that can occur in the ICU.

Draeger announced that the Draeger Fabius MRI anesthesia machine has received FDA clearance. The newest member to the family of Draeger anesthesia machines is designed specifically to meet the requirements for the Magnetic Resonance Imaging (MRI) environment. The Fabius MRI is designed for use with 1.5T and 3.0T MRI systems. An integrated Teslameter provides an acoustic alarm if the Fabius MRI is positioned within a field-strength greater than 40mTesla (400 Gauss). Contact draeger.com.

CLEARED FOR TAKEOFF

Teleflex Medical has received clearance from the FDA to market the Hudson RCI Neb-U-Mask, a respiratory device that allows for the concurrent delivery of aerosolized medication and a high concentration of medical gases to treat acute asthma exacerbations. The Neb-U-Mask allows the concurrent delivery of aerosolized medications and high concentrations of oxygen or heliox. The system is composed of an innovative wye design, featuring a nebulizer connection and MDI adaptor, a non-rebreathing mask with a 750ml gas reservoir bag, and color coded tubing. This patented design promotes positive patient outcomes by avoiding therapy interruption. The nebulizer connection features a valved port, which maintains a closed system when a nebulizer is not in use. This closed system design allows for delivery of high levels of oxygen or heliox gas mixtures. The system is available in both adult and pediatric versions. It is conveniently packaged with a Micro Mist nebulizer, allowing for a "grab and go" response in an emergency situation. Contact teleflex.com.

GROUNDBREAKING

Siemens Healthcare recently broke ground on a new state-of-the-art training and service facility at its location in North Carolina. The new facility is a planned 143,000-square-foot, six-story office building, scheduled to open in early 2010, which will house more than 500 technical and administrative support personnel. Siemens' commitment to the project includes a $57-million investment, as well as the addition of approximately 300 jobs. The North Carolina Department of Commerce estimates that over the next 10 years, the project will generate $594 million. In other Siemens news, the company has received FDA 510(k) market clearance for the Ysio, a new generation digital radiography system with a wireless detector (wi-D) for maximum positioning flexibility. Offering one digital radiography (DR) solution for virtually all clinical demands of the growing digital radiography market, the Ysio can be customized to suit the patient's needs, such as one or two detectors, with or without a patient table, and with fully automated or synchronized movements. Due to its versatility, the Ysio serves radiography needs no matter what the imaging volume, protocols, or patient profiles, and its performance features geared toward short examination times make it an ideal system for increasing daily patient throughput. Ysio is available in a variety of configurations: as a wall stand with an integrated detector, a wall stand and table system with a wireless detector, or even as a mixed detector solution for high throughput and flexibility. Contact siemens.com/healthcare.

TRUSTED

Maquet, Inc was awarded a three- year ventilator contract with HealthTrust Purchasing Group. The contract makes Maquet's SERVO ventilation platform available to HealthTrust members. HealthTrust is a group purchasing organization that supports over 1400 not-for-profit and for profit acute care facilities, plus ambulatory surgery centers, physician practices, and alternate care sites. Its members have an annual purchasing volume of more than $13 billion. Contact maquet.com/us.

PHEW

OxygenToGo provides oxygen equipment, advice and support for oxygen-dependent travelers. More than a simple rental agency, OxygenToGo is a medical services company that provides oxygen for oxygen-dependent travelers and travel providers. Most passengers and travel providers rely upon traditional, heavy steel oxygen tanks for supplemental oxygen. Traditional tanks are not only difficult for passengers and crew to handle, but add further cargo weight, increasing fuel costs. Recent safety concerns have arisen regarding the use of compressed oxygen tanks in transport. Oxygen dependent travelers not only require oxygen, but also equipment, advice and technical support from qualified medical personnel. OxygenToGo provides oxygen equipment for each passenger's needs from its large inventory, with an emphasis on portable oxygen concentrators (POCs). These FAA-, TSA- and DOT- approved devices provide limitless oxygen for every segment of the passenger's trip so they can be used seamlessly for ground, air and sea travel. POCs filter oxygen from the surrounding air only when the user requires it and do not store pressurized oxygen, thus eliminating the possibility of explosion. The DOT recently declared that all commercial flights, regardless of size, must allow users to bring a POC on board. As part of its screening services, OxygenToGo will verify and collect a valid, signed physician's prescription; verify adherence to airline regulations regarding seating, advance notice and documentation; as well as educate passengers on requirements regarding sufficient battery power and proper battery storage for their POC. OxygenToGo employs a staff of respiratory therapists and board-certified physicians who assess every passenger's medical condition. The staff also provides 24-hour technical and medical support to customers and travel providers. Contact OxygenToGo.com.

GET SMART

Clinical Foundations, an AARC accredited continuing education program, announced that more than 10,000 respiratory therapists have successfully participated in its self-study program and have earned CRCEs. Since its inception in 2006, Clinical Foundations has offered several modules focusing on a variety of respiratory diagnostic and treatment topics that are an integral part of clinical practice, including: Mechanical Ventilation and Humidification, Managing the Difficult Airway, Trends in Noninvasive Respiratory Support: Continuum of Care, Technological Advances in the Clinical Management of OSA, and Preventing Ventilator-associated Pneumonia. Over 35,000 certificates of completion have been issued to RTs for these five modules. The latest issue, Asthma Diagnosis, Treatment and Management is now available at clinicalfoundations.org. Saxe Healthcare Communications provides the program and is supported by an education grant from Teleflex Medical. Teleflex Medical, through the Hudson RCI brand of Respiratory Products.

KIDNAPPED (NOT)

RF Technologies announced it has installed its Safe Place Pediatric and Infant Security Solution at Waukesha Memorial Hospital to help protect infants and children from abduction. The tertiary care hospital's staff delivers around 2,300 babies per year. How RF's system works is that a lightweight transmitter is placed around a child's ankle or wrist. This allows the staff to monitor the child's whereabouts within the protected area. The transmitter sends a signal to receivers placed throughout the hospital. If the band is tampered with or if the infant or child is too close to a doorway, an alarm will sound. Hospital doors also immediately lock down. Safe Place also allows the hospital's staff to generate a variety of customized reports to help reduce alarms and to be ready for Joint Commission reviews at the touch of a button. Contact rft.com.

KEEPING COOL

The Dickson Alarm Thermometer for use in safeguarding temperature-sensitive drugs and vaccines, features tamper-resistant audible and visual alarms. It can monitor both refrigerators and freezers simultaneously. The thermometer provides a visual display of alarm that remains on even if temperatures are no longer out of range, alerting the need for remedial action. The alarm is tamper-resistant, and displays refrigeration conditions every five seconds. It monitors temperatures in the -58 to +158°F range. Contact dicksondata.com.

SEARCH ME

SearchMedica.com, the search engine for medical professionals, today announced the availability of PubMed's MEDLINE abstracts at its website. Now physicians can access abstracts from the 5,200 journals included in US National Library of Medicine's MEDLINE index. SearchMedica's MEDLINE abstracts link back to the Pubmed.gov website, which allows easy access to journal sites, including associated full text articles whenever available online. The new integration of MEDLINE resources simplifies the search process and provides authoritative clinical

information in fewer clicks. SearchMedica filters MEDLINE results to only connect medical professionals with practical resources. Specialists can refine their search into any of eight disease categories including cardiovascular, musculoskeletal, pediatric and respiratory disorders. Early feedback from SearchMedica's registered user base indicates the new interface is easier to use and more intuitive. Access to MEDLINE abstracts further enhances this functionality and provides specialists with additional clinical resources. The company also unveiled a new search category: Practice Management, which connects medical professionals with the best practice management resources available on the Web, including the financial, legal and administrative resources needed to effectively manage a medical practice. The Practice Management channel features content and advice from The American College of Physician Executives, PhysiciansPractice.com and the Centers for Medicare and Medicaid Services. SearchMedica.com was awarded the Silver Award for Outstanding Quality in the World Wide Web Health Awards, which are organized by the Health Information Resource Center and honor the best online health information. SearchMedica earned recognition in the category of Portal or Gateway site in the Professional class. SearchMedica provides free, open access to the web's most authoritative content for medical professionals, filtering out paid articles and consumer websites, making the research process more streamlined and productive. Contact searchmedica.com.

HOT & HUMID

Vapotherm has received 510(k) clearance from the FDA for its Precision Flow, the first high flow humidification system to integrate gas blending, flow control and humidification technology into one device for the optimal conditioning of nasal cannula inspired gases. Precision Flow was developed with extensive input from clinical professionals in neonatology, pediatrics and adult respiratory care. The result is a device that combines performance, safety and ease of use for optimal patient outcomes. The new device offers high flow therapy benefits, with improved ease of use and performance features. With the FDA clearance, the company has initiated full-scale production. Vapotherm also announced that it has secured $20.5 million in new equity financing. The financing will support the company's growth plans including new product development, sales expansion and the launch of Vapotherm's newest acute care Precision Flow device. Contact vtherm.com.

CLINICAL CASE STUDY

Significant Apnea and Bradycardic Episodes in Premature Neonate Alleviated by Micropump Nebulizer, by Matthew Bolinsky RRT-NPS. The author is an NICU Respiratory Supervisor. This case study was provided by Aerogen.

Baby Doe was born prematurely at the age of 26 weeks gestation. She was intubated immediately in the labor and delivery suite and gently ventilated using a T-Piece resuscitator. She was transported to the NICU and placed on mechanical ventilation for her first 21 days of life. On day of life 21, she was placed on nasal CPAP of 7 cmH_20 and 30% oxygen. While the results of her blood gases remained within normal limits, her chest x-ray showed streakiness as seen with moderate bronchopulmonary dysplasia (BPD). The more disturbing element of her care was that of significant apnea and bradycardic episodes with moderate frequency. These episodes required physical stimulation as well as increases in oxygen concentration.

Baby Doe remained on NCPAP and was ordered Budesonide 0.25 mg twice daily by her neonatologist. After contacting our Aerogen representative, he brought the Aeroneb Solo into our institution for a trial. We began delivering the ordered Budesonide on the infant and the results were remarkable. Twice daily she was removed from the NCPAP unit and given the medication via T-Piece resuscitator. This allowed delivery of continuous distending pressures as well as medication delivery. Within 48 hours of use we began to wean both her NCPAP pressure and oxygen. More significant than the weaning of support were the marked changes in her episodic events of apnea and bradycardia. She began to become much more stable, requiring very infrequent increases in oxygen concentration. Much to the surprise of the medical staff, Baby Doe did wean completely off her oxygen and was able to be discharged without oxygen, treatments, or monitors. The respiratory staff was convinced that her positive outcome was attributed to the nebulizer treatments delivered via the Aeroneb Solo. We have since purchased a unit for our use and will continue to deliver our medications in this manner.

GRAPHIC PRESENTATION

A new ventilator, which has taken a unique approach to monitoring the ventilatory status of the ventilator dependent patient, is now available from Hamilton Medical. The G5 and its onboard modes of (S)CMV, SIMV, SPONT, ASV, P-CMV, P-SIMV, APVcmv, APVsimv, DuoPAP, APRV, NIV is capable of ventilating virtually all intubated patients, including Neonates, Pediatric and Adults. The Hamilton G5's graphical user interface and its Ventilation Cockpit integrates 37 monitoring parameters into intuitive graphic representations that help you answer three basic questions in real time. Utilizing Intelligent Ventilation, the Ventilation Cockpit features two object oriented graphic representations. Visualizing the tidal Volume, in relation to predicted FRC, the Dynamic Lung panel displays the patient's real time lung compliance and bronchial tree which is super imposed over a "Normal" lung graphic that expands and contracts in synchrony. This graphic also displays patient effort, resistance, compliance and optional End-tidal CO_2 (CO_2 510k pending). The Vent Status panel monitors breath by breath patient activity, oxygenation and CO_2 elimination. Also displayed are visual representations of Oxygen %, PEEP, ExpMinVol, Pinsp, and the selectable parameters of RSB, % fSpont Rate, PO.1 and VariIndex as related to the patient and the current ventilatory support vs weaning status requirement. When the patient's ventilatory status enters the Weaning Zone, the light blue area, a timer will activate for each parameter and document the length of time the patient has been in the weaning zone. Once all user programmable "wean screen" parameters are met, a large green timer indicates the cumulative time potential withdrawal from mechanical ventilation is possible. The dynamic lung gives the bedside clinician an opportunity to visually assess the patient's lung compliance and airway resistance as ventilator adjustments are performed. As the patient's lung performance deteriorates, the lung inflation and appearance will deteriorate and as the airway resistance increases the airways will become

Continued on page 47…

A Big Wind

This article was provided by Dräger.

On Tuesday August 26th, the National Hurricane Center projected Hurricane Gustav to make landfall on the Louisiana Gulf Coast. They projected this storm would hit sometime early on Labor Day, which was September 1st as a Category 4 or even perhaps a category 5. It was widely believed Gustav would hit with winds of 150+ mph (241 kilometers/hr). Many Americans believe Hurricane Katrina was a worse case scenario for the city of New Orleans.

Hurricane Gustav was projected to be just that strong of a storm and it was on a truly worse case scenario projected path for New Orleans. This is why the Gulf Coast participated in the greatest mass evacuation in history. Over 2 million residents evacuated in less than three days. Lessons learned from Katrina would improve the response to future storms such as Gustav.

Having just launched its new Carina ventilator, Dräger through its local ventilation sales executive and marketing manager went immediately to work offering assistance to make these new ventilators immediately available in the event the Gulf region was to suffer a catastrophic landfall that would strike potentially affected hospitals.

Years ago, when Katrina hit the region, the shipment of merchandise was at a total standstill in the New Orleans metro area. It took weeks for hospitals to receive deliveries of all types of supplies and medical products. Knowing this could be the same situation with Gustav approaching, the need to be proactive, not reactive was all too apparent.

Frank Caminita.

Dräger dispatched 17 brand new Carina ventilators to the region for next day delivery, albeit expensive and perhaps maybe ultimately unnecessary—Americans learned that it is best to be prepared for the worst. When asked why Dräger would make such an effort for what remained an unknown at the time, Ed Coombs RRT, marketing manager for Dräger Ventilation stated, "It is the right thing to do. We want to support our respiratory colleagues from the Gulf region to the greatest extent possible."

Once he confirmed that the ventilators would arrive as planned in advance of the storm, the local ventilator representative, Frank Caminita, RRT contacted the Department of Emergency Preparedness for each of the Gulf States that could potentially be affected.

At that same time Ed Coombs notified the chief executive officer of the AARC Sam Giordano as to the actions Dräger was taking to proactively prepare for the storm. Sam then contacted all five of the presidents of the local state respiratory care societies within the Gulf States region to advise them of the resources Dräger was putting in place locally if needed. Sam asked each one of them to distribute this information to their member hospitals so this service could be best utilized if needed. To ensure that this assistance plan could be implemented flawlessly, Dräger rented a U-Haul trailer to deliver these ventilators to the affected areas. As the local ventilator sales executive, Frank proactively started calling hospitals with the highest probability of a direct hit to advise them that Dräger had devised this assistance plan if needed.

Dräger's Southeast regional manager, Dean Calderone organized Dräger's other local respiratory and anesthesia sales executives to be ready to go to affected areas should the need be necessary. Guy Ray, RRT, Robert Dutruch, RRT, and Nancy Hemmert, RRT were ready for the call if necessary for product training and support.

Left to right, Tamica Aguillard, Angie Welch, in back is Kevin Gobert and Jana Lazard. On the right, is Frank Caminita.

Additional easy reference guides were quickly printed and attached to the ventilators. Aware that if these vents were going to be needed for patients, it would be an impossible task to in-service every Respiratory Care Practitioner on such short notice, Dräger decided it would make the best possible effort to in-service beforehand, but during the storm it would have limited support.

Ed Coombs contacted the Intensive Care Online Network (ICON) to explain the response that Dräger was urgently undertaking to support the Gulf region during the crisis. He requested that ICON provide telephone support and clinical guidance should the need arise for customers who would have their personnel and resources stretched once again. ICON immediately supported this effort without hesitation. A "Carina hotline" was established to provide customers with 24/7 phone support in the event they had questions or needed other assistance.

The first call came on Friday August 29th. Jina Cook, Director of Respiratory Care at Lafayette General called and stated she had a need for the Carina ventilator. Lafayette General was one of the facilities which would be receiving evacuated patients from lower-lying hospitals. Cook was concerned that with the current resources and influx of patients, the hospital's ventilator supply would be exhausted. After a brief description of its features and functionality, Frank delivered a supply of Carina ventilators on Saturday—this was imperative due to the highways implementing "contra-flow" by 4 am Sunday, which meant that equipment couldn't be driven in-bound after that time.

Since Lafayette Hospital was in for a direct hit or possibly just west of the projected path, Frank and Jina decided that ten vents would be most appropriate. In the event other local facilities would need these machines the National Guard could deliver them.

St Tammany Parish Hospital also received Carina vents late Saturday evening prior to the storm. Lisa Hyde, Director of Respiratory Care agreed to house a cache of remaining ventilators for any area hospital. This staging of equipment allowed Dräger to provide ventilators in the path of a direct hit and additional ventilators on standby in close proximity to right side of the storm.

As Frank's own home was in the mandatory evacuation area, he had to head north towards Memphis with the remaining stockpile of Carina ventilators just in case additional calls came in requesting assistance. While traveling north, he heard on the radio an advertisement from NEMA (National Emergency Management Association). This agency was establishing an evacuation center in Jackson, MS for patients with special medical needs. Frank called NEMA to make them aware of the situation. NEMA has a website, aidmatrixnetwork.org, to organize efforts such as Dräger's.

Fortunately for the Gulf region, the storm did not strengthen as projected. Gustav made landfall as a Category 3 instead of a Category 4. Louisiana suffered massive power outages across the state; however, Baton Rouge was on the right side of the storm and they suffered significant power outages.

Fast forward to Friday September 5th: Adam North, Director of Respiratory Care at Our Lady of the Lake Hospital in Baton Rouge called Frank Caminita requesting ventilators, if possible. Adam mentioned that three of the area hospitals were closed and Our Lady of the Lake Hospital was receiving many additional patients. At the time, his hospital has a census of thirty-five ventilated patients, with only a few remaining ventilators on standby. Adam managed to borrow some neonatal vents from Woman's Hospital in Baton Rouge but had a need for adult vents. Within three hours, Dräger anesthesia sales executive Robert Dutruch, RRT was on site to deliver seven Carina ventilators. In-service education was provided to the staff along with the quick reference guides.

It is important to note after the news coverage of Hurricane Gustav even after four days from the storm making land fall, Baton Rouge still did not have power to the traffic lights and gasoline was not readily available.

In the wake of Hurricane Katrina, proactive planning and communication is paramount. Dräger executed this response plan on multiple levels and will continue to provide support to the respiratory care community everyday and especially when disaster strikes. The ventilators remain in the region for the threat of Hurricane Ike.

Albuterol Delivery Using 70%/30% Helium/ Oxygen (Heliox) Gas Mixture As A Source Gas: A Review

Daryl Rockwell, BA, RRT

Aerosolized bronchodilator therapy has long been the standard of care for resolving acute asthma attacks. This form of therapy in a continuous non-interrupted mode is a fairly common practice in severe cases. The use of Helium/Oxygen (Heliox) mixtures is also a widely accepted form of therapy for this same patient population deriving its benefit from a density lower than any FIO_2 mixture. This decreased density lowers airway turbulence and resistance further reducing the stimulation that can contribute to sustained bronchospasm. However, both forms of therapy are rarely given simultaneously without entraining another gas source (O_2 or room air). Previously, lack of equipment to allow for the safe use of both modalities concurrently has hindered both the research and clinical application.

Methods: Using an FDA approved device for titration of Heliox into a continuous medication nebulizer, we performed three independent bench tests using 70%/30% Heliox and a two-hour solution of 20 mg/hr Albuterol/Normal Saline (totaling 75cc). The first two comparative studies ran five continuous units simultaneously to determine the efficacy of nebulizing with Heliox. Following the allotted time (one-hour), the unit was weighed and results recorded. The third study was performed using the same calibrated equipment for each trial to eliminate discrepancy between regulators and flow meters. Before and after weights and times were documented. CONCLUSION: At 13 L/min., 70%/30% Heliox can consistently deliver 40 ml of 20 mg Albuterol solution per hour using the Flo-Mist Continuous Nebulizer (Smiths Medical, Carlsbad, CA).

Introduction

Asthma is a chronic respiratory disease that causes narrowing of the airways by two mechanisms: inflammation and bronchoconstriction. Together, these two processes result in wheezing, tightness of chest muscles, shortness of breath and, in extreme instances, even death.[1] Often overlooked is the key word "chronic." Too often asthmatics being treated for acute onset of symptoms report that they had asthma when they were younger and thought they had outgrown it or that it had gone away. This phenomenon can contribute to asthma sufferers' poor perception of severity of disease, its inappropriate treatment, and an increase in emergency department visits and fatalities. As outlined by Greenberger[2] for identifying asthmatics at risk for Near Fatal Asthma (NFA), patients and caregivers alike often contribute to delay of treatment and enabling of denial. According to the National Institutes of Health, asthma affected an estimated 14.9 million persons in 1995 causing over 1.5 million emergency department visits, about 500,000 hospitalizations and over 5,500 deaths. The rate of mortality among asthmatics has steadily increased over the past 20 years.[3]

Current conventional treatment for acute asthma exacerbation, depending on individual emergency departments, often include a varying combination of oxygen, inhaled bronchodilators, intravenous (IV) corticosteroids, isoproterenol, nebulized or IV terbutaline, magnesium sulfate, helium-oxygen (Heliox) and possibly even mechanical ventilation.

Heliox has been used as far back as 1935[4] for the treatment of asthma and has since generated many conflicting studies and reviews, some advocating, others disputing its value in improving

Criteria to identify patients with potentially fatal asthma

- Intubation for respiratory arrest or failure
- Respiratory acidosis without intubation
- Two or more hospitalizations for status asthmaticus in spite of long term oral corticosteroids
- Two episodes of pneumomediastinum or pneumothorax associated with status asthmaticus

Difficulties in management of patients with potentially fatal asthma

Physician factors

- Inaccurate estimation of severity of asthma
- Underutilization of essential corticosteroids for progressively severe asthma
- Prednisone phobia
- Lack of availability
- Excessive delegation of responsibility to patient regarding medication administration
- Lack of education regarding asthma
- Over utilization of theophylline or B-adrenergic agonists
- Creating excessively demanding regimens

Patient factors

- Noncompliance with medications or appointments
- Prednisone phobia
- Lack of accessibility to care
- Failure to seek care
- Delays in emergency services
- Low intellectual abilities
- Effects of abject poverty (e.g., no telephone or heat)
- Psychiatric conditions (e.g., depression, schizophrenia, bipolar disorders, anger, antisocial personality)
- Denial of disease
- Failure to remove animals from home environment as instructed
- Dysfunctional families

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Characteristics of clinical trials used in this article

Study & Reference	Methods Used	Criteria Used	Research Outcome	Discussion
Rose 2002 (11)	Patients were given three 2.5 mg Albuterol aerosolized treatments every 15 minutes prior to the use of Heliox	Spirometry	No difference between the uses of Heliox versus traditional therapy	Heliox was initiated only after and independent of brochodilator therapy. The authors speculated that patients with very severe symptoms (PEFR < 100 L/m) would probably be better responders
L'Her 2000 (36)	Patients were immediately initiated on inhalation of Heliox with nebulization of 5 mg terbutaline and 0.5 mg ipratropium bromide every 30 minutes using the same gas mixture in a closed system	Dyspnea visual scale, ABGs, lactate levels, and outcome parameters (intubation, mortality and morbidity rate, length of stay)	Inconclusive	The authors admit their trials were not definitive as the study was often terminated, perhaps prematurely, for fear of delaying conventional therapy and causing a worsening of symptoms
Kress 2002 (6)	Patients were given a total of three consecutive Heliox driven nebulized treatements of 0.5 ml of 0.5% albuterol mixed with 2.5 ml of 0.9% saline utilizing a closed system	FEV1	Heliox is beneficial	Results of a preliminary study using a system that allowed for entrainment of room air initially showed no difference between the control (oxygen as the source gas) and Heliox groups. A second study which prevented dilution of room air into the system produced results favoring the use of Heliox
Dorfman 2000 (13)	Heliox was titrated into a continuous nebulizer aerosolizing 0.45 mg/kg (maximum of 20 mg) of albuterol and 1.0 mg of ipratropium being powered by oxygen over one hour	%PEFR	Heliox has no benefit	Titrating Heliox into the gas supply dilutes the amount of Heliox reaching the airways and creates a higher density (Re) of inhaled gas than Heliox alone. Decreasing the beneficial properties associated with Heliox defeats the purpose of implementing its use
Carter 1996 (16)	Heliox was given independent of nebulized treatments of 0.5 mg albuterol every one to four hours	Heart rate, respiratory rate, SaO2, dyspnea score, clinical score, FVC, FEV1, PEFR, and FEF25-75	Heliox has no benefit	Heliox was not initiated until patients had already been treated for a minimum of six hours in the emergency department. Not being front line therapy, it is hard to establish what effect, if any, Heliox could have provided
Henderson 1999 (14)	A solution of 0.5 mg albuterol in 6 ml normal saline was aerosolized in Heliox at 10 L/m for a total of three treatments over 45 minutes	FEV1 and PEFR	Heliox has no benefit	The authors excluded asthmatics in severe distress (the same patient group Rose et al speculated would benefit the most from Heliox therapy). The authors used the same liter flows on the two study groups (oxygen versus Heliox) not taking into account the differences in Re, particle size or carrying capacity of the medication. They also failed to mention if the system used for the test group was closed, preventing further dilution of the Heliox by room air
Kass 1995 (31)	All test subjects had received three to five treatments of nebulized albuterol 2.5 mg per treatment prior to initiating Heliox	ABG drawn before and at a mean of 49.2±25.2 minutes after beginning Heliox	Heliox is beneficial for normalizing PaCO2 and PH	Lack of a control group prevents attributing the normalizaiton of PaCO2 and PH to Heliox alone. The treatments given prior to initiation of Heliox can not be ruled out as the major contributing factor for PaCO2 and PH to normalize
Schaeffer 1999 (8)	Mechanical support using Heliox for status asthmaticus patients	ABG	Heliox improves A-a gradient	There was more than a two-fold reduction in A-a gradient after administering Heliox an average of 90 minutes in patients undergoing mechanical ventilation. This study provides solid, measurable evidence to the benefits of Heliox

outcomes from asthma exacerbation. Some studies credit Heliox with correcting respiratory acidosis in status asthmaticus; increasing FEV1; pulsus paradoxicus; reducing A-a gradients and providing other clinical improvements.[5-10] Yet others cite no improvement in spirometry measurements or clinical disposition and felt the use of Heliox held no benefit for improving outcomes.[11-16] Four case reviews using Heliox reported benefits in averting intubations in patients earlier perceived to ultimately need mechanical ventilation.[6, 11, 17, 18]

Heliox is an inert gas with a lower specific gravity and lower viscosity than oxygen or air.[19] When inhaled alone, it has no known medical actions. It is available in various concentrations such as 60% helium/40% oxygen, 70%/30%, and 80%/20%.
The characteristics of Heliox make gas passage through the respiratory tract smoother, more laminar and less turbulent. In contrast, nitrogen, which makes up 78% of inspired air, is seven times denser than helium.[9] Heliox therapy allows carbon dioxide to diffuse 4-5 times faster, which decreases $PaCO_2$ without increasing peak airway pressures or respiratory rate.[20,21]

This document provides an analysis of several previous studies dealing with the use of Heliox in treating asthma exacerbation, evaluates the various methods used in those studies, and the findings that were obtained. Using information extracted from previous studies and reports as guidelines, a care plan specific to identifying and treating NFA was carefully developed at this institution to reduce poor outcomes and difficulties associated with the intubation of these patients.

Intubation and mechanical ventilation of severe asthma is not without complications of its own and can, in an attempt to avert

Characteristics of case studies used in this article

Case & Reference	Event	Conclusion	Discussion
Manthous 1995 (7)	A patient presents with severe exacerbation of asthma, which didn't improve with steroids, and continuous nebulized B-agonist treatments, experiencing increased work of breathing, tiring, and rising PCO2. Caregivers in the case agreed she would require intubation with mechanical ventilation. Heliox was administered in an attempt to avert intubation	Heliox with intermittent nebulized bronchodilator treatments and IV steroids continued and after 36 hours therapy was successfully withdrawn with no further need to consider intubation	Prior to the end of therapy, breaks from the Heliox were found to cause a return of patient discomfort and increased pulses paradoxicus
Kudukis 1997 (17)	Three separate cases where patients were nearly intubated due to deteriating status of their NFA	Clinicians involved in these cases felt that intervention and administration of Heliox was the common leading factor that averted intubation with these patients	An additional finding from all three cases was the decrease in patients PaCO2
Austan 1996 (18)	A patient thought to be experiencing NFA was being considered for intubation but refused, leading to the intervention of Heliox therapy	Intubation and mechanical ventilation was successfully avoided	The patients ability to rufuse intubation and alter the care givers initial treatment plan raises uncertainties as to the degree of the asthma severity. For this reason it is problematic to assume Heliox was the decisive factor in the patients' outcome and that prior therapies were starting to take effect
Martin-Barbaz 1987 (10)	Four case studies are presented citing clinical improvement and a return to normal ABGs following four hours of Heliox therapy	Heliox is beneficial	To put into perspective, this study is older, does not break down a time frame for improvement, and does not determine the onset severity level of exacerbation

one fatal condition, easily lead to another. Adverse consequences of intubation in asthmatics include hypotension, lobar collapse, pneumomediastinum, and pneumothoraces which have been documented to be found in up to 18% of intubated patients.[22] Intubation may secure an airway however it provides no benefit for the management of the underlying bronchospasm, which is the major pathophysiologic process in these patients. Mechanically ventilating asthma patients can provide a false sense of security especially when the patient is sedated and chemically paralyzed. A non-combative, sedated patient is often mistaken as having an improved condition when in reality he remains hyperinflated with increased bronchospasm secondary to flow turbulence, incomplete exhalation leading to air trapping, and increased interthoracic pressures as a result of increases in peak inspiratory pressures.

Classification of asthma severity

Clinical Features Before Treatment*		
	Symptoms**	Lung Function
Step 4 Severe Persistent	Continual symptoms Limited physical activity Frequent exacerbations	FEV1 or PEF </=60% predicted PEF variability >30%
Step 3 Moderate Persistent	Daily symptoms Daily use of inhaled short-acting beta2-agonist Exacerbations affect activity Exacerbations >/=2 times a week; may last days	FEV1 or PEF >60% predicted PEF variability >30%
Step 2 Mild Persistent	Symptoms > 2 times a week but <1 time a day Exacerbations may affect activity	FEV1 or PEF >/=80% predicted PEF variability 20-30%
Step 1 Mild Intermittent	Symptoms </=2 times a week Asymptomatic and normal PEF between exacerbations Exacerbations brief (from a few hours to a few days); intensity may vary	FEV1 or PEF >/= 80% predicted PEF variability <20%

* The presence of one of the features of severity is sufficient to place a patient in that category. An individual should be assigned to the most severe grade in which any feature occurs. The characteristics noted in this figure are general and may overlap because asthma is highly variable. Furthermore, an individual's classification may change over time.

** Patients at any level of severity can have mild, moderate, or severe exacerbations. Some patients with intermittent asthma experience severe and life-threatening exacerbations separated by long periods of normal lung function and no symptoms.

Many reports support the use of Heliox in asthma exacerbations as a means to reducing the work of breathing and correcting the acidosis attributed to status asthmaticus.[5,18] There is little research showing the use of Heliox continuously and in conjunction with aerosolized therapies in NFA in an effort to decrease morbidity and mortality, including the avoidance of intubation. Earlier studies involving test subjects typically used Heliox intermittently during treatment but not as a continuing, non-interrupted form of therapy. Much of the lack of concrete data to support continued use of Heliox is the fear of possibly harming the patient involved in the research by substituting an untested form of therapy over one with proven benefit. Previous studies made an effort to be unbiased and attempted to prove the benefits of Heliox without influence from other therapies, but that often meant terminating one form of therapy for another. A synopsis of the clinical trials and case studies researched for this article is included.

The use of bronchodilators in aerosol form is widely accepted as the most efficient method for delivery of bronchodilators for status asthmaticus. Heliox decreases turbulent flow and has been shown to improve deposition of medication in the smaller airways.[6,23,24] By combining uninterrupted delivery of both forms of therapy (Heliox and bronchodilators) simultaneously, it stands to reason that the treatment range is broadened thereby maximizing therapy.

Based on information gained from research, case studies, and our departments own bench tests, we developed a protocol using Heliox in a closed system as the source gas to deliver aerosolized bronchodilators. The protocol will provide a means to collect information without deviating from an accepted standard of care or subjecting participants to unknown risks. Data will be obtained by comparing the number of intubations and ICU admissions prior to implementing the Heliox protocol to those inpatients provided with Heliox-driven continuous bronchodilator therapy. Publishing characteristics and findings from previous clinical trials and cases and developing therapies modeled after our institution's Continuous Heliox/ Bronchodilator Therapy (CHBT) procedure could stimulate further research and/or studies in this arena.

Classification of asthma severity

Score	1	2	3	#
Oxygen Saturation	>94%	94%	<94%	
Inspired FIO2	Room Air	22-40%	>40%	
Inspiratory Breath Sounds	Normal	Unequal	Decreased or Absent	
Accessory Muscle Use	Absent	Moderate	Maximal	
Expiratory Wheezing	Absent	Moderate	Marked	
Cerebral Function	Normal	Decreased or Agitated	Confused, Combative, Not Cooperating	
Subjective Improvement After Bronchodilator	Improved	Min-Mod Improvement or Not Done	No Improvement or Worsening of condition	
Peak Flow/Spirometry Maneuver Before Therapy	Good Effort/>250 L/m	Mod Effort />150 L/m	Poor Effort/< 100 L/m or Unable to Perform	
History of Intubations	0	1	>1	
History of ED Admissions	<2 Past 12 Mo	2 or More Past 6 Mo	Within the Past Week	
History of Hospital Admissions	1 or < Past 12 Mo	>1 Past 12 Mo	1 or More Past 6 Mo	
			TOTAL	
A total score of ____ or greater meets criteria for implementation of Continuous Heliox Bronchodilator Therapy.				
Please refer to Procedure # ____				

Materials and Methods

Comparative analysis of published papers, studies, and articles from peer-review journals and texts were retrieved from a search of the medical literature. Further research was conducted utilizing a PubMed (MEDLINE) search using the following search terms: "asthma" and "helium-oxygen" or "Heliox." Included in the search were studies involving the use of Heliox both as an adjunct to therapy or in place of air or oxygen as a primary gas source to power medication delivery devices. Studies were identified as randomized, retrospective, controlled, experimental and blinded. The intent of the medical search was to examine the use of Heliox in earlier studies and to determine if others considered using Heliox in a closed delivery system. The use of Heliox had to be either a mechanism for treating status asthmaticus or as an alternative resource to prevent intubations of NFA. An uncertainty of deviating from established beneficial therapies in the treatment of status asthmaticus prevents many researchers from abiding to strict guidelines many studies require to be considered successful.

Risk factors for death from asthma

History of Severe Exacerbations
- Past history of sudden severe exacerbations
- Prior intubation for asthma
- Prior admission for asthma to an intensive care unit

Asthma Hospitalizations and Emergency Visits
- >/= 2 hospitalizations in the past year
- >/= 3 emergency care visits in the past year
- Hospitalization or emergency visit in past month

Beta2-Agonist and Oral Steroid Usage
- Use of > 2 canisters per month of short-acting inhaled beta2-agonist
- Current use of oral steroids or recent withdrawal from oral steroids

Complicating Health Problems
- Comorbidity (e.g., cardiovascular diseases or COPD)
- Serious psychiatric disease, including depression or psychosocial problems
- Illicit drug use

Other Factors
- Poor perception of airflow obstruction or its severity
- Sensitivity to Alternaria (an outdoor mold)
- Low socioeconomic status and urban residence

This resulted in many previous researches using Heliox to be labeled as improper, biased, or not fulfilling the requirements to consider the study valid. However, because of the lack of well-designed larger studies that defined the role of Heliox in the emergency department setting, information from all articles obtained in the search was considered useful. Subjective details in the researched studies included the use of various scales and guidelines to measure dyspnea comfort levels, hypoxia, and severity of the asthma exacerbation. Numerical data was obtained using arterial blood gases, spirometry, and peak flows.

In the Emergency and respiratory departments, the CHBT procedure provides another step in preventing intubation of patients presenting with NFA and not responding to established, non-invasive treatments. CHBT subjects have to meet the definition of severe persistent asthma as outlined in the asthma symptom severity guidelines adapted from the National Asthma Education and Prevention Program (NAEPP) and the table of indicators of severe asthma used by Jagoda et al. These patients were then placed into a Heliox Dyspnea Index, which was developed as a guideline to assist our emergency caregivers in the decision process of where patients fall in the treatment plan. The flow chart is based loosely on the Modified Borg Dyspnea Scale[25] and assists in determining the need of CHBT. Another tool to assist in the decision process is the 'Risk Factors for Death From Asthma' table published by the National Heart, Lung, and Blood Institute (NHLBI) [see Table 5]. The NHLBI places risk factors into five independent categories including history of exacerbations, intubations, and medications. Patients not initially considered exhibiting NFA but who met at least one criterion from each of these categories was seriously considered for CHBT.

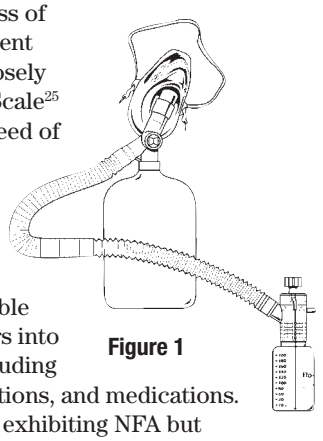

Figure 1

Heliox Bench Study Results

Tests #1 and #2

Sample #	1	2	3	4	5
Results (mg)	35.4	41.8	40.8	42.9	31.5

The mean from tests #1 and 2 is 38.48* ±5.06 and standard error is 2.07. At ±15% of the mean output, the low and high range is 32.71* and 44.25* respectively.

Test #3

Sample #	1	2	3	4	5	6	7	8	9
Results (mg)	41.2	43.1	44.8	36.9	39.7	39.9	42.9	43.0	41.3

The mean from test #3 is 41.4 ±2.7 and standard error is 0.93. At ±15% of the mean output, the low and high range is 35.19* and 47.61* respectively.
*Figures differ slightly from original abstract due to mathematical errors by the author discovered on rewrite.

The CHBT procedure calls for continuous aerosolization of 20 mg/hr mixture of ipratropium bromide 5 mg/ml and normal saline using 70%/30% helium-oxygen as the source gas to power the continuous device. In our studies, the Flo-Mist Continuous Medication Nebulizer (Smiths Medical, Carlsbad, CA—see Figure 1) was used. The device is FDA approved for delivery of continuous dosages of medication while providing the option to add a Heliox admixture as a secondary gas. This device offers a true closed system utilizing a reservoir that would not permit entrainment of room air while providing flows available to the patient at approximately 24 L/m when running Heliox through an oxygen flowmeter at 13 L/m. Similar studies involving other nebulizer brands have shown a decrease in total flow output when Heliox has been substituted for oxygen or air as the source gas. Sources cite a difference of at least 50% increased flow,[26] meaning that for every liter of desired output, the flowmeter needs to be reading 1.5 liters. Most continuous nebulizer systems run 12–15 L/min with oxygen or air as the source gas. If Heliox is to be used, the flowmeter must be set at 18-22 L/m minimum to achieve the same flow and delivery rate.

The Flo-Mist Continuous Nebulizer converts a liquid medication into an aerosolized form that is delivered directly to the patient for inhalation. Utilizing a non-rebreathing mask, it prevents dilution of inspired flow by room air. Attached to the mask is a reservoir bag that provides the patient with added volume above the set being delivered, if needed. According to the product insert, supplemental flows of Heliox being bled into the system need to be run at 22-32 L/m. This addition of Heliox into the delivery system has shown to improve outcomes.[6,7,9,10,17,18,21] Adding oxygen to the Heliox mixture increases specific gravity and density while decreasing the viscosity and laminar flow of the inspired gas.[19,26] In the airways, turbulence of gas flow is directly related to laminar flow and determined by the Reynold's number (Re) of the gas:

$$\text{Re} = \frac{[2(\text{airway radius})(\text{velocity})(\text{density of gas})]}{\text{Gas viscocity}}$$

Airway resistance also directly correlates to the amount of work of breathing and when gas flow is laminar, as it is with Heliox, resistance is reduced. Resistance can be calculated using the Poiseuille equation:

$$\text{Airway resistance} = \frac{[8(\text{tube length})(\text{gas viscosity})]}{3.14\ (\text{tube radius 4th power})^{19}}$$

Turbulent flow begins as Re exceeds 2000.[16] When the percent of helium delivered is decreased because of the addition of another gas, the result is a higher Re.[26] The main objective of the CHBT procedure is to maximize the benefits of Heliox therapy while reducing Re.

Bench tests were conducted to understand the effects of using Heliox as the source gas to aerosolize the medication from a Flo-Mist Continuous Medication Nebulizer. The first two series of tests were performed to evaluate the feasibility and effectiveness for helium to nebulize and deliver liquid medication at the same rate as oxygen. Each sample was run simultaneously for one hour using 70%/30% Heliox mixture. Through testing and published reports, we learned that an increased flow of Heliox was necessary in order to stay within the parameters of manufacturer guidelines for medication output. After determining Heliox as a source gas could stay within the +15% standard of error used by the manufacturer, a more refined bench test with multiple sample units but using the same Heliox regulator and flowmeter was performed. The flowmeter was set to a predetermined flow and calibrated using a Puritan Bennett PTS 2000 (Carlsbad, CA) calibration device. The flowmeter and Flo-Mist Continuous Nebulizer was attached to a 2-stage Heliox regulator (set and calibrated) at 50 psi. This in turn was attached to a 70%/30% Heliox "H" tank. Each nebulizer (nine different nebulizers were used for the study) was filled with a 20 mg/hr ipratropium bromide/normal saline solution for a total of 75 ml. Flow-Mist units were weighed dry using a metric scale (Melter Instrument Corp), filled with solution, and weighed again. They were then run at 13 L/m for one hour after which time they were reweighed. Total mean output after one hour for the nine samples was 41.4 +2.7.

Discussion

While it is important to study the advantages of one therapy over another, in an emergency department presentation of severe and near fatal asthma the possibility of compromising accepted monotherapy versus Heliox alone raises ethical and therapeutic concerns. The benefit of using Heliox in asthma exacerbations is already well documented. However, what interferes with most studies is the attempt to isolate the role of Heliox and just how much of a benefit it plays. Studies involving patients with regards to changes in standard practices raise ethical and therapeutic concerns. With the CHBT procedure as routine therapy for NFA, studies can focus on patient outcomes using the combination of therapies (Heliox and nebulized bronchodilators) versus attempting to determine benefits of one therapy (Heliox) over another (inhaled bronchodilators). The aim of research involving implementation of CHBT should be to show the effects on the number of ICU admissions, lengths of stays, and avoided perceived intubations while providing optimal therapy and not jeopardize patient safety or diminish the chance of collecting worthwhile data. Any studies evaluating the effects of Heliox continuous nebulization should evaluate the need of collecting data from invasive procedures such as ABGs. Documentation of arterial blood gas samples (ABGs) in status asthmaticus prior to and following therapy of Heliox is well established[5,8,17,29,30] and does not influence the immediate choice of therapy in the emergency room setting. To repeat this process at the expense of patient safety and comfort is unnecessary and would not shed any new information and therefore should not be deemed a priority. Also, the additional cost to the patient to repeat these tests for the sake of collecting previously well-documented data is morally unjustifiable.

Spirometry and Peak Flows (PF), normally the standard in

assessing results of bronchodilator therapy, are effort dependent maneuvers that are difficult for acutely ill asthmatics to perform accurately. Both of these factors bring to question the authenticity of the results of such maneuvers when placed into context of studies trying to determine the outcome of using Heliox. Asking patients to perform a procedure that can exacerbate their problem[27] or even lead to cardiorespiratory arrest[31] for the sake of a study would seem to contradict our main objective of improving one's quality of life or to do no harm. While some researchers argue spirometry and PF maneuvers generate bronchospasm,[32] others support the notion that patients often appear to experience a worsening of symptoms following a spirometry maneuver. Jagoda and colleagues admit to significant pulmonary air-trapping being serious enough of a concern to suggest that spirometry should be deferred until after treatment and improvement.[27] Another point that needs consideration is the methodology used to employ desired techniques. Enright discusses inaccuracy of test results because of improper coaching and consistency between test givers.[32]

Collaborative data collection nationally would help validate the use of CHBT and potentially limiting the need to intubate and mechanically ventilate NFA patients, ultimately improving outcomes and decreasing asthma morbidity. Further studies are needed to investigate particle size and concentrations of drug delivery using this product.

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The Hoover's Sign of Pulmonary Disease: Molecular Basis and Clinical Relevance

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In the 1920s, Hoover described a sign that could be considered a marker of severe airway obstruction. While readily recognizable at the bedside, it may easily be missed on a cursory physical examination. Hoover's sign refers to the inspiratory retraction of the lower intercostals spaces that occurs with obstructive airway disease. It results from alteration in dynamics of diaphragmatic contraction due to hyperinflation, resulting in traction on the rib margins by the flattened diaphragm. The sign is reported to have a sensitivity of 58% and specificity of 86% for detection of airway obstruction. Seen in up to 70% of patients with severe obstruction, this sign is associated with a patient's body mass index, severity of dyspnea and frequency of exacerbations. Hence the presence of the Hoover's sign may provide valuable prognostic information in patients with airway obstruction, and can serve to complement other clinical or functional tests. We present a clinical and molecular review of the Hoover's sign and explain how it could be utilized in the bedside and emergent management of airway disease.

Better clinical and bedside prognosticators of airway obstruction would be helpful as asthma and COPD are becoming increasingly prevalent in the population. COPD is the fourth leading cause of death in the United States behind coronary artery disease, malignancy, and cerebrovascular disease. In 2000, an estimated 10 million US adults reported physician diagnosed COPD. Data from the Third National Health and Nutrition Examination Survey (NHANES III), however, estimate that among 11 million US adults with evidence of low lung function, < 40% reported a diagnosis of COPD or asthma, suggesting that COPD is underdiagnosed. Acute exacerbations of COPD can result in ventilator failure, and patients with severe COPD or asthma are more prone to developing this complication. A clinical, quickly identified manifestation of respiratory failure is the Hoover's sign, which does not require expensive tests or waiting for radiological or biochemical results (such as arterial blood gases). Moreover, when patients presents with an acute exacerbation of airway disease in the emergency room or in a physician's office, they are less likely to tolerate laborious radiological examinations (such as computed tomograms) and pulmonary function tests (which require intense patient participation). It is in this situation that a positive Hoover's sign, in association with other clinical parameters, blood gases or peak expiratory flow tests is likely to assist in patient triage and management in emergency settings. We present a review of the clinical and molecular/structural basis of the Hoover's sign and explain how it could be utilized in the bedside and emergent management of severe airway disease.

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Case Report

Figure 1 demonstrates the chest wall findings in a 65 year old male long-term smoker who had frequent hospitalization for wheezing in spite of oral steroids. The patient's medications included prednisone (20 mg/day), formoterol and lisinopril. Examination revealed a thin, dyspneic Caucasian male. Pursed lip breathing, bilateral expiratory wheezing and Hoover's sign were present. Hoover's sign refers to the paradoxical inspiratory retraction of the rib cage and lower intercostal interspaces (Figure 1 Panels A and B). This patient had evidence of moderate airway obstruction and elevated residual volumes (Figure 1 Panels C and D). There was poor reversibility with bronchodilators. The patient had a low alpha-1 antitrypsin level of 83 mg/dl (N=90-200 mg/dl) and he was classified as a MZ phenotype. Figure 2 demonstrates the chest roentgenogram of

Table 1. Suggested Indices of Severity of Airway Obstruction

Physical Findings	Pursed lip breathing Intercostal retraction (Hoover Sign) Accessory muscle use Cyanosis **Hoover's sign?**
Laboratory Parameters	Pulmonary function (FEV1 and FEV1/FVC) Peak Expiratory Flow Rate Hypoxemia

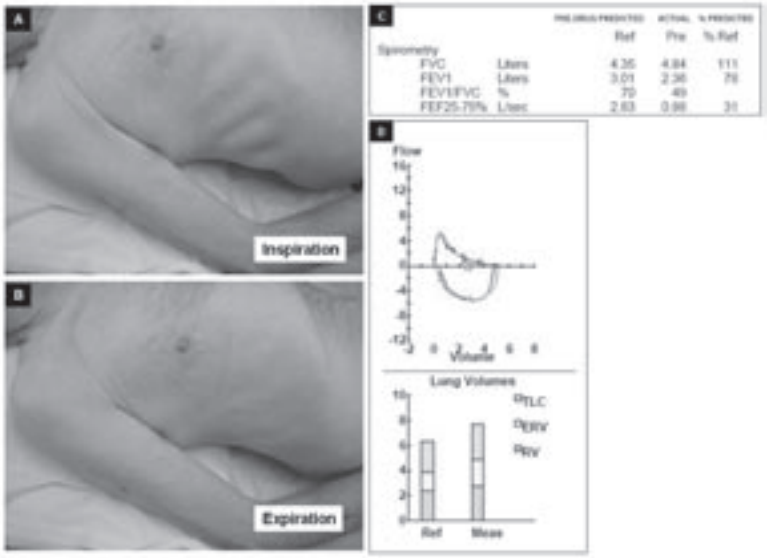

Figure 1. Hoover's sign refers to the paradoxical inspiratory retraction of the rib cage and lower intercostal interspaces (Figure 1 Panels A and B). This patient had evidence of moderate airway obstruction and elevated residual volumes (Figure 1 Panels C and D).

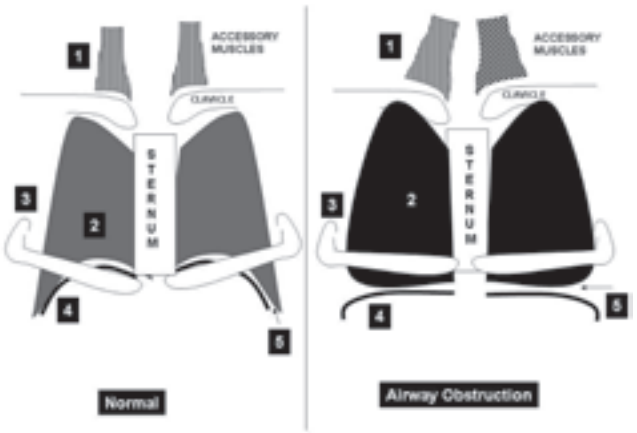

Figure 3 demonstrates the mechanism behind Hoover's sign. The numbers on the figure refer to the following: 1-accessory muscles, 2-hyper-expansion of the lungs, 3-alteration of rib orientation to horizontal 4-flattened diaphragm and 5-decreased zone of apposition (adapted from Mason: Murray and Nadel's Textbook of Respiratory Medicine, 4th Edition).

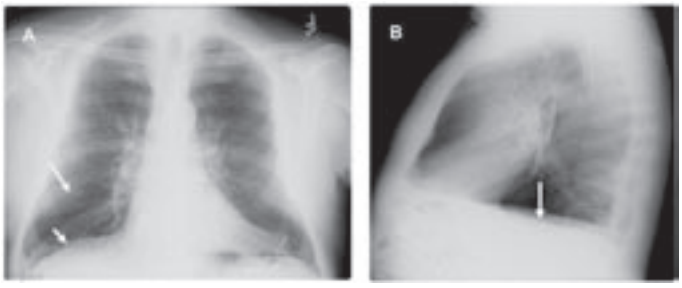

Figure 2 with A showing PA and B showing lateral views of the chest roentgenograms of the same patient. The arrow marks refer to the flattening of the diaphragm (white arrows), emphysematous changes (yellow arrow) and the decreased zone of apposition (red arrow).

the patient, with panel A being the postero-anterior and B lateral views of the chest roentgenograms of the same patient. The arrow marks refer to the flattening of the diaphragm (bottom left arrow), emphysematous changes (top left arrow) and the decreased zone of apposition (right arrow).

What is Hoover's sign? Originally described in 1920 by Hoover, this eponymous sign refers to the paradoxical inspiratory indrawing of the lateral rib margin which has been attributed to direct traction on the lateral rib margins by the flattened diaphragm. Normally, the costal margin moves very little during regular breathing, but, if it does, it moves outward and upward. In patients with obstructive airway disease there is a higher tendency for it to move paradoxically. In these patients, paradoxical movements of the sternum as well as of the abdominal wall may be seen. Garcia-Pachon et al., found Hoover's sign expression in 62 out of 82 patients with COPD (sensitivity of 76%), 3 out of 23 patients with asthma (13%) and in 3 out of 101 (3%) of patients with congestive heart failure. In a larger study of 157 patients, the same investigators demonstrated presence of Hoover's sign in 71 patients (45% of study population), and in 36%, 43% and 76% respectively of patients with mild, moderate or severe COPD. Garcia-Pachon also showed that patients with COPD and Hoover's sign tended to have a higher dyspnea index/score, have higher hospitalizations or emergency room visits than patients without the sign. It appears that Hoover's sign may provide excellent prognostication of severe COPD. In a multivariate analysis, severity of dyspnea, the patient's body mass index, numbers of exacerbations historically and numbers of prescribed drugs were independently associated with the sign.

The Hoover's Sign of Hysterical Paralysis, not to be confused with the sign being discussed, can be found in the neurological literature that describes a sign to separate organic from non-organic paresis of the leg. Involuntary extension of the paralyzed leg occurs when flexing the contralateral leg against resistance. The patient lies supine, the examiner's hand is placed under the non-paralyzed heel, and the patient is asked to elevate the paralyzed leg. In organic paresis the examiner feels a downward pressure under the non-paralyzed heel; in malingering no pressure is felt. This sign is not within the purview of the current review.

Studies by Gilmartin and Gibson suggest that transdiaphragmatic pressures play a major role in the pathogenesis of Hoover's sign. Figure 3 demonstrates the possible mechanism behind Hoover's sign. With emphysema secondary to airway obstruction, flattening of the diaphragm occurs. This leads to increased radius

of curvature, which in turn increases muscle tension. Secondary to the horizontal orientation of the diaphragm and the associated loss of the zone of apposition between the visceral and parietal pleurae, the force vector on the lower aspects of the ribs become inward rather than cephalad. This culminates in the lower rib cage motion directed inward on inspiration instead of outward, the paradoxical movement referred to as Hoover's sign. In an exacerbation, the presence of mucus and bronchoconstriction further increases airway resistance, work of breathing and lung inflation. This leads to more diaphragmatic flattening and exacerbation of the mechanisms mentioned above. It would be interesting to study molecular changes in the musculature such as expression of certain muscle genes and ultrastructural alterations in muscle but these have not been done.

Hoover's sign is a frequent finding in COPD, and the frequency increases with severity. The sign can also be present in patients with congestive heart failure, asthma, severe pneumonia (especially in children), bronchiolitis, as well as seen unilaterally in diaphragmatic paralysis, pleural effusion and pneumothorax. The Hoover's sign is reported to have a sensitivity of 58% and specificity of 86% for detection of airway obstruction in a study by experienced respiratory medicine specialists among a group of first year residents in family medicine. The study compared the accuracy of Hoover's sign detecting obstructive airway disease compared with traditional signs such as wheezing, rhonchi and/or reduced breath sounds. Observer agreement in the study (kappa statistic) was 0.74 for Hoover sign and was lower for the rest of the signs stated above. The Hoover's sign had a positive likelihood ratio of 4.16, which was higher than that of the other signs. Obstructive airway disease in the study was defined as an FEV1/FVC ratio of < 0.70. There have been no studies conducted on the sensitivity and specificity of Hoover's sign in asthma. There is no data available either on the cost savings that may be induced by using Hoover's sign as opposed to use of chest roentgenography, pulmonary function tests or arterial blood gases, for example. The duration of persistence of Hoover's sign, its appearance or disappearance in relationship to exacerbations and remissions and the influence of aggressive therapy on extent of retraction are hitherto unknown. Further studies would certainly improve insights into the pathogenesis of airway obstruction but probably would be unlikely to be done in this day and age of high technology and digital imaging.

Hoover's sign refers to the inspiratory retraction of the lower intercostal spaces. It results from alteration in dynamics of diaphragmatic contraction due to hyperinflation, resulting in traction on the rib margins by the flattened diaphragm. Seen in up to 70% of patients with severe obstruction, this sign is associated with body mass index, dyspnea and frequency of exacerbations. This sign can be an excellent marker for severe airway obstruction.

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Clinical Consequences of Asbestos-Related Diffuse Pleural Thickening: A Review

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Abstract

Asbestos-related diffuse pleural thickening (DPT), or extensive fibrosis of the visceral pleura secondary to asbestos exposure, is increasingly common due to the large number of workers previously exposed to asbestos. It may coexist with asbestos related pleural plaques but has a distinctly different pathology. The pathogenesis of this condition as distinct from pleural plaques is gradually becoming understood. Generation of reactive oxygen and nitrogen species, profibrotic cytokines and growth factors in response to asbestos is likely to play a role in the formation of a fibrinous intrapleural matrix. Benign asbestos related pleural effusions commonly antedate the development of diffuse pleural thickening. Environmental as well as occupational exposure to asbestos may also result in pleural fibrosis, particularly in geographic areas with naturally occurring asbestiform soil minerals. Pleural disorders may also occur after household exposure. High resolution computed tomography (CT) is more sensitive and specific than chest radiography for the diagnosis of diffuse pleural thickening, and several classification systems for asbestos-related disorders have been devised. Magnetic resonance imaging and flurodeoxyglucose positron emission tomography (PET) scanning may be useful in distinguishing between DPT and malignant mesothelioma. DPT may be associated with symptoms such as dyspnoea and chest pain. It causes a restrictive defect on lung function and may rarely result in respiratory failure and death. Treatment is primarily supportive.

Introduction

Millions of people worldwide have been exposed to asbestos. The commonest manifestation of asbestos exposure is pleural disease, including pleural plaques and diffuse pleural thickening (DPT). Malignant mesothelioma of the pleura and DPT are less common than plaques, both conditions are likely to become more common in the future. The overall prevalence of pleural disease including DPT is increasing due to the large number of workers who were exposed and the long latency of the disorder. The Worker's Compensation Dust Diseases Board of New South Wales acknowledges an increase in DPT cases from 65 cases in 2002 to 133 cases in 2006. This review is primarily aimed at clinicians. It summarises available information on diffuse pleural thickening (DPT), contrasting it with other types of pleural disease, discusses potential pathogenetic mechanisms, and summarises available evidence regarding its clinical consequences.

A link between pleural disease and asbestos exposure was first recognised in the 1930s but it was not until the 1960s that a distinction between diffuse pleural thickening and pleural plaques was made. Asbestos-related DPT refers to extensive fibrosis of the visceral rather than the parietal pleura, with adherence to the parietal pleura and obliteration of the pleural space (Figures 1 and 2). In contrast, the parietal pleura is primarily involved in pleural plaques (Figure 3). DPT has unique radiographic features and significant symptomatic and functional consequences for affected patients. It may cause exertional dyspnoea and has been associated with chest pain and in very rare cases with respiratory failure and death due to lung "constriction." Benign asbestos-related pleural effusions are believed to antedate the majority of cases of diffuse pleural thickening and to contribute towards disease progression. DPT may coexist with pleural plaques but has a distinctly different pathology, natural history and prognosis. Treatment is largely limited to supportive and symptomatic care, although rare case reports in the past have documented pleurectomy to be effective in a few progressive cases.

Epidemiology

The prevalence of DPT is difficult to adequately document as this disorder is asymptomatic in its earliest stages. Prospective studies of asbestos workers have shown DPT to occur in between 5-13.5% of workers between 3-34 years following first asbestos contract. In one large study of asbestos exposed insulators, where 58.2% of workers had pleural disease, DPT was rare compared with pleural plaques (5.5% vs 52.5%). The number of patients with DPT assessed for disablement benefit in the UK increased from 380 from April 2002 to 415 in 2004 (www.

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Table 1. Clinical differential diagnosis of asbestos related diffuse pleural thickening

Diffuse pleural thickening due to acute pleuritis:
Pneumonia
Tuberculosis
Empyema
Connective tissue disease
Drugs (eg. practolol, methysergide)
Fibrosing pleuritis
Post radiotherapy
Post-traumatic diffuse pleural thickening eg. haemothorax
Post-surgery (particularly coronary artery bypass grafting
Other diagnoses that may resemble diffuse pleural thickening:
Pleural plaques
Mesothelioma
Other pleural- based tumours

dwp.gov.uk; last accessed on 27 July 2007) and is likely to be an underestimate of the true prevalence. Lower numbers of cases reported prior to this (150 in 1991) are likely to partly reflect changes in the method of collecting statistical information as well as changes in diagnostic criteria, as cases of unilateral DPT have only more recently been included for compensation.

In New South Wales, Australia, the total number of DPT cases notified to the Surveillance of Australian Workplace Based Respiratory Events of NSW (SABRE NSW) Scheme until 2005 was 503, reaching a prevalence of 74.3 cases per million. The number of new cases notified to the Scheme in 2006 was 120 for DPT, 143 for mesothelioma and 240 for pleural plaques alone, although these figures also are likely to be underestimates.

Prevalence of DPT increases in a population from the time of first asbestos exposure, partly because of disease progression but also because calcification occurs, which allows easier detection. The latency (or the time between exposure to first diagnosis of disease) is variable. DPT can develop within a year from exposure to asbestos, usually following a benign asbestos related pleural effusion, but may also take 15-20 years or more to be diagnosed. This contrasts with the documented latency for the development of pleural plaques and asbestosis, which is generally longer at between 20-30 years, and malignant mesothelioma, which may have an even longer latency period of 40 years or more.

Asbestos-related pleural disease is well documented to occur after environmental exposure to asbestos. In areas such as Turkey where environmental exposure to asbestiform fibers is common, more than 50% of the population > 60 yrs of age may have pleural calcification and mesothelioma may also develop. Asbestos-containing "white" soil is used as a whitewash or plastering material and is found in the home environment, resulting in a reversal of the traditional male predominance in asbestos-related disease. DPT may occur in up to 11% of this population. Studies from China, Finland, and Corsica have all shown that pleural plaques are common, and one necropsy study reported plaques in 58% of cases of 288 urban men. The prevalence of both DPT and pleural plaques increases significantly with past occupational exposure to asbestos, duration and intensity of exposure. Thus, workers who have worked in occupations with heavy exposure (e.g. laggers, insulators) are more likely to have pleural disease than those with moderate or minimal exposures.

Table 2. Clinical characteristics of asbestos-related diffuse pleural thickening

Prevalence	5-13.5% of asbestos exposed people 3-34 years following first asbestos contact
Latency	Variable but can occur within 1 year of a benign asbestos associated pleural effusion. Usually 15-20 years
Frequency	Increases from the time of first exposure
Pathogenesis	Uncertain. Possible sequela of benign asbestos associated pleural effusion, recurrent bouts of asbestos related pleuritis or extension of parenchymal fibrosis into the pleura
Location	Usually bilateral, 1/3rd are unilateral Can extend to encase the lung, obliterating the pleural spaces, the fissures and the costophrenic recesses
Macroscopic appearance	Arises from the visceral pleura. Pale grey diffuse thickening of visceral pleura that may become adherent to the parietal pleura. Not sharply demarcated from the pleura, unlike pleural plaques.
Microscopic Appearance	Collagenous fibrous tissue
Symptomatology	Chest pain, dyspnea. Hypercapnic respiratory failure and death in severe cases
Pulmonary Function	Restrictive defect. Reduction in static lung volumes and compliance. Reduced transfer coefficient (TLCO) but a raised or maintained TLCO when corrected for alveolar volume (KCO)
Chest X-Ray Appearance	Smooth non interrupted pleural density extending over at least 1/4th of the chest wall Obliterates the costophrenic angles
HRCT Appearance	A continuous sheet of pleural thickening more than 5cm wide, more than 8cm in craniocaudal extent and more than 3mm thick
Associated Features	Rounded atelectasis, parenchymal bands
Treatment	Supportive, symptomatic, non invasive ventilation for respiratory failure
Differential diagnosis	Any cause of acute pleuritis can cause diffuse pleural thickening (see table 1). Chest trauma and surgery, Mesothelioma, other pleural based tumours, pleural plaques.

Although there are few studies which have concentrated upon the natural history of the disorder, it seems likely that after the initial episode of pleural inflammation, which may be mild or severe and accompanied by a pleural effusion, the condition then plateaus. In a minority of cases, recurring episodes of pleural inflammation may be the cause of further disease progression. Cessation of exposure is believed to slow progression, although information about this is limited.

Aetiology

Although this review concentrates on asbestos-related DPT, this is a diagnosis of exclusion. The differential diagnosis includes tuberculosis, previous chest trauma, especially haemothorax, previous surgery (eg coronary artery bypass grafting (CABG)), recurrent pleurisy eg due to repeated episodes of pneumonia, tuberculosis or rheumatoid arthritis, drugs (eg practolol, methysergide), fibrosing pleuritis, and post-radiotherapy (Table 1). A careful history should always be taken to exclude other causes of which post CABG is increasingly common. No reliable figures are available to assess the relative proportion of asbestos-related rather than non-asbestos related causes

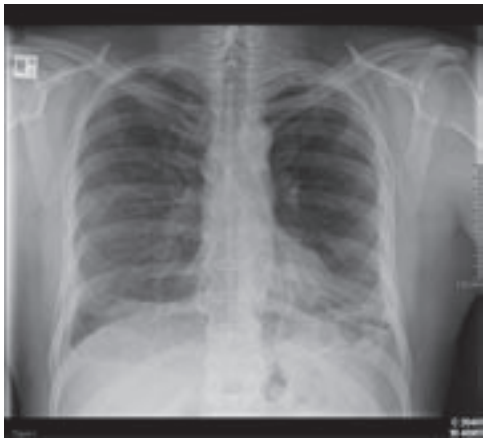

Figure 1. Postero-anterior chest radiograph demonstrating asbestos-related diffuse pleural thickening.

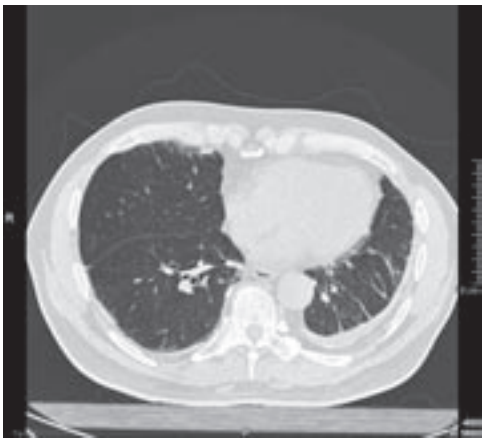

Figure 2. Computed tomography (CT) scan of the thorax demonstrating asbestosrelated diffuse pleural thickening. Note the "crow's feet" or parenchymal bands which are clearly seen on the left, and the overall reduction in lung volume.

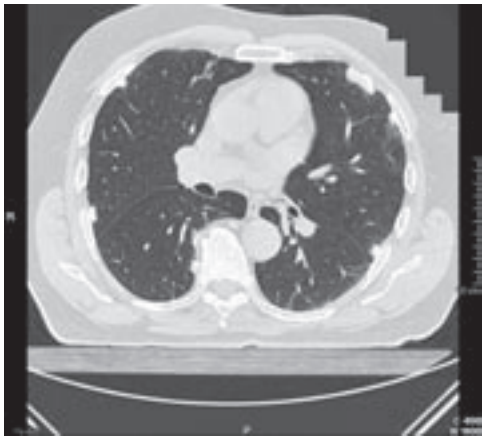

Figure 3. CT scan of the thorax demonstrating circumscribed calcified bilateral pleural plaques.

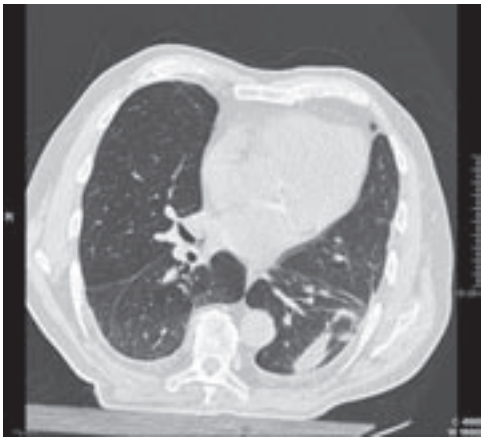

Figure 4. CT scan of the thorax demonstrating "folded lung" or Blesovsky's syndrome in association with diffuse pleural thickening.

but it is reasonable to assume that asbestos is responsible for the majority of cases where there is a documented history of asbestos exposure and the characteristic radiologic appearances are seen.

DPT can occur after exposure to all types of asbestos and its development is thought to be dose-related. Where asbestos fiber load burdens have been performed in the different asbestos diseases, these are highest for asbestosis. One autopsy study of asbestos fibers in 13 asbestos exposed cases of DPT found the proportion of shorter chrysotile fibers to be higher than longer amphibole fibers in partial pleura when compared to lung parenchyma. Total asbestos fiber counts in the parietal pleura were significantly lower than in the lung parenchyma and no differences were found between asbestos counts in subpleural versus central areas of lung. Sebatien et al also demonstrated that there was an increased frequency of short fibers and a decreased frequency of long fibers from lung to pleura and that the frequency of asbestos fibers in pleura compared to the parenchyma was low. He concluded that retention of asbestos fibers in the parietal pleura is related to fiber size and type, and that lung parenchymal retention is not a good indicator of pleural retention. Where comparative asbestos fiber burdens have been calculated, fiber counts are highest for asbestosis followed by DPT, pleural plaques and then malignant mesothelioma. In one study of 192 British naval dockyard workers (96 with DPT and 96 with pleural plaques) the average exposure ratings for DPT did not differ from those for pleural plaques. However, further analysis suggested that patients with bilateral DPT had significantly more exposure than those with unilateral disease. In one transmission electron microscopy (TEM) study of 44 workers from Wittenoom in Western Australia there was a median count of 207.5 uncoated fibers/gram (x 106) per gram of dry tissue in 44 deceased workers with asbestosis compared to 134.6 uncoated fibers/gram (x 106) in 53 with mesothelioma, 9.026 uncoated fibers/gram (x 106) with lung cancer and 0.92 uncoated fibers/gram (x 106) in the reference population. There are no electron microscopy studies from Australia comparing asbestos counts in DPT with other asbestos-related diseases. It has been postulated that pleural plaques develop due to intermittent asbestos exposure which allows time for fibers to be cleared to the pleura. In contrast to this, asbestosis is believed to occur due to heavy and more continuous exposure which overwhelms the fiber clearance mechanism.

Pathogenesis

How asbestos fibers reach the pleural space and cause pleural fibrosis is the subject of ongoing debate. Asbestos fibers may be inhaled, ingested or absorbed through the skin. Inhalation is by far the commonest route by which pathological consequences occur. The mechanism by which they reach the pleural space and cause a variety of different pathologies is controversial.

Fibers that are inhaled and pass through the conducting airways are deposited on the Type 1 alveolar epithelial cells that line the walls of the bronchiolar-alveolar duct bifurcations. These phagocytic cells cause migration or "translocation" of fibers into the interstitium, where the larger fibers like amphiboles are retained. This may in some patients induce a macrophage-induced alveolitis. Alveolar epithelial cell injury damages the fibroblasts and myofibroblasts, causing them to produce increased extracellular matrix. This can result in fibrosis (asbestosis). The ability of the lung to clear the fibers becomes overwhelmed. The shorter asbestos fibers like chrysotile are then transported to the pleural surfaces by macrophages through the lymphatics, where they induce acute pleuritis, pleural effusion and fibrosis. It has been postulated that fibers may also reach the pleural space via embolisation to the costal blood stream or by direct migration through the visceral pleura.

The mechanisms underlying why asbestos causes such a dense pleural fibrosis in DPT are gradually becoming understood. Injury caused by asbestos fibers induces subpleural fibroblasts and mesothelial cells to produce scar tissue and collagen deposition, resulting in subpleural thickening. It is still unclear why asbestos fibers which reach the pleura induce differing pathologies in individual patients, but is likely to be due to several mechanical, biochemical or genetic events. The response of the mesothelial cell to injury and the ability of it and the basement membrane to maintain their integrity is pivotal as to whether or not fibrosis occurs, and cytokines, growth factors and reactive oxygen species (ROS) are likely to play a role. Recent evidence from studies into other causes of pleural fibrosis suggests that upregulation of genes for pro-fibrotic mediators such as transforming growth factor beta (TGF-β) are important in asbestos-induced fibrogenesis. TGF-β and other cytokines such as tumour necrosis factor alpha (TNF-α) then cause disordered fibrin turnover, with increased fibrin formation and decreased and fibrin dissolution, resulting in the formation of a fibrinous intrapleural matrix. TGF-β is likely to be the most potent pro-fibrotic mediator, recruiting fibroblasts, and initiating matrix remodeling. In animal studies, intrapleural injections of TGF-β_2 rapidly induce pleural fibrosis and pleural sclerosis, with concomitant generation of reactive nitrogen and oxygen species (RNS and ROS), possibly acting via iron in asbestos fibers. These are cytotoxic and stimulate fibroblasts to synthesise extracellular matrix.

Another theory proposes that individual differences in the inflammatory response to asbestos determine whether pleural plaques or DPT develop. This is supported by several animal studies. One such study showed that after installation of intra-pleural asbestos, the presence of large numbers of pleural macrophages led to pleural plaque formation while their paucity resulted in DPT. Despite historical theories, it seems unlikely that direct mechanical irritation by asbestos fibers is responsible for the inflammatory infiltrate seen with asbestos. Inflammatory change is not seen at the site of pleural plaques, suggesting that this traditional explanation (irritation by fibers in the visceral pleura on the overlying pleura) may be incorrect. In DPT there is fusion of both pleural layers with loss of the submesothelial elastic tissue, suggesting that significant inflammation has already occurred.

On a clinical basis, there are several mechanisms by which diffuse pleural thickening has been postulated to develop: subsequent to benign asbestos-related pleural effusion, following recurrent bouts of acute pleuritis and/or extension of parenchymal fibrosis (asbestosis) to the visceral pleura.

Asbestos fibers can induce an acute exudative pleural effusion which may be symptomatic or asymptomatic. Approximately one third of these effusions may be eosinophilic. Benign asbestos related pleural effusions may precipitate the development of DPT via a complex interaction of inflammatory cells and cytokines locally within the pleural cavity. This could explain why approximately one third of cases of DPT are unilateral. Asbestos fibers which are coated in iron (asbestos bodies) are rarely found in pleural fluid, but they may occasionally be seen in pleural tissue. However, they are frequently seen in the lung tissue adjacent to DPT. The frequency of pleural effusions before the development of DPT has been reported to range between 31.4% and 37%. In a study of 2,815 insulators > 30 years from the onset of asbestos exposure, 20 had a past history of benign pleural effusion and of these, diffuse pleural thickening with blunting of the costophrenic angle was detected in 16. Pleural effusions may produce symptoms of an acute pleuritis (i.e. chest pain on exertion, fever, malaise and mild dyspnoea) or they may be asymptomatic. They generally resolve spontaneously and do not predict the development of malignant mesothelioma. The pleural thickening and fibrosis may increase with each subsequent episode of pleural effusion.

DPT may also develop due to recurrent episodes of asbestos-induced acute pleuritis in the absence of detectable pleural effusion. Here, a fibrinous matrix is laid down, matures and organizes into dense collagenous material. However, this may merely represent a milder degree of the same pleural inflammation responsible for recurrent effusions. This is difficult to confirm because serial chest radiology is not usually performed without clinical indication. Another theory as to the pathogenesis of diffuse pleural thickening is that it is an extension of the parenchymal fibrotic process to the visceral and parietal surface causing inflammation and fibrosis to the superficial or visceral pleural lymphatics. However, DPT and asbestosis are said to occur together in only 10.3% of cases and such a suggestion therefore does not account for the remaining 90% of cases.

Pleural plaques and DPT frequently coexist. However, they differ in their site of origin, appearance, extent, symptomatology, functional impairment and prognosis. Pleural plaques are discrete areas of relatively acellular and avascular pleural fibrosis that arise from the parietal pleura and the superior surface of the diaphragm. The most widely accepted theory for the development of pleural plaques is that the asbestos fibers travel via retrograde lymphatic drainage from the mediastinal lymph nodes to the retrosternal and intercostals lymphatics and thence to the pleural space. Another less plausible explanation is that fibers protruding into the pleural space cause local inflammation to the parietal pleural surface. Pleural plaques differ from diffuse pleural thickening in a number of ways. Unlike DPT, pleural plaques are sharply demarcated from surrounding structures.

They have a prolonged latency of at least 10 to ≥ 40 years and it is controversial whether they produce symptoms and functional impairment unlike diffuse pleural thickening. Some studies have shown that presence of pleural plaques may result in reductions of FVC but not the FEV1/FVC ratio. They are frequently incidentally detected on chest radiography and they are a helpful marker of previous asbestos exposure. Their presence is associated with a higher risk of malignant mesothelioma and lung cancer compared with workers with a similar exposure history but no plaques, but there is no evidence to suggest that they are in themselves pre-malignant.

Macroscopic Appearance

The lungs in DPT are surrounded by grey fibrous tissue, which blends with surrounding normal pleura. Unlike pleural plaques, DPT is not sharply demarcated and is often associated with fibrous strands ("crows feet") and parenchymal bands that extend into the lung parenchyma and lobular septae. These do not however represent asbestosis. Occasionally, pleural plaques may be superimposed on DPT and may also occur separately within the thoractic cavity. DPT is more extensive than pleural plaques. It may be unilateral or bilateral, and in contradistinction to pleural plaques it arises from the visceral not parietal pleura. DPT often results in dense adherence between parietal and visceral pleural layers. It may encase the lungs and obliterate pleural spaces, lobar fissures and the costophrenic recesses. Macroscopically, pleural plaques have a white or pale yellow shaggy "candle wax" appearance, very different from DPT. Microscopically they consist of acellular interwoven bundles of collagen. Central calcification may occur in mature lesions usually > 30 years old.

Clinical Findings

DPT has been reported as associated with a number of symptoms (Table 2). It is suggested that both DPT and pleural plaques are independently associated with exertional dyspnea. One study looking at a selected series of compensated patients with moderate to severe DPT found that 95.5% complained of breathlessness 65% of moderate breathlessness and 11% of severe breathlessness. A single case report has found diffuse pleural thickening to be associated with hypercapnoeic respiratory failure due to severe restrictive lung disease and death.

Chronic chest pain may also be a feature of DPT, although this is usually mild. Mild to moderate chest pain was noted in over half of the patients with moderate to severe DPT in a study of more severe cases. This was more frequent than in previous studies, probably because of the selected population. The pain is generally described as dull in character. In another study, patients with benign asbestos-related pleural and parenchymal disease appeared to have higher rates of chest pain, particularly anginal chest pain as assessed by a cardiovascular survey questionnaire. More severe pain seemed to be experienced in those with heavier asbestos exposure, older subjects and in retired workers. However, it is not clear if the incidence of ischaemic heart disease is truly higher in asbestos-exposed workers or if asbestos-related lung disease merely causes pain that resembles angina. The presence of radiographic pleural thickening has been shown to be a risk factor for death from ischaemic heart disease in subjects exposed to crocidolite from the Wittenoom population. One Swedish study reported a higher age and gender associated prevalence of calcified pleural plaques in patients with coronary artery disease (35%) compared with those with lung cancer (19%). The relative risk adjusted for age and gender was 2.19 (95% CI 1.44-3.32) among patients referred consecutively for coronary angiography compared with lung cancer patients. For this group, however, calcified pleural plaques showed no association with the severity of coronary artery disease, diabetes, hyperlipidaemia or smoking. It is unclear whether these results are due to confounding factors or whether there is a true etiological association.

Pulmonary Function

DPT may be associated with a "constrictive" deficit in pulmonary function. A reduction in static lung volumes and lung compliance with reduced transfer coefficient (TLCO or DLCO) and a raised or maintained transfer coefficient (KCO) occurs. This restriction may occur independently of the presence of asbestosis. The extent of DPT is strongly correlated with decreasing lung volumes, especially with residual volume, and less strongly with increasing transfer coefficient or KCO. Few longitudinal studies exist, but these have found no correlation between radiographic severity and longitudinal loss of lung function.

It has been suggested that restriction in DPT is due to adhesion of the parietal and diaphragmatic pleura in the zone of apposition between the diaphragm to the chest wall. This limits separation of the diaphragm from the rib cage during inspiration, which reduces the volume contributed by motion of the diaphragm to the chest wall. This limits separation of the diaphragm from the rib cage during inspiration which reduces the volume contributed by motion of the diaphragm and lower rib cage. It is thought that it is the reduction in movement of the lower rib cage that is the major cause of restriction, because the reduction in volume contributed by the diaphragm is partly compensated by flattening of its dome. Five HRCT scoring systems to measure the area and thickness of abnormal pleura have been reviewed by Copley et al. The extent of DPT on HRCT is strongly correlated with decreasing FVC and TLC and less strongly with increasing transfer coefficient KCO. However, in some patients the decreased DLCO suggests that pulmonary fibrosis may have been contributing to restriction.

The natural history of DPT is probably benign but this is difficult to assess as relevant studies either include a large proportion of cases of pleural plaques or concentrate on selected populations. In the longitudinal study of Yates et al, the pattern of lung function change was of an initial large loss of lung function followed by relative stability. There was further loss of lung function in a minority of cases.

Imaging

DPT is most commonly assessed by the plain chest radiograph, although CT scanning is increasingly superseding this tool. The chest radiographic appearance is of a continuous, irregular pleural shadowing which may extend up both chest walls and blunt one or more costophrenic angles. This density should extend over at least one quarter of the chest wall. The revised 2003 International Labour Office (ILO) Classification of Radiographs of Pneumoconioses provides a system for classifying pleural plaques and diffuse pleural thickening and for differentiating between these disorders. DPT is recorded only in the presence of, and in continuity with, an obliterated costophrenic angle. The earlier 1980 ILO version did not require obliteration of the costophrenic angle, which is now required. However, the chest radiograph even when accompanied by an oblique film is an insensitive index of disease severity.

It is well established that high resolution CT scanning is more sensitive and specific than chest radiography for the diagnosis of DPT, pleural plaques and asbestosis. It can detect early pleural thickening (ie 1-2 mm in thickness), and several classification systems have been devised. The most commonly used in Australia is that of Lynch et al. Here, diffuse pleural thickening is defined on HRCT as a contiguous sheet of pleural thickening more than 5 cm wide on transverse CT images, more than 8 cm in extent in craniocaudal images and more than 3 mm thick (Figure 2). Pleural calcification rarely occurs in DPT, unlike pleural plaques (Figure 3). HRCT should ideally be performed with prone views and at full inspiration to avoid dependant atelectasis in the posterior lung fields which may be confused with parenchymal fibrosis. A rare variant of apical diffuse pleural thickening in association with apical fibrosis has also been reported. The correlation of CT abnormality with symptoms has not been well investigated. Five methods of quantifying pleural thickening were compared by Copley et al in 50 patients with benign asbestos-related disorders. Comparable functional-morphological correlations were achieved by the different systems but the subjective simple CT system was easy to apply and useful for accurate assessment of the lung parenchyma. HRCT is also a sensitive method for assessing plaques, and is more specific than chest radiography for distinguishing DPT from other structures such as extrapleural fat.

Magnetic resonance imaging (MRI) and fluorodeoxyglucose (FDG)-positron emission tomography (PET) imaging scan may be useful in distinguishing malignant from benign pleural disease. Two studies of patients with pleural disease suggested that when signal intensity and morphologic features are assessed, MRI is superior to CT in differentiating benign and malignant pleural disease with a sensitivity ranging from 98-100% and a specificity of 92-93%. High signal intensity in relation to intercostals muscles on T2-weighted and/or contrast enhanced T1-weighted images was significantly suggestive of malignant disease. One study also suggested that MRI has a higher interobserver agreement compared with CT in detecting pleural thickening, pleural effusion and extrapleural fat. The agreement was however similar for the detection of pleural plaques and CT was superior for the detection of pleural calcification which is a marker of benign disease. PET can help distinguish between malignant pleural mesothelioma which has higher glucose avidity and benign DPT in patients where the two diagnoses coexist. A prospective American study of 28 patients referred for the evaluation of suspected mesothelioma demonstrated that a standardized uptake value for FDG of 2.0 used to differentiate between malignant and benign disease had a sensitivity of 91% and a specificity of 100%. However, some epithelial mesotheliomas had a glucose avidity that is very close to this threshold of 2.0. Another study of 63 patients with mesothelioma suggested that while PET did not identify the local extent of tumour or mediastinal nodal metastases it does detect extrathoracic metastases reducing the need for inappropriate thoracotomy. Moreover, one recent study has suggested that PET can predict survival in mesothelioma. PET needs to be used in conjunction with an anatomic imaging study like CT when staging mesothelioma. The cost and availability of MRI and PET are factors that may limit their use in some centres when compared with CT.

Associated Features

Several other features are frequently associated with DPT on HRCT in addition to pleural plaques. These include parenchymal bands and rounded atelactasis. Parenchymal bands are linear 2-5 cm long opacities extending through the lung to make contract with the pleura. These bands are areas of fibrosis along bronchovascular sheaths or interlobular septa and are generally related to moderate pleural fibrosis. Small pleura-parenchymal bands known as "crow's feet" are associated with focal rather than diffuse pleural thickening. The radiological appearances are different from asbestosis. Gevenois and colleagues distinguish between these features and those secondary to asbestosis, where septal and interlobular lines and honeycombing may be seen.

Rounded atelectasis may also occur in association with DPT. It is known as shrinking or contracted pleuritis, a pleuroma or "Blesovsky's" syndrome" (Figure 4). Rounded atelectasis is believed to be the result of infolding of the thickened fibrotic visceral pleura with collapse and chronic inflammation of the underlying lung parenchyma. The "comet sign," or a rounded mass connected by a fibrous band to an area of thickened pleura, is the pathognomonic HRCT feature. It can occur in response to any cause of acute pleuritis, but asbestos appears to be the commonest recognised cause. Symptoms generally only occur if the area of atelectasis is large enough to compromise lung function. The differential diagnosis of rounded atelectasis includes a peripheral lung cancer or a benign inflammatory pseudotumour. The latter, however, generally evolves more quickly.

Differential Diagnosis

There are several important differential diagnoses for asbestos-related DPT (Table 1). Any cause of acute pleuritis can cause pleural thickening which is clinically indistinguishable from that due to asbestos. Examples of these include tuberculosis, previous trauma, empyema, connective tissue diseases, drugs and surgery including coronary artery bypass surgery. These are much more likely to be unilateral, whereas although DPT can occur unilaterally, this is less common. Calcification may be heavy in post-tuberculous pleural thickening or that occurring after haemothorax. With past tuberculosis, upper lobe fibrosis may also occur along with bronchiectasis and evidence of old surgical procedures eg thoracoplasty. Upper lobe pleural thickening, especially when bilateral, is more likely to be due to old tuberculosis in older patients; however, upper lobe disease has also been described after asbestos exposure and there are no radiological features which are 100% specific. Clinical correlation is required, and a good occupational history is invaluable.

Because of the wide differential diagnosis for DPT, it is less specific for asbestos exposure than pleural plaques. The most important diseases which need to be distinguished from DPT and asbestos related chronic pleuritis and effusion are malignant mesothelioma, and of course tuberculosis in areas of high prevalence. Empyema should also be included, although features of sepsis are usually suggestive and the history more acute. Mesothelioma is unlikely when the chest pain is mild and persists for years with minimal or no clinical or radiographic progression. CT and MRI features which are more frequent in malignant disease include circumferential pleural thickening (>1 cm) with nodularity and irregularity of pleural contour as well as infiltration of the chest wall or diaphragm and mediastinal, pleural and/or nodal involvement. Involvement of the mediastinal pleura is thought to be more suggestive of mesothelioma than DPT. As discussed above, MRI and PET may be useful to distinguish malignant and benign pleural disease. Tuberculosis is more likely to be associated with fever, lymphocytosis and a history of hemoptysis. Differentiating between the different

causes of pleural disease can be very difficult and should include all possible information including that from pleural aspiration and/or cytology and biopsy where appropriate.

Management

Few data exist relating to optimal management of patients with DPT, probably because the condition is uncommon on its own. The majority of patients have not been shown to require ongoing respiratory specialist management and are treated symptomatically in primary care. The optimal management of more severe cases has not been well studied. Pulmonary rehabilitation has not been investigated in this area, and conventional respiratory therapies are likely to be ineffective other than analgesia where needed. There are reports of non-invasive ventilation being used to support patients with respiratory failure due to diffuse pleural thickening, but this is rarely required unless other pathologies exist. It has also been suggested in the past that patients with DPT might benefit from decortification because they have increased elastic recoil and a normal diffusing capacity when corrected for alveolar volume, but surgery has been rarely applied. However, patients with asbestos-related disease often have other co-morbidities which preclude surgery, and surgical treatment is unlikely to be appropriate if clinically significant asbestosis is present. Significant pleural disease is associated with a higher rate of post-operative complications and therefore most surgeons are reluctant to embark on such a procedure. However, surgery may be highly effective for patients with pleural disease due to other causes. This has not, however, been formally studied for asbestos-related DPT.

Conclusions

DPT is now a well recognised consequence of asbestos exposure and benign asbestos related pleural effusions, although it is probably under-recognised and reported. It may cause dyspnoea, chest pain, respiratory failure and a "constrictive" pattern on pulmonary function testing, but is usually only mildly symptomatic. It has distinctive features macroscopically, histologically and on HRCT. DPT may coexist with pleural plaques and has a distinctly different pathology with a different natural history, radiology and prognosis. Treatment is largely limited to supportive and symptomatic care. The incidence of this disease is currently rising and total numbers are likely to exceed those of malignant mesothelioma in the future. Thus, more clinicians are likely to be involved in its management and further research is required to better elucidate its natural history, radiology and treatment.

Extrathoracic Airway Hyperresponsiveness as a Mechanism of Post Infectious Cough: Case Report

Nicole M. Ryan, Peter G. Gibson,

Abstract

Post-infectious cough is a common diagnosis in people with chronic cough. However, the specific infectious aetiology and cough mechanisms are seldom identified. We report a case of chronic cough after Mycoplasma pneumoniae lower respiratory tract infection with extrathoracic airway hyperresponsiveness as the cough mechanism. Extrathoracic airway hyperresponsiveness may be a common mechanism in postinfectious cough which may be useful both diagnostically and therapeutically since chronic cough with extrathoracic airway hyperresponsiveness responds to speech pathology treatment.

Background: Post-infectious cough is a common diagnosis, especially in primary care settings, although a specific infectious aetiology is rarely confirmed. Aside from pertussis, the role of other infectious agents in chronic cough is poorly understood. In specialist clinics chronic cough occurs in association with asthma, rhinitis, gastro-oesophageal reflux (GERD), and ACE inhibitor use.[1] However, even in these settings, a respiratory infection is often reported at the onset of chronic cough. Extrathoracic airway hyperresponsiveness (EAHR) represents variable extrathoracic airflow obstruction following inhalation provocation testing.[2-6] It manifests as a fall in inspiratory airflow during challenge with histamine, exercise, or hypertonic saline. EAHR is a feature of cough due to ACE inhibitor use,[2] rhinosinusitis[3,4] and GERD,[5] and possibly asthma.[6] The mechanism of post-infectious cough is not known, however, upper airway sensory hyperresponsiveness might be one important mechanism in driving cough in some entities of CC[7] and this current case suggests that EAHR may be a useful objective marker and relevant mechanism in post infectious cough.

Case Presentation: A 60 year old non-smoking male presented to the Emergency Department with a nonproductive cough and cold symptoms. For the past week he had been confined to bed and reported severe bodily pain, a troublesome cough and shortness of breath when showering and toileting. His temperature was 38.6°C. Physical examination of the chest was unremarkable and chest radiograph showed increased bronchial markings centrally. Arterial Blood Gas results breathing room air were: pH 7.46, pCO_2 4.6 kPa, pO_2 6.9 kPa. He was commenced on oral roxithromycin 150mg bd, inhaled salbutamol 100ug 2 puffs qid, and analgesia, and continued pre-existing carbamazepine 300mg bd for controlled epilepsy (a recent onset condition) and thyroxine 50/100mcg on alternative days for hypothyroidism which had developed five years prior. He was subsequently changed to oral azithromycin 500mg, improved and was discharged on day 5. Acute and convalescent serology confirmed recent infection with Mycoplasma pneumoniae (antibody titre 1:1280 (ref range <1:40).

At a seven week follow-up visit he described persistent cough, inspiratory dyspnoea, voice changes (characteristics common to paradoxical vocal cord movement (PVCM) and EAHR disorders) and fatigue. Hypertonic saline provocation test was requested and conducted 2 months later.

Spirometry was FEV_1 84% predicted, FVC 86% predicted, FEV1/FVC 78%; and FIF50% 5.22 L/sec. Hypertonic (4.5%) saline provocation challenge identified EAHR with attenuation of the inspiratory flow curve. The FIF50% decreased by 39% to 3.20L/s at a cumulative saline dose of 10.59mL (figure 1, solid line). The fall in FEV_1 (12%) was within normal limits. A trial of fluticasone/salmeterol and nedocromil sodium was commenced.

The patient's cough and dyspnoea had greatly improved by three months. One year later the cough had resolved completely and an inspiratory/expiratory flow volume curve was normal. There was no EAHR or bronchial hyperresponsiveness after repeat hypertonic saline challenge (figure 1, dotted line), fall in FEV_1 remained within normal limits (8%) and laryngoscopy showed no posterior chinking during inspiration and no paradoxical vocal cord movement (PVCM).

Discussion

This case report describes Mycoplasma pneumoniae respiratory tract infection as a cause of persistent cough, occurring in

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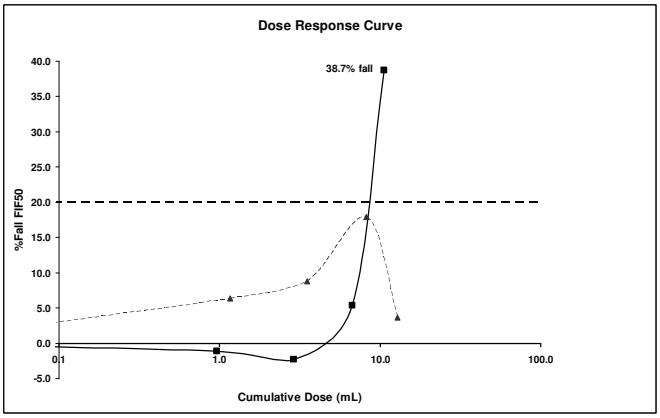

Hypertonic saline provocation dose response curve for FIF50% prior to treatment (demonstrating extrathoracic airway hyperresponsiveness) and after treatment.
Solid line=pre treatment
Dotted line=post treatment

association with EAHR. EAHR was demonstrated by a 39% fall in inspiratory flow during hypertonic saline challenge. The cough resolved as the EAHR resolved. Extrathoracic airway sensory hyperresponsiveness might be an important mechanism in driving cough in some entities of chronic cough (CC).[7] This case report extends these data to show that transient EAHR can occur with post infectious cough.

It has previously been proposed[8] that some patients with CC sustain vagal injury from respiratory infection and that airway hyperresponsiveness may persist beyond resolution of the acute upper respiratory tract infection (URTI). This hyperresponsiveness could decrease the cough threshold to irritating stimuli resulting in higher susceptibility to chemical or mechanical stimulation of the cough reflex. Transient post-infectious bronchial (intrathoracic) hyperresponsiveness is well recognised.[9] This case report identifies transient EAHR as an additional relevant mechanism associated with post infectious cough.

These observations have implications for the treatment of post infectious cough. There may be a role for inhibition of neuropeptide release, by cromoglycate, nedocromil, or specific neuropeptide antagonists in post infectious cough. Fontana et al[10] evaluated the effects of nedocromil sodium administration on cough threshold in a placebo controlled study of healthy subjects. They found a significant increase in cough threshold values after nedocromil and an unaffected result after placebo suggesting that nedocromil sodium administration may be useful for treating cough, especially when the use of centrally acting antitussive drugs should be avoided. These agents are also of benefit in ACE Inhibitor cough, which is associated with EAHR. Also, given the similarity between PVCM and EAHR,[11] adapting techniques used by speech language therapists that were developed for PVCM may be of benefit for post infectious cough with EAHR. In PVCM the vocal cords adduct episodically and involuntarily during inspiration. This phenomenon leads to reduced inspiratory airflow associated with signs of stridor and a perception of dyspnoea characterised by the inability to inspire sufficient air.[12] EAHR is thought to be the primary underlying pathophysiology of PVCM.[13] Speech language therapy has been shown to be a successful treatment in chronic persistent cough. Vertigan et al[14] conducted a randomised placebo-controlled trial in 87 patients with CC persisting despite medical treatment. Half of these patients had EAHR and symptoms of PVCM. Patients were randomly assigned to receive either a specifically designed speech pathology intervention or placebo intervention. Participants in the treatment group were found to have a significant reduction in cough with 88% having a successful outcome compared to 14% in the placebo group. In a comprehensive literature review, Gallivan et al[15] presented cases of episodic paroxysmal laryngospasm with definitive diagnosis by videolaryngoscopy of paradoxical vocal cord adduction during inspiration and extrathoracic airway obstruction by attenuation of the inspiratory portion of the flow volume curve. Prior to this, Christopher et al[16] identified 5 patients with a functional disorder of the vocal cords that mimicked attacks of bronchial asthma, that is paroxysms of wheezing and dyspnoea refractory to standard asthma therapy. During episodes of wheezing, the maximal expiratory and inspiratory flow-volume relationship was consistent with variable extrathoracic obstruction. Laryngoscopy confirmed adduction of the true vocal and false vocal cords. While during asymptomatic periods the maximal flow-volume relationship and laryngoscopic examination were normal. Patients were not aware of the vocal-cord dysfunction, which uniformly and dramatically responded to speech language therapy where they were taught to focus attention away from the larynx and the inspiratory phase of breathing during episodes of wheeze and dyspnoea.[16] EAHR may be a useful objective assessment measure to characterise laryngeal dysfunction in chronic cough.

EAHR can be assessed during inhalational provocation challenge. We prefer the use of hypertonic saline to assess EAHR as it is known to provoke neuropeptide release from nonadrenergic-noncholinergic nerves, which are prevalent in the larynx. Inhaled histamine to assess EAHR has been successfully used before[6] where the histamine concentration causing a 25% fall in mid-inspiratory flow was used as the respective threshold of EAHR. It was found that patients presenting with cough as the sole symptom had significantly greater probability of having EAHR. Histamine can however cause oedema of the vocal cords furthering our preference for hypertonic saline stimulus. Methacholine challenge appears to be a less sensitive stimulus for EAHR. This is likely because of its specific action on cholinergic receptors in airway smooth muscle, and unproven action on laryngeal responses. Exercise can also be used to assess EAHR, although quantification of the stimulus may be more difficult.

Our male patient had pre existing hypothyroidism which has been associated with idiopathic chronic cough and airway inflammation.[17] This is unlikely to be the primary cause of cough in the patient as the cough developed after a well-documented Mycoplasma pneumoniae lower respiratory tract infection that occurred some 5 years after the onset of hypothyroidism. Further there is a female predominance in cases of idiopathic CC and its association with mild chronic lymphocytic airway inflammation.[18] It is however possible that a pre-existing auto-immune lymphocytic bronchitis had a permissive effect on the occurrence of post-Mycoplasma chronic cough. Prospective studies would be helpful in evaluating this possibility.

Conclusion

Post infectious cough can occur with EAHR. There are opportunities to further investigate the frequency and treatment of EAHR as a mechanism of post-infectious cough with speech pathology.

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progressively narrow and redden to alert the clinician that a clinical intervention is warranted. As the lung is adequately recruited and ventilated, the dynamic lung will fully expand and a green border will be achieved if normal respiratory mechanics are achieved or restored. Contact hamilton.com.

GO TO GUY

RF Technologies, a leading provider of radio frequency identification monitoring systems and healthcare monitoring solutions, announced it has named Warner (Chuck) Pyne III to the position of Vice President of Sales and Marketing for its Hospital Solutions Group. Pyne brings 28 years of sales management experience to RF Technologies. Most recently, he was General Manager and Vice President of Dynamic Imaging Solutions Sales. Previously, he was with Philips Medical Systems North America for approximately six years and held a number of sales positions in various business units, his last position being Vice President of Sales, Cardiology IT. Earlier, he was with Fuji Medical Systems, where he held positions in sales, operations and product management. Pyne received his Bachelor of Arts in Business Administration from Muhlenberg College in Allentown, PA. RF Technologies is a leading provider of comprehensive, integrated RFID Safety and Security systems, Wi-Fi RTLS systems, and healthcare enterprise solutions. Contact rft.com.

GIVING THE BUSINESS

Business industry website MarketWatch reported: Cardinal Health, Inc said it is spinning off its clinical and medical products operations into one separate, publicly-traded company. The Dublin, OH corporation said the new company will be led by current vice chairman, David L. Schlotterbeck. Chairman and CEO R. Kerry Clark will continue to lead Cardinal Health through the spin-off and then will retire from the company. Clark will be succeeded by George S. Barrett, currently CEO of Healthcare Supply Chain Services. The proposed tax-free spin-off will be accomplished through a pro rata distribution to Cardinal Health shareholders. Covidien Ltd announced that it plans to implement a restructuring plan in fiscal 2009, resulting in pretax charges of about $200 million, starting in the first quarter. The health-care products maker said it expects to save about $50 million to $75 million on an annualized basis once the restructuring program is finished.

AT THEIR FINGERTIP

With the introduction of the Onyx II, Model 9560, the world's first interoperable fingertip oximeter with Bluetooth wireless technology, Nonin Medical has introduced a solution aimed to simplify healthcare and reduce skyrocketing costs through the promotion of remote monitoring. Designed for easy integration into medical ecosystems, numerous leading technology manufacturers are developing working interfaces for the revolutionary Onyx II 9560. Soon, patients and clinicians will easily be able to monitor vital signs in environments never before possible. This significant advance will also facilitate the development of a more simple, secure and cost-effective process of managing patient information by utilizing cell phones, PDAs and PCs, etc. Since its release in 1995, Onyx has become the most trusted name in fingertip pulse oximetry due to its ease-of-use, extreme durability and precision accuracy. The Onyx II, Model 9560 provides superior accuracy and versatility with its unique SmartPoint technology and Store and Forward capabilities. Contact nonin.com.

Factors Affecting Exhaled Nitric Oxide Measurements: The Effect of Sex

D. Robin Taylor, Piush Mandhane, Justina M. Greene, Robert J. Hancox, Sue Filsell, Christene R. McLachlan, Avis J. Williamson, Jan O. Cowan, Andrew D. Smith, Malcolm R. Sears

Abstract

Background: Exhaled nitric oxide (F_ENO) measurements are used as a surrogate marker for eosinophilic airway inflammation. However, many constitutional and environmental factors affect F_ENO, making it difficult to devise reference values. Our aim was to evaluate the relative importance of factors affecting F_ENO in a well characterised adult population.

Methods: Data were obtained from 895 members of the Dunedin Multidisciplinary Health and Development Study at age 32. The effects of sex, height, weight, lung function indices, smoking, atopy, asthma and rhinitis on F_ENO were explored by unadjusted and adjusted linear regression analyses.

Results: The effect of sex on F_ENO was both statistically and clinically significant, with F_ENO levels approximately 25% less in females. Overall, current smoking reduced F_ENO up to 50%, but this effect occurred predominantly in those who smoked on the day of the F_ENO measurement. Atopy increased F_ENO by 60%. The sex-related differences in F_ENO remained significant ($p<0.001$) after controlling for all other significant factors affecting F_ENO.

Conclusion: Even after adjustment, F_ENO values are significantly different in males and females. The derivation of reference values and the interpretation of F_ENO in the clinical setting should be stratified by sex. Other common factors such as current smoking and atopy also require to be taken into account.

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The authors wish to acknowledge the loyalty of each of the Study members of the Dunedin Multidisciplinary Health and Development Study, and the support of Michelle McCann and Professor Richie Poulton. Professor Temi Moffitt kindly permitted the use of data pertaining to cannabis smoking Reprinted from Respiratory Research, BioMed Central, © 2007 Taylor et al, licensee BioMed Central Ltd.

Background

Measurement of exhaled nitric oxide is increasingly recognised as an important addition to pulmonary function testing in clinical practice.[1] F_ENO may be used as a surrogate marker for airway eosinophilia,[2] and as an alternative to other more invasive or time-consuming assessments of airway pathology such as induced sputum,[2,3] bronchial lavage fluid,[4] or mucosal biopsy.[5-7] Against this background, F_ENO measurements are increasingly being used to clarify the aetiology of non-specific respiratory symptoms as well as monitor levels of inflammation in conditions characterised by airway eosinophilia.[8]

There are a number of demographic and biological factors which cause variation in F_ENO levels. The commonest are cigarette smoking[9,10] and atopy[11-13] with or without allergic rhinitis.[13,14] Others include age,[15,16] and IgE levels.[17] However, conflicting results concerning the importance of these factors has precluded a clear definition of so-called "normal" values. Buchvald et al. have reported reference values in a large population of children, but important biological confounders were evaluated only by questionnaire.[15] The same issues were addressed more recently in adults by Olin et al,[18] and Travers et al,[19] and Travers et al provided reference ranges which sought to take account of commonly encountered variables which affect F_ENO. However, there are some significant inconsistencies between these reports, not least in respect of the effects of sex on FENO. Clearly further data are needed so that routine FENO measurements can be interpreted appropriately. In the present study, comprising a well characterised cohort of nearly 1000 32-year old individuals born in Dunedin, New Zealand, we obtained detailed clinical and laboratory information regarding factors affecting F_ENO, and their potential relevance to reference ranges for F_ENO was evaluated.

Methods

The Dunedin Multidisciplinary Health and Development Study is a cohort study of 1,037 children (52% male) born between April 1972 and March 1973.[20,21] Follow-up assessments have been conducted at ages 3, 5, 7, 9, 11, 13, 15, 18, 21, 26, and at 32

Table 1: Mean values (with 95% confidence intervals) for FENO stratified by sex, smoking, atopy, rhinitis current wheeze and asthma.
*not all Study members underwent skin testing

All	All subjects, n=895 13.4 (12.9, 14.1)											
Gender	Male, n=471 15.3 (14.3,16.3)						Female, n=424 11.6 (11.0, 12.4)					
Smoking	Current smoker (smoked on the day of testing)		Current smoker (not smoked on the day of testing)		Ex-smoker or non-smoker		Current smoker (smoked on the day of testing)		Current smoker (not smoked on the day of testing)		Ex-smoker or non-smoker	
	n=133 8.8 (7.9, 9.7)		n=102 16.6 (14.7, 18.9)		n=236 20.2 (18.6, 21.9)		n=102 7.4 (6.7, 8.2)		n=58 12.3 (10.2, 14.7)		n=264 13.7 (12.8, 14.7)	
Atopy	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
	n=68 9.9 (8.6,11.5)	n=62 7.6 (6.7, 8.7)	n=61 19.8 (16.6, 23.6)	n=41 12.9 (11.1, 14.9)	n=141 24.8 (22.2, 27.7)	n=92 14.9 (13.6, 16.3	n=32 9.5 (7.8, 11.5)	n=69 6.7 (5.9, 7.5)	n=35 14.0 (10.6, 18.5)	n=23 10.0 (8.2, 12.2)	n=149 15.9 (14.4, 17.6)	n=114 11.2 (10.3, 12.2)
Rhinitis	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
	n=50 9.2 (8.0, 10.7)	n=83 8.5 (7.4, 9.7)	n=30 21.0 (16.0, 27.5)	n=72 15.1 (13.2, 17.4)	n=97 24.0 (21.2, 27.2)	n=139 17.9 (16.1, 19.9)	n=33 9.0 (7.5,10.9)	n=69 6.8 (6.0, 7.7)	n=23 13.4 (10.1, 17.8)	n=35 11.6 (9.0, 14.9)	n=116 16.1 (14.3, 18.0)	n=148 12.1 (11.1, 13.1)
Current wheeze	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
All	n=49 8.4 (6.9, 10.2)	n=84 9.0 (8.0, 10.0)	n=35 17.7 (13.4, 23.3)	n=67 16.1 (14.1, 18.5)	n=53 28.4 (23.0, 34.9)	n=183 18.3 (16.9, 19.9)	n=41 7.6 (6.4, 9.1)	n=61 7.3 (6.4, 8.4)	n=18 15.2 (9.4, 24.3)	n=40 11.1 (9.3, 13.3)	n=57 16.8 (14.2, 19.8)	n=207 12.9 (12.0, 13.9)
Taking ICS	n=8 8.0 (4.1, 15.6)	Nil	n=5 24.0 (12.7, 45.5)	n=1 72.9	n=17 27.5 (19.6, 38.7)	n=2 28.5 (NA)	n=3 8.8 (2.0, 40.0)	n=4 9.4 (1.9, 45.2)	n=3 32.4 (9.3, 112.0)	Nil	n=13 17.3 (13.1, 22.8)	n=3 17.8 (3.3, 96.9)
Not taking ICS	n=41 8.5 (6.9, 10.4)	n=84 9.0 (8.0, 10.0)	n=30 12.3 (16.8, 22.9)	n=66 15.8 (13.8, 17.9)	n=36 28.8 (21.9, 37.8)	n=181 18.2 (16.8, 19.8)	n=38 7.5 (6.2, 9.1)	n=57 7.2 (6.4, 8.2)	n=15 13.0 (7.7, 22.1)	n=40 11.1 (9.3, 13.1)	n=44 16.7 (13.6, 20.5)	n=204 12.9 (11.9, 13.9)
Current asthma	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
All	n=21 9.8 (6.9, 14.0)	n=112 8.6 (7.7, 9.5)	n=27 21.7 (16.5, 28.5)	n=75 15.1 (13.2, 17.4)	n=39 29.7 (23.7, 37.2)	n=197 18.7 (17.2, 20.4)	n=18 9.5 (6.5, 13.9)	n=84 7.0 (6.4,7.8)	n=10 28.0 (14.7, 53.3)	n=48 10.3 (8.9, 12.0)	n=41 15.7 (12.7, 19.5)	n=223 13.3 (12.4, 14.3)
Taking ICS	n=8 8.0 (4.1, 15.6)	Nil	n=6 28.9 (14.7, 57.0)	Nil	n=18 26.5 (19.1, 36.8)	n=1 58.3	n=5 11.0 (3.8, 32.2)	n=2 5.7 (0.5, 72.1)	n=3 32.4 (9.3, 112.0)	Nil	n=14 18.3 (13.8, 24.3)	n=2 12.0 (3.1, 47.4)
Not taking ICS	n=13 11.2 (7.1, 17.8)	n=112 8.6 (7.7, 9.5)	n=21 20.0 (14.6, 27.4)	n=75 15.1 (13.2, 17.4)	n=21 32.7 (23.5, 45.6)	n=196 18.6 (17.1, 20.2)	n=13 9.0 (5.8, 14.2)	n=82 7.1 (6.4, 7.8)	n=7 26.4 (9.9, 69.9)	n=48 10.3 (8.9, 12.0)	n=27 14.6 (10.8, 19.5)	n=221 13.3 (12.4, 14.4)

years, at which time 972 (96%) of 1,015 living Study members participated.

At age 32, study members were questioned about current and previous asthma, as well as symptoms of wheezing, cough, episodic shortness of breath, hay fever and rhinitis. Current asthma was defined as reported diagnosed asthma with symptoms in the last 12 months. Current wheezing was recorded as any wheeze in the last 12 months but excluding subjects with only one or two episodes each lasting less than 1 hour. Asthma treatment was any inhaled bronchodilator, corticosteroid or cromoglycate medication. Current smoking was defined as smoking tobacco cigarettes daily for at least one month during the previous 12 months, or smoking cannabis 6 or more times during the previous 12 months. Current smokers were further subdivided into two groups: those who did and did not smoke on the study day. Ex-smokers were defined as having discontinued for at least 12 months.

Height and weight in light clothing without shoes were measured to calculate body mass index (BMI) in kg/m^2. F_ENO was then measured on-line using a Logan LR 2000 series chemiluminescence analyzer (Logan Research Ltd., Rochester, England) in accordance with ATS/ERS guidelines at a flow rate of 50mL/sec.[22] Exhaled nitric oxide in parts per billion (ppb) was recorded continuously throughout expiration. Individual results were read at the first nitric oxide plateau and the mean of two acceptable tests was recorded. A third was obtained only where one or both of the first two were considered to be technically unsatisfactory. The NO recording was determined for each test by two observers on a separate occasion. The first 44 Study members were tested using a flow rate of 250mL/second and results were adjusted to 50mL/second using a previously validated formula.[23]

F_ENO measurements were obtained immediately prior to carrying out spirometry. Skin prick testing included house dust mite (D pteronyssinus), grass, cat, dog, horse, cockroach, wool, Aspergillus fumigatus, alternaria, penicillium, and cladosporium. A weal diameter 3 mm or greater than the saline control was considered positive. Atopy was defined as a positive response to one or more allergens. A blood sample was obtained for eosinophil count and total serum immunoglobulin E (IgE).

Statistical analysis: Study members who were pregnant at the time of assessment (n = 31) were excluded from all analyses. F_ENO measurements were not normally distributed, and were log transformed prior to analysis. Both univariate and multivariate linear regression analyses were performed to identify those factors which significantly affected F_ENO levels and to derive regression equations, with stratification for those factors which were shown to significantly affect exhaled nitric oxide levels.

Table 2: Mean values (with 95% confidence intervals) for FENO, stratified by smoking status and sex.

F_ENO (ppb) Mean 95% C.I.	All subjects	Males	Females
All Study members	n=895 13.4 (12.8, 14.1)	n=471 15.3 (14.3, 16.3)	n=424 11.6 (11.0, 12.4)
All current smokers (within last 12 months)	n=395 10.4 (9.7, 11.1)	n=235 11.6 (10.6, 12.6)	n=160 8.9 (8.1, 9.8)
Current smokers who smoked on the day of F_ENO testing	n=235 8.2 (7.6, 8.8)	n=133 8.8 (7.9, 9.7)	n=102 7.4 (6.7, 8.2)
Current smokers who did not smoke on day of F_ENO testing	n=160 14.9 (13.4, 16.6)	n=102 16.6 (14.7, 18.9)	n=58 12.3 (10.2, 14.7)
Ex-smokers (greater than 12 months)	n=107 16.0 (14.3, 17.8)	n=36 21.1 (17.6, 25.3)	n=71 13.8 (12.2, 15.7)
Never smokers	n=393 16.6 (15.6, 17.7)	n=200 20.0 (18.3, 22.0)	n=193 13.6 (12.5, 14.8)

The selection of appropriate linear regression models was based on maximum R-square and an examination of the residuals, to ensure an adequate model fit. Significant interaction terms ($p<0.05$) were retained in the model. Results are presented as anti-log values with 95% confidence intervals following back transformation.

Results

Eight hundred and ninety-five Study members completed the respiratory procedures in the Study. Of these, 471 (52.6%) were male, 486 (54.8%) were atopic, 349 (39.0%) had rhinitis/hay fever, 253 (28.3%) had current wheeze, 156 (17.4%) had current asthma, and 54 (6.6%) were using inhaled corticosteroid treatment. Three hundred and ninety five were current smokers (44.1%), of whom 235 (59.5%) smoked on the study assessment day prior to testing, and 107 were ex-smokers (12.0%). Two hundred and fifteen were cannabis smokers (24%), of whom 78 (8.7%) smoked cannabis alone.

The F_ENO values obtained from the Study population are shown in Table 1. Data relating to smoking status are shown in Table 2. F_ENO was on average 25% higher in males than females (males: 15.3 ppb [95% C.I.:14.3 - 16.3] versus females: 11.6 ppb [95% C.I.: 11.0-12.4]; $p < 0.0001$; Table 1). Unadjusted analyses revealed that, for all Study members, there were also significant differences in F_ENO in relation to height, FEV_1, FEV_1 % predicted and FVC (Table 3). However, none of these factors remained significant after stratifying by sex. In contrast, current smoking (on the day of testing), atopy, log IgE, history of rhinitis, and current asthma and the use of inhaled corticosteroids remained significant in both males and females.

In the adjusted regression analyses, significant predictors of F_ENO were sex, body mass index (BMI), current smoking (on the day of testing), atopy, current asthma, and the interaction between sex and smoking. Current wheeze was not a significant factor. This was perhaps because of the significant confounding relationship between current smoking (resulting in reduced F_ENO) and wheeze (p=0003).

After controlling for all of the significant factors affecting F_ENO, the sex-related differences in F_ENO remained significant ($p<0.001$). The factors which significantly affected F_ENO were different for males and females. For males, current smoking (all), current asthma, and atopy (any positive SPT ≥ 3mm over the negative control) were significant independent predictors of FENO. For females, while current smoking (all), current asthma, and atopy (any positive SPT ≥ 3mm over the negative control) were significant independent predictors of F_ENO, those females who were current smokers and also had asthma had an additional increase in their F_ENO (increased by 131%; $p = 0.001$; Table 4).

Based on these results, the equations for predicting F_ENO in our study cohort were:

For males: $\log F_ENO = 1.1932 - 0.3496$ current smoking (smoked day of testing) – 0.0940 current smoking (not smoked day of

Table 3: Factors affecting FENO by linear regression analysis, without controlling for any other factors. Magnitude of effect = change compared to reference group (females, non-smokers, non-atopics, nonrhinitics, non-wheezers, or non-asthmatics)

	All		Males		Females	
Factor	**Magnitude of effect***	**Significance**	**Magnitude of effect***	**Significance**	**Magnitude of effect***	**Significance**
Female Gender	0.7605	<0.0001	---		---	
BMI	1.0015	0.7571	1.0045	0.5600	0.9966	0.5503
Height	1.0013	<0.0001	1.0003	0.5859	1.0007	0.0969
FEV1	1.1315	<0.0001	0.9956	0.9328	1.0229	0.7230
FEV1 % predicted	0.9957	0.0166	0.9988	0.6422	0.9981	0.4432
FVC	1.1058	<0.0001	0.9832	0.6963	1.0443	0.4044
Current smoker (smoked on day of testing)	0.49600	<0.0001	0.43350	<0.0001	0.54337	<0.0001
Current smoker (within last 12 months, not smoked on day of testing)	0.90579	0.0825	0.82377	0.0091	0.89582	0.1945
Atopy (≥3mm)	1.6028	<0.0001	1.60363	<0.0001	1.5472	<0.0001
Log IgE	1.3897	<0.0001	1.3971	<0.0001	1.3235	<0.0001
Current rhinitis	1.3126	<0.0001	1.2868	0.0002	1.3670	<0.0001
Current wheeze	1.1009	0.0617	1.0906	0.2349	1.1004	0.1658
Current asthma	1.4132	<0.0001	1.4434	<0.0001	1.3495	0.0003
Using ICS	1.3904	0.0004	1.3780	0.0134	1.3755	0.0130

Table 4: Adjusted linear regression models with FENO as the dependent variable

Sample	Variables	Anti-log β-coefficient	p-value	R-square
All Study Members	Intercept	15.9	<0.0001	0.331
	Sex	0.69	<0.0001	
	Current Smoking — smoked on the testing day	0.45	<0.0001	
	Current Smoking — not smoked on the testing day	0.80	0.0014	
	Current Asthma	1.26	<0.0001	
	Atopy	1.41	<0.0001	
	Sex*Current Smoking— smoked on the testing day	1.32	0.0025	
	Sex*Current Smoking— not smoked on the testing day	1.10	0.3970	
Males	Intercept	15.60	<0.0001	0.343
	Current Smoking — smoked on the testing day	0.45	<0.0001	
	Current Smoking — not smoked on the testing day	0.81	0.0021	
	Current Asthma	1.25	0.0025	
	Atopy	1.45	<0.0001	
Females	Intercept	11.31	<0.0001	0.276
	Current Smoking — smoked on the testing day	0.57	<0.0001	
	Current Smoking — not smoked on the testing day	0.77	0.0022	
	Current Asthma	1.09	0.3460	
	Atopy	1.37	<0.0001	
	Current Asthma*Current Smoking— smoked on the testing day	1.13	0.4722	
	Current Asthma*Current Smoking— not smoked on the testing day	2.31	<0.0001	

testing) + 0.16511 atopy + 0.0973 asthma

(R^2 =0.3434).

For females: log F_ENO = 1.0533 – 0.2407current smoking (smoked day of testing) – 0.1160current smoking (not smoked on day of testing) + 0.0388*asthma + 0.1355*atopy + 0.0531*current smoking (smoked day of testing) asthma + 0.3630 current smoking (not smoked day of testing) asthma

(R^2 =0.2760) where, for the terms current smoking, atopy and asthma, yes = 1, and no = 0.

Using these equations, the predicted values and ranges (95% CI) for clinically important populations are presented in Table 5. For comparison, the actual values obtained from each subgroup of the study population are also presented.

Discussion

The results of the present study provide further evidence that sex is a major factor determining exhaled nitric oxide measurements. Without adjusting for other factors such as atopy, current smoking, and diagnosed asthma, the mean F_ENO levels in males were significantly higher than in females (p=0.0001). However, even after appropriate adjustments, this difference persisted. The magnitude of the difference was approximately 25%. This is clinically as well as statistically significant.[24]

A review of the literature provides somewhat conflicting data regarding this issue. It is important to take account of the different methodologies used for F_ENO measurements when making comparisons between studies, particularly with regard to expiratory flow rates. However, within studies, significant differences between males and females will still be valid, and the balance of evidence suggests that sex-related differences are indeed important. In early investigations, both Jilma et al.[25] and Tsang et al[26] reported sex-related differences whose magnitude (50% and 53% higher in males compared to females, respectively) was comparable to the present result. More recently, Olivieri et al. have reported higher levels in males, with an upper limit of normal of 28.8ppb, compared to 21.5 ppb for females.[27] Travers et al[19] reported that the mean F_ENO in males was 23% higher than in females (95% C.I. 7–43; p=0.004, n=191). In that study, the significance of the difference persisted even after controlling for height. In the study by Berry et al a similar highly significant difference between males and females was recorded.[28] However, in the largest study to date to focus on factors affecting F_ENO, comprising 2,200 subjects, Olin et al has presented contrasting results.[18] Although there was a male-female F_ENO difference in non-smokers amounting to 19%, this was not statistically significant in a multiple linear regression analysis in which adjustments for all other factors were included.[18] The reasons why the difference failed to reach statistical significance are unclear.

After adjusting for sex, we found that other anthropometric factors such as height and lung function were no longer significant factors affecting F_ENO. Previously it has been argued that sex-related differences in F_ENO result from differences in the surface area of airway epithelium, the major source of exhaled NO, and for which height is an important anthropometric correlate. Thus our results are perhaps surprising. However, given that plasma levels of nitrate, a product of NO metabolism, are similarly different between the sexes,[25,29] it seems unlikely that NO production in the airways is solely a reflection of differences in airway size, but rather reflects sex-related differences in endogenous NO production. This is consistent with the results of a twin study, which showed that genetic rather than environmental factors are more important in determining F_ENO.[30]

Our findings raise the question as to whether guidelines for the interpretation of F_ENO should be stratified by sex, and that reference ranges for males and females should be different. In

Table 5: Mean values and reference ranges for FENO (with 95% confidence intervals), based on prediction equations for males and females. For comparison, the measured values (with 95% confidence intervals) obtained in the Study members are provided

Population		Males		Females	
	FENO (ppb)		95% C.I.	FENO(ppb)	95% C.I.
Non-smokers, non-atopic, non-asthmatic	Predicted	15.6	14.1, 17.2	11.3	10.3, 12.4
	Actual	14.7	13.4 , 16.1	11.2	10.3, 12.2
Non-smokers, atopic, non-asthmatic	Predicted	22.6	18.3 , 28.0	15.4	12.6, 18.9
	Actual	23.1	20.4 , 26.2	15.6	13.9, 17.4
Non-smokers, non-atopic, asthmatic	Predicted	19.5	15.3 , 24.9	12.4	9.4, 16.3
	Actual	22.5	8.0 , 63.8	11.5	7.0 , 18.9
Non-smokers, atopic, asthmatic	Predicted	28.3	19.8, 40.5	16.9	11.5, 24.9
	Actual	30.4	23.9 , 38.7	17.2	13.5, 22.1
Smokers (not smoked on the day of testing), non-atopic, non-asthmatic	Predicted	12.6	9.9, 18.2	8.7	6.7, 11.3
	Actual	13.0	11.0, 15.2	9.6	7.8, 11.7
Smokers (not smoked on the day of testing), atopic, non-asthmatic	Predicted	18.2	12.8, 25.5	11.8	8.2, 17.2
	Actual	17.6	14.1, 22.0	10.9	8.7, 13.8
Smokers (not smoked on the day of testing), non-atopic, asthmatic	Predicted	15.7	10.7, 22.8	21.8	9.2, 51.8
	Actual	12.0	7.5, 19.5	16.0	0.3, 743.5
Smokers (not smoked on the day of testing), atopic, asthmatic	Predicted	22.8	13.6, 36.9	29.8	11.3, 79.0
	Actual	24.0	17.8, 32.4	32.3	14.6, 71.2
Smokers (smoked on the day of testing), non-atopic, non-asthmatic	Predicted	7.0	5.6, 8.8	6.5	5.1, 8.2
	Actual	7.3	6.4, 8.3	6.5	5.8, 7.3
Smokers (smoked on the day of testing), atopic, non-asthmatic	Predicted	10.1	7.2, 14.0	8.9	6.3, 12.5
	Actual	10.2	8.8, 11.8	8.9	7.3, 10.9
Smokers (smoked on the day of testing), non-atopic, asthmatic	Predicted	8.7	6.0, 12.5	8.0	3.8, 17.0
	Actual	8.9	7.3, 10.9	8.1	4.0, 16.4
Smokers (smoked on the day of testing), atopic, asthmatic	Predicted	12.6	7.6, 20.3	11.0	4.6, 26.0
	Actual	9.3	6.2, 13.8	10.9	6.6, 18.0

the paper by Olivieri et al. the authors propose that reference ranges should be stratified for sex.[27] Travers et al.[19] advocate reference ranges based on sex, smoking status and atopy, but not age or height. We concur with this view, and the reference ranges contained in Table 5 of the present paper are based on this approach. In the study by Olin et al.[18] similar to conventional pulmonary function tests, both age and height but not sex, were deemed to be significant, although reference values as such were not provided. All studies concur that smoking and atopy are important considerations, and both are included in the reference values given here and by Travers et al[19]

In fact, interpreting F_ENO levels in clinical practice is even more complex. Reference values which take into account background characteristics such as sex, atopy and smoking may indeed be useful in guiding the diagnosis of airways-related symptoms. In asymptomatic individuals, it is still possible that increased F_ENO reflects subclinical airway inflammation,[7,28] but this interpretation is less likely if appropriate reference values which take factors such as sex into account have been used in the first place. The interpretation of F_ENO levels in the context of ongoing management of diagnosed asthma is far from clear. Despite optimal anti inflammatory treatment, F_ENO levels may remain resolutely high,[31] and it is generally agreed that normalizing F_ENO in relation to reference values for a healthy population is not adesirable therapeutic aim.[8] This point is perhaps reflected in the results obtained in the present study, which showed that in non-smoking, atopic, male asthmatics, who were all clinically stable, the upper limit of the 95% confidence interval was 38.8 ppb, considerably higher than the levels obtained in non-smoking, atopic, male, non-asthmatics (28.2 ppb).

One of the weaknesses of our study is that the F_ENO measurements were obtained in individuals who were all aged 32 years. Thus it was not possible to explore the influence of age as a factor in the regression analyses or to conclude whether reference values ought to include it as a factor. Previous studies have reported that F_ENO rises with increasing age in children.[15,16,32-34] In adults, Olin et al[18] have reported that an effect of age also occurs: F_ENO was shown to increase over the age range 35 to 65 years, with the magnitude of effect similar to that of atopy. In contrast, in the study by Travers et al. no significant relationship was noted over a similar age range, but numbers were much smaller.[19] In children, it is suggested that the changes with age are attributable to increasing airway NO flux, probably reflecting larger airway surface area with growth.[34] If at all, any increase in F_ENO with age in adults is likely to be due to non-

anthropometric factors, and if the results from Olin et al are repeatable, this may be an important consideration.

In summary, our data confirm that differences in F_ENO between males and females are of sufficient magnitude that the interpretation of F_ENO should be stratified by sex. This approach should be incorporated into clinical practice. Other common and easily identified factors such as current smoking and atopy also require to be taken into account when interpreting F_ENO values in adults. Contrasting results from a number of studies still leave open the question as to whether age and height ought to be included in future reference equations. These outstanding issues add to the current challenges which still remain in the application and interpretation of F_ENO levels in clinical practice, and require further study.

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Editorial…continued from page 4

• "We use HMEs, we don't have problems with secretions and they're inexpensive."
That might be true from the clinician's perspective. I'm not so sure it's true from the patient's perspective. Absence of plugging and/or thick tenacious secretions does not mean you've achieved optimal humidity content or muco-ciliary clearance. Additionally, I've often seen saturated HMEs without obvious clogging cause dramatic increases in resistance.

Recently, I observed a patient failing a spontaneous breathing trial unless pressure support was at least 18cm. Simply removing the HME reduced the PS requirement to 5cm. Again, the HME was not visibly clogged.

• "We use an HME with low resistance and low deadspace so we're good to go." In reality, low resistance and deadspace often translates into a lousy humidifier. Low surface area (unless using more expensive hydrostatic electrostatic filter media) = low humidity content. Try the water test with your HME. Pour water into the HME in an amount roughly equal to the HME size. If the water pours through the other end, it's not absorbing moisture, so how can it possibly be returning moisture to the patient? Cheap is cheap. For example, "sponge" type HMEs are very inexpensive and can offer very low resistance and deadspace. Neither necessarily has anything to do with humidification performance without taking into consideration design of filter media and the materials the filter is constructed of. A better performing HME may reduce costs as the frequency of needing to replace the HME and/or switch to active humidification may be reduced.

• "We use HMEs exclusively." They either have read studies suggesting no advantage to heated systems or perhaps are aware there's no difference in VAP rates. This ignores other disadvantages of HMEs in select patients. For example, studies have shown that in borderline difficult to wean patients, the added minute volume requirement to correct for HME deadspace can mean the difference between weaning success and failure.[2] (Though one could make the case that a few cm of PSV could mitigate this.) Additionally, increased expiratory resistance could tip the balance in weaning patients with high levels of intrinsic PEEP. In ARDS patients whose plateau pressures are too high and/or pH goals cannot be met due to hypercapnia, the added deadspace due to an HME may be unwarranted.

Some practical recommendations:

- Educate yourself on the physical and chemical properties of HMEs. It's not enough to just look at size and resistance. Do the homework required to choose an effective HME
- Manufacturer's humidity specifications don't tell the whole story. Absolute and relative humidity specifications are typically measured at a fixed flow rate. Tidal volume size, minute volume, flow pattern and filtration efficiency all affect humidification performance.
- If you're going to use HMEs as your primary means of humidification, ensure compliance with a protocol that addresses contraindications and active humidification criteria. The protocol should also assess measurements of airway resistance.
- If you can't easily measure/document resistance with your ventilators, consider the need to change the HME daily to proactively prevent occlusion of the HME.
- If you're going to use heated humidification as your primary method, enforce a protocol/policy to require visualization of fogging (minimal condensation) in the tubing closest to the airway.
- Use heated wire circuits with a coaxial wire configuration to minimize condensate.

Can you have your cake and eat it too? A new product is now available in the US that combines the advantages of HMEs and heated humidification systems. "The HME booster" allows the clinician to convert an HME to an active humidification system. This system adds active humidification between the HME and patient airway. Since water is added at the patient airway, there's no water present in the circuit. There's no need to break the circuit to drain water. This avoids the expense of heated wire circuits, humidifier chambers and high cost of having heated humidifiers available for all patients. On a practical level, the ability to convert to active humidification in seconds may increase compliance with protocols. Additionally, water use is dramatically reduced as your not having to transport humidity from the ventilator across the ventilator circuit. (See http://www.hmebooster.com/index2.htm.)

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AARC Executive Preview

A look at companies exhibiting at AARC this year.
For an index of companies profiled, see page 64.

Roche

FEATURED PRODUCTS: The Roche cobas b 221 blood gas system with version 7.0 operating software, controlled with the new cobas bge link version 3.6 instrument software, will be showcased.

EDUCATIONAL OPPORTUNITIES: Journal articles and case studies addressing current blood gas testing trends will be available in the booth.

BOOTH PROMOS: For the eighth consecutive year, Roche Blood Gas is proud to sponsor the AARC Fun Run, scheduled for Sunday, December 14, 2008 at 7 am. All attendees are encouraged to stop by the booth and register for the 5K run/walk, which will take place on the road around the convention center. All finishers will receive an official Fun Run T-shirt. In addition to the Fun Run, there will be a drawing for a Littman stethoscope on Sunday, December 14. Another drawing will occur on December 15, for a hard-bound copy of Clinical Application of Blood Gases, by Shapiro et al. All attendees are encouraged to stop by the booth and register for both drawings.

WHY STOP BY? Healthcare providers will gain a greater understanding of the actionable information the cobas b 221 can provide with the configurable menu that has options for blood gas (pO_2, pCO_2 and pH), electrolytes (Na^+, K^+, Cl^-, Ca^+), metabolites (Glucose, Lactate, BUN), tHb/SO_2 and Co-oximetry (O_2Hb, HHb, COHb, MetHb, tHb, Hematocrit, Bilirubin) as well as enhanced applications of patient trended data and automated acid-base mapping trending. Learn how the cobas b 221, with the only FDA 501(k) clearance for testing pleural fluid pH, can help simplify regulatory compliance, and see how the cobas b 221 blood gas system, coupled with cobas bge link Instrument manager software, enables monitoring and control of up to four decentralized systems from one location. cobas bge link enhances operational efficiency of all connected systems through screen sharing to provide immediate real–time performance status, maintenance updates, and remote access for IT technical support 24/7.

Hydrate, Inc.

FEATURED PRODUCTS: Our feature product is the Hydrate OMNI humidification system with C-Force Technology which is a revolutionary humidifier based on novel technology used across virtually every application where heated, humidified gases are inhaled. This futuristic humidifier is now available in the United States and will be launched at this AARC Congress. The Hydrate OMNI's heart is a ceramic, porous disk where water is heated from liquid to vapor which then heats and humidifies gas. Water is precisely pumped to the disk independently of the heat so the therapist has control over both parameters and can actually set the humidity levels. Moreover, the system is smart so that all parameters are monitored and displayed. Aside from the Hydrate OMNI there hasn't been a step change in humidification since its introduction as a heated passover system in the 1970s. The time where clinicians had to assume adequate humidification is over.

EDUCATIONAL OPPORTUNITIES: Abstract and poster copies which provide insight into Hydrate OMNI's advantages over heated passover systems will be offered and discussed. Some of these will demonstrate dramatic improvement in humidification with different types of ventilation modes and some will illustrate the short falls of current systems.

BOOTH PROMOS: None! We won't lure therapists into a booth to see something they aren't interested in because they can win a prize.

WHY STOP BY? We will be demonstrating the Hydrate OMNI in both the ventilator and high flow gas (nasal cannula) applications and allow therapists to interact with it to see how unique, easy and effective it is. The Hydrate booth will be the only place therapists can see the future of humidification.

Bunnell Incorporated

EDUCATIONAL OPPORTUNITIES: Bunnell Incorporated will be distributing their three booklet pocket reference series that describes the What, Why and How of the Life Pulse High-Frequency Ventilator. The illustrated booklets explain in simple straightforward language what high-frequency jet ventilation is, why the Life Pulse is uniquely effective, and how to manage patients on the Life Pulse. Bunnell will also be distributing its new in-service training and educational DVD. The DVD contains a comprehensive training video with detailed components on patient management and clinical troubleshooting.

WHY STOP BY? Respiratory Therapy's readers will want to stop by the Bunnell booth to learn about the lung protective benefits of high-frequency ventilation. They will receive information about how HFJV is different from HFOV and the potential benefits of HFJV compared to HFOV. Finally, they will have the opportunity to discuss issues related to the clinical use of HFJV and have all their questions answered by one of our clinical specialists.

Cardinal Health

FEATURED PRODUCTS: At the AARC, Cardinal Health (formerly VIASYS Healthcare) will be featuring the Total Lung Care (TLC) range of ventilation products and in particular the EnVe, LTV

1200, and our new PureSom line of sleep therapy products. The newest addition to the Total Lung Care line of ventilators from Cardinal Health is the EnVe ventilator. The EnVe is a comprehensive, full feature, intensive care ventilator with our unique ActivCore technology. This ventilator is extremely compact and completely portable. The integrated full color LCD touch screen display and 4 hour hot-swappable internal battery, makes this ventilator fully wall independent. The comprehensive selection of modes, including noninvasive, integrated spontaneous breathing trial and active exhalation valve represent a major paradigm shift in critical care ventilation. Additionally, we will be showcasing many new additions and enhancements to the Pulmonary Diagnostic family and market driven enhancements to the best-selling LTV 1200. Our new line of PureSom sleep therapy products will be introduced and will include a broad range of devices and accessories.

EDUCATIONAL OPPORTUNITIES: This year, Cardinal Health is proud to support the AARC with the Application of High Frequency Oscillatory Ventilation seminar. This specialized seminar is designed to present information that is useful for new and experienced HFOV clinicians alike. All speakers are noted for their expertise in HFOV. Ruben Restrepo, MD, RRT will present on the technical aspects of HFOV. Henry Fessler, MD explores protocolized approaches to HFOV. And finally, Stephen Derdak, MD will summarize the clinical applications of HFOV based on underlying conditions such as pregnancy and head injured patients. Please join your colleagues on Saturday, December 14th to participate in the fascinating and useful seminar.

The new EnVe ventilator is a must see. The new ventilator system is the most compact, full-featured ICU ventilator on the market today. In fact, you can actually hold these critical care ventilators in the palm of your hand. Our PureSom sleep therapy offering is part of our constantly evolving sleep product line which has innovative products for polysomnography in the sleep center, for portable sleep monitoring as well as the complete line of sleep therapy products including devices, accessories and patient interfaces. In sleep there is always something new. As the market leader in Pulmonary Diagnostics, our PFT, Exercise and Spirometry line continue to deliver solutions to meet the complete spectrum of our customer's diagnostic needs.

B&B Medical Technologies

FEATURED PRODUCTS: B&B is introducing these new products: **Hybrid Baby Tape** and **Hybrid Pediatric Tape** are the only endotracheal tube securing products that combine the gentle qualities of hydrocolloid to safely adhere to tender skin with a specially formulated acrylic adhesive strip to tightly secure endotracheal tubes, NG/OG tubes, cannulas and small catheters. Latex-free and hypoallergenic, Hybrid Baby Tape and Hybrid Pediatric Tape dramatically improve the functionality, comfort and reliability of securing devices for infants and pediatric patients, respectively, while improving quality of patient care. Specifically designed for infant and pediatric applications, the tapes are precut to save the clinician time and enable a one-person application. Hybrid Baby Tape and Hybrid Pediatric Tape is flexible yet provides firm adhesion while also absorbing exudates. The skin-friendly hydrocolloid tape can easily be removed with water without damaging the skin. B&B Medical Technologies' Hybrid Tape collection is "Providing the Right Tape for the Right Hold." The tapes are used in the NICU, PICU, Labor & Delivery, the operating room and the emergency department, as well as in transport environments to secure artificial airways and other vital tubes and catheters. The benefits of the Hybrid Tape Collection are: • Convenience – ease of applications; time saving; pre cut tapes; all in one kit. • Cost effective – two tapes per package; secure hold; used to secure ETT, cannulas and OG/NG Tubes. • Safe – skin protective qualities; allows skin to breathe; latex free, hypo-allergenic; enhanced durability for tube protection. • Versatile – NICU and pediatric applications; contours to skin for secure fit; secures additional small tubes and cannulas; compatible for use in all clinical conditions. The **Test Lung** is a new, economical choice for providing high quality demonstration and testing applications on mechanical ventilators. The Test Lung simulates the respiratory system of an adult, providing nominal levels of resistance and compliance as well as a variable leak function to demonstrate patient-trigger function or the leak compensation of a respiratory system. The Test Lung is packaged with a 1 liter, latex free silicone ventilation bag, Test Lung Connector Kit and Rp5 Resistance. The 1 L Silicone Ventilation Bag is durable, easily removable and can be cleaned or sterilized as needed. The Test Lung Connector Kit adapts to all patient circuits and proximal airway flow sensors. It has three adapters, two with Luer Ports and caps, providing easy ability to demonstrate the ventilator's leak compensation performance and patient-trigger function. Compact in design and lightweight, each Test Lung is tested and validated for resistance and compliance in the application range and has a unique serial number to ensure its compliance with specification. As an added value to the Test Lung, the **Precision Resistor Kit** provides the precision adapters needed to simulate changes in airway resistance. The Kit contains three resistors: Rp5, Rp20 and Rp50. The Precision Resistor Kit can be cleaned and sterilized. Test Lung Benefits are: • Convenience – ease of use, no assembly required; packaged with adapters for ventilators. • Cost effective – solution for education, training and demonstration; easily replaceable ventilation bag for cleaning. • Safe – latex free, hypoallergenic materials. • Versatile – 1 liter ventilation bag; designed for use with most ventilators.

WHY STOP BY? Our exceptional attention to the needs of both respiratory patients and respiratory practitioners has resulted in a diverse and complementary array of products that leads the industry. B&B products are designed by respiratory therapists for respiratory therapists. Since 1985, B&B Medical Technologies has developed specialty airway management and nebulizer technology for infant, pediatric and adult patients. B&B Medical Technologies' product line includes the Hybrid Tape Collection, StabilTube, LockTite, E.T. Tape, and E.T. Tape II for adult/pediatric patients, bite blocks, TrachGuard, TrachStay, NEO2-SAFE, The Test Lung, Precision Resistor Kit, the HOPE Nebulizer and Sat Point pulse oximeters for adult and pediatric patients.

Medical Graphics Corporation

FEATURED PRODUCTS: Platinum Elite (Body Plethysmograph): The Plethysmograph's state of the art design and digital and enhanced technology represent the "Platinum Standard" for ease of use, patient comfort and reliability. CCM Express (Nutritional Assessment): The CCM Express provides true resting metabolic

measurement for ventilated and spontaneously breathing patients. The compact, mobile design with simple touch screen operation, gasless calibration and breath-by-breath analysis makes the CCM Express ideal for use in the hospital and private practice.

EDUCATIONAL OPPORTUNITIES: Annual Cardiorespiratory Diagnostics Seminar: This course will update participants knowledge of testing techniques, performance standards, quality assurance procedures and clinical applications for basic and advanced cardiorespiratory testing. The program format will include lectures, hands-on demonstrations and group discussions. Information will be available at our booth.

WHY STOP BY? Stop by to get hands-on time with our new products and speak with one of our representatives.

Vapotherm

FEATURED PRODUCTS: Vapotherm will feature the new acute care device, Precision Flow, at this year's AARC Convention. Precision Flow is the first high flow humidification device to integrate humidification technology and electronic gas blending in a single device. Precision Flow is FDA 510(k) cleared.

EDUCATIONAL OPPORTUNITIES: Vapotherm is dedicated to continued leadership in high flow education and research. In addition to field based educational and clinical support by our staff of Clinical Product Specialists, the Company offers several other educational services to the respiratory community including the Vapotherm Education Center (VEC), an e-learning platform with complimentary continuing education and technical training resources. The VEC can be accessed at vtherm.com. A new AARC accredited course, High Flow Therapy: Mechanisms of Action, will be available at the booth this year.

SPEAKERS: Tom Miller, PhD, Director of Clinical Research and Education for Vapotherm, will be available throughout the convention to discuss new research in high flow therapy as well as new educational offerings.

eVent Medical

FEATURED PRODUCTS: We will be showing the newest version of the Inspiration neonatal through adult ventilator with NCPAP with a rate as well as the Inspiration Ventilator's optional MiniWeb interface and Virtual Report Viewing System.

EDUCATIONAL OPPORTUNITIES: We will have a presentation on Sunday 14th discussing new ways of communication for ventilated patients.

SPEAKERS: We are working with Dr Chowdhury doing studies on Heliox and Infant Nasal CPAP with a rate.

BOOTH PROMOS: We will be demonstrating the MiniWeb Virtual Report Viewing System; and will also have a year-end sales promotion for NCPAP to be included as a standard item in every ventilator purchased.

WHY STOP BY? To see the latest technology for ventilator remote communication built into the Inspiration ventilator as well as a chance to see the first ventilator to have NCPAP with a rate as a standard mode.

Hamilton Medical

FEATURED PRODUCTS: In 2007, Hamilton Medical unveiled the Hamilton G5 Ventilator System and this year, we are providing the AARC membership the opportunity to see the new, enhanced features of the Hamilton G5, including Neonatal application, Heliox and $ETCO_2$. We will also be displaying the Hamilton C2 Ventilator System (pending 510(k)). The Hamilton C2 is a turbine driven transportable ventilator with all the features of Intelligent Ventilation which puts Hamilton at the leading edge of industry. Hamilton Medical will also be featuring the HME/Filter and HME Booster product line from Medisize. Hamilton's exclusive distribution agreement with Medisize allows us to address your humidification and filtration needs.

EDUCATIONAL OPPORTUNITIES: Hamilton Medical will be providing the Hamilton G5 Ventilator interactive simulator. This simulator enables clinicians to experience the Hamilton G5 and Intelligent Ventilation right on their own laptop.

BOOTH PROMOS: Back by popular demand the "Match and Win Game," which gives everyone a chance to win prizes including food, knowledge and travel. The grand prize is an Unrestricted Educational Grant to attend the 2009 AARC in San Antonio, TX.

WHY STOP BY? Everyone associated with respiratory healthcare understands that this dynamic field is constantly changing and Hamilton Medical remains at the forefront of the future of mechanical ventilation. Visit booth 970 to experience firsthand the features of Intelligent Ventilation, provided only by Hamilton ventilators. Hamilton Medical will have a clinical expert from Medisize in the booth to answer your HME/filter questions along with our expert sales and clinical team to address your ventilation needs.

Ambu Inc.

FEATURED PRODUCTS: The **Pentax AWS-S100**: A revolutionary videoscope device enables clinicians to visualize the vocal folds to place an endotracheal tube with ease. The **AuraOnce** with Removable Airway Connector**.** This version of the already popular Aura supraglottic airway will have a removable airway connector which allows the therapist to place an ET Tube through the device, during a difficult airway situation.

EDUCATIONAL OPPORTUNITIES: Training videos, training manikins, clinical study reprints.

BOOTH PROMOS: This year at AARC, Ambu Inc will feature the complimentary Ambu ResCue Key. This pocket size device is a terrific companion to accommodate any respiratory therapist when he or she needs to deliver CPR in any public setting. An ongoing promotion will feature our neonatal products sales campaign. The campaign includes both the Infant SPUR II resuscitator, with a neonatal sized electrode for diagnostic monitoring.

WHY STOP BY? We encourage every AARC attendee to stop by our booth in Anaheim, CA to visit the pioneers in manual resuscitation, and witness firsthand, the innovative products that are commercially available and on the product development horizon.

Hyperbaric America, LLC

FEATURED PRODUCTS: Hyperbaric America, LLC will be exhibiting our HA-34 monoplace hyperbaric chamber, part of our Presidential series of chambers.

WHY STOP BY? To review the unique features on Hyperbaric America, LLC's chambers.

MAQUET

FEATURED PRODUCTS: MAQUET will be showcasing the new SERVO-i—our flagship ventilator with its unique modular, plug-and-play platform that allows for fast upgrading to the latest innovations in mechanical ventilation. This year we will be focusing on the SERVO-i with NAVA. NAVA stands for Neurally Adjusted Ventilatory Assist and is an option for the SERVO-i. NAVA detects respiratory signals sent from the brain to the diaphragm and transmits those signals to the ventilator. This allows patients to receive the level of support best suited for them with each changing breath by controlling flow, pressure, volume and frequency. Other new products include the Heliox and MR options. Thanks to the low gas consumption of the SERVO-i, we will be offering one of the most cost efficient Heliox delivery systems available on the market today. The MR Option extends the use of the SERVO-i for conditional use in the MR examination room. Thus the SERVO-i can be used to provide advanced ventilatory care to critically ill patients using the same machine wherever they are in the hospital—in the ICU, MR suite or during transport between hospitals.

EDUCATIONAL OPPORTUNITIES: This year MAQUET will be offering live seminars in our booth to earn CRCE credits. They will last for one hour and cover the latest advancements in respiratory technology such as NAVA and Lung Recruitment. Visit maquet-training.com for more information regarding individual lectures and to register.

SPEAKERS: We are planning to present NAVA customer and patient experiences. Also, MAQUET clinical specialists will be giving one hour long CRCE accredited seminars.

BOOTH PROMOS: Dana Oakes, author of Critical Care Pocket Guides, will be present to autograph his latest book.

WHY STOP BY? Stop by the MAQUET booth to learn more about the latest advances in medical technology such as NAVA, Heliox and the MR option and to earn CRCE credits through in-booth seminars.

Opti Medical Systems, Inc.

FEATURED PRODUCTS: Recently OPTI Medical expanded the OPTI product line to include the OPTI Rhythm line of finger pulse oximeters. Our compact, versatile OPTI Rhythm pulse oximeters combine reliable performance with the simplicity and portability busy healthcare workers demand.

BOOTH PROMOS: Visit the OPTI Medical booth for a demonstration of the ComfortSampler arterial blood gas collection kit and receive a free sample. The ComfortSampler makes arterial blood collection simple, safe, and comfortable. Try the ComfortSampler for yourself at the OPTI Medical booth on our arterial puncture arm simulator.

WHY STOP BY? OPTI Medical offers the portable OPTI CCA-TS blood gas analyzer, the OPTI R blood gas analyzer with Auto QC, and the OPTI LION electrolyte analyzer. Each analyzer provides fast, lab-accurate results with simple intuitive operation. Stop by our booth for a demonstration and see how the OPTI line of products offers the ideal solution for your blood gas needs.

Ohio Medical

FEATURED PRODUCTS: Flowmeter, Care-e-Vac Lt (portable suction), O2 Blender.

EDUCATIONAL OPPORTUNITIES: Principles of Vacuum and Enhancing the Safety of Medical Suction Through Innovative Technology (white paper).

WHY STOP BY? To learn the importance of setting accurate vacuum levels to prevent over suctioning which can lead to potential tissue damage. Ohio Medical's Push-To-Set Vacuum Regulator has a built-in feature, Push-To-Set Knob, which saves time and improves patient safety by eliminating the need to pinch off patient tubing to set proper vacuum, making it a one-handed operation.

Electromed, Inc.

FEATURED PRODUCTS: Electromed, Inc is pleased to offer an exciting new vest therapy product which delivers HFCWO directed at establishing and continuing to clear human lungs. Mucus-free lungs promote enhanced lung health reducing the incidence of lung infections which can be so debilitating and a threat to life and quality of life. The new product is called the SmartVest Wrap. It is a very attractive innovation which utilizes a single airpulse hose, requires no complicated snaps or other fixtures, and provides "full coverage" pulse therapy 360 degrees about the chest and upper torso. Full coverage simultaneous pulsation assures that all lobes of the lungs are treated at the same time to foster loosening and mobilization of secretions. Materials construction and the overall innovative design of the SmartVest Wrap result in a high quality appearance and an ability to easily reverse the product so that a patient can be served from either the right or the left side of a bed or chair using the company's patented Single Hose Design. SmartVest Wrap is a single patient use product which may be discarded consistent with good infection control practice. It is compatible with any of the three generations of airway clearance products created, manufactured, and distributed by Electromed, Inc of New Prague, MN.

WHY STOP BY? Electromed CEO, Bob Hansen, invites physicians, respiratory therapists, nurses, and other attendees to visit the Company's booth. A complimentary Vest Light will be available along with the company's very popular SmartVest pen.

Philips Respironics

FEATURED PRODUCTS: The SideStream Plus Breath-enhanced Reusable High Efficiency Nebulizer and Sami the Seal pediatric character mask: The SideStream Plus breath-enhanced nebulizer features an easy-action inspiratory valve that opens on inspiration to boost medication delivery and closes on exhalation, preserving medication and reducing waste. Significantly less pressure is required to open the inspiratory valve compared to other breath-enhanced nebulizers making treatments easier for pediatric patients. Sami the Seal child-friendly character mask incorporates a vent design that blows medication away from the eyes, minimizing ocular deposition of aerosol medications during treatment.

EDUCATIONAL OPPORTUNITIES: New product sales aids.

SPEAKERS: Mike West, RRT, MBA, and Cheryl Nickerson, RRT, AE-C, Respironics, will be speaking on Respiratory Drug Delivery Contemporary Issues.

BOOTH PROMOS: Sami the Seal stress reliever.

WHY STOP BY? RDD continues to advance pulmonary aerosol delivery technologies. SideStream Plus and Sami the Seal, along with our MicroElite miniature jet compressor nebulizer system, expand our product solutions for the treatment of respiratory and non-respiratory diseases and are designed to provide comfort and convenience for the user.

Hill-Rom

FEAURED PRODUCTS: From a product standpoint Hill-Rom will be exhibiting their updated full line of disposable vest garments and our disposable air hoses for the acute care environment to aide in the minimization of cross contamination.

EDUCATIONAL OPPORTUNITIES: Hill-Rom will have booth representatives available to demonstrate and instruct participants on home and acute care products. Stop by and see our updated website and new patient stories. We will be giving away "sticky lungs" and disposable tape measures. We will also be offering promotional office supplies with company logo and contact information. Other offerings are being worked on—stop by and check it out.

WHY STOP BY? We are excited to discuss Medicare's expanded coverage of High Frequency Chest Wall Oscillation for many neuromuscular conditions and what this means for patients who require our product outside of the acute care setting. Hill-Rom received the 2008 Therapy Times Most Valuable Products award in Respiratory Therapy for the Wrap SPU Vest and The Vest System. The Wrap SPU Vest is a single patient use disposable product designed to minimize the risk of cross contamination and to ease product placement and removal for patients in acute and long-term care settings. The Vest Airway Clearance Model 205 was also the winner of the 2007 Medical Design Excellence Award. Both of these will be displayed at our booth—please stop by to see our full disposable line.

Dräger

FEATURED PRODUCTS: Dräger will be exhibiting the Evita XL with its new design and recently released 7.0 software, Oxylog 3000, Babylog, Savina, Carina, Carina Home Care, and the Infinity C700 for IT Workstation. These superior ventilation products are steadfastly advancing the field of respiratory care. Evita XL is the result of the latest model in modern ventilation, focusing on the patient's needs and offering increased comfort for critical care therapists and patients. The ventilator can easily be configured to meet the needs of ICU staff and enables work processes to be tailored to a patient's individual needs. A customized table displays the actual measured values and settings in the order of your protocol. Start-up ventilation modes, settings and function keys can also be configured to suit your daily routine. Oxylog 3000 offers both volume and pressure-based modes, for controlled, synchronized or spontaneous ventilation in the emergency room or during transport. When transporting critical care patients, the need to interrupt ventilation therapy is therefore eliminated. Non-invasive ventilation (NIV) reduces the need for intubation. Flow-time and pressure-time waveforms are shown on a high-contrast display, offering reliable patient monitoring. Oxylog 3000 is designed to be used both in the hospital and in the EMS environment. Babylog is used for harmonious ventilation of small children and the smallest pre-term babies. It has an advanced upgrade platform that has allowed it to keep pace with all new forms of treatment and clinical advances such as volume guarantee. Sensitive synchronization with gentle but precise support for spontaneous breathing reduces the work of breathing and makes the ventilation process much more comfortable for patients. Savina is a ventilator for adult and pediatric patients of all acuity levels. The machine's mobile capabilities enable continuity of therapy even during transport, and it also offers the option of invasive or non-invasive ventilation. It is specifically designed for areas with limiting surrounding conditions and can easily bridge periods of power failures and manage situations where no compressed air is present or is unreliable. The Carina ventilator offers both invasive and non-invasive capabilities. It is equipped for the emergency room, general ward, ICU or sub-acute facilities and features an internal battery that can operate independently of a high-pressure gas system. Its latest technology, known as "Synch Plus," will compensate for leakage and provide effective breath delivery. The Carina Home Care ventilator is intended to continue the treatment received in the hospital, at home, or in a long-term care facility. With a very low sound level, the Carina Home supports a calm and quiet environment for patients and their families. The unique user interface concept makes it easy to use for both the caregiver and the patient by giving each his or her own interface. The Infinity C700 for IT Workstation is part of the Infinity Omega and brings comprehensive patient data to the patient vicinity by displaying it on a 20" touch screen display. Infinity displays real-time monitoring and ventilation data together with networked data—such as lab results, DICOM/X-ray images, and patient/anesthesia data management system information.

EDUCATIONAL OPPORTUNITIES: Dräger will be holding user group meetings with Evita XL, Babylog and SmartCare users. These meetings will take place in a private business suite and will bring clinicians together to share information as well as their experiences with our ventilators. Our sales force will be signing customers up prior to and during the AARC Congress.

Readers should contact your local ventilator sales executive or Senior Marketing Manager Ed Coombs for more information at edwin.coombs@draeger.com or at (800) 437-2437 x2322.

SPEAKERS: Dräger will be featuring presentations from several of our clinical applications specialists who will be giving presentations on the following topics: SmartCare—Automated Weaning Program; Use of Airway Pressure Release Ventilation (APRV); and Use of Non-Invasive Ventilation with the Evita Ventilator.

BOOTH PROMOS: We will be distributing our Ventilation Solutions Brochure, which explains Dräger's products and the various ways we are helping to improve ventilation care. Also, our Evita and Oxylog trainers will be available to enhance training. To request educational materials, please contact your local sales rep or Clinical Applications Supervisor Phyllis Wilson at phyllis.wilson@draeger.com or (800) 437-2437 x4047.

WHY STOP BY? Readers should stop by our booth to learn all about the new and exciting activities at Draeger Medical, Inc., meet our new management team and view our latest products. The dedicated ventilator staff of Dräger will be happy to answer any questions they might have.

Instrumentation Laboratory

FEATURED PRODUCTS: Instrumentation Laboratory (IL), booth 354, will feature innovative products in Point-of-Care-Testing (POCT): • GEM Premier 4000 critical care analyzer with Intelligent Quality Management (iQM); • GEMweb Plus information management system; • GEM Premier 3000 with iQM; • GEM PCL Plus portable coagulation system.

EDUCATIONAL OPPORTUNITIES: IL will conduct an educational workshop on the "Effective Implementation and Management of a POCT Program." Participants will receive 1.5 CEU credits offered through the American Society for Clinical Laboratory Sciences (ASCLS) and the American Association for Respiratory Care (AARC). The workshop will bring together relevant voices of authority from both the hospital and academic settings to present the essential components for successfully implementing and managing a quality POCT program. Topics will include: quality management, patient safety, connectivity, and regulatory compliance. The session will conclude with a panel discussion among representatives from renowned U.S. hospitals who perform POCT. The workshop will take place on December 13, at the Hilton Anaheim, from 4:30pm to 6:30pm. To sign up and for more information please contact: Kari Jenkins: kjenkins@ilww.com.

SPEAKERS: IL's industry workshop will feature: • Dr Kent Lewandrowski, Director of Clinical Services (Anatomic and Clinical Pathology) and Associate Chief of Pathology at Massachusetts General Hospital, Boston, MA and Editor-in-Chief of Point of Care: The Journal of Near Patient Testing and Technology; • Dr Sharon L. Ehrmeyer, Professor of Pathology & Laboratory Medicine and Director of Medical Technology Program at University of WI; • John J. Ancy, MA, RRT, Senior Clinical Consultant for IL and former Director of Respiratory Services at St. Elizabeth's Hospital, Belleville, IL.

BOOTH PROMOS: Visitors of IL's booth will have the chance to enter the daily drawing to win a Canon PowerShot digital camera. In celebration of our 50th anniversary, we will also be offering a delectable celebratory treat.

WHY STOP BY? IL is celebrating our 50th anniversary and we are excited to present our "50 and Forward" program at this year's Respiratory Congress. IL will showcase our history of "firsts" in the industry with a large timeline graphic and a visual presentation. Come celebrate with us, learn more about our Passion & Results Award program and our commitment to the future of diagnostics. For more information on the 50 and Forward program and nomination forms for the Passion & Results Award, please visit our dedicated webpage: ilus.com/50forward.

Epocal, Inc.

FEATURED PRODUCTS: Epocal, Inc will be introducing the epoc Blood Analysis System, the next generation in point of care blood gas testing at this year's Respiratory Care Conference.

SPEAKERS: R. Rebecca L. Meredith, BS, RRT, RCP, Cleveland Clinic, Cleveland, OH.

WHY STOP BY? Attendees should stop by the Epocal booth (#355) to learn first hand how epoc Blood Analysis can revolutionize their hospital's blood gas testing process, reduce costs and help improve the delivery of patient care.

Vortran Medical Technology, Inc.

FEATURED PRODUCTS: We plan to exhibit and demonstrate our new VAR-Monitor that is designed specifically to monitor any non-cycling condition of the VAR (VORTRAN Automatic Resuscitator), and meets one of the alarm requirements specified in the AARC May 25, 2008 Guidelines for Acquisition of Ventilators to Meet Demands for Pandemic Flu and Mass Casualty Incidents. The VAR-Monitor will work with current VAR models and is easy to set up and use. The Monitor operates with a standard 9 VDC battery and is financially practical for all our existing VAR users to stockpile.

EDUCATIONAL OPPORTUNITIES: Demonstration of our products and services adds to the element of interactivity that connects the prospect to our future. Ongoing educational material available at the convention is our interactive CDROM containing a multimedia presentation for PC platform, which includes three instructional videos, brochures, and user guides in PDF for all VORTRAN products. Our CDROM will help answer questions on the operations and applications of our products and provide for future training needs. In addition to our CDROM, we'll have Educational Module Sponsorship program flyers for free CEUs that provide online continuing education, one contract hour (CEU) at no charge to medical professionals at accessce.com. The course title is, Gas Powered Automatic Resuscitator for Short Term, Emergency Ventilator. New educational modules are being developed for a workshop and information packet providing subject matter pertinent to mechanical ventilation in Disaster and Mass Casualty Incident (MCI) scenarios. The

NEW GEM® PREMIER™ 4000

So advanced, it's simple.

So simple, it's revolutionary.

Introducing the new GEM Premier 4000. Simply. Revolutionary.

It's the breakthrough whole blood analyzer with integrated CO-Oximetry that quickly provides consistent, accurate, lab-quality results throughout your hospital—in one easy-to-use, comprehensive solution. Minimal set-up. Virtually no maintenance. Remarkable flexibility for every testing need. With GEMweb® Plus you get central control over all testing processes, while iQM®, IL's patented intelligent quality management system, helps assure quality results and QC compliance 24/7, regardless of operator or testing location. The GEM Premier 4000 is revolutionizing blood testing—from the lab to the point of care.

Please contact your IL sales representative, at **1.800.955.9525**, or visit **www.ilus.com**.

Werfen Group | Instrumentation Laboratory

Instrumentation Laboratory is a company of Werfen Group IVD.

program will assist clinicians and serve as a re-certification tool with emphasis on the use of pneumatic ventilatory assist devices, and provide general ventilatory augmentation in high-impact disaster and MCI medical operations.

SPEAKERS: We are working with a preeminent expert in developing presentation programs and workshops that support clinician skills and a commitment to respiratory care, as well as foster guidance for the medical community charged with preparing for mass casualty and mechanical ventilation.

BOOTH PROMOS: We will be offering in-booth promotional giveaway items such as the classic YO-YO, which glows in the dark, and is again becoming one of the hottest items for all ages. The glow-in-the-dark YO-YO 72 (You're On Your Own for 72 hours) will be imprinted with a company logo and contact information. Our promotional giveaway items not only drive traffic to our booth, they create and keep our message awareness in the public eye.

WHY STOP BY? We recommend Respiratory Therapy readers stop by our booth (683) for the opportunity of obtaining a flyer for free online CEU, product setup instruction with demonstration, information for upcoming workshops, and to receive an Emergency Preparedness Readiness Checklist with a glow in the dark YO-YO 72 giveaway item.

Masimo

NEW PRODUCTS: This year, for the first time at AARC, we will be showcasing our two newest Masimo Rainbow SET noninvasive measurements and Pulse CO-Oximeters: Masimo noninvasive & continuous total hemoglobin (SpHbTM) is the first-and-only technology to enable continuous, real-time hemoglobin measurement without a painful needle stick and invasive blood draw—allowing clinicians to quickly detect chronic or acute anemia, identify occult bleeding earlier, and more effectively manage blood transfusions. SpHb, along with Masimo SET SpO_2, also allows for noninvasive real-time oxygen content (SpOCTM) monitoring, providing a more complete indication of your patient's oxygenation status. As part of the upgradable Masimo Rainbow SET technology platform, SpHb and SpOC join pleth variability index (PVITM)—a new method for noninvasive and automatic assessment of fluid responsiveness—as well as carboxyhemoglobin (SpCO), methemoglobin (SpMet), and the 'gold standard' measure-through-motion-and-low-perfusion SpO_2 and pulse rate measurements of Masimo SET. Masimo Pronto (pending FDA clearance) is a handheld hemoglobin spot check monitor that allows clinicians to noninvasively, and conveniently measure a patient's hemoglobin blood level in seconds, without having to draw blood, or wait for lab results. Pronto makes it safer, faster, and easier for health care professionals to measure hemoglobin levels on-the-spot—providing an opportunity for earlier and better clinical decision-making, improved patient safety, and reduced costs. In addition, Pronto may help to improve the accuracy of single-breath diffusion tests (Diffusion Capacity of the Lung for Carbon Monoxide—DLCO) by enabling pulmonary function technologists to immediately enter accurate, real-time hemoglobin measurements, instead of using default Hb values. Masimo Rad-87 is an easy-to-use, fully-featured bedside Pulse CO-Oximeter with a built-in 802-11a/b/g radio for bidirectional wireless communication with the Masimo Patient SafetyNet remote monitoring and clinician notification system. Featuring a simple, intuitive user-interface design with an easy-to-read, high-contrast display that allows clinicians to clearly see Masimo Rainbow SET measurements—even from across the room—the Rad-87 allows easy activation of many features with only a single touch, and its unique visual display allows users to quickly confirm if the alarm settings are appropriate for the patient environment. With flexibility in mind, Rad-87 is a cost-effective solution for clinicians who value ease-of-use and versatility, with breakthrough Masimo Rainbow SET noninvasive blood constituent monitoring capabilities—including noninvasive and continuous hemoglobin and oxygen content monitoring.

EDUCATIONAL OPPORTUNITIES: New educational materials being offered this year at the Masimo booth highlight the clinical benefits and accuracy of noninvasive & continuous total hemoglobin: SpHb Application Sheet—offers a summary of the clinical applications and benefits of SpHb in the surgical, critical care, and ED settings. SpHb Technical Bulletin—features a compilation of accuracy data gathered from three study sites.

SPEAKERS: This year, we are sponsoring a Respiratory Care Appreciation Party at the Anaheim House of Blues. AARC attendees must visit the Masimo booth to pick-up their VIP invitation.

BOOTH PROMOS: To celebrate the availability of noninvasive hemoglobin, we will be offering free hemoglobin spot check measurements to anyone visiting the Masimo booth. Also, AARC attendees who complete the Masimo booth presentation and tour will receive a sleek, new computer bag.

WHY STOP BY? Respiratory Therapy readers should stop by the Masimo booth #1831 to see noninvasive total hemoglobin in action, have their SpHb measurement taken, and pick-up their party invitation to a rocking good time at the Anaheim House of Blues.

Newport Medical Instruments

FEATURED PRODUCTS: Stop by the booth to see our critical care ventilator, the Newport e360. The e360 gives you all the critical care features you demand in a compact size that might surprise you. We call it Sophisticated Technology Made Simple. Simple to use, in less than 10 minutes you can learn to navigate the controls and graphics screens with ease. Sophisticated modalities include Automatic Leak Compensation, adjustable Slope/Rise and Expiratory threshold, Dual Adaptive Control and a Biphasic Pressure Release Ventilation breath style. In addition we will showcase the popular HT50 Ventilator. The HT50 has become a leader in the portable ventilator market. Reliable, durable and clinically effective for pediatric to adult patients, the HT50 is also meeting the needs for many emergency preparedness programs around the country and around the world. Stop by for the latest news on the exciting new technology we will be introducing.

SPEAKERS: This year our annual special educational presentation will again feature the world-renowned clinical researcher and physician, Marcelo Amato, MD, of the University of Sao Paulo, Brazil. Dr Amato is famous for his research into lung protective

ventilation strategies for ARDS patients. He is also known for his work in resolving dys-synchrony issues for spontaneously breathing patients during pressure support ventilation. Dr Amato's presentation will be held on Sunday evening from 5 to 6:30pm. Please join us for refreshments, appetizers, a stimulating presentation and the opportunity to earn Continuing Education (CE) credit. Afterwards, guests will have the opportunity to have a 'meet and greet' session with Dr. Amato.

Seating is limited, first come first serve, so be sure to get there on time. Stop by the booth for location and directions.

BOOTH PROMOS: Please do stop by the booth and enter to win an exceptionally unique gift item. We won't spoil the surprise—come by and see what we have for you.

WHY STOP BY? Newport Medical will be exhibiting in booth # 652. This year's meeting will be right in our back yard and we look forward to welcoming everyone to beautiful southern California. If ventilators are a part of your job then you need to put Newport Medical on your list of 'must see' exhibits at the 2008 AARC Congress. See you in Anaheim.

Philips Respironics

FEATURED PRODUCTS: The PerformMax Mask and PerfMax CapStrap interfaces are among the new products we'll feature at this year's conference.

EDUCATIONAL OPPORTUNITIES: Attendees are invited to visit our Education Station. This is where our education specialists highlight our training materials and the elearning.respironics.com Web site. We are intently focused on clinical education and training and value this time to demonstrate the many resources available, online and offline, to respiratory professionals.

BOOTH PROMOS: We will have our in-booth lectures over the course of the conference, with prizes for attendance. The 20-minute lectures are on a first-come first-served basis and cover a range of interesting topics. We encourage participants to arrive early. The seats fill up quickly.

WHY STOP BY? In addition to enhancing their knowledge of the advances in respiratory and critical care, readers are encouraged to stop by our booth to learn about our expanding operations as part of Philips Healthcare. We are excited to share our vision for the future of respiratory care. AARC affords us a unique opportunity to interact with numerous practitioners and also hear about their experiences and needs firsthand.

Respirtech

FEATURED PRODUCTS: RespirTech will be presenting a suite of single patient use jackets and wraps marketed under the ClearChest label. The products utilize a new proprietary polymer system specifically engineered for use in patient-contact medical supplies. Clear Chest jackets and wraps, used together with the inCourage system high frequency chest compression (HFCC) device, are available in three models to manage the full spectrum of airway clearance needs in both critical care and general medicine settings. New accessories will also be on display, including a convenient cart and travel bag.

EDUCATIONAL OPPORTUNITIES: RespirTech will be offering interactive demonstrations of the inCourage system and its full array of home and hospital jackets. Literature offerings will include Respirtech's newly revised Annotated Bibliography of HFCC studies and papers as well as reprints of recent articles on the value of the therapy in acute care medicine.

SPEAKERS: Members of the RespirTech team certified as respiratory care practitioners will be available for in-booth and individually scheduled break-away sessions to discuss clinical experience with the inCourage system.

BOOTH PROMOS: Booth visitors will be offered an opportunity to make arrangements for in-service demonstrations and/or AARC-approved CEU events for their facilities.

WHY STOP BY? Visitors to the RespirTech booth will be invited to examine and experience the latest advances in HFCC technology and product design. Our clinical and technical experts will be happy to discuss product applications and respond to questions and comments.

Aerogen

FEATURED PRODUCTS: We are very excited to be exhibiting our new single patient use disposable Nebulizer, the Aeroneb Solo. The Aeroneb Solo is a disposable version of the established Aeroneb Pro nebulizer favoured by leading ventilator manufactures and RT's as their high performance nebulizer of choice. The Aeroneb Solo provides effective dose delivery of physician-prescribed inhalation solutions for infants through adults requiring mechanical ventilation. It produces a fine particle, low velocity aerosol optimized for deep lung deposition with the increased flexibility of intermittent and continuous use.

EDUCATIONAL OPPORTUNITIES: As a leader in the field of aerosol science we promote continued education and research in the field and will continue our policy of supporting relevant Researcher and RT programs and studies which further knowledge of ventilator nebulization. We will be demonstrating our innovative technology and our exciting Aeroneb Micropump Nebulizer product line for pulmonary drug delivery. All our staff are on hand to answer any questions people may have regarding nebulization of the mechanically ventilated patient. Attendees can take away product information leaflets.

SPEAKERS: We are very pleased to have Dr Jim Fink, Fellow Scientist, Respiratory Therapy, with us at our booth.

BOOTH PROMOS: Following its huge success last year in Orlando we will again be inviting our customers and distributors to join us at our Irish Party Night in Anaheim. We will also have a competition to win a beautiful piece of hand crafted Irish Crystal.

WHY STOP BY? Readers should stop by our booth if they want to learn more about how to improve the quality of ventilated patients' lives through the use of our highly efficient nebulizers. We will demonstrate how our nebulizer range saves RTs valuable time as our products operate without changing patient ventilator parameters therefore not setting off ventilator alarms and can be refilled without interrupting ventilation. It may change the way you nebulizer forever.

Fisher & Paykel Healthcare, Inc.

FEATURED PRODUCTS: Fisher & Paykel Healthcare, Inc is pleased to be a participant in the AARC 54th International Respiratory Congress in Anaheim, CA. Being a market leader in several segments of the respiratory products market, we will be featuring a variety of new products and product concepts. From our respiratory continuum of humidification products, we will feature our Humidified High Flow segment of products for adults, pediatrics and neonates, including; Optiflow Nasal High Flow (Optiflow NHF) for adult and neonatal applications and Optiflow Trach High Flow (Optiflow THF). Optiflow NHF for adults and pediatrics, features our unique wide bore nasal interface that provides comfortable, humidified respiratory support with up to 50 liters per minute flow with minimal levels of system back pressure. The Optiflow THF is a unique tracheostomy adapter that provides the opportunity to deliver Optimal Humidity meeting the patient's inspiratory demand while keeping the stoma site dry. Another featured segment from our respiratory care continuum is our products for humidification of Non-Invasive ventilation including heated circuit kits and our line of vented full face and nasal masks. Fisher & Paykel NIV masks feature "bridge of the nose" vents that have been reported to reduce deadspace ventilation. The unique under the chin fit coupled with FlexiFit technology and wide area seal increases the likelihood of easy and quick fitting with a reliable seal. The full face mask also includes a combination anti-axphysiation/non-rebreather valve for added safety. From the Fisher & Paykel Neonatal products line, we will again feature the Neopuff Infant resuscitator, the original "T-Piece resuscitator," heated gas delivery systems and our unique resuscitation masks. The Neopuff promotes safe and effective ventilation during resuscitation by controlling delivery pressure, minimizing lung injury due to over distension. The resuscitation masks line includes sizes from 35mm, for the smallest micro-premie, to a 72 mm for term newborns and pediatrics. The wide flange seal requires minimal pressure to achieve a seal and is flexible to match any facial contour. At Fisher & Paykel Healthcare, we believe everyone should enjoy a good night's sleep. We've based our Obstructive Sleep Apnea business on this belief. To those who suffer from OSA and those who provide treatment for them, we bring SleepStyle, an innovative family of Auto-Adjusting and Continuous Positive Airway Pressure (Auto-Adjusting/CPAP) and interface solutions. The SleepStyle 200 Auto Series delivers outstanding clinical, patient-care and commercial results due to its innovative SensAwake technology and its unique ability to personalize sleep comfort to the needs of the patient. SensAwake uses flow to monitor patients' breathing patterns, senses the critical awake state and promptly reduces the delivered pressure to the most comfortable level. SensAwake together with the advanced auto-adjusting system personalizes treatment during sleep and awake states. SensAwake facilitates the return to sleep to increase sleep quality and ultimately improve therapy uptake. In addition, the Performance Maximizer software offers detailed efficacy reporting using recognized USB technology. From our Nasal interface product line, we are introducing a new generation of nasal masks The Zest Nasal Mask is small, quiet, and effortless to fit and use. The innovative design of the Zest Nasal Mask combines the Variable Thickness Silicone (VTS) technology, Easy-Clip Silicone Seal and Advanced Air Diffuser with proven technology that makes Fisher & Paykel Healthcare masks perform so well. We are also pleased to announce a new addition to our Full Face line of products, the Forma Full Face Mask. The all-new Forma Full Face Mask forms a superior seal and provides even more comfort with a greater range of movement through the active contouring of its new FlexiFoam Cushion. A new T-Piece adds stability to the stylized Mask Base, and works in harmony with the highly contoured Silicone Seal and Under-Chin Design to enhance sleep performance. With its ease of use and superior conforming seal, the Forma sets a whole new standard.

Apieron

FEATURED PRODUCTS: We plan to showcase the new Insight eNO System at the AARC. The Insight system measures exhaled nitric oxide, which is a marker of airway inflammation in people with asthma. It is a brand new medical device that is expressly designed for in-clinic application.

EDUCATIONAL OPPORTUNITIES: We plan to have several materials at the show to educate the attendees on this revolutionary new technology. It is currently being used by pulmonary care physicians and allergists, including several national clinics across the country. We are very excited to share the details of this technology for pulmonary labs everywhere and how people have benefited from it.

BOOTH PROMOS: We will be offering several special promotions to suit the varied needs that our customers have.

WHY STOP BY? With this technology you have the power to quantify airway inflammation with accurate eNO values; the power to visualize the inflammation status of your patients' airways and monitor the progression of their disease and how inflammation is changing over time; the power to optimize therapy, medication and to advance the overall management of asthma. Get the latest medical technology that is transforming asthma care now.

Index

The listings in this section are in the order received.

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