



Volume 3 Number 2 April-May 2008

Respiratory TherapyTM

The Journal of Pulmonary Technique

Home Oxygen
Checklists for Safety
Ventilation Strategies
Trigger Response
Oximetry Roundtable

A WORLD OF PRODUCTS FOR **B**BETTER **B**REATHING

STABILTUBETM
LOCKTITETM
E. T. TAPETM

NEO₂-SAFETM
INFANT CIRCUIT
MANIFOLD

BITE-PROOF BITE BLOCKTM
UNIVERSAL BITE BLOCKTM



BABY
E.T. TAPETM

TRACHSTAYTM
QUICKLOCKTM
TRACHGUARDTM

HOPETM NEBULIZER
ADULT & PEDIATRIC KITS
HELIOX REGULATOR

*Hoses in Tangles?
Cables in Chaos?...*
Get WRAP-SAFETM

Available from Finer Specialty HealthCare Product Providers Worldwide

B & B MEDICAL
TECHNOLOGIES 

Visit our Website at BANDB-MEDICAL.COM
or Contact Us Today Toll Free at 1.800.242.8778 or +1.916.331.5221
Fax Toll Free 1.877.810.8499 or +1.916.331.0161



Is your suction safe?

Ours was designed with your patients in mind.



- **Patented Push-to-Set™** – Built-in feature that eliminates the need for you to occlude patient tubing to set accurate vacuum levels
- **Quick-To-Max** – Only 2 turns from 0 to full wall vacuum
- **Quietest** on the market
- **Stat Set-up** – Intermittent mode starts in the “ON” cycle – No Waiting


Medical Corporation™
always there | for life



The most important part of Intelligent Ventilation®...



The Human Factor.

At Hamilton Medical, we believe the people using the equipment are just as important as the mechanical ventilator itself. We're dedicated to supporting each and every clinician every step of the way to help ensure the highest level of performance and patient safety available. Let us be a part of your crew and let's make mechanical ventilation as safe as commercial aviation.

Goto www.hamiltonG5.com
for Crew Training and Support

HAMILTON
MEDICAL

Holistic Oxygen Therapy, "Draft Oxygen" and Secret Thoughts From an Oxy-Moron

Mary Ann Couture, MS, RRT, NPS

Mary Ann Couture is a practitioner at Hartford Hospital, Hartford CT, in the department of Respiratory Care. She is also a clinical instructor with Goodwin College, East Hartford, CT.

Periodically, oxygen therapy is offered in public bars and holistic health spas. Either an oxygen concentrator, which can deliver approximately 5 liters per minute of 85-95% pure oxygen, or small oxygen tanks are commonly used for this therapy. The bars and spas that offer therapy tend to filter gas through jars with aroma therapy. This adds concern about bacterial contamination or inhaling oils that can lead to a serious inflammation of the lungs, known as lipoid pneumonia, among several other complications that can occur when oxygen is improperly dispensed.¹ The bottles may be set on top of a light source enhance a visual effect to market their product.

In their marketing, bars and spas may present false benefit claims for oxygen therapy. The Federal Food and Drug Administration, (FDA) has decreed that this naturally-occurring gas is a prescription drug when concentration is above ambient levels, under the Federal Food, Drug and Cosmetic Act 201(g)(1) of the [21 USC].² The FDA considers that improper use may harm some specific individuals.

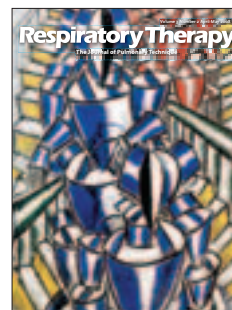
When we encounter oxygen therapy proprietors, we may have many questions about the quality of the therapy, and whether it is legal. Moreover, we may not realize what we should do about them. With the advent of certain legislative acts, the strength of the FDA to police this abuse may be weakened. This report explains benefits and hazards of supplemental oxygen, the abuse from mislabeling the therapy, and demonstrates how current legislation sets up a "perfect storm" that may render recreational oxygen therapy as a new financial windfall in spite of efforts to control the problem as an unregulated business.

Complementary therapies

In 1993, a sentinel article was presented in the New England Journal of Medicine which indicated that as many as 1 in 3 of 1,539 telephone respondents sought the use of complementary and alternative medicine therapies (CAM) for chronic conditions. The authors limited the list of therapies to 16 commonly used interventions, none of which was taught widely in US medical schools. Of those respondents, who used unconventional therapies, 72 % never informed their doctor. Yet, the number of these visits averaged 19 per year.³

Holistic therapy is a subgroup of CAM which may include aromatherapy, homeotherapy, naturopathy, dietary supplements and Chinese medicine. The purpose of treatment relates to pain or symptom relief. Spas may combine any subgroup as part of CAM therapy. There may be some benefits expressed towards certain CAM treatments, in general, but there is scant evidence for holistic benefits from many of these treatments. The evidence is hard to come by since full scientific review lacks serious funding. Many forms of CAM are offered in US health facilities in addition to patient medical care. Even after more than ten years of federally funded research in some areas, very little is known about whether most alternative therapies work at all and which methods are safe, except in the case of oxygen, where there is evidence that dates back as far as the late 1800s.

There seems to be little or no policing for the use of this particular CAM. Oxygen is labeled as a drug by the FDA, yet it does not seem to be regulated as such. This
Continued on page 11...



Respiratory Therapy
The Journal of Pulmonary Technique

Vol. 3 No. 2
April-May 2008

Table of Contents

ARTICLES

- 33 Prone Positioning During Ventilation
- 35 Lactic Acid Testing
- 36 Ventilator Technology
- 39 Trigger Response Time
- 43 Waveform Analysis
- 44 Asthma Management
- 49 Dealing With Death
- 54 Alcohol, Drugs and Ventilation
- 61 Coughing and Sleep Apnea

DEPARTMENTS

- 5 Editorial: Home Oxygen Therapy
- 15 Guest Commentary: Checklists & Safety
- 18 News
- 24 News Feature: Mass Casualties
- 25 Products
- 26 Oximetry Roundtable

Respiratory Therapy™

The Journal of Pulmonary Technique

Published six times each year by
Goldstein and Associates, Inc.
10940 Wilshire Blvd., Suite 600
Los Angeles, CA 90024 USA
Tel: 310-443-4109
Fax: 310-443-4110
E-mail: s.gold4@verizon.net
Website: www.respiratorytherapy.ca
Video website: www.rttv.ca

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

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

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

©2008 by Goldstein & Associates, Inc. All rights reserved. Reproduction in whole or in part without written permission is strictly prohibited.

Publisher
Steve Goldstein

Editor
Les Plesko

Senior Editor
Carol Brass

Assistant Editor
Laszlo Sandor

Design and Production Management
<http://accugraphics.net>

Editorial Advisory Board

Mohammed Al Ahmari, BSRT, MSc., RRT
Prince Sultan Military College
of Health Sciences
Al-Khobar, Saudi Arabia

Muhammad Aslam, MD
Clinical Fellow in Newborn Medicine
Harvard Neonatal-Perinatal Fellowship
Program
Children's Hospital Boston
Instructor in Pediatrics,
Harvard Medical School, Boston, MA

Larry Conway, RRT
North Mississippi Medical Center
Tupelo, MS

Ed Coombs, MA, RRT
Sr. Marketing Manager - Ventilation
Draeger Medical
Telford, PA

Antonio Esquinas, MD, PhD, FCCP
Intensive Care Unit
Hospital Morales Meseguer
Murcia, Spain

Dr. Javier Fernandez
Director of Clinical Affairs & Education
Respiratory Division Latin America
Miami, FL

Gerardo N. Ferrero, PT
Clinical Specialist, Latin America
Buenos Aires, Argentina

Surinder K. Jindal, MD
Postgraduate Institute of Medical
Education & Research
Chandigarh, India

Rebecca A. Mabry
General Sleep Manager
Viasys Healthcare, Yorba Linda, CA

Paul Mathews, PhD, RRT, FCCM,
FCCP, FAARC
Associate Professor, Respiratory Care
University of Kansas Medical Center
Kansas City, KS

Hossein Razavi, MD, FCCP
Pulmonary, Critical Care &
Sleep Medicine
St. Helena, CA

Daniel D. Rowley, BS, RRT-NPS, RPFT
Surgical/Trauma/Burn ICU
University of Virginia Medical Center
Charlottesville, VA

J. Kyle Schwab, MD
Medical Director
Louisiana Sleep Foundation
Baton Rouge, LA



Mobile pedestal
provides stability yet
requires minimal space

New! SmartVest Wrap™ Leading again with innovation.

Electromed, Inc., the leader in HFCWO innovation, announces the **SmartVest Wrap™** for use in acute care and transitional care settings.

The **SmartVest Wrap™** offers unique features designed with the patient and medical professional in mind. Ease of application, full-coverage versatility and reversibility make it the **smart** choice in ICU and transitional patient care.

Vigorous and effective airway clearance therapy is a cornerstone of good patient care. High Frequency Chest Wall Oscillation therapy (HFCWO) is an increasingly preferred and cost-effective method.

Contact us to schedule a demonstration
and to receive product and pricing information.



ELECTROMED, INC.
Creating superior care
through innovation®

502 Sixth Ave. N.W.
New Prague, MN 56071
Phone: 01-952-758-9299
Toll Free: 1-800-462-1045
Website: www.SmartWrap.info



Make compliance child's play

Compliance Made Fun

The clinically tested **Funhaler®** is a pediatric (18 months and older) small volume spacer that makes it fun and easier for young children to take their aerosol-based medication. Fits most pMDIs without needing adaptors.

www.funhaler.com



Designed with an internal spinner and whistle to improve the management of children's asthma.



Screening and Assessment

AllFLOW™ IQ Spirometer's is portable and easy to use. It accurately measures inspiratory and expiratory flow and volume to help with early detection of respiratory disease. Through one quick USB port connection to your PC, preview, print or store patient data.



Testing without Contaminants

AllFLOW™ Filters meet or exceed the highest standards in PFT filtering with minimal resistance and low dead space. The wide selection of color coded ports fit most equipment, enabling the professional to accurately obtain quality spirometry and lung function tests while reducing contamination.



Diagnosing and Training

The **In-Check™ DIAL** is an inhalation airflow meter with orifices designed to accurately simulate the resistance of popular inhaler devices. It is the only teaching and training device available for healthcare providers to use with patients on respiratory medication.



Efficient Delivery

Deliver medication more efficiently with the rigid **holding chamber** or the collapsible version for increased portability.

We carry many accessories suited for our quality respiratory products. To view our complete product line, please visit: www.alliancetechmedical.com



AllianceTech Medical, Inc.

Call us today! **1.800.848.8923**



EVERYBODY LOVES A COMFORTABLE FIT.

Introducing the PerforMax™ noninvasive ventilation face mask, the new standard for comfort and simplicity. Because of the unique perimeter seal, the PerforMax eliminates contact with the sensitive nasal bridge and annoying air leaks into the eyes. It is quick and simple to fit, and the clear field of vision may ease feelings of claustrophobia for many patients. Contact your Respironics representative or visit our Web site to learn why the PerforMax face mask is the clear choice for NIV.



PerforMax™

Envisioning tomorrow. Improving today.™

World's 1st Inline Oxygen Flow-Meter!

Distributed By:



Invacare Supply Group

*Oxyview™ is the most accurate flow-meter
powered by the flow of oxygen*

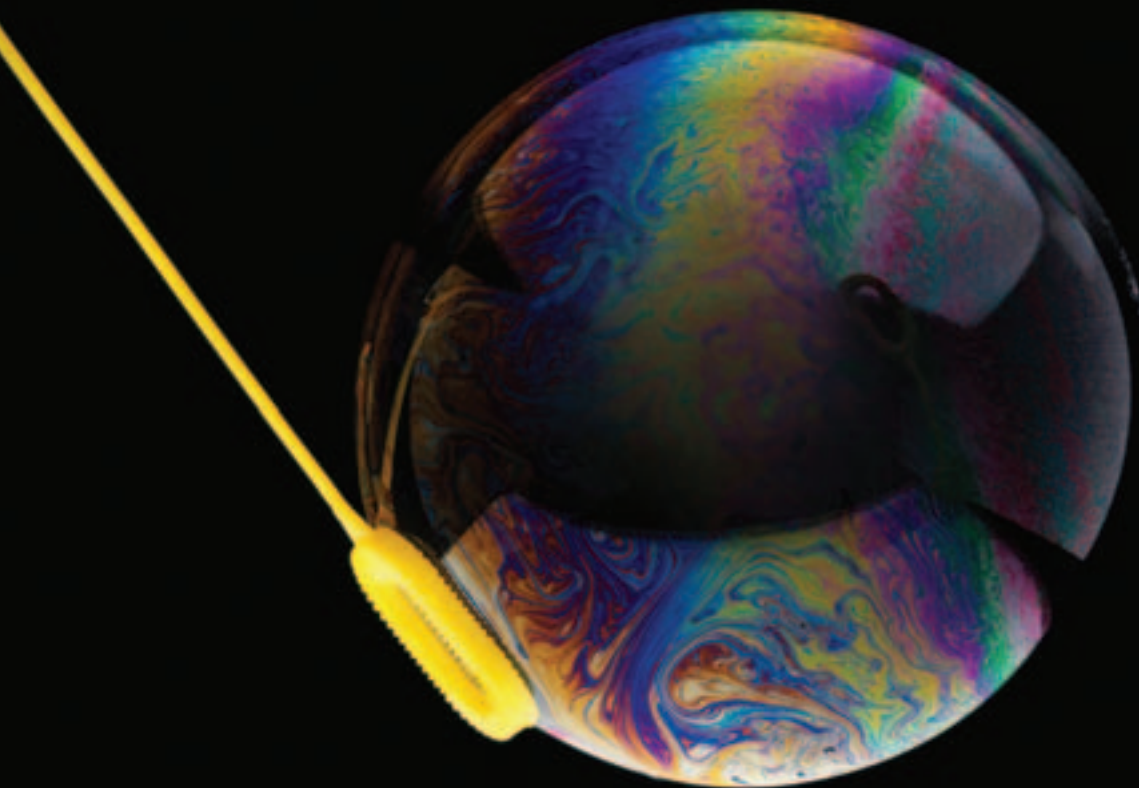


- ➔ Low cost flow-meter
- ➔ No batteries required
- ➔ For in-patient & out-patient use
- ➔ Instant verification of oxygen flow
- ➔ Gravity independent, works in any position
- ➔ Fits all respiratory devices

INGEN
TECHNOLOGIES, INC.

Call today to place your order!
Phone: 800.225.4792
Fax: 508.429.1581
www.invacaresupplygroup.com





PRECISION WITH EVERY BREATH

INTRODUCING BiPAP® AVAPS™ —

OPTIMAL NONINVASIVE VENTILATION, NATURALLY INSPIRED.

Don't compromise patient comfort or ventilation efficiency. Discover the advantage of BiPAP® AVAPS™ (Average Volume Assured Pressure Support) from Respironics. This exclusive technology, already proven successful in Europe, is designed to automatically and gradually adjust pressure support to meet changing patient needs and maintain an average tidal volume. Call 800-345-6443 to learn more about how you can place the comfort and safety of the BiPAP® AVAPS™ at your patient's fingertips.

BiPAP® AVAPS™



may be partly to blame from some technical loopholes based on recent Federal legislative acts. Whether certain CAMs work or not, there seems to be a clash of new technologies to manufacture oxygen therapy, and increased public use of CAM.

Oxygen complications

Medical oxygen is recommended for persons who have an oxygen saturation of <90%, which is measured by respiratory therapists or credentialed persons with equivalent training. Trained individuals have the ability to assess patients, recommend changes in therapy, and instruct caregivers.⁴ There are still a few harmful effects of oxygen. These are related to concentration, length of time in use, and some contraindications for certain medical conditions. Problems associated with oxygen administration can be found in the American Association of Respiratory Care, (AARC) clinical practice guidelines for oxygen administration in pediatrics and adults:

- Improper use of equipment may reduce the purity of the product. The masks and cannulas that are used may become contaminated. Most of these delivery devices to the patient come with a label for “single patient use,” policed by the FDA.
- Patients with some types of heart disease, asthma, congestive heart failure, pulmonary hypertension, and chronic obstructive pulmonary diseases, need to have their medical oxygen frequently monitored and oxygen prescribed carefully.
- Some state jurisdictions suggest that oxygen should not be given to some children or adults suffering from certain long-term heart defects such as single ventricle, or hypoplastic left-side of heart.
- A child's body habitus is smaller than an adult's. Children's ventilation capacity is also smaller. At 4 liters, the concentration of oxygen may be greater than 50% leaving children even more vulnerable to toxic effects from prolonged use.⁵
- Giving supplemental oxygen can “shunt” the balance of blood flow between the lung and the systemic blood flow, leaving the person more oxygen-hungry.
- The administration of supplemental oxygen to patients suffering from paraquat poisoning or to patients receiving certain chemotherapeutic agents such as bleomycin may result in pulmonary fibrosis.^{6,7,8}
- Persons receiving therapy for cancer may try to seek out these CAMs, especially if they are misinformed that oxygen relaxes them, improves emotional well-being or relieves stress.

Scope of the problem

Holistic programs need to be careful about their claims of health benefit. Several proprietors list most of the benefits from European spas' claims where oxygen therapy is not as well regulated. It seems that if one hears about a claim often enough, then the claim is presumed to be true, which may be the reason that similar false claims are repeated in advertisements and internet sites. (Table 1)

Some proprietors often state that their oxygen is not a medical gas and that it is offered strictly for recreational use, while others claim that there are medical benefits. Both claims would be against FDA regulations. The Federal Act provides for seizure of illegal products and injunctions against their manufacturers and distributors. The Act also accounts for misrepresentation of treatment by individuals who are not

medical practitioners. Other violations that are covered are misbranding oxygen as a new drug, or when claims from adding inhaled scents are considered “adulterated.”^{9,10}

Proper medical oxygen equipment is usually delivered by a licensed service company that provides equipment based on a doctor's prescription. The company should provide instructions on care and maintenance for the life of the product. However, this may change with current and proposed legislation. The licensed companies give general guidelines for cleaning the equipment and offer support for repairs. Yet, since some states do have allowances for holistic oxygen, a concentrator is easily available for about \$700 by just going online to Amazon.com, or the product can be shipped from international companies like Moorspa.com in Canada.

Critical issues in policy change

There are two areas, both regulated under the FDA, that can be addressed: 1) false claims in marketing a drug, and 2) ready access to oxygen-producing equipment that makes it relatively easy for bars to set up recreational oxygen, and for homeopathic agencies to claim oxygen therapy as a form of CAM. Moreover, there are three Federal Legislative Acts that may confound the issues and the future of distribution of oxygen equipment. The exclusive distribution of oxygen therapy by medical professionals may be in jeopardy due to a backlash from these regulations.

- Dietary Supplement Health and Education Act of 1994
This public law 103-417 was enacted by the 103rd Congress. It is frequently called the DSHEA Act. Senator Orrin Hatch (UT) originally sponsored this bill in an effort to amend the FDA to establish standards to dietary supplements with regards to scientific evidence in the benefit of health effects.¹¹ It consequently shifted the burden of proof to the FDA to present the scientific evidence in order to determine mislabeling and false claims. Two problems occurred based on this act. The first was that there was scant evidence to support many of the dietary supplements. Second, a backlash occurred since this act was enacted, and there has been an explosion of supplements on the market. This “sacred cash cow” has affected world-wide dialogue in trade practices. It opens the door for companies even outside of the US to sell supplements without the back up of scientific relevance and allows them to operate. Companies can market their products until the FDA shows its proof, but the agency does not always have the financial resources to assess each and every supplement.

But what does this have to do with oxygen? With homeopathic medicine so widespread and persistent, it is no wonder that holistic practitioners may feel that they can readily expand to “natural gases.” At most, the FDA can claim mislabeling and manufacture of a “new drug” when proprietors add inhaled flavors.^{9,10}

- Social Security Deficit Reduction Act of 2005
This law may be one of the most important for allowing spa oxygen to flourish and may be the most controversial on this subject. Procuring oxygen-producing equipment (concentrators and tanks) was previously limited to a prescription and rental use from a licensed vendor. The Social Security Deficit Reduction Act made changes to Medicare and Medicaid payment in order to reduce Federal spending over the next 5 years. It was signed by President George W. Bush in early 2006.

Are you oxy-smart or an oxy-moron

Several oxygen health benefit claims were assessed from European and US Spa web sources and handouts. A response is provided for each of the claims based on literature search. Some benefit claims could not be found anywhere in the medical literature, while others have half-truths buried within their claims.

Table 1: Benefits/claims from spas and bars

PROS	CONS
<p>Feel better with increasing oxygen levels Promotes relaxation, reduces stress. Heightens concentration, increases memory attention span and learning ability and improves creativity and verbal fluency</p>	<p>The National Center for Complementary and Alternative Medicine's mission is to explore practices under a context of evidence-based science. Safe practice of CAM added to conventional medical practices under a physician, doctor of osteopathy and allied health professions seek to decrease a patient's level of "discomfort" related to their diseases. Current research has shown no strong evidence for many CAM treatments as effective since the effects are not readily explained in scientific terms. Subjective statements such as "feels good" are subject to misinterpretation and become difficult to assess or explain in scientific terms.¹⁵</p>
<p>Natural remedy for the alleviation of the symptoms of hangovers, headaches, or migraines. Promotes better sleep and people wake up with more drive.</p>	<p>Sleep apnea is a condition that causes hypoventilation while asleep. The body either "can't breathe" due to excessive tissue in the neck or "won't breathe" because the brain signals from the brain are altered. It affects quality and quantity of sleep. This creates elevated levels of carbon dioxide and has a profound, systemic effect to the kidneys, heart, lung and brain as a chronic condition. If the body "can't breathe" or "won't breathe," then adding oxygen will not get into the bloodstream. Factors that increase risk of sleep apnea can include alcohol and tranquilizer consumption, which adds to hypoventilation and the brain's "won't breathe" response. Elevated carbon dioxide levels in the blood may cause symptoms of headache, forgetfulness, and confusion. Hangovers and headaches have a common connection with hypoventilation syndromes since alcohol is a respiratory depressant.^{16,17}</p>
<ul style="list-style-type: none"> • Faster recovery from injury by promoting cell regeneration • Strengthens the immune system. • Its natural antibiotic destroys harmful bacteria. • Cleanses the system to detoxify blood and increase circulation by oxidizing • Eliminates built up toxins and poisons. 	<p>These claims have some truth to them, but not at the level from oxygen that is received with spa treatment. Some of these claims may be based on hyperbaric oxygen therapy (HBO) where oxygen is delivered at pressures between 2-3 atmospheres above 760 torr. A state of hyperoxia with HBO is achieved when oxygen is forced into the plasma. This increased supply of oxygen may heal some wounds, restore white blood cell function and has some antimicrobial activity to specific bacteria that are sensitive to increased oxygen levels.^{16,18} Moreover, if oxygen had natural antibiotic properties and physicians were able to treat people with 100% oxygen, there would be scientific evidence published years ago on this subject.</p>
<p>Gives you fresher younger looking skin.</p>	<p>Since oxygen is being delivered to the nostrils, there is no added benefit. In addition, some long-term users of oxygen may experience skin irritation in the nares associated with the dryness of the gas.</p>
<p>Neutralizes toxins / displaces free radicals.</p>	<p>Free radicals have been the subject of many news articles on nutrition and cancer. Conclusions from clinical trials are still inconsistent. Free radicals are overactive molecules that can cause damage to tissue cells over time, which may lead to cancer. The literature suggests that antioxidants may stabilize these free radicals.¹⁹ As far as the claim goes, excess oxygen can actually increase the production of free radicals.²⁰</p>
<p>Aids in the treatment of allergies such as asthma, upper respiratory infections and sinus problems.</p>	<p>As oxygen comes out of the canister device, it is already filtered and dry. Whatever a person breathes beyond the 2-4 liters that is delivered via therapy, the total gas concentration becomes diluted through air entrainment. The short-term use of oxygen therapy may cause some individuals to claim that they feel better, since breathing the therapy gas has some level of filtration. It will not cure acute allergy symptoms and may prevent someone who needs emergency treatment to delay seeking treatment.</p>
<ul style="list-style-type: none"> • Improves athletic performance, energy booster. • Clientele includes marathon runners • Weight loss. 	<p>Sports participants may be out of breath because of a massive physical exertion and lactic acid build up. Lactic acid accumulates in the tissues as a result of anaerobic activity which actually helps the body burn more calories. Anaerobic activity may be beneficial for weight loss programs, but it is a benefit only to exercise and not from supplemental oxygen. Repetitive anaerobic exercise may improve oxygen and carbon dioxide gas exchange and reduce fatigue when properly done under a supervised exercise program. The only athletes who may need extra oxygen are those who work out at high elevations where atmospheric pressure is lower.^{1,20} Conversely, an effort is being made by athletes that is evidence-based to improve athletic performance and endurance. Athletes who sleep in low atmospheric environments, then train at low atmosphere, naturally build up a higher level of hemoglobin, which increases the red blood cells' oxygen carrying capacity (transport and consumption).^{21,22,23}</p>
<p>Decreases cravings for nicotine</p>	<p>Programs that are offered for smoking cessation such as Freedom from Smoking offered by the American Lung Association do not claim that oxygen therapy is a form of treatment.</p>
<p>Statement: "Alarming, medical research has indicated that oxygen deficiency is probably the greatest cause of degenerative diseases like cancer, atherosclerosis and diabetes. Increasing the quality and amount of oxygen in your life could be the smartest decision you'll ever make."</p>	<p>A minimum tissue oxygen level of 30 torr must be met for normal cell function. Lower levels from hypoxemia can cause damaged tissue and sometimes leads to infected tissue. Moreover, short periods of hypoxemia may lead to serious diseases like renal failure. In atherosclerosis and other vascular diseases, when the body is hypoxemic, the vessels in the heart and lungs can constrict. Normalizing oxygen levels when oxygen is given to correct the problem will relax the vessels.¹⁶ Otherwise, there was no literature found for the claim that oxygen deficiency is a cause of cancer.</p>

Medicare payments that existed prior to the enactment of the Deficit Reduction Act set limits to suppliers to 36 months of technical support for oxygen equipment under continuous use. After this period of time, the homecare equipment supplier transfers title to the patient. Additional payments from Medicare would only continue for some oxygen tanks and durable supplies. That means oxygen equipment supply changes from lease contracts to ownership regardless if the owner understands if the device still works properly. The burden of repair is shifted to the owner. In this particular case, the burden may be placed on an individual who may not fully be capable of handling this ownership. The 36 month countdown projects first ownership by January 2009.

How does this affect recreational use? The burden of this bill is already upon us by creating the legal loophole for spas and bars to purchase and own equipment that was previously limited to access by prescription.¹²

A repeal to amend part B of title XVIII of the Social Security Act to restore the reimbursement for oxygen equipment before enactment provision takes effect is in the works. The House version of the bill, HR 621, The Home Oxygen Patient Protection Act of 2007 was introduced in January by Rep Tom Price (GA). The Senate version, S 1484, was introduced by Senator Pat Roberts (KS). Legislative updates and information on how respiratory therapists can contact their elected officials are listed in the AARC website at <http://www.aarc.org/headlines/HR621.cfm>.

- Safe Medical Devices Act of 1990: S 3006

The Safe Medical Devices Act of 1990 may reveal a potential conflict between the Deficit Reduction Act, in its current wording, and the Federal Food, Drug, and Cosmetic Act: 21 CFR. In 1989, in anticipation of establishing a place for oxygen concentrators, Jim Dillard published, on an FDA website, a draft for Good Guidance Practice of February 1997. The content of that draft confirmed that oxygen was to be administered for disease states. He further added, "Oxygen conserving devices are prescription devices and must be labeled in conformance to 21 CFR Section 801.109. Both the device and its labeling will bear the prescription legend."¹³

The Safe Medical Devices Act of 1990 requires US medical facilities to comply with reporting and tracking requirements for deaths and serious illness or injuries associated with the use of medical devices. This Act, S 3006, was sponsored by Representative Henry Waxman (CA) and confirmed as HR 3095 in 1989 to amend the Federal Food, Drug and Cosmetic Act: 21 CFR. This bill allows for improvements in the regulation of medical devices. It is strictly limited to medical facilities. It requires manufactures of devices to keep track of device location and requires a manufacturer or a distributor to report any problems through post market surveillance.¹⁴

The conflict is present when the FDA issues warnings under 21 CFR while the Social Security Deficit Reduction Act of January 2006 and the Safe Medical Devices Act limits its power. Purchases of equipment from outside sources may not come under the scrutiny of the laws that were meant to protect patients under treatment from medical professionals and the healthcare facilities. However, since ownership of these devices is now possible, non-medical and non-trained personnel are excluded of these rules on reporting any post-market problems.

This leaves an unknowing public at risk for the problems of recreational or spa treatment with supplemental oxygen. It becomes a moot issue when ownership of equipment becomes involved. A "perfect storm" is brewing.

What can we do?

At best, medical professionals who have been trained in oxygen therapy and who recognize mislabeling may report violations to the FDA in a couple of ways:

Mandatory reporting can be addressed by contacting the Division of Surveillance Systems, Reporting Systems Branch by phone at (301) 594-2735 or FAX, (301) 827-0038. Written reports can go to:

FDA, CDRH, MDR User Reporting, P.O. Box 3002, Rockville, MD 20847-3002. The FDA Medical Device Reporting (MDR form 3500), which includes instructions and forms can be found on the Internet at <http://www.fda.gov/cdrh/mdr/> by following the links.

Summary

The FDA approves drugs on the basis of scientific data submitted by a drug sponsor to demonstrate that the drug is safe and effective. Oxygen is considered a drug and although oxygen therapy is not new, the FDA has to chase after Internet sales, bars and holistic centers that make false marketing claims. When claims are stated to "prevent, diagnose, treat, or cure disease," these statements alter the product's definition of oxygen to a drug, which can only be authorized by the FDA. State and Federal agencies do not have laws to protect consumers from the wasteful spending of money by individuals who wish to receive treatment from oxygen therapy, especially since oxygen-producing equipment like concentrators are so readily available on the market. Three Federal Legislative Acts precipitate this dilemma when ownership of medical equipment that manufactures supplemental oxygen becomes available.

Whether for CAM, or recreational use in bars, oxygen therapy may be dangerous for a few individuals. However, the dangers are compelling enough reason that this therapy should be banned from all uses except for evidence-based medical treatments for which it was intended. Physicians and allied health professionals who are certified to use oxygen for appropriate treatments become the first watchdogs for abuse, since they can recognize what is or is not a false claim without needing to search the literature. Ultimately, we are the ones who will most likely file the first report of a false claim or misuse. Unfortunately, if this is not done in a timely manner, someone may become injured.

References

- 1 Bren L. Oxygen bars: Is a breath of fresh air worth it? U.S. Food and Drug Administration FDA Consumer Magazine. November-December 2002. Available at http://www.fda.gov/fdac/features/2002/602_air.html Accessed on Dec. 20, 2007.
- 2 Federal Food, Drug, and Cosmetic Act. U.S. Food and Drug Administration. Available at <http://www.fda.gov/opacom/laws/fdcact/fdcact1.htm> Assessed Dec. 20, 2007.
- 3 Eisenberg DM, Kessler RC, Foster C, Norlock F E, Calkins DR, Delbanco TL. Unconventional Medicine in the United States — Prevalence, Costs, and Patterns of Use. New

- England Journal of medicine. 1993 January; 328(4): 246-52.
- 4 Oxygen Therapy for Adults in the Acute Care Facility — 2002 Revision & Update. AARC Clinical Practice Guideline. Respiratory Care. 2002; 47(6): 717-20. Available at <http://www.rcjournal.com/cpgs/otachcpg-update.html> Accessed Dec. 20, 2007.
- 5 Selection of an Oxygen Delivery Device for Neonatal and Pediatric Patients - 2002 Revision & Update. AARC Clinical Practice Guideline. Respiratory Care. 2002; 47(6): 707-16. Available at <http://www.rcjournal.com/cpgs/soddnppcpg-update.html> Accessed Dec. 20, 2007.
- 6 Oxygen Therapy. American Lung Association. November 2004. Available at <http://www.lungusa.org/site/apps/s/content.asp?c=dvLUK9O0E&b=34706&ct=2486673> Accessed on Dec. 20, 2007.
- 7 Fairshter RD, Rosen SM, Smith WR, Glauser FL, McRae DM, Wilson AF. Paraquat poisoning: new aspects of therapy. Q J Med. 1976; 45(180):551-65.
- 8 Ingrassia TS, Ryu JH, Trastek VF, Rosenow EC. Oxygen-exacerbated bleomycin pulmonary toxicity. Mayo Clinics Proc 1991; 66(2):173-178.
- 9 Certified Mail from Department of Health and Human Services to Aerobic Oxygen USA, FDA website. June 23, 2003. Available at <http://www.fda.gov/cder/warn/cyber/2003/CFSAaerobic.htm> Accessed Dec. 20, 2007.
- 10 Warning Letter Issued for Misbranded Oxygen. Center for Drug Evaluation and Research Bioresearch Monitoring (Summaries of warning letters). Center for Drug Evaluation and Research. FDA. 2006: 3-34 to 3-35. Available at http://www.fda.gov/ora/about/enf_story/ch3/default.pdf Accessed Dec. 20, 2007.
- 11 Dietary Supplement Health and Education Act of 1994. U.S. Food and Drug Administration. October 25, 1994. Available at <http://www.fda.gov/opacom/laws/dshea.html> Accessed Dec. 20, 2007.
- 12 Medicare Home Oxygen Patient Protection Act. American Association of Respiratory Care. Available at <http://www.aarc.org/headlines/HR621.cfm> Accessed Dec. 20, 2007.
- 13 Dillard J. FDA statement Good Guidance Practices and 1989 draft oxygen conserving device 5104 k. Review. U.S. Food and Drug Administration. Available at <http://www.fda.gov/cdrh/ode/guidance/583.pdf> Accessed Dec. 20, 2007.
- 14 Safe medical devices act of 1990 summary. Library of Congress, Thomas. Available at <http://thomas.loc.gov/cgi-bin/bdquery/z?d101:HR03095:@@D&summ2=1&%7CTOM:/bss/d101query.html%7C> Accessed Dec. 20, 2007.
- 15 What is CAM? National Center for Complementary and Alternative Medicine. 2007 February Available at <http://nccam.nih.gov/health/whatiscam/> Accessed Dec. 20, 2007.
- 16 Scanlan CL, Spearman CB, Sheldon RL. Egan's Fundamentals of Respiratory Care. Mosby, St. Louis (MO): Mosby Inc. 1995. Oxygen Therapy P. 702-41, Sleep apnea P. 821-2.
- 17 Casey KR, Cantillo KO, Brown LK. Sleep-Related Hypoventilation/Hypoxemic Syndromes. Chest. 2007 June; 131(6):1936-1948.
- 18 Sheridan RL, Shank ES. Hyperbaric Oxygen Treatment: A Brief Overview of a Controversial Topic. Journal of Trauma-Injury Infection & Critical Care. 1999 August; 47(2):426-435.
- 19 Antioxidants and cancer prevention fact sheet. National Cancer Institute. July 28, 2004. Available at <http://www.cancer.gov/newscenter/pressreleases/antioxidants> Accessed Dec. 20, 2007.
- 20 Marcus J. The truth about oxygen bars (editorial). Available at http://www.askmen.com/fashion/body_and_mind_60/89_better_living.html Accessed Dec. 20, 2007.
- 21 Johnson PC, Wagner PD, Wilson DF. Regulation of oxidative metabolism and blood flow in skeletal muscle: Summary report of the First ACSM Basic Science Specialty Conference, Indianapolis, IN, September 28-30, 1995. Medicine & Science in Sports & Exercise. 1996 March; 28(3):305-314.
- 22 LaRoche DP, Hill MR, Subudhi A W. Effectiveness of 10-day Altitude Training Camp on Red Blood Cell Indices. Medicine & Science in Sports & Exercise. 2002 May; 34(5) Supplement 1: 48.
- 23 Muir IH, Myhre LG, Salazar AB, Dahms T. Individual variation in responses of elite runners to 40 days of sleeping in simulated high altitude. Medicine & Science in Sports & Exercise. 2003 May; 35(5): Supplement:S115.

Checklists, Specialization, Safety, and Automation in the Intensive Care Unit

Jeff Borrink, BS RRT

Dr Atul Gawande, an author and general surgeon at Brigham and Women's Hospital in Boston MA, recently wrote an article in *The New Yorker* discussing how something very simple can transform the Intensive Care Unit (ICU): a checklist.

In his article, Dr Gawande writes about Peter Pronovost MD, PhD, a critical care specialist at Johns Hopkins hospital in Baltimore, MD, who is one of the first in medicine to recognize the power of a checklist to save lives in the ICU.

In 2001, Dr Peter Pronovost decided to tackle the problem of line infections in his ICU. He plotted out the steps to take when inserting a line, a checklist, in order to avoid a line infection. These steps had been well known and taught for years. Then he asked the nurses in his ICU to observe the doctors in the ICU put lines in for a month, and record how often they completed each step. As it turns out, at least one step was skipped in more than a third of patients.

The next month, nurses received backing from hospital administration to intervene if doctors didn't follow every step on the checklist. Dr Pronovost and his colleagues tracked what happened for a year afterward, and found that the ten-day line-infection rate went from eleven percent to zero. They calculated that the checklist had prevented forty-three infections, eight deaths, and had saved two million dollars in costs.¹ They subsequently tested other checklists in the ICU and found similar results.

Dr Pronovost observed that checklists provide two main benefits: help with recall, especially with mundane matters that are easily overlooked in patients, and explicitly laying out the minimum number of expected steps in a complex process.

Dr Pronovost was encouraged, and believed that his checklists could save lives, so he took his findings on the road, showing his checklists to doctors, nurses, insurers, etc, speaking in an average of seven cities a month. But for a variety of reasons, he found few who would accept his innovation.

The limited response to his checklist procedure was easy to

explain, but hard to justify. Some doubted the evidence. Some were offended by the suggestion that they needed a checklist because they were the expert. Checklists seemed to push against the traditional culture of medicine—expert audacity in complex environments and situations of high risk. According to Dr Gawande, “If a new drug were as effective at saving lives as Peter Pronovost's checklist, there would be a nationwide marketing campaign urging doctors to use it... Good medicine will not be able to dispense with expert audacity. Yet it should also be ready to accept the virtues of regimentation.”¹

According to Dr Pronovost, “The fundamental problem with the quality of American medicine is that we've failed to view delivery of healthcare as a science. The tasks of medical science fall into three buckets. One is understanding disease biology. One is finding effective therapies. And one is insuring those therapies are delivered effectively. That third bucket has been almost totally ignored by research funders, government, and academia. It's viewed as the art of medicine. That's a mistake, a huge mistake.”¹

Because Dr Pronovost is focused on work that is not normally considered a significant contribution in academic medicine, few other researchers are helping to extend his efforts and achievements. However, in 2003 the Michigan Health and Hospital association asked Dr Pronovost to implement three of his checklists in Michigan's ICUs. It became known as the Keystone Initiative. And in December of last year, the *New England Journal of Medicine* published a landmark article detailing the results from utilizing these checklists in the Michigan ICU's. According to the *New York* article, “The typical ICU cut its quarterly infection rate to zero. Michigan's infection rates fell so low that its average ICU outperformed ninety percent of ICUs nationwide. In the Keystone Initiative's first eighteen months, the hospitals saved an estimated hundred and seventy-five million dollars in costs, and more than fifteen hundred lives.”¹ Dr Pronovost's results from the Initiative have not gone unnoticed, and he has had requests to help New Jersey, Rhode Island, and the country of Spain do what Michigan did.

Checklists have been used successfully in other industries. The airline industry has been using checklists for years to reduce

Jeff Borrink is Clinical Specialist, Hamilton Medical.

pilot error and increase safety. As airplanes became substantially more complex over the years, lists with step-by-step checks for takeoff, flight, and landing were implemented to improve safety, rather than relying on pilot memory alone.

Healthcare, like airplanes has also become increasingly complex. And more of what hospitals do is critical care. According to Dr Gawande, “Substantial parts of what hospitals do—most notably, intensive care—are now too complex for clinicians to carry them out reliably from memory alone. ICU life support has become too much medicine for one person to fly.”¹

Our nation is at a crisis point in regards to quality healthcare delivery and patient safety. Checklists are not routinely used. Medical errors are common. In 1999, the Institute of Medicine (IOM) released a report, “To Err is Human: Building a Safer Health System.” According to the report, between 44,000 and 98,000 deaths may result each year from medical errors in hospitals alone. These errors are due to multiple factors, but most are considered preventable.”²

Publication of the IOM report triggered substantial public and private sector activity, including the formation of the National Patient Safety Foundation by the American Medical Association, the formation of a non-punitive sentinel events reporting system by the Joint Commission for the Accreditation of Healthcare Organizations, the establishment of new public-private partnerships by the Veterans Health Administration, creation of the Institute for Health Care Improvement “Preventing 5 Million Patient Injuries” campaign, creation of the Society of Critical Care Medicine’s “Right Care Right Now” campaign, creation of the National Coordinating Council for Medication Error Reporting and Prevention, formation of the National ePrescribing Patient Safety Initiative, and many others.

Most hospitals in the US have been putting error reduction strategies into high gear by reevaluating and strengthening checks and balances to prevent medical errors within their system since the release of the IOM study. Still, experts agree that there is much more work to be done.

According to Dr Gawande, “This is the reality of intensive care: at any point, we are as apt to harm as we are to heal. Line infections are so common that they are considered a routine complication. ICUs put five million lines into patients each year, and national statistics show that, after ten days, four percent of those lines become infected. Line infections occur in eighty thousand people a year in the United States, and are fatal between five and twenty-eight percent of the time, depending on how sick one is at the start. Those who survive line infections spend on average a week longer in intensive care. And this is just one of many risks. After ten days on the ventilator, six percent develop bacterial pneumonia, resulting in death forty to fifty-five percent of the time. All in all, about half of ICU patients end up experiencing a serious complication, and once a complication occurs, the chances of survival drop sharply.”¹

The medical profession has favored specialization over the years as a solution for the increasing complexity of healthcare. Training programs focusing on critical care have opened in every major American city in the last ten years. Responsibility has increasingly shifted to super-specialists, clinicians who have taken the time to practice one narrow thing until they can do it

better than others with lesser knowledge and ability.¹ Even many respiratory therapy departments have organized into separate specialty units or teams.

“Expertise is the mantra of modern medicine. As the intricacies involved in intensive care have mounted, responsibility has increasingly shifted to super-specialists. In the early twentieth century, you needed only a high school diploma and a one-year medical degree to practice medicine. By the century’s end, all doctors had to have a college degree, a four-year medical degree, and an additional three to seven years of residency training in an individual field of practice—pediatrics, surgery, neurology, or the like. Already, though, this level of preparation has seemed inadequate to the new complexity of medicine.”¹

“Intensive-care medicine has become the art of managing extreme complexity—and a test of whether such complexity can, in fact, be humanly mastered. Intensive-care medicine has grown so far beyond ordinary complexity that avoiding daily mistakes is proving impossible even for our super-specialists. The ICU with its spectacular successes and frequent failures therefore poses a distinctive challenge: what do you do when expertise is not enough?”¹

One solution for some of the complexity and patient safety issues for mechanically ventilated patients is automation through closed loop ventilation. ICU Mechanical ventilators have become more complex, requiring more expertise from the clinicians that operate them. To optimize ventilation and prevent harm, more expertise is required from the clinician in regards to pulmonary mechanics, monitoring, waveforms analysis, modes, controls, etc.

Proper delivery of mechanical ventilation falls into that ‘third bucket’ of medical science that Dr Pronovost was referring to: ensuring that therapies are delivered effectively. This bucket has been largely ignored, according to Dr Pronovost, and that is a huge mistake.

Numerous interventions are designed to prevent harm from mechanical ventilation, such as implementing lung protective ventilation strategies on day one, transitioning to a spontaneous breathing trial as soon as possible, etc. Strategies that mitigate ventilator induced lung injury (VILI), such as lower tidal volumes³ and low plateau pressures. Yet, in many instances these interventions that prevent harm are not implemented, or are implemented too late. ARDS patients are not always ventilated with a lung protective low tidal volume strategy.⁴ In fact, many times these patients are not even recognized and diagnosed with ARDS.⁵ Patients are not always assessed for their readiness to wean, sedation vacations are not always the norm, etc., all of which can create complications and safety issues for the patient. To make matters worse, forgotten steps, medication errors, mechanical breakdowns, inadequate staff training, fatigue, staffing shortages, etc, can all contribute to complications and patient safety issues for mechanically ventilated patients in the ICU. Adverse events and serious errors involving critically ill patients are common and often potentially life-threatening.⁶

Closed-loop ventilation can automatically implement many of the evidenced based medicine strategies designed to prevent harm from mechanical ventilation, and can improve patient safety. Closed-loop ventilation automatically ventilates to the

pulmonary mechanics of the patient, and adapts breath by breath to changes in mechanics.⁷ It allows the patient to spontaneously breathe as soon as they are able to, and can ensure faster weaning than conventional modes.^{8,9} It automates and streamlines many setting changes,^{8,9} therefore eliminating many errors that can occur, and it automatically implements safe ventilation rules which can improve patient safety and quality of care.

This approach to mechanical ventilation requires a paradigm shift when it comes to mechanical ventilation. It requires change. It requires changes in how mechanical ventilation is applied within the medical system or ICU. It requires changes in thinking from doctors, nurses, and respiratory therapists. It may also require additional training and expertise. It may require changes in our articles and documentation. It requires us as caregivers to take the time and initiative to evaluate the latest technology that is available, and make the required changes if that is what is in the best interest of the patient. It requires a "patient-centric" way of viewing mechanical ventilation as opposed to a "doctor-centric," "institution-centric," or "provider-centric" way of viewing mechanical ventilation. It requires the "third bucket" to be addressed.

About 90,000 people across the United States are in an ICU on any given day; 5 million Americans are in an ICU in any given year, and it is likely that almost all of us will be admitted to an ICU at some point in our lifetime.¹ We're all patients, or eventually may be at some point in time, which may place us all at risk of medical errors or complications. The ICU environment has become increasingly more complex, requiring more specialized training, with increasingly more complex medical equipment. Scores of clinicians must carry out thousands of steps correctly throughout our stay in the ICU in order to ensure our safe return to health. Checklists, specialization, and automation can help. "Going into an ICU, being put on a mechanical ventilator, having tubes and wires run into and out of you, is not a sentence of death. But the days will be the most precarious of your life. Intensive care succeeds only when we hold the odds of doing harm low enough for the odds of doing good to prevail."¹

References

- 1 Gawande A. The checklist. If something so simple can transform intensive care, what else can it do? *The New Yorker*. December 10, 2007.
- 2 Committee on Quality of Healthcare in America, Institute of Medicine. To err is human: building a safer health system. Washington D.C. National Academy of Sciences. 2000.
- 3 ARDSnet. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and acute respiratory distress syndrome. *N Engl J Med* 2000;342:1301-8.
- 4 Kalhan R. et al. Underuse of lung protective ventilation: Analysis of potential factors to explain physician behavior. *Critical Care Medicine*. 2006; Vol. 34, No. 2.
- 5 Ferguson N. et al. Acute respiratory distress syndrome: Underrecognition by clinicians and diagnostic accuracy of three clinical definitions. *Critical Care Medicine*. October 2005; 33(10) 2228-2234.
- 6 Rothschild J. et al. The critical care safety study: The incidence and nature of adverse events and serious medical errors in intensive care. *Critical Care Medicine*. August 2005; 33(8) 1694-1700.
- 7 Arnal J. et al. Automatic selection of breathing pattern using

adaptive support ventilation. *Intensive Care Medicine*. 11 September 2007.

- 8 Sulzer C.F. et al. Adaptive support ventilation for fast tracheal extubation after cardiac surgery: A randomized controlled study. *Anesthesiology*. 2001; 95: 1339-45.
- 9 Petter A.H. et al. Automatic « respirator/weaning » with adaptive support ventilation: the effect of duration of endotracheal intubation and patient management. *Anesth Analg*. 2003; 97: 1743-50.

Editor's Note: A follow-up editorial in *The Times* (12/30) by Atul Gawande revealed that the government has withdrawn funding from Johns Hopkins' checklist program. Gawande wrote, "The Office for Human Research Protections shut the program down, [saying] that introducing a checklist and tracking the results without written, informed consent from each patient and healthcare provider had violated scientific ethics regulations." Gawande noted, however, that "testing a checklist for infection prevention is not the same as testing an experimental drug... If the government's ruling were applied more widely, whole swaths of critical work to ensure safe and effective care would halt or shrink: efforts by the CDC to examine responses to outbreaks of infectious disease, the military's program to track the care of wounded soldiers, the campaign to reduce avoidable complications in 3,700 hospitals nationwide... Now that the work is becoming more systematic (and effective), the authorities have stepped in. And they're in danger of putting ethics bureaucracy in the way of actual ethical medical care."

□ April-May 2008

RESPIRONICS PURCHASED

Royal Philips Electronics of The Netherlands Friday said it is acquiring Respironics, according to the Wall Street Journal, for €3.6 billion (\$5.1 billion) in cash. In joint statements, the companies said they had reached a definitive merger agreement under which Philips will acquire all of Respironics' outstanding shares for \$66 a share. Over a 12-month period ending in September, 2007, Respironics reported sales of approximately \$1.2 billion. It has around 5,300 employees world-wide. Royal Philips makes a wide range of products from shavers and televisions to medical scanners and light-emitting diodes, and has in recent years transformed itself from an electronics manufacturing company into a technology company focused on lifestyle and health. In September '07, the company launched its "Vision 2010" strategic plan, under which it will simplify its structure into three core sectors: Philips Healthcare, Philips Lighting, and Philips Consumer Lifestyle. Several divestments have left the company with a cash pile of several billion euros. The company said Tuesday it would buy back up to €5 billion of its own shares. The tender offer isn't subject to any financing contingency, though it requires US and European Union regulatory clearances. Respironics will become the headquarters for Philips Home Healthcare Solutions group within Philips Healthcare.

FRESH AER

Aerogen has completed a management buyout from its US parent, Nektar Therapeutics. Under the terms of the deal, Nektar will maintain a minority share in the business. Aerogen specializes in drug delivery technology for the respiratory sector. Aerogen's core technology, the OnQ micropump aerosol generator, is currently used worldwide in nebulizers for drug delivery to patients in the intensive care and homecare settings. Distributed by Respironics, GE Healthcare, Maquet, Covidien and an independent distributor network, Aerogen's products are available in over 50 countries. Key markets include the US, Japan and Germany. Aerogen has advanced negotiations in several areas and plans to announce new partnerships with a number of US and European market leaders in both the medical field and commercial products area in the near future.

POISONED?

Masimo announced that the National Association of Emergency Medical Technicians (NAEMT) supports the use of 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. In a letter to its members and EMS professionals this month, NAEMT

highlighted that "failure to diagnose may lead to improper treatment and transport decisions for victims of carbon monoxide poisoning" and recommended proper CO training, along with noninvasive detection protocols for the recognition and management of carbon monoxide poisoning, 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 introduction of four new CO training programs, available free to NAEMT members online helps the association build awareness and promote adequate protocols for addressing this public health challenge. NAEMT joins other industry-leading emergency first responder associations, including the National Association of EMS Educators (NAEMSE) and the International Association of Fire Fighters (IAFF), who have recently issued similar recommendations that EMS and fire professionals "noninvasively screen patients for carbon monoxide poisoning that have had a suspected exposure, or present with any of the signs or symptoms of carbon monoxide poisoning." These organizations are examples of a growing trend within the emergency services industry and the convergence toward a new standard of care for the proactive screening of CO-exposed patients and emergency services personnel by newly developed Pulse CO-Oximetry technology. Too often, even the most skilled first responders can miss the chance to treat carbon monoxide poisoning early because until now there hasn't been a fast, accurate and noninvasive way to detect elevated levels of CO in the blood. However, with the Masimo Rainbow SET Rad-57 Pulse CO-Oximeter—the first and only technology capable of continuously and noninvasively measuring carbon monoxide levels in the blood—EMS professionals can easily detect carbon monoxide poisoning on the spot in just seconds with the push of a button, allowing for prompt and possibly life-saving treatment. In addition, the Masimo Rad-57 can also limit the likelihood of long-term cardiac and neurological damage that can result from non-fatal exposures. Studies have shown that even a single high level exposure, or prolonged exposure to low levels of CO, has the potential to cause long-term cardiac, neurocognitive and psychiatric damage. The National Fire Protection Association (NFPA) has also included CO screening by pulse CO-oximetry as part of a new national healthcare standard. The new standard establishes that any firefighter exposed to CO or presenting with headache, nausea, shortness of breath, or gastrointestinal symptoms should be measured for CO poisoning by pulse CO-oximetry or other approved methods.

UNWANTED ADVANCE

Chronic obstructive pulmonary disease is on the rise in women, according to a study by the University of Michigan. By 2000, the number of women dying from COPD surpassed the number of men. Researchers noted that the condition manifests differently in women than men in terms of the risk factors, symptoms, progression, and diagnosis. One of the major gender differences is that women tend to develop more airway obstruction, whereas men tend to develop a more emphysematic manifestation of the disease. It may reflect differences in exposures, or genetic differences in how males and females manifest damage... or not, researchers concluded. Women also seem more prone than men to developing COPD from exposure to cigarette smoke and smoke from biomass fuels used for cooking in many developing regions of the world. Women may be more susceptible to developing COPD, but they also predominate among COPD patients who have never smoked, and may have gender-linked genetic factors that predispose

them to developing the disease. Once sick, women are less likely to be correctly diagnosed or offered appropriate diagnostic tests, and they report more severe shortness of breath, more anxiety and depression and a lower quality of life as a result of the disease.

IDIOPATHIC

A study at Massachusetts General Hospital may have found a key mechanism underlying idiopathic pulmonary fibrosis. A specific molecular pathway appears responsible for key aspects of the scarring of lung tissue that characterizes IPF. Researchers said an agent that blocks this pathway is being developed as a potential cancer treatment, and they hoped to be able to test it in an animal model of IPF to determine whether it might be a candidate for trials in patients. About 50,000 new cases of IPF are diagnosed in the US each year. Theories about its cause have focused on chronic inflammation of the lungs, but recent evidence suggests that an abnormal healing response to lung injury may be responsible. The current study was designed to determine which specific chemoattractants were associated with IPF. Analysis of fluid from the lung surfaces of a mouse model suggested that the activity of lysophosphatidic acid, acting through its receptor LPA1, was responsible for attracting fibroblasts. A strain of mice lacking the gene for LPA1 did not develop pulmonary fibrosis when treated with a compound that usually causes the disease in the animals. Lung fluid samples from human IPF patients had significantly higher levels of LPA than control samples, and patient samples attracted fibroblasts while fluid from controls did not. In addition, an agent that blocks the LPA1 receptor eliminated the ability of fluid from IPF patients to attract fibroblasts. The results indicate that the LPA-LPA1 pathway is responsible for the abnormal migration of fibroblasts into the lungs in IPF, a crucial step in the development of fibrosis. This pathway appears to be involved in several steps in the development of fibrosis, including the leaking of blood vessels, which is why the LPA1 knockout mice are so dramatically protected. The goal would be to target this pathway.

CLINICAL STUDY

A recent clinical study posted on clinicalstudyresults.org, a website for current studies maintained by pharmaceutical firms compared ciclesonide and fluticasone use in patients with mild to moderate asthma (Comparison of ciclesonide (80 µg once daily in the evening) and fluticasone propionate (100 µg twice daily) in patients with mild to moderate asthma, Clinicaltrials.gov Identifier: NCT00163423, information provided by NYCOMED). A total of 48 main investigators participated in this international study at 48 centers located in Austria, Canada, Germany, Poland, and South Africa. The aim of the study, by Dr Ronald Dahl, Aarhus University, Denmark, was to compare the efficacy of 80 µg ciclesonide od in the evening vs 100 µg fluticasone propionate bid on lung function, time to the first asthma exacerbation, asthma symptoms, use of rescue medication, and quality of life in patients with mild to moderate asthma. In addition, the study was to provide information on the safety and tolerability of treatment with ciclesonide. The study consisted of a 2- to 4-week baseline period and a treatment period of 24 weeks. During the treatment period the patients were thus asked to visit the investigation site at intervals of 2, 4, 8, 16, and 24 weeks. Home morning and evening PEF (peak expiratory flow), asthma symptom scores, and use of rescue medication were recorded in patient diaries throughout the study period. In both treatment groups, asthma symptom scores

(daytime, nighttime, and sum), use of rescue medication, and asthma control variables improved during the treatment period. No statistically significant between-treatment difference was shown for the CIC80 to FP200 comparison with regard to asthma symptom scores, use of rescue medication, and asthma control variables. Asthma was the most common adverse effect leading to study discontinuation in each of the groups. No statistically significant difference between treatment with CIC80 and FP200 was seen for variables related to asthma control.

YOU SAY TOMOGRAPHY...

Computed tomographic pulmonary angiography (CTPA) may be a safe alternative to ventilation-perfusion scans for excluding the diagnosis of pulmonary embolism, although CTPA may detect more clots, according to a study by Dalhousie University, Halifax, Nova Scotia. CTPA was introduced as an alternative non-invasive test and has been adopted rapidly, despite some concerns about the sensitivity of this method. Researchers conducted a comparison of CTPA with V/Q scanning. The four-year trial included 1,417 patients considered likely to have acute pulmonary embolism. Patients were randomized to undergo either V/Q scanning (n = 716) or CTPA (n = 701). Of the patients randomized to CTPA, 19% were diagnosed with pulmonary embolism or deep vein thrombosis in the initial evaluation period; 14% of patients in the V/Q scanning group had a similar diagnosis. Both groups of patients were treated with anti-coagulant therapy. The overall rate of venous thromboembolism found in the initial diagnostic period was significantly greater (5%) in patients randomized to the CTPA strategy. Researchers said the data were reassuring, given previous reports of relatively low sensitivity of CTPA for the diagnosis of pulmonary embolism. Reported in JAMA, via Medical News Today.

NO BLEED NO BREATHE

Menopause is associated with lower lung function and more respiratory symptoms, especially among lean women, according to a new study in the Journal of Allergy and Clinical Immunology. Researchers studied a group of women aged 45-56 years who were not taking sex hormones. The women provided information about their lung health and menstrual history and BMI. The researchers found that women who had stopped menstruating had significantly lower lung function and more respiratory symptoms than women of the same age who were menstruating regularly. Lean women (BMIs of less than 23 kg/m squared) showed a greater risk for lung problems. The authors speculated that lower lung function in menopausal women could be explained by increased insulin resistance in menopause. Because insulin resistance is a proinflammatory condition, this could also explain the increase in respiratory symptoms associated with menopause. For more see jacionline.org.

VIRULENT

Researchers from Weill Cornell Medical College in New York say new molecular targets, so-called virulence factors that bacteria use to thrive once they are in the host, present an alternative means of stopping TB, leprosy and other bacterial illness. They've developed the first inhibitor of a key small molecule from Mycobacterium tuberculosis and Mycobacterium leprae, utilized to subvert human host's defenses and damage and invade human host's cells during infection. As such, there is now proof of principle for the inhibition of this virulence factor in bacteria cultured in the lab. The next step is to explore whether this inhibitor can stop these pathogens from

multiplying in a mouse host, curtailing infection. Researchers are moving beyond antimicrobials such as antibiotics to anti-infectives that may have no effect against the pathogen in the test tube but which do compromise its ability to infect and spread in the host. The Weill study focused on phenolic glycolipids (PGLs). *M. leprae* uses PGLs to damage and invade nerve cells during infection. Researchers hypothesized that drugs blocking PGL synthesis would reduce the adaptive fitness of PGL-producing *M. tuberculosis* strains in the human host by eliminating PGL-dependent immunomodulatory effects. These drugs may also diminish the ability of *M. leprae* to invade nerve cells and produce nerve function impairment. Researchers investigated and then elucidated a crucial, early step in PGL biosynthesis. They also pinpointed the key enzyme, FadD22, that is essential to that stage of the process. Follow-up work using both enzyme assays and *M. tuberculosis* assays confirmed that the new inhibitor does block the production of PGLs. Although it was technically not possible to test the inhibitor in *M. leprae*, that pathogen is very closely related to *M. tuberculosis*, so the researchers believe their agent would inhibit production of PGLs there, as well. Work is underway to come up with other, even more potent PGL biosynthesis inhibitors. Researchers say, with an eye to testing the best candidates in an animal model, that drugs targeting virulence factors are just one component of the paradigm shift in the antimicrobial drug discovery for the 21st century.

SLEEP TIGHTER

A new sedative drug has been shown to improve the sleep quality and comfort levels of intensive care patients, compared to the most commonly-used medication. US and UK researchers compared the effects of dexmedetomidine with the commonly used lorazepam. While lorazepam lessens discomfort, it has also been associated with an increased risk of brain dysfunction, including coma and delirium. New trials at Vanderbilt University are showing that dexmedetomidine can provide better sedation and analgesia while reducing these risks. Researchers administered either dexmedetomidine or lorazepam for up to 120 hours to 106 volunteer adult mechanically ventilated ICU patients and found that 30% fewer patients in the dexmedetomidine group experienced coma, and that this group also experienced an average of four more coma-free and delirium-free days over study days one to 12 than those using lorazepam. Dexmedetomidine also proved to be a more effective sedative, with 80% of the dexmedetomidine group sedated to the target level over the course of the trial, compared with 67% of the lorazepam group.

TO THE RESCUE

Home oxygen providers in the Midwest prepared for the deadly ice storm that struck earlier this week and responded with extra visits and contacts with patients receiving home oxygen therapy. In Missouri, where half the population was without power, Wilkinson Home Care Equipment filled and delivered more than 100 tanks in the last three days of the storm to keep its patients constantly supplied with oxygen. Wilkinson made daily runs 65 miles south to ensure that its outlying store had enough tanks to handle emergency needs. Response to the storm in Oklahoma was reported by Asthma & Respiratory Services of Tulsa. The company cares ventilator patients as well as oxygen patients. The company was prepared, since it learned from several major ice storms in previous years, and contacted its patients to make sure they were stocked up with oxygen before the storm hit. Family Medical Equipment in Altus, OK said it also used the

time prior to the storm to contact its customers and spent many hours delivering extra oxygen. In Iowa, a manager of Long Term Medical Supply traveled from home to home in the affected area to insure that his customers were safe and not afraid of their lack of power and inability to get to a safe place. He shuttled people to and took hot meals and blankets to elderly patients. The company noted that this was an area that some streets were impassable due to downed trees. When the manager couldn't get down roads, he made sure that he got in contact with customers somehow to make sure that they were okay. Reported by Medical News Today.

AS IF YOU DIDN'T ALREADY KNOW

Researchers at Monroe Carell Jr Children's Hospital at Vanderbilt, say they may have discovered a "new" option to help quiet children's coughs, by applying a study that showed that honey has some benefit in reducing cough symptoms. The study said that children who are given honey at bedtime had a 47.3% reduction in cough symptoms, while a honey-flavored syrup containing a common over-the-counter cough suppressant, dextromethorphan, had just slightly more effect than no treatment at all. The study used buckwheat honey, and the researchers noted that darker honeys such as buckwheat have more phenolic compounds than other varieties and that the associated antioxidant effect might have contributed to the good results. The long and short of it is what many people have been aware of for quite some time: a teaspoon of honey makes the coughing go down.

GO AROUND

Researchers at Sarasota Memorial Health Care System are working on the EASE (Exhale Airway Stents for Emphysema) Trial, an international, multicenter clinical trial to explore an investigational treatment that may offer a significant new, minimally-invasive option for those suffering with advanced widespread emphysema. The study focuses on airway bypass, which creates pathways in the lung for trapped air to escape and relieves emphysema symptoms. By creating new pathways for airflow with the bypass procedure, researchers hope to reduce hyperinflation and improve lung function. During airway bypass, physicians will use a flexible bronchoscope to go through the mouth into the airways. Then the physician will create new small pathways and place an Exhale Drug-Eluting Stent (Broncus Technologies) to allow the trapped air in the lung to escape. During the airway bypass procedure, physicians will first use a Doppler probe inserted through the bronchoscope to identify a site in the airway that is away from blood vessels. A special needle is then used to make a small opening and an Exhale Drug-Eluting Stent is placed in the passageway to keep it open. The procedure involves placing up to six drug-eluting stents. The total time of the procedure is approximately one to two hours. The procedure is still under clinical investigation, but early data suggest it may hold promise.

WATER UNDER THE BRIDGE

Bridgewater, NJ – Maquet has been working with the New England Aquarium Marine Animal Rescue and Rehabilitation Team to help save stranded sea turtles. Strandings of hypothermic juvenile sea turtles are an annual late autumn event on Cape Cod. For reasons that are not fully understood, many endangered young sea turtles become caught on the north side of Cape Cod and fail to migrate south. As water temperatures plummet in Cape Cod Bay, those sea turtles slowly

become hypothermic and float helplessly about the bay. If lucky, these gravely ill turtles with body temperatures as low as 45 degrees are washed ashore by strong northwest winds. Stranded sea turtles are brought to the New England Aquarium where the rescue and rehabilitation team treats them for hypothermia, dehydration, pneumonia and other opportunistic infections. For those sea turtles in critical condition, the aquarium veterinarian proposed utilizing a ventilator as a treatment method to aid in their recovery, and decided on Maquet's SERVO-i. Two sea turtles were trialed on the SERVO-i. The first turtle was intubated for one hour before becoming strong enough to be taken off the ventilator and was able to survive for an additional three weeks. The second turtle was intubated for two days but was in such poor health that the rehabilitation team knew it would not recover and made the decision to remove the sea turtle from the ventilator. While things didn't work out as planned, the aquarium expects to use the ventilator in future efforts.

PUTTING A "CAP" ON IT

Advanced Life Sciences Holdings, Inc announced positive results from Trial CL-05, the second of two pivotal phase III clinical trials designed to assess the safety and effectiveness of cethromycin, a novel once-a-day oral antibiotic for the treatment of mild-to-moderate community acquired pneumonia (CAP), the sixth leading cause of death in the United States. The primary efficacy endpoint of statistical non-inferiority in the clinical cure rate at the test-of-cure visit was achieved. The study results showed that cethromycin cured 94.0% of patients with CAP, compared to Biaxin (clarithromycin), a current standard of care treatment for CAP, which cured 93.8% of studied patients in the per protocol population. In the modified intent to treat population, cethromycin cured 83.1% of patients and Biaxin cured 81.1%. Cethromycin also demonstrated favorable safety results, with reported side effects similar to or less than those seen with Biaxin. Trial CL-05 was a double-blind, randomized, multi-center, multi-national, comparator phase III clinical study in which cethromycin was compared to Biaxin, an

approved antibiotic, in treating mild-to-moderate CAP. The trial design called for a seven-day course of therapy in which cethromycin was evaluated using a 300 mg once-daily dosing regimen compared to a 250 mg twice-daily dosing regimen of Biaxin. In the study, 584 adult patients were enrolled from clinics in the United States, Canada and South Africa. The Phase III CAP pivotal development program was comprised of two double-blind, randomized, well controlled, multi-center, multi-national, comparator trials designed to assess the safety and effectiveness of cethromycin in CAP patients compared to Biaxin. Trial CL-06 enrolled patients from clinics in Europe, South America and Israel and Trial CL-05 enrolled patients from the United States, Canada and South Africa. In both trials, cethromycin was evaluated using a 300 mg once-daily oral dosing regimen compared to 250 mg twice-daily dosing for Biaxin, both over a seven-day course of therapy. Biaxin is an FDA-approved standard of care antibiotic currently indicated for the treatment of CAP. The primary endpoint for both trials was the clinical cure rate at the test-of-cure visit (Day 14-21 post-initiation of dosing). The eligibility of patients for each trial was based on clinical signs and symptoms as well as chest X-ray results as evaluated by an independent radiologist. Extensive electrocardiogram and liver function test monitoring were incorporated into the study design in order to examine safety in these areas and add to the safety database established in previous cethromycin clinical trials.

In Trial CL-05, cethromycin met all efficacy endpoints and demonstrated a favorable safety profile:

Per protocol clinical cure rate (PPc)- cethromycin 94.0% (205/218) compared to Biaxin 93.8% (195/208) [-4.5, +5.1] (p>0.9999) PPc is defined as subjects who have completed the minimum required study medication, have confirmed clinical diagnosis of CAP supported by a positive chest X-ray and appropriate clinical signs/symptoms of CAP, and have had no other systemic antibacterial agents administered during or prior to the study period. Based on the 94.0% clinical cure rate for cethromycin being greater than 90%, a delta value of 10% or less on the lower bound and greater than zero on the upper bound [-4.5, +5.1] establishes non-inferiority. Under this analysis, the study met the clinical cure rate endpoint in the PPc population. Since p>0.05, there is not a statistically significant difference between cethromycin and Biaxin, which supports non-inferiority.

Pivotal Phase III Clinical Program Results Summary

Efficacy	Trial CL-05		Trial CL-06		Pooled Results		
	Cethromycin	Biaxin	Cethromycin	Biaxin	Cethromycin	Biaxin	Confidence Interval
Per Protocol Clinical Cure Rate (PPc)	94.0% (205/218)	93.8% (195/208)	91.5% (205/224)	95.9% (212/221)	92.8% (410/442)	94.9% (407/429)	[-5.4, +1.2]
Modified Intent-To-Treat Clinical Cure Rate (mITT)	83.1% (217/261)	81.1% (206/254)	82.9% (213/257)	88.5% (224/253)	83.0% (430/518)	84.8% (430/507)	[-6.4, +2.8]
Bacteriological Cure Rate (PPb)	95.9% (70/73)	97.1% (67/69)	89.1% (57/64)	96.8% (61/63)	92.7% (127/137)	97.0% (128/132)	NA

Safety	Trial CL-05		Trial CL-06		Pooled Results	
	Cethromycin	Biaxin	Cethromycin	Biaxin	Cethromycin	Biaxin
Diarrhea	4.5% (13/288)	4.1% (12/291)	5.0% (13/260)	4.7% (12/257)	4.7% (26/548)	4.4% (24/548)
Headache	2.4% (7/288)	3.1% (9/291)	3.1% (8/260)	6.2% (16/257)	2.7% (15/548)	4.6% (25/548)
Nausea	4.5% (13/288)	1.4% (4/291)	2.7% (7/260)	3.9% (10/257)	3.6% (20/548)	2.6% (14/548)
Vomiting	1.4% (4/288)	1.0% (3/291)	2.7% (7/260)	1.6% (4/257)	2.0% (11/548)	1.3% (7/548)
Abdominal Pain	1.4% (4/288)	1.4% (4/291)	1.5% (4/260)	3.1% (8/257)	1.5% (8/548)	2.2% (12/548)
Taste Disturbance	7.6% (22/288)	2.1% (6/291)	11.2% (29/260)	6.2% (16/257)	9.3% (51/548)	4.0% (22/548)
AE Discontinuations	4.2% (11/261)	2.8% (7/254)	1.6% (4/257)	2.8% (7/253)	2.9% (15/518)	2.8% (14/507)

Modified intent-to-treat clinical cure rate (mITT)- cethromycin 83.1% (217 subjects/261 subjects) compared to Biaxin 81.1% (206 subjects/254 subjects) [-4.8, +8.9] (p=0.5667). mITT is defined as subjects who received at least one dose of study medication and had a clinical diagnosis consistent with bacterial CAP confirmed by a positive pre-treatment chest X-ray and appropriate signs/symptoms. Based on the 83.1% clinical cure rate for cethromycin being between 80% and 90%, a delta value of 15% or less on the lower bound and greater than zero on the upper bound [-4.8, +8.9] establishes non-inferiority. Under this analysis, the study met the clinical cure rate endpoint in the mITT population. Since p>0.05,

there is not a statistically significant difference between cethromycin and Biaxin, which supports non-inferiority.

Per protocol radiographic success rate- cethromycin 92.7% (202 subjects/218 subjects) compared to Biaxin 92.3% (192 subjects/208 subjects) [-4.9, +5.6] ($p>0.9999$). Based on the 92.7% radiographic success rate for cethromycin being greater than 90%, a delta value of 10% or less on the lower bound and greater than zero on the upper bound [-4.9, +5.6] establishes non-inferiority. Under this analysis, the study met the radiographic success rate endpoint in the PPc population. Since $p>0.05$, there is not a statistically significant difference between cethromycin and Biaxin, which supports non-inferiority.

Modified intent-to-treat radiographic success rate- cethromycin 82.4% (215 subjects/261 subjects) compared to Biaxin 81.5% (207 subjects/254 subjects) [-6.0, +7.7] ($p=0.8195$). Based on the 82.4% radiographic success rate for cethromycin being between 80% and 90%, a delta value of 15% or less on the lower bound and greater than zero on the upper bound [-6.0, +7.7] establishes non-inferiority. Under this analysis, the study met the radiographic success rate endpoint in the mITT population. Since $p>0.05$, there is not a statistically significant difference between cethromycin and Biaxin, which supports non-inferiority.

Bacteriological cure rate- cethromycin 95.9% (70 subjects/73 subjects) compared to Biaxin 97.1% (67 subjects/69 subjects). The bacteriologically evaluable population for each arm of the trial was not powered to demonstrate statistical non-inferiority at a 95% confidence interval.

Percent of bacteriologically evaluable patients- approximately 33% of subjects in the per protocol population were bacteriologically evaluable. The Company believes that this percentage of bacteriologically evaluable patients is consistent with rates observed in precedent successful antibiotic drug approvals and that it will add to its existing bacteriologically evaluable patient database for cethromycin.

Discontinuation rate- from the modified intent-to-treat population, discontinuation rate due to adverse events was 4.2% for cethromycin and 2.8% for Biaxin.

Cethromycin demonstrated a favorable safety profile in Trial CL-05. The incidence of adverse events was not statistically different between cethromycin and Biaxin. The most common adverse events reported in patients receiving cethromycin were mild-to-moderate diarrhea (cethromycin 4.5%, Biaxin 4.1%), headache (cethromycin 2.4%, Biaxin 3.1%), nausea (cethromycin 4.5%, Biaxin 1.4%), vomiting (cethromycin 1.4%, Biaxin 1.0%), abdominal pain (cethromycin 1.4%, Biaxin 1.4%) and taste disturbance (cethromycin 7.6%, Biaxin 2.1%). No drug-related serious adverse events were observed in any study subject. Liver function tests and electrocardiogram monitoring in Trial CL-05 demonstrated no significant differences between subjects receiving cethromycin and subjects receiving Biaxin. This is consistent with the hepatic and cardiac side effect profile reported in previous cethromycin clinical trials.

Cethromycin is not approved as a treatment for CAP, and data from this analysis have not been reviewed by the Food and Drug Administration (FDA). Cethromycin has shown higher *in vitro* potency and a broader range of activity than macrolides against

Gram-positive bacteria associated with respiratory tract infections, and, again in *in vitro* tests, it appears to be effective against penicillin- and macrolide-resistant bacteria. Cethromycin has a mechanism of action that may slow the onset of future bacterial resistance. In addition to its utility in CAP, cethromycin is also being investigated for the prophylactic treatment of inhalation anthrax post-exposure. The FDA has designated cethromycin as an orphan drug for the prophylactic treatment of inhalation anthrax post exposure, but the drug is not yet approved for this or any other indication. For more contact advancedlifesciences.com.

IT'S BACK!

Rifapentine, the antibiotic which stopped commercial production years ago because of low demand, may be coming back as a potent, high-dose fighter against the most common and actively contagious form of TB. So say researchers at Johns Hopkins, who have revealed that studies in mice demonstrate that substituting higher and daily doses of rifapentine for another antibiotic, rifampin, cured mice two to three times faster than the much older, standard regimen of drugs that includes rifampin. Researchers say if tests in people confirm the findings in mice, the average time to clear the potentially fatal bacterial infection could be reduced from six months to three or less. Researchers said that what was especially advantageous is that Rifapentine is already government approved. Phase II clinical trials are set to begin by the middle of this year. Rifapentine was approved by the FDA in 1998 for treating widespread, drug-susceptible TB, and was initially developed as a once-weekly tablet. But the drug was never really considered effective in low doses when compared to the gold standard, daily, high-dose regimens with rifampin. Researchers investigated the high-dose potential of rifapentine because the drug was in the same class of drugs as rifampin, which is part of the standard antibiotic cocktail of rifampin, pyrazinamide, and isoniazid, a triple drug combo sold as Rifater, or with moxifloxacin in place of isoniazid. The research team tested seven different combinations of antibiotic drugs in hundreds of mice infected with active TB. Some were treated with the standard DOTS regimen, daily Rifater, while others took rifapentine in place of rifampin. Rifapentine, in daily amounts similar to what an adult human would take (600 milligrams), was also tested separately in combination with moxifloxacin- or isoniazid-based DOTS regimens. Blood and tissue testing were done over a six month period to see how quickly each drug combination rid the body of active TB. Treated mice were also tested three months later to check against any potential for relapse. After 10 weeks of drug therapy, mice taking rifapentine and moxifloxacin tested negative for active TB and remained so when retested three months later. Those treated with rifapentine and isoniazid also tested clear of the bacterium by 10 weeks, but were at least 10% more likely to relapse unless treatment persisted for another month. Meanwhile, the traditional DOTS regimen mostly took the full six months to work. Rifapentine remained in the blood in three times higher concentrations throughout treatment. Two more clinical trials are underway.

INSPIRATIONAL

Patients with severe COPD may benefit more from therapy that combines salmeterol and fluticasone than treatment with tiotropium, according to results from a long-term, multi-center study, "Investigating New Standards for Prophylaxis in Reducing Exacerbations" (INSPIRE) that directly compared the two

therapies. Researchers at the Royal Free & University College Medical School in London found no difference in the overall rate of exacerbations between treatment groups, but SFC treatment was associated with better health status, fewer patient withdrawals, and a lower mortality rate than occurred during tiotropium therapy. The researchers recruited 1,323 patients with severe COPD and randomized them to receive one of the two treatments for two years. They analyzed number and type of exacerbations, health status as measured by the St. George's Respiratory Questionnaire (SGRQ), lung function and study withdrawal rate. While exacerbation rates between the two treatment groups were statistically indistinguishable, there were differences in the treatment that the exacerbations required. Oral corticosteroids were used more often to treat the tiotropium group, whereas patients on SFC required antibiotics more frequently. Researchers said the study provided indirect evidence that these treatments affect apparently similar patients in different ways that influence clinical judgment. SFC patients also experienced a slightly higher overall quality of life and a post-hoc analysis revealed that more patients on SFC had a clinically significant improvement in health status than those on tiotropium therapy. Mortality was significantly lower in the SFC group during the study period, even though the trial was not designed to detect such a difference. There was more than a 50% reduction in the risk of on-therapy all-cause death at any time during the study period for the SFC patients. Patients undergoing SFC treatment were also significantly less likely to withdraw from the trial than others. Watson Pharmaceuticals, Inc announced that it has received final approval from the FDA on its Abbreviated New Drug Application (ANDA) for Ipratropium Bromide and Albuterol Sulfate Inhalation Solution in the 0.5 mg/3 mg strength. Watson's Ipratropium Bromide and Albuterol Sulfate product is the generic equivalent to Dey, LP's DuoNeb, which is indicated for the treatment of bronchospasm associated with COPD in patients requiring more than one bronchodilator. For more see "The Prevention of Chronic Obstructive Pulmonary Disease Exacerbations by Salmeterol/Fluticasone Propionate or Tiotropium Bromide." Jadwiga A., et al, American Journal of Respiratory and Critical Care Medicine Vol 177. pp. 19-26. For more on the drug mentioned above, contact watsonpharm.com.

GIVE 'EM AIR

Researchers at the Georgia Tech Research Institute (GTRI) have developed a sensor system that continuously monitors the air around persons prone to asthma attacks. Worn in the pockets of a vest, the new system could help researchers understand the causes of asthma attacks. "We are investigating whether we can go back after an asthma attack and see what was going on environmentally when the attack started," said Charlene Bayer, a GTRI principal research scientist. Although no one fully understands why certain people get asthma, doctors know that once a person has it, his/her lungs can overreact to environmental stimuli causing chest tightness or breathlessness, known as an asthma attack. The new sensor system measures airborne exposure to formaldehyde, carbon dioxide, ozone, nitrogen dioxide, temperature, relative humidity and total volatile organic compounds (VOCs). VOCs are emitted as gases from products such as paints, cleaning supplies, pesticide formulations, building materials and furnishings, office equipment and craft materials. In addition to detecting the seven environmental stimuli mentioned above, a special mesh filter collects particles. A pump pulls air through the filter so that the quantity of particles can be measured at the end of the

sampling period. The composition of the collected particulate can also be analyzed in the laboratory. The battery-powered system fits into the pocket of a vest and contains commercially available sensors that were integrated into a single system. The sensors were calibrated and tested in a large room-sized chamber that simulates real-world environmental conditions inside buildings. Coupled with sensitive mass spectrometers, the chamber allows the changing indoor air chemistry to be studied in detail. Another vest pocket device contains an electronic peak flow meter to periodically measure pulmonary function. When experiencing an asthma attack, the vest wearer notes what time it occurred and the levels of the chemical compounds at that time can be assessed. Contact gatech.edu.

BYE BYE BIRDIE

Officials in Washington State have warned that some cockatiels, as well as other pet birds that were shipped by a national distributor, may pose a risk to humans who are in contact with them. Approximately 20 PetSmart stores in 11 Washington counties have had birds delivered to them from this distributor. Some of these birds had tested positive for avian chlamydiosis. Infected humans can develop psittacosis (the human form of the disease). PetSmart removed all the birds it had received from the distributor. The company says it is treating exposed birds with antibiotics. Avian chlamydiosis is caused by *Chlamydophila psittaci*, a bacterium. Not all birds that become infected show symptoms of illness, but symptoms (in birds) are: lethargy, no appetite, weight loss, thick discharge from eyes and nose, and diarrhea. Susceptible birds are cockatiels, cockatoos, parrots and parakeets. The bacterium gets into humans via dust breathed in from dried bird droppings. An infected person will develop psittacosis. Symptoms include headache, fever, chills, cough, and muscle aches. There is an incubation period of 5-19 days. Psittacosis is usually mild, but can become serious if untreated with antibiotics. People can prevent the problem by keeping the cage clean. And watching the birdie.

ANIMAL FARM

Speaking of animals, recent research on what a study calls "farm women" has shown that contact with some commonly used pesticides in farm work may increase the risk of allergic asthma. Researchers noted that farm women were an understudied occupational group, and that more than half the women in the study by the National Institute of Environmental Health Sciences applied pesticides. The researchers assessed pesticide and other occupational exposures as risk factors for adult-onset asthma in more than 25,000 farmwomen in North Carolina and Iowa. They used self-reports of doctor-diagnosed adult asthma, and divided the women into groups of allergic (atopic) or non-allergic (non-atopic) asthma based on a history of eczema and/or hay fever. They found an average increase of 50% in the prevalence of allergic asthma in all farm women who applied or mixed pesticides. Although the association with pesticides was higher among women who grew up on farms, these women still had a lower overall risk of having allergic asthma compared to those who did not grow up on farms, due to what researchers called an under-understood "protective effect." Most pesticides were associated only with allergic asthma, even though non-allergic asthma is generally more common in adults. Some legal but rarely used compounds, such as parathion, were associated with almost a three-fold increase in allergic asthma. But even some commonly used pesticides were associated with a marked increase in allergic asthma prevalence. Malathion, for example, a widely used insecticide,

was associated with a 60% increased prevalence of allergic asthma. Of all the compounds examined, only permethrin, a commonly used insecticide that is used in consumer items such as insect-resistant clothing to anti-malaria bed-nets, was associated with both allergic and non-allergic asthma.

NEWS FEATURE

Mechanical Ventilation During Mass Casualty Events

Justin Tse, BS, RRT-NPS

Recent events have made me reflect on the preparedness of our hospitals during a mass casualty event. During the early morning hours of January 9th, intense fog and smoke made drivers on interstate 4 in Orlando unable to see anything which led to a 70 car pile up. Emergency medical responders had to cautiously enter the area. The potential for a large number of injured patients was stunning. Area hospitals had to respond to possibly large number of patients requiring mechanical ventilation. Many questions came to my mind. Do hospitals have enough ventilators for a major disaster and can they handle critical patients? Are there enough personnel to respond to such an emergency? What types of injuries could incoming patients have? How can we manage a large number of patients on ventilators with staffing shortages as they are? These are questions which we ask ourselves and try to prepare before the real thing happens. Let us try and answer some of these questions to see if we are prepared for a major event.

The first question is “do we have enough ventilators for a major disaster and can they handle critical patients”. There are many types of ventilators to choose from. You have pneumatic (single use—disposable) ventilators to transport ventilators to critical care ventilators. Each type has its advantages and disadvantages some of which is listed below.

Pneumatic	Transport	Critical Care
No electricity required	Require A/C power (usually has internal battery)	Require A/C power (usually has internal battery)
Small and easy to store	Anywhere from 8-20 lbs	Large and bulky
Limited or no alarms	High and low pressure alarms	Comprehensive alarm package
Limited modalities available	Volume or pressure control modes available	Comprehensive modalities available
Requires continuous education due to lack of use	Some have internal compressors	Some have internal compressors
Limited ability to manage complex patients	More expensive than pneumatic ventilators and more costly to store and maintain	Average cost over \$30,000
	Requires continuous education if not used frequently	Requires Preventative maintenance
	Requires preventative maintenance if used	Can handle a variety of patient disorders
	Can handle a variety of patient disorders	

The second question which came to mind was “are there enough personnel to respond to such an emergency.” The U.S. Bureau of Labor and Statistics in their monthly labor review states “Health care practitioners and technical occupations are projected to grow almost twice as fast as the average for all occupations. The increase in demand for health care practitioners and technical occupations is primarily the result of a growing and aging population. Technological advances in the medical field will lead to increased demand for more medical procedures and the workers who perform them.”¹ By 2016, the USBLS sees an increase of 22.6% for the need of respiratory therapist.¹ With the current shortages and an increased need for personnel, patient safety becomes an issue, not just for mass casualty but for normal operations.

What types of injuries could incoming patients have? With a 70 car pileup, trauma was the first to come to mind. Other problems I imagined were chemical injuries and respiratory disorders. In the January 2008 issue of Respiratory Care, Dr. Muskat discusses chemical exposure and its implications. “Exposure to chemical agents, both deliberate and accidental, over the past 100 years has resulted in the death of thousands and a significant number of casualties requiring hospitalization.”² Our highways and railways are the major transit for chemicals in the U.S. When accidents occur, the conditions of the area need to be assessed. Chemical exposure can affect not only the patients on scene but also the caregivers responding to the accident. Safeguards and protocols need to be in place for just such an emergency.

Having traveled to many hospitals in the US, a common theme I have run into is a shortage of staff for current patient assignments. How can facilities manage a large influx of patients? In this case, a major highway was closed due to the accident as well as weather conditions. Hospitals have developed disaster plans that call staff members to come in to respond to an emergency. If roadways are compromised, this can make such plans ineffective. Other issues regarding calling in personnel are whether that person being called can come in a timely manner. They may have family obligations which could prevent them from getting in immediately. If staff cannot get into the hospital facility, can the existing staff handle the incoming patients? . Do we have enough staff to monitor every patient’s dynamically changing condition and simultaneous deteriorations in patient status? Patient safety can be compromised. These are issues which are constantly being asked by health and governmental officials throughout the US.

Many systems are offered to take care of our patients and it is up to the hospital to choose the right one for the facility. Manufacturers are developing better technology to improve staffing efficiency. Closed loop controllers can help with patient care and free up the clinician to take care of sicker patients as well as monitor changes in a patient’s condition while the clinician is away. This could help alleviate current staffing shortages and improve patient care and safety.

Justin Tse is with Hamilton Medical. Editorial Note: since Justin wrote this article, the journal Respiratory Care’s January special issue “Mechanical Ventilation in Mass Casualty Scenarios” has been published. We encourage readers to review this issue. Some salient points raised include the need for ventilators capable of ventilating patients with ARDS per ARDSnet low Vt strategy and VE requirements. The authors indicate that the

disposable pneumatic ‘automatic’ type ventilators are not capable of ventilating these types of patients. They also discuss the need for ‘Intelligent’ ventilators that for example, ventilate patients based on ideal body weight, are simple to operate and identify the need for manufacturers to provide simple single page ‘cards’ for operation and ‘virtual’ computerized simulators to educate clinicians on ventilator operation.

References

1. Monthly Labor Review. November 2007 pgs 86-125. <http://www.bls.gov/opub/mlr/2007/11/art5full.pdf>.
2. Mass Casualty Chemical Exposure and Implications for Respiratory Failure. Volume 53, number 1, January 2008 pg 58-66.

PRODUCTS

IN THE BAG

B&B Medical Technologies now offers The Test Lung, a new, economical choice for providing high quality demonstration and testing applications on mechanical ventilators. The Test Lung simulates the respiratory system, providing nominal levels of resistance and compliance as well as a variable leak function to demonstrate patient-trigger function or the leak compensation of a respiratory system. The Test Lung is packaged with a 1 liter, Latex- free Silicone Ventilation Bag, Test Lung Connector Kit and Rp5 Resistance. The 1 liter Silicone Ventilation Bag is durable, easily removable and can be cleaned or sterilized as needed. The Test Lung Connector Kit adapts to all patient circuits and proximal airway flow sensors. The Test Lung Connector Kit has three adapters, two with Luer Ports and Caps, providing easy ability to demonstrate the ventilator’s leak compensation performance and patient-trigger function. The Test Lung is compact in design and lightweight. Each Test Lung is tested and validated for resistance and compliance in the application range and has a unique serial number to ensure its compliance with specification. A Precision Resistor Kit provides the precision adapters needed to simulate changes in airway resistance. The Kit contains three resistors: Rp5, Rp20 and Rp50. The Precision Resistor Kit can be cleaned and sterilized. The Test Lung and Precision Resistor Kit are the ideal tools for teaching and demonstrating mechanical ventilation in addition to performing ventilator verification testing in the respiratory care, biomedical labs and anesthesia departments. Contact bandb-medical.com.

SOLD

CHAD Therapeutics, Inc announced that its shareholders have approved the proposed sale for approximately \$5.25 million in cash of the assets related to CHAD’s oxygen conserving business to Inovo, Inc, a privately held manufacturer of oxygen regulators and conservers based in Naples, FL. The transaction was approved by more than 70% of the issued and outstanding shares. Over 99% of the shares represented at the meeting were voted in favor of the proposal. Earl Yager, CHAD’s President and CEO, said, “We intend to focus our future efforts on the sleep disorder market. We believe that our sleep products offer unique features that can improve the diagnosis and treatment of obstructive sleep apnea. We recently filed an application with the FDA for clearance to begin marketing the first of our sleep

products. With additional proprietary products in an advanced stage of development and a roadmap of additional product development opportunities based on our patented technology, we believe we have the opportunity to build CHAD’s position in this large and growing industry. In addition, we will continue to actively pursue the sale of our trans-filling assets.” Contact chadtherapeutics.com.

PATIENT PATENT

Vapotherm, the global leader in high flow oxygen therapy products, announced today that US patent rights have been validated for an apparatus used in the delivery tube technology for respiratory tract therapy. Reinforcing Vapotherm’s principal role in the industry, the US Patent No 7,314,046 B2 has been granted through 2022 and provides Vapotherm the right to prevent or exclude other companies from making, using, selling, or offering to sell or import the invention. The triple lumen design is the vital component for Vapotherm products as it helps deliver humidified air to the respiratory tract of patients. Used throughout all Vapotherm products, including the 2000i and the recently introduced Precision Flow, the apparatus allows Vapotherm to maintain the conditioned breathing gases to the patient and thus aid with respiratory tract therapy and treatment. The patient delivery circuit design is unique in the field and provides Vapotherm a competitive advantage through the delivery of optimally conditioned breathing gases all the way to the patient, whereas conventional approaches can result in significant temperature and humidity loss. For more information, contact vtherm.com.

READY FOR TAKEOFF

eVent Medical received FDA 510K clearance for its Heliox gas delivery by its Inspiration ventilator system. Heliox administration has been available on the Inspiration ventilator outside the US since 2006, and now the therapy will be provided to US customers. There have been a number of peer-reviewed medical publications demonstrating the utility of eVent’s Heliox delivery system on the Inspiration ventilator. Researchers have found the Inspiration ventilator—with its patented, compact block design—greatly reduces the consumption of Heliox when compared to other currently marketed older ventilator designs. The Inspiration does not have a bleed system that can waste large amounts of the gas even before it is delivered to the patient. Other studies have noted that the volume accuracy was maintained while using the sensor at the wye. With its expanding US and Canadian sales force, eVent Medical will begin marketing the Inspiration throughout the US with a focus on the pediatric areas that have the highest need for Heliox with asthmatic patients, and this will complement eVent’s dedicated Infant platform for the neonatal population of low birth weight babies. This new capability allows eVent Medical, a division of Kobayashi Medical America LLC, to further its mission of providing innovation and value to the clinical community. eVent Medical markets the Inspiration line of adult through neonatal ventilators with the most aggressive warranty and preventative maintenance programs in the industry—the Inspiration is truly recognized for its lowest cost of maintenance. Contact event-medical.com.

SET FOR SAN FRAN

Masimo announced the completion of UCSF Medical Center’s system-wide implementation of Masimo SET pulse oximetry and the Masimo Rainbow SET technology platform, establishing UCSF Medical Center as the first hospital to implement Masimo

Rainbow SET capabilities system-wide. Initially, UCSF Medical Center performed an extensive pulse oximetry comparison and found that Masimo SET obtained accurate and reliable oxygen saturation measurements under difficult conditions. UCSF clinicians also utilized new Masimo Rainbow SET technology to noninvasively and continuously measure physiologic and hemodynamic components that were previously only available by invasive tests. As a result, UCSF decided to expand the adoption of Masimo technologies beyond pulse oximetry to include the noninvasive patient monitoring capabilities of the Masimo Rainbow SET technology platform. Masimo SET provides continuous, accurate oxygen saturation measurements that reflect a patient's true status, even during low perfusion and motion. The new noninvasive measurement capabilities allow for more precise and timely diagnosis and treatment. From becoming the first in the world to successfully perform surgery on a baby still in the womb to developing life-saving treatments for premature infants whose lungs aren't fully developed, UCSF is now pioneering the application of new noninvasive measurements enabled by the Masimo Rainbow SET technology platform to help advance the care they deliver.

THE GREATEST OF EASE

ResMed today introduced its new Easy-Breathe technology into the United States and other Americas markets with the launch of the VPAP Auto bilevel device. Easy-Breathe technology combines a new motor with advanced software to make therapy nearly silent and extremely comfortable. First launched in Europe and Asia-Pacific in September, Easy-Breathe responds to patient breathing patterns with heightened sensitivity and reduces noise to less than 25 dB, more than 80% quieter than the leading competitor. The launch of Easy-Breathe at the European Respiratory Society conference created a sensation with its innovative, quiet motor technology, and ResMed noted that it expects a similar enthusiasm with the launch in the Americas market. The combination of whisper-quiet comfort in a compact system is truly a unique offering, comes in addition to ResMed adding the ultra-comfortable Easy-Breathe waveform for the launch of the VPAP Auto in the Americas. These features increase compliance, which benefits patients, HMEs and sleep specialists. The VPAP Auto offers comfortable bilevel therapy in ResMed's compact S8 platform. The VPAP Auto is able to deliver nearly silent therapy and greater pressure stability so patients sleep comfortably throughout the night, and synchronizes with the patient's normal respiration so that breathing feels more natural and comfortable. The Easy-Breathe pressure profile was originally developed for ResMed's advanced VPAP Adapt SV to deliver comfortable therapy for complex sleep disorders. The same comfortable pressure profile is ideal for all CPAP patients because, unlike the traditional square bilevel waveform, Easy-Breathe's profile recreates a patient's natural breathing pattern. Easy-Breathe features a dual-stage motor that delivers superior performance at half the effort, cutting device noise to less than 25 dB. Contact resmed.com.

GET THE POINT

An advanced, handheld creatinine monitoring system from Nova Biomedical enables simple, rapid, and accurate assessment of renal function by finger prick capillary blood sampling at the point of care. Incorporating new patented, Multi-Well test strip technology adapted from Nova's hospital glucose monitoring system, Nova StatSensor Creatinine allows creatinine to be measured with a simple 30 second test in the emergency department, radiology, oncology, or other point-of-care areas

where renal function must be assessed. StatSensor Creatinine measures creatinine and calculates estimated glomerular filtration rate (eGFR) by MDRD or Cockcroft-Gault equations. Creatinine with eGFR is a more accurate and sensitive measurement of kidney function than creatinine alone. In fact, the National Kidney Disease Education Program recommends reporting of eGFR with every creatinine measurement. StatSensor Creatinine offers easy, virtually painless capillary blood sampling on small, 1.2 microliter blood samples with fast, 30-second test results. StatSensor Creatinine provides excellent correlation to central laboratory reference methods over a wide measurement range from 0.03-12 mg/dL. StatSensor Creatinine interfaces seamlessly with hospital and laboratory information systems. Comprehensive instrument manager software provides management, control, and regulatory compliance, and allows the StatSensor system to be completely customized to the needs of each department within the hospital. Contact novabio.com.

OXIMETRY ROUNDTABLE

Roche Diagnostics

Information provided by Ernie Hobbs and Larry Healy, Marketing Managers, Point of Care Diagnostics, Roche Diagnostics.

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

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. Technical Aspects: Determination of Bilirubin on the Roche OMNI S, International Evaluation

Know sooner. Act faster.



Oxinet™ III Remote Respiratory Monitoring System Nellcor™ Oximetry Compatible with OxiMax™ Technology

Improve patient safety on your general care floor through early warning of respiratory distress.

- Monitor key respiratory parameters from a central display:
 - SpO₂, pulse rate
 - EtCO₂, respiration rate, FiCO₂
- Address JCAHO* National Patient Safety Goals:
 - 2007 Goal 2 to improve communication among caregivers
 - 2008 Goal 16 to improve response to changes in a patient's condition
- Support 2006 APSF** recommendation on safety during patient-controlled analgesia

* The Joint Commission www.jointcommission.org

** Anesthesia Patient Safety Foundation www.apsf.org



COVIDIEN

positive results for life™

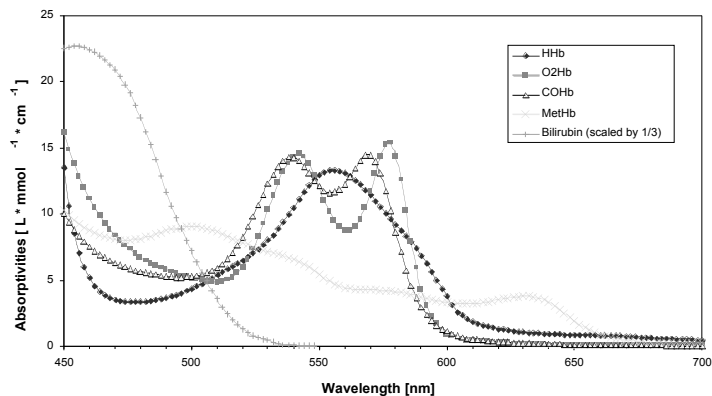
www.covidien.com | 1-800-635-5267

COVIDIEN, COVIDIEN with logo and ™ MARKED BRANDS are trademarks of Covidien AG. © 2008 Covidien AG. All rights reserved.

Workshop, October, 23 2003, Deutschlandsberg, Austria.

- 4 H. Hallemann et al. Technical Aspects of Bilirubin Determination in Whole Blood. Point of Care, The Journal of Near Patient Testing and Technology; Volume 4, March 2005.

Absorbance of Hemoglobin Derivatives and Bilirubin



Masimo Corporation

Information provided by Paul Jansen, VP of Strategic Marketing.

Tell us about the latest in R&D for oximetry.

For nearly 20 years, Masimo has been focused on a singular mission—to improve patient outcomes and reduce the cost of care by taking noninvasive monitoring to new sites and applications. Masimo Signal Extraction Technology (SET) provided clinicians with the first reliable oxygen saturation values during motion and low perfusion with significantly reduced false alarms. Now, Masimo has initiated the second oximetry revolution with Masimo Rainbow SET Pulse CO-Oximetry, an upgradeable platform that can not only measure oxyhemoglobin (SpO₂) and pulse rate, but additional blood constituents that previously required invasive procedures. Masimo Rainbow SET is the first and only platform capable of continuously and noninvasively measuring the toxic dyshemoglobins of carboxyhemoglobin (SpCO_{TM}) and methemoglobin (SpMetTM) as well as perfusion index (PI) and pleth variability index (PVI). While conventional pulse oximetry technologies use only two wavelengths of light and lack the sensitivity to determine dyshemoglobin levels, Masimo Rainbow SET uses multiple wavelengths of light to reveal a more comprehensive view of a patient's underlying physiology—enabling clinicians to make earlier and better clinical decisions, improve patient safety, and decrease costs.

Masimo is also innovating in the area of “smart alarms” that use multiple variables to trigger multi-dimensional (3D) alerts when an unnoticed and potentially dangerous change in patient status occurs, which include changes in measurements such as perfusion index (PI) that may indicate hypothermia, hypovolemia, shock and/or sepsis. With its innovations in technology, Masimo is empowering clinicians to do more with their Masimo devices by continuing to expand noninvasive measurement capabilities within an upgradeable platform. And because Masimo SET's SpO₂ solution is in more than 100 multiparameter monitors and 40 monitoring brands, hospitals can easily standardize their pulse oximetry solution across all clinical settings in a whole-house conversion. With an eye on the future, Masimo scientists are hard at work to deliver new

measurements and features that will continue to grow the platform's capabilities and benefits to the clinician.

How does oximetry and your oximetry product improve patient care?

Masimo SET pulse oximetry provides accurate oxygenation measurements even in the most challenging conditions of motion and low perfusion and dramatically reduces false alarms by over 90% when compared to conventional pulse oximetry. This has significantly improved the quality of patient care across clinical areas that rely on pulse oximetry—from the operating room to critical care to the emergency room. Masimo Rainbow SET now allows clinicians to continuously and noninvasively monitor blood constituents that previously required invasive procedures, decreasing the time to assess these factors and significantly increasing the number of patients that can be monitored. More than 40,000 people per year in the U.S. seek medical attention for carbon monoxide poisoning and the C.D.C. reports that each year more than 500 Americans die from unintentional CO poisoning. Masimo SpCO allows rapid spot-check assessment of carbon monoxide levels in patients with potential CO poisoning upon entry to the emergency department, enabling rapid and lifesaving treatment and eliminating missed diagnoses. Continuous SpCO monitoring also allows clinicians to detect elevated levels of carboxyhemoglobin caused by drugs used during surgery or present in high levels prior to or after surgery in smokers, increasing their cardiac ischemic risk. Over 30 drugs used in a variety of settings have been shown to contribute to methemoglobinemia, including anesthetics (such as cetacaine and xylocaine), certain antibiotics (dapsone and chloroquine), and benzene. Masimo SpMet allows clinicians to identify undetected acquired methemoglobinemia quickly, enabling earlier intervention to avoid brain damage or death. Pleth Variability Index (PVI) enables the detection of real-time changes in the perfusion index (PI), which may occur due to changes in volume status. Changing volume status can indicate a hyper- or hypo-volemic condition and the ability to continuously monitor and track changes in PVI may enable more effective titration of therapy.

Where and how do you see your product used most?

While pulse oximetry has a long history of use throughout the hospital and will continue to do so, conventional pulse oximetry was never practical for continuous monitoring on the general floor because of its high false alarm rate. Nevertheless, an enormous patient safety problem still exists on the general floor. According to the 2004 HealthGrades report, preventable deaths totaled 263,000, which equates to an average of one preventable patient death per week for the average U.S. hospital. 75% of these preventable deaths were due to “failure to rescue”—occurring most often on the general floor. The unmatched accuracy, reliability and low false alarm rate of Masimo SET pulse oximetry make it ideal to improve patient safety and reduce avoidable adverse events by monitoring both oxygen saturation and pulse rate on the general floor. The recently introduced Masimo Patient SafetyNet combines Masimo SET pulse oximeters in general floor rooms with an easy-to-use, open-architecture, and upgradeable system that wirelessly transmits user-defined oximeter alarms to a clinical assignment station. The clinical assignment station, which requires no direct supervision or additional staff, wirelessly routes any patient alarms to the pager worn by the responsible nurse, who is then able to immediately respond and initiate life-saving interventions at the patient's bedside. Masimo Patient

SafetyNet offers an effective solution to reduce adverse events and meets the 2008 Joint Commission safety goals for hospitals, requiring a mechanism that identifies physiologic changes and summons appropriate clinician response.

Discuss the cost effectiveness of oximetry use.

Masimo SET and the Masimo Rainbow SET technology platform offer multiple pathways to cost-effectiveness, including:

- Reduced burden on staff time—the reduction of false alarms with Masimo SET pulse oximetry reduces the burden on staff and allows them to spend more time caring for patients.
- Reduced morbidity related to avoidable adverse events—the use of Masimo SET pulse oximetry and Masimo Patient SafetyNet on the general floor may help hospitals reduce the number of adverse events, which, in turn may also reduce the costs associated with acute- and long-term treatment and their associated morbidity.
- Reduced sensor costs—the low perfusion monitoring capability of Masimo SET reduces the need to attempt multiple monitoring sites with multiple disposable sensors. In addition, Masimo advances in disposable sensor technology can translate to longer use per patient.
- Reduced capital costs—the upgradeable Masimo Rainbow SET platform with multiple noninvasive measurements from one sensor may eliminate the need to purchase additional devices. Clinicians can choose the measurements they need today and upgrade to future parameters when they become available (pending FDA clearance) without purchasing new capital equipment. With Masimo, hospitals can be confident that their investment in technology today won't become obsolete tomorrow.
- Reduced lab and diagnostic test costs - the ability to noninvasively measure SpMet and SpCO enabling the immediate discovery of carboxyhemoglobinemia or methemoglobinemia may decrease the need for additional lab, diagnostic, and imaging tests.
- Increased revenues—in patients eligible for reimbursement, new coding guidelines may allow for reimbursement for the measurement of SpCO and SpMet.

What type of training and customer assistance do you offer?

Masimo understands technical questions cannot wait until the next business day, which is why we offer 24 x 7 technical support and one of the largest teams of dedicated clinical specialists in the industry. When you choose Masimo, you get a business and clinical partner committed to your success—both before and after the sale. In addition, with comprehensive training tailored to your unique requirements and online training tools through Masimo U, we ensure that the initial and ongoing training for your entire staff is as smooth and rewarding as possible.

How do you perceive the role of oximetry in the future?

With Masimo's current and planned innovations, we believe oximetry's future is brighter than ever. By expanding the clinical relevance of oximetry, we believe that oximetry will play an expanded role throughout the hospital with continuous monitoring from admission to discharge, supported by:

- Multiple noninvasive blood constituent and hemodynamic measurements (SpO₂, PI, pulse rate, SpCO, SpMet, PVI, and future measurements)
- Continuous patient monitoring expansion to the general floor
- Comprehensive features that allow clinicians to set

- preferences and alarms specific to each patient's condition
- Upgradeable and expandable capabilities that allow the platform to grow as clinicians' needs grow.

Radiometer America

Information provided by Alan Beder, Manager of Scientific Affairs.

Tell us about the latest in R&D for oximetry.

In 1998, Radiometer pioneered the measurement of CO-Oximetry from 6 wavelengths to a continuous spectrum. This allowed a system that could automatically correct for many of the interfering substances that plagued conventional products while allowing the measurement of fetal hemoglobin and total bilirubin. The current R&D focus at Radiometer has been to maintain the gold standard performance achieved with the benchtop instruments on a compact POC platform. This has been achieved on the ABL80 FLEX through the replacement of the bulky halogen source with a compact LED. The other technical challenge has been harnessing the light that is now dispersed in a much smaller space. A significant effort has gone into refining the algorithms to maintain lab-quality performance.

How does oximetry and your oximetry product improve patient care?

The measurement of pO₂ gives the caregiver just a part of the oxygenation picture, since it only is an indication of oxygen uptake by hemoglobin. It does not provide information about O₂ transport or release to the tissues. A blood gas analyzer like the ABL80 FLEX can provide this true picture.

Discuss the cost effectiveness of oximetry use.

Providing the caregiver with a more accurate clinical picture of their patient's oxygenation status is only possible with the addition of CO-Oximetry. The incremental cost for a hospital to add CO-Oximetry to a Radiometer blood gas analyzer is nominal, as is the operating cost. Radiometer's patented hemolyzing cuvette is maintenance-free, providing further cost effectiveness.

What type of training and customer assistance do you offer?

Radiometer maintains an educational website about the clinical importance of CO-Oximetry at www.deep-picture.com.

How do you perceive the role of oximetry in the future?

The availability of CO-Oximetry at the POC will ensure caregivers are making the correct clinical decisions. Further utilization of total bilirubin will allow neonatal caregivers the opportunity to save precious blood for these patients.

Onyx Works!



Onyx® II
Fingertip
Pulse Oximeter

For Your Most Challenging Patients

Onyx II® – the original all-in-one digital fingertip pulse oximeter – works for your most challenging patients. Its superior accuracy is trusted by clinicians worldwide for spot checks on a wide range of patients from pediatric to adult, light to dark skin tones, and good to low perfusion.

Onyx II puts vital signs within reach anywhere, anytime. Learn how by visiting www.nonin.com/study/cottage for a copy of the Santa Barbara Cottage Hospital study showing decreased costs, enhanced patient care and time savings.



www.nonin.com

800.356.8874 +1 763.553.9968



NONIN
✓ Where People Make the Difference

Nonin's Onyx II Fingertip Pulse Oximeter in the Emergency Department Results In Decreased Costs, Enhanced Patient Care and Time Savings

Denise McDonald, BSN, CEN, MSNc

Abstract

This study was designed to assess the utility of the addition of a small, all-in-one digital fingertip pulse oximeter, Onyx II by Nonin Medical, Inc, in the Emergency Department (ED).

Methods: The study was conducted at a level II trauma center. All ED rooms are fully-equipped with pulse oximetry. For three months, all ED caregivers were provided an Onyx II. **Results:** Cost of disposable pulse oximeter sensors during the study were reduced by 48%. Overall, 76% of the caregivers indicated a time savings due to the use of Onyx II, an average savings of 26 minutes per caregiver per shift, with greater time savings noted for triage caregivers. Enhanced patient care was noted by 75% of the caregivers, attributed to quicker triage; accurate readings on a wide-range of patients (e.g. patients with low-perfusion and children); and availability of readings when monitors were not accessible or were malfunctioning. Ninety-eight percent (98%) of the caregivers found Onyx II to be easy to use. Six-months following the study period, the vast majority of caregivers continued to use Onyx II on a regular basis.

Introduction

Oxygen saturation monitoring through pulse oximetry (spot-check or continuous) is a standard of care in most Emergency Department (ED) settings. Multiparameter, non-invasive monitoring devices or portable equipment is often the only choice available for simple pulse oximetry spot-checks. Loss of time and inefficiencies result as caregivers search for portable equipment or over-utilize elaborate monitoring systems. Added noise from nuisance alarms and cost of disposable sensors are additional limitations to the use of these devices in the ED. We hypothesized that the addition of a small, all-in-one digital fingertip pulse oximeter, Onyx II by Nonin, in the ED would decrease overall oximetry costs without decreasing quality of patient care.

Methods

The study was conducted at Santa Barbara Cottage Hospital (SBCH), a level II trauma center within the Cottage Health System. SBCH has a 240-bed capacity, with a 25-bed ED. Annual ED patient volume is 1500 trauma patients and 40000 patients

Denise McDonald is Clinical Manager Emergency & Trauma Services, Santa Barbara Cottage Hospital, Santa Barbara, CA.

Figure 1: Disposable Sensor Expenses

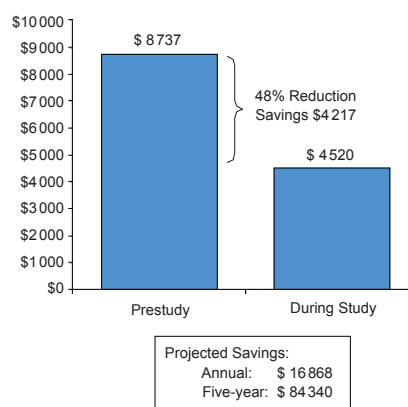
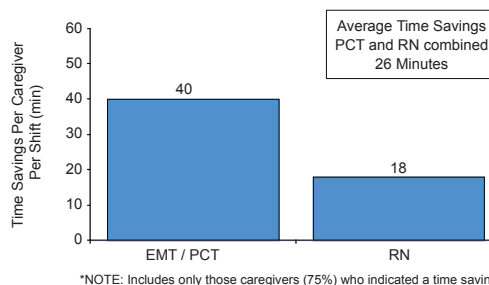


Figure 2: Average Time Savings In Minutes Per Caregiver Per Shift*



*NOTE: Includes only those caregivers (75%) who indicated a time savings.

overall, with a 23% admission rate. ED staffing includes 64 full-time employees consisting of approximately two-thirds registered nurses (RN) and one-third patient care technicians (PCT). The patient care ratio is three to one, excluding non-urgent patients. All ED rooms are fully-equipped with state of the art multiparameter vital sign monitoring equipment which include pulse oximetry. The fingertip pulse oximeter chosen for this study was Nonin's Onyx II because of the compact design, long battery life and proven accuracy.^{1,2}

The device can be carried in a pocket or attached to a stethoscope, belt or lanyard making it as unobtrusive as

possible for the ED personnel who may already be required to carry a number of necessary tools.

The study was designed to assess cost-effectiveness, device durability and caregiver acceptance and satisfaction with the addition of Onyx II in a fully-equipped ED. Onyx II was to be used for routine and spot-check SpO₂ readings as the caregiver felt necessary. For three months, all ED caregivers were provided an Onyx II to carry with them, allowing pulse oximeter assessment anytime and anywhere. Training on use and care of the devices was provided to all staff. Caregivers were not required to use Onyx II, but rather were given the opportunity to use it in the course of the work shift.

Direct costs of disposable pulse oximeter sensors were collected for a three-month period prior to the study and for three months during the study to evaluate cost savings. Caregivers were surveyed throughout the three-month study period to assess durability, utility and satisfaction with Onyx II.

Results

Direct costs of disposable pulse oximeter sensors were significantly decreased by the addition of Onyx II in the ED. Disposable sensor costs decreased from \$8737 for the three-month period prior to the study to \$4520 during the three-month study. This savings of \$4217, representing a 48% reduction in disposable sensor expense, was in conjunction with a higher patient census.

Other than the initial purchase, there were no incremental costs associated with the Onyx II. No Onyx II devices were lost or stolen during the study. As anticipated, none of the devices required service. There were no malfunctions or defects during the study or for up to six months following the study.

An indirect cost-savings was noted in time. Overall, 76% of the caregivers indicated there was a time savings due to the use of Onyx II, an average savings of 26 minutes per caregiver per shift. Time saved was related to the number of readings taken per shift and was noted to be higher for triage caregivers. PCT caregivers had an average time savings of 40 minutes as compared to RNs who noted a savings of 18 minutes.

The size of the Onyx II allowed each caregiver to conveniently carry a device. This resulted in quick and efficient monitoring of patients. Time savings were noted by 76% of caregivers as a result of decreased search time for portable equipment and quick attachment to patients. Time saved by not having to look for equipment can be spent providing direct patient care. Onyx II is also quickly cleaned between uses.

Onyx II's ability to provide quick and accurate readings in a wide range of patients and settings proved valuable. Onyx II's design allows for accurate use in pediatrics and low perfusion patients. The facility continues to use the Onyx II devices on nearly all pediatric patients, regardless of the availability of the multiparameter monitors. The pediatric patients found the device interesting and less intimidating. With recommended finger size ranging from 0.3 inches to 1.0 inches (0.8 – 2.5 cm) in thickness, we found Onyx II able to accommodate the typical pediatric patient's finger without problems.

Anecdotally, caregivers reported a confidence in Onyx II readings being more consistent with the clinical signs and

symptoms of the patients. This assessment was based on caregiver assessment of clinical signs and symptoms. Similarly, Onyx II provided assessments when the multiparameter units failed to register a reading due to low perfusion or monitor malfunction.

Conclusion

The addition of Nonin's Onyx II, a small, fingertip pulse oximeter, to the ED setting results in a 48% reduction in disposable sensor costs, time savings of 26 minutes per caregiver per shift and patient care enhancement. Caregivers reported satisfaction with ease of use and convenience of Onyx II.

Acknowledgements: This project was supported by Nonin Medical, Inc. Minneapolis-based Nonin, a privately owned company specializing in the design and manufacture of physiological monitoring solutions, distributes its products to health and medical professionals in more than 125 countries and to over 90 OEM partners. Since 1986, Nonin has developed a broad product line of pulse oximeters, capnographs, sensors, accessories and software for use by medical professionals. Its industry-leading capabilities in signal processing, sensor design and an innovative combination of features not available in competitive products are the foundation of its success.

References

- 1 Bickler, P, et al. Effects of skin pigmentation on pulse oximeter accuracy at low saturation. *Anesthesiology*. 2005 Apr;102(4):715-9.
- 2 Terre-Bouscoulet L, et al. Precision and accuracy of "a pocket" pulse oximeter in Mexico City, *Revista de Investigacion Clinica*, 2006 Jan-Feb;58(1):28-33.

Prone Positioning of Extremely Low Birth Weight Neonates During Mechanical Ventilation Results in Slightly Higher pCO₂ and slightly lower pH

Daniel D. Woodhead, RT; Diane K. Lambert, RN; Nancy Schmutz, RN; Camille Allen, RT; Jill Hildebrand, Vickie L. Baer, RN; and Robert D. Christensen, MD

Abstract

Introduction: In general, the Newborn Intensive Care Unit (NICU) bedside nurses and/or respiratory therapists change the body-position of each mechanically ventilated premature infant every three to four hours. We postulated that in the prone position, the chest wall of small preterm infants is less mobile, which can lead to reduced chest ventilatory excursions and decreased ventilation.

Methods: We conducted an historic cohort study, tabulating all blood gas values of mechanically ventilated neonates with gestational ages of 23 to 30 weeks, at McKay-Dee Hospital during the past five years. Data were categorized according to three weight groups; ≤ 1000 grams; 1001-1500 grams; and > 1500 grams.

Results: Ninety-six patients that required mechanical ventilation for more than three days, had multiple arterial blood gasses in multiple positions, were not transferred to another hospital, and survived to discharge, constituted this study. No position-associated differences were seen in neonates > 1000 grams. Fifty-two weighed ≤ 1000 grams and received high-frequency ventilation. While in the prone position, their pH was lower (7.29 ± 0.09 ; mean \pm SD) than while supine, right-down, or left-down (7.34 ± 0.09 , $P < 0.0001$). The 95% confidence interval (CI) for decrease in pH while prone was 0.03-0.05 pH units. Also, while in the prone position, their pCO₂ was higher (53.8 ± 13.6 torr) than while in the other three positions (47.4 ± 11.6 ; $P < 0.0001$; 95% CI 5.2-8.4 torr). Similar findings were observed for 53 neonates ≤ 1000 grams on conventional ventilation; the pH while prone was 7.30 ± 0.08 vs. 7.32 ± 0.07 in the other three positions ($P < 0.0001$, 95% CI 0.02-0.04 units), and the pCO₂ while prone was 53.2 ± 8.6 vs. 49.7 ± 9.9 in the other three positions ($P < 0.0001$, 95% CI 1.7-5.3 torr).

Conclusions: When providing care to mechanically ventilated ELBW neonates, one can anticipate slightly lower pH values and slightly higher PCO₂ values in the prone position.

Introduction

Periodically changing the body-position of a critically ill, mechanically ventilated, neonate is a common component of pulmonary and developmental support.¹⁻⁴ It seems that most NICUs advocate changing the position of such patients about

every three to four hours, and four positions are typically used—supine, right side down, left side down, and prone. We postulated that among very low birth weight neonates (VLBW; < 1500 grams birth weight), the prone position can render the chest wall less mobile, which might lead to reduced chest ventilatory excursions and decreased ventilation. If this is so, it might be manifested by an increase in the pCO₂ and a decrease in the pH. We postulated that any consistent trends toward reduced ventilation in the prone position would be worth knowing about, so this could be anticipated when arterial blood gasses from such patients are interpreted. Our hospital records include the position of the neonate when the blood gas was obtained; therefore we conducted an historic cohort study to assess any association between body position of mechanically ventilated preterm neonates and arterial blood gas results.

Methods

Data were collected from patient flow-sheets of neonates ≤ 30 weeks gestation mechanically ventilated during the years of 2002 to 2006. Patients were included only if they required mechanical ventilation for more than three days, had arterial blood gasses measured in multiple positions, were not transferred to another hospital, and survived to discharge. Data from all such patients were tabulated into three groups based on weight; ≤ 1000 grams; 1001-1500 grams; and > 1500 grams. Data collected included date of birth; gestational age; birth weight; infant weight for each day while on mechanical ventilation; ventilator mode, infant position; and arterial blood pH and pCO₂ while in the various positions. The pH and pCO₂ values while in various body positions were compared using an unpaired Student *t* test. The McKay-Dee Hospital Institutional Review Board approved the study.

Results

During the years 2002 through 2006, 94 patients required mechanical ventilation for more than three days, had arterial blood gasses in all four positions, were not transferred to another hospital, and survived to discharge. The records of these 94 were reviewed for this study.

Patients weighing > 1000 grams had no position-associated differences in pH or pCO₂. However, among those weighing ≤ 1000 grams, consistent differences were observed (Table). These differences were seen whether the patients were ventilated using a high frequency ventilator ($n=52$) or using a conventional ventilator ($n=53$) (11 were in both groups, because

The authors are with Intermountain Healthcare, Neonatal Intensive Care Unit, McKay-Dee Hospital Center, Ogden, UT, USA.

data were obtained before and after they changed from high-frequency to conventional ventilation).

When ELBW neonates on high frequency ventilation were in the prone position, their pH was lower (7.29 ± 0.09 ; mean \pm SD) than in the supine, right-down, or left-down positions (7.34 ± 0.09 , $P < 0.0001$). The 95% confidence interval (CI) for decrease in pH while prone was 0.03-0.05 units. Also, while in the prone position, their pCO₂ was higher (53.8 ± 13.6 torr) than while in the other three positions (47.4 ± 11.6 ; $P < 0.0001$; 95% CI 5.2-8.4 torr). Similar findings were observed for 53 neonates ≤ 1000 grams treated with conventional ventilation; the pH while prone was 7.30 ± 0.08 vs. 7.32 ± 0.07 in the other three positions ($P < 0.0001$, 95% CI 0.02-0.04 units, and the pCO₂ while prone was 53.2 ± 8.6 vs. 49.7 ± 9.9 in the other three positions ($P < 0.0001$, 95% CI 1.7-5.3 torr).

Discussion

Mechanically ventilated preterm infants are routinely subjected to periodic changes in position. Our study suggests that among those weighting >1000 grams, such positioning has no consistent effect on pH or pCO₂. However, in ELBW neonates, prone positioning results in a small but consistent increase in pCO₂ and decrease in pH. We do not interpret this finding as contraindicating prone positioning of ELBW neonates. In fact, these changes, which are probably clinically insignificant, could be outweighed by benefits to periodic prone positioning. Such benefits might include better pulmonary toilet, better oxygenation, and better neurodevelopment.^{1,2,5,6}

The effect of position on ventilation and oxygenation of ELBW neonates is a complex matter involving many variables. For instance, the compliant chest wall of an ELBW neonate might be better stabilized by prone positioning,⁶ and such stabilization might provide for better synchrony with the ventilator, and with an increase in tidal volume and minute ventilation.⁷⁻⁹ However, this benefit has not been observed in all studies,^{10,11} but rather an increased work of breathing is generally reported. Another

issue affected by position might be ventilation/perfusion mismatch. In some neonates prone positioning might serve to improve this parameter while in others it might be worsened. Another issue complicating the interpretation of position and ventilation was reported by Heinrich et al, who observed that when an infant was prone with the head turned to the left, ventilation in the left lung decreased, while no difference was noted if the head was turned to the right.¹² We were unable to assess any association of head position with arterial blood gas results, because the head position was not recorded in our data. Another complicating issue is whether the abdomen is relatively free or relatively restricted while in the prone position. However, Wagaman et al reported no such effect on lung compliance, tidal volume, or minute ventilation.⁵

Two previous studies, using transcutaneous CO₂ measurements, are consistent with our present observations. Namely, Schwartz et al¹³ studying VLBW infants, and Bozynski et al studying neonates 570 to 1360 grams, found higher transcutaneous CO₂ measurements while in the prone position.¹⁴

We recognize many shortcomings and pitfalls in the present study. Among these, the retrospective nature of the study leaves us uncertain about the timing of the observed changes. Specifically, we are uncertain how soon to expect changes in pH and pCO₂ after making a position change, and we are uncertain if these effects are relatively transient or persist until the position is changed. Also, we are not clear regarding the relevance of head position (to the right vs. to the left) on pCO₂ and pH of prone ELBW neonates. Moreover, we are uncertain regarding whether the relative freedom of the abdomen has an effect on the results. Despite these problems and uncertainties, we maintain that our overall finding can be of value to those who interpret arterial blood gasses of mechanically ventilated ELBW neonates, giving them the anticipation of a minor increase in pCO₂ and decrease in pH, in the prone position.

Continued on page 42...

Table. The effect of body-positioning on pCO₂ (torr) and pH (U) of arterial blood of neonates weighing <1000 g while on conventional ventilation (n=52) or high-frequency ventilation (n=53).

Positioning	Conventional Ventilation		95% CI vs. prone	P Value vs. prone	High Frequency Ventilation		95% CI vs. prone	P Value vs. prone
	Mean	S.D.			Mean	S.D.		
Right Side pCO ₂	49.7	9.7	1.6-5.4	0.0004	47.3	11.9	4.6-8.6	0.0001
Left Side pCO ₂	48.8	9.0	2.6-6.3	0.0001	47.8	10.2	4.2-8.0	0.0001
Supine pCO ₂	48.2	10.1	3.0- 6.9	0.0001	46.0	10.7	6.1- 9.7	0.0001
Prone pCO ₂	53.2	8.6			53.8	13.6		
Right Side pH	7.34	0.08	-0.06 -0.03	0.0001	7.33	0.09	-0.05 -0.03	0.0001
Left Side pH	7.32	0.06	-0.04 -0.02	0.0001	7.32	0.08	-0.05 -0.02	0.0001
Supine pH	7.33	0.08	-0.05 -0.02	0.0001	7.34	0.09	-0.07 -0.04	0.0001
Prone pH	7.30	0.08			7.29	0.09		

The Clinical Utility of Lactic Acid Testing with ABGs in the Neonatal Setting a Case Study

Doug Wilder, RRT

Case

A 19 year old female presented to the hospital with increasing labor pains and delivered an otherwise normal 3 lbs. neonate. The neonate was placed under an infant warmer with an Oxyhood at 100% O₂.

After a period of one hour the patient's respiratory rate increased to 60 with mild retractions noted.

A blood gas was ordered and run on the Roche cobas b 221 < 6 > blood gas system.

The following results were reported:

Parameter	Reported Value	Neonatal Normal Ranges
pH	7.331	7.35 – 7.50
PCO ₂	44.3	35 – 45
PO ₂	225.0	50 – 80
HCO ₃	22.9	22 – 26
tHb	20.5	13 – 22
SO ₂	99.5%	< 90
Glu	60	80 – 120
Lac	6.2	< 2.0

Assessment

The patient has a normal SO₂ of 99.5% normal PCO₂, normal HCO₃, and all electrolytes were in normal range. Based on ABG values and physical appearance, the patient appeared normal with increased respirations attributed to its premature condition. Upon closer review of the ABG results along with the lactic acid level of 6.2 mmol which is three times the upper limits of the normal range, the patient was diagnosed with Infant Respiratory Distress Syndrome. This syndrome increases the breathing rate in response to incomplete lung development characterized by reduced amounts of lung surfactant, cyanosis, the formation of a glassy membrane over the alveoli and pulmonary collapse. As respiration increases inspiratory muscles work harder to provide oxygen. The increased muscle activity results in utilization of glucose and increase in lactic acid in the bloodstream due to the inefficiency of the neonatal liver to convert the lactic acid to pyruvic acid.

Treatment

The patient was transferred to the NICU administered Bicarbonate, Glucose, Surfactant and placed on nasal CPAP overnight. The nasal CPAP was removed the next day.

Conclusion

Lactic acid and glucose as part of a neonatal ABG panel provides greater diagnostic capabilities in assessing and treating Infant Respiratory Distress Syndrome and related conditions.

Recommendation

All NICU blood gas analyzers should have the ability to run lactic acid and glucose like the Roche cobas b 221 < 6 > system. All neonatal blood gas panels should include lactic acid and glucose as a standard of care in the neonatal setting.

Connectivity and Ventilator Technology Improve Patient Outcomes

Facility Report: Anmed Health Medical Center

Physicians at AnMed Health Medical Center do not need to stand at their patients' bedsides in the ICU to check the parameters on their ventilators. They can do so from anywhere they have access to a computer terminal—whether that is in the hospital or on its campuses, their offices, or even their homes during off hours.

Such connectivity is part of the 600-bed, four-hospital system's leading-edge philosophy that has been driving its care since its founding in 1908.

Located on a 16-acre campus near downtown Anderson, AnMed Health Medical Center is a teaching hospital that serves people living and working in eight counties in southwestern South Carolina, an area known as the Upstate, and eastern Georgia.

"Even though a lot of people may never have heard of Anderson, South Carolina, we have always thought of ourselves as leading-edge," says Peggy Deane, RN, Senior Vice President for Patient Care Services, who has been with the health system for 35 years.

As part of its progressive philosophy, the hospital has been working toward a paperless environment. It is already paperless once the patient leaves the hospital, and it expects to reach that goal on the floors within five years.

When it comes to respiratory care, the hospital is well on its way toward its goal of having all medical records be electronic.

Fleet of SERVO ventilators integrated with electronic medical records improving patient care: AnMed Health has 26 SERVO ventilators in its fleet. In early 2005, the hospital's information technology department connected its ventilators to its facility-wide computer system, so that all respiratory records can be produced and stored electronically. Even though the hospital has three generations of SERVO ventilators, it was able to easily integrate the entire fleet.

All information for this article was provided by Maquet, Inc. The views, opinions, and assertions stated by the AnMed staff members in this article are strictly those of the clinicians and administrators, and do not necessarily reflect the views of MAQUET.

The project took less than four months, including building an ethernet port in each ICU patient room so that the ventilators could be connected to the system, says Darrell Hickman, Chief Information Officer for the hospital. Green cables were used for the ethernet to distinguish it from the other cables needed to run critical-care equipment.

The hospital employs a Nursing Informatics Applications Specialist, Sheila McLaurin, RN. After listening to the needs of RTs and physicians, McLaurin was able to program the system so that they could click on just one button and have all the data from the ventilator pop onto the computer screen. "With one click, they can see up to 20 data points," she says. "The old, time-consuming way was to do it one at a time."

"Whatever is on the ventilator is charted in real time," adds Scott Small, RRT, RCP, Clinical Manager for Respiratory Services, who has been with the hospital 12 years.

Electronic medical records help improve care because they save time and reduce chances for errors, Hickman says.

"The closer you push acquisition of data to delivery of care, the better it is because it makes the data more immediate and accurate," he says.

Connectivity allows therapists to spend more time caring for patients, weaning them off ventilators: The hospital administrators are convinced that the connectivity between the ventilators and information systems has improved the accuracy and efficiency of its respiratory services, and thus, patient care throughout the health system.

Most importantly, Small says, the connectivity allows the respiratory therapists to spend more time caring for patients and less time charting numbers. "It has turned our therapists back into therapists instead of data-entry people," he says.

"Because the data is entered automatically, the therapists can spend more time caring for patients and weaning them off the ventilators."

The electronic system also allows Small to be more efficient as



An RT views his patient's respiratory data from a computer in his office



Caroline Cox, respiratory therapist, and Dr. Charles Thompson, pulmonologist, discuss the patient's ventilator data in the ICU

a clinical manager—he is responsible for 11 respiratory therapists in the department, which has 77 full-time equivalents.

"I can sit at my desk in the morning and find out what every patient is on without having to visit all four ICUs. I can prioritize who I need to see first, and I am better prepared when I do go see the patients," he says. AnMed has 46 intensive-care beds: 19 in its medical ICU; 15 in coronary care; six in cardiovascular; and six in neuro-ICU. Its emergency unit sees nearly 85,000 patients a year.

The hospital's advanced information system in conjunction with the SERVO ventilators also allows physicians to make more informed clinical decisions, which have improved patient outcomes, Small says. From anywhere in the system, a physician can see trend data from the last 12 hours and decide whether to remove a patient from the ventilator. "The system provides a much better picture of the patient's overall status than what a physician can see in a few minutes during rounds," Small says.

Network allows pulmonologists to respond faster, more efficiently: AnMed Health has respiratory management protocols in place that allow its therapists to make some adjustments to ventilators as needed. When physicians need to make adjustments, they can look at the patient's respiratory parameters from any computer terminal connected to the network system. Not having to wait for the physician to get to the ICU has resulted in less time on the ventilator for many patients, Small says.

Physicians often will stop Garrick Chidester, Vice President for Network Development, and tell him they appreciate having the



"They [the doctors] say the connectivity makes it possible for them to get the data they need to make more informed clinical decisions faster and more efficiently."
Garrick Chidester, Vice President for Network Development



"...we have always thought of ourselves as leading-edge."
Peggy Deane, RN, Senior Vice President for Patient Care Services

ability to connect from wherever they are when they are paged.

"They say the connectivity makes it possible for them to get the data they need to make more informed clinical decisions faster and more efficiently," he says. "In the end, the patients are the ones who benefit the most."

The connectivity also makes it easier for the hospital to recruit respiratory therapists because most RTs want to work where they do what they were trained for, not where they have to be clerks much of their shift, Small says. "I have always believed that we were able to recruit RTs here because we give RTs more input, more involvement in the care of patients," agrees Chidester, who has been with the health system for 23 years.

The vast majority of ventilator patients at AnMed Health can be weaned in about three days, says Wanda Perry, RRT, RCP, M.Ed, who has been Director of Respiratory Care for the last four years. That is a low length of stay, she says.

While connectivity clearly has helped to reduce ventilator stays for many patients, Perry says, the functional capabilities of the SERVO-i ventilators they have in their fleet also play an important role. The Open Lung Tool (OLT) is one such advantage with SERVO technology.



Wanda Perry, RRT, RCP, M.Ed, Director of Respiratory Care for the last four years, stands by a SERVO-i, which has helped the hospital to improve outcomes



"I can prioritize who I need to see first, and I am better prepared when I do go see the patients." Scott Small, RRT, RCP, Clinical Manager for Respiratory Services

Open Lung Tool allows AnMed to take advantage of window of opportunity for weaning: SERVO-i ventilators, the newest in the SERVO product line by MAQUET, have a unique Open Lung Tool (OLT) that provides the clinicians with the parameters they need to more easily perform lung recruitment maneuvers. Its graphic user interface provides information about end inspiratory pressure (EIP) and PEEP pressures, and inspiratory and expiratory tidal volume as well as dynamic compliance. Seeing these parameters, the clinician can analyze the extent of opening and closing the alveoli.

"There's a window of opportunity to take the patients off the ventilator and you don't want to lose that," Perry says. "The OLT allows us to take advantage of that opportunity."

Thirty-five patients were studied from January through June 2006. By utilizing OLT and a lung recruitment protocol, the AnMed Health team noticed a significant decrease in peak inspiratory pressure (PIP) and a significant increase in dynamic compliance; no changes in heart rate or arterial blood pressure were noted. "Our outcomes data validates using a lung

Anmed Health Lung Recruitment Data
January 1 – June 30, 2006

Parameters	Pre-Lung Recruitment	Post-Lung Recruitment	p-value (t-test)
PIP (Mean)	29.86	26.74	0.002
PEEP (Mean)	7.89	11.31	0.0001
Cdyn (Mean)	27.49	33.30	0.001
(A-a)D02 (Mean)	329.59	206.84	0.0001
RR (Mean)	15.74	17.20	0.05
HR (Mean)	96.00	96.37	0.64
Art. BP Syst (Mean)	124.57	125.31	0.86
Art. BP Diast (Mean)	62.20	64.46	0.26

recruitment maneuver as a ‘best practice’ strategy during mechanical ventilation,” Perry says.

SERVO-i’s OLT takes the guesswork out of lung recruitment, making it a safer and shorter procedure, says Small, who reports on the hospital’s use of the tool at meetings of respiratory care professionals.

In his presentations, Small tells colleagues the OLT is like a GPS guide to ventilating pressures. “It’s really a map that tells us what ventilating pressures we need to be ventilating our patients at. I could have found them without the OLT but it would have been a much longer process,” he says. “The OLT takes the guesswork out and that’s what makes our job so much easier now.”

Shorter ventilator stays result in fewer respiratory

complications and lower costs: The ability to wean patients from ventilators more quickly is critical because every day a patient is on a ventilator, the chances of complications grow exponentially, Perry says. Reduced ventilator stays mean a lower rate of ventilator-associated pneumonia, a common complication of mechanically ventilated patients. “We have a very low rate of ventilator-associated pneumonia because we are able to get our patients off the ventilator quickly,” Perry says.

The reduction in ventilator time also is cost-saving because patients who are on ventilators for a length of time are more likely to need medical procedures such as tracheotomies, Perry says. Tracheotomies are one of the most expensive, diagnostic related groups (DRGs) in any hospital, Small notes. “The average tracheotomy patient is in the hospital for more than 40 days, so if we can eliminate the patient getting a tracheotomy, it’s a significant savings to the healthcare system.”

Because visitors to Anderson see a small community, they are often surprised to learn it is home to a major medical system offering leading-edge technology, Chidester says. However, he says, “If you just look at our respiratory department, it’s been a consistent philosophy for us to be cutting-edge.”

“Having the connectivity and the OLT,” Small adds, “I know we are positively affecting patient outcomes.”

Comparison of Trigger Response Time With and Without a Simulated Airway Leak

Cyndy Miller RRT, data collected by Jim Seeley, RRT

Introduction

The Newport HT50 Ventilator offers technological advances that enable it to handle sicker, more challenging pediatric and adult patients in comparison with other portable ventilators. It provides more reliable support of the patient's inspiratory effort and ventilation needs which can impart greater overall synchrony between patient and ventilator throughout the entire breath cycle. The HT50 employs pressure triggering. Some have proposed that flow triggering is superior to pressure triggering on a portable ventilator. This is an oversimplification of the issue.

PEEP (Positive End Expiratory Pressure) is a clinical necessity for many patients who are ventilated with portable ventilators and nearly every one of these patients has an airway leak, usually by design, in order to facilitate speaking and protect the trachea from erosion that would be caused by a tightly fitting tracheostomy tube.

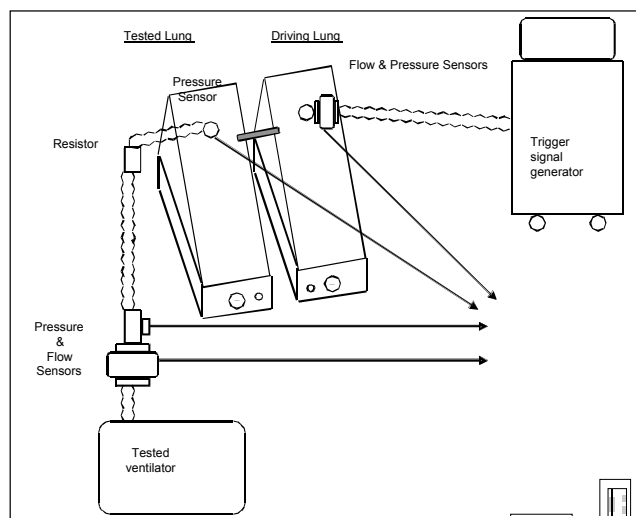
If this elevated end expiratory airway pressure is not held constant by the ventilator between breaths because an airway leak causes airway pressure to fluctuate during the exhalation period, the pressure or flow-triggering system may mistake the unstable signal for a patient trigger effort. This is called auto-triggering. In this case, the user has two choices: eliminate the use of PEEP (in spite of clinical necessity) or adjust the trigger setting so that it is insensitive to patient effort in order to prevent auto-triggering caused by the unstable signal.

Whether it is flow or pressure triggered, a ventilator should respond reliably and quickly to the patient's inspiratory trigger effort in real life situations that include both the use of PEEP (positive end expiratory pressure) and the presence of airway leaks. It is possible to provide a responsive triggering system, which can co-exist with PEEP and airway leaks using either a flow trigger or pressure trigger signal but neither signal guarantees good results in and of itself under these conditions.

We propose that it is the combination of leak compensation, baseline pressure (PEEP) management and trigger algorithm employed by a ventilator that either allows it to meet the triggering goal or keeps it from meeting the triggering goal when leaks and PEEP are present.

Purpose

The purpose of this investigation was to compare the trigger response times during spontaneous breathing (with PEEP and both with and without a simulated leak) of four portable ventilators: Newport HT50 Ventilator (pressure trigger and leak compensation/baseline pressure management), Pulmonetic LTV Ventilator (flow trigger and leak compensation), PB Achieva Ventilator (flow trigger), and PB LP10 Ventilator (pressure trigger).



Methods

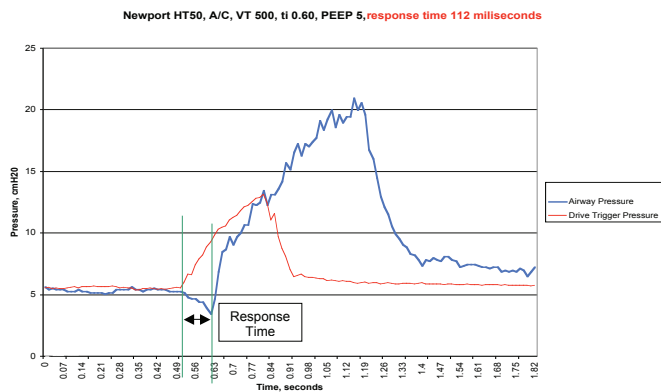
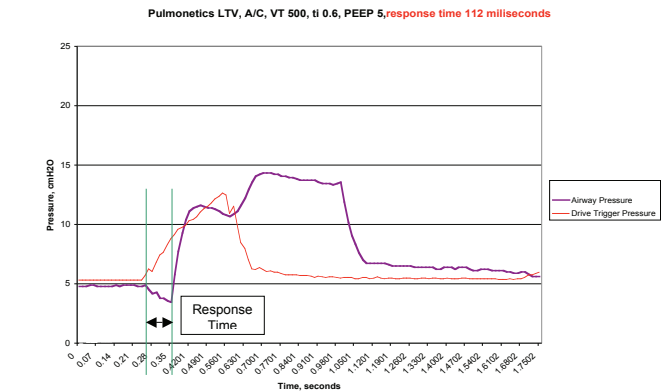
A drive-dependent (labeled driving and tested above) spontaneous breathing lung was used to model patient simulations. Flow and pressure sensors were used to electronically record the pressures at the driving lung, which represents the trigger effort, and the tested lung, which represents the tested ventilator response to trigger effort. ASTM standards were used to establish the simulated patient compliance and resistance levels as well as the tested ventilator settings for breath delivery. PEEP of 5 cmH₂O was added in every simulation. Each ventilator was tested with and without a simulated physiologic airway leak of 2.5 L/min at 25 cmH₂O airway pressure. Before each recorded measurement, trigger was adjusted to the point of auto-triggering, then backed off to the most sensitive setting without auto-triggering and allowed to stabilize for 2 minutes. The driving and tested pressure waveforms were superimposed so as to be able to measure the time from when the driving ventilator started the trigger effort

Cyndy Miller is Director Clinical Education, Jim Seeley is Product Manager, Newport Medical Instruments.

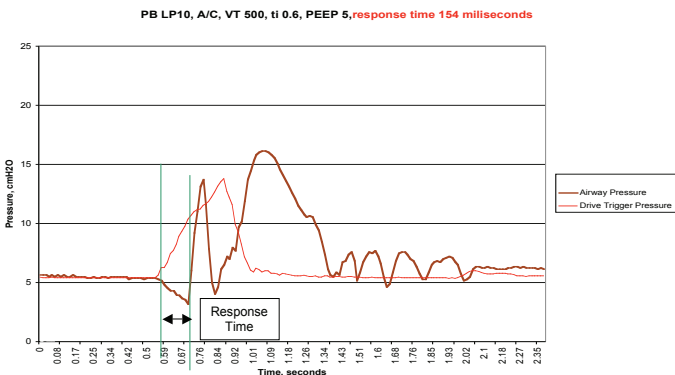
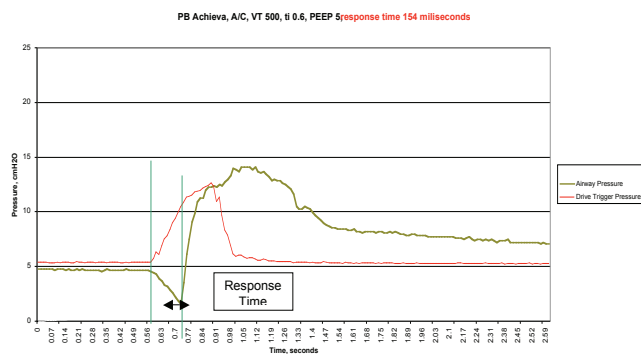
and when the tested ventilator responded to the effort. This duration of time, from trigger effort to tested ventilator response was recorded as Response Time.

Results

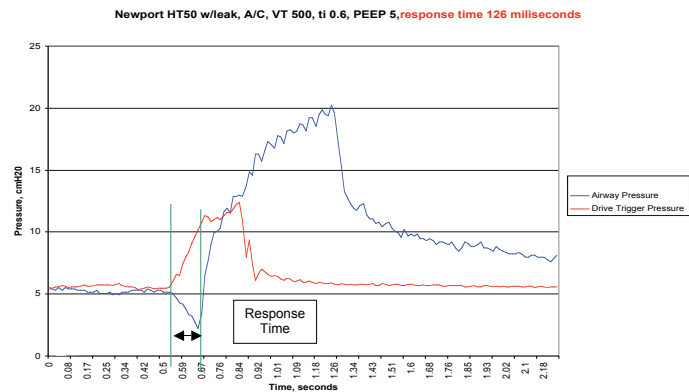
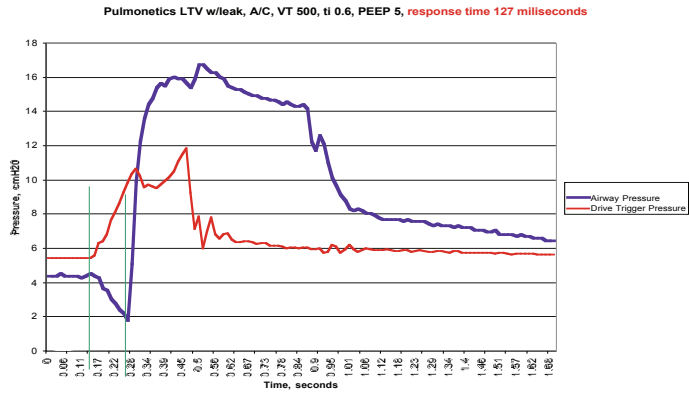
Test results for Pulmonetic LTV and Newport HT50 with “no leak.”



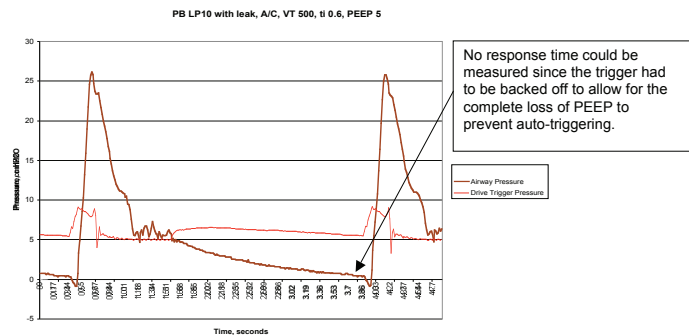
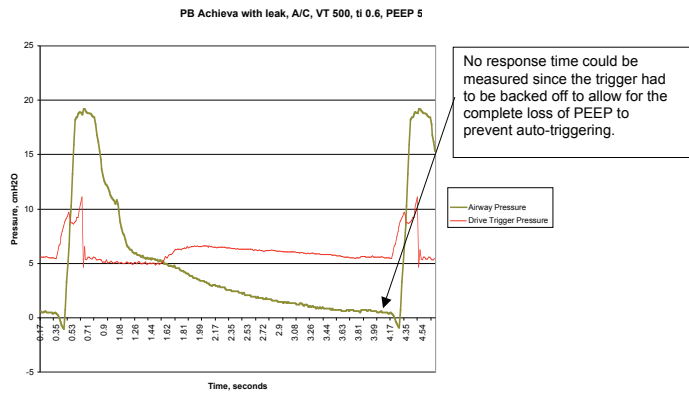
Test results for PB Achieva and PB LP10 with “no leak.”



Test results for Pulmonetic LTV and Newport HT50 with “leak.”



Test results for PB Achieva and PB LP10 with “leak.”



Summary of Results

Ventilator	Trigger Signal	Leak Compensation	Response Time (no leak)	Response Time (with leak)
Newport HT50	Pressure	Yes	112 ms	126 ms
Pulmonetic LTV1000	Flow	Yes	112 ms	127 ms
PB Achieva	Flow	No	154 ms	N/A (could not test)
PB LP10	Pressure	No	154 ms	N/A (could not test)

The Newport HT50 with pressure triggering and the Pulmonetic LTV1000 with flow triggering had identical response times when no leak was present and nearly identical response times with a leak present (HT50 was slightly faster). They both provided effective leak compensation/baseline pressure management and in spite of the fact that they used different signals for triggering, they equally met the clinical goal of providing effective and reliable response to trigger effort with PEEP in use, with or without the presence of a leak.

The PB LP10 with pressure triggering and the PB Achieva with flow triggering had identical response times when no leak was present but the response time was 42 milliseconds longer than the HT50 and LTV1000 Ventilators. Neither the PB LP10 with pressure triggering or the PB Achieva with flow triggering was able to meet the clinical goal of providing effective, reliable triggering with a leak present because neither was able to maintain a stable baseline pressure of 5 cmH₂O under these conditions. The pressure and flow trigger settings had to be adjusted to a less sensitive value to prevent auto-triggering when a leak was present.

The speed and reliability of the trigger response on the four ventilators tested was not based on which signal, pressure or flow, that is employed for recognition of patient effort. The two ventilators that triggered faster were those with newer, more advanced technology. The newer technology also allowed these ventilators to trigger quickly and reliably with a clinically relevant leak present.

The fact that pressure triggering systems can respond as quickly, or in some cases, more quickly than flow triggering systems is supported by a number of peer reviewed journal articles.

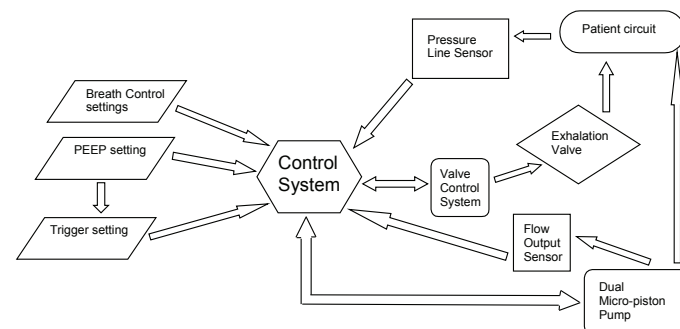
This author suggests that ventilators should be evaluated based on performance characteristics due to technological hardware and software design rather than on the type of signal used for triggering.

Technical Description of Newport HT50 Ventilator Technological Advances that Facilitate Fast Reliable Triggering

Newport does not contend that either flow triggering or pressure triggering is best, but that either can be used in conjunction with today's technology to provide a ventilator that responds quicker and supports better than more basic ventilators. Newport has chosen the pressure trigger for the HT50 Ventilator because of technology that enables the pressure trigger to respond quickly to the patient's effort while facilitating a more robust system that stands up to the daily rigors found in pre or post ICU use.

The HT50 Ventilator has a built-in (internal), servo-controlled, dial in PEEP (earlier defined as Positive End Expiratory Pressure) feature while some other ventilators still use an external, detachable PEEP valve. The external, circuit-based PEEP valve must be disassembled and reassembled for cleaning, then set to an appropriate position for a given patient. There is chance for error during assembly and during adjustment and either can result in providing the patient with a different level of PEEP than prescribed by the physician. Ventilators with external PEEP valves do not "know" where the PEEP is supposed to be set at (since the PEEP is not part of the ventilator only part of the breathing circuit), so the ventilator has no facility for alarming if PEEP has changed due to a circuit assembly or adjustment problem.

Following is a technical description of how the Newport HT50 Ventilator bias flow and servo control of PEEP (including leak compensation) function.



After setting up the HT50 ventilator with a new breathing circuit for patient use, the user performs an exhalation valve calibration. The calibration is an automatic < 45 second process that has two important functions: 1) It tests the circuit assembly for leaks. 2) It performs a 6 point pressurization of the circuit in order to establish a pressure linearization curve for accurately servo controlling PEEP, Pressure Control and Pressure Support levels during patient ventilation.

The user inputs breath control settings, including PEEP and Trigger, using controls on the front panel. A two step process for each control change minimizes the possibility of accidental changes. The dual micro-pistons which are used to generate the airflow to the patient and also to generate the pressure in the exhalation valve are feedback controlled by the CPU according to the user input breath control variables. During inspiration, the exhalation valve is closed and all airflow from the HT50 is delivered to the patient, allowing for monitoring delivered volumes for all breaths, mandatory and spontaneous. During exhalation, when PEEP is set > 0 cmH₂O the micro-pistons pressurize the back side of the exhalation valve diaphragm to

generate the user-set PEEP level (feedback controlled by a proximal pressure transducer) in the breathing circuit. The micro-pistons also provide ~7 L/min of continuous flow through the breathing circuit to keep baseline pressure stable and compensate for airway leaks. Two pressure transducers (one at the mainflow outlet and one at the proximal port) monitor pressure in the breathing circuit at all times. If during exhalation the PEEP monitored in the circuit differs from the user set PEEP value, the CPU changes the pressure on the back side of the exhalation valve to correct the PEEP value that is applied to the patient. If the CPU cannot successfully correct the PEEP value due to a massive leak or obstruction, alarms (low or high baseline pressure) result with a message in the monitor window indicating the nature of the alarm condition. The Trigger (Ptrig), which is also user set on the front panel, is a pressure setting with a resolution of 0.1 cmH₂O. The Ptrig setting (minimum setting = 0 cmH₂O) represents the amount of negative pressure change from the user set baseline that will result in a recognition of patient trigger effort.

Pressure monitored through the proximal port is displayed on the pressure gauge continuously. Peak, mean and baseline (PEEP) pressures may be digitally displayed in the monitoring window. During patient inspiration, all airflow to the patient is monitored, allowing for tidal volume monitoring from breath to breath and also, for minute volume monitoring. The user sets high and low minute volume alarms. A low minute volume alarm results in back up ventilation, which resets when the patient's minute volume reaches the low alarm setting + 10%.

Using a closed, feedback controlled system for PEEP, pressure support and pressure control increases patient safety because appropriate alarm thresholds may be set to alert a caregiver to a change in patient compliance due to a mucus plug (low minute volume) or a change in leak (high inspiratory minute volume alarm, low baseline alarm or low peak airway pressure alarm).

If the patient develops a mucus plug while being ventilated in pressure control, the airway pressure waveform will not change; therefore, the peak pressure alarm will not be violated. Since delivered volume will decrease when the patient develops a mucus plug in pressure control, a low minute volume alarm will be violated and alert the caregiver. A ventilator that offers pressure support and/or pressure control but no volume monitoring cannot provide the same level of patient safety. If secretions cause a decrease in tidal volume on a ventilator without breath by breath volume monitoring, the ventilator has no way of detecting the problem or of warning the caregiver of the resulting hypoventilation.

Conclusion

Results demonstrate that under conditions simulated by this spontaneous breathing lung model, it is not the type of signal used (flow or pressure) by the ventilator for triggering that establishes the speed and reliability of the trigger response. Instead, the technological aspects of ventilator design determine whether or not a ventilator with pressure trigger or flow trigger meets the clinical goal of providing fast and reliable trigger with PEEP in the presence of a leak.

References

- 1 R. Branson. Understanding and implementing advances in ventilator capabilities. Respiratory system, Current Opinion in Critical Care; February 2004,10(1):23-32.

- 2 R Goulet, D Hess and RM Kacmarek. Pressure vs flow triggering during pressure support ventilation. Chest 1997;111;1649-1653.
- 3 R. Branson. Understanding and implementing advances in ventilator capabilities. Respiratory system, Current Opinion in Critical Care; February 2004,10(1):23-32.

Prone...Continued from page 34

References

- 1 Itakura Y, Ogawa Y. Effect of body position on tidal volume and minute ventilation in very low birth weight infants. Acta Paediatr Jpn. 1998;40(6):555-557
- 2 Heaf DP, Helms P, Gordon I, Turner HM. Postural effects on gas exchange in infants. N Engl J Med. 1983;23;308(25):1505-1508
- 3 Vaivre-Douret L, Ennouri K, Jrad I, Garrec C, Papiernik E. Effect of positioning on the incidence of abnormalities of muscle tone in low-risk, preterm infants. Eur J Paediatr Neurol. 2004;8(1):21-34
- 4 Symington A, Pinelli JM. Distilling the evidence on developmental care: a systematic review. Adv Neonatal Care. 2002;2(4):198-221
- 5 Wagaman MJ, Shutack JG, Moomjian AS, Schwartz JG, Shaffer TH, Fox WW. Improved oxygenation and lung compliance with prone positioning of neonates. J. Pediatr 1979;94:787-791.
- 6 Hutchison AA, Ross KR, Russell G. The effect of posture on ventilation and lung mechanics in the preterm and light-for-date infants. Pediatrics 1979;64:429-432.
- 7 Wolfson MR, Greenspan JS, Deoras KS, Allen JL, Shaffer. Effect of position on the mechanical interaction interaction between the rib cage and abdomen in preterm infants. J Appl Physiol 1992;72:1032-1038
- 8 Maynard V, Bignall S, Kitchen S. Effect of positioning on respiratory synchrony in the non-ventilated pre-term infants. Physiother Res Int 2000;5:96-110
- 9 Crane LD, Snyder JE, Knight P, Phillips JB, Cassady G. Effects of position changes on transcutaneous carbon dioxide tension in neonates with respiratory distress. J Perinatol. 1990;10(1):35-37
- 10 Fox RE, Viscardi RM, Taciak VL, Niknafs H, Cinoman MI. Effect of position mechanics in healthy preterm newborn infants. J Perinatol 1993;3:205-211
- 11 Levy J, Habib RH, Liptsen E, Singh R, Kahn D, Steele AM, Courtney, SE. Prone versus supine positioning in the well preterm infant: effects on work of breathing and breathing patterns. Pediatr Pulmonol 2006;41:754-758
- 12 Heinrich S, Schiffmann H, Frerichs A, Klockgether-Radke A, Frerichs I. Body and head position effects on regional lung ventilation in infants: An electrical impedance tomography study. Intensive Care Med. 2006;32:1392-1398
- 13 Schwartz FC, Fenner A, Wolfsdorf J. The influence of body position on pulmonary function in low birthweight babies. S Afr Med J 1975;49:79-81
- 14 Bozynski ME, Naglie RA, Nicks JJ, Burpee B, Johnson RV. Lateral positioning of the stable ventilated very-low-birth-weight infant. Effect on transcutaneous oxygen and carbon dioxide. Am J Dis Child. 1988;142(2):200-202

Waveform Analysis: Assessing the “Trigger” Phase

Paul Garbarini

It seems like yesterday that when rounding on ventilator patients in the ICU, patients commonly were unable to trigger ventilator breaths. Current generation ventilator trigger systems impose less work on the patient during the trigger phase. Microprocessor controlled valves, improved pressure transducers, proximal sensors and flow triggering systems reduce the work to trigger and improve response times. My personal observations are that the incidence of auto-cycling has increased with the advent of improved triggering systems.

We'll use the following waveforms to illustrate assessment of the triggering phase:

In figure 1, the top violet waveform is flow and the bottom yellow waveform is pressure. The mode is Volume Control. Missed patient triggers are at the red arrows.

Flow waveform - note the 'seesaw' up & down flow pattern w/o breath delivery (pt. is only moving gas in circuit, not triggering)

Pressure waveform - note the negative deflections (below PEEP/'dips' w/o breath delivery.

Autopeep - if present, pt must overcome autopeep to trigger. Consider titrating PEEP upwards to counterbalance autopeep and assess whether the patient can trigger with additional PEEP.

Are the patient efforts too weak or ineffective due to paradoxical respiratory pattern? Look and feel - look at chest/abdomen. Place thumb on sternum and pinky on abdomen while looking at waveforms. Assess sedation and respiratory drive.

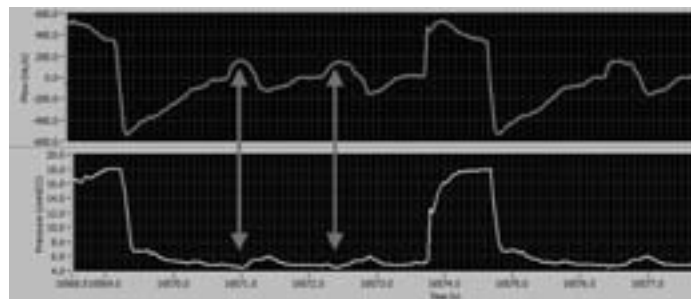


Figure 1. Assessing Missed triggers

In figure 2, the mode is Pressure Control in a passive patient with a set control rate of 12. The time scale is a 10 second sweep so there should be only 2 breaths delivered in 10sec. Note there's no deflections or dips during the expiratory phase for the 1st 4 breaths. The last breath is clearly patient triggered as there is a clear negative deflection in pressure immediately prior to breath delivery.

Increase the trigger sensitivity. Whether utilizing a pressure or flow trigger, this means lowering the setting (to a less negative value if pressure trigger or a lower 'flow trigger' setting if flow trigger).

Consider switching to a flow trigger as these systems impose less work than flow trigger systems, though current generation ventilators which allow for proximal pressure triggering can perform quite well.

Check for leaks. If the PEEP level is downward sloped during the expiratory phase, check for leaks or a malfunction/misalignment of the expiratory valve if applicable. If leaks are present and cannot be resolved, set the trigger to less sensitive values to compensate for leaks. This is especially true for flow triggered systems.

Look at EKG /SpO2 waveforms. Does triggering match heart rate - cardiac pulsations/balloon pumps can cause autocycling due to pressure changes in the chest.

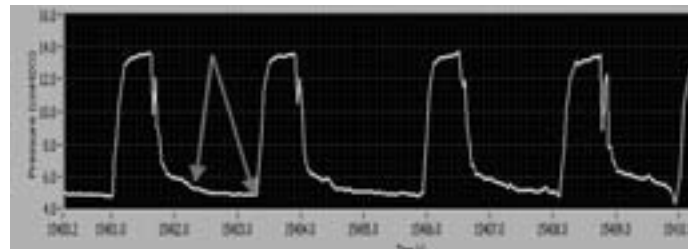


Figure 2. Autocycling

The author is Clinical Manager, Hamilton Medical.

Features of Asthma Management: Quantifying the Patient Perspective

John Haughney, Monica Fletcher, Stephanie Wolfe, Julie Ratcliffe, Roger Brice, Martyn R. Partridge

Abstract

Background: In the management of asthma, features of care important to patients may not be fully appreciated. This study quantifies the importance of different features of asthma management from the patient perspective. This may assist in the development of personalised management strategies.

Methods: We used the technique of discrete choice experiment (DCE). Patients over 18 years of age with asthma, prescribed and taking medicine at step 3 of the UK guidelines were recruited from 15 general (family) practices in three areas of the UK. 147 evaluable questionnaires were returned from a total of 348 sent out. The outcome measures were the relative importance to patients of features of asthma management and the impact of changes in asthma management, as measured by utility shift between the features tested.

Results: The largest shift in mean utility values was recorded in “number of inhalers” and “use of inhaled steroid.” Use of a personal asthma action plan was ranked next highest.

Conclusions: This study suggests that adults with moderate or severe asthma would trade some improvements in symptom

relief in favour of, for example, simpler treatment regimens that use as few inhalers as possible and a lower dose of inhaled steroid.

Background

Patient “self management” or “self care,” a concept that enables patients to take a guided but ultimately personal involvement in the management of their condition, is an increasingly debated element of healthcare provision. It is particularly relevant as the prevalence of long term conditions increases and growing numbers of people desire a more active role in their own care with a less paternalistic approach from healthcare professionals.¹ Effective self care has the potential to improve clinical outcomes and reduce use of healthcare resources.^{1,2}

Asthma is an ideal condition in which to strive for improved patient outcomes by optimising self management because it typically fluctuates over time, with symptoms and exacerbations that can potentially be minimised with self monitoring and appropriate adjustment of treatment.^{3,4} Self management of asthma is currently suboptimal in many patients, with around 50% self managing in ways that differ from recommended guidance.⁵⁻⁷

A key step in improving the self management of asthma is to understand what patients consider important. Patient education programmes designed to improve self care have traditionally centred on what health professionals consider to be important, for example, lung function, asthma symptoms and bronchodilator use in asthma.⁸ Previous research has shown that patients have different perceptions of asthma compared to health professionals and that education tailored to meet patients’ perceptions is more likely to change behavior.⁷

This study was designed to quantify the relative importance of features of the management of asthma from the patients’ perspective. We used discrete choice experiment methodology, a type of conjoint analysis that has been shown to be a rigorous survey technique for eliciting preferences.⁹ It is increasingly being used to identify patient and public preferences for health care.^{10,11} The technique allows respondents to choose their preferred option between hypothetical scenarios designed to reflect the different attributes that real world decisions would

John Haughney is with the Department of General Practice and Primary Care, University of Aberdeen; Monica Fletcher is Chief Executive, Education for Health, Warwick; Stephanie Wolfe is Respiratory Nurse, Thorpewood Medical Group, Norwich. Julie Ratcliffe is with the department of Health Economics and Decision Science, University of Sheffield; Roger Brice is Research Director, Adelphi Group Ltd, Macclesfield; Martyn Partridge is Chair in Respiratory Medicine, Imperial College, London, UK. The authors wish to thank Jill Whatling for help with designing the study, Adrian Vickers for assistance with the principal analyses and Amanda Lee for additional statistical analysis. They also thank Susan Mayor for editorial support during development of the manuscript. The authors have several competing interests. Please see BioMed Central under the name of the article for a list. This study was funded by an unrestricted educational grant from AstraZeneca, the research was carried out entirely independently of the funders, who had no part in the design, administration, analysis or publication plan for the study. Reprinted from BioMed Central, BMC Pulmonary Medicine, © 2007 Haughney et al., licensee BioMed Central Ltd. This is an open access article distributed under the terms of the Creative Commons Attribution License.

Attribute	Levels	Description	Constraints
Symptom relief provided by your treatment	<ul style="list-style-type: none"> ➤ Completely ➤ Mostly ➤ A little 	ORDINAL	Completely <ul style="list-style-type: none"> > Mostly > A little
Inhaled steroid dose	<ul style="list-style-type: none"> ➤ Always a low dose ➤ High dose when required but generally as little as possible ➤ High and regular steroid use 	NOMINAL (with constraints)	Always low > Always high (no other assumptions made)
Use of a written personalised asthma action plan (PAAP)	<ul style="list-style-type: none"> ➤ Full written instructions are provided by your doctor or nurse on how to recognise worsening asthma and how to alter your therapy yourself ➤ Brief written note is provided on how to take your medication ➤ No written instructions are provided 	NOMINAL	None
Asthma crisis management	You are encouraged to: <ul style="list-style-type: none"> ➤ Manage an asthma crisis yourself whenever possible ➤ Attend your local GP in the event of an asthma crisis ➤ Attend hospital in the event of an asthma crisis 	NOMINAL (with constraints)	GP>Hospital Yourself>Hospital (no assumption on Yourself v GP)
Number of different inhalers	<ul style="list-style-type: none"> ➤ A single inhaler is provided to you which contains all the inhaled medication you need for the management of your asthma ➤ No more than two inhalers are provided for the management of your asthma ➤ Three inhalers are provided to you for the management of your asthma 	ORDINAL	1>at most 2>3
Controlling your asthma symptoms	You are encouraged to: <ul style="list-style-type: none"> ➤ Change your own therapy in response to changes in your symptoms without consulting a doctor or a nurse ➤ Speak to a doctor or nurse before making changes to treatment 	NOMINAL	None

Table 1: Attributes and levels included in the study and constraints applied prior to analysis

contain, and to make trade offs between these attributes to reveal their preferences. This technique of revealing preference through choice is a truer representation of real life decision-making and as such may be a better tool for establishing preference than data based on the ranking or rating of individual components of asthma management.¹²

Characteristics	Mean (SD) or n (%)
Age (missing=1)	53.2 (16.2)
Male gender	48 (32.7)
Asthma duration	
< 12 months	0
1 to 4 years	14 (9.5)
5 to 10 years	33 (22.4)
More than 10 years	100 (68.0)
English is first spoken language (missing=2)	143 (97.3)
Difficulty of questionnaire (missing=2)	
Very	4 (2.7)
Moderately	20 (13.8)
Slightly	29 (20.0)
Not	92 (63.4)

Table 2: Descriptive characteristics of respondents (n = 147)

	Responder		Non-responder	
	Number	Mean (SD) or percentage	Number	Mean (SD) or percentage
Age	147	53.2 yrs (16.2)	201	45.2 yrs (15.9)
Female Gender	99	67%	129	64%

Table 3: Characteristics of responders compared to non-responders

A clearer understanding of such preferences may help healthcare professionals tailor an acceptable personalised management of asthma with their patient and consequently move nearer to controlled asthma.¹³

Methods

We carried out a discrete choice experiment (DCE) to determine the characteristics of long term asthma management that patients consider most important, requiring them to make choices between hypothetical scenarios and thus reveal their preferences.

To ensure a reasonable spread both geographically and socioeconomically, 15 general practices from three geographical areas of the United Kingdom (UK) (West of Scotland, Norfolk, Gloucestershire), with a total population of 116,000 patients, took part in the study. Nursing staff at each practice identified all patients on treatment step 3 or above in the British Asthma Guidelines (regular use of inhaled steroid and other therapies)¹⁴ who had received a prescription for asthma in the last 12 months, were over 18 years of age, and were believed to be able to understand and complete the questionnaire used in the study. The patients identified were included in a practice held "asthma register." The diagnostic criteria for inclusion in this register were likely to be variable. In many cases, a diagnosis of asthma will have been given and accepted without formal, objective evidence of asthma. This scenario is consistent with standard UK practice. Patients on UK asthma guideline treatment step 3 or above were chosen because their asthma management, by definition, is more complex than those at treatment steps 1 and 2.

Attribute	Individual Level RI	Aggregate Level RI
Number of Different Inhalers	21.9%	29.3%
Inhaled Steroid Dose	20.3%	21.1%
Use of a Written PAAP	17.0%	12.3%
Asthma Crisis Management	15.2%	15.0%
Controlling Your Asthma Symptoms	14.4%	6.1%
Symptom Relief Provided by Your Treatment	11.3%	16.3%

Table 4: Relative Importance (RI) of Attribute Ranges Tested

A sample was selected by allocating each patient a unique identification number and then by the use of a random number generator computer program. The number selected from each practice varied according to total eligible patient numbers, with a maximum of 30 patients per practice. A total of 348 questionnaires were mailed. A traditional power calculation is not appropriate in calculating a sample size for a DCE, where rules of thumb and experience drive the sample size decision. The accepted rule of thumb for our experimental design (nine tasks and two alternatives per task per respondent and no more than three levels in any one attribute) is that the sample size should be in excess of 83.¹⁵

The questionnaire presented respondents with nine pairs of choices (see figure 1 and additional file 2)—the discrete choice experiment. Socio-demographic information was also collected.

The key attributes for this discrete choice experiment were drawn from a previous study which included qualitative interviews with more than 400 patients with asthma.¹⁶ We chose six attributes highlighted by patients as being the most important considerations in their long term asthma management. These were: importance of gaining relief of asthma symptoms from treatment; dose of inhaled steroid; the availability and content of a written personalised asthma action plan; locus of crisis (exacerbation) management; number of inhalers prescribed for routine use; and response to a deterioration.

We chose and assigned what we considered to be plausible and realistic levels for the six attributes that represent scenarios commonly found in asthma management. Table 1 lists the levels chosen for each of the attributes.

A design program used in the statistical software SAS¹⁷ was used. This software produces a manageable number of combinations of attributes and their respective levels (or scenarios) to develop a survey questionnaire, balancing the statistical requirements with the need to avoid overburdening the respondent with work. A total of nine pairs of choices were produced. For each pair of scenarios, respondents were asked to indicate the one they would most prefer when considering how their asthma should be managed (see figure 1).

Using the techniques described in additional file 3, the overall relative importances of attributes at both individual and aggregate (group) levels, and shifts in utility values between each level within each attribute were calculated (see additional files).

Results

A total of 148 questionnaires were returned after one reminder, of which one was returned blank, from a total of 348 sent out, giving a useable response rate of 43%. Table 2 summarises the sociodemographic characteristics of the study population, while table 3 compares basic characteristics of responders with non-responders. Non-responders, by definition, did not consent to their involvement in the study. Consequently, a more detailed comparison of characteristics or features of responders and non-responders was not possible. The Relative Importance results are presented in Table 4. The outputs shown throughout are the means of the parameters calculated at the level of individual respondents. The means at aggregate level demonstrating relative importance were also calculated and are included for comparison, displaying where a non-homogenous response occurs. Figure 2 shows the importance that respondents placed on changes between different levels within-attributes. The degree of importance is seen by changes in utility values for levels within the attributes. All 11 successive within attribute transitions were statistically significant ($P < 0.05$), with the single exception of changing the management of an asthma crisis from “yourself” to “visiting a GP/nurse.” Those changes with the highest relative negative impact on respondents’ views of their asthma management were: changing from no more than 2 to 3 inhalers; change in steroid dose from “low but high when needed” to “always high”; being encouraged “to visit a hospital for crisis management” rather than being encouraged “to manage yourself” or “attend the local GP surgery”; symptom relief provided by current treatment changing from “completely” to “mostly”; and changing from 1 to 2 inhalers.

Discussion

The study emphasizes the importance of keeping treatment regimens simple. The results showed that adults with moderate or more severe asthma considered that a simple treatment regimen was the most important consideration in the longterm management of their condition, rather than symptom control without compromise. For example, two of the top five highest utility shifts between levels related to the number of inhalers they needed to use. Changing from no more than two to three inhalers had the highest relative negative impact on respondents’ views of their asthma management. While noting the caveats of the relative importance analysis, number of inhalers was ranked the most important attribute of asthma management at both the aggregate (29.3%) and individual levels (21.9%), suggesting a reasonably homogenous view.

This preference for simpler treatment and fewer inhalers confirms in a more systematic and rigorous way preferences for “fewer drug treatments” and “just one inhaler” reported in a previous pan-European study⁷ and confirms the findings from patient interviews in our previous study.¹⁶ Asthma is only one part of people’s lives and treatments that may need to be taken for decades and should be offered in the simplest format. Willingness to pay from the patients’ perspective—another factor that may influence treatment preference—was not addressed in this study; the cost of therapy to patients may be less important in the UK than in other healthcare settings; it was not rated highly as an issue in our qualitative study.¹⁶

The factor that patients rated as being of next highest relative importance, and which had the second greatest utility shift, was the dose of inhaled steroid. Scope for lowering the steroid dose

When considering your asthma management, if you were offered the choice between scenario A or B, which would you most prefer?

Choice 2	A	B
Symptom relief provided by your treatment	Complete	A little
Inhaled steroid dose (either in low dosage, plus a long-acting inhaled beta-agonist, or in high dosage)	A high regular steroid dose	Always a low steroid dose
Use of a written personalized asthma action plan*	Full written instructions are provided by the doctor or nurse on how to recognise worsening asthma and how to alter your therapy yourself	A brief written note is provided on how to take your medication
Asthma crisis management	You are encouraged to attend hospital in the event of your asthma worsening	You are encouraged to attend your local GP surgery in the event of your asthma worsening
Number of different inhalers	No more than two inhalers are provided to you for the management of your asthma	Three inhalers are provided to you for the management of your asthma
Controlling your asthma symptoms	You are encouraged to change your own therapy as required without having to consult a doctor or nurse	You are encouraged to speak to a doctor or nurse before making any changes to your treatment

*A "personalized asthma action plan" is a written plan, given to you by your doctor or nurse, which tells you how to recognise your asthma is worsening and how you should alter your treatment yourself

Which group A or B mostly fits with your preferences?

Please tick the box A or B that contains the statements that are most important to you. This may not be the column that has the most statements you agree with, but will have the ones you feel most strongly about. You may have to select some statements you would rather not choose because they are linked to the GROUP that you prefer overall.

A ☐ B ☐

Figure 1

without loss of asthma control has previously been described¹⁸ and the addition of an inhaled long-acting beta agonist often permits better control and use of a lower dose of inhaled steroid.¹⁴

Use of a personalized asthma action plan came next in patients' ranking of relative importance of the attributes of asthma management that they were asked about. A discouragingly small number, only 12 (8%) of respondents, indicated that they held a written personalized asthma action plan—two centers each accounted for three of these patients and a further six practices each had one patient with a plan. This low number of patients with an action plan is similar to that found in previous studies¹⁹ and is disappointing, especially because it has previously been shown that even those without plans would feel comfortable adjusting therapy themselves.¹⁶ Written asthma action plans have been shown both to improve outcomes³ and to improve compliance with asthma therapy,²⁰ to be cost-effective,²¹ and are strongly recommended in asthma guidelines.¹⁴ It may be that lack of familiarity with the nature and benefits of using a personalized plan, by both medical professionals and patients, may have influenced these results, and that a greater knowledge would increase the popularity and use of what may be the single most important non-therapeutic intervention in asthma management. In this study, patients indicate a desire for "brief" rather than "full" written instructions.

The next ranked factor was asthma crisis management. The utility analysis showed that patients preferred to avoid attending hospital even in the event of a crisis, a theme we have reported in a different disease area and population.²² Knowledge of patient preference can inform the clinician but will not, of

course, be the only factor to consider when deciding how and where to manage an acute exacerbation of asthma.

Perhaps surprisingly, controlling asthma symptoms was ranked lower in patients' ranking of importance, and relief of symptoms was considered least important in the range of attributes tested. However, this does not mean that people with asthma do not consider symptom relief important, but indicates that respondents considered it less important than the other attributes of asthma management they were asked to rank. This suggests that patients were prepared, at least to some extent, to trade off elements of efficacy for what they perceived to be other benefits, such as lower doses of inhaled steroids.

Both "asthma crisis management" and "controlling your asthma symptoms" had higher relative importance statistics when determined by the individual level method than by the aggregate level method. This means that there was a division of opinion within respondents as to which level in each of these two attributes was the most desirable.

There was some variation between respondents in the extent to which they wanted to manage their own asthma symptoms. Nearly two-thirds put a higher utility value on being encouraged to "change your own therapy" than "speak to a doctor or nurse before making changes to treatment" in the attribute of controlling asthma symptoms. This indicates a split

between patients wanting a collaborative/active role in making changes to their asthma therapy and those wanting a more passive role, at a similar level to that reported previously.²³

One of the greatest strengths of this study is the use of discrete choice experiment methodology, which is a rigorous method of eliciting preferences. Previous studies have demonstrated that respondents tend to behave in an internally valid and consistent manner when answering DCE questions.²⁴ The study explored patients' preferences between only the attributes and levels that were offered, but these had been identified as being important from patients interviewed in a previous study.¹⁶ The majority of the respondents found the questionnaire easy to complete, although it is possible that the type of questionnaire and the task, which is likely to have been unfamiliar to recipients, influenced the overall response rate.

Another possible limitation to the study is that the majority of respondents were female (65%) and aged over 55 years (48%). However, this is similar to previous studies exploring adult asthma patients' attitudes to their treatment.^{9,23} Responders were generally older (mean age 55 years) than non-responders (mean age 45 years) ($P < 0.01$), but there was no statistically significant difference in gender between respondents and non-respondents ($P = 0.3\%$).

Conclusion

Taking a flexible, patient-centred approach to asthma management means focusing on issues that patients consider important. Our study indicates that this means making treatment as simple as possible, with as few medications and inhalers as can achieve symptom control—ideally fewer than

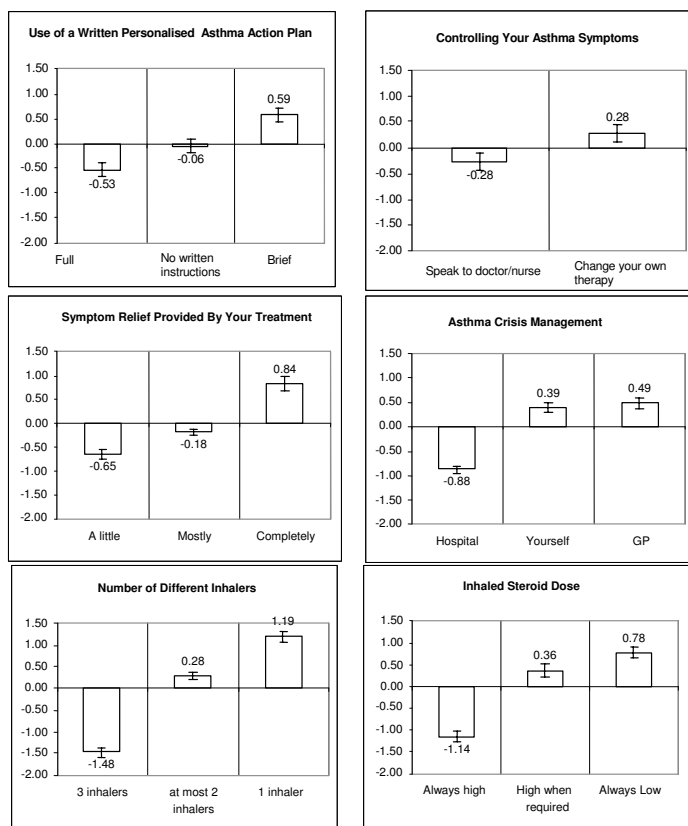


Figure 2

three, or even two, inhalers. It also means using the lowest dose of inhaled steroid that can effectively control asthma and avoiding hospitals for emergency care, as well as minimizing asthma symptoms. There is clearly room for improvement in increasing the number of patients receiving personalised asthma management plans, which should improve outcomes by increasing compliance.

References

- Barlow J, Wright C, Sheasby J: Self-management approaches for people with chronic conditions: a review. *Patient Educ Couns* 2002;48:177-187.
- Lorig KR, Sobel DS, Stewart AL, Brown BW Jr, Bandura A, Ritter P, Gonzalez VM, Laurent DD, Holman HR: Evidence suggesting that a chronic disease self-management program can improve health status while reducing hospitalization. A randomized trial. *Med Care* 1999;37:5-14.
- Gibson PG, Powell H, Coughlan J, Wilson AJ, Abramson M, Haywood P, Bauman A, Hensley MJ, Walters EH: Self-management education and regular practitioner review for adults with asthma. *Cochrane Database Syst Rev* 2002;(3):CD001117.
- Partridge MR, Hill SR: Enhancing care for people with asthma: the role of communication, education, training and self-management. 1998 World Asthma Meeting Education and Delivery of Care Working-Group. *Eur Respir J* 2000;16:333-348.
- van Es SM, le Coq EM, Brouwer AI, Mesters I, Nagelkerke AF, Colland VT: Adherence-related behavior in adolescents with asthma: results from focus group interviews. *J Asthma* 1998;35(8):637-646.
- Osman LM: How do patients' views about medication affect their self-management in asthma? *Patient Educ Couns* 1997;Suppl 1:43-9.
- Hyland ME, Stahl E: Asthma treatment needs: a comparison of patients' and health care professionals' perceptions. *Clin Ther* 2004;26:2141-2152.
- Sweeney KG, Edwards K, Stead J, Halpin D: A comparison of professionals' and patients' understanding of asthma: Evidence of emerging dualities? *Med Humanit* 2001;27:20-25.
- Johansson G, Stallberg B, Tornling G, Andersson S, Karlsson GS, Falt K, Berggren F: Asthma treatment preference study: a conjoint analysis of preferred drug treatments. *Chest* 2004;125(3):916-923.
- Ryan M: Discrete choice experiments in health care. *BMJ* 2004;328:360-361.
- Ryan M, Farrar S: Using conjoint analysis to elicit preferences for health care. *BMJ* 2000;320:1530-1533.
- Lancaster K: *Consumer Demand: A New Approach*. New York: Columbia University Press;1971.
- Global Initiative for Asthma (GINA) Report, Global Strategy for Asthma Management and Prevention. Revised 2006. www.ginasthma.org.
- British Thoracic Society / Scottish Intercollegiate Guidelines Network: British Guideline on Asthma Management. *Thorax* 2003;58,Suppl:i1-i92.
- Orme B: *Getting started with Conjoint Analysis: Strategies for Product Design and Pricing Research*. Madison Wis: Research Publishers LLC; 2006
- Haughney J, Barnes G, Partridge MR, Cleland J: The Living & Breathing Study: a study of patients' views of asthma and its treatment. *Primary Care Respiratory Journal* 2004;13:28-35.
- Sawtooth Software: An Overview and Comparison of Design Strategies for Choice-Based Conjoint Analysis 2000. http://www.sawtoothsoftware.com/download/techpap/design_cbc.pdf (Date last accessed September 2006).
- Hawkins G, McMahon AD, Twaddle S, Wood SF, Ford I, Thomson NC: Stepping down inhaled corticosteroids in asthma: randomised controlled trial. *BMJ* 2003;326:1115.
- Greater Expectations? Findings from the National Asthma Campaign's representative study of the Needs Of People With Asthma (NOPWA) in the UK. *Asthma J* 2003;5(3).
- Gallefoss F, Bakke PS: How does patient education and self-management among asthmatics and patients with chronic obstructive pulmonary disease affect medication? *Am J Respir Crit Care Med* 1999;160(6):2000-2005.
- Gallefoss F, Bakke PS: Cost-effectiveness of self management in asthmatics: a one year follow up randomized, controlled trial. *Eur Respir J* 2001;17(2):206-213.
- Haughney J, Partridge MR, Vogelmeier C, Larsson T, Kessler R, Stahl E, Brice R, Lofdahl CG: Exacerbations of COPD: quantifying the patient's perspective using discrete choice modelling. *Eur Respir J* 2005;26(4):623-629.
- Caress AL, Beaver K, Luker K, Campbell M, Woodcock A: Involvement in treatment decisions: what do adults with asthma want and what do they get? Results of a cross-sectional survey. *Thorax* 2005;60(3):199-205.
- Ryan M, Gerard, K: Using discrete choice experiments to value health care: current practice and future prospects. *Appl Health Econ Policy Analysis* 2003;2(1):55-64.

In the Shadow of Bad News – Views of Patients with Acute Leukemia, Myeloma or Lung Cancer About Information, From Diagnosis to Cure or Death

Lena Hoff, Ulf Tidefelt, Lars Thaning, Göran Hermerén

Abstract

Background: Many studies have been published about giving and receiving bad messages. However, only a few of them have followed the patients all the way through a disease as is done in this study. Many studies have been written about patients' coping strategies. In this study we will keep within the bounds of coping through information only. The aim of the study is to investigate patients' views of information during the trajectory of their disease, whether their reactions differ from each other and whether they differ in different phases of the disease.

Methods: Twelve patients with malignant hematological diseases or lung cancer were followed with interviews from diagnosis to recovery or into the terminal phase or at most for two years. The method is qualitative, using semi-structured interviews.

Setting: Örebro University Hospital or the patient's home.

Results: All patients described themselves as well informed from the start but in later phases of their disease some of them came to express a great uncertainty about the progressing disease and about the approaching death. Most of them, regardless of whether they had a hematological malignancy or lung cancer, expressed a wish to be well informed all through the disease and even when the messages were bad. Different strategies for coping with information, however, affected how they then dealt with the information received. Four such coping strategies were found: 1) Information-dependent and accepting; 2) Information-dependent but denying; 3) Medically informed and accepting; 4) Medically informed but denying.

Conclusion: For several patients, there was an unmet need for information about the progressing disease and the approaching

death. To optimize the care of these patients it seems important that the physician is aware of patients' need for information even when the news is bad. Knowing the patient's information strategy could probably function as a key for the physician to communicate with patients on these matters.

Background

Many studies have been published about giving and receiving bad messages. However, only a few of them have followed the patients all the way through a disease as is done in this study. Many studies have been written about patients' coping strategies since the fundamental work of Lazarus & Folkman on stress and coping. In this work, however, we will confine ourselves to coping through information only, which of course is only a small part of the coping process as an entity.

Ptacek & Eberhardt reviewed studies published 1985–1996, studies about the importance of where, when and how bad messages should be delivered. Since 1996 a large number of additional studies have been published focusing on the disclosure of the diagnosis or when death is coming close or the impact of the social and cultural context for truth-telling, and that common beliefs about what a patient really wants to know could be misleading. It has also been found that a majority of patients do wish to be informed even when the messages are bad.

Some studies are close to the areas of inquiry of this study, as when van der Molen stresses information as a key coping strategy, Quirt et al analyse how patients with recently diagnosed lung cancer received and held on to information, Leydon et al and Yardly et al emphasized the importance of giving moderated and individualized information. Finally, there is the longitudinal study by The, et al, of patients with lung cancer, calling attention to information as a complicated process of interaction between the physician and the patient.

The chief contribution of this study is that, by following each patient over time, it becomes possible to notice changes, if any, in the patient's reaction to information during the disease. Secondly, this study adds partly new knowledge, compared to earlier studies, in that it focuses on and compares coping strategies of two different categories of patients: patients with

Authors Hoff and Hermerén are with the Department of Medical Ethics, Lund University; Tidefelt is with the Department of Medicine, and Thaning is with the Department of Pulmonary Medicine, Örebro University Hospital, Sweden. For full references, please go to BioMed Central on the internet and type the full name of the article. Reprinted from BioMed Central, BMC Palliative Care, © 2007 Hoff et al; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License.

Table 1: Study participants and number of interviews

Category of patient	Number of interviews	Sex	Age
7 Haematologic	44	3 men / 4 women	37-80 years
5 Lung cancer	44	2 men / 3 women	60-71 years

Table 2: The distribution of interviews

Patient	Diagnosis/Treatment 1	Treatment 2	Terminally	Totally
A	3	-	-	3
B	1	-	-	1
C	9	2	2	13
D	3	-	-	3
E	6	3	1	10
F	3	-	-	3
G	11	-	-	11
V	2	-	1	3
W	6	-	1	7
X	11	2	1	14
Y	8	2	1	11
Z	8	-	1	9
				88

malign hematological diseases and those with lung cancer. Thirdly, this study adds partly new knowledge, compared to earlier studies, in the way it focuses on patients' need for information all through the disease.

The aim of this study is to explore how patients belonging to two categories of disease relate to information given by their physicians from diagnosis to cure or until the transition to terminal care becomes obvious to the patient. The aims are to investigate patients' views of the information received:

- regarding the content
- regarding the way the information was given to them
- in the longitudinal perspective, all through the disease, and as death approaches
- to find out whether the patients' ways of reacting differ from each other, and if so, how.

Methods

The study consists of recurrent interviews with 12 seriously ill patients, 7 patients with malignant hematological diseases (acute lymphocytic leukaemia, acute myelocytic leukaemia, myeloma) and 5 patients with non-operable lung cancer diseases (adenocarcinoma and squamous cell cancer). Only 20% of patients diagnosed with acute leukaemia are estimated to be alive two years later. Some patients with myeloma get an aggressive form of the disease bringing them to death within a year, while others might live with good quality of life for more than ten years. Among patients with non-small-cell cancer only 3–7%, are alive 5 years later, while 50% die within 7 months.

As the patients were diagnosed at Örebro University Hospital, Sweden, they were consecutively asked to join the study. Of 11 patients with acute leukemia or myeloma, 10 were asked and 7 of them accepted. Of 9 patients with lung cancer, 7 were asked and 5 accepted. Exclusion criteria were if the patient was unable to give informed consent or understand the questions. The interview period was 2002–2005. The settings were either the hospital or the patient's home. The total number of

interviews was 88, lasting 5-90 minutes each, depending on the health of the patient. The intention was neither to interview the patients as soon as possible after they had received their diagnosis nor to follow the patients during the whole processes of their dying. The first interview was held from six days to six weeks after the diagnosis had been given to the patient and the interviews came to an end as soon as the patients said that they knew that they were about to die as no more treatment was possible to stop the progress of the disease.

A summary description of the participants and the number of interviews is presented in Table 1. The letters A-G in the following refer to patients with hematological diseases and the letters V-Z to patients with lung cancer.

The intention was to interview the patients with hematological malignancies every fortnight and the patients with lung cancer as they came for treatment three times monthly, but for various reasons the number of interviews came to differ among the patients. Two patients did not get the desired effect of their treatment and died rather soon, patient B only four days after the first interview and patient V after two months. Three patients were excluded from the study, patient F because she wanted to withdraw, A for geographical reasons and D as the interview questions seemed to hurt and upset him. Four patients reached the desired state of complete remission, but three of these relapsed and then went on with a second-line treatment. Only one patient did not relapse at all during the two years that the patient was followed. Seven patients were followed into the terminal phase. For the distribution of interviews, see Table 2.

The patients were recruited to the study during their medical visits. As soon as the physicians found it suitable the patients were given both oral and written information about the study by their physician. Following Swedish and international guidelines for medical research it was stressed that participation was voluntary and the patients could withdraw whenever they wanted without any negative consequences for their treatment.

Table 3: The categorization of the patients

Patient	1 Information- dependent and accepting	2 Information- dependent but denying	3 Medically informed and accepting	4 Medically informed but denying
A			X	
B	(X)			
C	X			
D			X	
E	X			
F			X	
G			X	
V	X			
W				X
X		X		
Y	X			
Z			X	

The research ethics committee of Örebro University Hospital approved the study.

All interviews, except for those with one patient, were tape-recorded, conducted and transcribed verbatim by the first author. During the interviews with the patient who did not approve of the tape recorder, notes were taken on the basis of which the interview was reconstructed, which the patient was given the opportunity to read. The taping of another three interviews unfortunately failed, due to technical problems, but notes were taken and a reconstructed interview was read to the patient (C: 6). The other times (D: 2, X: 11) the most important questions were recapitulated in the next interviews held. Each interview consisted of 5–7 questions. The very first interview followed the interview guide. Depending on what the patient said and what happened to the patient, new questions emerged.

Analysis: The study is qualitative, with a hermeneutic approach. The steps taken in the analysis were inspired by Kvale and to some extent also by Graneheim and Lundman. Firstly, all typed material was read through. Then the material not containing information and messages relevant to the purpose of this study was excluded. The remaining material was divided into three domains of investigation: the disclosure of the diagnosis and information during the first treatment, during a second treatment, and terminally. As soon as they were transcribed, all the taped interviews were listened to once again to assure conformity. Then the process of coding started, piece by piece. During the process of coding, a co-reader checked that the codes summed up the text passages. Codes with similar contents, not necessarily confirming each other, were brought together into different investigation areas. One such area was how the patient came to deal with the information received. Then four possible patterns emerged, four kinds of strategies for coping with information—the four categories.

Results

Patients' views of information: All the patients expressed appreciation for the straightforward way they had been informed about diagnosis, prognosis, treatment plans, possible side effects, complications, and a recurrence of the disease. One patient, though, thought that she could have been informed openly but in a more cautious way. "They (the physicians) just came by and told me. Was it Christmas Day? Anyhow, one of the days of Christmas... They could have told me this more nicely, I think" (X: 1). The diagnosis was a surprise to everyone, except to patient B. This patient said: "I did understand. I did know...

there is only the choice of recovery or death" (B: 1). Not all patients could give the proper name of their diseases, but they all knew it was either about a malignant hematological disease or lung cancer, and without treatment they would all have been dead within a few weeks or a couple of months. They had all been informed about the prognosis of their disease; yet, one patient made an effort to talk about the disease as if it was of no such danger to her. Then she was asked if she knew of anyone who had got the disease acute leukaemia. She said she did. They had both died (A: 2, A: 3).

However, four patients out of five with lung cancer got a sudden, remarkable—but temporary—recovery shortly after the treatment had started. After this only one of the patients, and only once more, talked about the incurableness of the disease (X: 8) but as their health started to decline they all, except patient W, were wondering about the reasons behind that (Z: 4–8, Y: 5–8, X: 8–13, V: 2).

On the other hand, as treatment went on the patients came to express an adjustment of being in treatment, which made them fear less about a recurrence of the disease. Now, they thought they knew what another treatment would be like. "If I will relapse, I will relapse... but that day, that sorrow. It is no big deal if I have to go through it once more" (C: 9). "I do understand that the cancer could come again, but I am not worried if I have to go back to the hospital. Now, I know what it would be like." (E: 6).

Patients' views when the disease is in recurrence: For one of the patients with leukemia the information about suddenly declining test results came abruptly and without warning (C: 10), while for another the relapse was no surprise at all. This patient had been following the slowly declining test figures. When the relapse was confirmed by a bone marrow test, it was what the patient had already suspected (E: 9).

To the patients with lung cancer the recurrence of cancer started in quite a different way. These patients were all hit by different kinds of diseases, such as thrombosis (Z), recurrent pneumonia and dyspnea (Y, X), colds and high fever (W). This seems to have made it difficult for the patients to understand when the cancer was in progress and when not. They all came to express a great uncertainty. "It is like standing at a crossroads, not knowing which way to go" (Y: 5). Sometimes it happened that they felt really ill but all the same got good news about the tumour. "Yes, (they say) the tumour has shrunk! ... I

must say I had expected a little more sad news. I was prepared, as you can see (pointing at her toilet bag), that they would keep me here" (Z: 8). Sometimes these patients did ask their physicians about the cancer. "But he couldn't tell for sure! I do hope it's not the cancer coming on again!" (X: 12). The patient was then asked whether, if it was the cancer coming back, she would have wanted to know about it or not. The answer was: "Yes I would ... I would ... but, honestly I don't think he was lying to me ... but he said he couldn't promise" (X: 12).

Patients' views in the terminal phase: Two of the patients, C and V, received the information verbally from their physician that the treatment had failed and that other treatment was considered to be of no use. However, patient V had to ask to get this information. "They don't tell you very much. You have to ask..." (V: 3). Patient E seemed to have become aware of the transition to the terminal phase, not from what her physician told her but mainly because of the declining values of the test results. The transition to the terminal phase seems in no way to have been obvious to the patients with lung cancer. Even when feeling worse they were told, from time to time, that the tumour had not been growing (Z: 9, Y: 10, X: 11, W: 4). Not until the very last part of their lives did the X-rays reveal the progress of the cancer. Patient Y did not talk about his death as being close and inevitably terminal until only four days before he died (Y: 11). Patient X said that even if she might not have been given straight information about the nearness to death, she understood. "I do not think he has told me so very straight, but he held my hand and so ... so I did understand what it was all about" (X:14). Another patient declared that he was all right only three days before his death. "We even talked about his 70th birthday, which was to come three months later" (W: 7).

The patients followed into terminal phase were asked if they had talked with their physicians about death. They had not. Except for one patient, they hadn't talked about when death probably was to come: "They say up to six months or so, if I'm lucky. Nobody knows, it might be only three" (C: 12). Patient V said: "I ask quite often how long it will take before I die, but they're not able to answer! I find that very strange. I would have appreciated if there were some kind of statistics. I suppose there are, but they don't want to tell me" (V: 3). However, even if they had not consulted their physicians, several of these patients still had an understanding of when death was probably about to come, which turned out to be rather accurate. Only one patient turned his back on the whole question. He was not in the least interested in knowing. Death would come, as death comes to everyone (W: 7).

Patients' strategies for coping with information: Different strategies for coping with information affected how the patients came to deal with the information received. Four such coping strategies were found: information-dependent and accepting, information-dependent but denying, medically informed and accepting and medically informed but denying.

The first type is exemplified by those patients who carefully followed every test value of hemoglobin, thrombocytes, neutrophile leukocytes, bone marrow tests, X-rays, spirometries etc. Their coping strategy is called information-dependent and accepting, and their strategy may be illustrated by quotations like: "I find everything about this disease and the treatment of it interesting" (C: 2), or "I have been asking all the time, first the nurses, and if they haven't been able to answer, I have asked the

doctors. I do want to know what is going on" (C: 8). One of the patients told her husband every test result, from which he made statistical diagrams so that they could closely follow every change in the values (E: 4). These patients continued to express their need for information all through the disease, even when the information was sad, and they continued to follow every test result most carefully. During second-line treatment, as in the terminal phase, these patients could, just as before, give the exact figures from the results of the tests taken (C: 10, C: 11, C: 12, E: 7, E: 9, E: 10).

Patient X illustrates the second coping strategy, information-dependent but denying. Like patients C and E, this patient wanted information, but then held the information back. In the first interview this patient said that she was informed and that she had understood but now she tried to repress it all (X: 1). In the following interviews she often returned to the fact that she did know, but continued by saying: "then you have to deceive yourself, you know" (X: 4). When this patient understood that death was near, the reaction was: "Well, the thing now is to handle it in a positive way" (X: 14). When asked what this could mean, the answer was: "You have to deny it" (X: 14). The patient held on to this information-dependent but denying strategy in all phases of the disease.

The third coping strategy is called "medically informed and accepting." These patients also appreciated being informed but they came to deal with the information received in another way than did the patients categorized as information-dependent. While the information dependent patient followed every single test result most carefully, memorizing every value number, the medically informed patients never took such an interest in each test taken. They reckoned that they would be informed when there was something they ought to know about. "Actually, you can't keep it all in your head. It's too much" (F: 3). "I'm not one of those who checks up the test results. They'll tell me, I suppose, if there's something I should know" (G: 11). These patients found the focusing on every test result somewhat tiring and sometimes they criticized their doctors for being "too medical" or "too focused" on the test values figures and numbers. "Too medical ... I was unlucky meeting a real medical doctor, so to speak" (D: 3). "Yes ... it's a little too technical" (G: 6). However, of these patients, only patient Z was followed into the terminal phase, so it is hard from this study to tell how well these patients held on to their strategy. What was seen in this study was that two of the patients came to change their strategy slightly to the strategy of denying; Patient G, after being told that she had been very close to death, which she had not been aware of (G:9); however, in the next interview she was back as a non-denying patient. On the other hand, patient Z became all the more denying the more her health declined.

The patient using the fourth coping strategy, called medically informed but denying, denied the importance of the information received all through the disease. The patient approved of being informed: "I want to be informed right into the middle of my eye" (W: 1) but then he seemed to take little notice of the information received. "I need not die because of this. I could die for any reason!" (W: 5). Yet, this patient said that from the start he not only knew about the tumor in his lung, but also about the growth of metastases (W: 7). When asked about how to handle bad news he answered, as before, that he always wanted information as straight as possible. Then he was asked if there had been any bad messages in the physician's information today.

"No," he answered, "the thing is that there's no need for any more treatment. It's good as it is ... and I won't have to visit the hospital until the summer is over" (Z: 6). The patient died at the beginning of August.

Discussion

There is a point of knowing the patient's strategy for coping with information. But it is not in trying to classify them into any of the four categories found in this study, as there might be more strategies than these four which could perhaps have been discovered if other patients had been included. The very point of knowing the patient's strategy for coping with information, we think, is that the coping strategy could reveal a key to the physician about how to communicate with the patient in difficult matters such as information about progressing cancer and approaching death. This is especially true as we found that, irrespective of coping strategy, the need for information remained of great importance all through the disease, even when life was coming to an end. However, this is not congruent with the findings of some other studies such as the one by Leydon et al, where it is stated that patients vary in their attitudes towards information, with different needs at different times. There is little evidence for that in this study. We found that information for most of the patients was of great importance all through the disease, but that several patients expressed great uncertainty when life came close to an end.

The number of times participants were interviewed varied from 1–14. One might then have expected that the number of interviews could have affected the perceptions and reactions of the patients toward their disease, making a change in strategy for coping with information. As the health of the patients was declining, the attitudes to the disease were changing, but not attitudes to information. Only on some occasions did two patients change their strategy to the strategy of denying. This might also indicate that at least some patients had the ability to find "a way out" when facts were too hard to cope with. Otherwise they all held on to the strategy they had from the start.

One might also have expected that patients with lung cancer and hematological diseases would have reacted somewhat differently to the information given, revealing differences in when and how much they were informed. But we found people who were well informed and not so well informed in both kinds of patients, though the less well aware patients were more often found among patients with lung cancer. The reasons behind that need to be investigated further.

The age of the interviewees varied, from 37 to 80 years. The age could then have been of importance for the strategy of the patients but this was not found.

Finally one might have expected gender differences among the patients' attitudes to information, but no such differences were found.

The finding that patients were well informed from the start but not in later phases of their disease has been observed in the literature. Different explanations have been given, such as that it is due not only to the information given by the physicians, but also to the patient's ability to understand the verbal utterances of the physician, as well as to the patient's ability to cope with and integrate the bad news into his or her life. More research is

needed to find out whether the deficiency is due to a lack of information by doctors or to a lack of knowledge by patients for understanding the information provided.

How to deal with the lack of knowledge among patients? The answer to this question will obviously depend on the reasons behind the lack. Some patients might need further information, others might need to have the information explained, or repeated. Still other patients might need to cope with the information by leaving it behind them. Improved disclosure and the patients' right to obtain information about their condition can be supported by the principle of autonomy. Non-disclosure can be supported by the principle of beneficence. In a study by Schapira, the tension between those who favor complete disclosure and those who prefer more limited truth-telling is confirmed. Both practices, she says, can be justified ethically and both have received support in the published literature. We believe that the ethical justification is an act of balancing the pros and cons about what seems to be the best for the patient. But it has to be emphasized: what is found in many studies and confirmed in this one is that most patients want to be well informed even when the messages are bad.

To optimize care of patients, it seems important that, irrespective of the reason behind the lack of knowledge among patients, this lack of knowledge is recognized and as much as possible minimized by their physician. We believe that a patient with a better knowledge about approaching death is more able to make the necessary and desired practical, economic, social and spiritual adjustments and preparations in time before his or her death. Talking about death could probably harm some patients, at least in the short term, but if patients are as information-dependent, as shown in this study, and if the physicians are good at telling even sad news, as reflected in the interviews of this study, we are convinced that most patients would be relieved.

Limitations, trustworthiness and validity: In this study the first author had the unique opportunity to follow two groups of patients with severe disease over time. The patients, however, were not interviewed during the first shocking phase after having received their diagnosis. This might have affected the patients, so that they had a more positive attitude from the start, that is, to the information received, to the way it was given to them and to the informing physician.

As already noted only seven out of twelve patients, for various reasons, were followed into the terminal phase. The intention to maintain some regularity in following the patients could not always be realized. Some prearranged interviews had to be shorted or postponed for days, or even weeks, because of the patient's actual state of health.

A final important point is that not all patient strategies for coping with information were easy to identify. The patients in categories 1 and 4 were easy to identify, but not patients in categories 2 and 3. How to categorize these patients was very much a question of what to emphasize. By balancing the patients from one category to another, it became obvious where the patients fitted best.

Of course, the interview material can also be criticized for not being reproducible, as each interview reflects what the patients

Continued on page 60...

Prevalence and Impact of Alcohol and Other Drug Use Disorders on Sedation and Mechanical Ventilation: A Retrospective Study

Marjolein de Wit, Sau Yin Wan, Sujoy Gill, Wendy I. Jenvey, Al M Best, Judith Tomlinson, Michael F Weaver

Abstract

Background: Experience suggests that patients with alcohol and other drug use disorders (AOD) are commonly cared for in our intensive care units (ICU's) and require more sedation. We sought to determine the impact of AOD on sedation requirement and mechanical ventilation (MV) duration.

Methods: Retrospective review of randomly selected records of adult patients undergoing MV in the medical ICU. Diagnoses of AOD were identified using strict criteria in Diagnostic and Statistical Manual of Mental Disorders, and through review of medical records and toxicology results.

Results: Of the 70 MV patients reviewed, 27 had AOD (39%). Implicated substances were alcohol in 22 patients, cocaine in 5, heroin in 2, opioids in 2, marijuana in 2. There was no difference between AOD and non-AOD patients in age, race, or reason for MV, but patients with AOD were more likely to be male (21 versus 15, $p < 0.0001$) and had a lower mean Acute Physiology and Chronic Health Evaluation II (22 versus 26, $p = 0.048$). While AOD patients received more lorazepam equivalents (0.5 versus 0.2 mg/kg.day, $p = 0.004$), morphine equivalents (0.5 versus 0.1 mg/kg.day, $p = 0.03$) and longer duration of infusions (16 versus 10 hours/day medication, $p = 0.002$), they had similar sedation levels (Richmond Agitation-Sedation Scale (RASS) -2 versus -2, $p = 0.83$), incidence of agitation (RASS ≥ 3 : 3.0% versus 2.4% of observations, $p = 0.33$), and duration of MV (3.6 versus 3.9 days, $p = 0.89$) as those without AOD.

Conclusion: The prevalence of AOD among medical ICU patients undergoing MV is high. Patients with AOD receive

higher doses of sedation than their non-AOD counterparts to achieve similar RASS scores but do not undergo longer duration of MV.

Background

Sedative and opioid agents are routinely administered to critically ill patients to treat agitation and facilitate mechanical ventilation (MV).¹ Appropriate use of these agents is important as severe agitation is associated with prolonged MV and increased risk of self-extubation.² Excessive sedation administration is also associated with prolonged MV, and strategies aimed to limit oversedation have been found to decrease MV duration.³⁻⁷

Alcohol and other drug use disorders (AOD) affect 9.4% of the American population, and prevalence of these disorders in intensive care units (ICU's) ranges from 5 to 30%.⁸⁻¹¹ Unlike patients without AOD, evidence suggests that patients with AOD on MV may develop withdrawal syndromes if undersedated or with early withdrawal of sedation, and sedative agents have been found to reduce the duration of alcohol withdrawal delirium.^{12,13} However, the sedative requirements of patients with AOD have not been studied extensively.

Because there has been an increased focus recently on minimizing sedation to improve MV outcomes, and because patients with AOD may require a different approach to sedation while on MV, we designed a study to determine the prevalence of AOD and sedation needs among our medical ICU patients undergoing MV. We hypothesized that patients with AOD would require higher doses of sedatives and opioids, have more episodes of agitation, and require a longer duration of MV than those without AOD. The results of this study have previously been published in abstract form.¹⁴

Methods

The study was conducted in accordance with the ethical standards of the Virginia Commonwealth University's Office of Research Subject Protection and the Declaration of Helsinki of 1975, as revised in 1983. The study was approved by Virginia Commonwealth University Office of Research Subject Protection, Richmond, Virginia, and the need for consent was waived. The study was a retrospective cohort study of patient medical records. Medical patients admitted to our medical ICU

Authors de Wit and Jenvey are with Virginia Commonwealth University, Department of Internal Medicine and with the University's Division of Pulmonary and Critical Care Medicine, Richmond, Virginia, USA. Gill and Weaver are with the Virginia Commonwealth University Department of Internal Medicine, and Weaver is also with its Department of Psychiatry, Division of Addiction Psychiatry. Wan is with the University of Miami, Department of Medicine, Division of Pulmonary and Critical Care Medicine. Best is with Virginia Commonwealth University's Department of Biostatistics; Tomlinson is with the University's Department of Psychiatry, Division of Addiction Psychiatry. Reprinted from BMC Anesthesiology, BioMed Central. This is an Open Access article distributed under the terms of the Creative Commons Attribution License.

Table 1: Definition of Substance Dependence and Substance Abuse

Substance dependence is manifested by three or more of the following:
(i) tolerance, as marked by the need for larger doses to achieve intoxication or desired effect or markedly diminished effect with continued use of the same amount of substance;
(ii) development of withdrawal symptoms or use of substance to relieve or avoid withdrawal symptoms;
(iii) taking larger amounts or over longer periods than intended;
(iv) persistent desire or unsuccessful efforts to cut down or control substance use;
(v) spending time obtaining the substance, using the substance or recovering from its effects;
(vi) performing important social, occupational or recreational activities less frequently because of the substance;
(vii) continuing use of the substance despite knowledge of adverse physical or psychological problems.
Substance abuse is manifested by at least one of the following:
(i) recurrent use resulting in failure to fulfill major obligations at work, home or school;
(ii) recurrent use in situations in which it is physically hazardous;
(iii) recurrent substance-related legal problems;
(iv) continued use despite having persistent or recurrent social or interpersonal problems.

who required invasive MV were eligible for study participation. The medical ICU is a closed unit where patients have similar surroundings. All beds are located in close proximity to nursing stations and medical equipment. When monitoring equipment alarms, the alarm not only sounds at the nursing stations but also in all patient rooms. Only patients physically located in the medical ICU were eligible for study participation thereby assuring that the noise exposure was similar for all study patients.

Using a random number generator, patients were selected from a list of all patients undergoing MV in our medical ICU between October 2002, and June 2003. Study exclusion criteria were age < 18 years, duration of MV < 24 hours (to exclude those who required a short course of intubation for overdose), tracheostomy at the time of initiation of MV, transfer from another ICU service, location other than our medical ICU, or prisoners. If patients had multiple courses of MV during their hospitalization, only the first episode was evaluated. Sedation was managed according to our medical ICU algorithm and based on published recommendations.^{5,15} The sedation algorithm goals were to maximize the use of boluses, to minimize the duration of continuous intravenous infusion of sedation, and to treat pain with opioids. Weaning from MV was also standardized through the use of daily spontaneous breathing trials and was guided by bedside Nurses, Respiratory Therapists and Physicians.¹⁶

AOD was classified according to the substance used: alcohol,

benzodiazepines or barbiturates, heroin, opioids (other than heroin), cocaine, amphetamines, marijuana and other (excluding nicotine). Diagnosis of AOD was assigned if the disorder was present within one year previous to initiation of MV. Medical records were reviewed for the target admission as well as previous admissions and outpatient visits. To maximize diagnostic accuracy, experts in Addiction Medicine and Psychiatry assigned the diagnosis (MFW, JT). Diagnosis was established through review of toxicology results, medical records, and based on the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition TR (DSM IV-TR) (Table 1).¹⁷

Medical record: When physician notes explicitly documented the presence of alcohol or drug abuse, dependence, and/or addiction, the patient was classified as having AOD. When the terms abuse, dependence or addiction were not documented in the record, the patient was not diagnosed with AOD based on review of medical records alone.

Clinical diagnosis: Definitions of substance dependence and substance abuse as defined in DSM IV-TR are outlined in Table 1. If details in the medical history permitted, patients were diagnosed with AOD. For example, patients who presented to the Emergency Department with trauma and intoxication were diagnosed with AOD. As another example, patients with a history of withdrawal syndromes while on the inpatient ward were diagnosed with AOD. As a third example, patients with history of alcoholic cirrhosis who had consumed alcohol within the previous year were diagnosed with AOD.

Table 2: Richmond Agitation-Sedation Scale

Score	Term	Description
+4	Combative	Overtly combative or violent. Immediate danger to staff
+3	Very agitated	Pulls on or removes tube(s) or catheter(s), or has aggressive behavior toward staff
+2	Agitated	Frequent nonpurposeful movement or patient ventilator dyssynchrony
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	
-1	Drowsy	Not fully alert, but has sustained (>10 seconds) awakenings, with eye contact, to voice
-2	Light sedation	Briefly (<10 seconds) awakens with eye contact to voice
-3	Moderate sedation	Any movement (but no eye contact) to voice
-4	Deep sedation	No response to voice, but any movement to physical stimuli
-5	Unarousable	No response to voice or physical stimulation

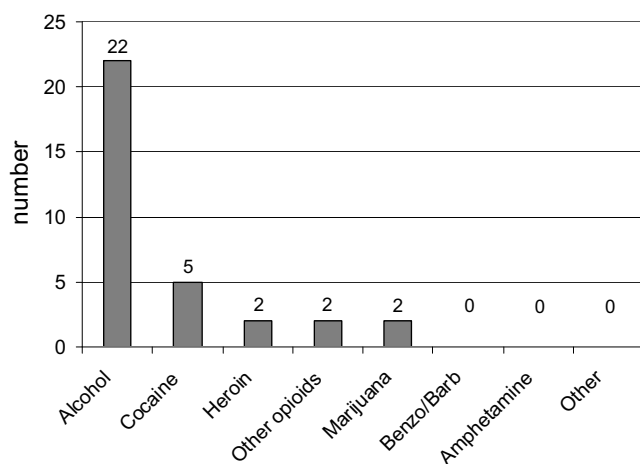


Figure 1
Distribution of substances implicated in alcohol and other drug use disorders. Benzo/Barb: benzodiazepines or barbiturates.

Toxicology results: If these revealed the presence of cocaine, heroin, marijuana, or amphetamine, patients were considered to have AOD. Patients with toxicology results that were positive for other opioids, benzodiazepines, or barbiturates were diagnosed with AOD if the substances were not administered by a healthcare professional prior to collection of urine or blood samples. Positive toxicology results for alcohol could be used only if they supported a clinical diagnosis (e.g. alcohol

withdrawal syndromes, alcoholic cirrhosis), and could not be used in isolation.

Investigators who collected the remaining data (MdW, SYW, SG, WJ) were blinded to the diagnosis of AOD. Similarly, Addiction Medicine (MFW, JT) experts were blinded to the remaining data.

Baseline characteristics of age, gender, race, ethnicity, reason for MV (which is also the reason for ICU admission and the major diagnosis), ratio of partial pressure of oxygen to fraction of inspired oxygen (P/F) positive end expiratory pressure (PEEP), and Acute Physiology Chronic Health Evaluation II (APACHE II) were collected.¹⁸ Because AOD patients may present with altered mentation, we adjusted APACHE II for Glasgow Coma Score (GCS; adjusted APACHE II = APACHE II - (15 - GCS)).¹⁹ Sequential Organ Failure Assessment (SOFA) was computed for the first day of MV and was also adjusted for GCS (adjusted SOFA = Respiratory score + Platelet score + Bilirubin score + Hypotension score + Renal score).²⁰ The total amount of sedatives and opioids administered during the course of MV was calculated, and duration of continuous intravenous infusion was recorded. Benzodiazepines and barbiturates were converted to lorazepam equivalents, and opioids were converted to morphine equivalents using referenced conversion formulas.^{21,22} Dose of propofol was also recorded and not converted to lorazepam equivalents because of unavailability of published data. We limited analysis to sedative and opioid administration with abuse potential and therefore did not record administration butyrophenones and phenothiazines. Sedation depth using Richmond Agitation-Sedation Scale (RASS, Table 2), as routinely

Table 3: Baseline Characteristics

	AOD	No AOD	p
n	27	43	
Age (years) (mean [95% CI])	50 [45.0; 55.8]	55 [50.6; 59.2]	0.20
Gender (n men/women)	21/6	15/28	<0.0001
Race (n African American/White/Asian)	20/7/0	22/19/2	0.12
APACHE II (mean [95% CI])	22 [18.2; 25.2]	26 [23.5; 29.0]	0.048
APACHE II excluding GCS (mean [95% CI])	13 [10.6; 17.1]	18 [15.1; 20.2]	0.07
SOFA (mean [95% CI])	8 [6.3; 9.3]	9 [7.5; 9.9]	0.33
Bilirubin* (mg/dl) (mean [95% CI])	2.2 [0.65; 3.85]	1.8 [0.52; 3.07]	0.65
Creatinine (mg/dl) (median, IQR)	1.1 [0.80; 2.20]	1.5 [1.10; 2.80]	0.10
P/F (mean [95% CI])	225 [177.4; 272.8]	218 [181.5; 254.2]	0.81
PEEP (cm H ₂ O) (mean [95% CI])	5 [4.4; 6.4]	5 [3.9; 5.6]	0.30
Reason for mechanical ventilation			0.46
Pneumonia/ALI	4	9	
Sepsis	1	4	
Delirium/Neurologic	7	10	
Asthma/COPD	3	4	
Upper airway obstruction	4	3	
Hemorrhagic shock	3	4	
Cardiac	1	4	
Cardiopulmonary arrest	1	2	
Drug overdose	3	0	
Other	0	3	

AOD: alcohol and other drug use disorders

CI: confidence interval

APACHE II: Acute Physiology and Chronic Health Evaluation II

GCS: Glasgow Coma Score

SOFA: Sequential Organ Failure Assessment

*Bilirubin: Total bilirubin measured in 14 patients with AOD and 22 patients without AOD

IQR: Interquartile range

P/F: Partial pressure of oxygen divided by fraction of inspired oxygen

PEEP: Positive end expiratory pressure

Table 4: Sedative and Opioid Doses

	AOD		No AOD		p
	Median	IQR	Median	IQR	
Lorazepam equivalents (mg/kg.day)	0.5	0.32–1.08	0.2	0.02–0.63	0.004
Morphine equivalents (mg/kg.day)	0.5	0.03–2.68	0.1	0.00–0.93	0.03
Propofol (microg/kg.day)*	0	0–28	0	0–14	0.81

AOD: alcohol and other drug use disorders

IQR: interquartile range

*33 patients received propofol, of which 12 had AOD

recorded by nursing staff every 4 hours, was collected.²³ Duration of MV, reintubation within 72 hours of extubation, unplanned extubation, placement of tracheostomy, ICU mortality, hospital mortality, hospital length of stay and ICU length of stay were recorded.

Data analysis: The primary aim compares patients with AOD to those without AOD. Duration of MV was computed using Kaplan-Meier method and compared by log rank. Normally distributed data were compared using two-group t-test. Non-normally distributed data were compared using Wilcoxon Test. A mixed-model repeated-measures ANOVA was used to compare sedation levels. The prevalence of AOD in the study was compared to that of the city of Richmond, Virginia (17.9%), using Chi-square.²⁴ ICU and hospital mortality rates as well as reintubation and tracheostomy rates were compared using Chi-square or Fisher's Exact test when appropriate. ICU and hospital length of stay were compared using log rank. Alpha was set at 0.05. Normally distributed data are reported as mean and 95% confidence interval (CI), and non-normally distributed data as median and interquartile range (IQR), or median and 95% CI.

Sample size calculation: We had a priori estimated the proportion of patients with AOD to be 30–40%. Study primary endpoint was total dose of sedative and total dose of opioids administered. Power analysis indicated that with 70 patients, we would be able to detect a 0.7 standard deviation difference with 80% power and a 0.85 standard deviation with 90% power.

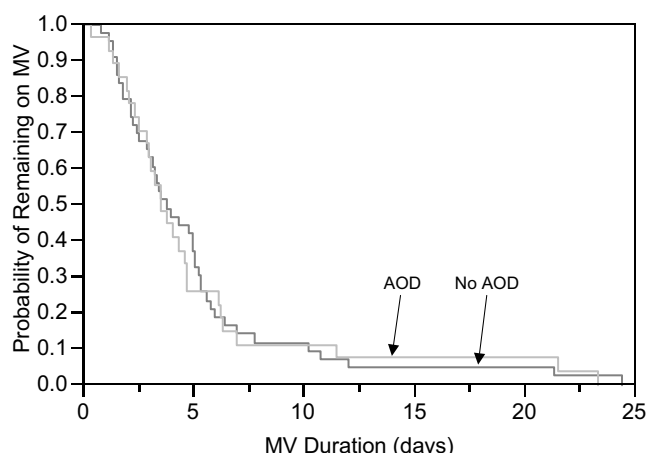


Figure 2
Kaplan-Meier estimate of probability of remaining on mechanical ventilation (MV) in patients with alcohol and other drug use disorders (AOD) and those without (No AOD).

Results: Three hundred fifty-three patients requiring MV were admitted to the medical ICU between October 2002 and June 2003. One hundred forty-nine patients selected by the random number generation algorithm were screened. Seventy-nine patients failed to meet the pre-specified inclusion criteria for the following reasons: age < 18 years (1), duration of MV < 24 hours (22), tracheostomy at the time of initiation of MV (2), transfer from another ICU (20), location other than medical ICU (24), prisoner (10).

Of the 70 patients meeting the inclusion criteria, 27 (39%) were diagnosed with AOD (Figure 1). The diagnosis of AOD was established based on toxicology results in 5 (19%), identification by the healthcare provider in the medical record in 16 (59%), and by the DSM IV-TR criteria in 7 (26%) patients. Of the 21 patients who underwent toxicology screens, 1 was positive for alcohol, 4 for cocaine, 5 for benzodiazepines, and 7 for opiates. All positive benzodiazepine and opiate screens could be accounted for by administration of medication prior to sample acquisition. No toxicology screen was positive for amphetamine, barbiturate, or cannabis.

Overall, alcohol was implicated in 22 cases (31%) and other drugs in 7 (10%). Of the 22 patients with alcohol use disorders, alcohol was the only implicated substance in 20 (91%) cases, while 2 patients had other drug use disorders (marijuana in 1 case and cocaine, opioids and marijuana in the second case). Of the 7 patients with other drug use disorders, heroin and/or cocaine were implicated in 5 patients. When comparing the prevalence of AOD in our medical ICU patients (39%) to the population prevalence of the city of Richmond (17.9%), the medical ICU rate was significantly higher ($p < 0.0001$).

Baseline characteristics for patients are outlined in Table 3. Patients with AOD were more likely to be male. Although one patient with AOD was intubated for delirium tremens, analyses revealed no difference in reason for MV between the two groups. Patients with AOD were less severely ill as measured by APACHE II, and adjustment of GCS suggested a trend toward lower severity of illness ($p = 0.07$). The two groups had similar Sequential Organ Failure Assessment (SOFA) scores on the first day of MV and adjusting for GCS did not change the results.

Patients with AOD were significantly more likely to receive benzodiazepines (27 out of 27 patients versus 39 out of 43, $p = 0.044$) and opioids (26 out of 27 patients versus 31 out of 43, $p = 0.006$) compared to patients without AOD. Administered opioids included morphine (AOD 15 versus non-AOD 21, $p = 0.38$), fentanyl (AOD 13 versus non-AOD 16, $p = 0.26$), hydromorphone (AOD 3 versus non-AOD 0, $p = 0.22$), and meperidine (AOD 0 versus non-AOD 1, $p = 0.39$). There was a trend toward increase

methadone administration in the AOD group (AOD 4 versus non-AOD 1, $p = 0.07$). The likelihood of receiving propofol was similar in the two groups (12 out of 27 versus 21 out of 43, $p = 0.72$). Table 4 summarizes the administered sedative and opioid doses. The group of patients with AOD received 2.5 times and 5 times the total doses of benzodiazepines and opioids, respectively, compared to the group without AOD. Propofol dose did not differ in the two groups. While the number of continuously infused sedatives and opioids was similar for AOD and non-AOD patients (2.1 versus 1.8, $p = 0.15$), the mean infusion duration in the AOD group was longer (16 hours/day medication, 95%CI [12.7; 18.3] versus 10 [7.6; 12.1], $p = 0.002$).

A total of 2381 RASS values were recorded during 362 days of MV for the 70 study patients. The number of assessments was similar between patients with and without AOD (28 observations, IQR [16.0; 39.0] versus 30, IQR [14.0; 40.2], $p = 0.89$). The mean RASS was similar among AOD patients (-2; 95% CI [-2.6; -1.6]) and non-AOD patients (-2; 95% CI [-2.4; -1.6], $p = 0.83$). However, AOD patients had a larger variance in RASS (3 RASS units, 95%CI [2.3; 3.7] versus 2, 95%CI [1.5; 2.6], $p = 0.049$), indicating larger fluctuations in sedation levels. Patients with AOD were not more frequently agitated as measured by RASS ≥ 3 compared to those without AOD (3.0% of observations, 95%CI [2.1; 4.2]% versus 2.4%, 95%CI [1.8; 3.2]%, $p = 0.33$).

AOD patients and non-AOD patients had similar MV duration (3.6 days, 95%CI [2.60; 4.71] versus 3.9, 95%CI [2.91; 5.14], $p = 0.89$) (Figure 2). Adjustment for gender, APACHE II, lorazepam equivalents, morphine equivalents, and duration of continuous infusions did not change the results. Because mortality on MV may be more a measure of time until death than outcome of mechanical ventilation management, we analyzed MV duration for ICU survivors and non-survivors. Twenty patients died in the ICU, 6 with AOD and 14 without AOD. The median duration of MV in non-survivors with AOD tended to be shorter compared to ICU non-survivors without AOD (AOD 3.6 days, 95% CI [0.43; undeterminable] versus non-AOD 5.4 days, 95% CI [2.22; 10.25], $p = 0.12$). Severity of illness in the two groups was similar as measured by APACHE II (AOD 32, 95% CI [23.7; 39.7] versus non-AOD 31, 95% CI [26.0; 36.4], $p = 0.92$) and SOFA (AOD 12, 95% CI [8.0; 15.0] versus non-AOD 11, 95% CI [8.3; 12.9], $p = 0.65$). Adjustment of APACHE II for GCS (AOD 23, 95% CI [15.6; 30.8] versus non-AOD 23, 95% CI [17.5; 27.5], $p = 0.88$) and adjustment of SOFA for GCS (AOD 8, 95% CI [5.4; 11.6] versus non-AOD 7, 95% CI [5.4; 9.5], $p = 0.55$) did not change severity of illness.

Fifty patients survived the ICU, 21 with AOD and 29 without AOD. Duration of MV for ICU survivors was similar for the two groups (AOD 3.8 days, 95% CI [2.36; 4.73] versus non-AOD 3.4 days, 95% CI [2.35; 4.82], $p = 0.87$). AOD patients who survived were less severely ill as measured by APACHE II (AOD 19, 95% CI [15.5; 22.3] versus non-AOD 24, 95% CI [21.0; 26.7] $p = 0.03$) but not SOFA (AOD 7, 95% CI [5.2; 8.2] versus non-AOD 8, 95% CI [6.6; 9.1], $p = 0.25$). APACHE II adjusted for GCS remained lower in the AOD group (AOD 11, 95% CI [8.2; 14.3] versus non-AOD 15, 95% CI [12.7; 17.9], $p = 0.045$). SOFA adjusted for GCS remained similar for the AOD and non-AOD group (AOD 5, 95% CI [3.7; 5.8] versus non-AOD 4, 95% CI [2.8; 5.3], $p = 0.40$).

There was no difference in the rate of reintubation (11% versus 9%, $p = 0.81$), tracheostomy (7% versus 2%, $p = 0.31$), or hospital

mortality (22% versus 40%, $p = 0.13$). ICU length of stay (6 days [3.4; 6.9] versus 6 days, 95% CI [4.4; 6.8], $p = 0.91$) and hospital length of stay (9 days, 95%CI [5.3; 11.9] versus 13 days, 95%CI [9.7; 18.2], $p = 0.11$) were similar between patients with and without AOD. There were no unplanned extubations.

Discussion

The current study reveals that nearly 40% of all mechanically ventilated patients in our medical ICU suffer from alcohol or other drug use disorders, with alcohol predominating. Additionally, our study found that AOD patients receive a greater amount of sedatives and opioids than their non-AOD comparators in order to achieve a similar degree of sedation. Despite this greater exposure to sedatives, the duration of MV was similar in the AOD and the non-AOD groups.

AOD is a common problem in our medical ICU, affecting 27 out of 70 (39%) of our long-term mechanically ventilated patients. The true rate in our patient population is likely to be even higher because of the retrospective nature of our study and because clinicians fail to diagnose AOD in 10% to 82% of patients.^{25,26} Our rate is substantially higher than that reported in the literature and may be explained by methodological issues. Other studies have examined rates of admissions directly attributable to AOD or have limited diagnosis to alcohol use disorders.^{9,10} We included all patients where AOD was either a primary or other diagnosis. The prevalence of AOD in our mechanically ventilated patients was significantly higher than that in the surrounding community, indicating that patients with AOD are at increased risk of requiring MV. This finding has also been demonstrated by others. Moss et al. have shown that patients with alcohol use disorders and sepsis are more likely to require MV compared to septic patients without alcohol use disorders.¹⁰ Saitz et al. have shown that patients with pneumonia who have alcohol use disorders are at increased risk of requiring ICU level care, and Suchyta et al. have shown that patients with AOD and other psychiatric disorders are overrepresented among ICU patients.^{11,27}

Alcohol was the most commonly implicated substance, which is similar to national findings, and our rate of 31% among MV patients is similar to the 30% reported in a prospective study by Moss et al.¹⁰ Also consistent with national findings, in 91% of all patients alcohol use disorders, alcohol was the only substance implicated.⁸ Among non-alcohol drug use disorders, cocaine and heroin, the two most common illicit drugs used in the city of Richmond, were the most commonly implicated substances in our patient population (5 out of 7 patients).²⁴ Not surprisingly, no patient was diagnosed with amphetamine use disorders, since these substances are more commonly used in the Western part of the United States than Virginia.²⁸ Additionally, the highest prevalence of amphetamine use disorders is in the age group 18–34 years old, which is generally younger than our study population.

Patients with AOD required 2.5 times more sedative and 5 times more opioid doses to achieve sedation levels similar to patients without AOD. They also received longer duration of infusions which likely resulted in higher plasma levels and suggest a high degree of tolerance.²⁹ Although no difference was seen in propofol dose, relatively few patients received this sedative. Since sedation was managed according to a standardized algorithm in our ICU, it is not likely that the higher dosages seen in the AOD patients were driven by a bias towards greater levels

of sedation in this population, but rather by the true need to achieve a pre-specified level of sedation. This is further supported by tolerance and increased metabolism through induction of the cytochrome P-450 enzyme system documented previously in this population.³⁰ Patients with AOD and those without AOD have similar bilirubin and creatinine, suggesting that lower doses in non-AOD patients are not accounted for by impaired metabolism and clearance. Additionally, P/F and PEEP were similar for both groups, suggesting no difference in lung injury and need for sedation.

Patients with AOD had duration of MV similar to patients without AOD. Patients without AOD had a higher number of patients with pneumonia, acute lung injury and sepsis, diagnoses that are associated with longer duration of mechanical ventilation.³¹ It is possible that this could have lead to a longer MV duration in the group of patients without AOD. Additionally, patients without AOD had higher severity of illness which may also have resulted in longer duration of mechanical ventilation compared to the group with AOD. It is conceivable that patients with AOD did not have a shorter MV duration because of the increased sedative and opioid requirement. The longer expected MV duration in the group of patients without AOD may have been eliminated by the increased sedative and opioid requirements in patients with AOD, resulting in similar MV duration in the 2 groups.

Our study has several strengths. The study was conducted at a large urban medical center, and patients were randomly selected. Diagnoses were established by clinical experts in Addiction Medicine who were blinded to the amount of administered sedatives and opioids and duration of MV. To minimize the bias in assigning an AOD diagnosis retrospectively, toxicology data and healthcare provider history were used whenever possible; when not available, very strict adherence to the definitions of the DSM IV-TR was established. Both sedation and weaning from MV are standardized in our ICU, thus eliminating the potential confounding effect of differential preference-based practices in this area on the outcomes of interest.

Our study has limitations. The diagnosis of AOD is difficult to establish in patients, and this is particularly problematic in non-verbal critically ill patients undergoing MV. Screening for AOD is not standardized in our ICU and is at the discretion of clinicians. In our experience, intensivists do not routinely determine the presence of these disorders in their patients. The definition of AOD is broad and includes behavioral and social aspects, and clinicians may focus on the aspects of physiologic dependence, tolerance and withdrawal during critical illness. Additionally, next-of-kin may not be forthcoming with information about AOD. These factors contribute to the underdiagnosis and misclassification of some study patients. Despite this limitation, we were able to determine significant differences between patients assigned a diagnosis of AOD and those not assigned this diagnosis, indicating that patients with AOD are different from those without AOD. The study sample was small; however, even the small number of charts reviewed had sufficient power to detect significant differences in the primary outcome, again supporting the findings that patients with AOD are quite different from their non-AOD counterparts. The study was limited to a single center's medical ICU, excluding patients in the surgical ICU, patients with primarily cardiac diagnoses, and trauma patients which may limit its generalizability.

Conclusion

Our study is the first to identify AOD as an important comorbidity that impacts sedation management while on MV. AOD patients require a greater amount of sedatives and opioids to achieve the same level of sedation. ICU clinicians need to be cognizant of the potential influence of AOD on the course and management of their mechanically ventilated patients, particularly in those ICU's that do not utilize a clinical practice guideline-driven sedation protocol, in order to avoid potential complications associated with over- or undersedation. Given a problem of such an extensive magnitude, AOD among MV patients needs to be studied further in prospective studies to gain a better understanding of how to improve sedation and other outcomes in these patients.

References

- 1 Arroliga A, Frutos-Vivar F, Hall J, Esteban A, Apezteguia C, Soto L, Anzueto A, International Mechanical Ventilation Study Group: Use of sedatives and neuromuscular blockers in a cohort of patients receiving mechanical ventilation. *Chest* 2005, 128:496-506.
- 2 Woods JC, Mion LC, Connor JT, Viray F, Jahan L, Huber C, McHugh R, Gonzales JP, Stoller JK, Arroliga AC: Severe agitation among ventilated medical intensive care unit patients: Frequency, characteristics and outcomes. *Intensive Care Med* 2004, 30:1066-1072.
- 3 Kollef MH, Levy NT, Ahrens TS, Schaiff R, Prentice D, Sherman G: The use of continuous i.v. sedation is associated with prolongation of mechanical ventilation. *Chest* 1998, 114:541-548.
- 4 Kress JP, Pohlman AS, O'Connor MF, Hall JB: Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *N Engl J Med* 2000, 342:1471-1477.
- 5 Brook AD, Ahrens TS, Schaiff R, Prentice D, Sherman G, Shannon W, Kollef MH: Effect of a nursing implemented sedation protocol on the duration of mechanical ventilation. *Crit Care Med* 1999, 27:2609-2615.
- 6 De Jonghe B, Bastuji-Garin S, Fangio P, Lacherade JC, Jabot J, Appere-De-Vecchi C, Rocha N, Outin H: Sedation algorithm in critically ill patients without acute brain injury. *Crit Care Med* 2005, 33:120-127.
- 7 MacLaren R, Plamondon JM, Ramsay KB, Rocker GM, Patrick WD, Hall RI: A prospective evaluation of empiric versus protocolbased sedation and analgesia. *Pharmacotherapy* 2000, 20:662-672.
- 8 Substance Abuse and Mental Health Services Administration, Office of Applied Research: Results from the 2004 National Survey on Drug use and Health: National Findings Rockville, MD: U.S. Department of Health and Human Services; 2005.
- 9 Baldwin WA, Rosenfeld BA, Breslow MJ, Buchman TG, Deutschman CS, Moore RD: Substance abuse related admissions to adult intensive care. *Chest* 1993, 103:21-25.
- 10 Moss M, Parsons PE, Steinberg KP, Hudson LD, Guidot DM, Burnham EL, Eaton S, Cotsonis GA: Chronic alcohol abuse is associated with an increased incidence of acute respiratory distress syndrome and severity of multiple organ dysfunction in patients with septic shock. *Crit Care Med* 2003, 31:869-877.
- 11 Suchyta MR, Hopkins RO, Beck C, Jephson A: Prevalence of alcohol abuse, drug abuse and psychiatric disorders in icu patients. *Am J Resp Crit Care Med* 2006, 3:A737.
- 12 Ip Yam PC, Forbes A, Kox WJ: Clonidine in the treatment of

- alcohol withdrawal in the intensive care unit. *Br J Anaesth* 1992, 68:106-108.
- 13 Mayo-Smith MF, Beecher LH, Fischer TL, Gorelick DA, Guillaume JL, Hill A, Jara G, Kasser C, Melbourne J, Working Group on the Management of Alcohol Withdrawal Delirium, Practice Guidelines Committee, American Society of Addiction Medicine: Management of alcohol withdrawal delirium. An evidence-based practice guideline. *Arch Intern Med* 2004, 164:1405-1412.
 - 14 de Wit M, Wan SY, Gill S, Best AM, Jenvey WI, Tomlinson J, Weaver MF: Effect of substance use disorders on sedation and mechanical ventilation. *Am J Resp Crit Care Med* 2006, 3:A736.
 - 15 Jacobi J, Fraser GL, Coursin DB, Riker RR, Fontaine D, Wittbrodt ET, Chalfin DB, Masica MF, Bjerke HS, Coplin WM, Crippen DW, Fuchs BD, Kelleher RM, Marik PE, Nasraway SA Jr, Murray MJ, Peruzzi WT, Lumb PD, Task Force of the American College of Critical Care Medicine (ACCM) of the Society of Critical Care Medicine (SCCM), American Society of Health-System Pharmacists (ASHP), American College of Chest Physicians: Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. *Crit Care Med* 2002, 30:119-141.
 - 16 Ely EW, Baker AM, Dunagan DP, Burke HL, Smith AC, Kelly PT, Johnson MM, Browder RW, Bowton DL, Haponik EF: Effect on the duration of mechanical ventilation of identifying patients capable of breathing spontaneously. *N Engl J Med* 1996, 335:1864-1869.
 - 17 American Psychiatry Association: Diagnostic and Statistics Manual of Mental Disorders. American Psychiatry Association editor. IVTR ed. Washington, DC 2000.
 - 18 Knaus WA, Draper EA, Wagner DP, Zimmerman JE: APACHE II: A severity of disease classification system. *Crit Care Med* 1985, 13:818-829.
 - 19 Teasdale G, Jennett B: Assessment of coma and impaired consciousness. A practical scale. *Lancet* 1974, 2:81-84.
 - 20 Vincent JL, Moreno R, Takala J, Willatts S, De Mendonca A, Bruining H, Reinhart CK, Suter PM, Thijs LG: The SOFA (sepsis-related organ failure assessment) score to describe organ dysfunction/failure. on behalf of the working group on sepsis-related problems of the European Society of Intensive Care Medicine. *Intensive Care Med* 1996, 22:707-710.
 - 21 Lacy CF, Armstrong LL, Goldman MP, Lance LL: Lexi-Comp's Drug Information Handbook. 13th edition. Hudson, Ohio: Lexi-Comp; 2004:1947.
 - 22 Cammarano WB, Drasner K, Katz JA: Pain control sedation and use of muscle relaxants. In *Principles of Critical Care* Second edition. Edited by: Hall JB, Schmidt GA, Wood LDH. New York: McGraw-Hill; 1998:90-97.
 - 23 Sessler CN, Gosnell MS, Grap MJ, Brophy GM, O'Neal PV, Keane KA, Tesoro EP, Elswick RK: The Richmond Agitation-Sedation Scale: Validity and reliability in adult intensive care unit patients. *Am J Respir Crit Care Med* 2002, 166:1338-1344.
 - 24 Thacker W, Turf E, Eller TJ: Measuring Alcohol and Other Drug Abuse Problems in Richmond, Virginia. Richmond, VA: Virginia Commonwealth University; 2001.
 - 25 Rumpf HJ, Bohlmann J, Hill A, Hapke U, John U: Physicians' low detection rates of alcohol dependence or abuse: A matter of methodological shortcomings? *Gen Hosp Psychiatry* 2001, 23:133-137.
 - 26 Rydon P, Redman S, Sanson-Fisher RW, Reid AL: Detection of alcohol-related problems in general practice. *J Stud Alcohol* 1992, 53:197-202.
 - 27 Saitz R, Ghali WA, Moskowitz MA: The impact of alcohol-related diagnoses on pneumonia outcomes. *Arch Intern Med* 1997, 157:1446-1452.
 - 28 Office of Applied Research, Substance Abuse and Mental Health Services Administration, Research Triangle Institute: Methamphetamine use, Abuse, and Dependence: 2002, 2003, 2004. Department of Health and Human Services; 2005.
 - 29 de Wit M, Best AM, Epstein SK, Greenblatt DJ: Lorazepam concentrations, pharmacokinetics, and pharmacodynamics in a cohort of mechanically ventilated icu patients. *Int J Clin Pharmac Therapeutics* 2006, 44:466-73.
 - 30 Feierman DE, Melinkov Z, Nanji AA: Induction of CYP3A by ethanol in multiple in vitro and in vivo models. *Alcohol Clin Exp Res* 2003, 27:981-988.
 - 31 Esteban A, Anzueto A, Frutos F, Alia I, Brochard L, Stewart TE, Benito S, Epstein SK, Apezteguia C, Nightingale P, Arroliga AC, Tobin MJ: Mechanical Ventilation International Study Group: Characteristics and outcomes in adult patients receiving mechanical ventilation: A 28-day international study. *JAMA* 2002, 287:345-355.

In The Shadow...continued from page 53

remembered about the past in a fleeting moment. However, each interview is a valuable source of information even if the results cannot be generalized. The methodology was chosen to be appropriate for the questions formulated. The intention was to follow as closely as possible the words of the patients, but there was always the possibility of misinterpretation or over-interpretation. To minimize such risks most interviews started with a short recapitulation of the previous one. Checking questions were also used (dialogic validity). Finally, all through the study, critical researchers, physicians and co-readers had critically read and checked the interpretations made (communicative validity).

Conclusion

The result of this study could help to improve health care, if it could make physicians

- more aware of the fact that there are patients whose need for information remains of great importance all through the disease, even in later phases and when life comes near to the end
- more aware that there is sometimes a lack of knowledge among patients, to be recognized and as much as possible minimized
- more aware that knowing the patient's strategy for coping with information could probably function as a key for the physician about when to communicate with the patient about progressing disease and about death coming near.

Obstructive Sleep Apnea: A Cause of Chronic Cough

Surinder S. Birring, Alvin J. Ing, Kevin Chan, Gavina Cossa, Sergio Matos, Michael D.L. Morgan, Ian D. Pavord

Abstract

Chronic cough is a common reason for presentation to both general practice and respiratory clinics. In up to 25% of cases, the cause remains unclear after extensive investigations. We report 4 patients presenting with an isolated chronic cough who were subsequently found to have obstructive sleep apnea. The cough improved rapidly with nocturnal continuous positive airway pressure therapy. Further studies are required to investigate the prevalence of coexistence of these common conditions.

Background: Chronic cough is one of the commonest reasons for presentation to respiratory clinics. Investigations are usually aimed at identifying the three most common causes of chronic cough: cough variant asthma, gastro-oesophageal reflux and upper airway cough syndrome.¹ In up to 25% of patients, the cause of cough remains unexplained after extensive investigations and treatment trials.²⁻⁴ Patients experience considerable physical and psychological morbidity. Here, we report 4 well-characterised patients referred to a general respiratory clinic with unexplained chronic cough who were subsequently found to have obstructive sleep apnea.

Case representations

Patient 1: A 52-year-old financial advisor was referred by his general practitioner with a 3-month history of productive cough. He described a severe barking cough that occurred both in the day and night time and was exacerbated by lying flat, strong odors and smoky atmospheres. He was prescribed multiple courses of antibiotics, which were unhelpful. He also complained of mild dyspnea on climbing hills but no wheezing. He had longstanding left nasal congestion without post-nasal drip following a broken nose in childhood and mild symptoms of gastro-oesophageal reflux. He had been diagnosed with hypertension and hypercholesterolemia two years previously for

which he was prescribed Bendroflumethiazide, Valsartan, Doxazosin and Cervistatin. He was an ex-smoker and accumulated a 15 pack-year smoking history. His clinical examination and physical findings were normal. Initial spirometry and chest radiograph were within normal limits (Table 1). His cough was thought to be due to gastro-oesophageal reflux and rhinitis so he was started on a prolonged course of topical nasal steroids and high dose proton pump inhibitor. Methacholine airway challenge test, induced sputum eosinophil cell count, high resolution computerized tomography (HRCT) scan and echocardiogram arranged to investigate asthma, eosinophilic bronchitis, bronchiectasis and left ventricular dysfunction were all normal (Table 1).

On review 6 and 12 months later his symptoms of rhinitis and gastro-oesophageal reflux had resolved but his cough persisted. No explanation for the cough was found and he discharged back to his general practitioner. He was re-referred back to the clinic 3 years later with daytime somnolence, lethargy, apneas and cough. In retrospect, he had mild daytime somnolence and lethargy at the time of initial presentation. He was noted to have a small oropharynx on external examination. Polysomnography was arranged that was consistent with the diagnosis of obstructive sleep apnea (Table 1). Nocturnal nasal continuous positive airway pressure (CPAP) therapy was commenced and he noticed an immediate improvement in cough and daytime somnolence. His cough resolved entirely within 6 weeks and he remains free of cough 12 months later. The initiation of CPAP therapy has also led to a reduction in anti-hypertensive medications and complete resolution of oxygen desaturation on repeat sleep study.

Patient 2: A 73 year-old housewife with an 18-month history of severe chronic cough was referred by her respiratory physician for a second opinion. The cough was predominantly dry, interfered with her daily activities and occasionally disturbed her sleep. She did not report other respiratory symptoms, postnasal drip or gastro-oesophageal reflux. Her past medical history consisted of diabetes, hypertension, atrial fibrillation and aorto-femoral bypass for peripheral vascular disease. Soon after the onset of cough, she was diagnosed as having severe obstructive sleep apnea with full polysomnography after admitting to symptoms of daytime somnolence, snoring and disturbed sleep (Table 1). She could not be persuaded to try CPAP therapy or alternative options and was more concerned about the chronic cough. She was an ex-smoker and stopped

Surinder Birring is with the Department of Respiratory Medicine, King's College Hospital, London. Authors Ing, Chan, and Cossa are with the Respiratory Investigation Unit, Concord Hospital, Sydney, Australia; Matos, Morgan and Pavord are with the Institute for Lung Health, Department of Respiratory Medicine, Glenfield Hospital, Leicester, UK. The authors wish to thank D.D. Vara (Head, Department of Respiratory Physiology, Glenfield Hospital) and Peter Rodgers (Head, Respiratory Function Unit, Concord Hospital) for assistance in characterization of some of the patients. Reprinted from Cough, BioMed Central. This is an Open Access article distributed under the terms of the Creative Commons Attribution License.

Table 1: Patient characteristics

	Patient 1	Patient 2	Patient 3	Patient 4
Age (years)	52	73	46	63
Gender (m/f)	M	F	F	M
Snoring	Yes	Yes	Yes	Yes
Nocturnal cough	Yes	Yes	Yes	Yes
Body mass Index (Kg/m ²)	35	32	37	33
Baseline cough VAS	90	95	50	80
Post CPAP cough VAS	0	5	0	0
Cough duration at OSA diagnosis (mo)	48	6	16	8
FEV ₁ (%predicted)	93	61	119	100
FEV ₁ /FVC (%)	78	70	84	83
PC ₂₀ mg/ml)	>16	nd	>16	>16
Sputum neutrophil (nr <65%)	89	-	91	87
Sputum eosinophil (nr <2%)	0.3	-	1.4	0.5
ESS preCPAP	7	14	15	15
ESS post CPAP	3	8	7	5
AHI baseline (per hour)	36	86	62	10 (4% SpO ₂ dips)
SpO ₂ (4% dips/hour) on CPAP	0.7	0	3	0
CPAP (cm H ₂ O)	12	12	8	6
CPAP compliance (mean hours/night)	6	4	7	6

NR: normal range; VAS: visual analogue score (0–100 mm worst); CPAP: continuous positive airway pressure; OSA: obstructive sleep apnoea; FEV₁: forced expiratory volume; FVC: forced vital capacity; PC₂₀: provocative concentration of methacholine causing >20% decline in FEV₁; ESS: daytime Epworth Sleepiness Scale (range 0–24, nr<11); AHI: apnoea hypopnoea index (nr< 5/hour); SpO₂: oxygen saturation

smoking 13-years previously, accumulating a 40-pack year smoking history. Clinical examination and chest radiograph were normal. Spirometry was consistent with a moderate restrictive defect consistent with obesity. Treatment trials with inhaled corticosteroids, short and long acting bronchodilators and high dose proton pump inhibitors were unsuccessful. Nasendoscopy, Ear-Nose-Throat evaluation, echocardiogram (normal left ventricular function) and bronchoscopy were normal. She had marked impairment of quality of life secondary to chronic cough as assessed with the Leicester Cough Questionnaire (Figure 1) and increased cough frequency measured with the Leicester Cough Monitor, a 24-hour ambulatory automated cough detection monitor (Figure 2).⁵⁻⁷ She agreed to try CPAP therapy at a subsequent follow-up clinic. She was admitted for a CPAP titration study and a pressure of 12 cm H₂O abolished snoring and apnoeas. She noticed a significant improvement in cough at the end of the first week on CPAP therapy. There was an 80% reduction in objective cough frequency at 6-weeks (672 vs 141 coughs per 24-hours) and a significant improvement in cough specific quality of life (Improvement in LCQ total score 8.2 which was greater than the LCQ minimal important difference of 1.3; Figures 1 and 2). She was able to resume regular activities after improvement of her cough.

Patient 3: A 46-year-old nurse was referred by her occupational health physician with a 1-year history of productive cough. The cough occurred through the day and night and there were no specific triggers or associated symptoms. There were no symptoms of dyspnea or wheeze. She did not complain of symptoms suggestive of rhinitis or gastro-esophageal reflux. A trial of inhaled corticosteroids and nasal steroids were unhelpful. Her husband commented that she recently started snoring but he had not witnessed apnoeas. She complained of lethargy that was associated with mild somnolence. She had pneumonia in childhood but was unable to give further details.

Her past medical history was otherwise unremarkable. She had never smoked and did not consume alcohol. On examination, she had evidence of retrognathia but was otherwise unremarkable. Chest radiograph and spirometry were within normal limits.

The initial differential diagnosis was cough secondary to asthma, eosinophilic bronchitis or bronchiectasis. Methacholine airway challenge test, induced sputum eosinophil cell count and HRCT were arranged and were normal (Table 1). Partial polysomnography (RM60 study: airflow, chest wall movement, oximetry, snoring, pulse) was subsequently arranged because of mild somnolence and snoring, which was highly suggestive of obstructive sleep apnea. Nocturnal nasal CPAP therapy was commenced and she noticed an immediate improvement in cough, lethargy and somnolence. The cough resolved within 5 days and she remains free of cough 15 months later. Repeat sleep study indicates complete resolution of oxygen desaturation on CPAP.

Patient 4: A 63-year-old office worker with the police force was referred by his general practitioner with a 4-month history of chronic productive cough. The cough was severe, occurred both day and night time and was worse lying flat. There were no dyspnea, wheeze or symptoms suggesting gastro-esophageal reflux and rhinitis. He was an ex-smoker with less than 2 pack year smoking history and did not consume alcohol. His past medical history was unremarkable. Clinical examination, chest radiograph and spirometry were normal.

The cause of cough was not clear. Methacholine airway challenge test and induced sputum eosinophil cell count were normal (Table 1). At 4-month review he complained of snoring and daytime somnolence. A pulse oximetry sleep study was arranged which was consistent with a diagnosis of obstructive sleep apnea. The cough and sleepiness improved significantly

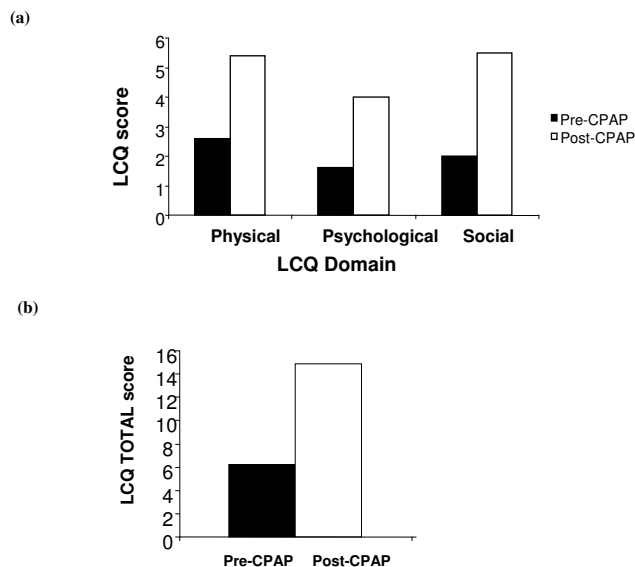


Figure 1 Improvement in cough specific quality of life after (continuous positive airway pressure) CPAP therapy in patient 2. (a) Leicester Cough Questionnaire (LCQ) Domain scores. (Higher score = better quality of life: QOL) (b) LCQ total score. (Minimal important difference 1.3; higher score = better QOL).

with nocturnal nasal CPAP after 2 days and the cough resolved completely 3 months later. At 15-month review after initiation of CPAP therapy, the patient does not complain of cough or somnolence.

Discussion

We report for the first time, four adult patients with obstructive sleep apnea that presented with a chronic cough. All patients had a rapid improvement of cough with CPAP therapy and are free of respiratory symptoms twelve months later. This suggests a link between cough and obstructive sleep apnea in these patients.

Obstructive sleep apnea was not apparent at presentation in our patients. The initial investigations were directed at determining the aetiology of chronic cough using a standardised diagnostic algorithm.⁸ These patients underwent assessment for the most common causes of chronic cough in non-smokers with normal chest radiograph and spirometry which are considered to be asthma, rhinitis and gastro-esophageal reflux disease. None of our patients were taking angiotensin converting enzyme

inhibitors. Daytime somnolence was present at initial consultation but this was not reported by patients or recognised by the physician. This symptom may have been masked by the severity of the cough and not considered by the physician since obstructive sleep apnea is not a recognised cause of chronic cough. It is only when typical symptoms of obstructive sleep apnea became apparent or progressed that polysomnography was requested and the diagnosis of obstructive sleep apnea established. The lack of clinical suspicion of obstructive sleep apnea at presentation with cough led to considerable delays in diagnosis and was over 3 years in one patient. Once CPAP therapy was initiated, there was a rapid improvement of cough and symptoms of obstructive sleep apnea within days. This is consistent with a case report of a three-year-old boy with chronic cough, snoring and upper airway obstruction on polysomnography in whom there was resolution of cough after commencing CPAP therapy.⁹

Patients with obstructive sleep apnea and cough are likely to have upper airway injury and inflammation resulting from snoring and frequent episodes of airway obstruction. Snoring and obstructive sleep apnea cause airway epithelial damage and inflammatory cell infiltration of the lamina propria.¹⁰ Our patients had a raised sputum neutrophil count consistent with inflammation in the large airways.¹¹ Patients with obstructive sleep apnea have raised concentrations of inflammatory mediators in the upper airways that may sensitize cough receptors leading to heightened cough reflex sensitivity analogous to that seen in cough due to asthma and eosinophilic bronchitis.^{12,13} Interestingly, subjects who snore are more likely to report a cough supporting the mechanism of airway injury causing cough in obstructive sleep apnea.¹⁴⁻¹⁸ It is possible that the cough may have resulted from mechanical causes and independently of airway inflammation since the effect of CPAP was rapid. Bonnet et al have described 5 patients with nocturnal cough and increased airway collapsibility secondary to bronchomalacia that responded to CPAP therapy.¹⁹ It is possible that this condition may have co-existed in our patients with obstructive sleep apnea.

Another potentially important mechanism of cough in patients with obstructive sleep apnea is gastro-esophageal reflux associated cough. Obstructive apnea episodes increase trans-diaphragmatic pressure that may lead to insufficiency of the gastric cardia and lower esophageal sphincter.²⁰ There is a higher incidence of gastro-esophageal reflux in patient with obstructive sleep apnea and CPAP therapy has been shown to reduce episodes of gastro-esophageal reflux.^{21,22} Another possibility is that CPAP therapy may be effective at reducing nocturnal gastro-esophageal reflux and associated cough independent of the presence of obstructive sleep apnea. Only patient 1 reported symptoms of gastro-esophageal reflux but his cough persisted despite a trial of high dose proton pump inhibitor. Gastro-esophageal reflux associated cough cannot be categorically excluded in our patients because we did not measure 24-hour esophageal pH or assess for the presence of non-acid gastro-esophageal reflux and this requires further study. Another possible cause of cough in our patients is rhinitis although none had symptoms or evidence of rhinitis on external examination at the time of diagnosis. However, "silent" rhinitis cannot be fully excluded in our patients. Finally, a general abnormality of upper airway reflexes is possible that leads to reduced upper airway tone and calibre and loss of inhibitory pathways of the cough reflex.²³

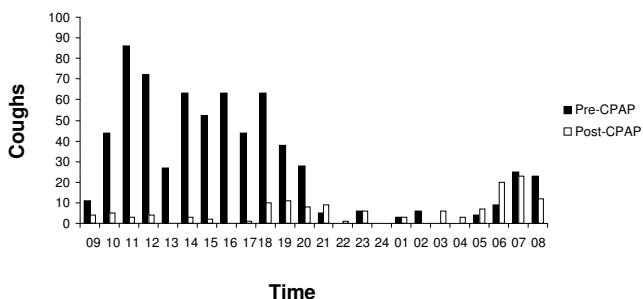


Figure 2 Decrease in cough frequency following CPAP in patient 2 assessed with the Leicester Cough Monitor (LCM).

Limitations of our study are the small number of patients studied and the diagnoses of obstructive sleep apnea were based on limited polysomnography and oximetry study in two cases. It is unlikely that these studies are false positives since both patients did not have a history of chronic obstructive pulmonary disease or heart failure where false positive studies are often seen. Furthermore, these studies are considered acceptable first line diagnostic studies in recent guidelines.²⁴ We are confident that our patients had obstructive sleep apnea since they had suggestive symptoms and good clinical and objective response to CPAP therapy. We were able to utilise recently available objective cough assessment tools in patient 2 to validate the presence of a frequent cough associated with impaired quality of life and a clinically significant improvement with CPAP therapy.⁵⁻⁷ This study suggests that objective coughing monitoring tools may be useful and responsive in patients with chronic cough and this requires confirmation in larger numbers.

Cough is likely to be a common symptom in patients presenting with obstructive sleep apnea. The prevalence of obstructive sleep apnea in patients presenting with a chronic cough is not known and deserves further study. The cause of cough remains unexplained in up to 30% of subjects referred to specialist cough clinics despite extensive investigations and it is likely that obstructive sleep apnea is missed in some cases. It is important to recognise this condition early because of its implications for driving and operating machinery and associated cardiovascular morbidity if left untreated. CPAP is a very effective therapy for obstructive sleep apnea associated cough, is well tolerated and resolution of cough was seen in all patients. Our preliminary series indicates that there is an association between cough and obstructive sleep apnea. Placebo controlled trials with CPAP will need to be performed to establish the value of this treatment modality for obstructive sleep apnea related cough.

References

- 1 Irwin RS, Baumann MH, Bolser DC, Boulet LP, Braman SS, Brightling CE, Brown KK, Canning BJ, Chang AB, Dicipinigitis PV, Eccles R, Glomb WB, Goldstein LB, Graham LM, Hargreave FE, Kvale PA, Lewis SZ, McCool FD, McCrory DC, Prakash UB, Pratter MR, Rosen MJ, Schulman E, Shannon JJ, Smith Hammond C, Tarlo SM, American College of Chest Physicians (ACCP): Diagnosis and management of cough executive summary: ACCP evidence-based clinical practice guidelines. *Chest* 2006, 129(1 Suppl):1S-23S.
- 2 McGarvey LP, Heaney LG, Lawson JT, Johnston BT, Scally CM, Ennis M, Shepherd DR, MacMahon J: Evaluation and outcome of patients with chronic non-productive cough using a comprehensive diagnostic protocol. *Thorax* 1998, 53:738-743.
- 3 Haque RA, Usmani OS, Barnes PJ: Chronic idiopathic cough: a discrete clinical entity? *Chest* 2005, 127:1710-1713.
- 4 Birring SS, Brightling CE, Symon FA, Barlow SG, Wardlaw AJ, Pavord ID: Idiopathic chronic cough: association with organ specific autoimmune disease and bronchoalveolar lymphocytosis. *Thorax* 2003, 58:1066-1070.
- 5 Birring SS, Prudon B, Carr AJ, Singh SJ, Morgan MD, Pavord ID: Development of a symptom specific health status measure for patients with chronic cough: Leicester Cough Questionnaire (LCQ). *Thorax* 2003, 58:339-43.
- 6 Matos S, Birring SS, Pavord ID, Evans DH: Detection of cough signals in continuous audio recordings using hidden Markov models. *IEEE Transactions on Biomedical Engineering* 2006, 53:1078-83.
- 7 Birring SS, Matos S, Patel RB, Prudon B, Evans DH, Pavord ID: Cough frequency, cough sensitivity and quality of life in patients with chronic cough. *Resp Med* 2006, 100:1105-9.
- 8 Brightling CE, Ward R, Goh KL, Wardlaw AJ, Pavord ID: Eosinophilic bronchitis is an important cause of chronic cough. *Am J Respir Crit Care Med* 1999, 160:406-410.
- 9 Teng AY, Sullivan CE: Nasal mask continuous positive airway pressure in the treatment of chronic nocturnal cough in a young child. *Respirology* 1997, 2:131-134.
- 10 Paulsen FP, Steven P, Tsokos M, Jungmann K, Muller A, Verse T, Pirsig W: Upper airway epithelial structural changes in obstructive sleep-disordered breathing. *Am J Respir Crit Care Med* 2002, 166:501-509.
- 11 Pizzichini E, Pizzichini MM, Efthimiadis A, Evans S, Morris MM, Squillace D, Gleich GJ, Dolovich J, Hargreave FE: Indices of airway inflammation in induced sputum: reproducibility and validity of cell and fluid-phase measurements. *Am J Respir Crit Care Med* 1996, 154:308-317.
- 12 Goldbart AD, Goldman JL, Veling MC, Gozal D: Leukotriene modifier therapy for mild sleep-disordered breathing in children. *Am J Respir Crit Care Med* 2005, 172:364-370.
- 13 Birring SS, Parker D, Brightling CE, Bradding P, Wardlaw AJ, Pavord ID: Induced sputum inflammatory mediator concentrations in chronic cough. *Am J Respir Crit Care Med* 2004, 169:15-19.
- 14 Lu LR, Peat JK, Sullivan CE: Snoring in preschool children: prevalence and association with nocturnal cough and asthma. *Chest* 2003, 124:587-593.
- 15 Nelson S, Kulnis R: Snoring and sleep disturbance among children from an orthodontic setting. *Sleep Breath* 2001, 5:63-70.
- 16 Corbo GM, Fuciarelli F, Foresi A, De Benedetto F: Snoring in children: association with respiratory symptoms and passive smoking. *BMJ* 1989, 299:1491-1494.
- 17 Bloom JW, Kaltenborn WT, Quan SF: Risk factors in a general population for snoring. Importance of cigarette smoking and obesity. *Chest* 1988, 93:678-683.
- 18 Larsson LG, Lundback B, Jonsson E, Lindberg A, Sandstrom T: Are symptoms of obstructive sleep apnea syndrome related to bronchitic symptoms or lung function impairment? Report from obstructive lung disease in North Sweden study. *Respir Med* 1998, 92:283-8.
- 19 Bonnet R, Jorres R, Downey R, Hein H, Maggnessen H: Intractable cough associated with the supine position body position. *Chest* 1995, 108:581-585.
- 20 Demeter P, Pap A: The relationship between gastroesophageal reflux disease and obstructive sleep apnea. *J Gastroenterol* 2004, 39:815-820.
- 21 Gislason T, Janson C, Vermeire P, Plaschke P, Bjornsson E, Gislason D, Boman G: Respiratory symptoms and nocturnal gastroesophageal reflux: a population-based study of young adults in three European countries. *Chest* 2002, 121:158-63.
- 22 Ing AJ, Ngu MC, Breslin AB: Obstructive sleep apnea and gastroesophageal reflux. *Am J Med* 2000, 108:120-125.
- 23 Kimoff RJ, Sforza E, Champagne V, Ofiara L, Gendron D: Upper airway sensation in snoring and obstructive sleep apnea. *Am J Respir Crit Care Med* 2001, 164:250-255.
- 24 SIGN: Management of obstructive sleep apnea/hypopnea syndrome in adults. 2003:1-35.

NO DOWNSIDE. ANY QUESTIONS?

Isn't it nice when your questions are answered?

At Vapotherm, we listened carefully to your questions and requirements for a high flow device.

Performance:

- Integrated flow control for 1 to 40 LPM
- Accurate FiO₂ management via electronic blender
- Up to 100% relative humidity
- Temperature range from 33-43°C

Safety:

- Medium and low priority alarms
- Fully disposable patient circuit
- Backup oxygen sensor
- Backup internal battery

Ease of Use:

- Five minute set-up
- One-button control for temp, flow and FiO₂
- Disposable patient circuit and simple wipe down
- No scheduled maintenance for 3 years for internal components

Patient Comfort:

- Simple nasal cannula interface
- Broad range of temperature control
- Flow range for neonatal through adult patients

We listened. We delivered.
Insist on Precision.

*This is Precision Flow.
Everything else isn't.*



Pending
FDA Clearance

A little bit of magic



Meet an amazing new item from Smiths Medical PM, Inc.: the compact, reusable Capnocheck® Capnometer. Direct your attention to this mainstream device for fully quantitative monitoring of patient ETCO₂ and respiration rate. The Capnocheck® is simple to use and has no strings attached – no cables to get in the way. Among its many talents: this portable device is ready to perform; it has a precision digital readout; and it's sensitive, even when CO₂ output is low. With no need for routine calibration, the Capnocheck® Capnometer is a real crowd pleaser.



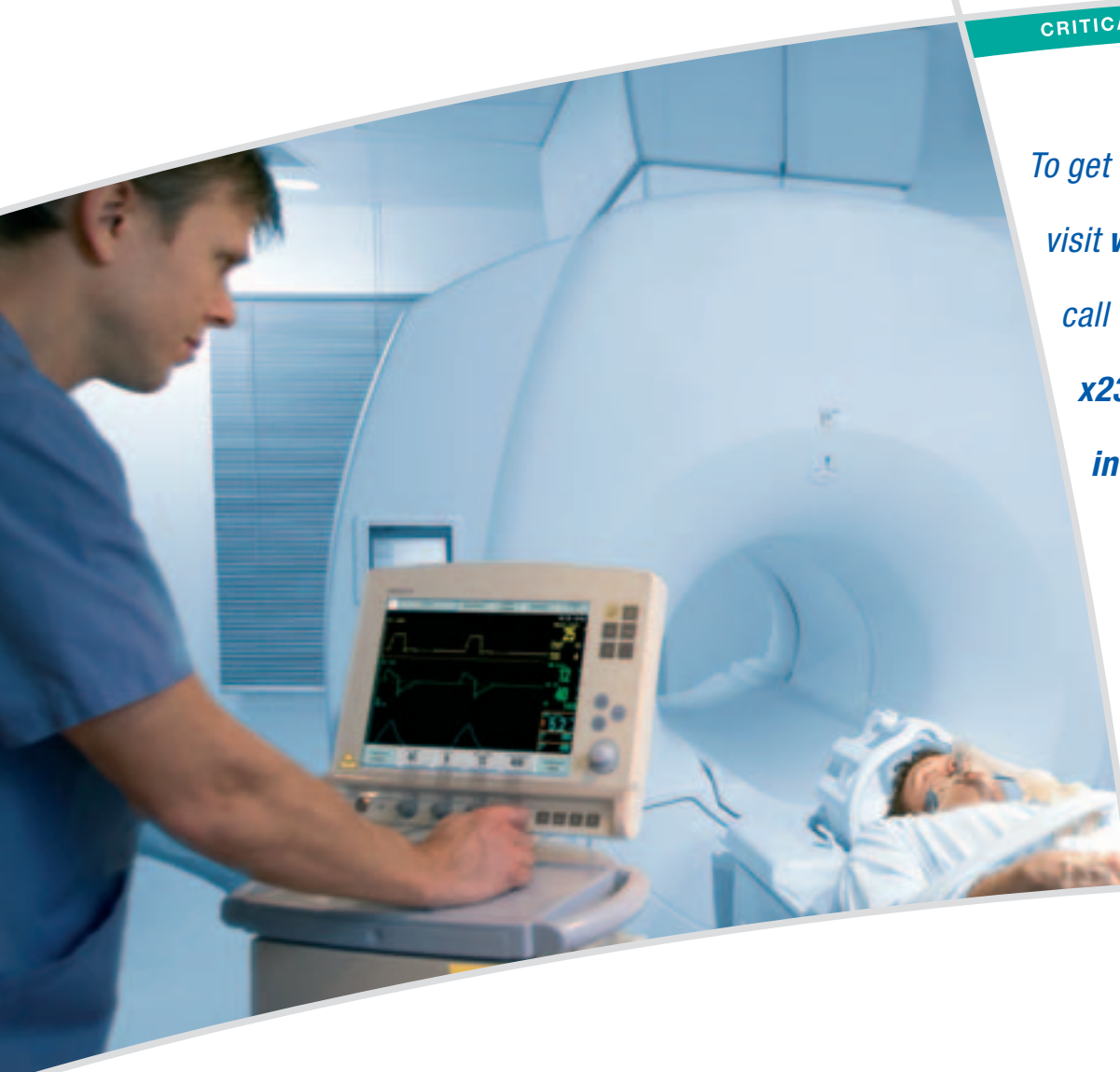
www.smiths-medical.com
800-558-2345

Smiths Medical, part of the global technology business Smiths Group
Capnocheck, BCI and the Smiths Medical design mark are registered trademarks of
the Smiths Medical family of companies. © 2007 Smiths Medical family of companies.
All rights reserved.

MAQUET

IMPROVE CLINICAL PERFORMANCE
IN THE MRI SUITE
SERVO-i FROM MAQUET

CRITICAL CARE



To get the MAQUET report,
visit www.mrivents.com,
call **1-888-MAQUET3**
x2306 or email
info@maquet-inc.com.

Critically ill patients on acute care ventilators often need MRI exams. Yet strong magnetic fields severely limit the types of medical devices that can be nearby.

Transferring patients out of the ICU and changing mechanical ventilators during transport can increase complications due to disconnection and lack of sophisticated ventilator support.



MR Conditional
symbol

The SERVO-i MR Environment Option from MAQUET can provide optimal ventilator support for any critically ill patient during MRI procedures. To get the MAQUET report, "Bridging the ICU and MRI Suite with Advanced Ventilator Support," visit mrivents.com, call 1-888-MAQUET3 x2306 or email info@maquet-inc.com.

SERVO-i MR Environment Option

MAQUET – The Gold Standard.



MAQUET, Inc.
1140 Route 22 East
Bridgewater, NJ 08807
1-888-MAQUET-3
www.maquet.com/us

MEMBER OF
THE GETINGE GROUP



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

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

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

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



Diagnostics

COBAS, LIFE NEEDS ANSWERS, AUTOQC and EQAP are trademarks of Roche.
©2006 Roche Diagnostics. All rights reserved. 574-31643-0606

<http://us.labsystems.roche.com>