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Editorial

TRUTH OR FICTION

While there are more medical journals than ever, they're also printing more lies, or so you'd glean from the nation's press. A New York Times story recently reported a huge surge in the number of journals aimed at particular segments of the healthcare community, most of them being published overseas. Concurrently, there's been no lack of press given over to stories about papers being planted in journals by writers with fiduciary connections to drug companies and medical product manufacturers. You can couple this with the South Korean cloning scandal, the dustup over article sponsorship at NIH, and, even as I write this, a revelation that Tamiflu may not be all it's cracked up to be.

According to Richard Smith, former editor for BMJ, "The problem lies with original studies, particularly the clinical trials, published by journals. A large trial published in a major journal has the journal's stamp of approval… These trials rarely produce results that are unfavorable to the [sponsoring] companies' products… Overall, studies funded by a company were four times more likely to have results favorable to the company than studies funded from other sources. In the case of the five studies that looked at economic evaluations, the results were favorable to the sponsoring company in every case." As if this wasn't bad enough, most of what you read, even if it's unbiased, may be just plain wrong. John Ioannidis, writing for PLoS Med, notes, "There is increasing concern that most current published research findings are false… Simulations show that for most study designs and settings, it is more likely for a research claim to be false than true. Moreover, for many current scientific fields, claimed research findings may often be simply accurate measures of the prevailing bias."

But let's face it, there's no such thing as a neutral, unbiased outlook. Human perception precludes a non-invested position from which any field can be evaluated, since there is always a de facto observer who cannot stand outside the perception to form a truly objective view. That's why, at Respiratory Therapy, we made the decision to be open to all points of view. Respiratory Therapy publishes all papers submitted by professionals in the field. Our goal is to present information to a well-informed audience in a timely manner. Our respondents are responsible for the accuracy of all information included in their submissions. We'll always provide the sources of all articles published in the journal so that there is never a misunderstanding as to the originator of the article. We believe our readers are astute enough to make the proper inferences about the validity of the information presented, based on the source, and to weigh the article accordingly. Respiratory caregivers make hundreds of judgments every day based on a variety of factors. That same level of expert judgment can easily be brought to bear on published research.

Les Plesko
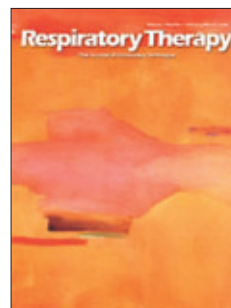
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News

HOPE FOR HACK ATTACKS

Vitamin 3D could improve asthma patients' responsiveness to steroids, according to a study at King's College London. According to the principal researcher, "This has major implications for how to treat patients with severe asthma." Steroids are often the only option, and they cause serious side effects, or they don't necessarily work. The effectiveness of vitamin co-therapy implies that steroids work by inducing the T-cells of the immune system to synthesize the signaling molecule IL-10. This molecule inhibits the immune responses that cause the asthma symptoms. Patients who are steroid-resistant don't produce IL-10, but when vitamin D3 is added to the culture medium along with dexamethasone, they do. Vitamin D3 is currently administered to patients with severe asthma to help prevent steroid-induced osteoporosis.

OR BREATHE THEM IN

Steroids, when inhaled, reduce airway inflammation, which leads to lower mortality rates from COPD. According to Dr. Donald Sin, who led a study at St Paul's Hospital in Vancouver, "Inhaled steroids have been controversial for a decade. They're clearly effective in asthma but some people in the COPD research community felt that the inflammation was quite different to asthma," and that the condition wouldn't respond to inhaled steroids." However, in trials of more than 5,000 patients, those assigned to steroid therapy had a reduction in mortality of about 25%. The researchers hope these results will end the steroid-COPD controversy.

WATCH OUT FOR DEATH!

The FDA called for stronger warnings on the labels for Advair, Serevent and Foradil that would say the drugs could increase the chances of severe asthma episodes that could result in death. The agency said long-acting beta 2-adrenergic agonists should only be used after other medicines fail to control asthma. GlaxoSmithKline, which manufactures Advair and Serevent, disagreed with the government, saying the proposal was inconsistent with effective standards of care. "These proposed labeling changes would reserve the most effective asthma treatment until after a patient has failed on other treatments and, therefore, may be at risk for severe outcomes," according to Glaxo. This last summer, the FDA decided the drugs were safe enough to remain on the market. Advair is Glaxo's top-selling product, at $4.5 billion last year. Sales of Serevent were $639 million and Foradil, $320 million.

CASS FOR VAP

CASS has been reported to be effective in reducing the incidence of VAP. Continuous Aspiration of Subglottic Secretions is made possible with the use of special endotracheal tubes containing an additional lumen to allow for the removal of secretions above the cuff. For CASS to be safe and effective, precision suction must be maintained in the 15 to 30 mm Hg range. Recent studies have shown that tenacious secretions can be more effectively removed using the new CASS Suction Regulator from Boehringer Laboratories, Inc. Developed in conjunction with respiratory professionals, this regulator includes a special pulse mechanism that moves secretions while protecting the patient from injury by effectively maintaining a safe applied level of suction. To find out more about protecting patients from Ventilator

Associated Pneumonia, contact Boehringer at (800) 642-4945, boehringerlabs.com.

FROM HERE TO INFINITY

Draeger Medical introduced new NICU capabilities for its Infinity Kappa XLT patient monitor. The Kappa XLT is a split-screen monitor that provides ClinicalVision, a comprehensive view of the patient's condition, on one large touchscreen display. This can result in a better informed nursing staff as a result of all clinically relevant information being displayed on one screen. The Kappa XLT presents physiological data without any compromising popups or obstructions. The other side of the split screen provides web-based access to hospital information system applications and reference material. There's also a video option that captures and records images of the baby and displays images in a real-time display. Integrated with a Draeger Medical infant ventilator, the Kappa XLT provides complete neonatal parameter support and facilitates easy assessment of apnea, bradycardia and desaturation. The monitor also offers Masimo technology. Contact draeger.com.

LEMONS FROM LEMONADE

Nellcor, losing its patent litigation case, reaffirmed its commitment to pulse oximetry leadership. Said Nellcor president David Sell, "We are disappointed by this decision, yet as an organization have been preparing for this potential outcome. As one of the earliest pioneers in pulse oximetry, Nellcor has consistently delivered technology advancements along with value and choice. Our OxiMax system remains the oximetry platform for the future. We plan to launch a new product line in the near future as part of the OxiMax system that includes bedside and handled monitors as well as OEM oximetry circuit boards that we will provide to other manufacturers of multiparameter monitoring device systems."

EAST MEETS WEST

The Masimo Corporation and Draeger Medical AG & CO KG announced the availability of the Masimo SET SpO2 SmartPod for Infinity patients. The Pod brings the advantages of Masimo's latest pulse oximetry technology because Masimo Signal Extraction Technology is accurate during low perfusion and most types of patient movement, including shivering, combativeness, movement and seizures, and aids in eliminating false alarms and detecting true alarms. The Infinity Masimo SET SpO2 Pod requires 510(k) review and isn't yet available in the US. The new technology was unveiled at Medica 2005 in Dusseldorf. For more contact masimo.com or draeger.com.

P TO P AGREEMENT

Puritan Bennett announced that its critical care business unit has been awarded a three-year agreement to provide intensive care ventilators to the Premier, Inc member hospitals and healthcare providers. Premier is a national alliance of 1,500 hospitals and health systems which lines up long-term purchasing agreements with manufacturers. Under the agreement, Puritan Bennett will continue to offer Premier group members discounted pricing on such items as its 840 ventilator system, and field service contractors with its Ventilator Field Service Program. The 840 offers ventilation to preemies through adults. Contact tycohealthcare.com.

SUMMING UP

Respironics reported successful international expansion in 2005, as well as the emergence of its Children's Medical

Ventures as a growth-driver. Additionally, Respironics made significant progress in fostering the development of advanced respiratory drug delivery and the screening, diagnosing and treatment of other sleep disorders. For the year ending June 30, net sales increased by 20% over the previous year. Domestic homecare product sales were driven by growth in the sales of sleep apnea therapy devices, masks and accessories. Respironics acquired 100% of the outstanding shares of Mini Mitter Company, Inc, which develops and sells sleep and physiological monitoring products to commercial sleep labs. The company changed its sales strategy from the BiPAP Vision Noninvasive Ventilation system from distributor-based to direct-sales. The company introduced its new BiPAP S/T Ventilatory Support System and its NeoPAP System. The PLV Continuum is the latest addition to the Respironics line of ventilation products.

CLOSING IN

Nektar Therapeutics announced that it has closed the acquisition of Aerogen, Inc. The acquisition broadens Nektar's pulmonary technology base by adding capabilities in aerosolized liquid drugs to Nektar's inhaleable powdered drugs. Aerogen's products are based on its OnQ Aerosol Generator technology. Its product line includes the Aeroneb Micropump Nebulizer. Nektar enables high-value, differentiated therapeutics with its drug delivery technologies.

LET IT FLOW

RAM Scientific announced the packaging of its SAFE-T-FILL blood gas capillary tubes with balanced heparin in a smaller quantity kit form. RAM's plastic blood gas capillary tubes have the same benefits as glass tubes, without the risks. The kit contains 50 tubes of 150 μL balanced heparin blood gas capillary tubes and 100 rubber endcaps for the tubes. The smaller quantity kit allows hospitals to be in compliance by simplifying the product purchase into a single item and bringing the acquisition cost down. Contact ramsci.com.

MAKING A SPLASH

VIASYS Healthcare made a splash at "Riverwalkin' for Respiratory Care" at AARC in San Antonio when it was presented with the prestigious 2005 Zenith Award at the International Congress. The Zenith Award recognizes five companies, out of more than 400 chosen by over 38,000 members of the AARC, that exemplify the utmost standards in excellence in the respiratory care industry. Also at this year's AARC, VIASYS was able to raise over $4,000 for the ARCF through its "Riverwalkin' For Respiratory Care" promotion. Visitors to the VIASYS booth at the congress received a free pedometer and a mileage card. They were invited to track their mileage while in San Antonio at the conference and return to the VIASYS booth prior to the close of the show. For every mile walked, VIASYS donated ten cents to the ARCF.

BUILT TO RESPOND

The *840* ventilator system is the flagship product in the Puritan Bennett line of critical care ventilators. It is responsive to patients and offers superior comfort, delivering sensitive, precise breaths to critically ill neonatal through adult patients. The *840* ventilator features a noninvasive ventilation (NIV) capability also designed for use on neonatal through adult patients with stable respiratory drives and which works with interfaces such as nasal masks, neonatal nasal CPAP prongs and full-face masks.

In addition, only the *840* ventilator has an integrated filter that enables the capture of SARS and avian flu virus particles. Our *SmartAlert*™ alarm system and self-tests allow users to meet stringent JCAHO standards, while the *840* ventilator's gas delivery engine provides excellent breathing synchrony for all patients, neonatal to adult. Contact (800) 635-5267, puritanbennett.com.

PEDIATRIC AWARD

Mary K. (Katie) Sabato, MS RRT, of Children's Hospital & Research Center Oakland, received the 2005 VIASYS Healthcare Neonatal and Pediatric Fellowship Award on behalf of the ARCF and VIASYS Healthcare. The fellowship is designed to foster projects in the field of neonatal and pediatric critical care.

In 2000, Katie was one of two respiratory care practitioners who partnered with a young Belizean pediatrician, Dr. Egbert Grinage, to provide mechanical ventilation for pediatric and neonatal patients in Belize. Traditionally, nurses in Belize would have to hand-ventilate pediatric patients—sometimes for as long as 48 hours. Katie was selected for this award for helping to secure ventilator equipment and providing mechanical ventilation and ventilator maintenance training to Belizean nurses and physicians.

"During our first trip we repaired an old donated ventilator just in time to use it on a premature baby who became Belize's first neonatal patient to survive on our mechanical ventilation

equipment," said Sabato. "The generous donations of companies like VIASYS Healthcare have resulted in better outcomes for children who would otherwise face inadequate or non-existing medical care."

Since 2000, medical teams have returned to Belize to continue to educate and support the medical staff at KH and Universal Medical Hospital. After initiation of this program, survival rates of ventilated babies at Karl Heusner Hospital have increased from 36% in the first year to 48% in 2004. Sabato's success inspired her colleagues at Children's Hospital & Research Center Oakland to work with her to create a medical missionary group, Medical C.A.R.E Inc., to help children of all nationalities. Next year, C.A.R.E. is planning to go to Nigeria to open that country's first pediatric cardiac center.

Becky Mabry, Senior Vice President Global Marketing for VIASYS Healthcare said, "VIASYS is committed to clinical education, research and to programs that enhance patient care. Katie Sabato has made a significant, long-lasting impact in a place where respiratory care resources are in short supply. VIASYS is proud to have had the opportunity to play a small part in that endeavor."

LETTER

RE: High Frequency chest Wall Oscillation for Individuals With Chronic Neuromuscular Weakness, Respiratory Therapy, Vol 1 No 1, December-January 2005/2006, 28-33.

FROM: Louie Boitano MSc, RRT. Pulmonary Clinic, Northwest Assisted Breathing Center, Department of Respiratory Care, University of Washington Medical Center. Seattle, WA.

The administration of an airway clearance modality should be based upon the understanding of the disease pathophysiology and how the particular therapy can benefit the patient. The author has indicated that the use of high frequency chest wall oscillation (HFCWO) can be beneficial to the respiratory health of neuromuscular patients with respiratory insufficiency by maintaining airway clearance and reducing the potential for morbidity and mortality associated with respiratory infection. Airway clearance therapy includes a variety of therapies that mobilize airway secretions, cough augmentation therapies that clear secretions from the airways and airway suctioning to clear secretions from artificial airways. Intrinsic lung diseases that affect airway muco-ciliary clearance function can result in pulmonary congestion and chronic respiratory infection. Secretion mobilization therapies can be very beneficial in augmenting the clearance of secretions in airway diseases including cystic fibrosis, bronchiectasis, ciliary dyskinesia, and other hyper-secretive pathologies where normal muco-ciliary clearance is encumbered. HFCWO has been found to be at least as good as other secretion mobilization therapies. Patients with intrinsic lung disease that affects normal muco-ciliary clearance generally do not have insufficient cough strength to clear

secretions and therefore cough augmentation therapy would not be indicated.

The pathophysiology of neuromuscular induced restrictive lung disease is quite different from that of intrinsic lung diseases. The signs and symptoms of neuromuscular respiratory insufficiency are chronic, progressive hypoventilation and associated lower lung field atelectasis, and insufficient cough strength secondary to diaphragmatic, chest wall and abdominal wall muscle weakness. Neuromuscular patients with respiratory insufficiency generally have no intrinsic pulmonary co-morbidity that affects airway muco-ciliary function. The limiting factor in the clearance of their pulmonary secretions is cough strength. Without adequate cough strength to clear secretions, neuromuscular patients are susceptible to pulmonary congestion. When cough strength is insufficient (peak cough flow <160 L/min) cough augmentation therapy can support adequate cough clearance to maintain pulmonary health[1]. Mechanical in-exsufflation has been found to be the most effective means of cough augmentation therapy for this patient population[2-4]. While secretion mobilization therapy has been commonly prescribed as maintenance therapy for neuromuscular patients with respiratory insufficiency, the evidence for this practice is limited. A global respiratory management approach that monitors ventilation sufficiency, corrects inadequate ventilation and supports adequate cough clearance, addresses the respiratory limitations associated with neuromuscular respiratory insufficiency[5-8]. Secretion mobilization therapy would be indicated if pulmonary congestion develops secondary to respiratory infection and in the subset of neuromuscular patients with airway disease that encumbers muco-ciliary function. Cough augmentation should

be used in conjunction with secretion mobilization to clear secretions in these patients. Mobilizing secretions without supporting adequate cough clearance may potentially result in asphyxiation. As the author indicates, in ALS and other neuromuscular diseases where progressive dysphagia develops secondary to bulbar dysfunction, there is a significant increase in the potential for aspiration related respiratory infection. The timely placement of a gastrostomy tube for nutrition, hydration and medication intake will be more effective in reducing the potential for aspiration related infection than a maintenance regimen of secretion mobilization therapy.

The author cites several studies showing both the effectiveness and acceptance of HFCWO compared to other secretion mobilization therapies in patients with intrinsic lung disease, most notably cystic fibrosis. While HFCWO has been shown to be an effective means of secretion mobilization for airway diseases that affect muco-ciliary transport, these studies alone do not provide substantiation to employ HFCWO for a completely different pathophysiology where muco-ciliary function is not encumbered. The author describes HFCWO as producing chest wall compression that creates a burst of air throughout the patient's airways resulting in a brief "cough-like" response that has been referred to as a "staccato cough". While the HFCWO induced rapid movement of air through the airway is designed to produce an airway shear force that mobilizes secretions, the characterization of this therapy as affecting a cough action may not be accurate. The author further states that HFCWO moves the mobilized secretions up through the airways where they can be coughed or suctioned. While HFCWO and other forms of chest physiotherapy may help a small number of neuromuscular patients with airway disease that encumbers secretion clearance, it does not support cough clearance which is the primary airway clearance limitation in this population.

The author describes mechanical in-exsufflation as a therapy that attempts to reproduce a cough maneuver by insufflation that inflates the lungs followed by immediate exsufflation that clears secretions from the lungs. She describes insufflation as having a potentially negative "muzzle loading" effect by blowing secretions into the distal respiratory tract. This conceptual idea is not supported by any reported physiologic observation. If the "muzzle loading" of secretions did occur with insufflation one would expect to find atelectasis in the lung fields distal to the impacted airways. Insufflation induced secretion impacted airways would potentially result in ventilation-perfusion abnormalities as well as an increased incidence of respiratory infection. We have prescribed mechanical in-exsufflation therapy for more than fifty neuromuscular patients with insufficient cough strength, as measured by peak cough flow, and have never observed iatrogenic related clinical symptoms associated with the use of this therapy. We have found no published reports of respiratory infection or ventilation-perfusion abnormalities associated with mechanical insufflation induced airway secretion impaction.

The author also states that patients with ALS often require mechanical ventilation, thereby rendering all of the airway clearance techniques, except HFCWO, unrealistic choices for regular periodic airway clearance. Mechanical in-exsufflation therapy is successfully used via tracheostomy for both ventilated and non-ventilated neuromuscular patients in a number of hospital rehabilitation centers. Our outpatient neuromuscular respiratory clinic program has four ALS patients

on long term home mechanical ventilation who use mechanical in-exsufflation. The patients all prefer mechanical in-exsufflation compared to airway catheter suctioning for both comfort and effectiveness in clearing airway secretions.

We appreciate the author's effort to support airway clearance therapy as a means of decreasing morbidity and mortality in neuromuscular patients with respiratory insufficiency. Secretion mobilization can be a beneficial respiratory therapy in addition to cough augmentation for those neuromuscular patients with airway disease and related co-morbidity that results in retained secretions and for neuromuscular patients hospitalized for pulmonary congestion.

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Arterial Blood Gases: Avoiding Preanalytical Errors to Improve Neonatal Assessment

Bruce Toben, RRT, NPS, Marcia L. Zucker, PhD

CLINICAL IMPORTANCE OF ARTERIAL BLOOD GAS ASSESSMENT

Frequent measurement of arterial blood gases (ABG) is a standard of care in the management of newborns suffering from acute respiratory failure, prematurity and congenital cardiac anomalies. In these critically ill patients, alterations in cardiopulmonary function can occur rapidly and ABG test results are used to guide the titration of oxygen, ventilatory support, hemodynamic resuscitation and acid-base balance. The successful administration of these therapies is essential in order to minimize morbidity and mortality in this subset of infants. Traditionally, the analysis of ABG has been conducted in a central laboratory using discrete blood samples, which are collected at the patient's bedside and transported to the lab for analysis. Recently, with the goal to improve patient care and expedite clinical interventions, ABG measurement has increasingly moved to point-of-care testing (POCT) using portable analyzers. The adoption of this technology has provided a means to isolate and eliminate sources of error in the testing, ultimately improving the quality of the clinical data.

PREANALYTICAL ERROR

Any variable which occurs prior to the actual analyte measurement is referred to as preanalytical error. In clinical practice, these technical errors can lead to erroneous measurements and be a source for misdiagnosis or inappropriate interventions. Preanalytical errors can result from incorrect sampling site preparation, improper collection procedures and inadequate specimen storage. Meticulous attention to blood collection techniques will ensure a true reflection of the patient's physiologic condition, allowing for appropriate interpretation of results.

It is imperative that when blood is drawn from an indwelling vascular access line, sufficient volume be removed before collecting a specimen to prevent contamination of the sample with the infusate. Traditionally, this waste sample is 3 times the

dead space of the access device.[1] Collecting capillary samples can be another source of preanalytical error. Arterializing the sample by warming the heel for 15-20 minutes prior to incision may not improve ABG correlation as once thought.[2] However if warranted, warming should be accomplished with a chemical heat pack, not warm wet compresses. The temperature of the wet compress decreases over time, reaching its lowest ebb just prior to blood collection. In addition, if the skin remains damp once the wet compress is removed, cooling of the skin over the sampling site could occur due to evaporation negating any positive effects of the procedure. It is important to remove the first drop of blood before filling the capillary device, avoiding squeezing, milking or flexing the foot. Doing such can increase venous admixture and produce a greater disparity in values.

Excess liquid sodium heparin in the collection syringe can reduce the pH of the blood and dilute the sample, resulting in lower PCO_2 and changing the measurable PO_2 level toward 159 mmHg.[3] The presence of air bubble(s) within the specimen or the introduction of air during analysis will decrease PCO_2, increase pH and drive the PO_2 closer to ambient air values. In the septic patient, a delay in analysis after collection or inadequate cooling of the sample in the transport/storage phase can cause "leukocyte larceny," which will reduce the specimen's pH and PO_2, and increase the PCO_2.[4]

Some blood gas analyzers measure additional metabolic analytes and practical knowledge of the cause for preanalytical error should also be discussed to avoid pitfalls in measurement. When sampling blood for lactate analysis, the RBC continues to undergo glycolysis, metabolizing lactate *in vitro* at a rate of approximately 0.01 mmol/L/min or 11.4% in the first 15 minutes post phlebotomy.[5] This can be a major source of error producing erroneously high lactate levels if not addressed. Analysis by POCT resolves this factor, but if POC analysis is not available, cooling the heparinized specimen in an ice water bath can retard lactate production. Grey-top blood collection tubes contain fluoride/oxalate, an effective lactate stabilizer. Blood stored in these tubes will provide accurate lactate results for up to eight hours at room temperature.[6] Erroneous blood lactate

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Table 1. CLIA guidelines for individual blood gas analyzers and acceptable ranges for sample values (excerpted from reference 12)

Analyte	Standard variance for each individual analyzer	If a known sample has this value…	Then this is the acceptable reported range
pH	± 0.04 units	7.40	7.36 to 7.44
PCO_2	± 5 mmHg or 8%*	40 mmHg	35 to 45 mmHg
PO_2	± 3 SD	100 mmHg	73 to 127 mmHg**

* Whichever is greater
** Based on a 9% SD

levels have been described in patients who were receiving crystalloid solutions. Infusion of lactated Ringer's increased lactate concentrations and non-Ringer's lactate solution reduced levels. These observations have been traced to inadequate dead space volume clearance procedures from the vascular catheter.[7]

The concentration of ionized calcium (iCa) varies inversely with pH due to its binding with albumin. Conditions that erroneously alter pH therefore have a direct effect on iCa accuracy. Blood samples that are cooled and/or hemolyzed have falsely higher concentrations of potassium (K^+). Excess liquid sodium heparin in the sample artificially raises the blood sodium (Na^+) measurement. Benzalkonium heparin is applied to some umbilical and pulmonary artery catheters to reduce the incidence of thromboembolic events. This composition of heparin exudes from the lumen of the catheters and can artificially raise cation results from analyzers using ion-selective electrodes.[8, 9] Hematocrit (Hct) analysis that employs the conductometry methodology is subject to preanalytical error if the sample is diluted with cardiopulmonary bypass priming solution.[10] Often, blood gas instruments calculate total hemoglobin (tHb) from the Hct result and therefore misleading information could be reported due to the same reason.

PHYSIOLOGIC CONSIDERATIONS

Compounding the preanalytical issues of blood analysis, ABG interpretation can be misleading due to alterations in the newborn's breathing pattern during sample collection. Tactile stimulation or the pain associated with specimen collection can cause hypocarbia from tachypnea or hypercarbia from breath holding. If the child is being supported by mechanical ventilation, abbreviated cycling due to pressure limiting with changes in functional positive end-expiratory pressure levels can also contribute to erroneous blood gas results. Most often, in remote lab testing, failure to record these conditions can lead to misinterpretation of ABG values and inappropriate patient care decisions.[11]

ACCURACY OF ABG RESULTS

ABG values should be comparable between analytic systems showing little between system bias, and repeated measurements of the same sample should be reproducible. Manufacturers are required to report precision and accuracy performance specifications of their analyzers and laboratories routinely confirm these claims. Proficiency testing, a requirement for

federal, state and independent accrediting agency certification, allows labs to periodically assess "blinded samples" and their performance compared to the reference "absolute" values. In addition, these results are also compared with values reported from other laboratories using the same reference instrument. Every analytical instrument has subtle variations in performance and differences of reported samples are expected. However, if significant variations outside of predefined limits are reported, identification of the cause and corrective action are required.

The Centers for Medicare and Medicaid Services (CMS) regulates all laboratory testing (except research) performed on humans in the US through the Clinical Laboratory Improvement Amendments (CLIA). The objective of the CLIA program is to ensure quality laboratory testing. CLIA has set guidelines defining the total acceptable variation for individual blood gas analyzers (Table 1). Based on these guidelines, the acceptable range of results for a single instrument can vary markedly. Laboratories may report differences for pH of 0.08 and PCO_2 of 10 mmHg on the same specimen using the same analyzer and still be within acceptable limits. Due to the volatility of the PO_2 measurement and the inability to consistently reproduce PO_2 data, CLIA has defined separate error limits for that analyte. Periodically, CLIA records the measured PO_2 values of the blinded samples sent to laboratories. Once all the results have been statistically tabulated, three standard deviations (SD) are calculated.[12] This statistical method will result in acceptance of 98% of all PO_2 values measured from all participating institutions. Thus, individual blood gas analyzers may report significant differences from the same blood sample, even in the face of a stable clinical condition.

RELIABILITY AND INTERPRETATION OF ABG VALUES

Blood gas and acid-base stability are presumed at the time an ABG sample is drawn. Based on the analyzed values, diagnostic and therapeutic decisions are made. However, in an acute disease stage, or when interventions specifically intended to promote hemodynamic resuscitation or pulmonary recruitment are applied, is it appropriate to make this assumption? Consider the following series of questions. Once high frequency oscillation ventilation is instituted on a premature infant, when are ABG values stable enough for analysis? After instilling a bolus of surfactant down an endotracheal tube, when should an

Photograph courtesy of Children's Hospitals and Clinics of MN.

ABG test be performed to establish the effectiveness of the therapy? How often should ABGs be assessed when titrating nitric oxide? The absolute answers to these valid clinical questions are unknown because each patient responds at different rates to the interventions applied. In addition, most cardiopulmonary dysfunctions are a dynamic process. Progressing pathophysiology and measuring the effective changes based on therapeutic modalities alter blood gases continuously. In many cases, estimating the physiologic status and monitoring disease management in the critically ill newborn is an attempt to hit a moving target.

IMPROVING ABG MEASUREMENT WITH POCT

Successful disease management necessitates that therapies are based on accurate diagnostic data which relates to the current physiologic condition of the patient. During periods of acute clinical change, the need for immediate intervention can preclude the luxury of a delay in receipt of test results. Such delays are often attributable to the process of ABG data collection. This time interval from sample collection to appropriate therapeutic intervention, referred to as the clinical turn-around-time (TAT) results from:

• Time to recognize the need to evaluate pH and blood gases
• Time to order an ABG test
• Time to summon technical staff to draw the blood specimen
• Time to acquire the blood specimen
• Time to transport the blood specimen to the laboratory
• Time to perform the ABG analysis
• Time to report the ABG results
• Time to interpret the ABG values and initiate a therapeutic intervention

The laboratory TAT (ie, time from receipt of specimen to reporting of test results) for blood gases has been reported to

be 19 minutes, with a range from 5 to 48 minutes.[13] It is obvious that the clinical TAT (ie, time from ordering an ABG to implementing intervention) must therefore be greater than 19 minutes, challenging our ability to react to sudden physiologic changes in a swift, decisive manner. In cases where rapid deterioration in pulmonary mechanics or hemodynamic function occurs, any delay to effectively intervene can contribute significantly to outcomes. With POCT, the improvement of TAT can lead to more rapid clinical interventions, especially important in the neonatal patient.

Point-of-care testing also helps satisfy the concern that the measured newborn's pH and blood gases are reflective of the actual physiologic state, whereas with remote lab testing, delays in getting ABG results increase the likelihood that decisions on disease management are being made on "old data." If the ABG was drawn prior to physiologic stability or if the V/Q shifted after the sample was drawn, the resulting intervention could be too aggressive, not aggressive enough, or even altogether inappropriate. In such events, therapy would need further modification requiring another ABG sample to determine the effectiveness and the need for additional action. The above chain of events can be expected to occur most often in the population of highest acuity, ironically where ABG data is most crucial and relied upon.

One such POCT system, IRMA TRUpoint, is capable of providing ABG results in less than 90 seconds. This portable, self-contained system can be easily brought to the infant warmer or incubator for bedside testing. Trained respiratory care practitioners, nurses and other allied healthcare professionals can operate the POC analyzer, thus eliminating many of the time consuming steps inherent in the laboratory testing model. By streamlining the results reporting aspect of the measurement, clinical interpretation and decision making

can occur at one time, at the bedside, while observing the infant. This methodology of diagnosis and disease management can reduce staff resources, thus allowing more time to be allocated to patient care. The IRMA TRUpoint system also includes a complete CLIA compliant quality control program.

SUMMARY

ABG assessment is a vital diagnostic test, critical in the management of newborns with acute respiratory failure, prematurity and congenital cardiac anomalies. Erroneous values caused by preanalytic errors and/or delayed TAT can compromise the accuracy of the data, leading to misinterpretation and faulty decision making. Due to the known variations in ABG values across different instruments, adherence to a common system in a hospital-wide setting helps ensure that accurate and consistent clinical decisions are made. Minimizing TAT promotes prompt reaction to changes in patient status and potentially reduces comorbidity. The use of POC blood analysis systems can markedly reduce the time to intervene, preventing further physiologic stress on the infant's marginal condition and hopefully improve clinical outcomes.

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Knowledge Based Weaning: Protocolized Care in the Weaning Process

Nader M. Habashi, MD, FACP, FCCP

Improving Intensive Care Unit (ICU) outcomes by reducing ventilator associated complications and ventilator days may warrant re-engineering the weaning process.[1] Alternative methods which assist clinicians in organizing and implementing accurate weaning processes may shorten the duration of ventilator dependence and positively impact ICU outcomes.[2] Knowledge based weaning (KBW) provides an alternative to the traditional weaning process.

A major challenge in the ICU is determining whether a patient is capable of weaning from the ventilator. Weaning patients from mechanical ventilation is initiated by the bedside clinician, not the ventilator.[3] Reductions in the level of ventilator support are typically performed once or twice a day during routine ventilator checks or at designated times, generally during daytime hours. The weaning process characteristically begins when the clinician believes the patient is able to tolerate less support, and is present to make appropriate changes in ventilator settings. Decisions to proceed with the weaning process by the respiratory therapist or physician are commonly intermittent and unstructured. Optimal ventilator settings during weaning are those which provide the lowest level of support and prevent excessive work of breathing and fatigue. Once committed to the weaning process, optimal ventilator settings should be maintained throughout. Progressive reduction of ventilator support requires frequent reassessment to determine whether to maintain, reduce or escalate ventilator support. Respiratory decompensation may not be recognized until significant fatigue has developed. Current methods of weaning rely on a reactive approach to detect inappropriate ventilator weaning. Excessive weaning may surpass the patient's ability to transition to less support, paradoxically prolonging ventilator dependence. Conversely, data suggests many patients are ventilated longer than necessary. Prospective, controlled studies have shown that greater than 70% of patients who tolerate a spontaneous breathing trial could be extubated successfully.[4,5,6] These studies advocate a spontaneous breathing trial to identify patients capable of being liberated from mechanical ventilation. In addition, studies reviewing self-extubation have documented a significant percentage of self extubated patients do not require reintubation. These studies suggest that care providers may not always recognize patients' readiness to be weaned and extubated.[7,8]

Complications from mechanical ventilation are associated with significant mortality, morbidity, increased ICU length of stay and ICU cost.[9] Ventilator associated lung injury and pneumonia are significant morbidities directly related to duration of ventilator dependence.[10] The need for continuous quality improvement has caused many ICU clinicians to focus on reducing ventilator days and complications from mechanical ventilation. In 1994, Esteban suggested that weaning from the ventilator accounts for up to 42% of the time a patient is mechanically ventilated.[11]

Multidisciplinary protocols can improve the weaning process through the implementation of a consistent, team approach.[12] Protocol based weaning defines and organizes a process for ventilator adjustments, expected outcomes, patient monitoring and patient care during weaning. Several studies have shown that implementation of protocols to aid the weaning process results in a significant reduction in ventilator days and cost.[2] Furthermore, reductions in ventilator days directly impacts ventilator associated complications. Successful protocol based weaning results from a coordinated approach using a multidisciplinary team rather than the mode of ventilator weaning. The multidisciplinary team approach to designing and implementing weaning protocols provides the opportunity to incorporate knowledge from several disciplines on how the weaning process affects patients. In addition, the multidisciplinary approach facilitates the coordination of care plans during the weaning process.[13] The multidisciplinary team should include nutritionists, pharmacists, physical and occupational therapists in addition to physicians, respiratory therapists and nurses. A diversity of clinical staff provides a well-rounded assessment of the patient, plan of care and

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expected outcomes. Effective protocols must balance adequate information to deal with the complexity of weaning and limit data overload for the clinician. If a protocol becomes too difficult to navigate, the protocol may not be utilized appropriately. Protocols with excessive detail may decrease their effectiveness, increase error rates and even limit successful implementation. Alternatively, if a protocol does not have enough detail, application may be limited to a narrow spectrum of patients, proving ineffective for clinical variability inherent in critical care patients.[14]

KBW computer software incorporates clinical logic and rules coupled to a knowledge base in order to automate the weaning process.[15] Automated weaning may provide several advantages over traditional methods of weaning. KBW facilitates data acquisition and monitoring, continually supplying information to the knowledge base. The knowledge base maintains current medical data and practice patterns from a multidisciplinary team to define and organize weaning.[16,17,18] The knowledge base engages the reasoning engine to provide rules for the weaning process. KBW provides the basis for organized, consistent and continuous weaning to reduce clinical variability. Furthermore, KBW allows the complexity of the weaning process to be transparent to the end user, improving the user interface. Improving the user interface has the potential to improve compliance, prevent process confusion and errors while limiting data overload.

Improved monitoring and trending coupled with a reasoning engine can guide therapy and allow weaning to progress over the entire 24 hour period. In addition, continuous monitoring provides trends of "smart alerts" which may signal impending weaning failure, providing a proactive weaning system. Reengineering the weaning process provides the potential to improve outcome while decreasing cost. KBW will provide a foundation for weaning in the 21st century.

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Utilization of an Automatic Mode of Ventilation (ASV) in a Mixed ICU Population: Prospective Observational Study

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INTRODUCTION

Adaptive Support Ventilation (ASV) is an automatic mode of mechanical ventilation that has been proven to simplify postoperative respiratory management[1,2] and to improve patient-ventilator interaction.[3] Prior to this study, there was no data available on routine ASV utilization in a large population of mixed intensive-care patients.

METHOD

This prospective observational study reports the use of ASV as the primary mode of ventilation in an 11-bed mixed ICU, over a 7-month period. While the clinician sets minute volume (as a percentage of the "ideal" minute volume: %MinVol), the ASV algorithm determines tidal volume and respiratory frequency based on respiratory mechanics, in such a way as to minimize the work of breathing.[4] Moreover, ASV encourages spontaneous breathing activity, providing full or partial ventilatory support. It is therefore well suited to use in the initiation, maintenance or weaning phase of mechanical ventilation. Contra-indications for ASV were noninvasive ventilation, bronchopleural fistula and Cheyne-Stokes breathing. The clinicians were allowed to switch to another mode of ventilation if the optimal tidal volume was not achieved despite a plateau pressure above 30 cmH$_2$O or in the case of patient-ventilator asynchrony. Data (Table 1) were recorded on a day-by-day basis (6 am daily) and analyzed each day of invasive ventilation. Results are given with mean ± SD.

RESULTS

Over the study period, 322 patients were admitted to the intensive care unit, amounting to 2,144 days of hospitalization. The mean IGS II was 46. There were 1506 days of ventilation (70%) with 1,349 days of invasive ventilation (89%).

ASV was used in 98% of invasive ventilation-days (Figure 1)
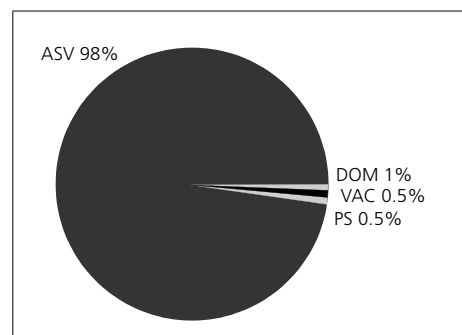
Figure 1: Modes of ventilatory support used. VAC: volume control, PS: pressure support, DOM: homecare ventilator.
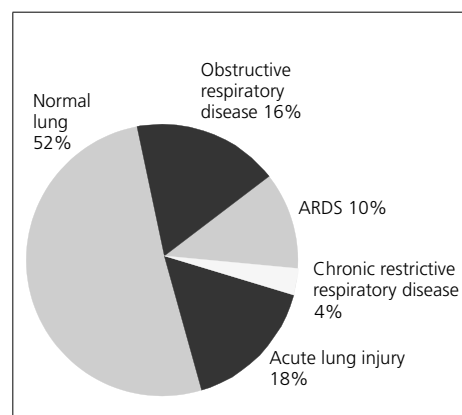
Figure 2: Indications for mechanical ventilation.

	Normal lung	Obstructive lung disease	ARDS	Restrictive lung disease	Acute lung injury
%ASV	116 ±25	119 ±29 NS	131 ±25 **	137 ±31 **	130 ±29 **
PEEP (cmH$_2$O)	5.2 ±1.5	6 ±2.5 **	9 ±3.3 **	5 ±1.7 NS	6.3 ±2.2 **
Peak pressure (cmH$_2$O)	22 ±6	24 ±7 **	30 ±6 **	27 ±6.7 **	25 ±6 **
Vt (ml)	516 ±131	585 ± 113 **	453 ± 112***	386 ± 91 **	503 ±109 NS
Ftot (C/mn)	17 ±5	16 ± 6 *	20 ± 6 **	23 ± 6 **	18 ±6 **
Fspont (c/mn)	9 ±10	9 ± 10 NS	6 ± 10 **	13 ± 13 NS	9 ±11 NS
I:E	0.50 ±0.17	0.41 ±0.15 **	0.62 ±0.27 **	0.54 ± 0.24 NS	0.48 ±0.17NS
RCe (s)	0.78 ±0.28	1.13 ±0.70 **	0.55 ±0.21 **	0.4 ±0.15 **	0.70 ±0.22 **
Cstat (ml/cmH$_2$O)	46 ±23	56 ±25 **	30 ±14 **	22 ±10 **	41 ±20 **
Rins (cmH$_2$O.s/l)	16 ±7	16 ±10 NS	17 ±7 NS	14 ±9 NS	16 ±7 NS
pH	7.40 ±0.07	7.37 ±0.09 **	7.29 ±0.14 **	7.37 ±0.11 NS	7.38 ±0.08 **
PaO$_2$/FiO$_2$	330 ±113	248 ±115 **	140 ±48 **	267 ±106 **	215 ±61 **
PaCO$_2$ (mmHg)	40 ±7	44 ±11 **	49 ±9 **	45 ±9 **	42 ±7 **
Vt/IBW (ml/Kg)	8.3 ±1.3	9.3 ±2.1 **	6.8 ±1.2 **	7.0 ±1.1 **	8.1 ±1.2 NS

Table 1: Breathing pattern, mechanics and gas exchange based on the underlying lung disease.
* $p < 0.01$; ** $p < 0.001$ between diseased lung and normal lung (using Mann-Whitney test).
% ASV: percentage of ideal minute ventilation, Vt: tidal volume, Ftot: total respiratory frequency, Fspont: spontaneous respiratory frequency, I/E: inspiratory expiratory ratio, RCe: expiratory time constant, Cstat: static compliance, Rins: inspiratory resistance.

including the weaning period. The %MinVol set was between 116% and 137%.

Indications for mechanical ventilation are detailed in Figure 2. Breathing pattern, mechanics and gas exchange based on the underlying lung disease (assessed by the physician in charge) are given in Table 1. Mean duration of ventilation and stay in intensive care are respectively 6.6 and 7.6 days. ICU mortality rate was 30% (predicted mortality 37%). No side effects were reported with the use of ASV.

CONCLUSIONS
The present prospective observational study found that the automatic mode of ventilation - ASV - was used in 98% of invasive-ventilation days, with patients suffering from very different types of underlying disease. There was only very occasional need to switch to an alternative mode of ventilation.

Although breathing patterns varied, depending on the underlying lung diseases, ASV consistently and automatically selected protective ventilation with low tidal volume for ARDS patients.

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Ventilation Procedures for Intensive Care Air Transports

Interview with Assistant Professor Dr Gerhard Kuhnle, Anesthesia Director of Intensive Care Transports, University of Munich hospital systems

Many metropolitan area hospitals are facing difficulties in densely populated urban areas: how to transfer intensive care patients to centers where there are open ICU beds or adequate staffing this week, or specialized centers for advanced treatment care needs. In addition to these logistics, transferring the ventilated patient from one ICU to another poses additional therapeutic challenges. The University Hospital System in Munich has defined a systematic approach to ICU patient treatment and transportation

How many intensive care patients are transported here on an annual basis?
In 2004 we had 1,900 patients by land and 860 by air transport, or a total of 2,760 patients. This represents primarily the area of Bavaria and Baden Wurttemberg, where we are receiving patients, but sometimes the patients can be transported from here, to Hamburg and Berlin.

What are the proportions of emergency and planned air transports of intensive care patients?
Of total patients in air transports, about two thirds are intensive care patients and about one third are from acute emergency situations. Of the intensive care patients, approximately 50% are emergency and 50% are planned transports. Most of these

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patients are coming from smaller hospitals in Bavaria and some are coming from central hospitals in Munich, smaller hospitals without special care units, or without cardiac or neurosurgery, for example.

Are these transports generally during daylight hours, or are they day/night transports?
Our helicopter and ambulance services run day and night. But at night, the helicopter primarily does emergency cases.

What is the average transport time for a ventilated patient by helicopter?
It depends entirely on the patient situation; we have flight times of a few minutes up to several hours. On one occasion last year, we took a ventilated patient from Marseilles to Munich, so it can vary. But in general, for the majority of intensive care patients, transport time is up to one hour in the air.

Which types of intensive care patient categories do you primarily transport by planned air transport?
There are a wide variety of intensive care cases: ARDS, infants, trauma, neurological cases and cardiac patients, heart failure, or pericardial infusion and coronary syndromes, coming from a peripheral hospital for specialized surgery. The infants are often premature, but there are also many full-term infants coming here for specialized surgery for congenital defects.

In these types of patient transports, what type of clinical performance is required from the ventilator?
It depends on the patient of course. Cardiac and neurological patients are often sedated and on controlled ventilation. In these patients it is pretty straightforward, since they have normal lungs, and normal resistance and compliance. But in the ARDS patients, we need a good intensive care ventilator, delivering pressure supported and pressure controlled therapy, or in very severe cases extracorporal membrane oxygenation (ECMO), also during the transport. Pressure controlled ventilation is also sometimes needed for infants.

Is there a profile or any type of clinical criteria intensive

care patients must fulfill to be transported by air?
The indication for air transport is dependent upon the patient. A patient with ARDS with unstable respiratory mechanics is stabilized on the ward of the remitting hospital. Other patients may be unstable and need hemofiltration, and then we try to transport them as urgently as possible. Each underlying disease or condition is different. We have no exclusion criteria, but I would not transport patients with acute bleeding, for example, or a ruptured aortic aneurysm. They require extensive blood transfusions, and that can be difficult to manage in the air. In our experience, almost every other patient, depending on their situation, may be transported by air or land. It is difficult to intubate or put in IV lines or a CVC during transport, but we have done this when necessary. If these types of interventions are needed, often we usually want to make sure that they are already in place prior to transport.

What are the types of ventilation strategies or modes commonly used during transport?
We have all modes of ventilation, protocols coming with high PEEP and high peak pressure, sedated patients, some patients with noninvasive ventilation by mask, for example with cystic fibrosis or lung fibrosis, coming to the transplant center here.

What is the normal range of trigger settings used during transport?
We try to determine what is good for that particular patient: for a patient on supported ventilation, we use flow triggering, which is best in my experience. But controlled ventilation is used for sedated patients, who are in the majority. Primarily, we try to maintain the same ventilation strategy initiated by the remitting hospital, continuing the same strategy during air transport until

the patient reaches our center here. However, there are cases where we try to adapt a good ventilation strategy during the transport. If the patient is not being optimally ventilated when we receive him, we titrate the settings and adjust to our own ventilation strategies enroute to this hospital.

What are some of the challenges in treating these ventilation patients in air transports?
The main challenge is the transport situation itself: you have a lot of equipment – several IV lines where you want to avoid disturbance, the ventilation circuit and tubes. The most important thing is to avoid leakage or disconnection in the ventilatory circle. In ARDS or ALI patients, the challenge is to improve patient oxygenation and recruiting lung area, or improving the ventilatory strategies of the remitting hospital.

What are the contrasts in ventilation treatment during air transport with an intensive care ventilator compared to traditional transport ventilators?
It is generally the same contrast that you have in the hospital, coming from the OR or in the ICU. Generally, uncomplicated and sedated patients do not require advanced ventilatory therapy. But if you have a patient with respiratory failure, whether in the ICU or in the air, you need a good intensive care ventilator. But since you never know what the next patient's condition will be, it is better to have both solutions – the intensive care ventilator for complex cases, and the transport ventilator for general cases. I think that only about 50% of our total transport patients require a sophisticated intensive care ventilator, but in those patients it is really a necessity. If we did not have it, we could not transport these patients. In air transports, we frequently use the intensive care ventilator even

in uncomplicated patients. The unit is already there and can simply be switched on. About 30% of our ventilated patients get hand ventilation from the remitting hospital to the ambulance or helicopter, where they are put on the intensive care ventilator and treated with supportive modes.

What types of preparations are needed for planned air transport of an intensive care patient; at the remitting hospital, and at Grosshadern where the patient is received?
It always depends on the underlying disease and the condition of the patient. Uncomplicated patients usually require no further preparation. Critically ill patients, on the other hand, with heart failure, respiratory failure or sepsis for example, often require hemodynamic stabilization, eg, catecholamines, improved ventilator strategies, nebulization of illoprost or NO ventilation, and sometimes insertion of central venous catheters or arterial catheters. The most demanding patients are the ARDS patients, since they are frequently in a critical and unstable condition when we receive them.

What are the average transport times by land?
We have a lot of transports from one Munich hospital to the other, for specialized types of surgeries. These transports are usually 30 minutes by land, and from ICU to ICU about 90 minutes. For hospitals in Bavaria outside of Munich, there can be a wider range of times. There can be extreme cases too: we had an intensive care patient transport to Bonn last year by land, when the weather did not permit air transport.

How big is the medical team that accompanies each intensive care patient by air?
In the majority of cases, the medical team consists of one doctor and one medic per patient. In some cases we might have three members in the medical crew. But it is a calculation of the crew weight and the total weight with fuel that determines how many medical team members the helicopter pilot will permit.

How do ventilated patients who are not sedated generally experience the air transport process?
I usually give a light sedation, but most of the patients are not nervous or fearful of the flight. They are generally comfortable, and they have headphones so they can talk with the medical staff members.

Can you give us an example of a "worst case scenario" for a ventilated patient during helicopter transport?
The worst case scenario is losing the airway in a patient who could not be intubated conventionally, for example a dysmorphic newborn, or discovering empty oxygen tanks and a patient with respiratory failure in need of an FiO2 of 1.0. What is the history behind the intensive care transport culture here at this institution? The first helicopter came in 1991, so we have a lot of experience with ARDS, transplant and emergency patients in air transports. Most strategies coming were the same for years, but some new ones from the ICU are also used in transport as well, such as; nitric oxide, noninvasive ventilation, lung recruitment and illoprost nebulization. Treatment strategies that are developing in the ICU are adapted for treating ICU patients in air transports. We had fewer emergency patients in 1991, and more planned transports at that time. But in recent years there has been a trend in Germany moving towards more emergency air transports. There are also more helicopters available now than there were ten years ago. Accidents outside the cities, or accidents at night, call for helicopter assistance.

What do you think will be the future trends in regard to transport of intensive care patients? Will there be increasing numbers, requirements or special demands in future?
The trend we have seen in recent years is one I think will continue. There are more and more critically ill patients being remitted by smaller hospitals to the large research centers. There are also more problems with intensive care department capacities that we are seeing more frequently, due to lack of beds or staff. Therefore the need for inter-hospital transfer with intensive care facilities will increase. In addition, the requirements for the quality of air transport will also increase, as well as the need for continuing therapy during air transport. Weight is the major problem for air transport, so every kilogram is important. Lighter weight and more advanced equipment to be used for more sophisticated ICU therapies is needed in future development to meet these future directions and trends.

The Politics of Health

Michel Foucault

THE POLITICS OF HEALTH IN THE EIGHTEENTH CENTURY

What the eighteenth century shows is a double-sided process. The development of a medical market in the form of private clienteles, the extension of a network of personnel offering qualified medical attention, the growth of individual and family demand for healthcare, the emergence of a clinical medicine strongly centered on individual examination, diagnosis, and therapy, the explicitly moral and scientific (and secretly economic) and the exaltation of "private consultation"—in short, the progressive emplacement of what was to become the great medical edifice of the nineteenth century. These things cannot be divorced from the concurrent organization of a politics of health or the consideration of disease as a political and economic problem for social collectivities, which they must seek to resolve as a matter of overall policy. "Private" and "socialized" medicine, in their reciprocal support and opposition, both derive from a common global strategy.

There were a number of distinct health policies, and various different methods for taking charge of medical problems: those of religious groups (the considerable importance, for example, of the Quakers and the various dissenting movements in England); those of charitable and benevolent associations, which operated rather like organs of surveillance of one class over those others which, precisely because they are less able to defend themselves, are sources of collective danger; and those of the learned societies, eighteenth-century academies, which endeavored to organize a global, quantifiable knowledge of morbid phenomena. Health and sickness, as characteristics of a group, a population, are problematized in the eighteenth century through the initiatives of multiple social instances, in relation to which the state itself plays various different roles.

Rather than being the product of a vertical initiative coming from above, social politics in the eighteenth century figures as a problem with a number of different origins and orientations, being the problem of the health of all as a priority for all and the state of health of a population as a general objective of policy.

The most striking trait of the eighteenth century consists in the displacement of health problems relative to problems of assistance. Schematically, one can say that up to the end of the seventeenth century, institutions for assistance to the poor serve as the collective means of dealing with disease. Medicine understood and practiced as a "service" operated simply as one of the components of "assistance." It was addressed to the category of the "sick poor." In economic terms, this medical service was provided mainly thanks to charitable foundations. Institutionally, it was exercised within the framework of lay and religious organizations. Sickness is only one among a range of factors—including infirmity, old age, inability to find work, and destitution—that compose the figure of the "needy pauper" who deserves hospitalization.

The first phenomenon in the eighteenth century we should note is the progressive dislocation of these mixed and polyvalent procedures of assistance. This dismantling is carried out or, rather, is called for, as the upshot of a general reexamination of modes of investment and capitalization. In this process of the gradual attenuation of traditional social statuses, the "pauper" is one of the first to be effaced, giving way to a whole series of functional discriminations (the good poor and the bad poor, the willfully idle and the involuntarily unemployed, those who can do some kind of work and those who cannot). The problem is to set the "able-bodied" poor to work and transform them into a useful labor force; but it is also to assure the self-financing by the poor themselves of the cost of their sickness and the temporary or permanent incapacitation. Thus, a complete utilitarian decomposition of poverty is marked out, and the specific problem of the sickness of the poor begins to figure in the relationship of the imperatives of labor to the needs of production.

This enables us to understand the main characteristics of eighteenth-century healthcare politics as follows:

1. The privilege of the child and the medicalization of the family. There are to be henceforth a whole series of obligations imposed on parents and children alike: obligations of a physical kind (care, contact, hygiene, cleanliness, attentive proximity), suckling of children by their mothers, clean clothing, physical exercise to ensure the proper development of the organism. The health of children becomes one of the family's most demanding objectives. From the second half of the eighteenth century, the family is the target for a great enterprise of medical acculturation.

The long campaign of inoculation and vaccination has its place in this movement to organize around the child a system of medical care for which the family is to bear the moral responsibility and at least part of the economic cost.

The medical politics outlined in the eighteenth century in all European countries has as its first effect the organization of the family or, rather, the family-children complex, as the first and most important instance for the medicalization of individuals. The family is assigned a linking role between general objectives regarding the good health of the social body and individuals' desire or need for care.

2. The privilege of hygiene and the function of medicine as an instance of social control. Medicine, as a general technique of health even more than as a service to the sick or an art of cures, assumes an increasingly important place in the administrative system and the machinery of power. A "medico-administrative" knowledge begins to develop concerning society and its health and sickness. There is likewise constituted a politico-medical hold on a population hedged in by a whole series of prescriptions relating not only to disease but to general forms of existence and behavior (food and drink, sexuality and fecundity, clothing, and the layout of living space).

The doctor becomes the great adviser and expert, if not in the art of governing at least in that of observing, correcting, and improving the social "body" and maintaining it in a permanent state of health.

In relation to these new problems, the hospital appears as an obsolete structure in many respects. A fragment of space closed in on itself, a place of internment of men and diseases, its ceremonious but inept architecture multiplying the ills in its interior without preventing their outward diffusion, the hospital is more the seat of death for the cities where it is sited than a therapeutic agent for the population as a whole. The hospital is perceived as an area of darkness within the urban space and it acts as a dead weight on the economy since it provides a mode of assistance that can never make possible the diminution of poverty.

Therefore, the hospital must become a functional element in an urban space where subject to measurement and control.

It is also necessary to organize the internal space of the hospital so as to make it medically efficacious, a place no longer of assistance but of therapeutic action. The hospital must function as a "curing machine." In a positive way, the space of the hospital must be organized according to a concerted therapeutic strategy, through the uninterrupted presence and hierarchical prerogatives of doctors, through systems of observation, notation, and record-taking. These make it possible to fix the

knowledge of different cases, to follow their particular evolution, and also to globalize the data that bear on the long-term life of a whole population, and finally, the substitution of better-adapted medical and pharmaceutical cures for the somewhat indiscriminate curative regimes that formed the essential part of traditional nursing. The hospital tends towards becoming an essential element in medical technology, not simply as a place for curing, but as an instrument, which, for a certain number of serious cases, makes curing possible.

Consequently, it becomes necessary in the hospital to articulate medical knowledge with therapeutic efficiency. In the eighteenth century, specialized hospitals emerge. The first maternity hospital was opened in London in 1749. In Paris, the Enfants Malades was founded in 1802.

Finally, the hospital must serve as the supporting structure for the permanent staffing of the population by medical personnel. Moreover, the hospital as a place of accumulation and development of knowledge must provide for the training of doctors for private practice. At the end of the eighteenth century, clinical teaching in the hospital—the first rudiments of which appear in Holland with Sylvius and then Boerhaave, at Vienna with Van Swieten, and at Edinburgh through the linking of the School of Medicine with the Edinburgh infirmary—becomes the general principle around which the reorganization of medical studies is undertaken.

THE BIRTH OF SOCIAL MEDICINE

State Medicine
"State medicine" developed primarily in Germany, at the beginning of the eighteenth century. At the end of the sixteenth century and the beginning of the seventeenth century, in a political, economic, and scientific climate characteristic of the epoch dominated by mercantilism, all the nations of Europe began to take an interest in the health of their populations. Mercantilism was not simply an economic theory, its overall object being to establish commercial exchanges that would enable Europe to achieve the greatest possible monetary influence and, thereby, to finance the maintenance of armies and of the whole apparatus that endows a state with real strength in its relations with others.

With this in view, France, England, and Austria began to evaluate the active strength of their populations. Thus, birth and death rate statistics appeared in France, and, in England, the great census surveys that began in the seventeenth century. But at the time, in both France and England, the only health interest shown by the state had to do with drawing up of tables of birthrate and mortality.

In Germany, on the other hand, a medical practice developed that was actually devoted to the improvement of public health. Frank and Daniel, for example, proposed, between 1750 and 1770, a program aimed in that direction; it was what was called for the first time a state "medical police."

The medical police consisted of:

- A system of observation of sickness, based on information gathered from the hospitals and doctors.
- The standardization of medical practice and medical knowledge. Then there emerged the idea of a

standardization of medical instruction and, more specifically, of a public supervision of training programs and the granting of degrees.

- An administrative organization for overseeing the activity of doctors.

All of this presupposed, of course, a subordination of medical practice to a higher administrative authority.

This state medicine did not have the objective of forming a labor force adapted to the needs of the industries that were then developing. It was not the workers' bodies that interested this public health administration, but the bodies of individuals insofar as they combined to constitute the state. Medicine was obliged to perfect and develop state strength, and this concern … implied a certain economico-political solidarity.

Urban Medicine

This second form of the development of social medicine is represented by the example of France, where at the end of the eighteenth century a social medicine appeared, seemingly not based on the state structure, as in Germany, but on an entirely different phenomenon—urbanization. Social medicine developed in France in conjunction with the expansion of urban structures.

In the second half of the eighteenth century, the need was felt to unify the city, to organize the urban corporate body in a coherent and homogeneous way, to govern it by a single, well-regulated authority. The fact that the city was not only a market center but also a place of production made it necessary to resort to homogeneous and coherent mechanisms of regulation.

The development of cities, the appearance of a poor, laboring population that was transformed during the nineteenth century into a proletariat, was bound to increase the tensions inside the cities. The coexistence of different small groups began to reduce down to a sort of confrontation between rich and poor, commoners and bourgeoisie; this resulted in more frequent urban disturbances and insurrections involving more and more people.

It was during this period that a feeling of fear, of anxiety about cities emerged and grew. For example, in reference to cities, the late eighteenth-century philosopher Pierre Jean George Cabanis said that whenever men came together their morals changed for the worse; whenever they came together in closed places their morals and their health deteriorated.

The life of the big eighteenth-century cities, especially Paris, provoked a series of panics. One might mention here the example of the Cemetery of the Innocents, in the center of Paris, into which the cadavers of those who lacked the resources or the social stature to buy or to merit an individual grave were thrown, one on top of the other. Urban panic was characteristic of a sanitary anxiety, the uneasiness that appeared as the urban machine developed. Measures had to be taken to control these medical and political phenomena, which caused the population of the cities to experience such intense anxiety.

As a result, a well-known but rarely employed model of intervention was appealed to—the model of the quarantine. It was to be applied when the plague or another serious epidemic disease appeared in a city.

The quarantine plan represented the politico-medical ideal of a good sanitary organization of eighteenth-century cities. Urban medicine, in the second half of the eighteenth century, with its methods of observation, hospitalization, and so on, was nothing but an improvement on the politico-medical schema of the quarantine that appeared at the end of the Middle Ages.

THE MAIN OBJECTIVES OF URBAN MEDICINE

Medicine's first objective consisted in analyzing the zones of congestion, disorder, and danger within the urban precincts. The initial objective of urban medicine was to study the accumulation and piling-up of refuse that might cause illnesses in the urban space. Graveyards were the main concern here. It was during this period that the individualized cemetery came into existence, that is, the individual coffin and the tomb reserved for the members of a family. It is often thought that, in modern society, the cult of the dead comes to us from Christianity. There is nothing in Christian theology that urges respect for the corpse. The individualization of the corpse, the coffin, and the grave appeared at the end of the eighteenth century not for the theologico-religious reasons having to do with respect for dead bodies but, rather, for politico-sanitary reasons having to do with respect for living ones, to protect the living from the harmful influence of the dead.

Secondly, urban medicine had a new objective—controlling circulation. Not the circulation of individuals but of things and elements, mainly water and air.

It was an old eighteenth-century belief that air had a direct influence on the organism because it carried miasmas. … The air was considered to be one of the great pathogenic factors. But how to maintain air quality in a city? The need arose to open up the avenues of the urban space in order to preserve the health of the population. Houses preventing air circulation above the streams and retaining the humid air on the slopes were systematically torn down.

The third major goal of urban medicine was the organization of what could be called distributions and sequences. Where to place the different elements necessary to the shared life of the city? The problem of the respective position of the fountains and sewers, the pumps and river washhouses was raised. This led to the first hydrographic plan of Paris, in 1742. When the French Revolution broke out in 1789, Paris had already been carefully studied by an urban medical police that had established directives for bringing about a veritable sanitary organization of the city. Public spaces, such as places of circulation, cemeteries, ossuaries, and slaughterhouses, were controlled starting in the eighteenth century.

It was precisely the analysis of water, of air currents, of the conditions of life and respiration, which brought medicine and chemistry into contact. The entry of medical practice into a corpus of physico-chemical science was brought about through urbanization. Scientific medicine did not grow out of private, individualized medicine, nor was it inspired by greater interest in the individual.

Urban medicine is not really a medicine of man, the body, and the organism, but a medicine of things—air, water, decompositions, fermentations. It is a medicine of the living conditions of the existential milieu.

The progression was not from analysis of the organism to analysis of the environment. Medicine went from analysis of the environment to that of the effects of the environment on the organism and, finally, to analysis of the organism itself.

With urban medicine there appeared, shortly before the French Revolution, the notion of salubrity.

Salubrity did not mean the same thing as health; rather, it referred to the state of the environment and those factors of it that made the improvement of health possible. Salubrity was the material and social basis capable of ensuring the best possible health for individuals. In connection with this, the concept of public health, hygiène publique, appeared.

LABOR FORCE MEDICINE

The third direction of social medicine can be examined through the English example. Poor people's medicine, labor force or worker's medicine, was not the first but the last objective of social medicine.

What characterized French urban medicine was respect for the private sphere and the rule of not having to regard the poor, the underclass, or the people as an element that threatened public health. Consequently, the poor or the workers were not thought of in the same way as cemeteries, ossuaries, slaughterhouses, and so on.

Urban activity depended on the poor. A city's poor people accomplished a certain number of tasks: they delivered the mail, collected the garbage, picked up old furniture, used clothing, redistributed or resold scrap materials, and so on. They thus formed part of urban life. In this era, the houses didn't have numbers and there was no postal service either. No one knew the city and all its nooks better than the poor; they carried out a series of basic functions such as water hauling or refuse disposal.

Insofar as the poor formed part of the urban system, like the sewers or pipes, they performed an indisputable function and could not be considered as a danger. But starting in the second third of the nineteenth century, the problem of poverty was raised in terms of menace, of danger.

During the French Revolution and in England during the great social unrest of the beginning of the nineteenth century, the destitute population transformed itself into a political force capable of revolting or at least of participating in revolts.

In the nineteenth century, means were found for partly replacing the services offered by the underclass, such as the setting up of a postal service and a transport system. These reforms were at the origin of a wave of popular disturbances launched against these systems, which deprived the most needy of bread and of the very possibility of living.

With the cholera epidemic of 1832, which began in Paris, then spread throughout Europe, a set of political and health fears occasioned by the proletarian or plebeian population crystallized. It was in this period that the decision was first made to divide the urban space into rich areas and poor areas.

In England—where industrial development was being experienced, and where, consequently, the formation of a proletariat was faster and more extensive—a new form of social medicine appeared.

It was essentially the Poor Law that made English medicine a social medicine insofar as this law implied a medical control of the destitute. Since the poor benefited from the welfare system, it became obligatory to subject them to various medical controls. With the Poor Law, an important factor in the history of social medicine made an ambiguous appearance: the idea of a tax-supported welfare. It made it possible to maintain a control by which the wealthy classes, or their government representatives, would guarantee the health of the needy classes and, consequently, protect the privileged population. In this way, an officially sanctioned sanitary cordon between the rich and the poor was set in place within the cities. Thus, the wealthy freed themselves of the risk of being victims of epidemic phenomena issuing from the disadvantaged class.

The Health Offices, which appeared in England in 1875, and were estimated to number a thousand toward the end of the nineteenth century, had the following functions:

- Control of vaccination
- Organizing the record of epidemics and diseases
- Localization of unhealthy places

In the second half of the nineteenth century, English medical control administered by the Health Offices provoked violent popular reactions and resistances, small-scale antimedical insurrections. Dissident religious groups were concerned with combating medicalization, with asserting the right to life, the right to get sick, to care for oneself, and to die in the manner one wished. This desire to escape from compulsory medicalization was one of the characteristics of these numerous apparently religious groups that were intensely active at the end of the nineteenth century, as they still are today.

In contrast to German state medicine of the eighteenth century, there appeared in the nineteenth century—above all, in England—a medicine that consisted mainly in a control of the health and the bodies of the needy classes, to make them more fit for labor and less dangerous to the wealthy classes. This enabled the creation of three superimposed and coexisting medical systems: a welfare medicine designed for the poorest people; an administrative medicine responsible for general problems such as vaccination, epidemics, and so on; and a private medicine benefiting those who could afford it.

The German system of state medicine was burdensome, and French urban medicine was a general plan of control without any specific instrument of authority; but the English system made possible the organization of a medicine with different features and forms of authority.

In Practice: Ethics Class

John Lantos

In our medical school, we teach ethics during the first year. We try to make it interesting by bringing in clinicians to discuss cases. Medical students do not like theory. Like William Carlos Williams, they want no ideas but in things.

This year, I once again gave the lecture on truth-telling, or as I have started to call it, "disclosure dilemmas." I try to cover the waterfront and review all the situations in which doctors have information they might choose not to share. We talk about whether students should introduce themselves as "doctor," whether any doctor should tell the patient it is their first time doing something, whether informed consent should include general outcome statistics, or those of the institution, or those of the individual doctor. We get into mandatory reporting requirements and the tensions they place on confidentiality. And, of course, we talk about delivering bad news, about giving bleak prognoses. Each area has zones in which things seem relatively black and white, and zones in which there are shades of gray.

During this winter quarter, I was also attending on the wards. When I came on service, one of the patients was an eight-month-old who was unable to eat by mouth. An ex-preemie, she'd had some birth asphyxia and a moderate intraventricular hemorrhage. Each month, the doctors tried to convince her mother that she would need a G-tube—a feeding tube inserted into her stomach through the stomach wall. At each discussion, the mother adamantly refused. So the baby had a nasogastric tube in place instead. She got all her nutrition, but it didn't seem like the best long-term solution. I arranged to meet with the baby's mother.

I started the discussion by asking her what she understood about her baby's condition. She looked at me suspiciously,

like she'd been down this road before, and like she wished I'd cut to the chase. But she was experienced enough, too, to know that she was going to have to humor me a little bit.

"My baby was a preemie and had some brain damage. They told me she might never see, hear, walk, or talk. But she's been doing better, much better."

"That's great," I said. "Babies are always surprising us. What have you noticed, in particular, as signs of progress?"

"Well, she's more alert, she smiles a lot more when she sees me, she's breathing more off the vent."

"That's fabulous. I think we're up to eight hours per day off the vent now. If we keep that up, we should have her home on just nighttime ventilation. That would make life a lot easier during the day."

"Yeah…."

"What about her eating by mouth?"

"Well, she's doing okay with that."

Our speech therapists had recently evaluated her. They said her suck and swallow reflexes were totally uncoordinated. Since she wasn't aspirating what she had in her mouth, they were continuing to work with her, but they thought there was no chance that she would ever be able to eat by mouth.

"One of the things I wanted to talk about," I said, "is getting a G-tube. Our speech therapists think it'll be months or years before she is able to eat by mouth. They're worried that the NG-tube will just cause problems during that time. It is uncomfortable, it may increase her chance of getting pneumonia, and she is starting to learn how to pull it out. Have you thought anymore about a G-tube?"

Mom stared at the floor, and her body

was tense. It felt as if the temperature was rising in the room.

"Look," she finally said, her voice now trembling with emotion, "after my baby was born, I thought she was going to die. When she was in the NICU, I took six months off work and I never left her bedside. I've been through everything with her. She had lines, she had chest tubes, she had surgery…." The mother paused. She seemed to be on the verge of tears. "And now, she's doing fine. And I just went back to work. I just don't want anybody cuttin' on my baby anymore. She's doing fine."

Back in ethics class, I described this interaction as an example of a situation where it was difficult to deliver bad news. A student raised his hand.

"But you didn't tell her the truth. Your speech therapists told you the baby would never eat. You told the mother it would take a while till she could eat. I thought you were encouraging us to tell the truth."

He was right. As so often happens when we go back and forth between practice and theory, the cases undermine the principles. We don't practice what we preach. Our behavior indicts our teaching.

As a teacher, I was happy that the student had noticed this and spoken up to point it out. As a role model, I was a little sheepish. I thought I could defend my conversation, but it would have been complicated, circuitous, casuistical. And after all, I wasn't completely sure whether it was my behavior or my theories that needed to change.

The next day, on rounds, the baby's mother was sitting beside the crib. She had a mysterious look on her face. She triumphantly informed me that her baby had taken five ccs by mouth the day before, more than she'd ever taken before. I was thrilled.

Early tracheostomy in closed head injuries: experience at a tertiary center in a developing country – a prospective study

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ABSTRACT

Background

An important factor contributing to the high mortality in patients with severe head trauma is cerebral hypoxia. The mechanical ventilation helps both by reduction in the intracranial pressure and hypoxia. Ventilatory support is also required in these patients because of patient's inability to protect the airway, persistence of excessive secretions, and inadequacy of spontaneous ventilation. Prolonged endotracheal intubation is however associated with trauma to the larynx, trachea, and patient discomfort in addition to requirement of sedatives. Tracheostomy has been found to play an integral role in the airway management of such patients, but its timing remains subject to considerable practice variation. In a developing country like India where the intensive care facilities are scarce and rarely available, these critical patients have to be managed in high dependency cubicles in the ward, often with inadequately trained nursing staff and equipment to monitor them. An early tracheostomy in the selected group of patients based on Glasgow Coma Score (GCS) may prove to be life saving. Against this background a prospective study was contemplated to assess the role of early tracheostomy in patients with isolated closed head injury.

Methods

The series consisted of a cohort of 50 patients admitted to the surgical emergency with isolated closed head injury, that were not considered for surgery by the neuro-surgeon or shifted to ICU, but had GCS score of less than 8 and SAPS II score of more than 50. First 50 case records from January 2001 that fulfilled the criteria constituted the control group. The patients were managed as per ATLS protocol and intubated if required at any time before decision to perform tracheostomy was taken. These patients were serially assessed for GCS (worst score of the day as calculated by senior surgical resident) and SAPS scores till day 15 to chart any changes in their status of head injuries and predictive mortality. Those patients who continued to have a GCS score of <8 and SAPS score of >50 for more than 24 hours (to rule out concussion or recovery) underwent tracheostomy.

All these patients were finally assessed for mortality rate and hospital stay, the statistical analysis was carried out using SPSS10 version.

The final outcome (in terms of mortality) was analyzed utilizing chi-square test and p value <0.05 was considered significant.

Results

At admission both tracheostomy and non-tracheostomy groups were matched with respect to GCS score and SAPS score.

The average day of tracheostomy was 2.18 ± 1.0038 days.

The GCS scores on days 1, 2, 3, 4, 5, 10 between tracheostomy and non-tracheostomized group were comparable. However the difference in the GCS scores was statistically significant on day 15 being higher in the tracheostomy group.Thus early tracheostomy was observed to improve the mortality rate significantly in patients with isolated closed head injury

Conclusion

It may be concluded that early tracheostomy is beneficial in patients with isolated closed head injury which is severe enough to affect systemic physiological parameters, in terms of decreased mortality and intubation associated complications in centers where ICU care is not readily available. Also, in a selected group of patients, early tracheostomy may do away with the need for prolonged mechanical ventilation.

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BACKGROUND

An important factor responsible for the high mortality in patients with severe head trauma is cerebral hypoxia. Mechanical ventilation is often required because of patient's inability to protect the airway, persistence of excessive secretions, and inadequacy of spontaneous ventilation. Tracheostomy plays an integral role in the airway management of such patients, but its timing remains subject to considerable practice variation. The complications associated with prolonged endotracheal intubation are increasingly being recognized and include injury to the larynx, trachea, and patient discomfort. In addition, endotracheal intubation often requires the administration of systemic sedation, with attendant complications. Finally the incidence of ventilator-associated pneumonia is related directly to the duration of mechanical ventilation – a complication that carries significant morbidity and mortality.

Paradoxically, although tracheostomy is frequently recommended in closed head injury patients, few studies have been carried out to assess the importance in this group of patients. Many studies recommend early tracheostomy to avoid serious oropharyngeal and laryngeal injury occurring from prolonged translaryngeal intubation though limited data is available to define the impact of early tracheostomy on duration of mechanical ventilation and hospital stay.

In a developing country like India, where even a tertiary care center like ours, is short of appropriate ICU facilities for patients with severe closed head injuries for all patients, these critical patients have to be managed in high dependency cubicles in the ward, often with inadequately trained nursing staff and equipment to monitor them.

We had observed that patients with severe head injury very frequently required prolonged intubation, primarily for airway protection after initial few days and due to fluctuating changes in airway reflexes patients often struggled with endotracheal tubes and required frequent use of sedatives.

With the underlying belief that early tracheostomy is beneficial, we searched the literature to find those objective factors (GCS and SAPS) which can be used early to separate those patients who will ultimately require tracheostomy from those that will not.

SETTINGS

The study was performed at a major tertiary care trauma centre in New Delhi, India. This 2200-bed hospital has an 8-bed medical/surgical ICU staffed by full-time, on-site intensivists 24 hours a day and 7 days a week. The hospital has a designated trauma service, including a consultant surgeon, available 24 hours a day. Medical care in the ICU is provided by the ICU team, with the trauma team being responsible for surgical aspects of care. In addition there is a 4-beded neuro-ICU for post-operative neurosurgical patients staffed by neurosurgeons. The surgical ward has 37 beds with a 6-bed high dependency cubicle.

The study was carried out following review with Institutional Review Board from July 2003 to November 2004. The series consisted of consecutive 50 patients who fulfilled the criteria of the study and underwent tracheostomy. First 50 case records from January 2001 that fulfilled the criteria of the study constituted the control group.

This study consisted of cohort of all patients admitted to surgery emergency with isolated closed head injury, that were not considered for surgery by the neuro-surgeon or shifted to ICU, but had GCS score of less than 8 and SAPS II score of more than 50 (predictive mortality more than 50%, calculated at http://www.sfar.org). The patients were managed as per ATLS protocol and intubated if required at any time before decision to perform tracheostomy was taken. Patients underwent NECT scan to find out any intracranial bleed and were managed as per the advice of neurosurgeon.

Those patients who continued to have a GCS score of <8 and SAPS score of >50 for more than 24 hours (to rule out concussion or recovery) were to undergo a tracheostomy with a standardized technique by the surgical resident. The following patients were excluded from the study

1) Children less than 12 years of age

2) Patients who underwent neurosurgical intervention, as these patients were later shifted to neuro-ICU

3) Patients who were shifted to the ICU as ventilator and / or ICU bed were available

4) Patients with poly trauma with other injuries besides closed head injuries, so as to constitute a homogenous cohort.

The control group was selected from previous admission records and only those cases were included in whom complete data so as to calculate serial SAPS II score were available, besides fulfilling the above criteria. This was to achieve a score matched control group as comparable to study group as possible and in order to eliminate confounding factors.

All these patients were assessed for mortality rate and hospital stay and 30 days (from the time of admission) mortality was taken in to consideration. These patients were also serially assessed for GCS (worst score of the day as calculated by senior surgical resident) and SAPS scores till day 15 to chart any changes in their status of head injuries and predictive mortality.

Surgical resident in the ward performed tracheostomy by the standardized technique using a high volume, low pressure cuffed tracheostomy tube. The patient was shifted to high dependency cubicle for monitoring and 2–3 hourly suction of the tracheostomy by the staff nurse. The nurse-patient ratio in the high dependency cubicle is 1:6. If patient required ventilatory support a small KV ventilator was arranged from ICU to supply 40% oxygen at a fixed rate and airway pressure. If that was not available the patients were put on continued Ambu-bag ventilation till a ventilator was arranged. Other resuscitation was carried as per the instruction of the ICU resident and neurosurgical resident, including use of sedatives.

All patients were to undergo flexible laryngoscopy within 24 hours of tracheostomy by an ENT senior resident for evaluation of endotracheal injury and at the time of extubation or tracheostomy removal.

A central venous access was established and daily routine investigations were sent for these patients. As and when the patient stabilized (SAPS II score <50), patient was placed in the general

ward with patient-nurse ratio of 1:15. A naso-gastric tube was placed and feeding started initially along with intravenous supplement and gradually only liquid diet through naso-gastric tube, providing 2200Calories a day was started. This was done till the patient gained adequate consciousness or oropharyngeal reflexes. The patient was also placed on water mattress with nursing attendants log rolling the patients every hour to prevent bedsores. The patients' attendants were gradually introduced to nursing care of the patient and taught precautions regarding hygiene and feeding. Staff nurses or surgical residents did tracheostomy care and dressing of the bedsores on a regular basis.

Special care was taken to prevent constipation and early switch from Foley's catheter to condom catheter drainage was done. Catheter care was done as long as Foley's catheter was in-situ.

Complications like fever, cough, blocked tracheostomy tube with sputum, bedsores and/or any other source of sepsis were dealt with as per standard protocol of culture sensitivity and appropriate antibiotic cover.

The patients were discharged only after

1) They regained adequate consciousness (GCS >13);

2) Patients not only improving in the GCS score but had a good SAPS II score Meanwhile attendants were adequately trained in patient care and patient gradually weaned off tracheostomy.

Patients were divided into two groups: those that underwent tracheostomy (T group) and those that did not (NT group). All the data was collected and comparisons between the two groups for continuous variables are expressed as means ± standard error of the mean, and were compared using two-tailed t-tests for unequal variance. Categorical variables are expressed as absolute and relative frequencies, and were considered statistically significant.

DISCUSSION

A tracheostomy is a proven adjunct in the care of head injury patients. Tracheostomy provides an early airway protection and seems to decrease the need for prolonged mechanical ventilatory support. Secondly, severe head injury patients require a prolonged time for recovery and the airway reflexes are rarely optimal. The association between the duration of intubation and risks of laryngotracheal injury is another important consideration in the timing of tracheostomy.

The tracheostomy tube facilitates pulmonary toilet and oral hygiene and has been shown to reduce the incidence of ventilator-associated pneumonia. Furthermore, a tracheostomy tube is less noxious for the patient emerging from coma and sedation can be more easily weaned off. In addition, tracheostomy reduces significantly the physiological dead space of ventilation and thereby the work of breathing. This is even more beneficial in a patient having labored breathing or deteriorating respiration and may prevent the use of mechanical ventilation altogether. Because of these benefits, early tracheostomies have been shown to reduce hospital stay. However to realize the benefits of early tracheostomy without performing unnecessary tracheostomies, appropriate patients must be identified early at the time of admission. Early oxygenation and ventilatory abnormalities can predict the need

for tracheostomy. However, head injury patients primarily require airway protection and not necessarily ventilatory support for pulmonary failure.

A study by Major et al showed that using objective scores such as GCS (less than seven) and SAPS (more than fifteen) score could aid in identifying those patients who will eventually require a tracheostomy for prolonged airway protection after blunt head trauma with high positive predictive value. However, they used day 4 scores of GCS and SAPS to determine the need for tracheostomy and performed the tracheostomy only after day 5. This way they not only excluded patients who were extubated but even those who died early, thus removing an important cohort who could benefit from tracheostomy. This skewed mortality data as severe head injury is associated with early mortality. In addition, these patients were admitted in ICU and were intubated already as per ATLS standards. Positive predictive value for GCS and SAPS score was 71%, and negative predictive value was 83%. Gurkin et al found two admission criteria (GCS <9 and ISS >24) to be predictive of the need for tracheostomy in those patients that remained intubated on day 7. Rodriguez et al noted a significant decrease in ventilator days and ICU days and hospital length of stay in patients who underwent tracheostomy within five days of intubation.

In a study by Sugerman et al several major trauma centers refused to participate in early tracheostomy (5 to 7 days) trial because they felt strongly, like we do, that either all severly injured patients should undergo tracheostomy within 2 to 3 days after injury or tracheostomy was not necessary for as long as 3 to 4 weeks after injury. In their study they found that head injury patients who underwent early tracheostomy had higher APACHE III scores but there was no difference in ICU LOS, pneumonia and death in these patients as compared to patients with late tracheostomy.

Lesnik *et al* retrospectively reviewed 101 adult patients with blunt injuries, 32 had tracheostomy within first 4 days and 69 underwent tracheostomy after 4 days. The author found that mean duration of ventilatory support was 6.0 days in early tracheostomy group versus 20.6 days in the late tracheostomy group ($p < 0.001$).

In a study by Bouderka et al a prospective study was conducted in patients with admission GCS of 8 or less, cerebral contusion on CT scan and GCS score of less than 8 on day 5. These patients were randomized into early tracheostomy and prolonged intubation. Besides demographic data admission scores SAPS, ICU stay duration of mechanical stay was compared. They concluded that early tracheostomy decreased total days of mechanical ventilation ($p = 0.02$). They agreed that choosing their criteria had the limitation of high mortality during the first week of hospitalization. They suggested that most of the patients did not require mechanical ventilatory support but were intubated mainly for airway protection. Early tracheostomy may provide an early alternative for airway protection and assist in early termination of mechanical ventilatory support and therefore reduce hospital stay for these patients.

In our opinion using admission data to support a decision several days later is flawed. This diminishes the benefits of early tracheostomy and makes the decision more straightforward and increases the chances of laryngotracheal injuries due to intubation.

Early tracheostomy may assist in early termination of mechanical ventilation and therefore, reduce the hospital stay and mortality. Currently, the decision to proceed to early tracheostomy is based on the attending trauma surgeon's preference. The consensus conference of 1989 recommended conversion to tracheostomy if the anticipated need for mechanical ventilation is more than 21 days. Such practice was based on earlier reports showing high tracheal stenosis rates with tracheostomy as compared with endotracheal intubation. However, the incidence of tracheal stenosis has decreased substantially with recognition of its aetiology and improvements in tracheostomy materials, design and management, particularly with the use of high-volume, low-pressure cuffs. Also, the complications associated with prolonged endotracheal intubation are increasingly being recognized, including injury to the larynx and trachea, and patient discomfort. In addition, endotracheal intubation often requires the administration of systemic sedation, with attendant complications.

Despite evidence to support the utility of early tracheostomy, few recommendations exist to facilitate identification of appropriate patients.

In a study by Arabi et al, 136 patients underwent tracheostomies, of which only 29 were early (seven days). The duration of mechanical ventilation was significantly shorter with early tracheostomy (mean ± standard error: $9.6 ± 1.2$ days versus $18.7 ± 1.3$ days; $P < 0.0001$). Similarly, ICU LOS was significantly shorter ($10.9 ± 1.2$ days versus $21.0 ± 1.3$ days; $P < 0.0001$). Following tracheostomy, patients were discharged from the ICU after comparable periods in both groups ($4.9 ± 1.2$ days versus $4.9 ± 1.1$ days; not significant). ICU and hospital mortality rates were similar. Using multivariate analysis, late tracheostomy was an independent predictor of prolonged ICU stay (>14 days). The very low mortality seen in the patients we studied may be explained by selection of proper candidates for tracheostomy, excluding those patients who were unlikely to survive. Hospital LOS in these patients was prolonged, reflecting their severe injuries that required lengthy rehabilitation periods.

Strengths of our study include prospective data collection ensuring complete data. The cohort was homogenous in that the decision for tracheostomy was not affected by other injuries (maxillofacial, neck) which may mandate early tracheostomy. Similarly the outcome in either group remained uninfluenced by systemic injuries. Our study included all patients with severe head injury (including those with early mortality) by virtue of doing early tracheostomy, unlike other studies which excluded such patients by doing tracheostomy on day 5 onwards. By taking SAPS II as a criterion, we tried not to overdo tracheostomies by including only those patients in whom the head injury was severe enough to affect systemic physiological parameters. Lastly, we have taken serial scores as criteria for tracheostomy rather than admission scores. However data extraction and analysis was retrospective. Because the database was not designed specifically to examine tracheostomy practices, certain issues were not documented, such as comparison with intubation and the type of tracheostomy done. Also, we did not compare the morbidity in the two groups. In addition, the study was conducted from one centre. A large multicentre randomized controlled trial in which patients are randomized to early versus late tracheostomy would be the ideal way to test the impact of procedure timing on resource utilization.

Inhaled Corticosteroids and Mortality in Chronic Obstructive Pulmonary Disease

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Background: Clinical studies suggest that inhaled corticosteroids reduce exacerbations and improve health status in chronic obstructive pulmonary disease (COPD). However, their effect on mortality is unknown. Methods: A pooled analysis, based on intention to treat, of individual patient data from seven randomized trials (involving 5085 patients) was performed in which the effects of inhaled corticosteroids and placebo were compared over at least 12 months in patients with stable COPD. The end point was all-cause mortality.

Results: Overall, 4% of the participants died during a mean follow up period of 26 months. Inhaled corticosteroids reduced all-cause mortality by about 25% relative to placebo. Stratification by individual trials and adjustments for age, sex, baseline post-bronchodilator percentage predicted forced expiratory volume in 1 second, smoking status, and body mass index did not materially change the results (adjusted hazard ratio (HR) 0.73; 95% confidence interval (CI) 0.55 to 0.96). Although there was considerable overlap between subgroups in terms of effect sizes, the beneficial effect was especially noticeable in women (adjusted HR 0.46; 95% CI 0.24 to 0.91) and former smokers (adjusted HR 0.60; 95% CI 0.39 to 0.93).

Conclusions: Inhaled corticosteroids reduce all-cause mortality in COPD. Further studies are required to determine whether the survival benefits persist beyond 2–3 years.

Chronic obstructive pulmonary disease (COPD) is a major global epidemic affecting 5–15% of all adults in industrialized countries[1,2] and accounting for over 3 million deaths each year worldwide.[3] Even more alarmingly, the global burden of COPD will escalate over the next 20 years as more people live longer and a greater number of individuals take up smoking, especially in developing countries. By 2020 the World Health Organization predicts that COPD will be the fifth most prevalent disease (currently twelfth) and the third most common cause of death worldwide (currently fourth).[3] Unfortunately, apart from smoking cessation, there is a dearth of management strategies available that can curb the rising impact of COPD. Smoking cessation improves the natural history of COPD. However, once COPD is established, many sustained quitters remain symptomatic and experience frequent exacerbations of their disease.[1] They also have evidence for persistent airway wall inflammation.[4] Thus, in symptomatic patients with COPD, additional treatments are indicated.

In view of the prominence and importance of airway inflammation in the pathogenesis of COPD,[5] anti-inflammatory drugs such as inhaled corticosteroids can potentially improve health outcomes in patients with the disease. However, a few short term physiological studies have failed to demonstrate

Table 1 Characteristics of individual studies at the time of randomisation

Study	No of patients	Age (years)	Women (%)	Current smoker (%)	FEV$_1$ (l)*	FEV$_1$ (% of predicted)*†	Mortality (%)	Follow up (months)	Drug/dose
LHS-2	1116	56 (7)	37	90	2.3 (0.6)	67 (13)	2.8	42 (5)	Triamcinolone (1200 μg/day)
CCLS	290	59 (9)	40	76	2.4 (0.8)	76 (18)	2.8	30 (12)	Budesonide (867 μg/day)
ISOLDE	751	64 (7)	25	48	1.4 (0.5)	49 (14)	13.7	34 (7)	Fluticasone (1000 μg/day)
EUROSCOP	1277	52 (8)	27	100	2.6 (0.7)	73 (13)	1.5	28 (13)	Budesonide (800 μg/day)
TRISTAN	735	63 (9)	28	50	1.4 (0.5)	46 (13)	2.0	10 (4)	Fluticasone (1000 μg/day)
Szafranski	403	64 (9)	18	30	1.0 (0.4)	36 (12)	3.5	9 (4)	Budesonide (800 μg/day)
Calverley	513	64 (9)	26	31	1.2 (0.5)	42 (15)	2.1	9 (5)	Budesonide (800 μg/day)
Total	5085	59 (9)	29	69	1.9 (0.8)	58 (19)	4.0	26 (15)	

LHS-2, Lung Health Study 2; CCLS, Copenhagen City Lung Study; ISOLDE, Inhaled Steroids in Obstructive Disease in Europe; EUROSCOP, European Respiratory Society Study on Chronic Obstructive Pulmonary Disease; TRISTAN, TRial of Inhaled STeroids ANd long acting β$_2$ agonists; FEV$_1$, forced expiratory volume in 1 second.
*Post-bronchodilator values.
†Values may differ slightly from the original publications because we applied Hankinson's prediction equation to all of the "raw" FEV$_1$ values.
Continuous variables are presented as mean (SD) and dichotomous variables as percentage of participants in each individual trial.

salutary effects of these medications on inflammatory indices in sputum,[6,7] as one might expect given their anti-inflammatory properties, and several long term trials have failed unequivocally to demonstrate a beneficial effect in modifying the long term decline in lung function.[8,9] Although several large clinical trials have evaluated the role of inhaled corticosteroids in COPD, none of them individually had sufficient statistical power to assess the effect of inhaled corticosteroids on all-cause mortality, and many did not report on mortality in their original publications. For this reason, prior meta-analyses, which relied on published grouped data, could not adequately evaluate mortality as an end point.[8-11] To overcome this deficiency and determine whether inhaled corticosteroids affect all-cause and cause-specific mortality in COPD, we pooled retrospective individual patient data from the seven large randomized controlled trials evaluating the effects of these medications in stable COPD over a period of at least 1 year. Because some of these trials selectively chose patients with COPD who were actively smoking at the time of enrolment (leading to the over-representation of active smokers), we also evaluated the potential effect modification by smoking status and several other factors including sex, age, and baseline lung function.

STUDIES INCLUDED: DESIGN AND TREATMENT

The Inhaled Steroid Effects Evaluation in COPD (ISEEC) study included patient level data from all clinical trials in which patients with stable COPD were randomly assigned to inhaled corticosteroids or placebo for at least 12 months. These trials included the Lung Health Study-2 (LHS-2),[12] Copenhagen City Lung Study (CCLS),[13] Inhaled Steroids in Obstructive Lung Disease in Europe (ISOLDE),[14] European Respiratory Society Study on Chronic Obstructive Pulmonary Disease (EUROSCOP),[15] Trial of Inhaled Steroids and long acting ß$_2$ agonists (TRISTAN),[16] and trials by Szafranski et al[17] and Calverley et al.[18] The full details of the individual trials have been published elsewhere.[12-18]

Participants in these trials were routinely seen at least every 3–6 months by study investigators. Mortality information was collected and collated by study personnel and recorded in the trial databases. Anonymized data collected from the seven individual trials were sent from each trial site to the central ISEEC coordinating centre where they were merged together for analytical purposes. We applied Hankinson's prediction equation to calculate percentage predicted forced expiratory volume in 1 second (FEV$_1$) across all studies.[19] Principal causes of death were classified on reports by study investigators and were categorized into four groups: cardiovascular, respiratory, cancer, and others/unknown.

STATISTICAL ANALYSIS

For the primary analysis we compared the efficacy of inhaled corticosteroids on all-cause mortality rates based on the original allocation of participants in the individual trials, regardless of whether they did or did not have complete follow up. This end point was chosen a priori. The participants in each trial were followed from the date of enrolment to the date of withdrawal (for whatever reason), death or study completion, whichever came first. In ISOLDE, complete mortality data were obtained on all study participants for 3 years through the UK Office of Population Statistics registry.[20] In LHS-2, mortality status was established by the investigators for study participants over the duration of the trial. For the other studies, complete mortality data were obtained only on those who completed the trials. Deaths that occurred after the withdrawal date were not ascertained except among those who developed a serious adverse event during the trial period and died before the full resolution of the serious adverse event had occurred.

Kaplan-Meier curves were generated to compare the time to death between the steroid and placebo arms, and the log-rank statistic determined the significance of differences between the curves. Cox proportional hazards regression modeling was used

Table 2 Baseline characteristics of study participants

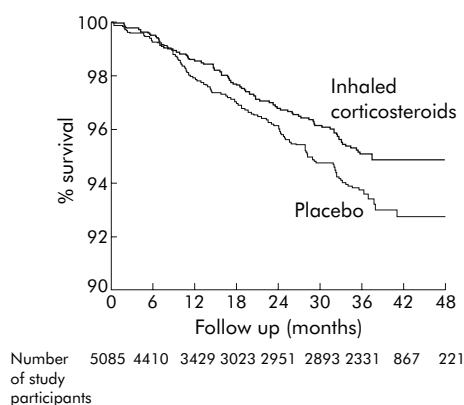|	Inhaled corticosteroids	Placebo
Number of participants	2543	2542
Age at enrolment (years)	59 (9)	59 (9)
Men	1798 (71%)	1810 (71%)
Body mass index (kg/m²)	25 (5)	25 (5)
Current smokers	1775 (70%)	1738 (68%)
Baseline post-bronchodilator FEV$_1$ (% predicted)	59 (19)	58 (20)
Length of follow up (months)	26 (15)	26 (15)

FEV$_1$, forced expiratory volume in 1 second.
Continuous variables are presented as mean (SD) unless otherwise specified.
Dichotomous variables are presented as number (% of column totals).

to estimate the relative effect of inhaled corticosteroids on all-cause mortality according to confounding variables. Hazard ratios (HR) and the nominal 95% confidence intervals (CI) were presented. We checked for the proportional hazards assumption visually and by including a time-interaction term to the model and the assumption was met (p = 0.741). In the adjusted model we stratified by individual trials which allowed hazard functions to differ for each trial. The model also controlled for age (in quintiles), sex, baseline post-bronchodilator percentage predicted FEV_1 (in quintiles), baseline smoking status, and body mass index (BMI; in quintiles) of the trial participants. Secondary analyses included subgroup analyses based on sex, baseline smoking status, and above and below median values for age, baseline FEV_1, and BMI. Competing risk models were used to evaluate the hazards of cause-specific mortality. All tests were two tailed in nature and were conducted using SAS 8.2 software (Cary, NC). Continuous variables are shown as mean (SD) unless otherwise indicated.

The characteristics of the trials included in the ISEEC are summarized in table 1. In total, data from 5085 participants were analyzed. None of the participants (including those who withdrew prematurely) was excluded from the analysis. The baseline characteristics of the trial participants are summarised in table 2. The mean (SD) age of the participants was 59.0 (9.3) years and the mean post-bronchodilator FEV_1 was 58.4 (19.5)% of predicted. Nine percent of the cohort (N = 436) were in the Global Initiative for Chronic Obstructive Lung Disease (GOLD)[1] class 4 (FEV_1 <30% of predicted); 28% (N = 1419) were in GOLD class 3 (FEV_1 30–49% of predicted); 49% (N = 2466) were in GOLD class 2 (FEV_1 50–79% of predicted); and 15% (N = 764) were in GOLD class 1 (FEV_1 80% of predicted). The mean bronchodilator response was 9 (12)% (0.13 (0.15) l) from pre-bronchodilator values. 71% of the participants were men and 69% were current smokers at the time of enrolment. In total, 973 participants (12%) withdrew prematurely from EUROSCOP, TRISTAN, and trials by Szafranski and Calverley and, as such, their vital status beyond the date of the study withdrawal could not be determined. In these trials, more participants withdrew prematurely from the placebo than from the steroid arm (21% in placebo versus 18% in the steroid arm; p = 0.006). The mean length of follow up was 26 (15) months; this was similar in the placebo and steroid arms of the trials.

Overall, 201 (4.0%) of the participants died during the trial period. Those who died during follow up were older (64 (7) years v 58 (9) years; p<0.001) and had lower post-bronchodilator FEV_1 (48% (17)% v 59% (19)%; p<0.001) at the time of randomisation than those who survived to the end of the study period. Male participants were more likely to die than female participants (4.5% v 2.6%; p = 0.002). The baseline BMI was similar between those who did and did not die during follow up (25 (5) kg/m² v 25 (5) kg/m²; p = 0.794).

Compared with placebo, participants assigned to inhaled corticosteroids had a lower risk of mortality (HR 0.75; 95% CI 0.57 to 0.99; fig 1.) Stratification by individual trials and adjustments for age, sex, baseline post-bronchodilator percentage predicted FEV_1, baseline smoking status, and BMI did not materially change the results (adjusted HR 0.73; 95% CI 0.55 to 0.96).

The effects of inhaled corticosteroids in the various subgroups are summarized in table 3. The beneficial effect of inhaled corticosteroids was especially noticeable in women (adjusted HR 0.46; 95% CI 0.24 to 0.91), former smokers (adjusted HR 0.60; 95% CI 0.39 to 0.93), and in those whose baseline post-bronchodilator FEV_1 was below 60% of predicted (adjusted HR 0.67; 95% CI 0.48 to 0.94). We chose this FEV_1 cut off because it was the median FEV_1 value. None of the interaction terms was significant at the p<0.05 level. Subgroup analyses based on GOLD severity classes showed that, in participants in GOLD classes 3 and 4, inhaled corticosteroids reduced mortality (adjusted HR 0.66; 95% CI 0.45 to 0.96). The effect was non-significant among participants in GOLD class 1 (adjusted HR 0.84; 95% CI 0.19 to 3.65) and 2 (adjusted HR 0.79; 95% CI 0.51 to 1.23). The effects of inhaled corticosteroids were similar between fluticasone, budesonide and triamcinolone, although the widths of the confidence intervals were different, reflecting the different sizes of the trials. We also performed subgroup analyses in which trials with a follow up time of 12 months or less were excluded. The results were similar whether trials were included or excluded in those with FEV_1 <60% of predicted. In such patients, the exclusion of these three studies resulted in an HR of 0.67 (95% CI 0.47 to 0.95). There was no significant heterogeneity in the HRs across the trials (p value for test of heterogeneity 0.93; fig 2.)

The principal causes of death are summarised in table 4 grouped into four major categories as described above. Most of the deaths were cardiorespiratory in nature (64% of all deaths). Approximately 21% of the deaths were from cancer. Of the 42 cases of carcinoma related deaths, 79% were attributed to lung cancer (N = 33). Other causes of death (including sudden deaths) and unknown causes accounted for the remaining 15% of deaths. Because of the small number of deaths in each category, none of the comparisons was significant at the p<0.05 level.

DISCUSSION

The most important and novel finding of this study is that treatment with inhaled corticosteroids is associated with a 27% reduction in all-cause mortality in individuals with stable COPD. The beneficial effects of these medications appear to be especially pronounced in women (adjusted HR 0.46) and former smokers (adjusted HR 0.60). However, none of the interaction terms was significant so the survival data in the various subgroups should be interpreted cautiously.

Figure 1 Comparison of Kaplan-Meier survival curves between patients treated with inhaled corticosteroids and placebo in COPD (log rank p = 0.039).
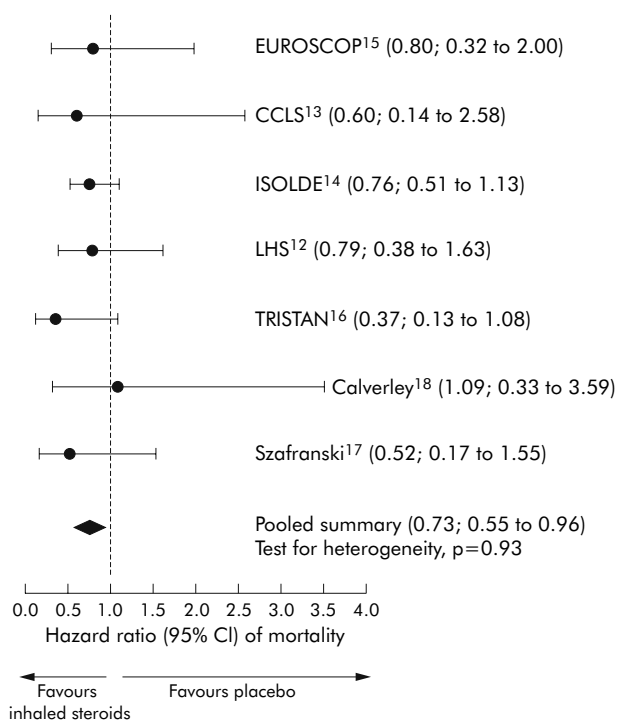
Figure 2 Forest plot of hazard ratios for all-cause mortality across the individual trials. Data are presented as point estimates with 95% confidence intervals.

This study has some limitations. Firstly, none of the primary studies included in the pooled analysis was designed to evaluate mortality as an end point, which imposed certain restrictions to the pooled analysis. For instance, five of the seven trials included in this pooled analysis did not ascertain mortality information on participants who withdrew prematurely from the trials. In these trials, participants were followed up to the date of withdrawal and any deaths occurring after this date were not recorded in the trial databases, except for those decedents who withdrew initially because of a serious adverse event from the study medication or placebo. As such, those who withdrew prematurely in these trials were recorded as "alive" at the final date of their assessment and any subsequent follow up period they were recorded as "missing." Data from the ISOLDE trial indicate that the placebo group is more likely to withdraw prematurely than the steroid group (53% v 44%; p = 0.008), and mortality is much more likely in those who withdrew prematurely than in those who remain in the trial (p<0.001).[20] It is therefore likely that, by not fully capturing deaths which occurred in the post-withdrawal period, we may have underestimated the true effect of inhaled corticosteroids because the rate of withdrawals was higher in the placebo arms than in the steroid arms of the trials and these participants tended to be sicker and to have a more rapid decline in FEV_1.[21] Indeed, in the trials in which complete mortality information was present (LHS-2, ISOLDE), inhaled corticosteroids were effective in reducing all-cause mortality in patients with COPD who had FEV_1 <60% of predicted (adjusted HR 0.60; 95% CI 0.40 to 0.91). In contrast, in the other five trials in which complete mortality data were not available for participants who prematurely dropped out, the adjusted HR was 0.69 (95% CI 0.37 to 1.30).

Secondly, there was a lack of information on long term serious adverse events. The trials included in this analysis were too

short to determine the long term effects of inhaled corticosteroids on such outcomes as hip fractures and glaucoma. In the short term at least, in the two trials that collected information on fractures (EUROSCOP and ISOLDE), inhaled corticosteroids did not appear to increase the risk of fractures (relative risk 0.70; 95% CI 0.36 to 1.38).[11] Thus, to assess formally whether the benefits in the current pooled analysis outweigh the adverse effects, there needs to be long term clinical studies to define better the risk of important side effects related to inhaled steroid treatment. A third limitation was the difference in investigational medications between the trials. It was reassuring that we did not observe any significant differences between the different formulations, suggesting a class effect of these medications on mortality. Because the trials used relatively homogeneous dosing schedules for specific inhaled corticosteroids, we could not determine whether different doses produced differential outcomes in COPD patients. Finally, as with most pooled and meta-analyses, publication bias is a source of concern. To mitigate this possibility we included all studies that met the inclusion and exclusion criteria, even those with a relatively short follow up period (12 months). We found three such trials. Their inclusion was also important to model accurately the effects of inhaled corticosteroids on mortality during the first 12 months of treatment.

The current study cannot determine the potential mechanisms by which inhaled corticosteroids reduce all-cause mortality in COPD. However, since exacerbations increase both the acute and long term risk of mortality in COPD,[22] these medications may confer survival advantage by reducing the frequency of moderate to severe exacerbations by nearly a third.[10] The beneficial effects on exacerbations are most obvious in participants with spirometrically defined moderate to severe disease.[23] It was in these participants (FEV_1 <60% predicted) that the effect of treatment on mortality was seen, and not in those individuals with less impaired lung function where death was infrequent. In addition, these medications improve the health status of participants with moderate to severe disease.[14] Reduced health status has been associated with both increased frequency of exacerbations[24] and mortality.[25] Inhaled corticosteroids also have a small effect on attenuating airway hyperresponsiveness,[12] which is found in 60–80% of patients with mild to moderate COPD.[26] Increased airway hyperresponsiveness has been linked to increased COPD mortality.[27] Interestingly, airway hyperresponsiveness is more common in women than in men with COPD.[26] The relative importance of these potential mechanisms requires further exploration.

This study was underpowered to evaluate the effects of inhaled corticosteroids on specific causes of mortality. However, there was a trend towards a lower risk of cancer related mortality for those randomised to inhaled corticosteroids. Whether or not this is a real effect will require further study. Chronic inflammation has been implicated in the development of malignant diseases.[28] In particular, cyclooxygenase COX-2 enzymatic activities may regulate immune responses that promote tumour growth.[29] Inhaled corticosteroids over 6 months have been shown to reduce prostaglandin E_2 levels, a product of COX-2 pathways, and to downregulate proto-oncogene (for example, BCL2) expression in the airways of smokers.[30] In murine models, corticosteroids modulate proto-oncogene expression and inhibit tumour growth by as much as 70%.[31] A prospectively randomised

Table 3 Comparison of inhaled corticosteroids and placebo for all-cause mortality per 100 patient-years in the various subgroups

	Inhaled corticosteroids	Placebo	Adjusted HR (95% CI)	p value for interaction
Overall	1.57	2.10	0.73 (0.55 to 0.96)	
Age (years)				
<60	0.57	0.93	0.60 (0.33 to 1.07)	0.443
≥60	2.91	3.67	0.77 (0.56 to 1.06)	
Sex				
Women	0.77	1.53	0.46 (0.24 to 0.91)	0.234
Men	1.93	2.36	0.80 (0.58 to 1.09)	
BMI (kg/m^2)				
<25	1.67	2.32	0.68 (0.47 to 0.99)	0.686
≥25	1.43	1.90	0.77 (0.50 to 1.17)	
Smoking status				
Current	1.23	1.44	0.87 (0.59 to 1.22)	0.231
Former	2.79	4.52	0.60 (0.39 to 0.93)	
Baseline FEV$_1$				
<60% of predicted	2.71	3.86	0.67 (0.48 to 0.94)	0.707
≥60% of predicted	0.83	0.91	0.90 (0.54 to 1.53)	
Length of study				
≤12 months	2.43	4.06	0.58 (0.31 to 1.10)	0.609
>12 months	1.46	1.86	0.77 (0.56 to 1.05)	
Study medication				
Fluticasone	3.61	5.18	0.70 (0.48 to 1.01)	0.944
Budesonide	1.04	1.33	0.73 (0.42 to 1.27)	
Triamcinolone	0.73	0.88	0.79 (0.38 to 1.63)	

Hazard ratios (HRs) were adjusted for age, sex, baseline post-bronchodilator FEV$_1$, smoking status, body mass index, and individual trial (see Methods section for details).

population of a similar size and follow up to this one will be needed to address these issues in patients with COPD.

Intriguingly, inhaled corticosteroids may be more effective in former than in current smokers. This pattern has also been observed in asthma.[32,33] Acutely in COPD, smokers have a lower therapeutic response to oral corticosteroids than former smokers.[34] It has been postulated that smoking induces a state of relative steroid resistance by increasing oxidative stress[35] and by upregulating production of various pro-inflammatory cytokines including interleukin-6 (Il-6), IL-8, IL-1ß, and monocyte chemoattractant protein-1.[36] Additionally, cigarette smoke appears to reduce histone deacetylase activity and its expression in alveolar macrophages, making these cells relatively resistant to corticosteroids since one of the principal targets of corticosteroid action is by switching off gene expression of inflammatory genes through the recruitment of histone decetylases.[37] Consistent with these findings, our data suggest that, for patients with COPD to experience maximal benefit from inhaled corticosteroids, cessation of smoking is of prime importance. Because the individual trials included in the current pooled analysis were originally designed and conducted at a time when anti-inflammatory drugs were thought to be most helpful in smokers with COPD, trials generally oversampled the smoking subpopulation of COPD patients. This may have attenuated (or even negated) the beneficial effects of inhaled corticosteroids observed in these studies.

In summary, the present pooled analysis indicates that inhaled corticosteroids are likely to be effective in reducing all-cause mortality in stable COPD. Further research is needed to understand better the molecular and physiological mechanisms by which inhaled corticosteroids reduce mortality in COPD.

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Table 4 Comparison of clinical characteristics of patients who died from various causes of mortality and the effect of corticosteroids for these causes of mortality

	Respiratory	Cardiovascular	Cancer	Others
Total number of deaths	69	60	42	30
Mean (SD) age (years)	66.1 (6.6)	63.5 (7.0)	63.8 (6.3)	63.6 (10.6)
Men	59 (85.5%)	50 (83.3%)	30 (71.4%)	23 (76.7%)
Baseline FEV$_1$ (% of predicted)	39.1 (13.1)	51.7 (17.1)	57.8 (17.0)	50.0 (17.7)
Adjusted HR (95% CI) for mortality between ICS and placebo groups	0.80 (0.50 to 1.28)	0.98 (0.59 to 1.62)	0.55 (0.29 to 1.03)	0.57 (0.27 to 1.19)

Hazard ratios (HRs) were adjusted for age, sex, baseline post-bronchodilator FEV$_1$, smoking status, body mass index, and individual trial (see Methods section for details).
FEV$_1$, forced expiratory volume in 1 second; ICS, inhaled corticosteroids.

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Improving Outcomes in ICUs

MOVING OUT OF THE ICU

Across the US, the dramatic rise in ICU bed utilization might be considered good economic news: filling hospital beds is generally good business for a hospital. But not in the case of long-term ICU beds. That's because most patients on ventilators are covered by Medicare, and hospitals receive the same flat DRG payment for these patients, whether they stay one day or six months. With many patients staying months at a time, hospitals are facing significant cost overruns.

Those trends became apparent at the Luther Midelfort — Mayo Health System, in Minnesota, where Mark Lindsay, MD, is chair of the department of pulmonary and critical care medicine. In 1997, Lindsay decided it would be a good idea to move many of these long-term ventilator patients from the hospital ICU to the ventilator unit at the Lakeside Nursing Home, which had vacancies. He calls it an example of "shared opportunities" for both facilities. Seven years later, the project is doing remarkably well. It has led not only to cost savings, but also to better care. "We're talking about millions of dollars," says Lindsay. "More importantly, we can dramatically improve the care of these patients."

The results are striking. From 1987 to 1997, the nursing home had 11 patients on ventilators. Only one patient was weaned successfully, and the majority died. Compare that with the results from 1997 to 2002, while the project was in place: the nursing home had more than 100 ventilator patients, and 67 percent of them came off their ventilators.

EMPOWERING STAFF

How did they do it? Lindsay points to training and dedication as major factors. His practice convinced a top respiratory therapist to move from his position at the hospital to become director of the nursing home's ventilator unit. It wasn't an easy decision for the therapist, says Lindsay, who says he was able to convince him by explaining that staff empowerment and other factors would lead to success.

One important success factor was introducing user-friendly protocols for weaning. "Protocol-based weaning is more effective than relying on physicians' orders," Lindsay explains. Another factor was something he learned at IHI: the concept of bedside rounds coupled with a goal sheet. Every Wednesday at 1 PM, the entire team — nurses, certified nurse assistants, respiratory therapists, social workers, and doctors, along with family members — meet at the patient's bedside. "It's key that everyone is on the same page for that patient," says Lindsay. And despite the fact that some of the patients have been on ventilators for five years or more, the team still asks each one about their needs and about any problems.

The program also emphasizes socialization and the importance of getting patients out of their rooms. "Most of them had never left their rooms in the ICU" in the hospitals they came from, Lindsay says. Using a simple trach collar to wean patients, the staff dresses them in regular clothes and gets them out of the unit.

Better patient care is just one of the benefits. These changes, among others, have reduced high turnover, which can approach 100 percent per year in some nursing homes. "Putting these partnerships together empowers staff," Lindsay says. "We have had very low turnover rates." The physician team that runs the ventilator unit at the nursing home also runs the ICU at one of the hospitals and gets production credit for the days spent caring for ventilator unit patients at the nursing home, so they have an economic incentive as well.

LIVES AND MONEY

The cost savings are considerable. Lindsay estimates that the program has saved the 20 participating hospitals some $18.5 million — based on 15,384 ventilator days, at $1,200 per day, with the DRG covering only the initial day. In contrast, the nursing home, which can collect reimbursement for its ventilator unit, spends $300 per ventilator day. Because of the economies of scale, among other factors, the program is profitable for the nursing home which has asked to expand the unit.

Lindsay emphasizes that the 67% weaning rate is real, and not the result of self-selection of patients. Among the nursing home patients, 28% have had neuromuscular diagnoses — those that predict the least likelihood of weaning — while other units, with lower weaning rates, had only 10 percent of patients with such diagnoses. Other units have had lower rates of successful weaning, at higher cost. This reinforces Lindsay's contention that "ICUs are not necessarily the best place" for patients chronically on ventilators.

He wanted to take the concept of shared opportunities beyond nursing homes. So he took it to a rural hospital, which, like many others, was having trouble competing with major medical centers. He wanted to develop a transitional care unit at the underutilized hospital for patients who were not on ventilators but were chronically ill. He received permission to conduct a six-month pilot program and began sending patients who needed rehabilitation from Luther Hospital, the major medical center, to the rural hospital. The program freed up beds at Luther and occupied beds in the rural hospital, which benefited both facilities.

With the influx of patients, along with the 1997 critical hospital designations that gave the rural hospital cost-based reimbursement, the rural hospital reversed a 10-quarter-long negative income streak in mid-2001. Since then, all but one quarter has been income-positive. "More importantly," says Lindsay, "4,500 patients were cared for, and we expanded and opened up new beds in the tertiary facility."

Lindsay says there are a number of other potential shared opportunities. He has worked with cardiovascular surgeons at his hospital on a post-CABG rehabilitation program. The surgeons weren't happy with the level of care their patients were getting in nursing homes, finding that they had frequent morbidities and readmissions to the hospital. When the cardiovascular rehabilitation program began, it had only one patient; today, it has an average of 12 patients, and the surgeons are so pleased with the results that they have committed to training additional staff in their protocols.

Lindsay cites the high rate of infections among nursing home patients as another area that could benefit from a shared project. "There really are tremendous opportunities to develop partnerships with nursing homes" and other facilities, says Lindsay. "If we don't invest in our nursing homes, it will impact our ability to discharge our patients safely from our hospitals," he adds.

EDITORIAL POLICY

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Discovery Labs

Robert J. Capetola, PhD

Robert J. Capetola is President & CEO of Discovery Labs

PRODUCTS

Surfactants are produced naturally in the lungs and are essential for breathing. Discovery Labs is developing a proprietary Surfactant Replacement Therapy (SRT) platform for multiple respiratory diseases. Our technology produces precision-engineered, completely synthetic surfactants that are designed to closely mimic the essential properties of natural human lung surfactant. We believe that through our technology, pulmonary surfactants have the potential to address respiratory diseases where there are few or no approved therapies available.

Our SRT pipeline is initially focused on the most significant respiratory conditions prevalent in the Neonatal Intensive Care Unit (NICU). Our lead product, SURFAXIN (lucinactant), has received an Approvable Letter from the US Food and Drug Administration (FDA) for the prevention of respiratory distress syndrome (RDS) in premature infants and is pending approval. Surfaxin is also under review for approval in Europe by the European Medicines Evaluation Agency. In addition to RDS, Surfaxin is being developed for the prevention of Chronic Lung Disease (CLD, also known as bronchopulmonary dysplasia) in premature infants. AEROSURF, aerosolized SRT administered through nasal continuous positive airway pressure (nCPAP), is being developed for neonatal respiratory failure.

The Aerosurf platform has the potential to apply SRT across many respiratory diseases with a less invasive delivery approach. Additionally, a broncho-alveolar lavage application of our SRT technology is being developed to address unmet needs in the critical care unit. We are conducting a phase 2 clinical trial to address acute respiratory distress syndrome (ARDS) in adults.

PATIENT CARE

Discovery Labs is committed to saving and improving the lives of the most fragile patients by advancing the standard of pulmonary medicine, leading with our SRT portfolio. Data from our RDS phase 3 pivotal trial showed an increase in patient survival favoring Surfaxin, compared to the most widely used, animal-derived surfactant in the United States. This data formed the hypotheses for a phase 2 clinical trial for the prevention of CLD in premature infants. Currently there is no FDA approved treatment available for CLD.

The Aerosurf platform holds the promise to produce a resilient pulmonary surfactant that reaches the deepest parts of the lung as an aerosol. We believe this will revolutionize the treatment of respiratory medicine through less invasive delivery while potentially reducing or eliminating the need for mechanical ventilation.

ADVANCES & TREATMENT

To date, the FDA has approved surfactants as replacement therapy exclusively for RDS in premature infants. Currently available replacement surfactants are animal-derived. Although animal-derived surfactants have advanced the standard of neonatal care, these products have risks for immunogenic effect and neonatal exposure to non-surfactant related proteins. Based on its completely synthetic composition, Surfaxin removes these potential risks.

Additionally, Surfaxin has demonstrated a favorable efficacy profile versus animal-derived surfactants. In our phase 3 pivotal trial, we showed a clear benefit over both Exosurf and Survanta, in our primary endpoint of RDS-related mortality. In addition, for the first time ever, Surfaxin has demonstrated a CLD benefit versus another pulmonary surfactant in terms of the treatment of RDS-related infants.

We believe that our precision-engineered surfactant can be manufactured in unlimited quantities, with a more consistent pharmaceutical grade quality compared to the animal-derived surfactants.

EDUCATION

Discovery Labs' goal is to become the preferred biotechnology partner in the neonatology and respiratory care communities. To achieve this goal, we are approaching the healthcare community with an intense focus on research and education. Our plans for investing in neonatology and respiratory related education include many traditional methods such as conference symposium, CME/CE sponsorship initiatives, and partnerships with relevant medical societies (AARC/NANN/PAS). One example of this commitment is NICUniversity, an online continuing education service created by some of the leading thought leaders in neonatology supported through an unrestricted grant from Discovery Labs.

Medical Science Liaisons (MSLs) play a key role interfacing between pharmaceutical companies and the opinion and thought leaders who influence how medicine is routinely practiced and prescribed. We currently have MSLs interacting in the neonatal medical community by educating and exchanging ideas among these thought leaders. In addition, we intend to have a highly experienced and well trained sales force which will focus its efforts on a targeted group of customers across the US.

THE ROLE OF CLINICIANS

Discovery Labs takes great pride in our long-standing collaboration with thought-leading clinicians from around the world. Many global thought leaders have been involved as advisors or investigators throughout the development of our SRT platform. This same philosophy has been adopted by our commercial team and utilized to obtain feedback and guidance on their efforts as they prepare to bring our unique surfactant replacement technologies to market. We will continue to rely on these valuable partnerships as we move forward with new products and enhance our current portfolio.

INTERNATIONAL MARKETING

At Discovery Labs we are committed to making our proprietary surfactant replacement technologies available outside of the

United States. As such, we have executed various strategies that involve the international markets. For example, we have utilized numerous multinational research sites for key clinical trials and have an ongoing partnership with Laboratorios del Dr. Esteve SA, one of the largest pharmaceutical companies in Southern Europe. We also plan to partner with additional companies in key international markets to ensure global availability of these life-saving medicines.

LOOKING AHEAD

Discovery Labs' vision is to become the global leader in pulmonary critical care biotechnology through the discovery, development, and commercialization of the highest quality, precision-engineered, life-saving medicines. We intend to become a fully-integrated biotechnology company through the implementation of a long-term business strategy which includes investing in manufacturing capabilities, building our own specialty pulmonary sales and marketing organization, securing aerosol generating technology and securing corporate partnerships for the development and potential commercialization of SRT in Europe and the rest of the world.

CONFERENCES, FORUMS, SEMINARS

Discovery Labs feels that these types of venues are excellent opportunities to introduce our products and technologies to the neonatology and respiratory medicine communities. As a biotechnology company, we are able to interact with a large percentage of the medical community and share our research achievements related to our pipeline of precision engineered technologies. As we anticipate gaining approval for Surfaxin and our pipeline of SRT products these venues will be a primary source of information-sharing with the healthcare community.

MAQUET

Ed Coombs

Ed Coombs is Director of Marketing/Product Management for MAQUET.

What led you to develop the Servo-i ventilator? That is, requests of clinicians, evidence of clinical need, enhancements in product development.
As the global leader in critical care ventilation, MAQUET has pioneered many advances in mechanical ventilation. The Servo ventilator line represents thirty years of technological innovation and clinical development of ventilatory treatment. For the Servo-i, over 1000 physicians, respiratory therapists, and nurses were asked to provide input on the mechanical ventilation practices. MAQUET's Servo-i is a software-based ventilator which allows for continuous update of the latest innovations. This ventilator platform is recognized in the market for the low work of breathing and superior patient comfort.

What level of user input has gone into the design and development of the Servo-i? How do you coordinate comments from clinicians and health care professionals into your design and production process?
MAQUET has an on-going commitment to research and development incorporating user input and world-renowned physician experts in critical care. Specialization in areas of lung recruitment, non-invasive ventilation, and patient-ventilator synchrony are highlights to MAQUET's current research

endeavors. There is a longstanding culture within the company to incorporate clinicians' feedback regarding ventilator performance and ideas to improve clinical outcomes in design engineering at the product's manufacturing site in Solna, Sweden. A worldwide market reference group meets regularly to discuss advances in mechanical ventilation, which then guides the process of product development.

What new features do you plan to add to your product in the future? What is your wish list for improvements or advances to this product in the short and long term?
Since the inception of the Servo-i, new features and functionality such as lung protective ventilation have been added every 9 to 12 months. MAQUET's latest updates in 2005 include the addition of an optional proximal airway sensor and continuous flow N-CPAP. In 2006, MAQUET plans to enhance the Servo-i's performance with a cost effective O2 analyzer and improvements in patient-ventilator synchrony. The open architecture design of the Servo-i allows for easy upgrades and enhancements through a software download. This guarantees lasting value as previous models of the Servo-i can be upgraded to the latest technology and innovative enhancements.

How did you determine the price of this product, and how do you apportion costs for R&D into the design/production/sales process?
The evolution of the Servo-i ventilator platform clearly demonstrates MAQUET's commitment to improving technology. This ultimately improves patient outcomes. MAQUET invests approximately 10% of its annual revenue into R&D. This investment and dedication to innovative mechanical ventilation solutions has been recognized and awarded within the mechanical ventilation industry. Currently MAQUET's research is focused on effective lung recruitment techniques, non-invasive ventilation, ARDS/VILI, and patient-ventilator synchrony. Every day MAQUET is finding new and innovative treatment modalities to improve patient outcomes.

Please discuss your company's quality control procedures that relate to the product in this profile. Also discuss the benefits of your quality control procedures for health care providers using your product.
Input from clinicians continues to play a key role in product development. MAQUET's leadership promotes an open dialogue with its customers and key industry leaders to gain feedback on product usage, clinical trends, and prevailing treatment modalities. Our organization is always in close communication with field staff, worldwide counterparts, and manufacturing teams. Our Quality and Regulatory Affairs department works closely with the FDA and other regulatory agencies to insure that all quality mandates are exceeded. Working together with our colleagues in Sweden, a quality program is maintained that ultimately benefits the end-user with improvements or enhancements that are critical to the clinical environment.

Many medical institutions and health care providers are increasingly adapting policies and routines to place environmental consciousness and ethics a top priority. MAQUET shares this environmental focus, and has a certified corporate environmental management system. Specific environmental objectives and policies in product development are implemented in manufacturing, as well as focus on cost-of-ownership for customers.

Please discuss any future related products that you are working on now. What would you estimate is the "shelf life" of the products discussed above?

The Servo-i ventilator was designed with an open architecture hardware and software design. This guarantees "backward compatibility" meaning that the Servo-i ventilators that are purchased today can be easily upgraded in the future as our technology and innovations are released. This is easily accomplished with a software download. The Servo-i Tryout Option program allows users to evaluate new options prior to purchase. Many hospital networks are signing long-term agreements known as our Preferred Partnership Agreements. Working with and for clinicians every day builds customer satisfaction and improved patient outcomes through technology and education. MAQUET is committed to this concept as it ensures the investment in Servo-i ventilator technology will continue to deliver lasting value to our customers.

If there are other aspects of design and development that you wish to discuss, please feel free to do so.

MAQUET encourages its users to provide their thoughts and feedback regarding the Servo-i in their clinical practice. For US clinicians, please feel free to contact the Director of Marketing/Product Management, Ed Coombs at edwin.coombs@maquet-inc.com. For international clinicians, please contact Martin Löfbom, Product Management at martin.lofbom@maquet.com.

Invacare

John Ledek

John Ledek is Vice President and Category Manager, Respiratory Group, Invacare.

Invacare's Respiratory Products in oxygen, sleep and asthma therapy are driven by innovation. Our products uniquely provide superior patient care in ways that are economically attractive for homecare providers and payers. We partner with clinicians, providers and patients to develop innovative product solutions that deliver the best clinical outcomes while reducing the total operating costs of providing this clinically superior care. A good example of this is Invacare's HomeFill Oxygen System. The patented HomeFill compressor enables oxygen patients to safely and easily fill their own portable oxygen cylinders in their homes. This ability to refill HomeFill cylinders gives the oxygen patient an unlimited supply of ambulatory oxygen and frees them from being dependent on weekly oxygen deliveries to their home. HomeFill gives patients their freedom back. No longer do oxygen patients have to wait at home for oxygen deliveries or worry about running out. They can now simply refill their small, lightweight HomeFill oxygen cylinder. The smallest HomeFill cylinder weighs just 3.6 pounds and lasts over four hours on a 2 LPM patient. Patients with an unlimited supply of ambulatory oxygen packaged in lightweight, inconspicuous cylinder and carrying bag can and do get out and enjoy life more. This increased ambulation improves respiratory health, increases survivability and maximizes the quality of life of the patient. HomeFill also delivers the lowest operating cost for the provider, enabling them to invest more in superior clinical care. Roughly 80% of the costs of providing oxygen therapy for an ambulatory oxygen patient is consumed in the weekly or biweekly deliveries of oxygen to the patient's home. These non-value added costs are eliminated when patients can refill their own lightweight cylinders with the HomeFill Oxygen System. Another example of Invacare's Respiratory Products delivering superior patient care is the Polaris EX CPAP with SoftX technology. The patent pending SoftX technology makes exhalation during CPAP therapy more comfortable for the patient by reducing the duration of the pressure spike experienced during exhalation. The result is increased patient comfort and ultimately better compliance with CPAP therapy. Since poor compliance drives up the cost of providing CPAP therapy, Invacare's Polaris EX with SoftX helps the homecare provider lower their operating costs while they improve patient comfort and compliance.

Invacare develops innovative products like HomeFill and the Polaris EX with SoftX by working closely with clinicians, providers and patients to better understand their needs and the challenges they face. For example, our Respiratory Clinical Manager, a registered respiratory therapist, works with physicians, therapists and researchers, some of whom serve on Invacare's Respiratory Medical Advisory Board, to develop superior product solutions and technologies that improve the current standards of care available to patients. These new product ideas are then tested and validated with patients and providers to ensure they deliver superior patient care. Invacare also works closely with respiratory professionals in associations and conferences like NAMDRC (National Association for Medical Direction of Respiratory Care), ASAA (American Sleep Apnea Association), the 6th Oxygen Consensus Conference and the AARC (American Association for Respiratory Care). Invacare also educates respiratory clinicians and other healthcare professionals through its Respiratory Education Programs that are conducted by Invacare's registered respiratory therapists around the country. These one day seminars offer CEU credits to respiratory professionals and provide the latest information on respiratory care and new product developments. Invacare's respiratory therapists also work with clinicians in the field every day to help keep them informed of the latest advances in respiratory products and technologies. It is this close interaction with respiratory clinicians, providers and patients that enables Invacare to develop innovative product technologies that improve patient care and reduce the cost of delivering this superior care.

Respironics

Bud Reeves

Bud Reeves is Marketing Manager, Hospital Division, Respironics, Carlsbad, CA

THE COMPANY AND ITS PRODUCTS

Respironics is a leading developer, manufacturer and distributor of innovative products and programs that serve the global critical care, respiratory and sleep markets. Focusing on emerging market needs, the Company is committed to providing valued solutions to help improve outcomes for patients, clinicians and healthcare providers. Respironics markets its products in more than 125 countries and employs over 3,800 associates worldwide with FY04 revenue of over $759M. Respironics is made up of 4 Divisions; Hospital, Homecare, Respiratory Drug Delivery, and International.

The Respironics Hospital Division provides our customers Total Ventilation Solutions(SM) via a wide range of products that treat patients, monitor the effects of that treatment, and manage data generated by that treatment. The Esprit is a full featured critical care ventilator that is used to provide ventilatory support to the most critically ill patients. It provides invasive and non-invasive ventilation capabilities in one product. The Respironics Vision is the world leader as a dedicated non-invasive ventilator with advanced functionality including built in oxygen blending, graphics, and the exclusive Auto-Trak leak compensation algorithm providing automatic triggering and cycling adjustments into inspiration and exhalation even in the face of changing leaks. Respironics provides a full line of mask interfaces from the Total Face Mask for emergency application to the Performa-Trak line of full face masks. The NICO2 monitor provides immediate data feedback that assesses the physiologic consequence of ventilator changes well before other monitoring methods. The measurement and trending of Volumetric CO2 and Vd/Vt can provide data on readiness of patients to be weaned from ventilation and assess efficiency of spontaneous breathing trials. Additionally, studies show that use of these measurements to fine tune ventilator settings may reduce length of ventilation time.[1] Our ALuRT (Advance Lung Recruitment Tool) may give clinicians significant feedback on appropriate setting of PEEP during treatment of ARDS. We have recently introduced NeoPAP into the Neonatal CPAP marketplace. This product features the Baby-Trak algorithm which provides dynamic pressure regulation even in the face of changing leaks. Additionally, NeoPAP provides integral humidification, oxygen blending, and alarms. Control of pressure takes place in the unit, so there are no cumbersome or heavy devices near the patient. Also, we have introduced a new line of infant-friendly interfaces that take advantage of the Baby-Trak leak compensation algorithm. Our Protocol Manager product has recently been introduced to the marketplace. This product manages data from many sources using handheld computers and integrates that data into already established protocols to assist the clinician in moving patients through those treatment protocols. Our weaning protocol is just one example of how Protocol Manager helps the clinician become more efficient in data management and patient care.

IMPROVEMENTS IN CARE

In our ventilation products, specifically the Esprit Critical Care Ventilator, the BiPAP Vision, and the NeoPAP Neonatal CPAP systems, we are committed to a concept called Free Breathing. We have built our triggering and cycling algorithms in all of our products to keep to this concept. The Esprit keeps to this concept by a feature called Flow-Trak, which allows the patient access to whatever flow they desire during a volume limited or pressure limited breath. Our BiPAP Vision employs a novel algorithm called Auto-Trak, which provides leak compensation, but also insures appropriate triggering and cycling in the face of constantly changing leaks without constant intervention by the clinician. NeoPAP, our new Neonatal CPAP product, uses an algorithm called Baby-Trak, which dynamically regulates set CPAP pressure and compensates for changing leaks, as well. This Free Breathing concept is meant to contribute to patient comfort in non-invasive as well as invasive ventilation. It also is designed to help to reduce time spent by clinicians constantly making ventilator adjustments to cycling and triggering.

R&D, EDUCATION

Respironics is committed to being a market needs organization. This means that we try to anticipate the needs of the marketplace even before the market realizes these needs exist. New product features are developed from suggestions by researchers, engineers, clinicians, and sales/marketing staff.

While many of our competitors are reducing or eliminating their clinical education and support staffs, Respironics' Clinical team is being expanded. We are especially proud of our clinical education department which is responsible for producing clinical education pieces, ensuring accuracy of product literature, and making sure our educational programs meet the needs of our internal and external customers. In addition to this group, we also employ an entire team of clinical experts, mostly RRTs that support all of our products in the field. When a customer is trained on a Respironics product, a medical professional, either RRT or RN, based on product application, is providing that training. Since Respironics is the worldwide leader in non-invasive ventilation, we provide CEU based NIV training as well as mask fitting workshops either on site or at major trade shows. In a recent MDBuyline survey, our customers ranked our Clinical applications training number one among ventilator manufacturers. Additionally, we offer product support training to BioMedical engineers so preventive maintenance and service can be performed by our customers.

TESTING AND TECHNOLOGY

The Respironics Hospital Division employs a full time Chief Medical Officer who also acts as our Director of Clinical Research. Any clinical research or product testing must follow a strict set of guidelines based on FDA rules. Generally, Respironics works with major teaching hospitals both inside and outside the US to accomplish clinical trials or customer preference testing.

Generally, advances in electronics that make products smaller, reduce costs, and increase efficiency will impact us the most. New advances in sensor technology which allow our products to measure faster and with greater accuracy will allow us to give our customers the products that they want to better manage their patients. Additionally, advancements in connectivity solutions, especially wireless, will provide our customers with the greater efficiency that the managed care environments demand.

SUCCESSES

I don't think that I can limit our successes to one specific institution, however here is one example. As you may know, Respironics pioneered a new generation of products for use in non-invasive ventilation with the BiPAP STD-30, then the Vision. South Miami Hospital presented an abstract at last years' AARC in New Orleans that demonstrated savings of millions of dollars attributed directly to their establishment of an effective non-invasive ventilation program using the BiPAP Vision. Many other hospitals around the country have reportedly experienced similar savings and continue to use non-invasive ventilation liberally in disease states where it has proven to be successful. Of course, many hospitals and patients are benefiting from our Critical Care ventilation, monitoring, and data management products, daily.

INTERNATIONAL/CONFERENCES/DEVELOPMENT

Much of the research that comes out of the international clinical community is the basis for product development at Respironics. Additionally, we do much of our basic clinical trials work, internationally.

The AARC is our biggest trade show and last year educational sessions on topics important to Respironics such as non-invasive ventilation, Volumetric CO2, and Transtracheal Augmented Ventilation were very well attended.

In my current position, I am not involved in day to day product development; however I serve as a conduit for information from our field sales force and our customers. I am also intimately involved in setting product specifications to be met during the development process and routinely meet with our "upstream" marketing group which works directly with our engineering team during the development process.

1. Continuous Advanced Respiratory Mechanics Decreases Length of Ventilation (LOV) in Infants and Children. Donna Hamel, RRT, RCP; Damian Craig, MS; Ira Cheifetz, MD., Duke Children's Hospital, Durham, NC; Presented at 2003 American Thoracic Society Conference.

Driving and Automobile Crashes in Patients With Obstructive Sleep Apnea/Hypopnea Syndrome

C. F. P. George

Driving is a complex task involving distinct cognitive, perceptual, motor, and decision making skills. After placing the vehicle on the road, the driver must constantly survey the ever changing roadway environment to keep the vehicle in the lane and moving at an appropriate safe speed. This surveillance involves two distinct visual tasks: estimating and responding to the oncoming curvature and controlling lane position. Driving is therefore a divided attention task involving speed and lane control as well as monitoring. To do this in a safe manner requires careful attention and alertness which can be problematic for patients with obstructive sleep apnea/hypopnea syndrome (OSAHS) or other sleep disorders.

Human error is a major determinant in automobile crashes with inattention, improper lookout, and other perceptual and cognitive errors accounting for up to 40% of such mishaps.[1,2] Sleepiness can lead to increased inattention and, not surprisingly, performance is often diminished in sleepy patients. The effects of sleepiness on various aspects of performance have been well documented. Indeed, depending on the task at hand, performance degradation due to sleepiness may be the same as, or greater than, that due to alcohol.[3,4] As a result, driver sleepiness is widely believed to be an important cause of road traffic injuries. Published estimates of the proportion of crashes attributable to sleepiness vary more than tenfold, from 1–3% in the US to 10% in France and over 30% in Australia.[6] The US National Highway Traffic Safety Administration (NHTSA) estimates that drowsiness is the primary causal factor in 100,000 police reported crashes each year, resulting in 76,000 injuries and 1500 deaths. These numbers represent 1–3% of all police reported crashes and 4% of fatalities.[5,7] Other sources have reported higher estimates. One UK study[8] concluded that 16–20% of motor vehicle crashes were sleep related based on police reported data, while another[9] arrived at a figure of 9–10% based on drivers' self-reports. While this variation reflects the

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quality of the data available, there is little doubt that drowsy drivers are involved in many motor vehicle crashes and motor vehicle injury accounts for a huge burden of death and disability. NHTSA estimates these crashes represent $12.5 billion in monetary losses each year.

The wide variation in estimates of sleep related crashes is due in part to the difficulty in determining the contribution of drowsiness to crash occurrence. In addition to "falling asleep at the wheel," drowsiness contributes to crashes by making drivers less attentive and by impairing performance levels. In other words, subjects do not have to fall asleep to have an accident. However, there is no objective field measure of sleepiness/fatigue which can be used to determine clearly if the crash is due to sleepiness. "Fall asleep crashes," however, have typical characteristics including:

- the problem occurs during late night/early morning or mid afternoon;
- the crash is likely to be serious;
- a single vehicle leaves the roadway;
- the crash occurs on a high speed road;
- the driver does not attempt to avoid a crash;
- the driver is alone in the vehicle.

Sleepiness has both homeostatic and circadian influences with the latter increasing sleep propensity at certain times of the day. Increasing sleepiness of a circadian nature is expected to produce increased motor vehicle crashes at certain times of the day as shown by recent Italian data (fig 1).[10]

While alcohol and/or obstructive sleep apnea/hypopnea syndrome (OSAHS) may be responsible for sleepiness while driving, there are many other risk factors for drowsy driving. Some of these are probably much more common than OSAHS as risk factors including sleep deprivation/chronic insufficient sleep or medications which increase sleepiness. Sleep related crashes are most common in young people who tend to stay up late, sleep too little, and drive at night. In a recent North Carolina study 55% of "fall asleep crashes" involved people aged
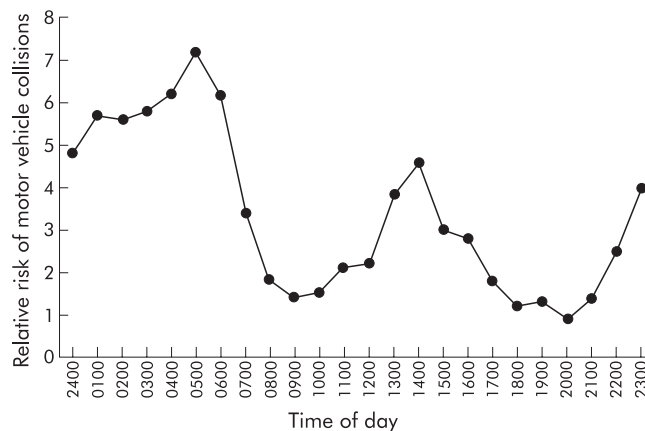
Figure 1 Relative risk of motor vehicle accidents by time of day. The increase in risk parallels the time of increased circadian sleepiness. Adapted from Garbarino et al.[10]

25 years or younger, mostly men.[11] Shift workers and especially night and/or rotating shift workers often suffer from poor quality of sleep as well as insufficient quantity of sleep. More than 25% of the US labor force performs some sort of shift work, particularly commercial vehicle operators.[12] Frequent business travelers—particularly those who drive through the night, in the early afternoon, or at other times when they are normally asleep—are at great risk. Driving alone or driving for long distances without rest breaks increases the risk of drowsy driving. It is important to recognize that these risk factors are not mutually exclusive. The sleep deprived business traveller with OSAHS is not an uncommon situation and the existence of two or more risk factors may synergistically increase the risk for drowsy driving and motor vehicle crashes.[13,14]

The first reports of motor vehicle crashes involving patients with OSAHS occurred in 1987.[15,16] Since then, numerous studies have suggested similar results using both subjective (self-report)[17–29] and objective (Department of Motor Vehicles) records.[30–33] Despite these multiple studies, the results have been criticised on epidemiological grounds.[34] Almost all studies have been cross sectional in nature with only one being case controlled;[32] there have been no prospective cohort studies to date. Several of the studies are subject to selection bias because they involve clinic patients. Information bias is also a concern because of a lack of similar information in the control groups. The confounding effects of age, sex, driving exposure, alcohol, and drug use were not adequately considered in most studies. Despite these limitations, most of the evidence continues to suggest that OSAHS confers an increased risk for driving.

These results are biologically plausible since patients with OSAHS are sleepy and inattentive, with reduced reaction times on reaction time testing which can lead to mistakes or mishaps while driving. As a result, many jurisdictions continue to require physician reporting to their local Department of Motor Vehicles regarding sleep disorders and fitness to drive.[35] Recent studies add further, if indirect, support to the hypothesis that patients with OSAHS have increased motor vehicle crashes. Data using both self-report [24,36] and objective records[37,38] indicate that treatment with continuous positive airway pressure (CPAP) markedly reduces the collision/crash frequency.

While the odds ratio for an automobile crash varies widely in the published literature (table 1) and while the crash rate is 2–4 times greater than in the population at large, the actual rate of crashes is still not that high. Many subjects seem never to have a crash. This should not be surprising since motor vehicle crashes are multifactorial in nature with sleepiness playing only a variable part. However, it is important to recognise the retrospective nature of the published data; ideally, physicians dealing with the issue of fitness to drive in patients with OSAHS need prospective data. If more than 65% of patients with OSAHS do not or will not have a crash, predicting the 35% at greatest risk is the current challenge. This has been part of the impetus for the development and testing of driving simulators in patients with OSAHS.

With advances in computer technology, various off-road driving simulators have been developed. These are cheaper and obviously safer than in-vehicle or on-road testing, and they allow a greater degree of experimental control and precision of performance measures without the interference of uncontrolled variables that operate in the real world. However, even the most sophisticated driving simulators do not provide all of the visual, vestibular, and proprioceptive changes that occur when turning a steering wheel and the vehicle changes course. Also missing in the laboratory environment is the subject's knowledge that the consequences of driving control responses affect his/her own safety. Most of the driver performance measures and all physiological evidence of driver fatigue can be gathered in either the simulator or in real driving environments. However, some measures such as lane tracking and yaw are more difficult to collect reliably in the open road environment

Many authors have examined the use of a number of simulators to measure driving performance in sleepy subjects. The complexities of these tests vary widely and, although the results have been generally congruent, the difference between sleepy subjects and controls varies considerably.

The Steer Clear, originally promoted as a driving simulator test,[39] is actually a choice reaction test and, while it requires the subject to maintain vigilance (a necessary factor for safe driving), it does not simulate driving. However, patients with OSAHS or narcolepsy have worse performance than control

Table 1 Motor vehicle crashes in patients with OSAHS

Study	Clinic patients (Y/N)	No of subjects†	Odds ratio (95% CI) for MVC	Accident rate (no/driver/year)
George[15]	Y	297 (27)	10.8 (2.4 to 27.2)	NA
Findley[16]	Y	64 (29)	7.4 (1.4 to 39.2)	0.05*
Young[30]	N	913 (221)	3.4 (1.4 to 8.0)	0.049*
Teran-Santos[32]	Y	254 (29)	8.1 (2.4 to 26.5)	NA
George[33]	Y	1163 (582)	1.9 (1.5 to 2.2)	0.09 (0.14)

*Calculated.
†Number with apnoea/hypopnoea index (AHI) >5 shown in parentheses.
NA = not available; MVC = motor vehicle crash; CI = confidence interval.

subjects[40] and other studies have confirmed this worse performance on the Steer Clear.[41,42] Although the magnitude of the difference in performance between patients and controls varies widely, none of these studies has shown any correlation between Steer Clear performance and crashes.

The Divided Attention Driving Test (DADT) includes a tracking task controlled by a steering wheel and a secondary visual search task.[43] In the DADT the tracking task is a variation of the subcritical tracking task, one of many psychomotor tasks developed to study performance and detect impairment due to fatigue, stress, or drug effects. This task is sensitive to fatigue resulting from hours of work among truck drivers.[44] The DADT was first validated using alcohol and then applied to sleepy patients with OSAHS or narcolepsy. Many, but not all, patients performed much worse than controls and performance in some patients was worse than controls impaired with alcohol. Moreover, performance was seen to improve when OSAHS was successfully treated with nasal CPAP.[45,46]

The Divided Attention Steering Simulation (DASS) involves steering, lane position, and secondary visual search. A computer derived image of the moving edges of a road that winds pseudo-randomly—white on black as in night driving—is presented so that, while driving, the eyes move between the far road in order to estimate the coming curvature and the near road to ensure accurate placement in the lane—two separate processes requiring different skills.[47] Patients with OSAHS perform badly on this simulator compared with matched control subjects,[48,49] and their collision and event rates improve with CPAP.[50]

STISIM is a personal computer (PC) based interactive driving simulator designed to represent a range of psychomotor, divided attention, and cognitive tasks involved in driving.[51] The overall simulation is fully interactive (the driver controls both speed and steering) and includes visual and auditory feedback, a vehicle dynamics model, and ability to modify the driving scenario to measure aspects of driver performance. On this simulator patients with OSAHS performed worse than controls on all performance measures including lane position variability, speed variability, steering rate variability, and crash frequency.[52] Simultaneous EEG measurements revealed increased lapses of attention in OSAHS and these correlated with crash frequency.

These data add support to the theory that inattention without overt episodes of falling asleep are all that are needed to produce crashes.

The Swedish Road and Traffic Research Institute driving simulator is an example of an advanced, hi-fidelity, moving base driving simulator. It is mounted in the driver's cabin of a Saab 900[53] and has a moving base system with four degrees of freedom of movement creating the same forces as those normally felt during driving. The system is fully interactive—that is, any action from the driver is fed into the computer which updates the visual presentation and creates the movement of the cabin and the momentum in the steering wheel. Using this sophisticated simulator, patients with sleep apnea performed much worse than controls while performance improved with successful treatment of OSAHS.[54,55]

Other simulators have assessed driving performance in normal subjects under the influence of alcohol and following sleep restriction to produce sleepiness. Despite the varying complexity of the simulation involved, the results of these off-road simulations are quite consistent in their outcome: driving performance is worse in sleepy subjects regardless of the cause of the sleepiness (disease state or sleep restriction). The magnitude of the decrements in driving performance is similar to that caused by alcohol. However, a more important question remains: can these results be extrapolated to and predict real world, on-road driving? If some patients perform well on the DADT or other simulators, it would stand to reason that some but not all patients with OSAHS will have on-road collisions. The data reviewed previously confirm this—many patients never have collisions. Moreover, when patients are treated (either by CPAP or uvulopalatopharyngoplasty), performance improved on the simulators[46,50,54,55] and, not surprisingly, the actual accident rates returned to normal.[38] The logical extension would therefore be that those who perform poorly on simulators are the ones who have the collisions and that, when they are treated and their simulator performance improves, they are the same patients who account for the reduced collisions. Unfortunately, the data for this final step are not yet available.

As a group, patients with OSAHS have a higher risk of having motor vehicle crashes. Since the causes of motor vehicle

crashes are multifactorial with sleepiness and decreased performance from OSAHS being only one factor, it stands to reason that the increased risk does not apply to all patients; indeed, some never have crashes. Performance on driving simulators is impaired in patients with OSAHS and improves with successful treatment, yet the predictive value of current systems is weak. Fortunately, motor vehicle crash rates return to normal after successful treatment of OSAHS. While research continues in an effort to identify high risk drivers, prompt treatment of OSAHS should remain the priority for the practicing clinician.

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Transcutaneous Monitoring: Back to the Future – An Important Adjunct to Care During High Frequency Oscillatory Ventilation

Sherry E. Courtney

High frequency oscillatory ventilation (HFOV) is often used in neonatal intensive care. HFOV has been shown to decrease bronchopulmonary dysplasia[1,2,3] in preterm infants and to be very effective in the treatment of persistent pulmonary hypertension of the newborn when used in conjunction with inhaled nitric oxide.[4] Other uses include pulmonary hypoplasia, air leak, and ventilation after abdominal surgeries such as gastroschisis closure.

Effective use of HFOV requires close attention to lung volume, with use of an "optimal value" strategy to open the lung and maintain it open.[5] Mean airway pressure is adjusted to minimize $FO_2(I)$ requirements without evidence of under- or overdistention on chest X-ray. Continuous pulse oximetry assists with adjustments of mean airway pressure and $FO_2(I)$.

Continuous assessment of CO_2 is also very important during HFOV. The oscillator is a powerful machine that can quickly drive arterial CO_2 to unsafe levels. Evidence is accumulating that suggests cerebral damage may result from hypocarbia.[6,7] Many infants on HFOV have indwelling arterial lines; however, frequent blood draws may be necessary to appropriately monitor CO_2 changes, leading to increased infection risk and/or anemia. A noninvasive, continuous estimate of pCO_2 during HFOV would be safer and more effective. Transcutaneous monitoring can provide this estimate.

Transcutaneous (tc) monitoring is not new; it has been available for well over twenty years.[8] Early machines were cumbersome and difficult to use. Accurate $tcpO_2$ assessment necessitated heating the skin to 43°C, which often led to skin burns in small preterm infants. After the advent of pulse oximetry, use of tc monitoring faded in most NICUs. Unfortunately, this led to "throwing the baby out with the bathwater," as $tcpCO_2$ monitoring also dramatically decreased despite the lack of a replacement for CO_2 monitoring such as pulse oximetry.

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Currently available tc monitors are small and easy to use. Importantly, they can be used to monitor both $tcpO_2$ and $tcpCO_2$, or either one separately. Even more importantly, use of $tcpCO_2$ alone can accurately be done at a monitor temperature of 40°C, thus not causing skin burns,[9] and site changes can be done as infrequently as every six to eight hours. The machine must simply be calibrated at the appropriate temperature.

The $tcpCO_2$ will correlate with the $pCO_2(aB)$ – that is, as one goes up the other goes up; as one goes down the other goes down. The "closeness" of the numbers will depend on the thickness of the skin and the perfusion of the site. The numbers are seldom identical, as they measure different things: one measures the $pCO_2(aB)$ of arterial blood and the other the CO2 diffusing from the cutaneous tissue. The numbers, however, will correlate (trend together).

It is important to check $tcpCO_2$ values with arterial blood gas samples or well-done capillary samples with each tc site change. A rising $tcpCO_2$ should always be considered a patient problem until proven otherwise. Something often forgotten is that an increasing $tcpCO_2$ may of and by itself indicate decreasing perfusion in the patient – perhaps sepsis or impending shock. Though the $tcpCO_2$ will still trend correctly, the $tcpCO_2$ will be considerably higher than the $pCO_2(aB)$ in a patient with significant circulatory compromise. In these cases the underlying cause of the problem must be treated.

"Something is wrong with the machine" is unfortunately often heard before evaluation of the patient has been done. A recent article, for example, documented the value of a rising $tcpCO_2$ in alerting staff to a pneumothorax well before acute decompensation of the patient.[10] A steadily rising or falling $tcpCO_2$ should prompt careful attention to reasons for under-or overventilation, not an immediate recalibration of the monitor or, worse, turning a blind eye to the readouts because "the machine is not working."

Troubleshooting the tc monitor is relatively easy. The calibration cylinder must contain sufficient gas and must be turned on

during calibration. The cable must be intact. The sensor must be remembraned as per the manufacturer's recommendations. Sufficient contact fluid must be placed between the skin and the sensor. Recalibration should be done every six to eight hours if only $tcpCO_2$ is being used. We have found every six hours to be the best in this circumstance; towards eight hours the contact fluid tends to evaporate, leading to spurious values. The sensor site should be changed every three to four hours if both $tcpO_2$ and $tcpCO_2$ are utilized. Heating of the sensor to 43°C is needed if the $tcpO_2$ is employed, and the site must be changed more frequently to avoid skin burns. A $tcpCO_2$ value of 0 or $tcpO_2$ of about 150 means the sensor has dislodged or an air bubble is under the sensor. These are the values expected for room air. $TcpCO_2$ values that jump about wildly indicate need for recalibration/remembraning. Steadily rising or falling values reflect patient status.

Though pulse oximetry has largely replaced the need for $tcpO_2$ monitoring, $tcpO_2$ monitoring can provide useful and complementary information should the practitioner choose to use it. High $pO_2(aB)$ should be avoided in most cases.[11,12] Because of the shape of the oxygen-hemoglobin dissociation curve, an oxygen saturation in an acceptable range could be associated with a $pO_2(aB)$ that is unnecessarily high. By the same token, a low or borderline saturation might be associated with an acceptable $pO_2(aB)$ because of shifts in the oxygen-hemoglobin dissociation curve and varying amounts of fetal hemoglobin. $TcpO_2$ monitoring can be very useful in titrating the $FO_2(I)$. Use of $tcpO_2$ monitoring requires more frequent site changes and close attention to the baby's skin to avoid burns. In most cases, however, the "burn" is a reddened area just under the sensor that heals without residua. Occasionally, tiny scars can result if the sensor temperature is too high or the sensor is left on the skin for too long. For a patient being started on HFOV, the $tcpCO_2$ monitor should be placed on the patient prior to instituting HFOV. Once the $tcpCO_2$ is stable and a correlating ABG has been obtained, HFOV can be started and the amplitude adjusted using the tc monitor. Severe hypocapnia, such as can occur with an inadvertently high amplitude or postsurfactant, can thus be entirely avoided. Hypercapnia from tube secretions, tube malposition, accidental extubation, pneumothorax or insufficient amplitude can also be quickly noted and appropriate interventions given. The $tcpCO_2$ monitor is also very valuable as the patient begins to wean, avoiding hypocarbia and allowing the staff to pace the wean appropriately.

Optimal use of HFOV should include concurrent use of $tcpCO_2$ monitoring to ensure prevention of hypo- and hypercarbia and timely interventions for both complications of therapy and patient weaning.

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Neonatal-Pediatric Application of Transcutaneous pO_2/pCO_2 Monitoring

Richard Williams

The application of transcutaneous pO_2/pCO_2 monitoring is essential in optimizing the ventilatory management of critically ill newborns. Application areas include high-frequency oscillatory ventilation initiation, transitioning modes of ventilation, and inter-facility transport.

In my experience, the transcutaneous pO_2/pCO_2 monitor is valuable in a variety of clinical situations that demand close observation by the healthcare practitioner of the ventilatory needs of the patient. There are at least three areas of application for transcutaneous monitoring in the neonatal-pediatric population.

- High-Frequency Oscillatory Ventilation (HFOV) Initiation
- Transitioning modes of ventilation
- Inter-facility transport

A prime example of a clinical situation that demands close observation by the healthcare practitioner is an infant that requires HFOV. The ability to monitor tcpCO$_2$ while initiating HFOV is crucial Adjusting the amplitude or Hz setting during the initiation of HFOV by monitoring tcpCO$_2$ is essential in decreasing the incidence of acute lung injury and potential neurological injury caused by lung overdistension. Manipulating the HFOV settings by utilizing a transcutaneous monitor allows the practitioner to maintain the pCO_2 levels of a patient within a designated range in an efficient manner without waiting for a blood gas result.[1] Implementing transcutaneous monitoring as a standard of practice during the initiation of HFOV for both neonatal and pediatric patients promotes a strategy that protects the lung from the problems associated with barotrauma.

Transitioning a patient between modes of ventilation is another example where the transcutaneous monitor can be beneficial. Infants and children that initially require HFOV will generally reach a point in their hospital course where they will need to transition to some form of conventional ventilation. The ability to fine-tune or make small changes on the conventional ventilator such as rate, peak pressure or tidal volume during the transition phase by monitoring tcpCO$_2$ allows the practitioner to increase the likelihood that the patient will tolerate the change successfully and avoid the problems associated with hyperventilation or hypoventilation.

Another area where the transcutaneous monitor has been beneficial is inter-facility transport. Infants with the diagnosis of Persistent Pulmonary Hypertension of the Newborn (PPHN) on Inhaled Nitric Oxide (INO) therapy that require inter-facility transport can be one of the most challenging and difficult patients to transport. The ability to monitor tcpO$_2$/tcpCO$_2$ levels in critically ill infants during transport allows the transport team to carefully observe the ventilatory status of the infant and intervene appropriately based upon the transcutaneous pO_2/pCO_2 values. In my experience, implementing transcutaneous pO_2/pCO_2 as a standard of practice during inter-facility transport of critically ill newborns promotes safety and efficiency in transport.

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Realizing Bioethics' Goals in Practice: Ten Ways "Is" Can Help "Ought"

Mildred Z. Solomon

A familiar criticism of bioethics charges it with being more conceptual than practical—having little application to the "real world." In order to answer its critics and keep its feet on the ground, bioethics must utilize the social sciences more effectively. Empirical research can provide the bridge between conceiving a moral vision of a better world, and actually enacting it.

Bioethics has been criticized for lacking relevance and for being naïve. Its principles and modes of justification are better suited to handling clinical matters at the bedside or policy issues related to new technologies than for grappling with arguably more profound moral problems like racism and human rights. Moreover, bioethical analyses often assume an implausible degree of rationality in human motivation and action. Getting from an ideal vision of the good to an embodiment of those ideals in practice depends as much on structural factors like power, money, and socialization as on espoused values and ideals.

It is not a coincidence that as these criticisms have been voiced, interest has been growing in the relationship between the social sciences and the bioethical enterprise. It is now well established that the social sciences have a lot to contribute to bioethics. One cannot define "the good"—and it might even be dangerous to try—without understanding context, intentionality, and outcomes, all of which the social sciences provide.

No one writing today would claim that empirical observations and normative analyses are wholly separate enterprises, wherein the social sciences simply serve bioethics' interests. Writing in the *Hastings Center Report* a few years ago, Robert Zussman observed that there are more normative assumptions and motives in social science research than social scientists acknowledge and more need for empirical, descriptive research than ethicists originally conceded. In the same issue, James Lindemann Nelson questioned the orthodox model of how "is" relates to "ought," according to which empiricists supply the

facts; moral philosophers, theologians, and humanists provide the values; and philosophers clarify relevant concepts and ensure valid argumentation. He criticized this view as too linear because "it keeps 'is' and 'ought' on their respective sides of the fence," and he called instead for "inverting the common wisdom about the relations between the normative and the descriptive."

But exactly *how* does empirical research in the social sciences relate to normative analysis? This essay is an attempt to give a more precise answer to that question. My goal is to reflect on the ways in which empirical research in the social sciences—both quantitative and qualitative—can be deployed to serve bioethics' goals.

My method is inductive and personal. I have worked as a social scientist doing research on values questions and moral uncertainty in medicine and health care with the goal of helping bioethics grapple with challenges in end of life care, organ donation, pain management, public health, and genetics. My work—including this essay—is therefore squarely located in what Raymond De Vries recently called the "social sciences in bioethics," which he distinguished from "the social sciences of bioethics." Social scientists who work *in* bioethics describe people's opinions, uncover how organizations work, or describe the impact of bioethical policies, thereby providing essential context to help bioethicists do their work. Sociology *of* bioethics is not interested in helping bioethics; instead, it studies it. Social scientists at this end of De Vries' continuum ask questions like: What were the social, political, historical, and economic factors that gave rise to the field? Is bioethics' real function to critique or to legitimize medicine?

In this essay, I look back at some of my own work in bioethics with an eye toward discerning the sorts of relationships to normative analysis that my research has exemplified, and I will try to infer a kind of taxonomy of the ways in which empirical research and bioethics can constructively relate. Since I am a social scientist of a particular bent—one who specializes in behavior change research—most of my work has involved needs assessments and intervention design and evaluation, aimed at

making improvements in individual and organizational behavior. One of the limitations of the approach I take in this essay is that it is based on what is essentially a convenience sample of cases. I offer the categories derived from these examples as a starting point for discussion. I hope that in reflecting on their own work, other empirical researchers in bioethics will modify, challenge, or add to this list.

TEN CONTRIBUTIONS
Zussman offered two ways in which the social sciences contribute to bioethics: by testing consequentialist claims, and by generating new normative concerns. I agree that empirical research functions in these ways, but the cases I present demonstrate a total of ten relationships, which I have organized into three categories. These examples illustrate that both qualitative and quantitative research in the social sciences can do far more than is currently acknowledged.

Most importantly, empirical researchers can help bioethicists realize their goals by developing the means *to move from moral vision and ethical analysis to ethically justifiable behavior*. In other words, social science research can make bioethics more effective. This is my first category.

Second, these examples also demonstrate that *empirical research can enrich the analytic process of moral justification itself* by testing consequentialist claims (as Zussman noted) and by helping us recognize which moral principles are most at stake in given contexts. Clarification of relevant moral principles comes from a deeper understanding of the meanings and actions that individuals situated in various cultural contexts intend, as well as from deeper understandings of power structures inherent in and between different social groupings—insights sociology, economics, anthropology, and other social science disciplines afford. In short, empirical research does not just confirm or disconfirm bioethicists' claims post hoc; it can be an integral part of moral justification itself.

Third, empirical research generates new normative concerns. This was one of Zussman's points. However, as I will attempt to illustrate, it seems to me that it does so in at least three ways that have not been distinguished, so far as I know.

FACILITATING THE MOVE FROM ETHICAL ANALYSIS TO ETHICALLY JUSTIFIABLE BEHAVIOR
Documenting gaps between espoused ideals and actual practice. My first day foray into descriptive research in bioethics was aimed at trying to understand why there was an apparent gap between recommended ethical policies and actual practice. By the late 1980s, 10 years had passed since the Karen Ann Quinlan case. Hundreds of similar cases had appeared, important national commissions had convened, and numerous policies had been published to guide decision-making about life-sustaining treatments. Yet one had only to pick up the paper to see that these guidelines were not offering substantial help at the bedside. Families were taking hospitals and physicians to court, and family advocacy groups like The Society for the Right to Die were forming out of frustration and fear that the health care system would impose burdensome technologies on dying loved ones.

In that environment, it seemed crucial to identify the barriers to sound decision-making near the end of life and to develop strategies for bringing practice more in line with existing normative guidelines. Conversely, the research might call some

of the guidelines into question by showing how policy-makers had been out of touch with clinical realities. To these ends, a team of researchers from Education Development Center (a nonprofit research and development organization) and The Hastings Center designed and conducted a national survey at seven geographically diverse hospitals and four nursing homes, as well as interviews and focus groups at Boston-based teaching hospitals, to explore clinicians' knowledge and attitudes of the prevailing ethical guidelines. These studies revealed that many physicians and nurses were unaware of, misunderstood, or disagreed with key national recommendations.

For example, while acknowledging the psychological difference between withholding and withdrawing life-sustaining treatments, most national recommendations held that these differences were not ethically salient and that clinicians would do better to initiate treatment and then withdraw it, if its burdens outweighed its benefits, than not try the treatment for fear that it could never be withdrawn. But only one third of the clinicians we surveyed agreed with this stance. Most who disagreed were simply unaware of or misunderstood prevailing guidelines; it was not that they had reached a different moral conclusion. National recommendations and clinicians' views also turned out to differ over the ethically troubling but commonly accepted distinction between "ordinary" and "extraordinary treatments," over "the doctrine of double effect" (which allows a physician to take an action that, while over-ridingly beneficial, may also have a foreseeable yet unintended negative effect), and over the withdrawal of artificial nutrition and hydration. Later surveys also showed that many clinicians profoundly misunderstood the U.S. Supreme Court's decision in the case of Nancy Beth Cruzan.

Revealing the nature of individual moral reflection and level of personal skill at ethical analysis. One of the most compelling findings from the survey research was that nearly half the clinicians reported acting against their conscience when providing care to the terminally ill, with nearly five times as many worried about overtreatment as were worried about undertreatment. This finding was important because up until then, media coverage of end of life cases had assumed that the problem was overzealous physicians committed to technology-driven rescue medicine. If the physicians themselves were worried about overtreatment, then what was locking them into doing things they thought were wrong?

In research I conducted on this apparent contradiction, I employed follow-up interviews to gain insight into physicians' thinking. Adapting a question that Carol Gilligan had found useful in her studies of moral development, I asked physicians, "Tell me about a time you just weren't sure what the right thing was to do with respect to using or forgoing life support." The interviews at one Harvard-affiliated teaching hospital resulted in about 1,000 pages of narratives about cases that had troubled the physicians and describing how the physicians had thought about their choices, what they had weighed, and what they finally decided to do. Nearly all of the physicians appeared to be deeply caring professionals who worried about their patients and were often filled with angst, especially about imposing treatments they thought futile and burdensome. But their narratives revealed an unfamiliarity with ethical concepts and forms of ethical concepts and forms of ethical analysis that could have helped them work through the choices confronting them and their patients.

These doctors felt they had to conceal their concerns about the wisdom of pursuing aggressive life supports. Some concealed their concerns because they held exaggerated misperceptions of their own legal vulnerability. Many others pursued aggressive, burdensome treatment for their dying patients out of an inchoate sense that they must, even if the interventions were not in the patient's best interest. These physicians seemed to assume that their only legitimate goal as technically proficient doctors was to use the tools of their trade to "save" patients, rather than to shepherd them through a terminal illness. Most of the physicians were uncomfortable talking about quality of life issues and questioned the legitimacy of doing so. They cloaked values questions in unnecessary and counterproductive technical medical language rather than directly discussing goals and values with patients and families; and they misperceived autonomy as a zero-sum game, wherein the more patients' rights were upheld, the more physicians lost power. They therefore interpreted the requirement to honor patient self-determination as a requirement to silence their own professional judgments. The narratives gave considerable evidence that these physicians were turning themselves into technicians, whose only job was to offer facts and let patients and families come to decisions pretty much on their own. No wonder they expressed qualms about the care they delivered.

Unlike the survey, this qualitative research did not just demonstrate that there was a gap between policy and practice. It was able to demonstrate, at least in part, *how* that gap was formed, expressed, and sustained: physicians' own language and lack of an appropriate cognitive framework impeded optimal ethical decision-making. Lack of a structure for thinking about moral choices at the end of life had gotten in the way of these physicians' ability to act in alignment with their own compassionate goals.

Describing the institutional and environmental context that mediates moral action. Although knowledge of ethical concepts and skill at ethical analysis is important, I and colleagues of mine asserted in an article published in 1991 that it could not alone create an institutional culture supportive of health care values and optimal end of life care. We based this claim on focus groups and direct observations in which we uncovered habitual practice patterns that undermined more thoughtful goal-setting for individual patients and revealed that in those institutions where nurses were granted more authority, conversations with families about their options near the end of life were more likely to occur. Survey data allowed us to quantify the extent to which physicians perceived legal vulnerability and how constraining the fear was to their practice. The data also revealed misconceptions about what was morally and legally permissible regarding decisions to use or forgo treatments. These direct observations and interviews suggested that a lack of accountability, with no one clearly in charge of end of life goal setting, contributed to technology-driven treatment that prolonged the dying process and undermined patients' wishes. As a result, in the technical assistance we later offered to hospitals around the country, we recommended strategies to encourage responsibility for goal setting, including mandatory family meetings, weekly interdisciplinary case review of patients currently in the hospital, and new roles for social workers.

Classic studies such as Charles Bosk's *Forgive and Remember*, Renee Anspach's study of the neonatal intensive care unit, and

Daniel Chambliss' study of hospital nursing provide other examples of how social science researchers' descriptions of institutional context can reveal the factors that impede or promote moral action within complex institutions. Still other examples would include studies that go beyond the walls of any one institution to look more broadly at factors in the larger environment, such as financial incentives, the number of hospital beds in a given region, patterns of financing and referral, and state and federal regulations.

Providing data to stimulate individual and institutional moral accountability. In addition to uncovering new knowledge, research can be a strategic asset for motivating change. Whenever possible, I share findings with participants—creating a feedback loop as a strategy for deepening their self-reflection and provoking both individual change and institutional accountability.

A target audience, particularly one composed of professionals in high-status positions who are typically granted great discretionary judgment in their professional behavior, is more likely to change its behaviors if the need for change is well established and personally relevant. The publication of clinical guidelines, whether based on evidence or professional consensus, does not achieve change by itself. Without data to prove that the problem is local—"here, in our own institution"—it is too easy to dismiss the problems as not relevant to "us."

In the end of life survey I mentioned earlier, participating hospitals were provided both the nationally aggregated data set and their own institution-specific data. Reported out at grand rounds, the local data helped galvanize quality improvement projects. Similarly, for a new national survey on pediatric palliative care that colleagues and I have recently completed, we provided local, disaggregated data to each participating children's hospital. When the institutions saw their own staff's concerns about inappropriate care of dying children, they launched plans to improve the quality of care.

When used as a strategic asset for motivating change, data can be either quantitative or qualitative. I know of one major managed care organization that radically redrafted its policies regarding access to hospice care for its non-Medicare members on the basis of just a few focus groups that documented the burdens a small number of their members faced.

Organizational ethics, now the subject of a large-scale effort at the health care institutions administered by the Veterans Administration, provides another opportunity to integrate moral vision and empirical research. Improving organizational ethics should begin with baseline descriptions of the organizational culture, identification of barriers to achieving aspirational goals, and articulation of likely points of leverage for making change. These research activities should proceed hand-in-hand with values-based goal setting.

ENHANCING ETHICAL ANALYSIS AND JUSTIFICATION

Testing consequentialist claims. When bioethicists suggest policy guidelines, they are usually trying to prevent potential harms that might befall patients or others. While thoughtfully deliberated, such guidelines nevertheless often emerge in anticipation of events, before anyone can be sure the potential harms are real. And sometimes the guidelines persist, taking on

a life of their own, while the conditions that motivated them change. Empirical research can provide evidence about whether the envisioned harms are genuine.

Work I recently did for The Institute of Medicine about its policy for "non-heart-beating organ donation (now referred to as "donation after cardiac death, or DCD) bears this out. Several commentators have expressed concerns about how patients might be harmed if DCD is broadly instituted, as the IOM has recommended. The main worry is that the prospect of donatable organs might encourage physicians or families to prematurely forgo life-sustaining treatments for gravely ill, incapacitated patients. The IOM asked me to design an evaluation process for measuring whether this occurs. I developed a three-pronged strategy that involves collecting data from families, clinicians, and the medical record in hospitals instituting DCD policies. The proposal, and a later editorial on the subject, reflect the view that when policy recommendations depend on strong, a priori claims about outcomes, empirical research is the only way to confirm whether the concerns are legitimate.

Validating, refuting, or modifying principles in the light of their relevance to moral agents. The 1990s saw the publication of a series of important cross-cultural studies of end of life decision-making. This research documented that many people—particularly, though not exclusively, from non-Anglo or non-European cultures—are more interested in filial duty and family responsibility than in self-determination. Being a good son or good daughter, protecting your parents or spouse from harm, and knowing that your children (or physician) will protect you when you are sick—these may matter more than the assurance that you can make all your health-care decisions yourself.

These cross-cultural studies have brought a variety of new moral issues to light, and they encourage more subtlety in our understanding of autonomy. The late Benjamin Freedman once called for "offering" autonomy, not "imposing" it. These studies confirm his intuition. Patients should be asked how much information they would like to have, and whether there are other family members whom the patient would like to have involved in the decision-making process. Clearly bioethics is and should be strongly committed to autonomy and patient decision-making, but as these studies show, cherished principles may not be equally salient to the very people whose rights and well-being bioethicists seek to protect.

Recognizing the relevance of otherwise neglected ethical principles. Empirical research can also be essential to the realization that an ethical principle is relevant to a given topic. The growing interest in collecting umbilical cord blood provides a case in point. Umbilical cord blood is a source of stem cells that can be used in treating leukemia and other devastating conditions, and these stem cells are much easier to obtain than stem cells harvested from bone marrow donors and are less likely to cause graft-versus-host disease, allowing the ability to transplant partially mismatched grafts.

IN the late 1990s the National Heart, Lung, and Blood Institute began establishing public banks to collect and store umbilical cord blood. At the time the public banks were being conceptualized, there were already well-established private for-profit banks that were recruiting pregnant women willing to pay to have their umbilical cord blood collected in the delivery room and stored for possible later use. My colleagues and I undertook

an analysis of the industry's websites and associated marketing materials, and we discovered important problems in how their messages were framed.

First, there were exaggerated claims of benefit to the baby itself. These ads were saying, both literally and through their imagery, should do this because someday it could save your baby's life." In fact, there had never been a reported benefit to a donating child; allogeneic use was far more likely. Second, the messages played on the parents' fear, sometimes with the overt taunt—"If you don't donate, are you adequately protecting your child's future health?" Such messages could erode the parents' confidence at precisely the worst possible time.

Based on this review, we proposed principles to guide the design of ethically appropriate recruitment campaigns. In addition to truthfulness and other obvious standards for ad campaigns, we called for "proportionality in message design." We meant to underscore the ethical importance of balancing the level of fear against the level of risk. For families with a high level of risk, program planners could use recruitment messages that introduced some appropriate caution. Fear-arousing messages would be wholly inappropriate for the general low-risk population. For most people, altruistic messages would be more appropriate. We published these recommendations along with key questions program designers could ask themselves to determine whether a message would meet these guidelines. For example: Is the level of fear appropriate to the level of risk? Do messages and dissemination strategies avoid coercion?

These questions, and the proportionality principle itself, are relevant not only to umbilical cord blood recruitment campaigns, but also to many other public communication campaigns, including efforts to protect people from HIV infection, automobile injuries, drug addiction, and smoking. One topic on which we have not yet had a public dialogue about the importance of proportionality and fear arousal in message design is the current federal communications campaign concerning public safety and terrorism.

GENERATING NEW NORMATIVE CONCERNS
Identifying and documenting new moral problems. Empirical research is vital for naming otherwise unseen or unrecognized moral problems. Hoffmaster, Bosk, Chambliss, and others have recognized the power of ethnography to uncover new moral issues worthy of bioethical attention. And of course it is not only ethnography that has something to contribute. Any systematic empirical investigation that studies harms or injustices can uncover new issues.

The intuition that something morally relevant is at stake usually drives research attention to a topic in the first place, but the existence of the problem and its nature cannot be confirmed without systematic exploration. For example, the apparent intractability of the "therapeutic misconception"—the misconception many subjects of medical research hold about the power of a clinical trial to bring them direct benefit—is just one case in point. Ethnographies of clinical decision-making, of the impact and meaning of illness on a person's sense of self, and of families' decisions to donate loved one's organs for transplantation are other examples of issues whose moral dimensions descriptive researchers have helped illuminate.

In his exploration of how "is" relates to "ought," James

Lindemann Nelson pointed to yet another way the social sciences can identify new moral problems. At their core, each discipline in the social sciences has central questions, methods, and often-tacit normative concerns, which he calls "epistemic values." These questions and values powerfully affect each discipline's direction and focus. Sociology, for example, is driven by its epistemic values to examine power differentials between groups or to question the historical development and the motives of professional elites. Nelson suggests that if bioethicists scrutinize the tacit epistemic values that different social science disciplines rely upon, they may well find a rich array of moral quandaries worthy of their attention. He calls on bioethicists to "look to the characteristic heuristic interests and procedures of the social sciences for different ways of understanding responsibilities—to look, in short, for the ethical messages that may be latent there."

More clearly specifying acknowledged problems. In addition to identifying and documenting new problems, empirical research can provide essential information about the context, meanings, and cultural surround of problems that are already acknowledged. One example is female clitorectomy. Most bioethicists actively call for abandonment of this practice on human rights grounds, while some anthropologists vigorously oppose that view on grounds of "cultural imperialism" or lack of cultural sensitivity. Yet neither camp would dispute that anthropological information about the practice is key to understanding it. And only by understanding its meaning from within the culture's frame of reference can those who advocate its abandonment hope to make progress. In fact, the progress now being made seems to depend on the leadership of indigenous women with strong local knowledge.

Anthropology has also been essential to the success of many public health interventions, from the introduction of oral rehydration therapies in African countries to condom promotion across the globe. In the early days of international public health interventions, before anthropologists were involved, public health messages tended to be simplistic and exhortative. They told people what to do but did not try to fit the message to the culture. Sophisticated public health interventions now begin with insights gleaned by anthropologists. Similarly, as bioethics has matured, it too has come to rely ever more on anthropologists—and sociologists and psychologists—to provide essential context and insight into the meanings that illness and health have for the people one hopes to serve.

Clarifying casual mechanisms. For decades we have known that African-Americans make far less use of health care services than European-Americans. However, in the absence of detailed research, many theories coexisted about what caused the disparity. Some of the theories suggested that much of the difference was due to cultural and economic differences within the African-American population itself—lack of insurance, distrust of the health care system, lack of transportation and other logistical problems associated with poverty. Fortunately, a large body of excellent empirical studies now point to a common predictor of lower health care utilization: failure on the part of physicians to refer African-American patients for critical screening tests and procedures at the same rate as they refer their white patients. This predictor was suspected but could not be confirmed before, and without such proof it could easily have been dismissed by the very people most in need of knowing it.

Identifying casual mechanisms is a complex undertaking. Nearly all social science research remains descriptive and associative; causality must be inferred. Ironically, the gold standard in research—the randomized controlled trial—often says very little about causality. RCTs can establish with the strongest degree of confidence that two phenomena are associated, but they cannot explain how they came to be associated—what the causal pathway was from independent to dependent variable. To make valid inferences about causality required either highly sophisticated studies, like the racial disparities work published in the IOM report, where many putative causal mechanisms are held constant and therefore ruled out, or qualitative research that uncovers the processes responsible for creating the observed associations.

In fact, qualitative research is often indispensable for revealing the causal mechanisms that led to a statistically significant effect, and its absence can be troubling. Consider the SUPPORT study, which found that an intervention ostensibly focused on improving advance care planning had no effect on patient outcomes. Publishing only the result of this RCT could give policy-makers the false impression that promoting advance-care planning is unwise. This conclusion would go well beyond the published data. To really understand what caused the effect reported, we need to know a lot more about how the intervention was carried out; qualitative data would be helpful for that kind of in-depth understanding.

Without knowing the causal mechanisms responsible for observed associations, it is easy to bark up the wrong tree. Premature abandonment of advance care planning could steer bioethicists in the wrong direction. Focusing on African-American alleged distrust of the health care system will not fix U.S. physicians' failure to refer for treatment. When either qualitative or quantitative research (preferably both in combination) supports valid inferences about causality, normative analysis is well-served and intentional research—aimed at achieving moral remedies—can focus on the right goals.

INTERCONNECTIONS
The first four functions of empirical research describe specific mechanisms by which social science research can help bioethics reach its own goals. Documenting gaps between espoused ideals and actual practice—the first of the social sciences' contributions discussed above—is a way of saying "change is needed." Revealing the nature of individual moral reflection (the second contribution) can stir greater personal reflection and encourage more sophisticated ethical decision-making. Descriptions of the institutional and environmental context that mediates moral action (the third contribution) identify barriers and opportunities for building more ethically responsive institutions. Providing individuals and institutions with data about their own behaviors and circumstances (the fourth) helps stimulate change.

The connections between empirical research and ethical justification can help bioethics better address deeply structured moral problems impinging on health and well-being. The fifth contribution (testing consequentialist claims) suggests that policies should always be scrutinized to gauge whether imagined harms are actually at stake. Not to gather such data, when it is available, is arguable an abrogation of the bioethicist's or policy-maker's responsibility. With the sixth and

seventh contributions (validating, refuting, or modifying principles and recognizing the relevance of otherwise neglected principles), empirical research can help ensure that the principles invoked really are those most relevant to the stakeholders and to the problem at hand.

Third, as noted at the start of this essay, commentators have criticized bioethics for having too narrow a set of interests. Clearly one benefit of more closely integrating the social sciences and bioethics would be the broader agenda that social science research could bring to the table—through research that uncovers new moral problems (the eighth contribution), explication of the morally salient context in which moral problems arise (the ninth contribution), or by revealing the causal mechanisms responsible for moral problems (the tenth contribution).

One caveat is worth noting here. Although the social sciences may help bioethics broaden its agenda and realize its aspirations, social scientists other than my special strain of behavior change specialists commonly eschew the role of reformers. While so much social science research may provide potentially stimulating data or reveal problems, barriers, and opportunities for change, the goal of social scientists is not to use the findings of research to create change, but rather to understand and interpret social phenomena. For this reason, Bosk claims that "there may be a built-in incompatibility between bioethical and sociological inquiry, and heightening this attention rather than attempting to deny it may very well be a useful contribution of the social scientist to bioethics." To echo De Vries' point, at least some social scientists should stand apart from the bioethical enterprise, the better to debunk its assumptions and critique its function as a new professional elite.

Social scientists who remain observant outsiders and ask unsettling questions undoubtedly provide great benefit. Yet surely bioethicists should not hesitate to take social science perspectives and tools into greater account. In their role as advocates for certain visions of the good, bioethicists need what empirical researchers can offer: a variety of powerful means for getting from here to there.

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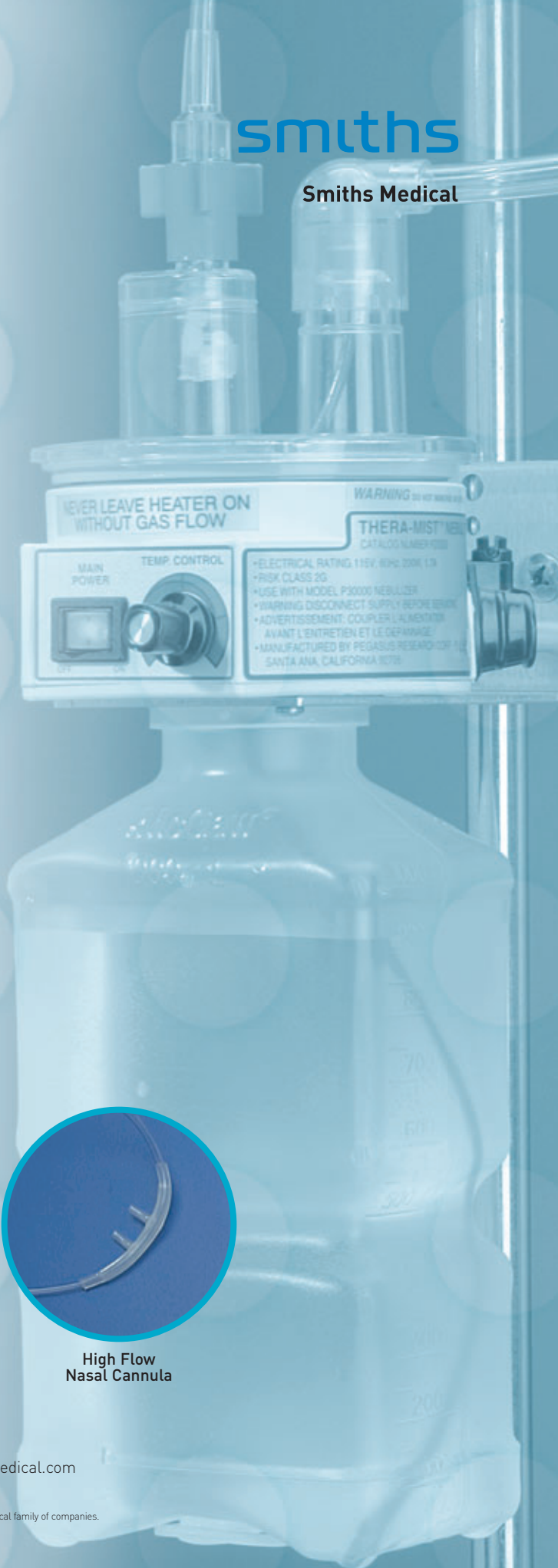
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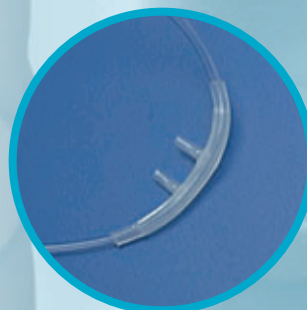
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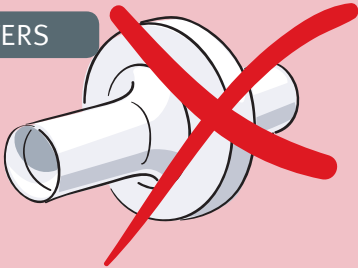**Smiths Medical**   800-258-5361   Fax: 603-352-3703   www.smiths-medical.com

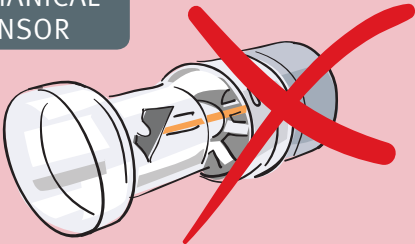# SPIROMETRY HAS NEVER BEEN EASIER!

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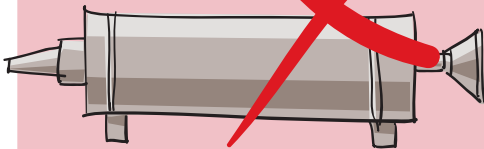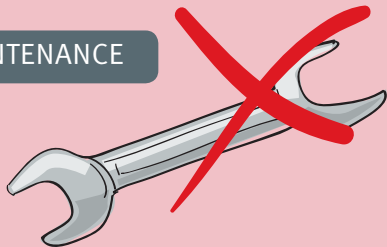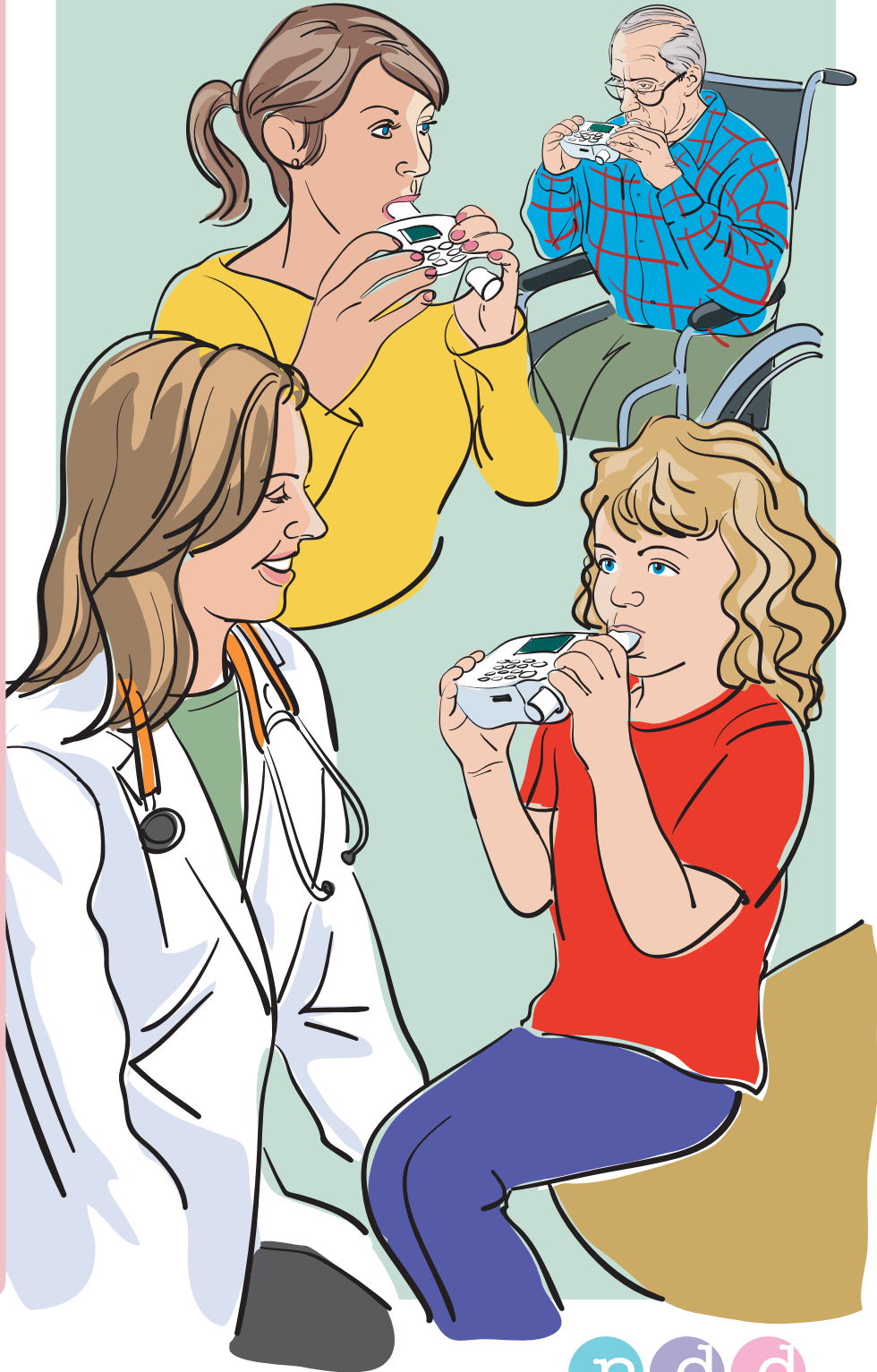
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