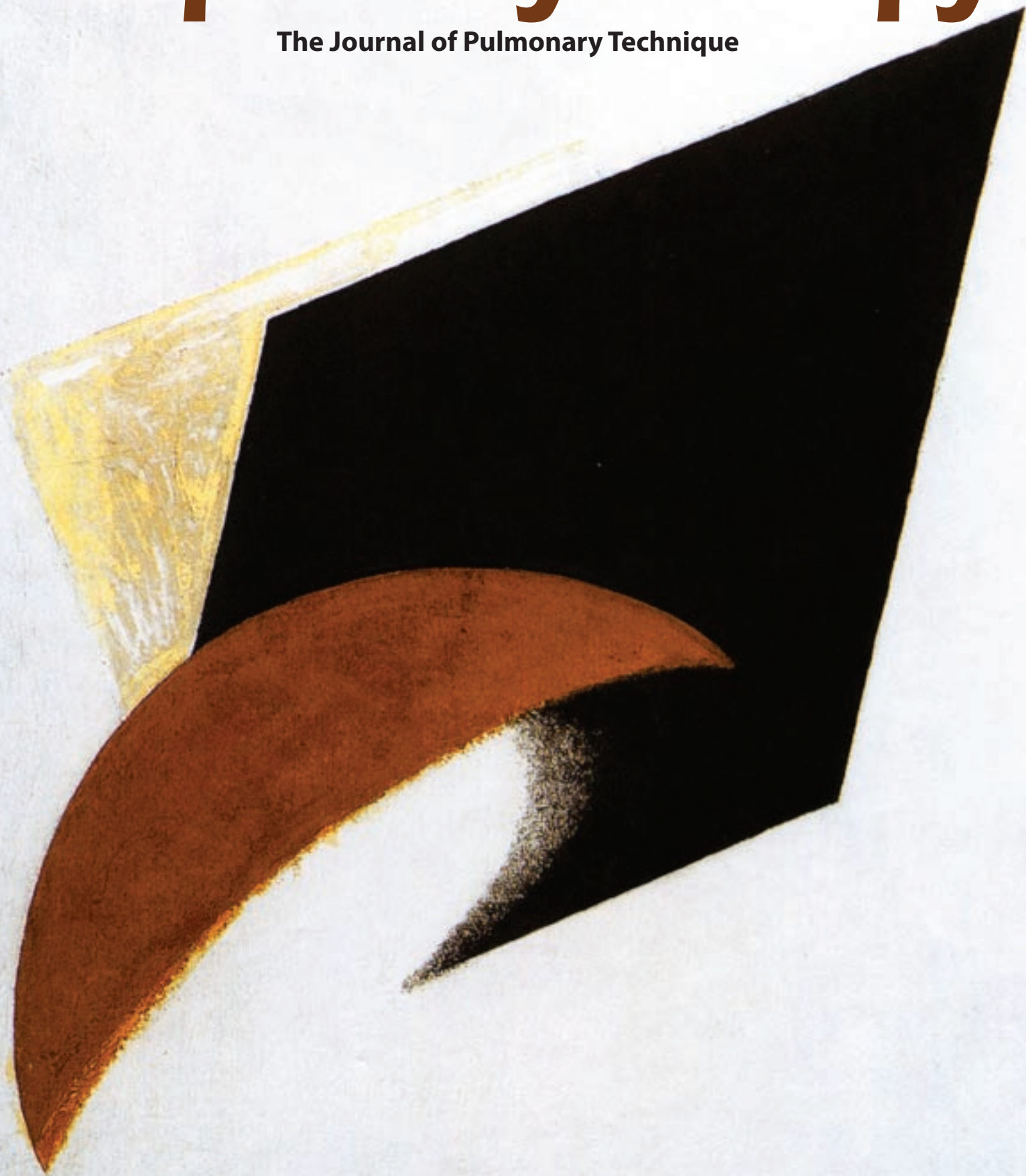


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* See, for example: Thille, A; Rodriguez, P; Cabello, B; Lellouche, F; Brochard, L; "Patient-ventilator asynchrony during assisted mechanical ventilation," Intensive care med., (226), 32:1515-1522, DOI 10. 1007/s00134-006-0301-8

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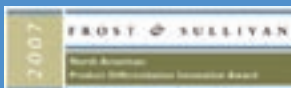


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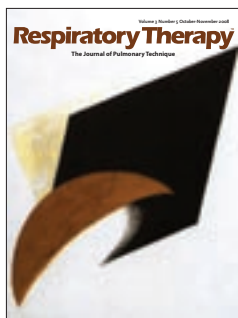


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Editorial

What Do You Care?

SARS, TB, Influenza—those who treat respiratory conditions are on the front lines of exposure to all kinds of danger—that's their job. And what do they think about it? A recent paper published in the online journal BMC Infectious Diseases sought to analyze the concept of "presumed consent" by which healthcare providers offer services to their patients, and the limits of consenting to risk and exposure. More than 300 frontline caregivers were questioned regarding their views and about the limits of occupational risk they'd be willing to assume.

Each year, the authors wrote, thousands of healthcare workers are adversely affected by psychological trauma stemming from months of anxiously awaiting the results of serological tests, tests made necessary due to potential infection incidents. The anxiety experienced by HCWs is related to the perception of risk from the incident and the resulting infection that may occur, and by the worry of what the reactions of others might be, such as colleagues, family, and friends, all who have to be informed. During this uncertain waiting period HCWs will frequently experience intrusive thoughts, problems concentrating, difficulty sleeping, frequent loss of temper, and a decrease in sexual desire, which can act as a catalyst to exacerbate any pre-existing and unresolved emotional issues. And if it turns out that the worker has indeed been infected by a contagion, the serious personal consequences to that worker can include the postponement of childbearing, damaged personal relationships, having to alter sexual practices, experiencing the side effects of prophylactic drugs, chronic disabilities, loss of employment, denial of worker compensation claims, possible need for a liver transplant, and premature death.

The idea of presumed consent implies that healthcare should be provided to patients who present risks to their caregivers, that contracting an infectious disease is part of the job, and that caregivers give their consent to this risk by *becoming* caregivers, though not without boundaries. But how much risk is too much? Of the healthcare providers surveyed, half stated that they understood that by choosing their profession they would be exposing themselves to an increased risk, 25% said they were unaware of any increased risks, but learned about it as part of their training, and a mere 6.5% said they didn't realize their risk exposure until they'd actually started to work. Thus, a clear majority knew what they were getting into. The percentage of participants who claimed that if they'd been aware of the risks earlier they wouldn't have chosen their profession was just 5%. The participants were also asked to react to the statement that, when people choose to practice these professions, they're required to accept all the attendant occupational hazards. More than half said there was a level where they didn't have to, and that certain exposures exceeded an acceptable level of risk. The aim of the study was to evaluate the claim that presumed consent constitutes the grounds for a moral duty to treat. The authors noted the mitigating conundrum that healthcare providers can't anticipate future levels of risk in their practice, and if there was little or no knowledge of a risk (such as the emergence of new types of tuberculosis that's resistant to treatment), then this mooted the premises of presumed consent. However, it can also be argued that the risk of uncertainty itself is a *de facto* part of the caregivers' assumed risk, and that it is never possible to be fully informed. Regardless, the premise of presumed risk is a shaky philosophical base for deciding acceptable levels of exposure. So how do caregivers decide this issue? The authors of the above study could only say that some new parameters for investigation need to be pursued, which isn't much of an answer. The authors do finally state that in terms of moral duty to provide care, "it seems that most HCWs are more concerned about the availability of protective measures than about whether they had been informed of a particular risk beforehand." And there is the answer. While healthcare providers are clearly aware of the risks inherent in their profession, they want to know that a risk exists, and what they can do to protect themselves.

Les Plesko, Editor

For a more detailed analysis, see the paper: "Can 'presumed consent' justify the duty to treat infectious diseases?" by Murat Civaner and Berna Arda, BMC Infectious Diseases 2008. You can access the article by going to BioMed Central and typing in the full title of the article.

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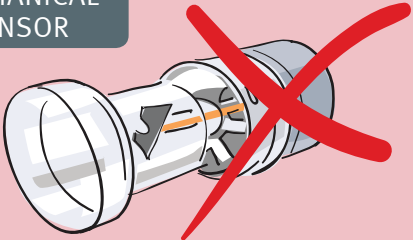
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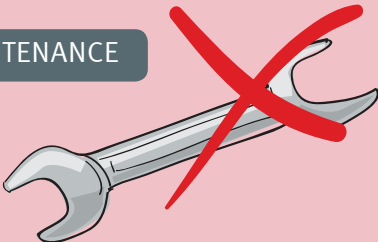
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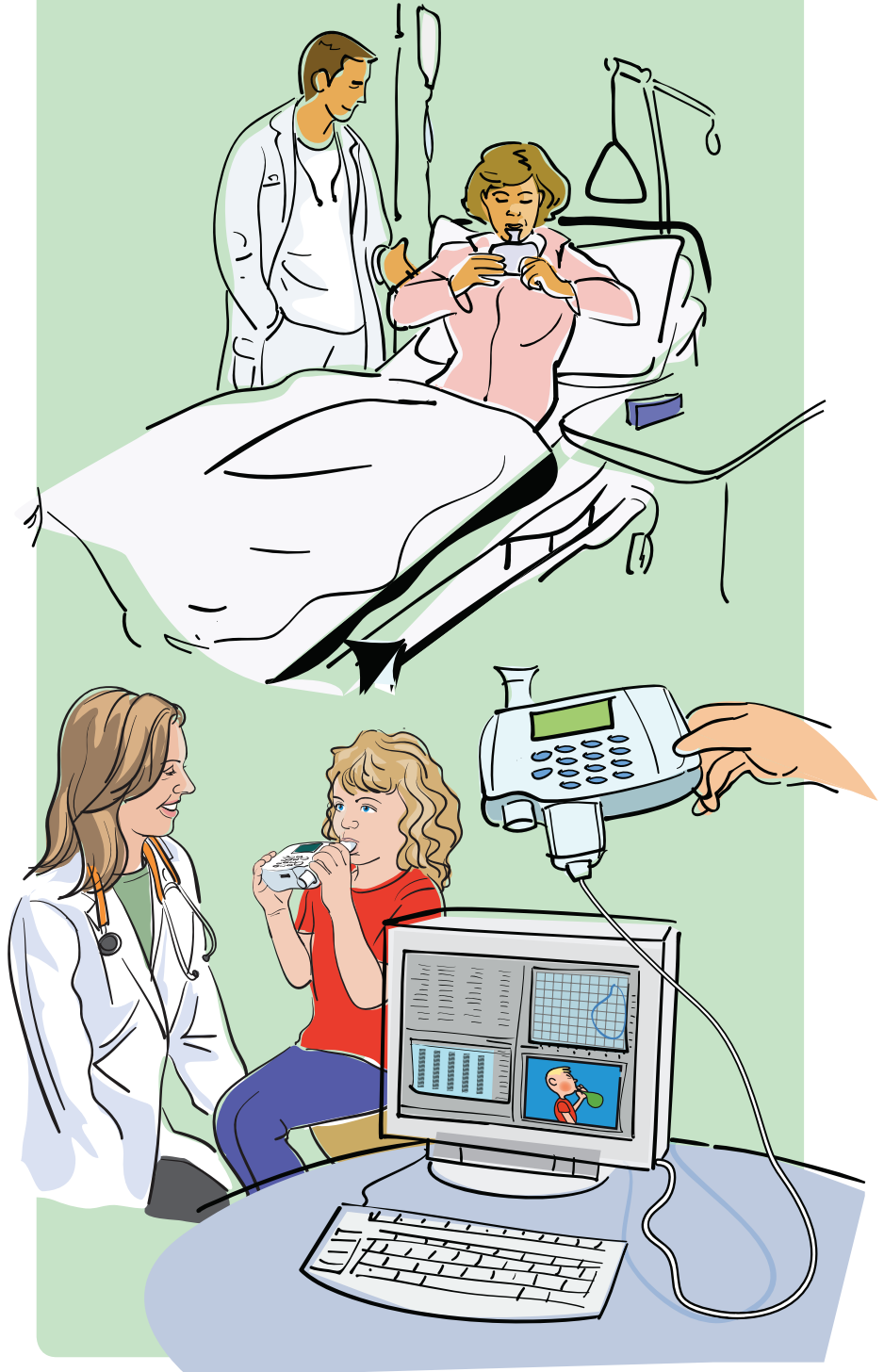
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News

□ October-November 2008

USE IT OR...

There are many studies that support the use of lung protective strategies in patients with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS). Yet, why do we underuse lung-protective ventilation (LPV)? "Failure to effectively implement evidence into clinical practice is one of the most important challenges in medicine."¹ In the April edition of *Respiratory Care*, Mikkelsen et al looked at this very problem. A retrospective cohort study was conducted using physician documentation to identify why LPV was not utilized in patients with ALI. LPV was defined as the use of tidal volume less than or equal to 7.5 ml/kg predicted body weight (PDW). Mikkelsen et al also looked at a sensitivity analysis with LPV defined as tidal volumes less than or equal to 6 ml/kg PDW. Eighty eight subjects were chosen by using the criteria defined by the American-European Consensus criteria for ALI. Of the 88 patients, only 75 were included in this study due to missing charts, expired, or no longer requiring mechanical ventilation.

This primary analysis revealed 32% of the subjects were utilizing LPV while only 16% used LPV transiently. Eight percent of subjects intended to use LPV but was not implemented. Other reasons why LPV was not used are as follows: metabolic acidosis (2.7%), change in clinical status (6.7%), diagnostic uncertainty (18.7%), and no documented explanation for why LPV was not used (16%).

The sensitivity analysis showed different results. Only 9.3% of the 75 patients were sustained on LPV while 16% used LPV transiently. The sensitivity analysis also showed an increase in intended LPV use, but failed implementation of 12%. Mikkelsen et al concluded "the majority of patients never received LPV at any point during the first 48 h of ALI, and that LPV, once initiated, is often discontinued."² They also stated, "Our study, the first to directly assess why physicians do not use LPV, suggests that uncertainty in making the diagnosis of ALI may be an important barrier to implementing and continuing LPV, and that physicians may prioritize limiting airway pressure to limiting VT."²

Closed loop mechanical ventilation can help improve the use of LPV. Adaptive Support Ventilation (ASV) employs lung-protective rules and adjusts the ventilatory pattern based on the patient's pulmonary mechanics and spontaneous respiratory activity to maintain preset minute ventilation (MinVol). MinVol is partitioned into targets for tidal volume and rate using the equation of Otis, based on the assumption that the optimal breath pattern results in the least amount of work of breathing such that the tidal volume applied results in lower plateau pressures being applied to patients in proportion to their degree of lung injury. By utilizing ASV in conjunction with PV Tools, LPV can be achieved 100 percent of the time.

References: 1. Institute of Medicine Committee on Quality of Health Care in America. *Crossing the Quality Chasm: A New Health System for the 21st Century*. Washington DC: National

Academy Press, 2001. 2. Mikkelsen MD, Mark E., Dedhiya MD; Pali M., Kalhan MD, Ravi; Gallop PhD, Robert J; Lancken MD, Paul N; and Fuchs MD, Barry D. Potential Reasons Why Physicians Underuse Lung-Protective Ventilation: A Retrospective Cohort Study Using Physician Documentation. *Respiratory Care*. April 2008; 53(4): 455-461. From the article, Lung-Protective Ventilation: How Often Do We Use It? by Justin Tse, RRT, NPS. Justin Tse is with Hamilton Medical. This article is reprinted from Hamilton's newsletter.

STAPH TEST

The FDA recently announced that it had cleared for marketing the first rapid blood test for Methicillin Resistant Staphylococcus Aureus (MRSA). This strain of staph bacterium has mutated over the years, becoming resistant to methicillin. The new test for MRSA cleared by the FDA is the BD GeneOhm Staph SR Assay. This test uses molecular methods to find out if a blood sample contains genetic material from the MRSA bacterium or the less serious staph bacterium. One big advantage of the test is that results are known within two hours versus having to wait more than two days. A clinical trial was done at five different locations prior to FDA clearance. During the trial, 100% of the MRSA-positive specimens were identified and more than 98% of the more common staph bacterium were identified. This test should only be used in patients with suspected staph infections. It should not be used to monitor staph infections as it does not qualify response to treatment. Test results should not be the sole basis for diagnosis of infection as it could reflect the presence of the bacteria in patients that have been treated successfully. The test does not rule out other complicating infections or conditions. The BD GeneOhm Staph SR Assay is manufactured by BD Diagnostics. Ref: <http://www.fda.gov/bbs/topics/NEWS/2007/NEW01768.html>. Provided by Melissa Turner, BA, RRT, Hamilton Medical.

LOOKING AHEAD

Patients who require prolonged acute mechanical ventilation (PAMV) are a large and resource-intensive population whose percentage increase in growth outpaces growth in the general US population and in overall hospital volume. A recent article published in *Critical Care Medicine* by Zilberberg M. et al, reported in Hamilton Medical's newsletter, projected the expected increase of adult PAMV cases through the year 2020. Patients requiring PAMV, defined as those requiring 96 or more hours of mechanical ventilation, have similar survival rates as those patients that require mechanical ventilation for ≤ 96 hours, yet those requiring PAMV consume approximately two thirds of hospital resources devoted to mechanical ventilation care. Because of this disproportionate resource utilization and shifting of United States demographics, it is helpful to be able to project growth in this patient population. Zilberberg M. et al projected that PAMV cases in the adult population will increase at a rate of 5.5% per year in the United States compared to just 1% growth per year in both the United States population and hospital admissions. This means that PAMV will more than double from approximately 250,000 cases in 2000 to 605,898 cases by the year 2020. The most rapid growth in PAMV can be expected among patients in the 45-64 age group, followed by the 18-44 age group, and then the 65-84 age group. Despite these age specific growth patterns, adult patients ≥ 65 years of age will continue to account for more than 50% of the adult PAMV population. In order to ensure resource development and allocation to take care of these patients, policy makers will need to factor this projected rapid growth in PAMV into

future resource and workforce planning. Furthermore, policy makers will have to deal with workforce shortages. Workforce shortages within the United States healthcare system, and more particularly within hospitals, are becoming a more and more prominent issue. It is projected that by 2020 there will be a shortage of more than one million nurses. Shortages of respiratory therapists, pharmacists, and intensivists are expected as well. Zilberberg M. et al concluded that due to the resource-intensive nature of these patients and the shifting of US demographics, strategies need to be developed to optimize care for these patients and to increase efficiency of healthcare delivery to this large and growing patient population. Reference: Zilberberg M. et al, Growth in adult acute prolonged mechanical ventilation: Implications for healthcare delivery, Crit Care Med Vol. 36, No. 5, 1451-55. Reported by Jeff Borink, BS, RRT, for Hamilton Medical.

CUFF 'EM

Jeff Borink writes in Hamilton Medical's recent newsletter about a recent pilot study by Poelaert et al, published in the Journal of Thoracic and Cardiovascular Surgery, which looked at whether the use of a polyurethane cuffed endotracheal tube could possibly reduce the risk of postoperative pneumonia after cardiac surgery. Microaspiration of contaminated supraglottic secretions past the endotracheal tube cuff is considered to be central in the pathogenesis of VAP. Better sealing of the upper trachea by the endotracheal tube cuff could possibly reduce this risk. Poelaert et al postulated that use of a polyurethane cuffed endotracheal tube would prevent early postoperative pneumonia by preventing this from occurring in a population of cardiac surgical patients. In this prospective, single-blind, randomized study, patients who were scheduled for routine or emergency cardiac surgery were divided into two groups. One group was intubated with a polyurethane cuffed endotracheal tube and the other group was intubated with the routinely used polyvinyl chloride cuffed endotracheal tube. A total of 134 patients were analyzed (67 in each group). Intensive care unit and hospital stays were not significantly different between the two study groups. Mortality was not different between the groups. However, the incidence of early postoperative pneumonia and empirical prescription of antibiotic therapy were significantly lower in the polyurethane group than in the polyvinyl chloride group (23% vs 42%, $P < .03$). Poelaert et al concluded that polyurethane cuffed endotracheal tubes can reduce the frequency of early postoperative pneumonia in cardiac surgical patients. Reference: Poelaert J. et al. Polyurethane cuffed endotracheal tubes to prevent early postoperative pneumonia after cardiac surgery: A pilot study. J Thorac Cardiovasc Surg 2008;135:771-776. The above is from Hamilton Medical's newsletter, by Jeff Borink, BS, RRT.

BOOM AND BREATH

Researchers at the University of Georgia and Emory University have discovered a link between thunderstorms and asthma attacks in the metro Atlanta area that could have a significant public health impact. While a relationship between thunderstorms and increased hospital visits for asthma attacks has been known and studied worldwide for years, this is the first time a team of climatologists and epidemiologists has ever conducted a detailed study. Researchers studied a database of more than 10 million emergency room visits in 41 hospitals in a 20-county area around Atlanta over an 11-year period, found a 3% higher incidence of visits for asthma attacks on days following thunderstorms. That seems insignificant, until one realizes that

3% equals quite a lot of people, out of the five million in the region, the researchers said. Then again, not all five million have asthma. However, in the US, 20-million do. While it's thought that thunderstorms clear the air, the researchers said winds from thunderstorms may create downdrafts that spread allergens. During the study period, there were 564 thunderstorm days, and 28,350 out of 215,832 emergency room visits for asthma occurred after a thunderstorm.

BONES OF NON-CONTENTION

Six-thousand year old bones excavated in Jericho are helping a joint Israeli-Palestinian-German research group combat tuberculosis. Researchers at the Kuvin Center or the Study of Infectious and Tropical Diseases at the Hebrew University of Jerusalem, are testing excavated bones for tuberculosis. Tuberculosis was well known in antiquity, and it's certainly hanging around, still causing three million deaths a year. Jericho was picked as the site for the researchers because TB is thought to come from first villages in the Fertile Crescent region about 10,000 years ago, and Jericho is one of the earliest towns on earth, dating back to 9,000 BC. By examining human and animal bones from this site, the researchers hope to see how the first people living in a crowded situation developed the diseases of crowds and how this affected the disease through changes in the DNA of both the microbes and the people. The bones used in this project were actually located in a box at Sydney University, and returned to Jericho, where they'll be studied along with new old bones. The research, sponsored by a grant from the German Science Foundation, will be conducted by the Hebrew University, Al Quds University and the Ludwig-Maximilians University, Munich. In Israel, researchers from both Al-Quds and the Hebrew Universities will devote their time exclusively to this project.

PASS THE SALT

Following a low-sodium diet doesn't have any effect on asthma, after all, according to a study by the University of Nottingham. A randomized, double-blind, placebo-controlled trial of 200 subjects compared the effect of changes in bronchial reactivity on asthma patients who followed a strict low-sodium diet and either received sodium supplements to approximate normal sodium intake of 80 mmol a day or a placebo for six weeks. Researchers hypothesized that the subjects on the low sodium intake would show improved clinical control of asthma symptoms based on a test of asthma activity, measures of lung function, asthma symptoms and use of asthma medication. However, no differences in any measures of asthma were found between the groups. This was the largest study to date about asthma and salt.

GUT TO CHEST

A microbial inhabitant of the human stomach may protect children from developing asthma, according to a new study among more than 7,000 subjects at NYU Langone Medical Center. While helicobacter pylori, a bacterium that has co-existed with humans for at least 50,000 years, may lead to peptic ulcers and stomach cancer, kids between the ages of 3 and 13 are nearly 59% less likely to have asthma if they carry the bug, the researchers report. H. pylori carriers in teens and children were also 40% less likely to have hay fever and associated allergies. The results are based on data gathered from 7,412 participants in the fourth National Health and Nutrition Survey conducted from 1999 to 2000 by the National Center for Health Statistics. The researchers noted that while asthma has been rising, the presence of H. pylori has been diminishing, due to antibiotics

and cleaner living conditions. Only 5.4% of children born in the 1990s were positive for *H. pylori*, and 11.3% of the participants under 10 had received an antibiotic in the month prior to the survey. When *H. pylori* is present, the stomach is lined with regulatory T cells that control the body's response to invaders. Without these cells, a child can be more sensitive to allergens. If a child does not encounter *Helicobacter* early on, the immune system may not learn how to regulate a response to allergens. Therefore, the child may be more likely to mount the kinds of inflammatory responses that trigger asthma.

PLACEBOS, PLEASE

People with asthma who use salmeterol are at a greater risk of non-fatal serious adverse events than those using placebos, according to a team of Cochrane researchers using data from 62,630 patients in 26 trials. Over a four to six month period, for every thousand people treated for asthma there were 45 who suffered a serious adverse event on regular salmeterol, compared to only 40 if a placebo inhaler was given. Over the last decade some researchers and practitioners have expressed anxieties that although salmeterol can relieve asthma symptoms, it could cause long-term problems. The authors recommend that people should follow the manufacturer's advice not to increase the dose of salmeterol during an exacerbation, and that salmeterol shouldn't be used as an alternative to inhaled corticosteroids.

PUKE AND PANT

Why people with asthma also suffer from GERD is the puzzle being solved by researchers at Duke University Medical Center. Studies have shown that anywhere from 50 to 90% of patients with asthma experience some aspect of GERD. Working with mice, researchers discovered that inhaling tiny amounts of stomach fluid that back up into the esophagus produces changes in the immune system that can drive the development of asthma. The researchers inserted minuscule amounts of gastric fluid into mice lungs, mimicking the human process of micro-aspiration, over a period of eight weeks. They compared these animals' immune systems with those of mice that were exposed to allergens but not the gastric fluid. The mice that had the gastric fluid in their lungs developed T-helper type 2 response, while the other mice mounted an immune reaction. The data suggest that chronic micro-aspiration of gastric fluid can drive the immune system toward an asthmatic response.

BIG SURPRISE

Immigrants from Southeast Asia, sub-Saharan Africa and parts of Latin America have high rates of active or latent tuberculosis, according to JAMA. CDC researchers analyzed data on TB among immigrants to the US from 2001 to 2006 and found that those from sub-Saharan Africa and Southeast Asia were at highest risk for the disease, with TB incidence of approximately 250 cases per 100,000 people. Immigrants from sub-Saharan Africa and Southeast Asia account for 22% of the foreign-born population but make up more than half of the TB cases among people born outside the US. In addition, TB cases among immigrants to the US increased by 5% from 1993 to 2006, accounting for 57% of all TB cases in the US in 2006. Researchers also found high rates of drug-resistant TB among immigrants from China, Peru, the Philippines and Vietnam. The CDC conducts an overseas screening process to detect active TB cases among people immigrating to the US, but about 30% of foreign-born people, including temporary workers, tourists, students and undocumented immigrants, don't undergo the process. Also, many latent TB cases do not become contagious

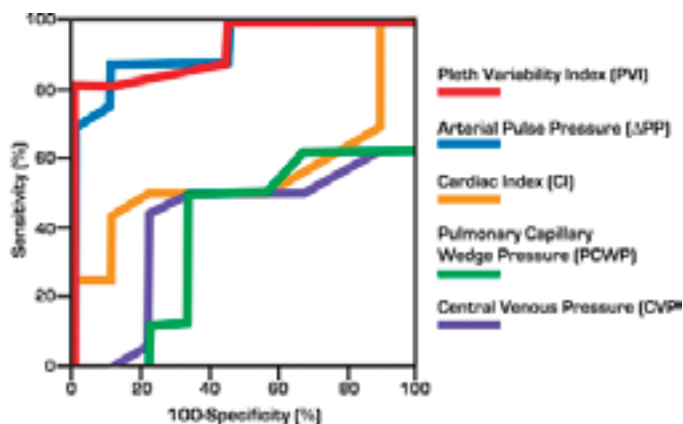
until after several years. (The above is from kaisernetwerk.org, © 2008 Advisory Board Company and Kaiser Family Foundation.)

FLUID RESPONSIVENESS

Masimo announced that a new clinical study, published in the June 2008 issue of the *British Journal of Anaesthesia*, concluded that under the study protocol Masimo's PVI measurement "can predict fluid responsiveness in mechanically-ventilated patients under general anesthesia." PVI is a new measurement available in the Masimo Rainbow SET technology platform that allows noninvasive, automated, and continuous monitoring of the variation in the pulse oximeter waveform amplitude during respiration.

In the study, a patient was defined as a "responder" if their cardiac index increased by 15% or more after administration of 500 ml of fluid. If cardiac index increased less than 15% after volume administration, the patient was defined as a "non-responder." Of the 25 patients evaluated in the study, 16 were considered responders and 9 were considered non-responders. PVI showed a similar accuracy (0.93 area under the curve, AUC) at predicting fluid responsiveness when compared to pulse pressure variation from an invasive arterial catheter (0.94 AUC) and superior accuracy when compared to central venous (0.42 AUC) or pulmonary capillary wedge pressure (0.40) (Figure 1). "PVI demonstrated high accuracy in discriminating fluid responders from non-responders—providing a unique opportunity to better manage a patient's fluid volume to optimize cardiac performance and organ perfusion," stated Maxime Cannesson, MD, lead researcher and anesthesiologist, Louis Pradel Hospital in Lyon, France. "Fourteen of the 16 patients who responded to fluid administration with a cardiac index increase of 15% or more had a PVI value of >14% before volume administration. All 9 patients who did not respond to fluid administration with a cardiac index increase of 15% or more had a PVI value of <14% before volume administration." According to a recent clinical study published in *Critical Care*, monitoring pulse pressure variation with an arterial catheter showed an ability "to decrease the duration of hospital stay, mechanical ventilation, and post-operative morbidity in patients undergoing high-risk surgery." While pulse pressure variation from an arterial pressure catheter is considered the gold standard for assessing fluid responsiveness, only a small minority of patients receive this type of catheter during surgery due to its invasiveness, complexity, and risk. In Dr Cannesson's study, Masimo PVI showed similar accuracy as pulse pressure variation at predicting fluid responsiveness but offers clinicians an easy and noninvasive assessment of fluid responsiveness in any patient undergoing surgery by simply using their existing noninvasive Masimo SpO₂ sensor with Masimo Rainbow SET monitors. Sources: Michard F, Teboul JL. Predicting fluid responsiveness in ICU patients: a critical analysis of the evidence. *Chest*. 2002 Jun;121(6):2000-8; Joshi G. "Intraoperative Fluid Restriction Improves Outcome After Major Elective Gastrointestinal Surgery." *Anesthesia Analgesia* (2005) 101:601-5; Cannesson M, Desebbe O, Rosamel P, Delannoy B, Robin J, Bastien O, Lehot JJ. "Pleth variability Index to Monitor the Respiratory Variations in the Pulse Oximeter Plethysmographic Waveform Amplitude and Predict Fluid Responsiveness in the Operating Theatre." *British Journal of Anaesthesia* 2008; 0: aen133v1-7; Lopes MR, Oliveira MA, Pereira VO, Lemos IP, Auler JO Jr, Michard F. "Goal-directed Fluid Management Based on Pulse Pressure Variation Monitoring During High-risk Surgery:

A Pilot Randomized Controlled Trial.” *Critical Care* 2007; 11: R100.



Adapted from Carsson M et al: *British Journal of Anaesthesia*, 2006 Jun 2 (Epub ahead of print)

Figure 1. Receiver Operator Characteristic (ROC) Curve for Diagnostic Accuracy of PVI Compared to Invasive Parameters

PRODUCTS

TESTING ONE TWO THREE

ARUP Consult is a first of its kind, no-cost resource for healthcare professionals, nurses, clinical decision makers and physicians in any diagnostic capacity. It supplements the diagnostic process of common and esoteric diseases or conditions by supplying current lab test suggestions and interpretations of more than 1,500 lab tests, more than 50 algorithms, links to PubMed, recommendations congruent with national guidelines and concise diagnostic advice. Through updates occurring bi-monthly, its information stays current with ever-evolving lab tests and discoveries, providing healthcare professionals accurate diagnostic knowledge at the point of care. ARUP Laboratories (a wholly-owned entity of the University of Utah) has produced ARUP Consult—a comprehensive laboratory test selection support tool to provide physicians with instant, up-to-date access for test ordering information. Since its introduction, ARUP Consult content and functionality has been updated every eight weeks. ARUP's goal was to put reliable and up-to-date laboratory testing and interpretation information in the hands of physicians at or very near the point of patient care. ARUP gives clinicians a single source of medical content necessary for diagnostic decision making. It can be accessed from any locale. Algorithms provide physicians with a visual, systematic process for diagnosing and monitoring a disease state, thus eliminating a shotgun approach to testing. Content is organized by disease categories, which allows the physician to diagnostically process the patient's symptoms and to differentiate among other possible diseases, and determine the appropriate laboratory tests to request for evaluating the patient. The site provides linked references to key journal articles, national guidelines, and other web sites. This resource is available at no charge; registration is not required and anyone with Web access can utilize the guide. ARUP combines several types of reference tools in one location and provides a laboratory tests available guide, diagnostic testing guide—detailed algorithms which serve as testing roadmaps for complex diseases and conditions, a disease states summary—a succinct, bulleted summary of various disease states along with diagnostic guidance, and a reference locator. The content is compiled and drafted by experts drawn from the University of

Utah's Department of Pathology and ARUP Laboratories' medical directors as well as a current practicing clinician. ARUP offers varied browsing and searching options. To see ARUP, go to arupconsult.com.

QUALITY IS NUMBER 1

Siemens Healthcare was recently ranked number one in service repair quality and service response time and received top vendor rankings in multiple imaging fields, including computed tomography (CT), positron emission tomography-computed tomography (PET-CT), and radiology information systems (RIS), according to the latest Quarterly User Satisfaction Report from data resource organization MD Buyline.

The report's 2008 second quarter rankings show that Siemens ranked first for service repair quality and service response time in its CT, PET-CT and cyclotrons, single photon emission computed tomography (SPECT) and SPECT-CT, mobile C-arms, and urological imaging service areas. Also of note are individual top ratings for the following Siemens products: magnetic resonance and mammography systems in the Installation/Implementation category, cardiology PACS in the "System Performance" category, and PACS in the "Integration" category. The MD Buyline Quarterly User Satisfaction Report determines vendor rankings based on user satisfaction composite ratings. The Siemens Healthcare service organization in the United States includes more than 1,300 Customer Service Engineers (CSEs) in eight regional zones. CSEs are supported by a parts distribution network which replenishes inventory daily at five regional parts depots and 12 local depots. The UPTIME Service Center operates 24 hours a day, 365 days a year, and handles more than two million calls annually. Contact siemens.com/healthcare.

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. Contact vtherm.com.

LIFE SUPPORT

RF Technologies is sponsoring a new training course on clinical safety. Following the guidelines set forth by the American Heart Association, the course certifies nurses in Advanced Cardiac Life Support specific to pregnant or newly delivered patients. In 2009, all OB nurses will need to be certified in ACLS. This course satisfies this requirement and is more pertinent for OB nurses as it was developed with them in mind. Upon completion of the two-day provider course, a nurse is certified and receives an AHA ACLS Provider Card. In addition, continuing education credits are awarded. A third day of training is available, which prepares new instructor candidates to teach the ACLS OB course. RF Technologies is partnering with the clinical instruction team from St Luke's Meridian Medical Center of Boise, ID, to provide the content and perform the actual training. RF Technologies was on-site at the AWHONN Convention to review ACLS OB courses and to discuss how

hospitals could implement the program. A second ACLS OB course was hosted by Waukesha Memorial Hospital ProHealth Care in Waukesha, WI. RF Technologies is a leading provider of comprehensive, integrated RFID Safety and Security systems, Wi-Fi RTLS systems, and healthcare enterprise solutions, including Code Alert Wandering Management, Wireless Call and Fall Management Solutions, Safe Place ED and Infant Security Solutions, and PinPoint RTLS Location-Aware Solutions. RF Technologies has been providing wireless RFID security systems to healthcare since 1987 and has an install base of over 10,000 healthcare facilities. Contact rft.com.

YOUR ORDER'S READY

Children's Healthcare of Atlanta, one of the country's leading pediatric healthcare systems, successfully implemented computerized physician order entry, a major component of the organization's electronic medical record (EMR) system. The new CPOE tools allow physicians, nurses and other clinicians to directly enter medication, respiratory and nursing orders themselves, expediting care and improving safety. In addition to knowing what medications a physician is ordering for a patient, Children's pharmacists now see the child's weight, medical condition, drug allergies and what other prescriptions the child is taking. Moreover, all of the information is legible because handwriting is no longer necessary. Children's Healthcare of Atlanta is implementing a robust and highly regarded EMR system developed by Epic Systems Corp. Children's is one of only a few top-tier children's hospitals to achieve a complete inpatient electronic record system. Other components of the EMR system include nursing documentation, physician documentation, medication administration and the electronic tools Children's pharmacy and radiology staff use to perform their day-to-day operations. Children's EMR system enables physicians to securely access patient information as soon as it is entered, regardless of where they are located in the hospital or even if they're logging in from their home, physician practices, or anywhere in the world. It allows employees and physicians to access the data simultaneously, including staff in other departments such as pharmacy, radiology and the lab, and enables staff to access information from all patient visits to Children's, regardless of the facility or past date. By 2010, Children's plans to integrate its current EMR tools with several others that it will implement in various outpatient and specialty care areas. Each software application is built to share a single storage area combining patient charts, physician orders, clinical notes, pharmacy information and other data. Contact choa.org.

FREE BIRD

OxygenToGo, the leader in direct-to-traveler oxygen services, announced their research report findings indicating that airlines can save money by reducing the onboard weight of equipment for oxygen-dependent travelers. Using market and in-house data, OxygenToGo concluded that using portable oxygen concentrators (POCs) instead of traditional oxygen tanks reduce the weight of oxygen equipment by at least 70% on short-haul flights and almost 85% on long-haul flights. With the high price of aviation fuel, these savings in weight correspond directly to a cost savings. In the near future, the demand for oxygen during travel is expected to rise sharply as physicians prescribe oxygen for both a broader range of medical ailments and the Baby Boomers who are preparing to retire and travel. These factors will dramatically increase the number of both rented and owner-provided POCs onboard aircraft. OxygenToGo offers a short-term rental program to assist airlines and their passengers

in easily obtaining a POC. Travelers in need of a POC will be directed to OxygenToGo via the airline's Web site or customer service staff. OxygenToGo has licensed respiratory therapists and board-certified physicians available at all times to ensure an appropriate match between passenger and equipment, as well as around-the-clock customer support for any technical or medical problems that the passenger may encounter. The POC is delivered to the passenger's home prior to departure, and OxygenToGo bills the fees directly to the passenger, removing the airline from all financial or logistical burdens. Contact oxygenotogo.com/airlines.

ON THE MOVE

Inovo Inc announced today that it has completed its relocation of CHAD Therapeutics' production and sales and marketing functions from California to Naples, FL. CHAD Therapeutics has been the leading innovator in the field of oxygen conservation since the introduction of the first conserving device in 1983. Today, CHAD offers the broadest line of electronic, pneumatic and disposable conservers on the market, and is uniquely positioned to meet the needs and preferences of a wide range of oxygen patients. Inovo has been a leading manufacturer of both regulators and conservers for the private-label market for over 10 years. Contact chadtherapeutics.com.

CHECKING IN

Smiths Medical PM, Inc offers the BCI Capnocheck capnometer. Unlike other capnometers, the Capnocheck capnometer does not need routine calibration. Powered by two AAA batteries, the device has multiple applications including intubation verification, an indicator for return of spontaneous circulation, routine airway management, ventilator transport and weaning. Unlike colorimetric and other qualitative mechanical devices, the Capnocheck capnometer provides a fully quantitative numeric value that is now recommended in the American Heart Association (AHA) 2005 guidelines. During resuscitation the Capnocheck capnometer can be an effective noninvasive indicator of cardiac output, CPR effectiveness, and indicator for return of spontaneous circulation. The device's simple operation and accuracy make it an invaluable tool in all areas of clinical practice. Contact (800) 558-2345, smiths-medical.com.

GAIN ON PAIN

Draeger Medical Inc announced the implementation of its Innovian Anesthesia information system at Walter Reed Army Medical Center's (WRAMC) new Acute Pain Medicine Center. The Draeger Medical anesthesia system will be used to monitor patient vital signs and create a real-time electronic medical record. The Acute Pain Medicine Center at WRAMC is transforming how the military treats pain by introducing regional anesthesia, whereby the use of high-tech nerve-blocking techniques prevents pain signals from reaching the patient's brain. This alleviates localized pain and prevents the development of maladaptive nerve pathways, which have the potential to cause chronic pain issues. Innovian Anesthesia integrates near real-time, life-critical information from patient monitoring, medical therapy devices and other ancillary information systems and gives clinicians fast access to patient data, which can minimize the duplication of efforts that often occurs with paper record systems. The Innovian technology improves the user's ability to monitor and document procedural events and notes as well as patient vital signs. Minimizing the time required for post-op notations allows physicians to treat more patients and frees anesthesiologists to focus on the patient instead of

documentation. Additionally, Innovian functions as a valuable research tool. Together with WRAMC's clinical question module, physicians can enter research questions for Innovian to track and compile data from all procedures. Contact draeger.com.

SAFETY FIRST

Masimo announced the first installation of the Masimo Patient SafetyNet remote monitoring and clinician notification system outside of a hospital setting. The East Tennessee Respiratory Center at Hillcrest North, a skilled nursing facility in Knoxville, TN, installed the Patient SafetyNet system after Respiratory Support Services (RSS), the center's respiratory care providers, outlined the significant clinical benefits that were possible with the system. After installation, the staff noticed an immediate reduction in false alarms by more than 60% and a marked reduction in hospital readmissions and acute care transfers, while the effectiveness of the ventilator weaning program and clinical efficiency has improved. Patient SafetyNet provides a new level of safety to patients in settings that preclude the level of direct surveillance required and recommended to preempt adverse events. Contact masimo.com.

IN AGREEMENT

Hamilton Medical, Inc has signed an agreement with Premier, one of the largest group purchasing organizations in the United States. Hamilton Medical's three-year agreement offers all Premier members access to contracts for Hamilton Medical's complete ventilation line. Owned by not-for-profit hospitals, Premier operates one of the leading healthcare purchasing networks and the nation's most comprehensive repository of hospital clinical and financial information. A subsidiary operates one of the nation's largest policy-holder owned, hospital professional liability risk-retention groups. Premier is working with the United Kingdom's National Health Service North West and the Centers for Medicare & Medicaid Services to improve hospital performance. Headquartered in San Diego, Premier has offices in Charlotte, NC, Philadelphia and Washington. For more information, visit premierinc.com. For more about Hamilton Medical, visit hamilton-medical.com.

STAT

A new software enhancement for Nova StatStrip Glucose and StatSensor Creatinine point-of-care monitoring systems allows off-line entry of POC test results for immediate data capture. With the enhanced NovaNet instrument manager software, operators can use StatStrip touchscreen to manually enter virtually any off-line POC test result, such as pregnancy or urinalysis, and use the meter as a POC communication device to transmit the information to the hospital's electronic database. The off-line entry capability saves time and labor compared to manually charting the result and then having to enter it later into the database. Contact novabio.com.

APPROVED

Actelion Ltd announced that Tracleer (bosentan), a dual endothelin receptor antagonist, has been approved in the European Union for the treatment of patients with mildly symptomatic pulmonary arterial hypertension (PAH WHO functional class FC II). Since 2002, Tracleer has been approved and available in the European Union for PAH patients with WHOFC III. Tracleer is the first PAH treatment ever to be investigated in a clinical study that exclusively enrolled patients with mildly symptomatic WHO FC II. This 185-patient randomized, double-blind, placebo-controlled study provided the

basis for this EU approval. The results from EARLY (Endothelin antagonist trial in mildly symptomatic PAH patients) published in *The Lancet*, document the relentlessly progressive nature of PAH, even in its early stages and highlight the need for earlier treatment and intervention in PAH management. The key results of the EARLY study were: PVR improved significantly, with a reduction of 22.6 after six months of bosentan compared with placebo. 6MWD increased by a mean of 19 meters. A significant 77% risk reduction in time to clinical worsening was seen after six months of bosentan treatment compared with placebo.

GET SMART

MAQUET, Inc recently sponsored a respiratory care symposium in conjunction with The California Society of Respiratory Care. Over 400 participants attended the event in downtown Los Angeles, making it the most widely attended MAQUET symposium to date. Topics pertained to respiratory care and the symposium was approved for 7 credit hours by the California Society for Respiratory Care. Among the speakers were Jonathan Marinaro MD from the University of New Mexico, Juan Boriosi MD from the University of California San Francisco as well as other doctors and RRTs who spoke on topics ranging from Bi-Vent ventilation and lung recruitment to law and professional ethics. Angel Pelayo, RRT and Lead Clinical Specialist for MAQUET spoke about the evolution of the company's NAVA technology, which allows the patient's own breathing and respiratory center in the brain to control the need for ventilation. The Neurally Adjusted Ventilatory Assist technology is available as an option on the company's SERVO-i ventilators. Contact MAQUETusa.com or MAQUET-training.com.

VEST-ED INTEREST

Hill-Rom announced it has received a 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 System is intended to help patients with respiratory conditions clear airway secretions. The 2008 Therapy Times award recognizes "products that—through their innovation, practicality and usefulness in the field—have had the greatest influence on today's therapy profession." Therapy Times is a multidisciplinary online resource for therapeutic professionals. "The Wrap SPU Vest provides respiratory therapists with a disposable option that is easy to fit, quick to place, and cost-effective," said Rollie Kitchens, manager, Global Strategic Marketing, Hill-Rom Respiratory Care. Contact hill-rom.com.

SPOTLIGHT ON BLOOD GAS

CO-OPERATING

Masimo Rainbow SET Pulse CO-Oximetry, the first-and-only technology platform capable of continuously and noninvasively measuring total hemoglobin (SpHb), provides real-time confirmation of hemoglobin levels, which may enable more efficient transfusion management during surgery, more timely detection of occult bleeding in ICU and trauma, and real-time anemia detection in any clinical setting. And, with additional noninvasive measurements available on the same platform—including carboxyhemoglobin (SpCO), methemoglobin (SpMet), oxygen content (SpOC), perfusion index, and pleth variability index (PVI), in addition to oxyhemoglobin (SpO₂), and pulse

rate—earlier detection and treatment of other potentially life-threatening conditions may be possible. Contact masimo.com, (800) 257-3810.

QUICK AND COMPACT

The Stat Profile Critical Care Xpress (CCX), from Nova Biomedical, measures blood gases, electrolytes, chemistry, hematology, and on-board co-oximetry in a single, compact analyzer. Individual tests include pH, PCO₂, PO₂, SO₂%, hematocrit, hemoglobin, sodium, potassium, chloride, ionized calcium, ionized magnesium, glucose, BUN, creatinine, lactate, and bilirubin. CCX can provide a full 20-test profile from a single 210-microliter sample in just 2 minutes, with simple push-button operation. CCX offers a number of innovative time and labor saving features, including automated maintenance, snap-in sensor and reagent cartridges, and on-board, automated controls. Integrated on-board data management software allows data capture, manipulation, and reporting, and simplifies regulatory compliance. Contact novabio.com, (800) 458-5813.

OPTIMUM

OPTI Medical Systems, Inc manufactures the OPTI line of portable analyzers for measuring time sensitive diagnostic assays including blood gas, electrolytes, ionized calcium, measured SO₂, tHb, and glucose. With the OPTI CCA-TS analyzer, obtaining accurate blood gas results is fast, easy and convenient. It's ideal for giving respiratory therapists and other clinicians a flexible solution for performing blood gas tests, on the bench top or at the bedside. It features the assays most needed by hospital clinicians, simple intuitive operation, and can be integrated with any HIS/LIS. Patented optical fluorescence technology virtually eliminates maintenance costs, test delays, and downtime. Contact (800) 490-6784, optimedical.com.

FAST RESULTS

The epoc Blood Analysis System is the first truly cost effective, enterprise-wide, point of care testing solution able to deliver caregivers lab equivalent, blood gas and electrolyte results at the bedside in just 30 seconds. The system is comprised of a portable epoc Reader and Host Mobile Computer, web-based epoc Data Manager and single-use epoc Test Cards. epoc System features include room temperature storage of test cards barcoded for quality and inventory management, internal, automated quality control, and secure, wireless capture and transmission of patient and quality test records to the epoc Data Manager and hospital LIS/HIS via HL7 interface. Contact epocal.com.

OXIMETRY ROUNDUP

IT'S A GEM

Instrumentation Laboratory's GEM Premier 4000 is the revolutionary critical care analyzer (BG, Electrolytes, Metabolites, Glu, Lac, Hct, tHb, O₂Hb, COHb, HHb, MetHb, sO₂, BUN, Creat, Total Bili, HCO₃⁻) with a complete, onboard CO-Oximetry panel for point-of-care and centralized testing. Using the IL 682 as a reference standard, the GEM Premier 4000 with integrated CO-Oximetry, fully analyses the sample, providing lab-quality results anywhere a hemoglobin panel is required. Self-contained cartridges incorporate all components for patient testing and are maintenance-free. Enhanced Intelligent Quality Management (iQM) on the GEM Premier 4000 includes CO-Oximetry parameters and automates quality control, continuously detects, corrects and documents, to assure

quality results and compliance, 24/7, regardless of operator or testing location. (The BUN, Creat, Total Bili and HCO₃⁻ are in development). Contact ilww.com.

SEEING STARS

Recently, the new E! Entertainment reality show called "Living Lohan" showed the Rad-57, by Masimo, being used on Ali Lohan (Lindsay's sister) after a small electrical fire at their home. Here's the link to watch it yourself: <http://www.youtube.com/watch?v=GyZU4pOG0z0>. Fast forward to 6:26 and you will see the firefighter pulling out the Rad-57 and at 6:30 you hear it beeping.

Is Pulse CO-Oximetry, invented by Masimo Corporation, now becoming a paramedic standard of care? Yes, the use of handheld noninvasive Pulse CO-Oximetry has just appeared in a significantly expanded chapter of the new 2009 edition of "Brady Paramedic Care, Principles and Practice." Published by Brady/Prentice Hall Health, this textbook is used for paramedic training in 95% of all programs worldwide, which establishes Pulse CO-Oximetry as a paramedic standard of care for noninvasive carbon monoxide (CO) screening and measurement. In this latest edition, the chapter covering the topic of carbon monoxide poisoning now includes this paragraph: "Because signs and symptoms of CO poisoning are so vague and nonspecific, CO exposure and poisoning is easy to miss. Failing to detect and diagnose CO poisoning can result in the patient being allowed to return to the contaminated environment with devastating outcomes. Missed CO poisonings are a particular area of legal liability for fire and emergency personnel. Because of the associated risk, and because of the insidious nature of CO poisoning, the use of CO-oximetry should be routine for all fire service and EMS personnel (Procedure 8-1)." It includes a photo of the Masimo Rad-57 next to this paragraph: Do you know about the new national standard concerning Carbon Monoxide (CO) screening? NFPA 1584 issued a new national standard establishing that "any firefighter exposed to CO or presenting with headache, nausea, shortness of breath, or gastrointestinal symptoms be measured for CO poisoning using a Pulse CO-Oximeter." The National Fire Protection Association (NFPA) Section 1584 sets the industry standard on the Rehabilitation Process for Members During Emergency Operations and Training Exercises.

NAEMT issued official guidance to NAEMT members and EMS professionals nationwide in late December 2007, calling for the development of written policies and procedures, at the state and local EMS levels, to implement "routine field screening protocols for the detection of elevated carbon monoxide (CO) levels in the blood of any patient presenting with suspected exposure or symptoms" by all field EMS personnel as a way to improve patient care and protect the public from the "significant public health hazard" of carbon monoxide. The National Association of Emergency Medical Technicians represents more than 25,000 paid and volunteer EMS workers from across the United States and 63 foreign countries who provide on-the-scene emergency care to populations around the world.

IAFF issued official guidance to 4,300 local union presidents in the United States and Canada in late November 2007, calling for routine "carbon monoxide (CO) screening by Pulse CO-Oximetry" for all fire fighters potentially exposed to CO and presenting with headache, nausea, shortness of breath, or gastrointestinal symptoms. The International Association of

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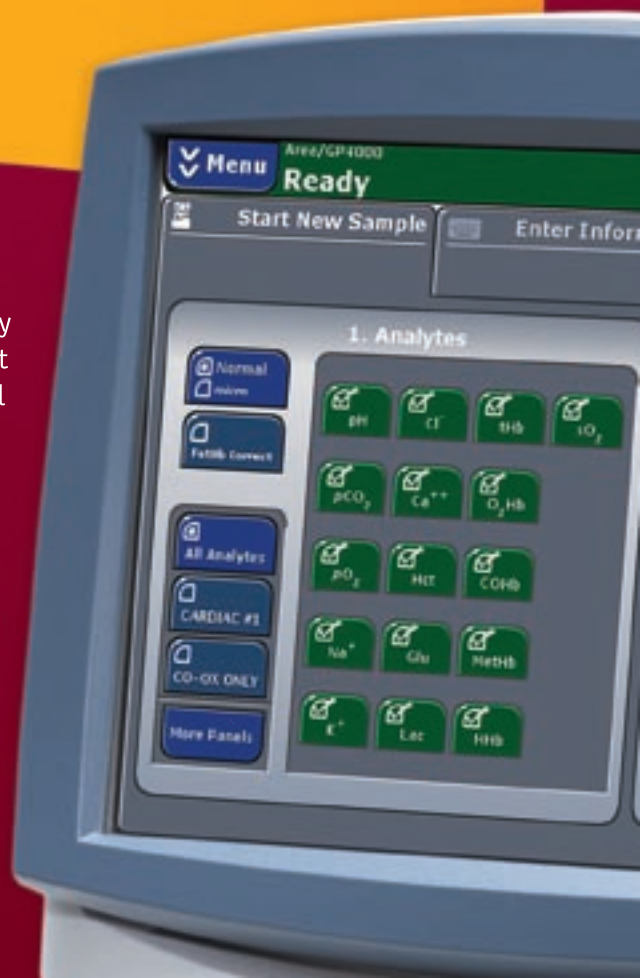
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Introducing the new GEM Premier 4000. Simply. Revolutionary.

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.

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Instrumentation Laboratory is a company of Werfen Group IVD.

Fire Fighters represents more than 287,000 (unionized) full-time professional fire fighters and paramedics who protect 85 percent of the nation's population.

NAEMSE issued official guidance to all its members in early November 2007, advocating carbon monoxide screenings for patients presenting with any of the signs and symptoms of carbon monoxide poisoning or suspected exposure. The National Association of EMS Educators is a professional trade association dedicated to quality EMS Education.

The National Academy of Clinical Biochemistry recommends that "clinicians routinely provide POCT of HbCO by CO-oximetry to screen patients with flu-like symptoms or headache in the emergency department for occult CO poisoning, particularly in communities where combustion is used for heating during the heating season. We found at least fair evidence that POCT of HbCO by CO-oximetry will lead to a correct and timely diagnosis of CO poisoning in patients who otherwise would have been missed." According to A.J. Heightman, editor in chief of *The Journal of Emergency Medicine*, recent carbon monoxide-related patient deaths "illustrate why EMS and fire response units, as well as hospitals and clinics, should have available to them the Masimo Rad-57." He added that widespread use of the technology would result in "minimizing the potential failure to detect CO poisoning and/or the misdiagnosis as food poisoning or flu, and also eliminating premature ED discharge that could result in patient deaths."

The Masimo Rad-57 Pulse CO-Oximeter offers noninvasive measurement of CO levels and enables on-site diagnosis of CO poisoning and the severity (no need to take blood and wait for lab results); rapid identification of necessary medical intervention/therapy to avert or minimize long-term health consequences of CO poisoning; more efficient management of care and triage of patients (those with critical CO levels can be immediately transported to hospital while non-critical CO levels can be treated at the scene with oxygen); and reduction in cost of care for CO-exposed patients by limiting unnecessary tests/diagnostics and getting to the proper diagnosis/treatment faster. Contact masimo.com.

PRODUCT REVIEW: WIRELESS OXIMETRY

The only wireless oximeter to meet all of the American Thoracic Society (ATS) guidelines for the Six-Minute Walk Test (6MWT), the NONIN Avant 4000 provides real-time monitoring without immediate patient contact. Conducting the 6MWT with the Avant 4000 allows patients to move at their own pace, resulting in a more accurate clinical evaluation. The technologist is able to focus more attention on the test administration while still monitoring the patient, resulting in decreased repeat testing and improved patient safety.

Clinical Setting: Cleveland Clinic is a not-for-profit, multi-specialty academic medical center that integrates clinical and hospital care with research and education. Founded in 1921, Cleveland Clinic was developed by four renowned physicians with a vision of providing outstanding patient care based upon the principles of cooperation, compassion and innovation. Today, Cleveland Clinic is one of the largest and most respected hospitals in the United States and worldwide. With over twenty physicians, the Pulmonary Institute treats a wide variety of lung disorders including asthma, chronic obstructive pulmonary disease, sarcoidosis, histoplasmosis, pulmonary fibrosis and

pulmonary hypertension. The Pulmonary Function Laboratory at the main campus is comprised of seven testing rooms and a staff of eight pulmonary function technologists who are respiratory therapists specializing in diagnostic testing. In 2006, this staff administered a total of 23,000 procedures on over 12,000 patients. Among these procedures are a variety of tests involving pulse oximetry, including assessment of oxygen saturation at rest and with exercise, titration of supplemental oxygen, altitude simulation tests and 6MWT.

The 6MWT is a simple, objective procedure that assesses the sub-maximal level of functional capacity. Pulse oximetry during a 6MWT provides valuable information about improvement or worsening of the patient's condition as well as information about when to terminate the test for safety reasons. ATS guidelines for the 6MWT call for the pulse oximeter to be lightweight (less than two pounds), battery powered and held in place so the patient does not have to hold or stabilize it.¹

The clinical protocol for the 6MWT at Cleveland Clinic is to attach the pulse oximeter sensor using either a digit or a forehead reflectance sensor and have a technologist carry the oximeter while walking just behind the patient. The technician also carries a stopwatch and a lap counter.

Clinical Solution: All this changed in 2006 with the evaluation of the NONIN Avant 4000 Bluetooth Wireless Oximeter. With this unique device, a module with pulse oximeter sensor attached is worn on the patient's wrist or forearm or can be placed in a pocket. Pulse oximetry results are transmitted to a table top display which can be placed anywhere within a 30 foot radius. The wrist module unit weighs 4.4 ounces and does not impede rapid walking.² Free from the tether of the sensor to oximeter cable, the technologist is able to focus more attention on test administration while still monitoring the patient.

Clinical Use/Implementation: The Avant 4000 has all of the standard features one expects from a clinical pulse oximeter: pulse signal quality assessment, high and low SpO₂ and heart rate alarms, and download capability. The display unit can be powered by line current or battery and can audibly signal each pulse detected—a feature that conveniently alerts all in the area that a walk test is in progress. This feature can also be silenced. The interference of a finite length of cable would often slow down the faster-walking patient if the technologist lagged behind. This would sometimes cause the final 6MWT distance to be artificially low and require a repeat test. The Avant 4000 has minimized the need for repeat testing and allows for a more accurate clinical patient assessment.

Avant 4000 Digital Pulse Oximetry System Specifications²: wrist module weight: 4.4 oz; SpO₂ and heart rate alarms; display dimensions: 7.25" wide x 5.5" high x 4.5" deep; audible signal of waveform detection; radius of transmission: 30' radius; memory: 33.5 hours; battery Life: Wrist Module—120 hours of continuous monitoring, display—18 hours of continuous monitoring.

The NONIN Avant 4000 meets ATS Pulse Oximeter Guidelines for the 6MWT: technician must not walk with the patient; lightweight, <2 pounds; battery powered; held in place such that stride is not affected; motion tolerant.

Clinic Staff and Patient Acceptance: Acceptance of the device by the testing staff was immediate and extremely positive.

Gone was the need to carry an oximeter and be within three feet of the patient during the 6MWT. Patients with normal functional capacity can be allowed to walk very quickly without feeling constrained by the attachment to a device carried by a technologist.

The Avant 4000 is easy to use. Training on device operation, facilitated by an informational CD, can be done in less than 30 minutes.

Summary: The only wireless oximeter to meet all of the ATS guidelines for the 6MWT, the NONIN Avant 4000 provides real-time monitoring without immediate patient contact. Conducting the 6MWT with the Avant 4000 allows patients to move at their own pace, resulting in a more accurate clinical evaluation. The technologist is able to focus more attention on the test administration while still monitoring the patient, resulting in decreased repeat testing and improved patient safety.

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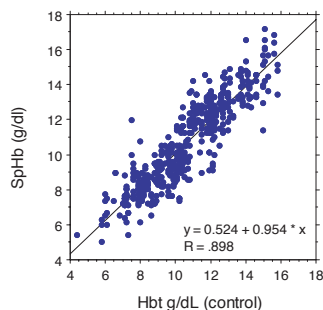
The above product review was provided by Kevin McCarthy, Technical Director, Pulmonary Institute, Cleveland Clinic. This article, in its original form, "NONIN Avant 4000 Bluetooth Wireless Oximetry: Increased Safety and Accuracy When Administering the Six-Minute Walk Test," was provided by NONIN, ©2008 Nonin Medical, Inc. All trademarks are the property of Nonin Medical, Inc. unless otherwise noted. Bluetooth and the Bluetooth Logo are registered trademarks of Bluetooth SIG, Inc.

CONTINUOUS NONINVASIVE MEASUREMENT OF HEMOGLOBIN VIA PULSE CO-OXIMETRY

This paper, by M.R. Macknet, S. Norton, P. Kimbal-Jones and R. Applegate, was presented at Society of Technology in Anesthesia 17th Annual Meeting, Orlando, FL. It was provided by Masimo.

Masimo Rainbow SET CO-Oximetry is the first patient monitoring platform that can provide fast, inexpensive and continuous measurements of carboxyhemoglobin, methemoglobin, oxyhemoglobin and pulse rate, noninvasively. This study tests the accuracy and reliability of a new noninvasive measurement parameter to be added to the Masimo Rainbow SET CO-Oximetry platform – total hemoglobin (SpHb).

The accuracy of the prototype Masimo SpHb device and sensor was tested in 19 surgery patients and 19 healthy volunteers. Individuals from both groups were monitored with an ASA standard monitor and fitted with a radial artery cannula and three Masimo prototype SpHb sensors, optically isolated from each other and connected to a data collection system. The healthy volunteers underwent a hemodilution protocol, which consisted of replacing one unit of blood with 30 ml/kg of saline. Data was collected during surgery or during the hemodilution protocol. Readings from the SpHb sensors were compared to readings from arterial blood gas draws taken at the same time. Bias, precision and Arms were calculated from the 458 data pairs comparing laboratory CO-Oximeter readings to the SpHb readings.

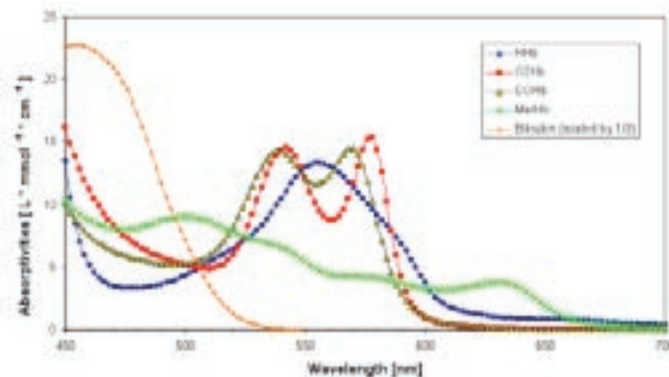


SpHb compared to Total Hemoglobin via laboratory CO-Oximetry; n=28	
Mean +/- SD	10.6 (+/- 2.3)
Range	4.4 - 15.8 g/dl
Bias	-0.039
Precision	1.09
Arms	1.09

The authors concluded: "This device is the first device developed that can continuously and noninvasively measure hemoglobin concentration in addition to the other common hemoglobin species and therefore provides a significant expansion to existing physiologic monitoring technology. Rapid measurement of hemoglobin would be extremely useful in many clinical scenarios. This technology in combination with methemoglobin and carboxyhemoglobin measurements should allow for significant advances in patient care."

LOOKING CLOSE

Enhanced spectrophotometric analysis of hemoglobin and bilirubin helps ensure accuracy of results. Spectroscopic analysis of hemoglobin and its derivatives (co-oximetry), in combination with blood gas analysis, provides actionable information about oxygen transport in human blood. The accuracy of the hemoglobin and bilirubin results depends on the performance of the co-oximetry technology. The co-oximetry module of the Roche cobas b 221 blood gas system measures both hemoglobin derivatives and bilirubin spectrophotometrically in the visible spectrum range (460nm to 660nm). Absorbance of the sample is measured at a total of 512 discrete wavelengths. The concentrations of hemoglobin, hemoglobin derivatives and bilirubin are determined by applying an accepted mathematical algorithm.¹ This enables the cobas b 221 system's co-oximetry technology to detect the presence of light-absorbing substances not covered by the reference spectra and to prevent incorrect values due to interfering substances from being reported.³ This advanced co-oximetry design helps improve the accuracy of patient test results, which is demonstrated by a high correlation with results from accepted clinical chemistry test methods.²



Absorbance of Hemoglobin Derivatives and Bilirubin⁴

References: 1. cobas b 221 reference manual version 8.0 pp 20, 21; 2. Rolinski, Boris et al. Evaluation of Total Bilirubin Determination in Neonatal Whole-Blood Samples by Multiwavelength Photometry on the Roche OMNI S Point-of-Care Analyzer. *Point of Care, The Journal of Near Patient Testing and Technology*; Volume4, March 2005.; 3. Schweiger, Gerd.

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RELIABLE DEAL

Smiths Medical has lowered the price of its most popular medical grade quality pulse oximeters. The BCI 3301 is a portable handheld monitoring system. Designed for simple, accurate spot-checking, it is ideal for use in outpatient clinics, emergency rooms, during emergency transport or for home care. The Digit Finger Oximeter delivers fast, reliable oximetry in a handy, pocket-size solution by combining the monitor and sensor into one unit. BCI brand products consist of a wide range of pulse oximetry devices in finger, handheld and bedside form factors that measure blood oxygen saturation in the blood and pulse rate. These products are known for their reliability and portability, and for providing clinicians with easy-to-use devices that aid in assessing and managing patients' vital signs. For more information, visit smiths-medical.com.

FLEXIBLE

Radiometer announced it has received 510(k) clearance from the Food and Drug Administration for its ABL80 FLEX CO-OX, a portable blood gas analyzer that brings speed and simplicity to the point-of-care. The ABL80 FLEX CO-OX accurately measures pH, blood gases, electrolytes, glucose and vital CO-oximetry parameters. The ABL80 FLEX CO-OX matches the CO-oximetry performance of Radiometer's benchtop analyzers, representing Radiometer's commitment to providing quality solutions for both laboratory and point-of-care testing. Radiometer's sophisticated CO-oximetry technology utilizes multi-wavelength technology for high measurement performance combined with an ultrasonic hemolysis process. Ultrasonic hemolysis offers advantages over chemical hemolysis, including low maintenance and zero risk of interference from chemical hemolyzing agents or partially hemolyzed red blood cells. In addition to lab-quality CO-oximetry, the ABL80 FLEX CO-OX provides: fast turnaround, with only 140 seconds between results; easy, cartridge-based testing; small sample size of 105 µL; fast start-up after installation of new consumables; portability, with full operation on battery power; minimal maintenance, with a self-cleaning sample inlet; automatic QC, with automated corrective actions; and full connectivity to the HIS/LIS. Contact radiometeramerica.com.

SPOTLIGHT ON SPIROMETRY

LEGENDARY

nSpire Health's all-inclusive KoKo Legend portable spirometer exceeds ATS/ERS 2005 standards. KoKo Legend redefines accuracy through technology and simplicity with Legend's intuitive color touch screen walking both patient and physician through standard testing procedures promoting superior patient test results. KoKo Legend utilizes a unique flexible orifice pneumotach which is extraordinarily precise at the low flow rates common in both pediatric and COPD patients. Choose built-in-printing or external office printing for 8½ x 11 reports. Easily transfer data into our KoKo PFT Spirometry software via a standard USB cable. For more information call (800) 574-7374, nspirehealth.com.

ON IMPULSE

Impulse Oscillometry (IOS) measures both spirometry and airways resistance in a quiet breathing mode, completely suitable from 2 of years age to adult. Flexible software encompasses a full set of age-specific predicted equations and allows for easy interpretation of results. IOS can be utilized as a standalone device or added to any VIASYS PFT product line. Researchers have demonstrated that IOS has proven to be more sensitive than spirometry in the early detection of small airways disease, broncho challenge testing, and post bronchodilator responses. Contact cardinalhealth.com.

IN THE BANK

Smiths Medical PM, Inc offers a complete line of diagnostic spirometry devices. They include the spirobank II and spirobank G handheld multifunction spirometers with graphic display, MiniSpir portable USB spirometer, Spirolab III spirometer with oximetry option, and pocket-sized spirotel device. Each uses turbine technology that does not need calibration, and is extremely sensitive to patient airflows. They provide real time graphical curves, automatic test interpretation, and quality control monitors. An internal temperature sensor provides automatic BTPS conversion. Pulse oximetry is an option on most models, with oxygen evaluation and overnight sleep screening modes standard. For more information, call (800) 558-2345 or visit smiths-medical.com/spirometry.

TAKE A LOOK

The SpiroDyn'rX (SDX), developed by the company Dyn'R, is a spirometer-plus-software system that helps more accurately position the organs around the respiratory system. By monitoring the respiratory movements of the patient and designating a visual representation "optimal inspiration zone" for the patient to achieve, the SDX aids in a more precise, and thus more effective, imaging or radiotherapy session. The SDX is composed of two parts: a spirometer and video glasses combination located in the imaging or treatment room, and software installed on a PC computer located in the control room. By sending data from the spirometer to the central computer, the software illustrates the levels of inhalation and exhalation by curves. The software detects the optimum inspiration level and automatically starts the respective device. Contact sdx.fr.

GOING PLATINUM

Medical Graphics Corporation, St Paul, MN, introduces the Platinum Elite Series plethysmograph providing complete spirometry, diffusion capacity, lung volumes by single breath diffusion, multiple breath diffusion and plethysmography, and airways resistance. The system can test pediatric through adult patients and the expanded seating space accommodates larger and tall patients with virtually no weight restriction. The system's advanced sensor technology is self-monitoring, self diagnostic and auto-adjusting to simplify system operation. New digital components offer the maximum in accuracy, reliability and serviceability. Each Platinum Elite comes with the latest release of Windows XP and Vista compatible BREEZESUITE software. Contact medgraphics.com, (800) 950-5597.

Non-invasive CO₂ Measurement in Ventilated Neonates: A Pilot Study

Shabih Manzar, MD, FAAP

Abstract

Background & Objective: Frequent blood gas analyses (BGA) are needed to monitor the pCO₂ during assisted ventilation. BGA are costly, invasive and a potential source of iatrogenic blood loss. We derived and validated the mathematical formula for estimating CO₂ from minute ventilation (Ve). The objective was to develop a non-invasive tool for continuous CO₂ monitoring.

Methods: A group of surfactant treated, mechanically ventilated extremely low birth weight (birth weight < 1000 grams) infants were selected. The minute ventilation (Ve) was measured by the pneumotachometer placed between the endotracheal tube and Y-piece using the AVEA ventilator. The mean Ve was calculated from the five-minute epoch. The arterial blood gas CO₂ (PaCO₂) obtained for a given time were matched to the mean Ve recorded for the same time period. A total of 54 observations were obtained from 20 infants during the first 12 hours of life. The linear regression model was used to derive a prediction formula for CO₂ from Ve. The formula was validated by applying it to a separate group of ventilated neonates. The calculated CO₂ (CalCO₂) was compared to simultaneously obtained blood CO₂. Twenty paired samples were analyzed.

Results: A negative correlation was noted between the Ve and PaCO₂, $r = -0.56$, $p = 0.001$. The prediction equation derived from the data was $CO_2 = 64.973 + (-0.0492) Ve$ or simply as: $CalCO_2 = 65 - 0.05 Ve$. On validation of the formula, a statistical significant correlation was observed between the PCO₂ and CalCO₂, $r = 0.92$, $r^2 = 0.86$, $p = 0.001$.

Conclusions: By using the formula: $65 - 0.05 Ve$, CO₂ could be reliably estimated from the measured Ve. This concept could be utilized as a valuable bedside tool for continuous CO₂ monitoring.

Introduction

Blood gas analysis (BGA) is frequently used to monitor the adequacy of ventilation and oxygenation during assisted ventilation. Due to the invasive nature of BGA and increased risk of phlebotomic losses, alternatives were developed. Transcutaneous (Tc) PO₂ and PCO₂ monitoring has been used

but due to the delicacy of the premature skin and labor intensive nature of Tc probes and calibration problems, these practices have fallen out of favor in the neonatal intensive care unit (NICU). Lately, pulse oximetry has emerged as a promising non-invasive tool to monitor oxygenation. Similarly, end tidal (ET) CO₂ measurement has been used as a surrogate of blood PCO₂.^{1,2} However, ET CO₂ monitoring was not adopted by many NICUs due to the device-associated dead space and need for extra monitoring equipment. The other potential alternative is to calculate the CO₂ from the alveolar ventilation (VA) using Gas Law, $PCO_2 = VCO_2 / VA \times k$, where k is 0.863, VCO₂ is carbon dioxide production.³ The evident problem with this formula is the measurement of the VCO₂ and VA in the clinical setting, making it unfeasible to use in clinical practice.

Pulmonary mechanics monitoring (PMM) is a built-in feature in most of the recent brands of ventilators and is being widely used in the intensive care units.^{4,5} With the use of PMM, many of the physiological measurements which were viewed as laboratory parameters are now available at the bedside. For example, the measurement of tidal volume (Vt) and minute ventilation (Ve) are reliably obtained at the bedside. The relationship between the Vte, Ve and CO₂ is well established (Figure 1). Based on this relationship and availability of bedside PMM, we hypothesized that a simple formula could be derived from the Ve for estimating CO₂ using the PMM.

Methods

The study was conducted at the John Stroger Hospital of Cook County, Chicago. The research protocol was presented to Scientific Committee of the Institutional Review Board and was exempted from review. The requirement for parental consent was waived in view of the observational nature of the study with no intervention on the infants. Also HIPAA (Health Insurance Portability and Accountability Act) waiver was obtained as study did not require any identification of the patients. No extra blood was drawn for the study purpose. The available blood gas values were utilized for the study.

Patients: First set of infants: We selected a homogenous group of neonates to simulate standard pulmonary setting. The group consisted of twenty extremely low birth weight (ELBW) infants, defined as birth weight less than 1000 grams. These infants had clinical and radiological evidence of respiratory distress syndrome. They received single dose of natural surfactant (Survanta, 4mL per 1000 grams) and were mechanically

Shabih Manzar is with the Division of Neonatology, Rockford Memorial Hospital, Rockford, IL. The author would like to thank the nursing staff and respiratory therapists of John Stroger Hospital of Cook County, Chicago, for their continuous support during the study.

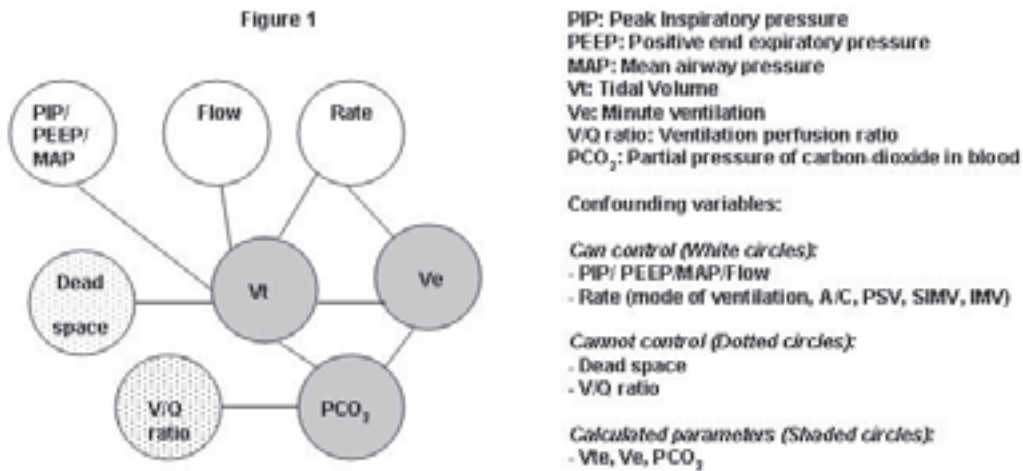


Figure 1: Schematic representation of relation between the Vt, Ve and PCO₂

ventilated using the AVEA ventilator. All infants were studied during the first 12 hours of life. Infants were excluded if they receive the second dose of Survant. The data on the ventilator settings and pulmonary mechanics were collected directly from the ventilator while PaCO₂ values were recorded from the daily flow sheet. A total of 54 BGA samples were available for final analysis (14 infants had three BGA in the first 12 hours while 6 had two BGA).

Second set of infants: This group comprised a heterogeneous group of infants ventilated for different respiratory conditions (gastroschisis-1 case, chronic lung disease-2 cases, respiratory distress syndrome-1 case, pneumonia-1 case). For validation of the derived mathematical formula, we compared the calculated CO₂ (CalCO₂) with the simultaneously obtained capillary CO₂ (PcCO₂). A total of 20 paired observations (4 each) were analyzed.

AVEA ventilator system: Setup: The AVEA ventilator system (Model No 16184, VIASYS Healthcare, Palm Springs, CA)⁶ was operated by certified respiratory therapists (RTs). The calibration and equipment check was done periodically by the RTs as routine and for potential problems. At admission, the time, weight and endotracheal tube (ETT) size and length were logged in by the RTs using the 'Setup' menu of the ventilator.

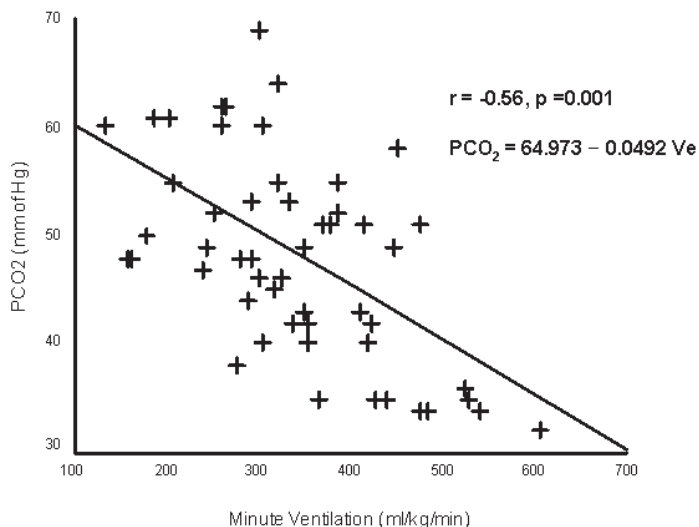


Figure 2: Scatterplot showing correlation between Ve and PCO₂

The AVEA ventilator has the feature of displaying up to 34 parameters on the 24-hour trend form recorded as one minute averaged value. The time is displayed in yellow while event values are displayed in green with asterisk at the time. Up to ten parameters could be seen at one time. The AVEA ventilator also has the feature of recording minute by minute spontaneous breath and mandatory breath separately and displaying these values simultaneously with the averaged Ve/kg values for that minute. The ventilator is also capable of recording the events. The blood drawn time is marked by selecting the Event drop down menu and selecting blood gas. The microprocessor stored all the values, including Ve, for that time in yellow color with the time marked with an asterisk. The information was retrieved and reviewed by using the "Trend" menu.

Measuring and minimizing variation in measurements:

All infants (first set) during the study period were ventilated by using the synchronized intermittent mandatory ventilation (SIMV) mode. The use of paralysis, sedation and analgesia during the first few hours of life in ELBW infants is not routinely practiced in our unit and is up to the attending's discretion. None of the infant received total parenteral nutrition or methyl-xanthines during the study phase. The total Ve (averaged for the minute) was measured by a low dead space

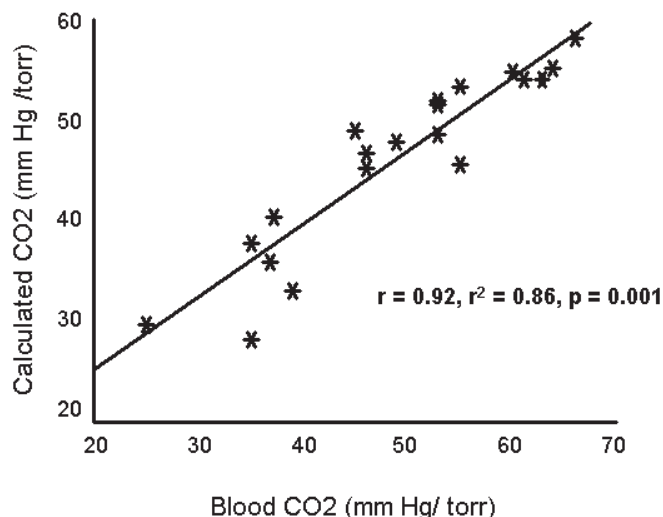


Figure 3: Scatterplot showing correlation between the blood and calculated PCO₂

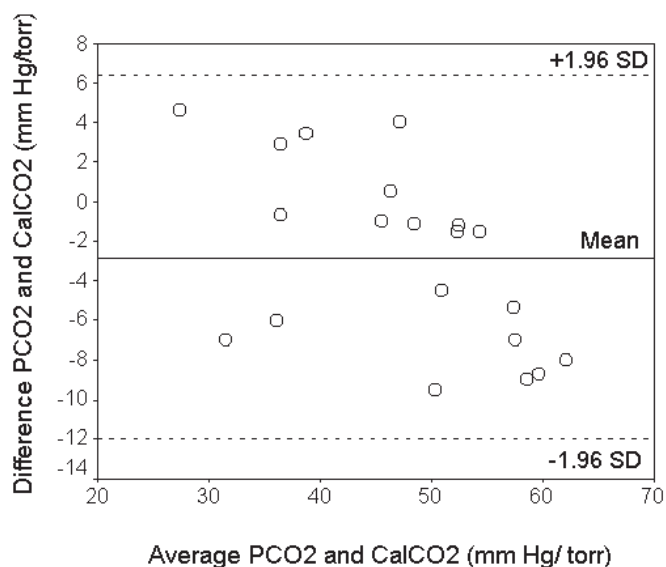


Figure 4: Bland – Altman plot

pneumotachometer (VarFlex) attached between the proximal end of the endotracheal tube and Y-piece. This flow sensor device has shown to give better volume measurement in infants.⁷ The principle is based on measuring the flow from pressure difference across the resistance. The flow (V') is measured in a tube with a small fixed resistance (R). The pressure drop ($P_1 - P_2$) across the resistance relates linearly to flow ($P_1 - P_2 = R \cdot V'$). A single-use pneumotachometer (PNT) was used for each neonate. The PNT was precalibrated and was checked periodically for occlusion by mucus or secretions. No endotracheal suction was performed 30 minutes prior to the blood gas analysis. No inline catheter was used during the study period. Breath greater than 10% leak was excluded from analysis. The total V_e was selected to be displayed on the monitor screen for reading. These measurements were automatically recorded on the computer-assisted microprocessor and were available for analysis for up to 24-hours recordings. As all the neonates studied were breathing spontaneously on SIMV ventilation, we use the total V_e (averaged for the minute ie Spontaneous V_e + Mandatory V_e) for analysis. To eliminate the chance of error in V_e per kg recordings, a manual check for the current weight was performed. Other parameters, including exhaled tidal volume and rate for the same epoch, were noted down. All observations were made by a single investigator (SM).

Using mean V_e for analysis: The mean V_e average of the five-minute recordings was used to study the relationship between the V_e and the PCO_2 . The matching procedure was: the blood gas done at 6.00 am was matched to the mean V_e obtained within the five minute period (± 2 minutes time frame) ie the average of V_e at 5.58 am, 5.59 am, 6.00 am, 6.01 am, 6.02 am. The time of blood gas drawn was recorded from 'Event' built-in feature of AVEA ventilator (marked with asterisk on the ventilator trend display) and/or by the time recorded on iSTAT (point-of-care blood gas analyzer) printout and nursing flow sheet. The time on iSTAT and AVEA ventilator are synchronized with the clock in the NICU.

Measurement of PCO_2 : The nurse taking care of the baby performed the blood gas analysis from the indwelling umbilical or radial artery catheter using the iSTAT blood gas analyzer (Princeton, NJ).^{8,9} We discarded the blood gas from analysis if intravenous sodium bicarbonate was given prior to the blood gas analysis. For the second set of infants we used the well

arterialized capillary sample (to comply with the IRB approved protocol and unit policy, no extra arterial stick was performed for the study purposes).

Sample size calculation and statistical analysis: Sample size calculation and power analysis was based on anticipated significant correlation coefficient of 0.60 between V_e and PCO_2 with α of 0.05 and β of 0.10. The sample size of 20 with power of 80% was obtained from the above input.^{10,11} SPSS version 7.5 was used for all statistical analysis. Pearson Correlation test and Linear Regression analysis was used where applicable. Bland-Altman plot 12 was used to further study any bias observed in the association.

Results

The mean V_e for the study cohort was noted to be 342 ± 104 ml/kg/min with $PaCO_2$ of 48 ± 9 mm of Hg/torr [6.4 ± 1.2 kPa]. A significant negative correlation was noted between the V_e and $PaCO_2$, $r = -0.56$ ($r^2 = 0.319$, adjusted $r^2 = 0.306$), $p = 0.001$. A similar correlation was noted between the exhaled tidal volume and $PaCO_2$ (Table 1).

Mathematical derivation of prediction equation: By keeping CO_2 as the dependent variable and using the linear regression equation ($Y = a + bX$), a prediction formula was derived as: $CO_2 = \{64.973 [57.813 \text{ to } 72.132, 95\% \text{ Confidence Interval}] + [-0.0492 (-0.069 \text{ to } -0.029, 95\% \text{ Confidence Interval})] V_e$ or $64.973 + (-0.0492) V_e$ or simply as: $CalCO_2 = 65 - 0.05 V_e$, where Y is the dependent variable, X is the predictor, a is the intercept and b is the slope (Figure 2). Correlation between the calculated CO_2 ($CalCO_2$) and blood CO_2 (PCO_2): A strong correlation was observed between the $CalCO_2$ ($65 - 0.05 V_e$) and simultaneously obtained PCO_2 , $r = 0.92$, $r^2 = 0.86$, $p = 0.001$ (Figure 3). The Bland-Altman plot showed a high repeatability between the two methods (Figure 4).

Discussion

The negative relationship noted between the V_e and PCO_2 has been reported earlier by Mathur¹³ using a heterogeneous group of forty mechanically ventilated neonates. Similarly, Greer et al¹⁴ have described an inverted parabolic relationship between the V_t and end tidal PCO_2 ($PETCO_2$), with the lowest $PETCO_2$ values at the extremes of V_t . $PETCO_2$ is a promising non-invasive parameter used to monitor adequacy of ventilation, however, measurement of $PETCO_2$ requires a separate analyzer (with infrared spectroscopy) and module (capnography). The former could be a potential source of additional anatomical dead space and the latter add extra cost to the care and may not be available readily in all NICUs. The other caveat with $PETCO_2$ is the reported variability with the simultaneously drawn blood gas values.¹⁵

Although we noted a significant negative relationship between V_e and PCO_2 but this relationship has limitations. With non-optimal V_e , physiological adjustments result in blunting of the regression curve. A high V_e results in over distension of the alveoli causing increased dead space thereby increasing the ventilation-perfusion (V/Q) mismatch while a very low V_e results in alveolar under ventilation and reversing the V/Q ratio. This phenomenon has been studied in Porcine neonates by Sakamoto et al.¹⁶ They observed widening of correlation between $PaCO_2$ and $ETCO_2$ with very high and very low tidal volumes.

Due to the technical limitation, we did not measure the dead

Table 1: Summary of the results

Number of observations	54
Birth weight (grams)	858 ± 87
Gestational age (weeks)	26 ± 0.53
V _{ie} (ml/kg)	6.3 ± 1.3
V _e (ml/kg/min)	342 ± 104
PaCO ₂ (mm of Hg/Torr)	48 ± 9
Rate (per minute; spontaneous + mechanical)	54 ± 13
Correlation coefficient between V _{ie} and PaCO ₂	r= -0.55, p= 0.001*
Correlation coefficient between V _e and PaCO ₂	r= -0.56, p= 0.001*
Correlation coefficient between V _{ie} and V _e	r= 0.54, p= 0.001*
Correlation coefficient between Rate and PaCO ₂	r= -0.20, p= 0.14

Results expressed as Mean ± Standard deviation

V_{te} (mL/kg): Exhaled tidal volume (milliliter /kilogram)

V_e (mL/kg/min): Minute ventilation (milliliter/kilogram/minute)

PaCO₂: Partial pressure of carbon-dioxide in arterial blood

r: correlation coefficient, *p < 0.05: statistical significant

space (DS). A potential argument could be raised about the accuracy of V_e measurements and its correlation with PCO₂ without controlling for DS. In clinical non-standardized setting it is difficult to measure the anatomical, alveolar or physiological DS using the Bohr method (anatomical DS = Alveolar CO₂ – Expired CO₂ / Alveolar CO₂ or physiological DS = Arterial PCO₂ – Expired CO₂ / Arterial PCO₂).¹⁷ However, we expect minimal DS ventilation in our first group of infants as they were all surfactant treated. It has been shown earlier that with the use of surfactant, the dead space to tidal volume ratio decrease considerably.¹⁸ The other alternative to obtain dead space free ventilation is the use of correction algorithm and dead space free flow-through technique but the former is possible in vitro and the latter has shown to have a very high inter-subject variability.^{19,20}

The study, being an observation study, has some limitations. We did not confirm the accuracy of the bedside V_e measurements with simultaneously in vitro measurements. In clinical setting it would be difficult to use the calibrated syringe to verify the V_e accuracy.

Similarly, we did not measure the metabolic component of CO₂ produced during oxidation or CO₂ bound to hemoglobin, hence the calculated CO₂ is not reflective of total CO₂ in the body. The other potential argument could be about the time delay between effective V_e and its influence on the CO₂. We studied the relationship within a five minute time frame which was arbitrary. The study was done in a single center using a single device which may be a source of bias. However, in view of the clinical significance of non-invasive CO₂ monitoring we expect further confirmatory studies, including a much wider spectrum of neonatal respiratory illnesses, from other centers that use different brand of ventilators.

In conclusion, the CO₂ could be calculated from minute ventilation by using a simple formula: 65 – 0.05 V_e. We speculated that the calculated CO₂ could be used as a non-invasive continuous CO₂ monitoring tool in mechanically ventilated neonates.

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Evaluating a Simulation-Based Neonatal Resuscitation Program

Daniel D. Woodhead, Robert D. Christensen

Introduction

The Neonatal Resuscitation Program (NRP) was introduced in 1987 as an educational collaboration between the American Academy of Pediatrics and the American Heart Association. NRP was designed as a standardized method of providing emergent assessment and care for newborn infants, and has been adopted by healthcare providers around the world.¹ In general, NRP instruction has been didactic, with practice sessions on resuscitation models used periodically throughout the classes.²

Simulation-based training has been embraced by organizations such as aviation, aerospace, police and fire departments, military service, and nuclear engineering.³ A simulation-based environment can provide visual, auditory, and tactile cues unavailable in classical didactic learning.^{4,5} Recent studies have shown that a simulation-based instruction in the healthcare profession can provide superior retention of essential skills.⁶

The Institute of Medicine and the Joint Commission on Accreditation of Healthcare Organization have recommended simulation-based medical training. On this basis, NRP simulation classes were begun in the northern region of Intermountain Healthcare in August of 2007. As part of introducing this new program, we performed two related studies. First, we sought to identify any specific skill-sets where performance after the class was seen to consistently be poor, so that additional education and training could subsequently be focused on strengthening those weak areas. Second, we sought to anonymously survey every class participant to identify the perceived strengths and weaknesses of the new NRP simulation-based program.

Methods

Seventy-seven health care professionals were enrolled in 11 NRP simulation classes, with a total of sixty-four scenarios. Class members included NICU respiratory therapists (n=14), NICU registered nurses (n=41), Labor and Delivery nurses (n=12), NICU nurse practitioners (n=1), neonatologists (n=1), and third year Family Residents (n=8). These individuals had 2-22 years of prior NRP experience. Information was collected by a single observer (DDW) regarding whether each of the five skill-sets was performed properly. These five sets were: 1) drying, stimulating and removing wet linen, 2) suctioning mouth and nose, 3) thirty seconds of effective bagging was performed before chest compression started, 4) proper bagging rate, and 5) proper chest

compression-bagging ratio (Table 1). A Fisher Exact was used to compare the dichotomous variable (performed properly, yes vs. no) of each skill-set with the other four skill-sets.

At the conclusion of the NRP simulation class an evaluation form with a Likert Scale (1 through 5, with 5 indicating excellent and 1 indicating poor), was completed by each student. The evaluation form contained 11 questions comparing the standard NRP class with the simulation NRP class. These questions were: 1) relevance to my practice in the hospital, 2) ability to engage my intellect, 3) ability to develop my behavior skills, 4) ability to transfer behavioral skills to the real environment, 5) ability to develop my technical skills, 6) ability to transfer technical skill to real environment, 7) ability to transfer critical thinking skills, 8) ability to transfer critical thinking skills to real environment, 9) builds confidence level in performing the steps of neonatal resuscitation, 10) would you recertify in a standard NRP course or a simulated NRP course and 11) overall, how would you rate the NRP simulation training? Responses were tabulated using means + SD and paired t-tests performed (Table 2). The study was approved by the Intermountain Healthcare Institutional Review Board.

Results

Of the five skill-sets evaluated, the one most often performed improperly was "suctioning of mouth and nose." The skill-set most commonly performed correctly was "proper chest compression-bagging ratio" (Table 1).

All 77 healthcare professionals completed the questionnaire. For each comparison, the simulation-based NRP classes were judged as superior to the standard classes (Table 2). All 77 participants responded that they would rather re-certify with the NRP simulation-based class than with the standard class.

Discussion

Since first introduced 22 years ago, NRP has served as a standard for resuscitation of newborn infants.¹ In each revision of the NRP program, an up to date evidence-based approach to resuscitation is taught.² Recent advances in NRP methodologies have been learner-focused, including incorporating simulation-based training into the curriculum.⁷⁻¹¹ Continued improvement of the NRP course depends, in part, on consistent re-evaluation of the performance of course participants. We recently introduced simulation-based NRP training into the northern region of Intermountain Healthcare, a health system including 18 hospitals with delivery services in the western United States. As part of this change, we sought to identify any consistently weak performance among the skill-sets taught in the classes. By using one evaluator to judge the performance of teams, we discovered

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	n	Drying, stimulating and removing wet linen	Suctioning mouth and nose	30 seconds of effective bagging before chest compressions	Proper bagging rate	Proper chest compression-bagging ratio
Teams	64	64% (41/64)	51% (31/61*)	64% (41/64)	67% (43/64)	81% (51/63*)
P value		0.447	0.006	0.447	0.436	0.002

Table 1. Performance of NRP skill-sets by teams of 77 health care professionals. The numbers below represent the percentage (and actual numbers) where each of five skill-sets was performed properly, as part of a simulation-based NRP course. P values compare the performance of that skill set with performance of the four other skill sets.

* Scenarios were presented such that these elements did not always apply to all 64 teams.

Questions	Standard NRP	Simulation NRP	P value
Relevance to my practice in the hospital	3.23 ± 0.79	4.95 ± 0.21	<0.0001
Ability to engage my intellect	3.09 ± 0.79	5.00 ± 0.00	<0.0001
Ability to develop my behavior skills	2.64 ± 0.80	5.00 ± 0.00	<0.0001
Ability to transfer behavioral skills to real environment	2.56 ± 0.79	4.98 ± 0.13	<0.0001
Ability to develop my technical skills	2.83 ± 0.85	4.97 ± 0.18	<0.0001
Ability to transfer technical skills to real environment	2.66 ± 0.84	4.97 ± 0.18	<0.0001
Ability to develop my critical thinking skills	2.73 ± 0.76	4.98 ± 0.13	<0.0001
Ability to transfer critical thinking skills to real environment	2.80 ± 0.78	4.98 ± 0.13	<0.0001
Builds confidence level in performing the steps of neonatal resuscitation	2.78 ± 0.74	5.00 ± 0.00	<0.0001

Table 2. Evaluation of the Standard vs. Simulation-based NRP classes by 77 health care professionals, using a Likert Scale (1 through 5, with 5 indicating excellent and 1 indicating poor)

that the suctioning of the nose and mouth was the procedure most often performed improperly. On the basis of that finding, we have added additional didactic and practice emphasis to this skill-set, as part of our next round of NRP classes.

A second part of our evaluative process, accompanying introducing simulation-based classes, involved learner evaluations, directly comparing the previous vs new simulation-based methods. The learners reported that simulation-based classes provided significantly better development of technical and cognitive NRP skills, improved communication, and facilitated teamwork.¹² In fact, without a single exception, the students all listed a preference to recertify in NRP using a simulation-based rather than a standard course.

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Predicting Extubation Failure

Jeff Borrink, BS, RRT

Prior to extubating a patient requiring mechanical ventilation, clinicians must try to determine whether or not the patient will be able to spontaneously breathe successfully post-extubation. Generally, an assessment is done to determine whether or not a spontaneous breathing trial (SBT) should be attempted. If a SBT is attempted and the patient does well, the patient is extubated. Weaning parameters, RSBi (f/V_t), ABGs, etc. are sometimes used to help make the determination to extubate. Even so, some patients fail to successfully breathe spontaneously post-extubation, and must be re-intubated and mechanically ventilated, despite having successfully passed a SBT prior to extubation.

A recent study by Dr. Babak Mokhlesi et al, published in the December issue of *Respiratory Care*, discussed the use of a clinical prediction rule to help predict which patients might fail extubation, despite successful completion of a SBT.

Mokhlesi performed the prospective observational cohort study at Northwestern Memorial Hospital in Chicago, Illinois. They observed six hundred and seventy three (673) consecutive patients who received mechanical ventilation during a fifteen month period. One hundred and twenty two (122) patients were ventilated for at least two days, and did not undergo withdrawal of support or tracheostomy. These patients were followed post extubation to identify who required re-intubation within 48 hours. Sixteen patients (13%) of the one hundred and twenty two patients required reintubation within 48 hours.

In a multivariable logistic regression model, three clinical variables independently predicted re-intubation within 48 hours of extubation. According to Mokhlesi et al, the three clinical variables that predicted reintubation were: moderate to copious endotracheal secretions (moderate secretions-suctioning required every 2-4 hours, copious secretions-suctioning required several times per hour), Glasgow Coma Scale score ≤ 10 , and hypercapnia ($\text{PaCO}_2 \geq 44\text{mmHg}$) during the SBT.

Mokhlesi et al concluded that with their clinical prediction rule that incorporates the assessment of mental status, endotracheal secretions, and pre-extubation PaCO_2 , clinicians can predict who will fail extubation despite a successful SBT. Furthermore, patients who have one or more of these risk factors may require a longer observational period in the intensive care unit following extubation.

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Can Asthma Control Be Improved by Understanding the Patient's Perspective?

Rob Horne, David Price, Jenn Cleland, Rui Costa, Donna Covey, Kevin Gruffydd-Jones, John Haughney, Svein Hoegh Henrichsen, Alan Kaplan, Arnulf Langhammer, Anders Østrem, Mike Thomas, Thys van der Molen, J. Christian Virchow, Siân Williams

Abstract

Background: Clinical trials show that asthma can be controlled in the majority of patients, but poorly controlled asthma still imposes a considerable burden. The level of asthma control achieved reflects the behavior of both healthcare professionals and patients. A key challenge for healthcare professionals is to help patients to engage in self-management behaviors with optimal adherence to appropriate treatment. These issues are particularly relevant in primary care, where most asthma is managed. An international panel of experts invited by the International Primary Care Respiratory Group considered

the evidence and discussed the implications for primary care practice.

Discussion

Causes of poor control: Clinical factors such as exposure to triggers and concomitant rhinitis are important but so are patient behavioral factors. Behaviors such as smoking and nonadherence may reduce the efficacy of treatment and patients' perceptions influence these behaviors. Perceptual barriers to adherence include doubting the need for treatment when symptoms are absent and concerns about potential adverse effects. Under-treatment may also be related to patients' underestimation of the significance of symptoms, and lack of awareness of achievable control.

Implications: Three key implications for healthcare professionals emerged from the debate. First, the need for simple tools to assess asthma control. Two approaches considered were the monitoring of biometric markers of control and questionnaires to record patient-reported outcomes. Second, to understand the reasons for poor control for individual patients, identifying both clinical (eg rhinitis) and behavioral factors (eg smoking and nonadherence to treatment). Third was the need to incorporate, within asthma review, an assessment of patient perspectives including their goals and aspirations and to elicit their beliefs and concerns about asthma and its treatment. This can be used as a basis for agreement between the healthcare professional and patient on a predefined target regarding asthma control and a treatment plan to achieve this.

Summary: Optimum review of asthma is essential to improve control. A key priority is the development of simple and effective tools for identifying poor control for individual patients coupled with a tailored approach to treatment to enable patients to set and achieve realistic goals for asthma control.

Background

Asthma is a chronic inflammatory disease of the airways, resulting in widespread but variable airflow obstruction in response to a variety of stimuli.¹ Airflow obstruction is usually reversible, either spontaneously or with treatment, though remodelling may lead to irreversible structural changes.

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Table 1: Reasons for poor control

Co-morbidity (e.g. rhinitis, COPD)
Severe therapy-resistant disease
Ongoing exposure to triggers (e.g. occupational asthma, pets, mite etc)
Inadequate assessment
Misdiagnosis
Inadequate treatment
Ineffective delivery of treatment (e.g. poor inhaler technique)
Limited treatment effectiveness (e.g. smoking interfering with steroid actions)
Inadequate use of action plans
Low patient and physician expectations
Low adherence with agreed asthma therapy
Functional and psychological problems affecting willingness to use therapy
Over-reliance on complementary/alternative treatment
Not attending medical consultations
Patients do not perceive symptoms as indicative of poor control

National and international guidelines clearly state that the aim of asthma management is to achieve and maintain control.^{1,2} Controlled asthma is characterized by minimal or no symptoms during the day and at night, no asthma attacks, no emergency visits to physicians or hospitals, minimal need for reliever medications, no limitations on physical activities and exercise, nearly normal lung function and minimal or no side-effects from medication.

With the medical treatments currently available, it is possible to achieve control in the majority of patients with asthma, at least in the artificial setting of a clinical trial.³ However, in the real world where patients make choices that may reflect conflicting priorities, asthma still imposes a considerable burden on healthcare systems, largely as a result of poor control.

There is evidence, from a 10 year Finish study, that enhancing the delivery of healthcare services, can improve asthma control⁴ but, in most countries, poor control remains a significant burden for patients and the healthcare system. An analysis of nine studies conducted in Australia, Canada, France, Sweden, UK and USA showed that around one third of the direct costs of asthma, and three-quarters of the total costs of asthma, were a consequence of uncontrolled disease.⁵ In a US study conducted in 1993, the average cost per patient ranged from US\$47 for those with controlled disease, to US\$7,030 for those with uncontrolled symptoms.⁶ A survey in the UK found that the annual cost of a patient who experienced an asthma exacerbation (indicative of uncontrolled asthma) was more than 3.5 times the cost of those who did not experience an attack (£381 vs. £108).⁷ International studies have confirmed the high cost of managing exacerbations.^{8,9}

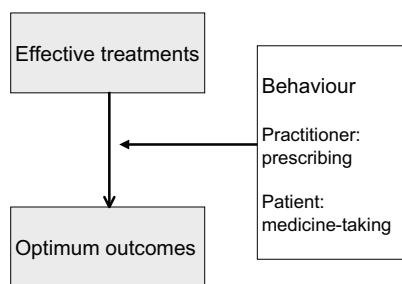


Figure 1. Patient and healthcare professional behaviour affects asthma control.¹⁰

There are many possible reasons for poor control (Table 1). However, regardless of the underlying causes, the level of control achieved reflects the behavior of both healthcare professionals and patients (Figure 1).¹⁰ Healthcare professionals need to conduct asthma reviews and take appropriate action if control is poor. Patients need to engage in self-management behaviors with optimal adherence to appropriate treatment. Differences in the perspectives of patients and healthcare professionals could affect their behaviors and consequently the achievement of asthma control. It may be possible for healthcare professionals to improve asthma control by achieving a greater understanding of the patient's perspective.

These issues are of particular relevance in primary care, where the majority of patients with asthma are managed. An international panel of general practitioners, respiratory physicians, patient representatives and others with an interest in asthma control, under the auspices of the International Primary Care Respiratory Group (IPCRG), considered the evidence about patient perspectives and discussed the resulting implications. This report summarizes the discussion.

Discussion

Presentations by group members on different aspects of asthma control resulted in a wide ranging discussion that crystallized around three key questions.

1. What levels of asthma control are patients currently achieving?
2. What are the common causes of poor control?
3. What are the main patient-related determinants of asthma control?

Each of these questions is addressed, below.

1) What levels of asthma control are patients currently achieving?

Large population-based studies, varying in methodology and funding, suggest that a substantial proportion of patients with asthma currently experience suboptimal levels of asthma control. The AIRE (Asthma Insights and Reality in Europe) study, involving over 2,800 people with asthma in France, Germany, Italy, Netherlands, Spain, Sweden and UK, found that asthma symptoms are part of everyday life for many patients.¹¹ More than half (56%) of the respondents (identified by telephone interviews of randomly selected households) suffered daytime symptoms in the last 4 weeks, and around one in three respondents experienced sleep disruption due to asthma at least once a week. Among the 753 children (<16 years) surveyed, 28% suffered night time symptoms in the previous month, with 61% needing to use their rescue medication.

Findings consistent with the AIRE study have been reported from the INSPIRE (INternational aSthma Patient Insight REsearch) study.¹² This study, conducted in eleven countries (Australia, Belgium, Canada, France, Germany, Italy, Netherlands, Spain, Sweden, UK, USA), included 3,415 adults with asthma treated with inhaled corticosteroids, recruited via their physicians and interviewed by telephone. Nearly three-quarters of the patients (74%) used a short-acting bronchodilator every day and half of all patients (51%) had at least one exacerbation requiring medical intervention in the past year. The mean number of asthma worsenings was 16 in those patients with uncontrolled asthma, compared with 6 in patients with well-controlled asthma.

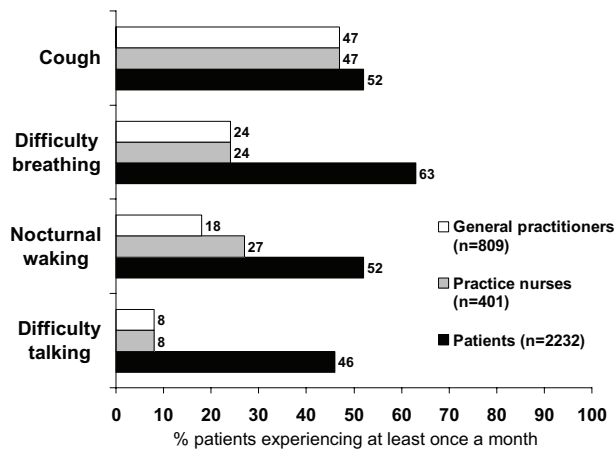


Figure 2. Healthcare professional and patient perspectives of the occurrence of asthma symptoms.¹⁶

2) What are the common causes of poor control?

There are many reasons why asthma may be poorly controlled, both clinical and behavioral. Important clinical factors include the genetic characteristics of the individual, type of asthma (eg aspirin-sensitivity, neutrophilic activity), co-morbidity (eg dysfunctional breathing, allergic rhinitis).^{13,14} The behavior of both clinicians and patients is also an important determinant of the level of asthma control achieved.

The behavior of clinicians is vital in making an accurate diagnosis and prescribing the best treatment but also in carrying out appropriate review of progress and subsequent control.¹⁵ Healthcare professionals may have limited awareness of symptom prevalence. In the AIR (Asthma in Real life) study, general practitioners substantially underestimated the prevalence of asthma symptoms (Figure 2).¹⁶ Furthermore, healthcare professionals may have difficulties estimating levels of asthma control.^{17,18} Clearly, there is a need for healthcare professionals to appreciate the widespread occurrence of poor asthma control.

Patient behaviors are also key as the level of asthma control is influenced by adherence to treatment and other self-management behaviors¹⁹ and smoking.²⁰ Patients' may also fail to consult their doctor. A UK survey found that 10% of asthmatic patients had seen no health professional about asthma in the previous 3 years.²¹

3) What are the main patient-related determinants of asthma control?

Patient expectations, aspirations and goals. Patients may unnecessarily accept symptoms, assuming that frequent symptoms, exacerbations and lifestyle limitations are an inevitable consequence of having asthma.²² In the AIRE

study, the majority of patients considered themselves to have controlled asthma, yet symptom levels showed control failing to reach the levels expected by management guidelines.¹¹ Patients may not realize that effective treatments are available. This was demonstrated in a study of 517 patients in the UK.²³ While 58% of patients reported that they were very satisfied with the standard of their asthma management, this fell to 33% after being shown the standards that patients can expect, as detailed in international guidelines. Such work implies that there is a need to raise patient expectations by increasing awareness of the quality of life that could be attained.

What level of control do patients want to achieve?

When asked about the things that they most dislike about asthma, patients most report symptoms such as cough, breathlessness, and lifestyle restrictions.¹⁶ In a study of patients with asthma, 55% of respondents reported that they would find a written action plan helpful,²³ though another study reported that 45% of patients neither had nor wanted regular asthma review.¹⁵ Some of the goals that patients say they want are apparently contradictory (e.g. they may want few symptoms and no impact on activities, but do not want to take medication that could help achieve this). In real life, patients make choices between different attributes of the disease and its treatment, trading off one aspect for another – just as they may choose between consumer goods that offer different features at different costs. Discrete choice experiments allow integration of these different aspects in one measure by presenting patients with a choice of scenarios, each of which includes the key characteristics at different levels. Health technology assessment agencies, such as NICE, may use information from discrete choice experiments to understand the issues that matter to patients.²⁴

A discrete choice experiment showed that patients were willing to experience higher levels of wheeze and sleep disturbance to avoid cough and breathlessness.²⁵ However, patients who have not experienced an exacerbation may not rate avoidance of an attack as highly as those who have suffered one, possibly because of the pronounced impact of an exacerbation on quality of life.²⁶ Discrete choice experiments have also been used to assess patient preference for different treatment regimens²⁷ and for autonomy in decision-making in asthma management.²⁸

Patient goals and asthma control

Currently, asthma control is measured in ways defined by healthcare professionals (e.g. use of reliever medication, lung function, need for unscheduled healthcare). However, these standard methods use surrogate markers that do not seem to be necessarily relevant to the individual patient. In contrast, psychological treatments routinely use patient-defined goals, achievement of which can be seen by both patient and healthcare professional as markers of improvement. For example, an agoraphobic patient may set a goal of walking to the

Table 2: Current methods used to imply level of asthma control

Measure	Comments
Symptoms	Day, night, exercise-induced
Lung function	% predicted, % variability
Healthcare resource use	Rescue medication, oral steroids, emergency consultations, hospitalisation
Bronchial hyperreactivity	Not suitable for routine clinical use
Biomarkers	Sputum eosinophils, exhaled NO
Health status	Numerous questionnaires available

Table 3: Ideal features of a tool to assess asthma control

Convenient to perform
Objective measure of asthma control
Simple Numeric value
Give a clear Target to guide treatment
Reliable, valid and responsive to changes in asthma control over time
Able to predict Outcomes
Complementary to Lung function tests

shop to buy a newspaper each day. Identifying and using patient goals has been shown to encourage patient involvement, which may lead to better adherence with therapy.²⁹ It is also consistent with the view that effective therapy is that which satisfies the patient's goals and expectations.³⁰

Few published studies have explored this issue in asthma with the exception of two recent studies. In the first study³¹ in 329 adults with asthma, patients were asked to name up to three personal goals, achievement of which would indicate to them that their asthma treatment was effective. One year later, patients were asked to score the extent to which they had achieved their goals. Most patients (92%) were able to set three goals. Themes from patient-named goals were categorized qualitatively, subject to inter-rater reliability, with key words identified for each theme. Four main themes were identified: reducing activity limitation (named by 60% of participants), reducing asthma symptoms (named by 52% of patients), avoiding/reducing exacerbations (named by 46% of patients), and 38% wished to reduce their use of relief treatment. Within these themes, patients could name more specific behavioral goals (eg avoiding use of out-of-hours service, being able to play more sport). Patient-set goals appeared to be responsive to change. When asked to score the achievement of their goals at the end of the study, 49% of participants considered that they had achieved or partially achieved their own goals of treatment.

In the second study of 83 patients with exercise-induced asthma treated using montelukast or placebo, patients were also able to set their own goals.³² The nature of these goals was very similar to that found previously, falling into four themes of reducing activity limitations, asthma symptoms, exacerbations and use of medication. These were more sensitive to change than the responses to the Royal College of Physicians' three questions.³³

Patient adherence to treatment and other aspects of self-management

Patients may not take the medications they have been prescribed, contributing to poor disease control. Regardless of age, gender and socioeconomic status of patients, and type and severity of disease, non-adherence rates of over 30% have consistently been noted across chronic illnesses³⁴ and with even higher rates of nonadherence to inhaled corticosteroids.³⁵ Non-adherence may be lower for more complex regimens, but significant non-adherence remains even when the frequency of dosing is reduced.^{36,37} Furthermore, providing clear information – although essential – is not enough to guarantee adherence.³⁸

Nonadherence is best thought of as a variable behavior, rather than a trait characteristic: most people are nonadherent some of the time. Nonadherence can have both intentional and unintentional causes. Unintentional nonadherence arises from capacity and resource limitations that prevent patients from implementing their decisions to follow treatment

recommendations and involves individual constraints (e.g. poor inhaler technique, problems remembering doses etc) and aspects of their environment (eg problems of accessing prescriptions, cost, competing demands etc). Intentional nonadherence arises from the beliefs, attitudes and expectations that influence patients' motivation to begin and persist with the treatment regimen.³⁷

Patients' common-sense beliefs about treatment and perceptions of asthma

Patients' self-management of their asthma is strongly influenced by their 'common-sense' beliefs about illness and treatment.³⁹ Patients do not blindly follow treatment advice even when it comes from trusted parishioners. Rather they evaluate whether the advice makes common sense in the light of their own understanding and beliefs about the illness and treatment.⁴⁰ Patients' adherence to medication is particularly influenced by the way in which they evaluate their personal need for medication relative to their concerns about potential negative effects of taking it. The utility of this simple necessity-concerns framework in explaining nonadherence has been shown in studies across a range of chronic illnesses,⁴¹⁻⁴³ including asthma.⁴⁴

Patients are more likely to doubt the necessity of treatment if they do not perceive a good fit with their common-sense understanding of their illness and symptoms experiences relative to expectations.^{45,46} A study of adherence to ICS in community-managed asthma patients in the UK showed that for many patients, the medical model of asthma as a chronic condition requiring daily preventer treatment was perceived to be at odds with their symptomatic experience of asthma as an episodic condition (eg my asthma isn't there when I don't have symptoms). These patients were more likely to doubt their personal need for daily ICS and were significantly less adherent.⁴⁵ Moreover, patients' concerns about potential adverse effects of medication become more salient when they doubt the necessity of treatment.⁴⁰ Patients' concerns about prescribed treatment extend beyond the experience of side effects to include more abstract worries arising from negative beliefs about pharmaceuticals such as the potential for dependence and long-term effects.⁴⁷

Mistrust of orthodox therapies may be one reason why many patients resort to unproven complimentary or alternative treatments for asthma. Surveys have shown high levels of use of such treatments by asthmatics in spite of a poor evidence base for efficacy.⁴⁸

Patients' beliefs about asthma and its treatment may be a hidden determinant of nonadherence when they are not volunteered in the consultation. If healthcare professionals are not aware of patient beliefs and hold different (sometimes opposing) beliefs about the nature of the illness and its appropriate treatment, then the consultation is unlikely to lead to successful outcomes. Where people lack information they may have inaccurate and uninformed views on the illness. They may also ignore missing information, devalue a treatment option, or make inferences based on the limited information they do have. Although patient beliefs govern their attitudes towards therapy, these beliefs are not fixed and can be changed through education and negotiation.⁴⁹ Finally, other psychological factors such as anxiety and depression may influence patient behaviour and asthma control.⁵⁰ Socioeconomic status⁵¹ and ethnicity⁵² are also important.

Table 4: Criteria for selecting patient-based outcome measures [65]

Criteria	Comments
Appropriateness	Match to the specific purpose and question to be addressed
Reliability	Reproducible and internally consistent
Validity	Measures what it purports to measure
Responsiveness	Sensitivity to changes of importance to patients
Precision	Number and accuracy of distinctions made by the instrument
Interpretability	How meaningful the scores are
Acceptability	How acceptable to the respondents
Feasibility	Effort, burden and disruption to staff and clinical care

Implications for practice

Three implications for health care professionals emerged from the debate on the patient's perspective of asthma control. The need:

1. For simple tools to assess and monitor asthma control;
2. To identify the patient-related reasons for poor control;
3. To incorporate patient perspectives into the routine review of asthma in primary care

Each of these implications is discussed in turn, below.

1) Assessing and monitoring asthma control

Severity vs. control

Management guidelines for asthma, as with many other diseases, include treatment algorithms based on severity of disease, as defined by the clinical features before treatment or by the treatment given.^{1,2} Severity usually refers to the degree of underlying pathology. Deciding the severity of asthma is not always easy.⁵³ When respiratory specialists were shown a number of case studies and asked to assign the severity of the asthma for each case, there was considerable disagreement.⁵⁴ The inherent variability of asthma also presents problems for classification of severity.⁵⁵ Severe asthma, defined as persisting symptoms despite high levels of treatment, is likely to have a number of underlying reasons, including psychological and adherence factors.⁵⁶

Although the factors indicating control may be the same as those indicating severity (e.g. persistent symptoms, impaired lung function, high bronchodilator use, oral steroid use, unscheduled consultations, hospitalisations, life-threatening attacks), there is a difference in the two concepts. Patients with severe asthma can be well-controlled, while those with mild underlying disease can show signs of poorly controlled disease. Changing the management plan to one based on control and the goals of patients may show improved outcomes compared to a plan based on severity.

Hospital-based studies have suggested that outcomes may be better with treatment algorithms based on parameters that are more closely linked to control than usual symptom-based management protocols. There is a reduction in exacerbation rate, although a higher inhaled corticosteroid load received, in patients given treatments that optimize reduction in bronchial hyperreactivity, rather than treatment on the basis of symptoms.⁵⁷ Likewise, a treatment strategy based on normalisation of sputum eosinophil levels resulted in reduced exacerbations compared to standard management protocols, without increasing steroid exposure.⁵⁸ A randomized controlled trial conducted in New Zealand used a management

strategy incorporating exhaled nitric oxide (NO) readings and achieved control that was at least as good as that obtained with a guideline-based approach but using a lower inhaled steroid dosage.⁵⁹ The GOAL study used a strategy based on the combined aims of treatment given in the GINA guidelines,¹ and showed that the majority of patients treated with individually titrated doses of inhaled corticosteroids, either alone or in combination with long-acting beta₂-agonist, could achieve and maintain control.

The need for simple valid and reliable measures of asthma control

In many chronic diseases, healthcare professionals have a philosophy of treating to achieve a predefined target level in a surrogate marker that indicates good control. However, in asthma, there is currently no simple, clear, accepted target measure that healthcare professionals can aim to achieve, and that patients can use as a reliable indicator of treatment effectiveness. Instead, asthma control is currently implied in a number of ways (Table 2).

Assessment of asthma has traditionally been based on parameters noted in management guidelines, such as lung function and symptoms. However, there is little correlation between commonly measured objective measurement of lung function using peak flow meters or spirometry and the level of symptoms or quality of life impairment perceived by patients,⁶⁰ and less easily measured parameters such as lung hyperinflation may show better correlations with symptoms such as breathlessness.⁶¹ This may be due, in part, to other factors that influence perception of symptoms, such as concomitant anxiety, depression and socioeconomic status.⁵¹ The demonstration of variability and reversibility of airflow limitation confirms asthma but the absence of these features at a given moment in time does not preclude the diagnosis.

A simple tool is required to assess asthma control accurately. The tool needs to be quick to use in primary care, where the majority of patients with asthma are managed by a range of healthcare professionals, in brief consultations. The ideal features of an asthma control tool are summarized in Table 3. Two approaches can be considered: monitoring of biometric markers of control and development of questionnaires to record patient-reported outcomes.

Biometric markers assess factors associated with the pathogenesis of asthma. The definition of asthma encompasses airways hyperresponsiveness and inflammation, which may both be more closely linked to asthma control than traditional measures of symptoms and lung function. Measurements of bronchial hyperreactivity have higher sensitivity and specificity

for the diagnosis of asthma than measurements of diurnal variation in peak flow.^{62,63} Exacerbations occur more frequently in patients with high bronchial reactivity, compared with those with reduced bronchial reactivity, though there is poor correlation between bronchial hyperreactivity and markers of inflammation. Bronchial hyperreactivity can be assessed by direct challenge (eg inhalation of histamine or methacholine) or indirectly (eg using exercise, or inhalation of hypertonic saline or mannitol). However, measurements of bronchial hyperreactivity are time consuming, and require appropriate equipment and healthcare professional expertise as well as patient cooperation, limiting the value of the approach as a practical measure of control. There is some interest in the use of mannitol BHR but this approach has yet to be fully evaluated in primary care.

Inflammation is central to the pathogenesis of asthma, with anti-inflammatory treatment forming the basis of asthma management. New technological developments enable non-invasive measurement of inflammation. Eosinophil count estimations in spontaneously produced or induced sputum can be measured as a marker of control, though the method requires appropriate expertise and laboratory support so is not currently suitable for use in routine primary care. Another surrogate measure of inflammation is exhaled nitric oxide (NO). NO is produced in low levels by airways epithelial and endothelial cells, but inflammatory cells contribute to greatly increased levels, explaining the observed correlation between NO-levels and eosinophilic inflammation.⁶⁴ Until recently, exhaled NO estimations necessitated the use of expensive monitoring equipment restricted to secondary care and research settings. However, technological advances have resulted in the development of inexpensive, handheld monitors to record exhaled NO, which are potentially available for use in primary care. This biometric method for assessment of control has some promise and is currently being evaluated.

Patient-based outcome measures

Patient-based outcome measures (Table 4)⁶⁵ may be useful to assess asthma control. A number of such tools have been developed that involve questioning the patient about outcomes achieved. Such tools may be generic or disease specific. Generic measures, such as the EQ-5D,⁶⁶ are often easy to use, brief and acceptable to both patients and practitioners. They also capture the impact of comorbid conditions (which are common in patients with asthma) and allow comparison across patient groups and therapies. However, asthma-specific outcome measures are more sensitive than generic measures to disease-specific aspects of health-related quality of life and the effects of asthma treatments.

There are a number of asthma-specific patient-based measures available that vary in characteristics, technical validity and ease of use. The Rule of Two consists of three items covering asthma symptoms and rescue medication use, each of which is answered with 'yes' (= 2 points) or 'no' (= 1 point) so that summing the answers gives a score ranging from 3 (= poor control) to 6 (= good control).⁶⁷ Although some validation of the instrument has been carried out, there is no information on a minimal important difference and limited data on responsiveness. However, the instrument is quick and easy to use in consultations. The 30-second test is widely used in Canada, where it is recommended in management guidelines.⁶⁸ Although the six questions are easy and quick to answer with yes/no, responsiveness has not been determined. The Royal College of Physicians three questions

are validated against other tools, widely used in the UK and recommended in management guidelines.³³ With the questions requiring simple yes/no answers, the method is quick and easy to use in clinical practice. Tools such as the Asthma Control Test (ACT),^{69,70} and the Asthma Control Questionnaire (ACQ)^{71,72} are also useful, and show good correlation with each other.^{53,73} The ACT is shorter, requires no calculations and includes a question on the patient's view of control so gives a useful insight into the patient perspective. Both the ACT and ACQ are validated tools that are reliable and responsive to changes in asthma control over time, and provide a single numerical indication of control that has the potential to provide a target to drive management, analogous to that of a blood pressure measurement or a lipid measurement for management of hypertension or dyslipidaemia. Both measures have the potential to influence long-term asthma outcomes, raising expectations for asthma management and facilitating the achievement of asthma control.

2) Identifying and addressing patient-related reasons for poor control

Identifying poor asthma control is the first step in improving it. The next step is to establish the reasons for poor control in individual patients. This should include an assessment of whether patient behaviors such as smoking or treatment nonadherence might be contributory factors. Patients may be reluctant to admit smoking or nonadherence if they believe that this will offend the clinician. However, asking adherence questions in a supportive manner, which sanctions nonadherence, can overcome this problem leading to more accurate reports.⁴⁵

It is also important to identify the specific reasons for nonadherence in individual patients. One of the reasons why previous interventions to improve adherence have met with limited success⁷⁴ is that they have taken a 'one-size fits all' approach, rather than individualising the approach to meet the specific needs of the patient.³⁷ Interventions to facilitate optimum adherence with asthma therapy are likely to be more effective if they are individualized and address perceptual barriers (eg patient beliefs and expectations) as well as practical barriers (eg regimen convenience, ability to use inhaler devices).⁴⁵

Healthcare professionals can provide information about illness and treatment. However, unless the information given has an impact on patients' common-sense beliefs about the illness and treatment, it will not change patient behavior. Healthcare professionals should ask about current illness and treatment beliefs. Although patient beliefs govern attitudes towards therapy, these beliefs are not fixed and can be changed through education and negotiation, leading to a better understanding of asthma that may promote more effective self-care behaviors.⁴⁵ In short, what people believe about their asthma may affect how they cope with it, and tailored education is the first stage. A three-step approach, covering perceptions and practicalities, has been suggested to facilitate optimal adherence to appropriately prescribed treatment.⁷⁵ This suggests that healthcare professionals should:

- 1) provide a common-sense rationale for the necessity of treatment that is consistent with the patient's common-sense model of asthma and their goals for asthma control
- 2) elicit and address specific concerns about treatment
- 3) prescribe a convenient treatment regimen tailored to address

practical barriers to adherence (e.g. correct inhaler technique, use of combination inhalers to reduce inhaler load (if indicated)).

Identifying and addressing misplaced health beliefs (eg asthma is an episodic disease) may be helped by tailoring education to the patient's own needs and goals. Explicitly eliciting patient goals and using these as a basis for treatment and education may allow professionals to identify more effectively what is important to the patient and allow the patient to assess meaningful changes in their asthma. The importance of the patient in their own self-care is increasingly recognized, with development of initiatives to support self-care.⁷⁶ Teaching physicians to improve interactions with patients can result in greater ability to address patients' fears about asthma medication and improvement in asthma control.⁷⁷

3) Incorporating patient perspectives into the routine review of asthma in primary care

The identification of non-adherence as a cause of poor control, and the factors contributing to poor adherence, has increased recognition of the need for individual patient-centred reviews. However, there are increasing resource constraints in primary care. Currently, asthma reviews are often not standardized in structure and data collection, are not comprehensive, fail to address the needs and expectations of patients, are ineffective at reducing morbidity and mortality, and are poorly attended.

The Minimal Asthma Assessment Tool (MAAT) is under development as a method to address some of these issues, and to help prioritize patients for primary care review by identifying poor asthma control and the causes of poor control for individual patients.⁷⁸ The MAAT consists of a brief 2-page questionnaire covering patient views about preventer inhalers, actual use and perceived side-effects, how asthma affects the individual, and issues likely to affect asthma control such as smoking and comorbid rhinitis. An international study is planned to evaluate use of the MAAT. The development of effective tools to facilitate more efficient, patient-centred review of asthma in primary care is vital to improving asthma control and patient quality of life.

Summary

It is possible to improve current levels of asthma control if healthcare professionals do four things:

- 1) use appropriate, patient-centred tools to assess control
- 2) identify the reasons for poor control in individual patients
- 3) work with patients to design individual treatment plans that address poor control and the causes of poor control, taking account of patient goals and aspirations
- 4) monitor outcomes and take appropriate action through regular review

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To Prone or not to Prone?

Jeff Borrink

A recent article published in *Critical Care Medicine* by Alsaghir et al, reviewed the effectiveness of prone positioning (PP) compared to supine position (SP) with respect to mortality, oxygenation, length of time on mechanical ventilation, and ventilator associated pneumonia (VAP) for patients with acute respiratory distress syndrome (ARDS). Dr. Alsaghir et al performed a systematic literature review of 63 articles, and then performed a meta-analysis of five randomized, controlled, human studies that assessed the effect of PP as compared with SP on mortality and improvement in oxygenation in patients with ARDS.

PP showed significant and persistent improvement in the PaO₂/FIO₂ ratio compared to the SP group. There were no significant differences in the number of days on mechanical ventilation between the two groups. No significant changes in the incidence of VAP were found between the PP group and the SP group. And no major adverse effects of PP were found.

Although each of the studies included in the meta-analysis had some limitations, primarily related to sample size and power, Dr. Alsaghir et al concluded that, overall, PP did not reduce mortality significantly, but it did improve oxygenation. In a subgroup of patients with higher severity of illness, the PP group did have reduced mortality as compared to the SP group. Because the authors were unable to identify any major adverse events of PP from the meta-analysis, and PP is a relatively simple and inexpensive intervention, they concluded that it should be considered early in the management of ARDS, especially for patients with a higher severity of illness. However, they concede that definitive recommendations require that this hypothesis be examined in a properly designed prospective trial.

Reference

Alsaghir A. H. et al: Effect of prone positioning in patients with acute respiratory distress syndrome: A meta-analysis. *Critical Care Medicine* 2008; Vol. 36, No. 2: 603-609.

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Laboratory Summary Report: Performance Observations of the Rainbow “Pulse CO-Oximeter”

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Background

While providing the normal functionality of a pulse oximeter for non-invasively monitoring functional oxygen saturation (SpO_2), Masimo’s recently introduced multi-wavelength “Pulse CO-Oximeter” device is advertised to additionally provide accurate monitoring of carboxyhemoglobin (COHb) and methemoglobin (MetHb) levels in the blood. Based in part on a published letter to the editor reporting inaccuracy of the non-invasive Pulse CO-Oximeter’s COHb measurements,¹ and the fact that the manufacturer’s accuracy claims for COHb and MetHb did not clearly indicate whether those accuracy levels applied during conditions of reduced arterial oxygen saturation,[†] we wished to further explore the performance of this system in individuals who had mild to moderately reduced oxygen saturation levels (ie elevated levels of deoxyhemoglobin in the arterial blood). Furthermore, we wanted to investigate if there are differences in the system’s SpO_2 accuracy provided by the sensor’s extra wavelengths. Covidien commissioned a study (as summarized below) to independently evaluate performance of the Masimo Rainbow SET system - specifically, to assess SpO_2 , SpCO (fractional COHb) and SpMet (fractional MetHb) accuracy over the 70%-100% oxygen saturation range.

The evaluation was conducted by Clinimark in Louisville, Colorado, an independent testing facility experienced in conducting in vivo pulse oximetry desaturation studies for research purposes and regulatory submissions. Study protocols, Institutional Review Board (IRB) approval, laboratory procedures, and data collection were managed by the test facility. This report summarizes the procedures used in the study, presents data collected in the study, and provides observations regarding the data.

Methods

Following IRB approval and subject informed consent, 13 volunteers were studied (ages 20-44 years, 130-195 lbs, with light to dark pigmentation and a mix of smokers and non-smokers). The subjects were healthy with normal blood constituent levels and perfusion as indicated by the CO-Oximetry data and pulse oximetry strength at the sensor site. Each subject

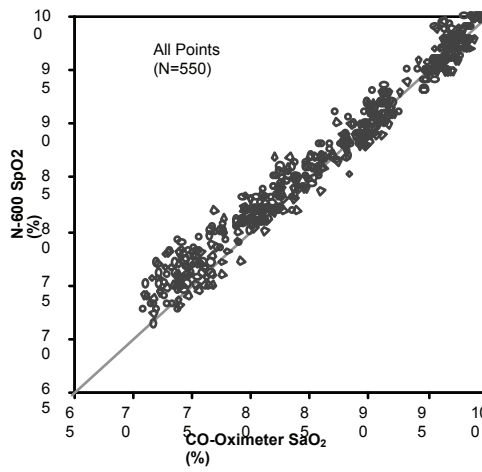
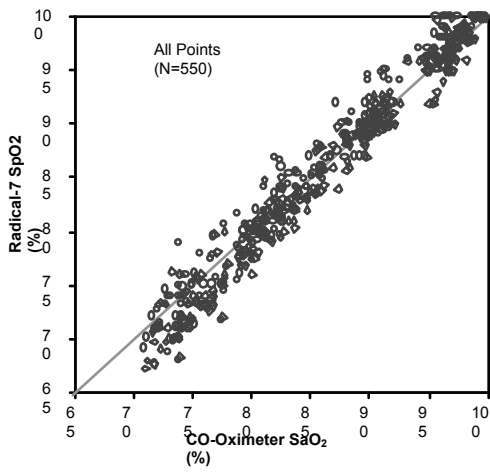
was cannulated in the left arm with an indwelling radial artery catheter for blood sampling. Two Masimo Radical-7 (rainbow R25 adhesive sensors) and two Nellcor N-600 (Max-A adhesive sensors) systems were placed on each subject. New sensors were used on each subject. All sensors were placed and connected to their respective monitors according to the manufacturers’ labeled Instructions-For-Use and prior In-Service Training.

Hypoxemia was induced in each subject by varying the fraction of inspired oxygen (FIO_2), creating stable oxygen saturation levels between 100% and 70% SaO_2 (stability was assessed using SpO_2 readings from a fifth pulse oximeter). The COHb and MetHb levels within each subject were not actively altered; their individual values remained stable over the data collection period. Both hands remained stationary throughout the arterial blood draws. SpO_2 , SpCO and SpMet values as available from the pulse oximeters were collected via computer simultaneous with blood drawn from the indwelling catheter. For each stable oxygen saturation level, approximately five arterial blood samples were collected approximately 20 seconds apart, targeting up to 25 blood draws per subject. Samples were immediately analyzed with a bench-top CO-Oximeter* to measure the arterial oxygen saturation (SaO_2), fractional carboxyhemoglobin (FCOHb) and fractional methemoglobin (FMetHb) levels for comparison with SpO_2 , SpCO and SpMet readings, respectively. Accuracy was computed as the root-mean-square of the pooled reading differences (A_{rms}). All procedures followed the methods outlined in ISO9919:2005.

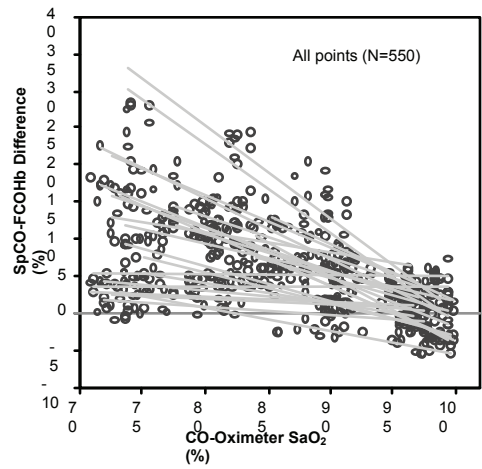
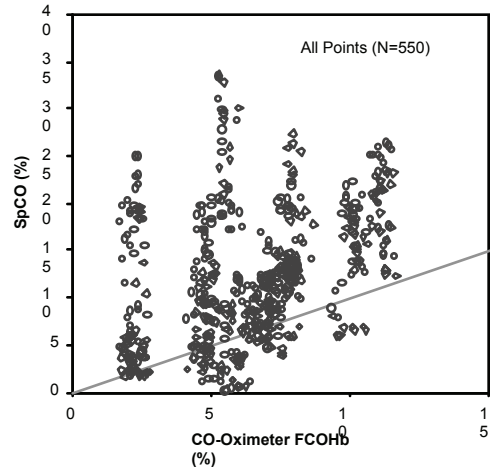
Results & Observations

The 13 volunteers enrolled in the study included a mix of non-smokers and smokers, providing an FCOHb range of 1.8% to 11.7% per laboratory CO-Oximeter. Subject FMetHb ranged between 0.1% and 0.9%. There were 275 blood samples drawn during stable reading periods, spanning a 71.0%–99.9% SaO_2 range and yielding 550 data pairs for analysis of each system. The Radical-7 displayed “low SpCO confidence” messages during some of the monitoring periods while continuing to post SpCO values; Observation 4 below offers analysis that excludes these data pairs.

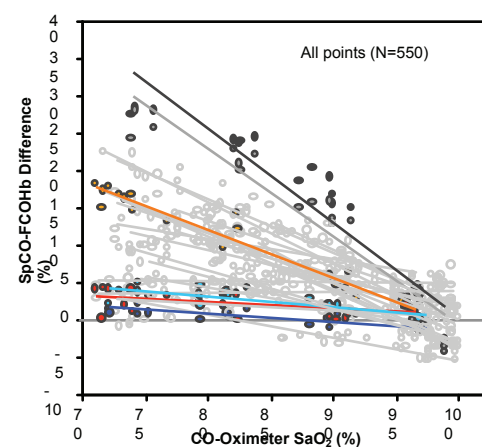
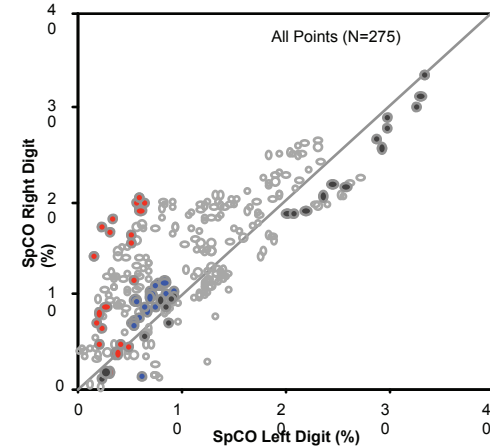
This article was provided by Covidien, which makes the Nellcor product mentioned in the article.



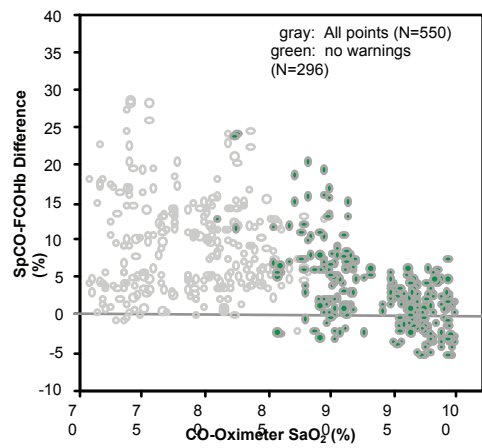
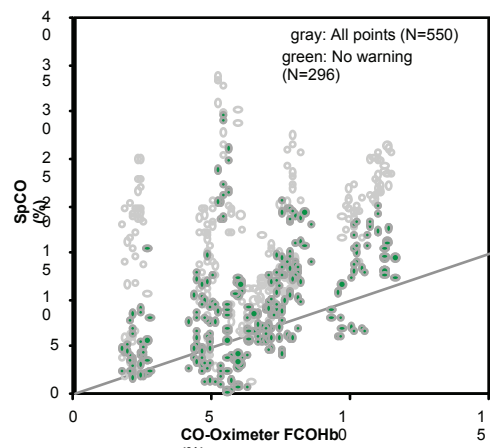
Observation 1: SpO₂ accuracy for the Radical-7/R25 ($A_{rms}=1.8\%$) and N-600/Max-A ($A_{rms}=1.6\%$) were both consistent with their labeled accuracy claims of $A_{rms} \leq 2\%$ SpO₂, even when including subjects with elevated FCOHb levels. In these observations, the COHb did not meaningfully influence the SpO₂ correlation to SaO₂ (Note: Neither SaO₂ or SpO₂ are direct measures of fractional oxyhemoglobin, FO₂Hb.)



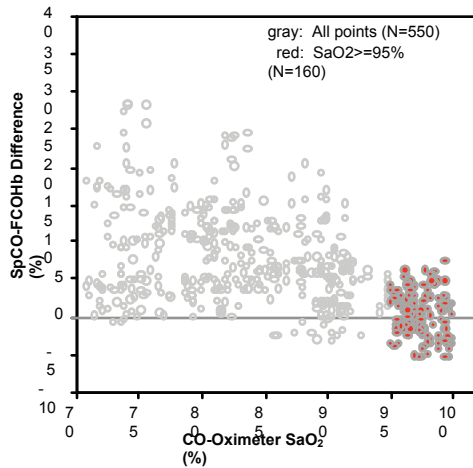
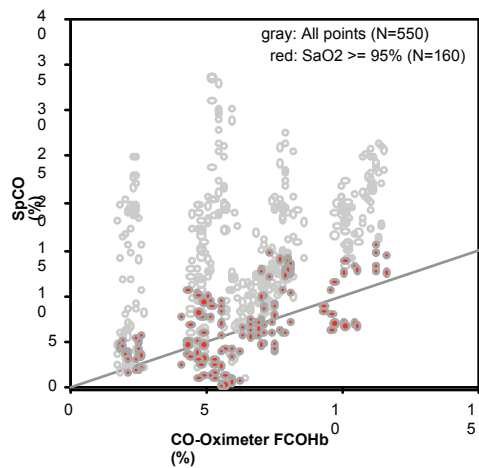
Observation 2: Radical-7 SpCO readings were significantly affected by the subjects' SaO₂ levels. The left graph below plots SpCO versus CO-Oximeter FCOHb for all data. A_{rms} accuracy for all points was 8.6%. The right hand graph plots the SpCO error versus blood SaO₂, indicating the 26 individual regression lines.



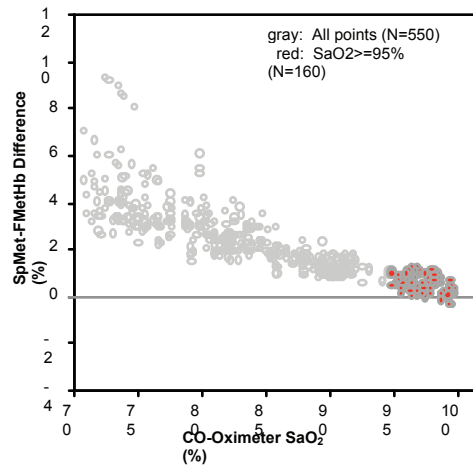
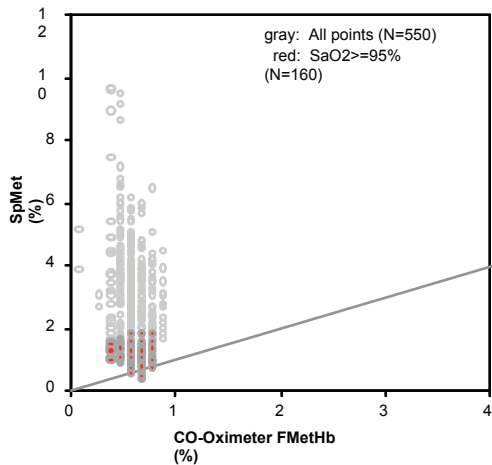
Observation 3: SpCO consistency between two simultaneously-placed Radical-7 systems varied among subjects. The graph on the left plots all observations, highlighting similar or disparate readings in three subjects (blue, black and red points). The graph on the right compares these subjects' SpCO readings to CO-Oximeter SaO₂, along with their individual regression lines (blue/aqua, black/grey, red/orange pairs).



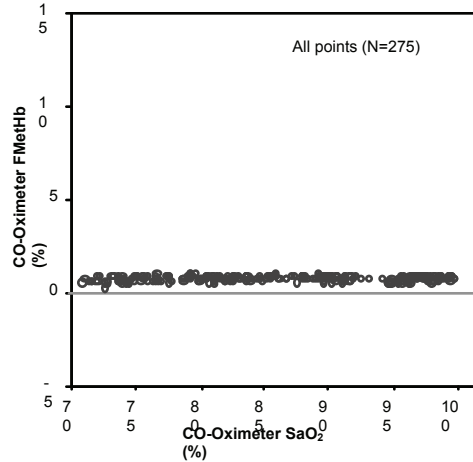
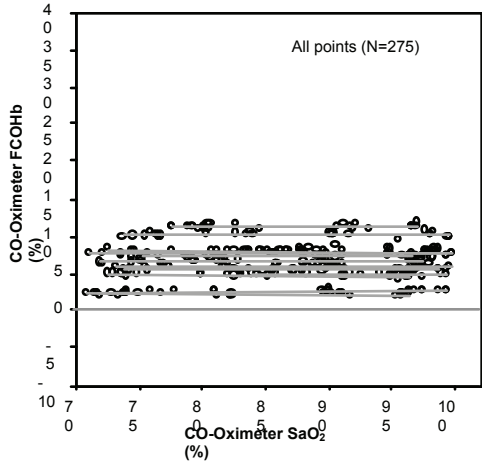
Observation 4: Excluding observations made during display of "low SpCO confidence" messages (typically at the lower SaO₂ levels) improves accuracy. Green points in the graphs below indicate observations made while no messages were displayed. A_{rms} improves to 5.7%, though remains outside the manufacturer's specified accuracy. (Open gray circles indicate the excluded data.)



Observation 5: Best performance in tracking FCOHb occurred at the highest SaO₂ levels. The solid red points in the graphs below indicate the observations made with blood SaO₂ ≥ 95%. A_{rms} for this set of observations was 3.0%, more in line with the manufacturer's specified performance.



Observation 6: Similar behaviors were seen with the SpMet readings (though available data is limited to FMethb < 1%). A_{rms} for all readings was 2.5%; including only SaO₂ ≥ 95% data improves A_{rms} to 0.5%.



Observation 7: The bench-top CO-Oximeter did not show SaO₂-dependence in FCOHb and FMethb readings – each individual's readings were stable across the SaO₂ span. (FCOHb vs. SaO₂ regression lines are shown for each of the 13 subjects in the left hand graph below.)

Conclusion

The Masimo Radical-7 Rainbow SET system reported SpO₂ values similar to the Nellcor N-600 two-wavelength pulse oximeter in comparison to blood SaO₂. Although not statistically significant, the N-600 was more accurate.

Both the SpCO and SpMet measurements of the Radical-7 were most accurate and consistent with the manufacturer's specifications when the subject's SaO₂ levels were 95% or higher. However, there was a clear correlation of each of these parameters becoming increasingly less accurate with a higher bias as the subjects became more hypoxemic.

†According to the user manual, the Radical-7's accuracy claims

for COHb and MetHb are ± 3% and ± 1% respectively; however, the claims do not indicate whether or not the COHb or MetHb accuracy levels are the same regardless of the concurrently occurring oxygen saturation levels.

*IL-682, Instrumentation Laboratories, Lexington, MA. Data analyses using values simultaneously measured with an OSM-3 Hemoximeter (Radiometer, Westlake, OH) were not meaningfully different than the results presented here.

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On the Front Lines: The Vital Role of Respiratory Care in Preparedness and Response

Frank G. Rando

This is Part II of a two-part article.

Clinical outcomes and salvageability in mass casualty medical management depend on a number of variables of which the availability of prepared medical personnel and resources that can be mobilized rapidly and efficiently are critical factors.

The availability and deployment of Disaster Medical Assistance Teams (DMATs) and the Strategic National Stockpile (SNS), which contains medical equipment, supplies and pharmacological agents will require time to deploy to an affected area, and then supplies, equipment, pharmaceuticals must be distributed. Therefore, HCFs are expected to operate in a stand-alone mode for 72 hours, and possibly longer, before Federal resources are in place.

The Joint Commission (JCAHO), now recommends a minimum of 96 hours to sustain critical healthcare infrastructure and resources, as the new standard in healthcare emergency preparedness. This move is a direct result of lessons learned during Hurricanes Katrina and Rita. In addition, as a forward-deployed asset of the SNS, CHEMPACKS have been made available to some municipalities to treat victims of chemical agent toxicity, and many EDs, hospital pharmacies, first responder vehicles and EMS systems possess Mark-I autoinjector kits (NAAKs) that contain atropine and pralidoxime (2-PAM Chloride). The Mark-I autoinjector system dispenses 2 mg of atropine and 600mg of pralidoxime chloride (2-PAM Chloride) IM and serves to reverse the cholinergic effects of organophosphate and carbamate pesticides and militarized nerve agents such as sarin (military nomenclature-GB) soman (GD), tabun (GA) and VX, which are all organophosphate compounds.

Organophosphates and carbamates bind to and inhibit acetylcholinesterase enzymes, allowing acetylcholine to accumulate at receptor sites, which induces excess cholinergic activity.

Signs and symptomatology of organophosphate and carbamate toxicity result from the accumulation of acetylcholine at muscarinic and nicotinic receptor sites in the peripheral and central nervous systems.

Muscarinic signs and symptoms include diarrhea, urination, miosis, bronchorrhea, bronchoconstriction, bradycardia,

emesis, lacrimation and sialorrhea (excessive salivation). The mnemonic "DUMBELS" can be used to memorize the signs and symptomatology of cholinergic pesticide/nerve agent toxicity.

The acronym "SLUDGEM" salivation, lacrimation, urination, defecation/diarrhea, gastrointestinal emptying, miosis (pin-point pupils) may also be used to refer to the signs and symptoms of cholinergic pesticide/nerve agent toxicity. The nicotinic signs and symptomatology consist of muscle fasciculation, weakness, fatigue, diminished respiratory effort, respiratory effort, tachycardia, hypertension, and hyperglycemia.

These adverse physiological effects occur due to excessive stimulation of nicotinic acetylcholine receptors at the neuromuscular junction and autonomic ganglia. Atropine will mitigate the muscarinic effects of organophosphate/carbamate pesticide and nerve agent toxicity, however, it will not reverse the nicotinic effects. Pralidoxime (2-PAM Chloride) reactivates acetylcholinesterase, serves as an antidote for organophosphate poisoning and it is effective at restoring muscle activity and respiratory effort. The endpoint of atropine therapy is the drying of secretions, particularly respiratory secretions, and reversal of pulmonary edema. It is evident that mass poisoning with a cholinergic pesticide or weaponized nerve agents (pesticides can be used as low-grade nerve agents by terrorists, as well) could require vast reserves of pharmacological agents including oxygen, airway management and ventilatory support elements.

Because nerve agent or cholinergic pesticide toxicity induces excessive secretions and bronchospasm, it may be necessary to administer atropine to reduce respiratory secretions which could be copious, and bronchospasm. This would vastly facilitate ventilatory efforts and improve gas exchange by decreasing airway resistance and secretion production. Airway suctioning/secretion removal would also be of paramount importance.

Beta-2 agonists, such as albuterol, would also be useful in treating reactive airways and reversing bronchospasm. In severe pesticide or nerve agent toxicity, seizures can be expected, and administration of an anticonvulsant such as diazepam will be needed. Convulsant Antidote for Nerve Agent or "CANANA" (military nomenclature) in autoinjector form is available to deliver an IM injection of 2ml of diazepam (Valium) to control seizure activity.

It is imperative that RCPs/RTs become cross-trained to administer antidotal therapy for nerve agents/cholinergic pesticides and other hazardous materials that may impact respiratory function, such as hydrogen cyanide or hydrogen sulfide. Members of the AARC Disaster Response Committee, now the Disaster Response Roundtable, have initiated a Mark-I autoinjector training program and 50 autoinjector trainers are available on a loan basis to be utilized in training programs for RCPs/RTs throughout the Nation. RCPs/RTs can be expected

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to treat a variety of clinical conditions ranging from acute exacerbations of asthma to mass trauma caused by terrorist bombings. RCPs/RTs must be well versed in tactical and disaster medicine and the AARC and credentialing bodies need to work together to establish a sub-specialization credential in emergency preparedness and disaster medicine.

An extended scope of practice for RCPs/RTs in mass casualty events is mandatory. While the emphasis will be on respiratory therapeutics, airway management and ventilatory support, the RCP/RT may be expected to function as a multi-skilled health professional utilizing a variety of patient care skills sets, such as establishing IV lines, performing pleural decompression, and assisting with triage and other procedures.

The RCP/RT may be one of the first health professionals to recognize unusual syndromes or cluster presentations that would serve as indicators of bioterrorism-related illnesses, emerging infectious diseases or chemical agent toxicities (toxidromes). This would require didactic and practical training in the medical management of hazardous materials exposures and weapons of mass destruction events.

Bioterrorism-related illnesses and emerging infectious diseases would require further training in syndromic recognition and surveillance, basic epidemiology, infection control, microbiology and pathophysiology of bioterrorism-related illnesses and emerging pathogens, medical management of biological casualties, including chemo- and immunoprophylaxis, antibiotic/antiviral therapies, and other related topics.

Some indicators and complications arising from bioterrorism-related illnesses and emerging pathogenic and infectious diseases include flu-like symptoms, pneumonias, sepsis, coagulopathies (eg, viral hemorrhagic fevers such as Ebola, Marburg and Lassa), mediastinitis (inhalational anthrax), descending paralysis/neuromuscular dysfunction/respiratory paralysis (botulinum toxin), catastrophic airway necrosis, non-cardiogenic pulmonary edema/ARDS/multiple organ failure (ricin toxin), hemoptysis/sepsis (pneumonic plague), dermal lesions, multisystem failure, bone marrow failure, inhibition of nucleic acid synthesis (tricothecene mycotoxins/T-2), vesicular lesions/centrifugal rash/sepsis/viremia (smallpox). All of these biological casualties would require the administration of respiratory therapeutics and physiological support. Mass casualties exposed to Clostridium botulinum toxin, for example, may need ventilatory support for extended periods of time, even months, as acetylcholine must be regenerated to sustain normal neuromuscular function. Therefore, weaning protocols must be re-examined and adjusted to meet the challenges of mass casualty ventilatory support.

Vigilant prevention and surveillance for nosocomial infections such as ventilator-associated pneumonia (VAP) is essential to minimize morbidity and mortality. Education and training for hazardous materials and chemical agent exposures and toxicities would include a basic understanding of the physical and chemical properties of hazardous materials and chemical warfare agents (CWAs), toxicology and pathophysiology of chemical exposures, decontamination operations, personal protective equipment (PPE), recognition of toxidromes and medical management, including pharmacological interventions.

The most common exposure pathway (route of exposure) in hazardous materials incidents and for WMD agents is

inhalational. Other exposure pathways include injection, dermal and ocular absorption, and ingestion. Often, the human lung is the target organ, and due to its exposure and large surface area, the respiratory system serves to facilitate systemic absorption for systemic toxicants.

For toxic industrial chemical inhalational exposures that result from irritant gases such as ammonia, chlorine and phosgene, water solubility plays an important role due to the aqueous medium present in the respiratory tract. Ammonia, for example, is a highly water soluble irritant gas that can induce upper airway effects, including airway obstruction, while chlorine gas is moderately water-soluble and phosgene is slightly water-soluble and mainly affects the peripheral airways resulting in delayed-onset, non-cardiogenic edema. After contact with moist mucosal membranes, ammonia reacts with water to form a strong alkali, ammonia hydroxide, which is highly corrosive and causes liquefactive necrosis/saponification of the tissue. Massive exposures can bypass the absorptive surface area of the upper respiratory tract and result in extensive injury to the lower and peripheral airways, including the alveoli. Early intubation is indicated in these scenarios due to impending glottic/laryngeal edema. In some cases of acute obstruction, a surgical airway may be required.

For acid gases, such as chlorine, administration of nebulized sodium bicarbonate has been found effective in safely buffering hydrogen chloride formation, for example, counteracting potential corrosive damage and alleviating symptoms such as chest tightness and cough. For hydrofluoric acid (HF) inhalation, the administration of aerosolized calcium gluconate is a viable therapeutic intervention. The classic, clinical hallmark for phosgene toxicity is delayed-onset, non-cardiogenic pulmonary edema/ARDS caused by slow formation of hydrogen chloride (HCl), inactivation of enzymes and oxidant damage to the alveolar-capillary membrane. This causes alveolar-capillary leak and non-hydrostatic and non-cardiogenic pulmonary edema.

Mechanical ventilation with positive end-expiratory pressure (PEEP) may be indicated for edemogenic effects and ARDS. Bronchodilators and corticosteroids are used judiciously to treat reactive airways, and corticosteroids have been employed to prevent the development of bronchiolitis obliterans in toxic inhalations. Hyperbaric oxygenation (HBO) may be indicated for victims exposed to cyanide, as well as carbon monoxide, however, mass HBO therapy is impractical for mass casualties.

The aftermath of mass chemical exposures and chemically-associated illness may result in acute and chronic respiratory dysfunction requiring urgent evaluation via pulmonary function testing and bronchoscopic examination. The RCP/RT will also be expected to perform, assist, interpret and evaluate pulmonary diagnostic studies.

While industrial accidents may be more likely, it must be understood that toxic industrial chemicals and materials (TICS/TIMs) may be used by terrorists as weapons of opportunity and convenience and that your facility and community must include this possibility in their risk and threat assessments and vulnerability analysis. The pre-event use and interpretation of plume dispersion/chemical behavior models, such as CAMEO and the integration of this data into healthcare facility emergency planning is vital.

Planners and clinicians should realize that the first battlefield

CWAs used in modern warfare were chlorine, phosgene and cyanide, all available TICs used in commerce and industry. The clinical management of blast-related trauma will require a basic comprehension of explosives, explosion kinematics, and the pathophysiology and clinical manifestations of explosive incidents, statistically, the preferred attack method of terrorists. Injury patterns with pulmonary barotrauma caused by the primary blast wave can be expected, along with penetrating injuries, crush injury/compartment syndrome, cranial, extremity and ocular trauma. Hollow viscus rupture, air embolism leading to cerebral, coronary or pulmonary embolization, pneumothorax, hemothorax and other complications may be present due to the mechanisms of injury.

Traumatic amputations and visceral injury from acceleration and deceleration forces are common. Tympanic membrane rupture may be a significant indicator of pulmonary barotrauma, because this disruption results from a blast wave insult of approximately 360 mmHg (7 psi). "Blast lung" is life-threatening due to widespread alveolar damage, ARDS and ensuing respiratory failure. Burn trauma, inhalation of toxic combustion byproducts and intentional dissemination of radiological, biological or chemical agents are also possible, although biological agents and chemical agents may be destroyed by a high-yield explosion, heat and pressure.

Ionizing radiation (nuclear radiation) is the most widely studied and understood environmental agent and its biomedical effects are well documented. There has been ample opportunity to conduct basic and applied research in radiobiology, as well as longitudinal epidemiological studies of exposures due to the use and testing of nuclear weapons, accidental exposures, environmental contamination, and, unfortunately, human experimentation during the Cold War era. While the threat of global thermonuclear warfare may have subsided, the possibility of accidental or intentional radiological releases from nuclear sources are possible; as is the detonation of a radiological dispersal device or a dirty bomb, which is a conventional explosive device that has radiological material incorporated into it and is designed to disperse radioactivity into the surrounding area of detonation. The deterministic effects (acute radiation syndrome or ARS, immediate effects) and stochastic effects (chronic, long-term effects) have been and continue to be studied. The complications of radiological exposure may require critical care interventions and support, including respiratory therapeutics and ventilatory support. Radiological exposure can induce bone-marrow suppression, central nervous system and gastrointestinal damage and lead to sepsis, ARDS and multiple-organ system failure. Respirable particles and radioactive aerosols and gases can be inhaled and deposited in the respiratory system (incorporation) and radioactive particles, such as alpha emitters, may be retained in the lung and irradiate local tissue. This can lead to radiation fibrosis and radiogenic carcinoma of the lung. Also, acute radiological exposures may damage pulmonary endothelium leading to changes in cell permeability, alveolar-capillary leak and non-cardiogenic pulmonary edema. A small, crude improvised nuclear device or a radiological dispersal device can inflict substantial, concomitant physical injury complicated by radiological exposure and contamination. Injuries resulting from blast trauma, incendiary effects (thermal burns), toxic inhalation/airway injury structural collapse should be expected in these scenarios and planned for accordingly. Combined and complex injury matrices would be likely.

Natural disasters contribute greatly to morbidity and mortality in the US and abroad. We need only to witness the ravages of

Hurricane Katrina, the recent tsunami that resulted in excess of 100,000 deaths and the May 2008 cyclone in Myanmar and massive earthquake in China. Critical infrastructure loss, infectious diseases, environmental hazards, psychosocial implications, multiple physical trauma and other associated hazards abound in the aftermath of natural disasters. In mass casualty management, triage is paramount to determine treatment priorities. Triage, in French, translates into "to sort," which is to say "the sorting of casualties," a system perfected by the world's military forces. RCPs/RTs need to understand and apply the principles of triage which seeks to place casualties into treatment categories for appropriate disposition based on criticality, salvageability and available resources. In mass casualty events, triage is essential, as limited resources and personnel must concentrate on those with acute medical needs that require immediate clinical intervention.

The national standard for mass casualty triage is known as START (Simple Triage and Rapid Treatment). START is based on three assessed parameters: respirations, perfusion (via radial pulse) and mental status (RPM). Triage categories are immediate (red tag), delayed (yellow tag), minimal (green tag) and dead or dying (also known as "expectant" black tag). For example, a respiratory rate greater than 30 for an adult (tachypnea) places an individual into the "immediate" or red tag category, while an apneic victim who does not respond to a head-tilt airway maneuver is placed into the deceased category and the patient disposition is for the morgue/mass fatality management team. Similarly, a patient who may have normal respirations and a palpable radial pulse, but who presents with an altered mental status, would be also placed into the immediate category.

RCPs/RTs can participate in triage training that teaches START principles and technique for adults and pediatric patients. In multiple or mass casualty events, the Incident Command System (ICS) becomes activated which lends itself to a flexible organizational structure and essential management tool for any contingency, whether natural or man-made, whether internal or external. In the healthcare setting it is known as the Hospital Emergency Incident Command System (HEICS), and it should be standardized to complement the external ICS. The HEICS must also be compliant with the new National Incident Management System (NIMS). As of January 2001, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) has added a requirement to have common all-hazards command structures and Emergency Operations Plans that link to the community. The RCP/RT and other health professionals must have a firm foundation in the ICS, NIMS and the National Response Framework (NRF). The US Department of Homeland Security/FEMA offers free online training on the ICS, NIMS and NRF and other emergency management and emergency response topics at www.fema.gov and click on to the "Independent Study" section.

Suffice it to say that the RCP/RT profession and respiratory care departments have played and will continue to play active roles in healthcare and community preparedness and response in the future. The determination, willingness and sacrifices of RCPs/RTs, individually and collectively, in day-to-day healthcare delivery and in austere and challenging environments are well known and appreciated by many, including the highest levels of public health and public policy decision-making. But, most importantly, we make a difference to our patients and their loved ones. We must all be able to confront and manage conventional and asymmetric threats and provide quality health services under

the most austere and desperate conditions.

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Anxiety and Panic Fear in Adults With Asthma: Prevalence in Primary Care

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Abstract

Background: Patients may find it difficult to distinguish between the symptoms of anxiety and those of asthma. Findings are equivocal on whether there is a specific link between anxiety and asthma. The aims of this study were to i) to identify the prevalence of anxiety, depression and panic fear in adults with asthma compared with that of the general population ii) to investigate whether there is a specific relationship between asthma and anxiety.

Methods: An epidemiological survey of 872 adults with a diagnosis of asthma identified from six General Practices in Sheffield, England. Community postal survey using self-completion questionnaire.

Results: The response rate was 59%. People with asthma had higher mean Hospital Anxiety and Depression Scale (HADS) anxiety scores than UK norms with a higher proportion above the clinical cut-off. Mean HADS depression scores were significantly higher than UK norms and norms for a general population sample of people registered with the same practice. These effects were age-related with the relationship between asthma and psychological distress most marked over the age of 45. The prevalence of asthma-specific panic fear was 15.7%.

Conclusion: A significant minority of people have high levels of panic fear (as measured by the Asthma Symptom Checklist) associated with asthma. However, in adults with asthma there is also high prevalence of both generalised anxiety and depression (as measured by the HADS), suggesting that the link of anxiety to asthma may be part of a broader relationship between psychological distress and chronic disease rather than a specific one.

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Background

There has been considerable research on the relationship between asthma and anxiety. Recent reviews¹⁻³ of the literature describe an increased rate of psychological co-morbidity in adults with asthma including anxiety and panic symptoms. Although anxiety is a normal reaction to extreme dyspnea,⁴ and may even be functional in moderation,^{5,6} high levels of panic fear may lead both to exacerbation of the condition and poor management. For example, it has been demonstrated that panic may trigger an asthma attack through hyperventilation and airways cooling.⁷ Patients may find it difficult to distinguish between the symptoms of anxiety and those of asthma leading to inappropriate self-medication.⁸ A New Zealand study of management errors in acute severe asthma in adults found that most were related to patient behavior, and that panic and the overuse of beta-agonists were important contributory causes.⁹ In a study of the Asthma Symptom Checklist¹⁰ used in people with asthma recruited from general practice, the responses to the panic fear subscale predicted oral steroid intake and the authors concluded that the emotional impact of asthma showed a stronger association with aspects of asthma management than symptoms of dyspnea did. Similarly, anxiety has been shown to be related to levels of oral corticosteroid prescribing in near-fatal asthma patients.¹¹

Findings are equivocal on whether there is a specific link between panic and respiratory disorders including asthma. The high prevalence of panic-fear or anxiety symptoms in asthma populations does not in itself establish a specific link as this could be part of a broader relationship between any chronic disease and lowered psychological wellbeing. A Swedish research group found significant correlation of anxiety and depression with self-reported respiratory symptoms, but not objective asthma variables using the Hospital Anxiety and Depression Scale.¹² This finding was replicated in asthma patients treated in GP practices in the UK, where there were significant correlations of HADS anxiety and depression with self-reported symptoms from the Asthma Quality of Life Questionnaire, but not with objective measures of lung function.¹³ A recent review¹⁴ of the literature reported that the findings are inconclusive on whether people with asthma are more likely to be depressed than those without asthma. Although HADS anxiety has been estimated in community samples of adults with asthma, ASC panic fear, a measure of asthma specific anxiety, has previously been less frequently reported in community populations. The higher rates of panic in hospital attendees could be a selection bias of hospital attendance, in that these rates may be associated with attendance at hospital. This paper addresses the question of whether the higher levels of anxiety demonstrated in people with asthma is specifically

Table 1: Hospital Anxiety and Depression Scale anxiety: Comparison of asthma population survey data with population norms [22]

	Asthma Population	Population norm (Crawford et al)	Difference	95% CI	p-value
n	455	1792			
Median	7.0	6.0			
Mean (sd)	7.79 (4.45)	6.14 (3.76)	+1.65	+1.23 to +2.05	<0.001
% score 8+	47.3%	33.2%	+0.14.1%	+9.0 to +19.1%	
% score 8–10	20.9%	20.6%	+0.3%	3.7 to +4.7%	
% score 11–15	20.2%	10.0%	+10.2%	+6.5 to +14.4%	
% score 16+	5.9%	2.6%	+3.3%	+1.3 to +6.0%	

linked or whether it is part of a picture of reduced psychological well-being by exploring the prevalence, in adults with asthma, of anxiety and panic fear as well as the prevalence of depression which has not previously been conclusively established.

Research questions

1. What is the prevalence of anxiety, panic fear and depression in adults with asthma, irrespective of their consultation history?
2. Is this prevalence significantly higher than that found in a general population survey of health and illness in the same General Practices and with UK normative data?
3. Are anxiety scores rather than depression scores elevated, compared with the general population, to support the suggestion of a specific relationship between asthma and anxiety?
4. Does the comparison of anxiety and panic fear levels with those in clinic-based samples suggest a selection bias of hospital attendance in previous research?

Throughout this paper levels of anxiety, panic fear and depression are reported as assessed using generally agreed cut-off points on established measures (HADS and ASC) and not as clinically diagnosed psychological disorders.

Methods

A random sample of 872 adults with asthma was obtained from six General Practices (serving a population of 32,343 listed permanent adult patients) in Sheffield, England during 1998 and 1999. Practices were selected to represent a wide range of Townsend deprivation scores (from 4.9 to -2.6). The six practices had a total of 2169 adult patients between the ages of 18 and 65 with a diagnosis of asthma registered with them. A random sample of 872 (approximately 40% of registered adults with asthma) was identified using computer generated random numbers. Each patient received a letter from the GP inviting him or her to complete and return an enclosed questionnaire.

The questionnaire included demographic questions, and a screening tool comprising the Asthma Symptom Checklist (ASC) and the Hospital Anxiety and Depression Scale (HADS).

The ASC15 is a self-report questionnaire widely used in asthma research to assess subjective asthma symptomatology including panic-fear. It was derived from empirical cluster analysis in a hospital sample, replicated in a later study^{15,16} and has been validated in the UK.¹⁷ We used a nine item version of ASC panic fear with response options of 1 to 5 and a cut off score of 28 and above. The cut off was derived from conventional practice of considering an average item score of 3 or more to be in the clinical range.¹⁶ A more recent reevaluation of the ASC demonstrated that, although some of the items included in the panic fear scale may be redundant, the original five factors, including one representing panic-fear, were replicated and the internal consistency of the panic fear scale was good.¹⁰

The HADS is a brief (14 item) scale developed as a reliable, practical and valid tool for identifying and quantifying anxiety and depression in patients in hospital clinics.¹⁸ It has been extensively used in hospital and primary care patients and in the general population and reviews of its use confirm its value as a case finder for anxiety disorders and depression in these populations.^{19,20} The internal consistency of the HADS has been well demonstrated and optimal balance between sensitivity and specificity for HADS as a screening tool is achieved using a cutoff of 8+ for both HAD anxiety and depression subscales.²⁰

Strategies for increasing the response rate to postal questionnaires were employed²¹ including sending two reminders to non-respondents.

Comparison data: HADS anxiety and depression scores were compared with Crawford's community sample of 1792 UK adults.²² In Crawfords study HADS data were collected from 1792 members of the general adult population (females = 978,

Table 2: Hospital Anxiety and Depression Scale depression: Comparison of asthma population survey data with population norms [22]

	Asthma population	Population norm (Crawford et al)	Difference	95% CI	p-value
n	454	1792			
Median	4.0	3.0			
Mean (sd)	4.72 (4.08)	3.68 (3.07)	+1.04	+0.67 to +1.42	<0.001
% score 8+	22.3%	11.4%	+10.9%	+7.0 to +15.1%	
% score 8–10	13.0%	7.8%	+5.2%	+2.1 to +8.8%	
% score 11–15	7.9%	2.9%	5.0%	+2.7 to +8.0%	
% score 16+	1.3%	0.7%	+0.6%	-0.3 to 2.2%	

Table 3: Mean Hospital Anxiety and Depression Scale depression score: Comparison of asthma population survey data with Sheffield Health and Illness Prevalence Survey (SHAIPS) findings for the same six practices

		Total	Males	Females
All ages	Asthma	4.70	4.64	4.72
	SHAIPS (6 practices)	3.58	3.62	3.55
	p-value	<0.001	<0.01	<0.001
18–34	Asthma	3.34	3.33	3.36
	SHAIPS (6 practices)	3.02	2.73	3.23
	p-value	= 0.298	= 0.212	= 0.763
35–44	Asthma	3.39	2.92	3.73
	SHAIPS (6 practices)	3.45	3.38	3.51
	p-value	= 0.882	= 0.498	= 0.708
45–54	Asthma	6.24	6.66	6.02
	SHAIPS (6 practices)	4.18	4.60	3.85
	p-value	<0.001	= 0.025	<0.001
55–64	Asthma	6.44	6.97	6.12
	SHAIPS (6 practices)	4.21	4.48	3.97
	p-value	<0.001	<0.001	<0.01

males = 810). Participants were recruited from a wide variety of sources including commercial and public service organizations, community centres and recreational clubs. The mean age of the sample was 41.5 years (SD = 15.9, range = 18–91). Each potential participant received an introductory letter, a HADS form and a form for recording demographic variables. The refusal rate was approximately 18%.

HADS depression scores were also compared with those of patients from the same General Practices, a subset of the Sheffield Health and Illness Survey (SHAIPS).²³ SHAIPS was a postal survey of a representative sample of the population of Sheffield looking at health status and use of health services and included the HADS depression scale. It was carried out two years after the survey reported here. The sampling frame used was the local population health register which contains, amongst other data, the GP with whom the person is registered. Stratification was used to ensure that the sample was representative of the Sheffield population in terms of age, sex and electoral ward. It is likely that some individuals responded to both surveys but the number doing so is unknown.

Data analysis: Data analysis was undertaken using SPSS software (version 10). The chi2 test was used to compare proportions of clinically significant scores for HADS and ASC measures between men and women, chi2 for trend for differences by age group, and Spearman's rank correlation was used to determine any relationship between continuous age and HADS/ASC score. Analysis of variance was used to compare HADS anxiety and depression scores with data from the UK and the general population of Sheffield. t-tests were used for comparison of means. Ideally, multiple regression analysis would have been used to determine whether there were differences in HADS depression by age and sex between the study population and the general population of Sheffield. However, as we did not have access to the SHAIPS raw data we undertook individual t-tests on each age, sex combination.

Data oversight: The investigators who collected and analysed the data reported to, and were advised by, a data monitoring group independent of the researchers.

Results

Respondents: 461 completed questionnaires were received giving a crude response rate of 53%. After accounting for 89 questionnaires returned either undelivered or marked indicating that the recipient did not have asthma the adjusted response rate was 59%.

We had a higher proportion of responses from women – 38.3% of respondents were male and 61.7% female. This approximately reflects the sex distribution of the Sheffield population and a higher prevalence of asthma in women in Sheffield.²³

The mean age of respondents was 42.4 (S.D = 13.4) years, the median was 41 years and the range was 18–66 years. The % of respondents in each age group approximately reflects the age distribution of the Sheffield population except for a slightly lower response rate in the younger age group.²⁴

HADS anxiety: The proportion of patients with a HADS anxiety score of 10 or more was 31.6%. HADS anxiety score increased with age for both scores 8+ (chi2 = 10.602, p = 0.031) and 10+ (chi2 = 21.218, p < 0.001). There was no significant difference between men and women with respect to these proportions. However, there was a significant difference in mean HADS anxiety scores by sex (Mann-Whitney U = -2.916, p = 0.004). Women had a mean score of 8.2 (S.D = 4.5) compared with a mean score of 6.9 (S.D. = 4.3) for men. The proportion of people with asthma with anxiety at a level of possible clinical disorder (HADS anxiety score 8–10) is no different from the general population. However, the proportion with probable clinical disorder (scoring 11+), is double that in the general population. The cut off of 11+ is used here for direct comparison with UK normative data.²² Mean HADS anxiety scores were also significantly higher for the asthma sample, compared with UK norms (Table 1).

HADS depression: The proportion of patients with a HADS depression score of 10 or more was 13.6%. HADS depression score increased with age for both scores 8+ (chi2 = 47.988, p < 0.001) and 10+ (chi2 = 30.721, p < 0.001). There were no significant differences between men and women.

Mean HADS depression scores were significantly higher for the asthma sample, compared with UK norms (Table 2). The proportion of the asthma population with depression at levels of both possible and probable clinical disorder was significantly greater than UK normative data (Table 2).

Mean HADS depression scores were also significantly higher for the respondents of our survey compared with Sheffield general population data, for the total sample, and for men and women separately (Table 3). This effect was accounted for by the older age groups (45–54 years and 55–64 years): see Table 3.

The proportion of the asthma population sample with high HADS depression scores was significantly higher for all categories:- 8+ and 11+ (Table 4).

Asthma specific panic fear: The prevalence of asthma-specific anxiety from the ASC Panic Fear score was 15.7% (62/395). Women were significantly more likely than men to experience panic fear associated with asthma: 19.2% (46/239) compared with 10.6% (16/151, Mann-Whitney U = -2.498, p < 0.05). The mean panic-fear ASC score (S.D.) was 17.9 (8.5) overall and 16.7

Table 4: Prevalence of Hospital Anxiety and Depression Scale (HADS) depression: Comparison of asthma population survey data with Sheffield population norms. Standardised for age and sex

Study	Standardised prevalence (95% CI) of HAD depression:	
	8+	11+
Asthma (n = 441)	24.3% (20.5 to 28.5%)	9.2% (6.9 to 12.4%)
SHAIPS: Sheffield normative (n = 714)	12.2% (10.0 to 14.8%)	5.4% (4.0 to 7.4%)

(8.3) for men compared with 18.7 (8.7) for women. The range was 9 – 44. The mean score for women was significantly higher than that for men (Mann-Whitney U = -2.498, p = 0.012). There was a significant correlation between increase in ASC score and increased in age (r = 0.114, p < 0.05).

Discussion and conclusion

The results of this study clearly show that both the prevalence of anxiety and the level of anxiety experienced by people with asthma (as measured using the HADS) are higher than that of the general population. Almost one third of asthma sufferers experience anxiety at the level of probable clinical disorder, double that in the general population. The prevalence of anxiety is higher in women than in men with asthma and increases with age. A significant minority of people with asthma experience asthma specific anxiety as measured by the panic fear subscale of the Asthma Symptom Checklist. However, the fact that the prevalence of generalised anxiety and depression are high in this population indicates that anxiety experienced in asthma may be part of a broader picture of generalised psychological distress rather than indicating that panic has a specific role in asthma.

These results from a general population sample are important in that they support the evidence of panic reported previously for hospital attenders,^{11,25} demonstrating that the findings are not only seen in hospital attenders but generally for people with asthma. Our findings are consistent with those reported previously. Rimington¹³ found that 30% of patients with a diagnosis of asthma recruited through general practice had anxiety scores of 11 or more on the HADS suggestive of a clinical anxiety state, for inner city patients this rate was 40%. In the same study 10% of patients had HADS scores suggesting depression with mean scores (S.D) of 3.7 (2.7) and 6.0 (4.3) for suburban and inner city patients respectively compared with our findings of a mean HADS depression score of 4.72 (4.08). An Australian study²⁶ reported a prevalence of anxiety (scoring 8 or more on HADS) of 40% of patients with asthma. More-over the findings add weight to the evidence supporting increased levels of depression in asthma.¹⁴

The results also corroborate the general findings of high levels of panic experienced by people with asthma reported in a recent review.¹ Specific comparison of our results with other published studies is not straightforward as variations of the ASC panic fear subscale are used. The ASC mean scores reported in this paper are some-what higher than those reported for a comparable study¹⁰ of asthma patients recruited from General Practice but the significantly higher levels in women compared with men is replicated.

That higher levels of anxiety and depression are associated with increasing age in the asthma population is interesting. In other chronic conditions psychological distress has been shown to decrease with age,²⁷ as it does in the general population.²⁸ The

present findings may be explained by evidence that the level of depression experienced in asthma is related to the level of illness uncertainty.²⁹ It may be that older people may feel more uncertain about managing their asthma. An alternative explanation may be that psychological distress increases with increasing duration of asthma as reported previously in men.³⁰ However, the upper age limit in this study was 65 years so the older age group were somewhat younger than comparable studies.²⁷

In the present study, duration of illness was not recorded so that it is not possible to distinguish between association of asthma with age or duration of illness. It is also likely that a proportion of participants may have had Chronic Obstructive Pulmonary Disease which occurs from around 45+ years and has been shown to have a major impact on QOL and mood.³¹ This may explain the link between depression and age. In this study the GP diagnosis of asthma was not verified though the upper age limit was restricted to 65 as the likelihood of COPD increases significantly over 65 years.

A limitation of the study is that the sample was drawn from one UK city. Comparisons were made with data from the general population from the same GP practices indicating that the findings of psychological distress are related to the experience of asthma or chronic disease rather than being related to the specific location. However, a recent, comparable, community study reported a prevalence of 'possible' anxiety of 38% and 'probable' anxiety of 18.9% in people with asthma and prevalence levels of depression were no greater than controls.³² This was carried out in a relatively affluent rural, mainly Caucasian population, indicating that prevalence of psychological distress associated with asthma may vary with geographical and socioeconomic factors. An earlier study reported significant differences in the level of anxiety and depression experienced by people with asthma living in a suburban compared with an inner city location.¹³

A further limitation is that no attempt was made to assess the prevalence of clinically diagnosed anxiety, depression or panic fear in the population.

A strength of this study is the relatively large sample size, however it is acknowledged that lack of information related to possible non-response bias is a weakness. Care was also taken to ensure that the socio-economic demographics of the practice populations reflected that of the city as a whole.

Implications for future research and clinical practice: In our parallel study³³ into the management of anxiety in asthma, GPs had difficulties identifying clinically anxious patients. This indicates that anxiety related complications of asthma might not be recognised in general practice despite high prevalence levels. The screening tool used in this study could be used in

both general practice and hospital clinics to identify patients with asthma experiencing levels of anxiety that may affect their ability to manage their asthma. Once such patients are identified, providing effective interventions to meet their psychological needs may pose a challenge to community services. Further research is needed into effectiveness of interventions to help people with asthma manage the associated psychological distress, particularly interventions which can be delivered by those staff already in contact with patients such as the asthma clinic nurse.

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News

□ October-November 2008

SLEEP NEWS FEATURE: DISORDERED

REM behavior disorder (RBD) is a rare parasomnia and is very often misdiagnosed. It is characterized by the intermittent loss or impairment of REM sleep atonia and by the appearance of elaborate motor activity associated with vivid dream-enacting behaviors.

A group of subjects in whom the clinical history fulfilled the diagnostic criteria for REM behavior disorder (RBD) of the criteria of American Sleep Disorders Association and Sleep Research Society (1997) described here were identified in a sleep unit between March 2000, and June 2007. Eighteen patients, (12) men and (6) women with a mean age of 70.5 ± 11 years. They all had a history of dream-enacting behaviors with a mean duration of 5.5 ± 9.5 years. Behaviors included talking (100%), shouting (78%), punching (74%), gesturing (63%) and kicking (65.3%). Fifteen subjects fell out of bed and 11 suffered lacerations in the face. The frequency of episodes is variable, occurring once every 2 weeks to 4 times nightly for consecutive nights, and often increases over time.

Patients were interviewed regarding their sleep habits and underwent full PSG. The clinical evaluation of the patients consisted of a neurological examination, an interview, and an interview with the spouse. They also underwent a full laboratory and biochemical evaluation like a complete blood count, test of thyroid function etc, as well as an EEG, a brain MRI and psychometrics tests (BDI, MPPI).

Four patients diagnosed as idiopathic RBD and one of them developed Parkinson disease 9 years after appearing of RBD symptoms and 4 patients also suffered from sleep apnea. Nine patients who their MRI showed multi-infracts lesions and 4 patients also suffered from sleep apnea. Five patients suffered from drug-induced RBD (fluoxetine, paroxetine, mirtazapine, amadadine). One patient suffered from neurinoma of right acoustic nerve. On polysomnography, the atonia that normally accompanies REM sleep is disrupted by periods of sustained increased tone, increased phasic muscle activity, or both. Simple as well as complex coordinated movements of the extremities occur during REM sleep, whereas periodic and aperiodic movements of the extremities may occur during NREM sleep.

Diagnosis was delayed to our patients from 1 year to 14 years. Symptomatic RBD associated with several neurological disorders such as cerebrovascular diseases, or co-occur with neurodegenerative disorders such as Parkinson's disease and drug-induced cases. Extensive neurological evaluations in humans suffering from both idiopathic and symptomatic forms have not identified specific lesions; however, findings in some patients suggest that diffuse lesions of the hemispheres, lesions in the pontine territory, or primary brain-stem lesions may result in the RBD.

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HOW TO SCORE

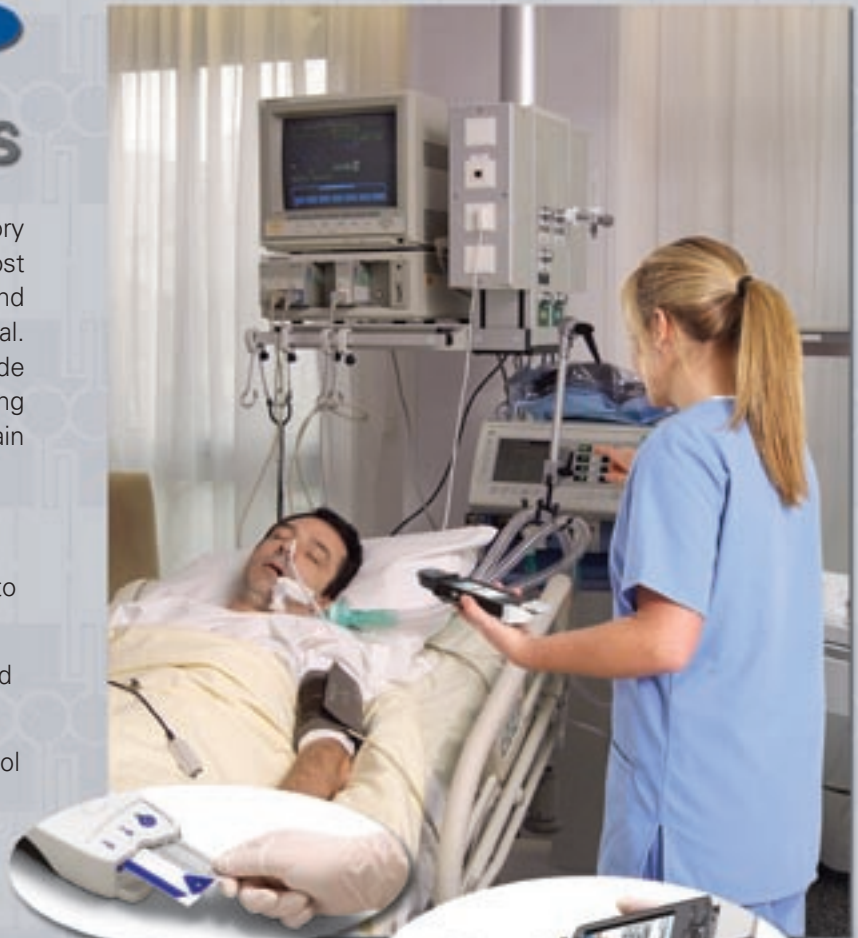
Visual sleep scoring is the obligatory reference for sleep analysis. An essential step in sleep scoring is sleep staging, according to a paper presented in *J Clin Sleep Med*. 2008 Apr 15;4(2):99-103, Rethinking sleep analysis, by H. Schulz. According to the article, this technique was first described in 1937 and later adapted three times: first, in 1957, after the detection of REM sleep, when electrooculography EOG was added; second, in 1968, when sleep staging was standardized and EMG was added; and third, in 2007, to integrate accumulated knowledge from sleep science, adding arousals and respiratory, cardiac, and movement events. In spite of the dramatic changes that have taken place in recording and storing techniques, sleep staging has undergone surprisingly few changes. [While] sleep staging was appropriate as long as sleep biosignals were recorded in the analog mode as curves on paper,

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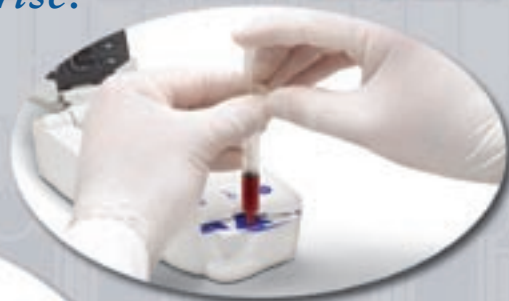


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this staging may be insufficient for digitally recorded and stored sleep data.

POKE IN THE EYE

OSA patients have extensive alterations in the brain's nerve tissue fibers that are insulated with myelin—a white, fatty sheath. The structural changes appear in brain regions that have functional importance for mood, memory and cardiovascular regulation, and in fiber pathways interconnecting these regions, according to researchers at the UCLA School of Medicine. Its study used 41 patients with moderate to severe OSA and 69 control subjects matched by age. Diffusion tensor was performed to analyze the microstructure of the brain tissue, and fractional anisotropy was derived to measure fiber integrity. Study subjects with OSA had lower FA in multiple areas of the brain including regions of the cerebellum, the thalamus and the prefrontal cortex. According to the authors, lower FA primarily represents damage, shrinking or loss of myelin in groups of axons. Such damage may affect the function of these brain regions, while similar changes to the fiber pathways may compromise the relaying of information between regions. The authors speculated that some of these changes result from the fluctuation of oxygen levels caused by pauses in breathing during OSA. The subjects with OSA averaged 15 to 101 partial or complete pauses in breathing per hour of sleep during one night of monitoring at the UCLA Sleep Disorders Laboratory. In a related study, the researchers reported finding that people with sleep apnea also have tissue loss in the mammillary bodies, brain regions that help store memory. The authors concluded that the structural changes likely represented injury that accumulated over time,

and couldn't say if these changes were permanent, or if they could be reversed by treating OSA. Reported by Medical News Today.

CAN'T SLEEP

Half of all older adults complain about trouble sleeping, and most don't bother to seek treatment, while those who do turn to medications or expensive, hard-to-access behavior therapies. Maybe they won't have to any more. UCLA researchers report that practicing tai chi chih, the Westernized version of a 2,000-year-old Chinese martial art, promotes sleep quality in older adults. In the study, 112 adults from 59 to 86 were assigned to one of two groups for 25 weeks. The first group practiced 20 simple tai chi chih moves; the second participated in health education classes that included advice on stress management, diet and sleep habits. Participants were asked to rate their sleep based on the Pittsburgh Sleep Quality Index. The study found that the tai chi chih group showed improved sleep quality and a remission of clinical impairments like daytime drowsiness and inability to concentrate, compared with those receiving health education. The tai chi chih participants showed improvements in their own self-rating of sleep quality, sleep duration and sleep disturbance.

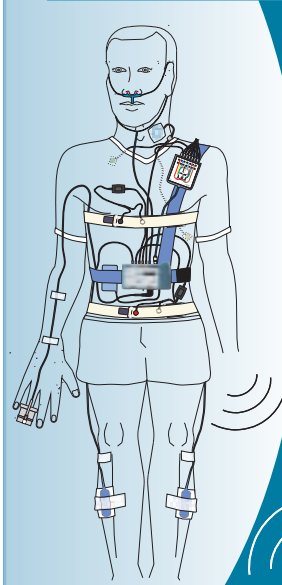
GOTTA PEE

Bladder problems may leave a mark on the brain by changing patterns of brain activity, possibly contributing to disrupted sleep and problems with attention, according to researchers at The Children's Hospital of Philadelphia. The research team mimicked the condition of an overactive bladder in an animal model by

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surgically constricting the outlet of urine from rats' bladders. They found that two small brain structures, the Barrington's nucleus and the locus ceruleus, developed abnormal activity as a result of the bladder obstruction. The locus ceruleus showed persistently high activity, and this resulted in an abnormal EEG recorded from the cortex, where high activity may result in disordered sleep, anxiety and difficulty in concentrating. The researchers noted that the brain circuits involving the locus ceruleus might be a useful target for drugs to improve attention and sleep patterns in patients with bladder dysfunctions, and also noted that other visceral diseases like irritable bowel syndrome may affect the same neural circuitry.

GOTTA SLEEP

Researchers at Washington University School of Medicine in St Louis have found a way to stop the spiral of sleep deprivation problems. When scientists genetically tweaked a part of the brain involved in learning and memory in fruit flies, the flies were unimpaired even after being deprived of sleep. Using fruit flies that enter a state comparable to sleep, researchers demonstrated that the flies had periods of inactivity where greater stimulation is required to rouse them. These periods begin at night and are cyclic, like human sleep, with cycles lasting 20 to 25 minutes. Like humans, sleep-deprived flies try to make up for lost sleep time by sleeping more the next day. To study the effects of sleep deprivation on learning, researchers ran the flies through a maze with two options: one lighted vial with bitter-tasting quinine in it and one darkened but quinine-free vial. Flies are instinctively drawn to light, but they want to avoid the unpleasant taste of quinine. In this test, flies have to remember that the lighted vial is the one with quinine, and then they have to suppress their natural instinct to fly toward that light. Flies allowed normal sleep learned to avoid the lighted vial, but sleep-deprived flies did not. However, sleep-deprived flies with extra dopamine receptors could still learn as if they had a full night's sleep.

NIGHTMARES

A recent report in the Los Angeles Times discussed the inordinate sleep problems encountered by veterans returned from Iraq. Mostly, the returnees were afraid to fall asleep because of distressing nightmares. The man profiled in the piece said he spent most of his time awake trying to stay awake by taking caffeine tablets, drinking caffeine drinks and playing video games. When he fell asleep, he said, he relived combat experiences, and had punched his fiancée in his sleep. Walter Reed Hospital noted that 36% of Army troops returning from Iraq were perpetually tired, had difficulty falling asleep, or slept too much. Seventy percent of vets treated for PTSD also have sleep problems.

APNEA = DEATH

Researchers at the University of Wisconsin-Madison followed a random sample of patients for 18 years and showed that those with sleep apnea had more than three times the risk of death from any cause compared to those who didn't, and that the risk went up when the condition was untreated. The researchers examined records of 1,522 people taking part in the ongoing Wisconsin Sleep Cohort Study and recruited a random sample of men and women aged from 30 to 60 years. The participants spent one night at the University's General Clinical Research Center where they underwent a polysomnography, from which their apnea-hypopnea index was calculated. For the follow up, the researchers reviewed state and national death records and found which participants had died and what was recorded as

the cause of death in each case. The results showed that 63 of the participants (4%) had severe sleep apnea at the start of the study, with an AHI of 30 or more, ranging from 30 to 97 apneas and hypopneas per hour. Seventy-six percent (1,157) had no sleep apnea, and their AHI was under 5. Eighty deaths were recorded, including 37 attributed to cancer and 25 attributed to cardiovascular disease and stroke. Twelve (19%) participants with severe sleep apnea died, compared with 46 with no sleep apnea. Participants who had severe sleep apnea had over three times the risk of dying due to any cause compared with people who did not have sleep apnea, a figure that went up to 4.3 when 126 people who reported regular use of CPAP were removed from the calculation. Hazard ratios for mortality due to any cause remained high even after adjusting for smoking, alcohol, sleep duration and total cholesterol, and severe sleep apnea was linked to increased mortality regardless of whether participants felt sleepy during the day. About 42% of the deaths among those with severe sleep apnea (5 of 12 deaths) were attributed to cardiovascular disease or stroke, compared to 26% of deaths among those with no sleep apnea. To read the complete study, see "Sleep-Disordered-Breathing and Mortality: Eighteen-Year Follow-Up of the Wisconsin Sleep Cohort," SLEEP, Volume 31, Issue 8, August 1, 2008.

PRODUCTS

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RESMED offers the following sleep products: The Swift LT nasal pillows system is light on the face, easy to use and fit, and provides personalized comfort and unparalleled quietness for users and their partners. Ideal for active sleepers, the Swift LT's compact and streamlined design minimizes facial contact while offering stability with a secure seal. The dual-wall nasal pillows, which sit on a flexible pillow base, seal softly to reduce airflow into the nasal passages, and the rotating barrel allows you to customize the perfect fit without over-tightening the headgear. Its flexible, lightweight tubing and optional tube retainer allows for side and back sleeping. Featuring a unique vent design and weighing only 2.3 oz, the Swift LT is the quietest and one of the lightest masks on the market. ResMed's S8 Series II with Easy-Breathe features a whisper-quiet motor and natural, comfortable waveform, making it the quietest device range available. With improved EPR, the S8 II delivers exceptional comfort in a compact design to suit the lifestyle of a patient and their bed partner. The nearly silent operation of the Easy-Breathe motor is sure to improve compliance and patient satisfaction. ResMed's S8 Series II includes the S8 Escape II, S8 Elite II, S8 AutoSet II and VPAPAuto. The Mirage Micro is the latest generation nasal mask from ResMed, providing personalized fit, seal and comfort for more users. Combined with ResMed's Mirage cushion technology, the Mirage Micro's unique MicroFit dial fine-tunes fit to suit each individual user. Intuitive to use for sleep professionals and users, the Mirage Micro includes two cushion sizes packaged together (except small) for fewer product codes and reduced inventory. With enhanced comfort and an improved fit range of over 95%, the Mirage Micro is the new benchmark in nasal masks. Contact resmed.com.

NETWORK LINKED

Electramed Corporation's Compumedics Sleep Products offers its E-Series comprehensive, network-linked amplifier system for sleep/EEG. The E-Series is a fully digital amplifier system with a standard network interface that is compatible with

most current personal computers. With 32, 44 or 64 channel configurations, these amplifier systems are appropriate for both full sleep and EEG data collection. Compumedics has developed a physiological amplifier that is built for the new age, designed to help your sleep and/or EEG lab take full advantage of high-speed computer networks. The Compumedics E-Series' Integrated TCP/IP architecture allows control and/or monitoring of E-Series amplifiers on the laboratory LAN from any computer on the network. You can monitor E-Series systems from your lab, your office, or even from remote sites. The system offers 44 amplified channels—32 referential, 12 bipolar; 8 inputs for ancillary devices; 3 channels from the available oximeter; 2 pressure signals from integrated transducers; nasal pressure flow signal; and CPAP or esophageal pressure. The E-series can be enhanced with the advanced Compumedics Digital Video Software. Fully integrated into the network, high resolution streaming video is also available. Compumedics Digital Video software utilizes network optimised MPEG-4 compression and is fully configurable for image size, frame rate storage and audio synchronization. Additional video features included pin-point area zooming, pan within the image frame and frame by frame advance. Compumedics also introduces Somté, a new investigative tool for "holter-style" recoding of a wide range of physiological data. Somté software provides comprehensive analyses to assist in understanding the nature and severity of the interrelated respiratory and cardiac diseases. The Somté is a compact pager-sized recorder with integrated, high resolution LCD display, high capacity data storage on a removable Compact Flash Card, and is powered by two AA batteries. An optional ECG analysis package is also available. Contact electrased.com.

SLEEP EXECUTIVE PROFILE

NSI

Describe your product(s) and its unique features.

NSI is a leading distributor of a wide range of neurological and sleep studies supplies required for electroencephalograph, evoked potentials, electromyography and sleep disorders testing. Products include, but are not limited to, air pressure transducers, snore sensors, electrodes, adhesive paste and gels for electrode application, educational materials and other necessities.

What sets your product apart from others in the field?

NSI offers the most complete and highest quality range of products designed to outfit your lab or clinic at the most affordable pricing.

Tell us how you utilize conferences, seminars and such to promote your product.

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SLEEP ROUNDTABLE

CleveMed

Response provided by Sarah Weimer, Product Manager, Sleep Systems, CleveMed.

Discuss your products for sleep testing, in the home and/or in-lab.

The Sapphire PSG and the Crystal Monitor PSG Series are wireless, handheld PSG systems, ideal for attended, unattended or remotely attended full PSG recordings. The Type III SleepScout exceeds AASM and CMS requirements for portable sleep monitoring making it ideal for home testing.

What are the latest product development trends in use for your product?

As portable monitoring is approved by more and more insurance providers, the possibilities for using CleveMed products continue to grow, including home testing and sleep evaluation in nursing homes. All of our sleep systems can be used for attended or unattended studies, giving the lab flexibility. CleveMed's systems are ideal for hospital inpatient testing. Pre-surgical assessment for sleep disordered breathing has been recommended by the American Society of Anesthesiologists and is becoming a requirement at many hospitals.

Please tell us about improvements in software and records management.

Crystal PSG 2008 includes tools for the new AASM scoring standards. We have also improved our automated respiratory event scoring which allows users to customize the scoring to best meet their lab standards.

What education and training support do you offer for clinicians and users?

Training is included in the purchase price of our PSG systems. Onsite training covers setup, data collection, scoring, reporting and troubleshooting. We offer 24 hour customer support. Support is offered through e-mail, phone and interactive web meetings.

How do reimbursement and regulatory issues affect the applications of your product?

CleveMed offers systems that can be used for attended and unattended testing using a type II or III monitor. Recent changes in home monitoring reimbursement will significantly grow our markets. Overall, we see a positive effect on how patients and doctors perceive home monitoring.

Grass Technologies

Response provided by Tina Pollard. Grass Technologies is an Astro-Med, Inc. Product Group.

Discuss your products for sleep testing, in the home and/or in-lab.

Grass Technologies has a complete product line for in-home and in-lab sleep testing. Grass Technologies offers three models for in-home recordings. The SleepTrek3 is our newest in-home, portable monitoring system. This 6-channel device meets the

requirements for a Type III portable monitor. Everything the customer needs to get started is included in the base system price, including amplifier, sensors, battery, memory card, wearable pouch, carrying case, and even software. There is an industry-leading 3-year warranty included with SleepTrek3. Grass Technologies also offers Type I and Type II portable monitoring devices. The AURA-PSG is our Type I device, with 25 total channels. EEG, EOG, EMG, EKG, Airflow, Effort, Snoring, Position, SpO₂, and Heart Rate typical of a full sleep study can be recorded with the AURA-PSG. The AURAPSG-LITE is our Type II device, with 16 total channels. The inputs for the AURAPSG-LITE are somewhat universal, so a good variety of channel types can be recorded to meet the specific customer's needs. The AURA-PSG and AURAPSG-LITE amplifiers are covered under our industry-leading Lifetime Warranty. Grass Technologies also offers two systems for in-lab sleep testing. The first is our AURA-PSG wireless system. In-lab, the AURA-PSG can be used to record up to 33 total channels. The amplifier is actually worn by the patient in a comfortable pouch, and all electrodes and sensors are connected directly to the amplifier. The reliable Bluetooth wireless transmission from the patient to the rest of the sleep system makes for an overall better PSG experience for the patient. There are no wires tying the patient to the bed—the patient is free to get up without interrupting recording. The very same AURA-PSG system can be used in-lab or out-of-lab depending on the customer's needs. Our second in-lab system is the CometPSG. The CometPSG has recording capabilities for up to 50 total channels. More than enough for extended PSG recordings, or those needing combined PSG/EEG systems. Both the AURA-PSG and CometPSG are covered under our industry-leading lifetime warranty.

What are the latest product development trends in uses for your product?

From a new product standpoint, at-home sleep testing has been at the forefront of conversation. CMS approved at-home sleep testing earlier this year and the SleepTrek3 is a product we introduced to meet the specific needs of a Type III portable monitoring device. Although some of the reimbursement and other approvals are still not finalized, we see significant interest in this type of product.

Please tell us about improvements in software and records management.

For 2008 Grass Technologies has been updating our sleep diagnostic systems and software to meet the new American Academy of Sleep Medicine (AASM) standards. This includes changes within the acquisition, review, analysis, and reporting. For records management, Grass Technologies continues to enhance our Database Explorer application for complete data/study management. Not only are improvements being made to help in the day-to-day use of our systems, but a new HIS/HL7 interface is available to help connect our sleep diagnostic systems to the hospital system.

What education and training support do you offer for clinicians and users?

Grass Technologies has always offered certain educational literature at no charge to our existing users and also teaching institutions. Visit our website, grasstechnologies.com/knowledgebase/educational.html, for more information. Regarding training for customers who have purchased our clinical systems, we provide technical training at the time of initial in-service and offer advanced training on-site or at our

“Heritage College.” Located at our world headquarters, the Heritage College option is a great resource for those looking for in-depth training on our clinical products or even training of a brand new technician or physicians on our systems. The college is no charge for our clinical customers.

How do reimbursement and regulatory issues affect the applications of your product?

In general, reimbursement has not been a factor in our sales of sleep monitoring systems to private labs and hospitals. With the advent now of portable home sleep testing (HST), final determinations have not as yet been formulated on just how much insurers will reimburse for unattended studies done in the home. We expect this to settle in the next couple of months. With regard to regulatory issues, we certainly meet all the requirements for FDA, ISO, MDD, UL, CSA as well as the requirements handed down by AASM. Our products are always prepared to meet the latest requirements.

Resmed

Response provided by Drew Terry, Director of Product Management.

Discuss your products for sleep testing, in the home and/or in-lab.

For home sleep testing, ResMed offers the simple yet powerful ApneaLink. This diagnostic tool measures high-resolution nasal flow, blood oxygen saturation, and heart rate. The software is designed to automatically produce a simple summary report with all of the information needed to determine if the patient requires treatment or should be referred to a sleep lab for further diagnosis. The ApneaLink is one of the only devices on the market that automatically detects Cheyne-Stokes breathing patterns—a clear indicator that the patient will require further analysis and advanced treatment using the VPAP Adapt SV.

In the sleep lab, ResMed offers a flexible suite of products that work in conjunction with the lab's PSG system to determine optimal treatment. The system includes a software controller, a titration flow generator, and a signal converter that sends information to the PSG system. Using ResMed's titration equipment, labs can deliver the same leading therapies that the patient will receive at home. Unique capabilities include: Easy-Breathe comfort and quiet technology; VPAP Adapt SV therapy for central sleep apnea; and automatic bilevel titrations.

What are the latest product development trends in uses for your product?

We have found that the driving factor for these products is simplicity. We believe the ApneaLink is the simplest diagnostic device on the market. A 1-2-3 setup procedure for the patient and simple download reports make it easy to identify patients who require treatment for OSA and patients who require a lab titration.

Please tell us about improvements in software and records management.

We recently added a software controller to our lab titration solutions. This allows sleep technicians to control the titration equipment from the same computer that they use to monitor therapy. This makes it very easy for the technician to monitor and adjust therapy on a real-time basis. In our ApneaLink software, in addition to the unique Cheyne-Stokes respiration

detection that I mentioned, we recently updated the hypopnea and apnea detection algorithms to comply with the most current AASM guidelines.

What education and training support do you offer for clinicians and users?

ResMed is well known for the excellent clinical support provided by our staff of clinical experts. Through this team we offer regular “webinars” and on-site training opportunities. We also offer technical support via telephone.

How do reimbursement and regulatory issues affect the applications of your product?

Medicare has clearly recognized the need to make therapy available to more patients who suffer from sleep disordered breathing. This means that more people are exploring opportunities for home testing. Many of these people will require additional diagnosis in the lab. ResMed is committed to the continued development of solutions to make the identification and treatment of patients simple and cost effective for our partners.

Nihon Kohden America

Response provided by Deidra J. Miltimore, Marketing Administrator, Nihon Kohden America, Inc.

Discuss your products for sleep testing, in the home and/or in-lab.

Nihon Kohden has developed a comprehensive line of sleep diagnostic equipment to cater to in-lab and Home Sleep Testing (HST) needs. Our in-lab solution includes our JE-912 and JE-921 amplifiers that fulfill the requirements of the AASM. Both amplifiers include a built-in pulse oximetry option, but the JE-921 amplifier offers the added capability of direct flow EtCO₂. Nihon Kohden was able to develop a miniaturized EtCO₂ sensor that allows it to be placed closer to the nose and mouth, thus reducing the cannula sample space. This design provides for more accurate real-time results while eliminating condensation problems experienced by side-stream EtCO₂ devices. The direct flow EtCO₂ probe also includes a built-in pressure transducer cannula, thus reducing the number of sensors placed on the patient face. Bridging the gap between in-lab and HST devices, Nihon Kohden offers the Trackit 18+8. The Trackit 18+8 grants a cost effective solution by providing the ability to record a full PSG in or out of the lab. Choosing the Bluetooth option for the Trackit 18+8, provides the in-lab studies to be collected wirelessly. The optional DC adapter provides a means of interfacing with any CPAP device. For portable sleep monitoring, we supply the Trackit SleepWalker and EOS devices. The Trackit SleepWalker is a scaled down version of the Trackit 18+8 and qualifies as a Type II/III device. It includes a Bluetooth option that affords the consumer the added benefit to monitor waveforms wirelessly prior to sending the patient home. The EOS is a price competitive Type III device that incorporates a multi-start feature that allows the user to determine whether to start the recording immediately, at a prescribed time, or by placing the pulse oximeter on the patient's finger. Nihon Kohden is also developing a new Type III device for release in 2009 called the NOMAD. The NOMAD will include an optional feature to notify the technician when a sensor has fallen off the patient. This monitoring feature will help minimize the need for repeat studies when key sensors fall off the patient, thus reducing costs while maintaining patient satisfaction.

Please tell us about improvements in software and records management.

Nihon Kohden strives to meet the needs of our customers and the sleep market. Product development centers around feedback from customers and emerging industry standards. The Polysmith software has been developed as a robust solution providing ease-of-use advantages. Polysmith is utilized in clinical research facilities as well as small sleep centers, which speaks to the scalability of the product. The Polysmith DMS database has been installed in over three hundred sleep centers and we currently interface with six different HL7 systems. The latest advances in our records management are encapsulated in the Polysmith DMS database. Starting in Polysmith 6, we have added the ability to attach files and documents to a patient in the database. Any text in the attached data is searchable from Polysmith DMS. Additionally, there is an integrated patient status to help facilities streamline workflow.

What education and training support do you offer for clinicians and users?

At Nihon Kohden, we realize the success of our product line is intertwined with customer education. We recognize that our system is most efficient when the customer understands the full potential of our system and when and how to employ it. Therefore, we provide rigorous in-service training at the time of installation and offer onsite customized courses. Nihon Kohden also offers a preparatory class for technicians seeking BRPT certification. In addition, we provide classroom courses covering the advance features of our product, customized report generation, and a biomedical course on Nihon Kohden products. For instances requiring immediate response, Nihon Kohden provides 24/7 phone support at no cost and offers remote support capabilities.

How do reimbursement and regulatory issues affect the application of your product?

Regulatory issues will generally impact the design and functionality of the product. However, reimbursement issues have really not impacted our customers' desire for a dynamic, high quality, and cost effective solution. Nihon Kohden actively seeks consumer feedback to enhance our products and software and anticipate their needs. This cooperative effort is reflected in our Polysmith software which provides a seamless workflow from scheduling to archiving. In our efforts to provide our customers with time saving cost effective solutions, the Polysmith program incorporates standard features such as a database, status tracking, auto-archive, and customizable sleep reports. We also offer an HL7/ADT interface to reduce redundant data entry from scheduling to medical records. Our advance database allows the site to mine for data and includes a document management system that allows for scanned and electronic documents to be attached to the patient file and searched by the database. This “manage attachments” feature provides physicians and staff easy access to documents that did not originate from our system. In addition, the Polysmith software interfaces with all of our in-lab and HST devices. By using a common software platform for all of our sleep devices, the customer is provided with a familiar user interface, thus reducing training time and costs.

Embla

Response provided by Kristen Pickard of Embla.

Please tell us about improvements in software and records management.

Embla's only business is sleep diagnostics, and we are focused on providing sleep diagnostic professionals a total system that optimizes the efficiency of their operation from the point of patient referral, to data acquisition and reports, to managing the patient follow through process. With this total system objective in mind, our development team has created the Enterprise Business Management solution. Combined with our sleep diagnostic system, the Enterprise Business Management solution allows us to offer a broad range of products for the sleep lab business. This range of products has recently been enhanced including the release of new AASM compliant RemLogic software, which is a combination of our renowned Rembrandt and Somnologica platforms into a single application that can be configured for a full PSG or home study. The Enterprise Business Management software enables optimal efficiency of managing patient data and information for both large, networked groups and small sleep centers alike. Enterprise software is compatible with Hospital or Practice Management applications, and allows the effortless generation of reports, questionnaires, and marketing trends using custom or standard fields. New features include "drag and drop" when building transcripts, and single point data entry to minimize errors and streamline workflow.

How do reimbursement and regulatory issues affect the applications of your product?

There have been several changes over the past year. The AASM published its new guidelines on scoring rules, and the CMS introducing the reimbursement of CPAP using home testing devices. Embla products have always supported AASM requirements and our newly released RemLogic system has already been through a successful sleep lab accreditation, with no "provisions" or comments. The new CMS rules have triggered the introduction of several new portable devices as some companies scrambled for market share in the home study arena. Our Embletta device has been the global leader of Level III devices, serving the unattended monitoring market in the rest of the world over the last eight years, and to the largest private healthcare delivery system in the US for the last seven. We are well versed in the requirements that home testing demands, which are reflected in our Embletta system, which has evolved based on feedback and experiences we've had while leading the unattended market for so many years. As the world standard in home sleep testing, the Embletta is also the product selected by the AASM for their proof of concept research on home testing.

What education and training support do you offer for clinicians and users?

Embla has a variety of training programs that are specifically designed to compliment the use of our products. We offer extensive onsite training to new customers at installation, and also to existing customers who may have experienced staff turnover or wish to learn about the more advanced features available in our products. Our comprehensive training courses are conducted at the customer site and may include several Clinical Application Specialists, many of whom are registered technologists. In addition to the on site training we offer extensive Web-based training that allows us to quickly address

issues in the field. The Web-based, instructor-led, and real-time training sessions are ideal for question and answer sessions with our Technical Support or Clinical Application Specialists, or to get new staff comfortable with our system, these conferences offer significant value for your training dollar with minimal disruption to your staff schedule or work day. Enterprise customers are also provided a significant amount of non-clinical training designed for the administrative staff responsible for scheduling, creating productivity reports, managing cancellation lists as well as other daily tasks that allow the sleep lab to run efficiently and smoothly. Whether you are a one bed facility or part of a multi-site hospital system with 30 beds, we can help improve your productivity and bottom line.

What are the latest product development trends in uses for your product?

Complex Sleep Apnea Syndrome (SAS) is a sleep disorder that is the simultaneous presence of upper airway obstruction and chemoreflex-driven respiratory oscillations during sleep. Complex SAS is encountered in 15-45% of the patients seen in a clinical sleep environment. The patient will appear to have predominantly mixed apneas and obstructed periodic breathing but during CPAP titration will reveal dangerous central apneas or Cheyne-Stokes breathing. Embla has recently developed technology that will assist clinicians to identify this disorder prior to the application of CPAP. Cardio Pulmonary Coupling is new technology recently developed by Beth Israel Deaconess Medical Center that creates a spectrograph of sleep that clearly phenotypes Complex Sleep Apnea in real time during the initial part of the sleep test, potentially saving clinicians time and the need for patients to revisit the sleep lab. A CPC analytical tool for use in RemLogic software is currently being developed by Embla Systems and will be available for sleep labs, clinicians, and technicians by Q4 of 2008. CPC technology provides a logical and physiologically understandable new method to aid in SDB differentiation, identification, treatment and management of SDB patients.

Dymedix

Response provided by Jim Moore, Marketing Communications for Dymedix Corporation.

Discuss your products for sleep testing in the home and/or in-lab.

Public awareness of sleep disorders has increased greatly in the last few years. As the magnitude of this problem receives more and more press the demand for sleep studies should and has increased with it. The availability of home sleep testing should have a very positive impact on the numbers of people tested. Dymedix is committed to working with the AASM, sleep physicians and technicians to see to it that these tests are performed to the highest standards available to achieve the best possible patient outcomes. With new innovative therapies on the horizon and the very effective current therapies, the overall health of the sleep disorder patient population will be greatly enhanced.

Dymedix is uniquely positioned as the only sensor company with a complete line of disposable sensors, covering all sensor needs for Types 1 through 4 of sleep diagnostic testing devices. Ease of use and patient comfort will be key to a positive outcome for these patients and Dymedix sensors have always been known for

these characteristics.

What are the latest product development trends in uses for your products?

Dymedix Corporation has introduced The Apollo Dual Airflow sensor, the world's first cannula free, thermo and pressure sensor. The problems with cannulas are legendary in the Sleep Industry, clogging and discomfort to mention but two. By combining two patented Polyvinylidene Fluoride Film (PVDF) segments in one sensor Dymedix has been able to replace the need for the age old thermister or thermocouple and the air pressure transducer. This revolutionary new approach to measurement of airflow is the first real advance in 20 years.

Dymedix has also introduced Perfect Fit, a respiratory impedance plethysmography system that is equivalent to respiratory inductance plethysmography in its ability to provide a summation channel that is equal to nasal prong pressure airflow. Our proprietary PVDF properties deliver accurate measurement of true paradoxical breathing and can identify RERA's flawlessly. Our connectivity works with virtually all PSGs and our low profile buckle ensures patient comfort.

How are your products different from others on the market?

The technology within Dymedix sensors is the first new concept in the sleep sensor market in the last 20 years. It is based on the science of Piezo and Pyro electric principles (not to be confused with piezo ceramic, a completely different concept) that were first discovered by the Currie Brothers over 100 years ago. However it wasn't until 1969 that Dr. Kuwai determined that processed polyvinylidene fluoride (PVDF) produced voltage in direct proportion to temperature change, pressure, noise and movement. PVDF is now used in many sophisticated applications such as rate responsive pacemakers, ultrasound, seismic accelerometers and advanced naval sonar to name a few. In 1998, our founder and Chairman, Peter Stasz, invented a sleep sensor using PVDF to accurately measure airflow, snore and movement. Our PVDF sensors were introduced to the market in 2001 and we now have a formidable customer base and are continuing to develop new applications for the sleep market. Better treatment starts with better data—better data starts with Dymedix. To learn more please contact Dymedix at (888) 212-1100 or dymedix.com, info@dymedix.com.

Compumedics USA

Tom Lorick

Response provided by Tom Lorick, VP of Marketing for Compumedics USA.

Discuss your products for sleep testing, in the home and/or in-lab.

Compumedics has a surprising array of products to suit every application in today's sleep diagnostic testing environment. We offer products for the traditional fixed bed sleep lab, ambulatory studies, home sleep testing and sophisticated advanced research applications. We realized a long time ago that a single amplifier/software combination will not offer the optimum solution for each of these distinctly different settings. That is why we offer IP based amplifiers (Our E-Series), WiFi wireless (Siesta), Bluetooth based (SomtéPSG) and small battery operated patient wearable devices for home use (Safiro and Somté). Our purpose built systems are robust and reliable in every situation and our

ProFusion PSG software is designed to easily scale to every application at hand.

What are the latest product development trends in uses for your product?

We recognized a demand for products designed for home sleep testing and for dual use EEG and PSG capable systems. Therefore our most recent product innovations have focused on cost-effective battery operated units suitable for the rigors of patient worn, home sleep studies and extended monitoring of EEG in a patient's typical daily environment. With a bent towards practical and cost-effective application of technology Compumedics can offer superior value for any application specific requirement.

Please tell us about improvements in software and records management.

Our ProFusion PSG3 Software Suite was just released in the past year and features a host of advancements over our previous versions. The result has exceeded our goal to provide a set of tools that ensure simple compliance with the newest AASM recommendations and that is customizable for each user requirement, whether acquiring, scoring or reporting studies. Our NeXus Lab Management Software is on its third generation with improved tools for HL7/EMR interface, and advanced queries among many enhancements. NeXus now supports a comprehensive Scheduling program that is designed to centralize and manage patient scheduling and lab utilization for sleep facilities ranging from one to a hundred or more beds and staff.

What education and training support do you offer for clinicians and users?

Our long-standing belief is that the happiest customers and the best systems come from having the best training from the very beginning as well as access to continuing education opportunities. As with our systems, we recognize that one solution cannot meet all needs, and that is why Compumedics offers customized on-site training in the customer facility, classroom based training at our world-class education facility in Charlotte, NC, standardized online training modules, customized online training, web based educational resources and regional training opportunities—all of which offer opportunities to earn AAST CEC credits. Training sessions are lead by our applications specialists who have a strong background in sleep and EEG and hold registries in their fields. We strive to match the content with the specific needs of each individual customer.

How do reimbursement and regulatory issues affect the applications of your product?

Two topics have really challenged our customers and sleep medicine in general in the past year: home sleep testing and AASM compliance. No other topic has so singularly thrown our customers and labs in to a state of confusion and angst as has the question of home sleep testing. After years of on again-off again rumors and promises, a definitive decision has finally been made, though the financial ramifications are still being settled. Compumedics has been here for our customers by having a scalable software suite that works with all of our amplifiers to deliver a wide ranging product line allowing our customers to grow and add the right systems for each application at the right price point.

Compumedics ProFusion PSG3 provides the perfect and easy answer to the topic of AASM compliance. Our ProFusion PSG3

was the first software from any manufacture to offer seamless, integrated compliance with the new AASM recommendations when introduced almost a year ago. As a company with a track record of “firsts” and practical innovations we strive to be ahead of the curve so our customers always have a solution for the inevitable changes in Sleep Medicine.

Philips Respironics

Response provided by Kevin Dorcak, US Marketing Manager, Diagnostics and Patient Monitoring, Sleep Disordered Breathing.

Discuss your products for sleep testing, in home and in the lab.

Well known for innovation in advanced sleep therapy systems and technologies for more than 30 years, Philips Respironics also leads the way in serving the needs of the sleep diagnostic market. Philips Respironics equips sleep and respiratory technicians with the latest in advanced in-lab PSG systems, full-featured portable testing devices, real-time portable screeners, and Pro-Tech's full-line of sensors to address level I to level IV testing needs. From the growing family of Alice diagnostic products (Alice 5, Alice LE and Alice PDx) to zRIP respiratory effort belts from Pro-Tech, Philips Respironics has the needs of sleep labs covered.

What are the latest product development trends in uses for your products?

In the current atmosphere of portable sleep testing, Philips Respironics is proud to introduce the newest member of the Alice family of diagnostic devices, the Alice PDx. The Alice PDx is a portable, diagnostic recording device for OSA screening, follow-up and diagnostic assessment of cardio-respiratory sleep disorders. This flexible and portable sleep system incorporates advanced features required to meet today's industry needs. It satisfies the portable testing requirements for levels II, III and IV and provides capabilities ranging from basic screening to advanced diagnostic evaluation. The Alice PDx enables your patients to be tested outside of the lab without compromising study results, helping you to avoid costs associated with retesting. The Alice PDx can be used in a sleep lab, clinical setting or a patient's home. The device is convenient for patients who are uncomfortable with, or have limited access to, a lab facility. It also increases the flexibility that facilities need for in- or out-of-lab services. Rather than having patients in need of sleep testing go untested, and lose revenue because of patients who cancel or never show, the Alice PDx provides an opportunity to retain patients who meet the criteria for portable testing. The Alice PDx device interface is easy to use, easy to understand and informative. Color-coded labels, located around the perimeter of the device, indicate where to connect the various sensor leads. The display shows the patient only the sensors that need to be connected. The sensor information and indicators are intended to help patients place the sensors correctly and reduce application errors. The patent-pending “Good Study Indicator” is based upon patient airflow and oximetry during the recording. The indicator enables a quick assessment of whether the study was properly performed in order to help minimize the need for retesting. These are just a few of the unique features that the Alice PDx offers to expand sleep testing outside of the Sleep Lab. For further information regarding the Alice PDx portable sleep diagnostic device or other diagnostic products from your “Total Sleep Solutions”

provider, Philips Respironics, please visit <http://www.philips.com/respironics>.

What education and training support do you offer for clinicians and users?

Philips Respironics dedicated diagnostic sales team, 24/7 technical and product support, and the specialized “Sleep VIP” customer service team, provide premium service and support to help lead the way in facilitating a healthy night's sleep for patients.

Cardinal Health

Discuss your products for sleep testing, in the home and/or in the lab.

The SomnoStar sleep diagnostic systems are well known for their comprehensive and flexible configuration. These systems are widely used in sleep disorders centers and laboratories around the world. The SomnoStar sleep disorders center or sleep lab systems have recently experienced a major evolutionary step with the introduction of the SomnoStar z4 amplifier and version 8.1 software. This amplifier functions as a network appliance and greatly improves interconnectedness. This system features 23 AC channels and 12 DC channels and also provides for digital video. The respiratory information can be obtained from a Calibrated Respiratory Inductance Plethysmography (RIP) system which provides real-time breath-by-breath Flow Volume Loop information that helps the clinician to identify airway obstruction. The software also provides a measurement of heart rate variability.

The SomnoStar product line also includes the SomnoStar Orbit, a Type 3 Home Sleep Testing System. This system provides 9 channels of information including respiratory effort with RIP technology, oximetry, pulse rate, airflow, body position and limb movement. The Orbit data can be downloaded into the SomnoStar software or others that accept its file format for easy scoring and documentation.

Please tell us about improvements in software and records management.

Our most recent software release addresses the new scoring guidelines issued by the American Academy of Sleep Medicine. These changes involved, for some, hardware modifications as well as software. The SomnoStar software now addresses the EEG referencing issues, labeling, flow measurements as well as all other requirements. The SomnoStar z4 provides the oximetry sampling frequency required and we have for many years provided RIP measurement of respiratory movement and this additionally includes a calibrated signal that provides a more meaningful signal to the clinician.

What education and training support do you offer to clinicians and users?

Cardinal Health has a dedicated team of educators and trainers that address the start-up as well of the on-going needs of sleep disorders centers and laboratories. This team is comprised largely of registered polysomnographic technologists and they provide both class room and on site training. In some cases the offering goes beyond the specific application as is the case of RIP and Flow Volume Loops. Here the training covers a more basic understanding of how the measurement is made and

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Sleep Structure and Sleepiness in Chronic Fatigue Syndrome With or Without Coexisting Fibromyalgia

Fumiharu Togo, Benjamin H. Natelson, Neil S. Cherniack, Jennifer FitzGibbons, Carmen Garcon, David M. Rapoport

Abstract

Introduction: We evaluated polysomnograms of chronic fatigue syndrome (CFS) patients with and without fibromyalgia to determine whether patients in either group had elevated rates of sleep-disturbed breathing (obstructive sleep apnea or upper airway resistance syndrome) or periodic leg movement disorder. We also determined whether feelings of unrefreshing sleep were associated with differences in sleep architecture from normal.

Methods: We compared sleep structures and subjective scores on visual analog scales for sleepiness and fatigue in CFS patients with or without coexisting fibromyalgia (n = 12 and 14, respectively) with 26 healthy subjects. None had current major depressive disorder, and all were studied at the same menstrual phase.

Results: CFS patients had significant differences in polysomnographic findings from healthy controls and felt sleepier and more fatigued than controls after a night's sleep. CFS patients as a group had less total sleep time, lower sleep efficiency, and less rapid eye movement sleep than controls. A possible explanation for the unrefreshing quality of sleep in CFS patients was revealed by stratification of patients into those who reported more or less sleepiness after a night's sleep (a.m. sleepier or a.m. less sleepy, respectively). Those in the sleepier group reported that sleep did not improve their symptoms and had poorer sleep efficiencies and shorter runs of sleep than both controls and patients in the less sleepy group; patients in the less sleepy group reported reduced fatigue and pain after sleep and

had relatively normal sleep structures. This difference in sleep effects was due primarily to a decrease in the length of periods of uninterrupted sleep in the a.m. sleepier group.

Conclusion: CFS patients had significant differences in polysomnographic findings from healthy controls and felt sleepier and more fatigued than controls after a night's sleep. This difference was due neither to diagnosable sleep disorders nor to coexisting fibromyalgia but primarily to a decrease in the length of periods of uninterrupted sleep in the patients with more sleepiness in the morning than on the night before. This sleep disruption may explain the overwhelming fatigue, report of unrefreshing sleep, and pain in this subgroup of patients.

Introduction

Chronic fatigue syndrome (CFS) is a medically unexplained condition occurring mostly in women and is characterized by persistent or relapsing fatigue that lasts at least 6 months and substantially interferes with normal activities. In addition to severe fatigue, one of the symptoms used for diagnosing CFS is unrefreshing sleep, and, in fact, this sleep-related problem is the most common complaint among patients with severe medically unexplained fatigue.¹ An obvious possibility is that patients with this problem have an underlying sleep disorder or substantial amounts of interrupted sleep which may be responsible for the genesis of the illness. This idea was supported by a recent longitudinal study that indicated that 20% of a carefully delineated group of CFS patients were found to have sleep apnea or narcolepsy, exclusions for the diagnosis of CFS.²

A number of reports of polysomnography in CFS patients were remarkable for finding high rates of these sleep disorders plus periodic leg movement (PLM) disorder,³⁻⁵ whereas several recent studies have found rates to be the same as in controls.^{6,7} One possible reason for this discrepancy is the existence of coexisting fibromyalgia (FM). None of these previous papers stratified their patient sample as to the existence of coexisting FM, and recent data indicate substantial amounts of sleep-disturbed breathing in patients with this disorder.^{8,9} FM is a medically unexplained syndrome characterized by four quadrant pain and multiple tender points and frequently occurs in conjunction with CFS.¹⁰ Hence, we evaluated polysomnograms (PSGs) of CFS patients with and without FM to determine

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Table 1

Selected sleep stage variables in healthy controls and chronic fatigue syndrome patients without sleep abnormalities

	Healthy	Chronic fatigue syndrome
Number	26	26
Age, years	38 ± 8	39 ± 8
Body mass index, kg/m ²	24.4 ± 4.8	24.9 ± 5.2
CES-D score	8 ± 7	17 ± 8 ^a
Sleep structure		
Time in bed, minutes	453 ± 33	438 ± 42
Total sleep time, minutes	385 ± 39	351 ± 54 ^a
Sleep efficiency ^b , percentage	85 ± 8	80 ± 10 ^a
Number of arousals per hour	8.2 ± 5.2	5.7 ± 4.9
Wakefulness, minutes	51 ± 38	61 ± 32
Stage 1, minutes	44 ± 18	33 ± 17 ^a
Wakefulness plus stage 1, minutes	96 ± 43	94 ± 35
Stage 2, minutes	225 ± 36	198 ± 33 ^a
Stage 3, minutes	29 ± 20	46 ± 23 ^a
Stage 4, minutes	5 ± 11	10 ± 15
Slow-wave sleep (stage 3 + 4), minutes	34 ± 26	56 ± 34
Stage REM, minutes	84 ± 25	64 ± 26 ^a
Sleep latency ^c , minutes	16 ± 18	26 ± 26
REM latency ^d , minutes	105 ± 49	127 ± 65
Median duration of sleep runs, minutes	15.6 ± 18.4	8.9 ± 5.7 ^a
Likert scale (0–15.5)		
Sleepiness		
Evening	6 ± 4	9 ± 5 ^a
Morning	1 ± 2 ^e	8 ± 4 ^a
Fatigue		
Evening	4 ± 4	11 ± 3 ^a
Morning	2 ± 2 ^e	9 ± 4 ^a
Pain		
Evening	1 ± 2	7 ± 5 ^a
Morning	0 ± 1	7 ± 5 ^a
Feeling blue		
Evening	1 ± 2	2 ± 2
Morning	0 ± 0 ^e	1 ± 3 ^a

Values are presented as mean ± standard deviation. ^aSignificantly different from healthy controls ($P < 0.05$, non-paired t test). ^bTotal sleep time/time in bed × 100%. ^cTime from lights out to sleep onset. ^dTime from lights out to first epoch of stage REM. ^eSignificantly different from evening ($P < 0.05$, paired t test). CES-D, Centers for Epidemiological Study-Depression; REM, rapid eye movement.

whether patients in either group had elevated rates of sleep-disturbed breathing (obstructive sleep apnea or upper airway resistance syndrome) or PLM disorder.

Another important issue was whether CFS patients would show abnormalities in their sleep architecture even if clinical sleep disorders were not present. Two studies have been done on patients with 'pure' CFS (that is, in patients with neither sleep disorder nor evidence of current depression, another illness that

can interfere with sleep) with differing results: one reported low sleep efficiency with increased periods of wakefulness in CFS¹¹ and the second found normal sleep architecture.¹² We decided to extend these studies and to determine whether the patient's subjective response to sleep, another source of variability in a clinical sample, might correlate with or predict sleep disturbance. Therefore, we also determined whether feelings of unrefreshing sleep were associated with differences in sleep architecture from normal.

Materials and Methods

Subjects: The subjects were 62 women (32 with CFS and 30 healthy controls) ranging in age from 27 to 56 years. Subjects older or younger than those selected were excluded because of age effects on sleep. There were no differences in age or body mass index between patients or controls (Table 1). Subjects were recruited either from our data set of prior research subjects or from the clinical practice of author BHN, who specializes in the care of these patients. Other patients were referred by their physician or were self-referred based on media reports about our research. All subjects initially completed an extensive health screening form¹³ that over the years has proven effective in identifying CFS patients (approximately 5% margin of error). This screening vehicle was also used to exclude patients taking antidepressants, opiates, steroids, hypnotics, and other sedatives, including benzodiazepines. Patients screening positive for CFS and controls indicating their health to be excellent or good—not fair or poor—arrived at our center, where they gave their informed consent and were approved by the medical school's institutional review board to participate in this research (n = 53 patients and 42 healthy controls).

Subsequently, each research subject underwent a complete medical history and physical examination, including a tender point evaluation, and a psychiatric diagnostic interview (Quick Diagnostic Interview Schedule, Q-DIS), all of which were administered by the study's advanced practice nurse (JF) under the supervision of BHN. The psychiatric interview¹⁴ was used to identify DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition)-based exclusionary disorders, including schizophrenia, eating disorders, substance abuse, or bipolar disorder,¹⁵ as well as major depressive disorder, a psychiatric disorder that can disrupt sleep.¹⁶ Finally, a set of blood tests was done to identify medical causes of fatigue. These tests included complete blood count with sedimentation rate, liver and thyroid function tests, Lyme antibody, anti-nuclear antibodies, rheumatoid factor, and C-reactive protein.

Following this evaluation, 21 patients and 12 healthy subjects were dropped from further study for the following reasons: inadequate criteria for CFS, 3 patients; use of exclusionary drugs, 6 patients; previously unappreciated medical illness, 1 patient and 2 controls; current depression, 5 patients; obesity, 1 patient; abnormal labs, 1 patient and 5 controls; moved or no longer interested, 3 patients and 2 controls; and technical or other problem, 1 patient and 3 controls. The remaining patients all fulfilled the 1994 case definition for CFS;¹⁵ of these patients, 14 also fulfilled the American College of Rheumatology criteria (1990) for FM.¹⁷

Procedures: Subjects were instructed to refrain from alcohol and caffeine ingestion and to avoid engaging in prolonged and/or strenuous exercise in the daytime of study nights; thereafter, subjects underwent one night of PSG recording in a quiet, shaded hospital room. Subjects went to bed at their usual bedtime (patients: 11:40 p.m. ± 1 hour 9 minutes; controls: 11:15 p.m. ± 1 hour 26 minutes) and slept until 7:15 to 8 a.m. the next morning.

Measurements: Subjects underwent full nocturnal polysomnography (Compumedics, Charlotte, NC) consisting of electroencephalogram (EEG) (C3/A2, O1/A2, and FZ/A2), electrooculogram (EOG), submental electromyogram (EMG), anterior tibialis EMG, a lead II electrocardiogram (ECG), thoracic and abdominal motion, airflow using a nasal cannula/

Table 2

Selected sleep stage variables in chronic fatigue syndrome patients with and without coexisting fibromyalgia

	CFS alone	CFS + FM
Number	14	12
Age, years	37 ± 9	41 ± 6
Body mass index, kg/m ²	23.3 ± 5.0	26.7 ± 6.0
CES-D score	17 ± 7	18 ± 10
Sleep structure		
Time in bed, minutes	440 ± 40	436 ± 46
Total sleep time, minutes	346 ± 60	358 ± 49
Sleep efficiency, percentage	78 ± 10	82 ± 9
Number of arousals per hour	6.2 ± 6.2	5.2 ± 3.2
Wakefulness, minutes	63 ± 27	59 ± 39
Stage 1, minutes	38 ± 20	27 ± 10
Wakefulness plus stage 1, minutes	101 ± 28	86 ± 41
Stage 2, minutes	203 ± 35	192 ± 30
Stage 3, minutes	35 ± 23	59 ± 16
Stage 4, minutes	10 ± 16	11 ± 15
Slow-wave sleep (stage 3 + 4), minutes	45 ± 34	70 ± 28
Stage REM, minutes	60 ± 22	69 ± 30
Sleep latency, minutes	31 ± 27	20 ± 24
REM latency, minutes	149 ± 77	101 ± 37
Median duration of sleep runs, minutes	8.5 ± 5.9	9.5 ± 5.5
Likert scale (0–15.5)		
Sleepiness		
Evening	10 ± 5	8 ± 3
Morning	9 ± 4	7 ± 3
Fatigue		
Evening	10 ± 3	11 ± 3
Morning	9 ± 4	10 ± 3
Pain		
Evening	6 ± 6	9 ± 3
Morning	6 ± 5	9 ± 4
Feeling blue		
Evening	1 ± 1	2 ± 3
Morning	1 ± 3	1 ± 2

Values are presented as mean ± standard deviation. CES-D, Centers for Epidemiological Study-Depression; CFS, chronic fatigue syndrome; FM, fibromyalgia; REM, rapid eye movement.

pressure transducer and an oral thermistor, and pulse oximetry. Analog signals for EEG, EOG, EMG, ECG, thoracic and abdominal motion, airflow, and pulse oximetry were processed on a real-time basis, using a Dell personal computer. Sleep was scored every 30 seconds by a single scorer according to standard criteria of Rechtschaffen and Kales.¹⁸ Sleep onset was defined as the first three consecutive epochs of sleep stage 1 or the first epoch of other stages of sleep. An arousal was defined

Table 3**Selected sleep stage variables in healthy controls and chronic fatigue syndrome patients who were either less sleepy or sleepier after polysomnography**

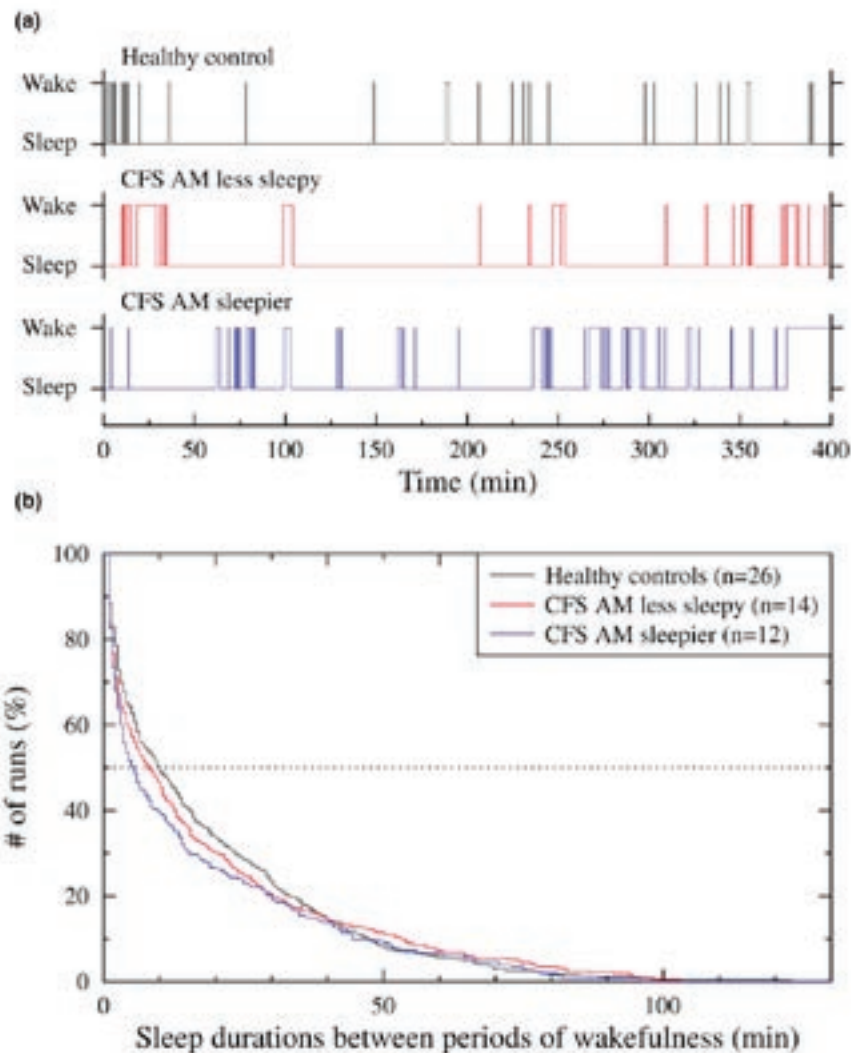
	Healthy	CFS a.m. less sleepy ^a	CFS a.m. sleepier ^a
Number	26	14	12
Age, years	37 ± 8	39 ± 8	39 ± 8
Body mass index, kg/m ²	24.0 ± 4.4	24.1 ± 5.7	25.8 ± 4.7
CES-D score	8 ± 7	20 ± 8 ^b	14 ± 7 ^{b,c}
Sleep structure			
Time in bed, minutes	453 ± 33	433 ± 41	445 ± 44
Total sleep time, minutes	385 ± 38	350 ± 50 ^b	353 ± 61 ^b
Sleep efficiency, percentage	85 ± 8	81 ± 9	79 ± 10 ^b
Number of arousals per hour	8.3 ± 5.2	4.8 ± 3.7	6.7 ± 6.1
Wakefulness, minutes	52 ± 38	64 ± 33	61 ± 35
Stage 1, minutes	45 ± 19	32 ± 12	34 ± 22
Wakefulness plus stage 1, minutes	96 ± 44	96 ± 34	95 ± 37
Stage 2, minutes	222 ± 34	195 ± 29 ^b	202 ± 38
Stage 3, minutes	30 ± 22	50 ± 20 ^b	41 ± 26
Stage 4, minutes	5 ± 11	13 ± 15	7 ± 15
Slow-wave sleep (stage 3 + 4), minutes	35 ± 26	63 ± 30 ^b	48 ± 37
Stage REM, minutes	83 ± 24	60 ± 18 ^b	69 ± 33
Sleep latency, minutes	16 ± 19	20 ± 20	32 ± 31 ^b
REM latency, minutes	107 ± 49	128 ± 64	126 ± 69
Median duration of sleep runs, minutes	15.6 ± 18.4	10.0 ± 6.7	7.9 ± 3.3 ^b
Likert scale (0–15.5)			
Sleepiness			
Evening	6 ± 4	12 ± 2 ^b	6 ± 5 ^c
Morning	1 ± 2 ^d	7 ± 4 ^{b,d}	10 ± 2 ^{b,d}
Fatigue			
Evening	4 ± 4	11 ± 3 ^b	10 ± 3 ^b
Morning	1 ± 2 ^d	8 ± 4 ^{b,d}	11 ± 3 ^{b,c}
Pain			
Evening	1 ± 2	8 ± 4 ^b	7 ± 5 ^b
Morning	0 ± 1	6 ± 4 ^{b,d}	9 ± 4 ^{b,c}
Feeling blue			
Evening	1 ± 2	2 ± 3	1 ± 1
Morning	0 ± 0 ^d	1 ± 3	1 ± 3

Values are presented as mean ± standard deviation. ^aData dichotomized based on difference between daytime and nighttime self-reported ratings of sleepiness ($P < 0.05$, analysis of variance [ANOVA]). ^bSignificantly different from healthy controls. ^cSignificantly different from CFS in the a.m. less sleepy group ($P < 0.05$, ANOVA). ^dSignificantly different from evening ($P < 0.05$, paired t test). CES-D, Centers for Epidemiological Study-Depression; CFS, chronic fatigue syndrome; REM, rapid eye movement.

according to standard criteria of the American Academy of Sleep Medicine¹⁹ as a return to alpha- or fast-frequency EEG activity, well differentiated from the background, lasting at least 3 seconds but no more than 15 seconds. Respiratory events were

defined as any combination of apnea and hypopnea lasting at least 10 seconds or airflow suggesting flow limitation lasting at least 10 seconds associated with an arousal. Apnea was defined as a reduction in airflow to less than 10% of waking level in the

Figure 1



Sleep-wake patterns and survival curves for the duration of every episode of sleep. **(a)** Representative sleep-wake patterns from one healthy control, one patient in the a.m. less sleepy group, and one patient in the a.m. sleeper group. In contrast to the control and a.m. less sleepy patient, the a.m. sleeper patient shows clustering of her arousals, which is documented in the accompanying panel. **(b)** Survival curves of every episode of sleep (that is, a bout of sleep preceded and followed by periods of wakefulness) for controls and patients in the a.m. less sleepy and a.m. sleeper groups for whole-night hypnograms stratified by the duration of the sleep episode. To compare sleep continuity between groups, all data from all subjects in each group were pooled and a group survival curve was generated using standard statistical techniques [22]. Patients in the a.m. sleeper group showed a significant shift toward shorter bouts of sleep ($P < 0.05$) compared with the other groups. CFS, chronic fatigue syndrome.

nasal cannula and absent airflow in the oral thermistor, and hypopnea was defined as a decrease in inspiratory airflow to less than 50% of waking levels. Flow limitation was considered to occur when there were two or more consecutive breaths (for an event duration generally greater than or equal to 10 seconds) that had a flattened or non-sinusoidal appearance but had peak inspiratory amplitudes that did not meet the greater than 50% reduction requirement of hypopnea. These events were required to end abruptly with a return to breaths with sinusoidal shape. The respiratory disturbance index (RDI) was defined as the total number of apneas, hyponeas, and flow limitation events per hour of sleep.²⁰ The RDI including the flow limitation events terminated by arousal has been previously shown to be nearly identical to the number of esophageal manometry events terminated by arousal, which have been called respiratory effort-related arousals.²⁰ Based on results by Ayappa and colleagues,²⁰ it was assumed that an RDI of greater than or equal to 18 events per hour was sufficient to account for excessive

daytime sleepiness on the basis of sleep-disordered breathing, and the diagnosis of sleep-disturbed breathing was then made for patients and healthy controls with this finding. PLMs were defined as four or more consecutive involuntary leg movements per hour during sleep, lasting 0.5 to 5.0 seconds, with an intermovement interval of 5 to 90 seconds. Patients were labeled as having Periodic Leg Movements in Sleep (PLMS) syndrome when the number of PLMs per hour (index) was greater than 5.

Sleep continuity: Sleep continuity was evaluated by generating a nonparametric survival curve calculated from the combined data within each group^{21,22} of the varying durations of sequential sleep runs (that is, continuous epochs of sleep separated from one another by epochs of wakefulness) and was expressed as the median duration of all continuous epochs scored as sleep in each subject. A run of sleep was defined using the sequence of epoch-based sleep stages represented in the hypnogram. A run began with a change from waking to any stage of sleep. A sleep

run continued until there was a change from any stage of sleep to waking. To compare sleep continuity between groups, all data from all subjects in each group were pooled and a group survival curve was generated using standard statistical techniques that take into account the multiple runs of sleep in each subject;^{21,22} this method was derived from an earlier one.²³

Subjective test: Subjects were asked to indicate their levels of perceived sleepiness, fatigue, pain, and feeling blue on separate 15.5 cm visual analog scales (0 to 15.5) given to them immediately before lights out and after awakening.

Depressed mood: The Centers for Epidemiological Study-Depression (CES-D) scale was used as an indicator of depressed mood. This 20-item scale required respondents to rate how often certain symptoms occurred during the past week on a scale from rarely or none (0) to most all the time (3). Items were summed to yield a total score. The higher the value, the more depressed the mood.

Statistical analyses: We dichotomized patients' data based on their self-reported sleepiness before and after sleep. We labeled those with more sleepiness in the morning than on the night before as 'a.m. sleepier' and those with less sleepiness in the morning than on the night before as "a.m. less sleepy." Changes of sleepiness before and after sleep as well as changes in the other variables captured via visual analog scale were assessed using the paired t test (Tables 1,2,3). Differences in measured variables between groups were assessed using the non-paired t test (Tables 1 and 2) or analysis of variance (Table 3). Post hoc analyses used Tukey Student range tests to adjust for multiple comparisons (Table 3). Interrelationships between subjective scales/psychological data and sleep structure were tested by simple Pearson correlation coefficients, and interrelationships between subjective scales were tested by least squares regression analyses. A P value of less than 0.05 was considered statistically significant.

Results

Evaluation of the PSG led us to exclude 10 subjects with clinically significant sleep abnormalities: 3 controls with RDIs of 26, 22.4, and 18/hour, 1 CFS patient with an RDI of 22.1/hour, 1 CFS/FM patient with an RDI of more than 40/hour, and 1 control, 3 CFS patients, and 1 CFS/FM patient with PLMs. We included 1 CFS patient and 3 healthy controls with RDIs of 10.4, 10.8, 10.1, and 9.5/hour, respectively, as these fall within the range seen in asymptomatic normal subjects in the study by Ayappa and colleagues.²⁰ This left a total of 26 CFS patients, 12 with comorbid FM, and 26 healthy control subjects.

Table 1 depicts the key PSG measures of the healthy controls and CFS patients. Total sleep time was significantly longer for healthy controls than patients as were the total durations of stage 1, stage 2, and rapid eye movement (REM) sleep, whereas total duration of wakefulness did not differ between healthy controls and patients. As a result, patients had a significantly lower sleep efficiency (that is, the percentage of the total time asleep after falling asleep relative to the time spent in bed) than healthy controls. However, sleep latency, defined as the time from lights out to the first three consecutive epochs of sleep stage 1 or the first epoch of other stages of sleep (that is, sleep onset), and total duration of slow-wave sleep (SWS) (that is, the sum of stage 3 and 4 sleep) did not differ significantly between groups. Data were also evaluated based on whether the patient

had CFS alone or CFS plus FM (Table 2). Patients with CFS plus FM had sleep structures similar to those of patients with CFS alone.

Table 1 also shows that sleepiness, fatigue, and pain before and after the PSG night were significantly higher in patients than healthy controls. Values for subjective a.m. sleepiness, fatigue, and feeling blue decreased compared with the evening in healthy controls, whereas none of these decreased for patients.

For patients, self-rated sleepiness, fatigue, and pain before sleep correlated positively with sleep efficiency ($r = 0.39, 0.59, 0.57$; $P < 0.05$) and duration of stage 4 sleep ($r = 0.48, 0.42, 0.56$; $P < 0.05$) and negatively with sleep latency ($r = -0.40, -0.42, -0.40$; $P < 0.05$); self-rated fatigue and pain correlated negatively with durations of wakefulness after sleep onset ($r = -0.50, -0.43$; $P < 0.05$) and wakefulness plus stage 1 sleep ($r = -0.50, -0.57$; $P < 0.05$). Self-rated fatigue correlated negatively with REM latency ($r = -0.49$; $P < 0.05$). Self-rated pain correlated positively with total sleep time ($r = 0.49$; $P < 0.05$) and durations of stage 3 sleep ($r = 0.49$; $P < 0.05$) and SWS ($r = 0.59$; $P < 0.05$). Moreover, change in self-rated sleepiness and fatigue over the night correlated positively with sleep latency ($r = 0.39, 0.49$; $P < 0.05$) and negatively with sleep efficiency ($r = -0.41, -0.54$; $P < 0.05$). Changes in self-rated fatigue over the night correlated negatively with total sleep time ($r = -0.39$; $P < 0.05$) and total duration of stage 3 sleep ($r = -0.41$; $P < 0.05$). No significant relations were found among any of these variables for the healthy control group. When we looked at correlations between self-rated variables reported after sleep and sleep stage variables, none was significant except that self-rated sleepiness after sleep correlated positively with duration of stage 2 sleep ($r = 0.48$; $P < 0.05$) for the healthy controls.

Patients in the a.m. sleepier group showed significantly longer sleep latency, poorer sleep efficiency, and shorter duration of median sleep run than healthy controls (Table 3). The survival curve of all sleep runs depicted in Figure 1 shows that patients in the a.m. sleepier group had a lower percentage of long runs of sleep than the other two groups and healthy controls (that is, less continuous sleep). For example, the proportions of runs lasting more than 10 minutes were 39.3%, 45.5%, and 49.0% for patients in the a.m. sleepier group, the a.m. less sleepy group, and healthy controls, respectively. The difference in temporal distribution of periods of wakefulness is evident from the representative data in Figure 1. Both the control subject and the a.m. less sleepy patient have periods of wakefulness that are spaced more evenly over time than is the case for the a.m. sleepier patient, whose periods of wakefulness appear bunched in time (Figure 1a). The frequencies of these bouts occurring after sleep onset did not differ among groups ($25 \pm 15, 21 \pm 5$, and 23 ± 7 for patients in the a.m. sleepier group, in the a.m. less sleepy group, and for healthy controls, respectively).

The existence of coexisting FM did not predict sleep quality for patients ($n = 7$ in the a.m. less sleepy group and 5 in the a.m. sleepier group). Patients in the a.m. less sleepy group had significantly higher CES-D scores than those in the a.m. sleepier group (Table 3).

Prior to going to sleep, the a.m. less sleepy patient group reported more sleepiness than both healthy controls and patients in the a.m. sleepier group ($P < 0.05$). On the morning after their night in the sleep lab, patients in the a.m. sleepier group had significantly more sleepiness, fatigue, and pain than both

healthy controls and patients in the a.m. less sleepy group ($P < 0.05$). Whereas fatigue and pain did decrease for patients in the a.m. less sleepy group, neither of these symptoms changed for patients in the a.m. sleepier group (Table 3). Visual analog scores for feeling blue showed minor differences among groups with little change after the night in the sleep lab (Table 3). Sleepiness and fatigue in both evening and morning were correlated ($P < 0.05$) in both patients and controls. Significant correlations were found for pain and fatigue reported in the evening and morning for patients but only in the evening for controls.

Discussion

CFS is diagnosed using clinical criteria and is therefore probably comprised of a heterogeneous patient pool. The data reported here indicate that some CFS patients have a problem with normal regenerative sleep, which may be responsible for the genesis of their symptoms. In this study, we reduced patient pool heterogeneity by studying women only during a fixed period of their menstrual cycle and after excluding patients with either major depressive disorder or PSG-defined sleep disorders. As a group, the patients studied showed evidence for sleep disruption in the form of significantly reduced total sleep time, reduced sleep efficiency, and shorter bouts of sleep than healthy controls. In comparison with controls, sleep in CFS had little effect on either self-reported sleepiness or fatigue. And, interestingly, for patients only, ratings of sleepiness and fatigue correlated well with total sleep duration and efficiency.

Stratifying patients as to the presence of comorbid FM did not further reduce the heterogeneity seen in the patients' sleep structure. However, asking them about their level of sleepiness before they went to sleep and immediately after awakening did. Dichotomizing the patients into a group that felt sleepier after a night's sleep than before sleep and a group that felt less sleepy after a night's sleep reduced the variability of the sleep records considerably. Those patients reporting less sleepiness after a night's sleep had sleep structures similar to those for healthy controls except for a shorter total sleep time and a commensurate reduction in stage 2 sleep; moreover, they reported their fatigue and pain to diminish following sleep. In contrast, patients in the a.m. sleepier group had the greatest abnormalities of sleep architecture, including poor sleep efficiency, longer sleep latency, and more disrupted sleep as manifested by a higher percentage of short-duration sleep runs, than either controls or patients in the a.m. less sleepy group (Figure 1).

The net effect of this sleep disruption may be the genesis of symptoms reported by this group of CFS patients. The effects of sleep disruption are well known to produce severe daytime fatigue, an example being patients with sleep apnea who have very disturbed sleep. In the case of CFS, neither arousals nor periods of wakefulness per se may be the problem so much as the pattern in which they occur. Patients in the a.m. sleepier group had a shift away from longer bouts of sleep to more frequent short-sleep bouts (that is, fragmented sleep, which may prevent them from falling back to sleep after awakening), resulting in their developing fatigue, unrefreshing sleep, cognitive problems, and achiness. These data appear to support the sleep continuity theory, which hypothesizes that good sleep quality requires longer periods of uninterrupted sleep.²⁴ Reduced energy and cognitive problems are known to occur in healthy controls who have normal sleep time despite disrupted sleep produced experimentally.²⁵ In addition, some studies in healthy

volunteers have reported increases in musculoskeletal pain and/or decreases in pain threshold after a period of sleep disruption or deprivation.²⁶⁻²⁸ We are currently testing the hypothesis that the process responsible for disturbing the sleep of this group of CFS patients is an imbalance of the cytokine sleep network (that is, sleep-producing and sleep-disrupting cytokines) in favor of sleep-disrupting cytokines.

One purpose of this study was to determine whether stratifying our patient sample into those with and without comorbid FM would explain discrepancies in the literature as to rates of sleep pathology. It did not. Regardless of the presence of FM, our findings were similar to earlier reports of rather low rates of sleep pathology in CFS.^{6,7} The low rates of sleep-disturbed breathing and PLMs we found in both patient groups are similar to those we found in our control group of sedentary women—rates that approached the values reported in the literature for unselected populations of healthy women.^{29,30} However, in our hands, we found low rates of sleep-disturbed breathing for patients with CFS alone or CFS plus FM.

Importantly, the rates we found for sleep disturbed breathing include data along the entire spectrum of sleep disturbed breathing from overt sleep apnea to the upper airway resistance syndrome. The monitoring technique we used for airflow, a nasal cannula and examination of the flow signal for the characteristic shape of flow limitation, should have detected subtle forms of sleep disturbed breathing in our sleep studies, but only rare occurrences of patterns of air flow consistent with flow limitation were found here. Thus, although we did not use the more invasive technique of esophageal manometry to detect respiratory effort-related arousals, our results do not support an association between subtle forms of sleep disturbed breathing and CFS, even when co-morbid FM is present. This conclusion contrasts with an earlier report of EEG patterns "related to subtle, undiagnosed sleep-disordered breathing" in patients with chronic fatigue.³¹ The apparent difference between these studies may relate to diagnostic specificity for CFS. All of our patients fulfilled the 1994 case definition for CFS, which requires their having disabling fatigue for at least 6 months plus at least four of eight infectious, neuropsychiatric, or rheumatological symptoms;¹⁵ the subjects in the earlier study just had fatigue of long duration. Thus, our study does not eliminate the possibility that some patients with severe fatigue alone may have this problem as a result of subtle forms of sleep-disturbed breathing.

In summary, based on sleep patterns as assessed by polysomnography, patients with CFS alone and CFS plus FM have a similar rate of diagnosable sleep disorders; in fact, neither group has rates of sleep disorders higher than those found in healthy controls. Thus, sleep-disturbed breathing, narcolepsy, and leg movement disorders are an uncommon cause of medically unexplained fatigue or pain syndromes. Moreover, after excluding those patients from further analysis, CFS and FM patients have similar sleep structures. Our results also suggest that, even when the rate of arousals is within the normal range, sleep quality may be affected by a decrease in the length of episodes of uninterrupted sleep.

Conclusion

CFS patients had significant differences in polysomnographic findings from healthy controls and felt sleepier and more fatigued than controls after a night's sleep. This difference was due neither to diagnosable sleep disorders nor to coexisting

FM but primarily to a decrease in the length of periods of uninterrupted sleep in the patients with more sleepiness in the morning than on the night before. This sleep disruption may explain the overwhelming fatigue, report of unrefreshing sleep, and pain of patients in this subgroup.

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Perception Versus Polysomnographic Assessment of Sleep in CFS and Non-Fatigued Control Subjects

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Abstract

Background: Complaints of unrefreshing sleep are a prominent component of chronic fatigue syndrome (CFS); yet, polysomnographic studies have not consistently documented sleep abnormalities in CFS patients. We conducted this study to determine whether alterations in objective sleep characteristics are associated with subjective measures of poor sleep quality in persons with CFS.

Methods: We examined the relationship between perceived sleep quality and polysomnographic measures of nighttime and daytime sleep in 35 people with CFS and 40 non-fatigued control subjects, identified from the general population of Wichita, Kansas and defined by empiric criteria. Perceived sleep quality and daytime sleepiness were assessed using clinical sleep questionnaires. Objective sleep characteristics were assessed by nocturnal polysomnography and daytime multiple sleep latency testing.

Results: Participants with CFS reported unrefreshing sleep and problems sleeping during the preceding month significantly more often than did non-fatigued controls. Participants with CFS also rated their quality of sleep during the overnight sleep study as significantly worse than did control subjects. Control subjects reported significantly longer sleep onset latency than latency to fall asleep as measured by PSG and MSLT. There were no significant differences in sleep pathology or architecture between subjects with CFS and control subjects.

People with CFS reported sleep problems significantly more often than control subjects. Yet, when measured these parameters and sleep architecture did not differ between the

two subject groups. A unique finding requiring further study is that control, but not CFS subjects, significantly over reported sleep latency suggesting CFS subjects may have an increased appreciation of sleep behaviour that may contribute to their perception of sleep problems.

Background

Chronic fatigue syndrome (CFS) is a complex illness defined by unexplained persistent or relapsing fatigue for ≥ 6 months that is not attributable to exertion and is not improved by rest. The fatigue must be accompanied by at least 4 of 8 defining symptoms (significant worsening of fatigue following exertion, unrefreshing sleep, impaired memory or concentration, muscle pain, joint pain, headache, tender cervical or axillary nodes, and sore throat) and the illness must cause substantial functional impairment.¹ Nearly all individuals with CFS report unrefreshing sleep at the time of diagnosis²⁻⁶ and self-reported sleep problems distinguish CFS cases from matched non-fatigued control subjects.⁷ In addition, complaints of non-refreshing sleep and difficulty getting to sleep or staying asleep remain common (decreasing from 95.4% to 79.2% and 81.4% to 75%, respectively, when CFS subjects are studied at 3 yearly time points after diagnosis.⁸ These complaints and their duration satisfy the definition for chronic insomnia as defined in an NIH Consensus Science Statement.⁹ However, while sleep complaints are a prominent component of CFS, major primary sleep disorders (narcolepsy and sleep apnea) are exclusionary medical conditions that preclude the research case definition of CFS.^{1,10}

Further, polysomnographic studies have not consistently documented sleep abnormalities in people with CFS.^{11,12} These observations raise the possibility that people with CFS perceive the quality of their sleep differently from well individuals; i.e., the prominence of self-reported sleep difficulties in CFS may reflect a heightened awareness of altered sleep physiology. Altered self-perception (sensitivity to internal signals) has been suggested to play a role in CFS,¹³ but few studies have explored the relationship between self-reported sleep quality and objective polysomnographic sleep parameters in persons with CFS. Fossey et al., 2004, contrasted sleep parameters obtained by polysomnography and sleep diaries, medical diagnoses, and results of structured interview and self-report measures between clinic-based subjects with CFS or narcolepsy, and

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those with no medical or psychiatric diagnoses. Their analyses, which included CFS subjects with sleep disorders identified by PSG and presence of insomnia, described the typical symptom and impairment profiles of the syndrome in CFS patients.¹⁴ A study of twins discordant for CFS found that those with CFS were significantly more likely to report insomnia and daytime sleepiness than their healthy siblings yet night time polysomnographic measurements and multiple sleep latency test (MSLT) did not differ between the groups. This led the authors to speculate that twins with CFS suffered from sleep-state misperception insomnia according to the 1990 International Classification of Sleep Disorders.¹⁴⁻¹⁶ The term sleep-state misperception insomnia has been replaced by the term paradoxical insomnia, which describes paradoxical relationships between objective and subjective sleep assessments in such patients according to the 2005 coding manual.^{17,18}

In the present study, we evaluated the relationship between subjective and objective measures of sleep alterations in persons with CFS and non-fatigued controls. As detailed previously,¹² we conducted overnight polysomnographic studies and daytime multiple sleep latency evaluation of 43 individuals with CFS and 43 non-fatigued controls. The study also included measures of participants' long term and short-term subjective reports of sleep quality. The following questions were addressed: 1) Are subjective sleep problems characteristic of CFS? 2) Is there objective evidence of abnormalities of sleep in CFS as defined by polysomnography? And, 3) Are there associations between subjective sleep problems and objective sleep abnormalities in persons with CFS? To avoid referral bias, a major limitation of studies that recruit CFS subjects from specialty clinics, we enrolled persons with CFS and non-fatigued controls identified from the general population of Wichita, Kansas.^{19,20} We also employed standardized criteria to define CFS and controlled for the use of medications known to affect sleep.

Methods

Participants: This study adhered to US Department of Health and Human Services human experimentation guidelines and received Institutional Review Board approval from the CDC and collaborating institutions. All participants gave informed consent. Between January and July 2003, we conducted a 2-day in-hospital study of adults identified with CFS from the general population of Wichita.¹⁹ The in-hospital study enrolled people who participated in the 1997 through 2000 Wichita Population-

Based CFS Surveillance Study.²⁰ The primary objective of the Surveillance Study was to estimate the baseline prevalence and 1-year incidence of CFS in Wichita, Kansas. Participants in the in-hospital study were fatigued adults with medically/psychiatrically unexplained chronic fatigue identified during the surveillance study. Fifty-eight participants had been diagnosed at least once with CFS and 59 had unexplained chronic fatigue that was not CFS. Controls were randomly selected from the cohort who participated throughout surveillance, who did not have medical or psychiatric exclusions, and who had not reported fatigue of at least 1-month duration; they were matched to CFS cases on sex, age, race/ethnicity, and body mass index. Upon admission to this study, subjects were re-evaluated for CFS symptoms and exclusionary medical and psychiatric conditions. The 43 who, at the time of the in-hospital study, met 1994 criteria for CFS comprise the cases in this report. Control subjects were 43 individuals who had never reported fatigue during the surveillance study, who were not fatigued at the time of entry into this in-hospital study and who had no exclusionary medical or psychiatric condition identified at the time of the study (following section). Because current classification of CFS was not completely in accord with recruitment classification, strict matching was not maintained, though cases and controls were demographically comparable. Thirty-six (84%) of the 43 with CFS and 38 (88%) of the 43 controls were women; most (40 CFS and 42 controls) were white; their mean ages were 50.6 and 50.3 years, respectively; and body mass index was 29.4 and 29.3, respectively.

Assessment and classification of CFS: We classified participants as having CFS at the time of the study based on the empirical application¹⁹ of the 1994 CFS research case definition.¹ We used the Multidimensional Fatigue Inventory (MFI)²¹ to evaluate fatigue status; we measured functional impairment with the Medical Outcomes Survey short form-36 (SF-36);²² and, we used the CDC Symptom Inventory²³ to assess frequency and severity of the 8 CFS defining symptoms. We defined severe fatigue as \geq medians of the MFI general fatigue (≥ 13) or reduced activity (≥ 10) scales. We defined substantial functional impairment as scores lower than the 25th percentile of published US population on the physical function (≤ 70), or role physical (≤ 50), or social function (≤ 75), or role emotional (≤ 66.7) subscales of the SF-36. Finally, subjects reporting ≥ 4 symptoms and scoring ≥ 25 on the Symptom Inventory Case Definition Subscale were considered to have substantial accompanying symptoms.

Table 1: Sleep disorders in CFS and non-fatigued controls

Sleep Disorders†	CFS (35)	NF (40)	p*
Obstructive Sleep Apnea (borderline)	3 (8%)	3 (7%)	/
Periodic Limb Movements	7 (20%)	8 (20%)	NS
Insufficient Sleep Syndrome	1 (2%)	0	NS
Delayed Sleep Phase Syndrome	0	1 (2%)	NS
MSLT Normal	16 (45%)	16 (40%)	/
MSLT Borderline	13 (37%)	15 (37%)	NS
MSLT Pathological	6 (17%)	9 (22%)	NS
Any Sleep Study Alteration	26 (48%)	28 (52%)	NS

* Chi-square test.

NF = Non-fatigued; MSLT = Multiple Sleep Latency Test.

† No cases of Bruxism, Central Sleep Apnea or Upper Airway Resistance Syndrome were identified.

Table 2: Sleep architecture in CFS and non-fatigued controls – Night 2 adjusted for medication use

	CFS n = 35	NF n = 40	p-value**
	Adjusted Mean*	Adjusted Mean*	
Total sleep time (min)	400.3	407.9	0.52
Sleep period time (min)	453.8	457.8	0.79
Latency to sleep onset (min)	21.3	17.1	0.47
REM latency (min)	98.4	106.8	0.40
Sleep efficiency (%)	88.3	90.2	0.32
Wake after onset (min)	53.8	44.0	0.69
Wake % Sleep Period	11.7	9.8	0.72
# Arousals	105.7	110.2	0.81
Arousal index	15.9	16.3	0.82
Stage 1 (% TST)	9.6	9.5	0.79
Stage 2 (% TST)	48.2	50.8	0.28
Stage 3/4 (% TST)	19.9	17.4	0.20
REM (% TST)	22.3	23.3	0.98
Alpha intrusion	0.29	0.49	0.11

*Mean values adjusted for medication use (yes/no).

** p-values generated using 2-factor analysis of variance

To assess whether medical conditions exclusionary for CFS (including untreated hypothyroidism, sleep apnea, or narcolepsy) had developed since the surveillance study, participants provided a standardized past medical history and a listing of current medications, underwent a standardized physical examination, and provided blood and urine for routine analysis. Medications that affect sleep were considered 'sleep medications' for the purpose of analysis and include: primary hypnotics (zolpidem, temazepam), narcotic analgesics (eg, hydrocodone, oxycodone, propoxyphene), anti-depressants (eg, citalopram, amitriptyline, imipramine, escitalopram, bupropion, venlafaxine, sertraline, paroxetine, fluoxetine), anti-anxiety (alprazolam), anti-histamines (eg, diphenhydramine, chlorpheniramine, promethazine), decongestants (eg, pseudoephedrine, guaifenesin), anti-convulsants (eg, topiramate, clonazepam), anti-sleep phase disorder (melatonin), blood pressure controlling (e.g., clonidine, midodrine), anti-psychotics (e.g., quetiapine, ziprasidone), stimulants (e.g., methylphenidate, modafinil), peristaltic stimulants (metoclopramide), and muscle relaxants (cyclobenzaprine).

To identify psychiatric conditions exclusionary for CFS (current melancholic depression, current and lifetime bipolar disorder or psychosis, substance abuse within 2 years and eating disorders within 5 years), licensed and specifically trained psychiatric interviewers administered the Diagnostic Interview Schedule for Axis I psychiatric disorders.

We classified participants meeting the 3 criteria (MFI, SF-36, and Symptom Inventory) for CFS and in whom no exclusionary medical (including sleep) or psychiatric conditions were identified as having CFS. Participants whose scores were in the normal range on all of the above mentioned instruments and who had no exclusionary medical or psychiatric conditions identified were classified as non-fatigued. Persons with exclusionary medical or psychiatric conditions were not included in the analysis.

Objective measures of sleep alterations: Sleep studies were

conducted in a 4-bed clinical research unit at Wesley Medical Center, Wichita, Kansas.¹² These sleep studies consisted of polysomnography on night #1, Multiple Sleep Latency Tests (MSLT) during the following day, and repeat polysomnography on night #2. Patients were asked to arrive 3 hours before their typical bedtime on night #1 to allow adequate time for electrode application and standard bio-calibrations. "Lights out" and "lights on" time were 22:00 and 7:00, respectively. MSLT began at 11:00 the following morning and consisted of three additional naps at 13:00, 15:00, and 17:00.

Daytime sleepiness was measured with the MSLT, which has demonstrated objective sensitivity to the effects of sleep deprivation, sleep fragmentation, sleep restriction, insufficient sleep hypersomnia, and in disease states such as sleep apnea and narcolepsy.^{24,25} Multiple sleep latency tests were performed and scored according to standard guidelines^{26,27} with the exception that four naps were recorded. The mean sleep latency on the MSLT was defined as the mean time from lights out to the first 30-second epoch scored as sleep. A sleep onset REM was defined as one or more epochs of REM sleep occurring within 15 minutes of the first epoch scored as sleep. We considered a mean sleep latency <5 min as pathological sleepiness, scores between 5–10 min as a degree of daytime sleepiness (borderline abnormal), and scores of 10–20 min as normal and a lack of daytime sleepiness. Because mean values on the MSLT may adversely be affected by a spurious sleep latency on a single nap opportunity²⁸ possibly due to what might be perceived as stressful inter-nap activities,²⁹ median values were also computed for each subject.

Measures of sleep architecture and diagnoses of primary sleep disorders were based upon data from MSLT and the second nocturnal polysomnography (to allow for sleep-lab habituation). Clinical outcomes of polysomnographic assessment and MSLT included obstructive sleep apnea, periodic limb movements, narcolepsy, insufficient sleep syndrome, primary/secondary insomnia, delayed sleep phase syndrome, bruxism, central sleep apnea, and upper airway resistance syndrome.

The polysomnographic outcome variables used in our analyses included: total sleep time (TST) (in min), sleep efficiency (% of time spent in bed asleep), the percentage of TST spent in non-REM (NREM) and REM sleep, latency to sleep onset (in min) to three consecutive epochs of sleep, and REM latency, defined as the time between the first epoch of any stage of sleep and the first epoch of REM-sleep. Brief arousals were scored following criteria set forth by the American Academy of Sleep Medicine, and the number of arousals expressed as a rate per hour of sleep adjusted for TST. Periodic leg movements both with and without accompanying arousals, were scored according to conventional criteria,³⁰ and expressed as an index of the rate of leg movements per hour of sleep, and a separately derived index of those accompanied by an American Academy of Sleep Medicine -defined arousal.³¹ We further recorded alpha intrusion, which was noted in review of 30-second segments. Polysomnography data were scored by an Emory University registered polysomnology technologist and interpreted by an Emory University Department of Neurology American Board of Sleep Medicine certified physician.¹²

Assessment of subjective sleep quality and sleepiness:

During the afternoon of their arrival at the hospital, subjects completed a self-administered questionnaire that explored themes and beliefs regarding sleep. The first two sleep specific

Table 3: Mean (SD) factorial scores and p-values for sleep questionnaire items in CFS and non-fatigued subjects

Factor pattern on sleep questionnaire items	CFS (n = 35)	NF (n = 40)	P *
	Mean factor scores (SD)†	Mean factor scores (SD)	
<i>F1 Insomnia</i> "How often trouble sleeping", "Waking up before you wanted to", "Sleeping for less than 5 hours", "Difficulty falling asleep", "Repeated awakenings", "Waking up not feeling refreshed", "Restlessness during sleep"	0.54 (0.8)	-0.48 (0.9)	.000
<i>F2 Sleepiness</i> "Falling asleep while sitting and talking", "Falling asleep while doing something, such as driving or talking", "Falling asleep in a car while stopped in traffic", "Falling asleep while sitting and reading", "Falling asleep as a passenger in a car", "Falling asleep while sitting quietly after a lunch", "Falling asleep while sitting inactive in a public place", "Trouble staying awake"	0.27 (1.2)	-0.24 (0.5)	.060
<i>F3 Physical/Somatic</i> "Nightmares or waking up frightened or crying out loud", "Waking up with aches, pains, or stiffness", "Sleeping more than nine hours", "Taking medication for sleep"	0.54 (1.0)	-0.48 (0.5)	.001
<i>F4 Apnea</i> "Interruptions to your breathing during sleep", "Falling asleep while lying down to rest in the afternoon"	0.09 (0.7)	-0.08 (1.2)	.865
<i>F5 Body Clock</i> "Working shifts", "Irregular bed time and/or wake-up time during the work week or weekdays"	0.13 (1.2)	-0.11 (0.7)	.610
<i>F6 Nasal Obstruction</i> "Loud snoring"	0.13 (1.1)	-0.12 (0.8)	.318

* 2-factor ANOVA, controlling for medication that influences sleep.

† A higher factor score represents more agreement on the sleep questionnaire items comprising the factor (i.e. more sleep complains)

questions, taken from the CDC Symptom Inventory,²³ queried frequency and intensity of unrefreshing sleep and problems sleeping during the past month. A score of 0 reflected no difficulty with unrefreshing sleep or no problems sleeping and the maximum score of 16 indicated the problem had occurred all the time and was severe.²³ The remaining 24 items of this questionnaire came from the Epworth Sleepiness Scale,³² which evaluates levels of excessive daytime sleepiness, and from the Toronto Sleep Assessment Questionnaire (SAQ),³³ which measures self-reported sleep quality.

Subjects completed four questionnaires (the Nap Booklets) after each nap on day 1, which assessed latency to fall asleep during each nap. Subjects also completed two questionnaires (the Sleep Booklets) the morning after each overnight study, which evaluated 1) perceived sleep quality the night before on a visual analogue scale from "Best possible sleep" (equals 0) to "Worst possible sleep" (equals 140); 2) latency to fall asleep (in min); and 3) total sleep time (in min).

Statistical analysis: Differences in categorical demographic data between CFS cases and non-fatigued controls were evaluated by Chi-Square or Fisher's exact test and continuous variables were compared by the t-test. Chi-Square test was also used for comparison CFS cases and non-fatigued controls in sleep study alterations. We used standard logistic regression analysis to regress CDC Symptom Inventory scores (unrefreshing sleep, problems sleeping) as well as Sleep Booklet scores (latency to fall asleep, total sleep time, sleep quality) and sleep medication use (yes/no) on case status (CFS/non-fatigued). Data from all

participants was evaluated by logistic regression; in addition the subgroup of subjects with no alterations noted in sleep studies (normal sleep) were evaluated separately.

A two factor analysis of variance (ANOVA) using a general linear model was employed to measure the association between cases status and medication use (yes/no) with polysomnographic variables. Log transformed values of polysomnographic variables were used when necessary to satisfy the assumption of normally distributed outcomes. Mean values for each polysomnographic variable were adjusted for medication use by utilizing the least squares method.

Paired samples t-tests were used to compare 1) mean sleep latency, as measured by the MSLT, and mean sleep latency, as evaluated by the Nap Booklets and 2) latency to fall asleep and total sleep time as measured by nocturnal polysomnography with latency to fall asleep and total sleep time as measured by the Sleep Booklets. Comparisons were done separately for the group of subjects with CFS and for the non-fatigued controls. P-values for the paired t-tests were adjusted for multiple comparisons using both a Bonferroni correction and by computing a false discovery rate.³⁴ Sleep questionnaire data from the SAQ© and the Epworth sleepiness scale were z-transformed for multivariate analyses. We used Principal Component Analysis (PCA)³⁵ with varimax rotation to evaluate which constellation of sleep symptoms represented the majority of the variance in sleep symptoms. Two-factor ANOVA was applied for comparison of factorial scores of sleep questionnaire items between CFS and non-fatigued groups, controlling for sleep medication use (yes/

no). Comparison of factorial scores was done for all participants as well as for the subgroup of subjects with normal sleep studies. Statistical significance for all tests was set at the 5% level. All statistics were computed using SPSS 12.0 (SPSS Inc, Chicago, IL).

Results

Clinically significant apnea and narcolepsy (exclusionary for CFS) were diagnosed in 11 subjects based on overnight and daytime polysomnographic studies.¹² These subjects were not included in this analysis.

The remaining CFS and control subjects were demographically comparable. Thirty (85%) of the 35 with CFS and 36 (90%) of the 40 controls were women; 32 CFS (91%) and all controls were white; their mean ages were 50.3 (range 27–69) and 50.5 (range 32–65) years, respectively; and mean body mass index was 28.7 and 29.2, respectively. Medication use was more common in CFS subjects compared to non-fatigued controls; 20 CFS subjects (57%) compared to 5 control subjects (13%) took medications that alter sleep.

Detailed polysomnographic findings have been reported in detail.¹² In brief, previously undiagnosed sub-clinical sleep disorders occurred similarly in both CFS and non-fatigued controls (Table 1). Minimal obstructive sleep apnea and periodic limb movements were the most common alterations and occurred similarly among those with CFS and the controls. MSLT results were also comparable between the two groups. Finally, there were no statistically significant differences in standard polysomnographic measurements between those with CFS and non-fatigued controls on either night 1 or night 2. Since the first night served as an adaptation to the sleep laboratory, Table 2 summarizes only the night-2 data adjusted for medication use. In addition, each group appeared to experience similar periods of wakefulness during the study night as recorded in the % wakefulness during the sleep period.

Our analysis included two questionnaire items from the CDC Symptom Inventory that assess subjective sleep qualities over the preceding month, unrefreshing sleep and problems sleeping (getting to sleep, not sleeping through the night, or waking up on time), as well as one question from the Sleep Booklet, evaluation of sleep quality (best possible sleep to worst possible sleep) during the PSG. In a logistic regression analysis, we found an association of CFS with higher frequencies of symptoms of unrefreshing sleep and problems sleeping ($p < .001$ for each item) as well as worse ratings of sleep quality ($p < .05$); these associations remained after adjusting for use of medications that affect sleep.

Among subjects with normal objective sleep studies, those with CFS still reported significantly higher frequencies of unrefreshing sleep and problems sleeping than did non-fatigued controls ($p < .001$ for each item). In addition, CFS subjects with normal sleep studies also rated their quality of sleep during night #2 significantly worse than non-fatigued controls ($p < .05$).

No significant differences between self-reported, as evaluated by the Nap Booklet, and the objective mean sleep latencies, recorded by the MSLT, were found for CFS subjects (Nap booklet score (\pm SE): 9.3 (\pm 0.9) minutes versus MSLT score : 7.2 (\pm 0.7) minutes, respectively; $t(7) = 1.7$, $p = .13$). In contrast, in non-fatigued controls, self-reported mean sleep latency was significantly longer than recorded mean sleep latency, MSLT

score (\pm SE): 10.8 (\pm 1.5) min versus Nap booklet score :5.8 (\pm 0.6) min, respectively; $t(16) = 2.9$, $p < .01$).

Similarly, self-reported mean latency to fall asleep in non-fatigued controls, as reported in the Sleep Booklets, was significantly longer than mean latency to fall asleep, as measured by overnight polysomnography. These differences were found both on night #1 and night #2 in control subjects, but were more pronounced on night #1. The mean latency to fall asleep on night #1 was 18.9 (\pm 3.5) minutes as measured by PSG, versus mean latency to fall asleep night described in the Sleep booklet 31.8 (\pm 5.2) minutes ($t(38) = 3.05$, $p < .005$). The mean latency to fall asleep on night #2 was 16.6 (\pm 3.5) minutes as measured by PSG, versus latency to fall asleep night described in the Sleep booklet of 23.7 (\pm 4.1) minutes ($t(38) = 2.4$, $p < .02$). In contrast, no significant differences between subjective and objective latency to fall asleep during overnight polysomnography, were found in CFS subjects on either night #1 or night #2. These results remained even after excluding those subjects taking medications that affect sleep. There was no significant difference in total sleep time, as estimated by the Sleep Booklets, and total sleep time, as measured by overnight polysomnography, in either non-fatigued controls or CFS subjects.

Using the conservative Bonferroni correction for multiple comparisons at the $\alpha = .05$ level, only the difference in night #1 sleep latencies in control subjects would remain significant. However, using the method of Benjamini and Hochberg and controlling the false discovery rate to $< 10\%$, then all 3 of the p -values reported above are still significant.³³ Together, these data suggest that altered perception of the latency to sleep onset is common in non-fatigued controls, but not in CFS patients.

Considering all items assessed by the SAQ and Epworth sleepiness scales, Principal Component Analysis (PCA) revealed six factors that accounted for the majority of variability in responses on the sleep questionnaire items. Table 3 shows the individual items comprising the six factors after a Varimax rotation with Kaiser normalization, the mean factor scores, and p -values for the differences between CFS and non-fatigued controls. A higher mean value for a factorial score represents more endorsement of the sleep questionnaire items comprising the factor (i.e. more sleep complaints). Factor score names were assigned to groups of questions comprising the different groupings based on the domains covered by the individual questions even though the questions were not designed with specific disorders or disturbances in mind. CFS cases had significantly higher scores in the Insomnia and Physical/Somatic factors compared to non-fatigued controls. CFS cases also had notably higher scores on the Sleepiness factor, although the difference was not statistically significant.

Differences in perception of sleep quality were even more pronounced between CFS cases and controls with normal objective sleep studies. CFS cases not only had significantly higher scores in the Insomnia (CFS: 0.51, non-fatigued: -0.56, $p = 0.001$) and Physical/Somatic (CFS: 0.41, non-fatigued: -0.42, $p = 0.013$) factors, but also in the Sleepiness factor (CFS: 0.39, non-fatigued: -0.27, $p = .004$).

Discussion

The major finding of this study is the documentation of the extent and nature of sleep complaints experienced by CFS subjects compared to non-fatigued controls in the absence of

differences in quantitative polysomnography and multiple sleep latency testing between the two groups. These findings are in agreement with previous clinic-based studies indicating that CFS patients perceive poor sleep in the absence of objective underlying sleep pathology.^{11,12,15,16} However, the somewhat paradoxical observation that controls and not CFS subjects, overestimated the time to fall asleep, has not been previously reported and deserves further exploration. This finding suggests that CFS subjects may more closely monitor their sleep behaviour and that may contribute to their perceived sleep problems. It is also possible that persons with CFS are more accurate in their perceptions of their generally impaired sleep than people who do not have insomnia (but may sleep badly from time to time). This finding should be validated in further studies.

Even though identification of insomnia per se was not a goal of the study, it is interesting to note that CFS subjects in this study who were identified by the presence of a prolonged syndromic illness and its consequences also fulfilled a general definition for insomnia.^{9,18,36} The symptom variables related to sleep (unrefreshing sleep and the 3 components of problems sleeping-getting to sleep, not sleeping through the night, or waking up on time) were identified by the patients themselves during the construction of the CFS symptom inventory.²³ Do these observations suggest that the CFS subjects have a problem with sleep efficacy, or that their descriptions of symptom association or our efforts to obtain information from them are inadequate? Are the CFS subjects identifying their impairments in terms of sleep based on the types of questions being asked with responses indicative of sleep problems not detected in the usual measures of sleep architecture?

These findings argue against the importance of readily identifiable sleep pathology contributing to the symptoms of CFS in the majority of CFS subjects. However, sleep disorders that may respond to clinical intervention should be evaluated in patients complaining of fatigue, and formal sleep studies are required in the evaluation of patients with suspected sleep disturbances. In clinical practice these disorders would have been considered as temporary exclusions of CFS and the patient re-evaluated after clinical re-evaluation.⁸ New clinical interventions in CFS patients await further delineation of possible mechanisms required to explain these differences, but they will likely be based on pharmacological and/or behavioural modalities. However, such interventions need to be based on a better understanding of sleep physiology and the influences of chronic illness and exclusion of primary sleep disorders.

Besides the theoretical issues addressed above, the present study is not without practical limitations. First, due to stringent selection criteria, our sample size was small, especially considering the number of variables examined. This circumstance limited the power to detect more subtle differences in responses to sleep questionnaire items between groups. Both CFS subjects and controls showed moderately impaired sleep quality (being in a research setting likely impaired sleep quality equally for both groups) and polysomnography is not an optimal measure of insomnia. Further studies with larger sample sizes are clearly warranted. Second, while sleep-altering medications were frequently used by both CFS subjects and controls, their use was more common among CFS subjects. Prescribed medications in CFS subjects may in turn have influenced CFS subjects' reports of sleep quality. Many published

studies of sleep in persons with CFS do not consider medication use. Our attempt to statistically adjust for differences in use of medications that affect sleep as a binary measure (use/non-use) might be inadequate to completely control for the confounding effect of medication use. However, our small sample size precluded conducting a stratified analysis among cases and controls who did and did not use medications that alter sleep or whether they medications induced or inhibited sleep. Finally, the mean duration of illness among CFS cases in this population was 7.3 years.¹⁹ Thus, findings in this study of prevalent CFS cases may not be applicable to those with a shorter duration of illness.

Conclusion

These findings suggest that alterations in standard objective sleep parameters do not explain the etiology of symptoms of unrefreshing sleep and presence of sleep problems reported by persons with CFS who do not have readily diagnosable sleep disorders. Further studies examining the causes of apparent altered sleep-state perception may be helpful in understanding CFS.

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how the FV Loops are generated. This level of understanding helps the clinician to understand the information that is being presented to them and how they can use it in titrating a therapeutic pressure level.

How do reimbursement and regulatory issues effect the applications of your product?

Recent changes in CPAP reimbursement that have been advanced by CMS have allowed for a more widespread use of home sleep testing (HST). The most recent version of the National Coverage Determination (NCD) still leaves many areas open for interpretation. These areas are now being addressed by the Local Coverage Determinations provided by the DME MACs. We now have a clearer picture of who can conduct HSTs and under what conditions. We also can see what types of devices can be used and what level of reimbursement is offered. While the CMS NCD addresses only about 15% of all sleep apnea patients, others will use it a guideline to revise their reimbursement of both sleep testing and sleep therapy. With declining levels of sleep disorders center and laboratory reimbursement for polysomnography this provides clinicians with less costly options for making a diagnosis of sleep apnea. By providing both the SomnoStar z4 sleep diagnostic system and the SomnoStar Orbit we can provide clinicians with the tools they need to manage their patients as cost effectively as possible. The only area that has not been addressed is the titration of CPAP. There is still no reimbursement code for autoCPAP therapy nor a policy from either AASM or CMS on the use of this mode of therapy for treatment or the determination of treatment levels.

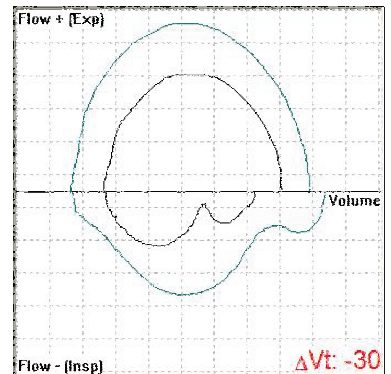
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